[PL1]

From optical to optoacoustic imaging: the time has come for broad clinical application

Vasilis Ntziachristos

Institute of Biological and Medical Imaging, Helmholtz Munich, Technical University of Munich

Optical and optoacoustic imaging have now progressed beyond critical boundaries in contrast and penetration depth of optical methods, enabling the use of light for a variety of research and clinical applications. The talk discusses advances in multi-spectral opto-acoustic tomography (MSOT) and optoacoustic mesoscopy and microscopy that impart unprecedented optical imaging performance in visualizing anatomical, physiological and molecular biomarkers in-vivo. In particular, we illuminate how MSOT visualizes biomarkers that relate to inflammatory and metabolic processes in a safe and portable manner, and the role of these biomarkers in addressing unmet clinical needs. Applications including imaging of breast cancer, brown fat activation or inflammatory conditions of the skin and bowels are showcased as examples of the clinical potential. We further highlight recent progress in the label-free imaging of molecules using Mid-IR Optoacoustic Microscopy (MiROM), a novel modality that pushes the limits of visualization in optical microscopy.

Vasilis Ntziachristos
Professor
Institute of Biological and Medical Imaging, Helmholtz Munich, Technical University of Munich, Germany

Professor Vasilis Ntziachristos studied electrical engineering at Aristotle University in Thessaloniki. Following his M.Sc. and Ph.D. in the Department of Bioengineering at the University of Pennsylvania, he was then appointed Assistant Professor and Director of the Laboratory for Bio-Optics and Molecular Imaging at Harvard University and Massachusetts General Hospital. Since 2007, he has served as Professor of Medicine and Electrical Engineering and the Chair of Biological Imaging at the Technical University of Munich and Director of the Institute of Biological and Medical Imaging at Helmholtz Munich. Prof. Ntziachristos is also currently Director of Bioengineering at the Helmholtz Pioneer Campus, and the Head of the Bioengineering Department at Helmholtz Munich. Prof. Ntziachristos is the founder of the journal Photoacoustics, regularly Chairs in international meetings and councils and has received numerous awards and distinctions, including the Karl Heinz Beckurts prize (2021), the Chaire Blaise Pascal (2019) from the Region Ile-de-France, the Gold Medal from the Society for Molecular Imaging (2015), the Gottfried Leibnitz prize from the German Research Foundation (2013), the Erwin Schrödinger Award (2012) and was named one of the world's top innovators by the Massachusetts Institute of Technology (MIT) Technology Review in 2004. In 2024, he has been elected as a new member of the German Academy of Sciences Leopoldina.Please also find his picture attached. You may use the provided photo (unchanged and by naming the copy right © Stephan Rumpf/Helmholtz Zentrum München) to announce his talk on your official website, but not for other things beyond that. Reproduction, modification, or omission of the copyright is not allowed

[PL2]

AI Enhanced Ultrahigh-Resolution Optical Coherence Tomography for 3D Cerebrovascular Imaging in Rodent Brain in vivo

Wensheng Cheng[1], Zhenghong Li[1], Hyomin Jeong[2], Qiaochu Wang[2], Congwu Du[2] , Haibin Ling[1]*, Yingtian Pan[2]*

[1]Depertment of Computer Science, [2]Depertment of Biomedical Engineering,

Stony Brook University, Stony Brook, NY 11794, USA

**hling@cs.stonybrook.edu, *yingtian.pan@stonybrook.edu*

Abstract: 3D optical coherence tomography angiography (OCTA) and Doppler tomography (ODT) is widely used to image subsurface vasculature and blood flow networks for various biomedical applications, owing to its noninvasiveness and high spatial resolution. However, the image fidelity of OCTA/ODT is severely degraded by background noise and artifacts.

To address these challenges, we develop and apply deep learning-based methods for post-processing to enhance 3D OCTA/ODT volumes. Firstly, we develop a network for joint noise and motion artifact reduction. Motivated by the slice-based acquisition process, where noise is largely independent across slices, we introduce a blind-slice self-supervised learning strategy that performs slice-wise denoising. Specifically, one slice is entirely masked and reconstructed from its neighboring slices. Furthermore, slices with minimal motion artifacts are selectively utilized to mitigate motion-related distortions. Second, we design a dedicated network to address shadow artifacts, which are primarily caused by light absorption and scattering along the optical path. To tackle this issue, we reformulate shadow removal as a vessel segmentation problem. Instead of explicitly modeling the complex physical formation of shadows, we focus on learning robust vascular representations. Specifically, we manually annotate vessel regions and train a neural network to extract clean and continuous vascular structures from raw OCTA volumes. The network is able to suppress shadow-affected regions while preserving anatomically meaningful vessel topology.

Extensive experiments on our self-collected OCTA datasets demonstrate the effectiveness of the proposed methods, achieving significant improvements in both quantitative metrics and qualitative visual quality. Comparative images of rodent cerebrovascular features both normal and diseased states will be provided

[PL3]

Low-coherence Biophotonics Imaging for the Brain

Xingde Li, Ph.D.

Professor of Department of Biomedical Engineering

Electrical and Computer Engineering, and Oncology

School of Medicine, Johns Hopkins University

Baltimore, MD 21205

Abstract: This talk will highlight our recent advances in using low-coherence light to explore the brain. We will focus on two scenarios: (1) intraoperative assessment of brain cancer infiltration in patients, and (2) real-time imaging of dynamic neural activities in freely-behaving rodents. In the first scenario (clinical-oriented), we developed a noninvasive, color-coded quantitative OCT (qOCT) technology that provides neurosurgeons with direct, real-time visual cues to maximize cancer resection while preserving healthy tissue. Results from more than 60 patients show excellent specificity and sensitivity (94% or better). In the second scenario (basic research), we created the first all-fiber-optic, head-mounted, ultracompact (~2.4 mm diameter) and ultralight (<1 g) two-photon fiberscopy platform, enabling high-resolution, large–field-of-view (~500 μm) imaging of neuronal activity in freely-walking/rotating mice. Detailed imaging results will be shared during the seminar, and, if time permits, we will also discuss other translational applications of these technologies for noninvasive, *in vivo* optical histology.

Xingde Li
Professor
Biomedical Engineering at Johns Hopkins University, USA

Xingde Li, PhD, is a Professor of Biomedical Engineering at Johns Hopkins University. After earning his PhD in Physics from UPenn and completing postdoctoral training at MIT, he joined the University of Washington in 2001. His research focuses on advancing biophotonics imaging for translational and fundamental applications. He has been actively engaged in the scientific community, serving on many professional society committees, chairing multiple international conferences, and holding several editorial roles, including the lead Founding Editor-in-Chief of BMEF, a Science Partner Journal. He is a Fellow of OPTICA, SPIE, and AIMBE.

[PL4]

Neurophotonic imaging to study drug addiction

Congwu Du and Yingtian Pan

Department of Biomedical Engineering, State University of Ney York at Stony Brook, Stony Brook, NY 11794, USA

Corresponding author e-mail address: congwu.du@stonybrook.edu

Abstract: Neuroimaging tools have expanded our capabilities for investigating the brain and the effects of drugs such as cocaine on neuronal and vascular function. The ability to distinguish cellular from vascular effects remains a challenge, partially due to the technical limitations of current neurotechniques to differentiate vascular from cellular effects with high spatiotemporal resolutions. To tackle such hurdles, we developed multimodality optical imaging platform that enables simultaneous imaging of hemodynamics (including cerebral blood flow - CBF, and hemoglobin oxygenation and deoxygenation) and intracellular calcium fluorescence (i.e., $Ca^{2+}{}_i$ as a marker of neuronal or astrocytic activity), thus allowing us to monitor the changes in large-scale cellular activity, cerebrovasculature, and tissue oxygen metabolism at high spatiotemporal resolution over a large field of view *in vivo*. By use of genetically-encoded $Ca^{2+}{}_i$ indicators and transgenic animal models, we are quantitatively image cell-specific $Ca^{2+}{}_i$ signaling and CBF network reactivity, thereby characterizing circuit- or pathway- interactions underlying brain dysfunction resulting from psychostimulants (e.g., cocaine) and drug addiction.

This presentation will provide an overview of neuroimaging techniques developed in our labs that are tailored to address technical challenges for studying neurotoxicity and addiction of cocaine, including its effects on neuro-astroglial-vascular (NAV) circuit within the medial prefrontal cortex (mPFC). We also summarize our recent findings in exploring astrocytes' roles that regulate neurovascular coupling under acute and chronic exposures, especially by incorporating our newly developed noninvasive model of cocaine self-administration in mice. We show that the integration of such neurotechniques provides new insights into neurobiological effects of cocaine on the brain, which could help to develop therapeutic intervention aimed at neuronal repair and minimizing brain ischemia resulting from drug abuse. These novel optical imaging modalities complement other neuroimaging tools, e.g., PET/MRI to measure cellular and vascular aspects of brain induced by drug addiction and other brain disorders (e.g., Alzheimer's Disease).

Congwu Du
Professor
Department of Biomedical Engineering, State University of Ney York at Stony Brook, Stony Brook, NY 11794, USA

Dr. Congwu Du received her PhD in Biomedical Engineering (BME) from the University of Luebeck, Germany and she is currently a professor at the Department of BME, State University of New York at Stony Brook. Her research focuses on developing the advanced optical techniques to address challenges related to the brain functional changes induced by drug addiction. She has over 100 scientific publications, and received many outstanding Awards. She is a fellow of American Institute for Medical and Biological Engineering (AIMBE), also serves on the editorial board of several journals in the fields in Neuropharmacology and Neuroscience.

Email: congwu.du@stonybrook.edu

[PL5]

Advances in tissue optical clearing

Valery V. Tuchin

Saratov State University, 83 Astrakhanskaya St., Saratov 410012, Russia

Federal Research Center "Saratov Research Centre of the Russian Academy of Sciences", 24 Rabochaya St., Saratov 410028, Russia

Tomsk State University, 36 Prospect Lenina, Tomsk 634050, Russia

Corresponding author e-mail address: tuchinvv@mail.ru

Abstract: The paper presents the physical principles of a method for optical clearing of biological tissues, which are considered dispersive media with strong multiple scattering and absorption of water molecules, proteins, hemoglobin, bilirubin, carotenoids, melanin, lipids, and other substances [1-5]. The method is based on short-term and reversible suppression of multiple scattering and absorption under the action of optical immersion agents, including dyes. The effectiveness of these methods for in vivo diagnostics using optical microscopy and tomography methods, such as optical coherence tomography (OCT), confocal microscopy, speckle interferometry, multiphoton microscopy, Raman spectroscopy, and polarization imaging, is discussed.
This study was supported by the RSF grant no. 23-14-00287-П.

References

[1] L. Oliveira, V. Tuchin, *The Optical Clearing Method - A New Tool for Clinical Practice and Biomedical Engineering* (Springer) (2019).

[2] V. Tuchin, D. Zhu, E. Genina (Eds.), *Handbook of Tissue Optical Clearing* (CRC Press) (2022).

[3] D. Zhu, V.V. Tuchin, *BME Front*. **5**, 0058 (2024).

[4] V.V. Tuchin, T. Dai, L.M. Oliveira, *Adv. Drug Delivery Rev*. **226**, 115699 (2025).

[5] W. Pang, …, Dan Zhu* , Valery V. Tuchin* , Jie Tian* , Cheng Ma* , Puxiang Lai*, Deep-tissue optics: Multidisciplinary innovations and emerging frontiers—A comprehensive review, PhotoniX Life, **1**(2), 2026

Valery V. Tuchin

Professor, corresponding member of the Russian Academy od Sciences

Saratov State University

Federal Research Center "Saratov Research Centre of the Russian Academy of Sciences",Tomsk State University, Russia

Valery V. Tuchin is the Head of the Department of Optics and Biophotonics and the Director of the Science Medical Center at Saratov State University. He is a Corresponding Member of the RAS, an Honored Scientist of the Russia, Fellow of SPIE and OSA, FiDiPro (Finland), and a laureate of awards: the SPIE Educator, OSA/SPIE J.W. Goodman Book Writing, OSA M.S. Feld Biophotonics, the Chime Bell, the National "Professor of the Year", the "Vyzov" Foundation's "Scientist of the Year", the regional "Vysota", and medals: the D.S. Rozhdestvensky, S.I. Vavilov, and A.M. Prokhorov. His publications have been cited over 48K times.

Email: tuchinvv@mail.r

[PL6]

Photoacoustic, Light-Speed, and Quantum Imaging/Physics

Lihong V. Wang, Ph.D., Bren Professor

Andrew and Peggy Cherng Department of Medical Engineering, Department of Electrical Engineering, California Institute of Technology

http://COILab.caltech.edu/

We develop sonic-speed photoacoustic tomography (PAT) to peer deep into biological tissue. PAT offers functional, metabolic, molecular, and histologic imaging across scales from organelles to entire organisms. We also develop light-speed compressed ultrafast photography (CUP), which records up to 219 trillion frames per second, far exceeding the capabilities of commercially available cameras. CUP can capture real-time images of the fastest phenomena in nature, such as light propagation, and can be slowed down to record slower events, such as neural conduction. In parallel, we explore quantum imaging and quantum physics.

PAT physically couples pulsed optical excitation with ultrasonic detection. Conventional high-resolution optical imaging of scattering tissue is confined to depths within the optical diffusion limit (~1 mm). PAT overcomes this limit, providing centimeter-scale penetration with high ultrasonic resolution and high optical contrast by sensing molecules. Its broad applications include early cancer detection and brain imaging. Since 2010, the annual PAT conference at SPIE Photonics West (about 20,000 attendees) has been the largest conference at that meeting.

With a single exposure, CUP can image transient events on time scales as short as tens of femtoseconds. Like traditional photography, CUP is receive-only and does not require specialized active illumination, unlike many other single-shot ultrafast imagers. CUP can be coupled to front-end optics ranging from microscopes to telescopes, enabling widespread applications in both fundamental and applied sciences, from biology to astrophysics and cosmology.

We study quantum entanglement, quantum imaging, and atomic physics. Entangled photons exhibit nonclassical characteristics and can be used for quantum imaging. Unlike classical optical imaging, quantum imaging has achieved super-resolution beyond the diffraction limit through coincidence detection. Because photons originate from atoms and molecules, we also investigate atomic physics at the interface between classical and quantum descriptions. For example, we found, perhaps surprisingly, that the Bloch equation, conventionally regarded as classical, yields the von Neumann and Schrödinger equations. We also developed a theory that models the multistage Stern–Gerlach experiment suggested by Heisenberg and Einstein more accurately than existing treatments.

Lihong Wang is Bren Professor of Medical and Electrical Engineering at California Institute of Technology. His book entitled “Biomedical Optics” won the Goodman Book Writing Award. He has published 630 peer-reviewed journal articles and delivered 650 keynote/plenary/invited talks. His Google Scholar h-index and citations have reached 170 and 125K, and he is #1 most cited scientist in optics and #4 in nuclear medicine and medical imaging according to Stanford/Elsevier. His laboratory was the first to report functional photoacoustic tomography, 3D photoacoustic microscopy, and CUP (world’s fastest camera). He received the NIH Director’s Pioneer, NIH Director’s Transformative Research, and NIH/NCI Outstanding Investigator awards. He also received the Optica Mees Medal, Optica Feld Award, IEEE Technical Achievement Award, IEEE Biomedical Engineering Award, SPIE Chance Award, and IPPA Senior Prize. He is a Fellow of AAAS, AIMBE, Electromagnetics Academy, IAMBE, IEEE, NAI, Optica, and SPIE. An honorary doctorate was conferred on him by Lund University, Sweden. He was inducted into the National Academies of Engineering and Medicine.

[TK-1] PIBM2026-0406-22

Evaluation of transplant liver viability with optical coherence tomography

Feng Yan[1], Qinghao Zhang[1], Yu Chen[2], Chongle Pan[1], and Qinggong Tang[1]

[1]Stephenson School of Biomedical Engineering, University of Oklahoma, Norman, OK 73019, USA

[2]Ministry of Education Key Laboratory of Optoelectronic Science and Technology for Medicine, Fujian Normal University, Fuzhou, Fujian 350117, P. R. China

Corresponding author e-mail address: yuchen@fjnu.edu.cn, cpan@ou.edu, qtang@ou.edu

Abstract: Human liver transplantation is severely constrained by a critical shortage of viable donor livers. In response to this shortage, marginal livers from extended criteria donors are increasingly used to expand the donor pool. Donor liver viability assessment remains limited by invasive, biopsy-based pathological sampling, and there is a need for more comprehensive and non-invasive evaluation techniques to meet the increasing demand for liver transplants. In this study, we propose the use of polarization-sensitive optical coherence tomography (PS-OCT) to perform a thorough viability evaluation across the entire surface of donor livers. PS-OCT imaging was conducted on multiple regions of human donor livers and the findings were cross-validated with histopathological evaluations. Machine learning and texture analysis were used to evaluate hepatic steatosis, fibrosis, inflammation, and necrosis from PS-OCT measurements in comparison with traditional pathological assessments, finding a correlation ($\geqslant$80%) between PS-OCT quantifications and pathology. Through normothermic machine perfusion and clinical transplantable liver imaging, PS-OCT imaging demonstrated a strong correlation with the functional performance of donor livers. PS-OCT offers a non-invasive assessment of liver viability by quantifying hepatic parameters across the entire donor liver, effectively complementing current pathological analysis. These results suggest that PS-OCT provides a robust approach to assessing donor liver viability, which could potentially decrease the discard rate of high-risk livers, thereby expanding the donor pool and reducing the inadvertent use of unsuitable livers for transplantation.

[TI-1] PIBM2026-0408-4

Influence of biomechanics on postoperative corneal asphericity after femtosecond laser refractive surgery

Xu Feng[1,2,3], Bingxi Wang[1,2,] Yinan Liao[1,2], Shichen Sun[1,2], Fengchen He[1,2], Zhuoyu Zhang[1,2], Zuowei Wang[1,2], Zimeng Zhou[1,2], Honghao Wang[1,2], Xiuli Liu[1,2], Xiaohua Lv[1,2], Shaoqun Zeng[1,2]

[1] Britton Chance Center for Biomedical Photonics, MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

[2] Department of Biomedical Engineering, College of Life Science and Technology, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

[3] xufeng@hust.edu.cn

Abstract: Corneal shape often changes after laser refractive surgery, represented by a decreased radius of curvature and an increased asphericity (Q-value). These changes may lead to increased higher-order aberrations, which in turn can cause night vision problems such as glare and halos. Clinical practice commonly employs population-based regression for postoperative aberration pre-compensation, but the precision is limited. This study hypothesizes that corneal mechanical deformation is a key factor in postoperative shape changes, yet direct experimental validation is currently lacking.

To test our hypothesis, fresh *ex vivo* porcine corneas were subjected to femtosecond laser ablation and compared with homogeneous phantom corneas. Optical coherence tomography and corneal topography were used to acquire pre- and postoperative corneal shapes. The radius of curvature and Q-value were fitted within the ablation zone, and finite element models were established to simulate shape changes.

Our experimental and simulation results both reveal that for homogeneous phantom corneas, the postoperative Q-value decreases. In contrast, for corneal models with higher central stiffness than peripheral stiffness, the postoperative Q-value increases, which is consistent with clinical observations. This suggests that heterogeneous stiffness distribution of the cornea could influence postoperative Q-value changes.

Based on these findings, this study demonstrates that corneal biomechanics have an impact on postoperative corneal shape. The proposed model can partially predict this trend. Future work requires accurate measurement of corneal stiffness distribution to enhance model predictability and provide a reference for personalized correction of higher-order aberrations.

[TI-2] PIBM2026-0525-1

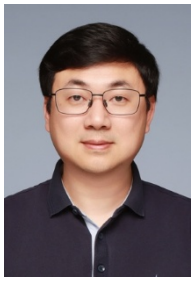
Stimulated Raman Histology for Label-free Cancer Diagnosis

Minbiao Ji[1]

[1]*Fudan University*

Corresponding author e-mail address: minbiaoj@fudan.edu.cn

Abstract: Rapid intraoperative diagnosis of human biopsy tissue is critically important for treatment strategy and timely decision-making. However, current standard histopathology is time-consuming and incompatible with fresh biopsies, such as gastroscopic biopsy and core-needle biopsy. We have integrated label-free stimulated Raman scattering (SRS) microscopy with various deep-learning algorithms to achieve instant and automated diagnosis of these biopsy tissues, enabling diagnostic classification, semantic segmentation, virtual staining and 3D volumetric histology. With the technical advances, we have demonstrated applications in multiple tumor types, including but not limited to brain tumor, gastric, prostate and breast cancers.



Minbiao Ji
Professor
Fudan University,China

Dr. Minbiao Ji received B.S. degree in Physics at Peking University, and his Ph.D degree in Physics at Stanford University, with his research focusing on ultrafast laser spectroscopy. Afterwards, he joined the research group of Prof. Sunney Xie at Harvard University as a postdoctoral research fellow, working on coherent Raman scattering microscopy. Minbiao Ji is currently a Professor in the Department of Physics **at Fudan University in Shanghai. His current research is focused on develo**ping novel nonlinear optical spectroscopy and microscopy tools to study biomedical problems and material sciences, including nonlinear optical microscopy, stimulated Raman scattering (SRS) microscopy and transient absorption microscopy for label-free tissue histology and AI-assisted disease diagnosis.

Email: minbiaoj@fudan.edu.cn

[TI-3] PIBM2026-0630-2

Functional Dynamic OCT and Applications

Jianbo Tang[1]*

[1]Department of Biomedical Engineering, Southern University of Science and Technology, Shenzhen, China

** e-mail address: tangjb@sustech.edu.cn*

Abstract: Dynamic imaging moves beyond static anatomy by capturing physiological processes, such as blood flow, cellular motion, and contrast agent kinetics, to reveal how the organ functions, enabling the early detection of dysfunction. A central challenge in this field is the quantitative analysis of these dynamic signals. This presentation will introduce the theoretical foundation for quantitative dynamic imaging based on the first-order field autocorrelation function (g1). I will detail our work leveraging this theory to develop dynamic optical coherence tomography (OCT) for imaging microvascular blood flow and assessing cell viability, with applications in studying cerebral vascular dysfunction and precision drug screening.

[TI-4] PIBM2026-0406-24

AI-Enabled Molecular Cytopathology Using Stimulated Raman Scattering Microscopy

Shuhua Yue[1]

[1]*School of Biological Science and Medical Engineering, Beihang University, Beijing 100191, China*

Corresponding author e-mail address: yue_shuhua@buaa.edu.cn

Abstract: Traditional cytopathology relies on chemical staining and morphological observation, suffering from limitations such as low sensitivity, strong subjectivity, and cumbersome workflows, making it difficult to meet the clinical demands for intraoperative rapid diagnosis and early cancer screening. This presentation will focus on our latest research advances in intelligent molecular cytopathological diagnosis technology based on stimulated Raman scattering (SRS) microscopy. Specifically, this study achieves precise segmentation of heterogeneous cells using DS-Cellpose, performs virtual H&E staining utilizing CycleGAN combined with structural similarity index measure (SSIM) loss, and employs contrastive learning to extract high-dimensional cellular features combined with multiple instance learning (MIL-XGBoosting) to identify malignant "signature cell clusters" exhibiting unique molecular metabolic characteristics. This technology has been validated in three clinical scenarios: intraoperative margin assessment for pancreatic cancer, peritoneal metastasis detection in gastric cancer, and early non-invasive screening for bladder cancer, achieving >90% sensitivity and <10 minutes detection time per case. The novel paradigm of "label-free SRS imaging – intelligent recognition – molecular diagnosis" established by this study provides an innovative solution for pathological diagnosis of human cancers.

Shuhua Yue（岳蜀华）

Professor

School of Biological Science and Medical Engineering, Beihang University,China

Dr. Yue got her bachelor's degree from Tsinghua University in China and her PhD degree with the advisor, Prof. Ji-Xin Cheng, from Purdue University in the US. She joined School of Biological Science and Medical Engineering at Beihang University in 2014. Her research focuses on the study of single cell metabolism by coherent Raman scattering microscopy and the translational research on precision disease diagnosis and therapy. She has published over 35 peer reviewed papers as the first or corresponding author on renowned journals, including Cell Metabolism, Science Advances, eBioMedicine, Advanced Science, etc. She has 11 issued patents and 2 of them have been successfully transferred. Her research is supported by multiple grants from the National Natural Science Foundation, including the Key Program, the Major Research Plan, and the National Key Scientific Instrument and Equipment Development Project. She was awarded the Young Investigator's Award by the WACBE World Congress on Bioengineering. She currently serves as committee members for Biomedical Photonics, Clinical Laboratory Testing, and International Affairs in Chinese Society of Biomedical Engineering, and organization committee member for SPIE Photonics West and SPIE European Conferences on Biomedical Optics.

[TI-5] PIBM2026-0406-23

Identifying molecular fingerprints for metabolic stress response and disease mechanisms by bond-selective microscopy

Hyeon Jeong Lee[1]

[1]*College of Biomedical Engineering & Instrument Science, Zhejiang University*

Corresponding author e-mail address: hjlee@zju.edu.cn

Abstract: Molecular-level diagnostic methods enable precise disease detection and classification while providing deep insights into pathological mechanisms. Among various molecular targets, lipids are frequently implicated in disease progression but exhibit extreme compositional and spatiotemporal heterogeneity. This complexity poses significant challenges for conventional omics approaches, which often struggle to track lipid dynamics within intact cells and tissues at sub-organelle resolution. In this talk, I will summarize our recent efforts to establish a high-resolution, chemical bond-selective imaging platform based on vibrational spectroscopy, primarily stimulated Raman scattering (SRS) microscopy, to decode the complex machinery of living systems. Using this platform, we identified specific spatio-spectral signatures for metabolic stress driven by both external environmental triggers, such as nanoplastic exposures, and internal pathological signals, such as cancers. These studies revealed significant alterations in lipid droplet compositions which, supported by mechanistic studies, serve as essential molecular signatures for evaluating metabolic stress and disease progression. Ultimately, these findings establish a basis for both environmental toxicology assessment and the early detection of metabolic diseases, bridging the gap between molecular spectroscopy and clinical diagnostics for precision medicine.

[TI-6] PIBM2026-0331-5

Label-free quantitative imaging of tissue chromophores with Spatial Frequency Domain Imaging (SFDI)

Yanyu Zhao[1]

[1]Beijing Advanced Innovation Center for Biomedical Engineering, School of Engineering Medicine, Beihang University, Beijing 100191, China

Corresponding author e-mail address: yanyuzhao@buaa.edu.cn

Abstract: New methods to measure and quantify tissue molecular composition and metabolism are a major driver of discovery in basic and clinical research. Optical methods are well suited for this task based on the non-invasive nature of many imaging and spectroscopy techniques, and the ability to utilize label-free endogenous absorption signatures of tissue chromophores including oxy- and deoxy-hemoglobin, water, lipid, collagen, and glucose. Despite significant advances in biomedical imaging, challenges remain in probing tissue information in a label-free, fast, and high-resolution manner. We'll present our recent studies on developing instrumentation and algorithms for high-speed non-invasive quantification of tissue optical properties and chromophore concentrations in a wide-field imaging format. Specifically, our work focused on an emerging diffuse optical imaging method called Spatial Frequency Domain Imaging (SFDI), and the extension of its methodology to other modalities. First, a high-resolution, label-free optical imaging method was developed to simultaneously measure water and lipids using the shortwave infrared (SWIR) wavelength region. Next, to break the speed bottleneck in terms of both measurement and image processing, new computational methods were developed to achieve 80× faster speed in measurement and over 300× - 100000× improvement in processing speed, without any additional cost in hardware. Finally, those methods were further generalized to other modalities including wavefront shaping and photoacoustic imaging, achieving light focusing through scattering media with 179× faster speed, and snapshot photoacoustic tomography with a single-element transducer (reducing the required number of transducer elements by two orders of magnitude). Taken together, the developed methods may substantially extend the available imaging contrasts and throughput for biological tissues, and provide opportunities for new preclinical and clinical applications.

Keywords: tissue optics, diffuse optics, chromophore concentration, spatial frequency domain imagin

[TI-7] PIBM2026-0529-1

Upconversion nanoparticles in biological labeling, imaging, and therapy

IrinaYanina[1]

[1]Institute of Physics, Saratov State University, Astrakhanskaya, 83, Saratov 410012, Russia

Corresponding author e-mail address: irina-yanina@list.ru

Abstract: Upconversion refers to non-linear optical processes that convert two or more low-energy pump photons to a higher-energy output photon. Owing to their small physical dimensions and biocompatibility, upconversion nanoparticles (UCNPs) can be easily coupled to proteins or other biological macromolecular systems and used in a variety of assay formats ranging from biodetection to cancer therapy. In addition, intense visible emission from these nanoparticles under near-infrared excitation, which is less harmful to biological samples and has greater penetration depths than conventional ultraviolet excitation, enhances their prospects as luminescent labels in bioimaging. This report explores and discusses the opportunities, challenges, and limitations that UCNPs exhibit as bioimaging probes and highlights applications with spatial dimensions ranging from the single nanoparticle level to cellular, tissue, and whole animal imaging. Our study investigated the differences in imaging depending on the accumulation of UCNPs in rat organs and tumor, based on their shell type, such as human serum albumin (HSA), HSA and folic acid (HSA+FA) or HSA, FA and cyanic dye Cy3 (HSA+FA+Cy3). We performed simultaneous rapid imaging of NPs using a standard microscope with field-excited luminescence excitation. We found that the nanoparticles accumulate more in tumors. Visualizing the nanoparticles accumulation boundaries is enabled by image processing. This type of particle may be promising for future clinical trials as well as photodynamic therapy (PDT), as it demonstrated a correlation between particle accumulation and tumor necrosis. When using UCNPs-HSA and UCNPs-HSA+FA, similar changes were detected in rat organs. There were differences in the kidneys depending on the type of particle that was used. When UCNPs-HSA+FA+Cy3 particles were injected into the internal organs, signs of circulatory disorders and minor morphological signs of kidney damage were observed. The data obtained will allow us to improve the method of PDT using nanoparticles and a photosensitizer (PS) with additional visualization..

Irina Yu. Yanina
Associate Professor
Saratov National Research State University, Russia

Irina Yu. Yanina received the Ph.D. degree in biophysics from Saratov National Research State University (SSU), Saratov, Russia, in 2013. She is authored 90 papers in peer-reviewed journals and in conference proceedings. From 2016 to present, she is an Associate Professor of Chair of Optics and Biophotonics at SSU. Her research interests include the development of optical methods of fat tissue destructive engineering, photodynamic/photothermal therapy, biomedical optics, nanobiophotonics, drug delivery, spectroscopy and imaging in biomedicine, optical and laser measurements. She has over 595 citations and an h-index of 12 (Scopus, January 2026)

[TI-8] PIBM2026-0630-3

Nanoparticle-Mediated Targeting of Pulmonary Metastases through an *In Vivo* Coagulation Cascade

Haiqiang Wang[1,2], Shiyuan Chen[1], Daiqin Chen[1,2*] and Xin Zhou[1,2,3*]

[1]State Key Laboratory of Magnetic Resonance Spectroscopy and Imaging, National Center for Magnetic Resonance in Wuhan, Wuhan Institute of Physics and Mathematics, Innovation Academy for Precision Measurement Science and Technology, Chinese Academy of Sciences – Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430071, China.

[2]University of Chinese Academy of Sciences, Beijing 100049, China.

[3]Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China.

Corresponding author e-mail address: chendychin@apm.ac.cn; xinzhou@wipm.ac.cn

Abstract: Pulmonary metastases are often small, disseminated, and poorly accessible to conventional nanoparticle delivery systems, creating major challenges for early imaging and targeted intervention. Here, we report an *in vivo* coagulation-assisted targeting strategy to enhance nanoparticle accumulation at pulmonary metastatic sites. In this approach, DMXAA pretreatment induces localized vascular disruption and fibrin deposition within metastatic lesions, thereby generating an inducible molecular target for CREKA-functionalized fibrin-targeted nanoparticles. Histological analyses, including H&E staining, Masson's trichrome staining, and immunofluorescence staining, confirmed DMXAA-induced hemorrhage and fibrin deposition in tumor tissues. Intravital two-photon imaging further showed that CREKA-modified nanoparticles accumulated efficiently at GFP-labeled pulmonary metastatic lesions, whereas control nanoparticles exhibited limited retention. This strategy enabled selective visualization of lung metastases by $^{1}H/^{19}F$ MRI in tumor-bearing mice, with negligible ^{19}F MRI signals observed in healthy control lungs. The MRI-positive regions were further validated by corresponding H&E-stained lung sections, confirming their association with metastatic lesions. Beyond molecular imaging, this coagulation-assisted targeting approach also supported selective mEGFP-LNP expression within pulmonary metastases, suggesting its potential for targeted nucleic acid delivery. Collectively, these findings demonstrate that activation of an *in vivo* coagulation cascade can remodel the metastatic microenvironment into a targetable niche, thereby improving nanoparticle delivery for both high-specificity imaging and localized therapeutic applications in pulmonary metastases.

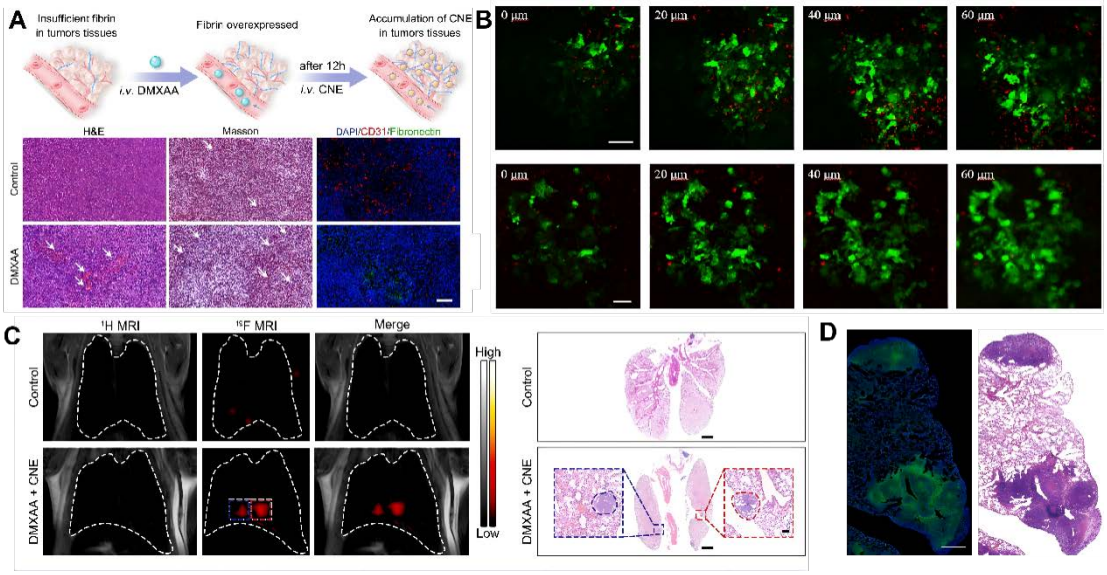


Figure 1. Nanoparticle-mediated amplification of pulmonary metastasis targeting through an in vivo

coagulation cascade and its applications. (A) Schematic illustration of pulmonary metastasis targeting through an in vivo coagulation cascade. DMXAA pretreatment induces fibrin deposition at tumor sites, thereby promoting the subsequent accumulation of CREKA-functionalized fibrin-targeted nanoparticles. H&E staining, Masson's trichrome staining, and immunofluorescence staining of tumor sections confirm DMXAA-induced hemorrhage and fibrin deposition within metastatic lesions. (B) Intravital two-photon imaging showing the accumulation profiles of CREKA-modified nanoparticles (top panel, scale bar: 100 μm) and control nanoparticles (bottom panel) at pulmonary metastatic sites with different depth using this strategy. Tumor cells were transfected with GFP (green, scale bar: 50 μm), and nanoparticle accumulation was indicated by DiD fluorescence (red). (C) $^{1}H/^{19}F$ MR images of healthy control mice and lung metastasis-bearing mice at 24 h after injection of DMXAA plus CNE NPs. Dashed rectangles indicate regions containing pulmonary metastatic lesions. Corresponding H&E-stained lung sections are shown below. Scale bar: 1.00 mm; inset scale bar: 100 μm. (D) Selective mEGFP-LNP expression in pulmonary metastases achieved using this coagulation-assisted targeting strategy. Scale bar: 500 μm

[TI-9] PIBM2026-0406-13

All-Optical IVUS-FFR Dual-Modal Imaging System for Precision Cardiovascular Care

Pu Wang[1]

[1]Beijing Advanced Innovation Center for Biomedical Engineering, School of Biological Science and Medical Engineering, Beihang University, Beijing, 100083, China.

Corresponding author e-mail address: 10318@buaa.edu.cn

Abstract: In cardiovascular disease diagnosis and treatment, intravascular imaging technologies are the core of precision medicine, irreplaceable in analyzing vascular wall morphology, assessing myocardial infarction risk, and guiding coronary intervention. However, mainstream techniques (intravascular ultrasound and optical coherence tomography) have flaws: they cannot balance high-resolution and large-depth imaging, failing to show deep structures and subtle lesions, and cannot accurately evaluate myocardial ischemia or plaque vulnerability, limiting diagnostic accuracy and treatment optimization. Thus, this project proposes an all-optical IVUS (AO-IVUS)-FFR dual-modality system. Leveraging AO-IVUS's ultra-wide bandwidth, it achieves high-resolution, large-depth imaging and simultaneous intravascular pressure measurement, enabling integrated structure-function assessment with one probe. Successful verification will allow one-time acquisition of plaque parameters, open a new path for atherosclerotic management, and elevate cardiovascular care.

[II-1]

Monitoring circulating melanoma cells by in vivo photoacoustic flow cytometry

Xunbin Wei[1]

[1] *Department of Biomedical Engineering, Peking University, China*

Abstract: Circulating melanoma cells, the prognosis marker for metastasis, are present in the circulation at the early stage. Compared with in vitro assays, in vivo flow cytometry is able to identify circulating tumor cells without drawing blood. Here, we have built in vivo photoacoustic flow cytometry based on the high absorption coefficient and monitoring circulating melanoma cells. Circulating targets in the blood flow are illuminated by high-pulsed repetition rate laser, followed by absorption of photons and generation of ultrasound to surroundings. We have built in vivo photoacoustic flow cytometry (PAFC) system to detect circulating melanoma cells in superficial vessels, which is useful for evaluating cancer stage and monitoring therapeutic effects.

Dr. Wei completed his post-doc at Harvard Medical School. He was a professor in Fudan University, China. From 2011-2019, he was a professor and chair in Department of Biomedical Instrumentation, School of Biomedical Engineering, Shanghai Jiao Tong University. Currently, he is a professor at Department of Biomedical Engineering, Institute of Clinical Advanced Medicine, Peking University. Dr. Wei is an SPIE Fellow, and recipient of Chinese Outstanding Young Scholar Award. He has published more than 100 peer-reviewed papers, including in Nature and PNAS. His interests include cancer detection by optical means, optical manipulation of cells, and light treatment of Alzheimer disease.

[II-2] PIBM2026-0515-1

Photobiomodulation Improves Cognitive Function in Sleep-Deprived Mice by Inhibiting the TLR4-Mediated Pyroptosis Pathway

Hongli Chen[1, *], Chunyan Ma[1, 2], Na Li[1, 2], Jianwu Dai[1], Xunbin Wei[3]

[1]State Key Laboratory of Advanced Medical Materials and Devices, Tianjin Key Laboratory of Neuromodulation and Neurorepair, Integrative Regeneration Laboratory, Institute of Biomedical Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, 300192, China

[2]State Key Laboratory of Separation Membranes and Membrane Processes & Key Laboratory of Hollow Fibre Membrane Materials and Membrane Processes, Tianjin Key Laboratory of Optoelectronic Detection Technology and Systems, Tiangong University, Tianjin, 300387, China

[3]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, the Center of Biomedical Engineering, Institute of Advanced Clinical Medicine, Institute of Medical Technology, Peking University Health Science Center, International Cancer Institute, Peking University, Beijing, 100191, China.

Corresponding author e-mail address: chenhli0107@163.com

Abstract: Sleep deprivation perturbs central nervous system homeostasis, resulting in neuroinflammation and cognitive impairment. Photobiomodulation (PBM), a non-invasive therapy using specific light wavelengths to modulate cellular metabolism and signaling, shows promise in cognitive enhancement. However, the neuroprotective mechanisms of 468 nm blue-light PBM in sleep deprivation-induced cognitive deficits remain unclear. Here, we used a sleep deprivation mouse model and lipopolysaccharide (LPS)-induced HT22 cell inflammation model to investigate the effects of 468 nm blue-light. Cognitive function was assessed through behavioral tests, while transcriptome sequencing (RNA-seq) analyzed differentially expressed genes (DEGs) and enriched signaling pathways after PBM. Biochemical and histological analyses measured neurotransmitter and inflammatory factor levels, neuronal damage and neuroinflammation, oxidative stress, and key proteins in the TLR4-mediated pyroptosis pathway. The role of this pathway was validated using the TLR4-specific inhibitor TAK-242. PBM markedly improved learning and memory, alleviated hippocampal neuronal damage, and downregulated inflammation-related genes and pathways. It inhibited microglial M1 polarization and astrocyte activation, reduced neuroinflammation, while decreasing reactive oxygen species (ROS) and enhancing superoxide dismutase (SOD) and catalase (CAT), mitigating oxidative stress. Importantly, it suppressed TLR4-mediated pyroptosis activation, with effects comparable to TAK-242. In conclusion, 468 nm blue-light PBM alleviates sleep deprivation-induced cognitive impairment by reducing neuroinflammation and oxidative stress via inhibiting the TLR4-mediated pyroptosis pathway, supporting its potential clinical application in sleep and cognitive disorders.

[II-3] PIBM2026-0605-2

Adaptive optics two-photon microscopy for deep-tissue imaging of immune cell dynamics

Sicong He

School of Life Sciences, Southern University of Science and Technology, Shenzhen, 518055

Corresponding author e-mail address: hesc@sustech.edu.cn

Abstract: Two-photon microscopy is widely used for deep-tissue imaging, but optical aberrations and scattering severely degrade resolution and signal, especially in weakly fluorescent or highly scattering environments. To overcome this, we have developed a novel adaptive optics (AO) method that is fast and robust to low signal-to-noise conditions. Using this AO-enhanced two-photon microscope, we have visualized immune and glial cell dynamics in their native microenvironments, including real-time tracking of microglial responses to nerve injury, subcellular imaging of glial calcium dynamics, and simultaneous observation of multiple immune cell types interacting during inflammation and tissue repair. Our AO technology provides a powerful tool for studying neuro-immune interactions, enabling deeper, clearer, real-time imaging without compromising the natural tissue environment.

Keywords: adaptive optics, two-photon microscopy, deep-tissue imaging, microglia, immune dynamics

[II-4] PIBM2026-0615-1

Photobiomodulation protects chronic kidney disease by inhibiting oxidative stress and inflammation

Ji Bian[1], Ann Liebert[2], Brian Bicknell[3], Xin-Ming Chen[1], Chunling Huang[*1], Carol Pollock[1*]

[1] Kolling Institute, Sydney Medical School, Faculty of Medicine and Health, University of Sydney, Royal North Shore Hospital, St Leonards, NSW 2065, Australia; jbia3972@uni.sydney.edu.au; dongjie.chen@sydney.edu.au; yzha9156@uni.sydney.edu.au

[2] Sydney Adventist Hospital, Wahroonga, NSW 2076 ann.liebert@outlook.com

[3] Brain and Mind Centre, Sydney University, Camperdown, NSW 2050, Australia; brian.bicknell@sydney.edu.au

Aim

To identify the protective mechanism of photobiomodulation (PBM) in managing chronic kidney disease (CKD).

Background

Novel therapeutic approaches for chronic kidney disease (CKD) are urgently needed, given the limitations of existing treatments. Photobiomodulation (PBM), a nonthermal light-based therapy, has been shown to reduce inflammation and oxidative stress, both of which are key contributors to CKD progression. However, its therapeutic potential in CKD remains largely unexplored.

Methods

In vitro, human proximal tubular cells (HK2 cells) pre-treated with low (4.32 J) or high dosage (8.64J) of PBM were then incubated with TGF-β1 (2 ng/ml) for 48 hours with or without PBM irradiation every 24h. In vivo, folic acid (FA)-induced CKD mice were treated with low dosage (7.2J) or high dosage (18J) of PBM 3 times per week for 2 weeks. SHAM treatments were identical but with laser diodes switched off. Renal function, fibrotic, inflammatory, and antioxidant markers were examined.

Results

In vitro, TGF-β1 significantly increased fibronectin, monocyte chemoattractant protein-1 (MCP-1), and tumor necrosis factor-α (TNF-α) expression, while reducing glutathione peroxidase 1 (GPx-1). These changes were significantly reversed by low-dose PBM ($P<0.05$), but not by high-dose PBM. In vivo, low-dose PBM, but not high-dose PBM, attenuated folic acid (FA)-induced kidney injury, as shown by significant reductions in blood urea nitrogen, 24-hour urinary albumin, and urine albumin-to-creatinine ratio ($P<0.01$). Low-dose PBM also significantly reversed FA-induced upregulation of fibronectin, collagen III, TGF-β1, MCP-1, TNF-α, F4/80, and CD68, and restored the expression of antioxidant enzymes GPx-1 and catalase ($P<0.01$). Conclusions

PBM attenuated chronic kidney injury via suppressing oxidative stress and inflammation at the appropriate dosage.

[AI-1] PIBM2026-0612-1

Upconverting nonlinearity enabled deep tissue super-resolution imaging

Fan Wang[1]

[1]School of Physics, Beihang University, Beijing, China

Corresponding author e-mail address: fanwang@buaa.edu.cn

Abstract: Super-resolution imaging has enabled nanoscale visualization in biological systems, yet achieving sub-50 nm resolution at depth typically requires complex optical architectures or computationally intensive reconstruction. Here, we present a unified nonlinear-response-enabled confocal nanoscopy framework that integrates image scanning emission saturation (ISES) nanoscopy with photon-avalanche (PA)-based signal decomposition to achieve sub-40 nm resolution in deep biological tissues. In the ISES modality, a 976-nm doughnut-shaped excitation beam is employed within an image scanning microscopy configuration to induce emission saturation, enabling point spread function (PSF) engineering and pixel-level confocal enhancement. This approach achieves a lateral resolution of 37 nm at imaging depths up to 200 μm. By simultaneously capturing high- and low-frequency components across detector pixels, Fourier-domain fusion preserves intrinsic frequency distributions while minimizing reconstruction artifacts in complex samples. Complementarily, we introduce a minimalist super-resolution strategy based on PA nanoparticles, where the nonlinear photoresponse of Tm^{3+}-doped probes is decomposed under sequential excitation intensities. This process selectively extracts higher spatial frequency components, enhancing resolution from 88 nm to 41 nm (λ /26) using a standard Gaussian-beam confocal system. The method enables direct visualization of nanoscale morphologies and resolves sub-diffraction biological structures with minimal computational overhead. By unifying saturation-based optical nonlinearity and avalanche-induced signal amplification, this work establishes a generalizable framework for deep-tissue super-resolution imaging. The approach balances spatial resolution, imaging depth, and system simplicity, offering a practical pathway toward low-cost, high-performance nanoscopy and guiding the development of next-generation nonlinear nanoprobes for in vivo applications.

[AI-2] PIBM2026-0331-6

Sparse scanning structured illumination microscopy (SS-SIM) for super-resolution imaging of thick samples

Peng Gao[1,2,*], Sha An[1,2], Xuhong Guo[1,2], Zhongxia Cai[1,2]

[1] School of Physics, Xidian University, Xi'an, China

[2] Key Laboratory of Optoelectronic Perception of Complex Environment, Ministry of Education, China

Corresponding author e-mail address: peng.gao@xidian.edu.cn

Abstract: Structured illumination microscopy (SIM) is a powerful super-resolution optical technique most suitable for live sample imaging. However, conventional SIM suffers from limited penetration depth (tens of micrometers) since its wide-field illumination is susceptible to sample scattering. To overcome this limitation, we developed a sparse scanning structured illumination microscopy (SS-SIM) as a super-resolution imaging technique for thick sample imaging. SS-SIM utilizes sparse fringe patterns generated by resonant scanning of a focused laser spot and synchronized intensity modulation. SS-SIM achieves a spatial resolution of 154 ± 12 nm, ~1.6-fold enhancement over conventional wide-field microscopy, across an imaging depth range from 0 to 200 μm for single-photon and 600 μm for two-photon excitation. We envision that our technique will find applications in imaging cells, tissues, and organisms, as well as other areas of the life sciences

[AI-3] PIBM2026-0624-2

Ultrasound and photoaocustic dual-modal imaging-guided deep penetration acoustic volumetric bioprinting

Qiangzhou Rong

Key Laboratory of Biomedical Information Engineering of Ministry of Education, Institute of Biomedical Photonics and Sensing, School of Life Sciences and Technology, Xi'an Jiaotong University, Xi'an 710049, China

Corresponding author e-mail address: qzrong@xjtu.edu.cn

Abstract: Acoustic volumetric bioprinting is an innovative and noninvasive additive manufacturing technology that enables rapid volumetric fabrication of intact living tissues via precisely modulated acoustic fields, overcoming the layer-by-layer printing limitations of traditional bioprinting methods. In this work, we develop a high-precision deep-penetration acoustic volumetric bioprinting method assisted by ultrasound-photoacoustic dual-modal imaging to address the low accuracy and shallow penetration defects of conventional acoustic bioprinting. By systematically optimizing acoustic field spatial distribution and implementing targeted energy attenuation compensation strategies, the proposed system achieves stable, high-resolution volumetric printing deep inside thick biological tissues. Real-time dual-modal imaging continuously captures tissue structural and functional information, providing dynamic feedback to calibrate acoustic parameters and greatly improving printing accuracy and spatial uniformity. Experimental results verify that the optimized system can reliably construct complex three-dimensional tissue architectures with excellent biocompatibility and high cell viability. This advanced technique significantly boosts deep-tissue manufacturing capability, offering a feasible and effective solution for in-situ tissue repair, regenerative medicine and precision biomedical fabrication.

[AI-4] PIBM2026-0408-2

A Study on a Highly Sensitive CRISPR-Based Single-Tube Dual-Gene Detection Method Using FWHT

Fei Hu[1,3,4], Fangning Wang[2,3,4], Yunyun Zhang[1,3,4]，Bo Zhang[1,3,4]，and Niancai Peng[1,3,4,5,*]

[1] School of Instrument Science and Technology, State Key Laboratory for Manufacturing System Engineering, Xi'an Jiaotong University, Xi'an 710049, Shaanxi, P.R. China.

[2] School of Mechanical Engineering, State Key Laboratory for Manufacturing System Engineering, Xi'an Jiaotong University, Xi'an 710049, Shaanxi, P.R. China.

[3] State Industry-Education Integration Center for Medical Innovations, Xi'an Jiaotong University, Xi'an 710054, Shaanxi, P.R. China.

[4] Key Laboratory of Advanced Biological Detection Technologies and Instruments of Shaanxi Province, Xi'an Jiaotong University, Xi'an 710054, Shaanxi, P.R. China.

[5] Xi'an Tianglong Science and Technology Co., Ltd., Xi'an 710018, Shaanxi, China.

Corresponding author e-mail address: pnc@mail.xjtu.edu.cn

Abstract: CRISPR-based molecular diagnostic technology offers high specificity and rapid response advantages. However, single-tube multiplex CRISPR detection faces challenges such as insufficient sensitivity and signal crosstalk while improving throughput. To address these issues, this study developed a single-tube dual-color orthogonal CRISPR detection system and introduced fast Walsh-Hadamard transform (FWHT) signal processing technology for weak fluorescence signal extraction. Based on the orthogonal substrate specificities of CRISPR-Cas12a and Cas13a, the ORF1ab and N genes of SARS-CoV-2 were simultaneously detected in a single tube. The mutual inhibition between the two systems was alleviated by optimizing reaction conditions. To solve the problems of weak fluorescence signals and low signal-to-noise ratio (SNR) at low target concentrations, a digital lock-in amplifier based on FWHT was designed and implemented. Using a "transform-first, mixing-second" architecture, the algorithm was programmed on the LabVIEW platform and the optimal Walsh waveform parameters were determined. Performance comparison shows that the SNR of this method is superior to conventional constant illumination and FFT-based methods under the same conditions. Experimental results indicate that the detection limits of the single-tube dual-color CRISPR system for the ORF1ab and N genes are both 1 copy/μL. After incorporating the FWHT method, the dual-gene detection sensitivity is improved to 0.5 copies/μL, which is comparable to qPCR. This approach provides an efficient and feasible signal processing pathway for improving the sensitivity of single-tube multiplex CRISPR detection.

[AI-5] PIBM2026-0619-1

SERS biosensing technology and liquid biopsy applications

Duo Lin[1]

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou 350117, China

Corresponding author e-mail address: duo@fjnu.edu.cn

Abstract: Surface-Enhanced Raman Spectroscopy (SERS) is an ultrasensitive nano-optical analytical technique. It retains the intrinsic "molecular fingerprint" detection capability of spontaneous Raman spectroscopy, while significantly amplifying the Raman scattering signals of target molecules adsorbed on the surface of nanometals via the localized surface plasmon resonance effect, enabling single-molecule detection. It boasts broad application prospects in the field of precise biomedical testing. This presentation will briefly introduce the development of SERS-based biosensors and the research progress in their detection of liquid biopsy biomarkers including exosomes, proteins and nucleic acids. It will focus on target self-localization methods and signal repeatability improvement strategies in label-free SERS biological detection. As for labeled SERS technology, the presentation will mainly cover advances in reporter molecule design, multi-signal amplification techniques, and multiplex quantitative detection of multiple analytes, as well as their exploratory applications in disease screening and therapeutic decision-making.

Duo Lin, Professor and Doctoral Supervisor, Fujian Normal University; Deputy Director of Key Laboratory of Optoelectronic Science and Technology for Medicine, Ministry of Education. His research mainly focuses on the development of Raman spectroscopy technology and its biomedical sensing applications. He has published 60 SCI papers as the first or corresponding author in authoritative journals including *Nature Communications*, *Laser & Photonics Reviews*, *Advanced Functional Materials* and *Photonics Research*. He has presided over 3 projects funded by the National Natural Science Foundation of China. He serves as Editor-in-Chief of the SCI journal *IET Nanobiotechnology*. His research achievements have won the First Prize of Fujian Provincial Science and Technology Progress Award and the First Prize of Science and Technology Progress Award from the Chinese Society for Optical Engineering (3rd-ranked completer).

[AI-6] PIBM2026-0330-2

Super-broadband stimulated Raman scattering spectroscopy and imaging

Jin Guo[1], Qiaozhi Yu[1], Haojie Zhang[1], Jiakai Wang[1], Hanqing Xiong[1]

[1]National Biomedical Imaging Center, College of Future Technology, Peking University, Beijing 100871, China

Corresponding author e-mail address: xiong.hanqing@pku.edu.cn

Abstract: Coherent Raman scattering (SRS) has emerged as a powerful quantitative contrast mechanism for chemical imaging in recent years. However, thanks to the high spectral quality of spontaneous Raman over large bandwidths, the very fundamental spontaneous Raman scattering still holds its superiority over CRS in simultaneously detecting a wide variety of biomolecules. In this talk, I will present a novel time-domain excitation strategy developed in our lab that provides identical spectra to the state-of-the-art spontaneous Raman over thousands of wavenumber ranges but is orders of magnitude faster in spectral acquisition speed. By encoding Raman free-induction decays into time-domain stimulated Raman loss (SRL) signals through few-cycle laser-induced quantum interference, we reconstruct the full-range Raman spectrum via Fourier transform of the time-domain SRL signal. This approach achieves natural-linewidth-limit spectral line shapes and enhanced sensitivity. I will discuss our progress in obtaining self-calibrated full-range Raman spectra and high-speed super-broadband Raman imaging, along with the advantages and limitations of this method for biomedical imaging applications.

Hanqing Xiong

Assistant Professor

National Biomedical Imaging Center, College of Future Technology,China

Dr. Hanqing Xiong has long been engaged in research on molecular spectroscopy and its applications in biomedical detection and imaging. His current research interests focus on developing high-throughput, universal biomedical measurement and imaging tools that can routinely acquire clinical big data capable of representing the health state for each individual in a label-free manner. Specific research directions include: (1) exploring new phenomena in molecular spectroscopy; (2) developing label-free optical measurement and imaging techniques based on molecular vibrational spectroscopy contrast, and designing related scientific instruments; (3) advancing ultrafast femtosecond laser technologies tailored for specific molecular spectroscopy applications. Since its establishment, his research group has published numerous papers in journals such as *Nature Photonics*, *JACS*, and *Light: Science & Applications*, and has filed or been granted several related invention patents.

[AI-7] PIBM2026-0406-25

What is hidden in water? Infrared-Raman-fluorescence microscopy reveals molecular signatures from nanoplastics to living systems

Delong Zhang[1]

[1]Zhejiang Key Laboratory of Micro-nano Quantum Chips and Quantum Control, School of Physics, Zhejiang University, Hangzhou 310058, China

Corresponding author e-mail address: dlzhang@zju.edu.cn

Abstract: Analytical biophotonics seeks chemically specific, quantitative, and dynamic molecular information from living systems in situ, yet current approaches remain limited by insufficient discrimination of spectrally similar species, inability to resolve physicochemical heterogeneity of individual particles, and the trade-off between chemical selectivity and imaging throughput in multimodal measurements.

To enhance chemical selectivity, quadrature phase-shifted polarization stimulated Raman scattering (QP^2-SRS) improves discrimination of closely related molecules such as cholesterol by accessing additional Raman tensor information beyond conventional measurements.

In parallel, mid-infrared photothermal (MIP) microscopy enables single-particle characterization of nanoplastics in bottled water, revealing substantial heterogeneity in polymer structure, crystallinity, and morphology, and demonstrating that particles with similar composition can occupy distinct physicochemical states.

To further increase chemical information content while maintaining imaging throughput, laser-scanning in situ pump–probe infrared and Raman excitation (LS-INSPIRE) microscopy integrates infrared, Raman, and fluorescence modalities within a unified platform, enabling simultaneous acquisition of complementary signals with intrinsic spatial co-registration. This capability supports isotopic tracing of newly synthesized lipids and proteins, quantitative mapping during development, and in vivo observation of neural and metabolic dynamics in *Caenorhabditis elegans*.

Together, these advances provide practical solutions toward comprehensive chemical analysis, linking improved molecular discrimination, particle-level heterogeneity, and real-time multimodal observation. This work establishes a general framework for connecting environmental chemical complexity with dynamic biological processes.

[AI-8] PIBM2026-0405-16

The Molecular Biophysics of EGFR and PDGFR Systems in Regulating their Distinct Kinetics of Biochemical Signals through FRET imaging study

Mingxing Ouyang[1]*, Linhong Deng[1], Shaoying Lu[2], Yingxiao Wang[2]

[1]Institute of Biomedical Engineering and Health Sciences, Changzhou University;

[2]Department of Bioengineering, University of California at San Diego & Department of Biomedical Engineering, University of Southern California (current address)

** mxouyang@cczu.edu.cn (presenter)*

Abstract;Growth factor receptors (GFRs) are one major pathway for signal exchanges between cells and their microenvironment, which results in broad cellular functions. Abnormal GFR kinase activities such as constitutive activation cause diseases including cancers, fibrosis and inflammation. Here we studied the regulatory mechanism on the distinct kinetics of EGFR and PDGFR signaling by combining Fyn FRET imaging. EGFR displayed transient activation in EGF-induced HeLa cells, while PDGFR showed sustainable activation in PDGF-induced MEF cells. Similar kinetics was observed in MEF expressing exogenous EGFR, or in HeLa expressing exogenous PDGFR. By swapping the extracellular domains between EGFR and PDGFR, the chimerical molecules were still sufficiently activated by EGF or PDGF stimulation, suggesting that ligand-induced changes in the extracellular domains could be transduced to the intracellular domains for kinase activation in these EGFR-PDGFR or PDGFR-EGFR chimeras. Interestingly, the activation kinetics of these chimeras showed consistency with the extracellular domains from EGFR or PDGFR. To further demonstrate whether biophysically disulfide-crosslinked PDGF dimer helps stabilize dimerized PDGFR for sustainable activation but not the case by monomeric EGF, mutations to destabilize PDGFR/PDGF dimerization did lead to less sustainable activation, while clustered EGF with biotin-streptavidin conjugation on microbeads induced more sustained EGFR activation. Our work revealed that the biophysical properties of EGFR-EGF and PDGRF-PDGF have crucial roles in regulating their distinct kinetics of biochemical signaling, which may be a considerable mechanism for clinical medicine development.

Keywords: molecular biophysics, biochemical activity kinetics, growth factor receptor, chimeric molecules, FRET imaging

[AI-9] PIBM2026-0403-1

Optical micromanipulation: from in vitro trapping to in vivo actuation

Hongbao Xin[1]

[1]Institute of Nanophotonics, College of Physics and Optoelectronic Engineering, Jinan University, Guangzhou 511443, China

**Corresponding author e-mail address: hongbaoxin@jnu.edu.cn*

Abstract: Optical micromanipulation has become indispensable for precise and non-contact handling of biological targets. However, conventional techniques are hindered by the diffraction limit, low throughput, and passive nature, restricting their application in complex biological environments. To address these challenges, we have developed two complementary strategies that bridge the gap from well-controlled in vitro trapping to active in vivo actuation. First, we developed two optical trapping methods based on opto-hydrodynamic cooperation and photon nanojet enhancement. By constructing flexible, stretchable, on-chip optical tweezers with orderly assembled microlenses on flexible substrates, we achieved high-throughput, precise manipulation of multi-scale bioparticles—from exosomes to cells—in complex in vitro settings. Second, we created optically controlled living-cell microrobots. By activating cellular ion channels with light, these biohybrid tools enable active, targeted biomedical operations inside living organisms, including pathogen clearance and photodynamic therapy. Together, these advances transform optical micromanipulation from a passive trapping tool into an active, multifunctional platform capable of operating in both in vitro and in vivo environments, opening new avenues for precision medicine at single cell level.

Hongbao Xin

Professor

Jinan University,China

Hongbao Xin is currently a Professor and Doctoral Supervisor at Jinan University, Vice Dean of the College of Physics and Optoelectronic Engineering, and Executive Vice Dean of the Institute of Nanophotonics. He received his Bachelor's and Ph.D. degrees from Sun Yat-sen University, and subsequently conducted postdoctoral research at the National University of Singapore and the University of California, Berkeley. He joined Jinan University in 2018, focusing on biophotonic manipulation. As first/corresponding author, he has published 48 papers in journals such as Nature Photonics, Nature Reviews Materials, Nature Communications, Light: Science & Applications, and Advanced Materials. He has been honored as a Youth Changjiang Scholar of the Ministry of Education and a World's Top 2% Scientist. He leads projects including the NSFC Original Exploration Program and the National Key R&D Program for Young Scientists. His awards include the Top 10 Social Impact Events in Optics in China, the Youth Science and Technology Award of the China Instrument and Control Society, the First Prize of Natural Science of Guangdong Province, and the First Prize of Optical Science and Technology of Guangdong Province. He serves as Associate Editor of Optics Express, Editorial Board Member of APL Photonics, and Youth Editorial Board Member for PhotoniX, Fundamental Research, JIOHS and other journals.

[AI-10] PIBM2026-0703-1

Ratiometric Polymer Dot Biosensor for Point-of-Care Metabolic Monitoring

Mingyue Gong[1], Zirui Zeng[1], Xiaoju Men[1,2], and Haobin Chen[1,2,3]

[1] School of Basic Medical Sciences, Central South University, Changsha 410013, China

[2] FuRong Laboratory, Changsha, 410078, China

[3] National Engineering Research Center of Personalized Diagnostic and Therapeutics, Changsha, 410083, China

Corresponding author e-mail address: chenhb@csu.edu.cn

Abstract: Long-term management of inherited metabolic disorders and ketogenic therapy requires frequent and accurate quantification of phenylalanine and β-hydroxybutyrate. Conventional methods are labor-intensive and instrument-dependent, limiting point-of-care use. Here, we report a ratiometric fluorescence platform using semiconducting polymer dots (Pdots) for two clinical applications: phenylketonuria screening and salivary ketone monitoring. The assay leverages specific dehydrogenases to convert target metabolites stoichiometrically to NADH. NADH quenches Pdot red emission via electron transfer while enhancing its blue fluorescence, producing a ratiometric B/R signal that self-corrects for optical interferences. A 3D-printed portable module with a 365 nm LED and a smartphone app enables automated image capture, RGB analysis, and real-time concentration readout. The system supports both microplate and test strip formats, and incorporates alternative camera or color sensor modules to ensure consistency across devices. In spiked plasma, phenylalanine detection showed a linear range of 0–2400 μM and a limit of detection of 0.29 μM. For salivary β-hydroxybutyrate, the dynamic range covered 0–5 mM and a strong correlation with blood values ($r = 0.89$, $p < 0.01$). This platform integrates molecular specificity, optical self-calibration, and smartphone analysis, offering a cost-effective and scalable solution for decentralized metabolic monitoring and personalized dietary management.

Haobin Chen

Professor

Biomedical Engineering at the Central South University,China

Haobin Chen is the Professor of Biomedical Engineering at the Central South University, Changsha. He obtained a B.S. in Microelectronics and a Ph.D. in Physical Electronics from the Jilin University at Changchun in 2013 and 2018. After completing postdoctoral research in Professor Daniel T. Chiu's laboratory at the University of Washington, Seattle, he started in the Spring of 2022 at the Central South University. He is the author of more than 60 publications and is the inventor on 6 issued patents. His research field of interest is activatable probes and nanomaterials for ultra-sensitive bioanalytical measurements and bio-optical applications.

[AII-1] PIBM2026-0605-1

Molecular Knowledge-Driven Cross-Fusion Transformer: A Generalized Multimodal Neural Network for Biomedical Data Integration

Liwen Chen[1], Jiong Ma[1]

[1] *Department of Optical Science and Engineering, School of Information Science 10 and Technology, Fudan University, Shanghai, China.*

Abstract: Unimodal identification methods fail to fully meet the precise needs for diagnosing meningitis. To overcome this limitation, we developed a generalized multimodal neural network for integrating heterogeneous biomedical data, which we termed the molecular knowledge-driven cross-fusion transformer (MKD-CFT) model. MKD-CFT constructs a novel two-dimensional interaction map through the interaction between protein peaks in mass spectrometry (MS) and molecular vibrations in Raman spectroscopy (RS). Leveraging directional cross-attention, multiscale convolution, and adaptive weighting mechanisms, this model achieves a true synergistic effect of $1+1>2$ while extracting long-range dependencies and capturing local neighborhood patterns from both modalities.

[NI-1] PIBM2026-0610-2

Ultrasound-triggered nitric oxide boosts neuromodulation efficacy and relieves Parkinson's symptoms in vivo

Siyi Lan[1,2], Zhen Yuan[1,2,*]

[1] Faculty of Health Sciences, University of Macau, Macau SAR 999078, China

[2] Centre for Cognitive and Brian Sciences, University of Macau, Macau SAR 999078, China

** Corresponding author: Prof. Zhen Yuan, Email: zhenyuan@um.edu.mo*

Abstract: Non-invasive neuromodulation technologies hold great promise for treating brain disorders, yet existing methods face trade-offs between spatial resolution, depth penetration, and mechanistic specificity. Transcranial ultrasound offers high spatiotemporal resolution but suffers from limited therapeutic efficacy when applied alone. Here, we developed ultrasound-responsive, NO-releasing nanoparticles (BP-B) that transiently open the blood–brain barrier (BBB) and confer neuroprotection upon ultrasound stimulation. Notably, we discovered that nitric oxide (NO) itself amplifies ultrasound-induced cortical neuronal activation when focused ultrasound targets to the subthalamic nucleus (STN) region, creating a positive feedback loop between drug delivery and neuromodulation. In a mouse model of Parkinson's disease, combined BP-B and ultrasound treatment significantly alleviated motor symptoms, an effect greater than that observed with ultrasound or BP-B alone. This work introduces a previously unexplored paradigm in which a single ultrasound-responsive nanoplatform integrates BBB opening, enhanced drug delivery, and synergistic neuromodulation, offering a non-invasive, toxicity-sparing strategy for neurodegenerative disease therapy.

Dr. Zhen Yuan is a Professor with Faculty of Health Sciences at the University of Macau and concurrently serves as the Head of the Centre for Cognitive and Brain Sciences with the university. Professor Yuan has achieved a series of internationally recognized in the fields of neuroscience and biomedical optics. He has published over 400 high-quality SCI-indexed papers in top journals including *Science Advances*, Nature Neuroscience,*Nature Communications*, Cell Reports, *Cell Reports Physical Sciences*, *Cell Biomaterials*, *Research*, *Microbiome*, *Translational Psychiatry*, *Biological Psychiatry*, and *Molecular Psychiatry*, *Advanced Materials*, *Small*, *Advanced Functional Materials*, *Nano Letters*, *Advanced Sciences*, *ACS Nano*, *Biomaterials*, *Nano Micro Letters*, *Angewandte Chemie International Edition*, *Theranostics*, *Optics Letters*, and *Applied Physics Letters*. His Google Scholar H-index is 65, with a total citation of around 13100.

Professor Yuan currently serves on the editorial board of *Quantitative Imaging in Medicine and Surgery* and Journal of Innovative Optical Health Sciences, and is also a Senior Associate Editor for *BMC Medical Imaging* and *Frontiers in Human Neuroscience*. He is a Fellow of Vebleo. He holds positions as a Standing Committee Member of the Biomedical Optics Committee of the Chinese Optical Society, Vice President of the Macau Society of Nuclear Medicine and Molecular Imaging, a Council Member of the Chinese Society for Anatomical Sciences, and a Council Member of the Chinese Neuroscience Society. He has received the China's Top Optics Research Award, led 18 national and provincial-level projects, and has filed/been granted 10 international and domestic invention patents.

[NI-2] PIBM2026-0401-1

Specific control of calcium channels via two-photon excitation

Hao He[1]

[1] Schotablol of Biomedical Engineering, Shanghai Jiao Tong University,

Shanghai 200030, P.R. China

Corresponding author e-mail address: haohe@sjtu.edu.cn

Abstract: Ca^{2+} channels can be externally activated by optogenetics, but it requires robust introduction of exogenous optogenetic genes. Here we present in vivo femtoSOC, a method for direct control of Ca^{2+} channels solely by ultrafast laser without the need for optogenetic tools or any other exogenous reagents. Specifically, by focusing and scanning wavelength-tuned low-power femtosecond laser pulses on the plasma membrane for multiphoton excitation, we directly induced photoexcited flavin bonding with cysteine in Orai1 that then polymerize to form store-operated calcium channels (SOCs). By this method, we achieve to activate an individual neuron in a cortical ensemble in layer 2/3 of the primary visual cortex (V1), which, in the absence of any visual stimuli, is sufficient to elicit visually percept-specific behaviors in awake mice, without co-activating other neurons in the ensemble in layer 2/3 of V1. Remarkably, the disruption of a single neuron within the ensemble temporarily paralyzes the entire ensemble and suspends behavioral responses to visual stimuli. However, the ensemble rapidly recovers its responsiveness and effectively maintains the internal representations necessary for these behaviors. Consequently, individual neurons in ensembles appear to function as fully functional units, redundantly supporting both the internal representations and the robustness of the entire ensemble. Furthermore, we reveal the existence of a Ca^{2+} channel in nuclear envelope (NE) by developing an optical technique, termed Ca^{2+} release in microdomain evoked by laser (CaMEL) that activates a local Ca^{2+} rise restricted to a cytosolic microdomain while maintaining intracellular Ca^{2+} homeostasis.

[NI-3] PIBM2026-0406-10

High-throughput two-photon microscope for multiparameter and quantitative brain function imaging

Shiwei Ye[1,*] and Wei Zheng[1]

[1]Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

[*]Corresponding author e-mail address: shiwei.ye@siat.ac.cn

Abstract: Large-scale recording of multiple dynamic behaviors and quantitative neurochemical concentrations with high spatiotemporal resolution is critical to understanding complex brain functions. Two-photon microscopy (TPM) is the excellent choice for brain function imaging because of its high resolution, deep tissue penetration, and favorable biosafety. However, current TPM is limited by a restricted field-of-view (FOV), an inherent trade-off between the imaging area and temporal resolution, and an insufficient amount of information obtained using only intensity recording.

In this study, we introduce the large-FOV, dual-region, two-photon fluorescence lifetime imaging microscopy (LD-2P-FLIM), which is characterized by a large space-bandwidth product (SBP) (resolution × FOV) and high data throughput (pixel number × frame rate), for multiparameter and quantitative brain function imaging. First, LD-2P-FLIM enables large-FOV (3×3 mm^2) and high-resolution (0.7-μm lateral resolution) two-photon imaging using only off-the-shelf optics with an effective adaptive optics strategy. Second, LD-2P-FLIM can simultaneously record neural activities in two arbitrarily selected regions across the whole large FOV using temporal multiplexing and two independent scan engines. Finally, by a home-made field programmable gate array (FPGA) module, LD-2P-FLIM can provide simultaneous two-region fluorescence lifetime images with a data throughput of up to 15.73 megapixels per second (512×512 pixels, 30Hz, two regions).

Benefitting from the large SBP and the high data throughput, various functional brain imaging experiments were conducted on awake mice using LD-2P-FLIM. We demonstrate LD-2P-FLIM in calcium imaging of neurons across multiple cortical areas, and synchronous observation of microglia and neuron. We apply LD-2P-FLIM to large-scale recording of neurovascular coupling at the same time and space under both physiological and pathological conditions. More importantly, for the first time, we show its unique capability in the quantitative imaging of calcium concentrations in a large neuronal population. The results suggest LD-2P-FLIM can advance functional neural imaging from a qualitative to a quantitative level.

[NI-4] PIBM2026-0609-1

Intervention of IL-6 signaling in the area postrema ameliorates cancer cachexia in mice

Yuanyuan Wang[1], Qingtao Sun[1*]

[1.] Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, China

Abstract: Interleukin-6 (IL-6) has been a crucial factor in inducing cancer cachexia. However, how peripheral IL-6 influences the brain remains poorly understood. Here, we show that neurons in the area postrema (AP) is a critical mediator of IL-6 function in cancer cachexia in male mice. We find that circulating IL-6 can rapidly enter the AP and activate neurons in the AP and its associated network. Remarkably, neutralization of IL-6 in the brain of tumor-bearing mice with an anti-IL-6 antibody attenuates cachexia and hyperactivity in the AP network and markedly prolongs lifespan. Furthermore, suppression of Il6ra, the gene encoding IL-6 receptor, specifically in AP neurons with CRISPR/ dCas9 interference achieves similar effects. Silencing Gfral-expressing AP neurons also attenuates cancer cachectic phenotypes and AP network hyperactivity. In addition, we developed a splice-switching antisense oligonucleotide (ASO) based therapy for treating cancer cachexia by reducing IL-6 receptor (IL-6R) expression in the brain. In mouse models of cancer cachexia, a single dose of a pair of ASOs, administered by intracerebroventricular injection after cancer onset, is sufficient to reduce IL-6R levels in the brainstem, ameliorate cachectic symptoms and extend survival. We also developed ASOs that suppress human IL-6R expression, paving the road for clinical studies. Our study thus provides a new approach for treating cancer cachexia.

[TO-1] PIBM2026-0518-1

Dual-mode endoscopic probe for optical coherence tomography and plasma ablation

Minghui Chen*, Haochen Hu

Shanghai Engineering Research Center of Interventional Medical Device, the Ministry of Education of Medical Optical Engineering Center, School of Health Sciences and Engineering, University of Shanghai for Science and Technology, Shanghai 200093, China

Abstract: A major challenge in minimally invasive endoscopic surgery is achieving precise tissue removal without causing excessive thermal damage to adjacent healthy layers. Traditional thermal ablation lacks real-time depth feedback, often leading to severe complications such as perforation. To address this, we present a novel dual-mode endoscopic probe that integrates optical coherence tomography (OCT) with low-temperature plasma ablation. The integrated probe features a compact diameter of 5 mm and a rigid length of 40 mm. For the imaging module, a piezoelectric bender driven at 278.5 Hz induces a single-mode fiber resonance, achieving a 1.88-mm lateral scanning range and a 20-μm lateral resolution at a 5-mm working distance. For the therapeutic module, a coaxial needle-shaped electrode was optimized through finite element analysis to ensure stable plasma generation at a low peak voltage of 120 V. Functional validation was performed on ex vivo porcine intestine tissues. Real-time OCT imaging provided precise, high-resolution visualization of the ablation progression. Furthermore, thermocouple measurements and histological (H&E) analysis confirmed that the plasma ablation maintained a low temperature, strictly restricting the thermal damage zone within the mucosal layer without carbonization. This study provides a highly promising and safe dual-mode integration strategy for future precise minimally invasive therapies.

Keywords: optical coherence tomography, plasma ablation, minimally invasive surgery, endoscopic prob

[TO-2] PIBM2026-0330-1

Advanced in Non-contact Optical Coherence Elastography

Yirui Zhu[1], Jiulin Shi[1], and Xingdao He[1]

[1]Jiangxi Key Laboratory of Optoelectronic Information Sensing Technology and Instruments, Nanchang Hangkong University, Nanchang, 330063, China

Abstract: The onset and progression of clinical diseases are closely associated with the biomechanical properties of biological tissues. Nevertheless, the in situ, non-contact, micron-scale high-resolution and high-sensitivity detection of longitudinal and shear moduli in biological tissues remains a crucial bottleneck that urgently needs to be addressed. Herein, we propose a non-contact optical coherence elastography (OCE) method that integrates air-coupled ultrasound transducer with optical coherence elastography. This paper presents a comprehensive overview of our research team’s pioneering contributions to non-contact optical coherence elastography, with particular emphasis on its translational potential for elastography of diverse biological tissues—including ocular and cerebral tissues. Furthermore, the manuscript critically evaluates the distinct advantages of non-contact OCE in quantitatively characterizing tissue elastic modulus, and outlines key opportunities and challenges for its clinical implementation.

Yirui Zhu, Associate Professor, School of Instrument Science and Optoelectronic Engineering, Nanchang Hangkong University

Ph.D. in Physics, visiting scholar at the University of California, Irvine / CSIC (Spain); has presided over 5 provincial and ministerial-level or above projects, including the National Natural Science Foundation of China (Category C), Key Research and Development Program of Jiangxi Province, and Natural Science Foundation of Jiangxi Province. In the past three years, has published more than 20 papers in journals such as Opt. L. Techn., BOE, APL, and J. Biop., including 2 cover papers, holds 3 authorized national invention patents, and won the Second Prize of Technological Invention of the Chinese Optical Society (ranked second). Research direction: functional optical coherence tomography technology and its applications

[TO-3] PIBM2026-0405-9

A novel fast and high resolution IVOCT image reconstruction method

Haiyi Bian[1,2], Hongnan Duan[1,2], Lei Liu[1], Xiaoteng Yan[3], and Xiupin Wu[4]

[1]Huaiyin Institute of Technology, Huai'an, Jiangsu 223003, P. R. China

[2]Nanjing Forssmann Medical Technology Co., Ltd., Nanjing, Jiangsu 210031, P.R. China

[3]The Second People's Hospital of Huai'an, Huai'an, Jiangsu 223003 P. R. China

[4]Shanghai University of Medicine and Health Sciences, Shanghai 201318 P. R. China

Corresponding author e-mail address: bianhaiyi@163.com

Abstract: Intravascular optical coherence tomography, as an effective technique for guiding percutaneous coronary intervention (PCI), relies on resolution and imaging speed as key technical indicators. To improve the speed and resolution, in this study, a linear relationship model between interference spectral frequency and depth was established, and support vector regression (SVR) was employed for spectral fitting. The sparrow search algorithm (SSA) was applied to optimize the hyperparameters, while partial least squares (PLS) was used to refine the predicted values, enabling more accurate reconstruction. By comparing the proposed method with conventional Fourier transform-based reconstruction, the experimental results demonstrate that the proposed method improves axial resolution by a factor of two and resolves structures that are only visible with full bandwidth. In addition, the proposed method provides consistent contrast and speckle statistics. Through a layered search strategy, the computational cost of spectral fitting is significantly reduced. Benefiting from the elimination of spectral resampling and the requirement of only a single spectral fitting step, the B-scan computation time is reduced to tens of milliseconds, which indicates that this method holds promise for fast, high-resolution OCT imaging, providing a feasible pathway for real-time biomedical imaging and the large-scale application of super-resolution OCT.

[TO-4] PIBM2026-0406-19

Accurate Extraction of OCE Elastic Waves and Motion Artifact Correction Based on Color Feature Segmentation and Double-Line Template Matching

Gangshi[1*], Zechen Cao[2], Yunfeng Wang[1], Xingdao He[2*]

[1] School of Information Engineering, Nanyang institute of Technology, Nanyang, 473004, China (8-point type,centered, italicized)

[2] Key Laboratory for Optoelectronic Information Perception and Instrumentation of Jiangxi Province, Nanchang Hangkong University, Nanchang 330063, P. R. China

Corresponding author e-mail address: Gangshi1145@163.com (Gang Shi), xingdaohe@126.com (Xingdao He)

Abstract: In vivo optical coherence elastography (OCE) is severely limited by motion artifacts in clinical applications. These artifacts reduce the quantification accuracy of Young's modulus and hinder the extraction of tissue mechanical properties. This paper proposes a pseudo-echo correction algorithm based on color feature segmentation (CFS) and double-line template matching (BTM). The CFS algorithm calculates the color moments of the multi-channel adaptive threshold by analyzing the RGB features of the OCE image, thereby accurately segmenting the artifacts and elastic waves; an image rotation strategy is also added to extract tilted elastic waves and reduce separation errors. The BTM algorithm suppresses background noise through Gaussian filtering, calculates the extreme values of column pixels to obtain the elastic wave center curve, and designs a double-line adaptive template for precise matching, while performing adaptive size adjustment. In the processing of simulated images, in vivo rabbit cornea and human skin experimental data, vibration displacement curves, HFI, and EWL-MSE are used as image quality evaluation indicators, and the elastic wave phase velocity deviation is used as the core performance indicator. The results show that the peak signal-to-noise ratio of CFS reaches 36.2 dB, and the effective no-echo mean square error of BTM is 47.3 dB; both can effectively eliminate artifacts and noise while retaining the characteristics of elastic waves. Compared with traditional methods, the phase velocity calculation deviation is significantly reduced, and the accuracy is improved. These robust algorithms can adapt to different OCE images of biological tissues, improve the accuracy of elastic wave extraction, and provide a reliable means for quantitative assessment of tissue mechanical properties in clinical practice, laying the foundation for accurate calculation of Young's modulus.

[TO-5] PIBM2026-0601-2

SERS-Enabled Liquid Biopsy for Precision Diagnostics

Jing Wang[1]

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, Fujian Normal University, Fuzhou, Fujian, China

Corresponding author e-mail address: jing.wang@fjnu.edu.cn

Abstract: Liquid biopsy is emerging as a powerful tool for the early detection, molecular classification, and treatment monitoring of diseases. However, its clinical translation remains challenged by the lack of robust biomarkers for complex diseases, the limited ability of single-analyte measurements to capture disease heterogeneity, the scarcity of high-performance affinity reagents for certain targets, and the difficulty of integrating multidimensional diagnostic information. To address these limitations, we have leveraged the molecular fingerprinting capability, multiplexing capacity, and high sensitivity of surface-enhanced Raman

scattering (SERS) to develop liquid biopsy technologies for diverse biomarker classes, including circulating tumor cells, extracellular vesicles, miRNAs, and circulating proteins. Three complementary technological pathways will be highlighted: (i) integrating proteomics-guided biomarker discovery with multiplexed SERS analysis for biomarker identification, validation, and disease classification; (ii) employing engineered recognition molecules, such as nanobodies, to enable highly sensitive and specific detection when conventional antibodies are unavailable or inadequate; and (iii) developing deep learning-driven multimodal fusion frameworks that combine SERS spectra with clinical parameters, metabolomics, and other complementary datasets to establish noninvasive diagnostic models for complex diseases. Together, these advances illustrate how SERS-based liquid biopsy can bridge biomarker discovery, molecular sensing, and artificial intelligence, accelerating the translation of precision diagnostics into clinical practice

[TO-6] PIBM2026-0402-3

Study on Correlation Indicators of Intestinal Barrier Function Based on the Combination of Multidimensional Metabolomic Data and Raman Spectroscopy

Qi Zeng[1,2,3,4*], Zexian Zhao[1,2], Xudong Zhou[1,2], Jinzhi Feng[5], Bin Guan[6], Xiaojia Hu[7] and Xueli Chen[1,2,3,4*]

[1] Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[2] Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[3] Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China.

[4] State Key Laboratory of Electromechanical Integrated Manufacturing of High-Performance Electronic Equipment, Xidian University, Xi'an, Shaanxi 710071, China.

[5] Hospital of Xidian University, Xidian University, Xi'an, Shaanxi 710071, China.

[6] Department of Pharmacy, Affiliated Wuxi Fifth Hospital of Jiangnan University, Wuxi, Jiangsu 214013, China

[1]Shanghai Nature ' s Sunshine Health Products Co. Ltd, Shanghai 200040, China

Corresponding author e-mail address: qzeng@xidian.edu.cn; xlchen@xidian.edu.cn

Abstract: The intestinal barrier plays a crucial role in maintaining intestinal homeostasis and host immune balance. Raman spectroscopy holds potential applications in the detection of intestinal-related diseases and the prediction of therapeutic efficacy. This study aimed to comprehensively evaluate intestinal barrier function by conducting a clinical cohort trial to investigate the protective effects of a plant-derived formula on human intestinal barrier function. Based on machine learning algorithms, a multi-dimensional intestinal barrier function assessment model was established from qualitative and quantitative perspectives, integrating routine blood, routine urine, biochemical indices, and Raman spectral data. Nine clinical indicators related with intestinal barrier function were screened. The top five main Raman spectral features of serum correlating with intestinal barrier integrity were identified, too. The evaluation models were established by various machine learning algorithms. For qualitative analysis, the evaluation model based on support vector machine (SVM) achieved optimal performance with accuracy of 0.97 and AUC of 1.000. For quantitative analysis, the D-lactic acid (D-LA) prediction model based on random forest (RF) performed best, yielding a test-set R^2 of 0.866 and RMSE of 0.701. Thus, quantitative evaluation model for intestinal barrier function could take D-LA as the primary marker and LPS as the auxiliary indicator. This study provides an auxiliary tool for elucidating pathogenesis, early screening, diagnosis, efficacy monitoring, and intervention evaluation of intestinal barrier-related disorders. And it could offer methodological support for intestinal pathophysiology research, drug development,

and detection technology optimization.

Keywords: Intestinal barrier, Raman spectroscopy, Multidimensional data, Machine learning, Evaluation model

[TO-7] PIBM2026-0601-1

Application of SERS-Based Multifactor Analysis of Extracellular Vesicles for Cancer Detection and Monitoring

Quan Zhou[1,2,*]

[1]College of Chemistry, Fuzhou University, Fuzhou, Fujian, China

[2]Fuzhou University Affiliated Provincial Hospital, Fuzhou, Fujian, China

**Corresponding author e-mail address: 935886885@qq.com*

Abstract: Extracellular vesicles (EVs) are nanoscale vesicles actively secreted by cells that carry diverse biomolecular cargo, including proteins, glycans, and nucleic acids. They play critical roles in tumor progression and immune regulation and have shown considerable potential in cancer screening, classification, and treatment monitoring. However, the complex origins and highly heterogeneous molecular composition of EVs, together with the interference of low-abundance signals in complex biological samples, limit the accuracy and robustness of their clinical applications.

To address these challenges, we proposed the concept of multifactor authentication (MFA) for EV analysis, which integrates multidimensional molecular and structural information to improve the reliability and specificity of EV identification in complex biological systems. Based on this concept, we developed a surface-enhanced Raman scattering (SERS)-based EV analysis platform and integrated microfluidic technologies to enable efficient EV enrichment and multiplexed biomarker detection.

This presentation will highlight the application of the SERS-based MFA strategy in three different disease settings. (1) To monitor therapy resistance during targeted treatment of melanoma, we established a liquid biopsy approach based on dynamic changes in EV protein phenotypes and revealed the association between epithelial–mesenchymal transition-related EV signatures and the development of resistance. (2) Through proteomic analysis, we identified and validated a panel of EV protein biomarkers that demonstrated excellent discriminative performance for early lung cancer detection. (3) To accommodate the analysis of different types of biomarkers, we optimized the molecular recognition strategy of SERS probes, enabling the parallel detection of EV proteins and glycans. The platform was subsequently validated using clinical plasma samples and demonstrated the ability to distinguish benign from malignant pulmonary nodules.

[TO-8] PIBM2026-0515-2

Bioinformatics-Driven SR-SIM with Machine Learning Quantifies Mitochondrial-ATP Spatial Features for Early Parkinson's Disease Prediction

Lihua Li[*], Zhongmin Yang[*]

Abstract：Parkinson's disease (PD) mechanisms remain elusive as conventional imaging cannot resolve transient subcellular metabolic fluctuations during prodromal stages. Clinical onset occurs only after irreversible dopaminergic neuron loss, highlighting the critical need to resolve early subcellular bioenergetic disruptions. We report an integrated biophotonic platform combining aggregation-induced emission (AIE)

probes, super-resolution structured illumination microscopy (SR-SIM), and machine learning to decode mitochondrial ATP architecture as a core early pathological driver of PD. Overcoming aggregation-caused quenching and phototoxicity, our AIE-SR-SIM system enables long-term, high-fidelity mapping of mitochondrial ultrastructure and ATP homeostasis in living neurons. From 3,000 SR-SIM images, we extract >50 quantitative morphometric, spatial, functional features of mitochondria and ATP. Using this high-dimensional bioinformatic feature library paired with a machine learning framework, we achieve single-cell stratification of pathological severity via mitochondrial bioenergetic fingerprints, and enable early PD drug efficacy prediction. This approach overcomes the limitations of conventional qualitative imaging that lacks quantitative predictive capability. Leveraging this optical-computational synergy, we performed a targeted phenotypic screen of ATP-modulating compounds, revealing region-specific therapeutic responses in neuronal axons and somas. We identify Vitamin B2 (VB2) and Nicotinamide Adenine Dinucleotide (NAD) as potent candidates that restore intracellular ATP architectures. Notably, VB2 effectively ameliorates early-stage phenotypes in both cellular and murine models by rescuing bioenergetic collapse. This work establishes a generalizable, mechanism-driven imaging–analytics pipeline for prodromal neurodegeneration research, and demonstrates that mitochondrial ATP architecture serves as an early biomarker and therapeutic target. Our integrated photonics–machine learning strategy provides a transformative toolkit for discovering next-generation disease-modifying therapies for PD and related disorders.

[TO-9] PIBM2026-0627-2

Hyaluronic acid-engineered infection-responsive liposomes achieve biofilm penetration and synergistic photothermal-photodynamic antibacterial therapy

Shisheng Cao[1], Zeqi Liu[1], Jiakang Zhao, Xiaoxi Dong[1] Jianwu Dai[1], Huijuan Yin[1*]

[1]Tianjin Key Laboratory of Neuromodulation and Neurorepair, Integrated Regenerative Medicine Laboratory, Institute of Biomedical Engineering, Chinese Academy of Medical Sciences& Peking Union Medical College, Tianjin, 300192, PR China

Corresponding author e-mail address: yinhj@bme.pumc.edu.cn

Abstract: Bacterial infections, particularly those caused by drug-resistant strains and biofilm-associated wounds, pose serious challenges in clinical treatment. Although phototherapy is a promising antibacterial approach, conventional photosensitizers suffer from poor stability, low photothermal conversion efficiency, and limited biofilm penetration. Herein, we developed an infection-responsive hyaluronic acid-modified cationic liposomal platform (HA@ICG@Lip) for synergistic photodynamic and photothermal antibacterial therapy. Elevated hyaluronidase (HAase) levels in infected tissues pecifically degrade the outer HA layer, triggering enzyme-responsive deshielding to expose the positively charged liposomal core, which enhances bacterial adhesion and deep biofilm penetration. Upon near-infrared irradiation, indocyanine green (ICG) generates reactive oxygen species and localized heat, inducing bacterial membrane disruption and biofilm disintegration. Moreover, ICG forms J-aggregates within the liposomal matrix, improving near-infrared absorption and photothermal conversion efficiency. In vivo, HA@ICG@Lip combined with 808 nm LED irradiation effectively eradicated mixed-species biofilm infections and accelerated wound healing. This study provides a polysaccharide-based, infection responsive phototherapeutic nanoplatform with potential for treating biofilm-associated infections

[TO-10] PIBM2026-0618-2

Review and prospects of corneal topography-guided personalized laser corneal refractive surgery

Shangbin Chen[1, 2], Chenxi Liu[2], and Shaoqun Zeng[*1, 2]

[1] Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, 430074,Hubei, China

[2] MOE Key Laboratory for Biomedical Photonics, Department of Biomedical Engineering, College of Life Science and Technology, Advanced Biomedical Imaging Facility, Huazhong University of Science and Technology, Wuhan, 430074, Hubei, China

**Corresponding autho: sqzeng@hust.edu.cn*

Abstract: With the continuous advancement of refractive surgery technology, personalized treatment has become a key factor in improving surgical outcomes and safety. As a core tool for assessing corneal morphology and optical characteristics, corneal topography has evolved from simple curvature measurements to high-precision three-dimensional tomographic imaging systems, further developing into AI-assisted analytical techniques, providing crucial support for personalized refractive surgery. This review systematically traces the development of corneal topography, elucidates its fundamental principles, and explores its applications in personalized laser refractive surgery, including preoperative screening, surgical plan design, intraoperative navigation, and postoperative visual quality assessment. This review further analyzes the challenges of corneal topography-guided personalized laser refractive surgery and provides insights into future directions, aiming to offer references for clinical and research purposes.

Keywords: corneal topography, personalization, laser refractive surgery, artificial intelligence, visual quality

[TO-11] PIBM2026-0629-2

A motion-tolerant method for biomagnetic measurements with moving subjects in unshield environment

Zeming Li[1,2], Wei Huang[1,3], Wen Luo[1,2], Li Wang[1,2], Fumin Guo[1,3], Yinan Hu[1,2] and Xin Zhou[1,2,4]*

[1]State Key Laboratory of Magnetic Resonance Spectroscopy and Imaging, National Center for Magnetic Resonance in Wuhan, Wuhan Institute of Physics and Mathematics, Innovation Academy for Precision Measurement Science and Technology, Chinese Academy of Sciences, Wuhan, 430071, Hubei, China.

[2]University of Chinese Academy of Sciences, Beijing, 100049, China.

[3]College of Life Science and Technology, Huazhong University of Science and Technology, Wuhan, 430074, Hubei, China.

[4]School of Biomedical Engineering, Hainan University, Haikou, 570228, Hainan, China.

Corresponding author e-mail address: xinzhou@wipm.ac.cn

Abstract: We present a motion-tolerant biomagnetic measurement approach based on optically pumped magnetometers(OPMs) for recordings with moving subjects. In a magnetically shielded room environment, the system provides an ultra-low-noise baseline and peak sensitivity, enabling stable extraction of neural signatures with high repeatability. In an unshielded environment, we combine a reference magnetometer, adaptive interference cancellation, and closed-loop field compensation to suppress power-line noise and motion-induced artifacts, enabling deployable, continuous measurements of MCG in realistic settings. Comparative results highlight a clear trade-off: shielded measurements favor ultimate sensitivity and precise spatial characterization, whereas unshielded measurements prioritize portability, real-time robustness, and

naturalistic monitoring. This method supports both laboratory-grade studies and scalable clinical or field applications of OPMs biomagnetism.

[TO-12] PIBM2026-0402-1

Biomedical Microwave-Induced Thermoacoustic Imaging

Huan QIN*

MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China

**Corresponding author e-mail address: qinghuan@scnu.edu.cn*

Abstract: This presentation introduces microwave-induced thermoacoustic imaging, a technique that employs a "microwave excitation-ultrasound detection" energy conversion mechanism to overcome the inherent depth limitations of conventional optical imaging in biological tissues. It enables non-invasive, high-resolution (hundreds of microns) imaging of living tissue at depths of several centimeters. We will elaborate on the newly established theory and technology of polarization-resolved microwave-induced thermoacoustic imaging, which has successfully achieved polarization anisotropy imaging of the myocardium and cerebral nerve fibers in vivo. This addresses the challenge of non-invasive detection of deep-seated microscopic pathological structures. Furthermore, the presentation highlights fundamental applied research findings, including structural and functional imaging of cerebral nerve fibers, rapid stroke typing and prognosis monitoring, and dynamic abdominal imaging. These findings provide a novel visualization approach for investigating the pathological correlations between microstructure and function in deep biological tissues.

[TO-13] PIBM2026-0406-26

Multispectral Photoacoustic Tomography for High-Precision Delineation of Thermal Ablation Zones in Subcapsular Hepatocellular Carcinoma

He Li[1], Wang Wenxiao[1], Li Qing[2], Zhu Shouping[1,3], and Wang Yihan[1,3*]

[1] the Engineering Research Center of Molecular and NeuroImaging of Ministry of Education, School of Life Science and Technology, Xidian University, Xi'an, 710126, China

[2] the Ultrasonic Diagnosis and Treatment Center, Xi'an International Medical Center, Xi'an, 710126, China

[3] the Innovation Center for Advanced Medical Imaging and Intelligent Medicine, Guangzhou Institute of Technology, Xidian University, Guangzhou, 510555, China

Corresponding author e-mail address: wangyihan@xidian.edu.cn

Abstract: Thermal ablation has become a standard treatment for early-stage hepatocellular carcinoma (HCC). However, for subcapsular HCC (SHCC) located within 1 cm of the liver surface, accurate delineation of ablation margins remains challenging, posing a significant risk of thermal injury to adjacent critical structures. Therefore, high-precision intraoperative monitoring of the ablation zone is essential for improving both treatment safety and efficacy. Existing imaging modalities have notable limitations, including insufficient functional contrast in ultrasound, post-procedural assessment in contrast-enhanced ultrasound, and limited intraoperative applicability of MRI and CT.

Multispectral photoacoustic tomography (MSPAT) enables combined structural and functional imaging by capturing ablation-induced changes in optical absorption. In this study, we investigate the feasibility of MSPAT

for deep-tissue SHCC ablation monitoring using fresh *ex vivo* porcine liver models (N = 6). To address the key challenges of light attenuation and spectral complexity in deep tissue, we develop a dedicated computational framework for precise ablation state differentiation: 1) a photon transport model integrating measured liver data with reference optical parameters to achieve centimeter-depth fluence compensation; 2) an unsupervised clustering model utilizing a hybrid "spectral angle-Euclidean distance" cost function to address the absence of prior ablation spectra; 3) a non-negative matrix factorization method combining spatial sparsity regularization and hierarchical iterative updating, specifically designed for the "coarse-grained" differentiation of typical ablation states. This robust unmixing method effectively avoids local minima under severe spectral overlapping and spatial co-localization, significantly enhancing boundary resolution and convergence efficiency.
Experimental results demonstrate stable reconstruction of a theoretical "three-zone" ablation structure (central necrotic, transition, and unablated zones). Validated against pathology, relative errors for the major axis, minor axis, and area are <5%, <4%, and <10%, respectively. This study verifies the feasibility of deep-tissue MSPAT and offers a highly translatable clinical strategy for high-precision intraoperative ablation margin assessment

[TO-14] PIBM2026-0402-7

Sparse-Sampling Photoacoustic Imaging and Artifact Suppression

Jiangbo Chen[1*], Kexin Chen[1], Congsen Li[1], Xiaobin Hong[1]

[1.] School of Mechanical & Automotive Engineering, South China University of Technology, Guangzhou, Guangdong, China

Abstract (in English): Photoacoustic imaging has emerged as a powerful modality for biomedical research by integrating optical contrast with ultrasonic penetration depth. High-speed implementations, including photoacoustic microscopy (PAM) and photoacoustic computed tomography (PACT), are essential for capturing rapid pathophysiological dynamics. In PAM, sparse sampling is often employed to accelerate imaging, but it introduces significant data loss, limiting reconstruction quality due to the constraints of existing algorithms. In PACT, image quality is often degraded by reconstruction artifacts arising from system geometry and inversion limitations. For sparse-sampling-based PAM, we propose a novel framework that exploits spatiotemporal information for high-fidelity reconstruction. Instead of treating system mechanical perturbations as detrimental, the framework exploits them as complementary cues. Specifically, a multi-frame reconstruction network utilizes inter-frame spatial shifts induced by inherent mechanical perturbations to enable super-resolution recovery from sparsely sampled data. To overcome the scarcity of fully sampled ground truth, pseudo-ground-truth data are generated by embedding deformation fields into duplicated static images, facilitating effective supervised training. By modeling spatiotemporal correlations, the network achieves superior performance in PSNR, SSIM, and LPIPS while remaining robust under high sparse-sampling rates. For PACT, a dynamic artifact suppression strategy based on pixel intensity consistency is introduced. Reconstruction artifacts vary with acquisition geometry, whereas true vascular structures remain stable. Exploiting this discrepancy allows the method to disentangle artifacts from underlying vascular features, yielding robust image enhancement. Experimental results demonstrate improvements in PSNR and SSIM over existing methods, alongside an ~100-fold increase in processing speed on large-scale datasets. Overall, these approaches provide an efficient and scalable framework for high-speed photoacoustic imaging, enabling real-time visualization and analysis of fast biological processes.

[TO-15] PIBM2026-0402-7

All-optical ultrasound detector for photoacoustic microscopy and computed tomography

Yuxin You[1], Pengfei Niu[1], and Yiwen Ma[1], Pengfei Zhang[1,*]

[1]School of Precision Instruments and Optoelectronics Engineering, Tianjin University, Tianjin, 300072, China

Corresponding author e-mail address: pfzhang@tju.edu.cn

Abstract: All-optical ultrasound sensors have recently emerged as promising candidates to replace conventional piezoelectric transducers in photoacoustic imaging, owing to their broad bandwidth, compact active area, and good compatibility with light excitation. While non-interferometric designs offer advantages in robustness, ease of fabrication, and multiplexing capability, their sensitivity is often limited by short acousto-optic interaction lengths. We demonstrate that “infinity reflection” provides an effective strategy to overcome this constraint. The core of our approach is a carefully designed optical cavity that enables the probe beam to undergo multiple round-trips within a confined region, thereby substantially extending the effective acousto-optic interaction path. When applied to beam-deflection ultrasound sensing, a direct side-by-side comparison reveals that this design achieves a 3.5-fold enhancement in sensitivity over conventional single-pass detection. Moreover, the development of large-scale optical ultrasound detector arrays and corresponding data acquisition system remains a major challenge. We thus developed an optical ultrasound line detector based on differential interference, demonstrating with 700 crosstalk-free virtual elements, a pitch size of 12.6 μm, and a bandwidth of 13.2 MHz at -6 dB. We further pioneered a camera-based readout architecture, enabling parallel data acquisition across all 700 channels, each achieving a sampling rate of 211 Ms/s and a precision of 12 bits.

[TO-16] PIBM2026-0406-12

Co-registered Real-Time Intravascular Photoacoustic/Ultrasound/Optical Coherence Tomography for Characterization of Lipid-Rich Carotid Plaques

Jinke Zhang[1], Haoxing Xu[1], Riqiang Lin[1], Chengyou Shu[1] and Xiaojing Gong[1]

[1] Research Center for Biomedical Optics and Molecular Imaging, Key Laboratory of Biomedical Imaging Science and System, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

Corresponding author e-mail address: xj.gong@siat.ac.cn

Abstract: Atherosclerotic carotid plaques with large lipid burden and thin fibrous caps are associated with elevated stroke risk. Currently, no single intravascular imaging modality can simultaneously resolve microstructural morphology, wall architecture, and lipid information. Here, we present a co-registered intravascular photoacoustic/ultrasound/optical coherence tomography system for real-time characterization of lipid-rich carotid plaques. Building on a previously developed trimodal imaging platform, the system integrates accurate frame-by-frame synchronization, electromagnetic-interference suppression, and a fully integrated catheter with an outer diameter of 0.9 mm and rigid length of 4.6 mm to achieve stable imaging at 20 frames per second. Lipid-sensitive photoacoustic imaging provides compositional contrast for plaque lipid mapping, ultrasound depicts the overall vessel wall and plaque burden, and optical coherence tomography delineates superficial microstructures such as the lumen boundary and fibrous-cap morphology. In ex vivo carotid specimens, the three modalities were spatially co-registered in the same cross section, enabling simultaneous visualization of plaque architecture and lipid distribution. The improved imaging speed reduced motion-induced

misregistration and supported continuous pullback imaging over clinically relevant lengths. Compared with single- or dual-modality approaches, the trimodal strategy provided more complete plaque characterization by linking deep structural information, high-resolution surface morphology, and lipid-specific contrast within one dataset. This work demonstrates the feasibility of real-time intravascular trimodal imaging for carotid atherosclerosis and highlights its potential for identifying high-risk plaque features, guiding specimen analysis, and advancing translation toward comprehensive vascular diagnosis.

Key words: intravascular photoacoustic imaging, intravascular ultrasound, optical coherence tomography, carotid atherosclerosis, lipid-rich plaque

[TO-17] PIBM2026-0331-8

Optical-resolution photoacoustic microscopy of tumor organoids

Yixuan Zhu[1], Qibo Lin[2], Qing Zhou[1], Jiaxing He[1], Xiongwei Wei[3], Maike Chen[2], Han Shan[2], Zeyu Chen[2], and Xiaofei Luo[1*]

[1]Department of Mechanical and Vehicle Engineering, Changsha University of Science and Technology, Changsha410114, China

[2] College of Mechanical and Electrical Engineering, Central South University, Changsha410013, China

[3] School of Microelectronics, Xidian University, Xi'an710071, China

**Corresponding author e-mail address: (xfl@csust.edu.cn)*

Abstract: Tumor organoids have emerged as advanced in vitro models that recapitulate the three-dimensional architecture and cellular heterogeneity of tumors, providing a promising platform for biological research and therapeutic evaluation. Accurate visualization of their three-dimensional morphology is essential for structural characterization and functional analysis. Optical-resolution photoacoustic microscopy (OR-PAM), which combines optical absorption contrast with ultrasonic detection, offers high-resolution imaging capabilities but remains limited by detection sensitivity when imaging weak signals from complex biological samples. In this work, we develop an OR-PAM system incorporating a high-sensitivity ultrasonic transducer for imaging tumor organoids. The proposed system improves signal detection while maintaining a compact system configuration. Imaging experiments were conducted on tumor organoids to evaluate system performance. The results demonstrate enhanced imaging contrast and improved visualization of structural features compared with conventional configurations. Three-dimensional imaging further confirms the capability of the system to resolve fine morphological details and capture structural variations in tumor organoids. These results indicate that the proposed system provides an effective approach for high-sensitivity OR-PAM imaging.

[TO-18] PIBM2026-0403-13

Fiber-optic Photoacoustic Imaging for Human Peripheral Microcirculation Dynamic Monitoring

Wei Li[1], Xue Bai[1], Yizhi Liang[1], Long Jin[2] and Bai-ou Guan[1]

[1]College of Physics and Optoelectronic Engineering, Jinan University, Guangzhou, China, 511400

[2]School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou, China, 510006

Corresponding author e-mail address: levis0513@163.com

Abstract: Effective imaging and monitoring of peripheral microcirculation are essential for the early detection of hemodynamic instability and organ dysfunction in ICU and intraoperative settings. However, existing techniques have significant limitations: macrocirculatory indicators such as blood pressure and heart rate cannot directly assess microvascular perfusion or oxygenation. Optical microscopy is restricted to superficial sites like tongue with shallow depth. Ultrasound patch technology suffers from limited spatial resolution, and cannot provide metabolic information.

To address these challenges, we developed a dynamic human microcirculation monitoring system based on a miniature fiber-optic photoacoustic probe. The system offers the following technical capabilities: (1) a 70 μm fiber-optic sensor achieving ultra-broadband omnidirectional ultrasound detection (0.3–80 MHz), with higher sensitivity and larger bandwidth despite a receiving area 300 times smaller than conventional piezoelectric transducers; (2) ~50 μm spatial resolution within 1 cm depth, enabling differential imaging of cross-scale vascular networks (40 μm–1.4 mm diameter); (3) multi-parameter hemodynamic characterization, monitoring dynamic responses at different depths including vessel diameter changes, hemoglobin concentration, and blood oxygen saturation.

The fiber-optic imaging probe can be integrated with other devices for multi-parameter synergistic monitoring. In free-movement and high-intensity cycling experiments, we successfully captured distinct dynamic responses from superficial to deep subcutaneous vessels, providing a new tool for understanding human microcirculatory regulation and clinical hemodynamic management.

Keyword: Photoacoustic imaging, Fiber optical sensing, Ultrasound detection, Microcirculation monitoring

[IO-1] PIBM2026-0617-4

Non-invasive modulation of meningeal lymphatics ameliorates ageing and Alzheimer's disease-associated pathology and cognition in mice

Miao Wang [1]，Feifan Zhou [1,*]

[1] School of Biomedical Engineering, Hainan University, Sanya 572025

Corresponding author e-mail address: zhouff@hainanu.edu.cn

Abstract: Meningeal lymphatic vessels (mLVs) have been shown to be involved in amyloid beta (Aβ) clearance, which is considered as a potential therapeutic target for Alzheimer's disease (AD). In this study, based on the superficial spatial distribution of mLVs, a near-infrared light is employed to modulate lymphatic drainage, significantly improving cognition of both aged and AD (5xFAD and APP/PS1) mice, and alleviating AD-associated pathology by reducing Aβ deposition, neuroinflammation and neuronal damage. Furthermore, transmission electron microscopy imaging and RNA sequencing data indicate amelioration of mitochondrial metabolism and cellular junction of meningeal lymphatic endothelial cells (mLECs) by light modulation. These studies collectively suggest that near-infrared light treatment can improve cognitive function by strengthening scavenging ability of mLVs through restoring mLEC function. In conclusion, lymphatic drainage potentiation by light promotes pathological remission and cognitive enhancement in aging and AD mouse models, which offers a potential amelioration strategy for neurodegenerative diseases.

[IO-2] PIBM2026-0610-1

Photobiomodulation: Regulation of Metabolic Function and Neuroinflammation in Diabetic Rats

Study on the regulatory effect of photobiomodulation on metabolic levels and neuroinflammation in diabetic rats

Hui Chen[1,2], Chunyan Ma[3], Ning Ma[4], Lina Chang[1], Yian Gu[1], Linlin Kong[1], Xin Wang[1], Qing He[1,*], and Hongli Chen[3,*]

[1]Department of Endocrinology and Metabolism, Tianjin Medical University General Hospital, Tianjin Medical University,Tianjin, 300052, China

[2]Xiangyang road subdistrict community health service center, Tianjin, 300111, China

[3]State Key Laboratory of Advanced Medical Materials and Devices, Tianjin Key Laboratory of Neuromodulation and Neurorepair, Institute of Biomedical Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, 300192, China

[4]Tianjin Medical University Cancer Institute & Hospital,Tianjin, 300060, China

Corresponding author e-mail address: hech69@163.com；chenhli0107@163.com

Abstract: Diabetes is a growing global health concern characterized by metabolic disturbances, including hyperglycemia, dyslipidemia, and insulin resistance, which contribute to severe complications such as cardiovascular and neurological disorders. Dysregulation of energy metabolism is considered a key pathological basis. Photobiomodulation (PBM), a safe and noninvasive therapeutic approach, has shown potential in modulating cellular metabolism; however, its role in systemic metabolic regulation in diabetes remains unclear. In this study, a diabetic rat model was established and subjected to near-infrared (808 nm)

and blue light (468 nm) PBM interventions. PBM was administered under controlled conditions, and metabolic parameters, including fasting blood glucose, glycated hemoglobin, lipid profiles, and free fatty acids, were measured. Behavioral tests were conducted to assess cognitive function. In addition, biochemical assays, histological examinations, and immunological analyses were performed to evaluate oxidative stress, neuroinflammation, pancreatic islet integrity, and hippocampal neuronal injury. The results demonstrated that PBM significantly improved fasting blood glucose, glycated hemoglobin, and lipid metabolism, as evidenced by reduced cholesterol and free fatty acid levels. PBM also markedly enhanced learning and memory performance and alleviated histopathological damage in pancreatic islets and hippocampal tissues. Furthermore, PBM effectively reduced oxidative stress and suppressed neuroinflammatory responses, as indicated by decreased reactive oxygen species levels and reduced activation of inflammatory markers. PBM also attenuated neuronal apoptosis. Mechanistically, these protective effects were associated with activation of the PI3K/AKT signaling pathway. Collectively, these findings indicate that near-infrared and blue light PBM ameliorate metabolic dysfunction, neuroinflammation, and neuronal injury in diabetic rats, highlighting its potential as a noninvasive therapeutic strategy for diabetes and its related complications.

[IO-3] PIBM2026-0403-2

SERS-AI strategy for rapid classification of CNS-related diseases

Dongjie Zhang[1,2,3*], Zhaoyang Cheng[1,2], Qi Zeng[1,2] and Xueli Chen[1,2,3,*]

[1] Center for Biomedical-photonics and Molecular Imaging, Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[2] Engineering Research Center of Molecular and Neuro Imaging, Ministry of Education & Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[3] Inovation Center for Advanced Medical Imaging and Intelligent Medicine, Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China

Corresponding author e-mail address: zhangdongjie@xidian.edu.cn; xlchen@xidian.edu.cn

Abstract: In recent years, non-invasive and dynamic monitoring technologies, represented by liquid biopsy, have emerged as one of the most promising frontiers for the early detection and diagnosis of CNS diseases. As a molecular vibration spectroscopy with high sensitivity and rapid detection characteristics, Surface-Enhanced Raman Spectroscopy (SERS) has been applied in various fields and has the potential to provide a rapid and highly sensitive diagnostic strategy for meningitis. Here, we propose a simple and reliable label-free CSF-induced SERS detection strategy and establish a machine learning (ML) model based on spectral information fused with baseline features, enabling rapid diagnosis and classification of meningitis. Stable and reproducible SERS spectra are obtained within 30 seconds by simply mixing colloidal silver nanoparticles (Ag NPs) with a CSF sample, achieving a relative standard deviation of signal intensity as low as 2.1%. Finally, an ML-assisted meningitis classification model is established based on the spectral feature fusion of characteristic peaks and baselines. Utilizing an optimized KNN algorithm, our model achieves a classification accuracy of 99% for autoimmune encephalitis, novel cryptococcal meningitis, viral meningitis, and tuberculous meningitis, while the baseline-corrected spectral data achieve an accuracy of 68.74%. The CSF-induced SERS detection method has the potential to provide a novel liquid biopsy approach for the diagnosis and early detection of various cerebral ailments.

Keywords: Raman spectroscopy, Machine learning, CNS diseases, Cerebrospinal fluid

[IO-4] PIBM2026-0617-6

Mesoscale imaging of liver vasculature and immune niches uncovers a nerve-associated portal macrophage subset

Zheng Liu, Mengli Xu, Zhihong Zhang

School of Life and Health Sciences, Institute of Biomedical Research, Hainan Province Key Laboratory of One Health, Hainan University, Haikou, China.

Abstract: The complex vascular architecture and diverse immune cell composition are essential for sustaining liver homeostasis. However, quantitative analysis of hepatic immunocyte distribution from single lobule to intact liver lobe levels remains a challenge. By combining liver whole-lobe imaging and single-cell RNA sequencing (scRNA-seq) of hepatic immune cells, we identified a CX3CR1+CD63+ liver portal area macrophage subset termed LPAMs, whose survival relies on CSF1R signaling under physiological conditions. Functionally, LPAMs efficiently capture hepatocyte-derived antigens and establish intimate interactions with periportal sympathetic nerves. Loss of LPAMs exacerbates sympathetic nerve degeneration and neutrophil infiltration, thereby aggravating pathological progression of hepatic nonalcoholic steatohepatitis. In summary, this study highlights a specialized nerve-associated portal macrophage, which is indispensable for maintaining liver immune homeostasis, and deepens the understanding of spatial macrophage heterogeneity in liver physiological and pathological processes.

Key words: Optical clearing method; Mesoscale whole-organ imaging; Liver Structure; LPAM; Liver immune homeostasis

[IO-5] PIBM2026-0428-1

Study on the Pathological Mechanisms of Sterile Inflammation Using Photoacoustic Detection and Imaging Technology

Tan Yizhou[1,2], Liu Chengbo[3], and Gu Ying[1,2]

[1]Laser Medicine Center, Hainan Hospital, Chinese PLA General Hospital, Sanya, 572013, China.

[2]Department of Laser Medicine, the First Medical Center, Chinese PLA General Hospital, Beijing 100853, China.

[3]Research Center for Biomedical Optics and Molecular Imaging, Key Laboratory of Biomedical Imaging Science and System, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen, 518055, China.

Corresponding author e-mail address: tanyizhou@126.com

Abstract: Our study focuses on two intractable sterile inflammatory diseases: knee osteoarthritis (KOA) and gouty arthritis (GA), which feature insidious early onset, undefined pathological mechanisms, and a lack of effective early diagnostic methods in clinical practice.

For KOA, we developed a customized photoacoustic spectral and ultrasound dual-modal system for non-invasive, label-free, radiation-free multi-dimensional evaluation of the infrapatellar fat pad (IPFP), a core inflammatory site of early KOA. Unlike conventional imaging that only provides structural information, our

system decouples IPFP-specific PA signals to characterize its fat content, tissue stiffness and blood oxygen metabolism, establishing a robust correlation with pathological alterations for early KOA diagnosis. Multi-center clinical trials are ongoing to translate this technique, alongside a wearable phototherapy device for KOA intervention.

For GA, we employed optical-resolution photoacoustic microscopy to dynamically monitor oxygen metabolism across the full disease course. We provided the first in-vivo dynamic evidence for the long-debated hyperoxia-hypoxia paradox, revealing that acute hyperoxia in the onset phase triggers severe inflammatory storms, while sustained hypoxia persists even after clinical symptoms resolve, with hypoxia-inducible factor (HIF) identified as a promising therapeutic target.

Out study demonstrates the significant potential of photoacoustic technology in elucidating sterile inflammation mechanisms and developing clinical theranostic strategies.

[IO-6] PIBM2026-0617-11

Targeted modulation of the meningeal lymphatic reverse pathway for immunotherapy of breast cancer brain metastasis

Yanfeng Dai[1*]

[1.]Hainan university, China

ABSTRACT：Treatment of tumor brain metastases (TBM) remains challenging due to the ineffectiveness of drugs in crossing the blood-brain barrier (BBB). Here, we proposed a potential strategy to target and modulate the meningeal lymphatic for immunotherapy of breast cancer brain metastases (BCBM) through peripheral administration. CT/fluorescence dual-modality imaging demonstrated that the phospholipid nanoprobe (α-PLNPs) through intracisternal magna injection effectively labeled and long-range tracked the meningeal lymphatic pathway from meningeal lymphatic vessels (MLVs) to periphery drainage cervical lymph nodes (CLNs). Interestingly, the reverse pathway from CLNs to MLVs was also successfully labelled with α-PLNPs through cervical subcutaneous injection, facilitating the noninvasive delivery of immunomodulators to the meningeal lymphatics. Given this, we used melittin carrying α-M-PLNPs to trigger the modulation of the meningeal lymphatic reverse pathway, which effectively prevents BCBM and prolongs the survival of mice through activating the antigen-presenting cells in the CLNs and promoting the migration of CD8+ T cells into the metastatic brain tumors. This study highlights the potential of meningeal lymphatic reverse pathway for the immunotherapy of BCBM, which holds a great promise for central nervous system diseases therapy without the need for drug delivery via BBB.

[AO-1] PIBM2026-0630-5

Development of a High-Sensitivity Piezoelectric Ultrasonic Transducer Based on PZT Thin Films for Deep-Sea Sonar Detection

Shi-Li Xiang[1*], Jun Liu[1*], and Tao Cheng[1*]

[1] Hubei Jiufengshan Laboratory, Wuhan, 430074, China.

Corresponding author e-mail address: xiangshili@jfslab.com.cn

Abstract: Deep-sea sonar detection is critical for underwater communication, navigation, and resource exploration, where acoustic waves are preferred over electromagnetic waves due to the low-pass filtering characteristic of seawater that causes severe attenuation of electromagnetic signals. This work presents a high-performance piezoelectric ultrasonic transducer fabricated by high-precision semiconductor manufacturing processes for deep-sea sonar applications. The transducer utilizes lead zirconate titanate (PZT) thin films as the piezoelectric sensing element, deposited on a Pt/Ti/SiO_2/Si substrate. The PZT film exhibits excellent crystalline quality with (100) preferred orientation, enabling high electromechanical coupling efficiency and low internal losses. The device operates on the principle of piezoelectric generation and detection of acoustic waves, where the resonance frequency shift induced by underwater acoustic signals enables accurate target detection and ranging. The transducer structure integrates interdigitated electrodes for acoustic wave excitation and reception, allowing real-time monitoring of underwater acoustic signals. Experimental results demonstrate that the fabricated PZT-based transducer achieves high transmitting voltage response and broad bandwidth, suitable for accurate underwater detection applications. Furthermore, the device architecture is compatible with standard MEMS fabrication processes, facilitating potential integration with on-chip signal processing circuits for compact and portable sonar systems. This work provides a promising pathway toward low-cost, high-sensitivity piezoelectric MEMS transducers for deep-sea exploration and underwater monitoring.

Keywords: Piezoelectric ultrasonic transducer, PZT thin film, Deep-sea sonar, Underwater acoustic detection, MEMS

[1] Sadeghpour, S., Kraft, M., & Puers, R. “Design and fabrication of a piezoelectric micromachined ultrasound transducer (pMUT) array for underwater communication,” Proceedings of Meetings on Acoustics, vol. 38, 045006, 2019.

[2] Abdullah, Z., Naz, S., Raja, M. A. Z., & Zameer, A. “Design of wideband tonpilz transducers for underwater SONAR applications with finite element model,” Applied Acoustics, vol. 182, 108293, 2021.

[3] “PZT 厚膜及高频超声换能器的研究,” 应用声学.

[AO-2] PIBM2026-0712-1

Ice-Interface Optothermal Tweezers for Programmable Cryogenic Assembly and Biosensing

Jiajie Chen[1*], Yonghong Shao[1], and Junle Qu[1]

[1] Key Laboratory of Optoelectronic Devices and Systems of Ministry of Education and Guangdong Province, College of Physics and Optoelectronics Engineering, Shenzhen University, Shenzhen, 518060, China

*Corresponding author e-mail address: cjj@szu.edu.cn

Abstract: Precise manipulation and programmable assembly of micro- and nanoscale objects are essential for the development of advanced photonic devices, functional materials, and biosensing technologies. Conventional optical and optothermal manipulation strategies are primarily confined to liquid environments, where our previously developed CRISPR-powered optothermal nanotweezers (CRONT) enabled highly specific single-molecule trapping. To extend optothermal manipulation beyond homogeneous liquids, we recently introduced optothermal ice–water interface management (OIIM), which exploits phase boundaries for universal, cross-scale analyte enrichment. Nevertheless, active and programmable assembly of multiple materials directly within a stable solid matrix remains highly challenging, owing to restricted object mobility, limited spatial control, and thermally induced structural instability.

Here, we introduce ice-phase optothermal tweezers (IOT), a cryogenic manipulation strategy that transforms the ice–water boundary from a passive enrichment interface into an active and programmable working platform. By generating a highly localized and dynamically movable melting zone within solid ice, IOT enables rapid, precise, and reconfigurable transport of diverse objects, including dielectric and metallic nanoparticles, biomolecules such as proteins and DNA, and trapped microbubbles. This capability allows programmable positioning and assembly of heterogeneous components with nanoscale precision, leading to the formation of hybrid multi-material architectures with tailored anisotropic and chiral optical responses.

By coupling the high mobility of transient liquid-like interfacial regions with the structural stability of the surrounding solid ice matrix, IOT provides a powerful route for cryogenic manipulation, programmable meta-structure fabrication, in situ optical characterization, and nanoscale biosensing. This ice-interface optothermal platform opens new opportunities for constructing complex functional assemblies under cryogenic conditions and for developing phase-boundary-enabled approaches to advanced photonic and bioanalytical applications.

References

[1] J. Chen et al., Nature Communications (2026).

[2] J. Chen et al., ACS Nano, 19, 39281–39291 (2025).

[3] J. Chen et al., Light: Science & Applications, 12, 273 (2023).

[AO-3] PIBM2026-0618-15

Gene-Editing Proteins-based highly sensitive gene detection technologies

Ru Huang[1], Feifan Zhou[1]

[1] State key laboratory of digital medical engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570100, China

Corresponding author e-mail address: zhouff@hainanu.edu.cn

Abstract: Molecular detection technology is a critical component of precision medicine. On one hand, molecular markers of major diseases, such as gene mutations, demand high sensitivity and accuracy from detection techniques. On the other hand, point-of-care testing (e.g., for pathogens) requires rapid, simple, and field-deployable methods. Gene-editing proteins, including the CRISPR/Cas system and Argonaute (Ago), have attracted considerable attention in molecular detection due to their programmable targeting capability and single-base resolution specificity, and they show great promise for point-of-care applications owing to their remarkable signal amplification capacity. Recently, our team has developed multiple gene detection technologies based on gene-editing proteins, including: (a) an electrochemiluminescence probe based on catalytically dead Cas9 (dCas9) for rapid identification of bacterial signature genes and highly specific recognition of tumor-associated mutations; (b) a primer-free exponential amplification system based on Ago

for zero-background detection of tumor-related mutations; (c) a multiplexed orthogonal cascade CRISPR/Cas system for simultaneous detection of two RNA markers in blood, enabling differentiation between bacterial and viral infections within 30 minutes. Furthermore, to address the challenge that pathogenic bacterial gene detection is hindered by complex sample preparation steps for point-of-care use, we have developed sea urchin-like magnetic beads for rapid bacterial lysis and nucleic acid extraction. Collectively, highly sensitive gene detection technologies based on gene-editing proteins hold substantial potential for further development and application in molecular diagnostics.

[AO-4] PIBM2026-0618-19

Engineering Functional Protein-Based Sensing Platforms for Biomedical Applications

Fang Liu and Feifan Zhou*

State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, Hainan 572024, China

Corresponding author e-mail address: zhouff@hainanu.edu.cn

Abstract: In the field of biomedicine, numerous critical challenges remain to be addressed. Inspired by the sophisticated mechanisms found in nature, we aim to harness the body's intrinsic molecular machinery to engineer functional proteins through precise and rational modifications. Building upon this strategy, we are committed to developing a diverse range of protein-based biotechnologies for applications in biosensing, disease diagnosis, and therapeutics, thereby providing innovative solutions for advancing biomedical research and clinical practice.

Our major research achievements include:

1. Development of target-activated signal amplification biosensors for ultrasensitive protease detection. By integrating target-responsive amplification strategies into biosensor design, we have established a highly sensitive platform for protease detection. This approach effectively overcomes the sensitivity limitations of conventional assays, enabling the accurate detection of trace levels of protease activity. Such capability holds significant potential for early disease diagnosis, biomarker discovery, and precision medicine.

2. Establishment of an orthogonal signal amplification strategy for multiplex nucleic acid detection. Through the implementation of orthogonal signal amplification mechanisms, we have achieved the simultaneous detection of multiple nucleic acid targets with high specificity and minimal signal crosstalk. This strategy addresses the challenges of limited multiplexing capacity and interference encountered in traditional methods, providing a robust platform for the comprehensive analysis of complex biological samples. It offers promising applications in disease diagnosis, dynamic disease monitoring, and molecular profiling, opening new avenues for next-generation biomedical diagnostics.

This work demonstrates the potential of leveraging engineered functional proteins and biomimetic strategies to create versatile biomedical platforms, contributing to the development of more sensitive, accurate, and efficient technologies for diagnostics, sensing, and therapeutic applications.

AI for Biophotonics

[AIO-1] PIBM2026-0410-1

AI-assisted quantitative brightfield microscopy for label-free phenotyping of appendix-derived gut organoids

Zhengyu Wu[1], Rongzhou Chen[2], Shaohua Ma[1,*]

[1] Institute of Biopharmaceutical and Health Engineering (iBHE), Tsinghua Shenzhen International Graduate School (SIGS), Tsinghua University, Shenzhen 518055, China

[2] Department of Electrical and Computer Engineering, University of Hong Kong, Pokfulam, Hong Kong SAR, China

** Corresponding author e-mail address: ma.shaohua@sz.tsinghua.edu.cn*

Abstract: Label-free organoid microscopy can provide rich morphological information, but reproducible extraction of high-value phenotypes remains limited by heterogeneous culture geometry, low-contrast brightfield images, and the lack of standardized computational analysis. Here, we present an AI-ready brightfield imaging and image-processing workflow for appendix-derived gut organoids cultured in microdroplet-constrained conditions. The framework couples longitudinal brightfield acquisition with segmentation-driven analysis, hybrid signal construction, and time-resolved phenotypic quantification, enabling consistent readout of organoid growth, cyst formation, wall thickening, darkening, shape irregularity, and fusion-associated internal edge redistribution from label-free images. To evaluate the workflow, we applied it across multiple perturbation regimes that alter organoid structural state, including density variation, matrix modulation, and cytoskeletal perturbation. The resulting image-derived feature trajectories separated cystic and differentiation-associated morphologies and sensitively captured fusion-related structural remodeling that is difficult to quantify by manual inspection alone. Importantly, selected image phenotypes remained consistent with supporting molecular measurements, indicating that the computational optical readouts reflect meaningful biological state changes rather than imaging artifacts. This study positions droplet-based organoid culture primarily as a standardized specimen format for computational microscopy rather than as the endpoint itself. The main contribution is a low-complexity, imaging-first framework for quantitative brightfield phenotyping that is compatible with AI-assisted segmentation, machine-learning-based feature extraction, and future multimodal optical sensing, including hyperspectral imaging. Such a pipeline can support diagnostic-oriented organoid analysis, image-based screening, and biomarker discovery in biomedical photonics.

[AIO-2] PIBM2026-0415-3

A Hybrid Deep Learning Model for Oral Disease Classification Based on Sub-Diffuse Reflectance Spectroscopy Technique

Limin Zhang[1,2], Siyi Zou[2], Jingyi Wang[2], Dongyuan Liu[1,2], Chenlu Liu[3,4] and Feng Gao[1,2]

[1]College of Precision Instrument and Optoelectronics Engineering, Tianjin University, Tianjin 300072, China

[2]State Key Laboratory of Precision Measuring Technology and Instruments, Tianjin University, Tianjin 300072, China

[3]Department of Oral Medicine, Tianjin Stomatological Hospital, School of Medicine, Nankai University, Tianjin, 300041, China

[4]Tianjin Key Laboratory of Oral and Maxillofacial Function Reconstruction, Tianjin, 300041, China

Corresponding author e-mail address: zhanglm@tju.edu.cn

Abstract: Oral mucosal lesions including Oral Leukoplakia (OLK), Oral Lichen Planus (OLP), and Oral Squamous Cell Carcinoma (OSCC) present significant diagnostic challenges due to overlapping clinical

features and the risk of malignant transformation. To provide a non-invasive and accurate diagnostic, this study proposes a hybrid deep learning framework for multi-class classification (Normal, OLK, OLP and OSCC) based on a sub-diffuse reflectance spectroscopy (DRS) designed using fiber-based Monte Carlo simulation and phase-lock-in technique. A total of 6035 sets of in vivo spectra were collected from 90 clinically confirmed patients and Spectral Ratio data were also derived based on original spectra. Principal Component Analysis-based preprocessing and Successive Projection Algorithm were first used to enhance data quality and extract informative spectral features. Subsequently, we introduced Res-BiLSTM-MHSA Net, a hybrid architecture integrating residual convolutional blocks, bidirectional Long Short-Term Memory units, and a multi-head self-attention mechanism to jointly capture spatial, sequential, and long-range dependencies within spectral data. The ablation experiments highlight the feature extraction and multi-class discrimination capabilities of the proposed model, with the DRw (washed-out diffuse spectra) dataset achieving the most outstanding performance. The model achieved an accuracy of 96.34% in stratified 5-fold cross-validation and 94.85% in an independent clinical cohort, demonstrating strong robustness and generalization. These findings underscore the potential of combining sub-diffuse reflectance spectroscopy with hybrid deep learning to enable rapid, non-invasive, and reliable identification of oral mucosal lesions, thereby supporting early diagnosis and clinical decision-making.

[AIO-3] PIBM2026-0403-2

SERS-AI strategy for rapid classification of CNS-related diseases

Dongjie Zhang[1,2,3]*, Zhaoyang Cheng[1,2], Qi Zeng[1,2] and Xueli Chen[1,2,3,*]

[1] Center for Biomedical-photonics and Molecular Imaging, Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[2] Engineering Research Center of Molecular and Neuro Imaging, Ministry of Education & Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[3] Inovation Center for Advanced Medical Imaging and Intelligent Medicine, Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China

Corresponding author e-mail address: zhangdongjie@xidian.edu.cn; xlchen@xidian.edu.cn

Abstract: In recent years, non-invasive and dynamic monitoring technologies, represented by liquid biopsy, have emerged as one of the most promising frontiers for the early detection and diagnosis of CNS diseases. As a molecular vibration spectroscopy with high sensitivity and rapid detection characteristics, Surface-Enhanced Raman Spectroscopy (SERS) has been applied in various fields and has the potential to provide a rapid and highly sensitive diagnostic strategy for meningitis. Here, we propose a simple and reliable label-free CSF-induced SERS detection strategy and establish a machine learning (ML) model based on spectral information fused with baseline features, enabling rapid diagnosis and classification of meningitis. Stable and reproducible SERS spectra are obtained within 30 seconds by simply mixing colloidal silver nanoparticles (Ag NPs) with a CSF sample, achieving a relative standard deviation of signal intensity as low as 2.1%. Finally, an ML-assisted meningitis classification model is established based on the spectral feature fusion of characteristic peaks and baselines. Utilizing an optimized KNN algorithm, our model achieves a classification accuracy of 99% for autoimmune encephalitis, novel cryptococcal meningitis, viral meningitis, and tuberculous meningitis, while the baseline-corrected spectral data achieve an accuracy of 68.74%. The CSF-induced SERS detection

method has the potential to provide a novel liquid biopsy approach for the diagnosis and early detection of various cerebral ailments.

Keywords: Raman spectroscopy, Machine learning, CNS diseases, Cerebrospinal fluid

[AIO-4] PIBM2026-0410-2

PanoMito: mapping mitochondrial heterogeneity from morphofunctional profiling to single-mitochondrion spatial transcriptomics

Karl Zhanghao[1]

[1]Assistant Professor, Eastern Institute of Technology, Ningbo

Corresponding author e-mail address: karl.hao.zhang@gmail.com

Abstract: Mitochondrial morphology and function are fundamentally linked, yet systematic investigation of this morphology-function relationship has been hindered by the lack of accurate segmentation tools and comprehensive benchmarks. Here we present PanoMito, an integrated toolbox built upon PanoMitoAtlas, the largest multi-modal dataset comprising >160,000 annotated instances across 15 species; and PanoMitoNet, a deep-learning framework unifying instance segmentation and unsupervised classification. PanoMitoNet achieves superior precision (AP50 of 63.6%) compared to existing methods. At single-mitochondrion resolution, PanoMito reveals extensive mitochondrial heterogeneity across species and cell types and uncover significant morphofunctional decoupling. Furthermore, through the application of pharmacological perturbations and temporal tracking, we identified mitochondrial subpopulations that exhibit unique stress resilience, maintaining high membrane potential and stability under stress. Finally, by combining PanoMito with in situ sequencing, we achieved single-mitochondrion spatial transcriptomics, providing a robust framework to dissect the complex interplay between mitochondrial architecture and molecular identity. By providing single-organelle resolution across morphology, function, and transcriptomics, PanoMito establishes a comprehensive, universally applicable framework for dissecting mitochondrial biology from model systems to non-model organisms.

[NO-1] PIBM2026-0403-8

Ultrasound Modulation of Visual Circuits in Mice Independent of Auditory Confound

Jiaru He[1], Jiejun Zhu[1], Xinxin Wang[2], Zihao Chen[1,3], Jin Yang[1,3], Zhen Yuan[2], Hongzhi Xu[4], Lei Sun[3], Zhihai Qiu[1]

[1]Guangdong Institute of Intelligence Science and Technology, Zhuhai 519031, P.R. China

[2]Faculty of Health Sciences/Centre for Cognitive and Brain Sciences, University of Macau, Macao SAR, P. R. China

[3]Department of Biomedical Engineering, The Hong Kong Polytechnic University, Hong Kong SAR 999077, P. R. China

[4]Department of Neurosurgery, Huashan Hospital, Shanghai Medical College, Fudan University,Shanghai, P. R. China

Corresponding author e-mail address: hejiaru@gdiist.cn

Abstract: Ultrasound neuromodulation, owing to its non-invasiveness, high penetration depth, and high spatial resolution, is widely regarded as a promising tool for clinical translation, with great potential in the treatment of brain diseases, brain function research, and brain–computer interface development. However, two key controversies persist in the field of ultrasound neuromodulation: (1) whether ultrasound exerts direct mechanical effects or merely triggers indirect auditory responses; (2) low-intensity ultrasound stimulation of the motor cortex commonly fails to induce obvious contralateral limb movements in animals. To address these controversies, this study established an ultrasound neuromodulation platform synchronized with a two-photon calcium imaging system, enabling real-time monitoring of large-scale neuronal calcium signals during ultrasound stimulation. Through systematic comparative experiments in normal and deaf mouse models, we found that ultrasound directly activates sparsely distributed “ultrasound-sensitive neurons” (UNs) in the visual cortex, and this sparse activation is sufficient to modulate broader visual circuits. Furthermore, inhibitory parvalbumin-positive (PV^+) neurons in the visual cortex exhibit higher susceptibility to auditory interference. These findings provide three major breakthroughs in the field of ultrasound neuromodulation: (1) direct in vivo evidence at the cellular level demonstrating that focused ultrasound, at the focal point, can directly activate neurons via mechanical effects rather than solely through auditory pathways; (2) revelation of the sparsity of ultrasound-activated neurons, explaining why low-intensity ultrasound can evoke local circuit responses but fails to induce obvious limb movements, especially in large animals and humans; (3) discovery that PV^+ neurons are more sensitive to auditory interference, offering critical guidance for future study design, parameter optimization, and result interpretation. In summary, this study experimentally decouples the direct mechanical effects of ultrasound from indirect auditory interference, clarifies that UNs are the core cellular substrate of ultrasound neuromodulation, and advances the mechanistic research in this field towards precision and depth.

[NO-2] PIBM2026-0506-1

Polarization-sensitive photoacoustic imaging

Zhenhui Zhang[1], and Sihua Yang[1]

[1]MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China [2]Guangdong Provincial Key Laboratory of Laser Life Science, College of Biophotonics, School of Optoelectronic

Science and Engineering, South China Normal University, Guangzhou 510631, China

Corresponding author e-mail address: shiyuj@scnu.edu.cn;

Abstract: Biological systems are intrinsically highly ordered architectures in which the molecular conformations of fibrillar proteins, collagen, and DNA play fundamental roles in physiological function. These ordered structures exhibit characteristic polarization-dependent optical responses, providing critical biomarkers for probing pathological processes and enabling early disease diagnosis. However, conventional optical polarization imaging techniques are fundamentally constrained by strong light scattering in biological tissues, limiting their applicability primarily to superficial or ex vivo specimens. To overcome this limitation, photoacoustic imaging leverages ultrasonic waves generated through optical absorption of biomolecules, enabling high-contrast imaging at substantially greater tissue depths. In our work, we first introduced polarization-sensitive photoacoustic microscopy for quantitative characterization of molecular ordering in biological tissues, and further advanced this framework into polarization-sensitive photoacoustic Mueller matrix imaging. These approaches enable the extraction of key vectorial parameters, including the degree of anisotropy and the orientation of transition dipole moments, thereby providing rich insights into biomolecular conformations and organizational states. We further demonstrate the utility of these techniques in quantitatively assessing burn severity through collagen anisotropy analysis and in visualizing β-amyloid plaque distributions associated with Alzheimer's disease. Collectively, these studies highlight the substantial potential of polarization-sensitive photoacoustic imaging for deep-tissue biomedical imaging and molecular-level pathological characterization.

[NO-3] PIBM2026-0509-1

Photoacoustic imaging and modulation of the brain lymphatic system

Zhiyang Wang[1,2], and Sihua Yang[1,2]

[1]MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China

[2]Guangdong Provincial Key Laboratory of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China

Corresponding author e-mail address: yangsh@scnu.edu.cn;

Abstract: The discovery of the brain lymphatic system, including the glymphatic system and meningeal lymphatic vessels, has provided a new theoretical framework for understanding waste clearance, immune regulation, and the pathogenesis of neurodegenerative diseases in the central nervous system. The brain lymphatic system plays a crucial role in maintaining cerebral metabolic homeostasis, clearing metabolic waste such as β-amyloid and tau proteins, regulating neuroinflammation, and sustaining neurovascular coupling. Dysfunction of this system has been closely associated with Alzheimer's disease, stroke, traumatic brain injury, and various neurodegenerative disorders. Therefore, achieving high-resolution visualization and precise modulation of the brain lymphatic system is of great significance for elucidating disease mechanisms and developing novel therapeutic strategies for brain disorders. Photoacoustic imaging possesses several unique advantages, including noninvasiveness, high sensitivity, multiparametric functional imaging capability, and the absence of ionizing radiation, demonstrating substantial potential for investigating the structure and function of the brain lymphatic system. Furthermore, when combined with multi-wavelength excitation and functional molecular probes, photoacoustic imaging enables dynamic monitoring of brain lymphatic drainage, cerebrospinal fluid circulation, and neurovascular activity, thereby providing an important tool for the early diagnosis and therapeutic evaluation of brain diseases. Beyond imaging, we further demonstrate that photoacoustic neuromodulation based on pulsed laser-induced ultrasound can generate localized mechanical

waves and acoustic effects, thereby activating mechanosensitive ion channels, modulating neuronal and glial cell activity, and further influencing cerebral blood flow, vascular pulsation, and brain lymphatic drainage.

[NO-4] PIBM2026-0407-4

A High-Synchronization Wearable fNIRS-EEG System for Investigating Neurovascular Coupling Dynamics at Millisecond Temporal Resolution

Dongyuan Liu[1], Yuke Wang[2], and Feng Gao[2,3]

[1]School of Artificial Intelligence, Tianjin University, Tianjin, China

[2]College of Precision Instruments and Optoelectronics Engineering, Tianjin University, Tianjin, China

[3]State Key Laboratory of Precision Measuring Technology and Instruments, Tianjin University, Tianjin, China

Corresponding author e-mail address: (liudongyuan@tju.edu.cn)

Abstract: We present a wearable fNIRS-EEG system that resolves the temporal mismatch between fast neural and slow hemodynamic signals for neurovascular coupling (NVC) studies. Using orthogonal encoding and cyclic decoding, it achieves synchronized acquisition at up to 1000 Hz (52 fNIRS, 32 EEG channels) with low noise (<0.28 mV), wide dynamic range (94 dB), and minimal cross-modal interference (<0.5%). Validated through phantom tests, physiological benchmarks, and an auditory study (n=18), the system captures millisecond neural events (e.g., P300 at 250 ms) alongside corresponding hemodynamic changes (peak DICE coefficient ~2.5 s), directly linking electrical and metabolic dynamics. This high-speed, wearable platform enables precise NVC investigation for BCIs and neurological research.

[NO-5] PIBM2026-0627-1

Two-Photon 3D Imaging of Optically Evoked Neural Activity at 100 Hz

Dongli Xu[1]

[1]Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology

Corresponding author e-mail address: mdonglixu@outlook.com

Abstract: Neuronal computation depends on how dendrites integrate synaptic inputs across three-dimensional arbors on millisecond time scales, yet conventional two-photon microscopy remains too slow to capture these dynamics in three-dimensional (3D) space. Here, we present dual-view Bessel two-photon projection microscopy (dv-B2PM), an all-optical imaging platform that combines high-speed Bessel beam scanning with simultaneous orthogonal projection detections. By acquiring paired projections of the same scanned volume, dv-B2PM preserves essential 3D spatial information while avoiding the speed penalties of sequential volumetric scanning. The system achieves 100 volumes per second over a 120 x 80 x 42 μm^3 field of view with submicron-scale optical resolution.

We integrated dv-B2PM with two-photon glutamate uncaging to visualize calcium dynamics in GCaMP8m-labeled neurons in live mouse brain slices. Localized uncaging near apical dendrites evoked calcium responses that transitioned from confined subthreshold activity to suprathreshold responses spreading toward the soma and additional dendritic branches as stimulation strength increased. Long-timescale spatiotemporal analysis indicated that Ca^{2+} dynamics reflected an uncaging-evoked dendrite-to-soma signal and delayed calcium changes consistent with soma-originating back-propagating action potential (bAP)-associated activity. On shorter timescales, two-dimensional wavelet analysis of calcium signals revealed spatially heterogeneous

Ca^{2+} transients with nominal frequencies of 5-40 Hz, exposing localized and propagating activity patterns across the dendrite.

These results demonstrate that dv-B2PM enables direct visualization of rapid, three-dimensional calcium dynamics across extended neuronal structures. By bridging high temporal resolution, volumetric coverage, and synaptic-scale spatial information, dv-B2PM provides a powerful approach for studying dendritic integration and activity propagation in intact neural tissue.

[NO-6] PIBM2026-0406-1

Synaptic level remodeling of basal forebrain PV projection in Alzheimer's Disease

Jiaojiao Tian[1], Miao Ren[2], Yingying Chen[3], Tao Jiang[4*], Xiangning Li[2, 4 *]

[1]Department of Clinical Laboratory, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan, China

[2]Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China

[3] MoE key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[4]HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215125, China

**Correspondence: taojiang@brainsmatics.org, lixiangning@hainanu.edu.cn*

Synaptic pathology is widely regarded as one of the earliest and most pivotal events in the pathogenesis of Alzheimer's disease (AD). Long-range projection circuits depend on highly organized synaptic connections across anatomically distributed brain regions to sustain learning and memory functions. Disruption at the synaptic level is therefore likely to constitute an initiating mechanism underlying large-scale circuit dysfunction. Nevertheless, the spatiotemporal patterns of synaptic degeneration within long-range projection circuits of defined neuronal populations throughout AD progression remain insufficiently characterized, hindering the identification of the earliest circuit elements susceptible to disease-related damage.

In the present study, we integrated viral labeling with fluorescence micro-optical sectioning tomography (fMOST) to reconstruct synapse-level projection maps of basal forebrain parvalbumin (PV) neurons across multiple stages of AD. Our analyses revealed marked early synaptic loss in the mammillary body and hippocampal formation, occurring before overt microenvironmental alterations became detectable in either the basal forebrain or its downstream target regions. In parallel, rabies virus-based retrograde tracing demonstrated a reduction in afferent inputs from multiple upstream brain areas, suggesting selective vulnerability of long-range PV neuronal circuits. Together, these findings indicate that basal forebrain PV projection networks undergo bidirectional degeneration during AD progression, affecting both incoming and outgoing circuit components.

In summary, this study establishes a stage-resolved atlas of synaptic degeneration for a specific neuronal population, uncovers region-dependent and age-related vulnerability patterns in long-range projections, and highlights potential circuit-level targets for early intervention in AD.

Keywords: Synapse degeneration, Alzheimer's disease, basal forebrain, PV neuron, whole brain

[NO-7] PIBM2026-0624-1

A dorsal subiculum-medial mammillary body pathway for spatial memory

Jianping Zhang[1, 2#], Mei Yao[3#], Tao Jiang[4], Anan Li[3, 4], Hui Gong[3, 4], Miao He[5*], Qingming Luo[1*], Xiangning Li[1, 4*]

[1] State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Haikou, China

[2] Department of Neurology, the First Affiliated Hospital of Chongqing Medical University, Chongqing, China

[3] Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan, China

[4] HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou, China

[5] Institutes of Brain Science, Department of Neurology, State Key Laboratory of Brain Function and Disorders and MOE Frontiers Center for Brain Science, Zhongshan Hospital, Fudan University, Shanghai, China

 # These authors contributed equally

**Correspondence: hem@fudan.edu.cn; qluo@hainanu.edu.cn; lixiangning@hainanu.edu.cn*

Abstract: The dorsal subiculum (dSub) and medial mammillary body (MM) are essential components of the extended hippocampal system, heavily implicated in spatial memory processes. However, the exact function of the prominent dSub-to-MM projection has remained ambiguous. Here, integrating c-fos mapping, fiber photometry, optogenetic manipulations and behavioral paradigms, we found that the monosynaptic connection between dSub and MM, rather than collaterals to other regions, is not only involved in spatial memory retrieval but also highly vulnerable to perturbations on activity level in both directions. In addition, we mapped the single neuron projectome of MM-projecting dSub neurons using fluorescence micro-optical sectioning tomography (fMOST). Our study unveiled that the individual dSub neuron extend efferent connections to the bilateral MM neurons, while also exhibiting substantial collateral projections to the retrosplenial cortex (RSP) and entorhinal (ENT). Our findings shed light on previously unknown subtypes and organizational principles of projection neurons in the afferent circuitry of the MM, thereby elucidating the circuit mechanism underlying the contribution of the dSub-MM circuit to spatial memory.

[TP-1] PIBM2026-0403-4

Intravascular OCT-Guided 355nm Laser Ablation for In-Stent Restenosis: A Preclinical Feasibility Study in a Porcine Heart Model

Site Luo[1*], Rui Zhu[2], Haiping Liu[2], Hongming Liu[1], Ruizhe Yang[1,]

[1] School of Health and Environmental Engineering, Shenzhen Technology University, Shenzhen, Guangdong, China

[2] Shenzhen Vivolight Medical Device & Technology Co., Ltd. Shenzhen, Guangdong, China

[*]Corresponding author e-mail address: Lost147258@163.com

Abstract: This study evaluated a novel integrated platform combining intravascular optical coherence tomography (IVOCT) and a 355 nm excimer laser ablation system for coronary stent assessment and in-stent restenosis (ISR) treatment in a fresh porcine heart model. The Cornaris® P80 IVOCT system and the CLA-355 nm laser ablation device, both manufactured by Shenzhen Vivolight Medical Device & Technology Co., Ltd., were used. Compared with the more established 308 nm excimer laser, the 355 nm laser offers higher photon energy, enabling more efficient tissue ablation with reduced thermal injury and improved safety profile. Following coronary stent implantation, agarose blocks were placed to simulate vascular plaque and neointimal hyperplasia. The P80 OCT system acquired high-resolution cross-sectional images of the stented segments, and three-dimensional reconstruction allowed quantitative assessment of stent deployment quality, including stent expansion, strut apposition distance, and symmetry index. Subsequently, the CLA-355 laser catheter was advanced to perform laser ablation of the simulated ISR lesions. Post-ablation OCT imaging was repeated to evaluate treatment efficacy, focusing on tissue characteristics (homogeneous, layered, or heterogeneous patterns), neointimal volume reduction (debulking effect), and mechanical integrity of the stent. Pre- and post-ablation comparisons demonstrated significant restoration of minimal lumen area, effective reduction of neointimal burden, and preservation of stent architecture without detectable strut damage, malapposition, or edge dissection. The 355 nm laser ablation successfully debulked the simulated neointimal tissue, as confirmed by improved lumen dimensions and reduced tissue area on OCT. These preclinical findings indicate that the Vivolight P80 OCT combined with the CLA-355 nm laser platform provides a feasible, high-precision diagnostic-therapeutic solution for comprehensive management of coronary ISR, from initial stent optimization to targeted debulking and immediate post-treatment verification, warranting further clinical investigation.

[TP-2] PIBM2026-0404-8

Energy spectrum calibration method for photon-counting Micro-CT and its application in mouse cerebrovascular imaging

Yihao Zhao[1], Enze Zhou[1,3], Feng Yi[1], Hanfei Xu[1], Tianwu Xie[2], Shaoyang Wang[1,*]and Qian Liu[1]

[1] State Key Laboratory of Digital Medical engineering, School of Biomedical engineering, Hainan University, Sanya, China

[2] Institute of Radiation Medicine, Fudan University, Shanghai, China

[3] MOE Key Laboratory for Biomedical Photonics, Wuhan national Laboratory for Optoelectronics, Huazhong University of Science and technology, Wuhan, China

wangshaoyang@hainanu.edu.cn

Abstract: Photon-counting CT enables material decomposition through multi-energy channels, showing immense potential for mouse cerebrovascular imaging. Accurate decomposition fundamentally relies on

precise base material calibration. This study proposes an accurate and convenient image-domain energy spectrum calibration method for photon-counting Micro-CT and explores its application in high-resolution mouse cerebrovascular imaging. The photon-counting Micro-CT system used in this research was developed in collaboration between our research team and Wuhan United Imaging Life Science Instrument Co., Ltd. The system operated at 80 kVp with two energy thresholds set at 15 keV and 30 keV to optimize the iodine K-edge effect. Using iodine and hydroxyapatite phantoms of varying concentrations, an interactive software tool was developed to extract CT values across energy bins. Base material attenuation coefficients were calculated via least-squares fitting of a linear attenuation model to construct a material decomposition matrix. For cerebrovascular applications, we evaluated ultra-high-resolution scanning at 10.5 μm of an ex vivo perfused mouse specimen and in vivo imaging at 22.9 μm using an iodine blood-pool contrast agent, followed by direct vascular extraction. The proposed calibration method demonstrated high quantitative accuracy, with concentration errors for hydroxyapatite and iodine phantoms remaining below five percent. For *in-vivo* imaging, the minimum resolvable vessel diameter reached 50 μm, clearly visualizing anatomical structures like the Circle of Willis. *Ex-vivo* ultra-high-resolution imaging successfully resolved vessels down to 25 μm. Furthermore, material decomposition enabled pixel-level separation of skull and blood vessels, overcoming traditional CT limitations in resolving vasculature near bone tissue. The proposed standardized calibration method simplifies the spectrum calibration workflow while maintaining rigorous accuracy. These imaging results compellingly demonstrate the significant advantages and promising prospects of photon-counting Micro-CT in overcoming bone interference and achieving ultra-high-resolution vascular imaging.

Keywords: Photon-counting computed tomography; Material decomposition; Energy spectrum calibration; Cerebral angiography; High-resolution imaging

[TP-3] PIBM2026-0404-9

Preliminary investigation of photon-counting micro-CT for *in-vivo* cerebrovascular imaging in mice

Feng Yi[1], Enze Zhou[1,3], Yihao Zhao[1], Hanfei Xu[1], Linhan Yang[1], Tianwu Xie[2], Shaoyang Wang[1,*] and Qian Liu[1]

[1] State Key Laboratory of Digital Medical engineering, School of Biomedical engineering, Hainan University, Sanya, China

[2] Institute of Radiation Medicine, Fudan University, Shanghai, China

[3] MOE Key Laboratory for Biomedical Photonics, Wuhan national Laboratory for Optoelectronics, Huazhong University of Science and technology, Wuhan, China

wangshaoyang@hainanu.edu.cn

Abstract: High-resolution in vivo cerebrovascular imaging is essential for studying the onset and progression of brain diseases. Photon-counting CT (PCCT) offers advantages in high spatial resolution, spectral imaging, and low-dose acquisition, showing great potential for material decomposition and angiographic imaging. However, its application in in vivo cerebrovascular imaging in mice remains limited. This study employed VivoVist™ barium-based nanoparticle contrast agent combined with a photon-counting micro-CT system to investigate cerebrovascular imaging in mice under different contrast agent doses and metabolic time points.C57 mice were used as subjects with VivoVist™ barium nanoparticles as the contrast agent. Three doses within the recommended range were compared to determine the optimal dose for cerebrovascular imaging, evaluated by contrast-to-noise ratio (CNR) and minimum resolvable vessel diameter. For longitudinal metabolic assessment, whole-body scans were performed at multiple time points post-injection using a

material decomposition algorithm to quantify contrast agent concentration changes and biodistribution.CNR of intracranial vessels increased substantially with dose, and the minimum resolvable vessel diameter improved accordingly. Head scanning time was approximately 10 minutes. Peak intracranial vessel concentration was reached immediately after injection, followed by a prolonged circulatory decay and near-complete blood clearance by 12–24 hours. Contrast agent progressively accumulated in the liver and spleen up to 120 hours post-injection. Material decomposition effectively separated skull from vessels, enabling precise extraction of periosteal vasculature that is not achievable with conventional CT.A dose of 0.25 mL with early post-injection scanning yields optimal image quality. This approach demonstrates clear advantages in low-dose acquisition, bone-vessel separation, and fine vessel resolution (~50 μm), establishing an imaging protocol for in vivo cerebrovascular studies in mice.

Keywords: Photon-counting CT； Low-dose imaging； *In-vivo* cerebral vascular imaging； Material decomposition；

[TP-4] PIBM2026-0405-7

Line-scan dynamic OCT for high-throughput label-free drug screening

Lingxuan Meng[1], Shuaibin Chang[1] , Xiuhua Zheng[1], and Jianbo Tang[1*]

[1]Department of Biomedical Engineering, Southern University of Science and Technology, 1088 Xueyuan Avenue, Shenzhen 518055, China

Corresponding author e-mail address: tangjb@sustech.edu.cn

Abstract: We present a line-scan dynamic OCT (LS-dyOCT) technique for label-free, high-throughput monitoring of intracellular dynamics in cultured tissue samples, dedicated to anti-cancer drug screening. Our approach enables rapid viability quantification of tissue slices based on line-scan acquisition and a theoretical model that quantifies subcellular motility via the normalized first-order field autocorrelation function ($g_1(\tau)$), which directly reflects metabolic activity without exogenous labels. Based on this technology, we demonstrate its application in anti-cancer drug screening on viable tissue slices. To support large-scale pharmacological assays, we further integrated a motorized stage and environmental controls for fully automated, serial scanning of multiple samples. Applied to anti-cancer drug screening on viable tissue slices, our system successfully detects differential drug responses and reveals synergistic effects of combination therapies. This LS-dyOCT technique provides a powerful, scalable platform for label-free pharmacological evaluation with strong potential for drug screening applications.

[TP-5] PIBM2026-0405-18

An electrothermal-MEMS-based large-field-of-view confocal laser endomicroscopy

Luyang Huang[1], Ting Pan[2],Silei Yu[3], Huikai Xie[4], and Qian Chen*

[1]School of Integrated Circuits and Electronics, Beijing Institute of Technology, Beijing 100081, China

[2]Chongqing Institute of Microelectronics and Microsystems, Beijing Institute of Technology, Chongqing 400000, China

Corresponding author e-mail address: 7520220182@bit.edu.cn

Abstract: Confocal laser endomicroscopy (CLE) enables in vivo histological imaging, but conventional distal scanners face trade-offs among driving voltage, imaging speed, and image fidelity. Electrothermal MEMS

micromirrors offer miniaturized size, light weight, low-voltage driving, high scanning speed, and large deflection angles, making them an optimal scanner for proximal laser confocal endoscopic imaging. Here we developed a handheld CLE probe integrating a miniaturized electrothermal MEMS mirror. The probe operates in quasi-static modes, achieving a lateral resolution of 1.5 μm, a large field of view up to 580 μm × 700 μm, and an imaging frame rate of 0.05 fps . Ex vivo and in vivo experiments were carried out to evaluate the imaging performance of probe. The imaging results of mouse skin, and internal abdominal organs demonstrate clear visualization of fine blood vessels, crypt structures, and mucosal lesions. Due to its high resolution, large field of view, and flexible imaging capabilities, this probe is expected to be used in future clinical endoscopy scenarios for minimally invasive or non-invasive in vivo histological diagnosis.

[TP-6] PIBM2026-0405-20

A MEMS-based handheld dual-modal microscope integrating photoacoustic and optical coherence tomography

Lei Zhang[1],Huikai Xie[2] and Qian Chen[3]

[1]School of Integrated Circuits and Electronics, Beijing Institute of Technology, Beijing 100081, China

[2]Chongqing Institute of Microelectronics and Microsystems, Beijing Institute of Technology, Chongqing 400000, China

Corresponding author e-mail address: 7520220182@bit.edu.cn

Abstract: Evaluating microvascular remodeling and tissue structure repair is critical for assessing skin injury and healing using optical coherence tomography (OCT) and photoacoustic microscopy (PAM). Here, we developed a MEMS-based handheld PA/OCT dual-modal imaging probe featuring a lightweight design (<200g), non-invasiveness, high-resolution, large field of view, and rapid three-dimensional imaging of skin tissue and vasculature. Ex vivo and in vivo experiments were performed to evaluate the imaging performance of the system and the probe. Results show that the probe achieves lateral resolutions of 17 μm (PA) and 37 μm (OCT), with an imaging field of view of approximately 5×5 mm^2 and an imaging depth of about 1-2 mm. Animal experimental results demonstrated the probe's excellent in vivo imaging performance. In the future, this handheld dual-modal probe holds potential for the diagnosis of skin diseases such as melanoma, scar cancer, psoriasis, burns.

[TP-7] PIBM2026-0406-5

Improving Deep Tumor Vasculature Detection in SBH-PACT via Coherence Factor-Based Beamforming

Wenjie Jia[1], Liya Hu[2], Tun Liu[1] and Ying Chen[1]

[1]Wuhan Union Photoacoustic Technologies Ltd. Wuhan, Hubei, China

[2]Department of Geriatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Corresponding author e-mail address: (wenjiejia@union-pa.com)

Abstract: Photoacoustic imaging (PAI) enables deep breast cancer detection by visualizing vasculature at hundred-micrometer resolution, leveraging differences in vascular density, distribution, and morphology between malignant and normal tissues. However, SBH-PACT, China's first commercial full-ring PAI system for

breast imaging, suffers from 4–5 times poorer longitudinal than in-plane resolution, causing coronal-plane tumor vascular images to be contaminated by adjacent-slice signals, particularly from superficial layers. Additionally, photoacoustic signals from skin-surface vessels are two to three orders of magnitude stronger than those from tumors deeper than 3 cm, leading to severe overlap between tumor vasculature and superficial artifacts, compromising segmentation accuracy and diagnostic reliability. To address these issues, we integrated simulations and clinical data to investigate how longitudinal resolution affects tumor detectability across depths. We then proposed a novel adaptive image reconstruction algorithm weighted by the Coherence Factor (CF). By optimizing acoustic source coherence metrics, the algorithm enhances longitudinal resolution and suppresses superficial artifacts, markedly improving contrast and boundary definition of deep tumor vasculature. Results demonstrate substantially improved tumor vessel identifiability and segmentation accuracy without degrading image quality. This advancement enhances SBH-PACT's clinical utility and supports precise, non-invasive PAI-based breast cancer screening.

[TP-8] PIBM2026-0406-7

Improving Deep Tumor Vasculature Detection in SBH-PACT via Active Interference Cancellation

Wenjie Jia[1], Liya Hu[2], Tun Liu[1] and Ying Chen[1]

[1]Wuhan Union Photoacoustic Technologies Ltd. Wuhan, Hubei, China

[2]Department of Geriatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Corresponding author e-mail address: (wenjiejia@union-pa.com)

Abstract: Photoacoustic imaging (PAI) offers a powerful means to detect deep-seated breast cancer by mapping vascular networks at a resolution of hundreds of micrometers, capitalizing on the distinct vascular density, distribution, and morphology that differentiate malignant lesions from healthy tissue. Nevertheless, SBH-PACT—the first commercial full-ring PAI system for breast imaging in China—exhibits an longitudinal resolution that is four to five times poorer than its in-plane resolution. This anisotropy causes coronal-plane images of tumor vessels to be contaminated by signal leakage from adjacent slices, particularly those originating from superficial layers. Moreover, signals from skin-surface vessels are two to three orders of magnitude stronger than those emitted by tumors located deeper than 3 cm, resulting in severe overlapping of tumor vascular signatures with superficial artifacts, which in turn undermines segmentation accuracy and diagnostic confidence. To tackle these challenges, we combined simulations with clinical data to explore how longitudinal resolution influences depth-dependent tumor detectability. Consequently, we developed an active interference cancellation technique grounded in the photoacoustic forward model and the least-squares method, realized via iterative reconstruction. This technique first identifies and extracts low-clinical-value superficial vascular targets from the original three-dimensional image, then employs the forward model to compute their respective acquisition data at each slice location. A weighting factor is subsequently applied to subtract these computed data from the measured acquisition data of the corresponding slices. By integrating this subtraction strategy with least-squares optimization and iterative reconstruction, our approach effectively suppresses superficial-vessel interference in deep-tissue imaging, thereby markedly enhancing the image quality of deep tumor regions.

[TP-9] PIBM2026-0406-9

An ultracompact 3D confocal laser endoscope integrated with an electrothermal MEMS micromirror featuring a central opening

Author name[1], Author name[2], and Author name[3]

Yu Silei、Pan Teng、Huang Luyang、 Xie Huikai、Chen Qian*

[1]Author affiliation and full address (8-point type, centered, italicized)

School of Integrated Circuits and Electronics, Beijing Institute of Technology, Beijing 100081

[2]Omit titles or degrees such as Dr., Prof., Ph.D., etc

[3]Avoid acronyms that are not internationally known

Corresponding author e-mail address: 7520220182@bit.edu.cn

Abstract: Confocal laser endomicroscopy (CLE) enables real-time, cellular-resolution imaging of biological tissues. However, conventional three-dimensional (3D) CLE imaging relies on mechanical translation of the objective lens or even the entire imaging probe to achieve optical sectioning, limiting probe miniaturization and clinical application. Here, we developed a ultracompact 3D CLE probe integrated with an electrothermal MEMS micromirror featuring a central opening. The probe adopts a folded optical path design and PCB-free packaging, with a rigid segment length of 13mm, a lateral resolution of 1μm, an axial resolution of about 10 μm, and a large filed of view of 330×360μm². Its true 3D imaging by actuating the MEMS mirror inside the probe, providing an axial scanning range of 45 μm and an axial step size of≤0.45μm. Animal imaging experiments further validate the probe's excellent optical biopsy performance. This work establishes a scalable, low-voltage, and fully integrated endoscopy for point-of-care in vivo 3D histopathology, demonstrating substantial translational potential in the early diagnosis of gastrointestinal cancers and intraoperative surgical guidance.

[TP-10] PIBM2026-0406-14

Common-path OCT–PDT integrated system with DMD modulation

Yejiong Shi[1,2], Bin He[1,2], Guoxi Ruan[3], Zhe Meng[3], Wenchao Liao[1,2], Zhangwei Hu[1,2], Ruizhi Xue[1,2], Pangi Yang[1,2], Weicheng Zhan[1,2], Letao Tan[1,2]and Ping Xue[1,2,*]

[1]State Key Laboratory of Low-dimensional Quantum Physics and Center for Atomic and Molecular Nanoscience, Department of Physics, Tsinghua University, Beijing, China

[2]Frontier Science Center for Quantum Information, Beijing, China

[3]Department of Neurosurgery, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine and Institute of Precision Medicine, Tsinghua University, Beijing, China

**Corresponding author e-mail address: xuep@tsinghua.edu.cn*

Abstract: Photodynamic therapy (PDT) is a promising approach for tumor treatment. However, the lack of real-time guidance, monitoring, and treatment-efficacy assessment remains a major barrier that limits further improvement of therapeutic outcomes. To address this limitation, we developed a common-path optical system integrating optical coherence tomography (OCT) with PDT. Leveraging real-time OCT and OCT angiography (OCTA) imaging, the system actively modulates a digital micromirror device (DMD) to precisely control the irradiation area, spatial shape, and illumination duration during PDT. This strategy minimizes collateral damage to surrounding normal tissues and enables continuous monitoring of vascular responses throughout treatment. The integrated, image-guided OCT–PDT platform enables real-time optimization of illumination duration and

supports more reliable efficacy assessment, improving treatment reliability.

[TP-11] PIBM2026-0406-16

All-Fiber Photoacoustic Endomicroscopy Reveals Layer-Specific Angiogenesis-Oxygenation Uncoupling in Experimental Colitis

Jinying Li [1,2,3†], Junye Bi [1,4†], and Di Zhang [1,3,5†]

[1] Jinan University, Guangzhou 510630, China.

[2] Department of Gastroenterology, The First Affiliated Hospital, Jinan University, Guangzhou 510630, China.

[3] State Key Laboratory of Bioactive Molecules and Druggability Assessment, Jinan University, Guangzhou 510630, China.

[4] Guangdong Provincial Key Laboratory of Optical Fiber Sensing and Communications, Institute of Photonics Technology, Jinan University, Guangzhou 510630, China.

[5] Department of Pathophysiology, School of Medicine, Jinan University, Guangzhou 510630, Guangdong, China.

Corresponding author e-mail address: lyz0528@jnu.edu.cn (Y. L.); thuangw@jnu.edu.cn (W. H.); tguanbo@jnu.edu.cn (B.-O. G.)

†These authors contributed equally to this work.

Abstract: Currently, the incidence of colorectal diseases in my country continues to increase, with a rising number of patients suffering from chronic bowel diseases such as colorectal cancer and inflammatory bowel disease (IBD). Clinical demand for high-resolution, functional, and real-time imaging technologies is becoming increasingly urgent. Traditional endoscopic techniques, such as white light endoscopy (WLE), narrow-band imaging (NBI), confocal laser endoscopy (CLE), and optical coherence tomography (OCT), primarily provide structural imaging. While these techniques can provide some information about lesions, they have significant limitations in quantitatively assessing microvascular function, oxygenation, and oxygen extraction dynamics, making it difficult to detect early microvascular changes or monitor functional recovery after treatment.

To address these challenges, we propose a novel all-fiber photoacoustic endoscopy (AFPEM) platform. This system integrates high-density fiber bundle scanning and broadband fiber ultrasound detection, employing a remote optical scanning architecture to achieve high-resolution, rapid dual-wavelength volumetric oxygenation imaging. The AFPEM system features a lateral resolution of 7.7 μm, an axial resolution of 67.5 μm, and a B-scan rate of 250 Hz, enabling efficient acquisition of microvascular structural information and real-time oxygenation monitoring. By quantifying vascular density, width, hemoglobin content, relative oxygen saturation (rsO_2), and oxygen extraction efficiency (OEF) in a colitis model, AFPEM revealed the "angiogenesis-oxygenation decoupling" phenomenon during acute inflammation.

Furthermore, AFPEM enables systematic analysis of different tissue layers, from superficial vascular remodeling to deeper metabolically active crypt regions (100-200 μm), thus achieving layer-specific quantification of vascular and oxygenation parameters. This method not only reveals early inflammatory changes but also provides precise diagnostic information for changes in mucosal healing and oxygenation status. In addition, it provides a new diagnostic tool for colorectal cancer staging, offering more biomarkers and imaging evidence to support clinical decision-making and reduce unnecessary biopsies.

[TP-12] PIBM2026-0406-18

In vivo whole-brain 3D ultrasound microvascular and photoacoustic molecular imaging with a standard linear array probe

Xiao Hu[1,2,3], Yachao Zhang[1,2,3,4,5*]

[1]The School of Biomedical Engineering (Suzhou), Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230026, China

[2]The Suzhou Institute of Biomedical Engineering and Technology, Chinese Academy of Sciences, Suzhou 215163, China

[3]Jiangsu Key Laboratory for Advanced Theranostics and Medical Instrumentation, Suzhou 215163, China

[4]Key Laboratory of Biomedical Imaging Science and System, Chinese Academy of Sciences, Suzhou 215163, China

[5]State Key Laboratory of Biomedical Imaging Science and System, Suzhou 215163, China

Corresponding author e-mail address: zhangyachao@sibet.ac.cn

Abstract: Simultaneous in vivo whole-brain imaging of 3D vascular structure, blood flow and molecular contrast is essential for dissecting neurovascular and pathophysiological dynamics across scales. Ultrasound imaging is sensitive to hemodynamics, while photoacoustic imaging provides molecularly specific contrast. However, achieving spatially co-registered volumetric imaging with both modalities remains challenging. Matrix-array based systems enable 3D imaging but require 512–1024 channels, increasing system cost and complexity, while linear-array probes suffer from limited elevational resolution. Here we present a whole-brain 3D ultrasound–photoacoustic imaging framework that combines a standard linear-array probe with an integrated X–Y–Z–R scanning platform and angular-spectrum reconstruction. Translational scanning defines the volumetric imaging range, whereas rotational acquisition expands k-space sampling to overcome angular-view limitations in dual-modal volumetric imaging. Selective angular-spectrum weighting further enhances vascular contrast. By coupling hardware-efficient rotational scanning with Fourier-domain reconstruction, our method substantially improves volumetric resolution, even under sparse angular sampling. We validated the approach in phantoms, healthy and glioma-bearing mice. The framework enables co-registered 3D ultrasound microvascular and photoacoustic molecular imaging, revealing interactions among hemodynamics, oxygenation and molecular signals across the whole brain. This approach provides an accessible route to high-resolution volumetric neurovascular and molecular imaging using conventional linear-array hardware.

[TP-13] PIBM2026-0406-21

Optical computing based on dispersion for low-cost 4D optical coherence tomography with 10MHz A-line rate

Ruizhi Xue[1,2], Chengming Wang[1], Yejiong Shi[1,2], Bin He[1,2], Wenchao Liao[1,2], Zhangwei Hu[1,2], Panqi Yang[1,2], Weicheng Zhan[1,2], Letao Tan[1,2], Yiran Shen[1,2], Kaiyu Zheng[1,2], Weicheng Zhan[3], Xiao Zhang[4,*], and Ping Xue[1,2,*]

[1]State Key Laboratory of Low-dimensional Quantum Physics and Center for Atomic and Molecular Nanoscience, Department of Physics, Tsinghua University, Beijing, China

[2]Frontier Science Center for Quantum Information, Beijing, China

[3]College of Electronic and Optical Engineering & College of Flexible Electronics (Future Technology), Nanjing University of Posts and Telecommunications, Nanjing, China

[4]School of Medical Technology, Beijing Institute of Technology, Beijing, China

Corresponding author e-mail address: zhangx@bit.edu.cn, xuep@tsinghua.edu.cn

Abstract: Four-dimensional (real-time three-dimensional) optical coherence tomography (4D-OCT) plays a critical role in nondestructive material inspection and biomedical clinical applications, enabling real-time feedback of material structures and intraoperative guidance. With the advancement of ultrafast swept-source lasers, line-scan speed no longer limits the implementation of 4D-OCT; however, the data processing speed for Fourier-transform-based swept-source OCT remains a primary bottleneck. Currently, the performance of GPUs limit the further improvement of 4D-OCT imaging speed, and the combination of ultrafast lasers and high-end GPUs results in high system costs, restricting the widespread application of 4D-OCT. To address this challenge, we propose and implement a dispersion-based optical computing approach, achieving real-time optical Fourier transformation of OCT signals at 10 MHz line speed under GHz-class modulation. This method allows data acquisition using commercially available cards and enables real-time three-dimensional rendering on a personal computer, thereby realizing a low-cost 4D optical-computation OCT system without relying on GPUs or swept-source lasers. We provide a theoretical explanation of the method and experimentally demonstrate quasi-video-rate real-time 3D rendering. This approach offers a feasible solution for low-cost, high-speed scan and real-time-processing 4D-OCT, with broad potential in industrial inspection and biomedical applications.

[TP-14] PIBM2026-0406-28

Multiphoton Microscopy Reveals Spatially Resolved Lamina Propria Collagen Alterations Beneath Esophageal Squamous Lesions

Qihang Zhou[1], Jianing Ouchen[1], Xiahui Han[1], Shanghai Jiang[4], Xuan Tao[1, 2], Tao Liu[1], Huihan Yi[3], Longhui Hou[1], Zufeng Liao[1], Aizhe Zhang[1], Jiaxin Zhu[1], Haodong Zhang[1], Jianxin Chen[1*], Jianhua Chen[4*]

1Key Laboratory of OptoElectronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, College of Photonic and Electronic Engineering, Fujian Normal University, Fuzhou 350007, China

2Department of Pathology, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China

3Fujian Key Laboratory of Precision Medicine for Cancer, Palmar Hyperhidrosis Research Institute, Department of Thoracic Surgery, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China

4Chongqing Key Laboratory of Optical Fiber Sensor and Photoelectric Detection, Chongqing University of Technology, Chongqing 400054, China

5College of Life Science, Fujian Normal University, Fuzhou 350117, China

Corresponding author e-mail address: chenjianxin@fjnu.edu.cn; kangdeyong@fjmu.edu.cn

Keywords

Esophageal squamous lesions, lamina propria, multiphoton microscopy, collagen, H&E-stained sections

Abstract: Collagen alterations in the stromal microenvironment are closely associated with epithelial neoplastic change. Previous multiphoton and second harmonic generation (SHG)-based studies of esophageal squamous lesions have mainly focused on group-level discrimination between diagnostic categories using extracellular matrix features. In contrast, the spatial heterogeneity of lamina propria (LP) collagen immediately beneath lesional epithelium compared with background LP within the same histologic section has been less directly explored. Because SHG signals predominantly arise from collagen-rich LP and submucosa on routine H&E-stained sections, multiphoton microscopy may provide a practical approach for assessing localized lesion-associated stromal alterations. In this preliminary, spatially paired observational study, routine H&E-stained sections containing esophageal squamous lesions were examined by multiphoton microscopy with specific attention to LP regions of interest. For each section, LP directly beneath lesional epithelium was compared with spatially separated background LP from the same slide. Collagen architecture was assessed on the basis of SHG-dominant signals, with attention to fiber orientation, continuity, compactness, and associated stromal features, including vascular and lymphocytic components. Imaging findings were interpreted together with corresponding histopathologic features. Background LP in non-lesional or less-involved areas typically showed curved and continuous collagen fibers, with an overall orientation parallel to the overlying epithelium and a reticular appearance. In contrast, lesion-associated LP exhibited localized collagen alterations beneath esophageal squamous lesions. These changes included reorientation of collagen fibers, disruption of the usual parallel organization, increased compactness or fibrotic deposition in carcinoma-associated LP, and enrichment of vascular or lymphocytic stromal components. In representative lesion-associated regions, LP collagen shifted from a relatively orderly reticular pattern to more vertically oriented, compact, elongated, or locally remodeled architectures, depending on the local lesional context of the overlying epithelium. These findings indicate that stromal alterations are spatially heterogeneous and locally linked to lesional epithelium rather than uniformly

distributed across the section. Multiphoton microscopy reveals spatially resolved collagen alterations in the LP beneath esophageal squamous lesions on routine H&E-stained sections. Beyond serving as a global extracellular matrix readout, LP collagen may provide localized microenvironmental information relevant to the overlying epithelial lesion. This spatially paired strategy may complement conventional histopathology by highlighting stromal heterogeneity that is not readily appreciated on routine review, and it supports future quantitative studies of lesion-associated versus background LP collagen as a potential imaging biomarker.

[TP-15] PIBM2026-0406-29

A non-rotary PZT-driven cone-mirror scanning endoscopic OCT/OCTA probe for intraluminal imaging

Rui Yuan[1], Riqiang Lin[1], Chengyou Shu[1], and Xiaojing Gong[1]

[1]Research Center for Biomedical Optics and Molecular Imaging, Key Laboratory of Biomedical Imaging Science and System, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

Corresponding author e-mail address: xj.gong@siat.ac.cn

Abstract: Optical coherence tomography (OCT) and OCT angiography (OCTA) have demonstrated strong potential for intraluminal imaging of tissue microstructure and microvasculature; however, conventional endoscopic OCT systems typically rely on proximal mechanical rotation, which introduces non-uniform rotational distortion and motion artifacts and limits the repeatability required for OCTA. In this work, we present a non-rotary endoscopic OCT/OCTA probe based on a piezoelectric transducer (PZT)-driven distal fiber scanning mechanism combined with a cone-mirror reflector. The distal fiber is actuated by a PZT to generate two-dimensional scanning, while the cone mirror redirects the beam to enable circumferential side-view imaging without mechanical rotation. This configuration eliminates the need for rotary joints and slip rings, thereby reducing system complexity and improving robustness. The probe is implemented on a 1310 nm swept-source OCT platform and supports repeated B-scan acquisition for OCTA. Compared with conventional rotational scanning approaches, the proposed design provides improved scanning stability and reduced motion-induced artifacts, which are critical for reliable angiographic imaging. Preliminary imaging experiments, including intraluminal imaging in small animal models, demonstrate the capability of the system to visualize layered tissue structures and microvascular networks. This work establishes a cone-mirror-based non-rotary endoscopic OCT/OCTA architecture and highlights its potential for stable and cost-effective intraluminal imaging applications.

[TP-16] PIBM2026-0414-1

Multiscale Imaging and Optomechanical Simulation of Femtosecond Laser Modification towards Presbyopia in Ageing Eye

Zhuoyu Zhang[1], Jionghang Zhang[1], Yujie Liu[1], Jiale Li[1], Honghao Wang[1], Yaping Shi[1], Xiaohua Lv[1], Xu Feng[1,\\], Shaoqun Zeng[1]

[1] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

\\Corresponding author e-mail address: xufeng@hust.edu.cn

Abstract: Presbyopia occurs in more than 90% of middle-aged and elderly populations. Its cause is the degradation of the dynamic focusing ability due to lens hardening with age. Currently, there is still a lack of effective clinical methods to improve the dynamic focusing ability in presbyopia, meaning the eye's accommodation ability cannot be restored. Previous studies have conducted preliminary explorations of laser-assisted anterior segment relaxation treatments, but these remain at an early stage. The core challenges include: (1) the lack of precise nonlinear ablation tools; (2) the characterization of crystalline lens optomechanical performance; (3) the quantitative imaging for cellular damage.

To address these cha, this study has developed the Femtosecond Laser Ocular Research Apparatus (FLORA), with large 3D scanning FOV >10×10×10 mm^3 and precise non-linear cavitation bubble with minimal size <10×10×50 μm^3. It can create micro-structures in anterior eye tissues to achieve mechanical properties modification. At the micro level, we developed Optical Transmission Tomography (OTT) microscopy for non-contact endothelial cell imaging and damage quantification. At the macro level, we developed Optical Coherence Elastography (OCE) to image the elastic wave and characterize the biomechanical properties changes induced by the fs-laser modification. Both of the proposed non-contact imaging tools can work *in situ* for the whole intact eyeball without any labeling. Besides, we proposed the finite element analysis (FEA) model with the “mechanics-shape-optics” coupling to understand the age-related lens accommodation changes in “Digital Twins” approach.

We demonstrated that after the fs-laser lentotomy (fs-lento) surgery the lens stiffness can be reduced ~25% which leads to an increase in dynamic accommodation amplitude exceeding more than 0.5 D. The technical system is expected to provide a feasible path for precise optical diagnosis and treatment of presbyopia in the future translation.

Key Words: femtosecond laser surgery, optical coherence elastography, optical transmission tomography, finite element anlysis

[TP-17] PIBM2026-0510-1

Robust hybrid feature-driven on-the-fly mapping enables freehand 3D panoramic photoacoustic angiography

Haishu Xin[1,2], Sihua Yang[1,2]

[1] South China Normal University, MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, Guangzhou, China.

[2] South China Normal University, Guangdong Provincial Key Laboratory of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, Guangzhou, China.

Corresponding author e-mail address: yangsh@scnu.edu.cn

Abstract: The vascular network defines the perfusion boundaries that are fundamental to surgical resection and functional preservation. Photoacoustic angiography (PAA) offers stereoscopic visualization and quantification of microvascular anatomy and hemodynamics in vivo, but existing implementations remain constrained in field of view and imaging speed, limiting the intraoperative utility. Here, we introduce a real-time PAA tracking and mapping strategy that estimates the six degree-of-freedom motion of a handheld probe and reconstructs panoramic three-dimensional vascular maps for surgical guidance. By associating geometric and intensity-based hybrid vascular features to prevent degeneracy, the method achieves robust online mapping with 99.67% accuracy, even under dynamic freehand operation. In rat radical gastrectomy, the approach expanded the imaging boundary by 42.3-fold to 50.84 mm^3 within 16.7 seconds, enabling panoramic microvascular visualization beyond the surgical field for preoperative planning, postoperative evaluation, and distal hemodynamic surveillance. This on-the-fly, freehand, and field-of-view–unconstrained PAA establishes a practical framework for vascular-focused surgical interventions, supporting precise and timely decision-making.

[TP-18] PIBM2026-0616-5

CFD/FSI-Guided Design and Optimization of a Pressure-Regulated Composite Glaucoma Drainage Stent

Ruonan Bian, Honghao Wang, Xiuli Liu, Shaoqun Zeng*

Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, China

sqzeng@hust.edu.cn

Abstract: Glaucoma drainage stents provide an alternative pathway for aqueous humor outflow, but passive drainage devices may suffer from insufficient flow regulation, hypotony risk, local flow concentration, and uncertain long term patency. In this study, a pressure regulated composite glaucoma drainage stent was designed and optimized using computational fluid dynamics and fluid structure interaction simulations. The proposed stent integrates four functional regions: an inlet guiding region, a slit membrane valve region, a gradual expansion region, and a distal micropore drainage region. Whole stent CFD and FSI simulations were performed to evaluate the pressure and velocity fields, outlet flow rate, and membrane deformation. Local FSI analysis was used to investigate the transient response of the slit membrane valve, while micropore CFD and gradual expansion analysis were conducted to compare drainage uniformity and structural safety. The simulation results showed that, at an inlet pressure of 15 mmHg, the outlet flow rate reached approximately 2.79 μL/min, which was close to the target value of 2.75 μL/min. The membrane valve reached stable deformation within 1.0-1.2 ms, and the peak membrane displacement was 5.86 μm, remaining below the 18 μm membrane thickness. Among the tested outlet configurations, the 8 × 30 μm micropore design achieved

the best comprehensive balance between drainage capacity, flow uniformity, and structural redundancy. The gradual expansion channel from 150 μm to 290 μm reduced local stress concentration compared with the equivalent diameter structure. These results provide simulation based evidence for the structural feasibility of a pressure regulated glaucoma drainage stent and support future prototype fabrication, in vitro validation, and in vivo evaluation.

[TP-19] PIBM2026-0617-9

Interfacial morphology shapes endothelial organization and function in a blood−brain barrier-on-a-chip

Zengting Li[1#], Qihang Yang[1#], Zhijun Tan[2#], Tingting Yu[1], Yufei Xue[2], Bo Peng[2,3*], and Dan Zhu[1*]

[1] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics - Advanced Biomedical Imaging Facility, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

[2] State Key Laboratory of Flexible Electronics (LoFE) & Institute of Flexible Electronics (IFE), Northwestern Polytechnical University, 127 West Youyi Road, Xi'an, 710072, China

[3] Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria 3052, Australia

[#]These authors contributed equally to this work

Corresponding author e-mail address: Bo Peng: iambpeng@nwpu.edu.cn; Dan Zhu: dawnzh@mail.hust.edu.cn.

Abstract: Organ-on-a-chip platforms incorporating hydrogels have emerged as powerful in vitro models for investigating human physiology and disease. In blood–brain barrier (BBB) and related barrier-on-a-chip systems, hydrogels serve not only as structural scaffolds but also as critical substrates for endothelial barrier formation. However, maintaining a stable and reproducible hydrogel interface during long-term culture remains challenging, and the extent to which interfacial morphology influences endothelial phenotype and barrier function remains unclear. Here, using a three-channel BBB-on-a-chip (μBBB) platform in combination with computational fluid dynamics simulations, high-resolution imaging, and transcriptomic profiling, we investigated how hydrogel interface morphology regulates endothelial organization and barrier function. We found that subtle geometric variations at the hydrogel interface substantially altered local shear stress distributions, with slightly protruded interfaces generating a more favorable microenvironment for endothelial alignment and organization. Building on these findings, we employed *in situ* photocrosslinking to stabilize the hydrogel interface. A flat or mildly protruded interface significantly improved endothelial viability, reduced cellular invasion into the hydrogel, and strengthened tight junction formation. Functionally, stabilized interfaces decreased barrier permeability by nearly an order of magnitude while enhancing efflux transporter activity. Transcriptomic analysis further revealed suppression of inflammatory signaling and angiogenic sprouting pathways, consistent with the establishment of a more quiescent and physiologically relevant endothelial phenotype. Taken together, our results identify hydrogel-cell interfacial morphology as a critical yet underappreciated determinant of μBBB performance and establish hydrogel interface engineering as a fundamental design principle for barrier-on-a-chip systems, providing a broadly applicable strategy for improving the physiological relevance and reproducibility of hydrogel-based organ-on-a-chip platforms.

[TP-20] PIBM2026-0618-4

High-speed swept-source optical coherence tomography for wide-field biomedical imaging and ocular dynamics

Yaping Shi[1]

[1] Britton Chance Center for Biomedical Photonics, MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China

Corresponding author e-mail address: ypshi@hust.edu.cn

Abstract: Optical coherence tomography (OCT) has become a regular clinical imaging modality, particularly in ophthalmology, and recent advances have expanded its role in biomedical imaging of vascular and microstructural diseases. However, most clinical OCT systems remain constrained by imaging speed, ranging depth, field of view, acquisition flexibility, and functional imaging capability, limiting broader in vivo applications in large, curved, or dynamically changing tissues. To address these limitations, we developed a high-speed swept-source OCT platform operating at A-scan rates of up to 600 kHz to expand the spatial and temporal imaging capabilities of OCT. The platform integrates synchronized high-speed acquisition, extended-range sampling, wide-field scanning, and phase-stable repeated measurements. To extend the usable ranging depth without sacrificing acquisition speed, multichannel delay sampling was introduced to increase the effective spectral sampling density, and a global k-space compensation algorithm was implemented to reduce distortion caused by electrical dispersion in high-speed electronic components. For complex surface topographies, adaptive contour tracking using an electrically tunable lens, a motorized optical delay line, and real-time surface profiling maintained focus and signal strength across curved regions. For large-area volumetric imaging, wide-field bidirectional scanning was combined with direction-specific geometric calibration and motion correction to improve acquisition efficiency and preserve spatial fidelity across expanded imaging regions. These advances enabled high-quality structural and OCT angiography imaging of facial skin that is difficult to assess using conventional clinical OCT, with imaging fields of up to 42 × 42 mm² and an axial range of up to 36 mm. Beyond anatomical imaging, rapid volumetric and phase-stable repeated acquisition enabled measurements of ocular dynamics, including stimulus induced optoretinographic responses and phase-resolved trabecular meshwork motion in the anterior chamber angle. Overall, this work extends OCT toward wide-field anatomical and dynamic functional imaging for broader biomedical and clinical applications.

[TP-21] PIBM2026-0707-3

NIR-II Fluorescence Surgical Navigation for Gastric Cancer: Systematic Preclinical Validation Toward Clinical Application

Xiaolong Liu[1], Zhe Feng[2], Jun Qian[2], Hui Lin[1]

[1] Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, 310016, China.

[2] State Key Laboratory of Extreme Photonics and Instrumentation, Centre for Optical and Electromagnetic Research, College of Optical Science and Engineering, International Research Center for Advanced Photonics, Zhejiang University, Hangzhou 310058, China.

Corresponding author e-mail address: 369369@zju.edu.cn

Abstract: The precise intraoperative delineation of gastric tumors and their micrometastases remains a significant challenge in surgical oncology. Conventional near-infrared I (NIR-I) imaging is often limited by suboptimal signal-to-background ratios and shallow tissue penetration. To address these limitations, we developed and comprehensively evaluated SPN01, a novel integrin αvβ3-targeted fluorescent probe designed

for the second near-infrared window (NIR-II, 900–1880 nm). SPN01 was engineered by conjugating a high-affinity RGD peptide to a net-neutral sulfonated cyanine-based fluorophore to minimize non-specific tissue interactions and enhance targeting precision.

In multiple preclinical models, SPN01 demonstrated superior optical properties, including high brightness and excellent photostability compared to clinically used indocyanine green (ICG). Systemic administration of SPN01 enabled real-time, high-contrast visualization of orthotopic gastric tumors and provided clear demarcation of tumor margins. Notably, the probe exhibited exceptional sensitivity in detecting occult peritoneal micrometastases as small as 0.5 mm and specifically identifying metastatic lymph nodes. The accuracy of the NIR-II fluorescence signals was validated through ex vivo histopathological analysis and immunofluorescence staining, confirming a strong correlation between SPN01 accumulation and integrin αvβ3 overexpression in both primary and metastatic lesions.

Furthermore, ex vivo incubation assays with fresh human gastric cancer specimens confirmed target-specific binding, reinforcing the clinical relevance of the probe. Comprehensive pharmacokinetic and safety studies in animal models revealed rapid dual-pathway (renal and hepatobiliary) clearance and no significant systemic toxicity. Following these preclinical findings, a first-in-human Phase I clinical trial was conducted, which confirmed the favorable safety profile of SPN01 in human subjects. These results suggest that SPN01-assisted NIR-II fluorescence-guided surgery is a promising translational strategy to improve the completeness of gastric cancer resection and enhance patient outcomes.

[TP-22] PIBM2026-0708-1

Orally Administered NIR-II AIEgen Nanoparticles for Targeted Gut–Brain Axis Photothermal Stimulation to treat Metabolic Dysfunction-associated Steatotic Liver Disease

Yujie Li[1], Hui Lin[1]

[1] Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, 310016, China.

Corresponding author e-mail address: 369369@zju.edu.cn

Abstract: Traditional organic fluorescent dyes have long faced the bottleneck of aggregation-caused quenching (ACQ) in biological imaging and phototheranostics — molecular fluorescence is significantly attenuated or even completely quenched in aggregated states or at high concentrations, while photosensitization efficiency is severely compromised. In contrast, Aggregation-induced emission luminogens (AIEgens) exhibit disruptive advantages: AIEgens display weak fluorescence in the monodispersed state, yet demonstrate markedly enhanced fluorescence emission in aggregated states (such as nanoparticle forms), while simultaneously achieving efficient heat generation.

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most prevalent chronic liver disease worldwide and is closely associated with obesity, insulin resistance, and dyslipidemia. Although vagus nerve stimulation (VNS) represents a promising non-pharmacological strategy for metabolic regulation, conventional implantable and transcutaneous electrical approaches are fundamentally hindered by surgical complications, current diffusion with poor spatial precision, off-target tissue activation, and the complete absence of real-time therapeutic feedback.

Here, we propose an orally administered near-infrared (NIR) AIEgen nanoparticle (AIE NP) stimulator for targeted photothermal regulation of the gut–brain axis to treat MASLD. Following oral administration, the engineered AIE NPs are designed to selectively accumulate within the gastrointestinal tract and adjacent vagal

sensory interfaces through surface modification. Upon external 808 nm laser irradiation, the nanoparticles generate localized mild hyperthermia, activating thermosensitive ion channels and modulating vagal afferent signaling to regulate appetite, glucose metabolism, lipid homeostasis, and liver function. Simultaneously, strong NIR-II (900-1880nm) fluorescence enables real-time visualization of nanoparticle distribution, while temperature-responsive fluorescence provides in situ feedback for photothermal dose monitoring, establishing a closed-loop, image-guided stimulation platform.

[IP-1] PIBM2026-0331-1

Single-molecule localization super-resolution microscopy reveals the organization CD47 in human erythrocytes

Leiting Pan

[1]*Key Laboratory of Weak-Light Nonlinear Photonics, Ministry of Education, School of Physics, Nankai University, Tianjin 300071, China*

Corresponding author e-mail address: plt@nankai.edu.cn

Abstract: The transmembrane protein CD47, also known as integrin-associated protein (IAP), is a key member of the “don’t-eat-me” signals on cell surfaces that help the cell evade elimination by the immune system. Previous immunofluorescence studies in CD47 on human erythrocytes and cultured cell lines have also suggested patchy, domain-like staining at the micrometer and sub-micrometer scales. In the present work, we used single-molecule localization super-resolution microscopy (SMLM) to resolve the distribution of CD47 at the nanoscale in human erythrocytes. We find that CD47 exists in randomly distributed monomers across the human erythrocyte membrane rather than in clusters as previously reported for mouse erythrocytes. Using 2nd antibody-induced crosslinking, it show that CD47 aggregates into stable clusters within minutes. By comparing with SMLM results of the fully mobile and the cytoskeleton-bound membrane proteins CD59 and glycophorin C under similar conditions, as well as devising two-color SMLM co-labeling and co-clustering experiments, we further quantitatively reveal an intermediate, self-limiting clustering behavior of CD47, elucidating its fractional (~14%) attachment to the cytoskeleton. Moreover, we report reductions in both the CD47 amount and its clustering capability in aged erythrocytes, hence a new insight into erythrocyte senescence. Together, the combination of STORM and 2nd antibody-based crosslinking unveils the unique self-limiting clustering behavior of CD47 due to its fractional cytoskeleton attachment.

[IP-2] PIBM2026-0408-1

Three-photon phosphorescence lifetime imaging of hypoxic tumor microenvironment

Jia Yu[1,2], Xueming Cao[1], Yufeng Gao[1], Na Xiao[1], and Wei Zheng[1,3]

[1]*Research Center for Biomedical Optics and Molecular Imaging, Shenzhen Key Laboratory for Molecular Imaging, Guangdong Provincial Key Laboratory of Biomedical Optical, Imaging Technology Key Laboratory of Biomedical Imaging Science and System, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences*

[2]*Institute of Translational Medicine, Ministry of Education Frontiers Science Center for Precision Oncology, Faculty of Health Sciences, University of Macau*

[3]*Corresponding author e-mail address: zhengwei@siat.ac.cn*

Abstract: The phosphorescence lifetime, due to its sensitivity to ambient oxygen molecules, is often used to detect changes in tissue oxygenation induced by physiological activities in biological tissues. Among the relevant techniques, two-photon phosphorescence lifetime imaging offers high spatial resolution and deep tissue penetration, making it particularly suitable for in vivo oxygen concentration imaging. However, limited by measurement speed, current two-photon phosphorescence lifetime approaches are often restricted to sampling at a limited number of points. To address this limitation, we propose a method based on three-photon phosphorescence lifetime imaging, which fully leverages the low repetition rate and long excitation wavelength

of three-photon excitation sources to enable rapid phosphorescence lifetime measurement and deep imaging. Using this method, we successfully mapped the oxygen concentration distribution in the tumor microenvironment of living mice.

[IP-3] PIBM2026-0415-5

Construction of photo/sono-responsive MOFs-based nanoplatform and their application in breast cancer therapy

Ke Gao[1], Qin Xu[1], Maojun Wu[1], and Dongbo Guo[*1]

[1]State Key Laboratory of Digital Medical Engineering, Sanya Research Institute of Hainan University, School of Biomedical Engineering, Hainan University, Sanya

572025, China

Corresponding author e-mail ： dongboguo@hainanu.edu.cn

Abstract: While carbon dots (CDs) have emerged as compelling candidates for tumor theranostics due to their exceptional biocompatibility and tunable optical characteristics, their clinical trajectory remains frequently hindered by aggregation-induced quenching and restricted penetration within the dense tumor microenvironment (TME). To overcome these challenges, we engineered a porous and biodegradable nanoplatform (CDs@ZIF-8/FA) by encapsulating CDs into a zeolitic-imidazolate-framework-8 (ZIF-8) matrix via a coordination driven self-assembly approach, followed by functionalization with folic acid (FA). As a porous material, ZIF-8 not only prevents the aggregation of CDs to preserves their intrinsic optical activity, but also enhances the sonodynamic activity and reactive oxygen species (ROS) generation ability of the CDs@ZIF-8/FA. Upon dual-stimulation with an 808 nm laser and ultrasound, the nanoplatform induces a ROS storm to boost apoptosis of breast cancer cells, which also exacerbates immunogenic cell death (ICD). The subsequent maturation of dendritic cells and extensive infiltration of cytotoxic T lymphocytes provoke a robust systemic immune cascade. Consequently, this engineered response successfully suppresses primary tumor growth and completely abates distal metastasis in mouse breast cancer. The targeted drug delivery of CDs@ZIF-8/FA is facilitated by interactions between FA and FA receptors in the surface of the tumor cell membrane. Importantly, the bright second near-infrared (NIR-II) fluorescence of the nanoplatform provides deep tissue and high contrast imaging capabilities to facilitate precise tumor delineation and real time therapeutic monitoring. Ultimately, this work delivers a versatile nanoplatform that seamlessly bridges NIR-II imaging guided sonodynamic therapy with robust immunotherapy, unlocking new avenues for precision oncology in breast cancer management.

[IP-4] PIBM2026-0417-1

Rational Design of a V-Shaped DNA-Targeted Photosensitizer Enables Endogenous DNA Damage-Driven cGAS-STING Activation and Systemic Antitumor Immunity

Yi Cai [1, #], Cai-Yun Wang [1, #], Min Dong [1, #], Zhang Lin [1], Cai-Qiang Liao [1], Ze-Jun Li [1], Tian-Yi Qin [1, *], Zhao-Hui Wang [1], *, Ya-Long Wang[1], * and Ming-Qiang Zhu[2]

[1]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Sanya Research Institute of Hainan University, Hainan University, Sanya, 572024, China.

[2] Wuhan National Laboratory for Optoelectronics, School of Optical and Electronic Information, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China.

[1, #]These authors contribute equally to this work.

Corresponding author e-mail address: qintianyi@hainanu.edu.cn; wangzhaohui@hainanu.edu.cn; ylwang@hainanu.edu.cn

Abstract: The cyclic GMP-AMP synthase–stimulator of interferon genes (cGAS-STING) pathway is a central driver of antitumor immunity, yet its safe and efficient activation in solid tumors remains challenging. Here we report a V-shaped photosensitizer, 2C6, that functions as an in situ DNA-fragmentation agent by directly targeting double-stranded DNA (dsDNA). Owing to its A–π–D–π–A molecular framework, 2C6 exhibits efficient reactive oxygen species (ROS) generation under low-power white-light irradiation. Photoactivation of 2C6 induces concurrent mitochondrial and nuclear DNA damage, leading to the accumulation of oxidized dsDNA fragments in the cytosol and subsequent activation of cGAS-STING signaling. In parallel, 2C6-PDT triggers pyroptosis and immunogenic cell death (NLRP3/IL-18 release, CRT exposure, ATP secretion, and HMGB1 release). In a murine 4T1 triple-negative breast cancer (TNBC) postsurgical residual model, a single intraoperative 2C6-PDT prevented local recurrence, established immune memory, and suppressed distant tumors and lung metastasis without immunoadjuvants. Collectively, 2C6 couples photoinduced DNA damage to cytosolic dsDNA sensing, type I interferon signaling, and adaptive immune activation through a defined cascade encompassing DNA damage, dsDNA accumulation, cGAS-STING engagement, inflammatory signaling, and immune-cell infiltration. Together, these findings demonstrate that rationally engineered DNA-targeted photosensitizers can convert localized photodynamic tumor ablation into a systemic photoimmunotherapeutic response, providing a strategy to transform immunologically “cold” tumors into immune-responsive states.

[IP-5] PIBM2026-0417-2

Structure-optimized cationic AIE photosensitizer-loaded gelatin/hyaluronic acid hydrogel for broad-spectrum anti-infective wound healing

Lu Zhang[1#], Yu-Jian Cai[1#], Quan Chen[1#], Xin-Zheng Liang[1], Tian-Yi Qin[1*], Zhao-Hui Wang[1*], Ya-Long Wang[1*] and Ming-Qiang Zhu[1,2]

[1]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Sanya Research Institute of Hainan University, Hainan University, Sanya, 572024, China.

[2] Wuhan National Laboratory for Optoelectronics, School of Optical and Electronic Information, Huazhong University of Science and Technology, Wuhan, Hubei 430074, China.

[1, #]These authors contribute equally to this work.

Corresponding author e-mail address: qintianyi@hainanu.edu.cn; wangzhaohui@hainanu.edu.cn; ylwang@hainanu.edu.cn

Abstract: Persistent disruption of the wound micro-environment hinders the healing of bacterial- and fungal-infected wounds. While photodynamic therapy (PDT) is promising, its efficacy is limited by aggregation-caused quenching (ACQ), poor performance in hypoxia, and rapid photosensitizer (PS) loss. To overcome these limitations, we developed a composite platform integrating a structurally programmable cationic aggregation-induced emission (AIE) PS into a GP-crosslinked hydrogel. By systematically tuning cationic valency and amphiphilic balance in triphenylamine-pyridinium-based AIE-PS, TPA-PY-C6, a moderately hydrophobic mono-cationic derivative, was identified as the optimal candidate. It overcomes ACQ, generates efficient Type I/II reactive oxygen species (ROS), and delivers broad-spectrum antimicrobial action. Incorporating TPA-PY-C6 into a GP-GLT-HA hydrogel to form TPA-PY-C6@Gel significantly improved local retention and controlled release at the wound site. In vivo, TPA-PY-C6@Gel effectively reduced microbial burden and accelerated wound closure. These benefits were driven by enhanced angiogenesis, improved re-epithelialization, and favorable immuno-inflammatory remodeling, characterized by reduced IL-6, increased IL-10, and a macrophage shift toward a reparative phenotype. Transcriptomic analysis confirmed the suppression of inflammatory programs and activation of tissue-repair pathways. Ultimately, coupling a structure-optimized AIE photosensitizer with a wound-adaptive hydrogel provides an effective strategy for infected wound treatment by combining potent anti-infective activity with micro-environment-oriented tissue repair.

[IP-6] PIBM2026-0616-1

A Systematic Integration Framework for Liver Single-Cell and Spatial Data Analysis

Shuwen Chen[1],Qi Pan[1], Zhihong Zhang[1,*]

[1]School of Life and Health Sciences, Hainan Province Key Laboratory of One Health, Collaborative Innovation Center of One Health, Hainan University, Haikou,Hainan 570228, China

Corresponding author e-mail address: zhzhang@hainanu.edu.cn

Abstract: The rapid growth of single-cell transcriptomic, and spatial transcriptomic datasets has substantially advanced investigations of liver biology. However, heterogeneity in data sources, experimental protocols, and analytical workflows limit standardized cross-modality integration and hinder systematic characterization of liver cellular heterogeneity.

In this study, targeting the construction of a comprehensive single-cell multi-omics deeply integrated database for the liver as the long-term goal, we focus on the integration of two core modalities: single-cell transcriptomics and spatial transcriptomics, and tackle key technical challenges in the integration process. We systematically

curated publicly available liver datasets from multiple species, developmental stages, physiological conditions, and disease states. A standardized preprocessing workflow, including quality control, normalization, dimensionality reduction, clustering, and cell type annotation, was applied to generate cross-modality integrated datasets for downstream analyses. Using these processed datasets, we constructed an integrated liver cell atlas and implemented an interactive web interface for data visualization and exploration.

The database enables users to visualize clustering results and major cell populations, compare cellular composition across biological conditions, and explore integrated transcriptomic, and spatial datasets within a unified framework. These functions provide an accessible resource for investigating liver cellular heterogeneity across diverse biological contexts.

In summary, this work presents a standardized integration pipeline for single-cell transcriptomic and spatial transcriptomic data, together with a preliminary web-based data resource and an integrated liver cell atlas. This resource facilitates data exploration and cell-type annotation, thereby providing a valuable foundation for future studies of liver homeostasis, development, and disease.

[IP-7] PIBM2026-0617-10

Deciphering the Spatiotemporal Evolution and Mechanisms of Subclonal Drug Resistance Heterogeneity in Liver Tumors via Multicolor Labeling Techonology

Jiahong Hu[1], Borui Li[2], and Zhihong Zhang[1]

[1]School of Life and Health Sciences, Hainan Province Key Laboratory of One Health, Hainan International One Health Institute, Hainan University, Haikou,

Hainan, China.

[2]Britton Chance Center and MoE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics-Huazhong University of Science and

Technology, Wuhan, Hubei 430074, China

Corresponding author e-mail address: zhzhang@hainanu.edu.cn

Abstract: Liver cancer is the third leading cause of cancer

[IP-8] PIBM2026-0617-8

Photo-empowered macrophage-based drug delivery system overcomes motility suppression and significantly enhances deep tumor drug delivery

Fuzhaoming[1], Wen Song[1], and Feifan Zhou[1] (10-point type, centered, bolded)

[1]School of Biomedical Engineering, Hainan University

Fuzhaoming@hainanu.edu.cn

Abstract: Recently, cell-based drug delivery systems emerge as highly promising alternatives in the field of antitumor therapy. These systems are characterized by their excellent biocompatibility, robust drug-loading capacity, and the ability to effectively traverse biological barriers. However, the immunosuppressive tumor microenvironment significantly weakens the motility of immune cells, which is crucial for efficient drug delivery. A novel photo-empowered macrophage-based (PEM) drug delivery system is successfully developed in this study. The system is modified with thylakoids extracted from spinach leaves. Upon stimulation with light of specific wavelengths, the thylakoids generate ATP through photochemical reactions, thereby significantly enhancing the motility of macrophages and effectively overcoming the limitations imposed by the tumor microenvironment. In this work, the PEM system is loaded with two antitumor drugs: doxorubicin (Dox) and tirapazamine (TPZ). The results demonstrate that the system not only significantly improves the delivery efficiency of drugs to deep tumor tissues but also greatly enhances antitumor therapeutic efficacy. Particularly after deep infiltration into tumor tissues, the PEM system efficiently eradicates hypoxic and drug-resistant tumor cells, showcasing remarkable performance. This innovative PEM strategy provides a new approach for deep tumor drug delivery and addressing multidrug resistance, holding great promise for a significant breakthrough in antitumor therapy.

[IP-9] PIBM2026-0618-1

Quantitative longitudinal investigation of non-alcoholic steatohepatitis in mice by photoacoustic microscopy

Jianshuang Wei[a], Xiaoquan Yang[a,b], Zhihong Zhang [a,b,*]

[a] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China

[b] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

Corresponding author e-mail address: zhzhang@hainanu.edu.cn(Zhihong Zhang),

Abstract: Non-alcoholic steatohepatitis (NASH) is a prevalent chronic liver disease characterized by significant alterations in liver microvascular structures, leading to microcirculatory dysfunction and potentially contributing to various extrahepatic complications. In this study, we propose a longitudinal investigative pipeline based on liver photoacoustic microscopy (LPAM), integrating optical-resolution photoacoustic microscopy (OR-PAM), a modular liver window (MLW), a custom 3D-printed liver imaging mount (LIM), and a dedicated vessel-sinusoid separation and analysis method. This pipeline enabled continuous monitoring and quantitative assessment of microvascular changes in a NASH mouse model over a six-week period. As NASH progressed, vessel density decreased by 64.18%, and hepatic sinusoid vessel coverage was reduced by 77.38%. Furthermore, hepatic sinusoidal volume, length, radius, tortuosity, and density declined by 87.29%, 83.92%, 21.86%, 71.57%, and 86.81%, Analysis of hepatic sinusoidal branches revealed a 51.80% decrease

in the fractal dimension of composite branches and a 54.90% increase in that of dead-end branches. These findings suggest that lipid accumulation and inflammatory responses contribute to the progressive deterioration of hepatic microvascular structures, thereby exacerbating vascular damage. LPAM offers a high-resolution, label-free imaging approach for dynamic monitoring of NASH-associated microvascular alterations. This study advances our understanding of hepatic microcirculatory changes in NASH and provides valuable insights for both basic research and clinical management.

[IP-10] PIBM2026-0618-3

A NIR-II AIEgen-Antibody Conjugate Enables Combined Photoimmunotherapy of Advanced Pancreatic Cancer

Jinxian Wu[1], Dingyuan Yan[2], and Feifan Zhou[3]

[1]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Sanya 572025, China.

[2]Center for AIE Research, Guangdong Provincial Key Laboratory of New Energy Materials Service Safety, College of Materials Science and Engineering, Shenzhen University, Shenzhen 518060, China;

[3]Key Laboratory of Biomedical Engineering of Hainan Province, One Health Institute, Hainan University, Sanya 572025, China

Corresponding author e-mail address: zhouff@hainanu.edu.cn

Abstract: Pancreatic cancer (PC) is a highly lethal malignancy, characterized by frequent late-stage diagnosis and limited response to available treatments. Photoimmunotherapy, which combines the localized tumor ablation of phototherapy with the systemic immune activation of immunotherapy, presents a promising strategy. However, its success is often hampered by insufficient accumulation of therapeutic agents at the tumor site. To address this challenge, we developed a novel antibody-photosensitizer conjugate, named α PD-L1@AIE, by conjugating a multifunctional phototheranostic agent with α PD-L1 antibody for targeted photoimmunotherapy of PC. The recommendation of α PD-L1 not only facilitates tumor-specific targeting but also acts as an immune checkpoint inhibitor. Upon 660 nm laser irradiation, phototheranostic agent enables NIR-II fluorescence imaging and simultaneously induces potent immunogenic cell death (ICD) via combined photodynamic and photothermal therapy. Following localized phototherapy, the released tumor-associated antigens from ICD initiate a robust anti-tumor immune response. Such a response is synergistically amplified by α PD-L1, which together alleviates immunosuppression via Treg cell depletion and M2-like macrophage repolarization, thereby promoting a marked increase in cytotoxic T lymphocyte infiltration and granzyme B production. Consequently, the aforementioned photoimmunotherapy approach effectively suppresses tumor growth and inhibits spontaneous metastasis, demonstrating a powerful and transformative paradigm for advanced PC management.

[IP-11] PIBM2026-0629-3

In Vivo Imaging Reveals the Immunomodulatory Role of Exercise in Alleviating Chronic liver disease

Hongying Jin[1], Jing Ai[1], Zhihong Zhang[1,*]

[1]School of Life and Health Sciences, Hainan Province Key Laboratory of One Health, Collaborative Innovation Center of One Health, Hainan University, Haikou, Hainan 570228, China

Corresponding author e-mail address: zhzhang@hainanu.edu.cn

Abstract: In recent years, the global incidence of metabolic dysfunction-associated steatotic liver disease (MASLD) has risen sharply. As a prevalent chronic liver disorder closely linked to unhealthy lifestyles, MASLD still lacks therapeutic agents with definite efficacy and mild side effects. Lifestyle intervention serves as an effective strategy to prevent and alleviate this disease.

This study aimed to investigate the immunometabolic mechanism by which treadmill exercise alleviate choline-deficient L-amino acid-defined high-fat diet (CDAHFD)-induced MASLD in mice. Experimental mice were randomly assigned to a sedentary control group (Sed) and a treadmill exercise group (ExT) with a 3-week intervention period. By combining intravital liver window confocal imaging, histological staining, in vivo photoacoustic imaging and ex vivo quantitative detection, we systematically evaluated hepatic lipid accumulation and liver morphological characteristics in mice, and verified that exercise could effectively relieve liver pathological injuries caused by MASLD.

In conclusion, treadmill exercise can reverse diverse pathological phenotypes of MASLD via regulating hepatic lipid metabolism. Future research will further elucidate the cross-regulatory axis of exercise-immunity-metabolism to identify novel therapeutic targets and intervention regimens for MASLD.

[IP-12] PIBM2026-0629-4

A Systematic Integration Framework for Liver Single-Cell and Spatial Data Analysis

Shuwen Chen[1],Qi Pan[1], Zhihong Zhang[1,*]

[1]School of Life and Health Sciences, Hainan Province Key Laboratory of One Health, Collaborative Innovation Center of One Health, Hainan University, Haikou,Hainan 570228, China

Corresponding author e-mail address: zhzhang@hainanu.edu.cn

Abstract: The rapid growth of single-cell transcriptomic, and spatial transcriptomic datasets has substantially advanced investigations of liver biology. However, heterogeneity in data sources, experimental protocols, and analytical workflows limit standardized cross-modality integration and hinder systematic characterization of liver cellular heterogeneity.

In this study, targeting the construction of a comprehensive single-cell multi-omics deeply integrated database for the liver as the long-term goal, we focus on the integration of two core modalities: single-cell transcriptomics and spatial transcriptomics, and tackle key technical challenges in the integration process. We systematically curated publicly available liver datasets from multiple species, developmental stages, physiological conditions, and disease states. A standardized preprocessing workflow, including quality control, normalization, dimensionality reduction, clustering, and cell type annotation, was applied to generate cross-modality integrated datasets for downstream analyses. Using these processed datasets, we constructed an integrated liver cell atlas and implemented an interactive web interface for data visualization and exploration.

The database enables users to visualize clustering results and major cell populations, compare cellular

composition across biological conditions, and explore integrated transcriptomic, and spatial datasets within a unified framework. These functions provide an accessible resource for investigating liver cellular heterogeneity across diverse biological contexts.

In summary, this work presents a standardized integration pipeline for single-cell transcriptomic and spatial transcriptomic data, together with a preliminary web-based data resource and an integrated liver cell atlas. This resource facilitates data exploration and cell-type annotation, thereby providing a valuable foundation for future studies of liver homeostasis, development, and disease.

[IP-13] PIBM2026-0630-1

Early evaluation of hepatocellular carcinoma and liver metastasis of melanoma by multi-functional photoacoustic imaging

Yifan Guo[1], Yanfeng Dai[1,*]

[1]School of Life and Health Sciences, Hainan Province Key Laboratory of One Health, Collaborative Innovation Center of One Health, Hainan University, Haikou, Hainan 570228, China

Corresponding author e-mail address: 182005@hainanu.edu.cn

Abstract: Early diagnosis and treatment of liver tumors pose great challenges to traditional imaging techniques. Photoacoustic imaging combines the high contrast of optics with the deep penetration advantage of ultrasound, enabling non-invasive, high-resolution and high-contrast imaging, making it a powerful tool for deciphering the structural and functional information of liver tumors. Accordingly, this study intends to establish a melanoma liver metastasis model and an orthotopic liver cancer model expressing photoacoustic proteins, to achieve non-invasive early identification of liver tumors and targeted immunotherapy via photoacoustic tomography.

Our results demonstrate that, relying on the intrinsic characteristics of melanoma, photoacoustic imaging can detect hepatic metastatic tumor lesions as small as approximately 0.3 mm without exogenous contrast agents, accompanied by increased vascular density and lower oxygen saturation than normal liver tissue. In mouse models of liver cancer transfected with photoacoustic proteins, photoacoustic imaging can clearly distinguish tumors from surrounding normal tissues.

Moreover, the developed melittin nanoparticles can significantly inhibit liver tumor growth after tail vein injection. This study analyzes parameters such as vascular density and blood oxygen saturation of the two types of tumors at different growth stages through photoacoustic imaging, and achieves integrated diagnosis and treatment combined with melittin-based nanomedicine. This research provides a novel strategy for the early evaluation of liver tumors, and holds important theoretical value and application prospects for improving the diagnosis and treatment of liver tumors.

Analytical Biophotonics

[AP-1] PIBM2026-0401-4

TCPP-loaded DNA nanospheres with electrocatalytic amplification: a microfluidic electrochemiluminescence sensor for rapid multibacterial detection

Chengli Zhang[1,2,3], Xiaolong Guo[4], Judun Zheng[2], Yi Feng[2], Wenjie Wu[1], Lunjing Liu[1], Jiang Xiao[1], Qingxian Li[3], Huiyi Yang[2], Jingru Wang[3], Jiajian Zhou[2]*, Yu Fu[1]*, Yuhui Liao[1,2,3]*

[1] Ningxia Medical University, Yinchuan 750004, P.R.China.

[2] Dermatology Hospital, Southern Medical University, Guangzhou 510091, P.R.China.

[3] Institute for Engineering Medicine, Kunming Medical University, Kunming 650500, P.R.China.

[4] Department of Laboratory Medicine, Zigong Fourth People ' s Hospital, Zigong 643000, P.R.China.

Corresponding author e-mail address: Email: liaoyh8@mail.sysu.edu.cn (Y.L.); hellfuyu@163.com (Y.F.); zhoujj2013@gmail.com (J.Z.).

Abstract: Rapid detection of multiple bacterial pathogens is essential for timely diagnosis and effective treatment of bacterial infections. Herein, we present a homogeneous electrochemiluminescence (ECL) microfluidic array for the synchronous detection of four bacterial pathogens: *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Klebsiella pneumonia*e, and *Pseudomonas aeruginosa*. The sensor is constructed from self-assembled DNA helical nanospheres loaded with tetrakis (4-carboxyphenyl) porphyrin (TCPP) as the ECL luminophore. In this "off-on" design, bacterial aptamers function as interlocking chains that maintain the nanosphere in a closed state. Upon specific recognition of target bacteria, the aptamers undergo conformational changes, triggering the opening of the nanosphere and the release of TCPP, which generates an enhanced ECL signal. Signal amplification is achieved by incorporating ceria nanoparticles (NanoCe), which leverage the Ce^{4+}/Ce^{3+} redox pair to promote electron transfer in the $S_2O_8^{2-}$—TCPP ECL system via electrocatalytic reactions, significantly improving sensitivity with a detection limit of $\leqslant$ 100 CFU/mL. Integrated with a microfluidic chip that preloads the four bacterial diagnostic reagents, the system enables simultaneous multibacterial detection within 45 min without the need for complex operations. Importantly, the ECL microfluidic array accurately quantified bacterial loads in clinical samples—including urine, blood, pleural fluid, and abdominal fluid—demonstrating 100% concordance with digital PCR results. This approach offers a rapid, user-friendly, and cost-effective diagnostic platform with strong potential for point-of-care applications in clinical settings.

[AP-2] PIBM2026-0402-4

Robust On-Axis Quantitative Phase Imaging via Stochastic Phase-shifting

Tao Yuan[1,3,4,5], Yachao Zhang[1,2,3,4,5]

[1]The Suzhou Institute of Biomedical Engineering and Technology, Chinese Academy of Sciences, Suzhou 215163, China

[2]The School of Biomedical Engineering (Suzhou), Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230026, China

[3]Jiangsu Key Laboratory for Advanced Theranostics and Medical Instrumentation, Suzhou 215163, China

[4]Key Laboratory of Biomedical Imaging Science and System, Chinese Academy of Sciences, Suzhou 215163, China 5State Key Laboratory of Biomedical Imaging Science and System, Suzhou 215163, China

Corresponding author e-mail address: (yuant@sibet.ac.cn; zhangyachao@sibet.ac.cn)

Abstract: Quantitative phase imaging (QPI) is vital for measuring cellular dry mass and dynamics without invasive staining, yet current technologies face a fundamental trade-off between spatial resolution and environmental stability. Off-axis interferometry suffers from lateral-resolution loss due to necessary Fourier-domain filtering, whereas on-axis approaches preserve optical bandwidth but remain highly sensitive to mechanical vibrations and thermal drift. Conventional solutions typically require complex stabilization systems that hinder the imaging speed or modify the Fourier plane of the optical system that introduces Halo artifact.

Here, we present stochastic phase-shifting microscopy (SPSM), a robust on-axis QPI modality designed specifically for vibration-prone environments. SPSM utilizes a balanced-path Mach-Zehnder interferometer with a spatially modulated spherical reference wave. Unlike conventional methods that treat random phase perturbations as noise to be suppressed, SPSM harnesses these stochastic shifts via a unique self-phase-registration strategy. This transforms a temporally disordered interferogram stack into a deterministic sequence through pointwise projection, eliminating the need for spatial-frequency filtering and retaining the system's full spatial bandwidth for sub-micrometre visualization.

Analytical modeling demonstrates that this process reduces vibration-induced noise by up to two orders of magnitude relative to the signal level for Gaussian-distributed random phase shifts. Experimentally, SPSM achieved nanometre-scale height measurements with 97.8%

accuracy relative to atomic force microscopy (AFM), even under uncontrolled perturbations exceeding 1 μm. Validation on yeast cells revealed sub-diffraction capabilities, resolving intracellular structures separated by only 135 nm. By eliminating the resolution-stability compromise, SPSM provides a practical framework for high-precision QPI in non-ideal laboratory settings. We conclude that SPSM paves the way for widespread adoption of high-resolution phase imaging outside specialized isolation rooms, facilitating reliable biophysical measurements without expensive infrastructure or active feedback loops. Consequently, this approach allows for the investigation of subtle biophysical processes that were previously inaccessible in standard optical setups.

[AP-3] PIBM2026-0402-6

Fluorescence Lifetime Imaging Based on Pulsed Interleaved Excitation

Huimin Jiang[1], Lixin Liu[1]*, Haoyang Yang[1], Jing Lu[1] and Peng Gao[2]

[1]School of Optoelectronic Engineering, Xidian University, Xi'an 710071, China

[2] School of Physics, Xidian University, Xi'an 710071, China

** Corresponding author e-mail address: lxliu@xidian.edu.cn*

Abstract: Fluorescence lifetime imaging microscopy (FLIM) provides quantitative information about the microenvironment of biological samples and has been widely applied in cell biology and medical diagnostics. The integration of time-correlated single photon counting (TCSPC) with laser scanning confocal microscopy (LSCM) enables high resolution fluorescence lifetime imaging. However, fluorescence detection often suffers from spectral crosstalk due to the coexistence of multiple fluorescent signals, which can compromise measurement accuracy. To address this limitation, we present a pulsed interleaved excitation (PIE)-based fluorescence lifetime imaging (PIE-FLIM) method for crosstalk-free dual channel fluorescence imaging. Using this approach, we successfully acquired and analyzed fluorescence lifetime data from dual-color fluorescent beads and COS7 cells, effectively eliminating inter-channel spectral crosstalk. Furthermore, we applied PIE-FLIM to monitor fluorescence lifetime changes in live COS7 cells at different physiological stages. Our results demonstrate that this method not only enables the discrimination of cellular states but also detects physiological alterations earlier than conventional morphology-based assessments. Therefore, this study provides a valuable approach for distinguishing apoptosis from necrosis at an early stage, which could significantly benefit mechanistic studies of disease and the development of therapeutic interventions.

[AP-4] PIBM2026-0403-7

Non-contact measurement of zebrafish heart rate based on video motion amplification and hybrid tracking

Jian Zou[1,*], Shufeng Zhuo[1], Kaihong Chen[1], Jingyi Zheng[1], and Zhifang Li[1,2]

[1]The Internet of Things and Artificial Intelligence College, Fujian Polytechnic of Information Technology, Fuzhou, Fujian, China

[2]Key Laboratory of Optoelectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, Fujian Provincial Engineering Technology Research Center of Photoelectric Sensing Application, College of Photonic and Electronic Engineering, Fujian Normal University, Fuzhou, Fujian, China

Corresponding author e-mail address: zoujian@fjpit.edu.cn

Abstract: Traditional methods for zebrafish heart rate measurement, such as electrocardiography and high-frequency ultrasound, suffer from several limitations including high invasiveness, physiological interference induced by anesthesia, operational complexity, and high cost. Moreover, these techniques are inadequate for assessing cardiac function under natural physiological conditions. To address these challenges, this paper proposes a non-contact method for zebrafish heart rate measurement based on video motion amplification and a hybrid tracking algorithm. The proposed method employs adaptive ROI tracking to precisely localize the cardiac region, followed by Gaussian pyramid decomposition and temporal bandpass filtering to extract subtle heartbeat-induced vibrations. Linear amplification of these signals enables visualization of pulse wave dynamics and accurate heart rate calculation. Experimental results demonstrate that this method enables high-precision heart rate measurement under natural physiological conditions without the need for anesthesia or physical contact, significantly reducing experimental interference and equipment cost. Furthermore, a

zebrafish temperature-heart rate response model is established based on this system, enabling quantitative analysis of arrhythmic characteristics induced by acute temperature changes. This approach provides a non-invasive phenotypic analysis tool for cardiac disease mechanism studies and drug-induced cardiotoxicity screening.

[AP-5] PIBM2026-0403-9

Multifocal structured illumination microscopy for arbitrary curved surfaces

Xinqi Mo, Danying Lin*, Bin Yu, and Junle Qu

Key Laboratory of Optoelectronic Devices and Systems of Ministry of Education and Guangdong Province, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen 518060, China

Corresponding author e-mail address: dylin@szu.edu.cn

Abstract: Super-resolution fluorescence microscopy has made rapid progress in recent years, becoming an indispensable tool for sub-cellular high-resolution imaging. Among various super-resolution techniques, multifocal structured illumination microscopy (MSIM) has emerged as a crucial instrument for biological dynamics observation due to its excellent optical sectioning capability and high resolution. However, traditional MSIM systems are limited by a finite depth of field. This inherent physical constraint necessitates time-consuming layer-by-layer scanning across a broad axial range when imaging samples with naturally curved surfaces, resulting in inefficient data acquisition that wastes significant time on non-target out-of-focus regions. To overcome this challenge, we have built upon our previously developed three-dimensional addressable scanning MSIM (3D AS-MSIM)—which utilizes an electrically tunable lens (ETL) and acousto-optic deflectors (AODs)—by incorporating a focal plane detection algorithm to acquire the 3D profile of the sample. Leveraging the high flexibility of 3D AS-MSIM, this approach enables scanning exclusively within the in-focus regions at different axial depths, effectively eliminating out-of-focus background and achieving efficient super-resolution all-in-focus reconstruction of complex curved surfaces. We anticipate that this technology will provide powerful technical support for the dynamic observation of biological structures with complex curved geometries.

[AP-6] PIBM2026-0403-10

NIR-II multifocal structured illumination microscopy with background suppression for deep-tissue super-resolution imaging

Yiwen He, Chenshuang Zhang*, Junle Qu, Bin Yu, and Danying Lin*

Key Laboratory of Optoelectronic Devices and Systems of Ministry of Education and Guangdong Province, College of Physics and Optoelectronic Engineering, Shenzhen University; Shenzhen, 518060, China

Corresponding author e-mail addresses: zhangcs@szu.edu.cn; dylin@szu.edu.cn

Abstract: Achieving high-resolution imaging in deep biological tissues remains challenging primarily due to the strong out-of-focus background and scattering-induced signal degradation. Although multifocal structured illumination microscopy in the second near-infrared window (NIR-II MSIM) improves penetration depth and realizes twofold spatial resolution enhancement, its imaging performance is still limited by the accumulated background fluorescence, which reduces image contrast and fidelity. Here, we present a background-suppressed NIR-II MSIM approach that integrates structured illumination technology with a single-frame computational enhancement strategy. By combining optimized multi-focal excitation patterns with targeted

suppression of defocused signals, the proposed method effectively mitigates the out-of-focus background while preserving the weak in-focus features of the sample. Experimental results demonstrate that this approach significantly improves image contrast and structural clarity in deep-tissue imaging scenarios. This work provides a robust and efficient solution for the super-resolution observation of deep biological structures without relying on deep learning algorithms, holding great potential for applications in deep-tissue biological imaging research.

[AP-7] PIBM2026-0403-11

High-spatiotemporal-resolution Interferometric Scattering Microscopy via Multifocal Structured Illumination

Ziming Huang[1], Hongying Chang[2],Guangpeng Ma[1], Hongwei Mi[2], Huiqun Cao[2], Danying Lin[1], Junle Qu[1] and Bin Yu[1,*]

[1]Key Laboratory of Optoelectronic Devices and Systems of Ministry of Education and Guangdong Province, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen 518060, China

[2]College of Chemistry and Environmental Engineering, Shenzhen University, Shenzhen 518060, China

Corresponding author e-mail address: yubin@szu.edu.cn

Abstract: While fluorescence microscopy has advanced nanoscale observation, it is constrained by labeling artifacts, photobleaching, and signal saturation. Interferometric scattering (iSCAT) microscopy offers a highly sensitive, label-free alternative; however, traditional point-scanning methods restrict spatiotemporal resolution. To address these challenges, this study proposes a novel imaging technique integrating multifocal structured illumination microscopy (MSIM) with iSCAT. This method utilizes a point array to excite sample scattering signals, effectively reducing ghosting artifacts caused by optical component reflections. By applying digital pinholes and pixel reassignment algorithms, the proposed system enables label-free, high-resolution, and long-time imaging. We have successfully constructed the MSIM-iSCAT system and conducted preliminary validation on lithium battery cathodes (LCO particles), verifying its reliability against scanning electron microscopy (SEM) references. The major conclusion of this research is that the MSIM-iSCAT approach provides a robust platform for real-time, nanoscale observation across diverse fields. The system is highly applicable for both the *in situ* electrochemical analysis of dynamic ion transport during battery charge-discharge processes and the three-dimensional tracking of nanoscale dynamics within living cells.

[AP-8] PIBM2026-0403-12

Raman Imaging Analysis of Shuang-Huang-Lian-Induced Immuno-metabolic Modulation and Cell Cycle Arrest in Macrophages

Mengjie Wang[1,2], Rui Wang[1,2], Dongjie Zhang[1,2,3,4], Lin Shi[1,2,3,4], Nan Wang[*1,2,3,4], Qi Zeng[*1,2,3,4], and Xueli Chen[1,2,3,4]

[1] Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[2] Xi ' an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[3] Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China.

[4] State Key Laboratory of Electromechanical Integrated Manufacturing of High-Performance Electronic Equipment, Xidian University, Xi ' an, Shaanxi 710071, China.

Corresponding author e-mail address: wangnan@xidian.edu.cn; qzeng@xidian.edu.cn

Abstract: Stimulated Raman scattering (SRS) microscopy is a label-free imaging technique with high chemical specificity. It has great potential for studying metabolic features in immune cells. In this study, SRS imaging was utilized to investigate the effects of Shuang-Huang-Lian (SHL) on the immune-metabolic characteristics of RAW264.7 macrophages. Biochemical assays and network pharmacology analysis were also performed to evaluate its phenotypic effects. SRS imaging showed that lipopolysaccharide (LPS) could induce macrophage polarization (M1). This was characterized by overexpressed saturated lipid content and abnormal cell morphology. In contrast, SHL did not induce inflammatory stimulation in non-polarized macrophages. No obvious pro-inflammatory metabolic reprogramming was observed. However, high concentrations SHL might alter the relative composition or spatial distribution of DNA and proteins in nuclear-associated regions. Further analysis showed that LPS significantly increased nitric oxide (NO) production ($P < 0.01$), as well as increased superoxide dismutase (SOD) activity ($P < 0.01$). In comparison, SHL did not significantly affect NO levels. And in SHL treated group, SOD activity remained close to that of the control group. These results suggested that SHL could maintain the redox homeostasis of immune cell.. Network pharmacology analysis showed that SHL treatment was enriched in pathways related to the cell cycle, lipid metabolism, and inflammation. These findings were consistent with the lipid changes and nuclear DNA/protein alterations observed by SRS imaging. Overall, the activity of SHL were mainly associated with regulation of the cell cycle and maintenance of metabolic and redox homeostasis. This study provided a metabolic imaging perspective for understanding the effects of traditional Chinese medicine on macrophage function.

[AP-9] PIBM2026-0403-14

Ribosome Affinity Carbon Dots for Live-Cell Imaging of Endoplasmic Reticulum

Jin-Xuan Fan*, Yuan-Di Zhao*

Huazhong University of Science and Technology, Wuhan 430074, Hubei, P. R. China

Corresponding author e-mail address: jxfan@hust.edu.cn

Abstract: The fluorescence imaging of ribosome-endoplasmic reticulum (ER) system is commonly by the complex intracellular environment and the non-specificity of ER receptors. Therefore, the development of novel targeting strategy is necessary to enhance the efficiency and precision of fluorescence dyes delivery to ribosome-ER system. In cell, ribosomes are dynamically binding with the ER and are present in considerable

numbers and distributed throughout the cell. Therefore, a strategy was designed to achieve ER fluorescence delivery by employing ribosomes as intracellular carries. Levofloxacin, which has low toxicity to eukaryotic cell was selected as ribosome anchoring moiety, and without interfering ribosome function. The surface-modified levofloxacin LT-CDs was synthesized for active target to the ER in the process of cell translation. The cell experiments shown that the LT-CDs have well biocompatibility, and effectively localized in the ER. This strategy provides a new hitchhiking idea for the labeling of organelles with subcellular structures and promotes further studies targeting organelles such as the endoplasmic reticulum-ribosome.

[AP-10] PIBM2026-0404-4

Quantitative analysis of maltodextrin adulteration in food additive ingredients based on Raman spectroscopy and machine learning

Shuo Huang[1,2,#], Youzhi Cao[1,2,#], Xudong Zhou[1,2], Zexian Zhao[1,2], Dongjie Zhang[1,2,3,4], Lin Shi*[1,2,3,4], Nan Wang[1,2,3,4], Qi Zeng*[1,2,3,4], Xueli Chen[1,2,3,4]

[1] Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[2] Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.

[3] Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China.

[4] State Key Laboratory of Electromechanical Integrated Manufacturing of High-Performance Electronic Equipment, Xidian University, Xi'an, Shaanxi 710071, China.

** Corresponding author e-mail address:shilin@xidian.edu.cn(Lin Shi);qzeng@xidian.edu.cn(Qi Zeng)*

Abstract: Maltodextrin is frequently applied as an illicit additive ingredient in high-value polysaccharide extracts to minimize production costs. As its structural homology to natural polysaccharides, conventional analytical assays often lack the specificity required for accurately detection. To address this problem, this study established a rapid, non-destructive quantitative method based on Raman spectroscopy combined with machine learning. Different concentrations of maltodextrin samples were prepared in solid and liquid forms by diluting with starch and water. 785 nm Raman spectroscopy was used to acquire the Raman spectra. Raw spectral data were optimization processed through featuring wavelet transform denoising, Savitzky-Golay smoothing, and adaptive iteratively reweighted penalized least squares (airPLS). The quantitative analytical models were established by four regression algorithms: Principal Component Regression (PCR), Partial Least Squares Regression (PLSR), Support Vector Regression (SVR), and a Convolutional Neural Network (CNN). And the predictive performance of these models was evaluated utilizing the coefficient of determination (R^2) and root mean square error (RMSE). For liquid samples, PLSR showed optimal predictive accuracy(R^2= 0.982, RMSE= 0.0378). In contrast, non-linear algorithms proved highly adept at modeling the strong signal scattering inherent to solid samples. Notably, the CNN model achieved the highest prognostic accuracy for solid mixtures (R^2 = 0.998, RMSE = 0.0073), closely followed by SVR (R^2 = 0.993, RMSE = 0.0192). The results demonstrated that Raman spectroscopy combined with machine learning architectures could achieve a highly sensitive and robust analytical paradigm for the rapid on-site screening and quantification of maltodextrin adulterants in food safety field.

[AP-11] PIBM2026-0405-3

Aspirin-Amide-Piperazine-Substituted Silicon Phthalocyanine for Dual Organelle-Targeted Photodynamic Therapy and Fluorescence Imaging

Hongshuo Liang[1],Weiqi Pan[1],Kuizhi Chen[2],Jianling Chen[1*],Yiru Peng[2*]

[1]Key Laboratory of Optoelectronic Science and Technology for Medicine of Ministry of Education, Provincial Key Laboratory for Photonics Technology, Institute of Laser and Optoelectronics Technology, Fujian Normal University, Fuzhou, China

[2]Fujian Provincial Key Laboratory of Advanced Materials Oriented Chemical Engineering, College of Chemistry and Materials, Fujian Normal University, Fuzhou, China

Corresponding authors e-mail addresses: jlchen@fjnu.edu.cn(J.Chen), yirupeng@fjnu.edu.cn(Y.Peng)

Abstract: Developing highly efficient photosensitizers with specific organelle-targeting capabilities is critical for improving the efficacy of tumor photodynamic therapy (PDT). Herein, an aspirin-amide-piperazine-substituted silicon phthalocyanine (Asa-PIP-SiPc) was rationally designed and synthesized for targeted fluorescence imaging and precise tumor therapy. Confocal fluorescence imaging demonstrated that Asa-PIP-SiPc exhibits efficient cellular internalization, with rapid uptake observed within 30 min at a concentration of 4 μM, along with a clear time-dependent uptake behavior. Colocalization studies further confirmed its dual-targeting capability toward lysosomes and the endoplasmic reticulum (ER), with Pearson's correlation coefficients of 0.80 and 0.74, respectively. Cytotoxicity assays revealed negligible dark toxicity, indicating favorable biocompatibility, while significant phototoxicity was observed upon irradiation, with a half-maximal inhibitory concentration (IC50) of approximately 200.12 nM. Flow cytometry analysis further demonstrated that low-dose Asa-PIP-SiPc (0.3 μM) induced substantial cell death under light irradiation, resulting in 55.59% apoptosis and 12.65% necrosis. Overall, these results highlight Asa-PIP-SiPc as an efficient dual-organelle-targeting photosensitizer for lysosomes and the ER, showing strong potential for synergistic imaging and targeted PDT, and offering promising prospects for precise tumor theranostics.

Keywords: Silicon phthalocyanine; Photodynamic therapy (PDT); Dual organelle targeting; Lysosome; Endoplasmic reticulum

[AP-12] PIBM2026-0405-6

A compact PSPR biosensing platform with multidimensional Stokes-parameter enhancement for biomolecular detection

Shuohong Weng[1], Yuanyang Xie[2] and Duo Lin[1*]

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou 350117, China

[2]Department of Physics and London Centre for Nanotechnology, King ' s College London, London, WS2R 2LS, UK

Corresponding author e-mail address: duo@fjnu.edu.cn

Abstract: Traditional surface plasmon resonance (SPR)-based optical biosensors have become essential analytical tools in life science and pharmaceutical research; however, they still suffer from limitations in detection dimensionality and sensitivity. To address these issues, we developed a compact propagating surface plasmon resonance (PSPR) sensing platform based on a self-assembled optical setup. A Kretschmann configuration was employed as the excitation structure, enabling flexible switching between intensity-interrogation and angle-interrogation modes. Combined with electromagnetic simulations, key parameters

including gold film thickness, incident angle, and excitation wavelength were systematically optimized to enhance refractive-index sensing performance. Furthermore, a Stokes-parameter-based polarization analysis module was introduced into the SPR system. By integrating a quarter-wave plate and a polarizer in the detection path, multidimensional information of the reflected light, including intensity and polarization states, was extracted. This strategy provides richer sensing parameters for chiral or polarization-sensitive analytes, thereby improving both detection resolution and sensitivity. The proposed PSPR sensing system has been successfully applied to antigen-antibody recognition and complementary nucleic acid hybridization detection, demonstrating promising potential for advanced biosensing applications.

[AP-13] PIBM2026-0405-11

Development of photo-induced pyroelectric-coupled SERS technology and its application in nasopharyngeal carcinoma subtyping

Yangmin Wu [1], Yanli Huang [1] and Duo Lin [*]

[1] Key Laboratory of OptoElectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou 350117, China.

Corresponding author e-mail address: duo@fjnu.edu.cn

Abstract: Owing to its ultrasensitivity and noninvasive nature, surface-enhanced Raman scattering (SERS)-based liquid biopsy has emerged as a promising optical strategy for early cancer screening. In particular, it offers a potential solution to the limitations of conventional screening methods for nasopharyngeal carcinoma (NPC) and provides a novel approach for noninvasive NPC screening and subtype classification. In this study, we developed a tunable $Ba(Ti_{0.89}Sn_{0.11})O_3$@Au pyroelectric-coupled SERS sensing chip. The chip generates a photothermally induced in situ pyroelectric field that promotes charge transfer within the system, thereby enhancing SERS performance. Experimental results showed that the signal intensity of the pyroelectric-coupled SERS chip was 60% higher than that of a pure pyroelectric SERS chip ($BaTiO_3$@Au) and 129% higher than that of a non-pyroelectric SERS chip (SiO_2@Au). Furthermore, by combining exosome SERS data with a multilayer perceptron (MLP) algorithm, the proposed platform effectively distinguished NPC patients from healthy controls and further discriminated among three NPC subtypes. These findings demonstrate the potential of pyroelectric-coupled SERS technology for noninvasive early NPC screening and subtype classification, providing a promising basis for future clinical translation.

[AP-14] PIBM2026-0405-13

An electrothermal MEMS micromirror-based and microrotating motor-based capsule OCT endoscope probe

Chenyang Zhou [1,2], Huikai Xie [1,2,*], Qian Chen [1,2,*]

[1]School of Integrated Circuits and Electronics, Beijing Institute of Technology, Beijing 100081,

[2]Chongqing Institute of Microelectronics and Microsystems, Beijing Institute of Technology, Chongqing 400000, China

**Corresponding authors: Huikai Xie (xiehuikai@bit.edu.cn), Qian Chen (chenqian8881229@163.com)*

Abstract: Optical scanning over a wide field-of-view (FOV) is essential for the diagnosis of luminal organ diseases, such as in gastroenterology. However, although traditional optical scanning approaches based on proximal mechanical actuators or micro motors enable circumferential endoscopic imaging, they still

suffer from motor noise and motion artifacts and cannot achieve precise three-dimensional imaging at a locally fixed position. Here, we developed a capsule OCT endoscope probe integrating a miniaturized electrothermal MEMS mirror and a micro motor for circumferential imaging, with a lateral resolution of about 25 μm and an axial resolution of about 5.50 μm. Within the probe, the MEMS micromirror performs a about 4 mm longitudinal linear scan, while the micro motor performs a rotational scan with a working distance of about 7 mm, generating a large FOV. The device achieves simultaneous circumferential and longitudinal scanning by combining the MEMS micromirror with the micro motor, featuring advantages of fast, wide-range, and flexible scanning imaging. This approach provides a compact, reliable solution for high-resolution circumferential scanning in endoscopic imaging, with potential applications in gastroenterology and other clinical domains that demand precise intraluminal assessment.

[AP-15] PIBM2026-0405-14

Fluoreneacetic Acid-Conjugated Silicon Phthalocyanine for Enhanced Cellular Uptake and Photodynamic Therapy in Pancreatic Cancer

Weiqi Pan[1],Hongshuo Liang[1],Kuizhi Chen[2],Jianling Chen[1*],Yiru Peng[2*]

[1]Key Laboratory of Optoelectronic Science and Technology for Medicine of Ministry of Education, Provincial Key Laboratory for Photonics Technology, Institute of Laser and Optoelectronics Technology, Fujian Normal University, Fuzhou, China

[2]Fujian Provincial Key Laboratory of Advanced Materials Oriented Chemical Engineering, College of Chemistry and Materials, Fujian Normal University, Fuzhou, China

Corresponding authors e-mail addresses: jlchen@fjnu.edu.cn(J.Chen), yirupeng@fjnu.edu.cn(Y.Peng)

Abstract: Developing novel photosensitizers with efficient cellular uptake and enhanced photodynamic therapy (PDT) efficacy is of great importance for the precise treatment of pancreatic cancer. In this study, a fluoreneacetic acid-conjugated silicon phthalocyanine (Caa-PIP-SiPc) was rationally designed and synthesized. In vitro confocal fluorescence imaging demonstrated that Caa-PIP-SiPc exhibited pronounced concentration- and time-dependent cellular uptake in BxPC-3 pancreatic cancer cells, with stable intracellular retention lasting up to 72h. Cytotoxicity assays revealed negligible dark toxicity, indicating favorable biocompatibility. In contrast, upon laser irradiation, Caa-PIP-SiPc showed significant phototoxicity toward BxPC-3 cells, with a half-maximal inhibitory concentration (IC_{50}) of approximately 268nM. Overall, these results highlight Caa-PIP-SiPc as a promising theranostic agent for integrated fluorescence imaging and photodynamic therapy, and provide valuable insights into the rational design of next-generation antitumor photosensitizers.

Keywords: Silicon phthalocyanine; Photodynamic therapy (PDT); Pancreatic cancer; Cellular uptake

[AP-16] PIBM2026-0405-15

Vision-driven optofluidics enables deterministic sample preparation for single-cell proteomics

Zonghao Li[1], Shuailong Zhang1, and Rongxin Fu[3]

[1] State Key Laboratory of Chips and Systems for Advanced Light Field Display, School of Integrated Circuits and Electronics, Beijing Institute of Technology, Beijing, 100081, China

[2] School of Medical Technology, Beijing Institute of Technology, Beijing, 100081, China

Corresponding author e-mail address: furongxin@bit.edu.cn

Abstract: Single-cell mass spectrometry (scMS) provides direct readouts of cellular phenotypes, but its sample preparation faces a fundamental technological dichotomy. Conventional continuous-flow microfluidics suffers from probabilistic Poisson loading, yielding mostly empty droplets, while precise robotic spatial arrays are hindered by low-throughput, serial processing bottlenecks. To overcome these limitations, we developed a vision-intelligence-driven optofluidic platform that operates as an array of spatiotemporally programmable microreactors for deterministic single-cell proteomics. This closed-loop system synergizes picoliter droplet compartmentalization, optoelectrowetting (OEW) digital microfluidics, and real-time deep learning. Operating on an open, unstructured photoconductive surface, the platform employs dynamic light patterns to actively route, sort, and merge sub-nanoliter droplets in massive parallel. Guided by a YOLO-based visual intelligence engine, the system achieves real-time, identity-driven sorting with >98% accuracy, enriching the purity of single-cell droplets in the working array to >95%. Furthermore, a Conflict-Based Search (CBS) path-planning algorithm ensures the collision-free spatiotemporal routing of hundreds of microreactors. We utilized this deterministic platform to perform automated, sequential on-chip cell lysis and enzymatic digestion within individual 524 pL droplets. Compared to conventional 1 µL in-tube protocols, this extreme spatial confinement accelerates reaction kinetics and drastically minimizes non-specific surface adsorption. Subsequent scMS analysis of these processed microreactors yielded high-fidelity, highly reproducible proteomic signatures, enabling the accurate machine-learning-based classification of distinct cell lines (HeLa, Jurkat, and HL-60). By seamlessly merging artificial intelligence with digital droplet microfluidics, this platform bridges the gap between high-throughput processing and programmable precision, establishing a highly scalable and robust front-end solution for advanced single-cell discovery.

[AP-17] PIBM2026-0405-21

Two-Photon Fluorescence Imaging of Gold Nanobipyramids for *In Vivo* Glioma Detection

Zhaoyi Li[1,2], Zhaoyang Cheng[1,2], Dongjie Zhang[1,2,3,*], and Xueli Chen[1,2,3,*]

[1] Center for Biomedical-photonics and Molecular Imaging, Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[2] Engineering Research Center of Molecular and Neuro Imaging, Ministry of Education & Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China

[3] Inovation Center for Advanced Medical Imaging and Intelligent Medicine, Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China

Corresponding author e-mail address: zhangdongjie@xidian.edu.cn; xlchen@xidian.edu.cn

Abstract: Gold nanoparticles have emerged as efficient multimodal bioimaging contrast agents due to their excellent biocompatibility, tunable localized surface plasmon resonance (LSPR) properties, and strong nonlinear optical responses. In this work, we investigate the application of two-photon fluorescence from gold nanobipyramids (AuBPs) for brain glioma imaging under femtosecond laser excitation. The polyethylene glycol-functionalized AuBPs exhibit high chemical and optical stability, enabling their use as two-photon nanoprobes for in vivo glioma imaging in live animals. We find that precisely tuning the size and morphology of AuBPs to match their LSPR absorption peak with the near-infrared excitation wavelength significantly enhances the two-photon fluorescence emission efficiency. After intravenous injection, the PEGylated AuBPs are delivered through systemic circulation to the brain glioma region, allowing the identification of abnormal tumor vasculature. Under 1035 nm femtosecond laser excitation, the AuBPs-PEG probes are used for deep imaging in an orthotopic mouse model of brain glioma. By systematically investigating the two-photon fluorescence signal across the 500-800nm emission band, we observe that the probes exhibit the strongest two-photon fluorescence emission at 747nm, effectively avoiding the biological autofluorescence window. This property significantly improves the imaging signal-to-noise ratio and imaging depth, enabling high-contrast identification and precise localization of the tumor region.

Keywords: Gold nanobipyramids, Two-photon fluorescence, Deep *in vivo* imaging, Tumor tissue

[AP-18] PIBM2026-0406-2

Super-broadband stimulated Raman scattering spectroscopy and imaging

Jin Guo [1†], Qiaozhi Yu [1†], Jiakai Wang [1†], Wenhao Yu [1], Zhuowen Wang [1] and Hanqing Xiong [1*]

[1] National Biomedical Imaging Center, College of Future Technology, Peking University, Beijing 100871, China

Corresponding author e-mail address: xiong.hanqing@pku.edu.cn; wenzhesi@bjmu.edu.cn.

Abstract: Spontaneous Raman scattering is widely used in biology and medicine, but it suffers from slow acquisition speed and fluorescence interference. Here we present super-broadband stimulated Raman scattering (SuperB-SRS), a time-domain technique that overcomes these limitations. By encoding Raman free induction decays into stimulated Raman loss via few-cycle laser-induced quantum interference, SuperB-SRS measures signals in the time domain rather than the frequency domain. This approach delivers Raman spectra identical to state-of-the-art spontaneous Raman over a thousand-wavenumber range, while being more than 100 times faster and naturally supporting simultaneous fluorescence detection. We demonstrate >100-fold

speed gain over spontaneous Raman for imaging biological tissue samples. With high spectral fidelity, natural-linewidth-limited resolution, broad bandwidth, and high sensitivity, SuperB-SRS provides a practical and powerful tool for high-speed Raman imaging in biomedical research.

[AP-19] PIBM2026-0406-3

Time-domain super-broadband stimulated Raman scattering spectroscopy and imaging

Jin Guo [1†], Qiaozhi Yu [1†], Jiakai Wang [1†], Wenhao Yu [1], Zhuowen Wang [1] and Hanqing Xiong [1*]

[1] National Biomedical Imaging Center, College of Future Technology, Peking University, Beijing 100871, China

Corresponding author e-mail address: xiong.hanqing@pku.edu.cn; wenzhesi@bjmu.edu.cn.

Abstract: Spontaneous Raman scattering is widely used in biology and medicine, but it suffers from slow acquisition speed and fluorescence interference. Here we present super-broadband stimulated Raman scattering (SuperB-SRS), a time-domain technique that overcomes these limitations. By encoding Raman free induction decays into stimulated Raman loss via few-cycle laser-induced quantum interference, SuperB-SRS measures signals in the time domain rather than the frequency domain. This approach delivers Raman spectra identical to state-of-the-art spontaneous Raman over a thousand-wavenumber range, while being more than 100 times faster and naturally supporting simultaneous fluorescence detection. We demonstrate >100-fold speed gain over spontaneous Raman for imaging biological tissue samples. With high spectral fidelity, natural-linewidth-limited resolution, broad bandwidth, and high sensitivity, SuperB-SRS provides a practical and powerful tool for high-speed Raman imaging in biomedical research.

[AP-20] PIBM2026-0406-8

High-throughput biomarker evaluation with serum C-H stretching transient stimulated Raman spectroscopy

Qiaozhi Yu[1], Hanqing Xiong[1*]

[1]National Biomedical Imaging Center, College of Future Technology, Peking University, Beijing, China

Corresponding author e-mail address: xiong.hanqing@pku.edu.cn

Abstract: Modern blood biochemistry analyzers play an essential role in disease diagnosis, but are resource-intensive and time-consuming. Studies on Raman spectroscopy have shown some progress in cost-effective blood analysis. However, spontaneous Raman (SR) suffers from low excitation efficiency and strong fluorescence interference. Coherent Raman could accelerate detection while eliminating fluorescence background, yet mainstream broadband techniques based on coherent anti-Stokes Raman scattering (CARS) are incapable of quantitative analysis due to the nonlinear concentration response and non-resonant background. Here we report a new profiling method to evaluate the biochemical information in large-scale human serum based on time-domain transient stimulated Raman scattering (T-SRS) spectroscopy. To demonstrate the practicality and efficiency of our system, we collected the spectra of serum samples from 2,212 different clinically subjects in C-H stretching region (i.e., 2800-3150 cm-1), and dug the underlying information of biomarkers mainly by classical partial least squares regression (PLS). Up to 20 independent biomarkers achieved correlation coefficient r larger than 0.5 in our prediction model, with 14 of them show strong correlation (r exceeded 0.7). Crucially, a systematic solution for model transfer between different T-SRS

systems was achieved. Cross-system validation across total 4,801 clinical serum samples confirmed the reproducibility of our results, demonstrating high transferability and paving the way for large-scale clinical deployment across different hospitals and communities.

[AP-21] PIBM2026-0406-20

Magnetically Enriched 3D Free-Standing Membrane Platform for Ultrasensitive SERS Detection of Pathogenic Bacteria

Minhang Zhu[a], Jiaxin Shi[a], Fasheng Zhang[a], Yubo Gao[a], Zufang Huang[a*]

[a]Key Laboratory of OptoElectronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, Fujian Normal University, Fuzhou 350007, China.

**Corresponding authors: zfhuang@fjnu.edu.cn.*

Abstract： Pathogenic bacterial infections pose a severe and persistent threat to global public health security, causing millions of deaths annually. It is projected that the health burden imposed by such infectious diseases will further intensify by 2050. Rapid and accurate identification of pathogenic bacteria is critical for implementing targeted antimicrobial therapy and curbing the spread of antibiotic resistance. Nevertheless, bacterial culture, regarded as the gold standard for pathogenic bacterial identification, is time-consuming, with test results typically obtainable only after 2 to 5 days. Current molecular detection technologies are plagued by complicated sample pretreatment and poor anti-interference capability in practical biological matrices. Surface-enhanced Raman scattering (SERS) technology has emerged as a highly promising tool in pathogen detection owing to its ultra-high sensitivity and excellent specificity. However, conventional SERS-based methods for pathogenic bacterial detection are still constrained by low signal stability, poor reproducibility, and difficulties in detecting low-abundance targets under complex physiological conditions. These drawbacks severely hinder their practical application in on-site rapid screening and clinical diagnosis. To further enhance the intensity and stability of SERS signals, a self-supporting membrane—a functional membrane system that requires no external support and maintains structural stability in liquid phases—was introduced. This report summarizes the application findings of exploratory surface-enhanced Raman scattering spectroscopic analysis combined with self-supporting membranes for the ultra-sensitive identification of Escherichia coli in complex matrices at low abundance levels. We present and experimentally verify the interaction between Escherichia coli and WGA-modified magnetic beads, along with the optimization of key parameters and corresponding outcomes. Moreover, by integrating SERS tags with magnetic enrichment technology and leveraging the directional aggregation effect of free-standing membranes (FSM), efficient enrichment and rapid detection of Escherichia coli in complex matrices are achieved.

Keywords: Surface-Enhanced Raman Scattering (SERS); three-dimensional liquid free-standing membrane (3D-FSM); SERS tags; Escherichia coli (E. coli) detection.

[AP-22] PIBM2026-0406-27

Efficient and Biocompatible Sperm Enrichment via Surface Acoustic Waves: An Exploratory Study

Zhaoyan He[1†], Haiyan Li[2†], Jiarui Wang[1], Ya Hu[1], Weida Su[1*], Shengrong Du[2*], Zufang Huang[1*]

[1] College of Photonic and Electronic Engineering, Key Laboratory of Opto-Electronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou 350117, Fujian, China;

[2] Reproductive Center, Fujian Maternity and Child Health Hospital, College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics, Fujian Medical University, Fuzhou 350001, Fujian, China

†These authors contributed equally to this work.

** Corresponding authors. suweida@fjnu.edu.cn (W. Su); dushengrong2001@126.com (S. Du); zfhuang@fjnu.edu.cn (Z. Huang).*

Abstract: Efficient and gentle sperm processing is essential for addressing male-factor infertility in assisted reproductive technology (ART). While acoustic manipulation offers a promising alternative to conventional centrifugation methods, its clinical adoption has been limited by a lack of frequency-specific operational criteria and comprehensive biocompatibility validation. Here, we present a highly efficient, non-contact acoustofluidic sperm enrichment platform driven by surface acoustic waves (SAW). By combining theoretical calculations of the κ-factor with microsphere-based modeling, we optimized the interdigital transducer geometry and identified 20 MHz as the critical frequency for maximizing enrichment efficiency.In clinical evaluations of 26 independent semen samples, our platform achieved an average sperm concentration increase of approximately 56%. Notably, clinically challenging low-concentration samples exhibited a remarkable 1.4-fold improvement. Comprehensive biocompatibility assessments via sperm chromatin dispersion assays confirmed that the acoustic field induces no significant impact on DNA integrity or velocity-derived kinematic parameters, including average path velocity, straightness, and wobble. These findings establish our acoustofluidic system as a rapid, biocompatible, and high-yield solution for sperm enrichment, overcoming the limitations of traditional methods and demonstrating strong translational potential for integration into standard ART workflows.

[AP-23] PIBM2026-0409-2

MBA-enabled SERS-LFIA for sensitive detection and quantitative analysis of SARS-CoV-2 RBD protein

Tang Qinglin[1] and Lin Duo[1]*

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou 350117, China

**Corresponding author: duo@fjnu.edu.cn*

Abstract: Lateral flow immunoassay (LFIA) is widely used for point-of-care testing due to its simplicity and rapid response; however, its limited sensitivity and lack of quantitative capability restrict broader applications. In this work, a simple strategy was developed to integrate surface-enhanced Raman scattering (SERS) into conventional LFIA by introducing 4-mercaptobenzoic acid (MBA) as a Raman reporter onto gold nanoparticles (AuNPs).

MBA-modified AuNPs were conjugated with antibodies to construct SERS-active nanotags without altering the basic structure of the LFIA strip. The MBA concentration was optimized, and 3 μM was selected as the optimal condition, providing strong Raman signals while maintaining nanoparticle stability.

Compared with conventional LFIA, the visual detection sensitivity showed no significant improvement; however, the SERS readout enabled sensitive and quantitative detection of SARS-CoV-2 RBD protein. A good linear relationship between Raman intensity at 1078 cm^{-1} and analyte concentration was obtained in the range of 50–2000 pg/mL ($R^2 \approx 0.997$). The practical detection limit was determined to be 50 pg/mL.

Furthermore, the assay demonstrated reliable detection performance in simulated biological samples, indicating good anti-interference capability. This work provides a simple and cost-effective approach to upgrade conventional LFIA into a quantitative detection platform.

[AP-24] PIBM2026-0412-1

Optical Bioensor Based on Fluorescent MgT MOFs and DNA Cube-Cas12a Coupled Signal Amplification System for Ultrasensitive Detection of CTCs

Abstract: Circulating tumor cells (CTCs) serve as pivotal biomarkers for early cancer monitoring, harboring abundant molecular information reflective of tumor tissues. Accurate quantification of these cells thus holds substantial clinical value. However, the scarcity of CTCs in early-stage cancer peripheral blood poses a significant hurdle. Thus, achieving ultrasensitive detection remains an urgent scientific priority. Herein, an ultra-sensitive fluorescent cytosensor integrating novel Mg2+-based fluorescent metal–organic frameworks (Mgb FMOFs) and DNA cube-Cas12a coupled signal amplification system (DCSAS) was developed.

To improve the sensitivity of the cytosensor, an ideal fluorescent signal tag, Mgb-FMOFs, was first synthesized via a one-pot solvothermal method, exhibiting bright yellow-green fluorescence under 365 nm UV irradiation. Subsequently, DCSAS was constructed to further improve the sensitivity. In DCSAS, an eight-branched DNA cube was designed, with one branch complementary to the EpCAM aptamer and the other seven branches complementary to seven crRNAs. CTCs competitively bind to the EpCAM aptamer, releasing the magnetic bead-captured DNA cube, which in turn activates seven Cas12a proteins. The DCSAS overcomes the Cas protein-to-target “1: 1 activation” limitation of traditional CRISPR systems, establishing a highly efficient 1: 7 activation mechanism. Furthermore, this multi-branched architecture effectively increases the local concentration of Cas12a, enhancing its collision efficiency with single-stranded DNA signal probes.

Based on the above strategy, the fluorescent cytosensor exhibited a good linear response in the range of 2 – 1000 cells/mL, with a limit of detection reaching the single-cell level. Meanwhile, benefiting from the high specificity of the aptamer, the sensor can effectively distinguish target CTCs from tumor cells of different origins. In summary, the fluorescent cytosensor developed in this study provided a new tool for the accurate detection of CTCs, and exhibited broad application prospects in early monitoring of tumor metastasis.

Keywords: Circulating tumor cells, fluorescent metal–organic frameworks, CRISPR technology, DNA cube, optical biosensor

[AP-25] PIBM2026-0412-2

Ultrasensitive optical biosensor based on fluorescent nanotrees and DNA molecular prison@Cas12a coupled signal amplification technology for precise detection of ctDNA

Fangzhu Zhou[1], Huawei Shen[1]

[1]Chongqing Key Laboratory of Sichuan-Chongqing Co-construction for Diagnosis and Treatment of Infectious Diseases Integrated Traditional Chinese and Western Medicine, Chongqing City Hospital of Traditional Chinese Medicine, Chongqing, 400021, China

Corresponding author e-mail address: huaweishen2022@163.com

Abstract: Precise detection of circulating tumor DNA (ctDNA) is of great clinical significance for early cancer screening and dynamic monitoring. However, ctDNA in peripheral blood during early-stage cancer faces severe bottlenecks including extremely low abundance, vulnerability to chemical damage, and strong background interference, which pose formidable challenges for its high-precision and high-sensitivity quantitative analysis. Thus, this study constructed an ultrasensitive fluorescent biosensor based on fluorescent nanotrees and DNA molecular prison-Cas12a coupled signal amplification system for precise detection of ctDNA.

To improve the sensing sensitivity, fluorescent nanotrees loaded with high-density fluorescent molecules were first prepared via nonlinear hybridization chain reaction (nlHCR) and served as high-efficiency signal output probes. Furthermore, by integrating DNA self-assembly and CRISPR-Cas12a technology, a cascade signal amplification strategy was designed. DNA tetrahedron was used as a “molecular prison” to precisely encapsulate double-stranded PAM sequences (dsPAM). In the presence of target ctDNA, the initial Cas12a could be activated, and its trans-cleavage activity would disrupt the DNA tetrahedron structure, continuously releasing dsPAM to trigger cascade activation of more Cas12a. This strategy breaks the inefficient 1: 1 activation mode between target and Cas protein in traditional CRISPR systems and establishes a novel 1: N cascade amplification mechanism. Meanwhile, the massively activated Cas12a cleaves fluorescent nanotrees through trans-cleavage reaction, releasing them from the solid-phase carrier into the supernatant, thereby realizing significant enhancement of fluorescence signals.

Under optimal conditions, the proposed fluorescent biosensor exhibits a good linear correlation toward ctDNA in the range of 10 – 10^6 aM, with a limit of detection as low as 5 aM. In addition, the developed biosensor displays outstanding specificity, which can accurately distinguish non-target double-stranded DNA with single-base mismatches and effectively eliminate complex background interference.

In summary, the proposed fluorescent sensing strategy provides a new method for ultrasensitive detection of low-abundance ctDNA, and shows broad application prospects in early cancer diagnosis, prognosis evaluation, and dynamic tumor monitoring.

[AP-26] PIBM2026-0415-1

NIR-II fluorescence lifetime mesoscopy for quantitative detection of tumor margins

Jiuling Liao[1*], Wei Zheng[1]

[1]Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, 1068 Xueyuan Avenue, Shenzhen University Town, Shenzhen, P.R.China

** jl.liao@siat.ac.cn*

Abstract: The fluorescence imaging in the second near-infrared (NIR-II) window is an emerging imaging technology that has the advantages of high tissue penetration depth and high signal-to-noise ratio. Driven by continuous advances in NIR-II fluorophores and detector technologies, NIR-II imaging has witnessed rapid development in both technical innovation and biomedical applications. We develop a novel NIR-II fluorescence mesoscopic imaging system based on f-θ scanning and confocal detection. In addition, we integrate fluorescence lifetime detection to enable in-depth analysis of fluorophore–environment interactions. Using this system, we perform high-resolution NIR-II imaging of cerebral blood vessels in intact mice without craniotomy. Moreover, by utilizing folate receptor-targeted indocyanine green nanoprobes (FPH-ICG), we achieve precise visualization of tumor margins in both mouse models and clinical samples. Importantly, in contrast to conventional NIR-II intensity imaging, NIR-II lifetime imaging offers a more reliable and accurate depiction of tumor margins, which is further validated by histopathological analysis.

[AP-27] PIBM2026-0528-1

Nanoplastics Detected in Hospital-Sourced Infusion System

William Ji[1], Licheng Wang[2], Liwu Zhang[2]

[1]No. 2 High School of East China Normal University

[2]Department of Environmental Science & Engineering, Fudan University

Corresponding author e-mail address: zhanglw@fudan.edu.cn

Abstract: Recent studies have highlighted the potential pathway of microplastic exposure through infusion therapy. However, the release of nanoplastics during this process remains poorly understood. In this study, three brands of hospital-sourced infusion products were analyzed for nanoplastic release using surface-enhanced Raman spectroscopy (SERS) combined with dark-field microscopy. A wide variety of nanoplastics, including polypropylene (PP), polyvinyl chloride (PVC), polystyrene (PS), polymethyl methacrylate (PMMA), polyethylene terephthalate (PET), polyamide (PA), and polyethylene (PE), was detected. Among them, PP and PVC nanoplastics were found at high concentrations, ranging from 7436 to 16439 particles per bag and 3914 to 7045 particles per tube, respectively. In addition to these dominant species, the combined concentration of the remaining five nanoplastics ranged from 17 to 68 particles per milliliter in the infusion solutions. This level of compositional diversity has not been previously reported, raising urgent concerns regarding nanoplastic exposure through infusion therapy and underscoring the need for further investigation.

[AP-28] PIBM2026-0604-2

Label-free detection of cellular drug responses based on dynamic light scattering imaging

Wanlin Xu[1], Linchun Xu[2], and Meiai Lin[1]

[1]Department of Biomedical Engineering, College of Engineering, Shantou University, Shantou, Guangdong, China

[2]Department of Hematology, The First Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, China

Corresponding author e-mail: meiailin@stu.edu.cn

Abstract: Triple-negative breast cancer (TNBC) is a highly heterogeneous malignant tumor. Deciphering its intratumoral heterogeneity at the single-cell level, along with the differential sensitivity to drug action, is essential for precision diagnosis and therapy. Dynamic light scattering (DLS), as a label-free optical method, is sensitive to changes in intracellular structures and holds potential for single-cell drug response analysis. However, the mechanism by which subcellular structural changes influence DLS signals remains unclear, and in particular, the sensitivity of DLS for detecting dynamic subcellular structural changes under drug action requires further investigation. This study aims to investigate the influence of subcellular structural changes on DLS by inducing functional and subcellular alterations in breast cancer cells through drug modulation, and to establish a DLS-based label-free analytical method for assessing drug response in breast cancer cells.

A DLS analyzer was developed and optimized for single-cell imaging, and TNBC cells were treated with the mitochondrial fission inhibitor Mdivi-1, the mitochondrial fusion agonist leflunomide, and the microtubule stabilizer paclitaxel, respectively, targeting different subcellular structures. The autocorrelation function method was used to analyze the DLS images. The results demonstrated that under 60 μM Mdivi-1 treatment, TNBC cell viability decreased to 52.15%, migration to 42.42%, and invasion to 27.55%. Concurrently, mitochondrial morphology transformed from fragmented pieces to web-like networks, causing the DLS decay rate to drop from 1.544 s^{-1} to 1.000 s^{-1}. Under 300 μM leflunomide, similar anti-tumor outcomes occurred alongside mitochondrial structural remodeling, where the DLS decay rate systematically fell from 1.802 s^{-1} to 1.373 s^{-1}. Under 40 nM paclitaxel, a microtubule stabilizer, the progressive evolution of cellular apoptosis was successfully triggered. Time-series analysis revealed that as cells transitioned through apoptosis, the DLS decay rate significantly accelerated from 1.348 s^{-1} in the relatively intact state to 3.951 s^{-1} in the terminal state. This result demonstrates that the DLS method has the capacity to capture the drug response status of cells.

In conclusion, the cell-based DLS method enables real-time, rapid, and sensitive quantification of multi-target subcellular dynamics and targeted drug responses. This non-invasive approach provides a potential tool for anti-tumor drug screening and early efficacy evaluation.

Keywords: Dynamic light scattering imaging, Triple-negative breast cancer, Mitochondrial dynamics, Cellular apoptosis, Drug efficacy evaluation

[AP-29] PIBM2026-0610-3

SAP FISH: Highly Specific and Sensitive Imaging for Single-Cell Spatial Quantification

Shujing Huang[1]

[1]Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics

Huazhong University of Science and Technology, Wuhan 430074, China

D202281303@hust.edu.cn

Abstract: High-resolution spatial transcriptomics technologies enable the systematic mapping of cell-type spatial architectures at the single-cell level, which is crucial for decoding the structural and functional complexities of biological tissues. However, existing detection methodologies based on in situ rolling circle amplification frequently fail to simultaneously satisfy the strict requirements for sensitivity and specificity, often exhibiting sparse signal spots and poor accuracy, thereby severely limiting their widespread application. To address this bottleneck, we systematically optimized the sequence design of padlock probes to achieve their stable anchoring, and based on this strategy, developed Stably Anchored Padlock FISH (SAP FISH). While effectively suppressing non-specific background signals, this technology significantly enhances the detection abundance of RNA molecules. Compared with conventional peer technologies, SAP FISH achieves over a tenfold increase in both signal-to-noise ratio and transcript detection efficiency. Furthermore, we applied this method to perform six rounds of sequential imaging on the mouse somatosensory cortex, successfully achieving the in situ spatial quantification of key cell-type marker genes. Taken together, our technology substantially enhances the precision of multiplexed spatial transcriptomics workflows, offering a powerful and reliable tool for future research in neuroscience and spatial molecular pathology.

[AP-30] PIBM2026-0616-3

Albumin-Resistant Background-Free NIR Fluorescence Imaging via Hydroxyl Radical-Specific Cascade Oxidative Cyclization

Deming He[†1], Minrong Huang[†1], Le Liu[1], Chiyuan Wei[2], Yuanqiang Sun[2], Xing Wei[1], Lingchao He[1], Feiyi Wang[3] and Wei Chen[1*]

[1] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[2] College of Chemistry, Henan Joint International Research Laboratory of Green Construction of Functional Molecules and Their Bioanalytical Applications, Zhengzhou University, Zhengzhou 450001, China

[3] Hubei Key Laboratory for Precision Synthesis of Small Molecule Pharmaceuticals & MOE Key Laboratory for the Synthesis and Application of Organic Functional Molecules, Hubei University, Wuhan 430062, China

Corresponding author e-mail address: w.chen@hust.edu.cn

Abstract: As the most harmful reactive oxygen species, hydroxyl radical (•OH) participates in various physiological processes. To elucidate its underlying biological functions, developing high-fidelity imaging probes for •OH with minimized false-positive signal has emerged as a research focus for chemists. However, the fidelity of current •OH-responsive probes are limited by three predominant sources of interference: biomolecule autofluorescence, inherent probe fluorescence, and false-positive signals induced by nonspecific serum protein-binding interactions. To break this dilemma, we reported a pioneering •OH-initiated cascade oxidative cyclization strategy for high-fidelity imaging of •OH. Utilizing this unique strategy, several

background-free fluorogenic probes **HRPO11** to **HRPO17** were rationally designed by fine-tuning the electron density and chemical reactivity of C=N bond, the novel •OH recognition site. Among these probes, **HRPO17** was selected due to its optimal chemosensing performance for •OH *in vitro* (192-fold). Furthermore, **HRPO17** successfully achieved the high-fidelity •OH imaging in the cellular lipid peroxidation, inflammation, and hepatic ischemia-reperfusion injury mice models. We anticipate that this fantastic cascade oxidative cyclization strategy can shed new light on developing albumin-resistant background-free fluorescent probes with improved imaging accuracy, and provide a robust tool for exploring •OH biology.

[AP-31] PIBM2026-0616-4

Unveiling Chain-Length Dependent Targeting for Rational Development of Mitochondrial Cristae Probes

Kaiqiang Liu, [1] Xiaohai Hu, [1] Ning Jing, [1] Lixin Niu, [2] Yu-Hui Zhang[1]*

[1]Britton Chance Center for Biomedical Photonics-MoE Key Laboratory for Biomedical Photonics, Advanced Biomedical Imaging Facility-Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, Hubei 430070, China.

[2]Key Laboratory of the Ministry of Education for Medicinal Resources and Natural Pharmaceutical Chemistry, National Engineering Laboratory for Resource Development of Endangered Crude Drugs in Northwest of China, and School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an 710119, People's Republic of China.

Responding Authors：zhangyh@mail.hust.edu.cn (Yu-Hui Zhang)

Abstract: Fluorescence super-resolution microscopy has enabled nanoscale visualization of mitochondrial ultrastructure; however, the development of mitochondrial cristae probes still relies heavily on empirical screening. Establishing a simple, efficient, stable, and broadly applicable targeting strategy for mitochondrial cristae remains a central challenge in the field. Here, by constructing a systematic probe library based on tetramethylrhodamine conjugated with alkyl chains of varying lengths (TMR-nC), we establish the intrinsic structure–activity relationship between alkyl-chain length and cristae-targeting performance.

We found that both cristae specificity and labeling stability strongly depend on alkyl-chain length, with TMR-11C achieving the optimal balance between cristae selectivity and membrane retention. More importantly, this chain-length-dependent design principle is readily transferable to multiple fluorophore scaffolds, including BODIPY and Cy5, demonstrating broad applicability. Guided by this principle, we further developed a series of multicolor mitochondrial cristae probes that are highly compatible with various live-cell dyes and fluorescent proteins for multiplexed imaging.

Using this probe set, we successfully visualized cristae remodeling during mitochondrial fission, captured transient interactions between mitochondria and cellular structures such as lysosomes and the cytoskeleton, and further visualized mitochondrial cristae within tunneling nanotubes. Overall, this work establishes a systematic alkyl-chain engineering strategy for mitochondrial cristae targeting, reveals a general molecular design principle underlying hydrophobic-chain-mediated inner membrane specificity, and provides reliable molecular tools for multicolor super-resolution imaging and long-term dynamic tracking of mitochondrial ultrastructure.

[AP-32] PIBM2026-0616-6

Thioxanthene-Based NIR-II Fluorophores and Ratiometric Probes for Bioimaging

Lingchao He[1], Xing Wei[1], Xian Zhang[1], Le Liu[1], Deming He[1], Wei Chen[1,*]

[1] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

Corresponding author e-mail address: w.chen@hust.edu.cn

Abstract: Near-infrared II (NIR-II, 1000–1700 nm) fluorescence imaging provides deep tissue penetration and high spatial resolution, but organic NIR-II fluorophores remain limited by the lack of versatile scaffolds combining long-wavelength emission, high brightness, and facile functionalization. General platforms for NIR-II ratiometric probes are also scarce. Here, we report a thioxanthene-based platform for bright NIR-II fluorophores and ratiometric probes. This platform enables dyes with large Stokes shifts and tunable properties. A representative fluorophore shows intrinsic dual emission under physiological conditions, enabling ratiometric sensing. Through modular functionalization, activatable probes were developed with stable ratiometric responses upon analyte activation. Importantly, in vivo NIR-II ratiometric imaging was achieved in both acute alcoholic liver injury and 4T1 tumor models for visualization of H_2Sn level fluctuations. Overall, this work provides a transferable scaffold and modular platform for NIR-II fluorophores and ratiometric imaging.

[AP-33] PIBM2026-0617-2

Hybrid confocal Raman micro-endoscopic imaging technology

Liu Peng lei[1], Yang Wei[1,]*, Liu Qian[1] , Fu Ling[1]

[1]School of Biomedical Engineering, Hainan University, No. 7 Daxue Road, Yazhou District, Sanya City, Hainan Province, 572024

**Email: wyang@hainanu.edu.cn*

Abstract: Traditional endoscopic imaging techniques face difficulties in simultaneously obtaining tissue cell-level morphological information and molecular chemical information, and Raman endoscopic probes often have weak detection signals and are easily affected by fiber-optic background noise. This project proposes research on a hybrid confocal Raman micro-endoscopic imaging technology, which will achieve an organic integration of anatomical imaging and functional imaging. This technology uses hollow-core anti-resonant fibers as low-background, wide-bandwidth transmission channels, combined with MEMS 2D scanning, a confocal microscopic endoscopic imaging optical path, a Raman spectroscopy acquisition module, and an image reconstruction algorithm to create an integrated platform for morphological imaging and molecular spectral detection within the same region. The system enables real-time visualization of tissue microstructures, single-point Raman molecular identification, regional Raman chemical imaging, and fused display of confocal microscopic and Raman images, thereby characterizing the distribution of biomacromolecular components such as lipids and proteins while acquiring cell-scale morphological images. This project overcomes the limitations of single-mode endoscopic imaging, which lacks biomolecular specificity, and traditional Raman endoscopy, which is constrained in spatial imaging. It will provide a novel multimodal optical technology solution for in situ detection, boundary recognition, and auxiliary diagnosis of lesions such as gastrointestinal tumors.

[AP-34] PIBM2026-0617-3

NSCLC-Induced Reorganization of Platelet α-Granules Drives a Machine Learning Diagnostic Platform for Early Cancer Detection

Ning Jing[1], Chuanjie Zhang[2], Jiajun He[1], Xiaohai Hu[1], Simei Zhong[1], Zelin Liu[1], Xiaowei Wu[2] and Yu-Hui Zhang[1]

[1]MOE Key Laboratory for Biomedical Photonics, Advanced Biomedical Imaging Facility-Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, China

[2]Department of Thoracic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Correspondence: Yu-Hui Zhang (zhangyh@mail.hust.edu.cn)

Abstract: Lung cancer remains the leading cause of global cancer incidence and mortality, with non-small cell lung cancer (NSCLC) accounting for 85% of cases. Early-stage NSCLC features a low tumor burden, rendering conventional screening tools inadequate. Low-dose computed tomography (LDCT) is widely used but suffers from a false-positive rate exceeding 98%. Consequently, indeterminate pulmonary nodules (IPNs) present a major clinical conundrum; their malignant potential cannot be definitively characterized via initial imaging, often leading to misdiagnoses and patient anxiety. Furthermore, conventional circulating blood biomarkers lack sufficient sensitivity and specificity for early-stage detection. Blood-based liquid biopsy has emerged as a promising, minimally invasive alternative. Platelets interact dynamically with tumors and are easily isolated, making them an excellent candidate. Our previous work demonstrated that at the subcellular level under structured illumination microscopy (SIM), the spatial distribution patterns of platelet alpha-granules undergo abnormal alterations in various malignancies, serving as a robust diagnostic feature. However, whether advanced characterization of alpha-granule distribution can enhance early NSCLC screening and differentiate benign from malignant IPNs—alongside the underlying molecular mechanisms—remains unknown. In this study, we optimized our platelet alpha-granule classification model to capture finer image details, significantly enhancing its discriminatory capacity. Utilizing this refined model, we conducted a large-scale analysis on a cohort of 716 participants, encompassing healthy volunteers, patients with radiologically indeterminate nodules, and NSCLC patients. Our method demonstrated exceptional performance in distinguishing early-stage NSCLC from non-cancer cohorts (accuracy: 87%). Remarkably, in a dedicated sub-cohort of 82 patients with radiologically ambiguous benign nodules requiring invasive confirmation, our approach achieved outstanding diagnostic accuracy (accuracy: 83%), significantly outperforming conventional clinical biomarkers (generally below 60%). Mechanistically, we discovered that protein X secreted within NSCLC-derived exosomes is a key driver of these aberrant alpha-granule distributions. Ultimately, this study provides a highly reliable, minimally invasive tool supporting early NSCLC detection.

Key Words: NSCLC, early detection, machine learning, liquid biopsy.

[AP-35] PIBM2026-0617-5

Phloxine B as a highly soluble absorbing molecule for enhanced in vivo tissue optical clearing

Jinkun Wang[1], Shaojun Liu[1], Xiang Zhong[1],Tingting Yu[1], Dan Zhu[1*]

[1]MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics-Advanced Biomedical Imaging Facility, Huazhong University of Science and Technology, China

Corresponding author e-mail address: dawnzh@mail.hust.edu.cn

Abstract: The high scattering properties of biological tissues severely limit the penetration depth of optical imaging techniques. Tissue optical clearing has emerged as an effective strategy to reduce light attenuation by improving refractive index matching within tissues. Recently, it has been demonstrated that strongly absorbing molecules can modulate the refractive index of aqueous media through the Kramers-Kronig relations, thereby enabling *in vivo* optical transparency. However, the widely used absorbing molecule tartrazine tends to precipitate at high concentrations, which compromises imaging quality and restricts its practical applicability *in vivo*. In this study, we aim to identify alternative absorbing agents with enhanced optical clearing performance and improved physicochemical stability. First, a simulation framework was established based on the Kramers-Kronig relations in combination with the Lorentz oscillator model to quantitatively describe the relationship between absorption spectra and refractive index modulation. Using this framework, candidate molecules with strong potential for scattering reduction in the red and near-infrared spectral regions were systematically screened. Subsequently, experimental validation was conducted across multiple levels, including tissue phantoms, *ex vivo* brain slices, chicken breast and bovine muscle sections as well as *in vivo* mouse ear. Among the candidates tested, Phloxine B exhibited superior optical clearing performance compared to tartrazine. Notably, it enabled enhanced transparency in living mouse ear vasculature without forming crystalline precipitates under ambient conditions, demonstrating improved solubility and stability, as well as greater suitability for *in vivo* applications. This study validates and extends the absorbing molecules-based tissue optical clearing strategy, and identifies Phloxine B as a promising candidate with superior performance, providing both theoretical guidance and experimental support for future research.

[AP-35] PIBM2026-0618-8

STIM1 Interacting with MCU at ER-Mitochondria Contact Sites Contributes to Mitochondrial Fission via Ca^{2} Transfer

Xiaohai Hu[1+], Xinxin Duan[1+], Yu-Hui Zhang[1*]

[1]MOE Key Laboratory for Biomedical Photonics, Advanced Biomedical Imaging Facility-Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology

** Corresponding author e-mail address: zhangyh@mail.hust.edu.cn*

Abstract: Mitochondrial fission is effectively regulated by the endoplasmic reticulum (ER) through molecular tethers that facilitate efficient ER-mitochondria communication; however, the molecular composition and regulatory mechanisms of these tethers remain largely elusive. Here, we reveal a new ER-mediated mechanism of mitochondrial fission. We demonstrate that Stromal Interaction Molecule 1 (STIM1), an ER-resident protein, plays a critical role in promoting mitochondrial fission through its coiled-coil (CC) domain and N-terminus working cooperatively. We also identify Mitochondrial Calcium Uniporter (MCU) as a novel STIM1

interacting partner. The STIM1-MCU complex, formed through the engagement between STIM1's CC domain and MCU's C-terminal region, mediates Ca^{2+} transfer from the ER to mitochondria primarily via STIM1's N-terminus and its interaction with MCU. Subsequently, the increase in mitochondrial Ca^{2+} level triggers the recruitment of Dynamin-Related Protein 1 (Drp1), ultimately driving mitochondrial fission. This study reveals that the STIM1-MCU complex not only serves as a key molecular tether between the ER and mitochondria but also functions as a Ca^{2+}-dependent regulator of mitochondrial dynamics, offering new insights into ER-mitochondria communication and mitochondrial dynamics regulation.

[AP-36] PIBM2026-0618-16

Rapid One-Step Construction of DNA-Functionalized Gold Nanoparticle Probes Enabled by Microwave Drying Synergy

Lixiang Guo†, Yanfeng Li†, Ruilin Gong†, Fang Liu* and Feifan Zhou*

State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, Hainan 572024, China

Corresponding author e-mail address: fangliu@hainanu.edu.cn; zhouff@hainanu.edu.cn

Abstract: DNA-functionalized gold nanoparticles (DNA-AuNPs), integrate the unique physicochemical properties of AuNPs with the high-specificity biorecognition capability of DNA, making them indispensable materials for biosensing and in vitro diagnostic assays. However, conventional fabrication strategies are generally plagued by time-consuming procedures (>48 h), tedious operations, and heavy reliance on thiol-modification, severely restricting their application in point-of-care testing (POCT). It is therefore of critical importance to develop a simple and efficient method for constructing DNA-AuNPs.

To address these challenges, we developed a microwave-drying-assisted one-step strategy that exploits the synergistic effect of microwave-induced dehydration and extreme molecular concentration to achieve rapid functionalization of AuNPs. Notably, the entire modification process can be completed within 10 min without any additional reagents. The resulting probes exhibited a high DNA loading capacity of up to 95 strands per particle, and maintained excellent colloidal stability under stringent conditions, including 0.6 M NaCl and a broad pH range of 6.0 to 8.5. More importantly, this strategy demonstrated remarkable sequence universality and substrate compatibility. It is not only compatible with phosphorylated DNA and long chain nucleic acids fragments exceeding 1000 bp in length, but also successfully achieves direct and efficient conjugation with EXPAR isothermal amplification products, thereby realizing on-demand customization of DNA-AuNP probes in laboratory settings and substantially expanding the range of compatible nucleic acid source and downstream application.

In summary, this microwave-assisted one-step modification strategy provided a rapid, straightforward, and versatile platform for the preparation of DNA-functionalized gold nanoparticles. By offering a universal solution for the functionalization of long nucleic acids and complex biomolecules on gold nanostructures, this technology holds significant promise for the development of next-generation POCT diagnostic reagents, biosensing systems, and translational nanobiotechnology applications with strong commercial potential.

[AP-37] PIBM2026-0618-20

High-strength porous hydrogels with sustained NO release properties for burn wound healing and microenvironment regulation

Xiaomin Ma[1]，Zhengyu Chen[1]，Wei Chen[1]，Ruorong Ran[1]，Junjie Wang[2,*]，Xingzhou Peng[1,*]

[1] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 572025, China

[2] NHC Key Laboratory of Tropical Disease Control, School of Life Science and Medical Technology, Hainan Medical University, Haikou 571199, China

Abstract: Delayed healing of burn wounds presents a major challenge in burn surgery. Severe thermal injury not only directly damages the skin's physical barrier and causes extensive tissue necrosis, but also leads to an imbalance in the local pathological microenvironment. At the same time, the wound is highly susceptible to infection by Staphylococcus aureus and Escherichia coli, which form persistent biofilms, causing prolonged stagnation in tissue repair. Faced with such a complex and dynamically evolving pathological microenvironment, conventional hydrogels generally suffer from poor mechanical properties and an inability to adapt to wound deformation; furthermore, traditional dressings struggle to respond to the physiological and metabolic fluctuations hidden deep within the wound bed. To address this, this study has developed a high-strength, porous composite hydrogel that combines excellent mechanical support with the ability to actively reshape the microenvironment. This system utilises acrylamide (AM) and polyethylene glycol diacrylate (PEGDA) to construct a three-dimensional network (APDA); simultaneously, through physical blending, the nitric oxide (NO) donor S-nitroso-N-acetylpenicillamine (SNAP) is incorporated, resulting in a composite hydrogel with biochemical intervention activity (APDAS). Physicochemical evaluation revealed that at a molar ratio of m(AM):m(PEGDA) = 10:1, the hydrogel exhibited excellent mechanical properties, with an elongation at break of 1371% and a tensile strength of 113 kPa, effectively alleviating mechanical compression of newly formed microvessels by the dressing. APDAS achieves active intervention in the microenvironment through the sustained release of NO molecules, enabling efficient degradation of bacterial biofilms, with inhibition rates exceeding 95% for both Staphylococcus aureus and Escherichia coli; The gel prepared from 0.2 mmol/L SNAP exhibited outstanding wound-healing promotion effects, with the migration rate of mouse fibroblasts (L929) reaching 40.9% (a 17.2-fold increase compared to the control group), and the luminal formation length of human umbilical vein endothelial cells (HUVEC) reaching 1.7 times that of the control group. Through the construction of a high-strength physical scaffold and active biochemical intervention with NO, this approach has successfully re-established a favourable microenvironment conducive to rapid healing of burn tissue, and has laid the foundation for the future development of smart wound dressings capable of dynamically responding to the physiological microenvironment.

Keyword： Hydrogels, NO therapy, angiogenesis, burn treatment

[AP-38] PIBM2026-0618-23

Ome zarr v0.5 lightweight visualization: a microscopic data sharing scheme better than zoomify

Zhencheng Ren[1]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, *School of Biomedical Engineering, Hainan University, Sanya 572025, China* [2]*HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215123, China.*

[3]*Wuhan National Laboratory for Optoelectronics, MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan 430074, China.*

Abstract: Remote sharing of large-scale microscopic imaging data has long relied on commercial formats such as zoomify. The tile architecture in this format has intensive requests and high server overhead, and scientific metadata such as physical scale will be discarded in the conversion process, which makes the data browsable but difficult to analyze quantitatively. Ome zarr v0.5 has become the next generation of open standards driven by the community by virtue of block storage, multi-scale pyramid and bloc lossless compression. However, it still lacks systematic engineering verification in format conversion and lightweight visualization deployment for large-scale data. This research completes the batch transcoding and visual verification of TB level multi-channel microscopic data based on high-performance cluster. The proposed distributed architecture natively supports the expansion processing of Pb level super large imaging data set, and adapts to the requirements of next generation ultra high throughput microscopic imaging data sharing. The system relies on nginx to provide static file services, and the front-end is based on vizarr to realize channel independent superposition and physical label interaction, and supports lossless scaling and multi-directional 3D slice browsing. Compared with zoomify ZIF format generated by the same data source, the comparative test is carried out under the same network conditions. The first screen data transmission volume of this scheme is reduced by 60%, the number of HTTP requests is reduced by 90%, and the server CPU consumption is very low. Meanwhile, the missing metadata in ZIF format is completely preserved in OME zarr scheme. In the mobile network environment, this scheme can realize low latency interactive browsing for multi-channel data. The whole deployment process can be reproduced at zero cost and open source synchronously, providing an effective solution for the transformation of biological microscopic imaging data from cluster standardization to fair online visualization.

Key words: ome zarr v0.5; Remote microscopic visualization; Multimodal imaging; Fair data; Lightweight deployment

[AP-39] PIBM2026-0621-1

Evaluation of SNSPD-based dual-detection system for time-resolved singlet oxygen luminescence and fluorescence detection

Shengdong Cui[1], Sen Wang[1], Xianzeng Zhang[1], Timothy C Zhu[2], and Zheng Huang[1]

[1]Ministry of Education Key Laboratory of Optoelectronic Science and Technology for Medicine, Fujian Normal University, Fuzhou, Fujian 350117, P. R. China

[2]Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, USA

Corresponding author e-mail address: huangz@fjnu.edu.cn

Abstract: Photoexcitation of photosensitizer can generate singlet oxygen ($^1O_2$) and fluorescence, which are important mediators in photodynamic therapy (PDT) and photodiagnosis. Although photosensitizer-mediated fluorescence emission is relatively strong, $^1O_2$ luminescence at 1270 nm is extremely weak, a sensitive NIR detection system is required for measuring $^1O_2$ luminescence. This study aimed to evaluate a superconducting nanowire single-photon detector (SNSPD) based dual-detection system for measuring photosensitizer-mediated $^1O_2$ luminescence and fluorescence. Q-switch laser of 532 nm was used as excitation source. The reference beam was directed to a photodiode to triggered the start channel of the time-resolved system, while the excitation beam was delivered to the sample. $^1O_2$ luminescence was collected, filtered, coupled into a single-module fiber, and detected by SNSPD. Fluorescence emission was collected through independent optical channel and recorded using a spectrometer or photodiode. The $^1O_2$ luminescence and fluorescence of domestic photosensitizer hematoporphyrin monomethyl ether (HMME) in different solvents were measured. Sodium azide, intralipid, and milk were used to investigate quenching and scattering effects. The system successful detected both $^1O_2$ luminescence and fluorescence at micromolar concentrations. Both signal intensities showed concentration-dependent behavior, while $^1O_2$ lifetime varied among different solvents, being longest in deuterium oxide and shortest in PBS. Sodium azide markedly reduced $^1O_2$ intensity and lifetime without affecting fluorescence or photosensitizer triplet-state lifetime. In scattering media, both signal intensities decreased with increasing scattering strength, whereas $^1O_2$ lifetime remained largely unchanged. The custom-built SNSPD-based dual-detection system demonstrated high sensitivity and reliability for simultaneous $^1O_2$ luminescence and fluorescence measurements, providing a useful optical tool for quantitative study of PDT-related $^1O_2$ dosimetry.

[AP-40] PIBM2026-0630-4

Needle-beam-assisted double-pulse laser capture microdissection with reduced collateral damage

Simo Tian[1], Zhiguo He[2], Dongshu Li[2], Fengqin Shang[1], Xiangning Li[2,3], Hui Gong[3], Qingming Luo[2], and Xiaoquan Yang[2,3]

[1]Wuhan National Laboratory for Optoelectronics, MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan 430074, China

[2]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China

[3]HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215123, China

Corresponding author e-mail address: xqyang@hainanu.edu.cn

Abstract: Laser capture microdissection (LCM) is essential for isolating specific cells from tissue sections, yet precise cutting in thick biological samples remains challenging due to limited depth-of-focus and collateral damage. Here, we propose a double-pulse laser capture microdissection method based on a needle beam (DPLM-NB) to address these limitations. A 60-μm-long needle beam is generated to extend the axial interaction range, while a double-pulse scheme with adjustable delay is employed to optimize energy localization. Numerical simulations based on a rate-equation model reveal that pre-excitation by the first pulse enhances energy coupling in the main-lobe region while suppressing side-lobe responses. Experimental results on 30-μm-thick frozen mouse brain sections demonstrate significant performance improvements. Compared to single-pulse Gaussian beam cutting, the proposed DPLM-NB method reduces the cutting width from 6.75 μm to 2.47 μm and lowers the threshold energy density from 5.02 J/cm² to 1.96 J/cm² at an optimal pulse delay of 1.0–1.3 ns. Furthermore, the method effectively mitigates side-lobe-induced collateral damage. These results indicate that DPLM-NB enables high-precision, low-damage microdissection suitable for downstream spatial omics analysis in thick biological tissues.

[AP-41] PIBM2026-0707-1

In vivo label-free investigation of mitochondrial dysfunction and collagen remodeling in vitiligo lesions

Xinhang Li[1], Junle Qu[2]

[1]Shenzhen Key Laboratory of Photonics and Biophotonics, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen, 518060, China

jlqu@szu.edu.cn

Abstract: Vitiligo is an acquired depigmenting skin disorder characterized by immune-mediated loss of melanocytes, while its in vivo microenvironmental alterations and treatment response heterogeneity remain unclear. In this study, multimodal nonlinear optical imaging was employed to investigate structural and metabolic changes in normal skin, stable vitiligo, and drug-treated lesions in vivo, aiming to identify microenvironmental signatures associated with disease activity and therapeutic sensitivity. A stable vitiligo mouse model was established using B16F10 cells combined with CD4 depletion antibodies, and compared with normal controls. Topical drug intervention was subsequently applied, followed by longitudinal in vivo imaging. Multimodal nonlinear optical imaging, including two-photon excited fluorescence (TPEF), second harmonic generation (SHG), and fluorescence lifetime imaging microscopy (FLIM), was used to characterize

structural and metabolic alterations in the model.Results showed persistent mitochondrial and metabolic abnormalities in stable vitiligo skin, accompanied by dermal collagen remodeling. Drug-sensitive regions exhibited early recovery of both metabolic and structural features.

[AIP-1] PIBM2026-0331-2

Quantitative Analysis of Cryptotanshinone in *Salvia miltiorrhiza via* MLR Background Correction of Raman Spectra

Huikang Wu[1,2,3], Rui Wang[1,2], Mengjie Wang[1,2], Dongjie Zhang*[1,2,3,4], Lin Shi[1,2,3,4], Nan Wang[1,2,3,4], Qi Zeng*[1,2,3,4], Xueli Chen[1,2,3,4]

[1] *Advanced Diagnostic-Therapy Technology and Equipment Key Laboratory of Higher Education Institutions in Shaanxi Province, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.*

[2] *Xi'an Key Laboratory of Intelligent Sensing and Regulation of trans-Scale Life Information, School of Life Science and Technology, Xidian University, Xi'an, Shaanxi 710126, China.*

[3] *Guangzhou Institute of Technology, Xidian University, Guangzhou, Guangdong 510555, China.*

[4] *State Key Laboratory of Electromechanical Integrated Manufacturing of High-Performance Electronic Equipment, Xidian University, Xi'an, Shaanxi 710071, China.*

Abstract: Raman spectroscopy shows significant potential for the quantitative analysis of active compounds in traditional Chinese medicine (TCM) extracts. However, in practical applications, strong spectral signals derived from solvents often mask the characteristic peaks of target compounds; Thereby compromising the reliability of analytical results. This study took the quantitative analysis of cryptotanshinone from Salvia miltiorrhiza extracts as a case study. A multiple linear regression (MLR) model was constructed to subtract the spectral background of methanol solvent, thus improving the accuracy of quantitative analysis. The MLR calibration model was established based on pure methanol spectra and a series of extracts with known concentrations of cryptotanshinone. This would enable the effective separation and subtraction of solvent interference signals. Subsequently, the background-corrected refined spectra were input into a convolutional neural network (CNN) for concentration regression analysis. Experimental results demonstrated that the MLR-based spectral correction strategy significantly enhances model performance. The prediction accuracy of cryptotanshinone concentration was increased from 75% based on original spectra to 86% after correction, highlighting the crucial role of background removal. In conclusion, the MLR-CNN combined strategy established a robust and data-driven quantitative analysis workflow. It achieved precise quantification of target active ingredients in TCM extracts under strong solvent interference conditions. This study provided an effective solution for the quantitative analysis of target components in complex systems via Raman spectroscopy.

[AIP-2] PIBM2026-0331-7

ARA-Net: Atlas-Guided Region Attention for Interpretable Alzheimer’s Disease Diagnosis from Structural MRI

Yuanqin Zhao*[a,b,c], Yu Zhang[d], Jinghong Hu[a], Jian Mao[e], Bisong Zhou[a], Zhuoyao Song[a], Tengfei Guo†[b], and Shaohua Ma†[a,c,f]

[1]Author affiliation and full address (8-point type, centered, italicized)

[a.]Institute of Biopharmaceutical and Health Engineering (iBHE), Tsinghua Shenzhen International Graduate School (SIGS), Tsinghua University, Shenzhen 518055, China.

[b.]Institute of Neurological and Psychiatric Disorders, Shenzhen Bay Laboratory, Shenzhen 518132, China.

[c.]Key Laboratory of Industrial Biocatalysis, Ministry of Education, Tsinghua University, Beijing 100084, China.

[d.]Institute of Integrated Circuits, School of Integrated Circuits, Tsinghua University, Beijing 100084, China.

[e.]Centre de Recherche sur l’ Inflammation, INSERM-U1149, Universite Paris-Cite, Facult´e de M´edecine Xavier Bichat, Paris 75018, France.

[f.]Key Laboratory of Active Proteins and Peptides Green Biomanufacturing of Guangdong Higher Education Institutes, Tsinghua Shenzhen International Graduate School, Shenzhen 518055, China.

Yuanqin Zhao, Ph.D. (first author); Yu Zhang, M.Sc.; Jinghong Hu, M.Sc.; Jian Mao, Ph.D.; Bisong Zhou, Ph.D.; Zhuoyao Song, Ph.D.; and Prof. Tengfei Guo(tengfei.guo@szbl.ac.cn) and Prof. Shaohua Ma(ma.shaohua@sz.tsinghua.edu.cn) as corresponding authors;

Abstract: Background. Deep learning has shown promise for Alzheimer’s disease (AD) classification from structural magnetic resonance imaging (sMRI), yet the absence of anatomically grounded explanations remains a critical barrier to clinical adoption and regulatory approval. **Methods.** We propose ARA-Net (Atlas-guided Region Attention Network), which integrates FreeSurfer-based parcellation of 21 brain regions with multi-head self-attention and anatomical regularization to produce region-level diagnostic explanations by design. A self-supervised pretrained 3D encoder and a three-component Attention-as-Biomarker framework-Region Discriminability Index (RDI), disease progression gradient, and Clinical Alignment Score (CAS)-quantify the clinical relevance of learned attention. We evaluated ARA-Net on 2,401 Alzheimer’s Disease Neuroimaging Initiative scans (cognitively normal: 750; mild cognitive impairment [MCI]: 1,156; AD: 495) via six-seed, five-fold cross-validation (30 runs), with external evaluation on IXI (n = 581) and OASIS (n = 99). **Results.** ARA-Net achieved a balanced accuracy of 67.1% (95% CI: 66.2-67.9%) and a macro area under the curve of 0.830±0.016, significantly outperforming baseline architectures ($p<0.01$, Wilcoxon signed-rank test). Attention weights differed significantly across diagnostic groups in 16 of 21 regions ($p < 0.01$), with eight regions exhibiting monotonic CN→MCI→AD gradients. Without region-level supervision, the amygdala emerged as a top-5 discriminative region (RDI = 0.67). Cross-dataset attention profiles generalized with cosine similarity exceeding 0.98, and error-conditioned analysis confirmed anatomically coherent attention under misclassification (CAS: 0.266 for MCI→CN errors vs. 0.267 for correctly classified MCI). **Conclusion.** ARA-Net demonstrates that atlas-guided region attention delivers clinically verifiable, dataset-independent interpretability for AD diagnosis, bridging the gap between algorithmic performance and clinical transparency requirements.

[AIP-3] PIBM2026-0402-2

Graph Convolutional Networks for Single-Shot Super-Resolution Reconstruction in Fibonacci Photoacoustic computed tomography

Zhibo Xiao[1,2], Xiali Gao[1,2], Yang Xiao[2], Fan Meng[1,2], Hao Huang[1,2], Xuanhao Wang[2,3,4], and Junhui Shi[1,2,3,4]

[1] College of Biomedical Engineering & Instrument Science, Zhejiang University, Hangzhou 310027, China

[2] Zhejiang Lab, Hangzhou 311100, China

[3] State Key Laboratory of Ocean Sensing, Hangzhou 311200, China

[4] xh-wang@zhejianglab.org

[5] junhuishi@outlook.com

Abstract: While photoacoustic computed tomography (PACT) delivers exceptional deep-tissue functional contrasts, the exorbitant cost and data-acquisition bottlenecks of fully sampled dense arrays hinder its widespread clinical translation. Consequently, systems often employ sparse, non-uniform configurations, such as Fibonacci spirals, which inevitably introduce severe aliasing artifacts and compress the effective imaging zone. Deep learning offers a pathway to digitally synthesize densely sampled wavefields from sparse single-shot acquisitions; nevertheless, conventional grid-based convolutional operators fail drastically when processing data from curved, non-Euclidean surfaces due to the inherent structural misalignment between rigid memory indexing and complex spatial reality. To bridge this fundamental gap, we introduce a physically-informed Graph Convolutional Network (ST-GCN) strictly tailored for non-standard PACT geometries. Instead of relying on sequential tensor indices, our approach mathematically conceptualizes the hemispherical probe as a complex interconnected network. Transducer elements act as graph vertices, linked via edges dictated exclusively by their real-world Cartesian coordinates. This topology-driven architecture empowers the network to propagate and aggregate spatiotemporal acoustic features along authentic physical pathways. Furthermore, we integrate a wave-equation-based penalty mechanism to ensure the computationally generated signals strictly adhere to acoustic propagation laws. Validated through in-vivo human hand experiments, ST-GCN successfully upsamples single-shot sparse data to emulate high-density mechanical rotational scans. The proposed framework profoundly suppresses background noise, recovers lost high-frequency spatial details, and broadens the reconstructable volume, paving a highly cost-effective route for high-performance 3D photoacoustic visualization.

[AIP-4] PIBM2026-0402-5

Automatic Identification and Precise Segmentation of Calcified Nodules in IVOCT Based on Self-Supervised Pretraining and Parameter-Efficient Fine-Tuning

Jinliang Hu, Qin Li

[1]School of Medical Technology, Beijing Institute of Technology, No. 5 Zhongguancun South Street, Haidian District, Beijing 100081, P.R. China

Corresponding author e-mail address: liqin@bit.edu.cn

Abstract: Calcified nodule (CN) is a challenging subtype of coronary calcified lesion in percutaneous coronary intervention, and its automatic identification and precise segmentation are of great importance for pre-procedural risk assessment, lesion quantification, and treatment planning. Intravascular optical coherence tomography (IVOCT), with its high spatial resolution, has become a key imaging modality for CN assessment.

However, CN in IVOCT images is characterized by complex morphology, irregular boundaries, and limited annotated data, which restrict the performance and generalization of conventional deep learning methods. To address these issues, this study proposes an automatic CN identification and precise segmentation framework based on self-supervised pretraining and parameter-efficient fine-tuning. First, large-scale unlabeled IVOCT data are utilized for domain-specific self-supervised pretraining to learn more discriminative vascular tissue representations. Then, parameter-efficient fine-tuning is performed on a small set of expert-annotated samples to enable efficient transfer and adaptation to CN identification and segmentation tasks. In addition, a joint identification-segmentation strategy is introduced to improve lesion localization and boundary delineation in complex regions. The proposed study aims to alleviate the bottleneck caused by expensive annotation and limited medical data, and to provide a feasible solution for intelligent CN analysis in few-shot settings, thereby supporting precise evaluation of coronary calcified lesions and clinical decision-making.

[AIP-5] PIBM2026-0403-3

H&E and MPM image fusion based on generative adversarial network for breast cancer diagnosis

Tao Liu[1], Lianhuang Li[1], Xuan Tao[1, 2], Qihang Zhou[1], Huihan Yi[3], Longhui Hou[1], Yaqi Chen[1], Yanbin Wu[1], Aizhe Zhang[1], Jiaxin Zhu[1], Haodong Zhang[1], Jianxin Chen[1*], Deyong Kang[4*]

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, College of Photonic and Electronic Engineering, Fujian Normal University, Fuzhou 350007, China

[2]Department of Pathology, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China

[3]Fujian Key Laboratory of Precision Medicine for Cancer, Palmar Hyperhidrosis Research Institute, Department of Thoracic Surgery, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China

[4]Department of Pathology, Fujian Medical University Union Hospital, Fuzhou 350001, China

Corresponding author e-mail address: chenjianxin@fjnu.edu.cn; kangdeyong@fjmu.edu.cn

Abstract: Breast cancer is one of the malignant tumors with the highest global recurrence rate, and accurate diagnosis is essential for improving patient prognosis. Current clinical practice relies primarily on H&E-stained sections to evaluate tumor cell morphology and tissue architecture. However, such sections cannot effectively image collagen fibers within the tumor microenvironment, despite evidence that collagen remodeling is closely associated with tumor invasion and metastasis. Although multiphoton microscopy (MPM) enables specific, high-resolution imaging of collagen fibers, integrating these data with cellular morphology to assist pathologists in comprehensive tumor assessment remains technically challenging. To address these challenges, we collected 2,610 paired H&E and MPM images. Fourier transform was first applied to precisely register the two imaging modalities. The registered images were then split into training and test sets at an 8:2 ratio, and a generative adversarial network–based fusion model was developed to achieve co-localized imaging of cellular morphology and collagen fiber architecture. Comparisons with several mainstream image fusion methods were performed. Qualitative analysis showed that the proposed model generated fused images that not only preserved nuclear structural details from H&E staining but also effectively visualized collagen fiber textures from MPM images. Quantitative evaluation using multiple metrics (e.g., information entropy, structural similarity) demonstrated that the model outperformed all compared methods across all measures, achieving superior fusion quality and information fidelity. In summary, this study presents a GAN-based fusion model for H&E and MPM images that effectively co-localizes and integrates cellular morphology with collagen fiber architecture,

providing pathologists with a more comprehensive view of the tumor microenvironment and holds promise for improving the accuracy of breast cancer diagnosis and progression assessment.

[AIP-6] PIBM2026-0403-5

ResMNet: an Efficient Multi-scale Mixed Convolutional Neural Network for OCT Retinal Image Classification

Minghui Chen,[1,*] Qian Cai,[1] Shuting Ke,[1] Wenfei Ma,[1] Jintao Niu,[1] and Zhensheng Gu[2,]**

[1]Shanghai Engineering Research Center of Interventional Medical Device, the Ministry of Education of Medical Optical Engineering Center, School of Health Sciences and Engineering, University of Shanghai for Science and Technology, Shanghai 200093, China

[2]Department of Ophthalmology, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200092, China

**cmhui.43@163.com, **13901912983@163.com*

Abstract: While traditional machine learning methods have been widely applied to retinal disease classification, deep learning algorithms demonstrate superior efficiency in analyzing optical coherence tomography (OCT) images. This paper introduces ResMNet, an enhanced residual block architecture designed for the automatic classification of four types of OCT retinopathy images. Unlike conventional approaches that rely on fixed small convolution kernels, ResMNet employs parallel multi-scale feature extraction within a single residual block by utilizing mixed convolution kernel sizes. Furthermore, to enhance feature representation, the 3×3 convolution in the ResNet bottleneck is replaced with a novel Pyramid Split-Channel Attention (PSCA) module. We utilized Grad-CAM to visualize and validate ResMNet's ability to focus on specific lesion regions. Using a private OCT dataset, we compared ResMNet against state-of-the-art architectures, including Vision Transformers and modern CNNs. Evaluating its performance in terms of accuracy, sensitivity, and specificity, our results demonstrate that ResMNet achieves superior diagnostic precision compared to these advanced baselines. Ablation studies confirmed that ResMNet achieves robust results across various metrics, demonstrating its superiority and effectiveness.

[AIP-7] PIBM2026-0403-6

A deep learning unmixing with spectral correction and noise reduction for multiplexed fluorescence imaging

Wensong Li, Yong Deng [*]

MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

Corresponding author e-mail address: ydeng@hust.edu.cn

Abstract: Multiplexed fluorescence imaging enables simultaneous labeling and discrimination of multiple target molecules within the same biological sample, facilitating multiplexed spatial mapping of molecular interactions and thus supporting cross-scale system-level analysis at the cellular, tissue, and organ levels. However, as the number of fluorophores increases, spectral overlap between their emission spectra introduces crosstalk in the acquired images, necessitating post-processing via spectral unmixing. In practice, severe spectral overlap, intensity heterogeneity among fluorophores, and measured spectral distortions pose significant challenges to existing unmixing methods. Traditional approaches often yield images with substantial artifacts and low accuracy, failing to effectively eliminate fluorescence crosstalk. To address these issues, we

propose a novel general-purpose high-accuracy unmixing method. Built upon traditional linear spectral unmixing, our method incorporates a spectral correction module to compensate for spectral distortions and a noise reduction module to mitigate spectral overlap and intensity heterogeneity. The whole architecture is unrolled iteratively into a trainable deep neural network. Experimental results on 8-color fluorescent beads and 7-color mouse brain slices demonstrate that our method significantly improves unmixing accuracy, producing images free of obvious structural artifacts or signal loss. This work provides a reliable tool for the widespread application of multiplexed fluorescence imaging.

[AIP-8] PIBM2026-0404-1

Cross-species and multimodal cell-state trajectory modeling in brain aging and Alzheimer's Disease

Changwen Yang[1], and Haiming Luo[3]

[1]Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, 430074, Wuhan, China

[2]MoE Key Laboratory for Biomedical Photonics, School of Engineering Sciences, Huazhong University of Science and Technology, 430074, Wuhan, China

[3] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China.

Abstract: Biophotonic technologies, including advanced optical imaging and spatially resolved molecular profiling, are generating unprecedented multimodal data for studying brain aging and Alzheimer's disease (AD). However, integrating these heterogeneous datasets to uncover dynamic, disease-relevant cellular processes remains a fundamental challenge. Here, we present a causal artificial intelligence framework that models brain aging and AD as a cross-species, cross-region, and multimodal cell-state trajectory problem, enabling unified analysis of biophotonics-derived data.

Our approach constructs a hierarchical latent trajectory model to capture the progression of cellular states across both normal aging and disease. At the global level, the model learns a shared progression axis with branching structures that distinguish conserved mechanisms from species-specific and region-specific pathways. At intermediate and local levels, it integrates cell-type composition, cellular community interactions, and gene regulatory programs derived from single-cell, spatial transcriptomics, and imaging-informed biophotonic measurements. To enhance interpretability, the latent space is explicitly decomposed into shared and modality-specific components using structured constraints and biological priors.

Crucially, we incorporate biologically informed causal structure into the trajectory model. Guided by established AD hypotheses, we impose a directed graph over key pathological processes, including amyloid accumulation, tau pathology, neuroinflammation, synaptic dysfunction, and cognitive decline. This enables the estimation of trajectory-dependent causal effects from multimodal observations, resulting in a causal trajectory graph that links cellular dynamics to disease mechanisms.

By unifying multimodal biophotonic data with causal AI, this work provides a principled computational strategy for studying neurodegeneration and may facilitate the discovery of mechanistic biomarkers and therapeutic targets.

[AIP-9] PIBM2026-0404-2

AI-Enhanced Lensless Portable Cell Counter

E Du,[1*] Weizu Zhang,[1] Zhipeng Huang,[1] Keming Tan,[1] Shiguo Li,[1], Weifeng Zhang,[1] Guoqing Wang ,[1] Shengfeng Zeng,[2]andShuhao Shen[2,*]

[1] School of Microelectronics, Shenzhen University of Information Technology, Shenzhen 518172, China.

[2]Xidian University, Guangzhou Institute of Technology, Guangzhou,510555, China.

Corresponding authors:

*E Du*due@sziit.edu.cn ;*

*Shuhao Shen *shenshuhao@xidian.edu.cn*

Abstract: We present a low-cost, stand-alone lensless cell counter based on a Raspberry Pi. Unlike conventional systems that rely on bulky microscopes or commercial handheld counters requiring a tethered computer, our device integrates on-board image reconstruction, a touchscreen display, and WiFi/Bluetooth modules to communicate directly with a cloud server and a mobile application—no external computer is required. The lensless design employs an RGB LED as the illumination source, enabling multi-wavelength (three-color) imaging. The Raspberry Pi computationally reconstructs light-intensity maps from raw diffraction patterns at each wavelength and fuses them to generate a full-color microscopic image, which is displayed on the integrated touchscreen. Furthermore, an embedded AI algorithm performs cell morphological recognition, allowing the system to analyze HE-stained tissue sections and distinguish between normal and cancerous tissues. Automatic cell counting results and classification outcomes are simultaneously uploaded to the cloud or a paired smartphone via wireless connectivity. Preliminary validation using cultured cell samples shows good correlation with manual microscopy for counting. The total hardware cost is approximately 2600 RMB (≈ 360 USD), substantially lower than commercial portable counters. The entire device is battery-powered and fits within a portable enclosure. This device is well-suited for point-of-care testing, field pathology screening, and STEM education, offering an affordable, connected, and truly portable solution for cell counting and tissue analysis in resource-limited settings.

[AIP-10] PIBM2026-0404-3

Anatomy-aware spatio-temporal implicit neural representation for continuous photoacoustic tomography reconstruction and segmentation

Yutian Zhong[1,2,3], Jinchuang He[1,2,3], Chaobin Hu[1,2,3], and Li Qi[1,2,3,*]

[1]School of Biomedical Engineering, Southern Medical University, Guangzhou, China

[2]Guangdong Provincial Key Laboratory of Medical Image Processing, Southern Medical University, Guangzhou, China

[3]Guangdong Province Engineering Laboratory for Medical Imaging and Diagnostic Technology, Southern Medical University, Guangzhou, China

**Corresponding author e-mail address: qili@smu.edu.cn*

Abstract: Photoacoustic tomography (PAT) is fundamentally limited in terms of spatial continuity and structural fidelity by sparse sampling along the axial direction, posing significant challenges for both volumetric reconstruction and downstream anatomical analysis. Existing approaches typically address super-resolution (SR) and segmentation (SEG) as independent tasks, overlooking their intrinsic structural coupling.

Here, we propose an anatomy-aware spatio-temporal implicit neural representation framework (AST-INR) to reconstruct continuous three-dimensional PAT volumes from discretely sampled low-resolution inputs while enabling precise multi-organ SEG. Specifically, the feature encoder based on an enhanced deep SR backbone first extracts rich representations from the low-resolution PAT volume. These features, together with spatial coordinates, are fed into a spatially-aware implicit neural representation network, which models PAT data as a continuous function over 3D space, enabling reconstruction at arbitrary inter-slice resolutions. To capture long-range dependencies while maintaining computational efficiency, we introduce a gradient-guided gating mechanism that identifies structurally complex regions based on intensity gradients. Conditioned on this gating, we design a locally aware spatial attention module that operates only on these challenging regions.

Based on the reconstructed high-resolution volumes, we develop a Hyper-Connection SEG network to achieve dynamic, input-dependent feature aggregation for accurate multi-organ delineation. Crucially, a structure-aware constraint is imposed to enforce consistency between intensity gradients and anatomical boundaries, promoting mutual enhancement between SR and SEG. Notably, by treating the axial dimension as a generic continuous variable that represents either spatial position or temporal evolution, AST-INR seamlessly generalizes to both spatial super-resolution and temporal enhancement tasks without any architectural modification.

Extensive experiments across multiple commercial PAT systems and anatomical regions demonstrate that AST-INR consistently outperforms state-of-the-art SR and SEG approaches. The results highlight the importance of jointly modeling structure and intensity, providing a new paradigm for continuous and anatomically faithful PAT reconstruction.

[AIP-11] PIBM2026-0404-6

Enhancing Ring-Array Ultrasound and Photoacoustic Dual-Modality Reconstruction via Self-Supervised Deep Learning-Based Signal Interpolation

Hao Huang[1], Zhibo Xiao[1], Xiali Gao[1]，Yang Xiao[2]，Fan Meng[1]，Xuran Zhou[1]， Xuanhao Wang[2]，Junhui Shi[2]

[1]College of Biomedical Engineering & Instrument Science, Zhejiang University, Hangzhou 310027, China

[2] Zhejiang Lab, Hangzhou 311100, China

Corresponding author e-mail address: junhuishi@zhejianglab.org

Abstract: Ring-array ultrasound (US) and photoacoustic (PA) dual-modality imaging provide complementary anatomical and functional information for biomedical applications. However, hardware constraints, defective transducer elements, and the need for accelerated acquisition frequently result in sparse spatial sampling. This undersampling introduces severe grating lobes, structural artifacts, and a degradation of overall image quality. While fully-supervised deep learning methods have shown significant promise in interpolating missing signals prior to image reconstruction, their reliance on vast, fully-sampled ground-truth datasets limits their practical applicability, particularly for in vivo scenarios where obtaining pristine reference data is highly challenging. To address this limitation, we propose a novel self-supervised deep learning framework for signal interpolation tailored to ring-array US and PA dual-modality reconstruction. Operating directly on raw radio-frequency (RF) channel data, our method leverages a masked modeling strategy. The network is trained to predict artificially masked subsets of the available sparse sensor data, learning the inherent spatio-temporal coherence and physical wave propagation characteristics without ever requiring fully dense ground-truth acquisitions. Experimental evaluations using both phantom and in vivo datasets demonstrate that the proposed self-supervised method effectively recovers missing channel information. Consequently, it significantly suppresses background artifacts while improving spatial resolution, image contrast, and signal-to-noise ratio (SNR) in both modalities. The reconstructed dual-modality images substantially outperform those processed with traditional interpolation techniques and achieve quality comparable to models trained with full supervision. In conclusion, this self-supervised approach offers a robust, data-efficient, and clinically translatable solution for mitigating undersampling artifacts, facilitating high-fidelity and high-frame-rate ring-array US and PA imaging.

[AIP-12] PIBM2026-0404-7

A Spectral-Adaptive Framework for Cerebrovascular Segmentation in Photon-Counting Micro-CT using 3D Foundation Models

Siyi Huang[1], Xiuping Liu[2], and Tianwu XIE[1]

[1] Institute of Radiation Medicine, Fudan University, 2094 Xietu Road, Shanghai 200032, China

[2]Guangdong Jiangmen Chinese Medicine College, No.4 Longwan Road, Pengjiang District, Jiangmen City, Guangdong Province, China

Corresponding author e-mail address: tianwuxie@fudan.edu.cn

Abstract: In high-resolution micro-CT, precise cerebrovascular segmentation is frequently compromised by intense signal overlap between contrast-enhanced vasculature and adjacent bony structures. Photon-counting micro-CT (micro-PCCT) addresses this challenge via material decomposition, yielding spectral priors such as discrete iodine and calcium maps. However, existing 3D foundation models are primarily optimized for single-channel inputs, leaving them unable to effectively exploit these multi-modal spectral cues. In this work, we

propose a spectral-adaptive framework designed to integrate material priors into pre-trained vessel foundation models through a streamlined channel-expansion strategy. This method effectively resolves segmentation ambiguities at bone-vessel interfaces while preserving the robust feature representation capabilities of the pre-trained backbone. Experimental results demonstrate that VesselSpec significantly outperforms single-channel baselines, achieving a 4 times Dice improvement in whole-brain segmentation, particularly in skull-adjacent regions. Furthermore, we introduce a spectral-aware annotation pipeline that leverages material decomposition to generate high-fidelity vessel ground truth with minimal manual effort, thereby addressing the critical shortage of public cerebrovascular datasets in the micro-PCCT domain.

[AIP-13] PIBM2026-0405-1

SwinUNETR-ADMM framework enhances zero-Shot 3D vascular photoacoustic imaging in vivo

Fan Meng[1,2], Junhui Shi[1,2]

[1] College of Biomedical Engineering & Instrument Science, Zhejiang University, Hangzhou 310027, China

[2] Zhejiang Lab, Hangzhou 311100, China

Corresponding author e-mail address: junhuishi@outlook.com

Abstract: Photoacoustic imaging technology combines the high contrast of optics with the deep penetration of ultrasound, demonstrating immense potential for applications in biomedical imaging. However, when imaging deep biological tissues, this technology is often limited by extremely low signal-to-noise ratios and reconstruction artifacts caused by undersampling or light attenuation. Traditional deep learning augmentation methods heavily rely on large-scale paired labeled datasets; however, in clinical diagnostics and in vivo animal experiments, obtaining high-quality “ground truth” labels is not only costly but also often difficult to achieve due to physiological motion and environmental interference. To address this challenge, this paper proposes a zero-shot learning augmentation framework that does not rely on external training data. This framework innovatively adopts a dual-view self-supervised learning strategy, deeply coupling the SwinUNETR network—which possesses powerful hierarchical feature extraction capabilities—with the classic PnP-ADMM optimization algorithm to establish a physics-model-driven iterative recovery mechanism. Experimental results demonstrate that this method can significantly suppress background noise and eliminate structural artifacts when processing 3D photoacoustic data. The framework performs particularly well in enhancing microvascular connectivity and contrast, enabling the detailed characterization of deep tissue vascular systems under fully unsupervised conditions. This provides an efficient and robust technical pathway for the clinical translation of multidimensional photoacoustic imaging.

[AIP-14] PIBM2026-0405-19

AI-driven label-free exfoliated tumor cells identification using hyperspectral single-cell optofluidic

Hanqi Hu[1], Zongliang Guo[1], Siyi Hu[3], Mengjie Li[2], Tao Zhao[1], Hang Li[1], Kangfu Chen[1], Shuailong Zhang[1,*], Haixia Li[2,*] and Rongxin Fu[1,*]

[1]Beijing Institute of Technology, CHINA

[2]Department of Clinical Laboratory, Peking University First Hospital, CHINA

[3]Suzhou Institute of Biomedical Engineering and Technology, Chinese Academy of Sciences, CHINA

Corresponding author e-mail address: furongxin@bit.edu.cn; haixia.li@pkufh.com; shuailong.zhang@bit.edu.cn

Abstract: Bladder cancer poses a significant global health challenge, characterized by its high recurrence rate and potential for invasive progression. Currently, cystoscopy remains the gold standard for diagnosis, enabling direct visualization and histological confirmation. However, its invasive nature, cost, and operator dependence cause patient discomfort and necessitate repeated surveillance—a particular concern given the disease's propensity for recurrence. While non-invasive alternatives like urine cytology offer high specificity, their low sensitivity, especially for low-grade or early-stage tumors, limits their utility as standalone tests. To address these challenges, we propose an integrated platform that combines hyperspectral imaging (HSI) with active-matrix digital microfluidics (AM-DMF) for the precise, label-free identification and sorting of exfoliated tumor cells in urine (UTCs). AM-DMF leverages thin-film transistor electrode fabrication techniques, enabling precise control over droplet volumes down to 3 nL and supporting large droplet arrays. This platform enables precise dynamic manipulation of micro-scale droplets, effectively addressing HSI's inherent lack of sorting capability. Concurrently, HSI contributes its unique strength by providing label-free biochemical identification based on intrinsic cellular spectral fingerprints, thus eliminating AM-DMF's traditional dependence on labels or morphological features. We establish an end-to-end framework combining YOLOv11-based cellular segmentation with ResNet-driven spectral classification, which effectively distinguishes UTCs from epithelial cells (EPCs) based on their intrinsic biochemical profiles. The biological significance of the model's decision-making was verified through Grad-CAM analysis, while its sorting reliability was further validated by biophysical assays, including hyperspectral variance mapping (HVM) and power spectral density (PSD) analysis. Our platform's label-free nature obviates the need for additional reagents, reducing external variables and enhancing diagnostic efficiency. By leveraging the intrinsic spectral properties of the cells, our system can perform cell sorting based on inherent biophysical characteristics, providing a more versatile and scalable solution for clinical applications.

[AIP-15] PIBM2026-0405-2

A deep learning framework with sparse masked pretraining for robust and generalizable ear feature detection

Yubiao Yue[1], Rui Zheng[2,3], Zhuonan Wang[1,4,5,6], Zhenzhang Li[1] and Lijun Bai[1,*]

[1]The Key Laboratory of Biomedical Information Engineering, Ministry of Education, Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xian, 710049, China.

[2]Department of Otorhinolaryngology-Head and Neck Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510630, China.

[3]Department of Allergy, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, 510630, China.

[4]PET-CT Center, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, China.

[5]School of Nursing, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi, 710061, China

[6]School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an, Shaanxi, 710049, China.

Corresponding author e-mail address: bailijun@xjtu.edu.cn

Abstract: Accurate localization of ear abnormalities and anatomical structures in otoscopic images is essential for interpretable AI-assisted ear assessment. We present an ear feature detection framework based on YOLO with self-supervised pretraining. Specifically, we construct OTO180K, a large-scale multicenter dataset containing 180,000 otoscopic images from 87,718 participants across nine medical centers, annotated with 751,927 bounding boxes for 11 ear features, including fungus, hyperemia, and perforation. In addition, we collect 1,774,816 unlabeled endoscopic images for self-supervised pretraining. We apply SparK, a sparse masked image modeling method, to pretrain the backbones of YOLOv8, YOLOv9, and YOLOv10, followed by supervised fine-tuning. Experiments show that self-supervised pretraining consistently improves all YOLO variants. On the internal test set, mAP improves by 9.87%, 8.48%, and 8.02% for YOLOv8, YOLOv9, and YOLOv10, respectively. YOLOv8-SSL achieves the best overall performance, with an mAP of 0.779. On three external retrospective datasets, it achieves mAP values of 0.752–0.763. On four prospective multicenter datasets, the model remains stable, with mAP values of 0.721–0.744. These results demonstrate that SparK-pretrained YOLO enables robust and generalizable ear feature detection in otoscopic imaging.

[AIP-16] PIBM2026-0405-22

Elucidating lipid droplet morphology-function relationships during photodynamic therapy via fluorescent probe imaging and deep learning-based instance segmentation

Bingyang Liu[1,3], Jianling Chen[1], Yiru Peng[2,*], and Hongqin Yang[1,*]

[1] Key Laboratory of Optoelectronic Science and Technology for Medicine of Ministry of Education, Fujian Normal University, Fuzhou, 350007, China

[2] Fujian Provincial Key Laboratory of Advanced Materials Oriented Chemical Engineering, Fujian Normal University, Fuzhou, 350007, China

[3] School of Mechanical and Electrical Engineering, Sanming University, Sanming, 365004, China

** Correspondence: Yiru Peng* (Email: yirupeng@fjnu.edu.cn); Hongqin Yang* (Email: hqyang@fjnu.edu.cn)*

Abstract: Lipid droplets (LDs) are dynamic organelles involved in cellular lipid metabolism and energy homeostasis, yet their remodeling under therapeutic stress remains incompletely understood. In this work, an integrated optical-computational framework is presented to examine LD morphology-function relationships

during photodynamic therapy (PDT). A dual-functional fluorescent probe (PP-SiPc) enables both LD-specific imaging and photosensitized reactive oxygen species (ROS) generation, allowing time-resolved observation of LD behavior under light irradiation. For quantitative analysis, a fine-tuned StarDist instance segmentation model, adapted to CLSM-acquired LD images, is employed to segment LDs, with preliminary results demonstrating effective resolution of densely distributed and morphologically heterogeneous LDs. Time-lapse imaging combined with computational analysis permits tracking of single-LD morphological changes across PDT progression. Our initial results indicate that LDs exhibit heterogeneous remodeling patterns, reflected by variations in number, size, roundness, and spatial distribution, which are associated with intracellular ROS levels and cell viability. In addition, modeling based on multi-parametric LD features suggests potential for distinguishing different PDT response states. Overall, this study outlines a fluorescence imaging-guided and computation-assisted strategy for examining LD dynamics under PDT, providing a basis for further investigation of organelle-level responses to therapeutic stress.

[AIP-17] PIBM2026-0405-4

Multi-Label Automatic Recognition of Tumor-Associated Collagen Signatures in Multiphoton Microscopy Images

Longhui Hou[1], Yaxuan Xiao[1], Tao Liu[1], Letian Tang[1], Qihang Zhou[1], Yaqi Chen[1], Xuan Tao[1, 2], Aizhe Zhang[1], Jiaxin Zhu[1], Xiahui Han[1*]

[1]Key Laboratory of OptoElectronic Science and Technology for Medicine of Ministry of Education, Fujian Provincial Key Laboratory of Photonics Technology, College of Photonic and Electronic Engineering, Fujian Normal University, Fuzhou 350007, China

[2]Department of Pathology, the First Affiliated Hospital of Fujian Medical University, Fuzhou 350005, China

Corresponding author e-mail address: hxiahui@fjnu.edu.cn

Abstract: Breast cancer is a prevalent malignancy with high recurrence risk globally. Multiphoton microscopy (MPM) has identified eight prognostically significant tumor-associated collagen signature (TACS) patterns at the invasive front of breast tumors. However, current TACS identification relies on subjective, time-consuming manual annotation, while existing automated methods are limited to small regions and single-label classification. To address this, we propose a multi-label automatic recognition model for large-scale MPM image analysis. Using 4,325 MPM images with five-fold cross-validation, we developed an EfficientNet-based model integrated with an attention mechanism for end-to-end multi-label classification of TACS1-8. Experimental results demonstrate that our model effectively focuses on TACS-relevant structures via attention heatmaps and achieves superior performance in accuracy, recall, and exact match ratio compared to mainstream methods, significantly reducing manual workload while enabling holistic TACS pattern assessment.

[AIP-18] PIBM2026-0405-8

Physics-Guided Quantitative Photoacoustic Tomography: decoupling from data dependency

Pengwei Han[1], Jiao Li[1,*]

[1]State Key Laboratory of Precision Measurement Technology and Instruments, Tianjin University

Corresponding author e-mail address: jiaoli@tju.edu.cn

Abstract: Quantitative photoacoustic tomography (QPAT) aims to overcome light attenuation and restore intrinsic absorption contrast in deep tissues. Existing methods rely either on complex multi-modal hardware, computationally expensive iterative optical inversions, or data-driven models that lack generalizability due to incomplete *in vivo* datasets.

To establish a universal framework for accurate QPAT, we propose a dual-stage, physics-informed quantitative reconstruction method. First, a grid-based partitioned training strategy is introduced to correct speed-of-sound aberrations, robustly recovering high-fidelity initial acoustic pressure distributions. Second, this corrected pressure drives a physical-neural inversion module. By directly coupling a neural network with a Monte Carlo optical forward model, this stage iteratively optimizes the absorption map to strictly satisfy the physical laws of light propagation, entirely eliminating the reliance on large training datasets.

We progressively validated this dual-stage approach. Initial phantom and ex vivo tissue experiments confirmed its quantitative accuracy and practical feasibility. To rigorously test its strong generalizability, we evaluated the framework across diverse in vivo cross-domain datasets acquired from various photoacoustic imaging systems, including point transducers, ring arrays, hemispherical arrays, and different illumination schemes. Across these highly heterogeneous systems, the proposed method successfully reconstructed quantitative absorption maps consistent with underlying physiological structures, without requiring hardware-specific priors or training data. Ultimately, this framework provides a robust, highly generalizable solution for mapping intrinsic optical properties, advancing the precision of deep tissue functional imaging.

[AIP-19] PIBM2026-0406-15

Physics-informed multi-encoder adaptive optics enables rapid aberration correction for intravital microscopy of deep complex tissue

Xiangzhang Cheng[1,2*], Bo Wang[2*], Li Luo[2], Zhaowei Sun[2,3] and Sicong He[2†]

[1]Department of Biomedical Engineering, Southern University of Science and Technology, Shenzhen, China.

[2]Department of Immunology and Microbiology, School of Life Sciences, Southern University of Science and Technology, Shenzhen, China.

[3]Division of Life Science, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China.

**These authors contributed equally*

†Correspondence: hesc@sustech.edu.cn

Abstract: Tissue-induced optical aberrations fundamentally constrain intravital microscopy in deep or complex biological specimens. While adaptive optics (AO) can compensate for these aberrations, conventional AO methods are limited by either guide-star dependency or slow correction speeds. Here, we develop MeNet-AO, a multi-encoder network-based AO method that enables rapid, guide-star-free aberration correction. By integrating a noise-resilient, structure-independent feature extraction model with a physics-informed multi-

encoder architecture, MeNet-AO jointly decodes multiple large-amplitude aberration modes from wavefront-modulated image pairs, achieving an effective balance between prediction accuracy and temporal efficiency. Validated in living organisms, MeNet-AO improves fluorescence imaging in zebrafish brain and eye, enhances neuronal calcium transients and direction selectivity in mouse visual cortex, and enables subcellular-resolution microglial calcium imaging through thinned-skull windows – revealing spatiotemporally heterogeneous signaling patterns previously obscured by skull aberration. The speed and robustness of MeNet-AO in low-signal and scattering conditions establish it as a versatile platform for dynamic subcellular imaging deep within native tissue environments.

[AIP-20] PIBM2026-0406-6

Enhanced Deep-Tissue Imaging Quality in Hemispherical PACT via Automated First-Arrival Wavefront Mapping for Speed-of-Sound Compensation

Xuran Zhou[1,2], Xiali Gao[1,2], Fan Meng[1,2], Hao Huang[1,2], Zhibo Xiao[1,2], Xuanhao Wang[2,*], and Junhui Shi[1,2,*]

[1] College of Biomedical Engineering & Instrument Science, Zhejiang University, Hangzhou 310027, China

[2] Zhejiang Lab, Hangzhou 311100, China

**Corresponding author e-mail address: xh-wang@zhejianglab.org*

junhuishi@outlook.com

Abstract: High-resolution deep-tissue imaging remains a cornerstone of non-invasive preclinical research, where Three-Dimensional Photoacoustic Computed Tomography (PACT) provides unparalleled functional and structural insights. However, inherent speed-of-sound (SoS) heterogeneity at the medium-tissue interface triggers severe wavefront aberrations, compromising the reconstruction of deep-seated microvasculature with significant geometric artifacts. While dual-SoS compensation models can rectify these distortions, conventional reliance on manual boundary segmentation is highly inefficient for high-throughput screening or real-time in vivo hemodynamic monitoring.To overcome these scalability limits in current PACT frameworks, we introduce an automated signal-domain segmentation architecture optimized for a high-density, 1024-element hemispherical transducer array. The algorithm achieves sub-millimeter boundary localization by automatically identifying the first-arrival photoacoustic peaks across individual A-lines, effectively mapping the acoustic transition interface directly from the raw sinogram, entirely eliminating the need for manual assumptions.To rigorously verify the boundary calculation accuracy, an irregular vascular phantom was utilized, demonstrating a near-zero deviation between the estimated interface and the ground truth. Leveraging this high-precision boundary data, our automated compensation scheme significantly sharpens deep-tissue vascular networks and suppresses off-focus clutter that plagues standard uniform-SoS reconstructions. This approach substantially enhances the imaging depth and quality of hemispherical PACT systems, offering a robust solution for high-fidelity in vivo imaging in acoustically heterogeneous biological environments.

Keywords: Photoacoustic, PACT, Speed-of-Sound Heterogeneity, Automated Boundary Segmentation

[AIP-21] PIBM2026-0407-1

Imaging Consistency Guided Aberration Correction for In Vivo Deep Tissue Optical Imaging

Yuxi Deng[1,2] and Zhenhua Hu[1,2]

[1]Beijing Key Laboratory of Molecular Imaging Technology Research and Translation, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China

[2]School of Artificial Intelligence, University of Chinese Academy of Sciences, Beijing 100049, China

Corresponding author e-mail address: zhenhua.hu@ia.ac.cn

Abstract: During in vivo deep-tissue optical imaging, complex aberrations are readily induced by tissue scattering, spatially heterogeneous refractive indices, and system mismatch, resulting in point spread function broadening, reduced image contrast, and attenuation of high-frequency details, which severely limits the accurate characterization of deep microstructures. To address the limitations of conventional aberration correction methods, which often rely on wavefront sensing, standard-sample calibration, or dedicated hardware compensation and thus suffer from high cost and limited response speed, we propose an imaging-consistency-constrained aberration correction method for in vivo deep-tissue imaging. Taking degraded images as input, the proposed method constructs a point-spread-function-guided imaging degradation and correction model. A physics-based point spread function forward network is introduced to characterize aberrations, and an image inversion and reconstruction network is further incorporated to unify aberration estimation and image restoration within a single optimization framework. On this basis, data consistency and local structure preservation constraints are imposed in the objective function to jointly suppress aberration-induced blur diffusion, edge distortion, and detail loss. Furthermore, to accommodate the spatially heterogeneous and depth-dependent aberration distribution in living tissues, a spatially adaptive iterative update strategy is employed to dynamically adjust the aberration compensation strength and restoration weights across different regions, thereby enhancing the recovery of weak-signal areas, low-contrast edges, and fine textural structures. Preliminary experimental results demonstrate that the proposed method achieves effective aberration compensation and image quality enhancement, yielding a peak signal-to-noise ratio of 29.2568 and a structural similarity index of 0.8343, which indicates favorable structural recovery capability and imaging fidelity. The proposed method does not require additional wavefront measurements or cumbersome pre-calibration, and offers good flexibility and adaptability, providing an extensible computational imaging strategy for high-quality in vivo deep-tissue optical imaging.

[AIP-22] PIBM2026-0407-2

A World-Model-driven Vision Speculation Framework for High-throughput Fluorescence Microscopy

Qiushi Huang[1,2], and Zhenhua Hu[1,2]

[1]Beijing Key Laboratory of Molecular Imaging Technology Research and Translation, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China

[2]School of Artificial Intelligence, University of Chinese Academy of Sciences, Beijing 100049, China

Corresponding author e-mail address: Zhenhua.hu@ia.ac.cn

Abstract: Achieving high-resolution fluorescence microscopy across a large field of view (FOV) is critical for biological research, yet conventional high-throughput imaging is hindered by the necessity of dense,

overlapping tile acquisition for seamless reconstruction. These redundant scanning protocols not only limit temporal resolution but also significantly increase phototoxicity risks. In this paper, we propose a paradigm shift by introducing a World-Model-driven Vision Speculation framework that enables seamless whole-FOV reconstruction from sparse, non-overlapping scans. We reformulate the scanning process as an agent interacting with a biological "world" and develop a World Model that learns the latent structural and spatial regularities of biological tissues. By encoding visual observations into a compact latent space and utilizing stage movement priors as action tokens, the model acts as a predictive engine capable of speculating the content of unobserved regions between non-overlapping tiles. This approach transforms the reconstruction process from reactive synthesis into proactive vision speculation based on a deep understanding of the sample's global context. Experimental evaluations on various biomedical datasets, including brightfield and Stimulated Raman Scattering imaging, demonstrate that our World Model framework significantly outperforms standard generative methods in maintaining long-range structural continuity and eliminating boundary artifacts. By bypassing the need for physical overlap, our method substantially increases imaging throughput while reducing light exposure, establishing a foundation for autonomous, environment-aware microscopy that can intelligently navigate and reconstruct complex biological landscapes for high-throughput clinical and research applications.

[AIP-23] PIBM2026-0407-3

Diffusion-Based Model for Fluorescence Image Enhancement

Jinze Zhao[1], Zhenhua Hu[2]

[1]Beijing Key Laboratory of Molecular Imaging Technology Research and Translation, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China

[2]School of Artificial Intelligence, University of Chinese Academy of Sciences, Beijing 100049, China

Abstract: Near-infrared imaging in the second window (NIR-II) has emerged as a powerful tool for deep-tissue biomedical imaging due to its reduced scattering, diminished autofluorescence, and enhanced tissue penetration. In particular, NIR-IIb imaging provides superior spatial resolution and higher signal-to-background ratio compared to NIR-IIa, enabling detailed visualization of fine anatomical structures such as microvasculature, organ boundaries, and small lesions. Despite its advantages, the clinical application of NIR-IIb imaging is severely restricted because most available NIR-IIb probes lack FDA approval, limiting their safe use in human studies and broader biomedical investigations. To address this challenge, we propose an unpaired image translation framework that converts NIR-IIa images into NIR-IIb-like representations without the need for paired training data. The framework models the cross-domain mapping as a progressive refinement process, where images are gradually transformed toward the target domain while preserving high-frequency details. This approach enhances training stability and mitigates artifacts commonly encountered in generative models. Additionally, a structure-preserving constraint is incorporated to explicitly maintain the consistency of anatomical features during translation, ensuring that the generated images faithfully reflect the underlying morphology of the original NIR-IIa images. Experiments demonstrate that the proposed framework effectively improves image contrast, reduces scattering-induced degradation, and enhances the visibility of fine structures. The generated NIR-IIb-like images exhibit high structural fidelity and clear visualization of features that are typically challenging to resolve in standard NIR-IIa images. By providing a reliable computational alternative to direct NIR-IIb imaging, this approach enables researchers and clinicians to obtain high-quality images without exposing subjects to potentially unsafe probes. Overall, the proposed method offers a practical and accessible solution for approximating NIR-IIb imaging, facilitating safer biomedical

imaging and supporting future studies in diagnostics, surgical guidance, and preclinical research.

[AIP-24] PIBM2026-0519-1

VesselSpec: Spectral-Adaptive Foundation Model for Cerebrovascular Segmentation in Micro-PCCT

Siyi huang[1], Enze Zhou[2], Yihao Zhao[2] , Zehao Yang[2], Yi Feng[2], Hanfei Xu[2], Linhan Yang[2], Shaoyang Wang[2], Qian Liu[2] and Tianwu Xie[1]

[1]Institute of Radiation Medicine, Fudan University, Shanghai, China,

[2]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering,

Hainan University, Haikou, China

Corresponding author e-mail address: tianwuxie@fudan.edu.cn

Abstract: Precise cerebrovascular segmentation in high-resolution micro-CT is often hindered by intense signal overlap between contrast-enhanced vasculature and bony structures. Photon-counting micro-CT (micro-PCCT) offers a solution through its material decomposition capabilities, providing spectral priors such as iodine and calcium maps. However, current 3D foundation models are typically optimized for single-channel inputs and cannot effectively exploit these multi-modal spectral priors. We present VesselSpec, a spectral-adaptive framework that integrates material priors into pre-trained vessel foundation models through a minimal channel-expansion strategy. This approach effectively resolves segmentation ambiguities at bone-vessel interfaces while preserving the backbone's robust pre-trained knowledge. Experimental results demonstrate that VesselSpec significantly outperforms single-channel baselines, achieving a 4.3 times Dice improvement in whole-brain segmentation including skull-adjacent regions. Furthermore, our spectral-aware annotation pipeline leverages material decomposition to construct vessel ground truth with minimal manual effort, addressing the lack of public cerebrovascular datasets for micro-PCCT.

[AIP-25] PIBM2026-0522-2

Segmentation of Cerebral Microvessels in Alzheimer's Disease Based on Mamba

Zhe Zhou[1],Yuxin LI[1],Weijie He[1],Fangqi Deng[1],Anan Li[2,3], Xiangning Li[3], Tao Jiang[2]

[1]Shaanxi Key Laboratory of Network Computing and Security Technology, School of Computer Science and Engineering, Xi'an University of Technology, Xi'an, 710048, China

[2]HUST-Suzhou Institute for Brainsmatics, Suzhou, 215123, China

[3]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 572025, China

Corresponding author e-mail address:liyuxin@xaut.edu.cn

Abstract: Pathological progression of Alzheimer's disease (AD) is closely associated with morphological abnormalities in the cerebral microvascular network. Accurate 3D segmentation of AD cerebral microvessels provides important quantitative evidence for investigating the pathological mechanisms of AD. Currently, whole-brain 3D high-resolution cerebrovascular imaging of AD can be achieved via lectin-specific fluorescence labeling and high-resolution fluorescence micro-optical sectioning tomography (HD-fMSOT), which provides a

stable data foundation for pathological studies of AD cerebral microvessels. However, images acquired by this technique still have multiple limitations: Aβ amyloid deposition in AD brain samples introduces extensive complex background noise, while fine microvessels with slender diameters and low imaging contrast are highly prone to structural connectivity breakage. These defects greatly increase the difficulty of accurate cerebral microvessel segmentation. To address the above challenges, we propose an automated 3D segmentation framework for AD cerebral microvessels based on the Mamba architecture. We built a U-shaped encoder-decoder backbone network with 3D convolutional residual blocks, **introduced the Mamba layer** to capture long-range spatial dependencies of the vascular network, embedded a Gated Spatial Convolution (GSC) module to extract fine local features of microvessels, and adopted a Focal-Dice joint loss function to simultaneously ensure the segmentation accuracy of low-contrast fine microvessels and the overall topological connectivity of the vascular network. Experimental results show that the proposed method achieves the optimal segmentation performance on the test set, and can effectively preserve the topological connectivity and structural integrity of the microvascular network. This framework can provide support for the neuropathological analysis of Alzheimer's disease.

Keywords: Alzheimer's disease, Cerebral microvessels, 3D image segmentation, Mamba, HD-fMSOT

[AIP-26] PIBM2026-0604-1

Intelligent identification of single-cell drug responses based on dynamic light scattering speckle videos

Cong Xiao[1], Wanlin Xu[1], Meiai Lin[1], and Xiangyuan Ma[1]

[1]Department of Biomedical Engineering, College of Engineering, Shantou University, Shantou, China.

Corresponding author e-mail address: maxiangyuan@stu.edu.cn

Abstract：Label-free, dynamic monitoring of single-cell drug responses is important for drug screening, dose–response analysis and the assessment of cellular functional states. Compared with conventional methods that rely on endpoint assays or exogenous labels, dynamic light scattering (DLS) speckle imaging can record drug-induced microscopic dynamic changes in cells under non-invasive conditions, providing a new source of information for analysing cellular pharmacological responses. However, single-cell DLS videos contain complex spatiotemporal fluctuation patterns. Their signal changes are often high-dimensional, nonlinear and strongly cell-specific, making it difficult for conventional feature-extraction methods to fully capture drug-related dynamic information. To address this challenge, we developed an intelligent method for identifying single-cell drug responses from DLS speckle-dynamics videos. The method takes high-frame-rate single-cell speckle videos as input and uses a two-stream feature-extraction architecture to learn spatial speckle-distribution features and temporal dynamic-change features separately. An interactive spatiotemporal feature-fusion strategy is then introduced to jointly model drug-response information across different dimensions. To evaluate the effectiveness of the method, we used highly invasive MDA-MB-231 breast cancer cells as the study model, collected DLS speckle-video data under different inhibitor and concentration conditions, and performed drug dose–response classification experiments. The experimental results show that the proposed method can effectively distinguish cellular response states induced by different concentrations of the same drug, and achieves good classification stability and applicability across multiple drug conditions. This study provides a data-driven analytical strategy for label-free and non-invasive monitoring of single-cell drug responses, and

offers a technical reference for future high-throughput drug screening, dose optimization and studies of cellular phenotypic dynamics.

[AIP-27] PIBM2026-0604-3

End-to-End Automated Characterization Framework for Dynamic Flow Light Scattering Videos Based on Deep Learning and Domain Adaptation

Pengfei Gao[1], Linchun Xu[2], Meiai Lin[1]

[1]Department of Biomedical Engineering, College of Engineering, Shantou University, Shantou, Guangdong, China

[2]Department of Hematology, The First Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, China

Corresponding author e-mail: baklala_xu@outlook.com

Abstract: The optical physical parameters of organelles, such as refractive index and size, reflect their structural characteristics and physiological states, and are of great significance for biomedical detection, cell-state assessment, and material characterization. Light scattering techniques capture spatial fringe patterns generated by the interaction between incident light and microscopic structures, providing a potential basis for label-free parameter inversion of microscale particles. However, conventional light scattering characterization methods commonly rely on iterative inversion algorithms, which are computationally complex, time-consuming, and sensitive to initial conditions, thereby limiting their applicability to high-throughput, automated, and real-time analysis.

In this study, we propose a deep learning-based end-to-end automated characterization framework for directly regressing key physical parameters of microsphere particles from dynamic flow light scattering videos. Built upon the physical principles of light scattering, the framework employs simulated data with well-defined parameter labels to construct a supervised training set and trains a VGG16 regression network via transfer learning. This enables the model to automatically learn the nonlinear mapping between scattering fringe patterns and particle physical parameters. To mitigate the domain discrepancy between simulated images and real flow light scattering images, including differences in fringe sharpness, image contrast, noise distribution, and background characteristics, a hybrid domain adaptation strategy combining image-level realistic augmentation and feature-level distribution alignment is further introduced. Experimental results demonstrate that the proposed end-to-end framework can effectively extract scattering representations associated with optical physical parameters. After realistic augmentation and domain adaptation calibration, the model achieves improved prediction stability and generalization performance on real microsphere and flow light scattering images.

This study provides a feasible deep learning approach for label-free, high-throughput, and automated characterization of optical parameters in microscale particles and organelle-related structures.

[AIP-28] PIBM2026-0617-7

A hybrid efficient Transformer network for gland segmentation in confocal laser endomicroscopy

Yifan Chen[1], Jingjun Zhou[1], and Qian Liu[1]

[1] School of Biomedical Engineering, Hainan University, Haikou, Hainan 570228, China

Corresponding author e-mail address: juingzhou@hainanu.edu.cn

Abstract: Gland segmentation represents a critical phase in the pathological diagnosis of digestive tract cancers via confocal laser endomicroscopy. However, due to high morphological variability and complex pathological backgrounds, traditional convolutional neural network (CNN) methods face limitations in capturing global context, while standard Transformer-based approaches suffer from heavy computational overhead and loss of local fine-grained details. To address these challenges, this paper presented a hybrid efficient Transformer network (HET-Net) to systematically minimize computational overhead while preserving segmentation fidelity. The proposed model incorporated a compound-scaled EfficientNet-B2 backbone as the feature encoder to substantively compress parameter redundancy from the foundational layers. At the deep layers of the network, a novel grouped self-attention bridge module was engineered; by leveraging a channel-grouping computational strategy, this module achieved low-cost, long-range global context dependency modeling while multiplying the reduction of computational complexity inherent to standard self-attention mechanisms. Furthermore, an adaptive channel calibration scheme was introduced within the skip-connection paths to modulate multi-scale feature alignment dynamically, effectively suppressing background noise. Extensive evaluations on a clinical database comprising 1,720 images from 114 subjects and the public GlaS dataset demonstrated that the network yielded Dice similarity coefficients of 91.72% and 90.71%, respectively. Meanwhile, HET-Net featured a parameter volume of merely 8.61 M, constituting approximately 27.7% of the classic U-Net model. Compared with mainstream frameworks such as U-Net, Swin-Unet, and TransUnet, the developed architecture achieved superior segmentation performance with a substantially lower parameter footprint, offering a high-efficiency paradigm for future computer-aided clinical diagnostic systems.

[AIP-29] PIBM2026-0618-11

Histological Feature Distillation for Unpaired CLE-to-H&E Virtual Staining

Dongfan Zhang[1], Jingjun Zhou[1], and Ling Fu[1]

[1]School of Biomedical Engineering, State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, Hainan University, Haikou, Hainan, China

Corresponding author e-mail address: zhou2j@hainanu.edu.cn

Abstract: Intraoperative histological assessment is crucial for surgical guidance and clinical decision-making. Confocal laser endomicroscopy (CLE) provides in vivo microscopic imaging at cellular resolution, but diagnostic interpretation still relies on hematoxylin and eosin (H&E) staining, the clinical gold standard. Recent advances in deep learning have demonstrated the feasibility of digital staining through supervised model training. However, the substantial modality gap between in vivo CLE and ex vivo H&E images prevents the acquisition of accurately paired data. To address this problem, we propose a self-supervised H&E-domain feature distillation framework for unpaired CLE-to-H&E virtual staining. Specifically, an H&E teacher encoder is first pretrained only on real H&E images and then kept frozen to encode domain-specific histological priors. During translation, the CLE-to-H&E generator is treated as the student and is guided to align generated virtual

H&E representations with real H&E images in the teacher's multi-layer feature space, thereby distilling histopathological characteristics learned from the H&E domain into the virtual staining process. Experimental results demonstrate that the proposed teacher-guided framework improves histopathological realism, preserves mucosal structures, and generates tissue representations with greater histological consistency with real H&E images, showing its potential for assisting CLE-based tissue interpretation.

[AIP-30] PIBM2026-0618-14

Deep learning-based super-resolution reconstruction and three-dimensional analysis of neuromuscular junction fluorescence volumes

Yujia Kang[1], Xizhi Meng[1],Tingting Yu[1],Zhengrui Wang[1],Yuening He[1], Dan Zhu*[1]

[1]MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics -Advanced Biomedical Imaging Facility, Huazhong University of Science and Technology, China

Corresponding author e-mail address: dawnzh@mail.hust.edu.cn

Abstract: Neuromuscular junctions (NMJs) are peripheral synapses formed by motor neuron axon terminals, skeletal muscle fibers, and terminal Schwann cells. Their innervation/denervation status and 3D morphological structure are important readouts of peripheral pathology associated with neuromuscular disease and aging. However, current NMJ assessment is usually performed on locally acquired high-resolution image volumes, from which morphology and colocalization metrics are quantified, making it difficult to capture spatially heterogeneous NMJ changes at the whole-muscle scale. Whole-muscle analysis therefore requires large-volume imaging, super-resolution reconstruction of fine junctional structures, and accurate quantitative analysis. In this study, we developed a deep learning method for NMJ super-resolution reconstruction and 3D morphometric analysis. Pixel-registered training data, comprising real low-resolution light-sheet volumes and corresponding high-resolution references, were constructed through cross-resolution registration and CycleGAN-based degradation modeling. For sparse and anisotropic NMJ volumes, we built a super-resolution reconstruction model with residual gated channel attention, an anisotropy-aware Mamba branch, and task-specific losses that enforce structural fidelity. On independent test volumes, the method increased ROI-based PSNR from 12.6 dB to 32.1 dB, ROI-based SSIM from 0.19 to 0.89, and MIP-SSIM from 0.27 to 0.95. Ablation experiments confirmed the effectiveness of these components in improving super-resolution reconstruction quality. We also developed NMJ Explorer, a reproducible platform for 3D NMJ quantification. It uses a postsynaptic-anchored segmentation strategy, restricts presynaptic signals to local colocalization regions, and outputs quantitative descriptors covering morphology and pre-/post-synaptic colocalization. The platform supports analysis of whole-muscle large-volume image data, generates NMJ density maps and spatial-distribution statistics, and enables cross-sample comparison through tiered confidence outputs and complete provenance records. Overall, this study extends NMJ analysis from local inspection to whole-muscle-scale, high-resolution, and traceable 3D quantification, providing reliable methodological support for NMJ studies in neuromuscular disease and aging.

[AIP-31] PIBM2026-0618-17

High-Resolution Photon-Counting CT Imaging and Systemic Mapping of the Mouse Cerebrovasculature

Zongyin He[1], Feng Yi[1], Enze Zhou[1], Shaoyang Wang[1], Qian Liu[1] and Ling Fu[1]

[1]School of Biomedical Engineering, State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, Hainan University, Haikou, Hainan, China

Corresponding author e-mail address: zongyinhe@gmail.com

Abstract: While Photon-Counting CT (PCCT) yields ultra-high-resolution cerebrovascular images, massive whole-brain datasets hinder fluent interaction and precise annotation. We propose Vessel-G, a 3D annotation system optimized for large-scale PCCT. It utilizes a novel "display-analysis separation" architecture: the display pipeline uses integer mapping and dynamic volume rendering for rapid interaction, while the analysis pipeline preserves floating-point precision for accurate tracking. Integrating block-wise ROI reading and asynchronous rendering overcomes interaction bottlenecks. Features include collaborative point-picking, SWC topological closed-loops, and deep-learning-assisted mask generation. Evaluations demonstrate a 50% reduction in GPU memory. Crucially, annotating complex mouse cerebrovasculature (1,383 nodes, 1,392 edges) was accelerated from weeks to 5 hours. Vessel-G establishes an efficient workflow from image browsing to label output, advancing cerebrovascular morphological analysis.

[AIP-32] PIBM2026-0618-22

Perceptual Reconstruction with Explainable Quality Assessment for High-Throughput Biomedical Imaging

Xinbo Zhang[1], Yihui Luo[1], Hongqin Liu[1], Anan Li[1], Chi Xiao[1*]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, 572025, China

xiaochi@hainanu.edu.cn

Abstract: High throughput biomedical imaging, such as fluorescence micro optical sectioning tomography (fMOST), enables sub micron whole brain structural imaging in mice but faces critical data quality challenges during prolonged acquisition due to equipment drifts and specimen variations. Manual inspection is subjective, delayed, and uninterpretable. To address this, we propose SFRR CLIP, an intelligent quality assessment and real time monitoring method based on perceptual reconstruction and multimodal semantic alignment. Built on the CLIP vision language model, SFRR CLIP integrates a wavelet based adapter (SFRRAdapter) that generates pseudo reference features online, and employs semantic modulation, band energy gating, and residual mask reconstruction to restore low quality images, classify their quality, and locate anomalies. Trained on 9,136 fMOST image pairs, our method achieves F1 scores of 0.964 (normal) and 0.899 (abnormal), outperforming FDP Net, AA CLIP, and other state of the art methods, while providing interpretable textual descriptions. Ablation studies confirm the contribution of each module. In deployed systems, manual attendance drops from 50% to 30% without increasing per section acquisition time. On the public VisA anomaly detection dataset, the model achieves an average AUROC of 95.7%, demonstrating strong generalization. Overall, this work offers online quality assessment, anomaly alerting, and text based quality control for long term high throughput imaging, providing practical technical support for data integrity in large scale brain imaging studies.

[AIP-33] PIBM2026-0618-24

PGRMamba: Geometry-Guided State Space Models for 3D Soma Detection in Large-Scale Whole-Brain Images

Zibin Cai[1], Rou Li[1], Yan Jiang[1],Jiamin Lin[1],Mengting Zhao[1,2],Anan Li[1,2,3],and Chi Xiao[1]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 572025, China.

[2]HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215123, China.

[3]Wuhan National Laboratory for Optoelectronics, and MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan 430074, China.

Corresponding author e-mail address: (xiaochi@hainanu.edu.cn)

Abstract: Constructing high-precision whole-brain connectomes and single-neuron morphology maps heavily relies on precise 3D soma detection. However, existing CNNs lack long-range spatial modeling, while Transformers suffer from quadratic complexity on large-scale high-resolution 3D whole-brain data. Furthermore, massive tubular axonal fibers and extreme soma density variations pose significant challenges. To address these issues, we propose Physics-Geometric Region-Gated Mamba (PGRMamba) with linear complexity. First, a Dual-Stage Filtering Block (DSFB) leverages 3D Difference of Gaussians priors to enhance spherical soma responses while suppressing tubular fibers. Second, a Geometric-guided Sparse Attention Module (G-SAM) is proposed to achieve targeted, lightweight long-range context modeling. Finally, a Gradient-Calibrated Affinity Loss (GCA-Loss) is introduced to mitigate structural noise and bolster robustness against sparse distributions. We evaluated PGRMamba on a newly constructed retrograde dataset (3D-NSD) and a public anterograde dataset (WMBSD) via strict leave-one-brain-out cross-validation. Extensive experiments demonstrate that PGRMamba achieves state-of-the-art performance. On 3D-NSD, it yields a 92.47% recall and a 92.35% F1-score. On WMBSD, precision, recall, and F1-score all exceed 96% (reaching 96.49%, 96.13%, and 96.31%, respectively), with a single-volume inference time of 0.20s achieving up to 220-fold acceleration over Cellpose-SAM. Notably, PGRMamba completes soma localization for an entire retrograde-tracing mouse whole-brain dataset at 1×1×2μm³ resolution in approximately 45 minutes on a single RTX 5880 Ada GPU, demonstrating its scalability for high-throughput whole-brain neuroscience analysis.

[AIP-34] PIBM2026-0618-25

Adapting MedSAM for Neuronal Soma Segmentation via Multi-Model Ensemble Self-Training

Liangbo Song ,Xiaoquan Yang ,Li Ma*

State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 570228, China

**mali@hainanu.edu.cn*

Abstract: To address the scarcity of annotated neuronal soma data, this paper proposes a segmentation method that adapts MedSAM through multi-model ensemble self-training. The core idea is to generate high-quality soft pseudo-labels that effectively highlight somata while suppressing background interference. Specifically, candidate soma centers are first extracted from predictions of multiple segmentation models, from which a distance map is constructed—this map yields high responses in soma-center regions and gradually decays toward low responses at boundary regions. For boundary pixels where the distance map alone

provides insufficient cues, a multi-model consistency score is adopted as the foreground probability to refine the pseudo-labels in these regions, compensating for the diminished response of the distance map at boundaries. Meanwhile, Voronoi partitioning is applied to explicitly set the dividing lines between adjacent somata as background, thereby mitigating cell adhesion artifacts. Building upon these pseudo-labels, we design an uncertainty-guided loss function that adaptively down-weights the contribution of low-confidence regions according to their estimated reliability, reducing the influence of potentially erroneous labels, and further refine the pseudo-labels through iterative self-training of MedSAM. Experiments on neuronal datasets from mouse and macaque brains demonstrate that the multi-model ensemble pseudo-labels significantly outperform predictions from any single model; fine-tuning various cell segmentation models with these pseudo-labels achieves performance closely approaching that of fully supervised training with ground-truth annotations; and ablation studies further confirm the necessity of jointly leveraging the distance map, multi-model consistency score, and Voronoi dividing lines, while also validating the effectiveness of the uncertainty-weighted loss and pseudo-label update strategy.

[AIP-35] PIBM2026-0618-27

Reconstruction and Automated Quantitative Analysis of Intestinal Villi from Three-Dimensional Optical Microscopy Images

Li Liu[1], Zhencheng Ren[1], Zixuan Zhou[1] , Anan Li[1 2 3],Chi Xiao[1 2]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 572025, China [2]HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215123, China.

[3]Wuhan National Laboratory for Optoelectronics, MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan 430074, China.

Abstract: Three-dimensional optical microscopic imaging enables the acquisition of continuous high-resolution spatial information from large-volume biological tissues, providing a powerful tool for the visualization and quantitative characterization of complex tissue microstructures. However, the dense distribution and complex morphology of intestinal villi make it difficult for conventional two-dimensional histopathology to preserve complete spatial information. Moreover, existing analytical methods are often unable to fully exploit morphological information contained in three-dimensional optical imaging datasets, limiting quantitative characterization of intestinal mucosal architecture.In this study, mouse small-intestine optical microscopy images were acquired using fluorescence Micro-Optical Sectioning Tomography (fMOST). A dual-scale analytical framework integrating a 4.5μm tissue-level scale and a 0.45μm single-cell scale was developed for reconstruction of the intestinal inner-surface topography and automated quantitative analysis. Deep learning-based segmentation combined with three-dimensional instance separation, skeleton analysis, and surface reconstruction was employed to achieve automated extraction of the intestinal epithelium and reconstruction of villus structures. At the tissue level, morphological parameters reflecting overall mucosal architecture were quantified. At the single-cell level, a microstructural parameter system was established to characterize epithelial surface features, enabling quantitative assessment of intestinal mucosal morphology across tissue and cellular scales.Experimental results showed that the nnU-Net model achieved a Dice coefficient of 0.9619 and an Intersection over Union (IoU) of 0.9267 on the test set. Validation using virtual villus phantoms confirmed the accuracy and stability of the proposed workflow. By integrating optical microscopy with intelligent image analysis, this study provides a new approach for morphological investigation

of complex gastrointestinal tissues. The proposed framework may serve as an optical characterization tool for intestinal disease model evaluation, drug-induced intestinal toxicity assessment, and spatial omics registration, while establishing a methodological foundation for future in vivo quantitative imaging of the entire small intestine using circumferential endoscopic scanning technologies.

[AIP-36] PIBM2026-0618-9

SparsePath-CTNet: A direction-aware hybrid network for sparse-view PCCT image reconstruction

Jiaxuan Xu[1], Jingjun Zhou[1], Shaoyang Wang[1], Enze Zhou[1] , Qian Liu[1] and Ling Fu[1]

[1]School of Biomedical Engineering, State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, Hainan University, Haikou, Hainan, China

Corresponding author e-mail address: zhou2j@hainanu.edu.cn

Abstract: Sparse-view photon-counting computed tomography (PCCT) has emerged as a promising low-dose imaging technique that enables multi-energy spectral imaging with reduced radiation exposure. However, angular undersampling inevitably introduces severe streak artifacts and structural distortions, posing significant challenges for high-quality image reconstruction. Although recent deep learning-based reconstruction methods have substantially improved sparse-view CT reconstruction, effectively preserving local anatomical details while suppressing globally distributed streak artifacts remains challenging.To address this issue, this study proposes SparsePath-CTNet, a U-shaped hybrid architecture with direction-aware Mamba for sparse-view PCCT reconstruction. The encoder and decoder adopt convolutional blocks for local feature restoration, while PathStateMixerMamba is introduced into the bottleneck layer to capture long-range spatial dependencies through horizontal, vertical, diagonal, and reverse path scanning. Experiments on 1/16-view and 1/12-view sparse sampling settings show consistent improvements over convolution-based, Transformer-based, and SSM-based methods, achieving average gains of 1.4 dB in PSNR and 1.0% in SSIM.

[AIP-37] PIBM2026-0629-1

OCTSAM: A joint denoising and segmentation framework for retinal OCT image analysis

Ji Bo[1,3], Yidi Wang[1,3], Sizhu Ai[2,3], Yuxin Zhao[3], and Xingdao He[1,3]

[1]Beihang University, Beijing 100191, China

[2]Tianjin University, Tianjin 300072, China

[3]Key Laboratory for Optoelectronic Information Perception and Instrumentation of Jiangxi Province, Nanchang Hangkong University, Nanchang 330063, China

Corresponding author e-mail address: 13834453612@163.com

Abstract: Optical coherence tomography (OCT) has become an essential imaging modality for diagnosing retinal diseases. However, severe speckle noise and complex retinal structures remain major challenges for accurate image segmentation. Existing foundation models, such as SAM and MedSAM, exhibit limited performance on retinal OCT images because they are not specifically designed to handle OCT-specific noise characteristics. To address these limitations, we propose OCTSAM, a joint denoising and segmentation framework that integrates a masked Swin Transformer-based denoising module with a Vision Transformer-

based segmentation network. The denoising module suppresses background noise while preserving fine retinal structures, and the segmentation module utilizes prompt-guided feature learning to improve retinal layer delineation. The proposed method was evaluated on six publicly available retinal OCT datasets covering multiple retinal diseases and imaging systems. Denoising performance was assessed using Peak Signal-to-Noise Ratio (PSNR) and Structural Similarity Index (SSIM), while segmentation performance was evaluated using Dice Similarity Coefficient (DSC) and Normalized Surface Distance (NSD). Experimental results demonstrate that OCTSAM consistently outperforms conventional denoising algorithms and state-of-the-art segmentation models, including SAM, MedSAM, and U-Net. The proposed framework achieves superior noise suppression while preserving retinal anatomical details and delivers more accurate and stable retinal layer segmentation in both internal and external validation. These results indicate that OCTSAM possesses strong robustness and generalization capability across different datasets and imaging conditions. The proposed framework provides an effective and reliable solution for automated retinal OCT image analysis and shows considerable potential for future clinical applications.

[AIP-38] PIBM2026-0709-3

Virtual DWI Synthesized from Non-contrast CT for Rapid Diagnosis of Acute Ischemic Stroke

Wenzhi Lv[1], Pengcheng Li[1,2]

[1]MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[2]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Sanya, Hainan, 572025, China

Corresponding author e-mail address: pengchengli@hainanu.edu.cn

Abstract: Non-contrast CT (NCCT) is the first-line imaging modality for evaluating acute ischemic stroke (AIS). Diffusion-weighted MRI (DWI) can reveal early ischemic changes that often remain subtle on NCCT within the treatment window. However, DWI suffers from longer scanning times, metal contraindications, and restricted availability, all of which may delay treatment. To bridge this gap, we propose an explicit transformation generative adversarial network (ETGAN) that synthesizes valuable DWI from NCCT scans. Our core innovation is an explicit semantic feature transformation that injects learned ischemic priors directly into the synthesis pipeline. Specifically, we introduce a Feature Transformation Module (FTM), pre-trained by cross-modal contrastive learning, to map NCCT features into an ischemia-aware pseudo-DWI feature space. By incorporating the pre-trained FTM, the generator explicitly transforms hierarchical NCCT features into pseudo-DWI features, which are aligned with real DWI through a dedicated feature loss. These prior-informed representations enable ETGAN to more accurately reconstruct early ischemic lesions in synthesized DWI. Additionally, an attention-enhanced discriminator focuses on ischemic regions and guides the generator to synthesize finer lesion details. Our proposed method was evaluated on public and in-house datasets, achieving high fidelity with SSIM scores of 0.946 and 0.905, respectively. Extensive experiments showed that ETGAN outperformed existing methods in both visual quality and quantitative metrics. Crucially, the synthesized DWI significantly improved neuroradiologists' diagnostic accuracy in identifying AIS from NCCT alone (p<0.001). Our model offers a promising solution for rapid and accurate AIS assessment when MRI is inaccessible or delayed.

Neurophotonics

[NP-1] PIBM2026-0401-2

OCT-based three-dimensional multiparametric imaging of the cerebral microvasculature with deep-learning-assisted vascular segmentation

Hengming Jing[1], Junxiong Zhou[1], and Jianbo Tang[1]*

[1]Department of Biomedical Engineering, Southern University of Science and Technology, Shenzhen, China

**Corresponding author e-mail address: tangjb@sustech.edu.cn*

Abstract: Accurate characterization of cerebral microcirculation is essential for understanding brain health and disease, yet existing optical imaging methods face significant challenges in achieving multi-parameter, three-dimensional quantitative detection. Here, we present an OCT-based framework that addresses these limitations by enabling three-dimensional multiparametric imaging of the cerebral microvasculature. The framework combines dual-repeat acquisition, first-order field autocorrelation (g1)-based analysis, and dynamic light scattering OCT to recover both vascular structure and blood flow velocity from the same region. A deep-learning-assisted segmentation step improves vascular network continuity, yielding high-quality three-dimensional masks that support robust skeletonization and graph construction. By integrating structural and flow information within a unified graph-based representation, the method allows quantitative assessment of vessel diameter, length, tortuosity, segmental flow speed, and blood flow transit time across the 3D network. Representative results demonstrate clear three-dimensional visualization and distinct differences in multiple structural and hemodynamic parameters between sham and Alzheimer's disease model mice. We believe this technique provides a useful tool for quantitative investigation of cerebral microcirculation and associated vascular alterations.

[NP-2] PIBM2026-0401-3

Working memory-related brain network dysfunction after stroke and its modulation by tDCS: A fNIRS study

Guo Qi[1], Ji Wenxuan[1], Song Zhenhua[2], Li Binbin[2], Wang Shaojin[3], Jie Jing[1*], Yin Ming[1*]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, Hainan 572024, China

[2]Rehabilitation Medicine Department, Haikou People's Hospital, Haikou, Hainan 570208, China

[3]General Practice Department, Haikou People's Hospital, Haikou, Hainan 570208, China

Corresponding author e-mail address: jiejing@hainanu.edu.cn, ming_yin@hainanu.edu.cn

Abstract： Stroke frequently results in persistent cognitive impairment, particularly working memory (WM) dysfunction. This study used functional near-infrared spectroscopy (fNIRS) to characterize WM-related network dysfunction after stroke and to investigate whether dorsolateral prefrontal cortex (DLPFC)-targeted transcranial direct current stimulation (tDCS) is associated with WM improvement and functional network reconfiguration. Two experiments were conducted. In Experiment 1, 17 stroke patients and 17 healthy controls

underwent fNIRS during resting state and a WM task. In Experiment 2, 53 stroke patients were assigned to the experimental group (n = 28) and the control group (n = 25). The experimental group received DLPFC-targeted tDCS for 5 consecutive days. Behavioral assessments were completed in both groups, and fNIRS was acquired in the experimental group before and after intervention to assess cortical activation, functional connectivity, and graph-theoretical network properties, together with brain–behavior association analyses. In Experiment 1, stroke patients exhibited prolonged reaction times (RT), decreased functional connectivity, and less efficient WM-related network organization than healthy controls. In Experiment 2, WM performance improved after intervention in the experimental group. fNIRS further revealed enhanced cortical activation, increased task-related functional connectivity (0.3177 to 0.3914), and more optimized network topology following tDCS. In addition, behavioral improvement was positively correlated with increased functional connectivity between the bilateral DLPFC ($r = 0.413$, $p = 0.029$) and between the left DLPFC and frontopolar area (FPA; $r = 0.406$, $p = 0.032$). These findings suggest that post-stroke WM dysfunction is associated with disruption of prefrontal-centered functional networks, and that DLPFC-targeted tDCS may support cognitive rehabilitation by promoting network reorganization.

Keywords Stroke, Working memory, Functional near-infrared spectroscopy, Transcranial direct current stimulation, Neural regulation

[NP-3] PIBM2026-0403-15

Dual-feature validated depth reconstruction enables accurate and fast two-photon volumetric imaging

Na Xiao[1,†], Yufeng Gao[1,†], Jinyi Liu[2,3], Xueming Cao[1], Yaozhang Sheng[1], Lina Liu[1], Jia Yu[1], Zhuo Du[2,3], Shiwei Ye[1,*], Hui Li[1,*], and Wei Zheng[1,*]

[1]Research Center for Biomedical Optics and Molecular Imaging, Shenzhen Key Laboratory for Molecular Imaging, Guangdong Provincial Key Laboratory of Biomedical Optical Imaging Technology, Key Laboratory of Biomedical Imaging Science and System, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

[2]Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing 100101, China

[3]University of Chinese Academy of Sciences, Beijing 100049, China

Corresponding author e-mail address: shiwei.ye@siat.ac.cn, hui.li@siat.ac.cn, zhengwei@siat.ac.cn

Abstract: Biological systems exhibit complex three-dimensional (3D) distributions and rapid dynamics, requiring high spatiotemporal resolution in vivo volumetric imaging. Two-photon microscopy (TPM) is a powerful tool for high-resolution 3D imaging of biological samples, but its volumetric imaging speed is fundamentally limited by the conventional layer-by-layer z-axis scanning method. Specially designed elongated point spread functions (PSFs), such as Bessel beam, vTwINS enable fast volumetric imaging and depth decoding, but struggle when signals from different depths overlap or have similar spatial profiles. This limitation reduces depth reconstruction accuracy and restricts current approaches to sparsely labeled samples. Here, we present dual-view gradient excitation TPM (Dvge-TPM), a fast volumetric imaging approach that utilizes a pair of elongated PSFs with engineered intensity imbalance and tilted geometry. In Dvge-TPM, the two PSFs generate laterally separated projections of the same emitter, and simultaneously encode the depth information in the fluorescence intensity ratio and the distance between the two projections. Both of these features monotonically change with depth, providing an internal consistency check and improving the accuracy and robustness of depth decoding. Dvge-TPM can resolve ambiguities caused by overlapping or similar projections, making it applicable to more complex biological samples. Dvge-TPM enables simultaneous depth

reconstruction over a 60 μm axial range with a depth error of only 1.37 μm (~2% of the total range). We further demonstrate its performance by tracking C. elegans nuclear division, monocyte/macrophage migration, and neuronal calcium dynamics, highlighting its potential for fast and accurate 3D imaging in complex biological systems.

[NP-4] PIBM2026-0405-5

High-Resolution Photoacoustic Tomography of Mouse Whole-Brain Microvasculature Enabled by Omnidirectional Fiber-Optic Ultrasound Sensing

Xue Bai[1], Yizhi Liang[1] and Bai-Ou Guan[1]

[1] Guangdong Provincial Key Laboratory of Optical Fibre Sensing and Communications, Institute of Photonics Technology, College of Physics and Optoelectronic Engineering, Jinan University, Guangzhou, 511400, China.

Corresponding author e-mail address: bx_jnu@163.com

Abstract: In this study, a novel fiber-optic ultrasound sensor is proposed, which exhibits an ultra-wide response bandwidth of 0.3–80 MHz and a 360° omnidirectional ultrasound reception angle. With a sensing area only 1/300 that of conventional piezoelectric detectors, the sensor achieves exceptionally high detection sensitivity, with an average noise equivalent pressure density of 1.5 mPa/ √ Hz. A linear-scanning photoacoustic tomography system constructed using this sensor enables high-resolution imaging of the coronal vascular structure in mice under craniotomy conditions. The system achieves an imaging penetration depth of 8 mm and a spatial resolution of 40 μm. It not only clearly visualizes microvascular networks smaller than 100 μm in the hippocampus and beneath the cerebral cortex, but also effectively addresses the challenge faced by traditional piezoelectric detectors of being unable to detect steeply inclined (perpendicular to the body surface) penetrating vessels due to limited reception angles, by virtue of the sensor's unique 360° omnidirectional reception capability, thus fully capturing the distribution of subcortical penetrating microvessels. The experimental results are cross-validated against magnetic resonance angiography (MRA), the gold-standard imaging modality, confirming the authenticity of the vascular patterns. Meanwhile, by exploiting the specific absorption differences of hemoglobin at 532 nm and 1064 nm, the system realizes dual-wavelength quantitative imaging of blood oxygen saturation, allowing clear discrimination between arterial and venous vascular distributions in brain tissue. This achievement provides a high-precision imaging tool for neuroscience research that integrates omnidirectional sensing capability and microvascular resolution.

[NP-5] PIBM2026-0406-1

Synaptic level remodeling of basal forebrain PV projection in Alzheimer's Disease

Jiaojiao Tian[1], Miao Ren[2], Yingying Chen[3], Tao Jiang[4*], Xiangning Li [2, 4 *]

[1]Department of Clinical Laboratory, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450052, Henan, China

[2]Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China

[3] MoE key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[4]HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou 215125, China

[*]Correspondence: taojiang@brainsmatics.org, lixiangning@hainanu.edu.cn

Abstract: Synaptic pathology is widely regarded as one of the earliest and most pivotal events in the pathogenesis of Alzheimer's disease (AD). Long-range projection circuits depend on highly organized synaptic connections across anatomically distributed brain regions to sustain learning and memory functions. Disruption at the synaptic level is therefore likely to constitute an initiating mechanism underlying large-scale circuit dysfunction. Nevertheless, the spatiotemporal patterns of synaptic degeneration within long-range projection circuits of defined neuronal populations throughout AD progression remain insufficiently characterized, hindering the identification of the earliest circuit elements susceptible to disease-related damage.

In the present study, we integrated viral labeling with fluorescence micro-optical sectioning tomography (fMOST) to reconstruct synapse-level projection maps of basal forebrain parvalbumin (PV) neurons across multiple stages of AD. Our analyses revealed marked early synaptic loss in the mammillary body and hippocampal formation, occurring before overt microenvironmental alterations became detectable in either the basal forebrain or its downstream target regions. In parallel, rabies virus-based retrograde tracing demonstrated a reduction in afferent inputs from multiple upstream brain areas, suggesting selective vulnerability of long-range PV neuronal circuits. Together, these findings indicate that basal forebrain PV projection networks undergo bidirectional degeneration during AD progression, affecting both incoming and outgoing circuit components.

In summary, this study establishes a stage-resolved atlas of synaptic degeneration for a specific neuronal population, uncovers region-dependent and age-related vulnerability patterns in long-range projections, and highlights potential circuit-level targets for early intervention in AD.

Keywords： Synapse degeneration, Alzheimer's disease, basal forebrain, PV neuron, whole brain

[NP-6] PIBM2026-0406-11

468 nm blue light ameliorates sleep deprivation-induced neuronal injury by modulating mitochondrial Complex I-mediated energy metabolism

Chunyan Ma[1, 2], Na Li[1, 2], Yutong Ye[1, 2], Xunbin Wei[3], Hongli Chen[1, *]

[1]State Key Laboratory of Advanced Medical Materials and Devices, Tianjin Key Laboratory of Neuromodulation and Neurorepair, Integrative Regeneration Laboratory, Institute of Biomedical Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, 300192, China

[2]State Key Laboratory of Separation Membranes and Membrane Processes & Key Laboratory of Hollow Fibre Membrane Materials and Membrane Processes, Tianjin Key Laboratory of Optoelectronic Detection Technology and Systems, Tiangong University, Tianjin, 300387, China

[3]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, the Center of Biomedical Engineering, Institute of Advanced Clinical Medicine, Institute of Medical Technology, Peking University Health Science Center, International Cancer Institute, Peking University, Beijing, 100191, China.

Corresponding author e-mail address: chenhli0107@163.com

Abstract: Sleep deprivation induces pronounced neuroinflammatory responses and mitochondrial dysfunction, leading to neuronal injury and cognitive impairment, and has emerged as an increasingly serious public health concern. with energy metabolism dysregulation recognized as a key pathological basis. Photobiomodulation (PBM) has emerged as a safe, non-invasive neuroprotective strategy; however, whether PBM alleviates sleep deprivation-induced neuronal injury through modulation of energy metabolism remains unclear. In this study, sleep-deprived mice were subjected to a seven-day 468 nm blue light PBM intervention (300 lux, 30 min per session, twice daily). In parallel, a corticosterone-induced HT22 cell injury model was established to further elucidate the molecular mechanisms underlying PBM-mediated neuroprotection. Cognitive function was assessed using behavioral tests, while biochemical, histological, and transcriptomic analyses were conducted to evaluate neuronal structure and function, neuroinflammation, oxidative stress, mitochondrial function, and energy metabolism. The results demonstrated that PBM significantly improved cognitive function and attenuated neuronal degeneration and apoptosis in sleep-deprived mice. PBM also effectively suppressed the overactivation of microglia and astrocytes, improved mitochondrial structure and function, and reduced oxidative stress. Notably, transcriptomic analysis revealed that PBM activated the oxidative phosphorylation pathway and upregulated genes and proteins associated with mitochondrial Complex I. Furthermore, PBM restored NAD^+/NADH redox homeostasis and re-established metabolic coordination between glycolysis and oxidative phosphorylation, thereby enhancing adenosine triphosphate (ATP) production. Inhibition of Complex I markedly diminished the neuroprotective effects of PBM, as well as ATP generation. Collectively, these findings indicate that 468 nm blue light PBM alleviates sleep deprivation-induced neuroinflammation, mitochondrial dysfunction, and neuronal injury by modulating mitochondrial Complex I-mediated energy metabolism. This study provides a theoretical basis for the application of PBM as a non-invasive therapeutic strategy for neuroinflammation-associated cognitive dysfunction.

[NP-7] PIBM2026-0406-17

Two-Photon Imaging Reveals Developmental Dynamics of Neurovascular Coupling in Neonatal Mice

Lijie Zhang[1,2], Jiaru He[1], Xiaoli Lin[1,3], Tingting Zhu[1,3], Hongrui Zhan[2*], Zhihai Qiu[1*]

[1] Guangdong Institute of Intelligent Science and Technology

[2] Department of Rehabilitation Medicine, The Fifth Affiliated Hospital of Sun Yat-sen University

[3] Beijing Normal University

Corresponding authors e-mail address: qiuzhihai@gdiist.cn; zhanhongrui@mail.sysu.edu.cn

Abstract: Neurovascular coupling (NVC), which refers to the vasodilation and increased blood flow accompanying neuronal activation, is a critical physiological process in the central nervous system and serves as the theoretical foundation for modern functional neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and functional ultrasound (fUS). In adult brains, enhanced neural activity leads to increased local blood flow. However, whether neonatal animals share identical neurovascular coupling (NVC) mechanisms with adults remains controversial. Previous assessments of functional hemodynamics in neonatal animals, including human infants and neonatal mice, have consistently observed abnormal or even inverted hemodynamic responses to stimulation. This study investigates NVC characteristics in unanesthetized neonatal mice using high spatiotemporal resolution two-photon microscopy. We synchronously recorded neuronal calcium signals and vascular/hemodynamic responses (arteriolar diameter, capillary red blood cell velocity) in the primary somatosensory barrel cortex (S1BF) of neonatal (P7-P21) and adult mice during both resting state and whisker stimulation. Crucially, local neural activity in early postnatal mice does not elicit substantial blood flow increases as observed in adult brains. Key findings include: 1) In P12-14 mice, neural activation after whisker stimulation induced small-amplitude delayed vasodilation, followed by significant constriction that impaired subsequent dilation; 2) P18 mice exhibited delayed vasodilation, while P25 mice displayed hemodynamic responses similar to adults but with reduced amplitudes; 3) Arteriolar diameters oscillated at 0.1 Hz during resting state in both P12-P18 and adult mice. This study elucidates the developmental trajectory of NVC in early postnatal stages, providing a critical theoretical foundation for interpreting functional neuroimaging data in developing brains and advancing our understanding of neurovascular interactions during brain maturation.

Keywords: neurovascular coupling, GCaMP imaging, two-photon imaging, cerebral hemodynamics, postnatal neural development

[NP-8] PIBM2026-0406-4

SPAD-Based Depth-Enhanced Diffuse Correlation Spectroscopy Combined with Near-Infrared Spectroscopy for Cerebral Hemodynamics Measurement

Quan Wang[1,2,3,4], Zhizheng Yuan[1,2], Hanqing Chen[1,2], Xunting Huang[1,2], Jing Wang[1,2], and Zhen Yuan[1,2,3,4]

[1] Centre for Cognitive and Brain Sciences, University of Macau, Macau SAR, China

[2] Faculty of Health Sciences, University of Macau, Macau SAR, China

[3] Zhuhai UM Science and Technology Research Institute, University of Macau, Hengqin, China

[4] University of Macau Advanced Research Institute in Hengqin, Zhuhai, China， Corresponding to: zhenyuan@um.edu.mo

Abstract: Accurate non-invasive measurement of the cerebral metabolic rate of oxygen ($CMRO_2$) remains challenging due to contamination from superficial tissue hemodynamics and the limited depth sensitivity of conventional optical techniques. To address this problem, we developed a hybrid system integrating a SPAD-based diffuse correlation spectroscopy (DCS) module with a frequency-domain near-infrared spectroscopy (FDNIRS) module. The SPAD-based DCS offers high photon detection sensitivity and an improved sampling rate, enabling faster acquisition of intensity autocorrelation curves ($g_2(\tau)$). Meanwhile, FDNIRS quantifies absolute tissue absorption (μ_a) and reduced scattering (μ_s') coefficients, from which oxy- and deoxy-hemoglobin concentrations ([HbO] and [HbR]) are derived. By combining the blood flow index (BFi) from DCS with [HbO] and [HbR] from FDNIRS, we calculated $CMRO_2$ based on the Fick principle. The system was validated using a two-layer liquid phantom with independent flow control, mimicking the scalp and cortical layers. Our results show that the SPAD-based configuration suppresses superficial flow contamination by over 85% compared to a conventional DCS system, enabling reliable extraction of deep cortical blood flow signals. In vivo measurements on healthy subjects will further confirm the system's ability to track dynamic $CMRO_2$ changes during breath-holding tasks. We conclude that this SPAD-based DCS-FDNIRS hybrid approach provides a robust, depth-enhanced solution for quantitative cerebral hemodynamic monitoring.

Key words: SPAD, DCS, FDNIRS, BFi, Cerebral Hemodynamic

[NP-9] PIBM2026-0408-3

Study on the regulatory effect of photobiomodulation on metabolic levels and neuroinflammation in diabetic rats

Hui Chen[1,2], Chunyan Ma[3], Ning Ma[4], Lina Chang[1], Yian Gu[1], Linlin Kong[1], Xin Wang[1], Qing He[1,*], and Hongli Chen[3,*]

[1]Department of Endocrinology and Metabolism, Tianjin Medical University General Hospital, Tianjin Medical University,Tianjin, 300052, China

[2]Xiangyang road subdistrict community health service center, Tianjin, 300111, China

[3]State Key Laboratory of Advanced Medical Materials and Devices, Tianjin Key Laboratory of Neuromodulation and Neurorepair, Institute of Biomedical Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, 300192, China

[4]Tianjin Medical University Cancer Institute & Hospital,Tianjin, 300060, China

Corresponding author e-mail address: hech69@163.com；chenhli0107@163.com

Abstract: Diabetes is a growing global health concern characterized by metabolic disturbances, including hyperglycemia, dyslipidemia, and insulin resistance, which contribute to severe complications such as cardiovascular and neurological disorders. Dysregulation of energy metabolism is considered a key pathological basis. Photobiomodulation (PBM), a safe and noninvasive therapeutic approach, has shown potential in modulating cellular metabolism; however, its role in systemic metabolic regulation in diabetes remains unclear. In this study, a diabetic rat model was established and subjected to near-infrared (808 nm) and blue light (468 nm) PBM interventions. PBM was administered under controlled conditions, and metabolic parameters, including fasting blood glucose, glycated hemoglobin, lipid profiles, and free fatty acids, were measured. Behavioral tests were conducted to assess cognitive function. In addition, biochemical assays, histological examinations, and immunological analyses were performed to evaluate oxidative stress, neuroinflammation, pancreatic islet integrity, and hippocampal neuronal injury. The results demonstrated that PBM significantly improved fasting blood glucose, glycated hemoglobin, and lipid metabolism, as evidenced by reduced cholesterol and free fatty acid levels. PBM also markedly enhanced learning and memory performance and alleviated histopathological damage in pancreatic islets and hippocampal tissues. Furthermore, PBM effectively reduced oxidative stress and suppressed neuroinflammatory responses, as indicated by decreased reactive oxygen species levels and reduced activation of inflammatory markers. PBM also attenuated neuronal apoptosis. Mechanistically, these protective effects were associated with activation of the PI3K/AKT signaling pathway. Collectively, these findings indicate that near-infrared and blue light PBM ameliorate metabolic dysfunction, neuroinflammation, and neuronal injury in diabetic rats, highlighting its potential as a noninvasive therapeutic strategy for diabetes and its related complications.

[NP-10] PIBM2026-0409-1

Sono-Magnetic-Activated Pyroelectric Catalytic Nanozymes for Glioblastoma Immunotherapy

Cong Wang[1,3], Yundi Wu[2], and Xilong Wu[1,3]

[1] State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Haikou 570228, China

[2]Key Laboratory of Tropical Biological Resources of Ministry of Education and Hainan Engineering Research Center for Drug Screening and Evaluation, School of Pharmaceutical Sciences, Hainan University, Haikou 570228, China

[3]Collaborative Innovation Center of One Health, Key Laboratory of Biomedical Engineering of Hainan Province, Hainan University, Haikou 570228

Corresponding author e-mail address: xilongwu@foxmail.com (X. Wu)

Abstract:

Glioblastoma (GBM) is one of the most aggressive and lethal malignancies of the central nervous system, characterized by extensive heterogeneity, diffuse invasion, severe hypoxia, and profound immunosuppression within the tumor microenvironment (TME). These features markedly limit the effectiveness of conventional surgery, radiotherapy, and chemotherapy, and also reduce the therapeutic efficacy of many reactive oxygen species (ROS)-based nanomedicines in deeply seated tumors. Pyroelectric catalytic nanomaterials have recently attracted increasing attention because they can convert thermal fluctuations into charge separation and ROS generation, thus offering a promising strategy for noninvasive tumor therapy. However, their catalytic efficiency and metabolic regulatory capacity still require substantial improvement for effective GBM treatment. Here, a sono-magnetic-triggered thermoelectric catalytic nanozyme, LFSH, is developed to overcome the complex TME of GBM. LFSH effectively suppresses charge-carrier recombination and enhances catalytic activity under alternating magnetic field (AMF) and ultrasound (US) stimulation. This sono-magnetic-thermal-electric synergistic activation promotes a pronounced ROS burst at the tumor site, thereby strengthening sonodynamic therapy and pyroelectric catalytic therapy. Notably, LFSH exhibits a quadruple catalytic network, including peroxidase-like (POD-like), and lactate dehydrogenase-like (LDH-like) activities. These enzyme-mimetic properties cooperatively deplete reducing metabolites, disrupt intracellular redox homeostasis, and weaken the antioxidant defense system of tumor cells. In addition, modulation of the lactate-glucose metabolic axis, together with NADPH exhaustion, induces disulfidptosis and further amplifies antitumor immune responses. Therefore, this sono-magnetic-triggered pyroelectric catalytic nanozyme provides a promising strategy for simultaneously regulating molecular metabolism and enhancing immunotherapy against deeply seated glioblastoma.

[NP-11] PIBM2026-0415-2

Histo-SFST: 3D Histoarchitectural Mapping of Pre-label-free Whole-organs at the Mesoscopic Scale Across Animal Species

Jingyi Che [1], Jiajia Wang[1], Xinle zhang[1], Yaoyuan Jiang[1], Xiaoyan Li[1], Chi Xiao[1], Xiaojun Wang[1]

[1]Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Haikou 570228, China.

xiwang@hainanu.edu.cn

Abstract: The mesoscopic-scale 3D architectonic mapping of intact organs across diverse animal species and experimental models is critical for elucidating the tissue organization and functional mechanisms that underpin complex biological activities. However, the conventional histological approaches remain limited to either 2D tissue sections or low-resolution 3D imaging due to technical barriers in both large-scale staining and high-resolution microscopic visualization of extensive tissue volumes. To address these challenges, we developed the Histo-SFST, a pre-label-free platform integrating surface fluorescence sectioning tomography (SFST) with ultrathin multicolor wash-free staining, enabling simultaneous in situ 3D visualization of diverse tissue architectures at whole-organ scale. Multicolor wash-free stains targeting overlapping or complementary tissue architectures were employed to expand the repertoire of visualizable histological structures, while ultrathin surface staining enabled uniform, high-contrast imaging that resolves fine structural details and highlights distinct color intensity differences between tissue architectures in color-merged images. We systematically validated its accuracy and comprehensiveness via side-by-side comparisons with conventional histochemical staining in mouse facial skin, demonstrated cross-species applicability for architectonic brain mapping in mice and monkeys, and confirmed its broad utility across mouse visceral organs. Overall, Histo-SFST provides a versatile tool for cross-species whole-organ 3D histoarchitectural mapping, with strong potential to advance anatomy, neuroscience, and pathology research.

Key Words： 3D histology, Pre-label-free, In situ, Ultrathin surface staining, Organ-wide, fMOST imaging

[NP-12] PIBM2026-0417-3

A head-mounted optically transparent skull (HOTS) window for deep transcranial imaging of the mouse cortex

Lina Liu[1,2], Yufeng Gao[1], Yuezhi He[1], Jiuling Liao[1], Yaozhang Sheng[1,4], Liang Wang[1], Shiwei Ye[1], Na Xiao[1], Xueming Cao[1], Ting Wu[1], Zonghua Wen[5], Jun Chu[1,3], Wei Zheng[1,3,*], and Hui Li[1,3,*]

[1]Research Center for Biomedical Optics and Molecular Imaging, Shenzhen Key Laboratory for Molecular Imaging, Guangdong Provincial Key Laboratory of Biomedical Optical Imaging Technology, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

[2]University of Chinese Academy of Sciences, No. 19(A) Yuquan Road, Shijingshan District, Beijing 100049, China

[3]Key Laboratory of Biomedical Imaging Science and System, Chinese Academy of Sciences, State Key Laboratory of Biomedical Imaging Science and System, Shenzhen 518055, China

[4]Medical School, Shenzhen University, Shenzhen 518060, China

[5]Department of Pathology, Shenzhen University General Hospital, Shenzhen 518055, China

**Corresponding author e-mail address: zhengwei@siat.ac.cn; hui.li@siat.ac.cn;*

Abstract: High-resolution two-photon imaging of the adult mouse cerebral cortex is severely limited by light scattering from the skull, which attenuates signals and restricts imaging depth *in vivo*. Although skull clearing methods provide optical access to the cortex through the intact skull, their practical performance remains constrained by limited clearing duration and suboptimal clearing reagents. Here, we present a head-mounted optically transparent skull (HOTS) window that combines a head-mounted cap with an optimized two-step skull-clearing procedure. The cap maintains clearing solutions over the skull, thereby avoiding prolonged anesthesia or physical restraint and enabling extended skull clearing for several hours in awake, freely behaving mice. The two-step clearing reagents (S1 and S2) were optimized through systematic chemical screening. Using HOTS, we achieved transcranial two-photon imaging of cortical structures to depths of up to ~800 μm below the pia, allowing visualization of layer 5 neurons and approaching the performance of open-skull windows. Importantly, HOTS enabled the detection of weak neural signals, including whisker-stimulation-evoked calcium transients and hindpaw electrical stimulation-evoked cAMP dynamics. Together, these results establish HOTS as a practical platform for deep transcranial structural and functional imaging through the intact skull.

[NP-13] PIBM2026-0508-1

Deep-Tissue Polarization Recovery via Dichroic Photoacoustic-Guided Wavefront Optimization

Wei Chen[1], Zhenhui Zhang[2], and SiHua Yang[3]

[1]MOE Key Laboratory of Laser Life Science & Institute of Laser Life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China

[2] Guangdong Provincial Key Laboratory of Laser life Science, College of Biophotonics, School of Optoelectronic Science and Engineering, South China Normal University, Guangzhou 510631, China

Abstract: Polarization is the core degree of freedom describing the vector properties of the optical field, carrying key information such as medium anisotropy, orientation orderliness, and vector light-matter interaction. However, in strongly scattering media, multiple scattering not only leads to the randomization of the optical field phase but also degrades the polarization state, causing rapid loss of polarization information during

propagation. Therefore, extracting deep localized polarization signals has long been a challenge. Although wavefront shaping technology has achieved the focusing of light transmitted through scattering media, existing methods mainly focus on scalar information such as light intensity or phase, and it is still difficult to solve the higher-order vector optical field control problem of deep polarization state recovery. This paper proposes a vector wavefront shaping strategy based on polarization optoacoustic feedback, utilizing the localized optoacoustic response encoded by the polarization-dependent absorption in the target region as feedback to achieve selective extraction of deep polarization information and recovery of the localized polarization state in strongly scattering media. Through joint optimization of the incident wavefront and polarization degrees of freedom, we have achieved localized polarization state recovery up to 16 scattering mean free paths in reflection mode. The results show that this method not only significantly extends the reachable range of deep polarization recovery but also enhances the interpretation ability of the polarization response of anisotropic absorbers. This work establishes a new physical path for extracting deep polarization information in strongly scattering media and promotes the expansion of wavefront shaping from scalar focusing to vector optical field control.

[NP-14] PIBM2026-0522-1

Efficient Web-Based Three-Dimensional Visualization Method for Large-Scale Cerebrovascular Networks

Fangqi Deng[1], Yuxin Li[1], Tao Jiang[2], Xiangning Li[3], Anan Li[2,3]

[1]Shaanxi Key Laboratory of Network Computing and Security Technology, School of Computer Science and Engineering, Xi'an University of Technology, Xi'an, 710048, China

[2]HUST-Suzhou Institute for Brainsmatics, Suzhou, 215123, China

[3] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya 572025, China

Corresponding author e-mail address: liyuxin@xaut.edu.cn

Abstract: Efficient three-dimensional visualization and online sharing of cerebrovascular atlases hold significant value for neuroscience research, neurodegenerative disease mechanism analysis, and drug development. The high-resolution three-dimensional structural information provides critical data support for understanding vascular spatial distribution and pathological evolution mechanisms. Compared to organs with relatively regular morphological structures, cerebrovascular networks not only exhibit intricate branching patterns but also demonstrate substantial morphological heterogeneity across different scales, imposing stringent requirements on the high-quality rendering and real-time interactive performance of online visualization systems. Traditional vascular visualization methods can be broadly categorized into two classes: parametric skeleton rendering methods based on centerline extraction and radius estimation, and triangular mesh surface reconstruction methods based on isosurface extraction. The former offers high computational efficiency but struggles to adequately represent fine vascular branches; the latter effectively preserves complex vascular morphologies yet faces substantial computational overhead and performance challenges in real-time interaction with large-scale datasets.This paper proposes a Web-based multi-resolution three-dimensional visualization method, developing an online vascular visualization system utilizing WebGL technology. The approach combines Tile-based organization with Level of Detail (LOD) techniques, with an adaptive tiling strategy for size and complexity-aware partitioning of 3D vascular data. This methodology enhances loading and interaction efficiency while maintaining rendering quality. Experimental results demonstrate that the proposed method enables visualization of large-scale vascular data within browser environments, significantly

improving rendering performance and interaction smoothness while ensuring overall structural continuity.

Keywords: Whole-brain vasculature, WebGL, Multi-resolution, Visualization

[NP-15] PIBM2026-0611-1

Analysis of Cerebral Microvascular Morphological Characteristics in Alzheimer's Disease Mice

Xinghai Wang[1], Yuxin Li[1], Fangqi Deng[1], Tao Jiang[2], Xiangning Li[3], Anan Li[2,3]

[1]Shaanxi Key Laboratory of Network Computing and Security Technology, School of Computer Science and Engineering, Xi'an University of Technology, Xi'an, 710048, China

[2]HUST-Suzhou Institute for Brainsmatics, Suzhou, 215123, China

[3] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya , 572025, China

Corresponding author e-mail address: liyuxin@xaut.edu.cn

Abstract: Alzheimer's disease (AD) is a central nervous system disorder characterized by cognitive impairment and neurodegeneration. In recent years, an increasing number of studies have shown that abnormalities in the cerebrovascular system are closely related to the occurrence and development of Alzheimer's disease, among which changes in the structure of cerebral microvessels are considered important factors affecting blood supply to brain tissue, metabolite clearance, and neurological function. Therefore, systematic quantitative analysis of microvascular morphological features is essential for elucidating cerebrovascular pathological mechanisms and identifying early biomarkers. In this study, we focuses on the cerebrovascular data of AD mice and constructs a set of analytical processes for the morphological characteristics of cerebral microvessels. First, we acquire cerebrovascular data from AD mice using high-definition fluorescence micro-optical sectioning tomography(HD-fMOST) and segment the cerebral vessels using a deep learning model to obtain complete three-dimensional vascular structures. Subsequently, we extract vascular data from selected brain regions of the segmented results, perform skeleton extraction and topological analysis on the vascular networks, and calculate multiple morphological metrics including vessel radius, branching angle, tortuosity, length density, surface area density, volume density, and distance transform. Experimental results demonstrate that the proposed method can effectively extract various morphological features of cerebral microvessels in AD mice, enable quantitative analysis of the structural complexity of vascular networks, and provide reliable analytical tools and data support for the study of AD-related cerebrovascular lesions. The established analytical pipeline can serve as a reference for mechanistic studies of cerebrovascular diseases and pathological analysis of related neurodegenerative disorders.

Keywords: Alzheimer's disease, Cerebral microvasculature, HD-fMOST, Morphology characteristics, Vascular network analysis

[NP-16] PIBM2026-0615-2

Whole-Brain Mapping of Cholinergic Circuits in Orofacial Motor Nuclei Revealing Ascending and Descending Dichotomy

Zhaoyang Meng[1], Hui Gong [2], Xiangning Li[2, 3]*

[1]Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan, China.

[2] HUST-Suzhou Institute for Brainsmatics, Suzhou, China.

[3] State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Sanya, China.

Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: Orofacial motor behaviors, including whisking, feeding, vocalization and facial expression, are fundamental for animal survival and social interaction. These behaviors are precisely orchestrated by the cholinergic neurons in brainstem motor nuclei which integrate extensive circuits to control multiple muscle groups. Decades of anatomical and functional investigations have well mapped the premotor circuits that relay descending motor commands to the motor nuclei, forming the classical framework of hierarchical orofacial motor control. However, emerging evidence has revealed that the motor nuclei extend cholinergic collateral projections within the central nervous system, challenging the long-held view that these nuclei function solely as effectors. Yet their brain-wide connectivity architecture and organizational rules at single-neuron resolution remain poorly understood. In this study, we systematically mapped the whole-brain input and output connectivity of cholinergic neurons in trigeminal motor, facial and hypoglossal nuclei using fluorescence micro-optical sectioning tomography (fMOST) at single-neuron resolution. We identified distinct topological input-output patterns across the nuclei, in which trigeminal motor and facial nuclei innervate regions spanning the midbrain, pons and medulla, while hypoglossal nucleus exhibits more restricted medullary connections. Furthermore, Single-neuron reconstruction data uncovered a unique subpopulation of centrally projecting cholinergic neurons separate from peripheral projection neurons with subtype-specific co-projection profiles. Collectively, our findings delineate the brain-wide topological connectivity of the cholinergic neurons in orofacial motor nuclei, establishing a bidirectional circuit framework for orofacial motor coordination that integrates both descending command and ascending feedback. This work renews the classical understanding of brainstem motor nuclei as simple effectors and provides a comprehensive anatomical foundation for deciphering the neural mechanisms underlying complex orofacial motor control.

[NP-17] PIBM2026-0616-2

Synthesizing 3D Pathological Volumes Using GANs with a Prior Reference Atlas from fMOST

Shang Wenkai[1], Liu Yibo[1]，Zheng Qinge[1]，Jiang Jialu[1]，Yang Shuhan[1]，Li Xiangning [1*]

[1]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University

Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: Pathological diagnosis remains the clinical gold standard, yet the current technological framework is hampered by a critical bottleneck. Conventional two

enhances the quality of two

resolution whole-brain data; however, a single macaque dataset can reach hundreds of terabytes, with neuronal signals accounting for less than 5% of the total. This massive redundancy severely hampers storage, transmission, and downstream analysis. Targeting sparsely labeled whole-brain neuronal data, this project designs an automated data cleaning and 3D efficient compression system. In the cleaning stage, neuronal morphology is acquired through maximum intensity projection, and neuronal positions are localized by combining a SegFormer segmentation network with morphological post-processing, ultimately achieving an average recall greater than 95% and a data retention rate below 5%. In the compression stage, an end-to-end compression framework based on a 3D dictionary entropy model is constructed, integrating multi-scale feature aggregation and a dictionary cross-attention mechanism. At a rate of 0.1 bpp, it achieves a PSNR of 48.57 dB and an SSIM of 0.981, with both encoding and decoding speeds exceeding 15 MB/s. Using this system, over 20 macaque whole-brain datasets and over 10 mouse whole-brain datasets have been cleaned. Compression was performed on one cleaned macaque dataset and one cleaned mouse brain dataset, with the storage size of the compressed data less than 0.5% of the original data. This system provides an efficient, high-fidelity engineering solution for large-scale brain atlas construction and cross-center data sharing.

[NP-20] PIBM2026-0618-12

Automated reconstruction and quantitative vectorization of whole-brain neuronal projection pathways from fMOST imaging data

Jinhong Jiang[1], Mengting Zhao[1*]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, 572025, China

**Corresponding author e-mail address: 996955@hainanu.edu.cn*

Abstract: Whole-brain imaging technologies such as fluorescence Micro-Optical Sectioning Tomography (fMOST) provide unprecedented opportunities for studying neuronal morphology and long-range connectivity at the brain-wide scale. However, accurate reconstruction of neuronal projection pathways from terabyte-scale imaging datasets remains challenging due to weak signals, discontinuous neurites, complex branching structures, and the high computational cost associated with large-scale data processing. In this study, we present a high-throughput intelligent analysis framework for automated neuronal reconstruction and neural circuit analysis from whole-brain imaging data. The framework integrates deep-learning-based neuronal signal segmentation, automated path reconstruction, and projection pattern analysis into a unified workflow. A ResNet50-based segmentation network is employed to enhance neuronal signal detection and generate high-quality probability maps from fMOST datasets. Subsequently, a Multi-Stencils Fast Marching Method (MSFM) is used to construct a global distance field for neuronal tracing. To balance reconstruction accuracy and computational efficiency, two complementary backtracking strategies are introduced: continuous gradient-descent tracing for high-precision reconstruction and a Parent Map-based discrete tracing method for large-scale projection analysis. The reconstructed neuronal structures are vectorized into standard SWC representations and registered to a brain atlas for quantitative characterization of projection patterns. Experimental results demonstrate robust segmentation performance with a Dice coefficient of 0. 89, IoU of 0. 81, Recall of 0. 91, and Precision of 0. 87. Reconstruction evaluation achieved an average coverage rate of 0. 97, and the miss and redundancy rates were both below 0. 05. Furthermore, projection analyses of external globus pallidus neurons successfully reproduced known projection motifs reported in previous whole-brain reconstruction studies, supporting the biological validity of the proposed framework. The

proposed approach enables efficient conversion of large-scale imaging data into quantitative neural circuit representations and provides a scalable tool for studying neuronal morphology, projection organization, and brain-wide connectivity.

[NP-21] PIBM2026-0618-13

Graph neural network analysis of mouse basal ganglia circuits based on voxel-level input connectivity networks

Jiamin Lin[1], Mengting Zhao[1*]

[1]State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province,School of Biomedical Engineering, Hainan University, Sanya, 572025, China

**Corresponding author e-mail address: 996955@hainanu.edu.cn*

Abstract: Basal ganglia (BG) circuits are essential for motor control, learning, and decision-making, and their dysfunction is closely associated with neurological disorders such as Parkinson's disease. Conventional region-of-interest-based connectome analyses can describe overall inter-regional projection patterns, but they often fail to preserve the spatially continuous topological organization within individual brain regions, limiting the identification of fine-grained functional subdivisions and inter-circuit integration in BG networks. In this study, we developed a voxel-level structural connectivity framework for mouse cortico–basal ganglia–thalamic circuits by integrating fluorescence micro-optical sectioning tomography (fMOST)-based retrograde viral tracing data with the STAM standard brain template. Retrograde tracing datasets were registered to the STAM space, voxelized, and assigned to anatomical regions using a majority-voting strategy. Signals from retrogradely labeled upstream somata were then normalized to construct directed and weighted connectivity matrices linking source voxels or regions to target injection experiments. We further modeled the voxel–experiment relationships as a heterogeneous graph using a graph neural network, in which voxel-level input patterns were learned through edge-weight regression. Leiden clustering was subsequently applied to the learned voxel embeddings to identify potential input-defined topological subregions within BG-related structures. The analysis showed that this framework captured canonical BG connections at the regional level, including cortico-striatal projections, direct and indirect pathways, and thalamic inputs. Furthermore, voxel-level representation learning combined with spatial mapping provides a new basis for resolving input heterogeneity and potential functional subdivisions within the same anatomical region. This study provides a computational strategy for high-resolution circuit modeling and fine-scale analysis of BG network organization.

[NP-22] PIBM2026-0618-18

Stage-dependent shifts in the causal contributions of cortical activity patterns during voluntary forelimb lever pushing

Qiao Tianyu[1], Li Xiangning[1*], Ren Miao[1*]

State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University

Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: Understanding how the cortex encodes complex continuous movements is fundamental to elucidating motor command generation, the involvement of sensory information, and the coordination of successive movement components. It may also provide a physiological basis for closed-loop brain–computer

interfaces that integrate neural recording and decoding with optical or electrical stimulation. Continuous movements are not a simple combination of individual motor parameters but consist of successive stages, including movement initiation, target contact, force modulation, and forelimb retraction. It is therefore important to determine how distributed cortical activity changes across movement stages and which activity patterns are causally required for specific movement components. Previous studies have used in vivo imaging and optogenetic manipulation to investigate mouse forelimb behaviors, including reach-to-grasp, lever-pull, and multistep reach–grasp–eat behaviors. These studies have shown that motor, somatosensory, and frontal cortical areas exhibit distinct temporal activity patterns during movement preparation, reaching, target contact, grasping, and forelimb retraction. Local cortical inhibition can delay movement initiation, alter movement trajectories, impair grasping, or interrupt ongoing movements, thereby establishing preliminary relationships between specific cortical areas and movement stages. However, most studies have focused on predefined cortical areas or broadly defined preparation and execution periods, and the coordinated dynamics of distributed and overlapping cortical activity patterns during continuous movements remain poorly understood. Whether imaging-defined activity patterns are causally necessary for behavior and whether their causal contributions shift across movement stages remain unclear. In this study, we established a voluntary forelimb lever-push task in mice and combined wide-field calcium imaging with multisite, stage-specific optogenetic inhibition to characterize the relationships between cortical activity patterns and successive movement stages and to determine whether their causal contributions change over the course of the behavior.

[NP-23] PIBM2026-0618-26

Single-Neuron Reconstruction Based on Dynamic Snake Convolution and Geometric Topology Repair

Ganghua Huang[1], Yan Jiang[1], Xinyi Cheng[1], Anan Li[1,2,3], Qingming Luo[1], Chi Xiao[1*]

[1] State Key Laboratory of Digital Medical Engineering, Key Laboratory of Biomedical Engineering of Hainan Province, School of Biomedical Engineering, Hainan University, Sanya, China

[2] HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou, China

[3] Britton Chance Center for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, MoE Key Laboratory for Biomedical Photonics, Huazhong University of Science and Technology, Wuhan, Hubei, China

**Corresponding author e-mail address: xiaochi@hainanu.edu.cn*

Abstract: Whole-brain single-neuron morphology reconstruction is essential for mapping neural circuit connectivity and understanding information processing in the brain. However, automated reconstruction from large-scale optical microscopy data remains challenging because of uneven fluorescence labeling, weak signals, complex background noise, and densely crossing neurites. In addition, block-wise processing of whole-brain datasets can introduce fiber discontinuities at block boundaries, while complex crossing regions may lead to false connections and topological errors. To address these challenges, this study proposes a single-neuron reconstruction framework that integrates dynamic snake convolution with geometric-topological repair. Dynamic snake convolution adaptively captures the local orientation of neurites and adjusts the receptive field shape, thereby improving the representation of thin, curved, and weak-signal neuronal processes. Geometric-topological repair further incorporates growth-direction consistency, curvature continuity, and spatial proximity priors to constrain the reconnection and structural repair of fragmented neurite segments, reducing the risk of false links in densely crossing regions. Experiments on fMOST whole-brain imaging data show that the proposed method achieves a single-neuron separation F1 score of 0.7491. Compared with

existing methods, the framework shows better structural continuity and robustness in complex crossing, weak-signal, and dense-fiber regions, providing technical support for large-scale neural circuit analysis and brain connectome mapping.

Keywords: single-neuron reconstruction; dynamic snake convolution; geometric-topological repair; single-neuron separation; optical microscopy imaging

[NP-24] PIBM2026-0618-28

The functional role of axonal projection patterns of mice primary visual cortex neurons in innate defensive behavior

Deyong Gong[1], Huijuan Lei[1], Zican Wang[1] , Zimin Dai[1], Jin Chang[1], Wei Zhou[1]

[1] Britton Chance Center and MoE Key Laboratory for Biomedical Photonics ,Wuhan National Laboratory for Optoelectronics , Huazhong University of Science and Technology

wzhou@mail.hust.edu.cn

Abstract: Visual threats are primary sensory cues that reliably evoke defensive behaviors. The superior colliculus（SC）serves as a critical node for generating defensive behaviors，receiving visual signals through two distinct pathways originating from retinal ganglion cells（RGCs） and primary visual cortex (V1). The RGC-SC pathway directly drives escape behavior, and the V1-SC pathway mediates fear-induced transient freezing. In addition, the V1-SC pathway sends collaterals to other visual threat-related regions including thalamus (TH) and striatum (STR), as confirmed by whole-brain axonal tracing. However, it remains unclear how axonal projection patterns of V1 neurons, defined by a specific combination of regions, participate in innate defensive behavior. By combining behavior assays, single-cell response properties and whole-brain projection mapping, we investigated how axonal projection patterns of V1 neurons modulate innate defensive responses. Axonal projection pattern heterogeneity supports the encoding of complex environment cues. This study converts the application of axonal projection patterns from mere anatomical descriptions to functional predictors of behavioral outcomes. The functional specialization of axonal projection patterns may facilitate precision in psychiatric conditions including anxiety and PTSD.

[NP-25] PIBM2026-0618-29

Distinct roles of apical and basal dendrites in shaping spatiotemporal tuning of mouse V1 pyramidal neurons

Zican Wang[1], and Wei Zhou[1]

[1]Britton Chance Center and MoE Key Laboratory for Biomedical Photonics

Huazhong University ofScience and Technology

Corresponding author e-mail address: wzhou@mail.hust.edu.cn

Abstract: Dendrites constitute sophisticated subcellular apparatuses specialized for afferent signal reception and active computation within neurons. Their multi-order arborization and topological architecture distributed across cortical tissue integrate information streams from heterogeneous synaptic inputs, which ultimately determine the functional tuning properties of individual neurons. In L2/3 pyramidal neurons of the mouse V1, the morphological architecture and firing activity of apical dendrites jointly determine the neuronal orientation

preference, whereas basal dendrites are essential for maintaining robust orientation selectivity in response to motion stimuli. How apical and basal dendrites modulate motion-related spatiotemporal tuning remains elusive. Combining in vivo two-photon calcium imaging and HD-fMOST, we systematically examined the correlations between dendritic morphology and motion visual responses. We confirmed both dendrite compartments contribute to spatiotemporal tuning, yet only basal architecture relate to orientation tuning (OSI). Morphological complexity, skeletal span and extension of apical and basal dendrites all correlate with spatiotemporal tuning (SF, TF, ST). First, the structural complexity of both apical and basal dendritic compartments exhibited statistically significant correlations with three core spatiotemporal tuning metrics, including spatial frequency (SF), temporal frequency (TF), and spatiotemporal tuning (ST). Such structure-function relationships exhibited distinct compartment-specific patterns: spatiotemporal tuning was associated with the peak number of Sholl crossings of apical dendrites (Peaks), whereas in basal dendrites, it was correlated with Sholl crossings of peripheral dendritic branches (Tips). Furthermore, dendritic skeletal span and extension degree both showed significant correlations with ST, whereas their relationships with SF and TF exhibited compartmental specificity. In addition, dendritic morphological features correlated with OSI were exclusively detected in basal dendritic compartments. Collectively, apical and basal dendrites do not independently process visual signals. Instead, they coordinate via compartment-specialized mechanisms to tune distinct visual features. This study provides a morphological reference for future investigations into the cellular mechanisms underlying multiscale parallel encoding of spatiotemporal visual encoding in dendrites.

[NP-26] PIBM2026-0618-5

Structural and functional dissection of retrosplenial cortex layer 5 neurons

Bimin Liu[1,2], Yuxiao Li[1,2], Miao Ren[1,2], and Xiangning Li[1,2]

[1]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Sanya, China.

[2] HUST-Suzhou Institute for Brainsmatics, JITRI, Suzhou, China.

Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: The cerebral cortex supports perception and information integration through spatiotemporally organized cross-regional and laminar circuit dynamics. General anesthesia is a special inhibitory state that disrupts cortical homeostasis, leading to a reversible loss of consciousness and intraoperative analgesia. It is widely hypothesized that anesthetics alter cortical network connectivity and impair information integration. Macroscopic imaging techniques, such as PET and fMRI, have revealed state-dependent alterations in functional connectivity between awake and anesthetized conditions. Advances in EEG and optical imaging have further elucidated alterations in region- and layer-specific neuronal activity. For instance, ketamine triggers low-frequency oscillations exclusively in the retrosplenial cortex (RSP), whereas layer 5 pyramidal neurons exhibit higher synchrony in spontaneous activity under various anesthetics. Nevertheless, population-level recordings are insufficient to resolve the precise regulatory patterns of specific neurons. In this study, two-photon microscopy combined with MOST imaging was utilized to dissect the structural and functional mechanisms by which RSP layer 5 neurons modulate information processing across different brain states.

[NP-27] PIBM2026-0618-6

A rapid vascular staining method for ex vivo thick tissues

Mengqi Ju[1], Miao Ren[1], Xiangning Li[1*]

State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: Three-dimensional vascular labeling of ex vivo thick tissues is an important technical basis for constructing vascular maps and analyzing pathological architecture. Current approaches mainly include vascular perfusion filling, immunofluorescent labeling, endothelial-associated lectin- or dye-based labeling, and whole-tissue imaging strategies combined with tissue clearing and optical sectioning. These methods have been applied in studies of the brain, tumors, and various parenchymal organs. However, their application to large-volume fixed specimens still faces common challenges, including limited deep penetration of probes, diffusion barriers formed by lipids and dense extracellular matrices, reduced tissue permeability after long-term fixation, and substantial differences in autofluorescence, vascular density, and preservation status across organs and species. These factors often result in discontinuous signals, high background, time-consuming procedures, and insufficient cross-sample applicability. To address these issues, we established a simplified rapid vascular staining workflow for ex vivo thick tissues. By optimizing delipidation conditions, dye concentration, incubation time, and pre-imaging processing, this method improves the continuity of vascular labeling and operational efficiency. The method enables vascular labeling of thick tissues within a relatively short time and is applicable to multiple organs from mice and macaques, as well as human pathological brain samples. This work provides a convenient approach for vascular mapping and pathological analysis of ex vivo thick tissues.

Keywords: vasculature; ex vivo tissue; membrane fluorescent dye; fMOST

[NP-28] PIBM2026-0618-7

Tissue processing strategy for continuous submicron-resolution imaging of cerebral vascular networks

Qiu Tingting, Liu Xiaonian, Ren Miao, Li Xiangning[*]

State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University Corresponding author e-mail address: lixiangning@hainanu.edu.cn

Abstract: Continuous three-dimensional imaging of cerebral vascular networks is needed to reveal vascular architecture and to understand vascular remodeling during brain development and disease. However, accurate whole-brain vascular imaging remains difficult because brain preparations contain mechanically heterogeneous interfaces, including the skull, meninges, and brain parenchyma. These interfaces are prone to tissue shrinkage, detachment, vascular deformation, and fluorescence loss during conventional embedding and processing, which compromises continuous reconstruction of microvascular networks at micron to submicron resolution. To address this problem, we developed an improved tissue processing strategy for whole-cerebrum vascular imaging. The strategy uses an ethanol-based stabilization treatment to enhance

tissue stabilization and to improve the mechanical integrity of elastin-rich interfaces, particularly around the dura–pia boundary. Combined with a preparation workflow compatible with fluorescence micro-optical sectioning tomography, this method enables continuous imaging from the skull surface to deep brain regions while reducing deformation and preserving vascular topology and fluorescence stability. This approach provides a practical solution for high-resolution reconstruction and quantitative analysis of cerebral vascular networks, and may support future studies of cerebrovascular development, physiological regulation, and pathological remodeling.

Keywords: cerebral vascular network; whole-brain tissue processing; submicron-resolution imaging; fluorescence micro-optical sectioning tomography

[NP-29] PIBM2026-0622-1

The Disinhibited Cortex as an Attractor: Altered Burst Initiation Reveals Focal Excitatory-Inhibitory Imbalance

Nan Li[a#], Rongxin Li[a#], Jing Li[a], Chaojia Chu[a], Dan Li[b], Hongtao Ma[c*], Weihong Lin[a*]

[a] Department of Neurology, The First Hospital of Jilin University, 1 Xinmin Street, Changchun, Jilin 130021, China

[b] Department of Radiology, The First Hospital of Jilin University, 1 Xinmin Street, Changchun, Jilin 130021, China

[c] Department of Anesthesiology, Weill Cornell Medicine, 1300 York Avenue, New York, NY 10065

[#]Nan Li and Rongxin Li contributed equally as the first authors.

Corresponding author:

Weihong Lin

E-mail: linwh@jlu.edu.cn

Hongtao Ma

E-mail: hom2001@med.cornell.edu

Abstract: The imbalance between cortical excitation and inhibition (E/I) underlies many neurological disorders; however, its early detection remains challenging. The burst suppression (BS) pattern, characterized by a globally suppressed cortical background punctuated by quasi-periodic bursts, provides a unique functional window. Under the BS state, wide-field imaging showed that bursts originated from discrete, flexible cortical foci and propagated in a stereotyped, highly synchronized manner. Given the established role of E/I imbalance in disrupting cortical synchrony and our prior observation that bursts preferentially arise near seizure focus, we hypothesized that a focal hyperexcitability would exert a concentration-dependent attraction on burst origin sites. To test this, we induced a graded, focal E/I imbalance in the cortex of mice (n = 26) via microinjections of the GABAA antagonist bicuculline at subconvulsive concentrations during anesthesia-induced BS. Our analyses revealed that focal disinhibition reconfigured BS dynamics across multiple scales. First, at the local level, burst-associated calcium transients at the injection site showed a tendency toward reduced waveform complexity and an increased amplitude of the initial response peak. Second, at the global level, the functional synchrony between the disinhibited focus and the rest of the cortex was disrupted. Critically, burst origin sites were progressively attracted towards the imbalance focus in a concentration-dependent manner. Quantifying this spatial clustering via hemisphere-specific hotspot analysis confirmed a stronger attraction effect in the ipsilateral hemisphere. Together, these results demonstrate that the spatiotemporal pattern of BS serves as a sensitive and quantifiable readout for detecting and localizing focal cortical E/I imbalance.

[NP-30] PIBM2026-0627-4

Sono-magnetic triggered enhancement of pyroelectric catalytic nanozymes activity: Inducing disulfidptosis and immunotherapy via regulating molecular metabolism

Cong Wang, Yundi Wu, and Xilong Wu

School of Biomedical Engineering. Hainan University, Haikou, China

wuxilong@hainanu.edu.cn

Abstract: Glioblastoma (GBM) is a prevalent malignant tumor in the central nervous system, presenting significant treatment challenges attributed to its intricate tumor microenvironment (TME). Pyroelectric nanostructures have shown promise in producing temperature-induced reactive oxygen species (ROS) via the pyroelectric effect, which holds potential for addressing deeply situated hypoxic tumors. This research designed a sono-magnetic triggered thermoelectric catalytic nanozyme $Lu_{0.01}Fe_{0.99}Te_2$@SnTe-PEI/HA (LFSH), for the complex TME. The nanozyme forms a Z-scheme heterojunction by leveraging the energy band structures of its nanomaterial components, effectively reducing charge carrier recombination and thereby enhancing catalytic efficiency in sonodynamic therapy (SDT) and pyroelectric catalytic therapy (PECT). The treatment mechanism involves the use of AMF to activate the PECT efficacy of the pyroelectric nanozyme, while US stimulation is employed to create a synergistic treatment approach combining sono-magnetic-thermal-electric modalities, leading to ROS surge at the tumor site. Notably, LFSH demonstrates quadruple catalytic network properties, including peroxidase-like (POD-like) enzyme, L-cysteine oxidase-like (LCO-like) activity, NADPH oxidase-like (Nox-like) activity, and lactate dehydrogenase-like (LDH-like) activity. These activities collectively participate in consuming reducing metabolites via cascade reactions, disrupting the antioxidant defense system of tumor cells, and intensifying cell damage. In addition, the regulation of the lactate-glucose metabolic axis via LDH-like enzyme activity, coupled with NADPH depletion triggers disulfidptosis in cells, thereby amplifying the antitumor immune response. The development of this sono-magnetically activated pyroelectric catalytic nanozyme not only enables simultaneous modulation of tumor metabolism but also offers a novel strategy for addressing deeply situated glioblastoma.

Keywords: Glioblastoma; Pyroelectric catalytic therapy; Sonodynamic therapy; Nanozyme catalyst; Disulfidptosis

[NP-31] PIBM2026-0709-1

A spatial selective optical regulation system for photothrombotic cerebral ischemia modeling

Tingyu Sun[1], Pengcheng Li[1, 2], and Jinling Lu[1]

[1] MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[2] State Key Laboratory of Digital Medical Engineering, School of Bliomedical Engineering, Hainen University, Sanva. Hainan, 572025, China

Corresponding author e-mail address: lujinling@hust.edu.cn

Abstract: Photothrombotic cerebral ischemia models serve as essential experimental tools for investigating the pathophysiological mechanisms underlying ischemic stroke and evaluating potential therapeutic strategies. By inducing selective thrombosis in targeted cerebral blood vessels through photosensitizer activation and laser irradiation, these models reproduce key pathological features of cerebral ischemia while offering high

reproducibility and minimal surgical invasiveness. Consequently, they have been widely applied in studies of cerebrovascular pathology, neurovascular remodeling, inflammatory responses, and neuroprotection. However, conventional photothrombotic ischemia modeling still faces several limitations. The illumination region is typically manually defined, resulting in insufficient spatial precision and limited adaptability for targeting cerebral vessels with complex morphologies. Moreover, the lack of real-time blood flow monitoring during thrombus formation prevents dynamic evaluation of vascular occlusion and reperfusion, making it difficult to precisely regulate the severity and stability of ischemic injury. These limitations compromise model reproducibility and may cause unnecessary damage to surrounding healthy tissues.To overcome these challenges, this study develops a spatially selective optical control approach based on a spatial light modulator (SLM). By digitally modulating the laser illumination pattern, the proposed system enables programmable and highly precise targeting of individual cerebral vessels with diverse geometries. Furthermore, laser speckle contrast imaging (LSCI) is integrated to provide real-time monitoring of cerebral blood flow during photothrombotic induction, enabling closed-loop regulation of vascular occlusion. The integration of spatial optical control and blood flow feedback allows simultaneous visualization, quantitative perfusion assessment, and precise manipulation of cerebral vessels within a single platform. Photothrombotic ischemia experiments demonstrate that the proposed system achieves vessel-selective cerebral ischemia induction with improved spatial precision, reproducibility, and controllability compared with conventional approaches. This platform provides a reliable and versatile tool for constructing experimental cerebrovascular disease models and facilitating mechanistic investigations of cerebral ischemia.

[NP-32] PIBM2026-0709-2

Title Time-scale-matched speckle contrast analysis for rapid OCT blood flow velocimetry

Yuanlong Wang [1], Jiachi Hong[1,2], Pengcheng Li[1,2] and Jinling Lu[1]

[1]'MOE Key Laboratory for Biomedical Photonics, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology, Wuhan 430074, China

[2]State Key Laboratory of Digital Medical Engineering, School of Biomedical Engineering, Hainan University, Sanya. Hainan, 572025, China.

Corresponding author e-mail address: lujinling@hust.edu.cn

Abstract: Quantitative OCT velocimetry of rapid blood flow is limited not only by scanning speed, but also by the temporal match between speckle decorrelation and the effective observation time. When moving scatterers decorrelate faster than the available temporal window, direct temporal fluctuation analysis becomes insensitive and may underestimate high-speed flow. We present a time-scale-matched speckle contrast analysis for OCT blood flow velocimetry, in which repeated A-line measurements at the same spatial location are integrated to generate intensity signals with controlled equivalent exposure times. In this formulation, the measured speckle contrast is determined by the exposure-weighted integral of the intensity autocorrelation function, while the underlying field autocorrelation reflects scatterer motion within the OCT resolution voxel. Therefore, velocity information can be recovered by selecting an equivalent exposure time that adequately samples the decorrelation process and by fitting the contrast using an exposure-time-dependent flow model. This strategy shifts the analysis from resolving every short-time fluctuation to extracting a robust statistical descriptor of motion-induced speckle dynamics. Using a swept-source OCT system with repeated A-line acquisition, we demonstrate depth-resolved rapid-flow velocimetry in controlled flow phantoms and representative biological imaging results. The method preserves the three-dimensional sectioning capability of OCT while expanding

quantitative sensitivity for high-speed vascular flow. This time-scale-matched framework provides a compact and practical interpretation of speckle-contrast-based OCT velocimetry and may support rapid hemodynamic assessment in biomedical imaging applications.