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## **Structural and functional mapping of whole-brain electrodynamics with photoacoustic imaging**

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Imaging brain voltage is essential for advancing our understanding of neural activity and for the diagnosis of neurological disorders. Although optical voltage imaging has made notable strides in recent years, it remains constrained by limitations in penetration depth, field of view, and the stability of voltage-sensitive dyes (VSDs). Photoacoustic imaging (PAI) offers a promising alternative, providing capabilities for deep-tissue, whole-brain imaging and real-time monitoring. To address current challenges, we developed a wide-field photoacoustic brain detection (WF-PABD) system incorporating a photostable voltage-sensitive dye (PA-VSD), enabling comprehensive mapping of voltage fluctuations across the mouse brain during epileptic episodes. Our findings demonstrate that PA-VSD allows high-resolution visualization of the entire cerebral microvasculature and delineation of cranial structures with strong contrast—even in low-blood-background scenarios. The system also facilitates extended seizure tracking and accurate identification of epileptic foci. Additionally, by analyzing temporal signal distribution and interregional correlations, we successfully delineated the pathways and direction of electrical signal propagation, offering valuable insights for chronic monitoring and the diagnosis of voltage-related neurological diseases. Beyond this, we further demonstrate the versatility of PAI across multiple clinical domains, including quantitative assessment of vascular microenvironmental changes during cupping therapy, evaluation of liver stiffness, monitoring the efficacy of microneedle-based drug delivery, and tracking tumor treatment response. These explorations aim to establish a theoretical foundation for the clinical translation of PAI technologies.

### **Short Bio:**



Prof. Puxiang Lai is currently a tenured Associate Professor at the Department of Biomedical Engineering at the Hong Kong Polytechnic University. His research centers around deep-tissue optical focusing, imaging, stimulation, and treatment. Current research projects include, but are not limited to, wavefront shaping, photoacoustic imaging, neuron stimulation, computational optics, and artificial intelligence. His research has fueled more than 100 top journal publications, such as Nature Photonics, Nature Communications, The Innovation, eLight, and Light: Science & Applications. He has been invited to give more than 100 seminars or invited talks worldwide. Dr. Lai was awarded the 12<sup>th</sup> National Talent Plan (Youth) and the 2016-2017 Hong Kong RGC Early Career Award. As a recognition for his contribution to the field, currently Puxiang serves as Associate Editor or Editor for a few premium journals, such as The Innovation, The Innovation Medicine, Journal of Visual Computing for Industry, Biomedicine, and Art (VCIBA), and Journal of Innovative Optics in Health and Science (JIOHS). He also serves as a Council Member of the World Association for Chinese Biomedical Engineers (WACBE), the Director of Chinese Laser Press (CLP)- Hong Kong Branch, and a Standing Committee Member of the Biomedical Optics Panel in the Chinese Optical Society, among other duties.