Research:

Adaptive Optics Microscopy for Fine Live Imaging

1. Towards the non-invasive imaging of brain networks and functions at high resolution

We developed a new microscope system combining three-photon excitation and adaptive optics capable of high-resolution in vivo imaging of fine neuronal structures in the mouse cortex through intact skull of mouse. We demonstrated the use of this platform to guide precise laser-mediated microsurgery through the intact skull and for accurate and sensitive functional calcium imaging of brain.

Related article:

“XXXX”, Nature Biotechnology,….

Related research grants:

General Research Fund (16102518): "High-resolution imaging of mouse brain in vivo through thinned skull cranial window based on adaptive optics wavefront correction"

Collaborative Research Fund (C6001-19EF): "High-resolution adaptive optics microscope system for live and deep imaging of biological tissues"

2. Deep brain imaging enabled by adaptive optics two-photon endomicroscopy

Optical deep brain imaging in vivo at high resolution has remained a great challenge. We developed an adaptive optics two-photon endomicroscopy providing a minimally invasive approach to image buried brain structures at high-resolution. A new precompensation strategy plays a critical role to correct aberrations over large volumes and achieve rapid random-access multiplane imaging. We investigate the neuronal plasticity in the hippocampus, a critical deep brain structure, and reveal the relationship between the somatic and dendritic activity of pyramidal neurons.

Related article:

“xxxxx”, Scince Advances, ….

Related research grants:

General Research Fund (16102518): "High-resolution imaging of mouse brain in vivo through thinned skull cranial window based on adaptive optics wavefront correction"

Collaborative Research Fund (C6001-19EF): "High-resolution adaptive optics microscope system for live and deep imaging of biological tissues"

3. Adaptive optics two-photon microscopy for structural and functional retinal imaging

In vivo fundus imaging offers non-invasive access to neuron structures and biochemical processes in the retina. However, optical aberrations of the eye degrade the imaging resolution and prevent visualization of subcellular retinal structures. We developed an adaptive optics two-photon excitation fluorescence microscopy (AO-TPEFM) system to correct ocular aberrations based on a nonlinear fluorescent guide star and achieved subcellular resolution for in vivo fluorescence imaging of the mouse retina. The AOTPEFM permits structural and functional imaging of the mouse retina with submicron resolution.

Related article:

“xxxxx”, Nature – Light: Science and Applications, ….

Related research grants:

General Research Fund (16103215): “In Vivo Adaptive Optics Multiphoton Microscopy for the Study of Retinal Ganglion Cell Death and Glaucoma”

General Research Fund (16102421): “In vivo visualization of structural and functional progression of retinal diseases at subcellular resolution in mouse models”

Multimdal nonlinear microscopy for biological imaging

1. In vivo imaging study of spinal cord injury

In vivo spinal cord imaging in mouse models without introducing immunological artifacts is critical to understand spinal cord pathology and discover effective treatments. We developed a minimally invasive intervertebral window by retaining the ligamentum flavum to protect the underlying spinal cord. By introducing an optical clearing method, we study neuron-glia dynamics following laser axotomy and observe strengthened contact of microglia with the nodes of Ranvier during axonal degeneration. By enabling long-term, repetitive, stable, high-resolution and inflammation-free imaging of mouse spinal cord, our method provides a reliable platform in the research aiming at interpretation of spinal cord physiology and pathology.

Related article:

“xxxxx”, Nature Communications, ….

Related research grants:

General Research Fund (16102920): “Development of advanced multimodal nonlinear optical microscopy for in vivo study of spinal cord injury”

Research Equipment Competition (REC14EG09): “High resolution stimulated Raman scattering (SRS) microscope system”

2. In vivo metabolic imaging and monitoring of adipose tissue

We investigated the metabolic characteristics of adipose tissues in live mouse model using a multiphoton redox ratio, fluorescence lifetime imaging technology and stimulated Raman scattering microscopy. Our study uncovered significant heterogeneity in the cellular structures and metabolic characteristics of thermogenic adipocytes in brown and beige fat. Subgroups of brown and beige adipocytes were identified based on the distinct lipid size distributions, redox ratios, fluorescence lifetimes and thermogenic capacities. The results of our study show that this label-free imaging technique can shed new light on in vivo study of metabolic dynamics and heterogeneity of adipose tissues in live organisms.

Related article:

“xxxxx”, Journal of Biophotonics, ….

Related research grants:

General Research Fund (16102518): “Label-free imaging of adipose tissue in vivo with integrated stimulated Raman scattering and two-photon fluorescence microscopy”

Research Equipment Competition (REC14EG09): “High resolution stimulated Raman scattering (SRS) microscope system”

3. Quantitative Imaging of Biological Dynamics by Stimulated Raman Scattering Microscopy

Quantitative methods to precisely measure cellular states in vivo have become increasingly important and desirable in modern biology. We developed a technique based on SRS microscopy of vibrational tags for quantitative imaging of lipid synthesis, lipolysis and biodistributions in live animals and cells. The technique aims to overcome the major limitations of conventional fluorescent staining and lipid extraction methods that do not provide the capability of in vivo quantitative analysis. Using a hyperspectral SRS (hsSRS) microscope and subtraction method, we demonstrated the unique capability of hsSRS microscopy in quantitative analysis of lipid metabolism in vivo. We reported a probe, named AIE-SRS-Mito, for imaging mitochondria in live cells via fluorescence (FL) and stimulated Raman scattering (SRS) imaging.

Related articles:

“xxxxx”, JACS, …

“xxxxx”, Analytical Chemistry, ….

General Research Fund (16102518): “Label-free imaging of adipose tissue in vivo with integrated stimulated Raman scattering and two-photon fluorescence microscopy”

Research Equipment Competition (REC14EG09): “High resolution stimulated Raman scattering (SRS) microscope system”

High-precision single-cell tracing

Heterogeneity broadly exists in various cell types both during development and at homeostasis. Investigating heterogeneity is crucial for comprehensively understanding the complexity of ontogeny, dynamics, and function of specific cell types. Traditional bulk-labeling techniques are incompetent to dissect heterogeneity within cell population, while the new single cell lineage tracing methodologies invented in the last decade can hardly achieve high-fidelity single-cell labeling and long-term in-vivo observation simultaneously. We developed a high-precision infrared laser-evoked gene operator heat-shock system to achieve precise single-cell labeling and tracing. In vivo study indicated that this system can precisely label single cell in brain, muscle and hematopoietic system in zebrafish embryo. Using this system, we traced the hematopoietic potential of hemogenic endothelium (HE) in the posterior blood island (PBI) of zebrafish embryo and found that HEs in the PBI are heterogeneous, which contains at least myeloid unipotent and myeloid-lymphoid bipotent subtypes.

Related articles:

“xxxxx”, eLife, …

“xxxxx”, Developmental Cell, ….

NSFC/RGC Joint Research Scheme (N\_HKUST603/19): “Study of the lineage relationship between hematopoietic stem cells and tissue-resident macrophages using a high-precision single-cell tracing technique”

Information about me:

Academic experiences and qualifications:

1997 - present: Assistant/Associate/Full Professor, Department of Electronic and Computer Engineering, The Hong Kong University of Science and Technology.

2006: Invited Professor, Swiss Federal Institute of Technology (Ecole Polytechnique Federale de Lausanne), Switzerland.

2005: Visiting Associate Professor, Beckmann Laser Institute and Department of Surgery, University of California, Irvine, USA.

1995 - 1997: Staff Scientist, Division of Biophysics and Bioimaging, Ontario Cancer Institute, Toronto, Canada.

1991 - 1994: Postdoctoral Research Associate, Department of Physics, University of California, Irvine, USA; British Columbia Cancer Research Center, Vancouver, Canada.

Selected recent publications: (no need to provide links)

1. Zhongya Qin, Zhentao She, Congping Chen, Wanjie Wu, Jackie K.Y. Lau, Nancy Y. Ip and Jianan Y. Qu, “Deep tissue multi-photon imaging using adaptive optics with direct focus sensing and shaping" , Nature Biotechnology , …
2. Wanjie Wu, Sicong He, Junqiang Wu, Congping Chen, Xuesong Li, Kai Liu and Jianan Y. Qu, “ Long-term in vivo imaging of mouse spinal cord through an optically cleared intervertebral window”, Nature Communications , V. 13, 1959 (2022).
3. Zhongya Qin, Congping Chen, Sicong He, Ye Wang, Kam Fai Tam, Nancy Y. Ip and Jianan Y. Qu, "Adaptive optics two-photon endomicroscopy enables deep brain imaging at synaptic resolution over large volumes", Science Advances, 30 Sep 2020: Vol. 6, no. 40, eabc6521 DOI: 10.1126/sciadv.abc6521
4. Zhongya Qin, Sicong He , Chao Yang, Jasmine Sum-Yee Yung, Congping Chen, Christopher Kai-Shun Leung, Kai Liu and Jianan Y. Qu, "Adaptive optics two-photon microscopy enables near-diffraction-limited and functional retinal imaging in vivo", Nature – Light: Science & Applications, (2020)9:79, <https://doi.org/10.1038/s41377-020-0317-9>
5. Sicong He, Ye Tian, Shachuan Feng, Yi Wu, Xinwei Shen, Kani Chen, Yingzhu He, Qiqi Sun, Xuesong Li, Jin Xu, Zilong Wen, Jianan Y Qu, " In vivo single-cell lineage tracing in zebrafish using high-resolution infrared laser-mediated gene induction microscopy", eLife 2020;9:e52024, DOI: 10.7554/eLife.52024