

Interferometric Ultra-high resolution imaging system

Interferometric microscopy achieves sub-15-nm 3D protein mapping deep in tissue with ~10× resolution gains.

Modern single-molecule super-resolution microscopy for biological tissues is often difficult due to optical scattering and aberrations. This limits the resolution and depth at which these tissues can be studied. Researchers at Purdue University have developed a system, termed 4Pi-BRAINSPOOT, for imaging deep biological tissues at ultra-high resolution. This technology comprises a novel optical system and algorithms for image processing that can achieve 10-fold higher resolution than conventional methods through tissues that are 5 times thicker. In addition, this imaging approach enables the quantification of protein distribution with sub-15-nm resolution in all three dimensions in a complex tissue specimen. It demonstrated the capacity to determine the molecular arrangements in various sub-cellular organelles and membrane morphology of individual dendritic spines through 50-micron mouse brain slices. This ultra-high-resolution approach allows researchers to decipher nanoscale organelle architecture and molecular distribution in both isolated cells and native tissue environments with a precision down to a few nanometers.

Technology Validation:

Comparative results inside 50-micron thick mouse brain samples indicate a 1.5-fold increase in coherent fringe contrast (from 0.25 to 0.38) and a 1.3-fold increase in signal-to-background ratio (from 80.1 to 106.9). 4Pi-BRAINSPOOT further enables a 60% reduction in out-of-focus background across 50-m thick brain sections.

Advantages:

- 10-20-fold improvement in resolution compared to conventional imaging
- 3-5-fold improvement in penetration depth in biological tissue vs. conventional imaging

Technology ID

2025-HUAN-70839

Category

Digital Health &
Medtech/Medical Image
Processing

Authors

Hao-Cheng Gao
Fang Huang
Fan Xu

Further information

Parag Vasekar
psvasekar@prf.org

View online



Applications:

-Biological tissue imaging

-Microscopy

TRL: 4

Intellectual Property:

Provisional-Gov. Funding, 2024-10-03, United States

Utility-Gov. Funding, 2025-10-03, United States

Keywords: Biological Imaging, Biomedical Engineering, Biotechnology, Deep Tissue Imaging, Interferometric, Microscopy, Ultra-high Resolution