

Investigating the brain extracellular space in live brain slices by super-resolution STED microscopy

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日時 令和5年 6月 29日 (木) 13:00~14:00

場所 東京大学医学部教育研究棟 13階 第5セミナー室

セミナー要旨

The brain extracellular space (ECS) is a continuum of interconnected channels and reservoirs. The ranges of ECS channel widths, lengths, and shapes easily exceed the morphological complexity of individual neural cells, so that on one hand the ECS is comparatively vast in extent, while at the same time its even more geometrically complex. The combination of spatial continuity and a fine mesh-like structure makes the ECS extremely difficult to visualize in live tissue, as conventional light-microscopy blurs out structural details beyond cell somata and large dendrites. Current data on ECS structure are therefore based largely on volume-averaging imaging techniques or electron microscopy in fixed tissue. Accordingly, our knowledge about ECS structure and dynamics is rudimentary.

In a step forward, we recently introduced super-resolution shadow imaging (SUSHI) to image the extracellular space in live brain slices by combining STED microscopy with fluorescent perfusion-labeling of the interstitial fluid (Tønnesen et al, Cell 2018). SUSHI reveals the complex geometry and dynamics of the ECS, while simultaneously outlining all cellular structures in the field of view as shadows. In this talk I will introduce STED microscopy for imaging in live organotypic mouse brain slices, and how we went from imaging individual neuronal synapses to also imaging the extracellular space. I will show preliminary results from a computational diffusion model we are establishing based on SUSHI images of the ECS, which may help us understand functional aspects of extrasynaptic signaling and metabolite clearance from dense parenchyma.

多数の皆様のご来聴をお待ちしております。