

Multiple Routes to 3D Imaging – Combining Information from Different Microscopy Modalities

K.S. Grusmayer^{1,2,3}, A. Descloux^{2,3}, V. Navikas², R. Wombacher⁴, K. Yserentant⁵, S.M. Leita⁶, K. Ibrahim^{2,7}, N. Riguet⁷, L. Feletti², D.P. Herten⁵, G. Fantner⁶, H. Lashuel⁷, A. Radenovic²

¹ Department of Bionanoscience and Kavli Institute of Nanoscience Delft, TU Delft, Netherlands; ² Laboratory of Nanoscale Biology, EPFL, Switzerland; ³ Laboratory of Biomedical Optics, EPFL, Switzerland; ⁴ Department of Chemical Biology, MPIImF, Germany; ⁵ Centre of Membrane Proteins and Receptors (COMPARE), College of Medical and Dental Sciences, Medical School & School of Chemistry, University of Birmingham, UK; ⁶ Laboratory for Bio- and Nano-Instrumentation, EPFL, Switzerland; ⁷ Laboratory of Molecular and Chemical Biology of Neurodegeneration, EPFL, Switzerland.

Abstract

Microscopy techniques, especially in fluorescence super-resolution imaging, present trade-offs, for example between resolution, acquisition speed and live-cell compatibility. I will present two strategies for 3D imaging: an image-splitting prism for simultaneous multiplane acquisition [1] and remote focusing via adaptive optics [2]. SOFI is an alternative to localization microscopy that analyzes spatio-temporal fluctuations in fluorescence by calculating higher-order cumulants, a quantity related to correlations. The method is less demanding in terms of fluorophore photoswitching and brightness, offering better time resolution and lower phototoxicity at the cost of a more moderate resolution gain. We exploit the synergy between super-resolution optical fluctuation imaging (SOFI) and self-blinking fluorophores for 2D imaging with up to 50-60nm resolution and for 3D imaging covering up to 10µm depth [1,2]. I will furthermore show how we combine the fluorescence-based molecule specific information with label-free 3D imaging to acquire complementary information e.g. about the topology of cells (scanning-ion conductance microscopy (SICM) [3]) and their morphology and dry mass (quantitative phase imaging [4]). I will give an outlook on the application of these techniques to study neurodegenerative disease and highlight how we leverage deep learning for label-free identification of the associated aggregates [5].

References

- [1] K. Grusmayer, Tomas Lukes, Theo Lasser, and Aleksandra Radenovic, ACS Nano 2020, 14, 7, 9156–9165; <https://doi.org/10.1021/acsnano.0c04602>
- [2] V. Navikas, A. C. Descloux, K.S. Grusmayer, S. Marion, A. Radenovic, Nanophotonics 2021, 000010151520210108. <https://doi.org/10.1021/acsp Photonics.1c00668>
- [3] V. Navikas, S. Mendes, K. Grusmayer, et al., Nat. Comm. (2021), 12, 4565.
- [4] A. Descloux, K. Grusmayer (equal contribution), ..Lasser, T., Nat. Photonics (2018), 12, 165–172.
- [5] Khalid A. Ibrahim, Kristin S. Grusmayer*, Nathan Riguet, Lely Feletti, Hilal A. Lashuel* and Aleksandra Radenovic*, under submission, <https://www.biorxiv.org/content/10.1101/2023.04.21.537833v1>