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

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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 10um 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

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