Improving super-resolution optical microscopy for (neuro-)biology

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Far-field optical super-resolution microscopy or nanoscopy techniques "super-resolve" features residing closer than the diffraction-limit by transiently preparing fluorophores in distinguishable (typically on- and off-) states and reading them out sequentially.
In coordinate-targeted super-resolution modalities, such as stimulated emission depletion (STED) microscopy, the state difference is created by patterns of light, driving for instance all molecules to the off-state except for those residing at intensity minima.
Expansion microscopy provides an intriguing alternative route by isotropically increasing the physical separation between fluorophores by embedding the sample in a swellable hydrogel [1] and thus increasing effective spatial resolution.
I will discuss the efforts of my recently founded group at IST Austria where we work as an interdisciplinary team of physicists, biologists, and neuroscientists to develop and apply methods that bridge spatial scales from the nanoscale molecular arrangements to the native tissue context and where we strive to characterize biological samples with high information content. To this aim, we further develop and employ STED microscopy and expansion microscopy [2] to enable nanoscale imaging deep in living and fixed tissues. To characterize cellular and molecular arrangements, we combine these with multiplexed labelling both at the protein and the RNA level.

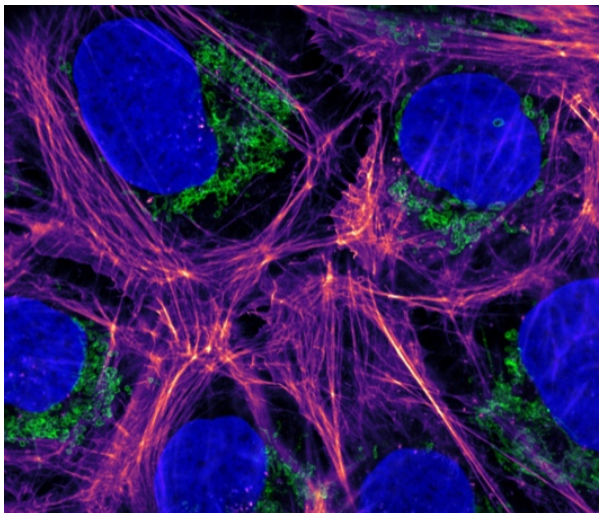

Figure: Dual colour STED image of cultured cells with actin (pink) and mitochondria (green) labelled. Nuclei are counterstained in blue.

[1] Chen, Tillberg, & Boyden, Science 347, 543 (2015)
[2] Truckenbrodt, Sommer, Rizzoli, & Danzl, Nature Protocols, in press (2019)