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## **Super-Resolution Light Microscopy in Physiology and Disease: Advances and Challenges**

Christoph Cremer<sup>1,2,3</sup>

<sup>1</sup>Institute of Molecular Biology (IMB), D-55128 Mainz/Germany; <sup>2</sup>Institute for Pharmacy and Molecular Biotechnology (IPMB), University Heidelberg & Kirchhoff-Institute for Physics (KIP), D-69120 Heidelberg/Germany; <sup>3</sup>Department of Physics, University Mainz (JGU), Germany

e-mail: [c.cremer@imb-mainz.de](mailto:c.cremer@imb-mainz.de); [cremer@kip.uni-heidelberg.de](mailto:cremer@kip.uni-heidelberg.de)  
[www.optics.imb-mainz.de](http://www.optics.imb-mainz.de)

Using super-resolution microscopy (SRM) approaches, both optical and structural resolution have been enhanced far beyond the conventional resolution limit. At the present state of the art, they allow the imaging of specific molecules inside biological specimen down to an optical resolution in the few nm range and a structural resolution down to the 10 nm regime. In this report, we shall review some examples of the present advances of SRM in physiology and cellular pathology and discuss the challenges still to be met to introduce such SRM technologies on a larger scale. In our experience, the present spectrum of such application examples comprises high resolution analysis of age dependent macula degeneration using structured illumination (SIM); of the disease related distribution of membrane bound receptors, transcription factors and intracellular microRNAs, or of virus-membrane interactions by single molecule localization microscopy (SMLM); the SRM monitoring of the repair of double strand DNA breaks induced by X-rays and heavy ion radiation on the single molecule level; the compaction status of individual disease related short DNA sequences by SRM based Combinatorial Oligonucleotide Fluorescence in situ Hybridization (Combo-FISH); the SRM analysis of chromatin texture in brain cancer cells; or the imaging of chromatin nanostructure changes induced in cardiomyocyte cells under ischemia conditions (oxygen and nutrition depletion). On this basis, we anticipate various methodological directions towards a broad medical application of SRM, such as large field of view imaging; high working distances (up to the cm range) compatible with super-resolution of 3D extended objects, such as cell spheroids or tissues; “nanoimaging” of multiple molecular target types (“multicolor SRM”); high throughput SRM to register thousands of cells in a short time, e.g. for diagnostics or pharmaceutical research; as well as the development of fast & reliable data evaluation modes (“Instant Nanoimaging”).