

Spectrally Assigned Localization Microscopy: A new lightoptical approach to study chromosome geometry on the nanoscale

C. Cremer*

**Universität Heidelberg, ¹Kirchhoff-Institut für Physik (KIP), ²Institut für Pharmazie und Molekulare Biotechnologie (IPMB), ³Bioquant-Zentrum, ⁴Interdisziplinäres Zentrum für Wissenschaftliches Rechnen (IWR); Institute for Molecular Biophysics/The Jackson Laboratory, Bar Harbor, ME*

One of the key issues of modern cell biology is the complex interplay between chromosome geometry, gene function and gene regulation. For this, detailed knowledge about the spatial organization of chromatin on the nanoscale, e.g. of active and inactive gene domains, should be highly relevant.

Until recently, however, the structural analysis of chromatin by farfield light microscopy methods has been limited to an optical resolution of about 200 nm (Abbe 1873). During the last years, several methods of lightoptical superresolution far field fluorescence microscopy (nanoscopy) have been developed.

The lecture will focus on Spectrally Assigned Localization Microscopy (SALM). Using a special SALM method, Spectral Precision Distance/Position Determination Microscopy (SPDM) with physically modified fluorophores, we achieved to measure the cellular distribution of appropriately labelled proteins and DNA sequences with a lateral effective optical resolution down to ca. 10 nm (about 1/50 of the exciting wavelength). Using a combination of SPDM and Spatially Modulated Illumination (SMI) microscopy, in addition an axial resolution of about 40 – 50 nm was obtained. Examples for the SPDM analysis of general chromatin nanostructure in human cell nuclei and of specific nuclear domains will be discussed.