Institute of Biophysics

Molecular Mechanisms of Transcription and Gene Regulation in Eukaryotes

Head: Jens Michaelis

Gene expression in eukaryotes is a complicated and highly regulated dynamical process. By looking at the key steps of this process in real time and at the level of single molecules, we are able to obtain mechanistic insight. Using single-molecule fluorescence resonance energy transfer (smFRET) and related techniques, we were able to obtain structural and dynamic information about one of the key enzymes of gene expression, RNA polymerase II. During this process we had to improve the methodology for such measurements in order to gain access to the quantitative information required for building models elucidating structure-function relationships. To achieve this, we developed the so-called Nano Positioning System (NPS) and applied it to open questions in the areas of transcription initiation, transcription elongation and, most recently, nucleosome remodeling.

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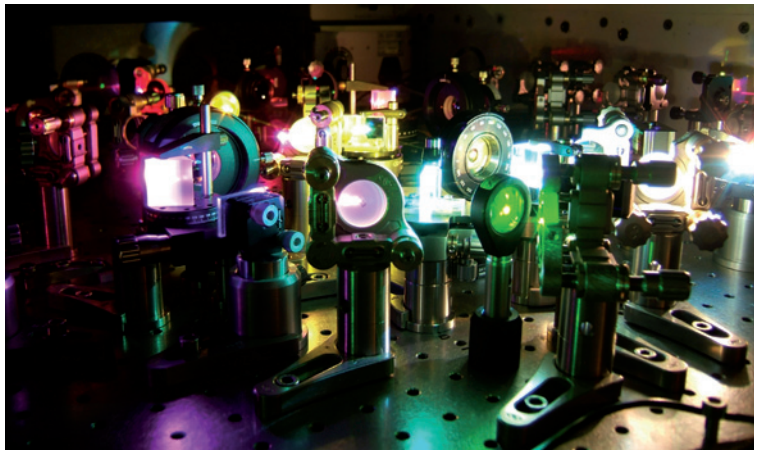
Rather than just looking at the structure and dynamics of single complexes, the intra cellular movement of complexes is also of interest for understanding the spatio-temporal regulation. We perform such experiments using single-molecule tracking techniques, thereby focusing on specific aspects, such as the position and mobility of certain factors during the cell cycle. By attaching fluorescent particles or even single dye molecules to such complexes, we can obtain position information on length scales down to a few nanometers in real time.

With the growing amount of information about gene expression available, the questions that are developing have also become more and more complex and, as a result, there is often the wish to study ever larger complexes and transient architectures. For this reason, we are also developing super-resolution optical fluorescence microscopy techniques in which the resolution limit of optical microscopy is overcome by turning fluorescent molecules on and off. By using these techniques one can bridge the length scale from that of single molecules to standard microscopy approaches covering the cellular level. Thus, we now have the complete toolbox for answering mechanistic questions regarding gene expressions in vitro as well as in living cells.



Setup of a super-resolution optical fluorescence microscope based on the principle of stimulated emission depletion (STED). The microscope was developed in the institute and now allows for the super-resolution imaging of two colors simultaneously with a resolution of about 30nm in x and y and about 80 nm in z.

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Selected Publications:

- *Torrano AA, Blechinger J, Osseforth C, Argyo C, Reller A, Bein T, Michaelis J, Bräuchle C (2013): "A fast analysis method to quantify nanoparticle uptake on a single cell level," Nanomedicine, doi: 10.2217/nnm.12.178.*
- *Bönisch C, Schneider K, Pünzeler S, Wiedemann S, Bielmeier C, Bocola M, Eberl C, Kuegel W, Neumann J, Kremmer E, Leonhardt H, Mann M, Michaelis J, Schermelleh L, Hake S (2013): "H2A.Z.2.2 is an alternatively spliced histone H2A.Z variant that causes severe nucleosome destabilization," Nucleic Acids Research, 40, 5951-5964.*
- *Treutlein B, Muschielok A, Andrecka J, Jawhari A, Buchen C, Kostrewa D, Cramer P, Michaelis J (2012): Dynamic architecture of the RNA polymerase II open promoter complex, Molecular Cell 46, 136-146.*
- *Grohmann D, Nagy J, Chakraborty A, Klose D, Fielden D, Ebright RH, Michaelis J, Werner F (2011): "The initiation factor TFE and the elongation factor Spt4/5 compete for binding to the RNAP clamp during transcription initiation and elongation," Molecular Cell 43, 263-274.*
- *Moffitt J, Osseforth C, Michaelis J (2011): "Time gating improves the spatial resolution of STED microscopy", Optics Express 19, 4242-4254.*
- *Muschielok A, Andrecka J, Brückner F, Jawhari A, Cramer P, Michaelis J (2008): "A Nanopositioning system for macromolecular structural analysis," Nature Methods 5, 965-971.*