

# Fast light-sheet microscopy for real-time mobility imaging of interacting proteins in living cells

*Doctoral or Master's thesis project in the Division Biophysics of Macromolecules*

## Project description

DNA packing into chromatin and its accessibility to proteins plays a central role in determining gene expression in normal and malignant states of the cell. We are interested in the physical mechanism of how proteins find their target on the DNA in the cell nucleus. In this project you will study the dynamics of fluorescently labeled proteins in living cells, using single molecule microscopy methods established in our group.

Our recently constructed light sheet microscope (1,2) takes an image of a two-dimensional cross-section of a cell by illumination with a flat sheet of light from a laser (<http://www.dkfz.de/Macromol/research/spim.html>). Series of images are taken by a fast camera, and the mobility and interaction of proteins analyzed by correlation techniques (3), yielding "mobility maps" of the proteins in the cell (4-7).

You will study the mobility and interaction of GFP-fusions of different proteins (transcription factors, nuclear receptors, cytoskeleton components) in live cells. The single molecule fluorescence data is then analyzed to characterize regions of different mobility, strong or weak binding, formation of protein complexes, etc. The mobility data will be compared with prediction from recent computer simulations (8).

The goal of the project is to understand: a. in general, how proteins can move through the cell nucleus to interact and find their binding target, b. how the function of signalling factors depends on their intracellular localization and c. how chromatin dynamics are affected by the cytoskeleton. This will provide important fundamental data for understanding the role of the spatial arrangement of the genome in determining normal and abnormal cell function.

## Desired qualifications

Our group is highly interdisciplinary, comprising biologists, physicists, chemists and mathematicians, and using molecular and cell biology, experimental biophysics, and computer modeling. This project addresses students interested in modern light microscopy techniques applied to cell biology. Interest in physics and sophisticated optical equipment would also be an asset. If you like an open and friendly atmosphere, you will be very happy in our group.

## References

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