Dynamic Structural Biology with an Optical Microscope

Philip Tinnefeld

Philip.tinnefeld@cup.uni-muenchen.de

Fluorescence superresolution microscopy has reached molecular resolution and starts complementing Fluorescence Resonance Energy Transfer (FRET) for obtaining dynamic structural information of single biomolecules and their interactions. To this end, I will introduce pulsed-interleaved MINFLUX microscopy that optimally uses the information of each detected photon to reach 1 nm localization precision with only 2000 photons.[1] Additionally, pMINFLUX provides the fluorescence lifetime information that we use, for example, for simultaneously tracking two independent molecules on the nanometer scale.[2] In combination with energy transfer to graphene-on-glass coverslips, pMINFLUX also offers 3D information.[3]

Recently, we discovered that DNA stands perpendicular on graphene. The defined orientation in combination with using graphene as an energy transfer acceptor is used to study DNA conformations including bending by bulges and induced by proteins such as DNA repair proteins. The technique even reveals single base-steps of O^6-alkylguanine DNA alkyltransferase diffusion along DNA.

References:

[1] L. A. Masullo, F. Steiner, J. Zahringer, L. F. Lopez, J. Bohlen, L. Richter, F. Cole, P. Tinnefeld, F. D. Stefani, *Nano Lett* **2021**, *21*, 840-846.
[2] F. Cole, J. Zähringer, J. Bohlen, T. Schröder, F. Steiner, F. D. Stefani, P. Tinnefeld, *bioRxiv* **2023**, 2023.2003.2024.534096.
[3] J. Zahringer, F. Cole, J. Bohlen, F. Steiner, I. Kaminska, P. Tinnefeld, *Light Sci Appl* **2023**, *12*, 70.