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High speed single molecule tracking on lipid membranes

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It is generally accepted that the cell lipid membrane is highly heterogeneous in local lipid and protein composition. This heterogeneity is believed to be induced by lipid-lipid, lipid-protein and protein-protein interactions and to be crucial for the high functionality of the membrane, e.g. for signal transduction. On the other hand, it is still a matter of debate how exactly the local organization of the membrane is mediated and on which spatial and temporal scales distinct structural features exist.

One approach to resolve this issue is to observe the motion of individual molecules in the membrane. In order to be able to draw conclusions from such measurements about the membrane molecular organization, a high spatial resolution on the order of the size of the probed molecule as well as a temporal resolution much faster that a typical membrane rearrangement time is required. We present a powerful single particle tracking approach based on interferometric scattering microscopy (iSCAT), which meets these requirements. By attaching small gold nanoparticles of ≤ 20 nm in diameter to lipid molecules and detecting their weak linear scattering signal by iSCAT, we are able to localize the position of the molecules with nanometer-accuracy at a temporal resolution of down to 10 μs.

Thus, with iSCAT it is possible to detect small-scale and short-time variations of the diffusion character of the probed molecule which opens the door to study membrane dynamics with unprecedented clarity. We present results from a systematic study on model lipid membranes and discuss possibilities of applying the method to diffusion measurements on cell membranes.

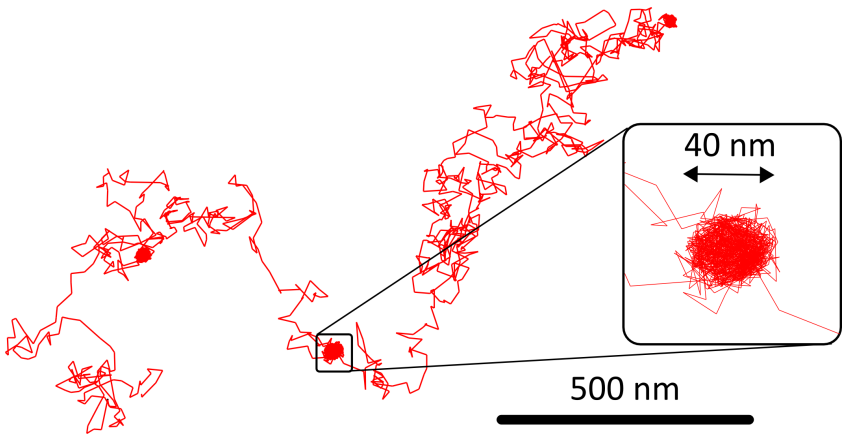

Figure 1: Trajectory of a 20 nm gold nanoparticle bound to a lipid molecule in a supported lipid bilayer. With iSCAT it is possible to detect small-scale and short-time confinements induced by the interaction of the bilayer with the glass support.