Albert-Ludwigs-Universität Freiburg

Physikalisch-Chemisches Kolloquium
Institut für Physikalische Chemie

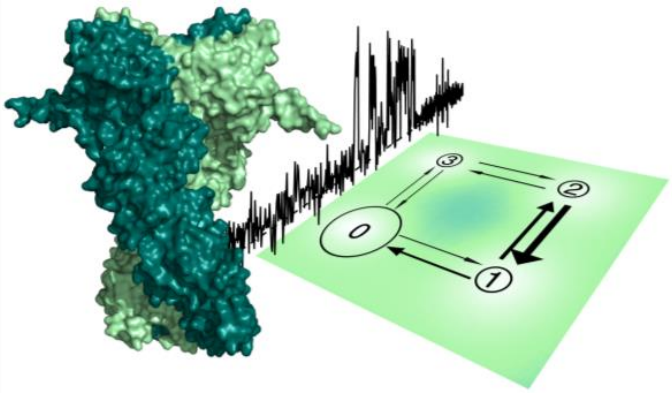
CENTRE FOR INTEGRATIVE BIOLOGICAL SIGNALLING STUDIES

SINGLE PROTEIN DYNAMICS: FROM FLUORESCENCE TO ELECTRICAL DETECTION

Dr. Sonja Schmid

BioNanoscience Dept., Kavli Institute of Nanoscience, TU Delft, NL

.



Proteins are the molecular makers in our body. They use diverse energy sources to perform specific tasks in a highly controlled and efficient manner. For an in-depth understanding of the energetics and diverse driving forces that govern protein machines, we still lack detailed, dynamic information on the molecular level.
Single molecule FRET is amongst the most popular biophysical techniques to observe individual proteins at work in real time. However, due to photo-bleaching, the observation time of *one single molecule* spans hardly more than 2 orders of magnitude, e.g. 10ms - 1s, or 1s - 100s. This makes quantitative kinetic analysis challenging. I will present here our solution to the challenge: a 2D machine-learning approach that extracts a maximum of information out of inherently noisy single-molecule trajectories. It has allowed us to pinpoint remarkable, mechanistic effects of the Hsp90 chaperone system, i.a. induced by a co-chaperone, drug candidates, macro-molecular crowding, or mutations.
Despite all experimental and analytical efforts, the time bandwidth of single-molecule fluorescence remains poor compared to protein dynamics occurring on much broader timescales simultaneously. An advantageous alternative is therefore *electrical* detection, spanning microseconds to hours in one experiment. We exploit this in an entirely new approach to protein kinetics, using a combination of solid-state nanopores with DNA origami. Specifically, we anchor the protein of interest to a DNA origami structure inside a nanopore and monitor its behavior electrically, by means of conductance changes over time. I will discuss our latest results obtained with this new & label-free single protein detector. In combination with existing 3D structures and MD simulations, it has the potential to reveal the kinetic & energetic origin of protein function at the sub-molecular level.

Monday 1 July 2019, 13.30

Hörsaal Physikalische Chemie (Albertstr. 23 a, 79104 Freiburg)

Guests are welcome