BP 27: Computational Biophysics

Time: Tuesday 9:30–11:45 Location: H43

Invited Talk BP 27.1 Tue 9:30 H43

Membrane proteins under voltage: simulations of ion channels and receptors at work — •Ulrich Zachariae — University of Dundee, Dundee, United Kingdom

Electrochemical ion gradients across biological membranes generate membrane voltage and drive the function of essential membrane proteins. We use sustained transmembrane electrochemical gradients in molecular dynamics simulations to investigate the function of ion channels and receptors under voltage. In our work on potassium channels, we find that a mechanism involving electrostatic interaction between close ion pairs in the ion selectivity filter underlies high-efficiency conduction near the diffusion limit. Evidence for the existence of close ion contacts additionally comes from crystallography. We show that this mechanism is also exquisitely selective for the conduction of potassium vs. sodium ions. Our simulations reveal the determinants of ion discrimination in the channels under actual permeation conditions.

While voltage sensing in ion channels is a widely studied phenomenon, the effects of membrane voltage on other membrane proteins are not as well understood. G-protein coupled receptors (GPCRs), which transduce signals across the membrane and form most human drug targets, have been shown to be regulated by voltage as well. However, the nature of the voltage sensor has remained elusive. Our simulations reveal the motion of a conserved voltage-sensor in class A GPCRs, whose functional implications will be discussed.

BP 27.2 Tue 10:00 H43

Electrochromic shift calculations reveal spectral tuning in animal rhodopsins — •Florimond Collette, Marcel Schmidt am Busch, and Thomas Renger — Institut für Theoretische Physik, Johannes Kepler Universität Linz, Altenberger Strasse 69, 4040 Linz, Austria

Rhodopsins are biological pigment-protein complexes found in photoreceptor cells of the retina. Within the framework of a two-step quantum chemical/electrostatic calculation scheme [1] that has recently been successfully applied to reveal the functional states of BLUF photoreceptors [2], we estimated absorption shifts of the retinal chromophore for a series of site-directed mutants. We eventually explain the variations of the maximal absorbance in the red- and green-sensitive visual pigments. Our results are in excellent agreement with recent experimental studies [3] and suggest that the maximum spectral sensitivity in animal rhodopsins is dominated by electrostatic tuning.

[1] T. Renger et al., *Photosynth. Res.* **116**, 367 (2013).
[2] F. Collette et al., *J. Phys. Chem. B* **118**, 11109 (2014).
[3] W. Wang et al., *Science* **338**, 1340 (2012).

BP 27.3 Tue 10:15 H43

The internal dynamics and early adsorption stages of fibrinogen investigated by molecular dynamics simulations — Stephan Köhler[1], Friederike Schmid[1], and •Giovanni Settanni[1,2] — [1]Johannes Gutenberg University, Mainz, Germany — [2]Max-Planck Graduate Center with the University of Mainz

Fibrinogen, a plasma glycoprotein of vertebrates, plays an essential role in blood clotting by polymerizing into fibrin upon activation. It also contributes, upon adsorption on material surfaces, to determine their biocompatibility and has been implicated as a cause of thrombosis and inflammation at medical implants. Here we present the first fully atomistic simulations of the initial stages of the adsorption process of fibrinogen on mica and graphite surfaces. The simulations reveal a weak adsorption on mica that allows frequent desorption and reorientation events. This adsorption is driven by electrostatic interactions between the protein and the silicate surface as well as the counter ion layer. Preferred adsorption orientations for the globular regions of the protein are identified. The adsorption on graphite is found to be stronger with fewer reorientation and desorption events, and showing the onset of denaturation of the protein.

BP 27.4 Tue 10:30 H43

Folding of small knotted proteins: Insights from a mean field coarse-grained model — Saeed Najafi and •Raffaello Potestio — Max Planck Institute for Polymer Research, Mainz, Germany

A small but relevant number of known protein structures features a knot. Understanding the process of folding from a swollen unknotted state to the biologically relevant native conformation is, for these proteins, particularly difficult, due to their rate-limiting topological entanglement. In this talk I will present and discuss a novel coarse-grained model, dubbed Elastic Folder Model (EFM), developed to contribute shedding some light on the problem of knotted protein folding. The EFM is a minimalistic, structure-based model where the information about the knotted conformation is encoded in bonded angular interactions only; this potential, which does not favor the formation of native contacts, is parametrized through a stochastic search scheme in parameter space. The optimal knotting pathways of the two smallest known proteins, obtained through this approach, are consistent with the results derived by means of coarse-grained as well as full atomistic simulations.

15 min break

BP 27.5 Tue 11:00 H43

Inferring Co-evolution in proteins and RNA by Maximum Entropy Based Approaches — •Alexander Schug — Karlsruher Institut für Technologie, Steinbuch Centre for Computing

Protein function often requires a protein to form a complex or adopt multiple conformations during its functional cycle. The increasingly ubiquitous availability of sequential information for many protein families has given rise to a Maximum Entropy based approach called Direct Coupling analysis [1], which traces amino acid co-evolution to extract contact maps out of only sequence information. This is sufficient information for the blind prediction of quaternary and tertiary protein [2,3] or RNA structures [4]. Residue co-evolution therefore guarantees the structural stability of a protein including its functional conformations. Similarly, we can infer mutational landscapes and capture epistatic couplings between residues, and assess the dependence of mutational effects on their sequence context [5]. We find an about 40% in explicative power as compared to approaches neglecting epistasis.

References
[1] Weigt M et al., PNAS (2009) 106, 67-72; F. Morcos et al., PNAS (2011) 108, E1293-E1301
[2] Schug A et al., PNAS (2009) 106, 22124-22129
[3] Dago A et al., PNAS (2012), 109: E1733-42
[4] De Leonardis E et al., NAR (2015), doi: 10.1093/nar/gkv932
[5] Figliuzzi M et al., Mol Biol Evol (2015), doi: 10.1093/molbev/msv211

BP 27.6 Tue 11:15 H43

Bending algorithms for soft objects: Challenge and bane — •Achim Guckenberger, Marcel Schraml, and Stephan Gekle — Biofluid Simulation and Modeling, Universität Bayreuth, Germany

Vesicles, capsules and red blood cells all share a common property, namely the resistance towards bending of their surface, an important ingredient for quantitative simulations. Unfortunately, accurate computation of these bending forces on typical surface discretizations such as flat triangles is far from being trivial.

Starting from the famous Helfrich model, we present and analyze five substantially different algorithms for the computation of the force density on triangulated meshes. Their quality is evaluated quantitatively by comparing with the analytically obtained values for the typical red blood cell shape. Furthermore, we consider the behavior of an elastic capsule in a linear shear flow using the boundary integral and the Lattice Boltzmann method. Comparisons with the existing literature are provided. We finally make a suggestion for the choice of the appropriate bending algorithm based on the presented results.

BP 27.7 Tue 11:30 H43

Exploring Gliding Motility: Model of Helical Transport of Cell Surface Proteins in Flavobacterium johnsoniae — •Mei-Hsien Tu[1], Hirofumi Wada[2], and Hsuan-Yi Chen[1] — [1]Department of Physics, National Central University, Jung-Li 32001 Taiwan — [2]Department of Physics, Ritsumeikan University, Kusatsu, 525-8577 Shiga, Japan

Cells of Flavobacterium johnsoniae exhibit rapid gliding on a solid surface powered by the migration of surface adhesive proteins SprB along a left-handed helical loop on cell surfaces. We develop a model of rigidly coupled adhesins on a helical loop to study the mechanism

of this gliding motility. The model takes into account the helical geometry of the loop and the stochastic binding/unbinding dynamics of SprB. The numerical calculations reproduce the main features for the movement of Flavobacterium johnsoniae observed in the experiments. Cell body translation along its long axis displays a bidirectional motion via spontaneous symmetry breaking as predicted in a previous simple one-dimensional model. However, this linear movement has a characteristic switching length comparable to cell length due to end effect. As a cell undergoes translation, the cell body rotates counterclockwise about its principle axis when viewed from its rear. Cells with helical loop that makes one full turn from one pole of the cell to the other pole show left-turn trajectories. Furthermore, SprBs with strong binding at a cell pole naturally introduce an asymmetric distribution of the force generation to uplift the cell body and achieve the end-over-end flipping.