BP 27: Computational Biophysics II

Time: Thursday 15:00–17:30 Location: BAR 0106

BP 27.1 Thu 15:00 BAR 0106

Spectral signatures of excess-proton waiting and transfer-path dynamics — •Florian Brünig[1], Manuel Rammler[1], Ellen Adams[2], Martina Havenith[2], and Roland Netz[1] — [1]Freie Universität Berlin, Department of Physics, 14195 Berlin, Germany — [2]Ruhr-Universität Bochum, Department of Physical Chemistry II, 44780 Bochum, Germany

Signatures of solvated excess protons in infrared difference absorption spectra, such as the continuum band between the water bend and stretch bands, have been experimentally known for a long time and have recently been used to analyze protonation dynamics in photoactive proteins. However, the theoretical basis for linking spectral signatures with the microscopic proton-transfer mechanism so far relied on normal-mode analysis.

We analyze the excess-proton dynamics in ab initio molecular-dynamics simulations of aqueous hydrochloric acid solutions by trajectory-decomposition techniques. The continuum band is shown to be due to normal-mode oscillations of temporary H_3O^+ complexes. The actual proton transfer between two water molecules, which for large water separations involves crossing of a barrier and thus is not a normal mode, is characterized by two time scales: Firstly, the waiting time for transfer to occur, which leads to a broad weak shoulder around 100 cm^{-1}, consistent with our experimental THz spectra. Secondly, the mean duration of a transfer event, which produces a rather well-defined spectral contribution around 1200 cm^{-1} and agrees in location and width with previous experimental spectra.

BP 27.2 Thu 15:15 BAR 0106

Lipid-based nanomaterials for RNA delivery investigated using molecular dynamics simulations — •David Noel Zimmer[1] and Giovanni Settanni[1,2] — [1]Physics Department University of Mainz — [2]Faculty of Physics and Astronomy Ruhr University Bochum

Lipid-based nanoparticles (LNP) are one of the most effective carriers in mRNA therapeutics. They are made of a mixture of ionizable, helper, and pegylated lipids encapsulating mRNA. While peg tends to remain on the surface of the nanoparticle, the structure of the core has not yet been well characterized. Experimental data point to a relative lack of order. The lipid composition of the formulation plays a key role in determining the effectiveness of the nano carrier. Small changes in the chemical structure of ionizable and helper lipids dramatically affect the efficiency of mRNA transfection. LNPs based on DLinDMA and DLinDAP, two ionizable lipids, showed significantly different transfection efficiencies, notwithstanding the very small difference in structure. Here, using a multiscale modeling approach, the behavior of lipid formulations based on these two lipids, cholesterol and DSPC or DOPE is examined aiming to provide an understanding of the interactions of lipids and mRNA. The simulations show that, despite DLinDAP binding affinity for mRNA is larger than DLinDMA, the overall interaction of the whole lipid formulation containing DLinDAP with mRNA is weaker, resulting in a larger average distance of the mRNA from the lipid bilayer. This shows that chemical optimization based only on mRNA-ionizable lipid interactions may not be sufficient for the development of more effective lipid formulations for RNA delivery.

BP 27.3 Thu 15:30 BAR 0106

Toehold-Mediated Strand Displacement in Random Sequence Pools — •Thomas Mayer, Lukas Oesinghaus, and Friedrich Simmel — School of Natural Sciences, Department of Bioscience, TU Munich, D-85748 Garching, Germany

Toehold-mediated strand displacement (TMSD) has been used extensively for molecular sensing and computing in DNA-based molecular circuits. As these circuits grow in complexity, sequence similarity between components can lead to cross-talk causing leak, altered kinetics, or even circuit failure. For small circuits, such unwanted interactions can be designed against. In environments containing a huge number of sequences, this becomes infeasible. Therefore, a general understanding of the impact of sequence backgrounds on TMSD reactions is of great interest. Here, we investigate the impact of random DNA sequences on TMSD circuits. We begin by studying individual interfering strands and use the obtained data to build machine learning models that estimate kinetics. We then investigate the influence of pools of random strands and find that the kinetics are determined by only a small subpopulation of strongly interacting strands. Consequently, their behavior can be mimicked by a small collection of such strands. Finally, we compare two established and a novel technique that speed up TMSD reactions in random sequence pools: a threeletter alphabet, protection of toeholds by intramolecular secondary structure, or by an additional blocking strand. We expect that our insights will be useful for the construction of TMSD circuits that are robust to molecular noise.

BP 27.4 Thu 15:45 BAR 0106

comparison of molecular dynamics simulations and neutron reflectivity experiments reveals strengths and weaknesses of current force fields for ionizable Dlin-MC3-DMA lipids — •Ibrahim Mohd[1,3], Jennifer Gilbert[2], Marcel Heinz[3], Tommy Nylander[2], and Nadine Schwierz[1,3] — [1]University of Augsburg, 86159 Augsburg, Germany — [2]Lund University, SE-22100 Lund, Sweden — [3]Max-Planck-Institute of Biophysics, 60438 Frankfurt am Main, Germany

Dlin-MC3-DMA (MC3) is one the most promising ionisable lipid for designing lipid nanoparticles (LNPs), which are used as drug delivery agents. Here, we provide force field parameters for cationic and neutral MC3 compatible with the AMBER Lipid17 force field. Subsequently, we carefully assess the accuracy of the current and existing MC3 force fields by providing a direct comparison to neutron reflectivity experiments of mixed lipid bilayers consisting of MC3 and DOPC at different pH. At low pH (cationic MC3) and at high pH (neutral MC3) the newly developed MC3 parameters in combination with AMBER Lipid17 for DOPC give excellent agreement with the experiments compared to existing MC3 models. With the currently parametrized MC3 parameters we are able to simulate MC3 containing LNPs in atomistic details and gain insights into the effect of pH and RNA cargo on the LNP structure. Combining molecular dynamics simulations, neutron reflectivity experiments and other scattering techniques is therefore a valuable step to drive the advancement of accurate atomistic force fields and to unravel the detailed structure of LNPs.

BP 27.5 Thu 16:00 BAR 0106

Simulation-based Parameter Inference for Large Scale Tumor Simulations — •Julian Herold[1], Eric Behle[2], and Alexander Schug[2] — [1]Karlsruhe Institute of Technology, Karlsruhe, Deutschland — [2]Jülich Supercomputing Center, Jülich, Deutschland

While clinical imaging of tissues focuses on macroscopic tumors, many experiments investigate only small clusters of cells. We aim on providing a scale-bridging link by performing large scale tissue simulations. We employ highly parallelized code in an HPC setting to simulate mm-sized virtual tissues such as embryogenetic zebrafish tissue or breast-cancer tumors with more than a million μm-resolved individual cells. We deploy Cells in Silico (CiS), which combines a cellular potts model with an agent based layer and is thus capable of accurately representing many physical and biological properties, such as individual cell shapes, cell division, cell motility, interactions with the extra-cellular matrix etc.

Using a model with such a strong representational capacity poses the task of adjusting a large number of parameters to reproduce experimental findings. Prior work has attempted to characterize the similarity between experimental and simulated data by extracting different features and using statistical tests to establish a distance measure. This work highlights how this difficult task can be circumvented by training neural networks to distinguish between experimental and simulated data while simultaneously optimizing the model parameters to maximize the error rate of the network.

15 min. break

BP 27.6 Thu 16:30 BAR 0106

Effects of chromatin fibers characteristics on cohesin mediated loop architecture — •Aymen Attou, TIlo Zülske, and Gero Wedemann — University of Applied Sciences Stralsund, System Engineering and Information Management, 18435 Stralsund, Germany

The spatial organization of DNA in eucaryotes starts at nucleosome chains forming chromatin loops that can cluster together establishing fundamental units called topologically associating domains (TADs).

TADs are an important factor for gene regulation by facilitation or repressing long range contacts in the genome. Those loops are formed and held together by a ring-shaped protein complex called cohesin together with the effect of CTCF. A loop has a residence time of several minutes. To clarify the spatial structure of a loop, we established a coarse-grained computer model of chromatin with a resolution of single nucleosomes integrating potentials describing CTCF and cohesin. We performed Metropolis Monte Carlo simulations combined with replica exchange procedure with regular spaced nucleosomes and experimentally determined nucleosome positions in presence of cohesin-CTCF as well as depleted systems as control for different loop sizes. We studied differences in the spatial structure and of contacts probabilities of different domains, what allowed us to understand the role of cohesin and CTCF, and their impact on the 3D structure of chromatin. This study also allowed clarifying how nucleosome positions can impact the conformations of the chromatin loops during the residence time of the loop anchor, with presumed consequences for transcriptional activity.

BP 27.7 Thu 16:45 BAR 0106

Theoretical investigations on enzyme-plasma interactions in the context of plasma-driven biocatalysis — •Hanna-Friederike Poggemann, Björn Kirchhoff, Timo Jacob, and Christoph Jung — Ulm University, Institute of Electrochemistry, D-89069 Ulm

Biocatalysis is an emerging field that has several advantages over classical catalysis. The use of enzymes as catalysts is not only more environmentally friendly, but also has potential to be more efficient than the conventional approach in industrial applications. Plasma-assisted biocatalysis is a specific subsection of this field, where a plasma source is used to provide a constant supply of the enzyme co-substrate H_2O_2 that drives the catalytic reaction. However, the use of plasma presents some challenges. The plasma species can alter the structure of the enzyme leading to changes in the catalytic reaction pathway or even deactivation of the enzyme. In a theoretical multiscale approach, we address the questions of how the plasma interacts with the enzyme and how this alters the catalytic reaction. To this end, we use reactive molecular dynamics simulations to investigate possible structural changes of the enzyme by plasma species. We also perform QM/MM hybrid simulations to further investigate the reaction pathway of the enzyme AaeUPO.

BP 27.8 Thu 17:00 BAR 0106

Diffusive properties in simulations of polydisperse sphere mixtures mimicking the inside of a cell — •Frank Hirschmann[1], Hender Lopez[2], Felix Roosen-Runge[3], and Martin Oettel[1] — [1]Institute for Applied Physics, University of Tübingen, Germany — [2]School of Physics and Optometric & Clinical Sciences, Technological University Dublin, Ireland — [3]Department of Biomedical Sciences and Biofilms-Research Center for Biointerfaces (BRCB), Malmö University, Sweden

The interiors of living cells contain a multitude of different-sized biomacromolecules at relatively high packing fractions. Diffusivity and transport properties in such crowded environments are highly influenced by hydrodynamic interactions. Thus, the time needed for proteins to come into contact with each other within the cell is determined by a complex interplay of polydispersity, size-distribution and crowding. In order to analyze such systems theoretically, we employ Brownian Dynamics (BD) simulations of polydisperse mixtures of hard spheres. Using results of Stokesian dynamics we approximate hydrodynamic interactions in our BD simulations by a simple multiplicative ansatz (equivalent to a hydrodynamic "renormalization" of the Brownian short-time diffusivity), which allows us to access the long-time limit of our system. We investigate resulting diffusion constants and survival probabilities, exhibiting non-trivial behavior.

BP 27.9 Thu 17:15 BAR 0106

Unwrapping trajectories of constant-pressure molecular dynamics simulations — •Jakob Tómas Bullerjahn[1], Sören von Bülow[2], Jérôme Hénin[3], and Gerhard Hummer[1,4] — [1]Department of Theoretical Biophysics, Max Planck Institute of Biophysics, Frankfurt am Main, Germany — [2]Linderstrøm-Lang Centre for Protein Science, Department of Biology, University of Copenhagen, Copenhagen, Denmark — [3]Laboratoire de Biochimie Théorique, Institut de Biologie Physico-Chimique, CNRS, Paris, France — [4]Institute of Biophysics, Goethe University Frankfurt, Frankfurt am Main, Germany

In molecular dynamics simulations at constant pressure, the size and shape of the periodic simulation box fluctuate with time. Special care is thus required when a particle trajectory is unwrapped from a projection into the central box under periodic boundary conditions into a trajectory in full three-dimensional space, e.g., for the calculation of diffusion coefficients. Here, we review and compare different schemes proposed for trajectory unwrapping, and specify the respective rewrapping scheme to put an unwrapped trajectory back into the central box. On this basis, we then identify a scheme in which the wrapped and unwrapped trajectory are mutually consistent and in which the statistical properties of the trajectory are preserved. We conclude with advice on best practice for the consistent unwrapping of constant-pressure simulation trajectories.