BP 32: Computational Biophysics II

Time: Friday 9:30–13:00 Location: H46

BP 32.1 Fri 9:30 H46

From slabs to cubes: finite size effects in biomolecular simulations — •Rodrigo F. Dillenburg and Martin Girard — Max Planck Institute for Polymer Research, Mainz, Germany

Coarse-grained simulations of intrinsically disordered proteins have become essential to the study of biomolecular condensates. Multiple choices of force fields, simulations techniques and box geometries have been employed in such studies, assuming that results will converge due to the law of large numbers. This assumption is, however, not automatically valid for all systems and needs to be carefully examined to assure the validity of the results. In our work we focused on the choice of box geometry (cubic or slab) and statistical ensemble (canonical or grand-canonical) and its effect on the phase behavior of systems undergoing liquid-liquid phase separation. Our results allow us to estimate if a system can be approximated by the thermodynamic limit or if finite size effects have to be taken into consideration. We are able to derive expressions for these corrections depending on the choice of system and are also able to relate it to condensate properties such as surface tension. Our results provide a rational approach to selecting the most appropriate simulation methods for a given system.

BP 32.2 Fri 9:45 H46

Interactions of Imidazolium with Elastin-Like Polypeptides: A Molecular Dynamics Study — •Julia Keil and Nico F. A. van der Vegt — Technische Universität Darmstadt, Germany

Biological buffers are commonly used to adjust the pH value of protein solutions and are typically assumed not to affect other properties of the system.[1] However, a series of experimental observations suggest buffer-specific effects on protein stability.[2] Despite these findings, studies on these effects remain limited, and the underlying mechanisms are still poorly understood.[2-4]

We performed molecular dynamics simulations at constant pH[4] to investigate the interactions between the buffer imidazolium (IMI) and elastin-like polypeptides (ELPs) that contain chemically different amino acids at their variable positions. Our analyses revealed a local accumulation of imidazole (IMI^{o}) around the ELPs and its hydrogen bonding to the ELP backbone, regardless of the ELP composition. In contrast, interactions with imidazolium (IMI^{+}) were found to depend on the ELP composition. A strong local accumulation of IMI^{+} was observed around ELPs containing negatively charged groups, accompanied by hydrogen bonding to their side chains. Conversely, local depletion of IMI^{+} occurred around ELPs with positively charged groups. As a result, the interactions of ELPs with IMI are determined by the specific composition of the ELPs.

[1] *Nat. Chem.* 2021, 13, 1023-1024 [2] *Curr. Opin. Colloid Interface Sci.* 2016, 23, 1-9 [3] *J. Pharm. Sci.* 2017, 106, 3, 713-733 [4] *J. Chem. Theory Comput.* 2022, 18, 10, 6148-6160

BP 32.3 Fri 10:00 H46

Graphite-based Bio-mimetic Nanopores for Protein Sequencing and Beyond — •Chandan K. Das and Maria Fyta — Computational Biotechnology, RWTH Aachen University, Aachen, Germany

Protein sequencing via nanopores offers a transformative approach to bioanalytics, but challenges remain, particularly in linearizing unfolded proteins and controlling translocation speed through solid-state nanopores. This study introduces a novel solution: biomimetic graphite-based nanopores designed with nanometer-sized pores featuring a constriction zone inspired by the alpha-hemolysin protein pore. All-atom molecular dynamics simulations demonstrate the nanopores' ability to achieve ion selectivity and generate electro-osmotic flow (EOF) within the pore lumen due to tailored surface charges. This innovation enables the detection of peptides at the single amino acid level by analyzing ionic current fluctuations during peptide translocation. A critical feature of this design is its capacity to balance hydrodynamic drag, induced by EOF, with electrophoretic force (EPF), facilitating peptide linearization and extending amino acid residence time within the constriction zone. These advancements significantly enhance sequencing resolution and accuracy. Beyond protein sequencing, this technology holds potential for diverse applications, including seawater desalination via electrodialysis and renewable energy generation through salinity gradient-driven ion separation. By providing a robust computational foundation, this study advances the development of graphite-based biomimetic nanopores, offering versatile solutions for bio/nanotechnological challenges and sustainable energy innovations.

BP 32.4 Fri 10:15 H46

Helical transition of protein chain: An in silico study — •tika ram bhandari and martin girard — Max Planck Institute for Polymer Research, Mainz, Germany

Structural transformations in biomolecular systems are critical for physiological functions, with folding and unfolding transitions governing numerous cellular activities. Misfolding of proteins, however, is a key factor in the onset of severe diseases, emphasizing the need for comprehensive studies to understand and control these processes. Computational simulations provide valuable insights into such mechanisms. Here, we employed coarse-grained molecular simulations coupled with Hamiltonian Replica Exchange method to investigate the disordered-to-helical transition of IM30, the bacterial counterpart of the ESCRT-III. By systematically varying the strength of hydrogen bonds, we simulated an in-silico denaturation process, enabling a detailed analysis of the structural properties underlying this transition. Furthermore, we explore the impact of point mutations on the protein's helical propensity using free energy calculations. These approaches provide a deeper understanding of the molecular mechanisms influencing folding behavior and highlights the role of specific mutations in modulating protein structure.

BP 32.5 Fri 10:30 H46

Towards modeling cellular environments from cryo-electron tomography by high-confidence 3D template matching — •Sergio Cruz-León, Jan Philipp Kreysing, Maziar Heidari, Beata Turoňová, Martin Beck, and Gerhard Hummer — Max Planck Institute of Biophysics, Max-von-Laue-Str. 3, 60438, Frankfurt am Main, Germany

The simulation of biologically realistic systems requires precise knowledge of the composition and spatial arrangement of biomolecules in situ. This information can be obtained from cryo-electron tomography (cryoET), which images the interior of intact cells in 3D. However, feature identification is limited by the low signal-to-noise ratio and anisotropic resolution of the tomographic data. In this talk, I will present our recent advances in high-confidence 3D template matching (hcTM) for cryoET [1] and how we use hcTM to generate simulation-ready molecular models directly from cells [1,2]. hcTM enables the automated and comprehensive detection of a wide variety of macromolecular complexes within crowded eukaryotic cells. The high-confidence molecular assignments have driven both technical advances [3] and biological discoveries [1,2], fostering robust connections between molecular functionality, spatial localization, and cellular context. Thus, hcTM paves the way for modeling and simulating the dynamics of biomolecules in their native environment.

[1] Cruz-León, et al., Nat. Comm., 2024 [2] Kreysing*, Heidari*, Zila*, et al., BioRxiv, 2024 [3] Tuijtel, et al., Sci. Adv., 2024

BP 32.6 Fri 10:45 H46

Membrane insertion and channel formation of alpha-latrotoxins — •Andreas Heuer[1], Azadeh Alavizargar[1], Björn U. Klink[2,3], and Cristos Gatsogiannis[2,3] — [1]Institute for Physical Chemistry, University of Münster, Germany — [2]Center for Soft Nanoscience (SoN), University of Münster — [3]Institute for Medical Physics and Biophysics

Latrotoxins are the main toxic component of the venom of black widow spiders. It is known that the they provide ion channels in the plasma membrane, allowing, e.g., for a strong influx of Ca2+ ions which may induce a burst of neurotransmitters. Despite its importance, microscopic information about the microscopic structure of latroxin pore formation remained elusive.

In this presentation it is shown how detailed information can be gained by a combination of cryoEM, AlphaFold and Molecular Dynamics (MD) simulations [1]. From this analysis we can identify a unique mechanism of membrane insertion and channel formation for the example of Na+ and Ca2+ transport. From the MD simulations it is possible, e.g., to elucidate the efficiency and the time-scales of the transport processes and to show why the channel is efficient in transporting mono- and divalent ions but not trivalent ions.

[1] Klink, B.U., Alavizargar, A., Kalyankumar KS, Chen M, Heuer A, Gatsogiannis C (2024) Nature Communications 15, 8551

BP 32.7 Fri 11:00 H46

Understanding the impact of functionalized gold nanoparticles (AuNPs) on the lipid bilayer and interfacial water through atomistic molecular dynamics simulations — •Haifa Al Mamari, Srinivasa Varanasi, and Issam Ali — Sultan Qaboos University, Department of Physics

Functionalized gold nanoparticles (AuNPs) show promise as drug delivery systems due to their customizable size, shape, biocompatibility, and surface modifications. However, crossing cell membrane barriers is a challenge, requiring efficient penetration for effective drug delivery. Interfacial water and ions play a crucial role in the interaction between AuNPs and bilayers, making it essential to understand the structural and orientational effects on lipid bilayers. This study explores how nanoparticle surface charge and lipid chemistry impact AuNP-lipid bilayer interactions, focusing on anionic (carboxylate) and cationic (quaternary ammonium) AuNPs with zwitterionic (DPPC), anionic (DPPG), and cationic (DPTAP) bilayers using molecular dynamics simulations.Our analysis shows that AuNPs significantly alter bilayer properties, impacting the area per lipid, membrane thickness, acyl chain order, electrostatic potential, dipole alignment, and head and tail tilt angles. These changes enhance water dipole alignment and modify electrostatic potentials, depending on the nanoparticles surface charge. These insights emphasize AuNPs' potential to reshape membrane properties, providing valuable guidance for nanoparticle-based therapeutic development.

15 min. break

BP 32.8 Fri 11:30 H46

Swimming by spinning: spinning-top type rotations regularize sperm swimming into persistently progressive paths in 3D — •Xiaomeng Ren and Hermes Bloomfield-Gadêlha — School of Engineering Mathematics & Bristol Robotics Laboratory, University of Bristol, BS8 1UB Bristol, UK

Sperm swimming is essential for reproduction, with movement strategies adapted to specific environments. Sperm navigate by modulating the symmetry of their flagellar beating, but how they swim forward with asymmetrical beats remains unclear. Current methods lack the ability to robustly detect the flagellar symmetry state in free-swimming spermatozoa, despite its importance in understanding sperm motility. This study uses numerical simulations to investigate the fluid mechanics of sperm swimming with asymmetrical flagellar beats. Results show that sperm rotation regularizes the swimming motion, allowing persistently progressive swimming even with asymmetrical flagellar beats. Crucially, 3D sperm head orientation, rather than the swimming path, provides critical insight into the flagellar symmetry state. Sperm rotations during swimming closely resemble spinning-top dynamics, with sperm head precession driven by the helical beating of the flagellum. These results may prove essential in future studies on the role of symmetry in microorganisms and artificial swimmers, as body orientation detection has been largely overlooked in favor of swimming path analysis. Altogether, this rotational mechanism provides a reliable solution for forward propulsion and navigation in nature, which would otherwise be challenging for flagella with broken symmetry.

BP 32.9 Fri 11:45 H46

Simulating Trypanosome Motility — •Florian Overberg, Gerhard Gompper, and Dmitry Fedosov — Theoretical Physics of Living Matter, Institute for Advanced Simulation, Forschungszentrum Jülich, 52428 Jülich, Germany

We investigate motility of the protozoan Trypanosoma brucei via numerical simulations, in which a trypanosome model is informed by experimental observations. The cell body is represented by a set of vertices distributed homogeneously on a pre-defined elongated surface, forming a triangulated elastic network of springs. This network model incorporates bending rigidity, area conservation, and volume conservation constraints. For the generation of propulsion, a flagellum is attached to the cell body. The flagellum consists of four parallel filaments, two of which are embedded in the body and used for generating a propagating bending wave. We examine the parasite behavior for various conditions, including different flagellum and body stiffnesses, beating frequencies, actuation wavelengths, and amplitudes. Our simulations yield swimming velocities and rotation frequencies around the swimming axis that are in a good agreement with experimental measurements. Additionally, we investigate the importance of various actuation characteristics, such as orientation of the beating plane and the stress-free conformation of the flagellum. We have also started to study parasite motility in a stationary blood suspension, which serves as a first step to understand trypanosome behavior in one of its natural environments such as blood vasculature.

BP 32.10 Fri 12:00 H46

Leveraging quantum data to advance machine-learning in (bio)molecular simulations — •Leonardo Medrano Sandonas[1], Mirela Puleva[2], Gianaurelio Cuniberti[1], and Alexandre Tkatchenko[2] — [1]TUD Dresden University of Technology, Germany. — [2]University of Luxembourg, Luxembourg.

The rapid advancement of machine learning (ML) applications in chemistry and physics has been driven by the increasing availability of comprehensive quantum-mechanical (QM) datasets. Recently, we introduced high-fidelity property data at the PBE0+MBD level of theory for both small [Sci. Data 8, 43, (2021)] and large [Sci. Data 11, 742, (2024)] drug-like molecules in equilibrium and non-equilibrium states. These datasets have been instrumental in advancing QM-based ML interatomic potentials [10.26434/chemrxiv-2024-bdfr0, (2024)] and enhancing semi-empirical (SE) methods [J. Phys. Chem. Lett., 11, 6835 (2020)], enabling accurate (bio)molecular simulations. In this presentation, we will discuss our recent efforts to improve the transferability and generalizability of the ML-corrected density functional tight-binding method. We demonstrate that equivariant neural networks significantly enhance the accuracy and scalability of ML-based many-body repulsive potentials trained on energies and forces of small organic systems. This approach facilitates the investigation of the energetic and structural properties of large drug-like molecules and molecular dimers. Hence, our findings indicate that combining ML with SE methods achieves both high accuracy and computational efficiency, paving the way for diverse applications in (bio)molecular simulations.

BP 32.11 Fri 12:15 H46

Calibrating 1D-0D Coupled Blood Flow Models: the potential of Neural Network based Surrogates — •Benedikt Hoock[1,2] and Tobias Köppl[3] — [1]Technische Universität München, School of Computation, Information and Technology — [2]Support by Computing Facilities of Leibniz-Rechenzentrum München — [3]Fraunhofer-Institut FOKUS, Berlin

Hydrodynamic models of the human arterial network can simulate the blood flow in parts or the whole body. The calculations can be simplified by solving the incompressible one-dimensional Navier-Stokes equations only for a set of larger vessels and coupling those at their outlets to a Windkessel model (*1D-0D approach*). Here, the right parametrization of the Windkessel parameters, i.e., the resistances and capacities, is crucial to obtaining realistic simulations. This can be done by calibrating the model parameters to match the model predictions with in-vivo blood pressure measurements. Since this requires many computationally expensive model evaluations, we test the potential of surrogates based on neural networks (NN). Once set up in an appropriate architecture, already ordinary fully connected NNs of moderate depth and width two can reproduce the simulations with high accuracy, advancing over e. g. the PINN approach due to their better trainability. We use these in an optimization algorithm to identify the target resistance and capacity with high precision in several test cases. Our efficient calibration scheme is an essential building block for an instantaneous visualization of the organ perfusion in a digital twin of a patient under different motion conditions on a digital treadmill.

BP 32.12 Fri 12:30 H46

MolecuTas: an ML platform for refining quantum properties and bioactivity of complex molecules — •Vicente Domínguez Arca[1,2], Jannis Krüger[2], Álvaro Vallejo Bay[3], Thomas Hellweg[2], and Luis Taboada Antelo[1] — [1]Biosystem and Bioprocesses Engineering, IIM-CSIC, Spain — [2]Physical and Biophysical Chemistry, Bielefeld University, Germany — [3]Applied Physics, University of Santiago de Compostela, Spain

The integration of machine learning (ML) and computational chemistry enables efficient prediction of quantum properties for complex molecules, crucial for advancing drug discovery and materials science. Our ML platform leverages Graph Convolutional Neural Networks (GCNNs) and the "sliding window" methodology to predict quantum mechanical parameters like partial atomic charges, overcoming traditional ab initio constraints. This approach scales to larger, biologically

relevant molecules, enhancing molecular dynamics simulations and rational drug design.

Focusing on marine saponins -complex thalassochemicals with unique sulfated glycoside structures- our platform improves charge distribution predictions, enabling precise simulations of bioactive interactions. These advances highlight the therapeutic potential of marine saponins in oncology, lipid metabolism, and immune modulation. By applying our platform to marine saponins, this research bridges computational and experimental workflows, fostering the discovery of novel thalassochemicals for applications in functional foods, pharmaceuticals, and sustainability.

BP 32.13 Fri 12:45 H46

Ab-initio optimization and AI-powered inference for parametrizing complex biological models under low data availability — •Thomas R. Sokolowski — Frankfurt Institute for Advanced Studies (FIAS), Ruth-Moufang-Str. 1, 60438 Frankfurt am Main, Germany

Early development unfolds under diverse circumstances and time scales, but always facing the impacts of inevitable biological noise. To cope with this, various developmental mechanisms evolved, with their differences shaped by physical and environmental constraints. In spite of decades of research, we still lack theories that explain these processes truly mechanistically. Increasing computational power allows for constructing developmental models with increasing complexity, but since corresponding experimental data is scarce, the parametrization of such models becomes a key problem itself. I will contrast two strategies for parametrizing biophysical models in development and beyond: optimization of normative theories, and Bayesian inference. I will present a framework that unifies both strategies in a mathematically rigorous fashion and enables quantitative transition between them. I will then present our results combining both strategies for understanding embryogenesis in two organisms: (1.) optimization of a spatial-stochastic model of the gap gene system in Drosophila, and (2.) elucidation of robust cell-fate assignment in early mouse embryogenesis via AI-powered simulation-based inference (SBI). Our results highlight distinct developmental strategies that emerged under the different circumstances faced by the two organisms.