BP 15: Computational Biophysics III

Time: Wednesday 9:30–12:45 Location: BAR/SCHÖ

BP 15.1 Wed 9:30 BAR/SCHÖ

Local chain stiffening regulates non-equilibrium maturation and clustering in biomolecular condensates — •Subhadip Biswas[1] and Davit A Potoyan[2] — [1]Iowa State University, Ames, Iowa, USA — [2]Iowa State University, Ames, Iowa, USA

Biomolecular condensates formed through liquid-liquid phase separation display complex structural and dynamical features that are essential for cellular organization, signaling, and aging. Using coarse-grained molecular dynamics simulations based on a polymer model with tunable local semiflexibility and sticker stickiness, we systematically examine how angular rigidity modulates aging and clustering within condensates. We investigate four regimes involving coupled variations of sticker/spacer stiffness and interaction strength. By quantifying structural heterogeneity, orientational ordering, and rheological responses, including oscillatory shear, Green-Kubo viscosity, and uniaxial deformation, we uncover distinct non-equilibrium behaviors and maturation pathways that emerge from local chain stiffening. These results highlight angular rigidity as a key regulator of condensate stability and internal organization, with implications for understanding condensate aging in cells and for designing programmable biomaterials.

BP 15.2 Wed 9:45 BAR/SCHÖ

Uncovering the thermodynamic principles of enzymatic regulation in biomolecular condensates with reactive simulations — •Enrico Lavagna[1], Francesco Delfino[1], Georgii Koniukov[1], Matteo Paloni[1,2], Luca Ciandrini[1,3], and Alessandro Barducci[1] — [1]Centre de Biologie Structurale (CBS), Montpellier, France — [2]Department of Chemical Engineering, Thomas Young Centre, University College London, London WC1E 7JE, United Kingdom — [3]Institut Universitaire de France (IUF)

Biomolecular condensates are dynamic cellular assemblies often regulated by energy-consuming processes such as post-translational modifications (PTMs). Nevertheless, the coupling between reaction dynamics and cellular spatial organization remains poorly understood at the molecular scale. Using a minimal, particle-based model, we investigate how phosphorylation controls condensate steady-state behavior. We find that condensate formation is regulated by the steady-state fraction of phosphorylated scaffold proteins, which increases with enzyme activity. This chemical regulation exhibits a non-linear, non-trivial dependence on the phosphorylation strength. Furthermore, reaction fluxes are spatially heterogeneous, with phosphorylation activity sharply peaking at the condensate interface. Our findings highlight novel, general features of chemically active biomolecular condensates. Moreover, we observe that incorporating local detailed balance is essential for understanding how energy-consuming reactions shape the steady-state properties of phase-separated systems.

BP 15.3 Wed 10:00 BAR/SCHÖ

Multiscale Simulation of Phosphofructokinase-1 Assemblies: From Transient Interactions to Large-Scale Assembly Formation — Mehrnoosh Khodam Hazrati, Tom Miclot, and •Stepan Timr — J. Heyrovsky Institute of Physical Chemistry, Czech Academy of Sciences, Prague, Czech Republic

Human phosphofructokinase-1 (PFK1)—a key glycolytic enzyme—forms filaments and localizes into large-scale assemblies that are thought to play a major role in the regulation of glycolysis. However, the molecular interactions driving this assembly and the precise mechanisms by which it regulates the pathway remain poorly understood. In this work, we combine three levels of description—atomistic, residue-level coarse-grained, and highly coarse-grained—to characterize interactions between PFK1 tetramers and to elucidate factors governing PFK1 assembly formation. Atomistic molecular dynamics simulations of PFK1 filament interfaces reveal specific side-chain interactions that are critical for filament stability. These insights enable us to improve the description of filament formation in residue-level coarse-grained models. Using the Martini 3 and OPEPv7 coarse-grained models, we further identify key regions mediating transient PFK1–PFK1 interactions and show that these include filament-forming interfaces. Finally, we construct a highly coarse-grained model that integrates information from the more detailed simulations. Using this model, we investigate the role of membranes in PFK1 filament formation and describe how filaments may affect the recruitment of other constituents into large-scale glycolytic assemblies.

BP 15.4 Wed 10:15 BAR/SCHÖ

Multiscale Approaches to Phase Behaviour and Mechanical Properties of Synthetic DNA Networks — •Aaron Gadzekpo[1], Xenia Schneider[1], and Lennart Hilbert[1,2] — [1]Karlsruhe Institute of Technology, Institute of Biological and Chemical Systems — [2]Karlsruhe Institute of Technology, Zoological Institute

DNA can be used as a programmable material whose sequence-level design governs emergent properties. However, approaches that link sequences to the macroscopic behaviours needed in biotechnology remain limited. Here, we integrate coarse-grained simulations, Bayesian optimisation, and graph-based rheology to connect sequence-encoded, molecular-scale parameters to network-level properties. We apply our methods to DNA nanomotifs, which are nanometre-sized, multi-armed molecules assembled from single strands. Network formation among nanomotifs via sticky-end overhangs enables phase separation into liquid-like condensates or the assembly of viscoelastic hydrogels. Our multiscale approaches reveal how nanomotif flexibility, affinity, and concentration govern network formation, phase behaviour, and viscoelasticity. By combining our approaches, we propose inverse design strategies to select sequences that yield targeted emergent properties.

BP 15.5 Wed 10:30 BAR/SCHÖ

Self-Assembly of KAHRP Spirals in Malaria-Infected Red Blood Cells — Devika Magan[1], Michael Lanzer[2], and •Ulrich S. Schwarz[1] — [1]Institute for Theoretical Physics, Heidelberg University — [2]Center for Infectious Diseases, University Hospital Heidelberg

Malaria infections alter the mechanical and adhesive properties of red blood cells (RBCs). To avoid clearance by the spleen, infected RBCs develop thousands of nanoscale protrusions called knobs, which stiffen the RBC and mediate cytoadhesion to the endothelium. A central player in this process is the exported parasite protein KAHRP. The parasite sends KAHRP to the RBC membrane skeleton, where it interacts with spectrin and actin to reorganize the local architecture. Strikingly, KAHRP also forms prominently sized spirals underneath the knobs, yet the physical principles governing their formation and how such structures might influence membrane mechanics are still not understood. In this talk, I present a coarse-grained, patchy-particle framework designed to explore how simple interaction rules can give rise to spiral formation. By tuning local binding geometry and torsional preferences, the model produces a rich variety of self-organized states, ranging from compact rings to extended curved chains. These simulations provide a starting point for connecting protein-level organization to cell-level mechanics. I will outline how this approach can be extended toward membrane-associated scenarios to investigate whether KAHRP assemblies can generate spontaneous curvature or store elastic energy - providing a path toward understanding their potential function during parasite cytoadhesion and egress.

30 min. break

BP 15.6 Wed 11:15 BAR/SCHÖ

From Data to Discovery: Machine Learning Force Fields for Fast and Accurate Ligand-Protein Screening — •Sergio Suárez-Dou[1], Miguel Gallegos[1], Hamza Ibrahim[2], Joshua T. Berryman[1], Andrea Volkamer[2], and Alexandre Tkatchenko[1] — [1]Department of Physics and Materials Science, University of Luxembourg, Luxembourg — [2]Data Driven Drug Design, Center for Bioinformatics, Saarland University, Germany

Pretrained Machine Learning Force Fields (MLFF) are transforming computational chemistry by combining speed and accuracy. In drug discovery, predicting binding energies and affinities is key to identifying viable candidates. Among MLFFs, SO3LR excels in both performance and efficiency, enabling accurate ligand binding predictions at low computational cost, surpassing semiempirical methods.

However, data coverage remains a challenge. While datasets like OMol25 and QCell offer broad molecular diversity, drug-like chemical space requires more targeted representation. To address this, we are developing a dataset optimised for docking evaluations, covering key regions of drug-like space. Our goal is a pretrained model capable of predicting drug-ligand affinities with PBE0+MBD DFT-level accu-

racy, bridging quantum precision with high-throughput screening and accelerating drug discovery.

BP 15.7 Wed 11:30 BAR/SCHÖ

Modelling Protein Dynamics with Machine Learned Coarse-Grained Models — •Klara Bonneau — Freie Universität Berlin, Germany

The most popular and universally predictive protein simulation models employ all-atom molecular dynamics (MD). However, understanding dynamical processes like protein folding, interactions, and aggregation requires accessing timescales beyond conventional MD capabilities. Coarse-graining (CG) accelerates simulations by focusing on essential degrees of freedom, but a universally predictive CG model for proteins remains elusive. Our work introduces the first thermodynamically consistent CG model that extrapolates to unseen protein sequences. By leveraging state-of-the-art machine learning techniques, we simulate the folding of unknown proteins, protein-protein interactions, intrinsically disordered proteins, and mutation effects. Current extensions include larger proteins and protein-ion/small molecule interactions, surpassing conventional MD timescale limitations. Additionally, explainable AI techniques enable us to interpret results and demonstrate that deep learning models capture physically consistent interactions.

BP 15.8 Wed 11:45 BAR/SCHÖ

Gradient-Estimating Gillespie Simulators for Parameter Inference in Stochastic Models — •Ludwig Burger[1], Annalena Kofler[2], Lukas Heinrich[3], and Ulrich Gerland[1] — [1]Physics of Complex Biosystems, School of Natural Sciences, Technical University Munich — [2]Max Planck Institute for Intelligent Systems, Tübingen — [3]Data Science in Physics, School of Natural Sciences, Technical University Munich

Stochastic models are ubiquitous in (biological) physics, yet fitting such parameterized models to experimental data remains challenging. While gradients in deterministic systems can be obtained efficiently through numerical or automatic differentiation, these tools cannot be directly applied to stochastic simulation algorithms such as the Gillespie algorithm, where sampling from a discrete set of reactions introduces non-differentiable operations. In this work, we adapt three gradient estimators from machine learning for use in Gillespie simulations: the Gumbel-Softmax Straight-Through estimator, the Score Function estimator, and the Alternative Path estimator. We extend all three estimators to address the specific requirements of gradient estimation in Gillespie simulations. We analyze the statistical properties of the estimators and highlight practical advantages and limitations in two representative systems: a minimal bimolecular association-dissociation model and the repressilator. Our results demonstrate that gradient estimators can be effectively integrated into the Gillespie algorithm, providing a systematic approach for gradient-based parameter inference in stochastic models.

BP 15.9 Wed 12:00 BAR/SCHÖ

Deep-Pose-Tracker: a unified model for behavioural analysis of *Caenorhabditis elegans* — •Debasish Saha[1], Shivam Chaudhary[1], Dhyey Vyas[2], Anindya Ghosh Roy[2], and Rati Sharma[1] — [1]Indian Institute of Science Education and Research Bhopal, Bhopal, India — [2]BRIC-National Brain Research Centre, Gurugram, India

The ability to respond to environmental stimuli by living organisms is essential for survival and adaptation. Locomotion and posture-based analyses of animals are commonly performed; however, manually performing these tasks is effort-intensive, time-consuming, and error-prone. Automation of this process is therefore crucial for accurate and fast detection. To this end, in this work, we report the development of Deep Pose Tracker (DPT), an end-to-end deep learning model to automate the study of posture dynamics and locomotion behaviour of *C. elegans*, a model organism useful to study neuroscience, genetics, drug design, *etc.* The DPT model enables automatic detection and tracking of these animals while measuring essential behavioural features like locomotion speed, orientation, forward or reverse locomotion, complex body bends as omega turns, and eigenworms (representing the overall posture dynamics in a low-dimensional space). Our DPT model can generate highly accurate data, with very high inference speed, while being user-friendly and robust to experimental variabilities. DPT, therefore, can be a valuable toolkit for researchers studying behaviour under different environmental stimuli.

BP 15.10 Wed 12:15 BAR/SCHÖ

Adaptive Determination of Cluster Number in Single-Cell RNA-seq — •Cornelius Miller, Felix Wehrenberg, Dominik Egger, and Sophia Rudorf — Institute of Cell Biology and Biophysics, Leibniz University Hannover, Hannover, Germany

Single-cell RNA sequencing (scRNA-seq) has transformed transcriptomic research by enabling gene expression profiling at the resolution of individual cells. The complexity and high dimensionality of scRNA-seq data pose substantial challenges for effective data interpretation. Current analysis pipelines often struggle with computational scalability and the subjective nature of parameter selection. Here, we introduce a comprehensive Python-based framework that automates key analytical stages while maintaining user flexibility. A critical innovation of this framework is the implementation of an adaptive clustering algorithm designed to estimate cluster count without prior knowledge. This method was specifically developed to define the number of distinct subpopulations in Mesenchymal Stem Cell (MSC) datasets, where cellular heterogeneity is often ambiguous. Furthermore, by leveraging parallelization, the proposed architecture handles high-dimensional datasets with improved latency compared to sequential execution. This approach resolves common ambiguities in defining cell types, offering a robust tool for unbiased exploratory data analysis.

BP 15.11 Wed 12:30 BAR/SCHÖ

AI-Guided Transition Path Sampling of Lipid Flip-Flop and Membrane Nanoporation — •Matthias Post and Gerhard Hummer — Max Planck Institute of Biophysics, Frankfurt, Germany

We studied lipid translocation (or *"flip-flop"*) between leaflets of a bio-membrane and the possible involvement of water nanopores via molecular dynamics simulation.[1] We used transition path sampling[2] within the AIMMD[3] framework to efficiently sample unbiased lipid flip-flops and pore formation. A neuronal network model was trained to predict the *"committor"*, that is the probability of a successful transition from a given microscopic conformational state. While coarse-grained DMPC lipids flip via tunneling through the intact membrane, atomistic (CHARMM36) simulations reveal that flip-flop requires the formation of metastable water pores. DSPC bilayers and plasma membrane mimetics[4] facilitate flip-flop via transient water threads or nanodroplets to cross a locally thinned membrane. Deep neural networks map the transition mechanism from a high-dimensional (660d) feature space to a nearly linear committor model, consistent with Cover's theorem[5] and the concept of dominant reaction tubes.[6]

[1] Post, Hummer, *arXiv.*2502.11894 (2025) [2] Bolhuis et al., *Annu. Rev. Phys. Chem.* **53**, 291-318 (2002) [3] Jung et al., *Nat. Comput. Sci.* **3**, 334-345 (2023) [4] Pogozheva et al., *J. Chem. Inf. Model.* **62**, 1036-1051 (2022) [5] Cover, *IEEE Trans.Electron. Comput.* **EC-14**, 326-334 (1965) [6] E, Vanden-Eijnden, *J. Stat. Phys.* **123**, 503-523 (2006).