# BP 20: Statistical Physics of Biological Systems I (joint session BP/DY)

Time: Wednesday 15:00–18:00 Location: H44

BP 20.1 Wed 15:00 H44

**Separating bio-condensates with surfactant-like proteins** — Jannik Kindermann and •Tyler Harmon — Leibniz Institute for Polymer Research, Dresden, Germany

Biocondensates are prevalent in cells as individual compartments that separate material and reactions in space. Many condensates share similar components and/or chemical interactions that drive their formation. This would suggest that the condensate:condensate interface would have a very low surface tension compared to the condensate:solvent interfaces. Supported by in vitro results, this leads to condensate-inside-condensate or dumbbell-like architectures which minimize the condensate:solvent interfaces. However, in vitro, condensates are most often isolated in space from each other. This could play important roles such as limiting the direct flow of material from one condensate to another. The mechanism in cells that separates droplets in space is unknown.

We show using simulations and theory that proteins or other biopolymers that have surfactant like molecular architectures can separate condensates in space. We show how robust this mechanism can be with respect to condensate specificity and the expression levels of surfactant-like molecules in cells.

BP 20.2 Wed 15:15 H44

**Phase separation in membranes and compartments with binding reactions** — •Riccardo Rossetto, Gerrit Wellecke, and David Zwicker — Max Planck Institute for Dynamics and Self-Organization

Biological cells exhibit a hierarchical spatial organization, where various compartments and membranes harbor condensates that form by phase separation. Cells can control the emergence of these condensates by affecting the physical interactions of the involved biomolecules, thus also tuning the binding affinity to the compartments. We describe this situation with a thermodynamically-consistent kinetic model considering passive and active binding reactions to elucidate their role in controlling the occurrence and timescales of phase separation in compartments. On the one hand, binding reactions can lead to the emergence of new equilibrium phenomena, such as re-entrant phase transitions and multistability. On the other hand, they can also affect the kinetics of phase separation. As a particular example, we consider protein droplets in cellular membranes when proteins can also unbind to the cellular bulk. For fast bulk diffusion, this leads to effective nonlocal transport, which fundamentally affects droplet dynamics. For instance, the seminal Lifshitz-Slyozov coarsening can be abolished. Furthermore, active binding reactions can both accelerate or fully suppress coarsening, leading to protein patterns on the membrane. The general conclusions from our model unveil fundamental mechanisms of phase separation in membranes and compartments, and will help us explain more biological observations in the future.

BP 20.3 Wed 15:30 H44

**Reconciling conflicting selection pressures in the plant collaborative non-self recognition self-incompatibility system** — Amit Jangid[1], Keren Erez[1], Ohad-Noy Feldheim[2], and •Tamar Friedlander[1] — [1]Faculty of Agriculture, food and environment, The Hebrew University of Jerusalem, Rehovot, Israel — [2]Einstein Institute for Mathematics, The Hebrew University of Jerusalem, Jerusalem, Israel

Complex biological systems should often reconcile conflicting selection pressures. Specifically, in systems relying on molecular recognition, molecules should recognize particular partners, but avoid others. Here we study how such selection pressures shape the evolution of the self-incompatibility system in plants. This system inhibits self-fertilization using specific molecular recognition between proteins, expressed in the plant female and male reproductive organs. We study the impact of these opposing selection pressures on the amino acid frequencies in these proteins' recognition domain. We construct a theoretical framework enabling promiscuous recognition between proteins and multiple partners each, as found empirically, and employ stochastic simulations. We find asymmetric responses to selection affecting mostly the female, but not the male protein composition. Using large deviations theory, we well-approximate the simulated frequencies and find agreement with genomic data. Our work offers a general theoretical framework to study the impact of multiple selection pressures, applicable to additional biological systems.

BP 20.4 Wed 15:45 H44

**Learning the Equilibrium Free Energy from Non-Equilibrium Steady States with Denoising Diffusion Models** — •Daniel Nagel and Tristan Bereau — Institute for Theoretical Physics, Heidelberg University, 69120 Heidelberg, Germany

Estimating accurate free energy profiles is crucial for predicting the behavior of complex molecular systems. While biased molecular dynamics simulations enhance the sampling of rare events, extracting reliable free energy landscapes from these simulations remains challenging. On the other hand, stochastic thermodynamics, i.e. the concept of entropy production, provides valuable insights into the dynamics of complex systems in non-equilibrium states. However, its computational complexity, due to dependence on time-dependent probability distributions, limits its application to smaller systems.

This work presents a novel approach that combines stochastic thermodynamics with the established machine learning technique of denoising diffusion models to efficiently estimate free energy profiles from biased non-equilibrium steady states. By linking the diffusion and simulation times, we show that the training objective, known as the score, can be decomposed into a non-trivial conservative contribution from the equilibrium potential and a trivial non-conservative part determined by external driving forces. To showcase the effectiveness of our approach and its ability to learn equilibrium free energy profiles, we apply it to a driven toy model and a Martini force field molecular dynamics simulation of a small molecule biased through a lipid bilayer.

BP 20.5 Wed 16:00 H44

**Multiple Pareto-optimal solutions of the dissipation-adaptation trade-off** — •Jorge Tabanera-Bravo and Aljaz Godec — Max Planck Institute for Multidisciplinary Sciences, Göttingen

Adaptation refers to the ability to recover and maintain "normal" function upon perturbations of internal or external conditions and is essential for sustaining life. Biological adaptation mechanisms are dissipative, i.e. they require a supply of energy such as the coupling to the hydrolysis of ATP. Via evolution the underlying biochemical machinery of living organisms evolved into highly optimized states. However, in the case of adaptation processes two quantities are optimized simultaneously, the adaptation speed or accuracy and the thermodynamic cost. In such cases one typically faces a trade-off, where improving one quantity implies worsening the other. The solution is no longer unique but rather a Pareto set—the set of all physically attainable protocols along which no quantity can be improved without worsening another. We investigate Pareto fronts in adaptation-dissipation trade-offs for a cellular thermostat and a minimal ATP-driven receptor-ligand reaction network. We find convex sections of Pareto fronts to be interrupted by concave regions, implying the existence of distinct optimization mechanisms. We discuss the implications of such "compromise-optimal" solutions and argue that they may endow biological systems with a superior flexibility to evolve, resist, and adapt to different nvironments.

**15 min. break**

**Invited Talk** BP 20.6 Wed 16:30 H44

**Centrosome positioning in cell migration and immune response** — •Heiko Rieger — Department of Physics and Center for Biophysics, Saarland University, Saarbrücken, Germany

Leukocytes are the key players of the immune system in eliminating pathogen-infected or tumorigenic cells. During these processes centrosome positioning plays a crucial role for establishing cell polarization and directed migration, targeted secretion of vesicles for T cell activation and cellular cytotoxicity as well as the maintenance of cell integrity. Here, we give an overview over microtubule organization and dynamics during immune processes and present models for centrosome repositioning during the formation of the immunological synapse and during cell migration. We focus particularly on actin-myosin crosstalk, which is involved in regulating the polarity and morphology of migrating cells and encompasses mechanical interactions, mediated by crosslinkers and molecular motors, as well as cytoskeletal

regulators. Based on recent experimental results we develop a computational whole-cell model involving dynamical microtubules that interact not only mechanically but also via signaling with an active cell boundary. A rich self-organized dynamical behavior emerges, comprising varying positions of the microtubule organizing center relative to the nucleus in the migration direction, varying migration characteristics and cell shapes, and complex migratory behavior in obstacle parks and microfluidic setups. Specific dependencies of these behaviors from parameters like the average microtubule length or the cell-boundary stiffness are predicted and compared with experimental observations.

BP 20.7 Wed 17:00 H44

**Modelling neuron growth dynamics and role of extra-cellular matrix** — •Pritha Dolai, Federica Furlanetto, Sven Falk, Marisa Karow, and Vasily Zaburdaev — Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg, Erlangen

Biological tissues are composed of cells embedded in extracellular matrix (ECM) and extracellular fluid. We study the role of cell-matrix interactions in the context of brain tissues and the mechanism of neuron growth through this matrix. We consider two modes for the neurite growth: linear growth by tip extension and growth by the traction force at the tip of the neurite with the ECM. In the second mechanism, growth happens solely due to the interaction of the growing appendages with the particles modeling the matrix. With an agent based model we recapitulate experimentally observed neuron growth patterns in healthy neurons and neurons with mutations corresponding to a disease state performed in organoid models. In experiments, neuron growth is quantified by the dynamics of the growing tips. Additionally we compare further growth characteristics such as track length and velocity of the tip, tortuosity, and angular correlation of growth direction. Our model provides mechanistic description of the neurite growth and can be useful in describing neuronal network formation during early development.

BP 20.8 Wed 17:15 H44

**Cellular morphodynamics as quantifiers for functional states of resident tissue macrophages in vivo** — •Miriam Schnitzerlein[1,2], Eric Greto[3,4], Anja Wegner[3,4], Anna Möller[3,4], Oliver Aust[3,4], Oumaima Ben Brahim[3,4], Stefan Uderhardt[3,4], and Vasily Zaburdaev[1,2] — [1]Department of Biology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) — [2]Max-Planck-Zentrum für Physik und Medizin, Erlangen — [3]Department of Medicine 3 - Rheumatology and Immunology, FAU und Universitätsklinikum Erlangen — [4]Deutsches Zentrum für Immuntherapie, FAU

Resident tissue macrophages (RTMs) perform essential tasks such as clearing cellular debris to ensure tissue homeostasis. Such actions are accompanied by morphological changes in cell shape which reflect their functional states. Until now, RTMs were mostly studied *in vitro*, even though their dynamic behaviour *in vivo* is fundamentally different.

We employed a high-resolution, intravital imaging protocol to generate dynamic data of *in vivo* peritoneal RTMs of mice. Next we built a custom image processing pipeline to assess RTM morphodynamics via a set of human-interpretable cell shape and size features. Those features could quantitatively and also qualitatively differentiate between cells in different activation states. Furthermore, we showed that unperturbed RTMs exhibit a wide range of morphodynamical phenotypes, constituting a naive morphospace of behavioural motifs. Analysing cells challenged by chemical stimulations or due to aging gave us insights into how RTMs respond and adapt to inflammatory stimuli.

BP 20.9 Wed 17:30 H44

**Slimming down through frustration** — •Martin Lenz — Université Paris-Saclay, CNRS, LPTMS, 91405, Orsay, France — PMMH, CNRS, ESPCI Paris, PSL University, Sorbonne Université, Université Paris-Cité, F-75005, Paris, France

In many disease, proteins aggregate into fibers. Why? One could think of molecular reasons, but here we try something more general. We propose that when particles with complex shapes aggregate, geometrical frustration builds up and fibers generically appear. Such a rule could be very useful in designing artificial self-assembling systems.

BP 20.10 Wed 17:45 H44

**RNA fitness prediction with sparse physics based models - A way to explore the sequence space** — •Christian Faber[1], Francesco Calvanese[2], Alexander Schug[1], and Martin Weigt[3] — [1]Forschungszentrum Jülich, Jülich, Germany — [2]Sorbonne-Université, Paris, France — [3]CNRS, Paris, France

The field of medicine uses macromolecules as a means of therapeutic intervention. Consequently, the functional attributes of these novel molecules are assuming greater significance. To complement the wet-lab experiments, we have devised a series of statistical physics based models that are capable of predicting the fitness of RNA molecules based on one- and two-point mutation scans. The experimental data were employed as training data to fit models of increasing complexity, commencing with an additive model and concluding with a model that accounts for global and local epistasis. The models were validated using fitness data from scans with higher order mutations of the wild-type. In contrast to conventional AI algorithms, the parameters of our models were designed for direct interpretation. In examining more distant sequences, we can distinguish the corresponding RNA family from random sequences with a high degree of accuracy. Moreover, the models facilitate interpretations of evolutionary processes and the significance of epistatic terms. Our model can be used to create a fitness landscape far beyond the experimental sequence space, thus identifying promising RNA molecules. Furthermore, the extension to the entire sequence space can be used as a blueprint for other molecules, providing a novel avenue for questions in biomolecular design.