BP 32: Statistical Physics of Biological Systems III (joint session BP/DY)

Time: Thursday 15:00–18:15 Location: BAR/SCHÖ

BP 32.1 Thu 15:00 BAR/SCHÖ

Efficiency of Droplet Formation and Dissolution by Chemical Reactions — •Gerrit Wellecke[1,2], Riccardo Rossetto[1,2], Jan Kirschbaum[1], and David Zwicker[1] — [1]Theory of Biological Fluids, Max Planck Institute for Dynamics and Self-Organization, Am Faßberg 17, 37077 Göttingen, Germany — [2]University of Göttingen, Institute for the Dynamics of Complex Systems, Friedrich-Hund-Platz 1, 37077 Göttingen, Germany

Droplets formed by phase separation are vital for intracellular organization, and cells often control the formation and dissolution of these droplets through chemical reactions. To understand how cells can influence droplets in space and time, we consider a ternary system that exhibits a bistability between homogeneous and phase-separated states. We use a thermodynamically consistent approach to describe the diffusive and reactive dynamics, which allows us to quantify the energy dissipation and entropy production during transitions between these states. We find that reaction-controlled droplet formation and dissolution in the bistable regime are fundamentally different processes. While droplet formation is generally aided by relaxation to equilibrium, we find that a droplet's size determines whether it is best dissolved internally or externally. Further, our model identifies plausible mechanisms by which cells may regulate their intracellular droplets, providing insights that could guide the development of synthetic soft matter systems with tunable droplet behaviour.

BP 32.2 Thu 15:15 BAR/SCHÖ

Size control and fluctuations of chemically active droplets — •Guido Kusters and David Zwicker — Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

Biological cells use liquid-liquid phase separation to dynamically compartmentalize their environment for various applications, many of which require size control. This process is challenging because (i) large droplets tend to grow at the expense of smaller ones, and (ii) thermal fluctuations can disturb droplets since cells are typically small and soft. Chemical reactions can, in principle, control droplet sizes, but there are no clear guidelines on how to robustly achieve size control. To provide guidelines, we consider a binary fluid model driven out of equilibrium by chemical reactions. We reveal two different classes of size-controlled droplets, depending on the ratio of droplet radius to the reaction-diffusion length. Moreover, we determine parameter regimes in which droplets become small. To study fluctuations in this case, we use fluctuation-dissipation arguments to predict the size fluctuations of size-controlled droplets, consistent with our numerical simulations. Taken together, our theory allows us to predict the chemical reactions necessary for maintaining small droplets, e.g., in biological cells or synthetic applications.

BP 32.3 Thu 15:30 BAR/SCHÖ

Anomalous diffusion and directed coalescence of condensates out of equilibrium — •Andriy Goychuk — Helmholtz Centre for Infection Research, Braunschweig, Germany — Lower Saxony Center for Artificial Intelligence and Causal Methods in Medicine, Hannover, Germany

Phase separation is ubiquitous in engineered and in biological systems. For example, biomolecular condensates contribute to the organization of the cytoplasm and nucleoplasm in cells. Here, I will first extend our understanding of textbook phase separation models by showing how condensates consisting of nonpolar molecules can effectively polarize and undergo coarsening by directed coalescence when subjected to a global drift, for example due to electrostatic potential gradients, chemical concentration gradients, or gravitation. Next, to better model the intracellular solution, I will incorporate viscoelastic stress propagation and nonequilibrium fluctuations. In this context, the Brownian motion of condensates has been barely explored despite being a cornerstone of statistical and colloidal Physics. If the active stresses, for example generated by molecular motors, have a different correlation time than the viscoelastic relaxation time of the solution, then the fluctuation-dissipation theorem is broken and the mixture is driven out of equilibrium. In this case, the size-dependence of the center-of-mass diffusion coefficient of the condensates can be either suppressed or enhanced, and the droplet can show superdiffusive motion. Together, these findings improve our understanding of the dynamics of domains in viscoelastic media and conserved order parameters in general.

BP 32.4 Thu 15:45 BAR/SCHÖ

A Minimal Theoretical Framework Linking Translation Activity to Stress-Induced Condensates — •Pascal S. Rogalla[1], Alessandro Barducci[1], and Luca Ciandrini[1,2] — [1]Centre de Biologie Structurale, Université de Montpellier, CNRS, INSERM, Montpellier, France. — [2]Institut Universitaire de France

The formation of intracellular membraneless organelles, such as stress-granule-like condensates formed via liquid-liquid phase separation (LLPS), is a common response to cellular stress. RNA, including mRNA, promotes the assembly of many of these condensates, while the resulting aggregation of mRNAs reduces their availability for translation and thereby modulates ribosome loading. This establishes a feedback loop between condensate formation and translational activity. Here we develop a minimal physical model that makes this coupling explicit by combining Flory-Huggins theory for LLPS with the Totally Asymmetric Simple Exclusion Process (TASEP) for ribosomal traffic on mRNAs. This hybrid framework provides a proof-of-principle description of how LLPS and translation dynamically influence one another. Our analysis reveals that the phase behaviour of both subsystems becomes mutually dependent: a low-occupancy ribosomal phase promotes mRNA aggregation, whereas a high-occupancy phase suppresses condensate formation. These results suggest that cells may regulate condensate formation through translation modulation and, conversely, that LLPS can reshape the translatome. This provides a first proof-of-principle framework for quantifying stress-induced reorganisation of the translational landscape.

BP 32.5 Thu 16:00 BAR/SCHÖ

Optimal sensing through phase separation — •Henry Alston[1], Mason Rouches[2], Arvind Murugan[2], Aleksandra Walczak[1], and Thierry Mora[1] — [1]Laboratoire de Physique, Ecole Normale Superieure — [2]The James Franck Institute & Department of Physics, The University of Chicago

Cells are constantly tasked with making accurate measurements of their surroundings. A paradigmatic example is the sensing of signalling molecule concentrations: the work of Berg and Purcell derived limits for the precision and speed of this sensing through ligand-receptor binding. However, recent experimental work has identified the formation of condensates (liquid droplets coexisting with the cell cytoplasm through phase separation) as a potential mechanism for selectively initiating downstream processes by effectively amplifying small concentration differences between competing signalling molecules. Using a minimal model for droplet nucleation and growth in a fluid mixture, we observe that phase separation can distinguish concentration differences of 1% in minutes, a significant improvement upon well-established pathways for precise concentration sensing.

BP 32.6 Thu 16:15 BAR/SCHÖ

Thermodynamics of DNA sequence recognition by a transcription factor — •Jonas Neipel[1,2,3], Anne Schwager[1], Yahor Savich[1,2,3], Douglas Diehl[1], Anthony A. Hyman[1], Frank Jülicher[2,3], and Stephan W. Grill[1,3] — [1]Max Planck Institute for Molecular Cell Biology and Genetics, Dresden Germany — [2]Max Planck Institute for the Physics of Complex Systems, Dresden Germany — [3]Center for Systems Biology Dresden, Dresden, Germany

Transcription factors (TFs) are proteins that regulate the transcription of genes by binding to specific genomic positions defined by the DNA sequence. The sequence of preference of a TF is typically characterized by a single sequence motif that maximizes binding affinity. However, eukaryotic TFs bind to a spectrum of low affinity binding sites that vastly outnumber canonical motif sequences in the genome. Here, we develop an Ising model of DNA sequence recognition that yields quantitative prediction of TF binding energies across sequence space for the human TF KLF-4. The model is parametrized by in vitro experiments, where we quantify relative binding energies for various sequences in a competitive assay using fluorescence anisotropy. Strikingly, we find that the thus fully parametrized thermodynamic model quantitatively predicts KLF-4 occupancy across the human genome. Finally, we discuss how this genomic energy landscape guides the formation of TF condensates.

15 min. break

BP 32.7 Thu 16:45 BAR/SCHÖ

Kinetic inference of entropy production — •Ivan Di Trelizzi — Max Planck Institute for the Physics of Complex Systems, Dresden, Germany

Nonequilibrium steady states, from planetary dynamics to biological processes, constantly dissipate energy to their environment, producing entropy at a constant rate. Quantifying this dissipation is key to understanding how far systems operate from equilibrium but remains experimentally challenging. I will present a new approach to infer entropy production directly from trajectory data, using measurable kinetic quantities known as traffic and inflow rate, without requiring knowledge of microscopic forces or fluxes. The method remains effective even under partial observation, providing a practical framework to quantify nonequilibrium behaviour in complex physical and biological systems.

BP 32.8 Thu 17:00 BAR/SCHÖ

Frequency-space trajectory Fisher Information to quantify sensitivity in complex living systems — •Zhiheng Wu[1] and Isabella Graf[1,2] — [1]European Molecular Biology Laboratory, Heidelberg, Germany — [2]Department of Physics and Astronomy, Heidelberg University, Heidelberg, Germany

Living systems sense their environment by stochastically mapping external signals onto internal states. For example, several animals including fruit flies and pit vipers encode small changes in the ambient temperature in terms of changes in the interspike time of neurons. The sensitivity of these measurements can be evaluated by the so-called Fisher information (rate). While living systems constantly adapt to changing environments, calculations of Fisher information have so far mostly focused on static signals and internal states. To evaluate measurement sensitivity in the non-static case, we evaluate the trajectory Fisher information and show that, under common assumptions, it can be expressed as an integral over frequency space involving the power spectral density. This expression provides a tractable way to quantify information in adaptive and complex biological systems and we discuss some interesting applications.

BP 32.9 Thu 17:15 BAR/SCHÖ

Ergodicity shapes inference in biological reactions driven by a latent trajectory — •Ricardo Martinez-Garcia[1], Benjamin Garcia de Figueiredo[2], Justin Calabrese[1], and William Fagan[3] — [1]CASUS-HZDR, Görlitz, Germany. — [2]Princeton University, Princeton NJ, USA. — [3]University of Maryland, College Park MD, USA.

Many natural phenomena, from intracellular reactions to predator-prey encounters, can be described as counts of events triggered at random intervals when an underlying dynamical system enters reactive regions of its phase space. These reactions control biological functions across scales, from cellular processes to ecosystem services and stability. We compute the exact distribution of inter-count times under the only assumption that the latent dynamical system is Markovian and ergodic, recovering widely used Poisson statistics as a limiting case. These results limit what information about the latent process can be inferred from a local detector, which we explore in two biophysical scenarios. First, in estimating an animal's activity from detector crossings, we show that mean counts may fail to capture movement parameters, encoded in higher-order moments. Second, we show that the variance of inter-reaction times imposes a fundamental limit on how precisely detector measurements can infer the size of an ensemble of trajectories, generalizing the Berg-Purcell limit for chemosensation. Overall, we develop a flexible framework for quantifying inter-event time distributions in reaction-diffusion systems that shows which properties of latent processes are inferable from observed reactions.

BP 32.10 Thu 17:30 BAR/SCHÖ

Information Bottleneck in Gene Regulation — •Marianne Bauer — TU Delft

Biological systems need to process information in order to perform specific functions. In the context of gene regulation, regulatory regions process transcription factor signals in order for cells to differentiate towards correct fates. Previously, we have shown that the information bottleneck (IB) framework provides a useful framework for understanding regulatory binding site regions. Here, I will discuss two recent collaborative advances to provide an improved biological understanding from IB based predictions. First, using two complementary models for clustering transcription factors at binding site sensors, we can study information transfer during early fly embryo development with local transcription factor clustering. We find that weak cooperativity or clustering can allow for maximal information transfer, especially about the relevant variable, and that weak clustering also allows the binding site sensors to achieve optimality consistent with the IB bound. Second, we investigate how optimal activation changes when multiple binding site elements can process information, and find that activation profiles consistent with IB optimality resemble gene expression profiles in the early fly embryo.

BP 32.11 Thu 17:45 BAR/SCHÖ

Binary karyotypes are universally selected for across cancers — •Lucija Tomašić[1], Shane A. Fiorenza[1], Hajime Okada[2], Thomas W. van Ravesteyn[3], Uri Ben-David[2], Geert J.P.L. Kops[3], and Nenad Pavin[1] — [1]Univ. of Zagreb, Zagreb, Croatia — [2]Tel Aviv University, Tel Aviv, Israel — [3]Hubrecht Institute, Utrecht, the Netherlands

Aneuploidy, an abnormal chromosome number, is a defining feature of most cancers, yet its vast diversity has made it difficult to identify universal evolutionary rules. By analyzing over 90,000 patient-derived cancer karyotypes using a new visualization approach and mathematical modeling, we uncover a simple organizing principle. Across cancer types, and even in yeast, aneuploid genomes overwhelmingly assemble into "binary karyotypes" composed of only two chromosome copy numbers. Despite the enormous space of theoretically possible chromosome configurations, these states dominate patient data, comprising more than three-quarters of observed karyotypes. Our model shows that this pattern arises from a modest but consistent fitness advantage of binary karyotypes over more complex configurations. This principle also provides insight into how aneuploid cells withstand stress responses, as binary karyotypes exhibit lower rates of tumor suppressor gene inactivation. Together, our results identify binary karyotypes as a conserved evolutionary class of aneuploidy, governed by global organizational rules that may reveal shared vulnerabilities across cancers.

BP 32.12 Thu 18:00 BAR/SCHÖ

Inertial instability of blood in cross microchannels — •Joséphine Van Hulle and Christian Wagner — Experimental Physics, Saarland University, Germany

A localized reduction of vessel diameter (stenosis) increases the local blood flow speed and can trigger downstream recirculation which promotes conditions for the vessel blockage (thrombosis). The role of fluid elasticity in these flows remains underexplored. We isolate the extensional effects using cross-slot microfluidics, which creates an elongation plane with a well-defined inertial instability. By varying the hematocrit and plasma composition, we show that red blood cell deformability and plasma viscoelasticity lower the critical Reynolds number for the onset of vortex formation. These results highlight that even weak elastic stresses of blood can favor recirculation, a characteristic rarely modeled but necessary for physiologically realistic arterial simulations.