CPP 45: Focus Session: Theoretical Modeling and Simulation of Biomolecular Condensates I (joint session CPP/BP)

Biomolecular condensates play a central role in many cellular processes and provide a fascinating example of self-organized, highly dynamic systems. Physical methods, particularly from statistical physics and soft matter, have emerged as valuable tools for understanding and predicting their fundamental properties. Conversely, the complexity and diversity of biological systems open new perspectives and challenges for physical modeling. This focus session will highlight current research at the interface of physics and biology, with an emphasis on theoretical modeling and simulation of the physics of biomolecular condensates.

Organized by Arash Nikoubashman, Tyler Harmon and Lukas Stelzl.

Time: Thursday 9:30–11:15 Location: ZEU/0260

Topical Talk CPP 45.1 Thu 9:30 ZEU/0260

Wetting transitions in biomolecular coacervates — •Susanne Liese[1], Tiemei Lu[2], Evan Spruijt[3], and Christoph Weber[1] — [1]University of Augsburg — [2]University of Oxford — [3]Radboud University

Biomolecular coacervates are liquid-like droplets that can interact with membranes and self-organize into complex structures. Understanding the principles governing their shapes and higher-order assemblies is crucial for controlling compartmentalization in biological and synthetic systems.

We present a theoretical framework describing the shape and organization of biomolecular coacervates interacting with membranes and each other. Large coacervate droplets adopt morphologies determined by the balance of surface tensions, from partial adhesion to full engulfment. Scaled membrane tension and droplet-membrane interactions predict transitions between spherical, lens-shaped, partially wrapped, and endocytosed droplets, with composition-dependent contact angles linking molecular properties to macroscopic shapes.

For multiphase coacervates, we model the impact of interfacial species on droplet organization. Enrichment of an interfacial component at phase boundaries drives partial wetting between droplets, promoting the formation of dimers and extended chains. Numerical simulations show that surface tension minimizes the contact area, straightening droplet arrangements and generating polymer-like behavior with bending stiffness and segment-length constraints.

CPP 45.2 Thu 10:00 ZEU/0260

Elastic regulation of biomolecular condensates — •Oliver Paulin and David Zwicker — Max Planck Institute for Dynamics and Self-Organization, Am Faßberg 17, 37077 Göttingen, Germany

In recent years, biomolecular condensates have emerged as a vital component of sub-cellular organisation. Here, we discuss the role that elastic interactions can play in regulating condensate size, count, and mechanical properties. First, we focus on the impact of 'external' elasticity that arises from a confining mesh such as the cytoskeleton. We find that the additional energetic cost of network deformations induced by condensate growth limits condensate size, and can even suppress condensate formation entirely. Additionally, when condensate size is comparable to characteristic heterogeneities of the network, non-local interactions may arrest thermodynamic coarsening and drive the formation of stable patterned states with an energetically selected length scale. Second, we study how 'internal' elasticity, resulting from the intrinsic viscoelasticity of condensate material, can inhibit condensate growth, but also impart condensates with mechanical strength. For the case in which condensate growth is driven by active incorporation of new material, we demonstrate how a delicate balance of material properties provides condensates with solid-like mechanical strength, without compromising their liquid-like ability to form and grow rapidly. For both examples, we construct dynamic continuum models that couple phase separation with elastic deformation, analysing the key parameters that control condensate form, and identifying how cells can use elasticity to fine-tune condensate behaviour to fulfil a specific function.

CPP 45.3 Thu 10:15 ZEU/0260

Phase Separation of a Nucleator in a Self Straining Active Filament Network — •Jakob Schindelwig[1], Quentin Bodinier-Lefranc[1,2], and Sebastian Fürthauer[1] — [1]Institute of Applied Physics, TU Wien, Lehargasse 6, 1060 Vienna, Austria — [2]Ecole polytechnique, Institut Polytechnique de Paris, Route de Saclay, 91120 Palaiseau, France

Many membraneless compartments of cells, such as stress-granules, form via liquid-liquid phase separation. In cells many compartments of the same type and similar sizes can coexist. Since this is inconsistent with equilibrium phase separation physics, we ask if active mechanics could explain this observation. We develop a model coupling dynamics of the droplet material to an active self-straining filament network. This model shows (i) arrested coarsening , (ii) oscillations, (iii) scale selection. We establish that our model is physiologically plausible by comparing to recent work on a phase separating nucleator of actin.

CPP 45.4 Thu 10:30 ZEU/0260

Active Transport as a Mechanism of Microphase Selection in Biomolecular Condensates — •Le Qiao, Peter Gispert, and Friederike Schmid — Institut für Physik, Johannes Gutenberg-Universität Mainz, D55099 Mainz, Germany

Cells control the size and organization of biomolecular condensates formed by liquid-liquid phase separation (LLPS), yet the underlying physical principles remain incompletely understood. We propose a transport-driven mechanism in which undirected motor-mediated motion along cytoskeletal filaments redistributes phase-separating components, generating an effective non-equilibrium long-range repulsion that arrests coarsening. This is explored using a minimal reaction-diffusion-transport model that captures the interplay between binding-release kinetics, diffusion, and active transport. A linear stability analysis and three-dimensional simulations reveal a transition from macroscopic to microphase separation at remarkably low binding/release fractions, corresponding to minute fractions of motor-bound proteins. Tuning motor binding rates b or transport velocities enables sublinear control of condensate dimensions ($L \sim b^{1/4}$) from nanometers to micrometers. This mechanism provides a simple physical route for spatially programmable condensate organization in living cells and active materials.

CPP 45.5 Thu 10:45 ZEU/0260

Positive feedback in chemically active droplets — •Xi Chen[1], Jens-Uwe Sommer[1,2], and Tyler Harmon[1] — [1]Leibniz Institute of Polymer Research, Dresden, Germany — [2]Dresden University of Technology

Biomolecular condensates are dynamic compartments that can be maintained far from equilibrium by active chemical reactions. Active condensates can be driven by phase-dependent reaction fluxes, for example via localized enzymatic activity, and thereby exhibit emergent behaviors that cannot be realized in equilibrium condensates. We analyzed condensates with positive feedback between phase separation and reactions: droplets enhance reactions, and the resulting products stabilize the droplets. We show that this feedback produces pronounced hysteresis, making droplets resilient to cellular fluctuations. We show the hysteresis persists across a broad range of reaction schemes and parameter choices, indicating that it is a robust feature of droplets with positive feedback. Condensates that form to satisfy transient cellular needs may benefit from such hysteresis, because it ensures that they persist long enough to carry out their functions despite fluctuating conditions.

CPP 45.6 Thu 11:00 ZEU/0260

Chemically driven simulations of enzymatic phosphorylation in protein condensates — •Emanuele Zippo[1], Dorothee Dormann[1,2], Thomas Speck[3], and Lukas Stelzl[1,2] — [1]Johannes Gutenberg University Mainz, Mainz, Germany — [2]Institute of Molecular Biology (IMB), Mainz, Germany — [3]University of Stuttgart,

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The condensation and aggregation of intrinsically disordered proteins (IDPs) in cells are governed by enzyme-driven, non-equilibrium processes. Kinases such as Casein kinase 1 delta (CK1d) phosphorylate proteins using ATP as chemical fuel, tuning intermolecular interactions and modulating condensate assembly. The neurodegeneration-linked protein TDP-43 undergoes CK1d-mediated hyperphosphorylation, proposed as a cytoprotective mechanism through condensate dissolution, yet the mechanisms underlying kinase-condensate interactions remain unclear. Using coarse-grained molecular dynamics simulations, we investigate how CK1d phosphorylates TDP-43 and how this reaction drives the structural reorganization and dissolution of its condensates. To ensure thermodynamic consistency in such fuel-driven simulations, we employ an automatic, generally applicable Markov state modeling framework. Post-translational modifications (PTMs), such as phosphorylation, can actively regulate condensate stability and suppress Ostwald ripening, offering a mechanism to control mesoscale structure in soft materials. Understanding such reaction-structure coupling in non-equilibrium environments is key to explaining cellular self-organization and designing biomimetic systems.