CPP 50: Focus Session: Theoretical Modeling and Simulation of Biomolecular Condensates II (joint session CPP/BP)

Time: Thursday 11:30–12:45 Location: ZEU/0260

CPP 50.1 Thu 11:30 ZEU/0260

Exponential Size Control in Biomolecular Condensates via Universal Scaling of Power-Law Distributions — •Yifan Huang[1], Chuan Tang[1], Haoyu Song[2], Bing Miao[3], and Qiyun Tang[1,4] — [1]Key Laboratory of Quantum Materials and Devices of Ministry of Education, School of Physics, Southeast University, Nanjng 211189, China — [2]School of Physics, Zhejiang University, Hangzhou 310058, China — [3]Center of Materials Science and Optoelectronics Engineering, College of Materials Science and Opto-Electronic Technology, University of Chinese Academy of Sciences, Beijing 100049, China — [4]Jiangsu Physical Science Research Center, Nanjing 210093, China

Power-law distributions are ubiquitous phenomena in diverse systems, whereas concomitant scale invariance hinders the exploration of precise size control for biocondensates in recent experiments. Using massive computer simulations and the kinetic theory of coalescence, we demonstrate that the cutoff volume can collapse all power-law distributions of biocondensates in different parameters onto one master curve. Remarkably, the cutoff size can increase exponentially by increasing monomer concentrations $R \sim e^{\phi}$, of which nanometer condensates in simulations can be extrapolated to micrometer droplets in experiments. The findings provide a new mechanism to rapidly tailor the biocondensates to appropriate sizes through power-law distributions, which can stimulate explorations in biological and other nonequilibrium systems

CPP 50.2 Thu 11:45 ZEU/0260

Droplet-assisted folding of long regulatory RNAs — Simon Doll[1], Lukas Pekarek[1], Fathima Ferosh[1], Jovana Vasiljević[1], Marcus Jahnel[1], and •Tyler Harmon[2] — [1]BIOTEC, Dresden, Germany — [2]IPF, Dresden Germany

Long regulatory RNA regions orchestrate complex cellular processes, including gene expression and epigenetic modifications. How these RNAs dynamically fold and refold in response to cellular signals remains poorly understood. Given that RNAs interact with ubiquitous RNA-binding proteins (RBPs) prone to form biomolecular condensates, we explore how protein droplets interacting along an RNA impact its folding process. Attached droplets prevent premature folding by competing with RNA:RNA interactions. When droplets dissolve due to cellular signals, capillary effects cause the RNA to collapse while refolding. We test this process of condensate-guided RNA folding by adapting established RNA secondary structure predictors to mimic various folding pathways and supplement this with coarse-grained simulations. We find that interactions with transient droplets robustly leads to the formation of long-range RNA contacts, which are otherwise hard to achieve. Our results compare favorably with available experimental data. We propose that this strategy, which we call droplet-assisted RNA folding, represents a previously unexplored mechanism for shaping RNA structures. Given the widespread propensity of RBPs to form condensates, this process could play a fundamental role in the structural organization, conditional reshaping, and functional regulation of long regulatory RNAs.

CPP 50.3 Thu 12:00 ZEU/0260

Simulation Insights into the Assembly of Polyplexes for RNA Delivery — •Jonas Hans Lehnen[1], Jorge Moreno Herrero[3], Heinrich Haas[3], Friederike Schmid[1], and Giovanni Settanni[1,2] — [1]Department of Physics, Johannes-Gutenberg University Mainz — [2]Faculty of Physics and Astronomy, Ruhr University Bochum — [3]BioNTech SE, Mainz

RNA-based pharmaceuticals proved successful with the COVID-19 vaccines and are now undergoing clinical trials for a broad range of therapeutic indications. Lipid-based nanoparticles (LNPs) have been used so far as delivery systems, although alternatives are still needed to meet efficacy and safety requirements across a broader range of applications. Polyplexes, formed by the self-assembly of cationic polymers with the anionic nucleic acids, constitute a valuable substitute, especially if precise control of the number and shape of the encapsulated RNA chains is possible. Here[1], we use molecular dynamics simulations of a coarse-grained polyplex model to show that the most important factors controlling it are the charge ratio between polyelectrolytes and RNA and their concentration during assembly. Close to the isoelectric point, the polyplexes are large, whereas in large excess of cationic polymer, their size decreases, allowing one RNA copy per nanoparticle. Our results are consistent with recent experimental work on polyethylenimine polyplexes.

[1] Simulation Insights into the Assembly of Polyplexes for RNA Delivery, Lehnen et al., Biomacromolecules (2025), DOI: 10.1021/acs.biomac.5c01219

CPP 50.4 Thu 12:15 ZEU/0260

Polymer-assisted condensation as key to chromatin localization — •Arghya Majee[1] and Jens-Uwe Sommer[1,2,3] — [1]Leibniz Institute of Polymer Research Dresden, Germany — [2]Institute for Theoretical Physics, TU Dresden, Germany — [3]Cluster of Excellence Physics of Life, TU Dresden, Germany

We put forward a novel mechanism [1] to account for the experimentally observed [2] positional shifts of chromosomes within the cell nucleus, which appear to be driven by compositional alterations in the nuclear lamina. By considering chromatin as a biomolecular condensate we demonstrate that the adsorption of the chromatin-binding proteins at the lamina leads to a wetting of the condensate while spreading of the chromatin on the lamina is avoided. This leads to the non-monotonous density profile of the polymer with respect to the surface which can be explained by the competition between the tendency of the protein component to wet the surface and the conformational restrictions of the polymer near the impenetrable surface. A change in the composition of the the lamina can lead to repositioning of chromatin towards the center of the nucleus. Our theory not only offers an explanation for specific chromatin conformation experiments, but also contributes to the broader understanding of wetting onto responsive surfaces in multi-component systems.

References:

[1] A. Majee and J.-U. Sommer, bioRxiv 2025.06.11.658974 (submitted).

[2] Amiad-Pavlov *et al.*, Sci. Adv. **7**, eabf6251 (2021).

CPP 50.5 Thu 12:30 ZEU/0260

Bridging Scales to Understand the Role of Ubiquitylation and Sumoylation in Protein Phase Separation — •Supriyo Naskar, Kurt Kremer, and Oleksandra Kukharenko — Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

The post-translational modifiers, such as mono- and poly-ubiquitins and SUMOs, are known for their ability to modulate protein-protein interactions by becoming covalently attached to other target proteins. Despite the high similarity in the tertiary structure and sequence, they differentially influence the target protein properties. In this work, we employed a multiscale simulation approach that encompasses atomistic to different levels of coarse-grained modeling techniques, combined with data-driven methods, to explore the structural differences and multidimensional energy landscapes of ubiquitin, SUMO, and their conjugates. We finally investigate the influence of distinct features of the targets and modifiers on protein phase separation and aggregation, providing molecular-level insight into the corresponding in vitro measurements and informing further experiments through the adjustment of relevant parameters.