BP 14: Focus Phase Separation in Biological Systems I (joint session BP/CPP)

Time: Tuesday 9:00–11:00 Location: BPc

BP 14.1 Tue 9:00 BPc

Intranuclear Phase Separation of a Chromatin Scaffolding Protein — •Davide Michieletto[1], Mattia Marenda[1], David Zwicker[2], and Jan Kirschbaum[2] — [1]University of Edinburgh — [2]Max Planck Institute for Dynamics and Self-Organization

The formation and regulation of phase separated condensates is now widely seen in vitro and cytoplasm, but far more challenging to observe and test in the cell nucleus. In this talk I will present recent work on an abundant nuclear RNA-binding protein called Scaffold Attachment Factor A, or SAF-A, that regulates chromatin decompaction at transcriptionally active loci through its interaction with RNA. Here I show that the intrinsically disordered RNA binding domain of SAFA * known as an RGG domain – undergoes phase separation upon transcriptional inhibition and that the size of the condensates can be controlled by tuning the amount arginine/lysine residues in the RGG domain. By expressing a longer, and closer to native, SAFA domain we observe that the phase separation is suppressed. To explain our findings, we propose an equilibrium model in which a slowly diffusing RNA substrate can sequester RGG fragments; upon transcriptional inhibition the freed up fragments can undergo phase separation via weak self-interactions.

BP 14.2 Tue 9:20 BPc

Quantitative phase microscopy enables precise and efficient determination of biomolecular condensate composition — •Patrick M McCall[1,2], K Kim[3,4], AW Fritsch[1], JM Iglesias-Artola[1], LM Jawerth[1,2], J Wang[1], M Ruer[1], A Poznyakovskiy[1], J Peychl[1], J Guck[3,4], S Alberti[3], AA Hyman[1], and J Brugués[1,2] — [1]MPI-CBG, Dresden — [2]MPI-PKS, Dresden — [3]TU Dresden — [4]MPI Science of Light

Many cellular processes rely on condensed macromolecular phases termed biomolecular condensates. Despite progress in measurements and theoretical descriptions of several condensate properties, an understanding of their most basic feature, composition, remains elusive. Here we combined quantitative phase microscopy and sessile droplet physics to measure the shape and composition of individual model condensates. This technique requires 1000-fold less material than traditional approaches, achieves a precision of better than 2 %, and does not rely on fluorescent tags, which we show can significantly alter phase behavior. The protein concentrations measured in three model condensates span a broad range, from 80 to 500 mg/ml, pointing to a natural diversity in condensate composition specified by protein sequence. We report salt- and temperature-dependent binodals as well as time-resolved measurements revealing that PGL3 condensates undergo a contraction-like process during aging. This leads to doubling of the internal protein concentration coupled to condensate shrinkage. We anticipate that this new approach will enable understanding the physical properties of biomolecular condensates and their function.

BP 14.3 Tue 9:40 BPc

Quantitative Theory for the Diffusive Dynamics of Liquid Condensates — •Lars Hubatsch[1,2], Louise M Jawerth[1,2], Celina Love[2], Jonathan Bauermann[1], Stefano Bo[1], T-Y Dora Tang[2], Anthony A Hyman[2], and Christoph A Weber[1,2] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

To unravel the biological functions of membraneless liquid condensates it is crucial to develop a quantitative understanding of the physics underlying their dynamics. Key properties of such condensates are diffusion and exchange of material with their environment. Experimentally, such diffusive dynamics are typically probed through the direct observation of the individual or collective motion of fluorescently labelled molecules. However, to date we lack a physics-based quantitative framework for the dynamics of labeled condensate components. Here, we derive the corresponding theory, building on the physics of phase separation, and quantitatively validate this framework via experiments. We showcase the accuracy and precision of our approach by considering space and time resolved data of protein condensates and two different coacervate systems. Strikingly, our theory can be used to determine the diffusion coefficient in the dilute phase and the partition coefficient, purely based on fluorescence measurements in the droplet.

BP 14.4 Tue 10:00 BPc

Interactions of droplets with polymer networks at the mesh and continuum scale — •Thomas J Boeddeker[1], Estefania Vidal[2], Kathryn A Rosowski[1], David Zwicker[2], and Eric R Dufresne[1] — [1]ETH Zurich, Zurich, Switzerland — [2]MPI DS, Göttingen, Germany

Phase-separation of biomolecules in cells takes place in a complex environment crossed by multiple filaments of the cytoskeleton or chromatin. Interactions between the emerging protein droplets and filaments take place over different length scales and may lead to motion and deformation of both network and droplet. In this shared talk, Thomas presents experimental work on the interactions of stress granules, a phase-separated protein-RNA droplet in the cytosol, with the heterogeneous microtubule network at the mesh scale. Inspired by observations in the cell, we then turn to synthetic gels where elastic effects produce ripening in stiffer materials leading to a dissolution front. Estefania presents a theoretical framework for the observed ripening in gradients of network stiffness at the continuum scale. Our combined results present an initial approach to understand the complex interactions throughout phase separation in an elastic network.

30 min. Meet the Speaker