

Dynamic molecular landscape of disordered translation factors: from molecular interactions to biomolecular condensates

Mikayel Aznauryan¹

¹ ARNA research unit and European Institute of Chemistry and Biology, INSERM U1212, CNRS UMR 5320, University of Bordeaux

Mikayel.aznauryan@inserm.fr

Biomolecular function often emerges not from a single defined structure, but from dynamic networks of weak and transient interactions. Intrinsically disordered protein regions (IDRs) exemplify this principle, using their flexible conformational ensembles to drive molecular recognition, self-assembly, and the formation of biomolecular condensates. Understanding how the molecular properties of IDRs and their interactions collectively generate biological organization requires approaches capable of capturing the dynamic structural heterogeneity at molecular resolution.

We use single-molecule fluorescence spectroscopy, combined with nuclear magnetic resonance spectroscopy, molecular simulations and live-cell imaging that provides a quantitative framework for probing biomolecular assembly across molecular scales. Using the translation factor eIF4B as a model system, we reveal how nanoscopic oligomeric clusters emerge from monomeric protein chains prior to macroscopic phase separation and nucleate the formation of condensates. These dynamic clusters are reminiscent of reverse micelles of block copolymers and are driven by the distinctive sequence composition of the long IDR of eIF4B. They are highly sensitive to ionic conditions, molecular crowding, and post-translational modifications, highlighting multiple mechanisms through which biomolecular condensation can be regulated. By resolving eIF4B conformational dynamics and self-association from monomers to condensates, we uncover a continuum of molecular states in which disorder and assembly coexist.