Bioinspired all-aqueous emulsions highlight tunability of subcellular compartmentalization

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Biomolecular condensates have been increasingly implicated in the spatiotemporal organization of cells. These condensates are non-membrane-bound organelles formed by multivalent interactions between biopolymers that selectively partition and concentrate molecules to control signaling and chemical reactions. Complex coacervation is a liquid-liquid phase separation (LLPS) emulsification process that has been extensively used as a model system for studying condensates. Likewise, this LLPS process occurs when the multivalent interactions of oppositely charged polymers under appropriate conditions are sufficient to form an aqueous, polymer dense, phase separate from the aqueous bulk with similar properties to condensates. Peptide-RNA coacervates can thus be studied as a model system to better understand the 'molecular grammar' of biopolymer primary structure as it relates to condensate formation.

Condensates leverage a variety of interactions including electrostatic, cation-π, and hydrophobic interactions to achieve sufficient valency for phase separation We designed a set of coacervate systems using peptides and nucleotide triphosphates to assess the differences in the formation, stability, and subsequent properties of coacervates with equal biopolymer charges and length to assess the implications of non-electrostatic interactions on coacervates. We found that these differential interactions, presumably differences in cation-π and π-π stacking, led to enthalpic stabilization and increased biopolymer enrichment within the coacervate phase. Similarly, cells leverage post translational modifications to dynamically modulate biopolymer valency by adding or removing functional groups. Arginine methylation, a modification wherein the guanidinium moiety of arginine is modified by adding two methyl groups, has been shown to impact condensates in vivo. We found that arginine methylation has a subtle effect on the complex coacervation process, in this case disrupting RNA secondary structure leading to a change in the phase diagram without substantially impacting the properties of the resultant phase. Overall, condensate formation with respect to non-electrostatic interactions can be studied in detail by complex coacervation.