

Minimal Peptide Sequences That Undergo Liquid–Liquid Phase Separation via Self-Coacervation or Complex Coacervation with ATP

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The simple (self-)coacervation of the minimal tryptophan/ arginine peptide sequences W_2R_2 and W_3R_3 was observed in salt-free aqueous solution [1]. The phase diagrams were mapped using turbidimetry and optical microscopy, and the coacervate droplets were imaged using confocal microscopy complemented by cryo-TEM to image smaller droplets. The droplet size distribution and stability were probed using dynamic light scattering, and the droplet surface potential was obtained from zeta potential measurements. SAXS was used to elucidate the structure within the coacervate droplets, and circular dichroism spectroscopy was used to probe the conformation of the peptides, a characteristic signature for cation– π interactions being present under conditions of coacervation. These observations were rationalized using a simple model for the Rayleigh stability of charged coacervate droplets, along with atomistic molecular dynamics simulations which provide insight into stabilizing π – π stacking interactions of tryptophan as well as arginine–tryptophan cation– π interactions (which modulate the charge of the tryptophan π -electron system). Remarkably, the dipeptide WR did not show simple coacervation under the conditions examined, but complex coacervation was observed in mixtures with ATP (adenosine triphosphate). The electrostatically stabilized coacervation in this case provides a minimal model for peptide/nucleotide membraneless organelle formation. These are among the simplest model peptide systems observed to date able to undergo either simple or complex coacervation and are of future interest as protocell systems.

Keywords:

peptides, coacervates

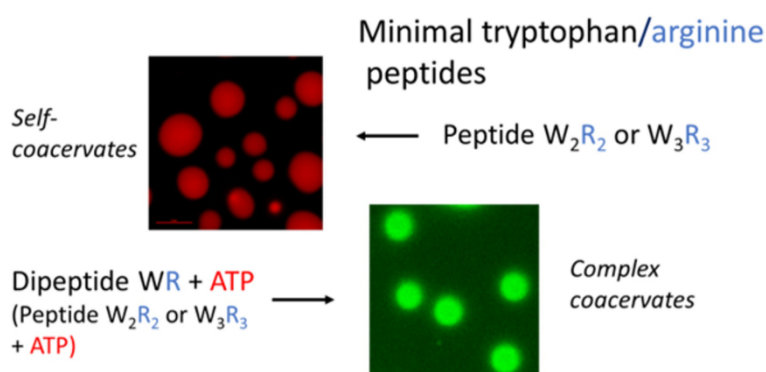


Figure 1. W_2R_2 and W_3R_3 self coacervates and $WR+ATP$ complex coacervates

References:

[1] V. Castelletto, J. Seitsonen, A. Pollitt et al., *Biomacromolecules*. 2024, 25, 5321–5331.

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