



Chirality Directs the Formation, Structure, and Function of Peptide Coacervates

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Chirality governs molecular recognition and assembly, yet its influence on condensed soft phases remains unknown. We show that stereochemical configuration directly regulates phase separation and internal organization in small-molecule coacervates formed by diphenylalanine derivatives. Homochiral peptides undergo coacervation at lower concentrations to form compact, ordered droplets stabilized by hydrogen bonding and π - π stacking, whereas heterochiral combinations yield more dynamic, permeable condensates. These differences extend to tripeptide systems, revealing a stereochemical control axis that defines droplet order, stability, and molecular selectivity. Thus, these results establish stereochemistry as a regulator of packing geometry and mesoscale organization in condensed phases, providing a general physical principle by which chirality programs order, fluidity, and molecular selectivity in soft matter.

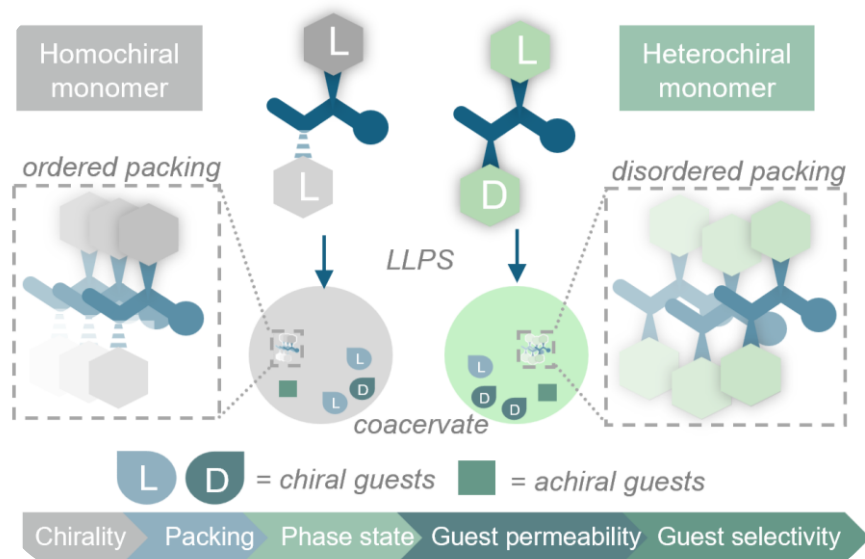


Figure 1. Chirality directs peptide coacervate formation by regulating molecular packing. Homochiral assemblies exhibit ordered packing, while heterochiral assemblies display disordered packing, leading to differences in condensate properties, guest permeability, and molecular selectivity.

References

1. L. Leon, G. M. Santiago, and E. Spruijt, *Commun. Chem.* **7**, 275 (2024).
2. M. Matsuo and K. Kurihara, *Nat. Commun.* **12**, 5487 (2021).