PEPTIDE SELF ASSEMBLY CONFERENCE 2026
MAINZ. GERMANY
FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Sticker–Spacer Molecules as Minimal Models for Coacervation: Linking Electronic and Structural Design to Phase Behavior

L. Lenz[1], M. Kumar[1], M. Kapidžić[1], S. Dhiman[1*]

[1] Department of Chemistry, Johannes Gutenberg University Mainz, Duesbergweg 10- 14, Mainz, 55122, Germany.
E-mail: llenz@students.uni-mainz.de

Biomolecular condensates form through multivalent, transient interactions between weakly interacting regions along intrinsically disordered proteins, driving liquid–liquid phase separation inside cells. Reproducing this behaviour with small, fully synthetic molecules offers a modular and synthetically tractable route to studying phase separation and to building protocell-like compartments. Such systems are typically described using a "sticker–spacer" framework, in which aromatic or hydrophobic "stickers" mediate intermolecular association while flexible, hydrophilic "spacers" connect them and modulate solubility. Despite the appeal of this design logic, the rules linking sticker electronics, spacer properties, and molecular flexibility to coacervate formation remain poorly understood, limiting the development of predictive design principles for small-molecule coacervates.

Here, we synthesized a library of sticker–spacer molecules in which a naphthalic anhydride sticker bearing substituents of varying electron-withdrawing strength (H, Br, NO_2) was connected to glycol-based spacers of varying length and flexibility. Varying the substituent allowed us to tune the electron-poor character, aromaticity, and hydrogen-bonding/dipolar behaviour of the sticker independently of its overall size, enabling us to probe how electron-withdrawing strength influences sticker–sticker association. By correlating substituent electronics and spacer design with the observed phase behaviour, we established structure–property relationships that link molecular architecture of aromatic stickers to macroscopic coacervation outcomes.

These findings position sticker–spacer molecules as a simple, chemically tunable model system for dissecting the molecular grammar of biomolecular condensate formation and provide design guidelines for engineering synthetic coacervates with tailored stability and morphology.