Solvation-by-design: amphiphile self-assembly and biomolecular adaptation in deep eutectic solvents

Adrian Sanchez-Fernandez[a]

[a]*Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS), Departamento de Enxeñaría Química, Universidade de Santiago de Compostela, Santiago de Compostela, Spain*

adriansanchez.fernandez@usc.es

Solvation has become a design principle, and deep eutectic solvents (DESs) perfectly exemplify this emerging paradigm. DESs are liquids formed through the mixture of simple molecular components (e.g. choline chloride and urea) in the absence of water or any other solvent [1]. In these, the intermolecular forces between the constituents elicit a marked depression in the melting point that stabilizes the fluid phase. Far from acting as passive media, DESs are increasingly recognized as task-specific 'cocktails' in which composition can be controlled to precisely modulate hydrogen-bonding networks, charge density, and solvophobicity. This allows to design DESs that can dictate solvation landscapes and specific solvent-solute interactions. This exceptional tunability makes DESs a unique framework in which we can interrogate phenomena ranging from self-assembly to biomolecular stability, adaptation and function, with implications spanning soft-matter science, biocatalysis and advanced biomedical formulation.

In our group *descaffold* , we exploit the design space to show that DESs can regulate matter across length scales. In amphiphile systems, they modulate self-assembly pathways by balancing the supramolecular interactions that define aggregate curvature and colloidal organization [2]. In proteins, they remodel folding and association landscapes [3], which can be induce gellation and expose new principles for biomolecular soft materials [4]. In nucleic-acid formulations, they create anhydrous environments that enhance stability, expanding the scope of transfecting systems beyond the constraints of aqueous media. If solvation can be engineered at will, then DESs may do more than expand formulation space—they may fundamentally redraw its boundaries.

Keywords:
Deep eutectic solvents, self-assembly, protein folding, gel formation

References:

[1] Hansen et al., *Chem Rev* **2021** , 121 (3), 1232-1285.
[2] Sanchez-Fernandez et al., *J. Am. Chem. Soc.* **2021** , 143 (35), 14158-14168.
[3] Sanchez-Fernandez et al., *J. Am. Chem. Soc.* **2022** , 144 (51), 23657-23667.
[4] Sanchez-Fernandez et al., *ACS Nano* **2024** , 18 (28), 18314-18326.