Order from the disorder with intrinsically disordered peptide amphiphiles

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The concept that a given amino-acid sequence will not form a 3D folded structure but still have biological functionality has developed only in the last ~15 years. The discovery rate and characterization of intrinsically disordered proteins have been increasing continually, becoming one of the fastest-growing areas of proteomics [1]. It is now estimated that over 50% of eukaryotic proteins contain large intrinsically disordered regions involved in a wide range of cellular functions, including transcription, translation, signaling, and regulation of protein assembly. Structural flexibility and plasticity originating from the lack of an ordered structure suggest a significant functional advantage for these proteins, enabling them to interact with a broad range of binding partners.

Amphiphilic molecules and their self-assembled structures have long been the target of extensive research due to their potential applications in materials design to biomedical fields. An emerging class of molecules, namely, peptide amphiphiles, combines key advantages and circumvents some disadvantages of conventional phospholipids and block copolymers.

In this talk, I present new peptide amphiphiles composed of an intrinsically disordered peptide conjugated to variants of hydrophobic domains [2]. These molecules termed intrinsically disordered peptide amphiphiles, exhibit a sharp pH-induced micellar phase-transition from low-dispersity spheres to extremely elongated worm-like micelles. I will present various experimental characterizations of the transition and propose a theoretical model to describe the pH response [Fig. 1]. I will also show the potential of the shape transition to serve as a mechanism for the design of a cargo hold-and-release application. Such amphiphilic systems demonstrate the power of tailoring the interactions between disordered peptides for various stimuli-responsive biomedical applications.

References

[1] T. Ehm, H. Shinar, S. Meir, A. Sekhon, V. Sethi, I. L. Morgan, G. Rahamim, O. A. Saleh, and R. Beck, *Intrinsically Disordered Proteins at the Nano-Scale*, Nano Future. **5**, (2021) 022501.

[2] G. Jacoby, M. Segal Asher, T. Ehm, I. Abutbul Ionita, H. Shinar, S. Azoulay-Ginsburg, I. Zemach, G. Koren, D. Danino, M. M. Kozlov, R. J. Amir, and R. Beck, *Order from Disorder with Intrinsically Disordered Peptide Amphiphiles*, J. Am. Chem. Soc. **143**, (2021) 11879.

Figures

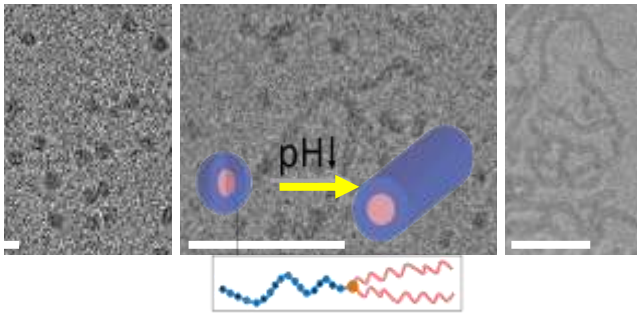

Figure 1: Cryogenic TEM of intrinsically disordered peptide amphiphiles transitioning via alternation of pH between isolated nanoscopic micelles to worm-like micelles.