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The CSI Chemistry Department Presents

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Bioinspired Supramolecular Systems Chemistry

Date: 3/7/2024 **Time: 2:30 PM** **Room: 6S-232**

Systems chemistry is a chemists attempt to create and study chemical complexity with a prospect to understand biological processes which are governed by metabolic reaction networks and a functional use of biological order and disorder. At its core it is an interplay between supramolecular interactions and reaction networks. The following presentation deals with my efforts in this direction starting from reaction networks controlling order in synthetic mimics of cytoskeleton. This is followed with expanding the understanding of biological order and disorder by exploiting reaction networks and amyloidal co-assembly with peptidic condensates. These components of the presentation are detailed below.

Cytoskeletal proteins are a network of biological fibers that can control their length and temporal profile precisely due to the strict metabolic control. Such a property is desirable in synthetic systems as you can make highly adaptable materials. We thus designed synthetic molecules that shuttle between its non-assembling and assembling form driven by reversible equilibrium in water. This imparts a unique control over aggregate nucleation and eventually leads up to precise control of their length polydispersity. Furthermore, coupling other networks to this reaction driven assembly we were able to design hydrogels that can emulate the cytoskeleton in its temporal properties.[1]

Following this, I will detail chemical systems with local order in globally disordered coacervates/biomolecular condensates that drive the cellular organization. Recent work has shown their involvement in a plethora of processes in vivo. Even though biomolecular condensates are globally disordered, they perform efficient biological functions through ordered domains present inside them. Understanding and ultimately controlling the local architecture of these liquid droplets is thus imperative if one were to gain deeper functional insights into their means of operation and apply them in diverse fields. We designed a multi-component system such that the interface between ordered and disordered domains is stabilized through a covalent connection of beta sheet-promoting and condensate-forming features. This allows beta sheet fibers to form exclusively inside the droplets and show clear fiber nucleation and elongation stages. This study shows for the first time that minimalistic ordered domains can be generated inside liquid droplets in a controlled fashion.[2]

The following presentation thus details the efforts in controlling the tryst between order and disorder in bioinspired systems using key principles of supramolecular systems chemistry.

[1] A. Jain, S. Dhiman, A. Dhayani, P. K. Vemula, S. J. George, *Nature Commun.* **2019**, *10*, 450.
[2] A. Jain, S. Kassem, R. S. Fisher, B. Wang, T.-D. Li, T. Wang, Y. He, S. Elbaum-Garfinkle, R. V. Ulijn, *J. Am. Chem. Soc.* **2022**, *144*, 15002-15007.

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