The interplay of physical and chemical events in peptide-based systems

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Biology utilizes both covalent chemistry and physical assembly to achieve the complex behaviors associated with living systems. The field of systems chemistry has been inspired by biological systems, constructing and analyzing systems that are simpler than biology, while still embodying biological design principles. Due to the multiple phenomena at play, it can be difficult to predict which phenomenon will be dominant and when. Conversely, there may be no single rate-limiting step, but rather a reaction network that is difficult to intuit from a purely experimental approach. Mathematical modeling can help to sort out these issues, although it can be challenging to build such models, especially for assembly kinetics.

Here I will discuss our collaborative work with the Lynn group on peptide-based systems, which utilizes an acetal linkage to create modified peptides containing reversible covalent bonds. Such reversibility is a hallmark of biological systems, enabling reconfiguration in a dynamic environment. As the peptides react, a physical phase transition is triggered, and within the new droplets, new reactions are promoted. The droplets grow, and at a critical size peptide assembly is triggered, selecting out a single oligomer length through an autocatalytic growth process. Our mathematical modeling indicates that elementary reaction expressions can describe the kinetics, although the rate constants depend on the local transient environment. Feedback is another key design principle in biological systems, and with a reaction network having peptide assemblies, it should also be possible to catalyze new reactions that can provide further feedback to the reaction network.