Sequence Specific Phase Separation using Dynamic Peptide Library

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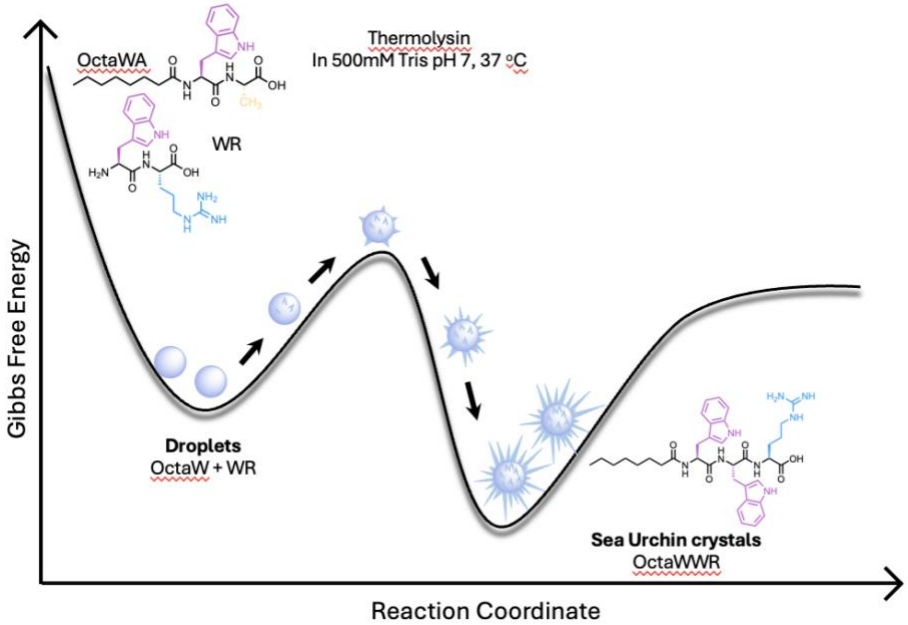
Compartmentalization is a feature that allows cells to perform multiple functions simultaneously. This can be achieved through liquid-liquid phase separation (LLPS).[1] The Early Earth was a mixture of various components, including amino acids, fatty acids, nucleotides, and others. It is most probable that compartmentalization made the existence of life possible by segregating reactions into different, distinct spaces. Similarly, here we are trying to couple compartmentalization to reaction networks using the Dynamic Peptide Library (DPL) approach. In a DPL, the enzyme thermolysin can reversibly break and form bonds to yield a mixture of peptides.[2] In our system, a product peptide sequence undergoes phase separation, giving rise to droplets that act as compartments for further elongation and sequence-specific peptide synthesis. Our design consists of a fatty acid chain (C_8) with a dipeptide sequence that can phase separate in an enzymatic reaction. In the current work, we have thus created a microreactor from simple building blocks for peptide synthesis, making it relevant to the origin of life scenario.



(1) Slootbeek, A. D.; Haren, M. H. I. van; Smokers, I. B. A.; Spruijt, E. *Chem. Commun.* **2022**, *58* (80), 11183–11200.
(2) Pappas, C. G.; Shafi, R.; Sasselli, I. R.; Siccardi, H.; Wang, T.; Narang, V.; Abzalimov, R.; Wijerathne, N.; Ulijn, R. V. *Nat. Nanotechnol.* **2016**, *11* (11), 960–967.