A DNA-driven assembly strategy for a decodable biohybrid block copolymer library

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Soft materials made from synthetic copolymers are applicable to a broad scope of biomedical applications, particularly in peptide stabilization for peptide-based therapeutics. However, identifying specific copolymers that best serve a desired application is currently a time-intensive process. One approach to identifying copolymers is to screen a copolymer library, but due to synthetic restrictions and the use of low-throughput screening methods, current library strategies are limited in size to several hundred members.

To overcome these challenges, we are currently developing a novel library of biohybrid block copolymers, where DNA tethers are responsible for both directing copolymer assembly and barcoding the identity of each copolymer. This strategy allows us to quickly synthesize a library of over 10,000 members at once and screen the library at high-throughputs using next-generation DNA sequencing.

Our DNA-driven copolymer assembly strategy was studied computationally using NUPACK, a published algorithm used to predict the binding interactions of a set of nucleic acid strands. We modelled our biohybrid copolymers as a test tube of DNA strand sequences which were then analyzed using NUPACK. Results verified that our barcoded DNA sequence design drives favorable and specific assembly of each copolymer member. These promising results allow us to move forward with implementing our DNA sequence design in library synthesis, which we will use to screen copolymers for peptide stabilizing activity.