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

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Background

Copolymer Library

Current synthetic copolymer libraries are limited in library size and screening throughput. Our strategy uses DNA to assemble a large block copolymer library at once while encoding information about each copolymer's identity for high-throughput screening.

High Throughput Screening using Next-Generation DNA Sequencing

Peptide Stabilization

Synthetic copolymers have been shown to stabilize peptides, particularly for peptide therapeutics such as insulin. A robust copolymer library would allow us to quickly identify and optimize copolymers for peptide stabilization.

Project Overview

NUPACK Analysis Algorithm

The NUPACK Analysis Algorithm can predict the assembly behavior of a set of interacting DNA strands. We modelled our biohybrid copolymers as DNA sequences in order to predict assembly behavior using NUPACK.

Favorability of Assembly

Will blocks favorably assemble into a full block copolymer complex?

Specificity of Assembly

Will tethers bind to their specific staple complements, based on the barcode?

NUPACK Model and Predictions

NUPACK generated structure of a sequence model of the copolymer assembly. This 13-strand complex includes 7 polymer blocks and 6 staples.

NUPACK Predicted Yields for a Full Copolymer Assembly

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<tr>
<th>Yields</th>
<th>3-block</th>
<th>5-block</th>
<th>7-block</th>
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<tbody>
<tr>
<td>99%</td>
<td>96%</td>
<td>84%</td>
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Key Findings:
- Copolymers with more blocks assemble less favorably.
- The largest copolymer size our design supports (7-blocks) can still assemble at good yields.
- As equilibrium, the reaction mixture has a bimodal distribution between the full assembly and the smaller complexes. May allow us to purify our fully assembled copolymers based on size.

Acknowledgements:
The Knight Group @ UNC Chemistry, UNC Longleaf Computing Cluster, The NUPACK Team, Taylor and Gold Research Fellowship

References: