

UNIVERSITY OF RHODE ISLAND
Department of Chemistry
SEMINAR

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Room 105 – Beaupre Center

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Synthesis and Sequencing of
Sequence-Defined Biotic and
Abiotic Polymers

HOST

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Synthesis and Sequencing of Sequence-Defined Biotic and Abiotic Polymers

There is little argument that many of the grand achievements of biotechnology, biochemistry, and chemical biology stem from advances in synthetic organic chemistry embodied in the development of solid-phase synthetic approaches for proteins and nucleic acids. Of equal importance to the synthesis of the biopolymers, however, are methods for their sequencing. Revolutions in nucleic acid sequencing have led to single molecule and Next-Gen parallel methods. Similar advances in protein sequencing have lagged behind. In collaboration with the Marcotte group at UT Austin, we have created a single-molecule peptide sequencing routine referred to as fluorosequencing. Therein, peptides are N-terminal captured, the amino acids selectively labelled with fluorophores, C-terminal differentiated, and then placed on TIRF microscope for rounds of Edman degradation. The development and implementation of the organic chemistry necessary in the method will be discussed. On another topic, the ribosome is Nature's synthesis machine for creating sequence-defined polyamides, i.e., peptides/proteins. This machinery has previously only been shown to generate analogous linkages, such as esters. Given this limitation, we have extended Nature's machinery to make repetitions of complex heterocyclic rings, such as pyridazinones. Further, the sequencing of sequence-defined polymers, other than nucleic acids and proteins, shows promise as a new paradigm for data storage. We have devised the first use of oligourethanes for storing and reading encoded information. As a proof of principle, an approach will be described using a text passage from Jane Austen's *Mansfield Park*. It was encoded in oligourethanes and reconstructed via chain-end degradation sequencing. We developed Mol.E-coder, a software tool that utilizes a Huffman encoding scheme to convert the character table to hexadecimal. The passage was capable of being reproduced wholly intact by a third-party, without any purifications or the use of MS/MS, despite multiple rounds of compression, encoding, and synthesis. Overall, this presentation will highlight the interplay and utility of synthesis and sequencing in sequence-defined polymers.

