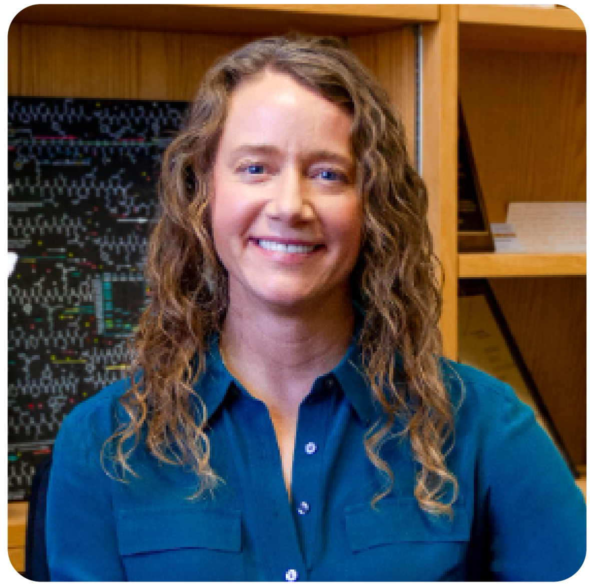
Penn Engineering
University of Pennsylvania
Chemical and Biomolecular Engineering

Spring 2023 Seminar Series

THERESA M. REINEKE

"Tunable Multifunctional Macromolecules via Parallel Experiment and Computation: from Drug and DNA Delivery Vehicles to Sustainability"

Wednesday
March 22, 2023
3:30 PM
Wu and Chen Auditorium
Levine Hall



Prager Chair in Macromolecular Science
Distinguished McKnight University Professor
University of Minnesota

ABSTRACT
Multifunctional macromolecules have a tremendous impact on a multitude of applications. For example, the development of polymer excipients can improve the solubility and bioavailability of intractable drugs, nucleic acid delivery vehicles have promise to promote selective genome editing, and materials from sustainable monomers may lower the environmental impact of plastics. While the materials function is diverse across these fields, the synthetic principles are similar and should be readily tunable for each specific application while remaining biologically and environmentally benign. Modern polymer chemistry and engineering offers numerous pathways for tailorable materials development and a multitude of rich monomer functionality (high heteroatom content and stereochemistry), composition, molecular weight, and architecture (linear, statistical, block, brush), where engineering is now hindered by the infinite design space. To this end, we have coupled parallel experimental workflows with computation and/or machine learning to effectively understand structure-activity trends, mechanisms, and rapidly discover high performance structures. For example, we have applied these techniques to design delivery vehicles for Cas9 ribonucleoprotein (RNP), plasmid (pDNA), and combination payloads. A library of statistical copolymers has been synthesized and systematic variations in physicochemical properties and trends for encapsulation/delivery of RNP and pDNA payloads were examined in parallel. Structure-function correlations underlying cellular internalization, editing efficiency, gene expression, and cellular toxicity of the polymer-payload formulations were probed through machine learning approaches. This workflow allowed rapid identification of successful architectures that outperform commercial reagents, achieving nearly 60% editing efficiency via non-homologous end-joining. Furthermore, the data set allowed us to uncover the physicochemical basis of delivery performance, offering understanding of divergent requirements for successful delivery of RNP and plasmid payloads. Our work demonstrates the power of combinatorial synthesis and high-throughput characterization methodologies coupled with data science approaches to discover promising macromolecules and structure-property relationships that would have otherwise remained inaccessible to intuition.

BIO
Theresa M. Reineke is the Prager Chair in Macromolecular Science and Distinguished McKnight University Professor in the Department of Chemistry at The University of Minnesota. She also holds graduate faculty appointments in the Departments of Chemical Engineering/Materials Science and Pharmaceutics. She received a B.S. Degree from the University of Wisconsin-Eau Claire, a M.S. Degree from Arizona State University, and a Ph.D. from The University of Michigan. She then received a National Institutes of Health Postdoctoral Fellowship to further her research background at the California Institute of Technology prior to beginning her independent faculty career. Her research group is focused on enabling fundamental and applied technology advancements of polymers in the fields of gene therapy and genome editing, drug delivery, and sustainability. She has published over 170 peer reviewed manuscripts, has numerous patents, and manages a large group of researchers funded by several corporate, private foundation, and national funding agency grants. Reineke has received several awards, including the 2009 National Institutes of Health Director's New Innovator Award, 2012 Outstanding New Investigator Award from the American Society of Gene and Cell Therapy, 2017 Carl S. Marvel Creative Polymer Chemistry Award from the American Chemical Society Division of Polymer Chemistry, 2018 was awarded the DuPont Nutrition and Health Sciences Excellence Medal, and most recently the 2022 Arthur C. Cope Scholar Award from the American Chemical Society. She has cofounded two start up biotech companies: Techulon, Inc. and Nanite, Inc. She has also served as Associate Editor of ACS MacroLetters and Chemical Science and in 2023 became Editor-in Chief of Bioconjugate Chemistry. She also currently serves on the Editorial Advisory Boards of the peer-reviewed journals Biomacromolecules, Bioconjugate Chemistry, Polymer Chemistry, and ACS Applied Polymer Materials.