UCI Samueli School of Engineering

Department of Materials Science and Engineering

UNIVERSITY OF CALIFORNIA, IRVINE

DEPARTMENT OF MATERIALS SCIENCE AND ENGINEERING

Is Proud To Host A Seminar By

"Illuminating microstructure-dependent binding and delivery of nucleic acids via gradient copolymerization and field flow fractionation"

DATE
Thursday, November 19, 2026

TIME
2:00 PM – 3:00 PM

LOCATION
McDonnell Douglas Engineering Auditorium

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Department of Chemical and Biological Engineering

Colorado School of Mines

Abstract: Therapeutic nucleic acids such as plasmids pDNA and genome editor ribonucleoproteins (RNPs) such as CRISPR/Cas9 promise to improve the lives of millions of people suffering from genetic disorders. However, nucleic acids confront intracellular delivery barriers such as cellular uptake, endolysosomal processing, or nuclease-mediated degradation, which curtail their therapeutic functionality. Engineered viral vectors can overcome these challenges but are difficult to manufacture at scale and prohibitively expensive. Polymers, in contrast, can be economically mass-produced and designed to minimize immune responses. Synthetic advances, particularly in reversibly deactivated radical polymerization, help chemists access arbitrary combinations of compositions, lengths, architectures, and repeat unit spatial distributions, offering unprecedented control over polymer properties. Here, we demonstrate that the spatial distribution of lipophilic cations governs the complexation pathways and biological performance of polymer–pDNA and polymer–RNP complexes (polyplexes). Previous research focused on block/statistical copolymers, whereas gradient copolymers, where the density of lipophilic cations diminishes (gradually or steeply) along polymer backbones, remain underexplored. We engineered gradient copolymers that combine the polyplex colloidal stability of block copolymers with the transfection efficiency of statistical copolymers. We synthesized length- and compositionally equivalent gradient copolymers (G1–G3) along with statistical (S) and block (B) copolymers of 2-(diisopropylamino)ethyl methacrylate and 2-hydroxyethyl methacrylate. We mapped how polymer microstructure governs pDNA loading per polyplex, pDNA conformational changes, and polymer–pDNA binding thermodynamics via static light scattering, circular dichroism spectroscopy, and isothermal titration calorimetry, respectively. While gradient steepness is a powerful design handle to improve polyplex physical properties, augment pDNA delivery capacity, and attenuate polycation-triggered hemolysis, microstructural contrasts did not elicit differences in complement activation. Our work demonstrates that gradient polymerization is a powerful and under-utilized tool to optimize multiple design objectives in polycation-mediated nucleic acid delivery. For RNP delivery, we observed stark microstructure-dependent differences in polymer–RNP binding affinity, trends that propagated across genome editing assays and cellular uptake. We established that chemical and electrostatic heterogeneity along polymer backbones is essential to achieve high editing efficiencies. In the second part of the talk, we will demonstrate how asymmetric flow field flow fractionation (AF4) illuminates hitherto unsuspected solution properties of polyplexes. We will also describe how AF4 is a powerful analytical and preparative tool to realize the potential of polymeric gene delivery.

Bio: Ramya has been a tenure-track Assistant Professor in the Department of Chemical and Biological Engineering at the Colorado School of Mines since Jan 2022. Her lab applies functional polymer synthesis, advanced characterization, and statistical modeling to engineer polymeric nanocarriers for genome editor delivery and polymer coatings that direct and interrogate cell behavior. In 2023, she was awarded an NIH R21 to develop polymer coatings for mesenchymal stem cell engineering. In 2025, she won three early career awards: NSF CAREER, NIBIB TrailBlazer and NIGMS ESI MIRA. She also won student-nominated awards for teaching and mentoring. She has authored 25 publications (in journals such as ACS Nano, JACS Au, Biomacromolecules, Macromolecules, ACS AMI, ACS Macro Letters) and 3 patents. She is a member of the American Chemical Society, American Institute of Chemical Engineers, and the Society for Biomaterials. Outside work, Ramya enjoys long-distance running, baking naturally fermented bread, and reading literary fiction.