# CHEMICAL ENGINEERING

DISTINGUISHED YOUNG SCHOLARS SERIES


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# Elucidating Protein Corona Composition and Dynamics on Nanoparticles in Biological Environments


**ABSTRACT:** Engineered nanoparticles are increasingly used for biological sensing, imaging, and delivery due to their distinctive optical and physical properties. Specifically, DNA functionalized single-walled carbon nanotube (DNA-SWCNT) probes operate at spatiotemporal scales necessary to capture information on chemical signaling, such as neurotransmission in the brain.[1] The critical – and often overlooked – challenge with these nanoscale tools is understanding the fundamental mechanisms of interaction between the nanoprobe and the system they are designed to query. When a nanoparticle enters a biological system, the surface becomes rapidly coated with proteins to form the "protein corona". Binding of proteins to the nanoparticle disrupts intended nanoparticle functionality and leads to unpredictable in vivo outcomes (Fig. 1).


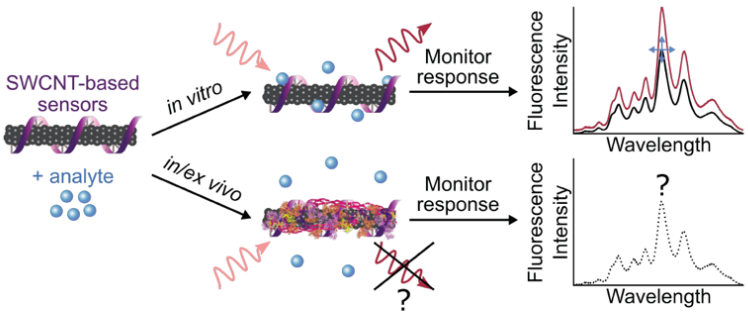


Figure 1: Protein corona formation unpredictably affects performance of SWCNT-based fluorescent nanosensors applied in biological environments.

A comprehensive understanding of the protein corona remains a paramount barrier to successfully implementing nanotechnologies within biological environments. Herein, I present multimodal characterization of (i) protein corona composition on DNA-SWCNTs in relevant biological media, (ii) timescales and driving forces of formation, and (iii) kinetics of protein adsorption to DNA-SWCNTs in solution (Fig. 2). I have optimized a platform to characterize protein corona composition formed on DNA-SWCNTs by proteomic mass spectrometry to determine abundant and differentially enriched vs. depleted corona proteins.[2] By

varying incubation conditions of DNA-SWCNTs in biofluids, I have investigated the role of electrostatic and entropic interactions driving selective protein corona formation. To study the dynamic exchange of biomolecules on the SWCNT surface, I have developed a multiplexed fluorescence assay that enables real-time tracking of biomolecule adsorption and desorption events.[3] This corona exchange assay is generic towards the study of various biomolecules exchanging on the SWCNT surface and enables study in solution rather than on a surface-immobilized, less biologically relevant, setting.[4]

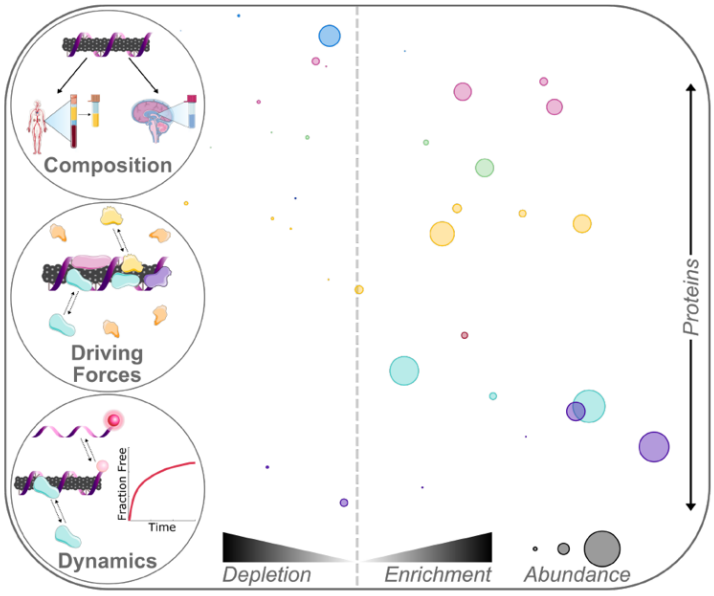


Figure 2: Studying characteristics of the protein corona formed on nanoparticles will provide insight into the high failure rate of *in vitro* validated nanobiotechnologies translated to *in vivo* application.

Understanding the corona composition, timescales and driving forces of formation, and corona dynamics under relevant solution conditions informs design and synthesis of nanotechnology-based tools applied in protein-rich environments. Although corona formation can impair nanobiotechnology efficacy, it also presents an opportunity to create improved protein-nanoparticle architectures by exploiting selective protein adsorption to the nanoparticle surface. In this work, I develop techniques and analyses that directly characterize the in-situ protein corona microenvironment and employ this knowledge towards rational design of nanobiotechnologies.

**BIOGRAPHY:** Rebecca is an NSF Graduate Research Fellow pursuing her PhD in UC Berkeley's Chemical and Biomolecular Engineering Department. Her current research with Professor Markita Landry focuses on engineering fluorescent carbon nanomaterial-based sensors to probe biological systems. In her PhD, Rebecca aims to understand the mechanisms and effects of protein adsorption on nanosensors functioning in biological environments and apply this knowledge to develop more robust nanosensors. Rebecca has received awards for her research including the CAS Future Leader Award and ACS Women Chemists Committee/Merck Research Award. Prior to her PhD, Rebecca graduated with her BS in chemical engineering with honors from Brown University in 2016, where she worked with Prof. Peterson on heterogeneous catalysis for biofuel production. Through numerous summer research experiences, she has ventured from the tall glass towers of pharmaceutical drug development in Boston, down to the mud in Tennessee riverbeds to analyze nutrient bioavailability. Beyond research, Rebecca is actively involved in leading local science outreach programs that encourage participation in STEM, including Expanding Your Horizons and Bay Area Scientists in Schools. She is passionate about mentoring undergraduate students in research and teaching college and graduate level courses.

**LECTURE 1:00 - 2:00 Zoom**
**Networking Hour on Zoom Following**

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[1]Beyene, A. G., McFarlane, I. R., Pinals, R. L. Landry, M. P. Stochastic Simulation of Dopamine Neuromodulation for Implementation of Fluorescent Neurochemical Probes in the Striatal Extracellular Space. ACS Chem. Neurosci. 8, 2275–2289 (2017)
[2]Pinals, R. L. et al. Protein Corona Composition and Dynamics on Carbon Nanotubes in Blood Plasma and Cerebrospinal Fluid. bioRxiv.2020.01.13.905356 (2020) doi:10.1101/2020.01.13.905356.
[3]Pinals, R. L., Yang, D., Lui, A., Cao, W. Landry, M. P. Corona Exchange Dynamics on Carbon Nanotubes by Multiplexed Fluorescence Monitoring. J. Am. Chem. Soc. (2019) doi:10.1021/jacs.9b09617.
[4]Alizadehmojarad, A. A. et al. Binding affinity and conformational preferences influence kinetic stability of short oligonucleotides on carbon nanotubes. bioRxiv 2020.02.08.939918 (2020) doi:10.1101/2020.02.08.939918.