

UNDERSTANDING THE STABILIZATION OF PROTEINS IN HETEROGENEOUS SURFACE ENVIRONMENTS

Joel L. Kaar, Department of Chemical and Biological Engineering, University of Colorado, USA
joel.kaar@colorado.edu

Key Our group is broadly focused on understanding and controlling the intersection of biology and materials at the molecular level. This intersection is critical in many areas of biotechnology where proteins and enzymes are integrated into or in constant contact with materials, including biocatalysis, tissue engineering, drug delivery, biosensing, and therapeutic protein formulation. In line with this interest, we have developed a novel approach to elucidate the structure and transient behavior of protein molecules at the solution-solid interface based on dynamic single-molecule tracking. This approach, which is uniquely sensitive to structural and interfacial dynamics, includes the use of high-throughput tracking of protein molecules by means of internal reflection fluorescence (TIRF) microscopy in combination with intramolecular as well as intermolecular Forster resonance energy transfer (FRET). Notably, in this approach, as many as 10⁶ protein molecules are tracked as they adsorb, desorb, diffuse, and simultaneously undergo conformational changes and/or intermolecular associations, permitting the statistical identification of dynamic, spatial, and population heterogeneity. The subsequent correlation of these dynamic behaviors on a molecule-by-molecule basis via large-scale multivariate analyses, moreover, provides new insights into the connection between interfacial dynamics and protein structure. In this talk, I will discuss our recent results applying this approach to elucidate the molecular mechanisms involved in the stabilization of proteins through intentionally creating chemical heterogeneity in polymer brush and lipid bilayer surfaces. Additionally, I discuss how this understanding can be extended to design biomaterials that have improved biocompatibility.