INTERFACIAL STUDIES OF SURFACES AND PROTEINS

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ABSTRACT

The objective of this research was to demonstrate and quantify the effect of interfaces on protein adsorption and aggregation. Proteins interact with interfaces in many applications and invariably adsorb onto or are affected by these surfaces. How proteins behave at various interfaces is of fundamental importance in protein folding/unfolding and protein fouling phenomena. These processes are relevant for medical and industrial applications. In this study, we demonstrate that interfaces can play a role in adsorption and aggregation. First we studied protein fouling behavior of a model foulant, BSA, on a reversibly switching photoresponsive surface and static surfaces modified with zwitterionic charged monomers. We demonstrated how by changing the surface chemistry protein-surface interaction can be reduced. Next, we focused on protein-protein interactions (protein aggregation) and chose human insulin as a model protein. We used small angle neutron scattering (SANS) during the early stages of *in vitro* fibrillation of insulin, to establish the structure of the "critical nucleus" of the insulin fibril. Using different additives that affect the kinetics of oligomer formation, we also demonstrated that although the kinetics of the nucleus formation is dependent on a specific system, they all followed a universal pathway. The stabilizing effect of dissolved sugars and the accelerating effect of solid hydrophobic surfaces on the fibrillation kinetics were also observed. An array of analytical techniques such as contact angle goniometry, UV-visible spectroscopy, circular dichroism, atomic force microscopy, fluorescence spectroscopy, Fourier transform infrared spectroscopy and small angle neutron scattering was employed. We also established a new assay (A_{600}) for quantifying fibrillation.