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**Towards a Deeper Understanding of Protein Resistance:
Characterizing Water/Surface and Protein/Surface Interactions by In
Situ Neutron Reflectometry**

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Materials which are resistant towards adsorption of proteins from biological media are of crucial importance in biotechnology and biomedical applications. The most outstanding protein resistant properties are exhibited by surfaces containing poly- (PEG) and oligo(ethylene glycols) (OEG), $(-O-CH_2-CH_2-)_n$. For surface-grafted PEG, protein resistance is associated with an unfavorable change in the free energy when a protein approaches the surface and thereby compresses and dehydrates the polymer chains. However, this mechanism cannot explain the inertness of rigid, and thus conformationally restricted, OEG terminated alkanethiolate self-assembled monolayers (SAMs). Proposed models suggest the importance of water/SAM interactions at the surface or relate protein resistance to repulsive electrostatic forces. Due to its capability to characterize biological interfaces in situ, neutron reflectometry provides a unique tool to address fundamental questions of protein repulsion. We have studied the importance of interfacial water layers between inert SAMs and the bulk water phase to repel proteins. Temperature dependent studies on the OEG/water interface reveal, that a previously observed, density reduced water phase in the vicinity of the SAM cannot account for the protein resistant properties of the films. Moreover, neutron reflectometry has been used to investigate protein/surface interactions employing biomolecules in their native state and natural environment. Room temperature measurements on protein resistant films of OEG in contact with bovine serum albumin (BSA) solutions reveal the presence of an extended protein depletion layer between the SAM and the bulk protein solution. The results are compared to the strength and range of repulsive forces measured by AFM.