INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	**SHIVAM TIWARI**
Roll Number	:	**156107039**
Programme of Study	:	**Ph.D.**

Thesis Title: **Protein-Surface and Protein-Ligand Interactions: Insights from Atomistic Simulations**

Name of Thesis Supervisor(s)	:	**Prof. Katha Anki Reddy**
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SHORT ABSTRACT

Proteins are one of the most abundant and essential class of organic molecules present in the living systems. Their role in the sustenance and growth of life is unique. However, proteins can turn toxic and unfavourable if they are displaced from their native form or present in an undesirable environment. In this thesis, we perform a computational investigation of protein's interaction with various surfaces and chemical entities in varying environments. Various roles of protein are explored in this thesis, ranging from, as a foulant in a desalination membrane, as a cell invader to toxic β plaques causing cell damage. Specifically, in the first part (first two chapters) of the thesis, the protein plays a role of a membrane foulant. We investigated the reason for differences found in fouling of reverse osmosis (RO and a forward osmosis (FO) membrane with lysozyme protein. We explained the role of hydration repulsion and electrostatic interactions in the differences found in FO and RO fouling. we studied the interaction of SARS-CoV2's spike protein (which plays a crucial role in cell entry of the CoV2 virus) with the montmorillonite surface, a clay mineral. Substantial damage to the secondary structure of spike protein is observed in the presence of a mineral surface. In the last two chapters, protein is in the form of toxic β sheets, responsible for a range of age-related dementia. Mechanism of binding and disaggregation of Aβ fibrils with a novel peptidomimetic compound was investigated. The compound showed a strong binding on Aβ fibril via hydrophobic interactions and significant destruction of the fibril's β sheet content. Finally, the interaction between A β fibrils and lipid bilayer was studied using a prodrug peptide β-Aspartyl. The study showed that β-Aspartyl inhibits the interaction between A β fibrils and lipid bilayer. The study also showed the role of π-π stacking and cation-π interactions in binding β-Aspartyl on fibrils.