Role of Surface Chemistry on Protein Conformation at Solid-Liquid Interfaces

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The formation of dense, linear arrays (fibrils) by biomolecules is the hallmark of many degenerative diseases, such as Alzheimer's and type-2 diabetes. Protein fibrils have also attracted interest as building blocks for new materials. It has long been recognised that surfaces can affect the fibrillation process, with the effect of surfaces dependent on both surface chemistry and protein structure[1]. As the behaviour of proteins on surfaces depends on the complex interplay of many different effects (e.g. protein sequence, surface physiochemical properties, protein mobility) and understanding this requires detailed microscopic information. In this presentation work using molecular dynamics simulations the conformation of intrinsically disordered proteins on surfaces will be discussed. This will focus on typical fibril forming proteins, human Islet Amyloid Polypeptide (hIAPP)[2] and amyloid beta fragments[3], on a range of material surfaces. Notably hIAPP adopts largely alpha-helical conformations on hydrophobic surfaces (Figure 1), which are unfavourable for fibril formation. This is consistent with experimental observation that hydrophobic surfaces inhibit hIAPP fibrillation[4]. Understanding the relationship between surface properties and protein conformation can help us decipher the mechanism of protein fibrillation on both naturally-occurring (e.g. cell membrane) and synthetic surfaces.

REFERENCES

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FIGURES

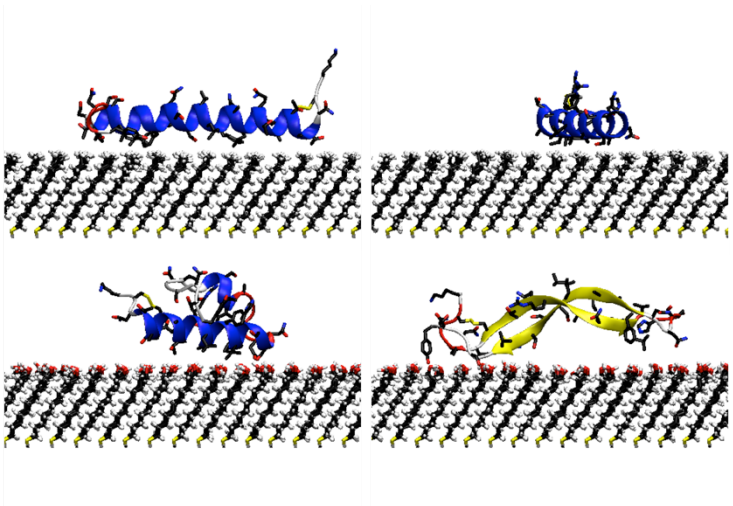

Figure 1: Typical conformation of human Islet Amyloid Polypeptide on hydrophobic (top) and hydrophilic (bottom) surfaces.