Insulin at interfaces – beyond the hydrophobic-hydrophilic dichotomy

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Human Insulin is a relatively small peptide (51 amino acids) which plays a major role in controlling glycemia in the human body. It is also a model protein for understanding protein unfolding and aggregation into fibril-like structures called amyloid which are the hallmark of many degenerative diseases such as diabetes, Alzheimer's and Parkinson's, but also occur during purification, storage and delivery of protein-based drugs.

Amyloids are frequently formed at interfaces, ranging from cell membranes to syringes, in particular if those interfaces are hydrophobic. The main driver for adsorption at hydrophobic interfaces is the entropy gain from excluding water at the interface. The handwaving explanation of why proteins unfold suggests that this adsorption makes it more favourable for hydrophobic amino acid side chains that are normally buried inside the protein structure to attach to the surface which causes unfolding.

Using a range of vibrational spectroscopies, we made the surprising discovery that hydrophobic interfaces can actually stabilise the native structure of insulin at both air-water and water-solid interfaces [1,2] and that unfolding only occurs well above room temperature. We suggested that the interface inhibits fibril formation because it protects the aggregation-prone hydrophobic domains on the insulin monomer by adsorption on the hydrophobic surface. We have since found that this stabilisation of the native structure occurs on a large variety of interfaces, ranging from model functionalised silicon wafers, to porous functionalised silica beads used in reverse phase liquid chromatography and fabrics such as cotton and polyester.

In this talk I focus on how this protection mechanism depends on the precise chemical nature of the interface and whether we can use surface chemistry to control protein aggregation at interfaces.

[1] S. Mauri, T. Weidner, H. Arnolds, "The structure of insulin at the air/water interfaces: monomers or dimers?" Phys. Chem. Chem. Phys. 16 (2014) 26722

[2] S. Mauri, M. Volk, S. Byard, H, Berchtold, H. Arnolds, "Stabilization of Insulin by Adsorption on a Hydrophobic Silane Self- Assembled Monolayer" Langmuir 2015, 31, 8892