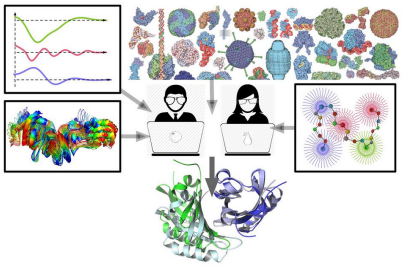

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Spontaneous formation of cushioned model membranes promoted by an intrinsically disordered protein

Histatin 5 (Hst5) is a histidine-rich, 24 amino acid protein, classified as an intrinsically disordered protein (IDP). It contains 7 histidines, an amino acid sensitive to charge regulation. The histidines can titrate and gain a positive charge, making the protein highly cationic. Hst5 is a salivary protein found to play a crucial role in fungicidal activity, and its activity to inhibit the growth and viability of *Candida albicans* has been evaluated using a variety of techniques. We have found that when exposed to a solid supported bilayer, the protein spontaneously forms a cushion below the bilayer and lifts it from the solid support.
The results obtained from neutron reflectometry and QCM-D have shown that the interaction between the peptide and the lipid bilayer is completely governed by electrostatic effects. This was done by changing the charge content in the bilayer and the ionic strength of the buffer. At low ionic strength, the peptide penetrates the bilayer and cumulate close to the solid silica substrate underneath the lipid bilayer. We suggest a mechanism of the formation of the cushion where the histidine residues are charged up by the solid substrate, as well as the charged bilayer. The protein can then penetrate the bilayer without disrupting the lipid-lipid interactions, and adsorb to the solid substrate, which releases counterions bound to the substrate. This counterion release increases the osmotic pressure and lifts the bilayer from the substrate.

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