

Exploring the Interactions of Ions, Peptides, and Proteins with Lipid Membranes

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Biological membranes often contain negatively charged lipids such as phosphatidylserine, phosphatidylglycerol, phosphatidic acid, and gangliosides. The head groups of these lipids can strongly interact with positively charged amino acids from peptides and proteins (i.e. Arg and Lys residues), metal cation from the extracellular solution, as well as positively charged drug molecules. These negatively charged lipids are highly regulated within cells and are highly abundant in certain organelles while almost completely absent in others. Moreover, their concentration within a particular leaflet of a given membrane is often tightly regulated. Despite the high degree of control of lipid composition within cells, little is often known about the reason for it or even the specific nature of ligand-receptor binding interaction with such moieties. To remedy this, we have employed a combination of spectroscopic techniques (Figure 1), microfluidic platforms, monolayer and planar supported bilayer architectures to explore the specific biophysical chemistries of these interactions. This includes the development of a novel analytical tool that employs a pH sensitive fluorophore to probe subtle changes in the surface potential of lipid bilayers upon ligand or ion binding. Both

thermodynamic and molecular level details of these systems have been obtained. The results reveal that binding can be highly dependent on the concentration of specific lipids within the membrane. Moreover, the presence or absence of various uncharged lipids can also greatly influence the binding properties. Interestingly, specific interactions involving hydrogen bonding, charge transfer, and hydrophobic interactions often dominate over simple electrostatic effects.

Figure 1. Monitoring water structure next to a lipid monolayer containing phosphatidylserine (PS) and phosphatidylcholine (PC) lipids by vibrational sum frequency spectroscopy.

