

Artificial membranes get charged

As early as the seventeenth century, scientists realized that some sort of a fatty membrane must surround cells to keep their contents from spilling over. The molecules in the membrane, known as lipids, were known to be made up of a water-loving “head” portion and a long, water-fearing “tail” region. It took over two centuries after that, however, to understand that the cell membrane took the form of a lipid bilayer, which consists of two rows of lipid molecules with the water-fearing tails standing end to end, so as to avoid any contact with water, and the water-loving heads facing outwards. But even a hundred years after the discovery of the bilayer, many of its complexities still remain mysterious. Today, cell membranes are often studied using artificial lipid bilayer structures that act as simple, yet relevant models for the real thing. In a paper recently published in *Biointerphases*, Ralf Zimmerman and his colleagues carefully describe how the charge of a lipid bilayer supported on a silicon surface—one of many models for a real cell membrane—changes in response to the external environment.

The charge in a lipid bilayer is important to understand in detail for many reasons. The charge determines how proteins can bind to the membrane, how cells attach to surfaces and how drugs or DNA can be delivered inside a cell. A negatively charged cell membrane, for instance, would be more likely to attract positively charged proteins. Since only the lipid headgroups of the bilayer are exposed to external environment, the researchers measured what is known as the zeta potential to see how the charge on these headgroups changed as they varied the pH (the level of acidity) and the concentration of the external salt solution. They discovered two interesting phenomena. Firstly, the charge changed dramatically as the external salt solution changed in acidity. Secondly, the charge also appeared to drive a change in the fluidity of the membrane.

At all salt concentrations, the bilayers started out with a positive charge in highly acidic solutions of pH 2, became neutral at pH 4 and turned negative as the acidity decreased to pH 9. Because the lipid headgroups contain both acidic and basic moieties that should charge up in about equal and opposite directions when the solution is neither too acidic nor too alkaline, the observed changes were rather unexpected. The changes were caused, the researchers concluded, by the very ions that make up water itself. These positively and negatively charged water molecules (known as hydronium and hydroxide ions) were probably fixating onto the lipids at different levels of acidity to change the charge. And since water always breaks up into hydronium and hydroxide ions, it could well be doing the same thing to real cell membranes.

The changes in the charge of the bilayer also appeared to compel the bilayers to alter the mobility of the lipids in them. To measure this mobility, the scientists added lipid molecules that had been tagged with a fluorescent dye to the bilayer, then locally bleached the dye to create a dark spot, and finally watched the fluorescence recover as tagged lipids from the surrounding region drifted into the dark spot. At alkaline pH levels, the bilayer was fluid, with lipid molecules being able to move around relatively unconstrained. But at the point where the bilayer took on a neutral charge (at pH 4), its mobility also changed, becoming less fluid and more like a gel at lower pH levels. So in addition to all the possible effects on protein or cell binding, this work shows that alterations in charge also appear to affect the intrinsic nature of a lipid bilayer.

Understanding these artificial, controlled lipid bilayer systems is essential before delving into the far more complex world of real membranes, and Dr. Zimmerman plans to extend these studies to probe bilayers made up of different lipid molecules that perhaps more closely resemble the real thing. Furthermore, lipid bilayers could have applications beyond being models for cell membranes. Because of how they change in response to the environment, they could be used as biological sensors to detect anything from changes in acidity to protein binding. Even a hundred years after their discovery, lipid bilayers look set to stay in the news.

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“Charging and structure of zwitterionic supported bilayer lipid membranes studied by streaming current measurements, fluorescence microscopy, and attenuated total reflection Fourier transform infrared spectroscopy,” Ralf Zimmermann, David Küttner, Lars Renner, Martin Kaufmann, Jan Zitzmann, Martin Müller, and Carsten Werner