pH EFFECTS ON LIPID BILAYER STRUCTURES: A COMPUTATIONAL STUDY

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The study of biological membranes has been for quite some time a challenging endeavour for researchers, who must exploit a variety of methodologies. In recent years, molecular modelling is probably the field of research that has more enthusiastically contributed with information at the atomic level. A detailed description of a lipid bilayer has to take in consideration all important factors that affect in some way the membrane behaviour and stability. pH is recognizably one of these factors even though it is usually forgotten due to the high complexity in terms of modelling.

The presence of negatively charged groups in the membrane gives rise to a surface electrostatic potential. The negative charges come mainly from anionic lipids that are prone to protonation under certain conditions. It is not so uncommon to find this fact neglected in the literature. Many studies, both experimental and theoretical, tend to "simplify" the problem by using in their membrane models neutral (usually zwiterionic) phospholipids. In the available modelling studies on anionic and negatively charged lipids, their negative charges are fixed. This is usually justified with the fact that the pK_a values are too low to allow for any (even partial) protonation. This approach can be compromised, to a certain level, if we take in consideration that biological membranes can share protons as "acid-anion" dimers and those anionic lipids thus trap and conduct protons along the headgroup domain of bilayers that contain such anionic lipids (1). The "acid-anion" mechanism suggests that some of these anionic lipids can retain protons at higher pH values, hence altering their structural properties.

In this work, we present a new method that allows the inclusion of pH in molecular dynamics simulations of lipid bilayers. The results on the application of the method to a lipid bilayer constituted by oleic acid will be presented.

1. T. H. Haines, *Proc. Nat. Acad. Sci. USA,* 80, 160 (1983)