Protons at the membrane water interface

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Proton diffusion along biological membranes is vitally important for cellular energetics. The diffusivity of the interfacial proton is almost as large as that in bulk water (1). Protons migrate without significant contributions from jumps between ionizable groups on the membrane surface (2). The presence of structured water at the boundary of a hydrophobic phase appears to be sufficient (3). This observation seems to be at odds with the substantial Gibbs activation energy barrier $\Delta G^{\ddagger}_{r}$ that must oppose proton release from the membrane in order for long range interfacial diffusion to occur. Here we determined $\Delta G^{\ddagger}_{r}$ from Arrhenius plots of (i) protons' surface diffusion constant and (ii) the rate coefficient for proton surface-to-bulk release. Therefore we photo-released protons from a membrane patch at different temperatures and monitored their arrival at a distant patch. The results disproved that quasi-equilibrium exists between protons in the near-membrane layers and in the aqueous bulk. Instead, non-equilibrium kinetics is consistent with this experiment. $\Delta G^{\ddagger}_{r}$ only contains a minor enthalpic contribution that roughly corresponds to the breakage of a single hydrogen bond. Conceivably, its dominating entropic component originates from the hydrogen bond orientation of surface water molecules that strongly favors proton movement towards the membrane, as indicated by *ab initio* molecular dynamics simulations. The simulations mirrored the large *in vitro* $\Delta G^{\ddagger}_{r}$, and they revealed a back-and-forth shuffling of the excess proton between the proximity of the phosphate groups and the interfacial water layers, which suggests high proton mobility. Taken together, this work reconciles the delayed proton surface-to-bulk release with protons weak bonding to surface water molecules.

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2. Springer A, Hagen V, Cherepanov DA, Antonenko YN, & Pohl P (2011) Protons migrate along interfacial water without significant contributions from jumps between ionizable groups on the membrane surface. *Proc Natl Acad Sci U S A* 108(35):14461-14466.
3. Zhang C, *et al.* (2012) Water at hydrophobic interfaces delays proton surface-to-bulk transfer and provides a pathway for lateral proton diffusion. *Proc Natl Acad Sci U S A* 109(25):9744-9749.