

Electronic Supplementary Information

Water channel formation and ion transport in linear and branched lipid bilayers

Shihu Wang and Ronald G. Larson
Department of Chemical Engineering, University of Michigan
2300 Hayward Street, Ann Arbor, Michigan 48109-2136

Theoretical Models for Critical Electric Field

Many different theoretical models have been put forward to explain electroporation since 1970s, including the hydrodynamic models, the elastic model, the viscohydroelastic model, the phase transition model, the aqueous pore formation model, and many others.^{1,2} Here we adapt the aqueous pore formation model to describe the formation of barrel stave and toroidal pores from our simulation. We have made the following assumptions.

- The interfacial tension between the hydrophobic lipid bilayer interior and water depends on the pore size. Glaser et. al.³ have derived the following equation to describe the interfacial tension $\sigma(R)$ as a function of the radius of hydrophobic pore R :

$$\sigma(R) = \sigma_0 I_1(R/\rho) / I_0(R/\rho) \quad (1)$$

where $I_n(x)$ are the modified Bessel functions of n -th order: $I_n(x) = i^{-n} J_n(ix)$; $\sigma_0 = 0.05$ N/m is the constant interfacial tension between a planar hydrophobic surface with water; and $\rho = 1$ nm is the characteristic length over which the properties of water undergo a gradual transition from the interface to the bulk.⁴

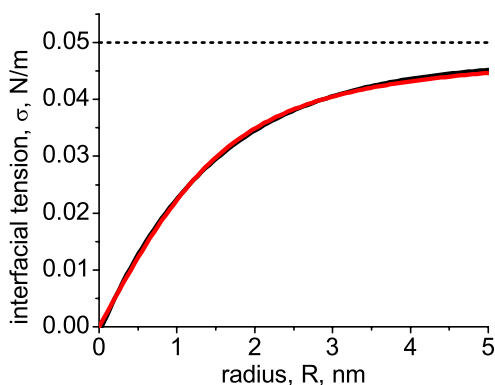


Fig. S1. Interfacial tension between hydrophobic pores and water as a function of pore radius. The red line is calculated using eq. (1) with $\sigma_0 = 0.05$ N/m and $\rho = 1$ nm. The black line is the fitting using eq. (2). The dashed line indicates $\sigma_0 = 0.05$ N/m.

The dependence of $\sigma(R)$ as a function R is shown in Fig. S1. As is seen, when the pore size is small, $\sigma(R \ll \rho) = R\sigma_0/2\rho$ while when pore size is large, $\sigma(R \gg \rho) = \sigma_0$. Since we need to differentiate this relationship in what follows, here we fit this result for $\sigma(R)$ vs. R (with $R \leq 10$ nm) by the following expression:

$$\sigma(R) = \left[0.04678 - 0.04795 \times \exp(-0.681R) \right] \times 10^{-9} \quad (2)$$

Please note 10^{-9} is used to convert the units of $\sigma(R)$ to N/nm and the units of R to nm. Eq. 2 gives an excellent fit to Eq. 1 as shown in Fig. S1.

The line tension for the DPPC membrane is taken to be $\gamma=3\times 10^{-11}$ N from a previous molecular dynamics simulation⁵ and is here assumed to be independent of pore size for simplicity.

- b. The capacitance of the water inside the lipid bilayer is given by

$$C_w = \epsilon_w \epsilon_0 \frac{\pi R^2}{h_0}$$

where h_0 is the thickness of the lipid bilayer; $\epsilon_0=8.854\times 10^{-12}$ F/m is the permittivity of vacuum; $\epsilon_w=68$ is the relative permittivity of the water at $T=310$ K. Note that the relative permittivity of water is extrapolated linearly from the dielectric constant of SPC/E of 71 at $T=298$ K and of 51 at $T=373$ K.⁶

- c. The applied electric field in GROMACS is E in units of V/nm.
d. Assuming the water pore is cylindrical, the number of water molecules inside the pore with a radius of R is given by:

$$N_{water} = \pi R^2 h \rho N_A / m$$

where h is the height of the pore ($h=1.6$ nm to be consistent with the cutoff of 0.8nm used in our simulations); Avogadro's number is $N_A=6.02\times 10^{23}$ mol⁻¹; the water density is $\rho=992$ kg/m⁻³; and the molar mass of water is $m=18$ g/mol. We plug in these numbers, rearrange the equation and derive the radius of the pore in terms of number of water molecules inside the pore as:

$$R = 0.0755 \sqrt{N_{water}} \quad (3)$$

- e. The thickness of DPPC lipids is 3.8 nm and that of DPhPC is 3.4 nm.

For a *barrel-stave pore*, the sum of the interfacial and electrostatic free energy needed to open the pore of radius R and fill it with water in the presence of an electric field is:

$$F_R = 2\pi R h_0 \sigma(R) - \frac{1}{2} C_w E^2 h_0^2 = 2\pi R h_0 \sigma(R) - \frac{\epsilon_w \epsilon_0}{2} \pi R^2 E^2 h_0 \quad (4)$$

Taking the derivative of F_R with respect to R, we have:

$$\frac{\partial F_R}{\partial R} = 2\pi h_0 \sigma(R) + 2\pi R h_0 \frac{\partial \sigma(R)}{\partial R} - \epsilon_w \epsilon_0 \pi R E^2 h_0 \quad (5)$$

Letting $\frac{\partial F_R}{\partial R} = 0$, to obtain the critical field for opening the pore, we have

$$2\sigma(R) + 2R \frac{\partial \sigma(R)}{\partial R} = \epsilon_w \epsilon_0 R E_C^2$$

We solve the equation above and obtain the critical electric field E_C to hold open a barrel-stave pore of radius R:

$$E_C = \sqrt{\frac{2\sigma(R) + 2R \frac{\partial \sigma(R)}{\partial R}}{\epsilon_w \epsilon_0 R}} \quad (6)$$

From eq. (2), we obtain

$$\frac{\partial\sigma(R)}{\partial R} = 0.03265 \times \exp(-0.681R) \times 10^{-9} \quad (7)$$

Plugging in the known values of ε_0 and ε_w , eq. (2), eq. (3) and eq. (7) into eq. (6), we get:

$$E_C = \sqrt{\frac{10.57 - 10.83 \times \exp(-0.0528 \times \sqrt{N_{water}}) + 0.572 \times \sqrt{N_{water}} \times \exp(-0.0528) \times \sqrt{N_{water}}}{5.27 \times \sqrt{N_{water}}}} \quad (8)$$

The free energy to open a *toroidal pore* of radius R and fill it with water in the presence of electric fields is:

$$F_R = 2\pi R\gamma - \frac{1}{2}C_w E^2 h_0^2 = 2\pi R\gamma - \frac{\varepsilon_w \varepsilon_0}{2} \pi R^2 E^2 h_0 \quad (9)$$

where γ is the line tension, as mentioned above. Again, taking the derivative of F_R with respect to R gives

$$\frac{\partial F_R}{\partial R} = 2\pi\gamma - \varepsilon_w \varepsilon_0 \pi R E^2 h_0 \quad (10)$$

and letting $\frac{\partial F_R}{\partial R} = 0$ we get:

$$2\gamma = \varepsilon_w \varepsilon_0 R E_C^2 h_0$$

Solving the above equations, we get the critical electric field E_C to hold open a toroidal pore of radius R:

$$E_C = \sqrt{\frac{2\gamma}{\varepsilon_w \varepsilon_0 R h_0}} \quad (11)$$

Plugging in the known values of ε_0 and ε_w , γ , h_0 , and eq. (3) into eq. (11), we get:

$$E_C = 0.347 \times N_{water}^{-0.25} \quad (12)$$

Eq. (8) and Eq. (12) are compared in the main text with the simulations results.

References

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