Evidence of conducting hydrophobic nanopores across membranes in response to an electric field

SUPPLEMENTARY INFORMATION

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Electrostatic Properties:

The electrostatic potential 3-dimensional maps $\Phi_j(\mathrm{r},\Delta V)$ for the simulations were generated using the PME method as implemented in NAMD.[1] In this scheme, the potential is obtained by solving the Poisson's equation:

$$\nabla^2 \Phi_j(\mathrm{r},\Delta V) = -4\pi \sum_i \rho_i(\mathrm{r})$$

where ρ_i is the point charge approximated by a spherical Gaussian of inverse width s and the sum running over all atoms in the system. We considered a grid of 1.5x1.5x1.5 $Å^3$ and s = 0.25 $Å^{-1}$.

The average of $\Phi_j(\mathrm{r},\Delta V)$ over x and y provides the electrostatic potential profile along the membrane normal. This one dimension profile may also be derived directly from the MD simulations as a double integral of the charge distribution of all atoms averaged over the membrane plans, $\rho(z)$, as $\phi(z) - \phi_0 = -\varepsilon_0^{-1} \iint \rho(z'')dz''dz'$. As a reference, φ(z) is set to zero in the upper electrolyte. Considering the present protocol, φ(z) show plateau values in the aqueous regions. The difference between the plateau values at the two electrolytes corresponds to the TM potential ΔV.

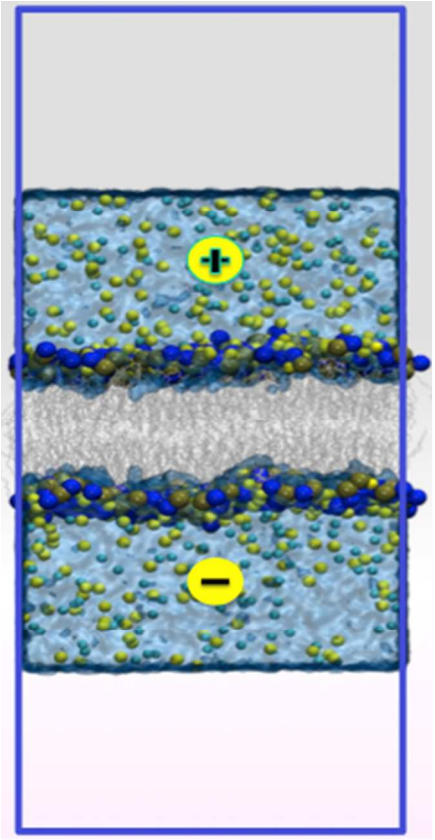

Figure S1: Molecular dynamics simulations setup of the system using the charge imbalance method. One single bilayer is surrounded by water baths (maintained at 250mM NaCl). The original cell is expanded in the direction perpendicular to the bilayer allowing for the creation of water air interfaces. ΔQ is imposed between the lower and upper bath.

Sim. n°	ΔV/Init. ΔV/Fin. [V]	Length [ns]	Pore Nature	Pore opening time [ns]	Pore Lifetime [ns]	Ion Exchange	Observation
1	3.1/3.1	10.1	NO				
2	3.5/3.5	16.0	NO				
3	3.5/3.5	25.0	NO				
4	4.0/0.61	27.0	Hydrophilic	7	Inf.	5 Na/1 Cl	Pore stable after 12 ns. 1 lipid flip-flop
5	3.7/0.5	27.0	Hydrophilic	Immediate	Inf.	7 Na	Restart from the end of sim. 4. Opening and conduction of the same pore
6	4.0/0.91	20.0	Hydrophobic	4	14	5 Na/1 Cl	
7	4.0/0.84	32.0	Hydrophobic	5	13	4 Na/1 Cl	2 lipid flip/flops
8	4.0/0.98	33.0 52.0	Pore defect	6	Inf.	4 Na/2 Cl	One lipid headgroup from lower leaflet is stabilized in transmembrane position. Pore still stable at the end of the simulation
9	4.0/0.54	33.0	Pore defect	3	Inf.	6 Na/1 Cl	One lipid headgroup from lower leaflet is stabilized in the membrane
10	4.0/0.86	32.0	Pore defect	5	18	6 Na/1 Cl	Several lipid headgroups from upper leaflet is stabilized in the membrane
11	4.0/0.43	34.0	Hydrophobic	5	12	7 Na/1 Cl	
12	4.0/0.15	38.0	Hydrophilic	16	Inf.	4 Na/1 Cl	
13	4.0/0.84	33.0	Hydrophobic	8	9	6 Na	1 lipid flip/flop Some lipids are stabilized in a TM position and return to the interface when the pore closes
14	4.45/0.84	22.0	Hydrophobic	1	13	4 Na/4 Cl	
15	4.45/0.80	7.5	Hydrophobic	1.5	4.5	5 Na/3 Cl	One lipid headgroup from lower leaflet is stabilized in transmembrane position
16	4.9/1.25	24.4	Hydrophobic	2	4	7 Na/1 Cl	One lipid headgroup from lower leaflet is stabilized in transmembrane position

Table S1: Characteristics of the pores forming in POPS bilayers following the application of high transmembrane voltages from MD simulations**.**

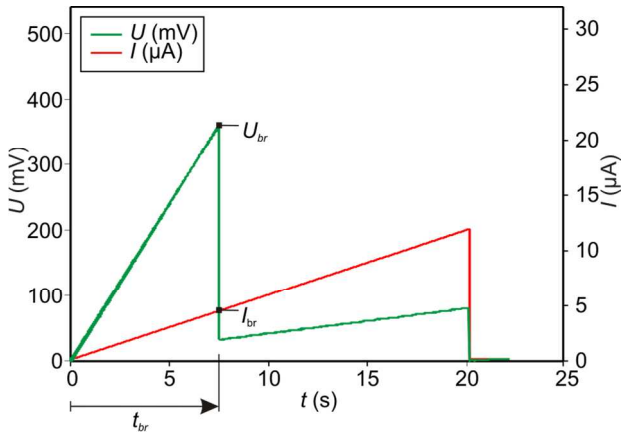

Figure S2. Breakdown voltage U_{br} determination by linear rising current signal.

k (μA/s)	N	U_{br} (mV)	I_{br} (μA)	t_{br} (s)
0.5	8	450 ± 152	9.26 ± 2.87	17.26 ±5.12
1	5	330 ± 44	7.00 ± 0.91	6.99 ± 0.90
4	6	451 ± 137	9.51 ± 2.85	2.37 ± 0.71
8	5	367 ± 36	7.72 ± 0.71	0.98 ± 0.07
10	5	334 ± 43	7.06 ± 0.84	0.61 ± 0.25
20	5	402 ± 85	8.48 ± 1.75	0.34 ± 0.08

Table S2. Breakdown voltage (U_{br}), breakdown current (I_{br}) and the lifetimes (t_{br}) for POPS planar lipid bilayers exposed to linear rising current signals of different slopes (k). Values given are mean ± standard deviation. Number of measurements N in each experimental group is given in the second column.

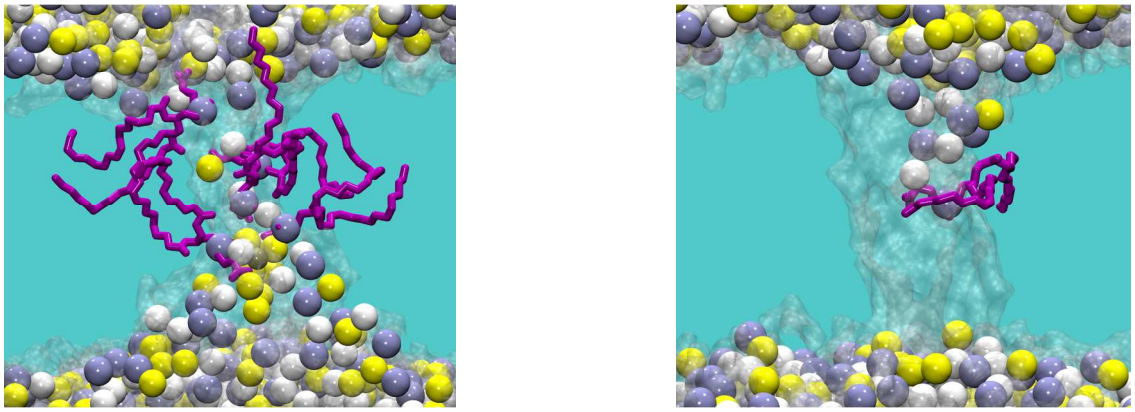

Figure S3: (Left) Typical hydrophilic pore (snapshot from simulation n° 4). (Right) Typical hydrophobic pore presenting a defect in the upper leaflet (snapshot from simulation n° 10).

Movie S1: Translocation of one lipid trough a hydrophobic pore (simulation n° 13).

Movie S2: Simultaneous translocation of two lipids trough a hydrophobic pore (simulation n° 7).

REFERENCES

(1) Aksimentiev, A.; Schulten, K. *Biophys. J.* **2005**, *88*, 3745–3761.