Biophysical Journal, Volume 96

Supporting Material

Determinants of Water Permeability Through Nanoscopic Hydrophilic Channels

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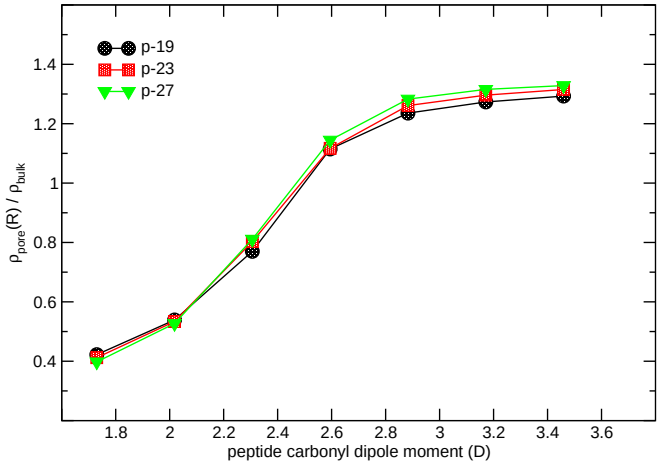
Supporting information - Determinants of water permeation. Portella and de Groot, *Biophys. J.*

1 Normalized pore water density for polyalanine channels



μ (D)	p-19	p-23	p-27
1.72971	0.42218	0.41208	0.39785
2.01799	0.53903	0.53374	0.52706
2.30628	0.76993	0.80303	0.81099
2.59456	1.11485	1.11698	1.14455
2.88285	1.23558	1.26110	1.28284
3.17114	1.27313	1.29627	1.31552
3.45942	1.29295	1.31529	1.32837

Table 1: Pore water density for the studied polyalanine model channels, normalized to the density of bulk water, as function of the peptide backbone carbonyl dipole moment.

2 Details for gramicidin and aquaporins simulations

We used full atomistic molecular dynamics simulations to obtain estimates for the water pore densities in natural occurring water channels, such as gramicidins and aquaporin channels. Here we report on the set up of the simulation systems.

For all simulated systems, interactions between all atoms were described by means of the OPLS all-atom force field (1, 2), and water molecules were described by the TIP4P model (3). The DMPC and POPC force field parameters were taken form Berger *et al.* (4). All simulations were performed using the GROMACS 3.3.1 simulation software (5, 6). Electrostatic interactions were calculated with the particle mesh Ewald method (7, 8). Short-range repulsive and attractive dispersion interactions were simultaneously described by a Lennard-Jones potential, using a cut-off length of 1.0 nm. The Settle (9) algorithm was used to constrain bond lengths and angles of water molecules, and LINCS (10) was used for all other bonds and angles, allowing a time step of 2 fs. The temperature in the simulations was kept constant by separately coupling the peptide, the lipid molecules, and the water molecules together with the ions to an external heat bath at 300 K (11) ($\tau = 0.1$ ps). The pressure in the simulations was kept constant by a weak anisotropic coupling ($\tau = 1$ ps) to a pressure bath of 1 atm. Average pore radii were computed using the program HOLE (12). Pore occupancies used to determine the reported water pore densities were extracted from the equilibrated trajectories.

For gramicidin channels, initial structures for gA in the helical dimer conformation and the linked MDg were taken from protein database entries 1MAG (13) and 1TKQ (14), respectively. After energy minimization in vacuum, the channels were embedded in a previously equilibrated dimyristoylphosphatidylcholine lipid bilayer containing 124 lipids, solvated by ∼3600 water molecules. To insert the channels in the DMPC bilayer, an initial cylindrical hole was made by removing two lipids in the central position from each layer. A molecular surface of the gA was used to define a region from which the lipid molecules should be expelled. A modified version of the GROMACS simulation package was used to expel the lipids by means of force normal to the molecular surface (15). After a cavity was formed in the bilayer, the peptide was finally incorporated and an energy minimization was carried out with the peptidic backbone kept fixed. The same process was repeated for midigramicidin.

After the insertion of the peptides in the membrane, the backbone of the peptides was kept fixed by means of position restraints to equilibrate the interface between the channel and the membrane. After 2 ns of molecular dynamics simulations, the position restraints were removed and the channels were allowed to freely diffuse within the membrane. The simulation time for gA amounted to 100 ns, and to 90 ns for MDg.

The simulation set-up for aquaporin water channels Aqp-1 and GlpF was done as previously reported in Hub *et al.* (16). The effective radii and the normalized water occupancy were extracted from 20ns equilibrium simulations.

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