**Computational Details**

The simulated outer membrane slabs consisted of monolayers of 72 LPS and 180 DPPE molecules. Six outer membrane slabs were simulated with different metals as counterion (Table I). Alkali ($Na^+$ and $K^+$), alkaline earth ($Mg^{2+}$, $Ca^{2+}$ and $Ba^{2+}$) and transition ($Zn^{2+}$) metals were chosen based on having either similar ionic radii and different charge states, or vice-versa. While hydration properties of force-field based metal ions may not always be quantitatively accurate, our choice of cations having similar ionic radii and different valences is expected to mitigate minor inaccuracies arising from the model. Atomic coordinates for the initial configurations were taken from a LPS membrane pre-equilibrated for 600-ns.[1] A multiple-step protocol was previously developed to construct and equilibrate LPS membranes.[2] The $Ca^{2+}$ couterions in the equilibrated system were replaced by the divalent and monovalent cations investigated in this study. The excess of monovalent cations was added by replacing water molecules. These monovalent cations rapidly migrated from the solvent to the negatively charged LPS membrane. Two simulations were performed for the LPS membrane containing $K^+$ ions starting from different configurations in order to reproduce the lamellar to non-lamellar transition. The atomic parameters for the carbohydrates and phospholipids are from Kirschner *et al*.[1] and for the cations parameters come from the AMBER99 force-field.[3] The systems were further equilibrated for 100 ns with production runs for additional 100 ns or longer. Periodic boundary conditions were applied to the systems based on a rectangular box containing the fully-hydrated LPS-DPPE bilayer in the *xy* plane and normal to the *z* axis. The TIP3P water model[4] was used as in our previous simulations of LPS membranes.[1, 2, 5-7] All bond lengths in the solute were kept constant using the LINCS[8, 9] algorithm, and the water geometry was maintained with the SETTLE[10] algorithm.

Simulations were performed in the isothermal-isobaric ensemble (NPT) with a time step of 2 fs, and in the absence of any external surface tension parameter. The center of mass motion was removed at every step. Temperatures of the solute and solvent were separately coupled to a Berendsen thermostat[11] at 300 K with a relaxation time of 0.4 ps. The pressure was maintained by weakly coupling[11] the particle coordinates and box dimensions in the $xy$ plane and along the $z$ axis separately to a pressure bath at 1.0 bar by means of semi-isotropic coordinate scaling with a relaxation time of 0.4 ps and a compressibility of 4.5 x $10^{-5}$ (kJ $mol^{-1}$ $nm^{-3})^{-1}$ as appropriate for water. Bond lengths between hydrogen and heavy atoms, and the geometry of the water molecules were constrained using the linear constraint solver algorithm with a tolerance of $10^{-4}$.[8] The generalized reaction field correction and a cutoff of 1.4 nm were used for both vdW and long-range electrostatic interactions with a permittivity dielectric constant of 66.[12, 13] In all cases, the pair list for short-range nonbonded and long-range electrostatic interactions were updated with a frequency of 5 timesteps. The present long-range scheme has been previously used for validation of the LPS force field parameters. In addition, exploratory simulations using Ewald summation approach overestimates the order parameter of hydrocarbon chains in LPS membranes. This preliminary finding is consistent with previous reports that Ewald summation methods may display non-negligible structural overstabilization.[14, 15] Furthermore, recent studies have shown that the effect of small changes in force field parameters on the structure and dynamics of a membrane bilayer is more significant than the treatment of the long-range electrostatic interactions using reaction field or Ewald summation. Nevertheless, a systematic comparison of the two approaches would be required to further characterize their influence on the dynamics of LPS membranes.[16] Configurations of the trajectory were recorded every 2 ps. Property analysis were

carried out for the last 70 ns of simulations, unless noted. The software package Gromacs v.4.04 and v.4.5.3 was used for all simulations and trajectory analysis.[17, 18] Coordinates and trajectories were visualized with the software VMD 1.86.[19]. Structural properties[20, 21] were analyzed and averages were calculated over 72/180 LPS/DPPE molecules. The area per acyl chain was calculated by dividing the box dimension in the x-y axis by the total number of lipid molecules in each leaflet of the bilayer. Mass partial densities of cations, phosphorus atoms, water oxygen, carboxylate and acyl chains were calculated along the axis normal to the bilayer. Radial distribution functions g(r) were calculated for the distance between cations and the oxygen atoms in the water molecules, the phosphorus atoms in the phosphate group, and the carbon atom in the carbonyl group. Values were averaged over the final 70 ns of simulations. Deuterium order parameters $S_{CD}$ for the acyl chains were calculated over the last 150-ns simulation period from the elements of the order parameter tensor. The order parameter elements is defined as $S_{CD} = < (3\cos^2\theta - 1)/2 >$ where $\theta$ is the angle between the molecular axis given by two consecutives carbon atoms and the lipid bilayer normal plane. In perfectly ordered lipid chains, the angle between the C-D bonds in the acyl chain and the bilayer normal is 90° with $S_{CD} = -0.5$. For $S_{CD} = 0$, the C-D bond is either permanently at an angle of 0° or random. $S_{CD}$ values are reported as $-S_{CD}$ or $|S_{CD}|$. All the others analyses were made with the GROMACS v.4.5.3 simulation package.[17]

**Movie of the lamellar to non-lamellar transition for K⁺-LPS membrane**

The movie shows the transition from lamellar to non-lamellar arrangement for the LPS membrane containing K⁺. The movie covers 250 ns after the equilibration of the system. The full system was replicated along the x-axis whereas water molecules and

cations were replicated also along the z-axis. This representation shows the water

molecules penetrating the membrane, followed by the K$^+$ ions.

## Cited References

1.      K. N. Kirschner, R. D. Lins, A. Maass and T. A. Soares, *J. Chem. Theory Comput.*, 2012, **28**, 14849–14854.
2.      T. A. Soares and T. P. Straatsma, *Mol. Simul.*, 2008, **34**, 295-307.
3.      J. Wang, P. Cieplak and P. A. Kollman, *J. Comput. Chem.*, 2000, **21**, 1049-1074.
4.      W. L. Jorgensen, J. Chandrasekhar, J. D. Madura, R. W. Impey and M. L. Klein, *J. Chem. Phys.*, 1983, **79**, 926-936.
5.      R. D. Lins and T. P. Straatsma, *Biophys. J.*, 2001, **81**, 1037-1046.
6.      T. A. Soares, R. D. Lins and T. P. Straatsma, *J. Braz. Chem. Soc.*, 2008, **19**, 312-320.
7.      T. P. Straatsma and T. A. Soares, *Proteins: Struct., Funct., Genet.*, 2009, **74**, 475-488.
8.      B. Hess, *J. Chem. Theory Comput.*, 2007, **4**, 116-122.
9.      B. Hess, H. Bekker, H. J. C. Berendsen and J. G. E. M. Fraaije, *J. Comput. Chem.*, 1997, **18**, 1463-1472.
10.     S. Miyamoto and P. A. Kollman, *J. Comput. Chem.*, 1992, **13**, 952-962.
11.     H. J. C. Berendsen, J. P. M. Postma, A. DiNola and J. R. Haak, *J. Chem. Phys.*, 1984, **81**, 3684-3691.
12.     I. G. Tironi, R. Sperb, P. E. Smith and W. F. van Gunsteren, *J. Chem. Phys.*, 1995, **102**, 5451-5459.
13.     J. W. Essex, *Mol. Simul.*, 1998, **20**, 159-178.
14.     R. D. Lins and U. Rothlisberger, *Journal of Chemical Theory and Computation*, 2006, **2**, 246-250.
15.     L. Monticelli and G. Colombo, *Theor. Chem. Acc.*, 2004, **112**, 145-157.
16.     D. Poger and A. E. Mark, *J. Chem. Theory Comput.*, 2012, **8**, 4807-4817.
17.     B. Hess, Kutzner, C., van der Spoel, D., Lindahl, E., *J. Chem. Theory Comput.*, 2008, **4**.
18.     D. van der Spoel, E. Lindahl, B. Hess, G. Groenhof, A. E. Mark and H. J. C. Berendsen, *J. Comput. Chem.*, 2005, **26**, 1701-1718.
19.     W. Humphrey, A. Dalke and K. Schulten, *J. Mol. Graphics*, 1996, **14**, 33-38.
20.     W. F. van Gunsteren, D. Bakowies, R. Baron, I. Chandrasekhar, M. Christen, X. Daura, P. Gee, D. P. Geerke, A. Glattli, P. H. Hunenberger, M. A. Kastenholz, C. Ostenbrink, M. Schenk, D. Trzesniak and N. F. A. van der Vegt, *Angewandt. Chem.-Intl Ed.*, 2006, **45**, 4064-4092.
21.     W. F. van Gunsteren, D. Bakowies, R. Burgi, I. Chandrasekhar, M. Christen, X. Daura, P. Gee, A. Glattli, T. Hansson, C. Oostenbrink, C. Peter, J. Pitera, L. Schuler, T. A. Soares and H. B. Yu, *Chimia*, 2001, **55**, 856-860.