Supplementary Material (ESI) for Chemical Communications

Supporting Information:

The effect of sodium chloride on poly-L-glutamate conformation

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SIMULATION METHODOLOGY.

The initial structure of poly-L-glutamate (PGA) was created using the Molden program[i] as an ideal α-helix with Ramachandran dihedral angles $(\Phi,\Psi)=(-60°,-45°)$ for all neighbour residuals. The positions of the side-chain residual atoms were chosen to provide the most compact conformation for given van der Waals radii of the atoms. This structure served as a reference structure for the Solvent Accessible Area (SAS) data shown on the Fig.1 in the main text of the paper. Another reference structure – an extended PP II helix were created with the same program providing the Ramachandran angles $(\Phi,\Psi)=(-80°,+155°)$ for all neighbour residuals. The positions of the side-chain residual atoms were chosen to provide the most extended conformation for given van der Waals radii of the atoms.

The molecule was placed in the centre of a cubic simulation cell contained 10 200 SPC/E water molecules for simulations of the solution. To create the 0.3 M sodium chloride solution we randomly substituted 154 water molecules in the simulation cell by 77 sodium chloride pairs.

For molecular dynamics simulations we used GROMACS 3.3 software[ii,iii] running on eight 2.7 Gz CPUs on a parallel cluster. The electrostatic interactions were treated with use of Particle-Mesh Ewald summation algorithm[iv] with 1.0 nm real-space cut-off. For integration of the equations of motion the standard Verlet algorithm was used with a time step of 2.5 fs. The systems were coupled with a heat bath of 300 K temperature using Berendsen thermostat. [v]

Firstly, for each system we constrained positions of the PGA backbone atoms with flexible harmonic constrains and performed a preliminary 1 ns molecular dynamics simulation run to equilibrate positions of water and ions. The harmonic constant for these constrains was equal to 1000 kJ/(mol*nm). Due to the flexibility of constrains and strong repulsive electrostatic interactions between the side chains, the final conformations of PGA after these preliminary simulations were less compact and more exposed to the solvent than the reference α-helix (see Fig. 1 in the main text). Then for each system we have run 200 ns productive molecular dynamics simulations at NVT conditions. The trajectories were saved each 2 ps. In both water and brine we assumed that all the PGA side-chain carboxylic acids were ionised, and the PGA N-terminus was also ionised. The non-zero charge of the simulation cell was neutralised by a homogeneous background charge density ("charge jelly") of the opposite sign and with the same magnitude when integrated across the simulation cell. [4]

To check whether or not this way of neutralisation affect the results on compact PGA conformation in the solution we performed an additional 200 ns of the brine solution where there were 77 sodiums and only 56 chlorides, so, the net charge of the system was equal zero. The results on comparison of the SAS values of these two simulations are presented on Fig. 1 here. As one can see from the figure, there is no significant difference between these two curves.

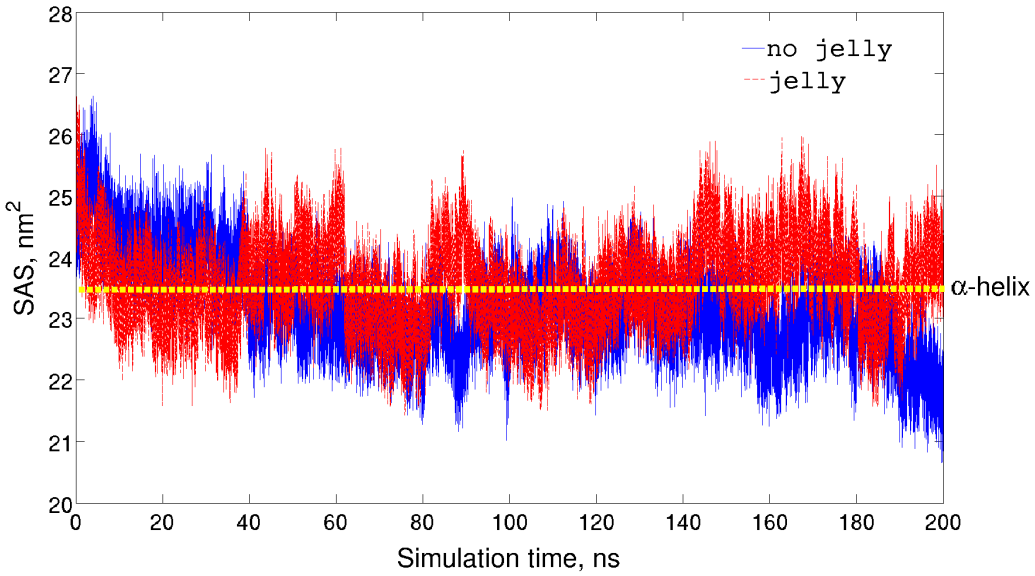

Figure S1. Solvent-accessible surface (SAS) area of PGA in 0.30 M NaCl solution against simulation time for two different ways of the simulation cell neutralisation. Solid line – the simulation cell was neutralised by different numbers of added ions (references as 'no jelly'). Dashed line - the simulation cell had the same numbers of sodiums and chlorides and has been neutralised by the electrostatic jelly (referenced as 'jelly'). The SAS values for an ideal α-helix shown by horizontal dashed line.

The molecular dynamics trajectories were analysed by the GROMACS analysis tool[iii] (calculations of Ramachandran angles and SAS values). The Matlab program [vi] was used for some additional statistical analysis and plotting the figures except of molecular graphics which were designed with the VMD molecular visualisation & analysis program.[vii]

[i] G. Schaftenaar, J. H. Noordik, *Journal of Computer-Aided Molecular Design* 2000, **14**, 123.
[ii] H. J. C. Berendsen, D. van der Spoel, R. van Drunen, *Comput. Phys. Commun.* 1995, **91**, 43-56.
[iii] E. Lindahl, B. Hess, D. van der Spoel, *Journal of Molecular Modeling* 2001, **7**, 306-317.
[iv] T. Darden, D. York, L. Pedersen, *J. Chem. Phys.* 1993, **98**, 10089.
[v] H. J. C. Berendsen, J. P. M. Postma, W. F. van Gunsteren, A. Dinola, J. R. Haak, *J. Chem. Phys.* 1984, **81**, 3684-3690.
[vi] http://www.mathworks.com/
[vii] W. Humphrey, A. Dalke, K.Schulten, *Journal of Molecular Graphics* 1996, **14**, 33-38.