Ion counting from explicit solvent simulations and 3D-RISM

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Convergence of preferential interaction parameters

Preferential interaction parameters (PIPs) can be calculated using KB integrals, as done for 3D-RISM and NLPB, or using the two-partition method, which is convenient for MD. The convergence of both methods have a distance dependence that can be examined using cRDFs and applying the KB approach. The convergence of Eq 3 as a function of radial distance without long-range correction is shown in Figure S1. All three simulation methods have a similarly long-ranged g(r) and a discernible non-zero slope is still evident in $\Gamma^{+}(r)$ at r = 40Å. This gives an indication of both the extent of the solvation box required to achieve the desired precision, as used for MD and NLPB, or the need for a long-range correction, such as 17 used for 3D-RISM.

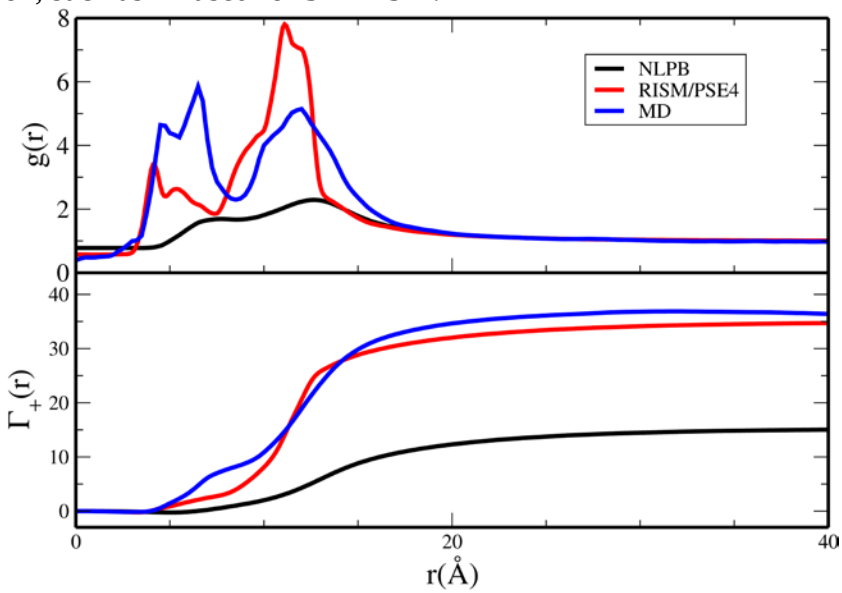

Figure S1. Cylindrical radial distribution function, g(r), (top) and its corresponding preferential interaction parameter, $\Gamma^{+}(r) = 2\pi h \int_0^r (g(r)-1) r' dr'$ (bottom) from MD, 3D-RISM and NLPB. The KB integrals reach their limiting values for r~40Å.

Numerical Precision of 3D-RISM Calculations

Numerical precision of 3D-RISM calculations depend on the grid spacing, residual tolerance and solvation box size. For a given, solvation box, a grid spacing of 0.5 Å and residual tolerance of 10-6 provide PIP precisions lower than 10-3 ions. The buffer region between the solute and nearest box edge, which determines the size of the solvent box, is then the only remaining determinate of numerical precision. The extent of the solvent buffer required to achieve the desired precision varies with salt concentration. Figure S2 shows the sodium PIP dependence on buffer size at 0.1, 0.01 and 0.005 M NaCl for 3D-RISM-KH. Differences are calculated relative to the largest buffer size tested at each concentration. The closure approximation used was found to have negligible effect on the precision. Note that the PIP for sodium is always over-estimated as the box size is reduced.

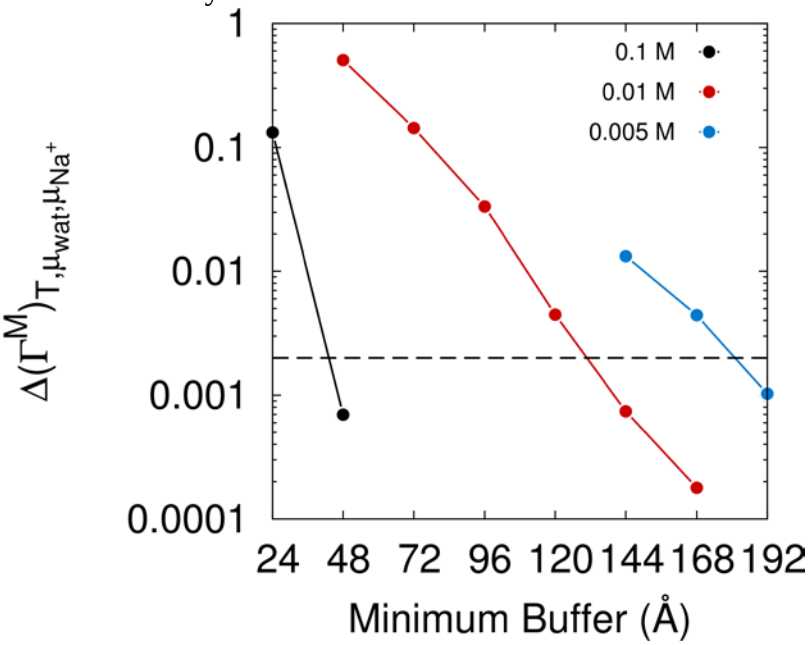

Figure S2. Difference in PIP for 3D-RISM-KH as a function of solvent box buffer size. Differences are calculated relative to references buffer sizes of 70 Å (0.1M NaCl), 192 Å (0.01M NaCl) and 216 Å (0.005M). The horizontal dashed line indicates a difference of 0.002 ions from the reference calculation.

Impact of closure relation on ion counting estimates from 3D-RISM

The PSE-4 closure relation used in the main manuscript is part of the partial series expansion of order-*n* (PSE-*n*) family of closures(1) that approximate the hypernetted-chain equation (HNC)(2) by including *n*-terms of a Taylor expansion. PSE-4 was the highest-order closure that could be converged in this study. In Figure S3 we compare the ion counting concentration profiles for lower order closures :KH or PSE-1, PSE-2 and PSE3. Irrespective of the salt concentration, the preferential interaction parameter increase with the number of terms included in the expansion. This behavior is consistent with attractive interaction being enhanced as the PSE-n closure approximation approaches the HNC.

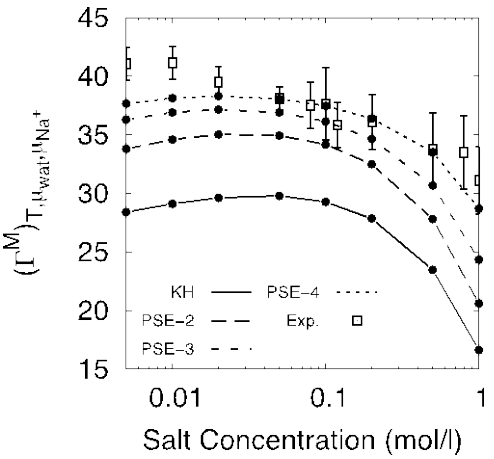

Figure S3: Closure dependence of sodium preferential interaction paramters for 3D-RISM calculations. Experimental results from (3).

Force Field	Duration (ns)	$M^{(2)}_{NaCl}$	$M^{(2)}_{H2O}$	M_{NaCl}
0.7 NaCl				
JC:TIP3P	100	0.7298	53.4867	0.7109
JC:TIP4P-Ew	150	0.7288	53.8447	0.7157
JC:SPC/E	120	0.7452	54.8205	0.7287
0.2 NaCl				
JC:TIP3P	100	0.1829	53.8635	0.1731
JC:TIP4P-Ew	100	0.1830	54.0004	0.1752
JC:SPC/E	120	0.1842	53.9492	0.1739

Table S1. Summary of the explicit solvent simulations and key properties. $M^{(2)}_{NaCl}$ and $M^{(2)}_{H2O}$ are the molarities of sodium chloride and water in the bulk; see text for discussion on determining the properties of the bulk. M_{NaCl} is the salt molarity if calculated by dividing the number of moles with the total volume of the cell.

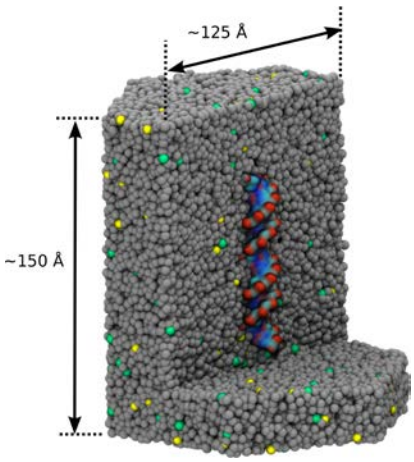

Figure S4 Section through the molecular dynamics simulations box. A single B-DNA molecule (shown in surface representation) is placed in a hexagonal prism periodic box that extends ~60 Å in the direction perpendicular on the DNA main axis and 30 Å in each direction along the main axis from the DNA. Water is represented as gray spheres, sodium ions as yellow spheres, chloride ions as green spheres.

Salt Concentration (M)	Requested Buffer (Å)	Actual Buffer (Å)
0.005	192	192.696 x 214.708 x 227.678
0.01-0.05	144	147.696 x 169.708 x 173.678
0.1-5	48	50.196 x 49.708 x 53.678

Table S2. Summary of 3D-RISM calculations. The requested buffer sizes reported here were automatically increased the actual buffer size to evenly distribute memory for parallel calculations and satisfy FFT grid size constraints. To maximize the parallel efficiency of the 3D-RISM code, the DNA molecule was oriented along the z-axis. However, due to the load balancing requirements of the parallel implementation, the buffer region was typically larger than requested by a small amount as it was automatically increased to the minimum buffer size that gave an even distribution of memory among parallel processes and ensure the grid dimensions were multiples of small prime numbers for the FFT calculation. The size of the buffer region required was found to be independent of the closure used and only depended on ion concentrations.

Salt Concentration (M)	Grid Dimensions (Å)	Grid Spacing (Å)
0.005-0.05	514 x 514 x 610	2
0.1-0.5	257 x 257 x 353	1
1-5	129 x 129 x 225	1

Table S3. Summary of NLPB calculations.

$M^{(2)}_{NaCl}$	0.18-0.2M		0.7-0.8M	
	$\Gamma^{(M)}_{Na^+}$	$\Gamma^{(M)}_{Cl^-}$	$\Gamma^{(M)}_{Na^+}$	$\Gamma^{(M)}_{Cl^-}$
Experiment	36.1(3.1)	-11.8(2.3)	33.5(3.7)	-15.5(3.1)
MD JC:TIP3P	33.2(0.6)	-12.8(0.6)	21.0(1.1)	-25.0(1.1)
MD JC:SPC/E	36.1(0.5)	-9.9(0.5)	25.3(1.1)	-20.7(1.1)
MD JC:TIP4P	36.0(0.6)	-10.0(0.6)	29.3(0.7)	-16.7(0.7)
3D-RISM JC:SPC/E	36.6	-9.4	31.2	-14.8
NLPB	31.7	-14.3	19.2	-26.8

Table S4. Estimation of preferential interaction parameters from MD, 3D-RISM and NLPB and comparison with experiment.

1. Kast, S.M., and T. Kloss. 2008. Closed-form expressions of the chemical potential for integral equation closures with certain bridge functions. J. Chem. Phys. 129: 236101.

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