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Macromolecular crowding and the importance of proper hydration for the structure and dynamics of protein solutions

Supplementary Information

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Interaction matrix

		H_2O #1	H_2O #2	H_2O #3	UBQ #1	UBQ #2	UBQ #3
H_2O #1		$U_{elec\,1,1}$ + $U_{SD\,1,1}$	$U_{elec\,1,2}$ + $U_{SD\,1,2}$	$U_{elec\,1,3}$ + $U_{SD\,1,3}$	$U_{elec\,1,4}$ + $U_{SD\,1,4}\,\lambda$	$U_{elec\,1,5}$ + $U_{SD\,1,5}\,\lambda$	$U_{elec\,1,6}$ + $U_{SD\,1,6}\,\lambda$
H_2O #2		$U_{elec\,2,1}$ + $U_{SD\,2,1}$	$U_{elec\,2,2}$ + $U_{SD\,2,2}$	$U_{elec\,2,3}$ + $U_{SD\,2,3}$	$U_{elec\,2,4}$ + $U_{SD\,2,4}\,\lambda$	$U_{elec\,2,5}$ + $U_{SD\,2,5}\,\lambda$	$U_{elec\,2,6}$ + $U_{SD\,2,6}\,\lambda$
H_2O #3		$U_{elec\,3,1}$ + $U_{SD\,3,1}$	$U_{elec\,3,2}$ + $U_{SD\,3,2}$	$U_{elec\,3,3}$ + $U_{SD\,3,3}$	$U_{elec\,3,4}$ + $U_{SD\,3,4}\,\lambda$	$U_{elec\,3,5}$ + $U_{SD\,3,5}\,\lambda$	$U_{elec\,3,6}$ + $U_{SD\,3,6}\,\lambda$
UBQ #1		$U_{elec\,4,1}$ + $U_{SD\,4,1}\,\lambda$	$U_{elec\,4,2}$ + $U_{SD\,4,2}\,\lambda$	$U_{elec\,4,3}$ + $U_{SD\,4,3}\,\lambda$	$U_{elec\,4,4}$ + $U_{SD\,4,4}$	$U_{elec\,4,5}$ + $U_{SD\,4,5}$	$U_{elec\,4,6}$ + $U_{SD\,4,6}$
UBQ #2		$U_{elec\,5,1}$ + $U_{SD\,5,1}\,\lambda$	$U_{elec\,5,2}$ + $U_{SD\,5,2}\,\lambda$	$U_{elec\,5,3}$ + $U_{SD\,5,3}\,\lambda$	$U_{elec\,5,4}$ + $U_{SD\,5,4}$	$U_{elec\,5,5}$ + $U_{SD\,5,5}$	$U_{elec\,5,6}$ + $U_{SD\,5,6}$
UBQ #3		$U_{elec\,6,1}$ + $U_{SD\,6,1}\,\lambda$	$U_{elec\,6,2}$ + $U_{SD\,6,2}\,\lambda$	$U_{elec\,6,3}$ + $U_{SD\,6,3}\,\lambda$	$U_{elec\,6,4}$ + $U_{SD\,6,4}$	$U_{elec\,6,5}$ + $U_{SD\,6,5}$	$U_{elec\,6,6}$ + $U_{SD\,6,6}$

Interaction matrix of a symbolic system composed of three water molecules and three UBQ molecules. Each box stands for a matrix entry and contains the shape/dispersion interaction plus the electrostatic interaction between the specified pair of molecules. Diagonal entries contain intramolecular interactions. Pairs of the same molecular species are organized in blocks. The font colour marks water-water (blue), protein-protein (red) and water-protein (green) interactions. The sum over all entries gives the system's total non-bonded potential energy.
It is important to note that λ scaling is applied to the green block only.

Implementation of the λ-scaling

This section lists the non-bonding parameters adjusted by λ-scaling. In CHARMM, shape/dispersion interactions are modelled as Lennard-Jones potentials

$$U_{\mathrm{SD}} = \sum_{i=1}^{N-1} \sum_{j=i+1}^{N} 4\epsilon_{ij}\{(\frac{\sigma_{ij}}{\mid \vec{r}_i - \vec{r}_j \mid})^{12} - (\frac{\sigma_{ij}}{\mid \vec{r}_i - \vec{r}_j \mid})^{6}\} \tag{1}$$

with pair-wise distance parameter σ_{ij} and potential well depth ϵ_{ij}. The force fields, however, contain atomic parameters σ_i and ϵ_i which are converted to the pair interaction parameters by the Lorenz-Berthelot relations:

$$\sigma_{ij} = \frac{1}{2}(\sigma_i + \sigma_j) \tag{2}$$

$$\epsilon_{ij} = (\epsilon_i \epsilon_j)^{\frac{1}{2}} \tag{3}$$

λ-scaling, as it is used both in Bests and Mittals preceeding study[1] and this one linearly alters the pair-wise potential well depth ϵ_{ij}:

$$\epsilon_{ij}^{\text{scaled}} = \lambda \epsilon_{ij} \tag{4}$$

The table below summarizes the scaling of the atom type force field parameters by $\lambda = 1.1$, imposed on the force field *post festum* via NBFIX command. The first column contains the SPC/E oxygen, the only atom in this water model exerting shape/dispersion interaction. The second column contains the CHARMM36[2–5] atom types used to model proteins such as UBQ.

atom type 1	**atom type 2**	ϵ_{ij}	σ_{ij}
OT	C	-0.142283	3.777
OT	CA	-0.113503	3.7694
OT	CC	-0.113503	3.777
OT	CD	-0.113503	3.777
OT	CE1	-0.11187	3.867
OT	CE2	-0.108529	3.857
OT	CP1	-0.06067	4.052
OT	CP2	-0.100609	3.952
OT	CP3	-0.100609	3.952
OT	CPH1	-0.095927	3.577
OT	CPH2	-0.095927	3.577
OT	CS	-0.142283	3.977
OT	CPT	-0.134982	3.637
OT	CY	-0.115909	3.767
OT	CAI	-0.115909	3.767
OT	CT	-0.06067	4.052
OT	CT1	-0.076742	3.777
OT	CT2	-0.10152	3.787
OT	CT2A	-0.10152	3.787
OT	CT3	-0.119813	3.817
OT	H	-0.09201	2.0015
OT	HA	-0.063631	3.097
OT	HB1	-0.063631	3.097
OT	HB2	-0.071785	3.117
OT	HE1	-0.075533	3.027
OT	HE2	-0.069174	3.037
OT	HB	-0.063631	3.097
OT	HC	-0.09201	2.0015
OT	HP	-0.074305	3.1352
OT	HR1	-0.09201	2.677
OT	HR2	-0.09201	2.477
OT	HR3	-0.037888	3.245
OT	HS	-0.135662	2.227
OT	HA1	-0.091005	3.117
OT	HA2	-0.079104	3.117
OT	HA3	-0.06646	3.117
OT	N	-0.191855	3.627
OT	NC2	-0.191855	3.627
OT	NH1	-0.191855	3.627
OT	NH2	-0.191855	3.627
OT	NH3	-0.191855	3.627
OT	NP	-0.191855	3.627
OT	NR1	-0.191855	3.627
OT	NR2	-0.191855	3.627
OT	NR3	-0.191855	3.627
OT	NY	-0.191855	3.627
OT	O	-0.14861	3.477

OT	OB	-0.14861	3.477
OT	OC	-0.14861	3.477
OT	OH1	-0.16731	3.547
OT	OS	-0.16731	3.547
OT	S	-0.287782	3.777
OT	SM	-0.264453	3.752
OT	SS	-0.294108	3.97

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