# Towards capturing cellular complexity: Combining encapsulation and macromolecular crowding in a reverse micelle

## **Supplementary Information**

Philipp Honegger and Othmar Steinhauser

### **1** Convergence of the *NVT* simulation

The starting geometries of the simulation boxes were first energetically relaxed using the steepest-descent gradient method. Following this, the initial equilibrations of the systems were performed as NpT ensembles of 4 ns until the length of the cubic simulation box converged. This is necessary to know the equilibrium density of the simulation box.

This equilibration was followed up with the trajectory production as NVT ensemble, altogether covering  $300ns \times 5$  replica  $\times 3$  scaling levels = 4.5 microseconds. However, large and slow molecules such as ubiquitin and complicated systems such as RMs are known to be plagued by long equilibration processes, where the system needs to dissipate surplus energy to reach its equilibrium. For instance, the protein seeks its optimal conformation and its preferred location within the reverse micelle which takes dozens of nanoseconds.<sup>1</sup>. Since all subsequent analyses of the trajectory require equilibrium conditions, the system was controlled for convergence on the basis of a series of properties, *e.g.* radial distribution functions (RDFs) shown below. The water-protein curves explain why we decided to discard the first 200 ns of each replicum and use the last 100 ns only.



#### 2 $\lambda$ -scaling

Bests and Mittals<sup>2</sup>  $\lambda$ -scaling approach consists of modifying the Lennard-Jones potential  $U_{ij}$  between two atoms i and j

$$U_{ij}(r_{ij}) = 4\epsilon_{ij} \left\{ \left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^6 \right\}$$
(1)

with  $r_{ij}$  as the interatomic distance,  $\sigma_{ij}$  as the repulsive/attractive switching distance and  $\epsilon_{ij}$  as the potential well depth. In  $\lambda$ -scaling, the potential well depth  $\epsilon_{ij}$  is then adjusted by multiplication:

$$\epsilon_{ij}^{\text{scaled}} = \lambda \epsilon_{ij} \tag{2}$$

To date, there is no extensive screening study optimizing  $\lambda$ , but Best and Mittal found that  $\lambda = 1.1$  considerably improves protein-protein behaviour, hence we used this value in this study as well.

Technically, CHARMM does not store pair Lennard Jones parameters  $\sigma_{ij}$  and  $\epsilon_{ij}$ , but single-particle parameters  $\sigma_i$  and  $\epsilon_i$  designated for each atom type individually. Upon force field construction, pair-wise Lennard Jones parameters  $\sigma_{ij}$  and  $\epsilon_{ij}$  are obtained via the Lorenz-Berthelot relations forming the arithmetic and the geometric means respectively:

$$\sigma_{ij} = \frac{1}{2}(\sigma_i + \sigma_j) \tag{3}$$

$$\epsilon_{ii} = (\epsilon_i \cdot \epsilon_j)^{\frac{1}{2}} \tag{4}$$

The parameter  $\epsilon_{ij}$  is then simply modified *post festum* using the NBFIX command to overwrite the nonbonded parameters evaluated by CHARMM based on the CHARMM36 force field.<sup>3-6</sup> The two tables below list the NBFIX commands employed for the half-scaled ( $\lambda_{UBQ} = 1.1$ ,  $\lambda_{surfactant} = 1.0$ ) and the fully scaled ( $\lambda_{UBQ} = 1.1$ ,  $\lambda_{surfactant} = 1.1$ ) system, respectively.

atom type 1	atom type 2	$\epsilon$	σ
ОТ	С	-0.142283	3.777
OT	CA	-0.113503	3.7694
OT	CC	-0.113503	3.777
ОТ	CD	-0.113503	3.777
ОТ	CE1	-0.11187	3.867
ОТ	CE2	-0.108529	3.857
ОТ	CP1	-0.06067	4.052
OT	CP2	-0.100609	3.952
ОТ	CP3	-0.100609	3.952
ОТ	CPH1	-0.095927	3.577
ОТ	CPH2	-0.095927	3.577
ОТ	CS	-0.142283	3.977
ОТ	CPT	-0.134982	3.637
ОТ	CY	-0.115909	3.767
ОТ	CAI	-0.115909	3.767
ОТ	CT	-0.06067	4.052
ОТ	CT1	-0.076742	3.777
OT	CT2	-0.10152	3.787
OT	CT2A	-0.10152	3.787
OT	CT3	-0.119813	3.817
OT	Н	-0.09201	2.0015
OT	HA	-0.063631	3.097
OT	HB1	-0.063631	3.097
ОТ	HB2	-0.071785	3.117
OT	HE1	-0.075533	3.027

NBFIX commands for the half-scaled system

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	Ν	-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	0	-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

NBFIX commands for the fully scaled syste
---

atom type 1 atom type 2	$\epsilon$	σ
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
ОТ Н	-0.09201	2.0015
OT HA	-0.063631	3.097
OT HB1	-0.063631	3.097
OT HB2	-0.071785	3.117

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 HA1 -0.091005 3.117   OT HA3 -0.06646 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 NP -0.191855 3.627   OT NP -0.191855 3.627   OT NP -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 <th>OT</th> <th>HE1</th> <th>-0.075533</th> <th>3.027</th>	OT	HE1	-0.075533	3.027
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 HA1 -0.091005 3.117   OT HA2 -0.079104 3.117   OT HA2 -0.079104 3.117   OT HA2 -0.079104 3.117   OT N -0.191855 3.627   OT NC2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NP -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR3 -0.191855	OT	HE2	-0.069174	3.037
OT HC -0.07201 2.0015   OT HP -0.074305 3.1352   OT HR1 -0.09201 2.677   OT HR2 -0.09201 2.477   OT HR3 -0.03788 3.245   OT HS -0.135662 2.227   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 NH2 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT OR -0.14861 3.477   OT OS -0.14861	OT	HB	-0.063631	3.097
OT HP -0.074305 3.1352   OT HR1 -0.09201 2.677   OT HR2 -0.09201 2.477   OT HR3 -0.035662 2.227   OT HA1 -0.091005 3.117   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 NR1 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NH3 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.1918	OT	HC	-0.09201	2.0015
OT HR1 -0.09201 2.677   OT HR2 -0.09201 2.477   OT HR3 -0.037888 3.245   OT HA1 -0.09105 3.117   OT HA2 -0.079104 3.117   OT HA2 -0.079104 3.117   OT HA2 -0.0191855 3.627   OT N -0.191855 3.627   OT NC2 -0.191855 3.627   OT NH2 -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 NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT OB -0.14861 3.477   OT OB -0.14861 </td <td>OT</td> <td>HP</td> <td>-0.074305</td> <td>3.1352</td>	OT	HP	-0.074305	3.1352
OT HR2 -0.09201 2.477   OT HR3 -0.037886 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 NH2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT OR -0.14861 3.477   OT OB -0.14861 3.477   OT OB -0.14861 <td>OT</td> <td>HR1</td> <td>-0.09201</td> <td>2.677</td>	OT	HR1	-0.09201	2.677
OT HR3 -0.037888 3.245   OT HA -0.135662 2.227   OT HA1 -0.091005 3.117   OT HA2 -0.079104 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 NH2 -0.191855 3.627   OT NH3 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT OR -0.14861 3.477   OT OB -0.14861 3.477   OT OS -0.14861 <td>OT</td> <td>HR2</td> <td>-0.09201</td> <td>2.477</td>	OT	HR2	-0.09201	2.477
OT HS -0.135662 2.227   OT HA1 -0.09105 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 NH1 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OG -0.14861	OT	HR3	-0.037888	3.245
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 NH2 -0.191855 3.627   OT NH2 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OS -0.284782<	OT	HS	-0.135662	2.227
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 NH3 -0.191855 3.627   OT NH3 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OS -0.16731 3.5447   OT SS -0.284782 <td>OT</td> <td>HA1</td> <td>-0.091005</td> <td>3.117</td>	OT	HA1	-0.091005	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 NH2 -0.191855 3.627   OT NH3 -0.191855 3.627   OT NP -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT OC -0.14861 3.477   OT OB -0.14861 3.477   OT OS -0.16731 3.547   OT S -0.294108 3.972   OT CG202 -0.134298 <td>OT</td> <td>HA2</td> <td>-0.079104</td> <td>3.117</td>	OT	HA2	-0.079104	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 NH2 -0.191855 3.627   OT NH3 -0.191855 3.627   OT NP -0.191855 3.627   OT NP -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT O 0 -0.14861 3.477   OT OB -0.14861 3.477   OT OS -0.16731 3.547   OT OS -0.16731 3.547   OT S -0.287782 3.772   OT CG202	OT	HA3	-0.06646	3.117
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 NP -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NR3 -0.191855 3.627   OT O -0.14861 3.477   OT OC -0.14861 3.477   OT OS -0.16731 3.547   OT S -0.287782 3.777   OT SS -0.287782 3.777   OT CG321 -0.10152 3.787   OT CG334 -0.19374 <td>OT</td> <td>Ν</td> <td>-0.191855</td> <td>3.627</td>	OT	Ν	-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 NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -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 OS -0.16731 3.547   OT S -0.287782 3.777   OT S -0.287782 3.777   OT CG321 -0.10152 3.787   OT CG324 -0.134298 3.477   OT CG334 -0.01951 <td>OT</td> <td>NC2</td> <td>-0.191855</td> <td>3.627</td>	OT	NC2	-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 NR1 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR2 -0.191855 3.627   OT NR3 -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 OS -0.16731 3.547   OT S -0.287782 3.772   OT SM -0.264453 3.752   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG311 -0.076742 </td <td>OT</td> <td>NH1</td> <td>-0.191855</td> <td>3.627</td>	OT	NH1	-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 NR3 -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 OS -0.16731 3.547   OT OS -0.16731 3.547   OT S -0.287782 3.772   OT SM -0.264453 3.752   OT CG202 -0.134374 4.0612   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374 <td>OT</td> <td>NH2</td> <td>-0.191855</td> <td>3.627</td>	OT	NH2	-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 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 OC -0.14861 3.477   OT OS -0.16731 3.547   OT OS -0.16731 3.547   OT OS -0.16731 3.547   OT SM -0.287782 3.777   OT SS -0.294108 3.97   OT CG202 -0.134298 3.477   OT CG321 -0.10152 3.787   OT CG321 -0.10152 3.787   OT CH3 -0.190531	OT	NH3	-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 NY -0.191855 3.627   OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OS -0.16731 3.547   OT S -0.287782 3.777   OT SM -0.264453 3.752   OT SS -0.294108 3.97   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.787   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374	OT	NP	-0.191855	3.627
NR2 -0.191855 3.627   OT NR3 -0.191855 3.627   OT NY -0.191855 3.627   OT OY -0.191855 3.627   OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OS -0.16731 3.547   OT S -0.287782 3.777   OT S -0.287782 3.752   OT SS -0.294108 3.97   OT CG302 -0.134298 3.477   OT CG321 -0.10152 3.787   OT CG334 -0.19531 3.8805   OT CH3 -0.19531 3.8805   OT CH3 -0.19531 3.8805	OT	NR1	-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 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 3.952   OT CG2O2 -0.134298 3.477   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG321 -0.134374 4.0612   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT HGA1 -0.09201 2.0015   OT HGA1 -0.08	OT	NR2	-0.191855	3.627
NY -0.191855 3.627   OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OC -0.14861 3.477   OT OC -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   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG324 -0.119043 3.992   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT HGA1 -0.09201 2.0015   OT HGP5 -0.09201 2.0015<	OT	NR3	-0.191855	3.627
OT O -0.14861 3.477   OT OB -0.14861 3.477   OT OC -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   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT HGA1 -0.09201 2.0015   OT HGP1 -0.09201 2.0015   OT HGP5 -0.09201 2.477   OT MG3PO -0.1918	OT	NY	-0.191855	3.627
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   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG334 -0.19433 3.992   OT CH3 -0.19531 3.8805   OT HGA1 -0.091005 3.117   OT HGA1 -0.09201 2.0015   OT HGP5 -0.09201 2.477   OT HGP5 -0.09201 2.477   OT HGP5 -0.09201 2.477   OT HGP5 -0.09201 2.477   OT HGP5 -0.09	OT	0	-0.14861	3.477
OT OC -0.14861 3.477   OT OH1 -0.16731 3.547   OT OS -0.16731 3.547   OT OS -0.16731 3.547   OT S -0.287782 3.777   OT SM -0.26453 3.752   OT SS -0.294108 3.97   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT HGA1 -0.091005 3.117   OT HGA2 -0.080259 3.117   OT HGP1 -0.09201 2.0015   OT HGP5 -0.09201 2.477   OT NG3P0 -0.191855 3.627   OT OG302	OT	OB	-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   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.777   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT CH3 -0.19531 3.8805   OT HGA1 -0.091005 3.117   OT HGP1 -0.080259 3.117   OT HGP1 -0.09201 2.477   OT NG3P0 -0.191855 3.627   OT OG2D1 -0.14861 3.477   OT OG302 -0.135662 3.427   OT OG311	OT	OC	-0.14861	3.477
OT OS -0.16731 3.547   OT S -0.287782 3.777   OT SM -0.264453 3.752   OT SS -0.294108 3.97   OT CG202 -0.134298 3.477   OT CG311 -0.076742 3.787   OT CG321 -0.10152 3.787   OT CG334 -0.119043 3.992   OT CH2 -0.134374 4.0612   OT CH3 -0.19531 3.8805   OT CH3 -0.19531 3.8805   OT HGA1 -0.091005 3.117   OT HGA2 -0.080259 3.117   OT HGP5 -0.09201 2.0015   OT HGP5 -0.09201 2.477   OT OG302 -0.138662 3.427   OT OG302 -0.1386027 3.542   OT OG311 -0.188027 3.542	OT	OH1	-0.16731	3.547
OTS-0.2877823.777OTSM-0.2644533.752OTSS-0.2941083.97OTCG202-0.1342983.477OTCG311-0.0767423.777OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGP1-0.092012.0015OTHGP1-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG311-0.1880273.542OTOG312-0.148613.527	OT	OS	-0.16731	3.547
OTSM-0.2644533.752OTSS-0.2941083.97OTCG2O2-0.1342983.477OTCG311-0.0767423.777OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGP1-0.092012.0015OTHGP1-0.092012.477OTNG3P0-0.1918553.627OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	S	-0.287782	3.777
OTSS-0.2941083.97OTCG2O2-0.1342983.477OTCG311-0.0767423.777OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	SM	-0.264453	3.752
OTCG2O2-0.1342983.477OTCG311-0.0767423.777OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	SS	-0.294108	3.97
OTCG311-0.0767423.777OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.148613.527	OT	CG2O2	-0.134298	3.477
OTCG321-0.101523.787OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG302-0.1356623.427OTOG311-0.148613.527	OT	CG311	-0.076742	3.777
OTCG334-0.1190433.992OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	CG321	-0.10152	3.787
OTCH2-0.1343744.0612OTCH3-0.195313.8805OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	CG334	-0.119043	3.992
OT CH3 -0.19531 3.8805   OT HGA1 -0.091005 3.117   OT HGA2 -0.080259 3.117   OT HGP1 -0.09201 2.0015   OT HGP5 -0.09201 2.477   OT NG3P0 -0.191855 3.627   OT OG2D1 -0.14861 3.477   OT OG302 -0.135662 3.427   OT OG311 -0.188027 3.542   OT OG312 -0.14861 3.527	OT	CH2	-0.134374	4.0612
OTHGA1-0.0910053.117OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	CH3	-0.19531	3.8805
OTHGA2-0.0802593.117OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	HGA1	-0.091005	3.117
OTHGP1-0.092012.0015OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	HGA2	-0.080259	3.117
OTHGP5-0.092012.477OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	HGP1	-0.09201	2.0015
OTNG3P0-0.1918553.627OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	OT	HGP5	-0.09201	2.477
OTOG2D1-0.148613.477OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	ОТ	NG3P0	-0.191855	3.627
OTOG302-0.1356623.427OTOG311-0.1880273.542OTOG312-0.148613.527	ОТ	OG2D1	-0.14861	3.477
OTOG311-0.1880273.542OTOG312-0.148613.527	ОТ	OG302	-0.135662	3.427
OT OG312 -0.14861 3.527	ОТ	OG311	-0.188027	3.542
	ОТ	OG312	-0.14861	3.527

#### References

- [1] M. Schmollngruber, D. Braun, D. Oser and O. Steinhauser, Phys. Chem. Chem. Phys., 2016, 18, 3606–3617.
- [2] R. B. Best, W. Zheng and J. Mittal, J. Chem. Theory Comput., 2014, 10, 5113–5124.
- [3] D. Beglov and B. Roux, J. Chem. Phys., 1994, 100, 9050.
- [4] A. D. MacKerell Jr., D. Bashford, M. Bellott, R. L. Dunbrack Jr., J. D. Evanseck, M. J. Field, S. Fischer, J. Gao, H. Guo, S. Ha, D. Joseph-McCarthy, L. Kuchnir, K. Kuczera, F. T. K. Lau, C. Mattos, S. Michnick, T. Ngo, D. T. Nguyen, B. Prodhom, W. E. Reiher, B. Roux, M. Schienkrich, J. C. Smith, R. Stote, J. Straub, M. Watanabe, J. Wlorklewicz-Kuczera, D. Yin and M. Karplus, *J. Phys. Chem. B*, 1998, **102(18)**, 3586–3616.
- [5] A. D. MacKerell Jr., M. Feig and C. L. Brooks III., J. Am. Chem. Soc., 2004, 126, 698–699.
- [6] R. B. Best, X. Zhu, J. Shim, P. E. Lopes, J. Mittal, M. Feig and A. D. MacKerell Jr., J. Chem. Theory Comput., 2012, 8(9), 3257–3273.