Electronic Supplementary Information

CHARMM all atom force field employs a Lennard-Jones (6-12) function to describe Van der Waals interactions. This potential is a combination of attractive and repulsive contributions. The repulsive term describes internuclear electrostatic repulsion and short-range repulsive forces (or exchange forces) between electrons with the same spin. The attractive term is due to dispersion forces, which in turn are due to instantaneous dipoles arising during the fluctuations in the electron clouds. The form of the potential energy function of two interacting atoms is:

$$V_{vdW} = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

Where r is the distance between the two atoms, σ is the collision diameter (the distance at the zero energy) and ε is the Lennard-Jones well depth. For a q atom and a c atom, these empirical parameters are expressed from the Lorentz-Berthelot mixing rules:

$$\sigma_{qc} = \frac{1}{2}\left(\sigma_{qq} + \sigma_{cc}\right)$$

$$\varepsilon_{qc} = \sqrt{\varepsilon_{qq}\varepsilon_{cc}}$$

Van der Waals interactions are also important to well describe the interaction between QM and MM regions in hybrid QM/MM enzyme simulation. The Van der Waals parameters relative to the QM atoms of the FAAH-oleamide complex, applied in all the simulations performed, are reported in the table below. These are consistent to those reported in the combined parameter file (CHARMM22 for protein, CHARMM27 for lipid) par_all27_prot_lipid.prm.

For further details see www.charmm.org

ATOM NAME	ATOM TYPE	e (kcal mole^{-1})	s (Å)	Notes
O1	O	-0.120000	1.700000	Oleamide
C1	CC	-0.070000	2.000000	Oleamide
N2	NH2	-0.200000	1.850000	Oleamide
H	H	-0.046000	0.224500	Oleamide
H1	H	-0.046000	0.224500	Oleamide
C18	CTL2	-0.056000	2.010000	Oleamide
C2	CTL2	-0.056000	2.010000	Oleamide
C3	CTL2	-0.056000	2.010000	Oleamide
H6	HAL2	-0.028000	1.340000	Oleamide
H7	HAL2	-0.028000	1.340000	Oleamide
H4	HAL2	-0.028000	1.340000	Oleamide
H5	HAL2	-0.028000	1.340000	Oleamide
H2	HAL2	-0.028000	1.340000	Oleamide
H3	HAL2	-0.028000	1.340000	Oleamide
CB	CT2	-0.055000	2.175000	Ser217
HB1	HA	-0.022000	1.320000	Ser217
HB2	HA	-0.022000	1.320000	Ser217
OG	OH1	-0.152100	1.770000	Ser217
HG1	H	-0.046000	0.224500	Ser217
CE	CT2	-0.055000	2.175000	Lys142
HE1	HA	-0.022000	1.320000	Lys142
HE2	HA	-0.022000	1.320000	Lys142
NZ	NH2	-0.200000	1.850000	Lys142
HZ1	HC	-0.046000	0.224500	Lys142
HZ2	HC	-0.046000	0.224500	Lys142
CB'	CT2	-0.055000	2.175000	Ser241
HB1'	HA	-0.022000	1.320000	Ser241
HB2'	HA	-0.022000	1.320000	Ser241
OG'	OH1	-0.152100	1.770000	Ser241
HG1'	H	-0.046000	0.224500	Ser241
HQL1	HQ	-	-	Link atom
HQS1	HQ	-	-	Link atom
HQS2	HQ	-	-	Link atom
HQM1	HQ	-	-	Link atom