

Supporting information

Table 1. Average D-RESP charges for COP in water compared to in HIV-protease.

Atom	COP/water	COP/PR
C ₁	-0.06790	-0.07308
C ₂	-0.06001	-0.05625
H ₃	0.04318	0.07469
H ₄	0.07775	0.07161
C ₅	-0.09356	-0.09427
H ₆	0.06263	0.04958
C ₇	-0.07984	-0.05522
H ₈	0.06770	0.07729
C ₉	-0.04947	-0.06856
H ₁₀	0.07432	0.00821
C ₁₁	0.01133	-0.01666
C ₁₂	0.02852	-0.01654
C ₁₃	-0.00609	-0.01084
C ₁₄	-0.04399	-0.04829
H ₁₅	0.04539	0.02503
H ₁₆	0.02721	0.01065
H ₁₇	0.00490	0.04026
H ₁₈	0.03683	0.02322
H ₁₉	-0.02459	-0.00659
H ₂₀	0.02705	-0.09034
C ₂₁	-0.01376	-0.03618
C ₂₂	0.07508	0.10038

O ₂₃	-0.11241	0.02036
H ₂₄	0.22899	0.32640
C ₂₅	-0.00117	-0.01967
O ₂₆	-0.45040	-0.43867
O ₂₇	-0.03935	-0.04593
C ₂₈	0.08861	0.05317
C ₂₉	0.00647	0.01798
C ₃₀	-0.02065	0.00664
H ₃₁	-0.05810	0.08284
H ₃₂	0.06176	0.01876
C ₃₃	-0.00914	-0.00144
H ₃₄	0.02574	-0.01260
H ₃₅	-0.00236	0.06253
C ₃₆	-0.00998	-0.01872
H ₃₇	0.01991	-0.00974
H ₃₈	0.00127	0.03241
C ₃₉	-0.00635	-0.01777
H ₄₀	0.00093	0.00468
H ₄₁	0.04945	-0.00163
C ₄₂	-0.00409	-0.00847
H ₄₃	0.02036	0.03846
H ₄₄	0.00137	-0.02113
C ₄₅	-0.01154	-0.02488
H ₄₆	0.07109	0.05633
H ₄₇	0.00781	-0.00781

Table 2. Average group charges for COP in water and in HIV protease.

Group	COP/water	COP/PR
Cyclooctane	0.13748	0.17820
pyranone	-0.21794	-0.02216
CH	0.05557	-0.10688
Phenyl	-0.01387	-0.08266
Alky group	0.03966	0.03344
OH	0.11658	0.34670

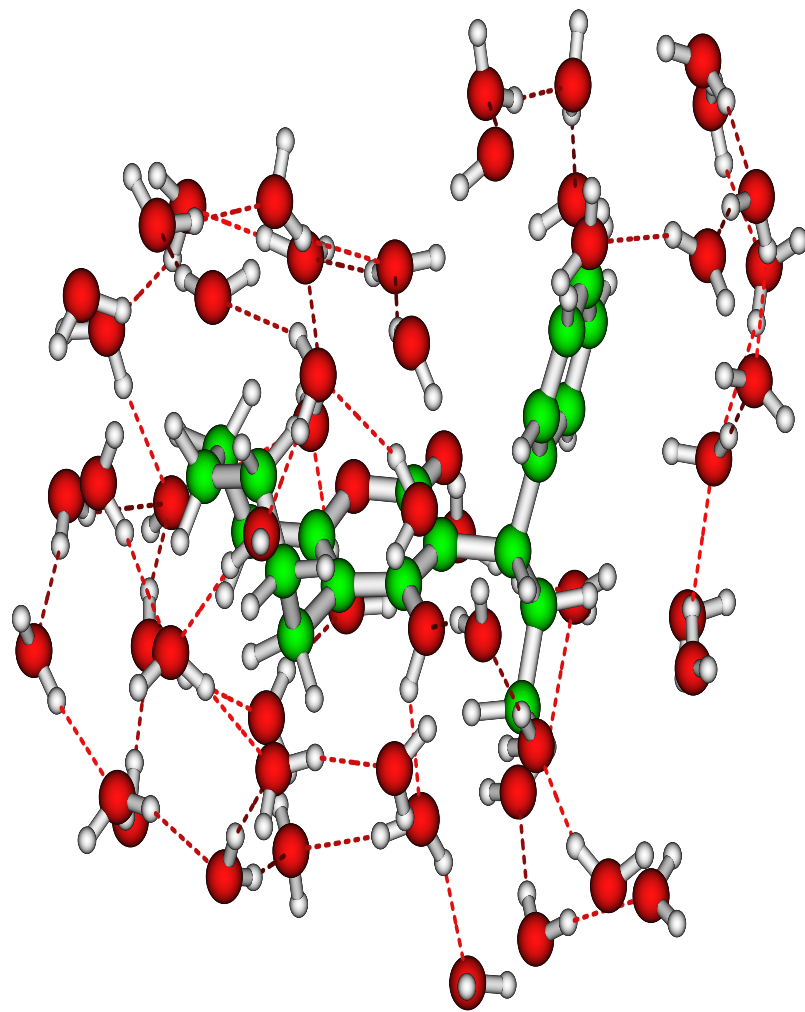


Figure 1: COP molecule and water solvents included upto third solvation shell in the $g_{X-COM}(r)$ rdf. calculation.