CM5239 Tutorial 5 - Molecular Mechanics & Molecular Dynamics

(1) For the two lowest energy conformations of *n*-butane, the MM2 force field calculations yield the individual strain energy terms (kcal mol^{-1}):

term	A	B
stretch	0.15	0.16
stretch-bend	0.05	0.07
bend	0.29	0.63
torsion	0.01	0.44
vdw	1.68	1.75
total	?.??	?.??

Of the conformations A and B, which is the lowest in energy? According to the MM2 force field, what are sources of energetic preference for the lowest energy conformation?

(2) Suppose you are going to invent a new force field method, **MMHC**, for saturated compounds containing carbon and hydrogen only. Assume the following strain energy terms: (1) harmonic approximation for bond stretch, (2) harmonic approximation for angle bend, (3) 3rd order Fourier series for torsion, and (4) Lennard-Jones potential for nonbonded interaction, are used for the **MMHC** force field.

(a) List down all the force field parameters required for the **MMHC** method.

(b) What sort of data would you use for force field parametrization?

(c) Suggest two ways to improve the reliability of the **MMHC** method.

(3) With the use of the table of coordinates (in Å) given below and the following force field parameters: k_r = 700 kcal mol^{-1} $Å^{-2}$, r_0 = 0.93 Å, k_θ = 100 kcal mol^{-1} rad^{-2} and θ_0 = 104.5°, what is the stretch-strain energy for water at this geometry? What is the bend-strain energy for water at this geometry? What is the total strain energy for H_2O at this geometry? [Use harmonic approximation for both bond stretching and angle bending terms ($E = \frac{1}{2}kx^2$)]

atom	x	y	z
O	0.0	0.0	0.0
H_1	0.0	–0.65	0.60
H_2	0.0	0.65	0.60

(4) You are conducting a research project on the dynamics of protein-ligand interactions using molecular dynamics (MD) simulation. Your goal is to investigate the binding mechanism of a small molecule inhibitor to a target protein implicated in a disease pathway. Design a computational workflow, from system preparation to analysis and interpretation of simulation results, outlining the steps you would take to perform and analyze the MD simulation of the protein-ligand complex.