10.637: IN CLASS WORKSHEET, LAB 2

This worksheet should be filled in to the best of your ability during in-class time and returned to myself or the TA at the end of the class period on 09/21/23 or uploaded to Canvas by 11:59PM EDT (Thu). Please answer questions to the best of your ability. You may work with a partner and ask questions, but you must hand in your own work.

Name: Wenhao He

A. Stacked benzene

	single benzene energy (kJ/mol)	stacked benzene energy (kJ/mol)	binding energy (kJ/mol)	inter-benzene or C-C distance (Å)
MMFF94	70.058	226.278	86	3.020
GAFF	19.9033	57.6357	19	3.021

What additional constraints could help with this optimization? angle = 90: 1-13-14 ; angle = 90: 1-13-18 ; angle = 90: 13-1-2 ; angle = 90: 13-1-6 ;

Circle one underlined choice in each of the following four questions:

How does the **GAFF** binding energy compare to the CCSD(T) reference:

Is it an overestimate or underestimate?

What about the **GAFF** separation distance:

Is it an overestimate or underestimate?

How does the **MMFF94** binding energy compare to the CCSD(T) reference:

Is it an overestimate or underestimate?

What about the **MMFF94** separation distance:

Is it an overestimate or underestimate?

B. More chemically diverse molecules and conformer searching

Molecule	Conformer	FF	E_{tot} (kJ/mol)	Dihedral Angle (degrees)
Butane	anti	GAFF	4.606	180.0
Butane	gauche	GAFF	7.03153	67.8
Butane	anti	MMFF94	-21.2521	180.0
Butane	gauche	MMFF94	-17.9773	65.3
1,2-ethanediol	hydrogen bond gauche	GAFF	2.63333	57.3
1,2-ethanediol	anti	GAFF	8.50248	180.0
1,2-ethanediol	regular gauche	GAFF	11.1894	68.1
1,2-ethanediol	hydrogen bond gauche	MMFF94	67.262	59.0
1,2-ethanediol	anti	MMFF94	79.4417	180.0
1,2-ethanediol	regular gauche	MMFF94	86.8163	77.1

Based on the table from the previous prompt, why is the gauche conformer lower in energy for 1,2-ethanediol?

because of hydrogen bond

How strong is the 1,2-ethanediol hydrogen bond (in the unit of kJ/mol) according to MMFF94? According to GAFF? MMFF94: -8.5 ; GAFF: -19.6

C. Remdesivir models for hydrogen bonds compared to 1,2-ethanediol:
Based on the table below, rank the hydrogen bond strengths (1, 2, 3):
__3__ 1,2-ethanediol __1__HB in tetrahydrofuranyl ring of remdesivir model __2__ HB between ring and free hydroxyl on remdesivir model

remdesivir model 1) (HB) energy: 441.121	**remdesivir model 2) (no HB) energy:** 476.301	**HB energy (1-2):** -35.5
remdesivir model 1) (HB) energy: 441.121	**remdesivir model 3) (two HBSs) energy:** 425.877	**HB energy (3-2):** -15.3

If you wanted to strengthen binding between a drug molecule and a protein by 75 kJ/mol, and you knew the protein had up to 8 hydrogen bond acceptors in the active site, how many hydroxyl groups should you add to the druglike molecule assuming they would form intermolecular hydrogen bonds with the protein? __8__
Explain your reasoning: __by experiemtn, inter molecular HB is about 10 kJ/mol, so we need 8*10 > 75__

D. Accessing and getting familiar with the Linux command line.
What is the last number reported when these variables are **3** and **4?** 64079