Solutions for Project I, Chem5021/8021, Spring 2005 (**30 points total**)

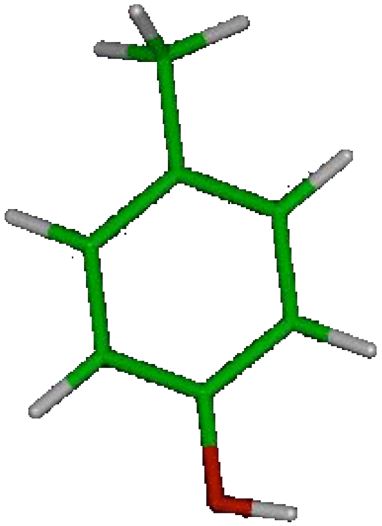
1a (5021). (15 pts). The topology file for the molecule p-cresol is constructed by making use of the protein residue, Tyr, as a template. First, atoms in the amino group and in the carbonyl group, as well as the a-hydrogen, are deleted. Then, the CA atom is changed to HB3, and the atom type for the CB is replaced by the CT3 type. To balance the overall charge and keep the "CHARMM convention" that an aliphatic hydrogen atom has a partial atomic charge of +0.09 e, the partial atomic charge for the CB atom (which is the methyl group in p-cresol) is assigned to a value of –0.27. The remaining components in the tyrosine residue are kept.

To obtain the initial Cartesian coordinates, the IC table for this "residue" is modified, and the final topology file is attached in the end as an appendix.

As it turns out, no additional parameters are needed to optimize the structure by energy minimization. The energy minimization was accomplished by performing 200 steps iteration using the adopted-basis Newton-Raphson optimizer, after which the energy change was zero, and net gradient was also zero. No further checks, nor optimization with other optimization options were made at this point.

The optimized structure is given below, in Problem 2, which was obtained by an additional 15 steps energy minimization using the Newton-Raphson method. Key structural parameters are indicated.

2a (5021). (15 pts). The optimized structure (after 200 steps of ABNR iteration) from problem 1 was first read, and then, subjected to 15 steps of energy minimization using the Newton-Raphson optimizer. The final energy change between steps and the final gradient are both zero.



After this further optimization, a force field calculation was performed to obtain the normal mode vibrational frequencies. After diagonalization of the force constant matrix (Hessian), the first 6 vibrational frequencies are exactly zero and there are no negative frequencies either, suggesting that the geometry of p-cresol has been fully optimized. To analyze qualitatively the major components of the first non-zero (or lowest) vibrational frequency, the eigenvectors of modes 7 through 12 were printed.

From the components in the internal coordinate representation, it was clear that the dihedral angle torsinal about the methyl group has the largest component for vector #7. Consequently, a projection of all eigenvectors was made on this torsional degrees of freedom (corresponding to HB3-CB-CG-CD1). Indeed, the projections demonstrated that it is eigenvector #7 that has the largest value, consisting of 98.9%, which confirms the initial speculation. The lowest eigenvalue for mode #7 is 23.0 cm^{-1}, and this mode can be confidently assigned to correspond to the torsional motions of the methyl group in p-cresol.

It is interesting to note that if a projection of the calculated eigenvectors onto the hydroxyl torsional angle, it is found that mode #10 (288.0 cm^{-1}) has 50.2% contribution from this motion, and mode #11 (337.6 cm^{-1}) has 41.4% contribution, also from this torsion. Thus, the normal motions of mode #10 and #11 are closely coupled.

1b (8021). (10 pts). The residue topology file for the molecule CHEM8021 (someone may want to write the IUPAC name) is a bit more complicated to construct than p-cresol, but it can also be constructed by making use of the protein residue, Tyr, as a template.

First, the C_α and H_α atoms are removed (which I found it to be easier, but you may want to work it around it differently). The amino group in the original Tyr residue topology file is kept, and then a new methyl group is added in the end of the atom definition.

The CHARMM force field uses the convention that the amino group and the alpha carbon and its hydrogen are grouped together to have a net charge of zero, and that the carbonyl group itself has a net charge of zero. Thus, to keep this convention (and that for aliphatic hydrogens with 0.09 e) a partial charge of –0.02 e is required for the carbon atom attached to the amide nitrogen. The remaining partial charges are straightforward and obvious to assign.

To obtain the initial Cartesian coordinates, the IC table for the CHEM8021 “residue”, which is called PR1B, needs to be modified to accommodate the new atoms, and the final topology file is attached in the end as an appendix. Note that you are not required to make a self-consistent internal coordinate (IC) table to generate the Cartesian coordinates, but it would be a good exercise. You can certainly use “insightII” to get the Cartesian coordinates.

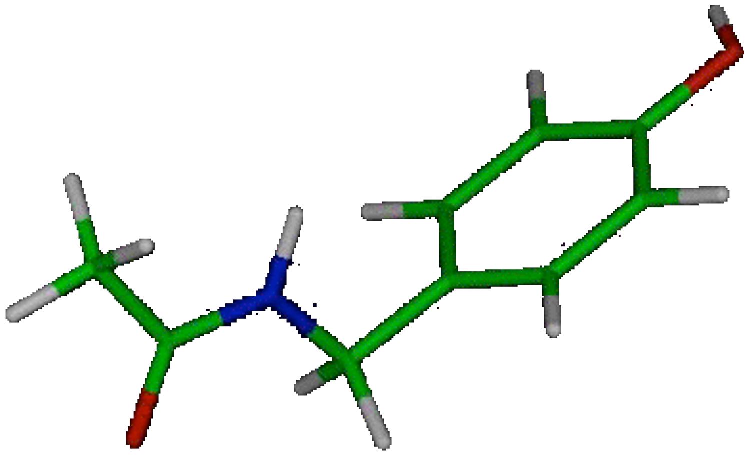
There is one angle parameter missing, corresponding to the angle type of “CA-CT2-NH1”, which was estimated by an analogous type “CC-CT2-NH1”. This new angle parameter is added to the standard CHARMM parameter file at the end of the angle parameter list. When energy minimization was requested, it was found that two dihedral angle parameters were missing also; they are “C-NH1-CT2-CA” and “H-NH1-CT2-CA” combinations, and they are replaced respectively by the “C-NH1-CT2-CC” and “H-NH1-CT2-CC” types. The energy minimization was accomplished by performing 300 steps iteration using the adopted-basis Newton-Raphson optimizer, after which the energy change was 0.002 kcal/mol, and net gradient was also 0.07 kcal/mol-A. This was stopped. No further checks, nor optimization with other optimization options were made at this point.

The optimized structure is given below, in Problem 2, which was obtained by an additional 100 steps of ABNR, and 15 steps energy minimization using the Newton-Raphson method. Key structural parameters are indicated.

2b (8021). (10 pts). The optimized structure (after 200 steps of ABNR iteration) from problem 1 was first read, and then, subjected to 100 steps of ABNR and 15 steps of energy minimization using the Newton-Raphson optimizer. The final energy change between steps was 0.0027 kcal/mol, and the final gradient was both zero.

After this further optimization, a force field calculation was performed to obtain the normal mode vibrational frequencies. After diagonalization of the force constant matrix (Hessian), the first 6 vibrational frequencies are almost zero, with the largest value of 0.00003 cm^{-1} and there are no negative frequencies beyond these 6 “zero” frequencies, suggesting that the geometry of CHEM8021 has been fully optimized. To analyze qualitatively the major components of the first non-zero (or lowest) vibrational frequency, the eigenvectors of modes 7 through 12 were printed.

From the components in the internal coordinate representation, it was not immediately possible to identify the major components for vector #7 since three dihedral angles have relatively the same contributions. Two of them correspond to the torsional angle about the methylene carbon and amide nitrogen atoms. Thus, a projection of eigenvectors to this torsional angle was made, along with projections to the methyl group rotation, and the hydroxyl group rotation.



The lowest vibrational frequency has a value of 23.2 cm^{-1}. The projections reveal that mode #7 has about 60% of C-N torsional and mode #8 (33.3 cm^{-1}) has 40% C-N torsions. The remaining modes have zero contributions from this torsional motion.

The next two modes (#9 and #10, both about 60 cm^{-1}) are mainly due to the methyl torsion, and the hydroxyl torsion has largest projections from modes #15 and #17, which are about 300 cm^{-1}, similar to that found in p-Cresol above.

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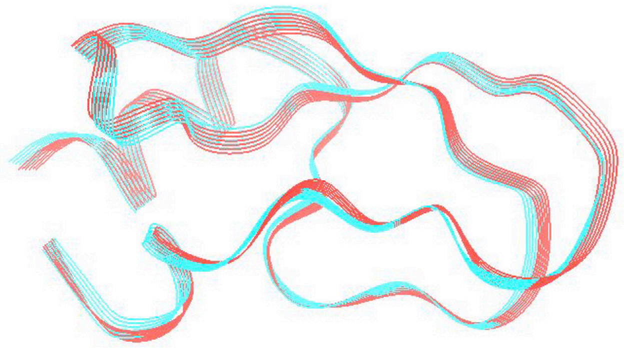
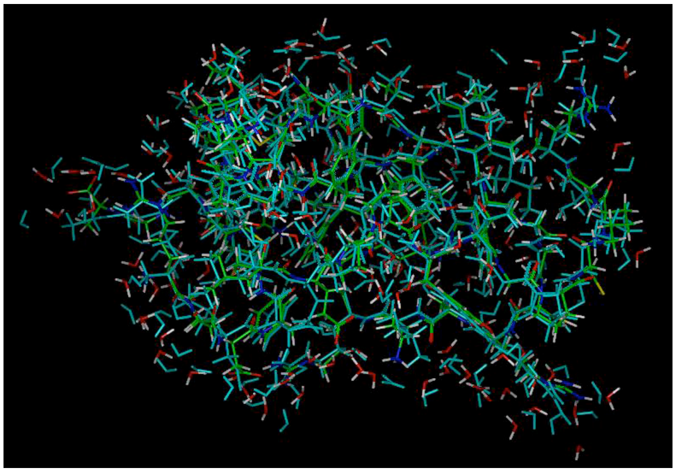
3 (10 points). I have extensively commented, in the input files in the chemta directories, the procedure and various ways of constructing the protein structure for BPTI. You can compute both the RMS for all atoms between the optimized and the crystal structure, which is 1.1 angstroms, and the RMS for the backbone atoms, which is 0.46 angstroms. Obviously, the backbone atoms have much smaller overall changes in the energy minimization than the side change atoms. A snap-shot of the structure after just 500 steps of ABNR energy minimization is shown below. Note that this is far from fully optimized.



Ribbon diagram of the backbone trace for the minimized (red) and crystal (blue) structures.



All atom comparisons. The minimized structure is colored by atom types.