1.   PURPOSE OF THE EXPERIMENT

This project will further your exposure to PC-Spartan for modeling molecular properties. In particular, you will investigate the electronic structure of polyenes and porphyrins and will learn how to use results of molecular orbital calculations to predict the (qualitative) spectroscopic properties of molecules.

2.   A(nother) BRIEF TOUR OF COMPUTATIONAL CHEMISTRY METHODS

It is now possible to predict the structure and reactivity of small and large molecules with computers. Computational chemists often work very closely with experimental chemists to develop better theoretical tools with better predictive power. The synergy between theory and experiment is very important: it is often the case that a computer model may explain a puzzling experimental result. In the pharmaceutical industry, computational chemists are often asked to predict the structural features that lead to an efficient drug by considering the nature of a receptor site.   Then, organic chemists synthesize the proposed molecules, which are in turn tested by biochemists for efficiency.   The process is often iterative, with experimental results feeding back into the calculations, which in turn generate new proposals for efficient molecules, and so on. As a result, computer-aided molecular modeling is a tool with which every well-educated chemist should be acquainted.

Molecular models are mathematical entities generated via the application of the laws of physics to chemical systems. The chemist is often asked to choose between classical and quantum mechanical models.

Molecular mechanics and **molecular dynamics** methods use Newtonian mechanics. The molecule is seen as a collection of hard spheres (the nuclei) connected by flexible springs (the chemical bonds). Electrons are not taken into account explicitly and, as a result, thermochemical properties such as the heat of formation, ΔH_f^o, cannot be calculated. The preferred structure of a molecule is obtained by minimizing the so-called **steric energy**, which is a measure of steric repulsion between spheres or between springs. Therefore, these classical models are only useful for comparing conformational isomers of a given molecule. Molecular mechanics and dynamics are very fast methods that use minimal computer resources. They are still viable tools for the study of very large molecules such as proteins and nucleic acids.

Quantum mechanical models are generated via **semi-empirical** or **ab initio** methods.   They solve the Schrödinger equation for the entire molecule by making different approximations. Semi-empirical methods (such as the AM1 and AM1-SM2 methods) make use of experimental data to characterize mathematically atoms of

different elements. The results are reliable to the extent that these parameters do not change from molecule to molecule and to the extent that the experimental data are reliable. Ab initio methods do not depend on empirical parameters. Much of the work in developing these methods comes from developing appropriate mathematical forms for the atomic orbitals of different elements. The goal is to generate molecular structures that agree with experiment.

Because the electronic structure of the compound is calculated explicitly, quantum mechanical methods lead to reasonable predictions of structure and thermochemical properties. Semi-empirical methods are a bit less accurate than but are faster than ab initio methods. When used judiciously, semi-empirical methods (e.g., AM1) can give great insight into structure and reactivity of even moderately large molecules. Furthermore, there exist good semi-empirical methods (e.g., AM1-SM2) for the simulation of solvent effects on structure and reactivity. We will use the AM1 and AM1-SM2 semi-empirical methods and (occasionally) the 3-21G ab initio method in this course because they are relatively fast and versatile.

Chemists and computer scientists are constantly working on new molecular modeling methods. For example, hybrid methods that take advantage of the best features of classical and quantum mechanical methods are currently being developed to increase the accuracy and speed of simulations of large molecules such as proteins. At the same time, computers are getting faster and better. There are already prototype virtual reality systems that allow chemists to manipulate (literally) molecules in a three-dimensional virtual molecular environment. Indeed, computational chemistry is a field with a great future!

3. PREDICTING THERMODYNAMIC AND KINETIC PROPERTIES FROM MOLECULAR MODELS

Although we will not investigate thermodynamic and kinetic properties in these experiments, it is useful to know how molecular modeling can be used to predict such important reaction parameters as enthalpy changes, equilibrium constants, and rate constants. Semi-empirical methods can calculate the **heat of formation** of a molecule directly, often in units of kcal/mol. As a result, the enthalpy changes of reactions may also be predicted by subtracting the total enthalpy contribution due to reactants from the total enthalpy contribution due to products. Ab initio methods calculate the **total energy**: the energy of a hypothetical reaction that forms a molecule from a collection of nuclei and electrons. Total energies are always negative and are expressed in atomic units (a.u.). The conversion factors are:

$$1 \text{ au} = 627.5 \text{ kcal/mol} = 2625 \text{ kJ/mol} \tag{1}$$

The energy change of a reaction may be calculated as:

$$\Delta E_{reaction} = E_{product1} + E_{product2} + \ldots\ldots - E_{reactant1} - E_{reactant2} - \ldots\ldots \tag{2}$$

It is also possible to estimate the equilibrium constant, K, of reactions according to the following procedures. First, we express K in terms of the standard free energy change $\Delta G_{reaction}$:

$$K = \exp(-\Delta G_{reaction}/RT) \tag{3}$$

where R is the gas constant and T is the absolute temperature. At room temperature (298 K) and for $\Delta G_{reaction}$ in a.u., we have:

$$K \ = \ \exp\,(\text{-}1060\;\Delta G_{reaction}) \tag{4}$$

In turn, $\Delta G_{reaction}$ is given by:

$$\Delta G_{reaction} \ = \ \Delta H_{reaction} \ \text{-} \ T\Delta S_{reaction} \tag{5}$$

For reactions where the change in entropy may be neglected and where $\Delta H_{reaction} \approx \Delta E_{reaction}$, we can write:[1]

$$K \ = \ \exp\,(\text{-}1060\;\Delta E_{reaction}) \tag{6}$$

Total energies may be used to calculate energies of activation of reactions:

$$\Delta E^{\ddagger} \ = \ E_{transition\ state} - E_{reactant1} - E_{reactant2} \ \text{-} \ \ldots\ldots \tag{7}$$

Once $\Delta E^{\ddagger}$ is calculated, the rate constant, $k_{reaction}$, of the reaction may be estimated by using the Eyring equation:

$$k_{reaction} \ \approx \ (k_B T/h)[\exp(\text{-}\Delta E^{\ddagger}/RT) \tag{8}$$

where k_B Boltzmann's constant and h is Planck's constant. At room temperature and for $\Delta E^{\ddagger}$ in a.u., we have:

$$k_{reaction} \ = \ 6.2 \text{ x } 10^{12}\ \exp(\text{-}1060\;\Delta E^{\ddagger}) \tag{9}$$

4.   PROCEDURES

You will use the molecular modeling program PC-Spartan, which is installed only on the computers in the Chemistry Department's P-Chem Laboratory (Holroyd 301). You may not access these programs from the University network.

Spartan is a very flexible program that allows you to draw the molecule on the screen, generate the preferred structure via computation, and then visualize the results in a number of ways. For example, you may look at ball-and-stick models to get a sense of the general placement of the bonds and nuclei, or you may generate electron density maps, which give you a sense of how the electrons are distributed in the molecule. Among the properties you may calculate are: the heat of formation, the dipole moment, the energies of molecular orbitals, formal charges, electrostatic potentials, etc.

Getting acquainted with the software. You will work in groups of two. In the lab, you will find copies of the following:

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[1] Among the many reactions that meet these criteria are gas phase reactions where the number of moles of gas molecules does not change.

- "PC Spartan Tutorial and User's Guide"
- "A Laboratory Book of Computational Organic Chemistry" by W.J. Hehre, A.J. Shusterman, and W. Wayne Huang.

You may not remove these books from Holroyd 301. Whenever in doubt, consult the User's Guide for information about menu options, running calculations, and displaying results. Of course, you can always consult me. You have already attended a brief tutorial on the use of the software; below I summarize the basic steps for running a molecular orbital (MO) calculation with Spartan.

Guidelines for MO calculations with Spartan.

- Draw the molecule and minimize it in the Builder. Save it when prompted to do so to your own folder on the disk. IF YOU SAVE IT TO THE DEFAULT FOLDER, OTHER GROUPS MAY ACCIDENTALLY VIEW YOUR RESULTS. THIS IS NOT ALLOWED UNDER THE RULES OF THIS ASSIGNMENT.
- Open the Setup menu and choose Calculation.
- Set up a Geometry Optimization at the appropriate level (e.g., AM1, AM1-SM2, or 3-21G(*) level). In the Options box, enter PRINTMO.
- Open the Setup menu again and choose Surfaces.
- Set up calculation of the required number of HOMO-x, HOMO, LUMO, and LUMO+x surfaces.
- Open the Setup menu and click on Submit.
- When the calculation is done, choose Display, then Surfaces.
- Add the surface you wish to visualize and click OK.
- To view another surface, you must first deselect the current surface, and then add the new surface in the Display Surfaces dialog box.
- In order to obtain the MO energies, you must display the numerical output of the calculation. Choose Display, then Output. A window displaying numerical data should appear. If it does not, it may be because the output file is too long. In this case, open the output file with Word. The output file is a text file that is saved to the same folder where you saved your molecule data.
- To find the HOMO and LUMO in the output file, follow these procedures:
  - Near the top of the file, find the number of electrons that were used in the calculation.
  - Divide this number by 2, since there can be no more than two electrons per orbital.
  - The result is the orbital number that corresponds to the HOMO.
  - The LUMO is the next orbital in the order.
  - The energy of each MO is under "eigenvalues" and is given in atomic units.

Electronic structure of polyenes. Linear polyenes, of which β-carotene (shown below) is an example, are important biological co-factors that participate in processes as diverse as vision, photosynthesis, and protection against harmful biological oxidations. When β-carotene is oxidized *in vivo*, it breaks down in half and forms two molecules of retinal (vitamin A), which is a precursor to the visual pigment in rhodopsin.
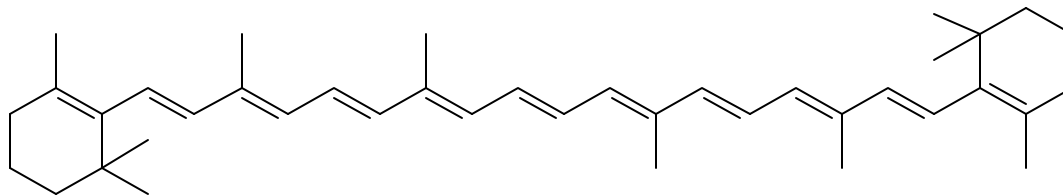
Let us gain some insight into the modulation of spectroscopic properties by structure in linear polyenes by solving the following problems:

a. Optimize the structures, visualize the HOMO and LUMO, and calculate the HOMO-LUMO gaps for the following molecules: (i) ethene; (ii) 1,3-butadiene; and (iii) 1,3,5-hexatriene. Use the 3-21G(*) method.

b. For each molecule, count the number of bonding interactions and antibonding interactions in the HOMO. Which HOMO's (if any) are "pure" bonding orbitals? Which HOMO's (if any) are non-bonding (equal number of bonding and antibonding interactions)? What effect does the extent of conjugation have on the HOMO energy?

c. Repeat the analysis of part (b), but now focus on the LUMO's.

d. From your results, make the appropriate choices below:
    "*For linear polyenes, the electronic absorption spectrum shifts to the (**blue/red**) as the number of **p** electrons (**increases/decreases**) and as the length of the conjugated system (**increases/decreases**).*"

Effect of solvent on the electronic spectrum of acetone. Let us explore the origin of solvent effects on electronic spectra, with acetone as a model.

a. Optimize the geometry of acetone at the AM1 level and calculate the energies of the π, n, and π^* orbitals of acetone. This calculation corresponds to acetone in the gas phase, since a solvent was not included explicitly. Note that AM1 calculations report energy in units of kcal/mol.

b. Repeat the calculation, but now at the AM1-SM2 level. This procedure simulates the effect of water as a solvent.

c. Which orbital is affected by water most strongly? Why do you think this is the case?

d. Compare the gaps between the n-π^* and π-π^* orbitals in both cases. Which of the electronic transitions is affected more strongly by water?

Electronic structure of porphyrins. The porphine dianion, shown below, is a tetra-pyrrole macrocycle that forms the core of many important biological molecules, such as the heme group and chlorophylls. The four pyrrole nitrogens form a cavity into which metal ions can bind (by coordinate-covalent bonds between the metal and the nitrogens); these are the so-called metalloporphines or metalloporphyrins. Alternatively, protons may bind to the negatively charged nitrogens, forming the so-called free-base porphyrins.

Martin Gouterman, of the University of Washington, proposed (in the 1960's) that the spectroscopic properties of porphine dianion, free-base porphine, and metallo-porphines may be understood at least qualitatively by considering four orbitals: the HOMO-1, HOMO, LUMO, and LUMO+1 orbitals. The first two are occupied and nearly degenerate and the last two are unoccupied and degenerate when the macrocycle is perfectly square

planar (e.g., the porphine dianion and metalloporphines where the metal is right at the center of the cavity). Let us investigate Gouterman's four-orbital model.
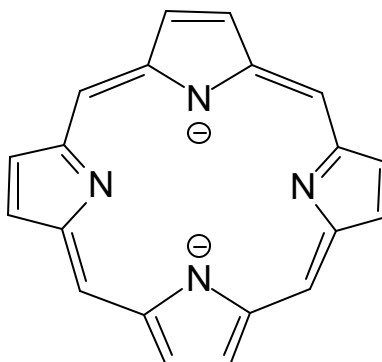
a. Optimize the geometry of free-base porphine (don't forget the protons!) AM1 level.
b. Visualize the HOMO-1, HOMO, LUMO, and LUMO+1 orbitals and calculate the HOMO-1-HOMO, HOMO-1-LUMO and HOMO-LUMO gaps.
c. Now replace each of the hydrogens at the *meso* carbons (the carbons that bridge adjacent pyrrole groups) with fluorine atoms and repeat steps (a) and (b). Did the shape of the orbitals change? How did the energy gaps between orbitals change? Based on the shapes of the orbitals, can you rationalize why the gaps changed in the way that they did? Does the absorption spectrum of free-base porphine occur to the red or to the blue of the absorption spectrum of fluorinated free-base porphine? (Hint, you will need to find references)
d. Now replace each of the hydrogens at the *meso* carbons with methyl groups and repeat steps (a) through (c).
e. Based on your work so far, discuss the effect of electron-withdrawing and electron-donating *meso* substituents on the electronic absorption spectra of free-base porphine. In your discussion, enumerate the effects and discuss their origins in the context of the Gouterman four-orbital model.   Now repeat for a zinc(II)

5.   THE LABORATORY REPORT

This is an abbreviated report, to be formatted according to the guidelines in the Lab Report Handout
 More specifically, it should consist of:
*   A title followed by the name(s) of the student(s) who completed the experiment.
*   A *Results* section, where you tabulate the data for each experiment. You may also choose to include print-outs of structures. However, include structures only if you believe that they are required to strengthen your arguments in the *Discussion* section. Please give a title and a number to each table. Also, please number and caption each figure.
*   A *Discussion* section, where you answer the questions posed above for each experiment.
*   *Acknowledgments* and *References*