CHEM1030 Quantum Chemistry Practical A:
Equilibrium geometry and molecular volume of cocaine

Introduction

The task of refining the molecular geometry from some initial guess (provided by chemical intuition) amounts to finding the minimum of the molecular energy with respect to the atomic coordinates:

$$\{\vec{r}_1, \vec{r}_2, ...\} = \underset{\{\vec{r}_1, \vec{r}_2, ...\}}{\arg\min} E(\vec{r}_1, \vec{r}_2, ...) \tag{1}$$

where $\vec{r}_k = \begin{bmatrix} x_k & y_k & z_k \end{bmatrix}$ are Cartesian coordinates of the k-th atom. In the discussion below $\vec{R}$ symbol will be used to denote the vector containing all coordinates of all atoms. The minimum with respect to $\vec{R}$ is called *equilibrium geometry* because static forces on each atom at the energy minimum are zero. Basic quantum chemistry software packages usually calculate molecular geometries using *gradient descent* type methods, in which the geometry is updated by stepping down the energy gradient:

$$\vec{R}^{(n+1)} = \vec{R}^{(n)} - k \cdot \text{grad}\left[E(\vec{R})\right] \tag{2}$$

where k is the step length. The reverse (note the minus sign) of the gradient is used as the descent direction because gradient itself

$$\text{grad}\left[E(\vec{R})\right] = \begin{bmatrix} \dfrac{\partial E}{\partial R_1} & \dfrac{\partial E}{\partial R_2} & \dfrac{\partial E}{\partial R_3} & \cdots \end{bmatrix} \tag{3}$$

is defined as the vector pointing in the direction in which the function grows most steeply. More sophisticated software packages use Newton methods, where the geometry is updated using a procedure that takes into account the curvature of the surface using a matrix of second derivatives called the *Hessian*:

$$\vec{R}^{(n+1)} = \vec{R}^{(n)} - \mathbf{H}^{-1}\text{grad}\left[E(\vec{R})\right] \qquad H_{nk} = \frac{\partial^2 E}{\partial R_n \partial R_k} \tag{4}$$

Energy itself is computed using a large variety of methods – in this practical we will use the semi-empirical PM6 method and density functional theory (DFT), which are both fast (they cut a few corners with the Schrödinger equation and avoid a full quantum mechanical calculation) and reasonably accurate (formation energies for CHNO molecules are generally within 6 kcal/mol from their experimental values).

Molecular volume is computed for the optimized geometry by associating with each atom a sphere of a certain radius (the atomic radii are determined from crystallography or DFT calculations) and calculating the total outer volume of the resulting set of interlocking spheres.

Recommended literature

1. J.B. Foresman, A. Frisch, *"Exploring chemistry with electronic structure theory methods"*, Gaussian Inc., 2003.

2. A.R. Leach, *"Molecular modelling: principles and applications"*, Prentice Hall, 2001.

3. F. Jensen, *"Introduction to computational chemistry"*, Wiley, 2007.

4. A. Hinchliffe, *"Molecular modelling for beginners"*, Wiley, 2008.

5. *"Quantum Chemistry"* – IK's online lecture course, http://spindynamics.org/support.php

Geometry specification and optimization

1. Launch GaussView (Start Menu/Your School Software/Chemistry/GaussView 5.0/GaussView). The following windows will appear:
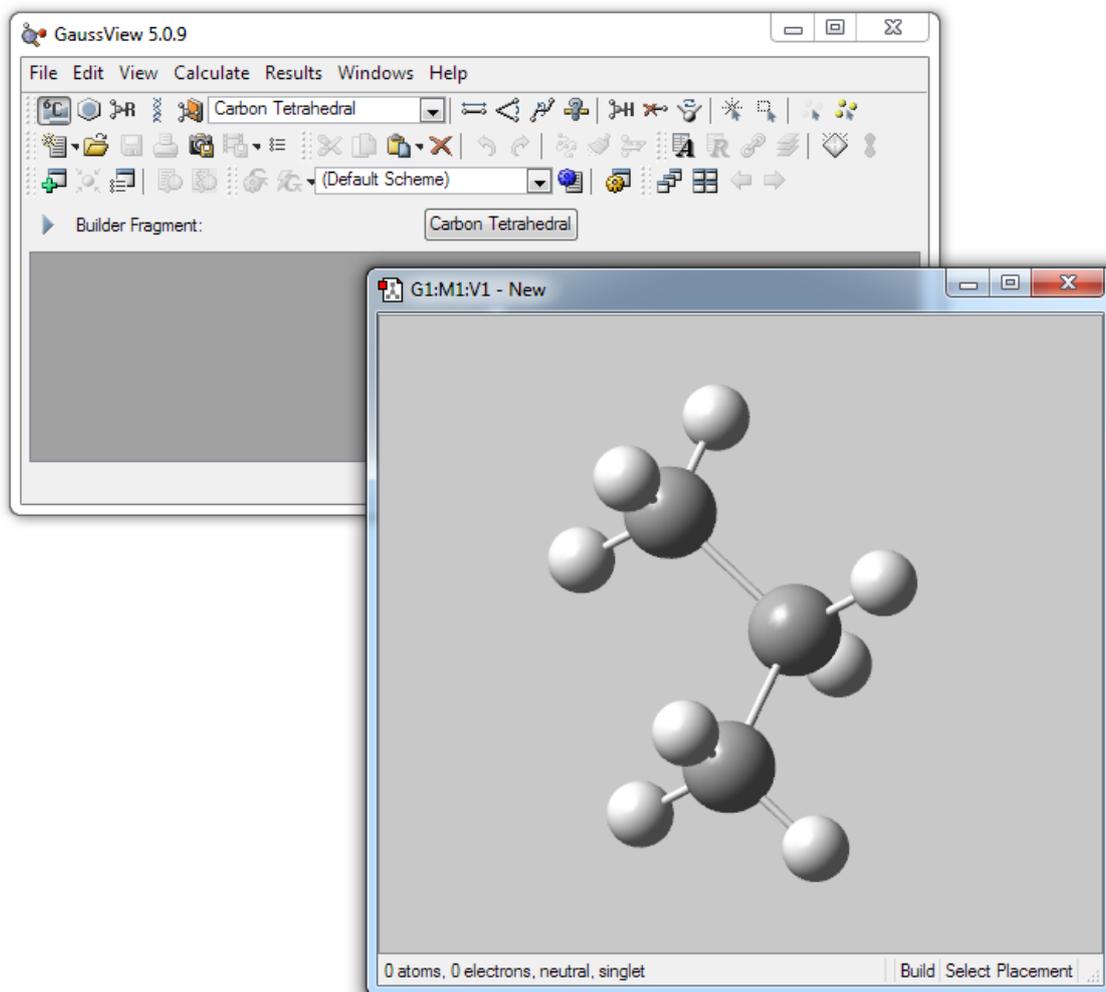

The left one is the *control window* (file load and save operations, calculation options, tool selectors, *etc.*) and the right one is the *canvas*, on which the molecule is drawn.

Click once in the middle of the canvas window. A methane molecule would appear. Click once on any of the hydrogens. Methane would be transformed into ethane. By selecting different atoms and groups in the control window and clicking on various parts of the molecule in the canvas, a variety of structures may be drawn. Use bond length, bond angle and dihedral angle buttons in the control window to refine your drawings.

Molecular structure drawing functionality in GaussView is quite intuitive – as a practical exercise, try drawing an ethanol molecule and changing various aspects of its geometry, deleting and re-adding atoms and adding various substituents in place of the hydrogen atoms. Make sure you are comfortable with structure drawing before moving on to the next step.

2. Open a new canvas window in GaussView (*File / New / Create Molecule Group*) and draw the cocaine molecule. This will take considerable effort – real molecules are more crowded in 3D space than their stick representations suggest. Include a screenshot of your molecule into your report.

G1:M1:V1 - New

43 atoms, 162 electrons, neutral, singlet   C1 Modify Dihedral Select Atom 1
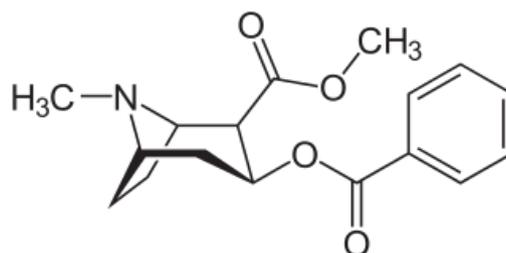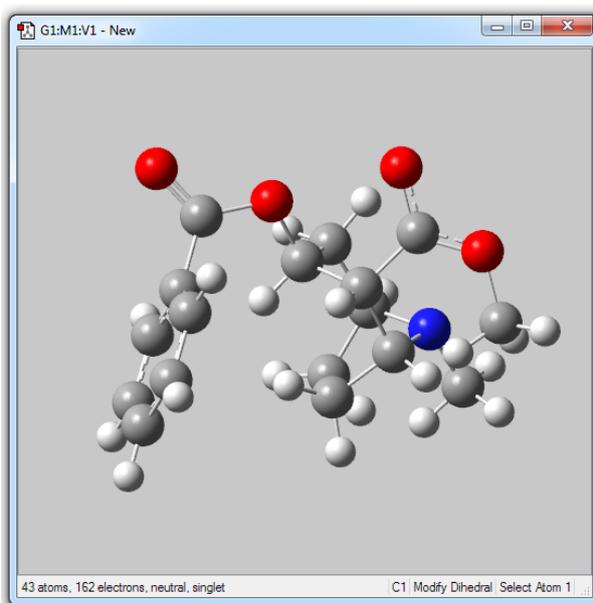
3. Perform molecular geometry optimization using PM6 method in vacuum: launch Gaussian interactive job setup window (*Menu / Calculate / Gaussian Calculation Setup*), select *Optimization* in the *Job Type* tab, in the *Method* tab set method to *Ground State Semi-Empirical Default Spin PM6*, then click *Submit* button. The program will ask you for the name of the calculation output ("log") file. Choose an easily recognizable file name and some reasonable location, for example Desktop. Let Gaussian calculation run its course. If Gaussian returns an error, check for atom collisions and invalid valences in the structure you have drawn.

4. Open the log file in GaussView (tick the *Read Intermediate Geometries* box in the file open window) and inspect the resulting molecular geometries – there would be a few dozen, starting from the geometry you have provided and ending with the energy minimum geometry. Then click *Menu / Results / Optimization* and inspect the energy and the gradient curves produced by the optimization process. Both the energy and the gradient curve should be decaying. Export both curves into text files, read the text files into a scientific plotting package and include the corresponding graphs into your report.

5. Inspect the final geometry and comment on the geometry changes that occur during the energy optimization process. Choose five or six common bond types and plot your calculated bond lengths (measure them on the optimized geometry) against the corresponding bond length in the crystallographic structure of cocaine (*cocaine.cif* file), which is available on Blackboard. Make a conclusion on the practical accuracy of the semi-empirical methods for molecular structure refinement.

G2:M1:V1 - Optimization Plot

Plots

**Total Energy**

RMS Gradient Norm
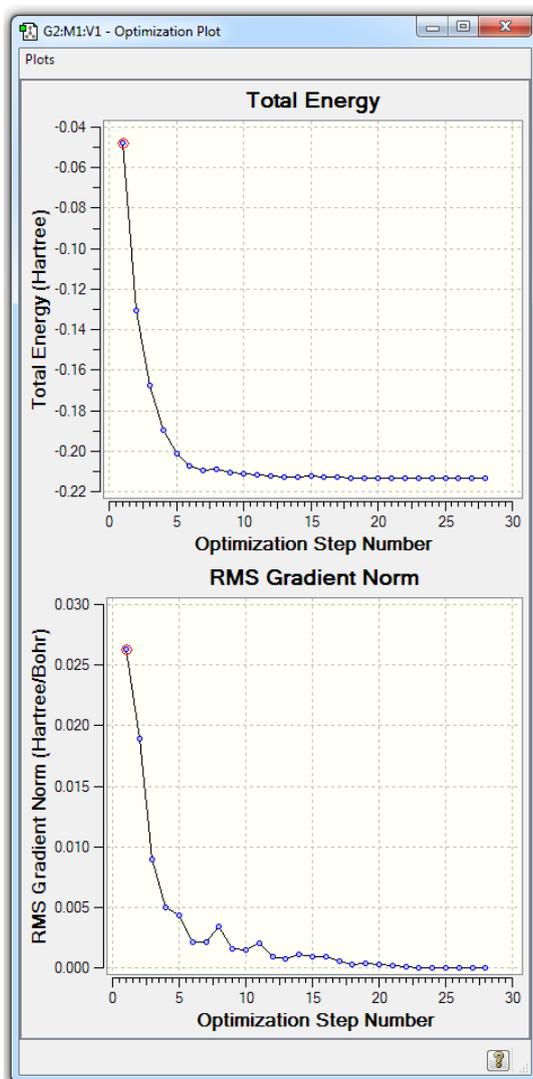
Molecular volume calculation

Open the geometry optimization log from the previous section and scroll GaussView geometry window to the last geometry. Open the interactive job setup window (*Menu / Calculate / Gaussian Calculation Setup*) and select *Energy* in the *Job Type* field (make it absolutely certain that you do it because a geometry optimisation at this level of theory can take days). Then click on the *Method* tab and select *DFT B3LYP cc-pVDZ* as the calculation method.
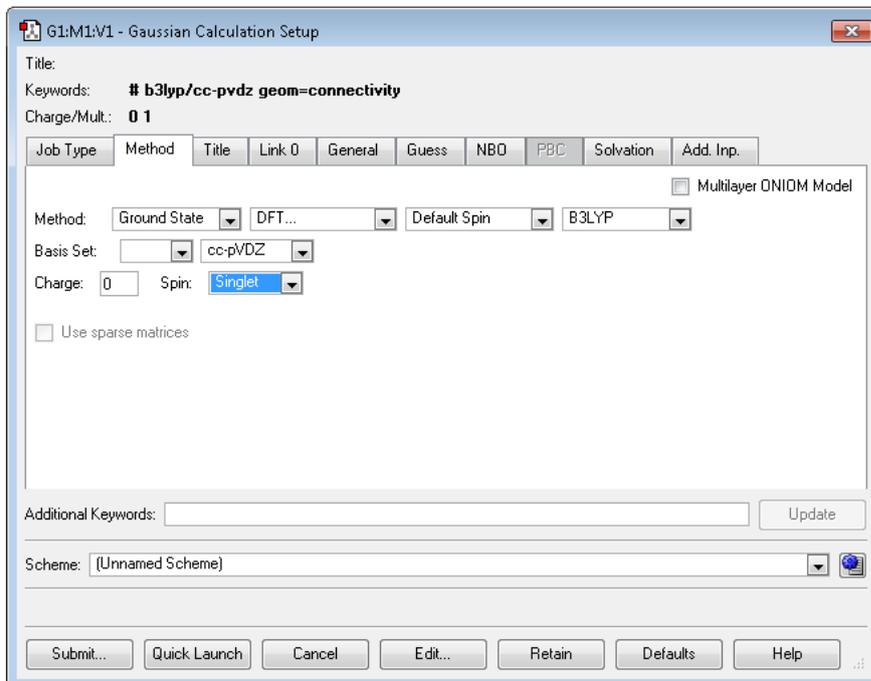
Click the *Solvation* tab and set the solvation model to *IEFPCM* and solvent to *Water*.
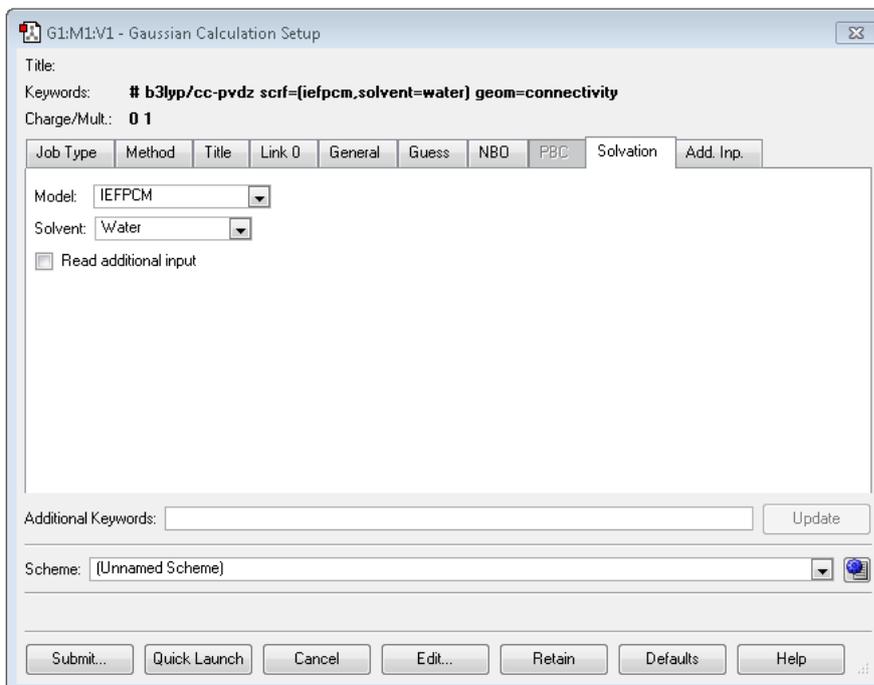
Click the *General* tab and tick the *Additional Print* box (make sure you do it, otherwise the molecular volume would not appear in the log file). Click the *Submit* button at the bottom of the window, specify log file name and location and let the calculation run its course. When the calculation finishes, open the

log file with a text editor (WordPad is a good choice on Windows systems) and scroll to the item titled *GePol: Cavity volume*. Record the molecular volume in cubic Angstroms and convert it to SI. From the molecular volume data you have obtained estimate the density of crystalline cocaine and comment on the expected accuracy of value that you get.

Report preparation

Write a 1500-word report, containing a brief introduction into the quantum mechanical methods you used for the calculation (PM6 for the geometry, PCM DFT B3LYP/cc-pVDZ for the molecular volume) and into the geometry optimization technique (gradient descent) used by the program. Briefly summarise your results and comment on the accuracy of the numbers you have obtained. Outline practical difficulties that are likely to be encountered in the experimental measurement of cocaine molecular volume and compare the estimated cost of an experimental measurement to the cost of a quantum mechanical calculation.

It is strongly recommended that you explore *LaTeX* as a way of preparing your reports and *Origin* as a way of creating scientific plots – *LaTeX* is a *de facto* standard in academic writing and *Origin* is a sophisticated scientific data analysis package. Both are something a good chemist ought to know and both are available on the standard University workstations. For personal use, *LaTeX* is freely available online for all major operating systems and *Origin* may be downloaded from the iSolutions software page.

Expectations

Given the nature of this assignment, there is no assessment of pre-labs, interim report, lab book or measurement data records. The mark for this practical will be based entirely on the submitted report. The following marking scheme will be applied to reports:

Feature	Maximum mark out of 100
Introduction: objectives and problem setting	5
Introduction: description of methods	10
Molecule drawing in GaussView	5
Energy and gradient convergence plots	10
Bond length plot (X-ray against PM6)	5
Bond length accuracy discussion	15
Molecular volume and density figures	10
Molecular volume and density accuracy discussion	15
Report: quality of writing	10
Report: quality of typesetting	5
Report: quality of references	10

Word count deviation in excess of ±10% from 1500 words will incur a 10-point penalty. At least five references are expected. References should contain academic journal articles as well as books. Web links in the reference list will incur a 5-point penalty.

The completed report for this practical must be submitted online as a single PDF file by the deadline indicated in the course coordinator's email. Penalties will be applied for late submission. Submissions more than five working days late will receive zero marks.