

Ollscoil na hÉireann, Gaillimh
National University of Ireland, Galway

SUMMER EXAMINATIONS, 2002

THIRD SCIENCE EXAMINATION

CH314 CHEMINFORMATICS AND VALIDATION

Professor J. Evans
 Professor R.N. Butler
 Professor M.J. Hynes
 Professor P. McArdle
 Dr. J. Simmie
 Dr. N.W.A. Geraghty

Time allowed: **Two** hours

Attempt **two** questions from each section

Use **separate answer books** for Sections A and B

Marks: All questions carry equal marks

Section A

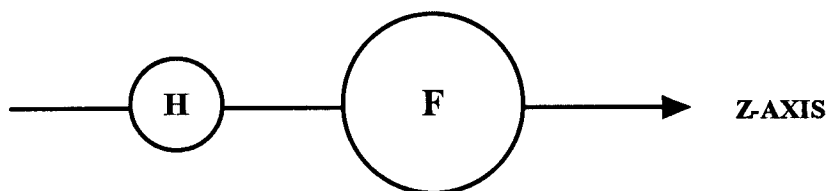
1. Answer (a) and (b).

- (a) Tetranitrocubane, $C_8H_4(NO_2)_4$, has recently attracted interest as a potential high-energy fuel and/or explosive. Outline briefly the computations that you would make to see whether tetranitrocubane has that potential.

[10 marks]

- (b) Geometry optimisation of the hydrogen fluoride molecule with the semi-empirical method AM1 revealed five molecular orbitals as:

		MO #1	MO #2	MO #3	MO #4	MO #5
F	2S	0.92860	0.31006	0.00000	0.00000	-0.36771
F	2PX	0.00000	0.00000	1.00000	0.00000	0.00000
F	2PY	0.00000	0.00000	0.00000	1.00000	0.00000
F	2PZ	-0.07750	0.75380	0.00000	0.00000	0.75352
H	1S	0.17763	-0.43364	0.00000	0.00000	1.00800



What do the terms: (i) *geometry optimisation*, and (ii) *semi-empirical* mean?

[10 marks]

Sketch one of these orbitals and describe it in your own words.

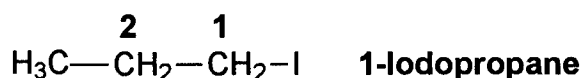
[5 marks]

Turn over

2. Answer **each** of the following;

- (i) Describe the type of information that is available on the Cambridge Crystallography Data Base and on the Protein Data Bank. [4 marks]
- (ii) If you were asked to provide atomic coordinates for the active site of lysozyme, which would be suitable for use in modelling the interaction with potential lysozyme blockers, what criteria would you use to select suitable data? [4 marks]
- (iii) What is the difference between the cost of using these two data bases? [2 marks]
- (iv) Name three important file formats used for atomic coordinate data. [3 marks]
- (v) When a file has been downloaded what is the simplest way to tell if an atom coordinates are in fractional or Cartesian coordinates? [4 marks]
- (vi) What type of molecular orbital calculations are suitable for transition metal complexes? Give a short explanation of your answer. [8 marks]

3. Describe **in general terms** how you would carry out the systematic conformational analysis of 1-iodopropane using molecular modelling software such as *Spartan*.



[10 marks]

Sketch the potential energy diagram that would be obtained as a result of rotation about the C₁-C₂ bond in 1-iodopropane. Draw Newman projection formulae for **all** the minima and maxima. [9 marks]

Discuss the factors affecting the energy of the minima and maxima. [6 marks]

4. Write notes on **each** of the following:

- (a) Conformational searching. [7 marks]
- (b) The evaluation of angle strain and bond strain using molecular mechanics. [6 marks]
- (c) The structure of **any two** conformations of cyclohexane and why they differ in energy. [6 marks]
- (d) The factors affecting the conformation of unbranched alkanes and how these are affected by the length of the chain [6 marks]

Turn over

Section B

5. Outline the procedures necessary to validate an analytical method for use in a pharmaceutical plant selling product into the U.S. [25 marks]
6. Given the accuracy and reliability of modern equipment and the use of powerful software, why is validation still a necessary and integral part of pharmaceutical manufacturing? [25 marks]
7. Write an essay on cleaning validation. [25 Marks]
8. Answer (a) and (b)
 - (a) In the context of electronic data and information, explain what you mean by the following terms (i) 'closed systems' (ii) 'open systems' and (iii) electronic signature'. [6 marks]
 - (b) Describe the main features of 21 CFR 11. [19 marks]