



Autumn Examinations 2010 / 2011

Exam Code(s)	3BS9, 3BPM
Exam(s)	Third year Chemistry and Third year Biopharmaceutical Chemistry
Module Code(s)	CH328
Module(s)	Molecular Modeling and Drug Design
Paper No.	
External Examiner(s)	Professor Paul Seakins
Internal Examiner(s)	Professor Paul V. Murphy Professor Leif A. Eriksson Professor Rob Woods
<u>Instructions:</u>	Answer <u>four</u> questions: <u>One</u> from each Section
	All questions carry 100 marks
Duration	2 hours
No. of Pages	2
Discipline(s)	Chemistry
Requirements	None

Section A

Molecular Mechanics / Structure (answer one of the two questions – 100 marks)

1. Which five terms make up a general Molecular Mechanics Force Field?
2. Computer simulation methods allow us to study the energetics and dynamics of biomolecular systems such as proteins. One of the most important steps in the set-up of a molecular simulation is the choice of an accurate 3D starting structure of the protein. Structures determined by X-ray crystallography are generally a good choice.
 - a. Explain why it is preferable to start molecular simulations from high-resolution 3D structures (Suggestion: you can draw a 2D conformational energy profile to highlight the concept of local energy minima also known as energy “traps”).
 - b. What online archive allows you to search and retrieve protein 3D structures?

Section B

Quantum Chemistry (answer one of the two questions– 100 marks)

3. Explain, in a few sentences, each of the following terms:
 - a. Transition state
 - b. QM/MM
 - c. PM3
 - d. Hamiltonian
 - e. Molecular orbital
4. Explain three different ways in which solvent effects can be taken into account in computational modeling, and what advantages/disadvantages they have.

Section C

Bioinformatics (answer one of the two questions– 100 marks)

5. Explain the main features of Homology modelling of a protein structure, starting from the gene sequence.
6. Molecule **A** has been designed to bind protein **P** and to prevent (or inhibit) the interaction between protein **P** and its natural ligand, molecule **B**. What thermodynamic function would tell you if molecule **A** is a competitive inhibitor relative to molecule **B**? Name two computer simulation methods that you can use to obtain such thermodynamic function.

Section D

Molecular Dynamics Simulations (answer one of the two questions– 100 marks)

7. Monte Carlo (MC) and Molecular Dynamics (MD) are two different simulation techniques. Both MD and MC can be used to explore the conformational space of biomolecules. Briefly outline the main characteristics of these two techniques and discuss the aspects in which they differ.

8. What are the fundamental steps in the set-up of a MD simulation of a generic biomolecular system? Discuss briefly the significance of each step.