BIRKBECK COLLEGE

(University of London)

Advanced Certificate in the Principles of Protein Structure

Date: Thursday 2nd September 2010

Time: 3 hours

Start time as per instructions to local exam centre

Students will be expected to answer 6 of the 10 short questions in section A, and 4 of the 8 long questions in section B. They will be advised to spend 1 hour on section A and 2 hours on section B.

Short questions are worth 6 Marks.

Long questions are worth 18 Marks.

Each question must start on a new page and the question number written at the top of each sheet.

Section A: Ten Short Questions

Six questions only to be attempted from section A

(Suggested time 10 minutes on each)

A1. Answer all parts;

a) What is the CORN Law and why is Gly the exception to this Law? {2 Marks}

b) Why is Pro unique conformationally and so acts as a helix breaker? {2 Marks}

c) Name the two amino acids that contain sulphur. How could they assist in stabilising a tertiary structure? {2 Marks}.

A2. Draw schematically, including any hydrogen bonding, the following;

a) Parallel and anti-parallel beta sheets. {2 Marks}

b) A trans- and cis-peptide. {2 Marks}

c) Left handed alpha helix and the dipole. {2 Marks}.

A3. Explain how the oligomeric structure of haemoglobin enables it to release oxygen in muscle tissues. {6 Marks}.

A4. Draw topology diagrams for;

a) A TIM barrel. {3 Marks}

b) A single gamma crystallin domain. {3 Marks}.

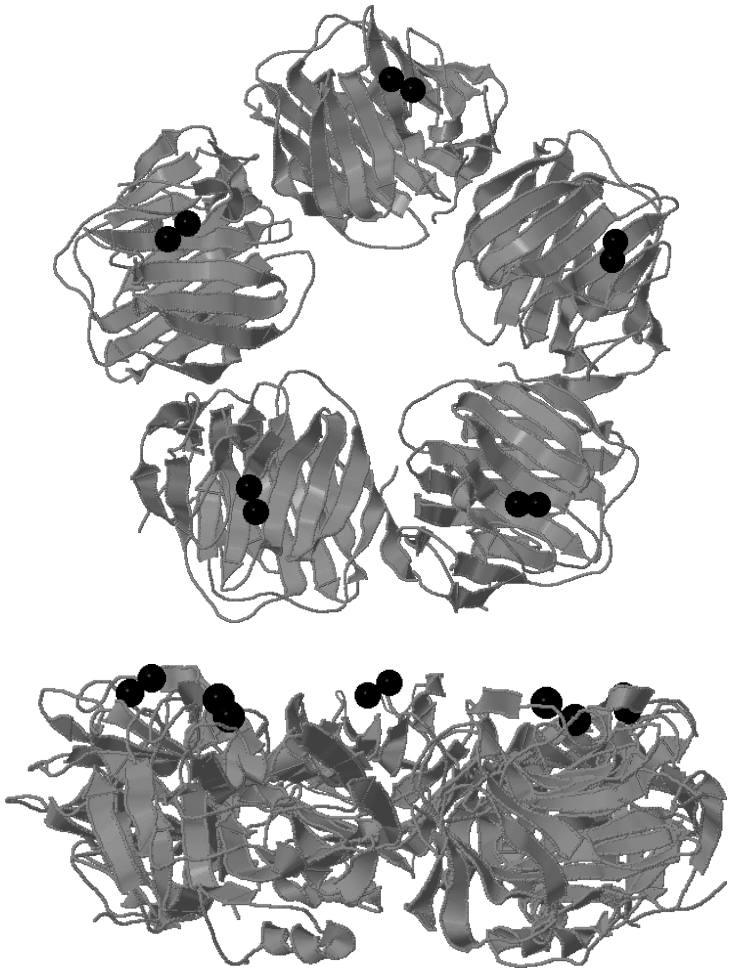
Section A: Continued

A5. The figure below shows two views of an oligomeric protein comprised of identical chains. The black spheres depict calcium atoms.

a) What is the quaternary structure of this oligomer? {1 Mark}

b) What is the point group symmetry of the oligomer? {2 Marks}

c) Indicate how the symmetry of this oligomer impacts on its interaction behaviour. {3 Marks}.



Section A: Continued

A6. a) Give two examples of types of information that you would expect to gain from examining a multiple alignment of polypeptide sequences from a family of proteins. {2 marks}

b) List one amino acid pair that you would expect to be associated with a high score in a PAM or BLOSUM matrix (i.e. that can be "switched" during evolution with little or no functional change to the protein) and one amino acid pair that you would expect to be associated with a low score. Explain in one sentence each the reasons for your choices using the chemical structures of the side chains concerned. {4 marks}.

A7. Describe how a protein can interact with DNA. {6 Marks}.

A8. Answer all parts;

a) Describe the topology of a G-protein coupled receptor and its relationship to the plasma membrane. {3 Marks}

b) Where does the G-protein bind? {1 Mark}

c) Name two types of signalling ligands that activate the receptor. {1 Mark}

d) Describe briefly the structure of one signaling ligand. {1 Mark}.

Section A: Continued

A9. Describe the properties of the hydrogen bond and indicate the most common examples found in proteins. {6 Marks}.

A10. Describe the involvement of the human immune system in the development of;

a) an allergic reaction {3 Marks}

b) an autoimmune disease {3 Marks}

and in each case, give one example of a molecule that gives rise to the abnormal response.

Section B: Eight Long Questions

Four questions only to be attempted from section B

(Suggested time 30 minutes on each)

B11. Define in one sentence each the terms “genome” and “proteome”. {2 marks}

Explain in detail how bioinformatics is used to study the genome and proteome of a pathogenic bacterium such as *Mycobacterium tuberculosis*, and what scientists can expect to learn from such an analysis. Name and describe very briefly some of the bioinformatics tools that are used in such an analysis. {12 marks}

List two characteristics of a bacterial protein that make it a good drug target, and give a reason for each choice. {4 Marks}.

B12. Describe the role of the following during the synthesis and life cycle of a protein molecule {3 marks each}:

ATG start codon

Spliceosome

Ribosome

Hsp60 chaperonin

Ubiquitin

Proteasome

Section B: Continued

B13. a) Survey the range of inner and outer membrane protein structures that form pores or channels {10 Marks}

and

b) In the case of the inner membrane pores or channels indicate how the different structures contribute to their role of passing ligands across membranes. {8 Marks}.

B14. a) Describe the active sites of a serine protease and an aspartic protease {6 Marks each}

and

b) Describe how inhibition of an aspartic protease is used to make a drug to combat HIV. {6 Marks}.

B15. Discuss the structure and function of Haemagglutinin and its role in influenza infection. {18 Marks}.

B16. Describe in detail, with diagrams if necessary, the structures of both the MHC Class I and Class II molecules. Pay particular attention to the similarities and differences between the structures, and the way in which each type of molecule binds its peptide antigen. {12 Marks}

Making reference to your answer above, where necessary, describe the process through which MHC molecules present peptides on the surface of antigen-presenting cells and how that may lead to an immune response. {6 Marks}.

Section B: Continued

B17. For the 20 usual L-amino acids found in proteins give the following information for each of them;

a) The three letter code and the amino acid name. {6 Marks}

b) The chemical nature of each amino acid and draw the structure of the side chain. {12 Marks}.

B18. Discuss the classification of protein folds used in the CATH database and give one example for each type;

a) Mainly Alpha. {4.5 marks}

b) Mainly Beta. {4.5 marks}

c) Mainly Alpha-Beta. {4.5 marks}

d) Small Proteins. {4.5 marks}.