BIRKBECK COLLEGE

(University of London)

Advanced Certificate in the Principles of Protein Structure

Date: Wednesday 17th September 2008

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 fresh page and the question number written at the top of the sheet.

Section A: Ten Short Questions

Six questions only to be attempted from section A

(Suggested time 10 minutes on each)

A1. Illustrate each of the following;

i) Cis and trans prolines (2 marks).

ii) Tyrosine side-chain, indicating the Greek names for all the atoms (2 marks).

iii) The 3_{10}-Helix (2 marks).

A2. Give both the full amino acid name and the single letter code for the following amino acids;

i) Gly (1 mark).

ii) Arg (1 mark).

iii) Phe (1 mark).

iv) Trp (1 mark).

v) Ser (1 mark).

vi) Met (1 mark).

Section A: Continued

A3. Describe briefly the following;

i) Social software (2 marks).

ii) Blog (2 marks).

iii) Wiki (2 marks).

A4. Outline the main criteria used for classification of protein domains in the CATH protein database.

A5. Describe what is meant by the information that two proteins are;

i) homologs (1.5 marks).

ii) orthologs (1.5 marks).

iii) paralogs (1.5 marks).

What can be deduced about the structures and functions of a pair of proteins that are orthologs (1.5 marks)?

A6. Describe the sequence repeat in collagen and indicate how it contributes to the formation of a parallel triple helix.

A7. What is the function of eukaryotic RNA polymerase II? Name some of the other protein components that it interacts with in order to perform this function.

Section A: Continued

A8. In one sentence define the characteristics of the following;

i) Enzymes (1.5 marks).

ii) Transcription factors (1.5 marks).

iii) Receptors (1.5 marks).

iv) Transport proteins (1.5 marks).

A9. Describe or draw the structure of a porin molecule. What type of organisms are porins found in, and where are they found within those organisms? Briefly, what is their function?

A10. Draw a schematic diagram of the structure of the immunoglobulin IgG, labelling the major secondary structure component of each domain. Mark on your diagram the location of the antigen binding site. What is unusual about the sequences that bind antigen?

Section B: Eight Long Questions

Four questions only to be attempted from section B

(Suggested time 30 minutes on each)

B11. Discuss protein tertiary structure in relation to the underlying protein secondary structure elements.

B12. Name three common ligands that interact with proteins. Describe the structure of two protein domains of different structure that interact with different ligands, and name those ligands. Indicate a function for each protein bound to its ligand.

B13. Draw a diagram of an asymmetric object (to represent a protein domain). Show how it can be arranged as a dimer with a 2-fold axis. Choose an example of a protein dimer that has a catalytic site close to the 2-fold axis and describe how it works. Give an example of a protein that has four polypeptide chains, describe its symmetry, and indicate its function. Give an example of a protein that has sixty polypeptide chains, describe its shape and symmetry, and indicate its function.

B14. Outline the role of molecular chaperones during the lifecycle of proteins within a human cell (13 marks). How are proteins degraded (5 marks)?

Section B: Continued

B15. i) Explain in detail the inter-atomic forces involved in the formation of a hydrogen bond. Sketch a typical hydrogen bond between two water molecules, marking on it the range of inter-atomic distances and angles expected in hydrogen bonds.

ii) List the amino acids in each of four categories; those with side chains containing hydrogen bond donors only, acceptors only, both donors and acceptors, and neither. In globular proteins, where are side chains involved in hydrogen bonding more likely to be found, and why?

B16. Discuss the DNA-binding protein families and the structure of the DNA-binding motifs. Describe the helix-turn-helix motif family in more detail using bacteriophage lambda cro repressor, the trp repressor and catabolite gene activator protein (CAP).

Section B: Continued

B17. i) Describe in detail the structure and function of mammalian rhodopsin and name its ligand.

ii) Mutations in rhodopsin cause many cases of retinal degeneration and blindness. Speculate, with reasons, about the location and type of mutations in this protein that are most likely to cause disease.

iii) Proteins with the same topology as rhodopsin form a large and ubiquitous family with the same generic function; proteins in this family are targets for many useful drugs. Name this family and the protein complex it binds to, and describe the generic function of the protein family. Name one protein in this family with a known three-dimensional structure and one disease that drugs which target this protein are used for treatment.

B18. What is a subunit vaccine, and how does it differ from more conventional vaccines? Explain in detail how the bioinformatics and structural biology of the immune system are being used to help select proteins and peptides that are good candidates for inclusion in subunit vaccines, relating your explanation where possible to the molecular processes involved in immune function.