Birkbeck College

University of London

School of Crystallography

Advanced Certificate in Principles of Protein Structure

Date: Thursday 25th September 2003

THREE HOURS TOTAL

Answer **FOUR** questions only (45 minutes each, total three hours).

Write your answer for each question in a separate answer book.

Record both the question number and your examination number on the cover of **EACH** question book used.

Make sure that each question number is clearly marked on each answer page in the book.

1. Name one amino acid in each of these categories:

i) Very hydrophobic
ii) Part hydrophobic and part hydrophilic
iii) Very hydrophilic

Explain briefly how a hydropathy plot is calculated from a protein sequence. What might this tell you about the location of the protein within a cell?

Sketch roughly the type of hydropathy plot that you would expect to see for a protein in the G-protein coupled receptor family. Label the sequence positions where you would expect to find transmembrane helices.

2. What does it mean to say that two proteins are homologous? How do homologous proteins differ from analogous ones?

Give a detailed description of how the program BLAST can be used to select sequences from a database that are similar to a given protein sequence. What output does BLAST produce, and how is it interpreted?

What other programs and tools can you use to determine which of the more marginal "hits" from a BLAST run are truly homologous to your original protein? Give reasons for your choices.

3. Discuss the role of hydrogen bonds, salt bridges, hydrophobic interactions and disulphide bridges in protein structure.

4. In 1902 Emil Fischer and Hofmeister demonstrated that proteins are polypeptides. What are the 20 building blocks that make up these polypeptides? Draw each, indicate their individual chemical characteristics and suggest how this would affect their location in a folded protein.

5. Discuss primary, secondary, tertiary and quaternary structure using the structure of haemoglobin as an example; and discuss how tertiary and quaternary structure change in the haemoglobin allosteric mechanism.

6. Draw a Ramachandran plot indicating the areas for right-handed alpha helix, beta-sheet and left handed alpha helix.

Draw the molecular structure for each listed below;

i) Type I and II beta turns
ii) Zinc finger
iii) Beta-alpha-beta motif – and comment in two or three sentences about its "handedness"
iv) Greek Key
v) EF hand

7. Discuss the architecture of the icosahedral viruses in relation to the theory of quasi-equivalence and the triangulation number, T.

8. Discuss, with illustrations, the components of thin and thick filaments of skeletal muscle at the molecular level. Show how these structures act together as molecular motors during the contraction cycle.

9. Discuss the principles involved in the packing of secondary structures within proteins.

10. Discuss the increasing structural complexity from glucagon, Rop, ferritin and myohemerythrin, to the membrane proteins bacteriorhodopsin and the L and M subunits of the photosynthetic reaction centre of the purple bacterium *Rhodopseudomonas*.

11. Describe the structure of the IgG and the Immunoglobulin fold. What are the three main classes of Antibody binding sites found and what molecular forces are involved in antigen binding?