1 Reading assignment 2. Introduction.

Read the Introduction (pp. XVI-XIX) and answer the following:

1. Name five physiological processes where proteins participate.

   Metabolism, transport, immune response, signal transduction and cell cycle.

2. What is the most common cause of endogenous diseases?

   Malfuctioning of proteins.

3. How do life-saving drugs act?

   By interfering with the action of a faulty or foreign protein by keeping it from performing its function. It competes directly with the substrate occupying the site where action occurs, or it binds in a different location of the protein surface, modifying the geometry of the active site and making the protein unable to perform its biochemical function.

4. What is the traditional process of drug discovery? What is the success rate of this process?

   By trial-and error, testing thousands of randomly selected compounds for their ability to interfere with the function of a protein or with a biological process. The rate of success of this process is rather low, it is estimated that only one out of a thousand active molecules makes it to the pharmacy bench.

5. How can the knowledge about proteins aid in the process of drug development?

   Differences between the genetic background of individuals might cause the protein of a specific individual to be less sensitive to the effect of a drug or cause the drug to have side effects. If we had a deep structural understanding of our complete proteins list, we could screen drugs in a virtual computer simulated system and detect a substantial proportion of these problems beforehand, increasing substantially the effectiveness of medical approaches.

6. Name two experimental methods for finding the precise arrangement of every atom of a protein. Do they work for every protein?

   X-ray crystallography and NMR spectroscopy. First one requires the protein or the protein complex under study to form a reasonably well ordered crystal (feature not universally shared by proteins). And the second needs proteins to be soluble and there is a limit to the size of protein that can be studied.

7. What is the topic of the book?

   The learning from the analysis of known protein structures and how this knowledge can be used to attempt the prediction of unknown protein structures. However, the accuracy of a predicted model is not comparable with that achievable by experimental methods, so it is important to understand their limitations.