

Unit 7: Structural and Computational Biology

Long Questions

DESCRIPTIVE QUESTIONS

APPLICATIONS OF STRUCTURAL BIOLOGY

Q1. Define structural biology, describe its applications.

Ans. Definition: Structural biology deals, with the study of three dimensional (3D) structures of macromolecules (including proteins and nucleic acids) at atomic levels.

Importance: It provides the detailed information about the structure of **biomolecule**, its **functions**, **dynamics** and **interaction with ligands** and other macromolecules.

Applications of structural biology: Structural biology has a wide range of applications especially in the field of medical research. Some of these are discussed here.

1. Determining the Active sites and Domains

Structural biologists can **determine the three-dimensional (3D) structures** of macromolecules such as proteins and nucleic acids. The 3D structures reveal the exact location, shape, and environment of the active sites and **different domains** (distinct structural units with independent functions) of macromolecules.

Example

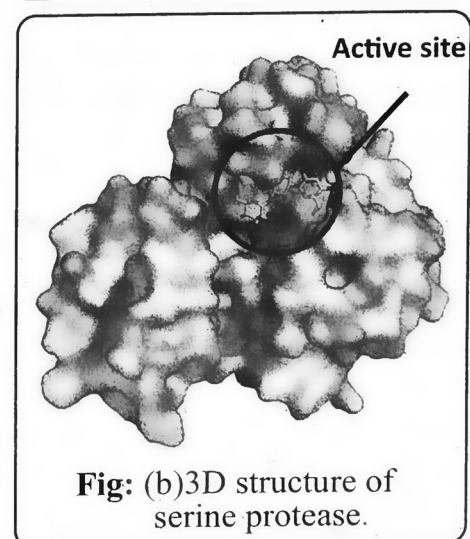
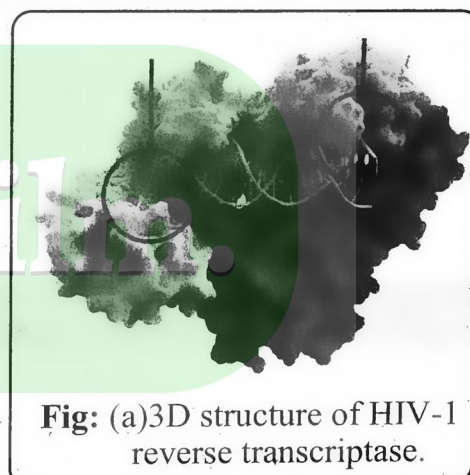
For example, structural studies of the enzyme **HIV-1 reverse transcriptase** have identified its polymerase domain (which synthesizes DNA).

RNase H domain (which breaks down the RNA strand of RNA-DNA hybrids).

Significance

- Knowing the location and structure of these domains has helped in the **design of antiviral drugs** that specifically target them.
- Similarly, the structure of serine proteases

★ **Note:** All questions and paragraphs marked with a star ★ are explanations of the Box Information provided in the textbook.



reveals its well-defined **active site**, which is responsible for breaking down peptide bonds.

2. Identifying Drug Targets: Structural biology helps scientists find the right place on a disease-causing molecule where a drug can work. These places are usually proteins and are called **drug targets**. By studying the 3D shape of these proteins, scientists can find specific spots where a drug can attach and stop the protein from working.

Example

For example in COVID-19, scientists used **structural biology** to study the spike protein of the coronavirus (SARS-CoV-2). This protein helps the virus to enter human cells.

Significance

By knowing its 3D structure, scientists identified it as a **drug target**. Thus, they designed vaccines and medicines that block the spike protein, preventing the virus from infecting more cells.

3. Identifying Host-Pathogen Interactions

Structural biology also helps in understanding how **pathogens** (like viruses or bacteria) **interact with the host's body cells**. This is called **host-pathogen interaction**.

By studying the 3D structures of both the pathogen and the host cell proteins, scientists can see how the pathogen attaches to and enters the host cell, and which molecules are involved in the process.

Example

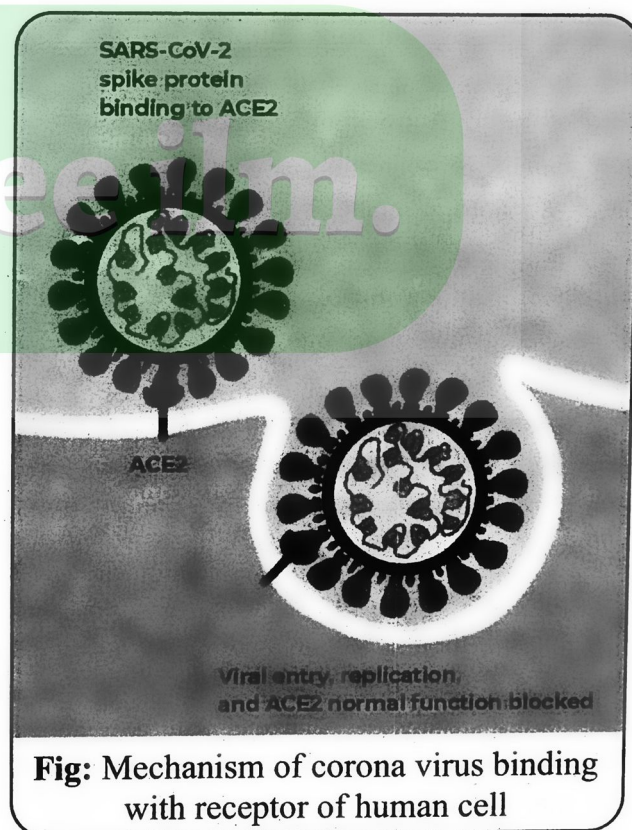
For example, structural biologists studied the **spike protein of coronavirus**, which sticks out from the surface of the virus. They also looked at a protein on **human cells** that acts as **receptor** of virus spike protein. So, the scientists discovered exactly how the virus enters human cells.

Significance

This information was vital in developing the drugs that can bind with receptor proteins. Such drug inhibits the interaction of the virus with the receptor and consequently blocks the entry of virus into the host cells.

4. Identifying Protein Misfolding

The functionality of proteins depends on the correct folding into three dimensional shapes. Several diseases (including cystic fibrosis, Parkinsons, Alziemer's) originate due to **incorrect folding of proteins**. Structural biology provides understanding of intricate folding pathways and how misfolding leads to the diseases.



X-RAY CRYSTALLOGRAPHY

Q2. Write a note on principle and working of x-ray crystallography.

Ans. Discovery: X-ray crystallography was developed in 1912 by **William Henry Bragg** and **William Lawrence Bragg**. They were awarded 1915 Nobel Prize in Physics for their work. Since then it has been **used to analyse the diverse substances** including minerals, salts, metals, proteins, carbohydrates, nucleic acids and vitamins.

Principle

In this technique, **x-rays beam strikes crystal atoms** and molecules in the crystals diffract the x-rays beam in specific directions. From the angles and intensities of diffracted beams, a **3D picture of electron density** within the crystals are produced. The electron density is exploited to create 3D structure of the molecule.

Working of X-ray Crystallography

In order to understand the working of X-ray crystallography. Let us take the example of protein structure determination. The method can be divided into **following steps**.

(i) Protein Crystallization

Protein crystallization means turning a **purified protein into a solid crystal form**. Crystals are needed because they arrange protein molecules in a regular, repeating pattern, which is important for getting a clear image during the X-ray process. To make crystals, scientists slowly **mix the protein with special solutions** that cause the protein molecules to stick together in an orderly way. This process can take hours, days, or even weeks. It often requires **careful control of temperature, pH, and salt concentration**. Once a clear and stable protein crystal is formed, it can be used in the next steps.

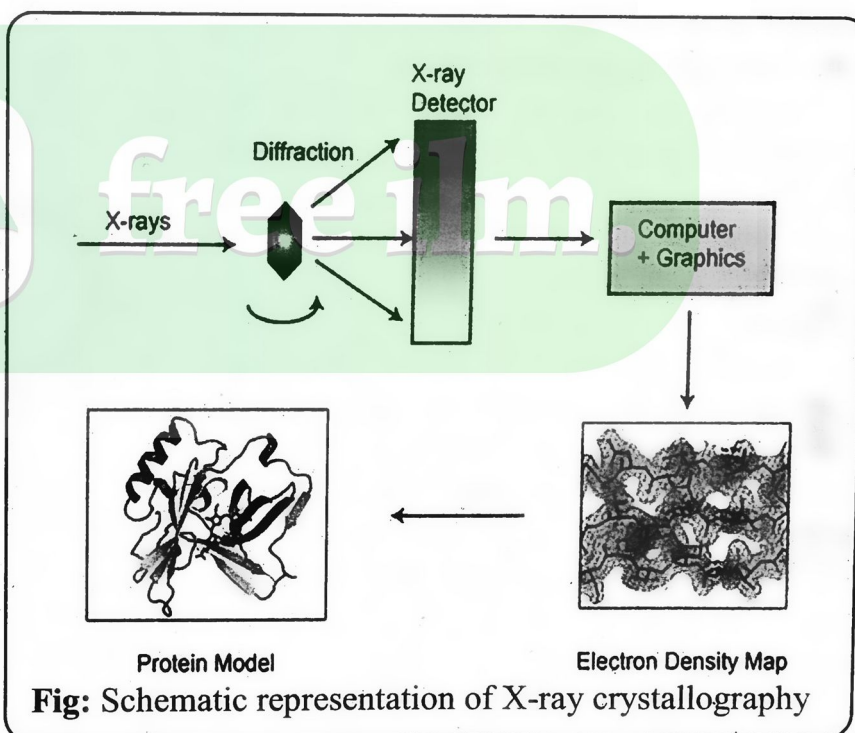


Fig: Schematic representation of X-ray crystallography

(ii) Production of a diffraction pattern: Once a good quality crystal is formed, it is mounted on the x-ray machine. The x-rays beam is bombarded at the crystal at various angles. The atoms in the crystal diffract the x-rays beam and a diffraction pattern (which is a series of spots) is created on the detectors.

(iii) Creating density map: The angles and intensities of these spots contain information about the arrangement of atoms in the crystal. Diffraction pattern is used to make a density map.

(iv) **Determination of protein structure:** Then the data is analyzed mathematically by using computational programs. These calculations transform data into the 3D structure of protein.

COMPUTATIONAL BIOLOGY

Q3. Define computational biology. Describe its major areas and applications.

Ans. Definition

Computational biology is an interdisciplinary field that uses computational techniques and tools to solve biological problems. It **integrates** knowledge from **biology, computer science, mathematics, and statistics** to analyze and interpret biological data.

Importance of Computational Biology

The importance of computational biology lies in its ability to handle large datasets, uncover hidden patterns, and generate predictive models that can lead to new biological insights and applications.

Major areas

In the computational biology include:

(i) **Genomics** is the study of genomes, which are the complete set of DNA within a single cell of an organism. Genomics involves **sequencing, assembling, and analyzing** the **function and structure of genomes**. It helps in understanding genetic variations, gene function, and evolutionary relationships.

(ii) **Proteomics** is the large-scale study of proteins, including their structures and functions. Proteins are essential molecules that perform many functions within organisms.

Proteomics **aims to map the entire set of proteins** (the proteome) produced by an organism and understand their interactions and roles in cellular processes.

(iii) **Bioinformatics** is the application of computer technology to manage and analyze biological data. Bioinformatics tools and techniques are used to store, retrieve, and analyze DNA, RNA, and protein sequences.

Applications of Computational Biology

Though computation biology has vast application, some of these are discussed here.

(i) **Drug Discovery:** Computational biology helps in identifying potential drug targets and simulating the effects of drugs on biological systems. It accelerates the drug discovery process by predicting how drugs interact with proteins and other molecules.

(ii) **Genetic Research:** By analyzing DNA sequences, computational biology helps identify genetic variations associated with diseases. It aids in understanding the genetic basis of diseases and can lead to the development of personalized medicine.

(iii) **Evolutionary Biology:** Computational tools are used to compare genetic information across different species, helping to reconstruct evolutionary relationships and understand the process of evolution.

Q4. What are databases in biology? Briefly describe key databases of computational biology.

Ans. Databases: In biology, databases are **organized collections of biological data**, including **genetic sequences, metabolic pathways, protein structure** and other related information.

Key Databases: Here are some of the key databases used to analyze nucleic acid and proteins.

1. GenBank:

It is a comprehensive public **database of nucleotide sequences and supporting bibliographic and biological annotations**. It provides access to a vast repository of DNA sequences from various organisms, facilitating genetic research and comparative genomics.

GenBank: <https://www.ncbi.nlm.nih.gov/nucleotide/>

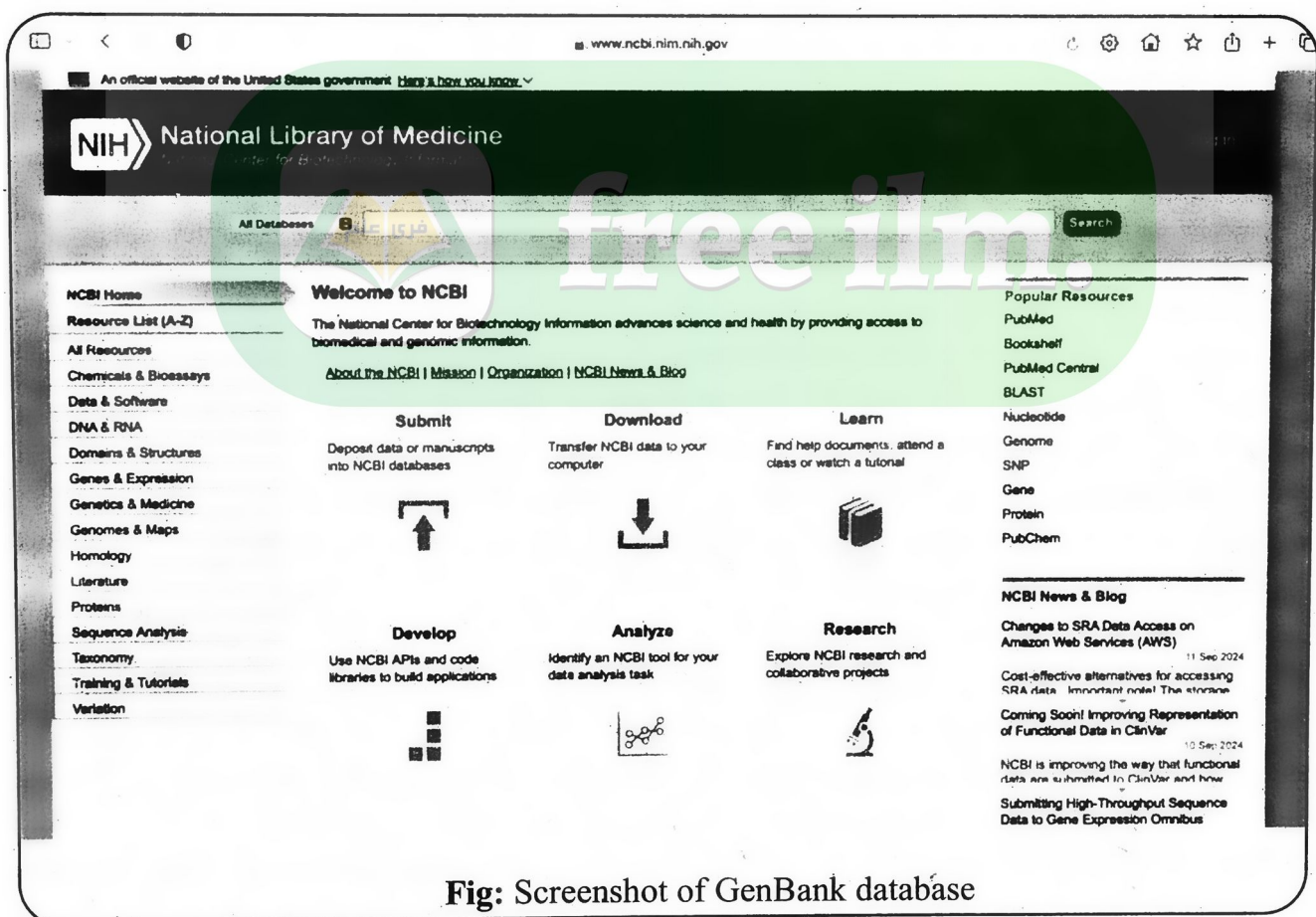


Fig: Screenshot of GenBank database

2. Protein Data Bank (PDB)

This database provides **3D structural data of large biological molecules**, such as proteins and nucleic acids. It is important for studying the structures of macromolecules, understanding their functions, and designing drugs that target specific protein structures.

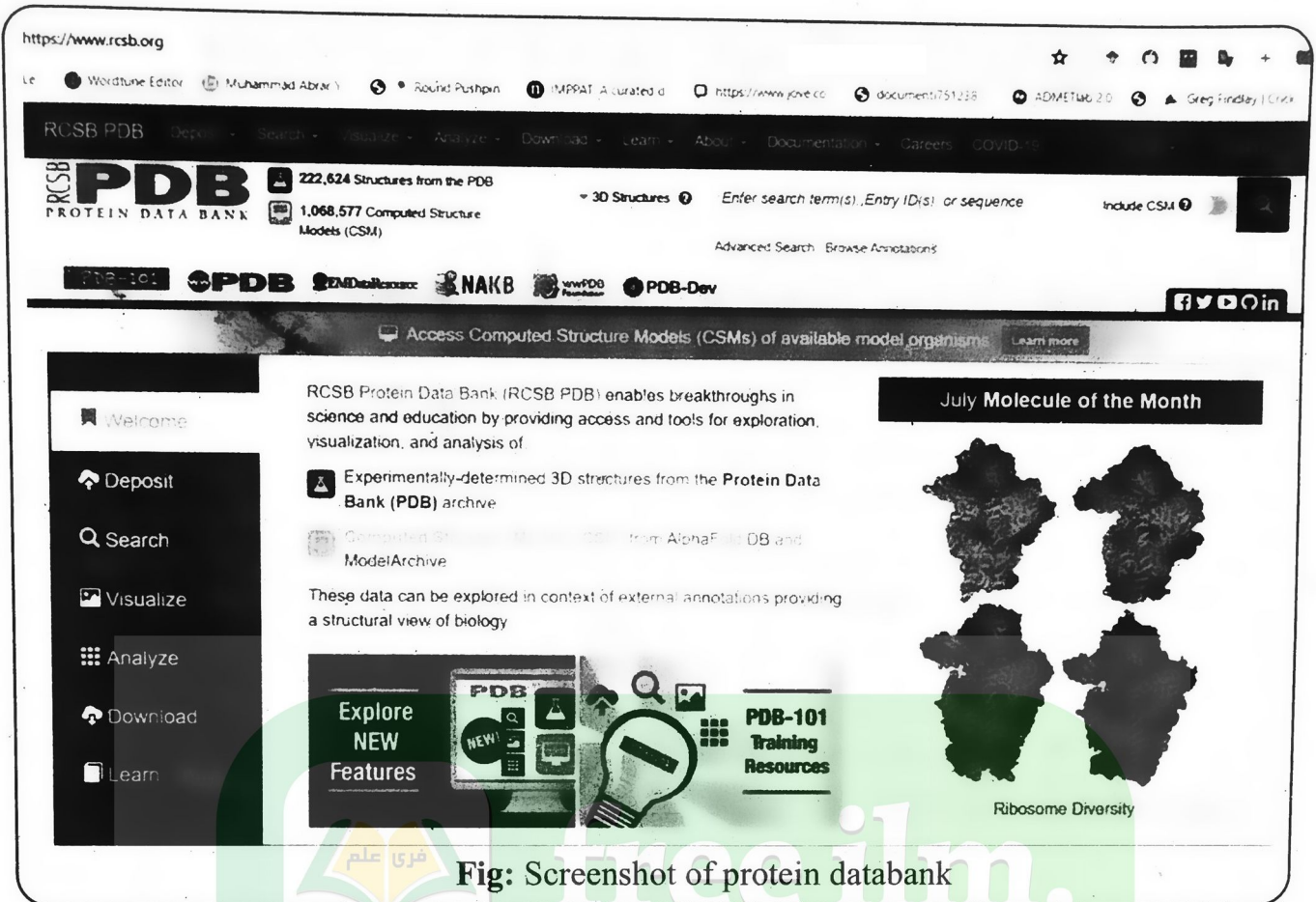


Fig: Screenshot of protein databank

3. Ensembl

It is a **genome browser** providing information on genome sequences, gene models, and comparative genomics for various species. Ensembl helps to access and visualize genomic data, supporting studies in genomics and evolutionary biology.

Q5. Describe some key algorithms being used in data analysis in biology.

Ans. Algorithms: In biology, algorithm refers to a systematic and step by step computational procedure or set of rules designed to solve specific biological problems or to analyze data.

Key Algorithms

The following are the algorithms being in data analysis.

1. BLAST (Basic Local Alignment Search Tool)

- It is used for comparing primary biological sequence information, such as the **amino-acid sequences** of proteins or the **nucleotides of DNA sequences**.
- It helps identify homologous sequences, predict functions of unknown genes, and study evolutionary relationships.

2. FASTA: It is a sequence alignment tool that compares a query sequence to a database of sequences to find regions of similarity. It is used for searching protein and nucleotide databases, identifying sequence homology, and analyzing sequence alignments.

SEQUENCE AND STRUCTURAL HOMOLOGY

Q6. What is sequence homology? Describe its categories and applications?

Ans. Sequence homology: Sequence homology refers to the similarity between DNA, RNA, or protein sequences due to **shared ancestry**.

Categories of homologous sequences

Homologous sequences have evolved from a common ancestral sequence and can be categorized into two main types:

- i) **Orthologs:** Sequences in **different species** that originated from a common ancestral gene during speciation. Orthologs often retain the same function across species.
- ii) **Paralogs:** Sequences within the **same species** that originated from gene duplication. Paralogs can evolve new functions even if they originally arise from the same ancestral gene.

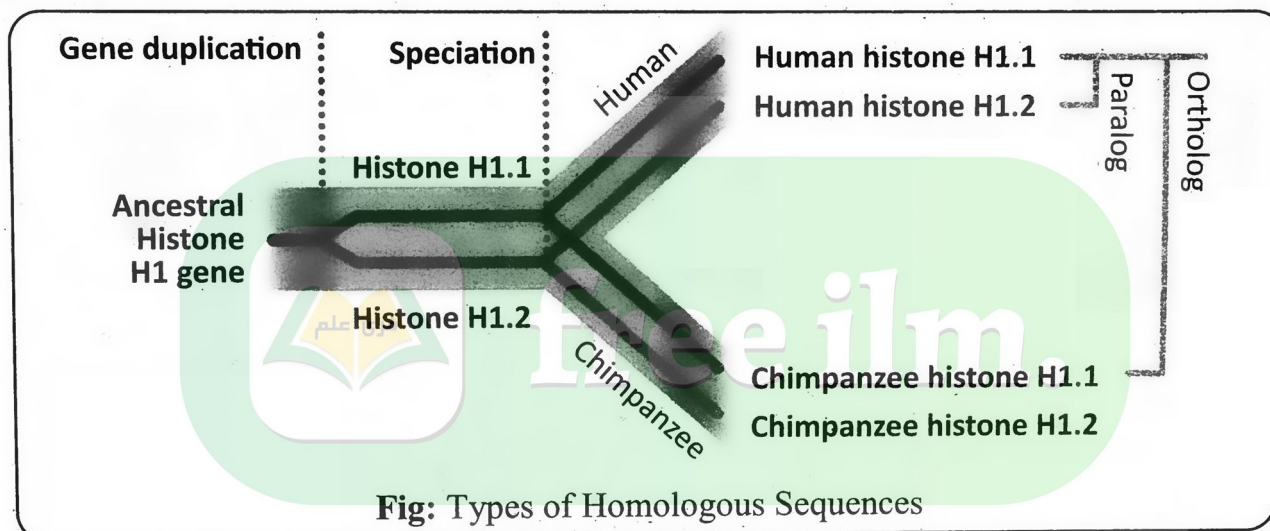


Fig: Types of Homologous Sequences

Applications of sequence homology

- Sequence homology provides an insight into the **evolutionary relationships** between organisms.
- By comparing homologous sequences, scientists can **infer the evolutionary history and divergence of species**.
- Sequence homology provides a **clue about the function of an unknown gene or protein**. If an unknown gene/protein is homologous to a gene/protein with a known function, it is likely to have a similar function.
- Identifying homologous genes involved in diseases across different species helps in **understanding disease mechanisms** and developing treatments.
- Homologous genes in model organisms can be studied to **gain insights into human diseases**.

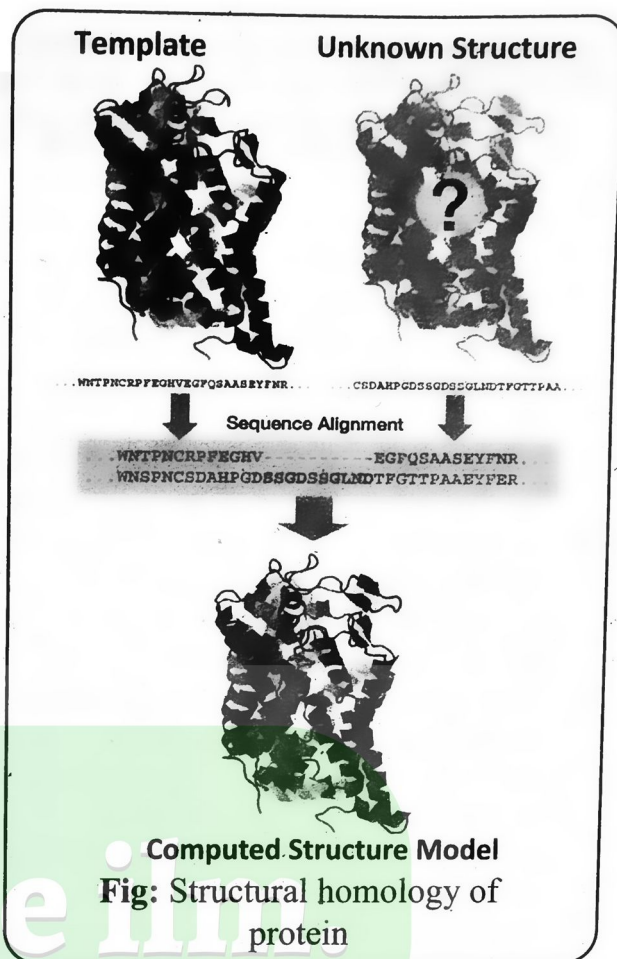
Q7. Define structural Homology. Discuss how studying structural homology benefits mankind.

Ans. Structural Homology

Structural homology refers to the **similarity in the three-dimensional structures of proteins** or other macromolecules due to shared ancestry. Proteins with similar structures often perform similar functions, even if their sequences are not highly similar.

Significance

- The three-dimensional structure of a protein **provides critical information** about its function.
- Understanding structural homology helps in **predicting the function** of newly discovered proteins.
- Structural homology is **crucial in drug designing** as drugs are often designed to interact with specific protein structures.
- Understanding the **structural relationships** between proteins can help in **designing more effective drugs**.
- Also studying the structural homology of proteins helps in understanding the **evolutionary processes** that shape protein functions and interactions.



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