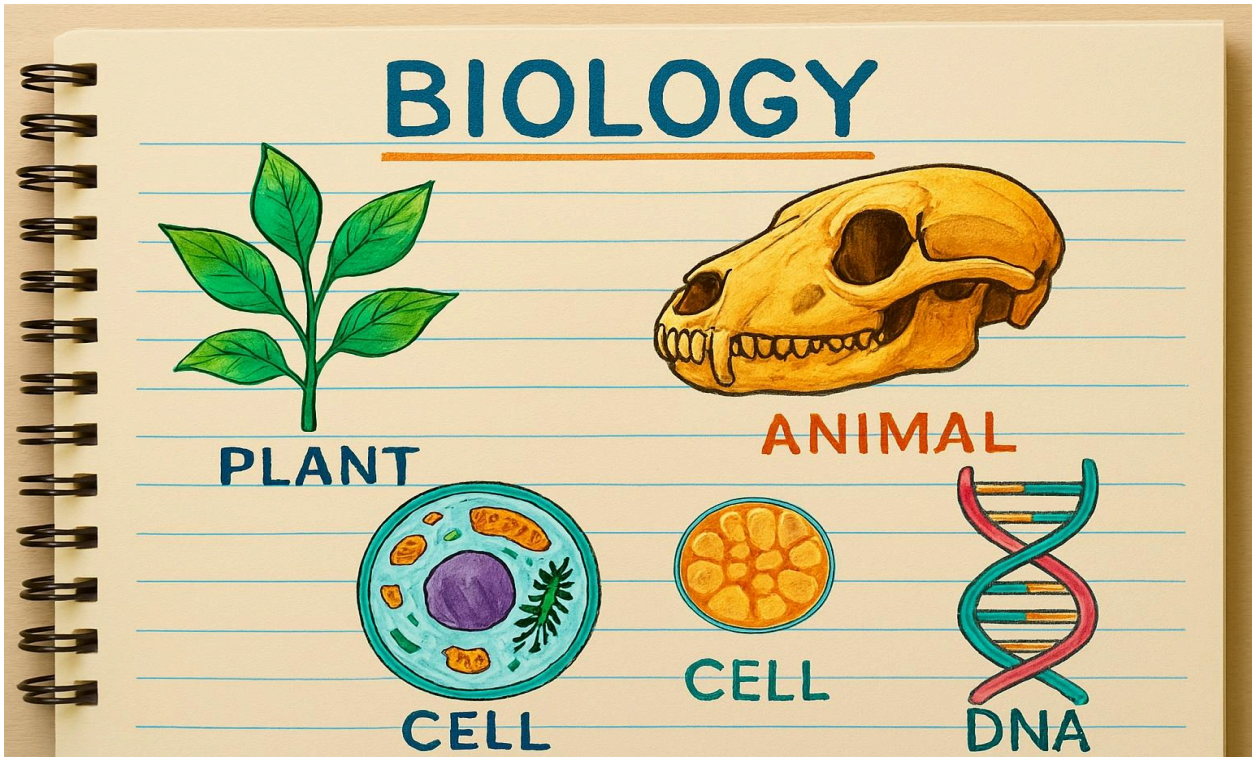


Class: 11th

Subject: Biology

Chapter 7: STRUCTURAL AND COMPUTATIONAL BIOLOGY

❖ Important MCQs:

1. Structural biology is the study of:

(a) Chemical reactions in cells

(b) Three-dimensional structures of macromolecules at atomic level ✅

(c) Energy production in cells

(d) Transport of molecules in cells

2. Structural biology mainly studies which macromolecules?

(a) Lipids and vitamins

(b) Proteins and nucleic acids ✅

(c) Minerals and hormones

(d) Carbohydrates and fats

3. Structural biology provides information about the:

(a) Structure and function of biomolecules ✅

(b) Only metabolic reactions

(c) Only genetic mutations

(d) Only cell division

4. Domains in macromolecules are:

(a) Chemical bonds

(b) Distinct structural units with independent functions ✅

(c) Energy producing structures

(d) Parts of chromosomes

5. The polymerase domain of HIV-1 reverse transcriptase is responsible for:

(a) Breaking peptide bonds

(b) Synthesizing DNA ✅

(c) Destroying RNA

(d) Producing proteins

6. RNase H domain of HIV-1 reverse transcriptase:

(a) Synthesizes RNA

(b) Breaks RNA strand of RNA-DNA hybrid ✅

(c) Produces ATP

(d) Repairs DNA

7. Structural biology helps scientists to identify:

(a) Active sites of enzymes ✅

(b) Blood cells

(c) Vitamins

(d) Minerals

8. Active site of an enzyme is the region where:

(a) Energy is stored

(b) Chemical reaction takes place ✅

(c) DNA replication occurs

(d) Protein folding occurs

9. Drug targets are usually:

(a) Lipids

(b) Carbohydrates

(c) Proteins of pathogens ✅

(d) Minerals

10. In COVID-19 research, scientists studied the structure of:

(a) Envelope protein

(b) Spike protein of coronavirus ✅

(c) DNA polymerase

(d) Hemoglobin

11. Spike protein of coronavirus helps the virus to:

(a) Produce energy

(b) Enter human cells ✅

(c) Destroy antibodies

(d) Replicate DNA

12. Interaction between pathogen and host cell is called:

(a) Enzyme inhibition

(b) Host-pathogen interaction ✅

(c) Protein synthesis

(d) Metabolism

13. Structural biology helps scientists understand:

(a) How viruses enter host cells ✅

(b) How blood circulates

(c) How digestion occurs

(d) How plants grow

14. Protein misfolding may lead to diseases such as:

(a) Malaria

(b) Parkinson's disease ✅

(c) Cholera

(d) Typhoid

15. Correct folding of proteins is important for:

(a) Color of proteins

(b) Proper functioning of proteins ✅

(c) Storage of minerals

(d) Production of vitamins

16. X-ray crystallography was developed in:

(a) 1905

(b) 1910

(c) 1912 ✅

(d) 1920

17. X-ray crystallography was developed by:

(a) Watson and Crick

(b) William Henry Bragg and William Lawrence Bragg ✅

(c) Mendel and Darwin

(d) Pauling and Hodgkin

18. William Henry Bragg and William Lawrence Bragg received the Nobel Prize in:

(a) 1910

(b) 1915 ✅

(c) 1925

(d) 1930

19. X-ray crystallography is used to analyze:

(a) Only proteins

(b) Only minerals

(c) Different substances including proteins, nucleic acids and vitamins ✅

(d) Only metals

20. In X-ray crystallography, X-rays strike the:

(a) Liquid sample

(b) Crystal sample ✅

(c) Gas sample

(d) Cell membrane

21. When X-rays strike the crystal, atoms in the crystal:

(a) Absorb the X-rays

(b) Diffract the X-rays in specific directions ✅

(c) Destroy the X-rays

(d) Reflect the X-rays completely

22. The pattern formed after diffraction of X-rays is called:

(a) Reflection pattern

(b) Diffraction pattern ✅

(c) Molecular pattern

(d) Structural pattern

23. The diffraction pattern is used to create a:

(a) Genetic map

(b) Density map ✅

(c) Chromosome map

(d) Metabolic map

24. Protein crystallization means:

(a) Converting protein into liquid form

(b) Turning purified protein into a solid crystal form ✅

(c) Breaking protein molecules

(d) Producing enzymes

25. The final step in X-ray crystallography is:

(a) Protein purification

(b) Production of diffraction pattern

(c) Creating density map

(d) Determination of protein structure using computational analysis ✅

26. Computational biology is an interdisciplinary field that combines:

(a) Biology and chemistry only

(b) Biology, computer science, mathematics, and statistics ✅

(c) Physics and chemistry only

(d) Botany and zoology only

27. The main purpose of computational biology is to:

(a) Grow microorganisms

(b) Analyze and interpret biological data using computational tools ✅

(c) Study plant growth

(d) Perform laboratory experiments

28. The ability of computational biology to handle large datasets helps to:

(a) Reduce laboratory work

(b) Discover hidden patterns and predictive models ✅

(c) Produce proteins

(d) Destroy viruses

29. Genomics is the study of:

(a) Proteins

(b) Lipids

(c) Complete set of DNA (genome) in an organism ✅

(d) Vitamins

30. Proteomics is the large-scale study of:

(a) DNA molecules

(b) Proteins and their structures and functions ✅

(c) Carbohydrates

(d) Hormones

31. Bioinformatics is the use of computer technology to:

(a) Produce drugs

(b) Manage and analyze biological data ✅

(c) Study cell division

(d) Destroy pathogens

32. Computational biology helps in drug discovery by:

(a) Producing vaccines directly

(b) Predicting how drugs interact with proteins and molecules ✅

(c) Killing bacteria

(d) Growing cells

33. GenBank database mainly stores:

(a) Protein structures

(b) Nucleotide (DNA) sequences ✅

(c) Vitamins

(d) Enzymes

34. Protein Data Bank (PDB) provides information about:

(a) DNA mutations

(b) 3D structures of proteins and nucleic acids ✅

(c) Plant cells

(d) Metabolic reactions

35. BLAST algorithm is used to:

(a) Produce DNA molecules

(b) Compare biological sequences such as DNA and proteins ✅

(c) Destroy harmful genes

(d) Store protein structures

36. Sequence homology refers to the similarity between:

(a) Cells and tissues

(b) DNA, RNA, or protein sequences due to shared ancestry ✅

(c) Organs of animals

(d) Chemical reactions in cells

37. Homologous sequences evolve from:

(a) Different ancestral genes

(b) A common ancestral sequence ✅

(c) Random mutations only

(d) Environmental factors

38. Orthologs are sequences that:

(a) Occur within the same species

(b) Originate from gene duplication

(c) Occur in different species from a common ancestral gene ✅

(d) Have no evolutionary relationship

39. Orthologs usually:

(a) Perform completely different functions

(b) Retain the same function across species ✅

(c) Exist only in bacteria

(d) Exist only in plants

40. Paralogs are sequences that:

(a) Occur in different species

(b) Originate from gene duplication within the same species ✅

(c) Are found only in viruses

(d) Have identical structures

41. Sequence homology helps scientists to:

(a) Study evolutionary relationships between organisms ✅

(b) Produce enzymes

(c) Destroy harmful genes

(d) Create new cells

42. If an unknown gene is homologous to a known gene, it is likely to:

(a) Have a similar function ✅

(b) Stop functioning

(c) Destroy other genes

(d) Produce energy

43. Studying homologous genes in model organisms helps scientists to:

(a) Grow plants faster

(b) Understand human diseases ✅

(c) Produce vitamins

(d) Increase metabolism

44. Structural homology refers to similarity in:

(a) DNA sequences only

(b) Three-dimensional structures of proteins or macromolecules ✅

(c) Cell membranes

(d) Metabolic pathways

45. Structural homology is important in:

(a) Food digestion

(b) Drug design and predicting protein function ✅

(c) Energy production

(d) Blood circulation

📘 EXERCISE

SECTION 1: MULTIPLE CHOICE QUESTIONS

1. Generally, the function of a protein depends on its:

(a) One-dimensional structure

(b) Two-dimensional structure

(c) Three-dimensional structure ✅

(d) Four-dimensional structure

2. The protein domains are:

(a) Functional and structural units within protein ✅

(b) Secondary structural elements

(c) Linear sequences of amino acids

(d) Specific regions for post-translational modification

3. The first step in X-ray crystallography experiment is:

(a) Compute an electron density

(b) Build a model of your molecule

(c) Measure a diffraction pattern

(d) Grow a crystal ✅

4. What is the primary role of computational biology?

(a) Using computer algorithms to analyze data ✅

(b) Identifying genetic mutations

(c) Studying protein functions

(d) Analyzing the expression patterns

5. Which computational approach is used to predict protein structure based on amino acid sequence?

(a) Multiple sequence alignment

(b) Homology modelling ✅

(c) Clustering analysis

(d) BLAST searches

SECTION 2: SHORT QUESTIONS

1. Define domains of the protein.

Answer:

Protein domains are distinct structural and functional units within a protein. Each domain can fold independently and often performs a specific function in the protein.

2. How does coronavirus enter the host cells?

Answer:

Coronavirus enters host cells through its spike protein. The spike protein attaches to a receptor protein on the surface of human cells, allowing the virus to bind and enter the host cell.

3. Define genomics.

Answer:

Genomics is the study of the complete set of DNA (genome) of an organism. It includes the sequencing, structure, function, and analysis of genes.

4. Differentiate between genomics and proteomics.

Answer:

Genomics:

Genomics is the study of the complete set of DNA (genome) in an organism and focuses on genes and genetic variations.

Proteomics:

Proteomics is the large-scale study of proteins, including their structures, functions, and interactions in a cell.

5. What is GenBank? Describe it briefly.

Answer:

GenBank is a public database of nucleotide sequences (DNA). It stores DNA sequences from many organisms along with biological information, helping scientists in genetic research and comparative genomics.

6. Write a short note on Protein Data Bank.

Answer:

Protein Data Bank (PDB) is a database that provides three-dimensional (3D) structural data of biological macromolecules such as proteins and nucleic acids. It helps scientists understand molecular structure, function, and drug design.

SECTION 3: LONG QUESTIONS

🌟 **Q1: Describe the applications of structural biology.**

❖ **Answer:**

Structural biology is the study of three-dimensional (3D) structures of macromolecules like proteins and nucleic acids at the atomic level. The function of a biomolecule depends on its 3D structure, so structural biology is crucial in understanding biological processes. It has several applications, particularly in medical research, drug design, and understanding diseases. The main applications are:

1. Determining Active Sites and Domains

- Structural biology allows scientists to determine the 3D structure of proteins and nucleic acids.
- This helps to identify active sites (where reactions occur) and domains (independent structural units with specific functions).

Example:

HIV-1 reverse transcriptase has:

1. Polymerase domain – synthesizes DNA
2. RNase H domain – breaks RNA in RNA-DNA hybrids

- Knowledge of these domains allows scientists to design drugs that specifically inhibit these functions.
- Another example: Serine proteases have a defined active site for breaking peptide bonds.

2. Identifying Drug Targets

- Structural biology helps in finding specific spots on disease-causing molecules (usually proteins) where drugs can bind.
- By studying the 3D structure, drugs can be designed to block the protein's function.

Example:

- In COVID-19, the spike protein of SARS-CoV-2 was studied.
- Drugs and vaccines were designed to block the spike protein, preventing viral entry into human cells.

3. Studying Host-Pathogen Interactions

- Helps understand how pathogens (viruses or bacteria) interact with host cells.
- Comparing 3D structures of pathogen and host proteins shows:
    - How the pathogen attaches to the host
    - Which molecules are involved

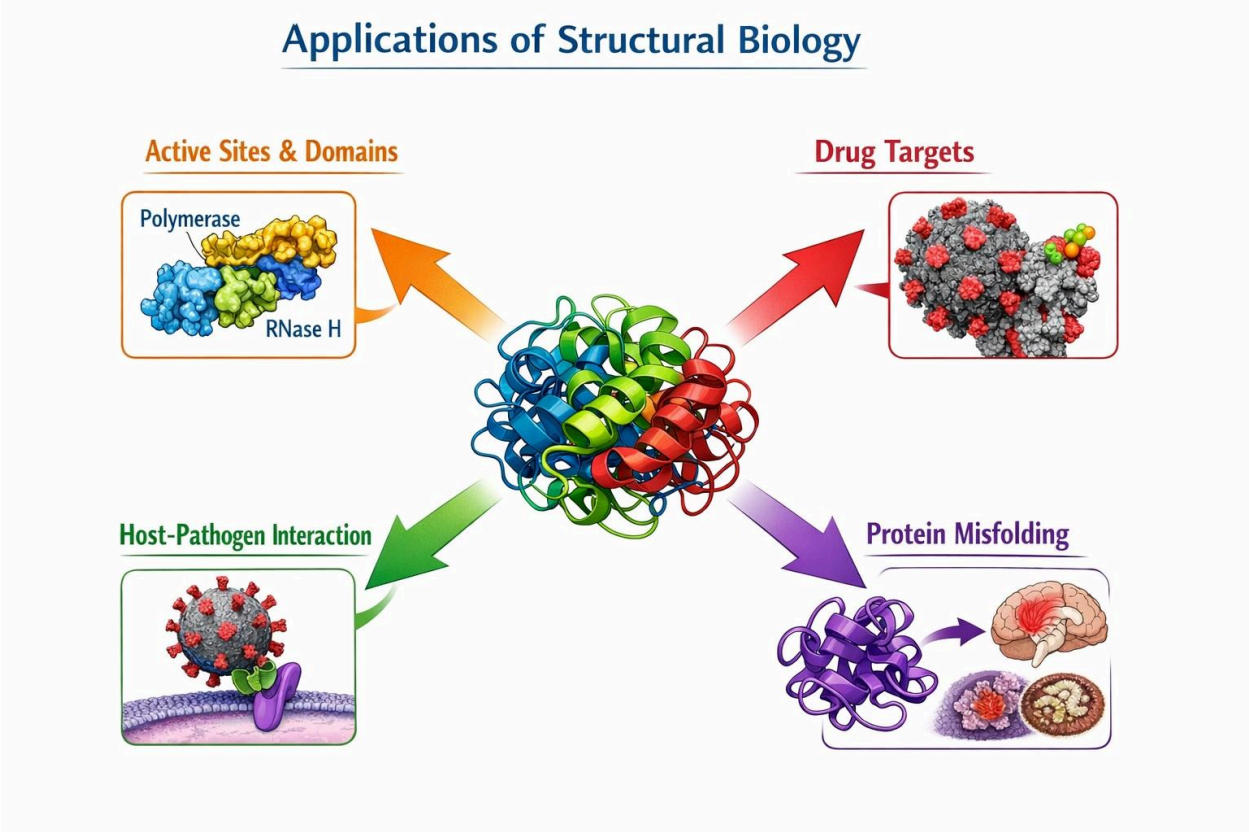
Example:

- Coronavirus spike protein binds to human receptor protein.
- Drugs can be designed to block this interaction, preventing infection.

4. Understanding Protein Misfolding

- Proteins must fold into correct 3D shapes to function.
- Misfolding causes diseases like:
    - Cystic fibrosis
    - Parkinson's disease
    - Alzheimer's disease
- Structural biology helps study folding pathways and understand how misfolding leads to disease, aiding drug development.

Diagram:



✦ **Summary:**

Structural biology is essential for:

- Identifying active sites and domains in proteins
- Drug discovery and vaccine development
- Understanding host-pathogen interactions
- Studying protein misfolding diseases

✅ By analyzing 3D structures, scientists can predict functions, design effective drugs, and understand complex biological processes.

🌟 **Q2: Write a note on principle and working of X-ray crystallography.**

❖ **Answer:**

X-ray crystallography is a technique used to determine the three-dimensional (3D) structure of molecules, especially proteins, nucleic acids, and other macromolecules, at atomic resolution. It helps in understanding the arrangement of atoms, active sites, and structural domains, which is essential for drug design and biological research.

Principle of X-ray Crystallography:

- X-ray crystallography is based on the diffraction of X-rays by the regular arrangement of atoms in a crystal.
- When a beam of X-rays strikes a crystal, atoms in the crystal diffract the X-rays in specific directions.
- The angles and intensities of the diffracted beams are recorded to produce a 3D electron density map.

- From this electron density map, the 3D structure of the molecule can be determined.

✅ In simple terms: X-rays + crystal ⟶ diffraction ⟶ electron density ⟶ 3D molecular structure

Working / Steps of X-ray Crystallography:

1. Protein Crystallization:

- Purified protein is converted into a solid crystal.
- Crystals are necessary because they arrange molecules in a regular, repeating pattern, giving a clear diffraction pattern.
- Crystallization requires careful control of temperature, pH, and salt concentration.

2. Production of Diffraction Pattern:

- A good quality crystal is mounted on the X-ray machine.
- The X-ray beam is directed at the crystal from different angles.
- Atoms in the crystal diffract the X-rays, producing a diffraction pattern (spots) on a detector.

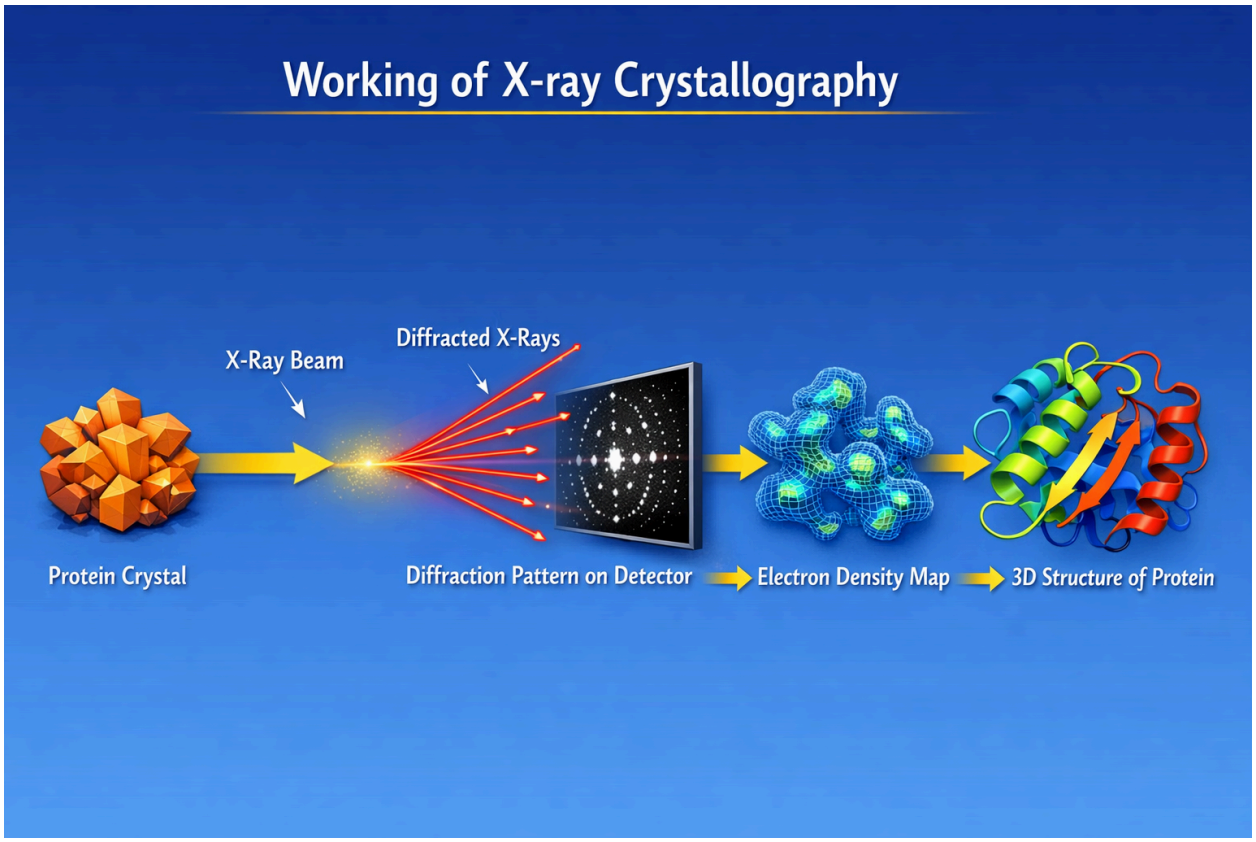
3. Creating Electron Density Map:

- The angles and intensities of diffraction spots provide information about atom positions.
- Computational programs are used to create a 3D electron density map.

4. Determination of Molecular Structure:

- The electron density map is analyzed to build a 3D model of the molecule.
- This model reveals structural details, including domains, active sites, and binding pockets.

Diagram:



✦ **Summary:**

X-ray crystallography is a powerful tool to determine the 3D structure of macromolecules. Its principle is based on X-ray diffraction by crystals, and its applications include:

- Studying protein and nucleic acid structures
- Understanding biological functions
- Designing drugs and vaccines

✅ **Steps:**

1. Protein crystallization
2. Diffraction pattern production
3. Electron density map creation
4. Structure determination

🌟 **Q3: Briefly describe key databases of computational biology.**

❖ **Answer:**

Computational biology uses databases to store, retrieve, and analyze biological data such as DNA, RNA, and protein sequences. These databases are essential for genetic research, protein structure analysis, and drug design. The main databases are:

1. GenBank:

- GenBank is a public database of nucleotide sequences (DNA).
- It provides access to a vast repository of DNA sequences from various organisms.
- Researchers use GenBank for:
    - Genetic research
    - Comparative genomics
    - Identifying genetic variations and functions of genes

Website: https://www.ncbi.nlm.nih.gov/nuccore/🔍

2. Protein Data Bank (PDB):

- PDB provides 3D structural data of macromolecules, including proteins and nucleic acids.

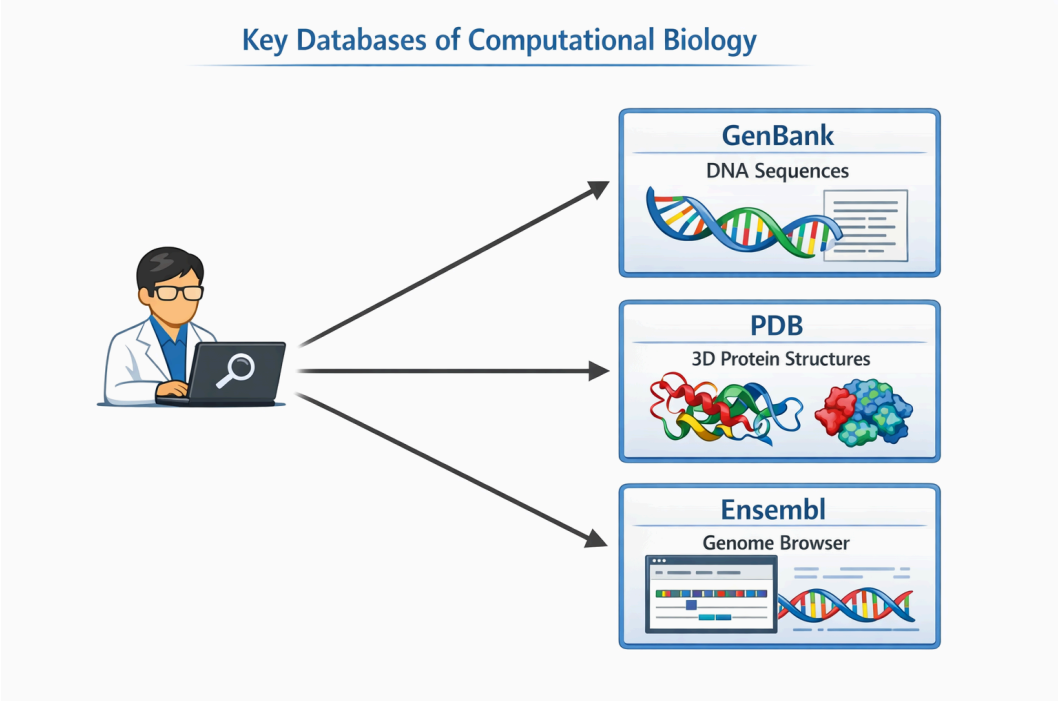
- Important for:
    - Studying molecular structures
    - Understanding protein function
    - Designing drugs targeting specific protein structures

Contains electron density maps and 3D coordinates of molecules.

3. Ensembl:

- Ensembl is a genome browser that provides information on genome sequences, gene models, and comparative genomics for various species.
- **It helps in:**
    - Accessing and visualizing genomic data
    - Supporting studies in genomics and evolutionary biology
    - Understanding gene structure and function across species

Diagram:



✦ **Summary:**

Key databases in computational biology provide organized, searchable, and annotated biological data.

- GenBank ⟶ nucleotide sequences (DNA)
- Protein Data Bank (PDB) ⟶ 3D structures of proteins and nucleic acids
- Ensembl ⟶ genome sequences, gene models, and comparative genomics

✅ These databases are critical for research in genomics, proteomics, evolutionary biology, and drug design.

INQUISITIVE QUESTIONS

🌟 **Q1: Consider there is a pandemic of a new unknown disease, and the causative agent is a virus. You also know that the virus belongs to X family. How can structural biology be helpful in preventing the disease?**

❖ **Answer:**

Structural biology studies the three-dimensional (3D) structures of macromolecules, such as proteins and nucleic acids, at atomic resolution. In the case of a new viral disease, structural biology can play a critical role in understanding the virus and preventing the disease. The following points explain how:

1. Determining Viral Protein Structures

- Structural biologists can determine the 3D structures of viral proteins, including surface proteins like spike proteins.
- Knowing the exact shape, active sites, and binding domains allows scientists to identify potential targets for drugs or vaccines.

Example: Similar to SARS-CoV-2, the spike protein structure helps in designing vaccines and antiviral drugs.

2. Identifying Drug Targets

- By studying the active sites of viral proteins, researchers can design drugs that specifically bind and inhibit these proteins.
- Structural biology allows rational drug design, reducing time and cost in the development of antiviral therapies.

3. Understanding Host-Virus Interactions

- Structural biology helps to see how viral proteins interact with host cell receptors.
- Scientists can design inhibitors or antibodies that block the virus from entering host cells, preventing infection.

4. Vaccine Design

- Structural knowledge enables the design of vaccine antigens that mimic the viral protein structure.
- This helps the immune system recognize and neutralize the virus efficiently.

5. Predicting Mutations and Variants

- By analyzing structural data, researchers can predict how mutations may affect viral protein structure.
- This helps in updating drugs and vaccines against emerging viral variants.

✦ **Summary:**

Structural biology can help prevent a pandemic caused by a virus by:

- Determining viral protein 3D structures
- Identifying drug targets
- Understanding host-virus interactions
- Assisting in vaccine design
- Predicting effects of mutations

✅ In short, structural biology provides critical molecular insights that guide drug development, vaccine design, and prevention strategies.

🌟 **Q2: Suppose you find an unknown protein and determine its amino acid sequence by Edman degradation or mass spectrometry. How can you exploit computational biology to predict the structure and function of the protein?**

❖ **Answer:**

When a protein's amino acid sequence is known, computational biology provides powerful tools to predict its structure and function without extensive laboratory experiments. The approach can be divided into the following steps:

1. Sequence Comparison (Homology Search)

- Use databases like GenBank or Protein Data Bank (PDB).
- Apply algorithms like BLAST or FASTA to compare the unknown sequence with known sequences.
- If the protein shows homology with known proteins, its function and possible structure can be inferred.

Example:

- An unknown protein sequence similar to a kinase in PDB suggests it may also function as a kinase.

2. Structure Prediction

- Use homology modeling or ab initio methods to predict the 3D structure of the protein.
- Homology modeling builds a 3D model based on a similar known protein structure.
- Computational tools predict folding patterns, domains, and active sites, which are critical for function.

3. Functional Annotation

After predicting the structure, bioinformatics tools can:

- Identify active sites or binding pockets
- Predict enzymatic or signaling functions
- Suggest possible interactions with other proteins or ligands

4. Protein-Protein and Protein-Ligand Interaction Analysis

- Use computational tools to simulate interactions of the protein with other molecules.

- Helps in drug design or understanding metabolic pathways.

5. Evolutionary and Phylogenetic Analysis

- Compare the sequence across species using genomic databases.
- Helps determine evolutionary conservation of functionally important regions.

✦ **Summary:**

Computational biology allows prediction of structure and function of an unknown protein using:

1. Sequence homology searches (BLAST/FASTA)
2. 3D structure prediction (homology modeling or ab initio)
3. Functional annotation (active sites, domains, interactions)
4. Interaction studies (protein-protein, protein-ligand)
5. Evolutionary analysis (conserved regions and functional inference)

✅ This approach saves time, reduces experimental costs, and provides insights for drug design, disease study, and functional characterization.

🌟 **Q3: Homology models of macromolecules differ from experimentally determined structures of the macromolecules. Please comment.**

❖ **Answer:**

Homology modeling is a computational technique used to predict the three-dimensional (3D) structure of a macromolecule, usually a protein, based on its sequence similarity to a known protein structure (template). While homology models are extremely useful, they differ from experimentally determined structures obtained through methods like X-ray crystallography, NMR spectroscopy, or cryo-electron microscopy.

1. Basis of Prediction vs Experiment

Homology models are predicted using computer algorithms. They rely on the sequence similarity of the unknown protein to a known template protein. The accuracy of the model depends on how similar the sequences are and how precise the alignment is. In contrast, experimentally determined structures are obtained by directly measuring the molecule at an atomic level, which provides high-resolution structural details.

2. Accuracy and Detail

Homology models are generally good at predicting the overall fold and arrangement of domains, but they may not accurately depict loop regions, side-chain positions, or subtle structural features. Experimental structures, however, show precise atomic positions, including side chains, hydrogen bonds, and interactions with ligands or other molecules.

3. Applications and Limitations

Homology models are very useful for:

- Predicting general protein function

- Designing mutant proteins
- Identifying potential drug binding sites

However, they have limitations and cannot replace experimental data when high-precision structural information is needed, such as for detailed mechanistic studies or drug development requiring exact atomic contacts.

Experimental structures, being directly measured, serve as a gold standard for validating any computational predictions.

✦ **Summary:**

Homology models differ from experimentally determined structures because they are computational predictions, whereas experimental structures are directly measured and highly accurate. Homology models are approximations useful for function prediction and drug design, but they require experimental validation for detailed structural studies.

✅ **Key Point:** Homology models guide research, but experimental structures provide reliable atomic-level details.

🌟 **Q4: Draw a flow chart to describe the steps involved in drug development till its prescription.**

❖ **Answer:**

Drug development is a systematic and stepwise process that transforms a scientific discovery into a medicine that can be safely prescribed to patients. The process can take 10–15 years and involves multiple stages:

1. Identification of Drug Target

- **Goal:** Find the molecule in the body (like a protein, enzyme, or receptor) responsible for causing the disease.
- **Methods Used:** Structural biology, computational biology, genomics, proteomics.
- **Importance:** Correct identification ensures the drug will act specifically on the disease-causing pathway.
- **Example:** The spike protein of SARS-CoV-2 is a drug target for COVID-19 therapies.

2. Drug Discovery / Lead Compound Identification

- Goal: Find or design a chemical compound that can interact with the target.

Approaches:

- High-throughput screening: Testing thousands of compounds in the lab.
- Rational drug design: Using 3D structures of the target protein to design molecules that fit the active site.

Outcome: A lead compound that shows potential therapeutic activity.

3. Preclinical Testing

- **Goal:** Assess the safety and efficacy of the lead compound before human testing.
- **Methods:**
    - **In vitro studies:** Using cells in a laboratory to test drug activity.

    - **In vivo studies:** Using animal models to assess safety, toxicity, and metabolism.
- **Importance:** Ensures the drug is safe and effective enough to proceed to human trials.

4. Clinical Trials (Human Testing)

Goal: Test the drug in humans under controlled conditions. Conducted in three phases:

Phase I:

- Small group of healthy volunteers.
- Tests safety, tolerable dose, and side effects.

Phase II:

- Larger group of patients with the disease.
- Evaluates efficacy and optimal dose.

Phase III:

- Large-scale testing in diverse patient populations.
- Confirms safety, efficacy, and compares with existing treatments.

Importance: Ensures the drug is both effective and safe for human use.

5. Regulatory Approval

Goal: Obtain approval from authorities (e.g., FDA, EMA) to sell the drug.

Process:

- Submit all preclinical and clinical data.

- Regulatory agencies evaluate for safety, efficacy, and manufacturing quality.

Outcome: Approval allows legal marketing and prescription of the drug.

6. Manufacturing and Quality Control

- **Goal**: Produce the drug on a large scale while ensuring high quality, purity, and consistency.
- **Importance**: Prevents contamination and ensures patients receive the correct dose and formulation.

7. Prescription / Marketing

- Goal: Make the drug available to patients through healthcare professionals.
- Post-marketing surveillance: Monitors long-term effects and rare side effects in the general population.

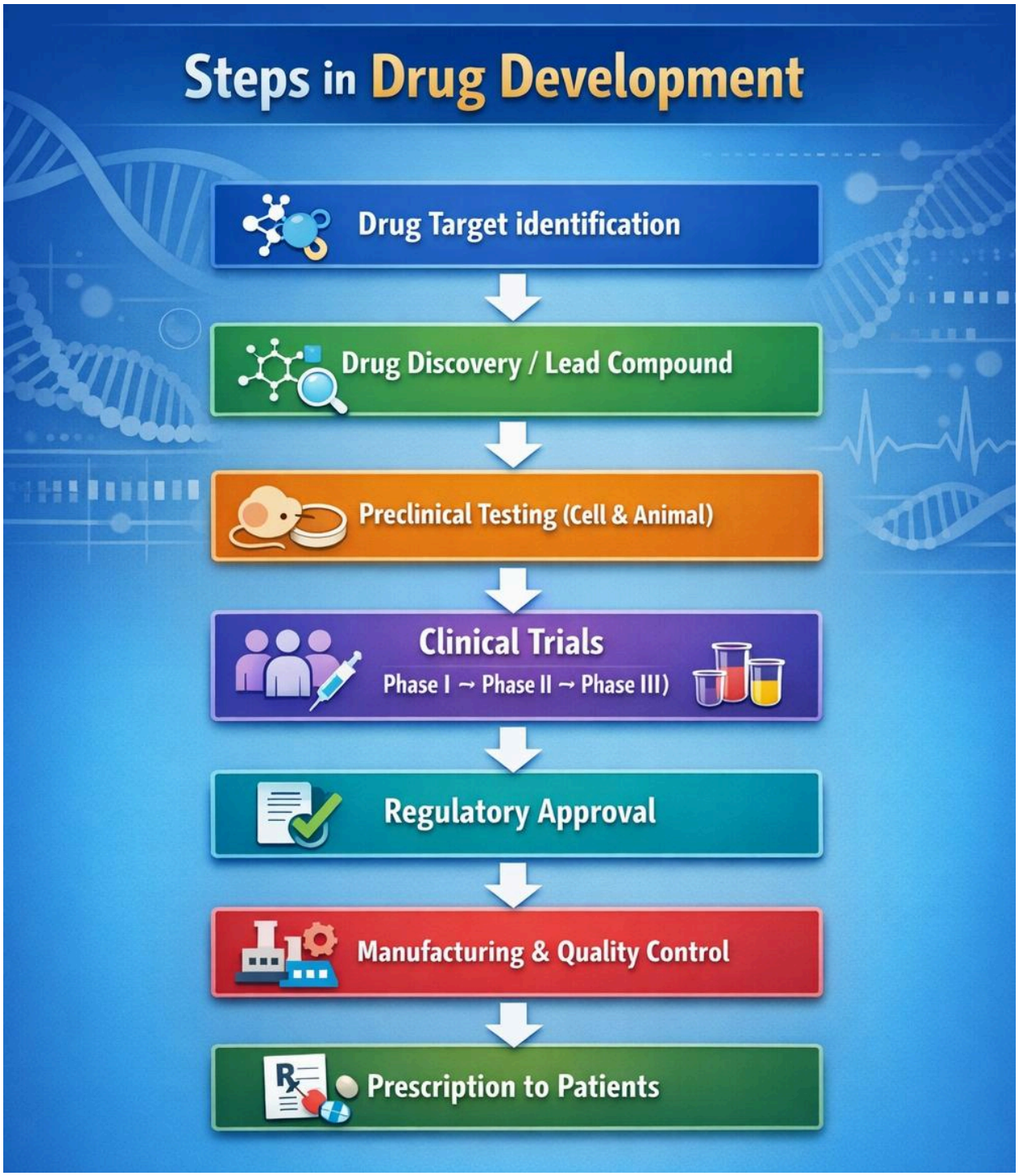
✦ **Summary:**

The drug development process is a careful, multi-step procedure designed to ensure safety, efficacy, and quality of medicine:

- Target Identification ⟶ Drug Discovery ⟶ Preclinical Testing ⟶ Clinical Trials ⟶ Regulatory Approval ⟶ Manufacturing ⟶ Prescription

✅ Structural biology and computational biology are key tools for target identification, drug design, and predicting interactions, speeding up the process and improving accuracy.

Flow Chart Concept (Visual Layout):



Note:

This chapter is designed to provide a solid foundation of knowledge, with the goal of deepening understanding and encouraging further exploration of the subject. The content has been carefully selected to support effective learning and inspire students to engage with the topic more deeply.

Author: Muhammad Asghar

Purpose: To contribute to education by offering insightful and valuable content that enhances learning and understanding.

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