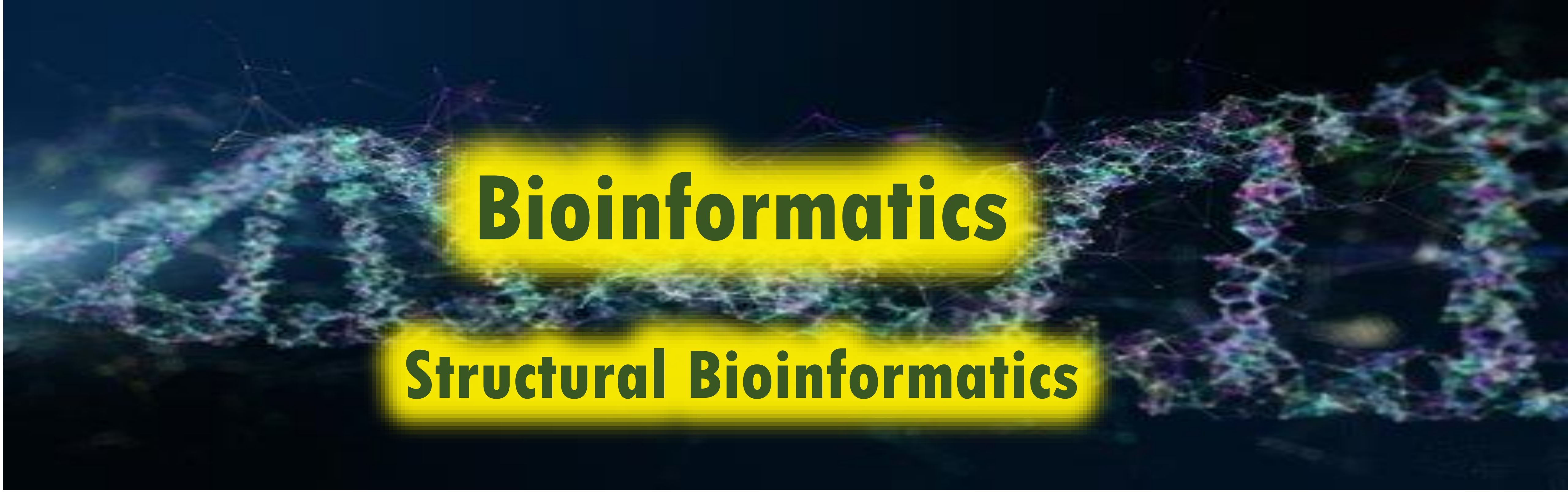
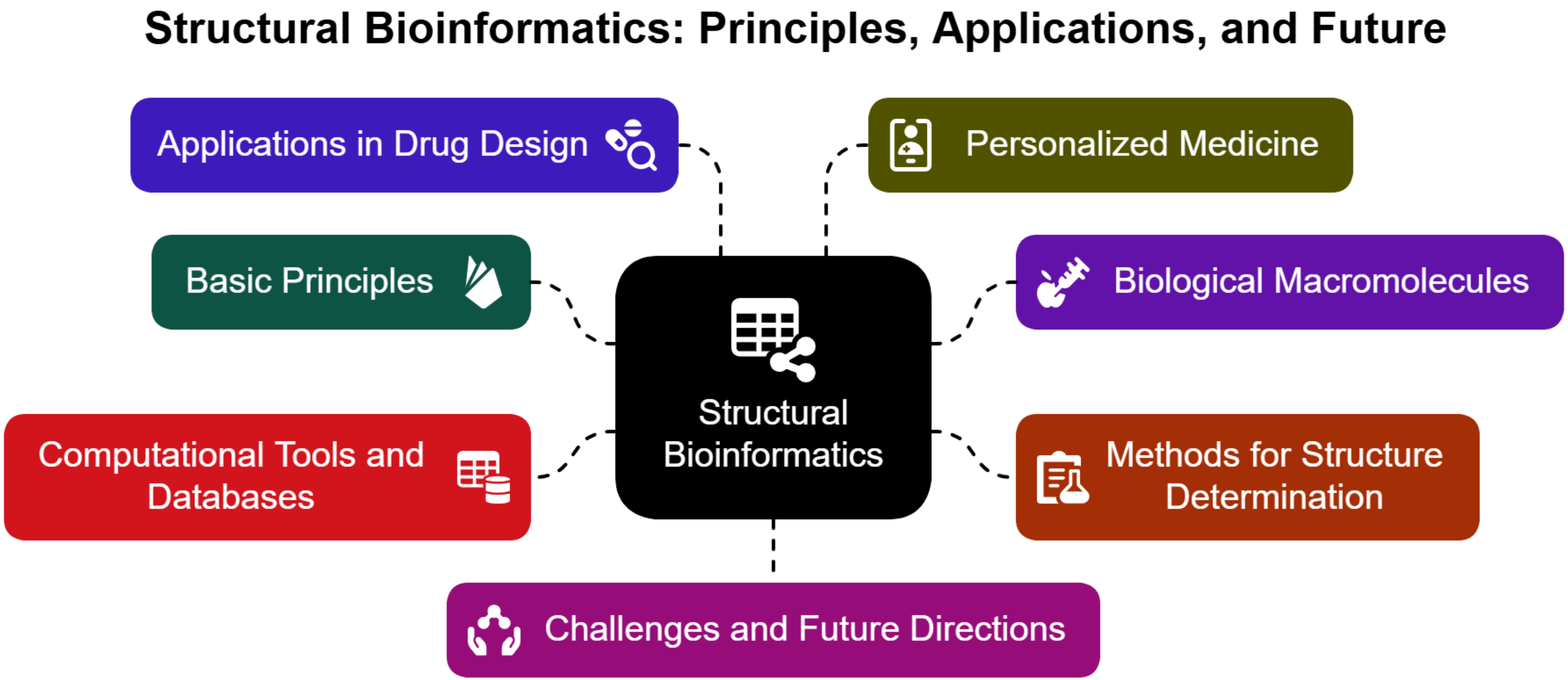


Bioinformatics

Structural Bioinformatics

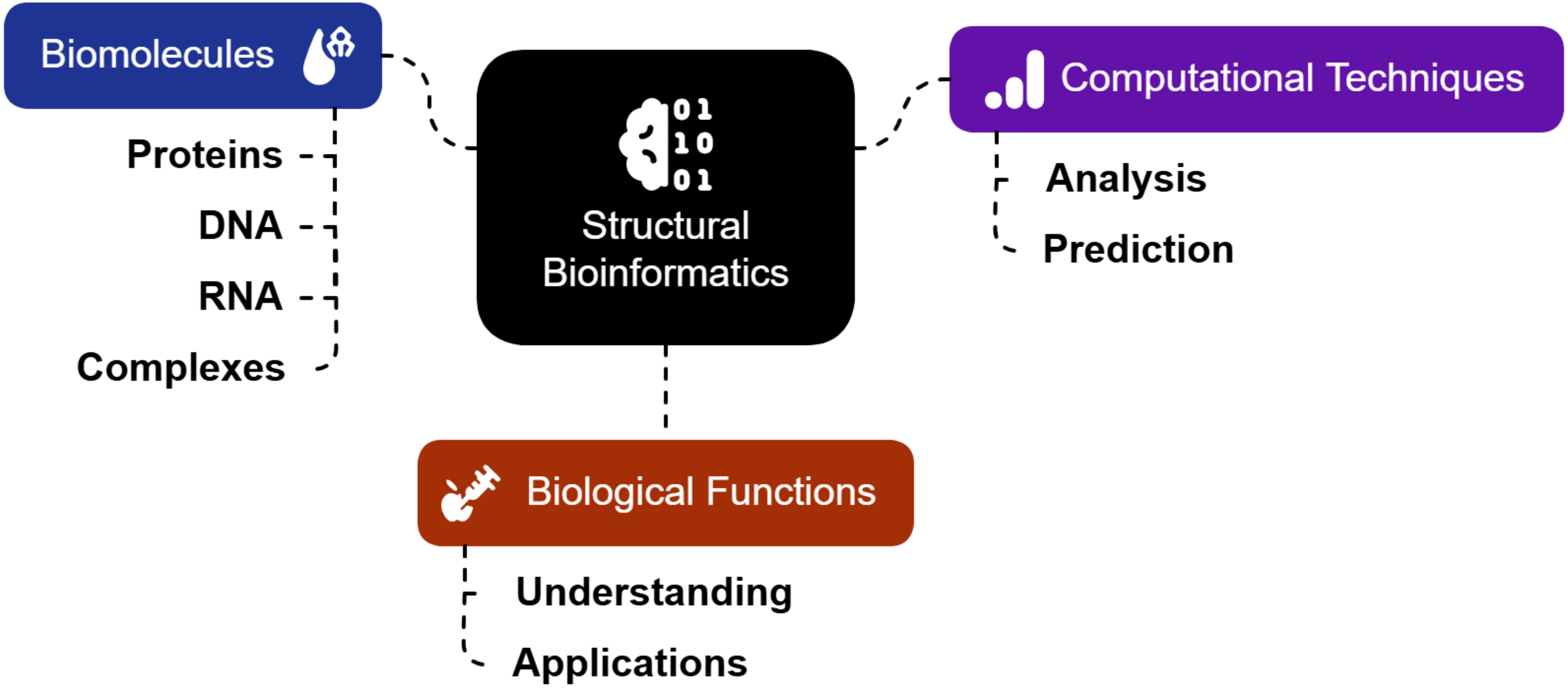
Assis. Prof. Dr. Labeed Al - Saad

The objectives



What is Structural Bioinformatics?

Structural Bioinformatics: Integration of Biology and Computation



What is Structural Bioinformatics?

Structural Bioinformatics: Tools, Techniques, and Applications

Structural Bioinformatics

Computational Tools
- Molecular Dynamics
- Homology Modeling
- Docking

Applications
- Drug Design
- Protein Engineering
- Genetic Variant Interpretation

Experimental Data
- X-ray Crystallography
- Cryo-EM

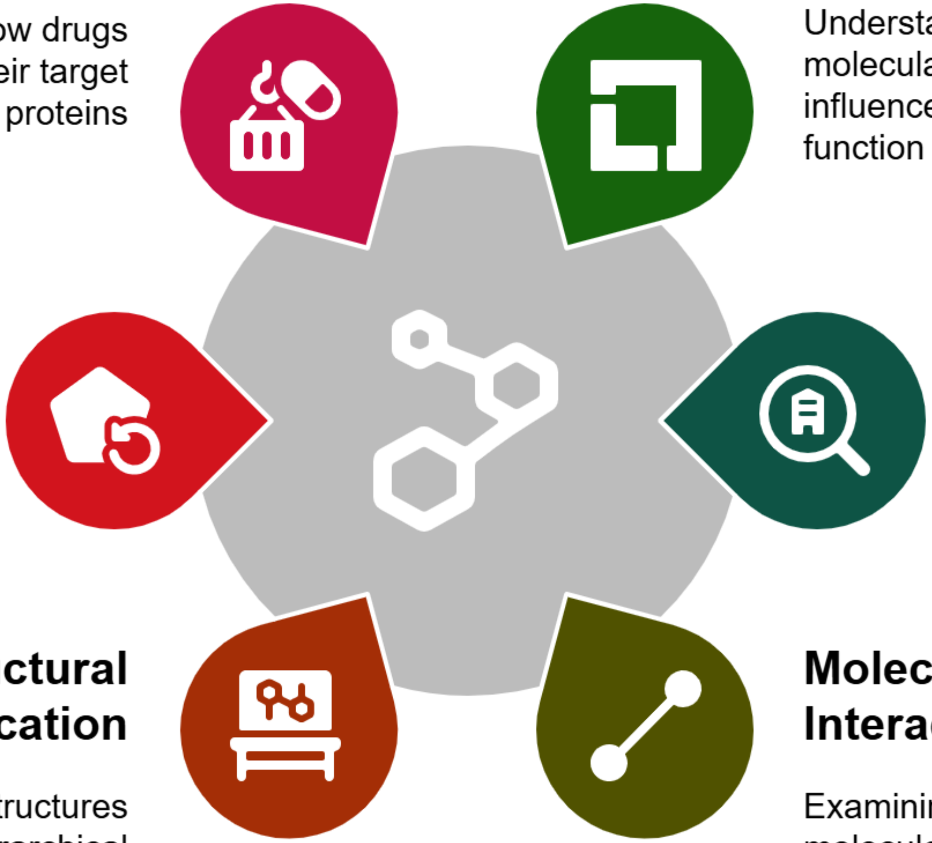
Principles of structural bioinformatics

Protein-Ligand/Drug Docking

Analyzing how drugs bind to their target proteins

Structure-Function Relationship

Understanding how molecular structure influences biological function



Dynamics & Flexibility

Studying the movement and adaptability of molecules

Structure Determination & Prediction

Techniques to elucidate and predict molecular structures

Structural Classification

Organizing structures into hierarchical categories

Molecular Interactions

Examining how molecules interact at the atomic level

Structure Determination in Biochemistry

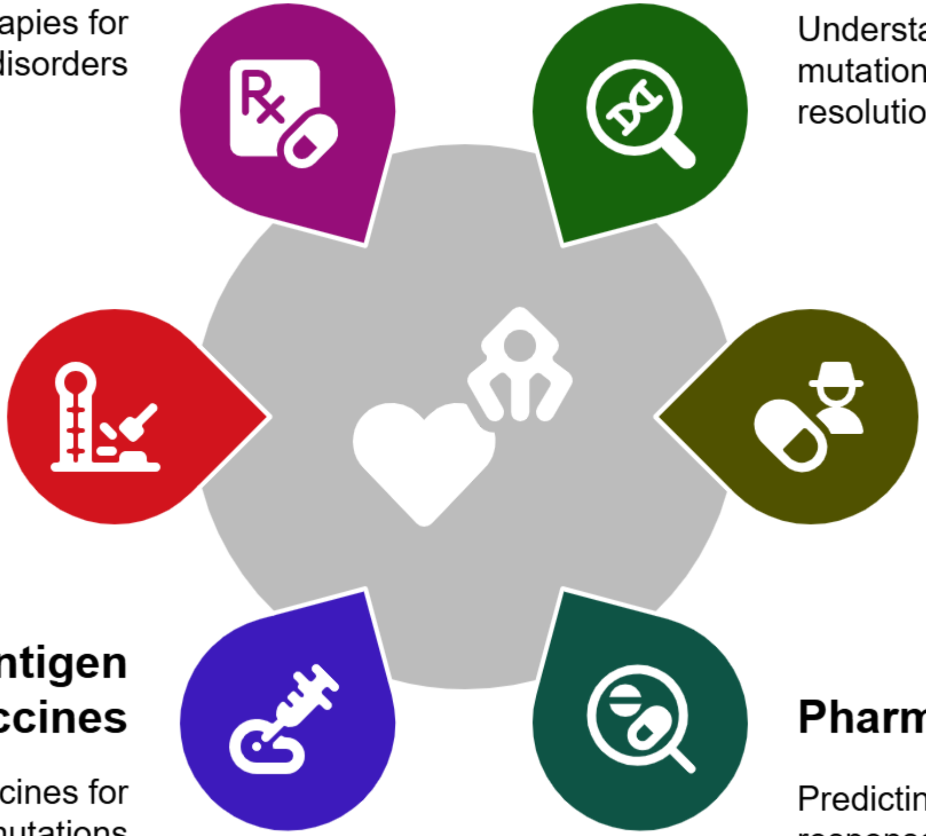
Structure Determination Methods

- **Experimental Methods**
  - X-ray Crystallography
  - Cryo-Electron Microscopy
  - NMR Spectroscopy
  - Electron Crystallography
- **Computational Methods**
  - Homology Modeling
  - Ab Initio Modeling
  - Molecular Dynamics Simulations
  - Docking
- **Hybrid Approaches**
  - Integrative Modeling
  - AI-Augmented Methods

Comparison of Methods

Method	Resolution	Sample State	Size Limit	Key Advantage
X-ray Crystallography	0.8–3.0 Å	Crystal	None	Atomic detail
Cryo-EM	2.5–4.0 Å	Solution (frozen)	>100 kDa	No crystallization needed
NMR	1.5–2.5 Å	Solution	<50 kDa	Captures dynamics
AlphaFold2	1–5 Å*	In silico	None	No experimental data required

Structural Bioinformatics in Personalized Medicine



Rare Disease Therapies

Developing therapies for rare genetic disorders

Genetic Variants

Understanding mutations at atomic resolution

Drug Resistance

Overcoming mutations that block drug binding

Drug Personalization

Matching drugs to unique protein variants

Neoantigen Vaccines

Designing vaccines for tumor-specific mutations

Pharmacogenomics

Predicting drug responses based on genetics

Key Technologies Enabling Personalized Medicine

Technology	Application	Example
AI Structure Prediction	Model patient-specific mutant proteins	AlphaFold2 for *TP53* mutations in cancer
Molecular Docking	Match drugs to mutant targets	Imatinib for *BCR-ABL1* mutants
Cryo-EM	Study patient-derived protein complexes	Immune receptor-antibody interactions
MD Simulations	Test drug binding kinetics	HIV protease inhibitor resistance

Challenges and Future Directions in Structural Bioinformatics

High Impact

Dynamic Modeling

Dynamic modeling is crucial for high-impact structural predictions.

Interdisciplinary Collaboration

Interdisciplinary collaboration enhances high-impact advancements in bioinformatics.

Challenges

Future Directions

Ethical AI

Ethical AI poses challenges with low immediate impact.

Improved Computational Methods

Improved computational methods promise future low-impact innovations.

Low Impact

Comprehensive Questions

1. Explain the principle of the "structure-function relationship" in biomolecules. Provide examples of how structural disruptions (e.g., misfolded proteins) lead to disease, and name tools used to visualize these relationships.
2. Compare X-ray crystallography, Cryo-EM, and NMR spectroscopy in terms of workflow, resolution, sample requirements, and limitations. Use specific examples (e.g., insulin, SARS-CoV-2 spike protein) to illustrate your answer.
3. Describe the steps involved in homology modeling and ab initio modeling. How do tools like SWISS-MODEL and AlphaFold2 differ in their approaches? What validation metrics ensure model accuracy?
4. How do molecular dynamics (MD) simulations and molecular docking contribute to drug discovery? Discuss software tools (e.g., GROMACS, AutoDock Vina) and applications like virtual screening.
5. What role do databases like CATH, SCOP, and PDB play in structural bioinformatics? Why is evolutionary conservation critical for predicting protein function?
6. Explain how structural bioinformatics enables personalized medicine. Use HER2-positive breast cancer (trastuzumab) and EGFR-mutant lung cancer (osimertinib) as case studies.

Comprehensive Questions

7. Discuss the challenges of validating computational models in structural bioinformatics. How do RMSD and Ramachandran plots address these challenges?
8. How does structural bioinformatics address drug resistance in diseases like leukemia? Include examples such as the BCR-ABL1 T315I mutation and the drug ponatinib.
9. Analyze the "Comparison of Methods" table from the PDF. How do resolution, sample state, and size limitations influence the choice between X-ray, Cryo-EM, NMR, and AlphaFold2?
10. What are the future challenges for structural bioinformatics? Discuss the roles of dynamic modeling, ethical AI, and interdisciplinary collaboration in advancing the field.


THANK YOU!