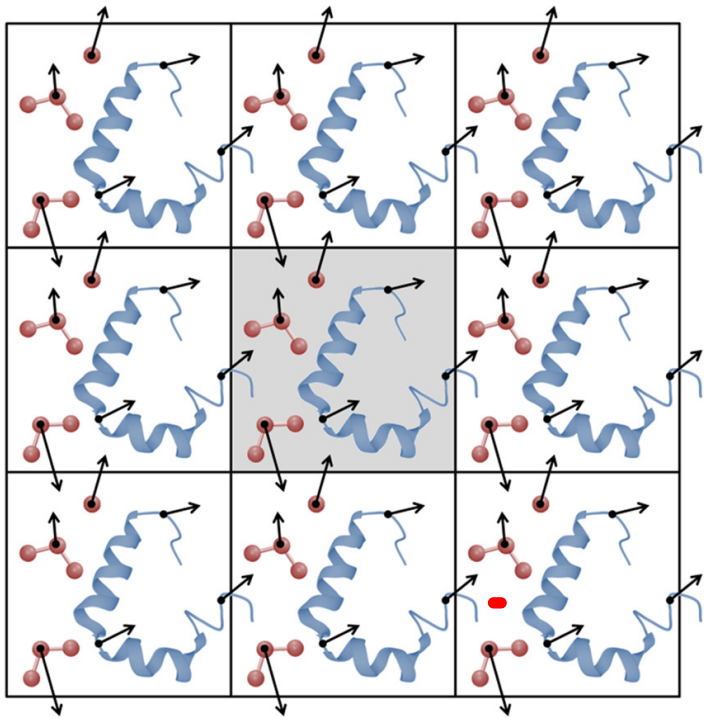
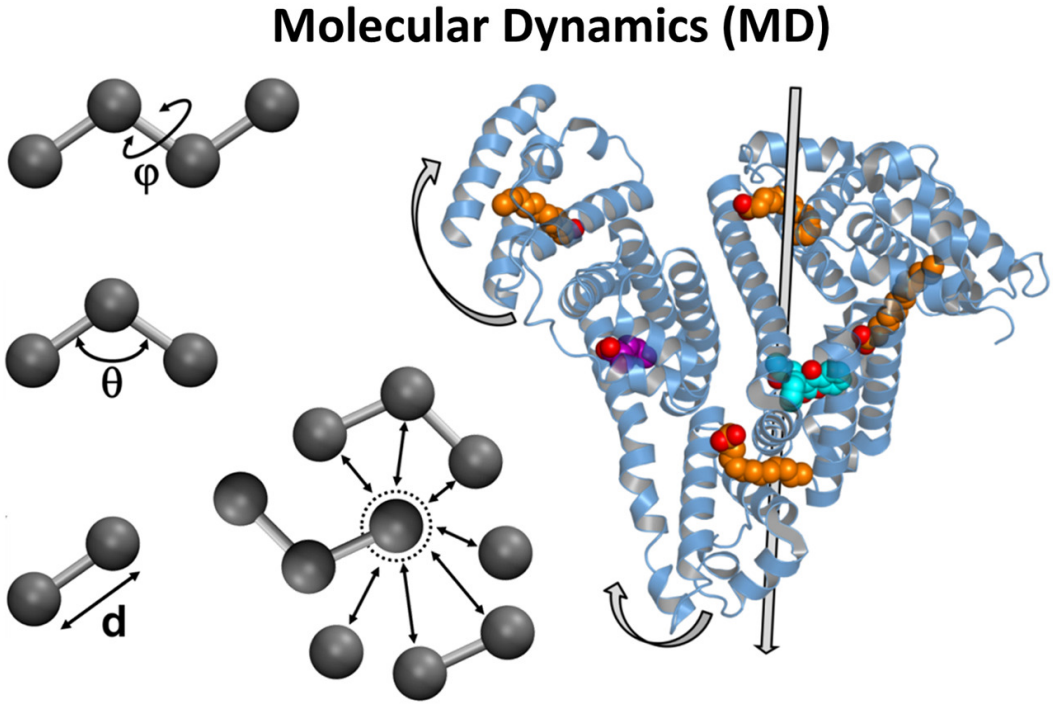
Introduction to molecular visualization of proteins





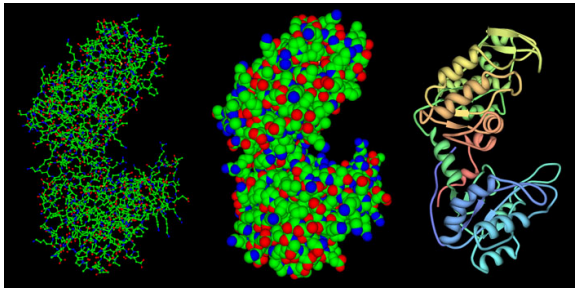
BBA-Proteins Proteomics, Volume 1870, Issue 3, 1 March 2022, 140757

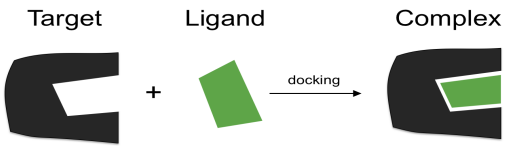
MolSimBioMed: An Introduction to Molecular Dynamics Simulations & Docking for Biomedical Applications

- Course instructors:
  - Dr. hab. Adolfo Poma Bernaola
  - Dr. Luis Fernando Cofas-Vargas
- Course type:
- ECTS credits: 4
- Total hours: 30 h (15 x 2 h)
- Language: English

Key course objectives

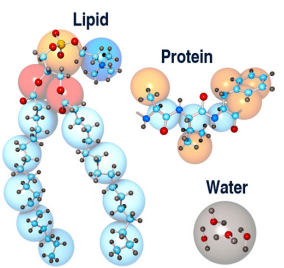
- Understand molecular visualization and structure preparation
- Learn molecular docking and molecular dynamics (MD) simulations
- Use MD tools like GROMACS and AMBER
- Analyze ligand-protein interactions
- Explore coarse-grained simulations for large biomolecular systems





FAST. FLEXIBLE. FREE.
GROMACS

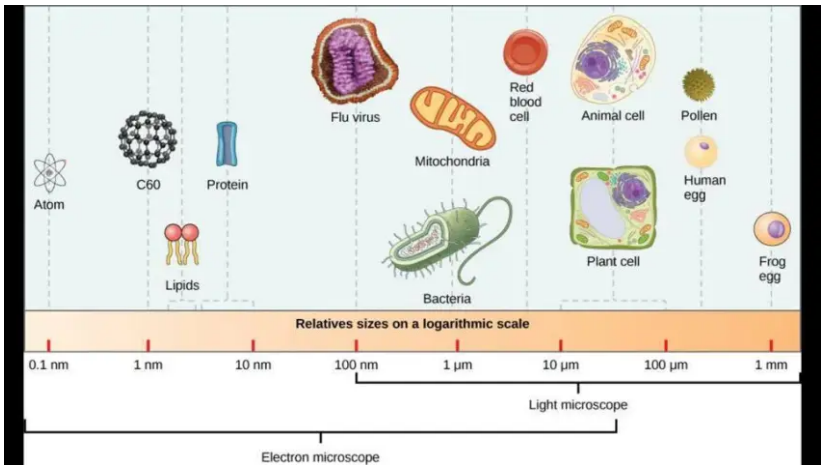
AmberTools23

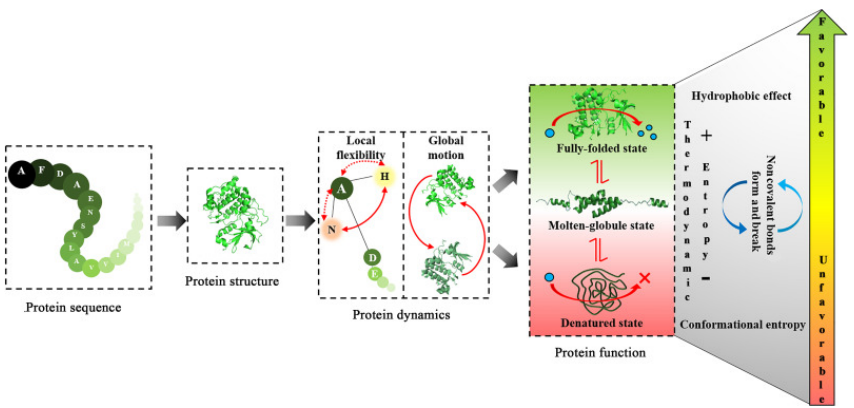


Chem. Rev. 2016, 116, 14, 7898–7936

Why do we model molecular systems?

- Molecular structures are too small for conventional microscopes (< 200 nm)
- Bridging the gap between experiments and predictions
- Understanding biomolecular function: Structure-Function relationship
- Predicting interactions
- Complementing experimental methods: X-ray, NMR, Cryo-EM

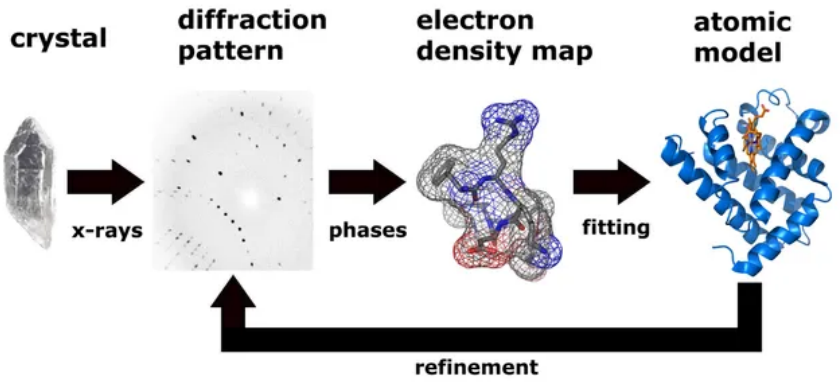


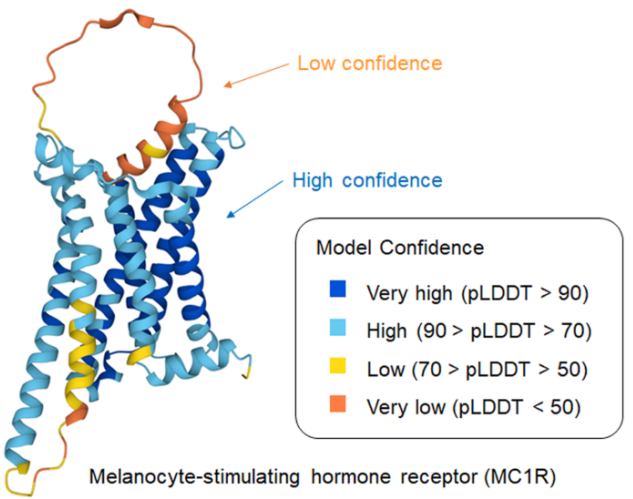


Microbial and Natural Macromolecules, Synthesis and applications, 2021, 755-809

The evolution of structural biology and molecular modeling

- 1960s-1970s:
  - X-ray crystallography and NMR
    - Need for a structured way to store atomic coordinates → PDB format (Protein Data Bank) was born
- 1980s-1990s:
  - Molecular dynamics simulations begin using XYZ, and PDB file formats
    - New experimental methods refine structure determination
- 2000s-present:
  - Cryo-EM revolution: needed better formats for large molecular assemblies
  - AI-based methods (AlphaFold, RoseTTAFold) change how we predict protein structures

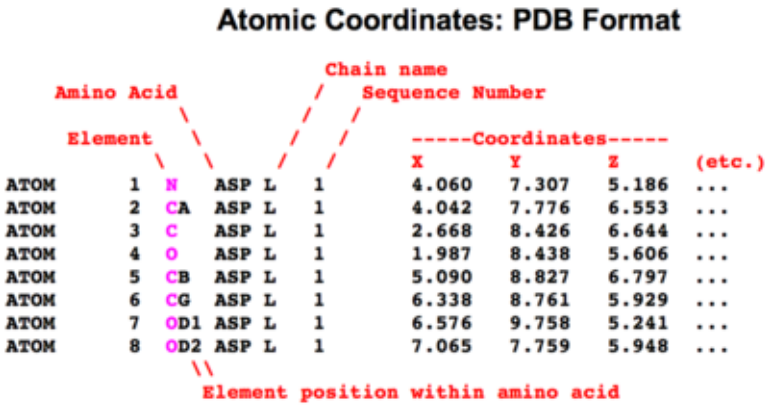


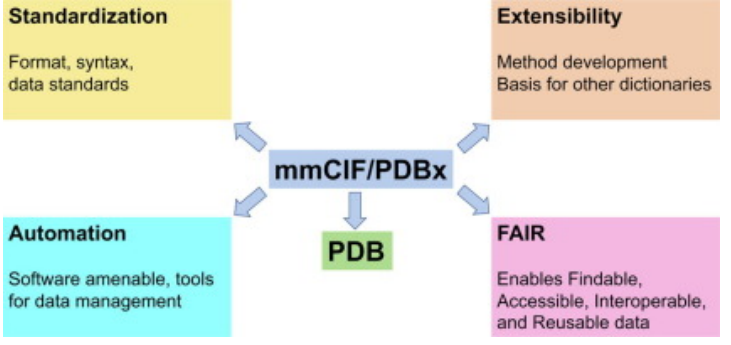


J Hum Genet 69, 477–480 (2024).

Why are molecular structure formats important?

- Molecular structures must be stored and analyzed computationally
- Standardized formats (PDB, XYZ, CIF, mmCIF) allow easy sharing and simulation
- Each format has historical reasons behind it:
  - PDB: first widely used format for proteins structures (X-ray, NMR)
  - MmCIF: needed for large molecular complexes (Cryo-EM)

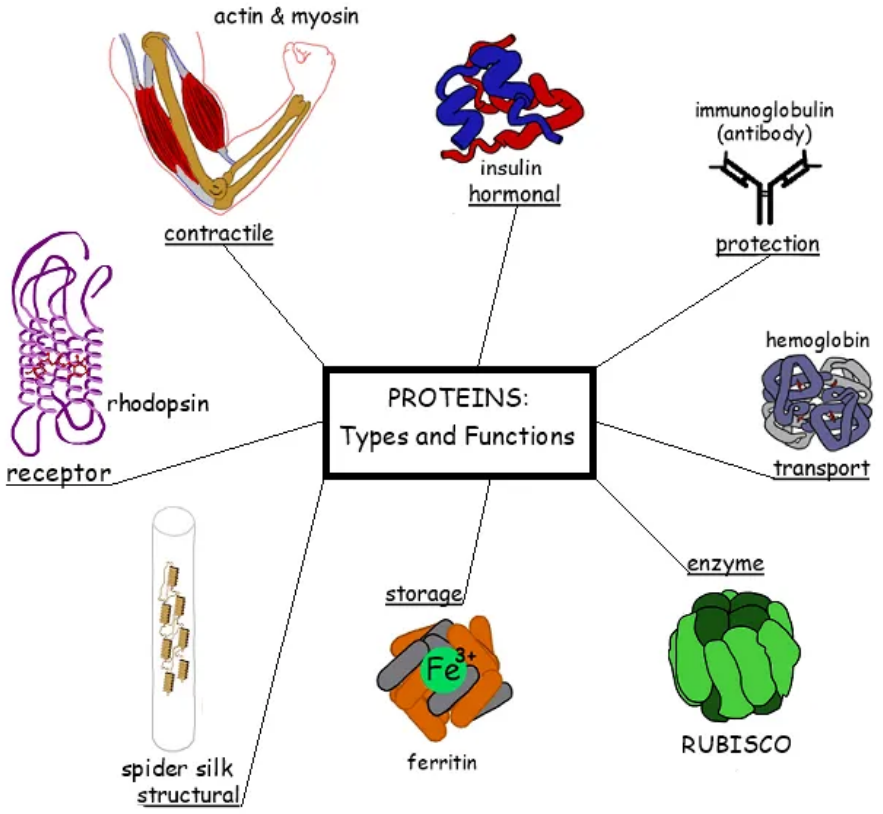




JMB, 2002, 343, 11, 167599

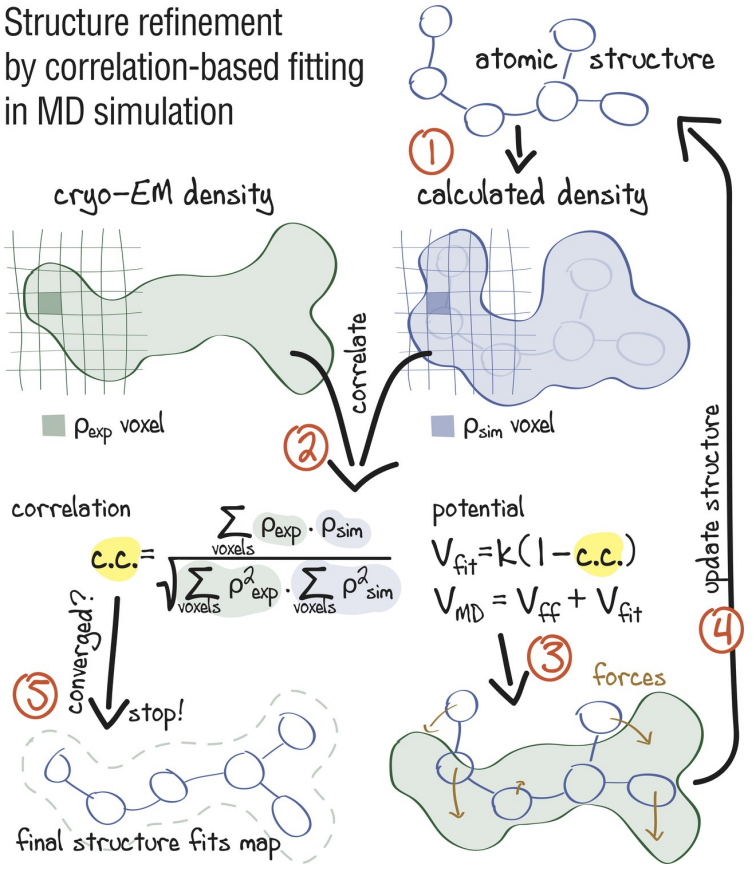
Principles of Structure-Functions

- Why structure is important?
  - The shape and flexibility of a molecule dictate its biological function
- Why do we simulate?
  - Many biological process involve dynamics that are not capture in static structures
  - Simulations allow us to observe how molecule move and interact over time



Linking experiments to models

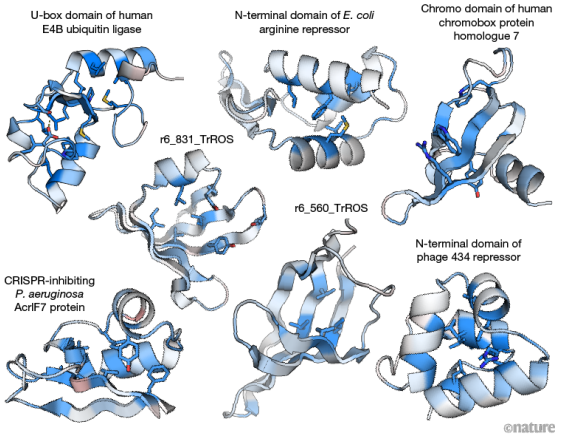
- Experiments give us static snapshots (X-ray, NMR, Cryo-EM)
- Simulations let u s explore molecular motions and interactions
- Modern structural biology integrates experiments with computational models
  - Cryo-EM provides a low-resolution density map → Molecular modeling refines atomic details
  - Experimental binding assays → Docking simulations predict binding sites and affinities

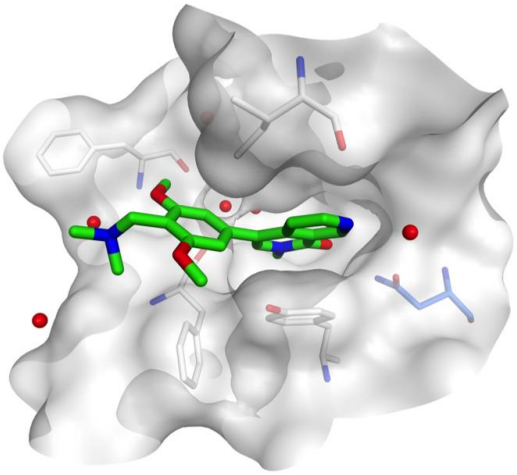


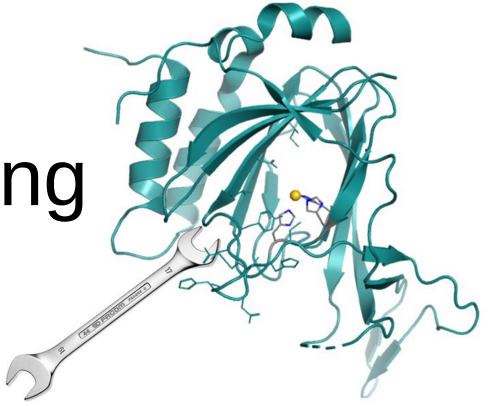
eLife 8:e43542.

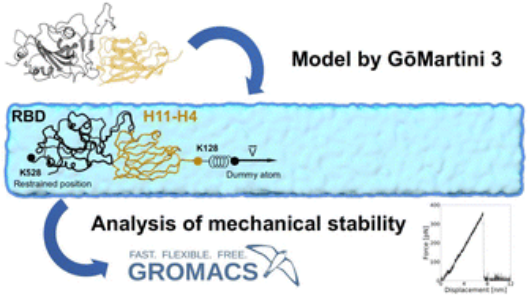
Applications in biomedical sciences

- Protein folding and stability
- Drug binding and discovery
- Pathogen interaction studies
- Biomolecular engineering
- Nanomechanics









Summary

- Modeling is neccesary because experimental methods provide partial information (static picture)
- Molecular structure determination evolves alongside experimental techniques
- Modeling allow the dynamics exploration of biological systems based on the structure-function relationship