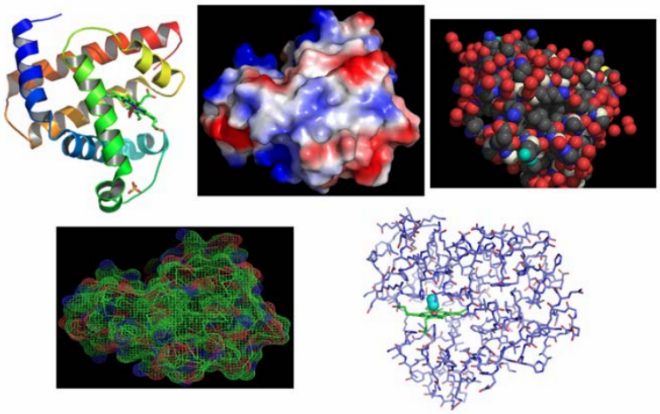
CHAPTER OVERVIEW

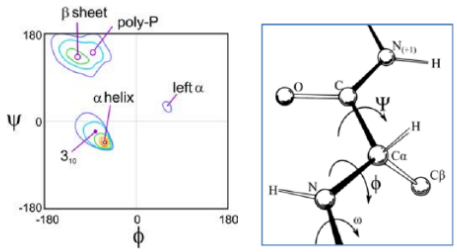
7: Statistical Description of Macromolecular Structure

There are a number of ways in which macromolecular structure is described in biophysics, which vary in type of information they are trying to convey. Consider these two perspectives on macromolecular structure that represent opposing limits: atomistic vs. statistical.

1. **Atomistic**: Use of atoms, small molecules, or functional groups as building blocks for biomolecular structure. This perspective is rooted in the dominant methods used for studying macromolecular structure (90% X-ray crystallography; 10% NMR). It has the most value for describing detailed Ångstrom to nanometer scale interactions of a chemical nature, but also tends to reinforce a unique and rigid view of structure, even though this cannot be the case at physiological temperatures. The atomistic perspective is inherent to molecular force fields used in computational biophysics, which allow us to explore time-dependent processes and molecular disorder. Even within the atomistic representation, there are many complementary ways of representing macromolecular structure. Below are several representations of myoglobin structure, each is used to emphasize specific physical characteristics of the protein.



2. **Statistical/physical**: More applicable for disordered or flexible macromolecules. Emphasis is on a statistical description of molecules that can have multiple configurations. Often the atomic/molecular structure is completely left out. These tools have particular value for describing configurational entropy and excluded volume, and are influenced by the constraints of covalent bonding linkages along the chain. This approach is equally important: 30–40% of primary sequences in PDB are associated with disordered or unstructured regions. Conformational preferences are described statistically.



Statistical Models

- Structure described in terms of spatial probability distribution functions.
- There may be constraints on geometry or energy functions that describe interactions between and within chains.
- We will discuss several models that emerge for a continuous chain in space that varies in stiffness, constraints on conformation, and excluded volume.
  - Segment models: random coils, feely jointed chain, freely rotating chain
  - Lattice models: Flory–Huggins theory

- Continuum model: worm-like chain
