Structural Bioinformatics (C3210)

Introduction to Structural Bioinformatics

Structural Bioinformatics

Structural Bioinformatics is an interdisciplinary field that deals with the three dimensional structures of biomolecules. It attempts to model and discover the basic principles underlying biological machinery at the molecular level. It is based on the assumption that 3D structural information of a biological system is the core to understanding its mechanism of action and function. Structural bioinformatics combines applications of physical and chemical principles with algorithms from computational science.

Major areas:

◆ protein and nucleic acid 3D structure determination
◆ prediction of protein 3D structure from sequence
◆ protein structure validation
◆ protein structure comparison and alignment
◆ protein and nucleic acid structure classification
◆ inferring protein function from structure
◆ prediction of protein-ligand interaction
◆ prediction of protein-protein interactions
◆ development of databases

Challenges in the Post Genomic Era

The completion of the human genome project (first draft 2000, completed 2003) and other genome projects were the first step towards a comprehensive understanding of life at the molecular level.

One of the key issues is the characterization of structure and function of proteins with a view to using the findings in the discovery of novel and effective therapeutic treatments.
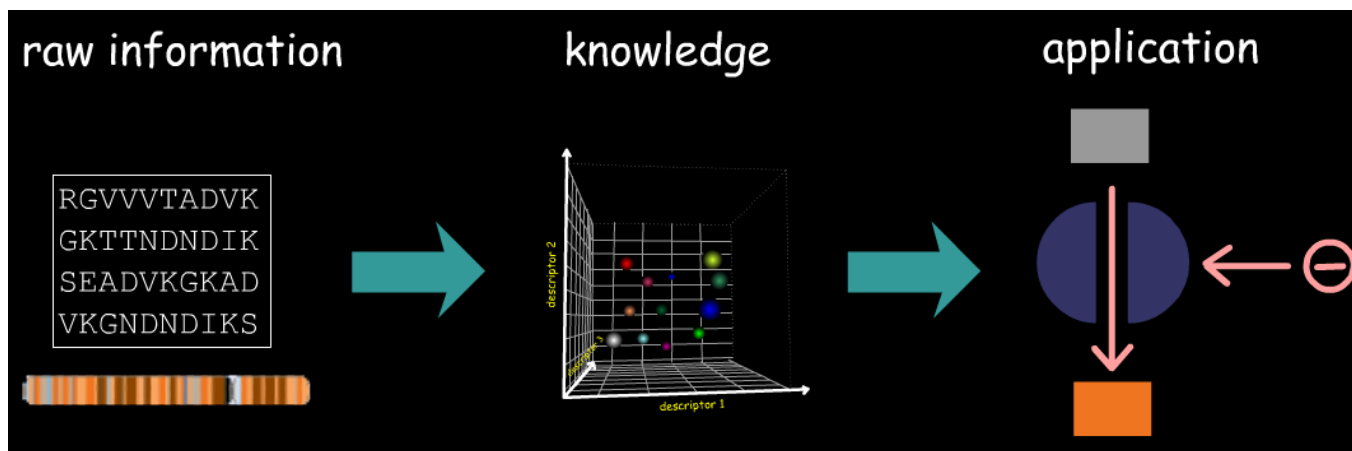
Structure-function paradigm

Structural Bioinformatics is based on the protein structure-function paradigm, which states that the function of a macromolecule is dictated by its 3D-structure.
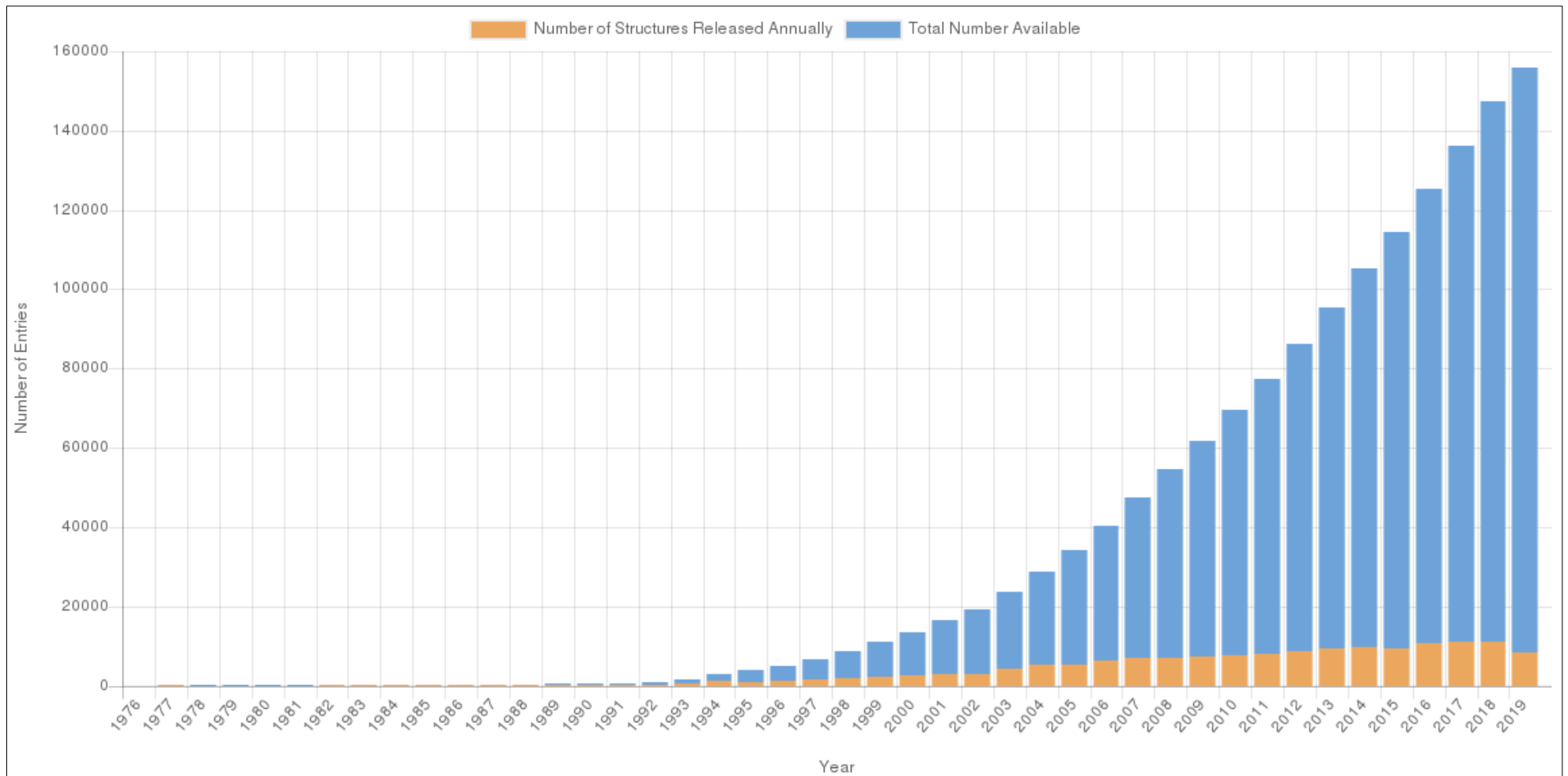
The challenges for our post genomic era towards a systematic understanding of life are:

- to obtain the 3D structures of all the proteins encoded in the genomes
- to decode their function based on their structure
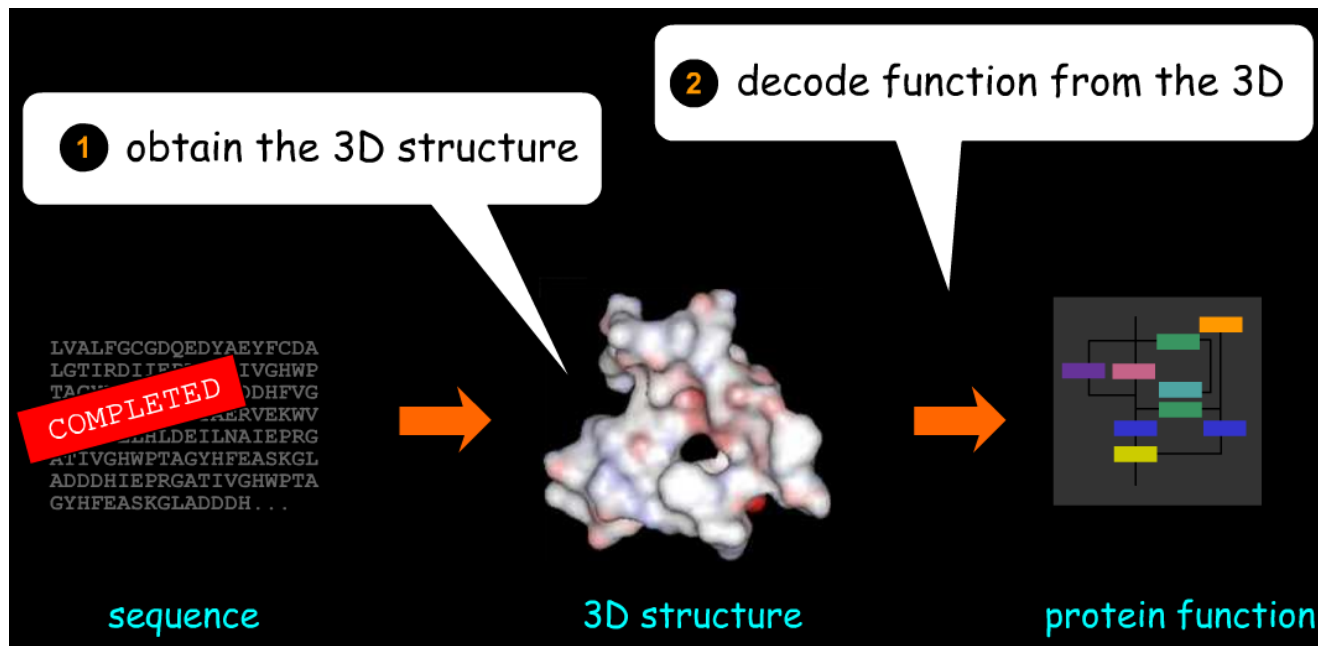
Solved 3D Structures Growth

Total number of determined 3D structures of proteins is approx. 156 000 (September 2019)

Is Structure Sufficient to Predict Function?

Proteins are not static; to fulfill their function they undergo a wide range of motion and conformational rearrangements. The knowledge of a static structure may not be sufficient to understand its biological function. An important component of structural bioinformatics is the development of experimental and computational methods (such as molecular dynamics) that sheds light on the dynamic behavior of biological systems. These methods simulate the way biomolecules behave, specifically recognize each other, interact and trigger biological events at the molecular level.
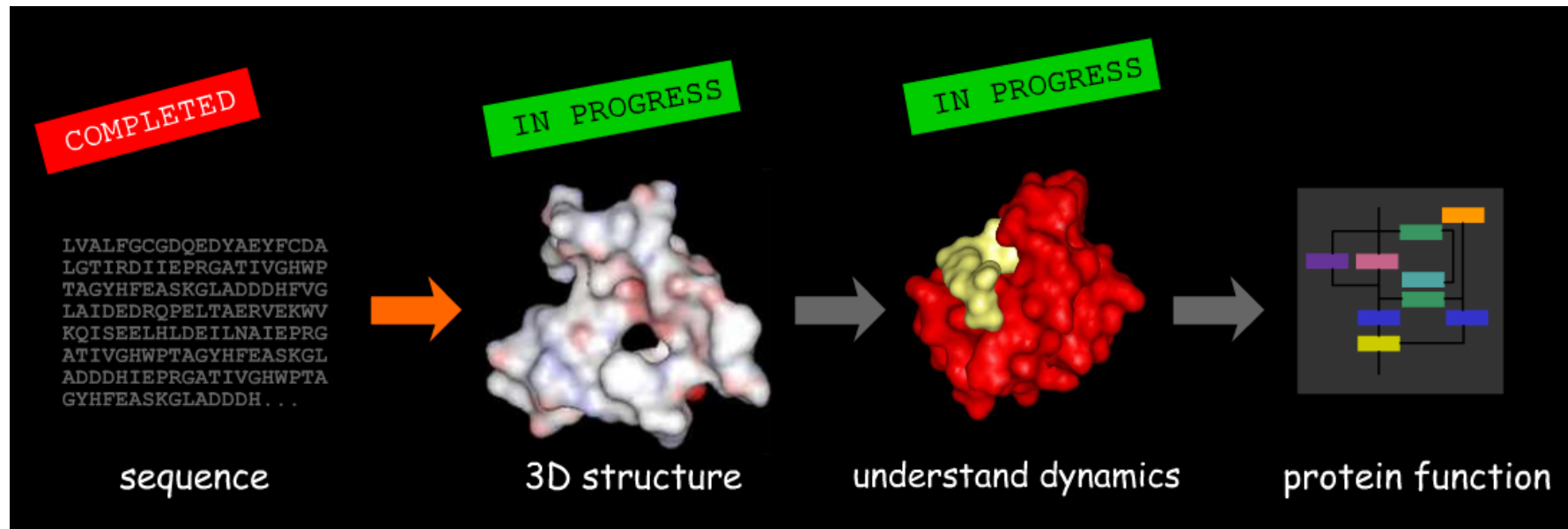
Biomolecules in the Cell

The two most important biomolecules present in our cells are proteins and nucleic acids.
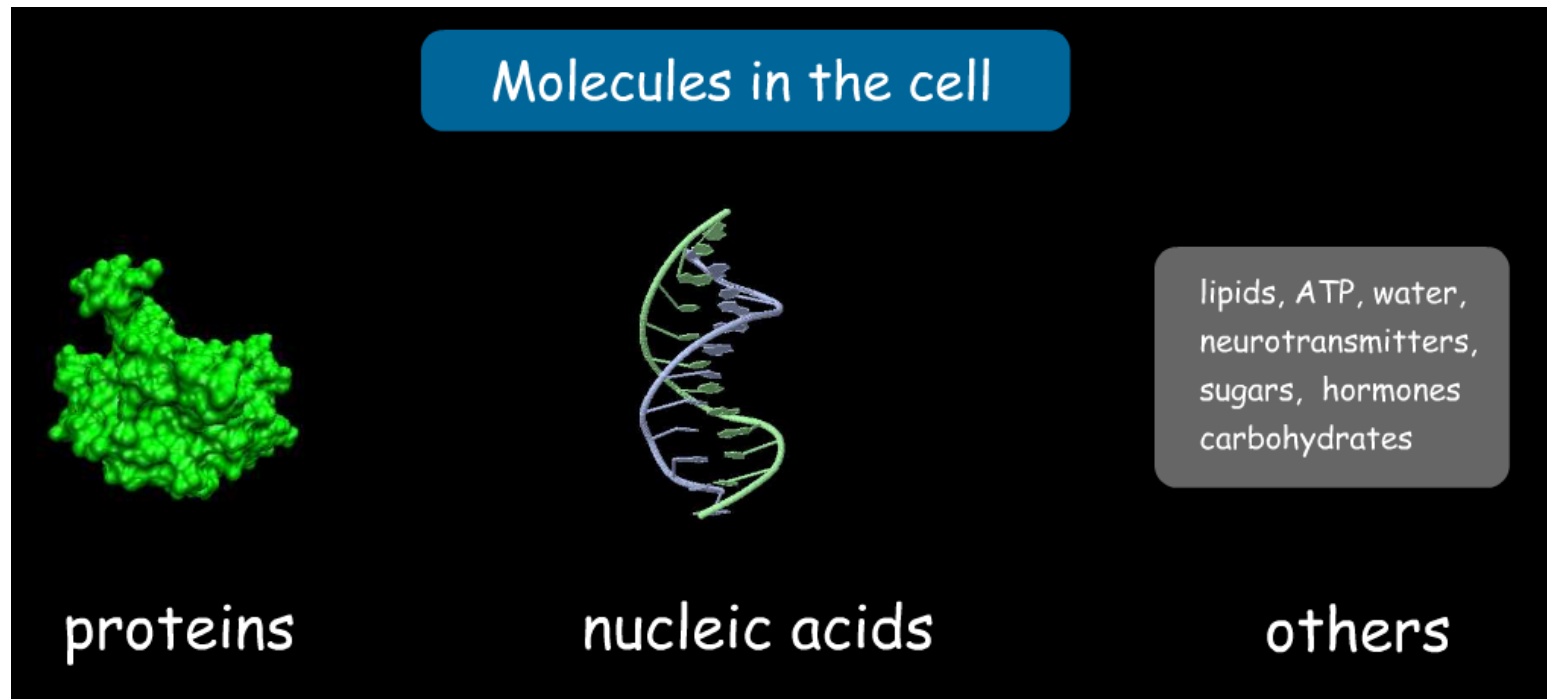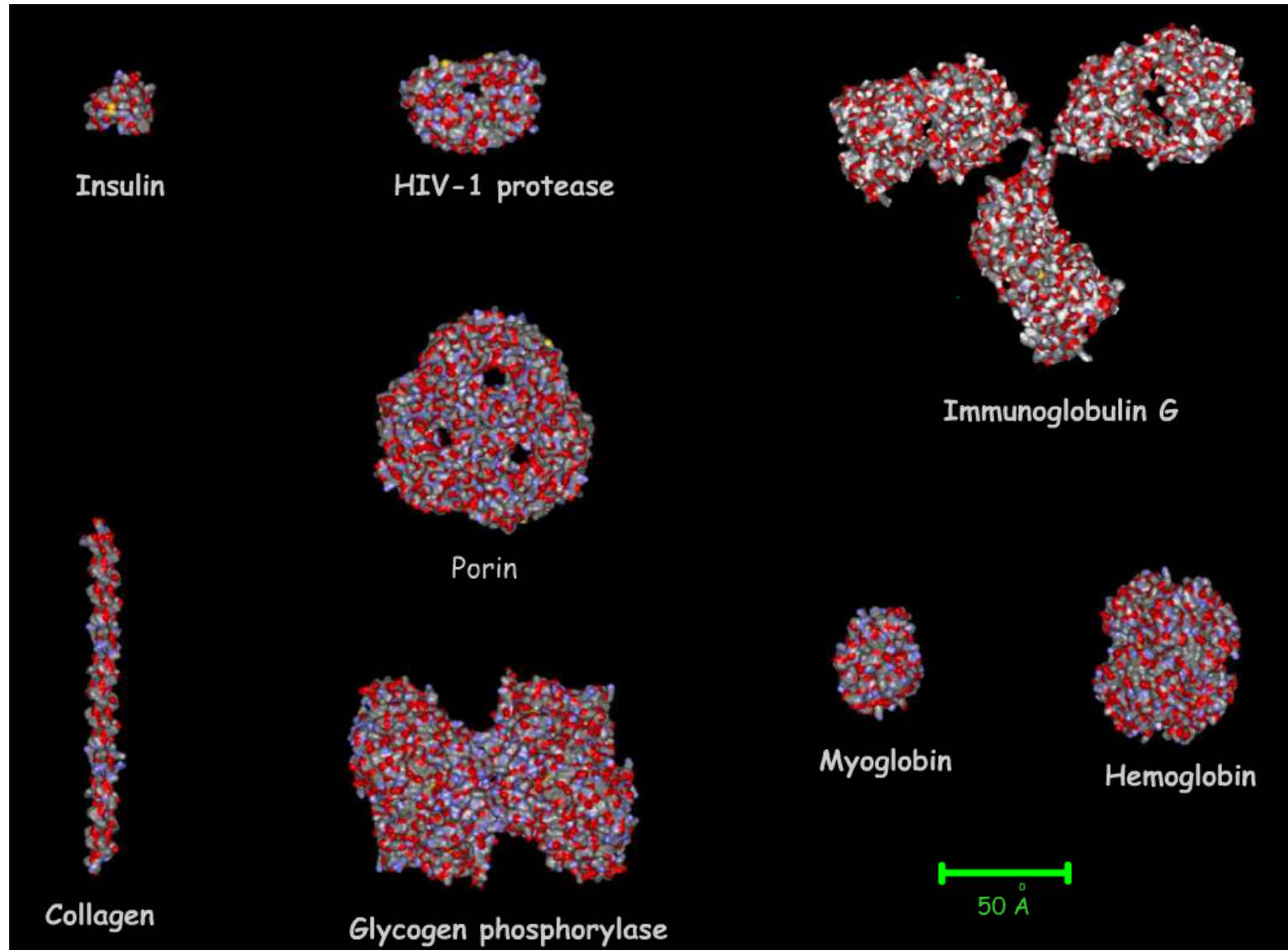
Proteins

Proteins form the very basis of life. They are the most abundant macromolecules in living cells. Thousands of different proteins can be found in a single cell, and proteins have been identified in all parts of all cells. Proteins affect virtually every property that characterizes a living organism.
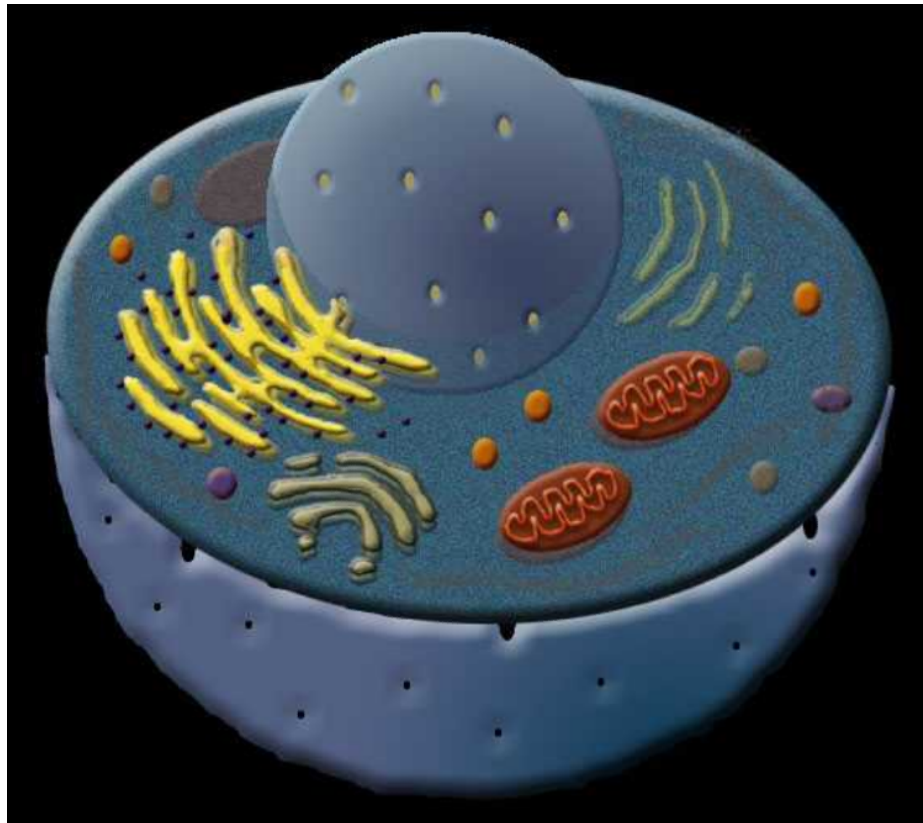
Structural Diversity of Protein Structure

The great diversity of the functional properties of proteins is directly related to their subtle three-dimensional structures. Every protein has a unique 3D structure that determines its function.

Insulin

HIV-1 protease

Immunoglobulin G

Porin

Collagen

Glycogen phosphorylase

Myoglobin

Hemoglobin

50 Å

Nucleic Acids

Nucleic acids are the information carriers in the cells. This information is stored in the form of long polymer chains. Although the information they carry is one-dimensional, it is essential to understand the 3D structure of nucleic acids. This structure dictates their organization, functions and interactions with proteins.

Structure of DNA is made of two helical strands of polynucleotides.

Due to its nature, this helix contains grooves which are preferred sites for proteins and other molecules to interact with the DNA.