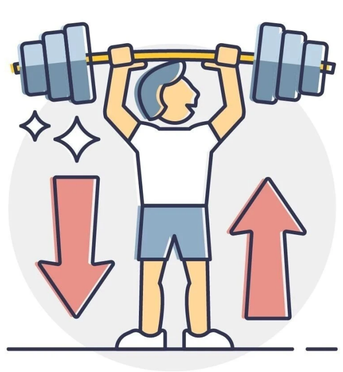
Structural Biology

Ruchika Bajaj, PhD
Membrane Protein Biologist

Why do we eat proteins ??

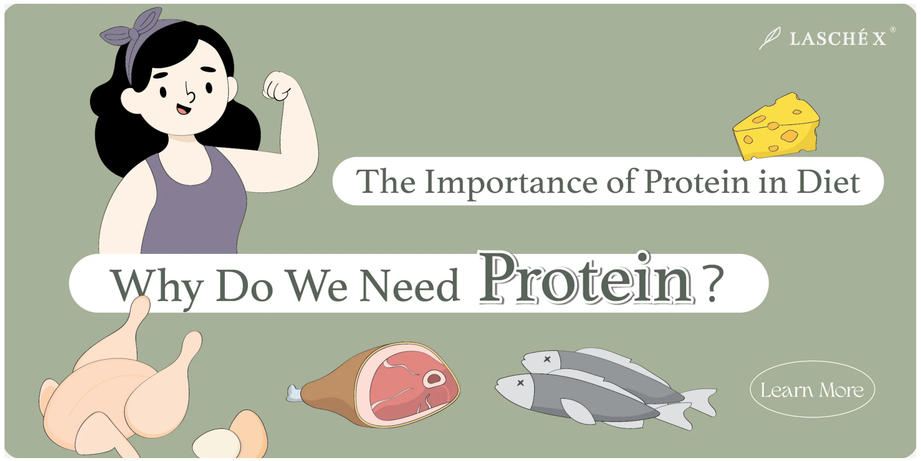
Digestive enzymes help facilitate chemical reactions

Antibodies support immune function

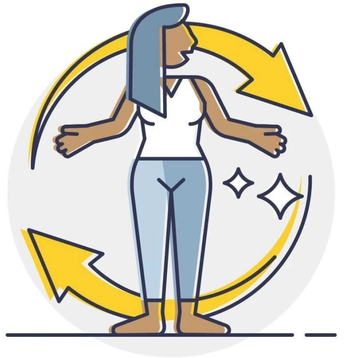


Support muscle contraction and movement

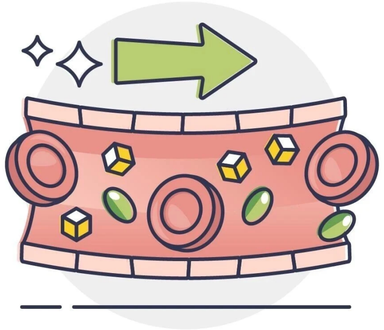
Support the regulation and expression of DNA and RNA



Provide support to the body

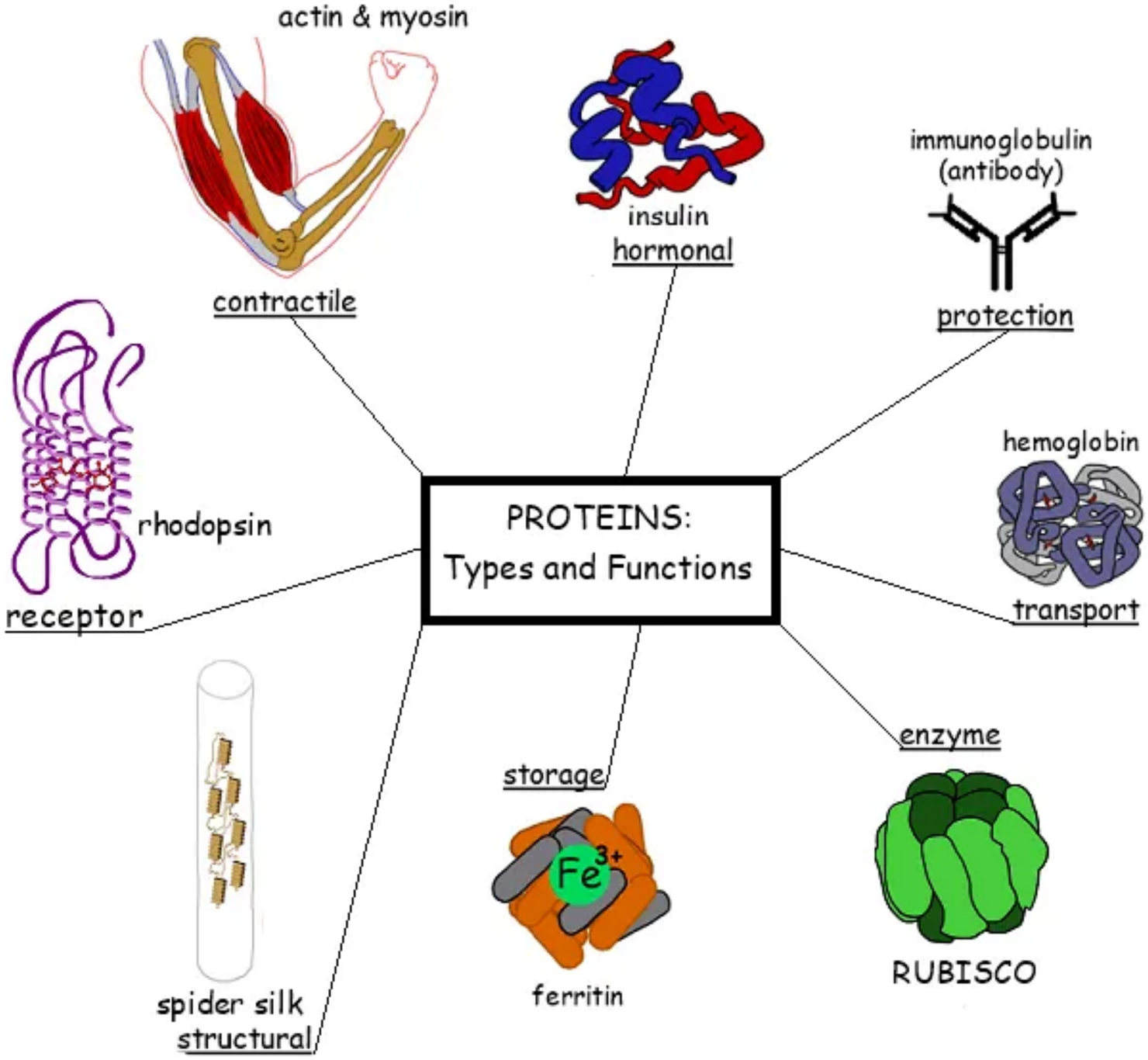


Hormones help coordinate bodily function



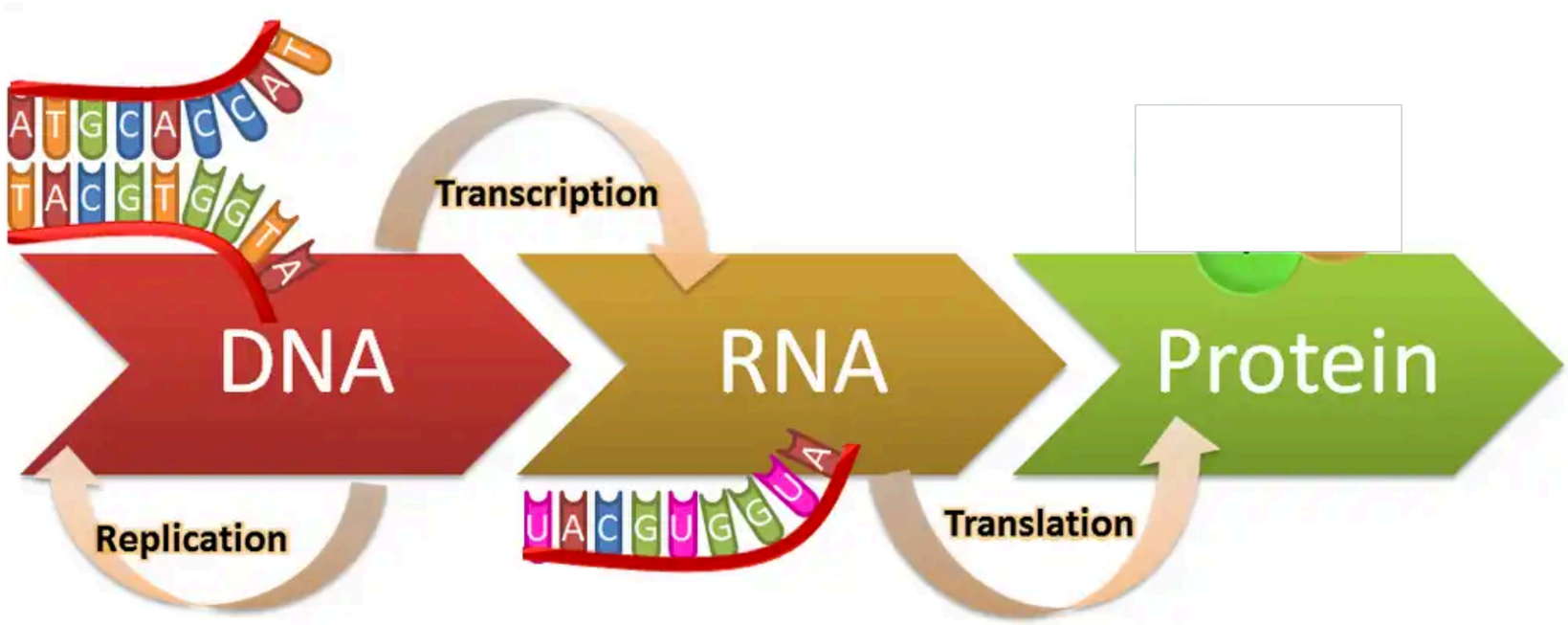
Move essential molecules around the body

Functions of protein

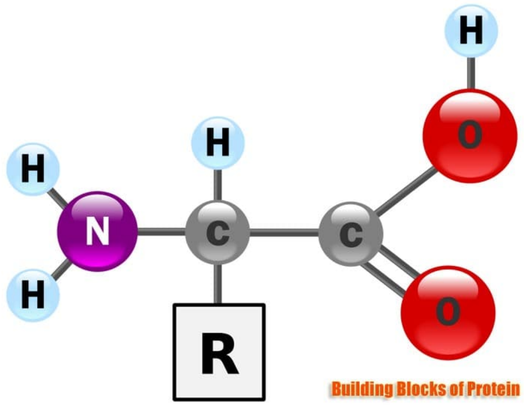


Central Dogma: Proteins : the building block of life

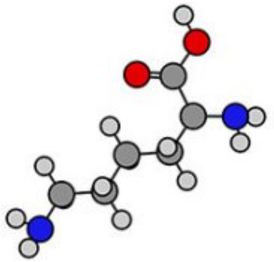
Central Dogma

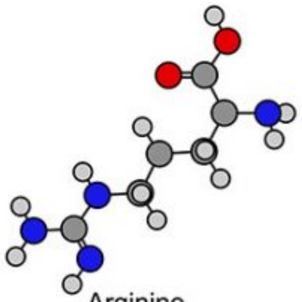


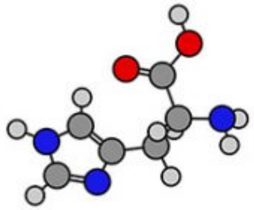
Amino acids : building blocks of proteins



Positively charged

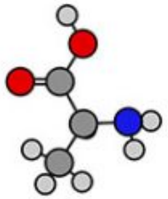

Lysine

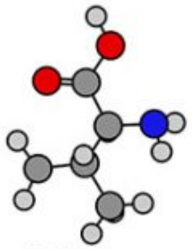

Arginine

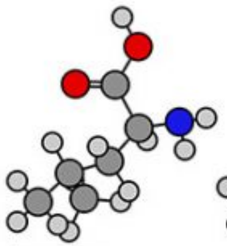

Histidine

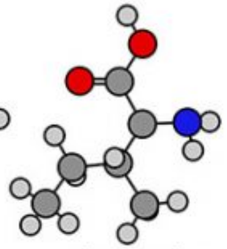
Non-Polar

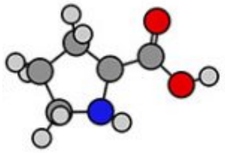

Glycine


Alanine

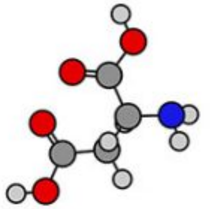

Valine

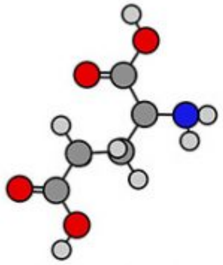

Leucine


Isoleucine

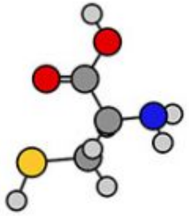

Proline

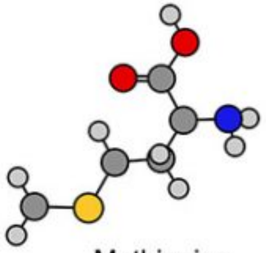
Negatively charged

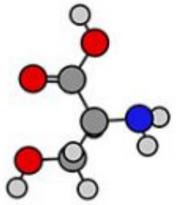

Aspartic acid

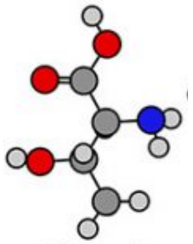

Glutamic acid

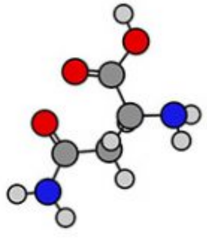
Polar

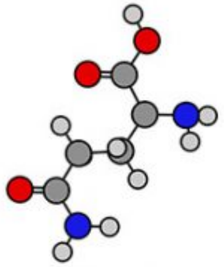

Cysteine


Methionine

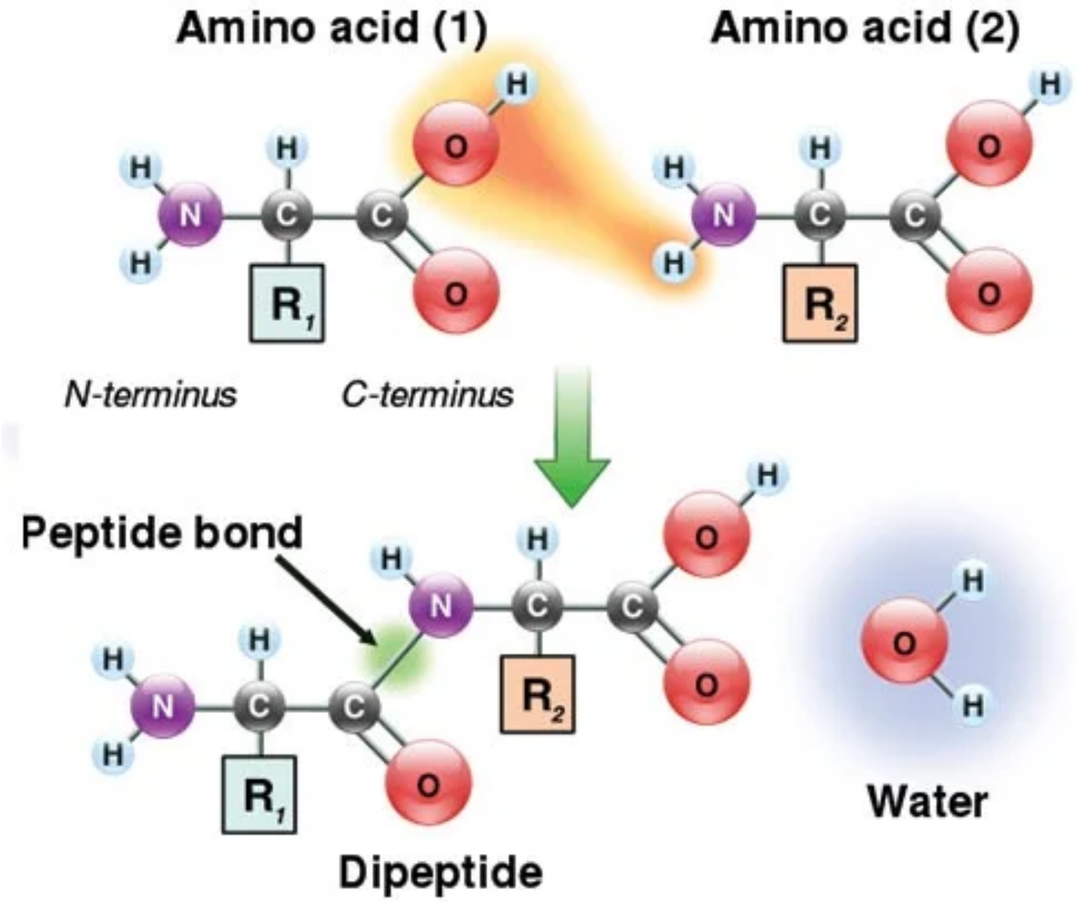

Serine

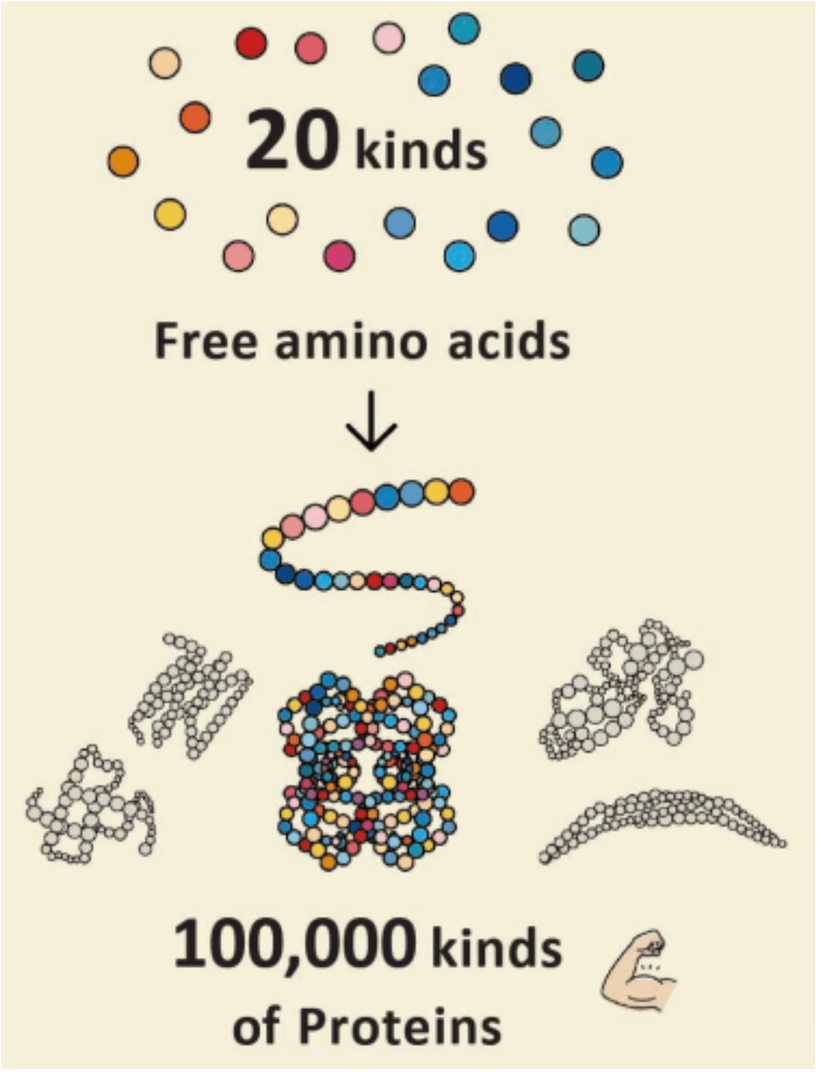

Threonine


Asparagine

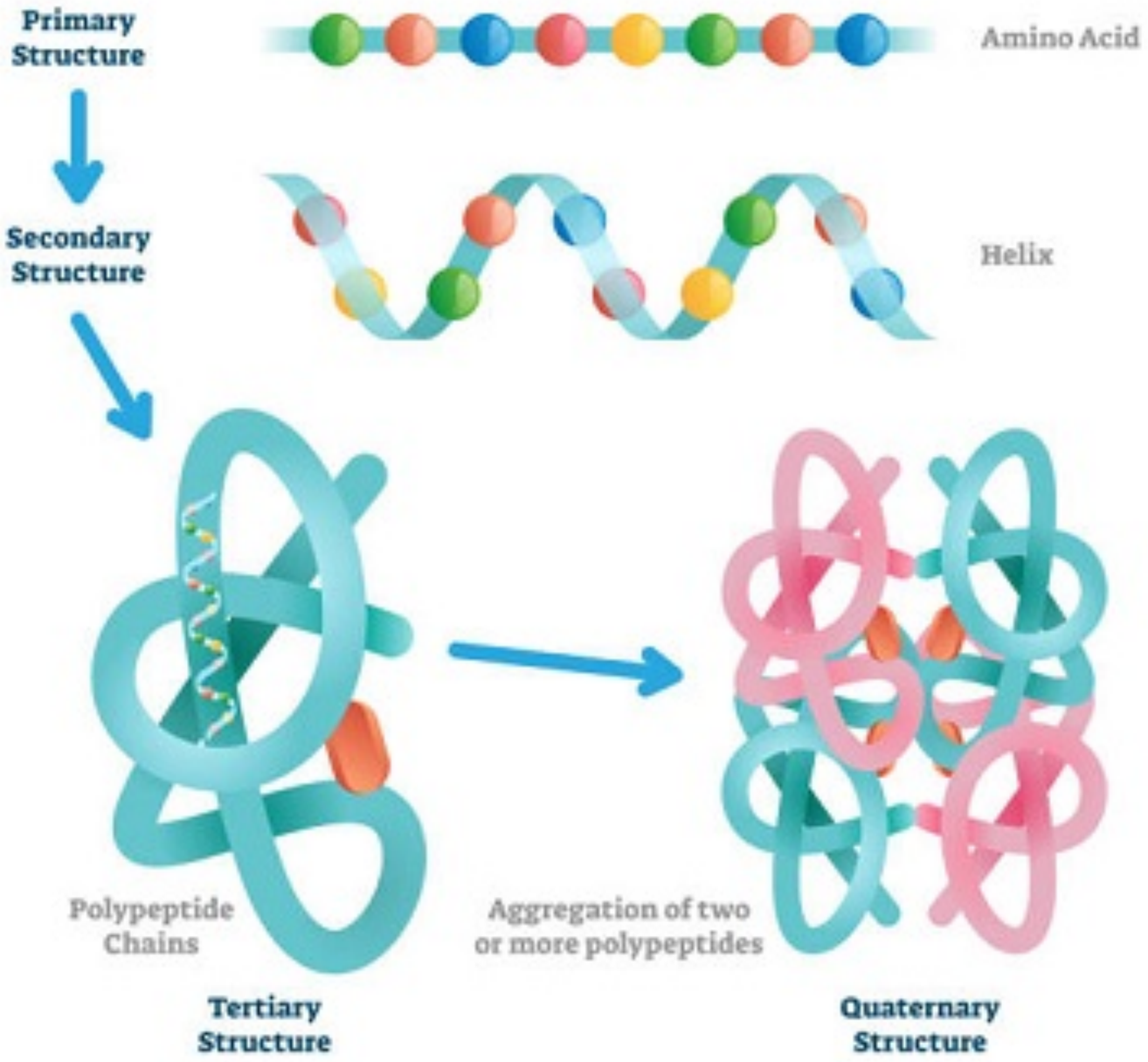

Glutamine

The peptide bond connects amino acids to build peptides

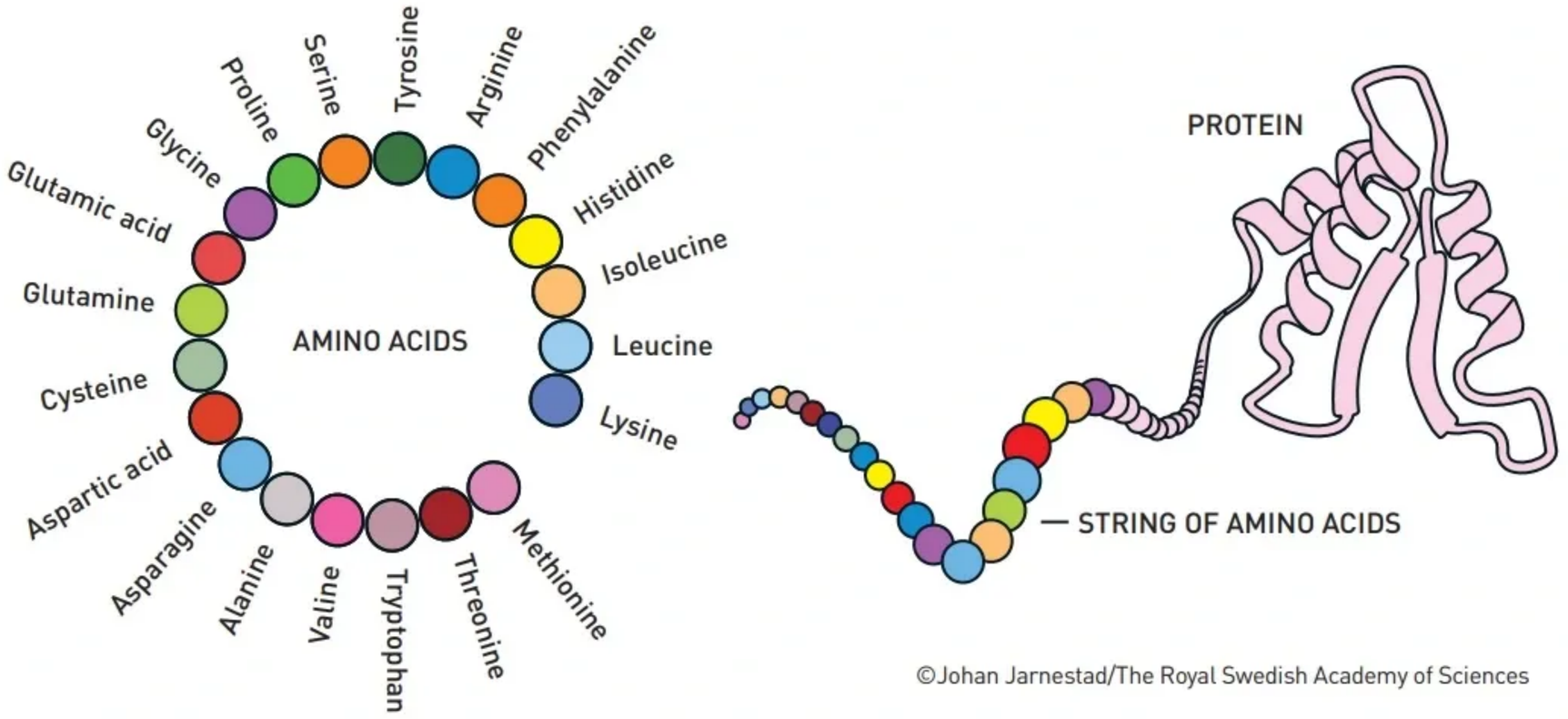




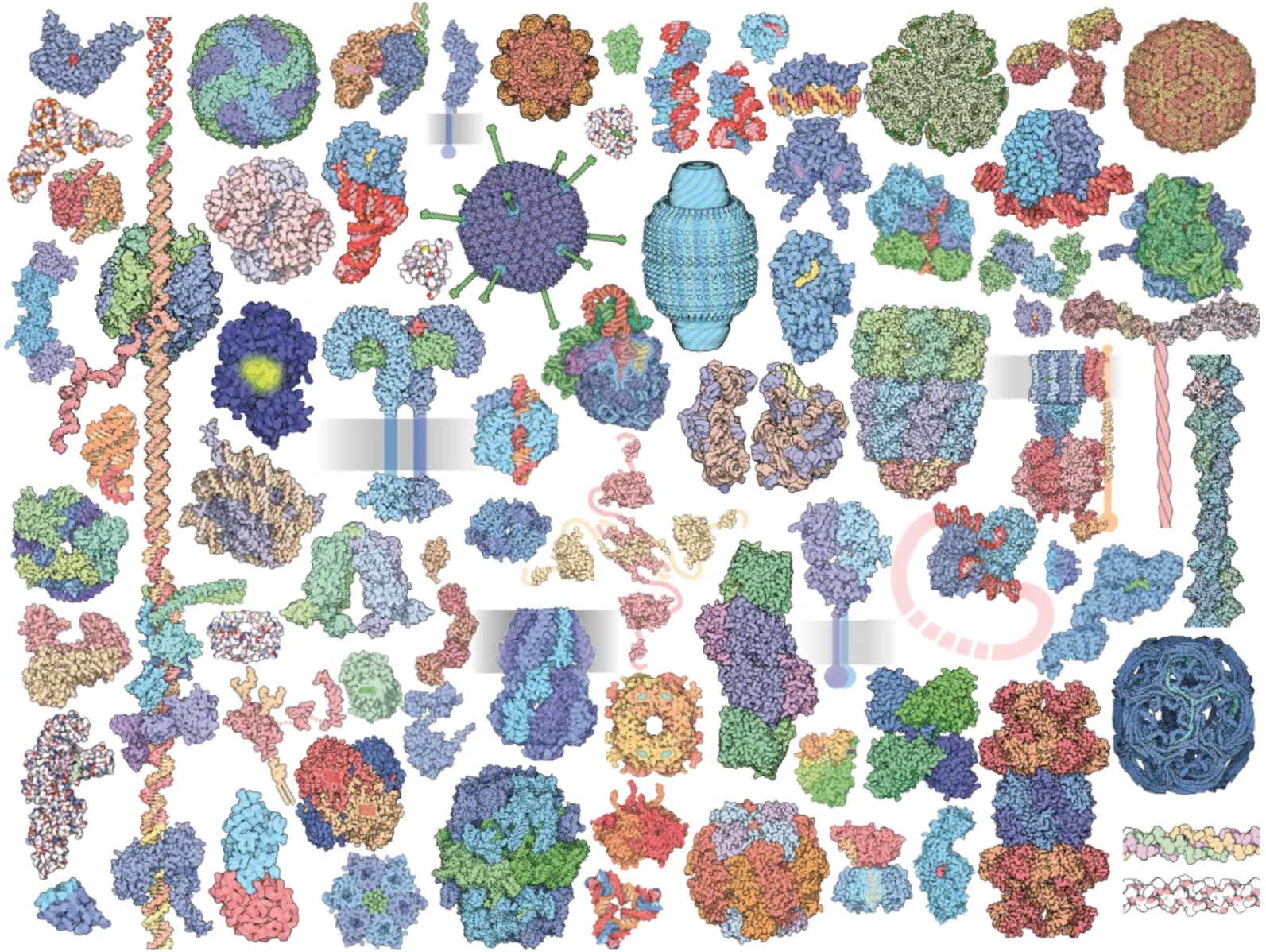
Levels of protein structure



The Folding Problem

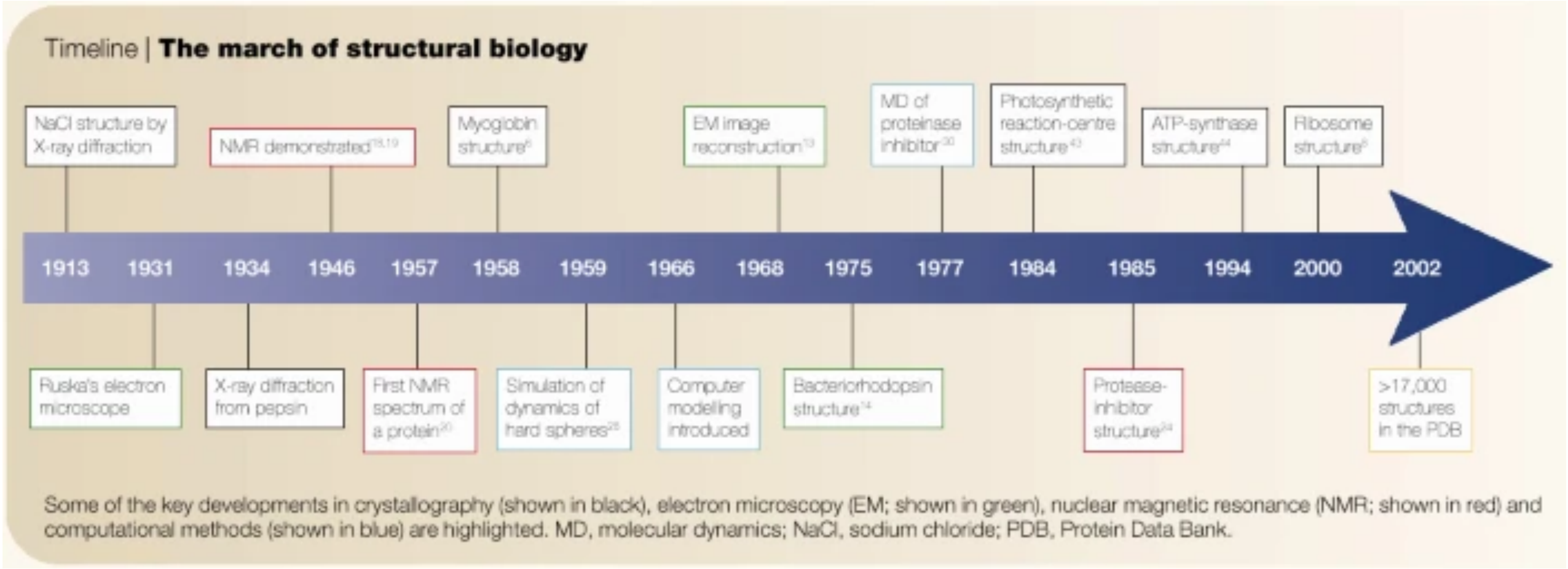


A variety of protein structures



Structural Biology is a mature science

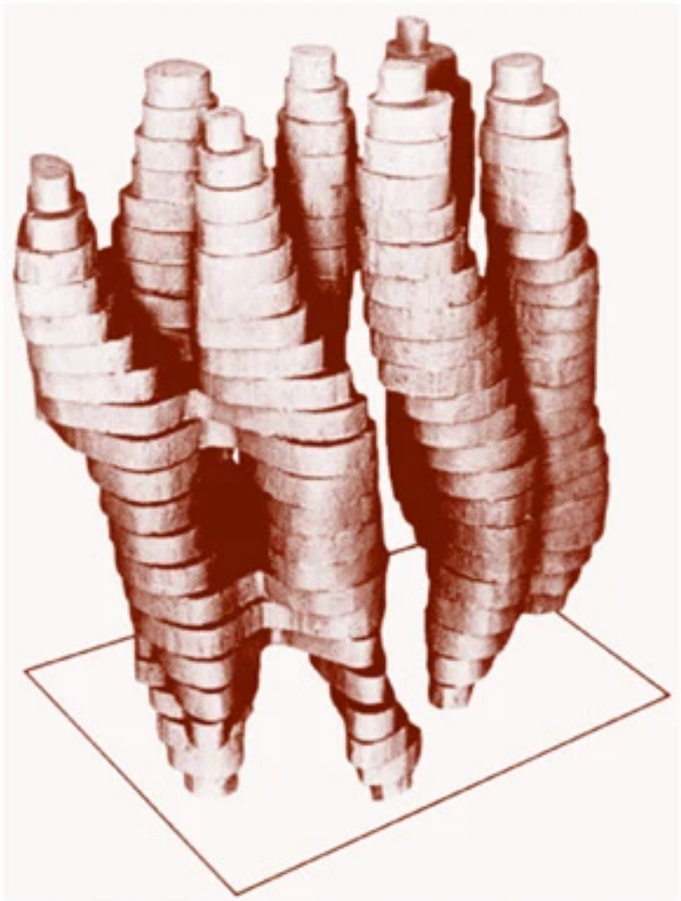
Structural biology is the study of the molecular structure and dynamics of biological macromolecules, particularly proteins and nucleic acids, and how alterations in their structures affect their function. Structural biology incorporates the principles of molecular biology, biochemistry and biophysics.



Some of the key developments in crystallography (shown in black), electron microscopy (EM; shown in green), nuclear magnetic resonance (NMR; shown in red) and computational methods (shown in blue) are highlighted. MD, molecular dynamics; NaCl, sodium chloride; PDB, Protein Data Bank.

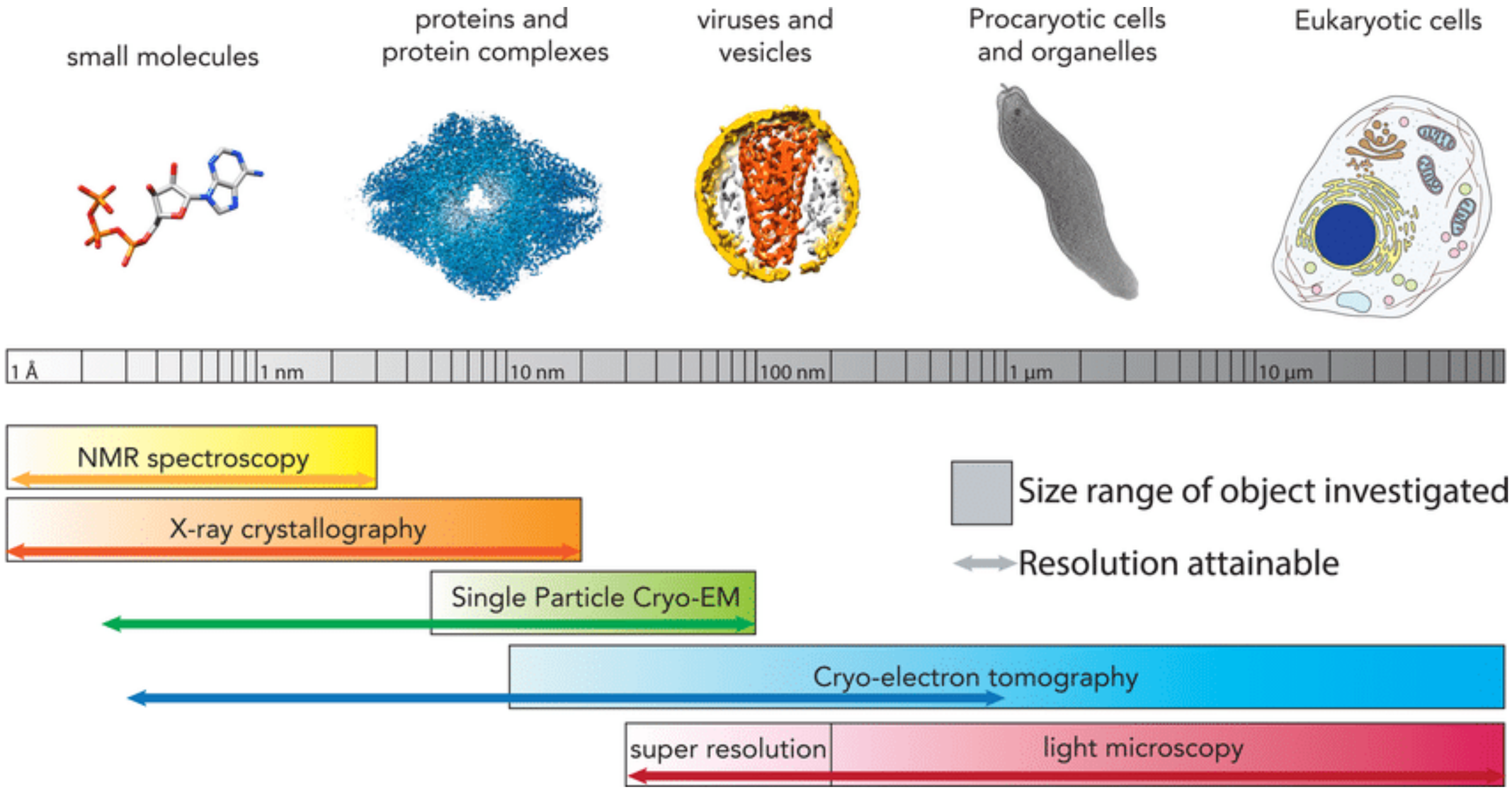
First structures in Structural Biology

1962 of Max Perutz with his balsa-wood model of haemoglobin, and John Kendrew with his wire model of myoglobin. Models were derived from X-ray data. The resolution of the myoglobin data (1.4 Å). the haemoglobin data were derived at a lower resolution (6.0 Å).

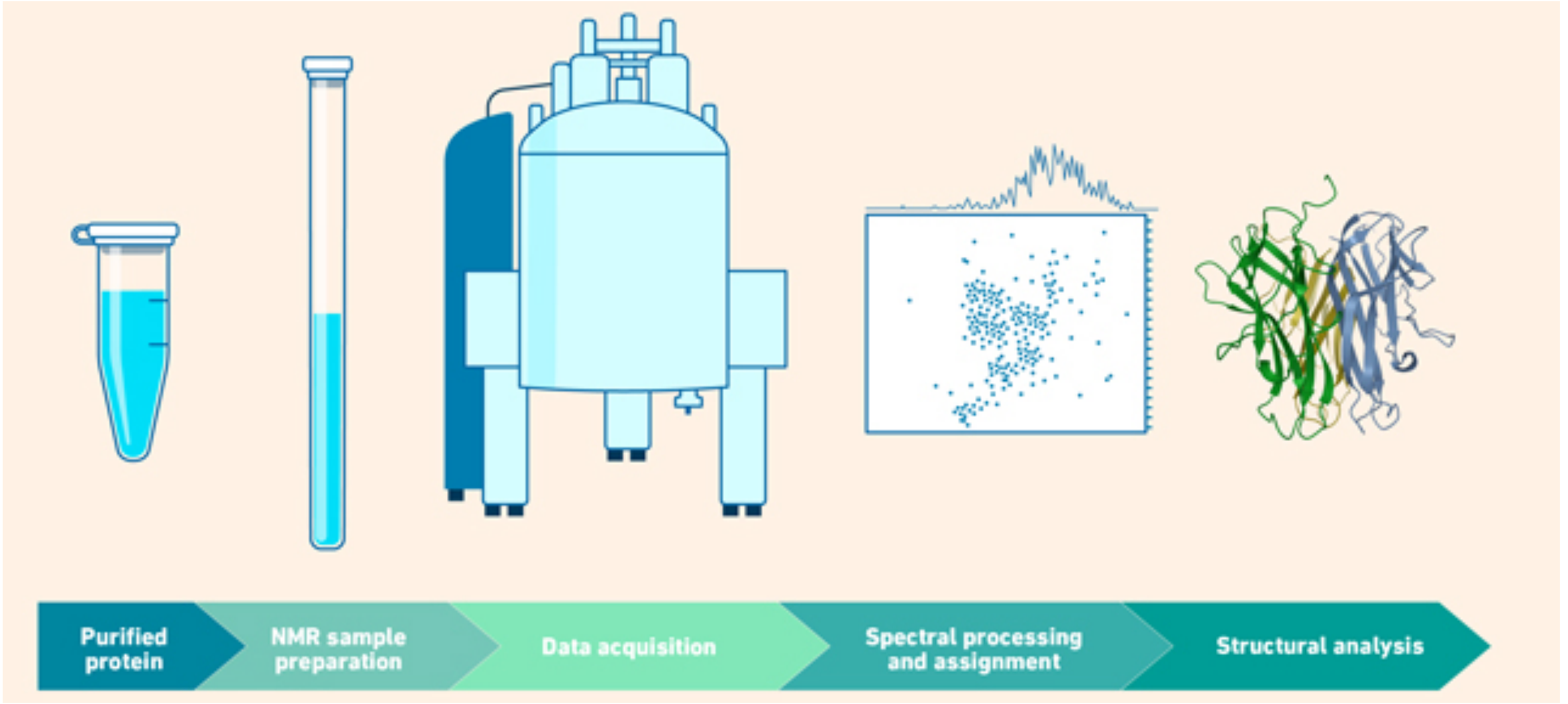


Nature Reviews | Molecular Cell Biology

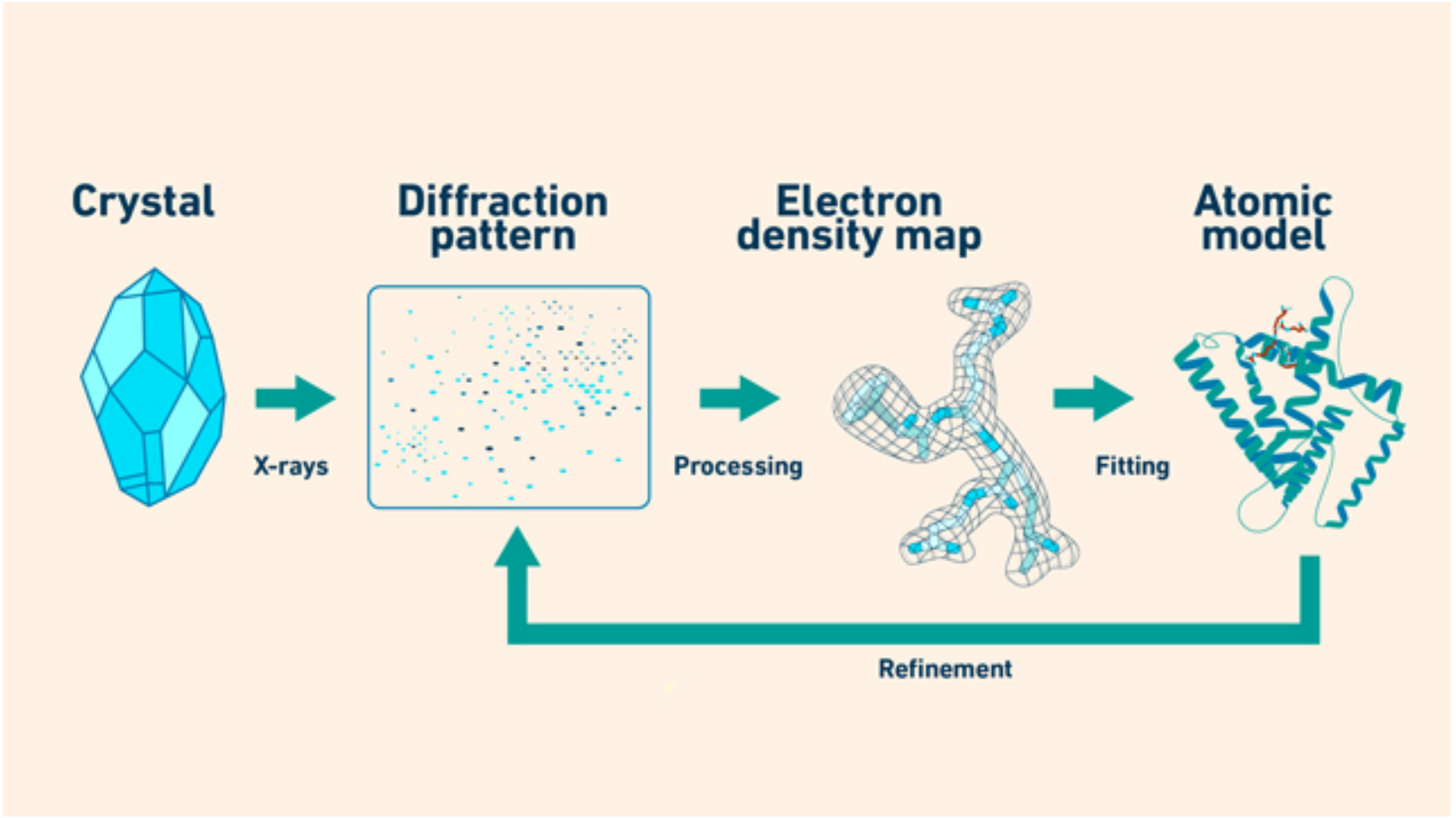
Key Techniques in Structural Biology



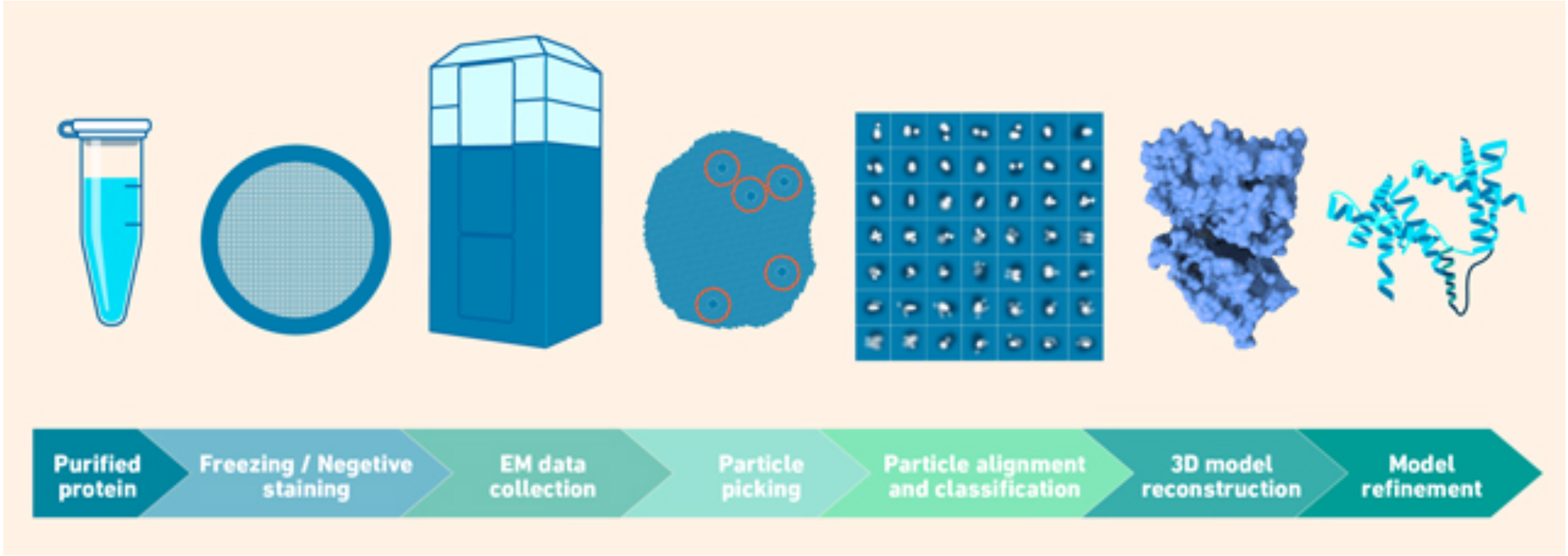
Nuclear Magnetic Resonance



X-Ray Crystallography

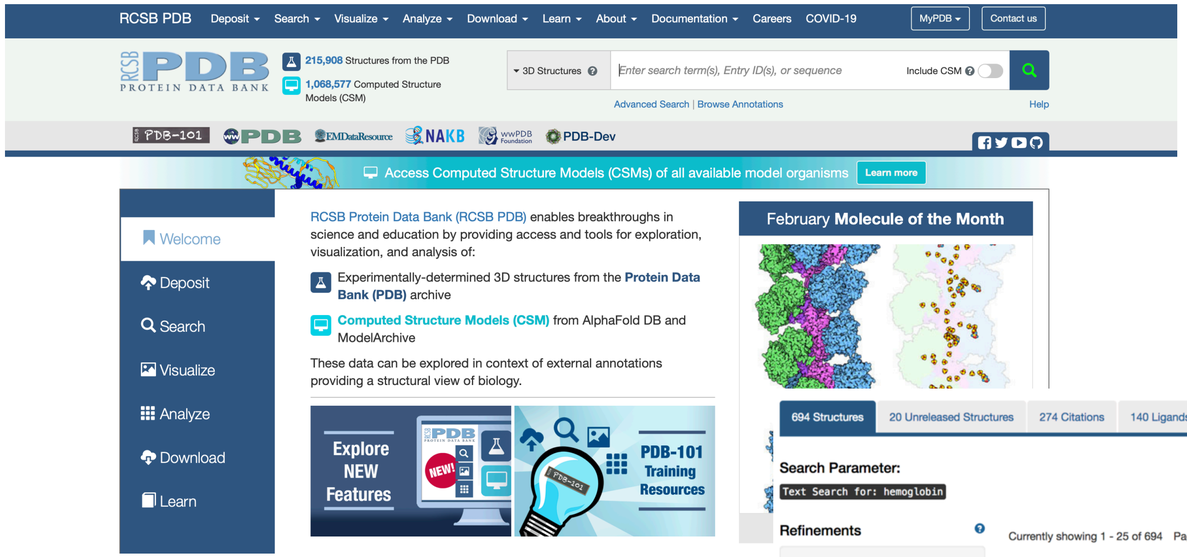


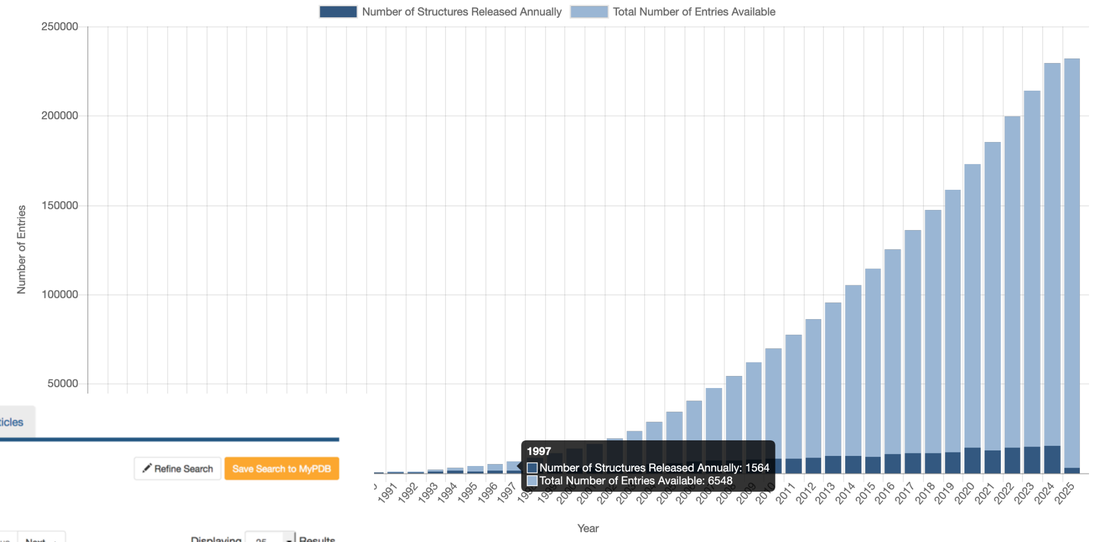
Cryo-electron microscopy

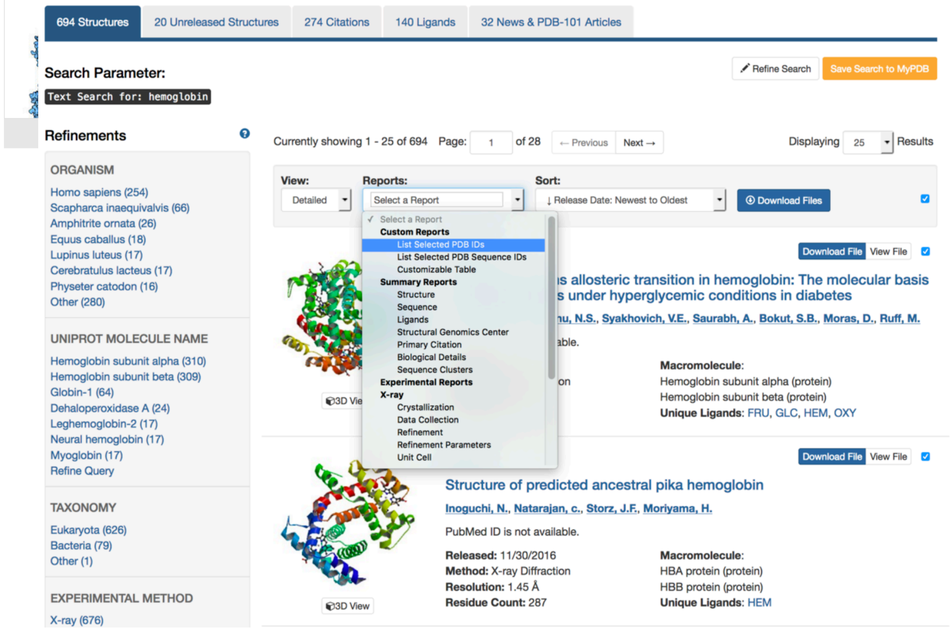


Protein Data Bank: The protein repository

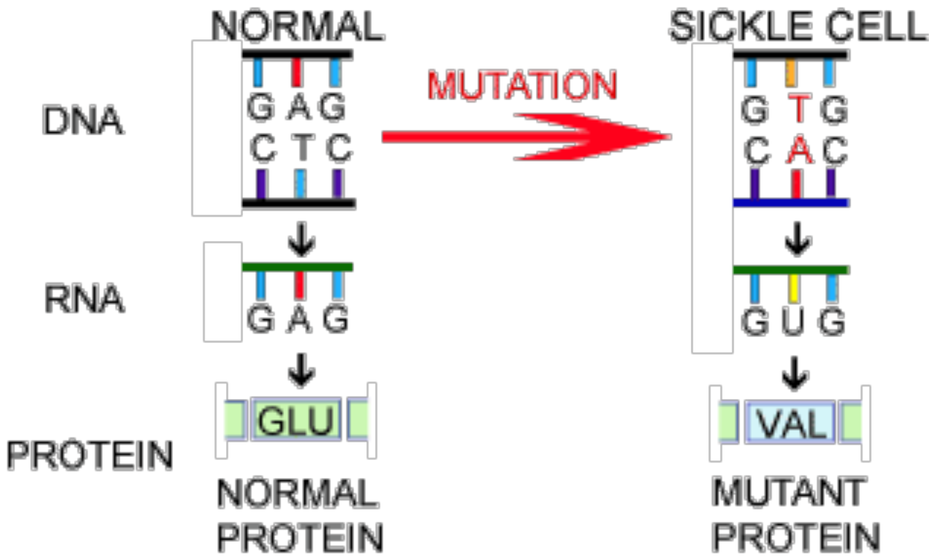
Protein Data Bank: https://www.rcsb.org/

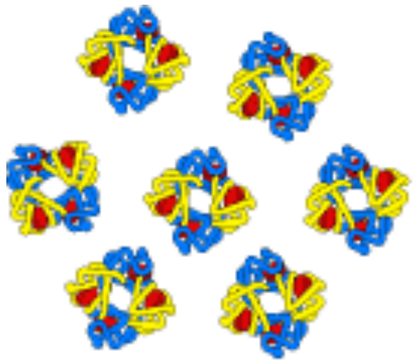




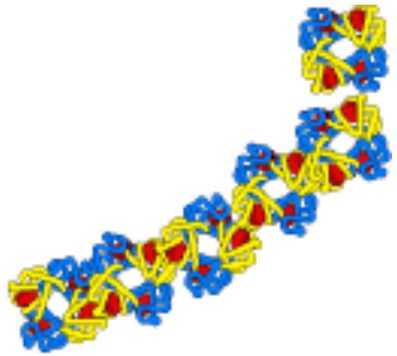


The impact of mutation on structure-function of protein

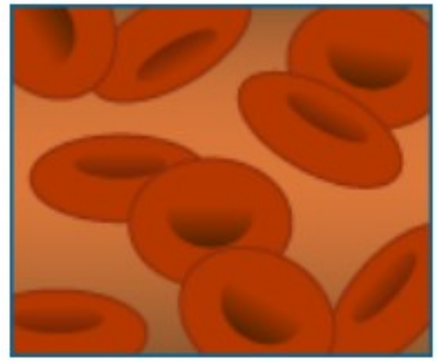




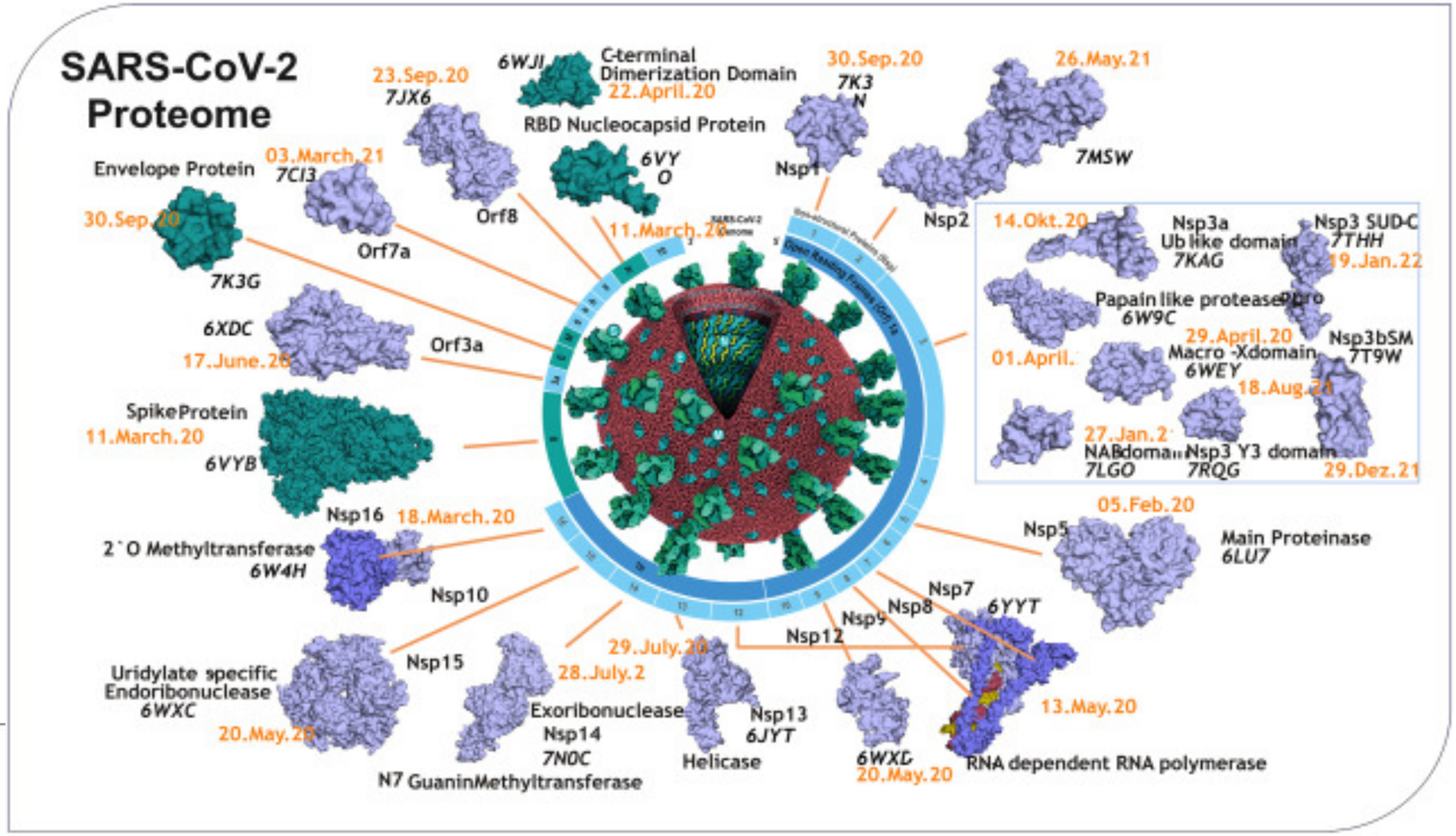
NORMAL HEMOGLOBIN

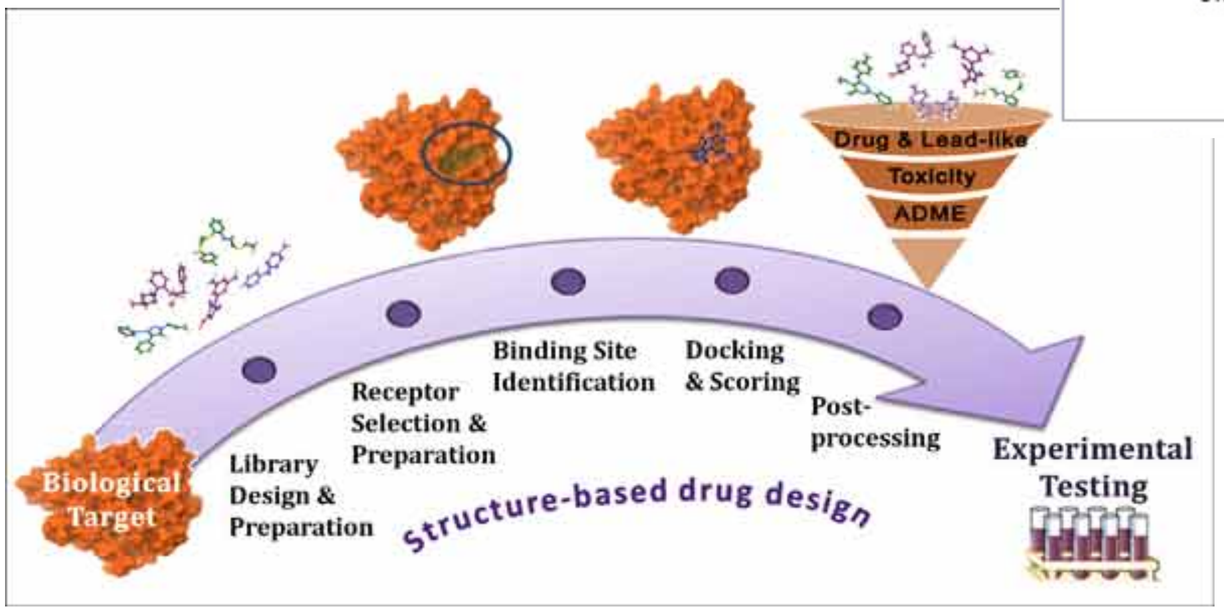


CLUMPED HEMOGLOBIN

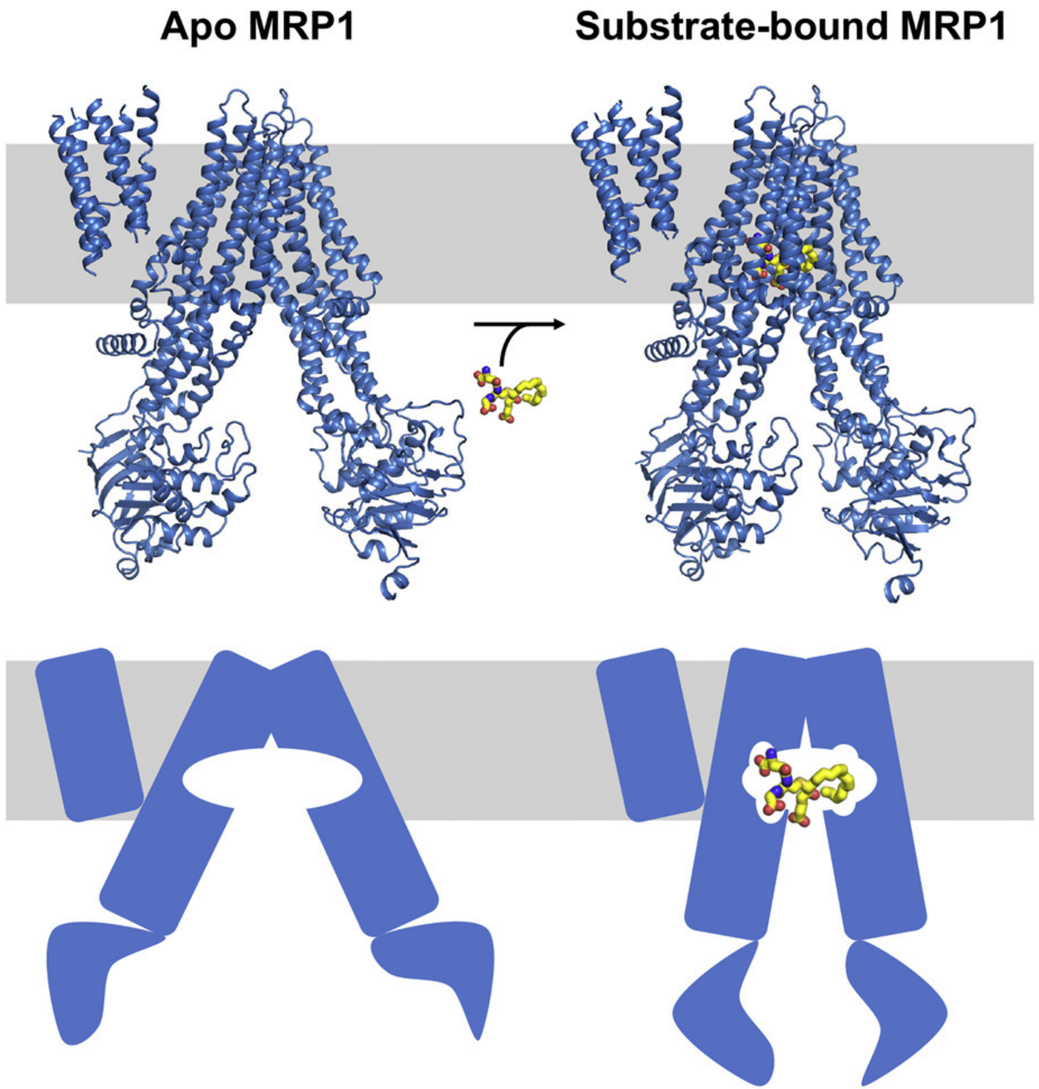


Structure-based drug designing

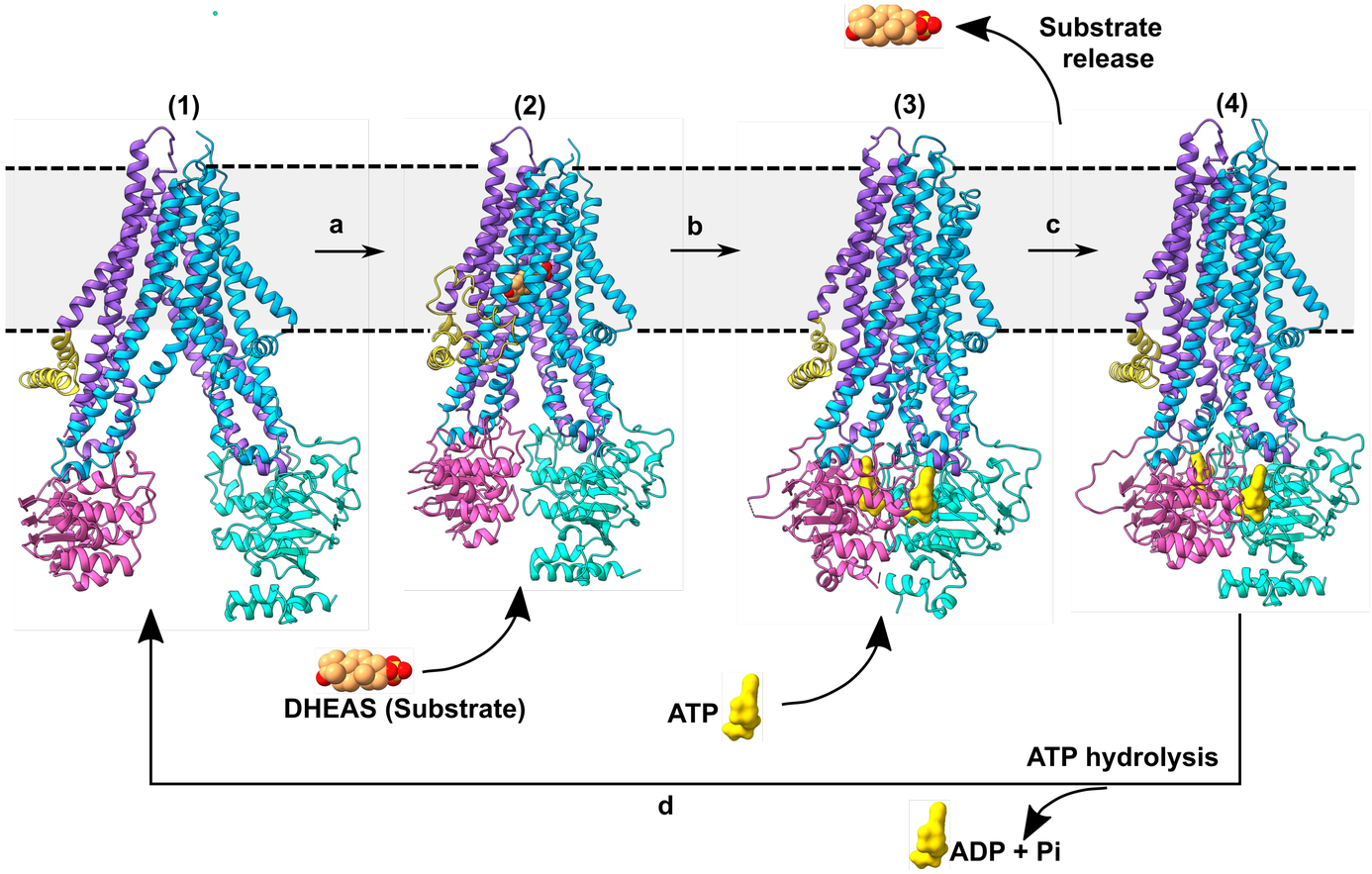


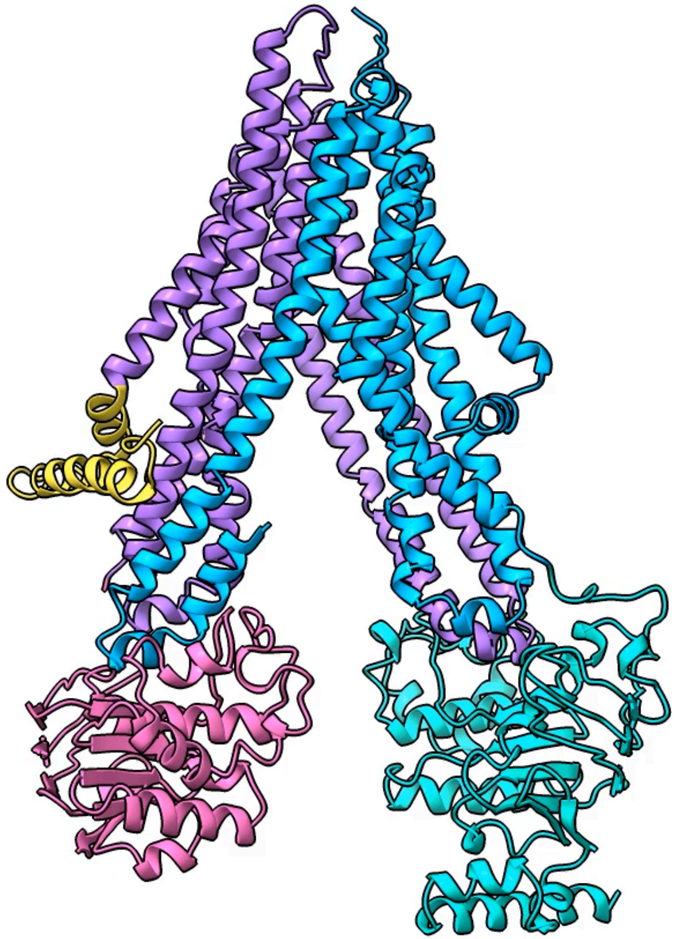


Conformational changes on ligand binding

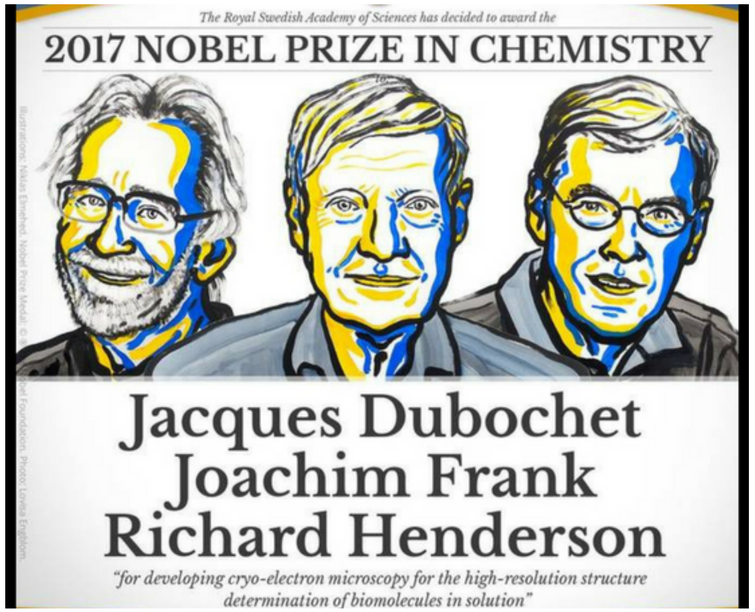


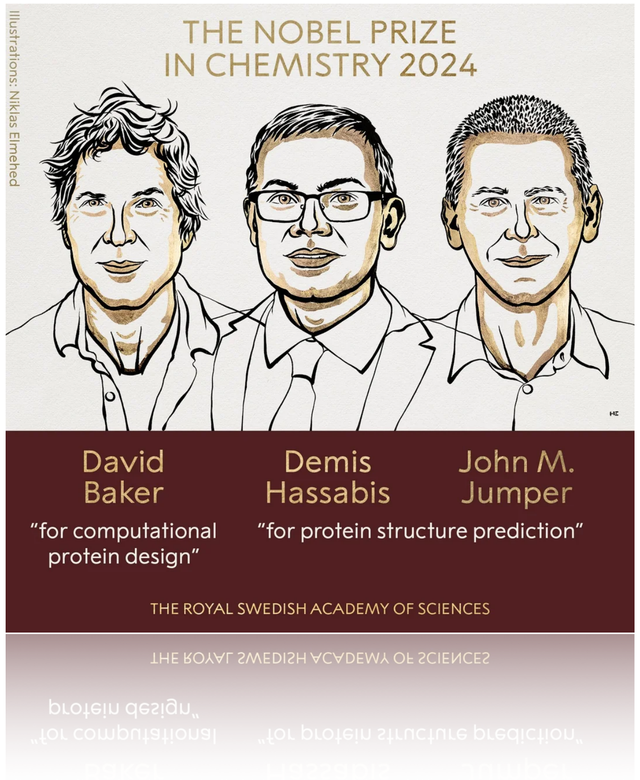
Structure-functional relationships - catalytic cycle of protein





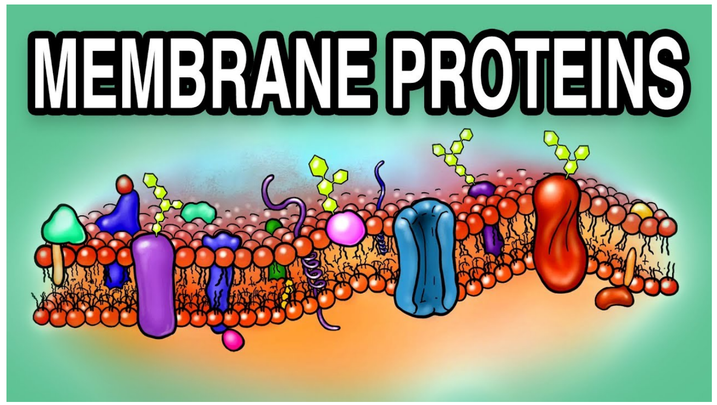
Recent Nobel prizes in Structural Biology

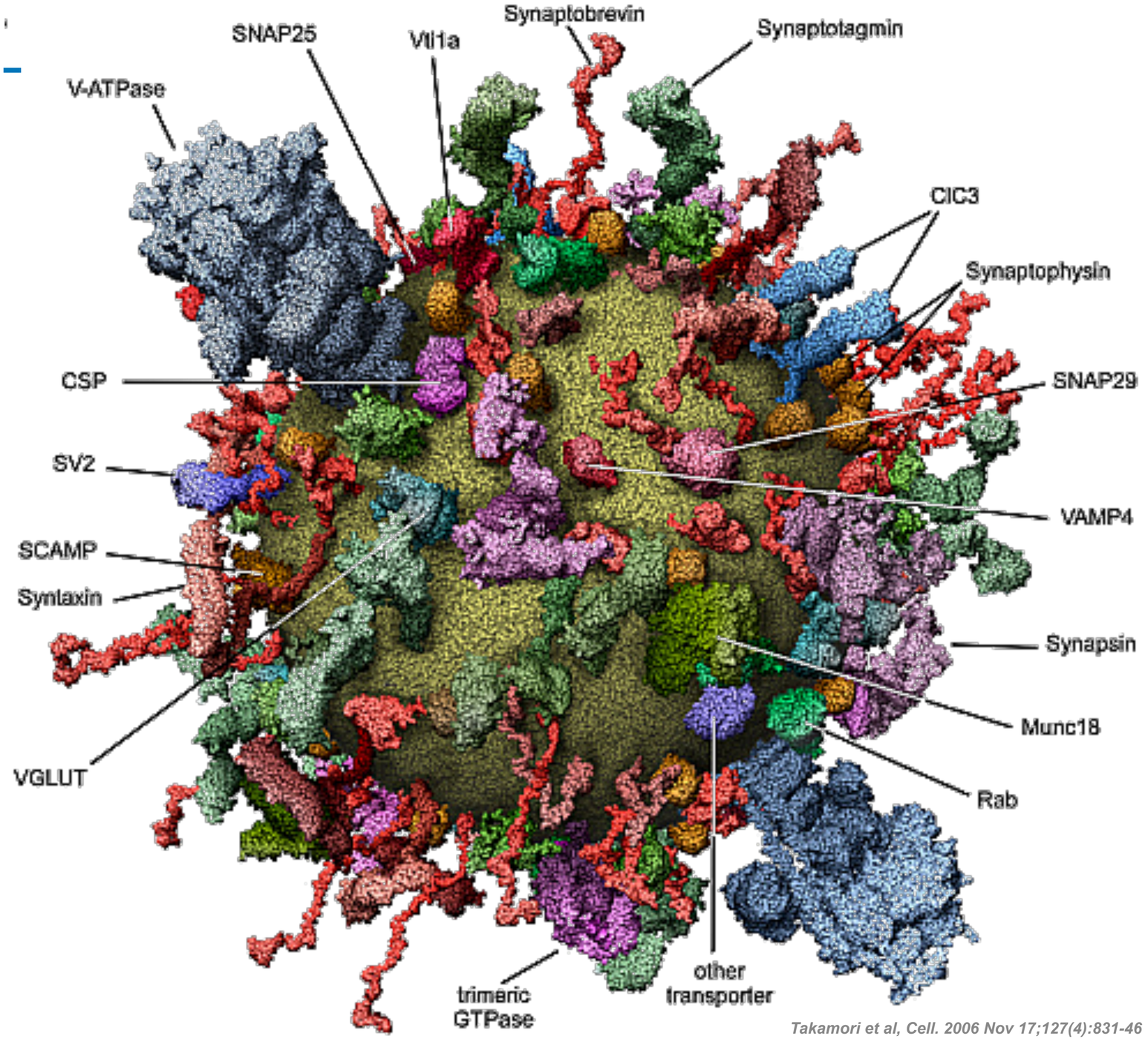




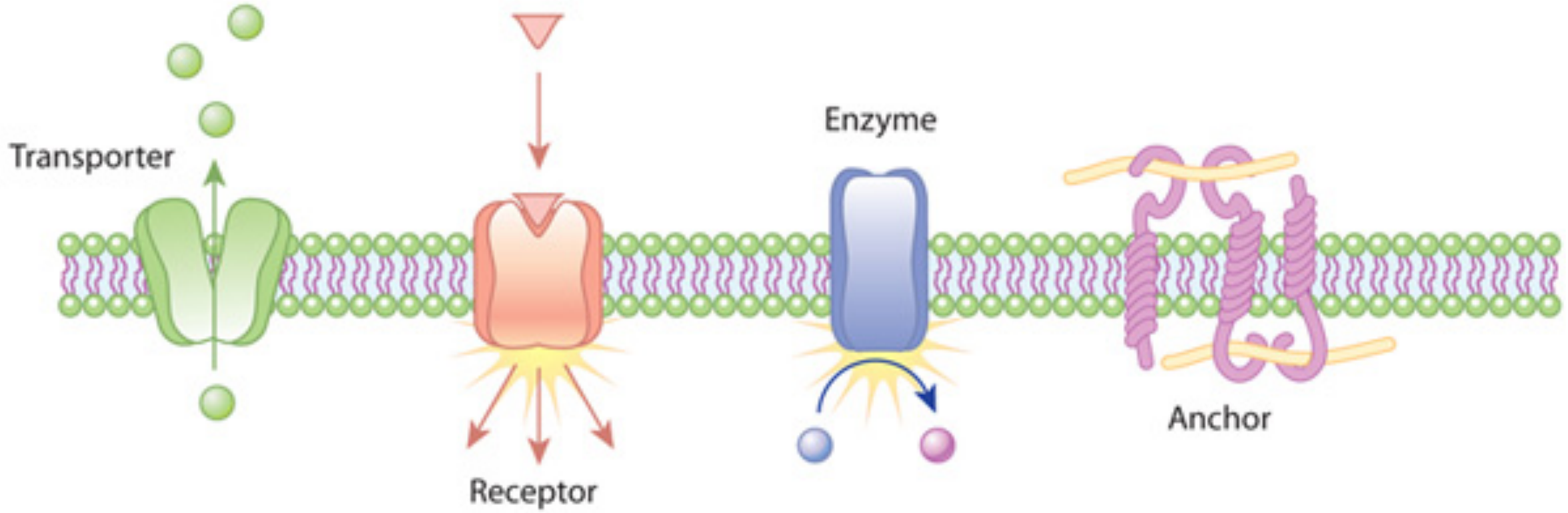
Questions

A special class of proteins - Membrane Proteins





Takamori et al, Cell. 2006 Nov 17;127(4):831-46


Transporter
Receptor
Enzyme
Anchor

Proteomics

Ruchika Bajaj, PhD
Membrane Protein Biologist

One gene is not equal to one protein

Genome

all genes in an organism

Transcriptome

all transcripts in an organism

Proteome

all proteins in an organism

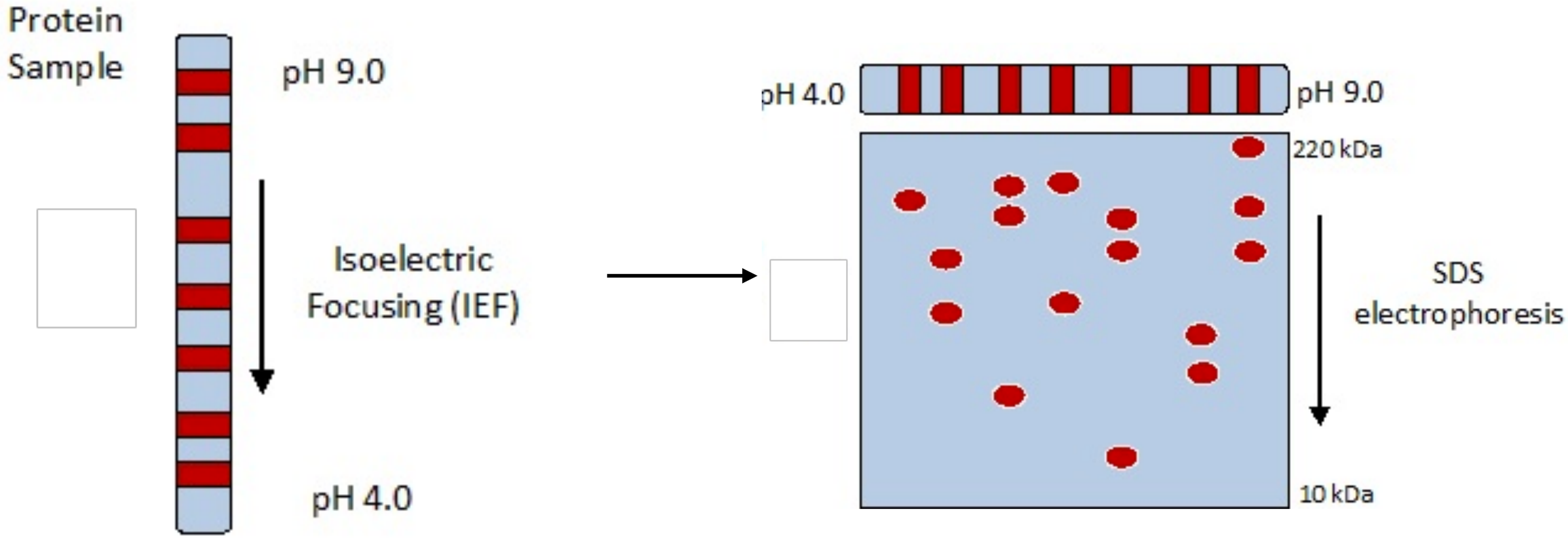
alternate splicing
mRNA editing
alternate promoters

proteolysis
post-translational modifications

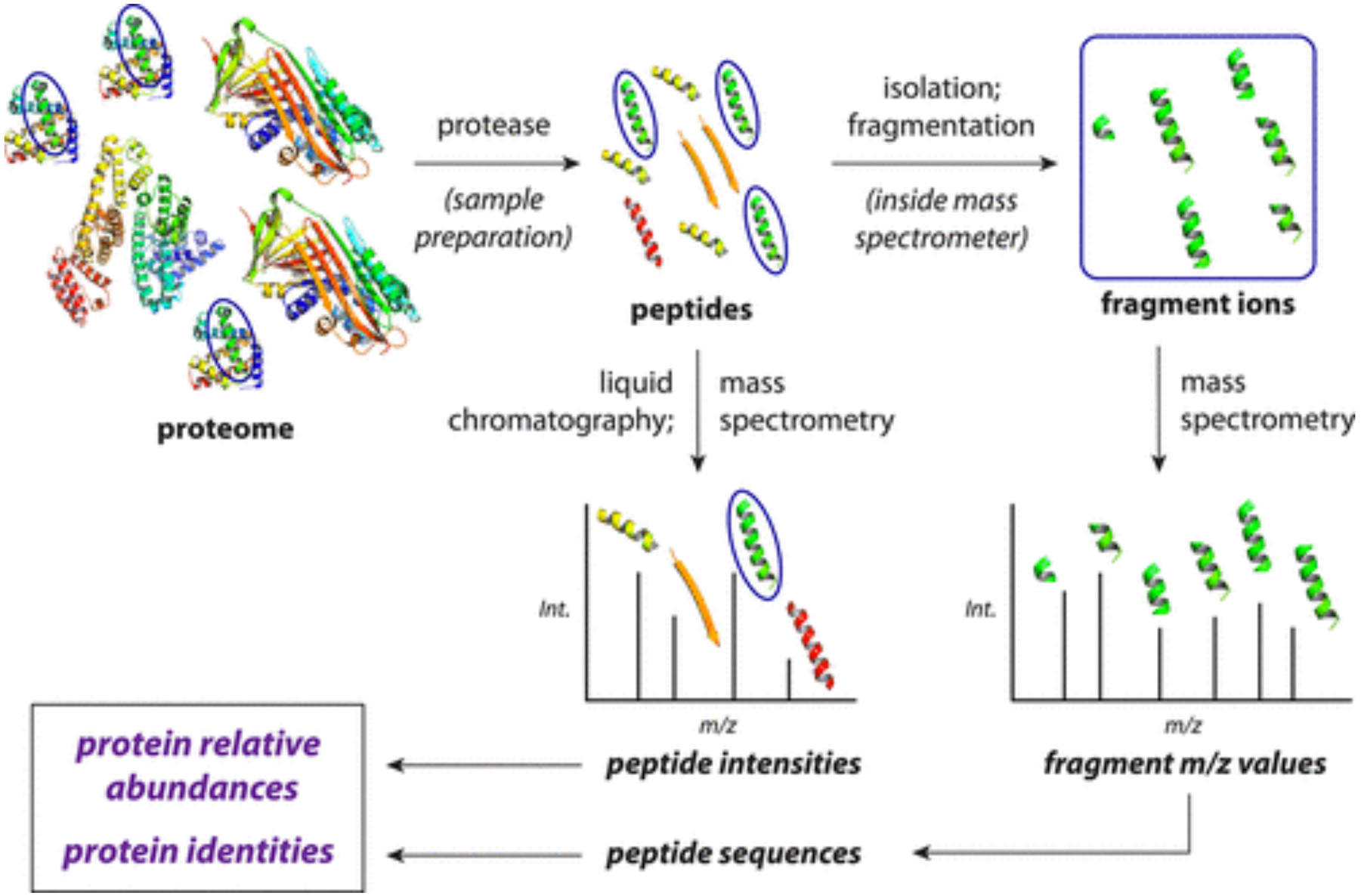
Proteomics can tell a lot of things

- protein identification
- protein function
- protein expression levels
- post-translational modifications
- protein localization and compartmentalization
- protein-protein interactions

Old proteomics using 2D Gel Electrophoresis



New generation proteomics uses mass spectrometry

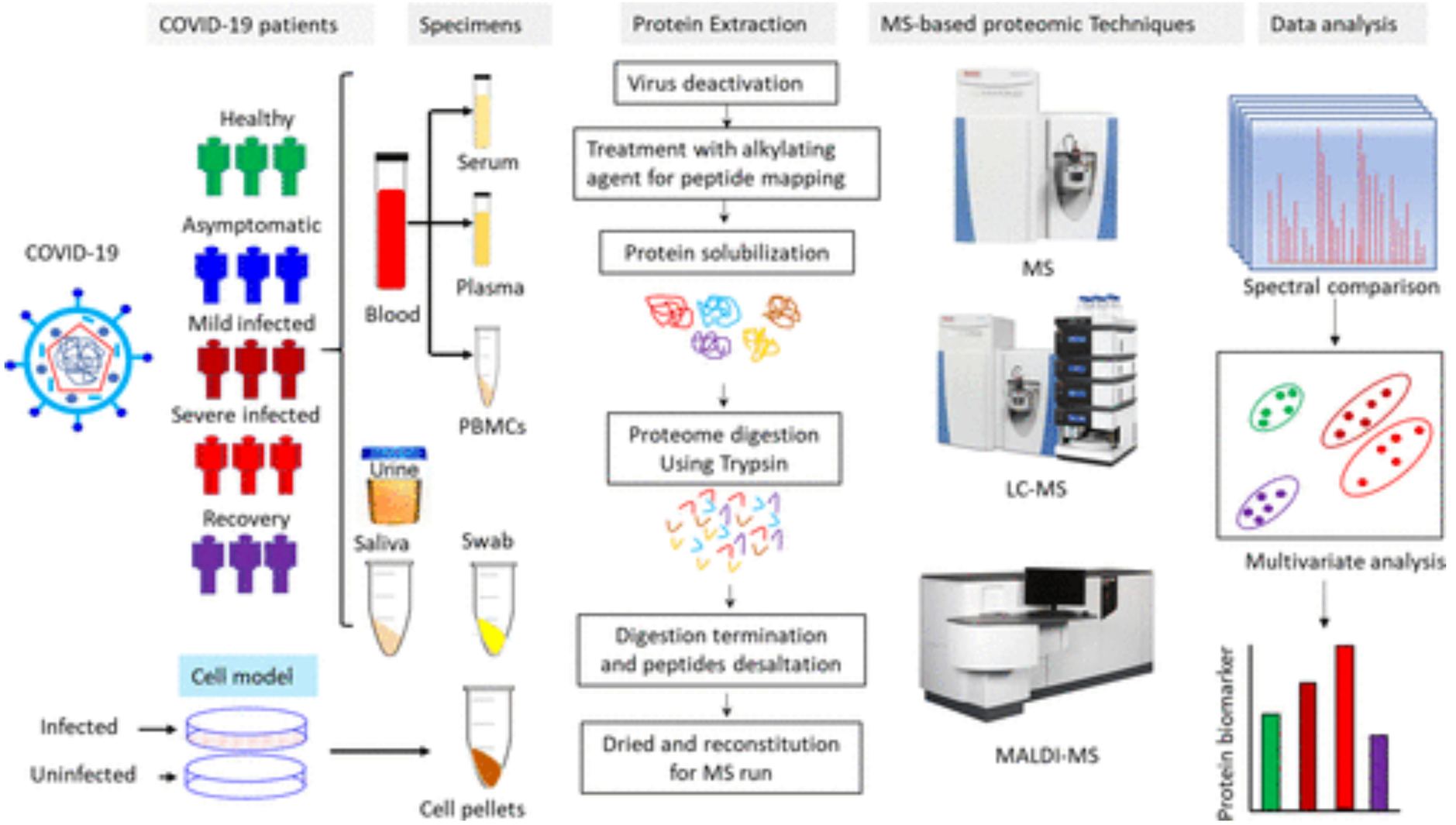


J. Proteome Res. 2023, 22, 7, 2151–2171

Applications of Proteomics

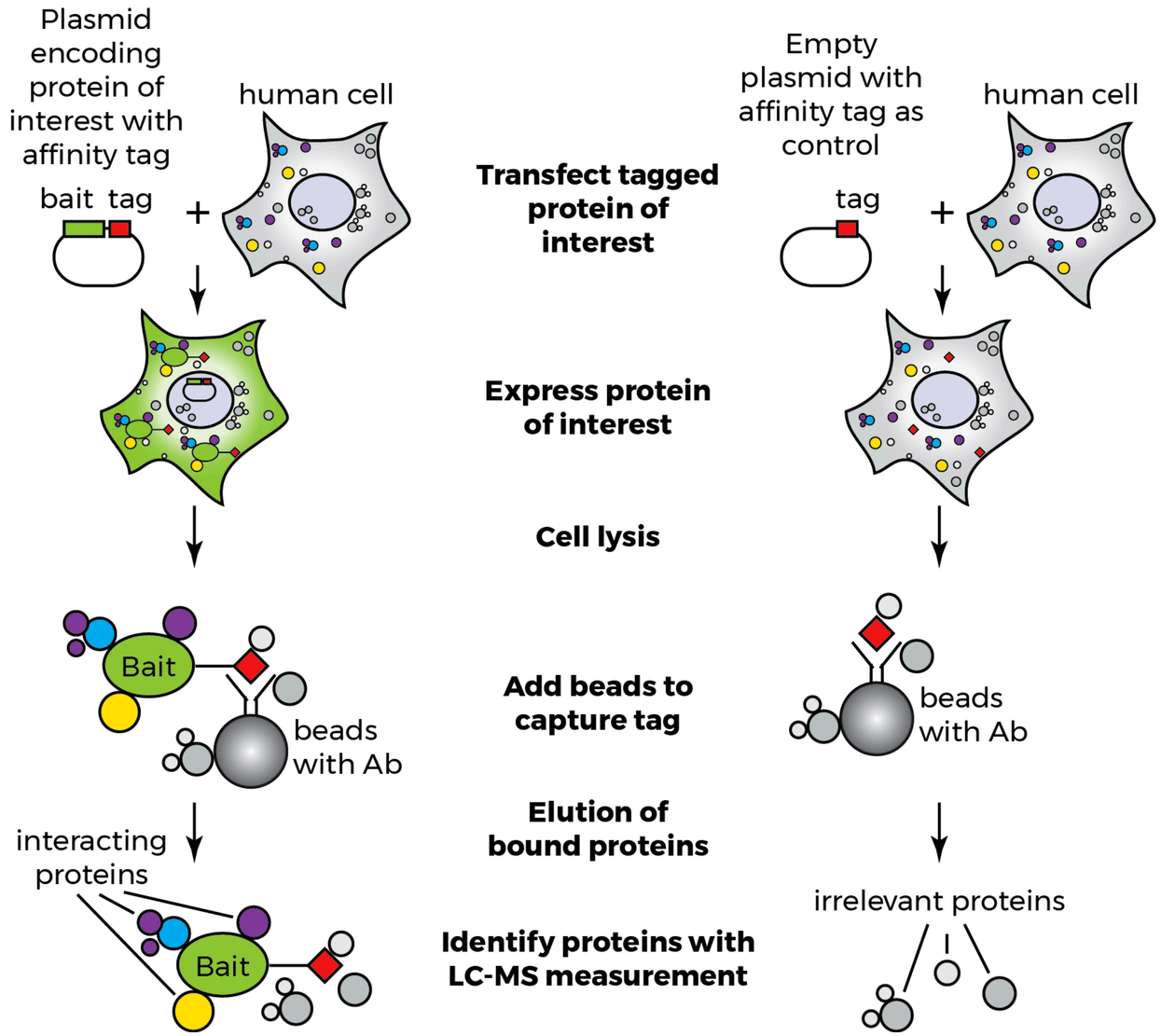
- Characterize protein - molecular weight and structural information
- Protein fingerprinting, Peptide mass fingerprinting - gives a set of peptides
- Identification of disease related biomarkers -diagnostic tool

Identification of disease biomarkers



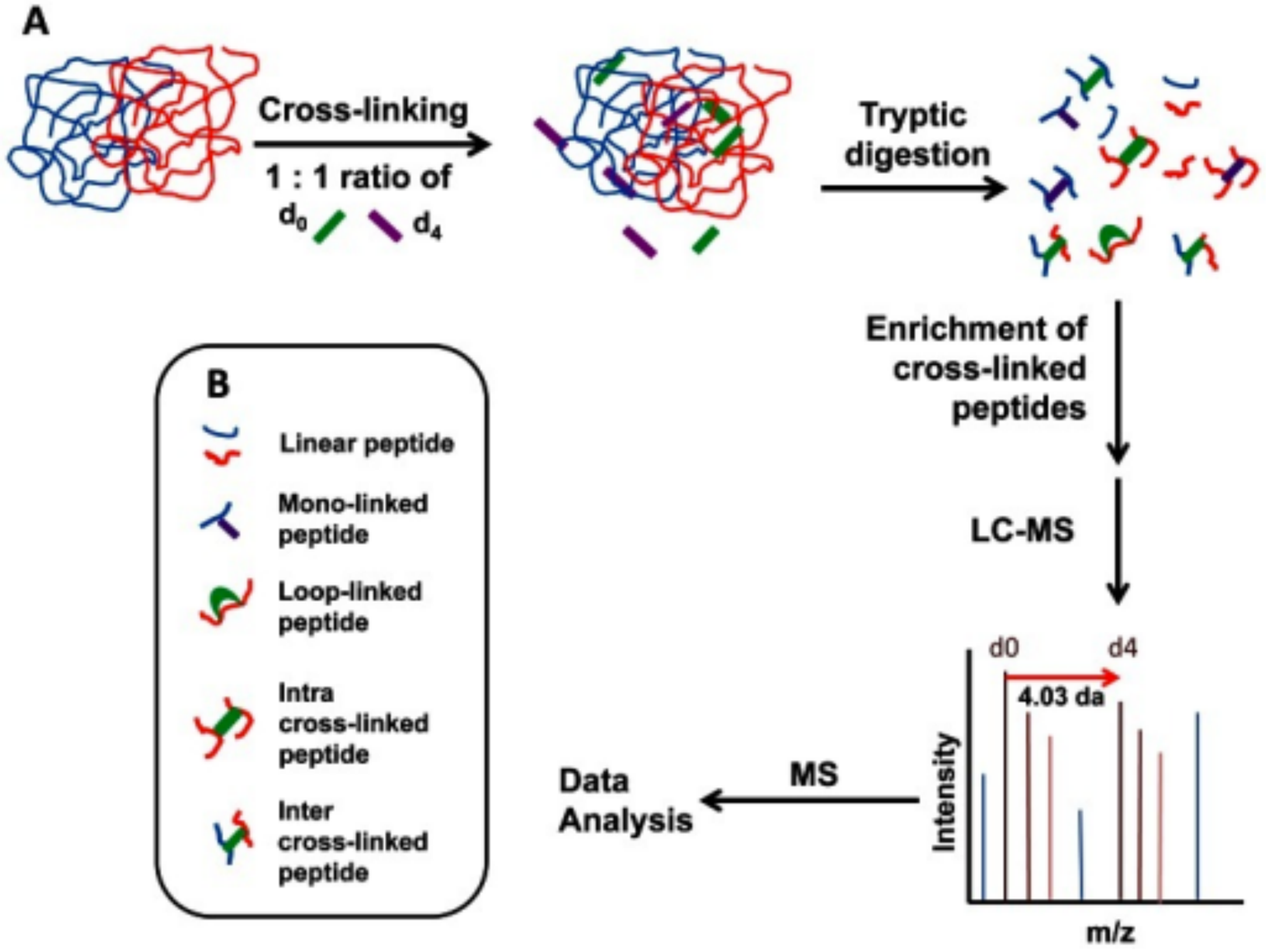
J. Am. Soc. Mass Spectrom. 2020, 31, 10, 2013–2024

Identifying interactions of a favorite protein



Krogan lab website

Identification of protein-protein interaction



PLoS One. 2013; 8(6): e65610.

Questions