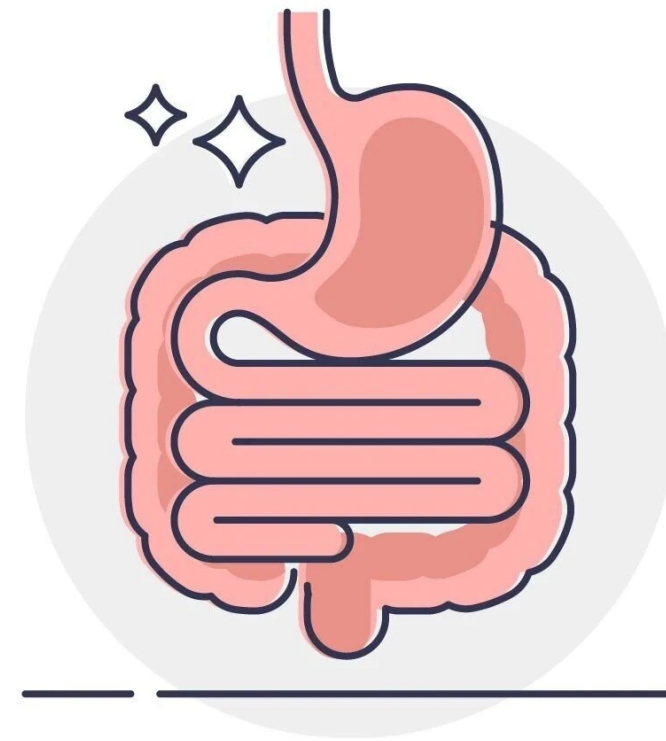


Structural Biology

Ruchika Bajaj, PhD
Membrane Protein Biologist

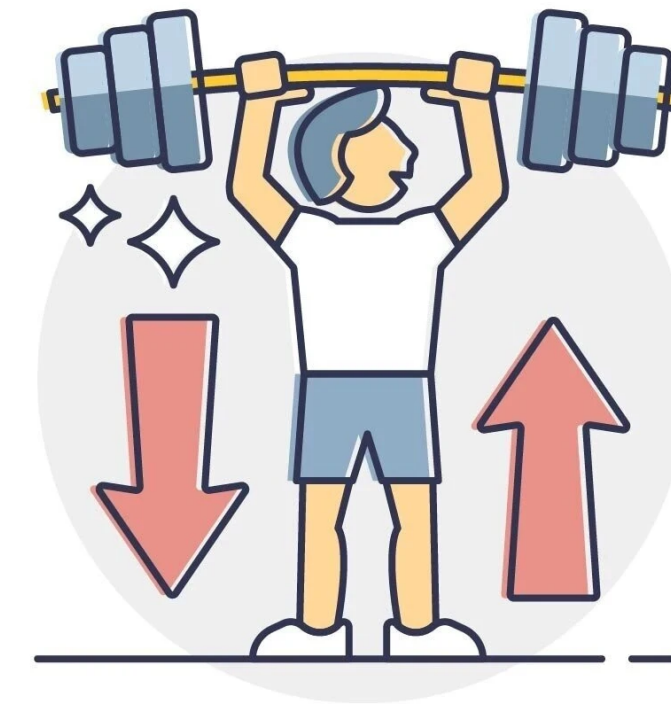
Why do we eat proteins ??



Digestive enzymes help facilitate chemical reactions



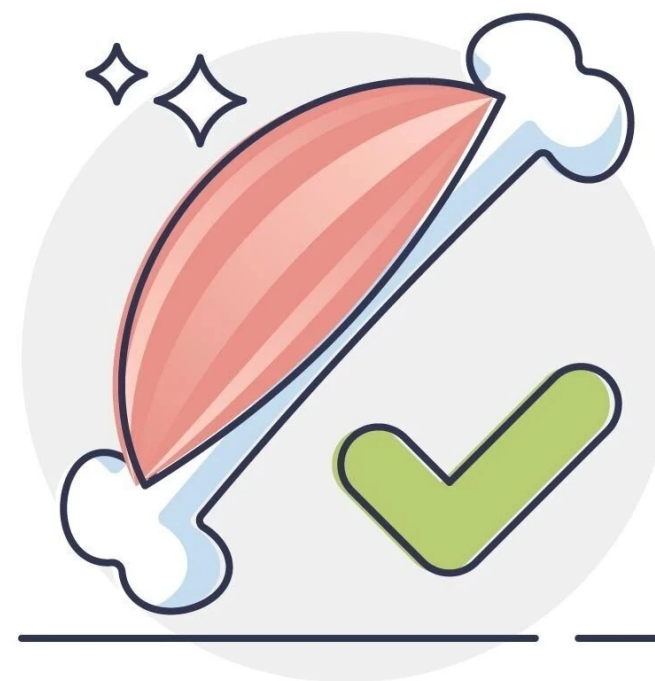
Antibodies support immune function



Support muscle contraction and movement



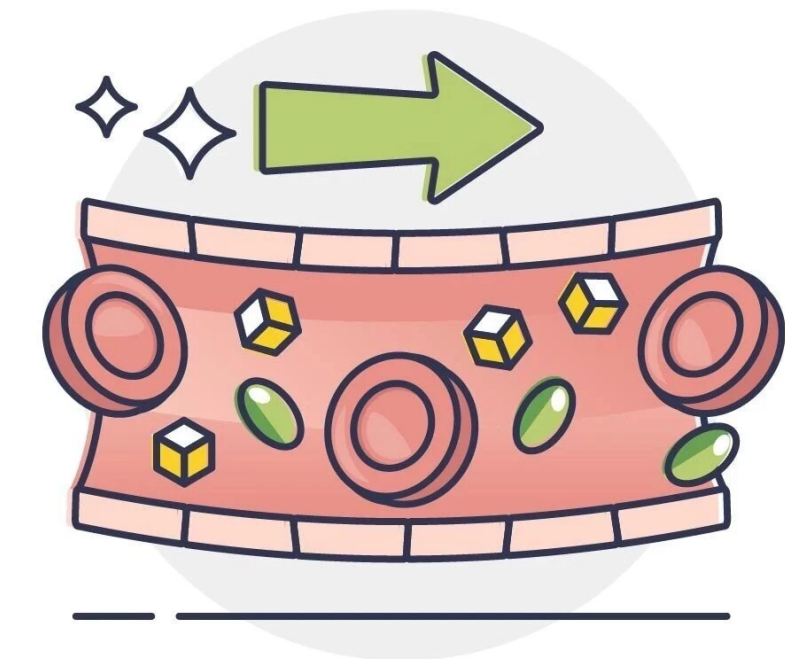
Support the regulation and expression of DNA and RNA



Provide support to the body



Hormones help coordinate bodily function



Move essential molecules around the body

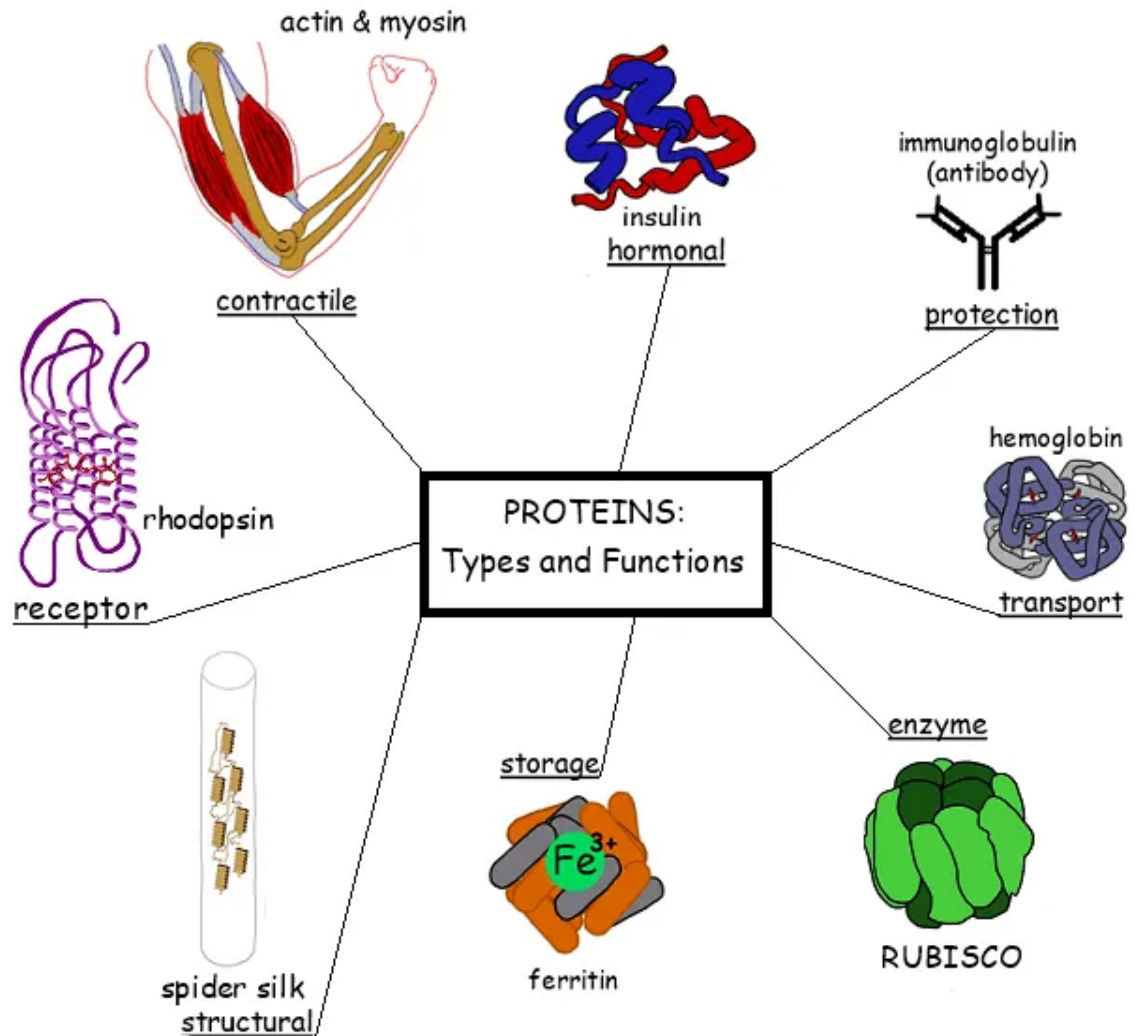
LASCHÉ X[®]

The Importance of Protein in Diet

Why Do We Need **Protein**?

Learn More

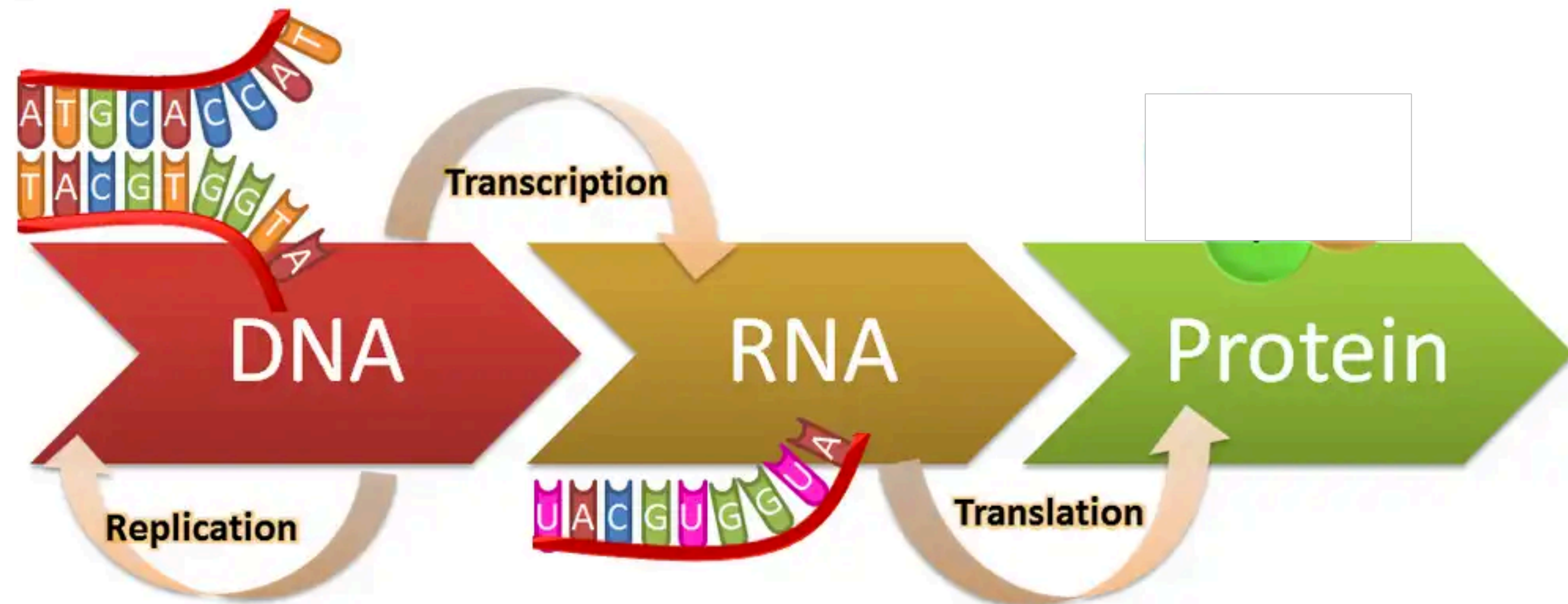
Functions of protein



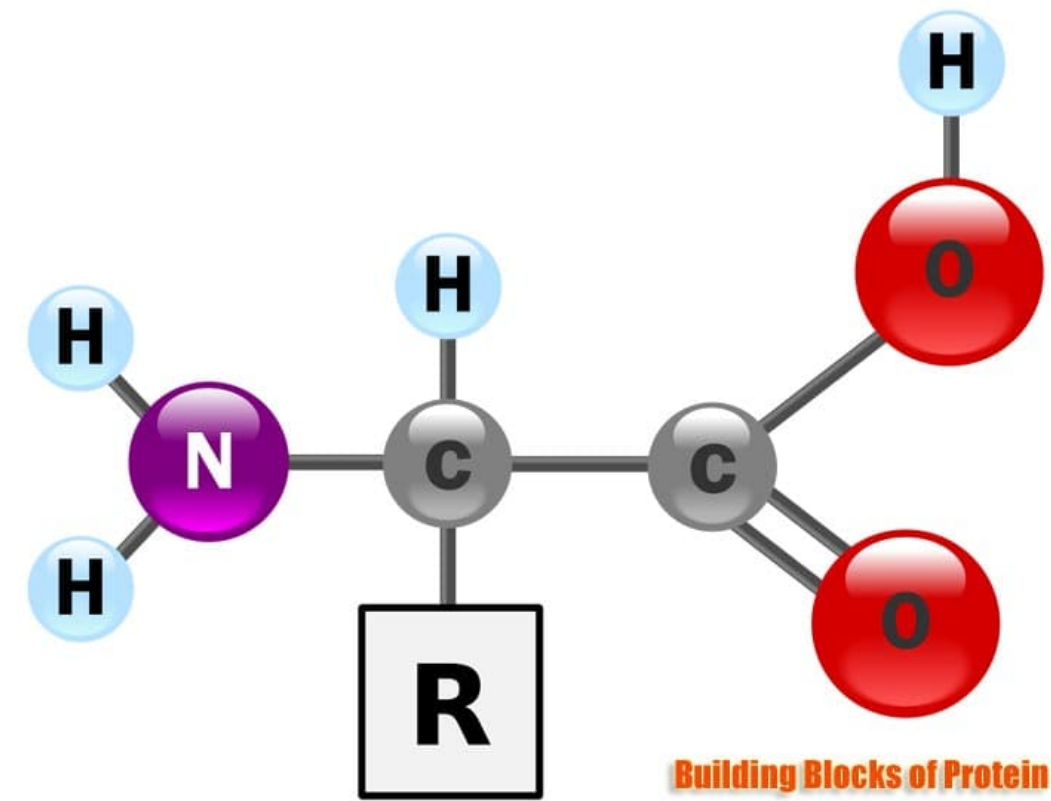
Central Dogma: Proteins : the building block of life



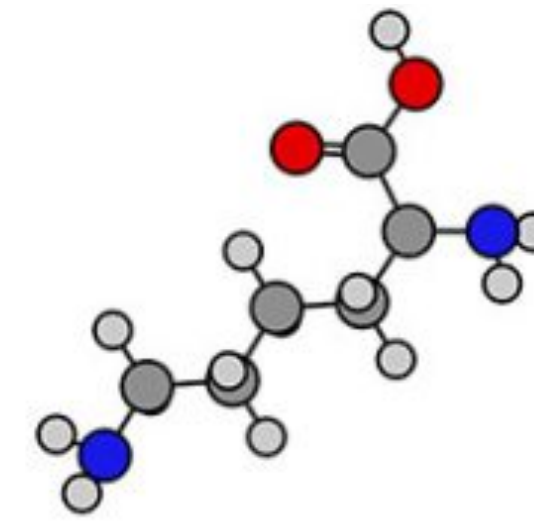
Central Dogma



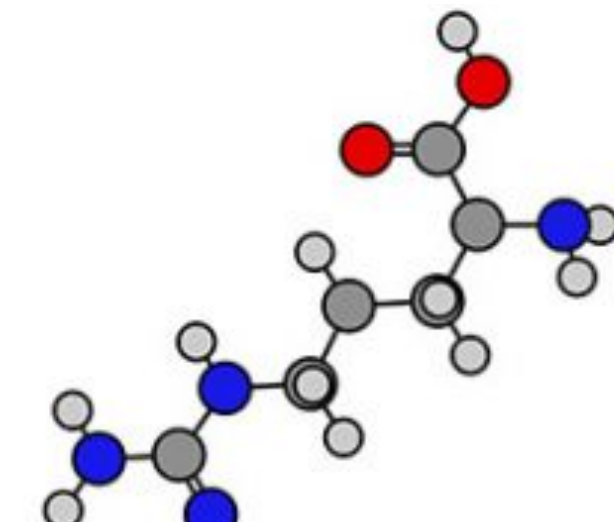
Amino acids : building blocks of proteins



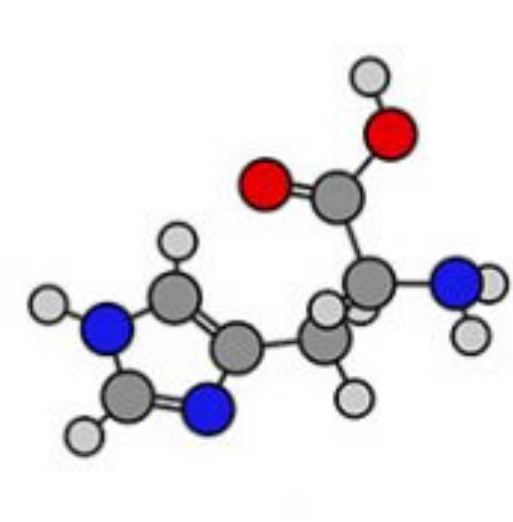
Positively charged



Lysine

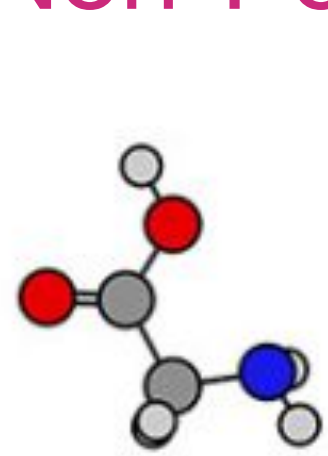


Arginine

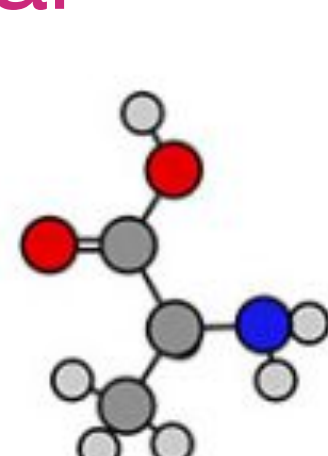


Histidine

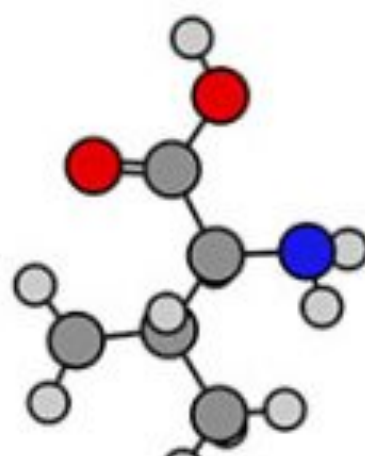
Non-Polar



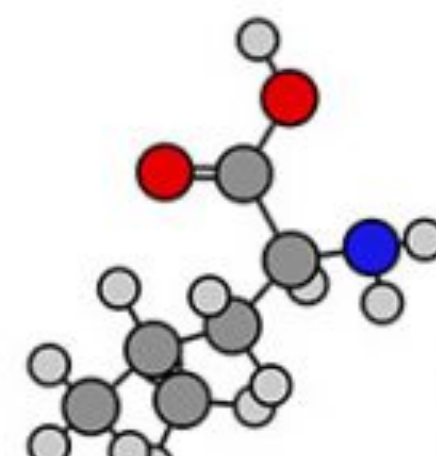
Glycine



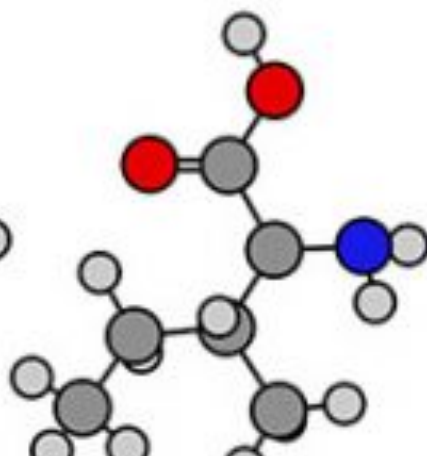
Alanine



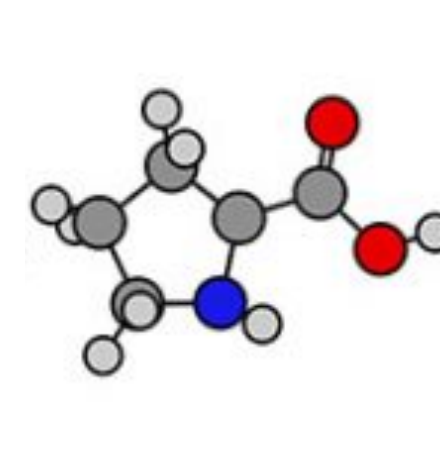
Valine



Leucine

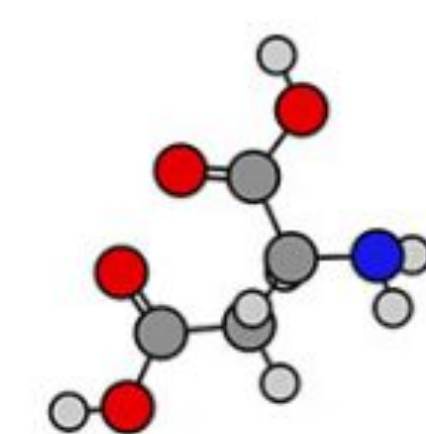


Isoleucine

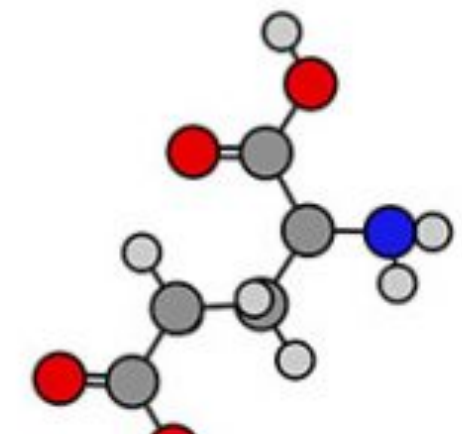


Proline

Negatively charged

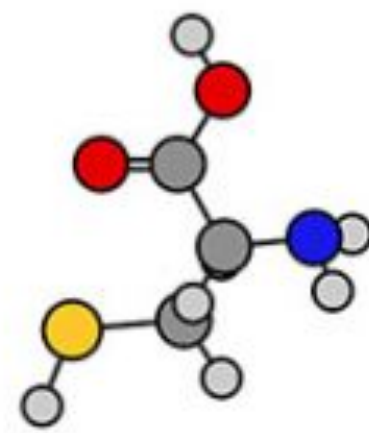


Aspartic acid

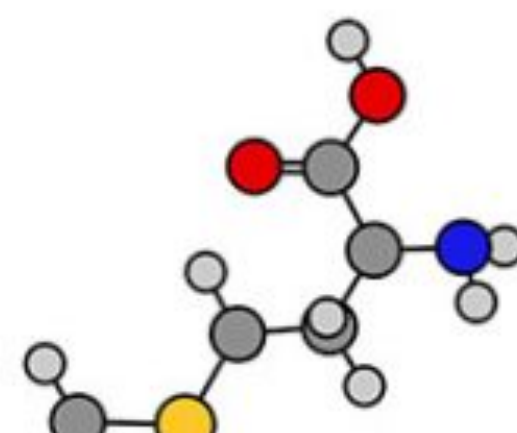


Glutamic acid

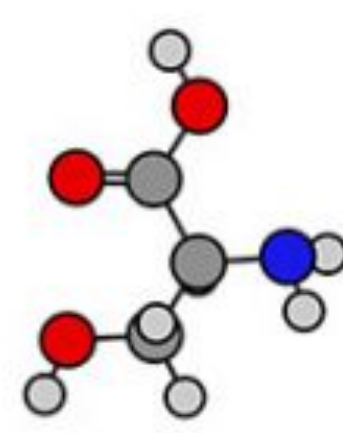
Polar



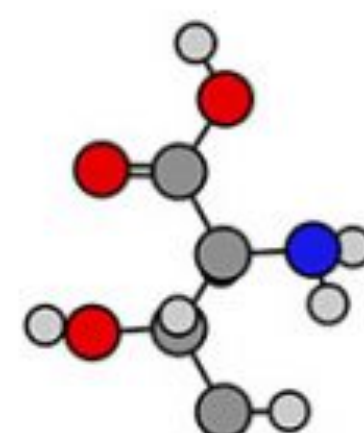
Cysteine



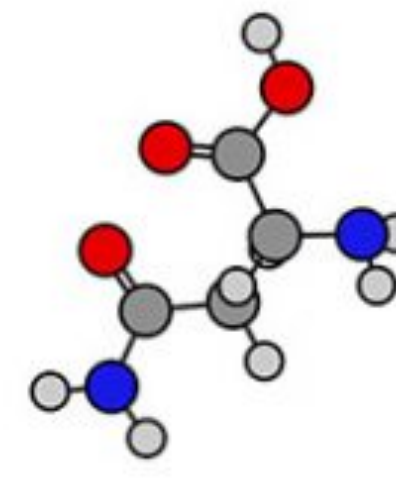
Methionine



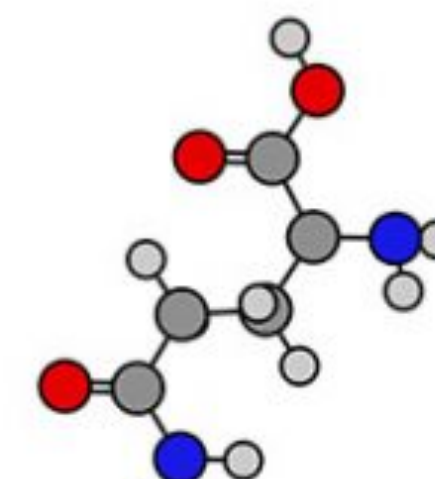
Serine



Threonine

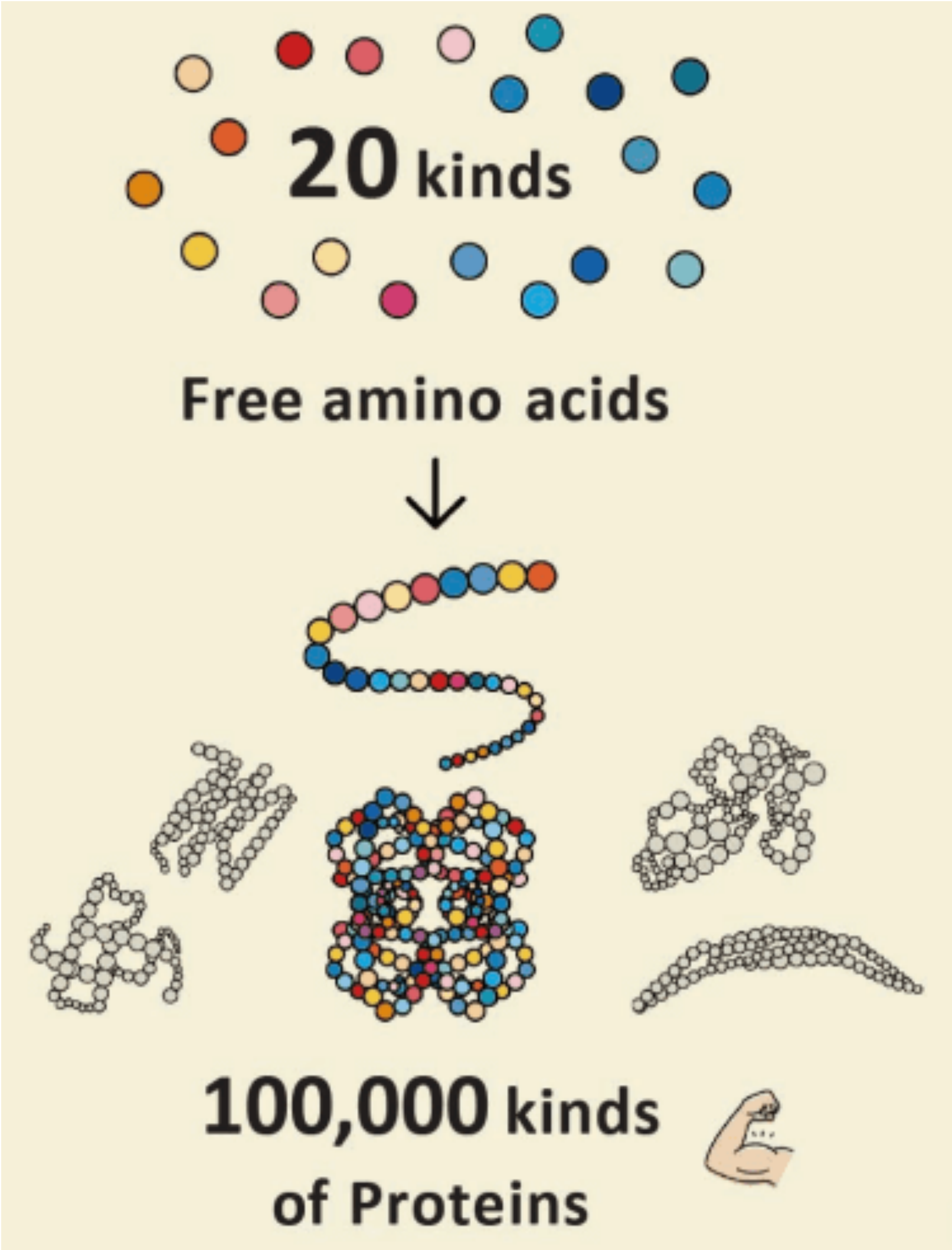
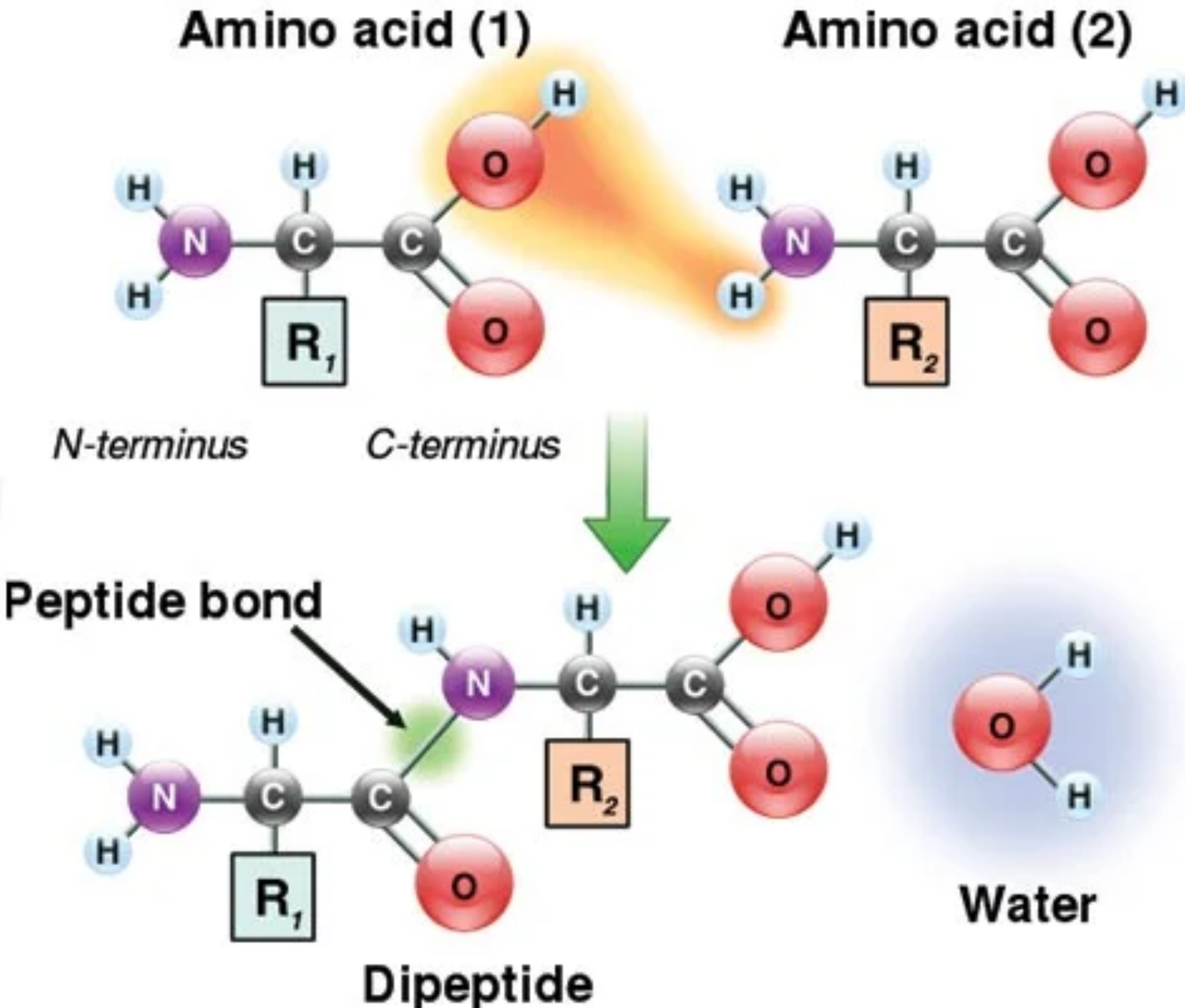


Asparagine

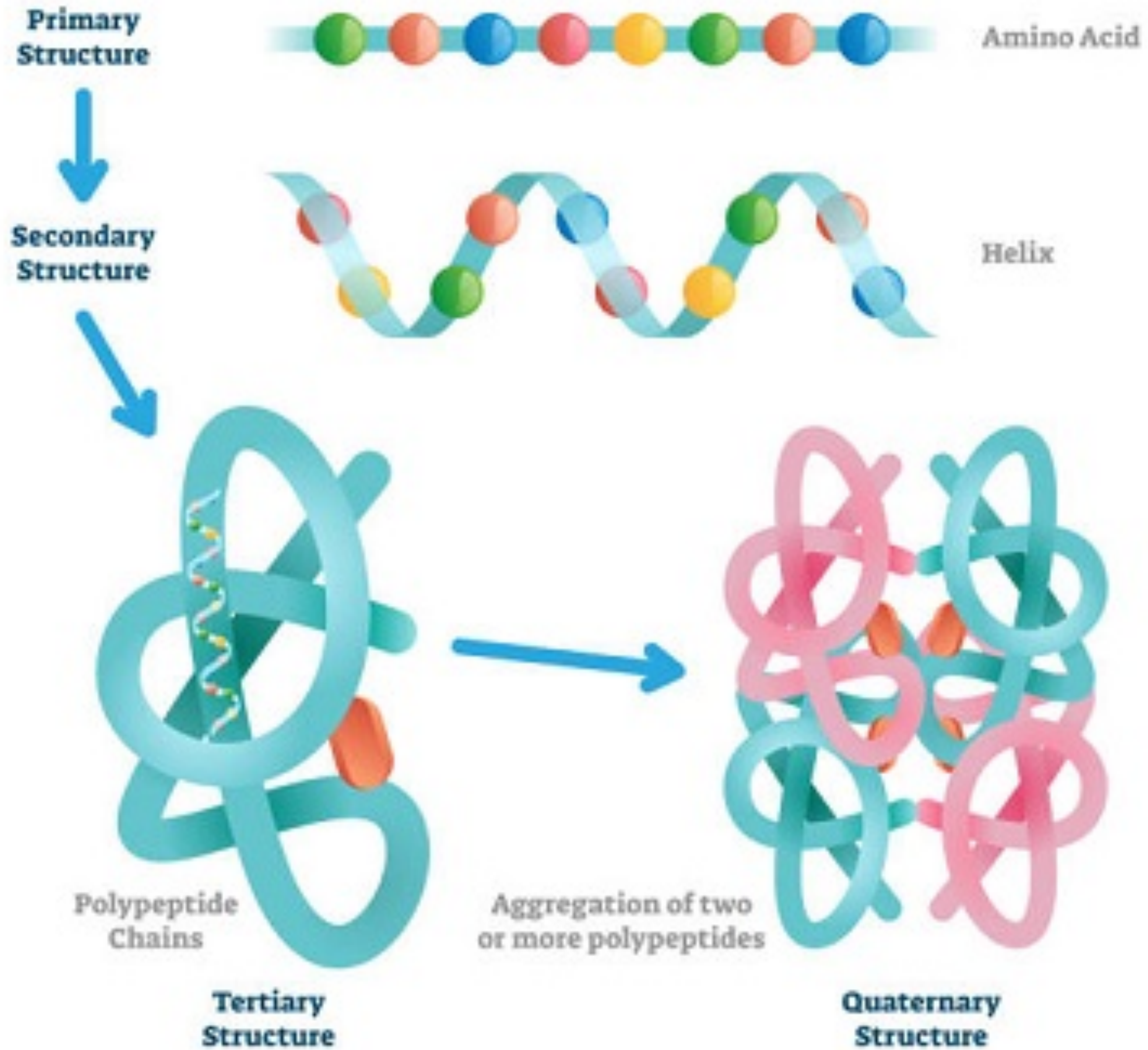


Glutamine

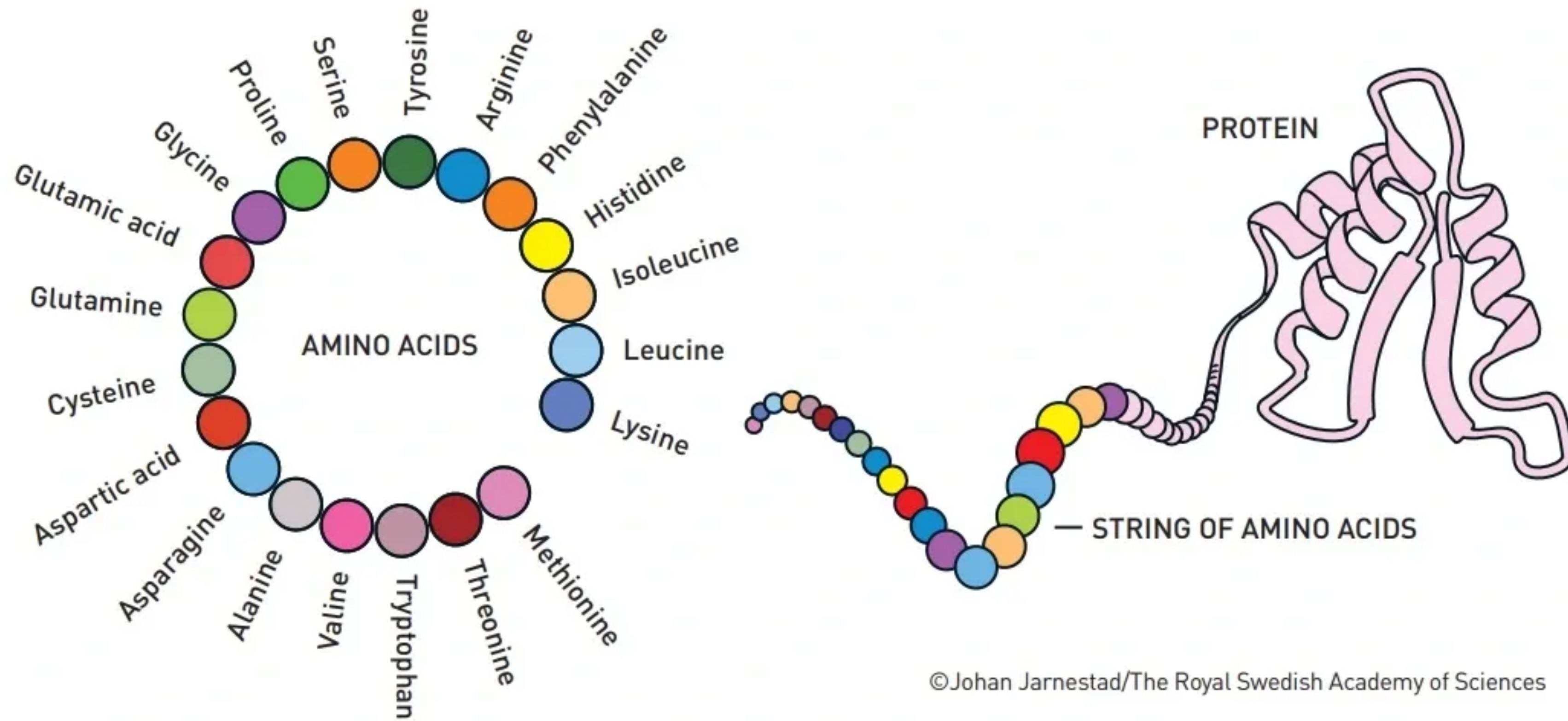
The peptide bond connects amino acids to build peptides



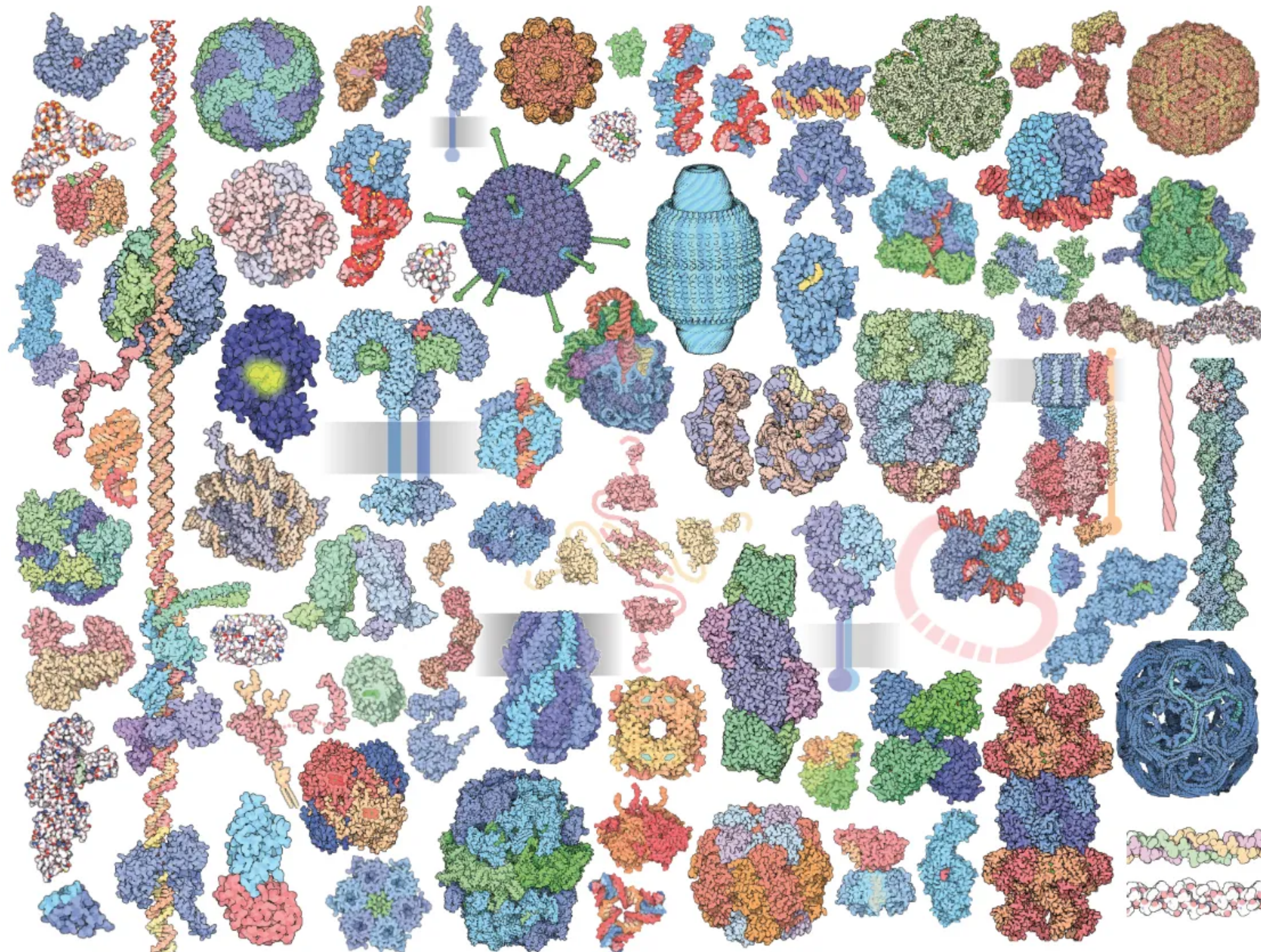
Levels of protein structure



The Folding Problem



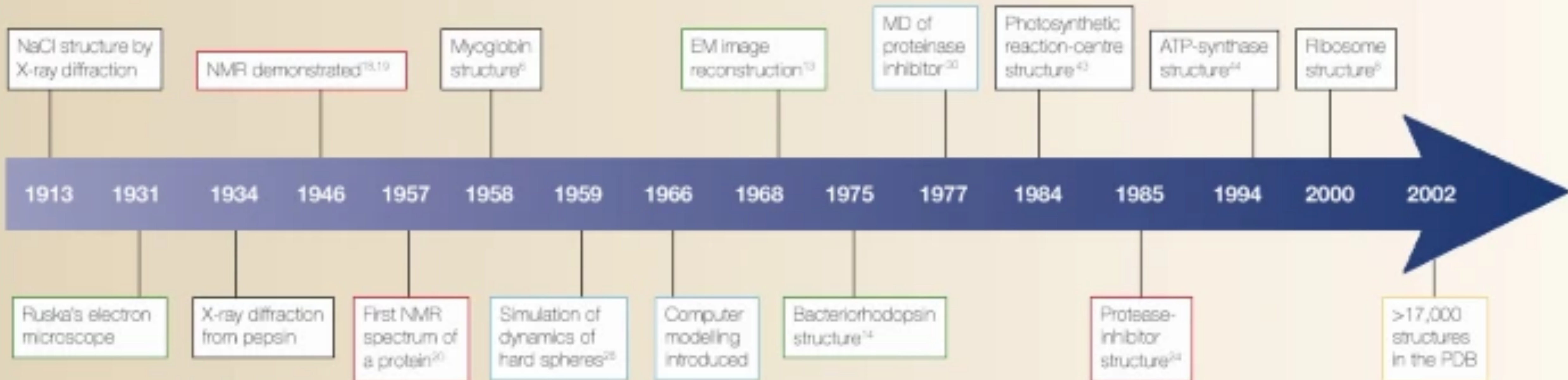
A variety of protein structures



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.

Timeline | **The march of structural biology**

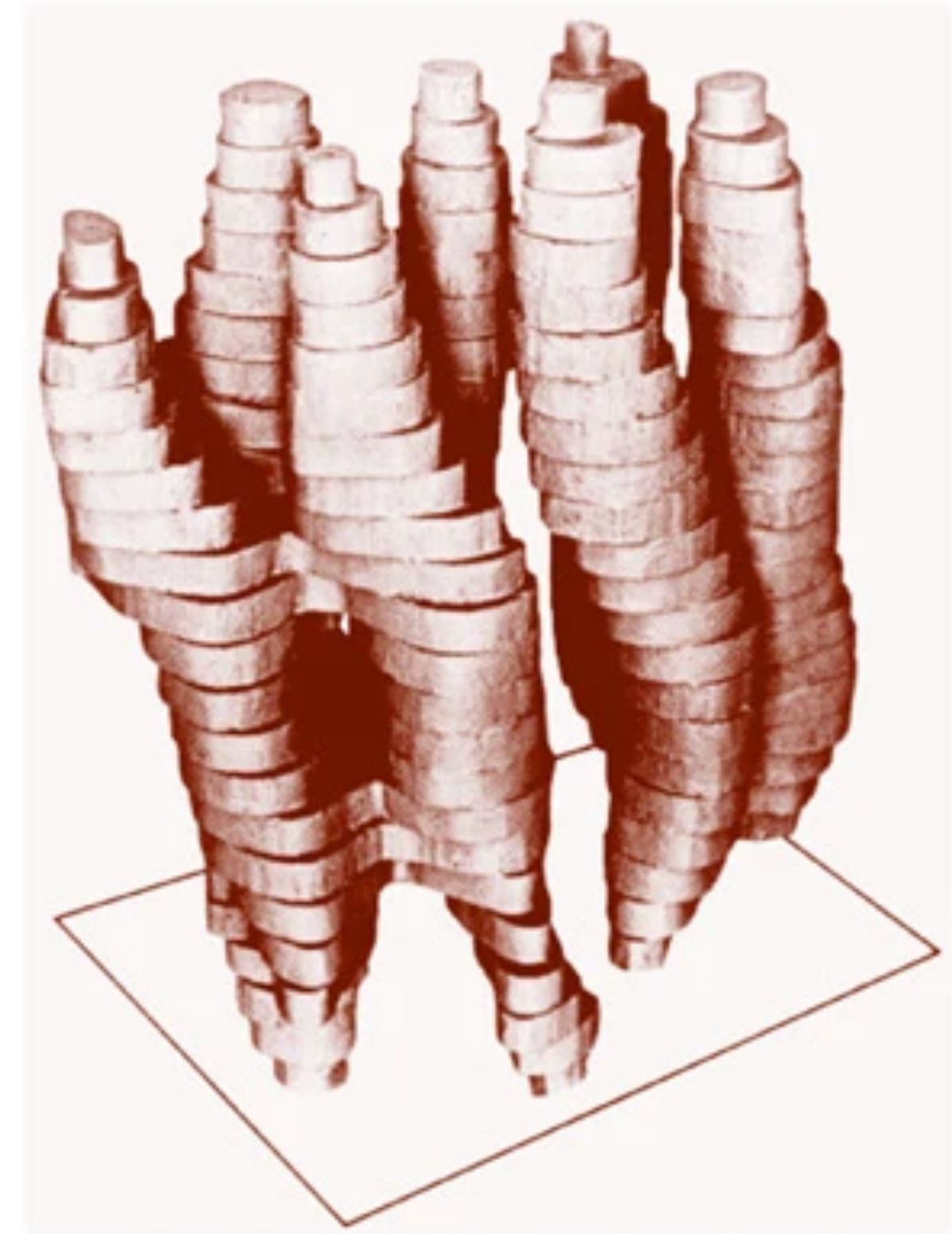


Some of the key developments in crystallography (shown in black), electron microscopy (EM; shown in green), nuclear magnetic resonance (NMR; shown in red) and computational methods (shown in blue) are highlighted. MD, molecular dynamics; NaCl, sodium chloride; PDB, Protein Data Bank.

First structures in Structural Biology



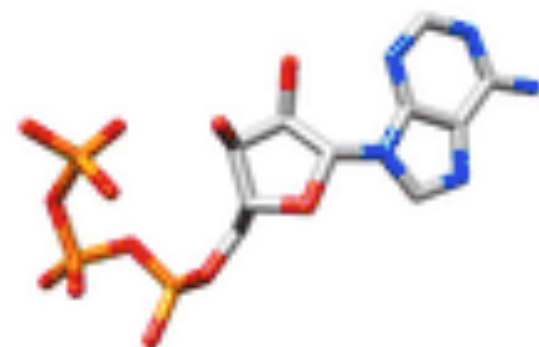
1962 of Max Perutz with his balsa-wood model of haemoglobin, and John Kendrew with his wire model of myoglobin. Models were derived from X-ray data. The resolution of the myoglobin data (1.4 Å). the haemoglobin data were derived at a lower resolution (6.0 Å).



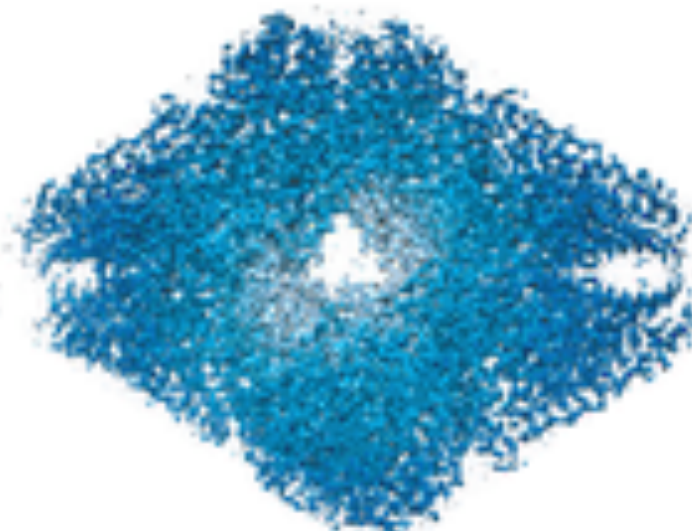
Nature Reviews | Molecular Cell Biology

Key Techniques in Structural Biology

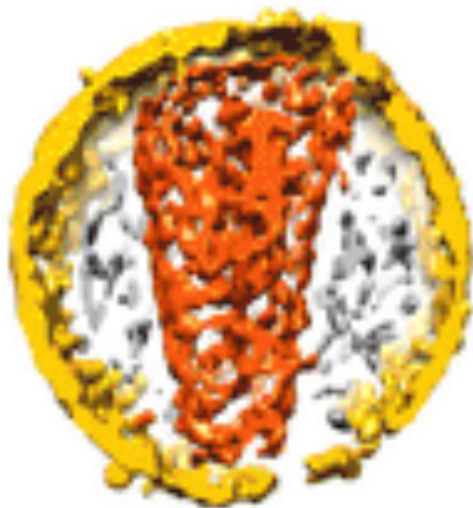
small molecules



proteins and protein complexes



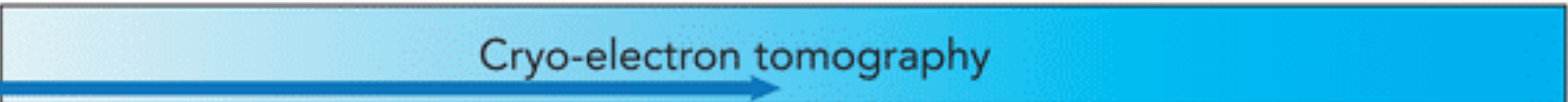
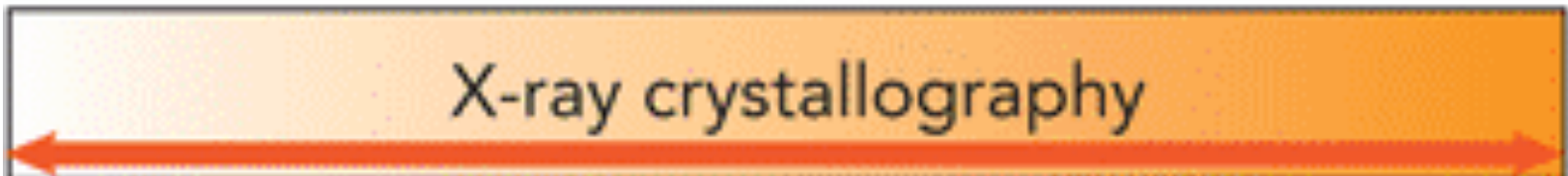
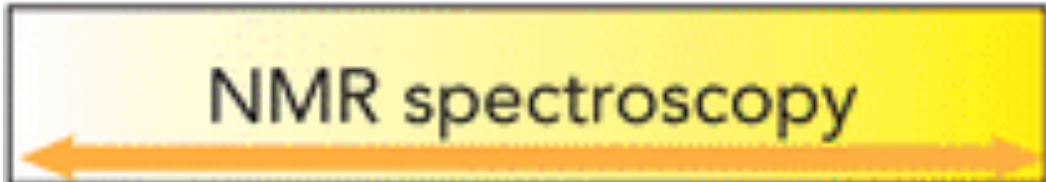
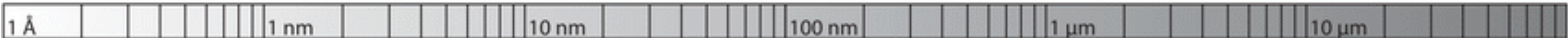
viruses and vesicles



Procaryotic cells and organelles

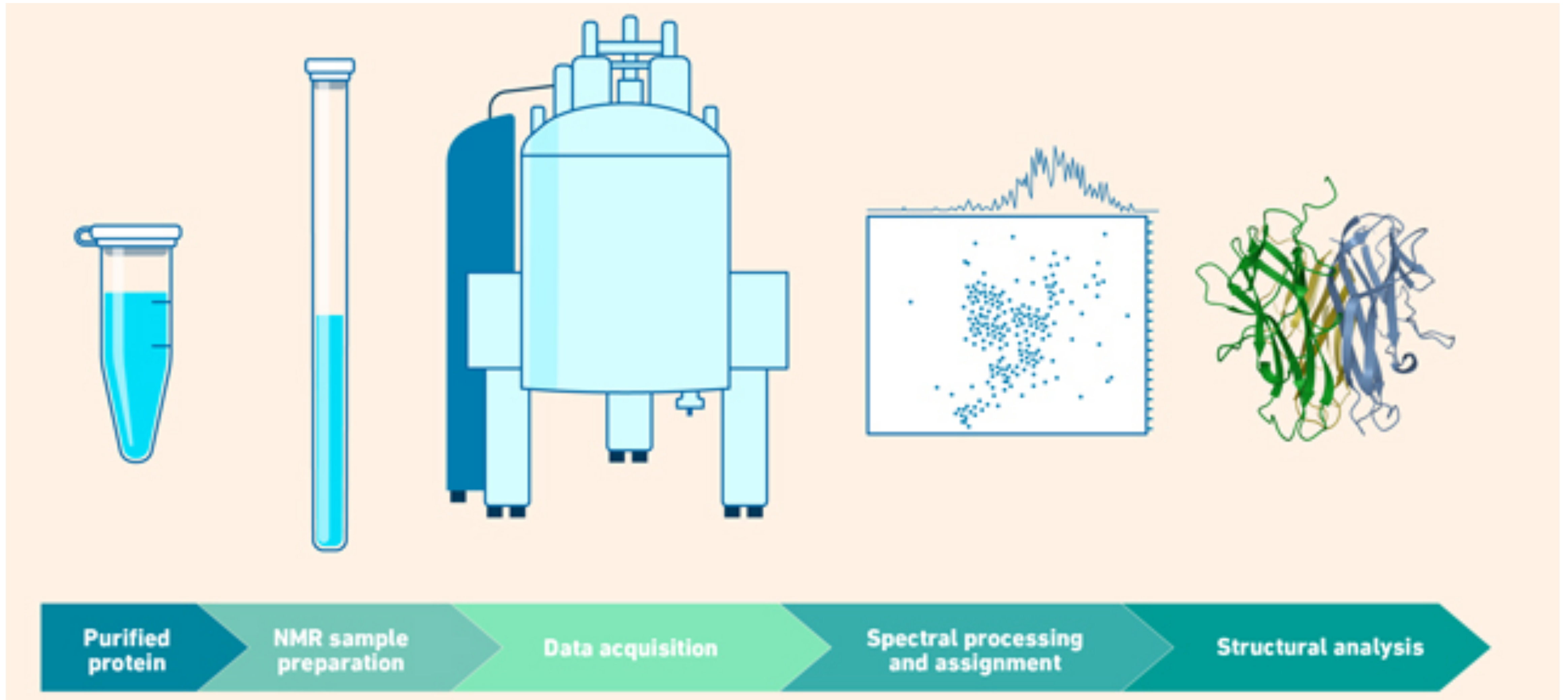


Eukaryotic cells



Size range of object investigated
Resolution attainable

Nuclear Magnetic Resonance



X-Ray Crystallography

Crystal



X-rays

Diffraction pattern



Processing

Electron density map



Fitting

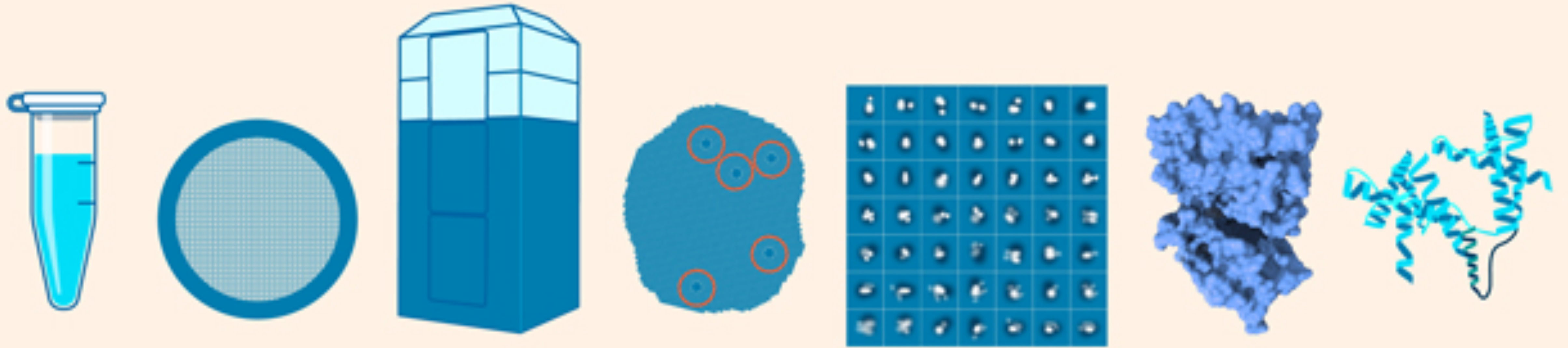
Atomic model



Refinement



Cryo-electron microscopy



Purified protein

Freezing / Negative staining

EM data collection

Particle picking

Particle alignment and classification

3D model reconstruction

Model refinement

Protein Data Bank: The protein repository

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

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RCSB PDB PROTEIN DATA BANK 215,908 Structures from the PDB 1,068,577 Computed Structure Models (CSM)

3D Structures Enter search term(s), Entry ID(s), or sequence Include CSM

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RCSB Protein Data Bank (RCSB PDB) enables breakthroughs in science and education by providing access and tools for exploration, visualization, and analysis of:

- Experimentally-determined 3D structures from the Protein Data Bank (PDB) archive
- Computed Structure Models (CSM) from AlphaFold DB and ModelArchive

These data can be explored in context of external annotations providing a structural view of biology.

Explore NEW Features

PDB-101 Training Resources

February Molecule of the Month

694 Structures 20 Unreleased Structures 274 Citations 140 Ligands 32 News & PDB-101 Articles

Search Parameter: Text Search for: hemoglobin

Refinements

ORGANISM

- Homo sapiens (254)
- Scapharca inaequivalvis (66)
- Amphitrite ornata (26)
- Equus caballus (18)
- Lupinus luteus (17)
- Cerebratulus lacteus (17)
- Physeter catodon (16)
- Other (280)

UNIPROT MOLECULE NAME

- Hemoglobin subunit alpha (310)
- Hemoglobin subunit beta (309)
- Globin-1 (64)
- Dehaloperoxidase A (24)
- Leghemoglobin-2 (17)
- Neural hemoglobin (17)
- Myoglobin (17)
- Refine Query

TAXONOMY

- Eukaryota (626)
- Bacteria (79)
- Other (1)

EXPERIMENTAL METHOD

- X-ray (676)

Currently showing 1 - 25 of 694 Page: 1 of 28

View: Detailed Reports: Select a Report Sort: Release Date: Newest to Oldest

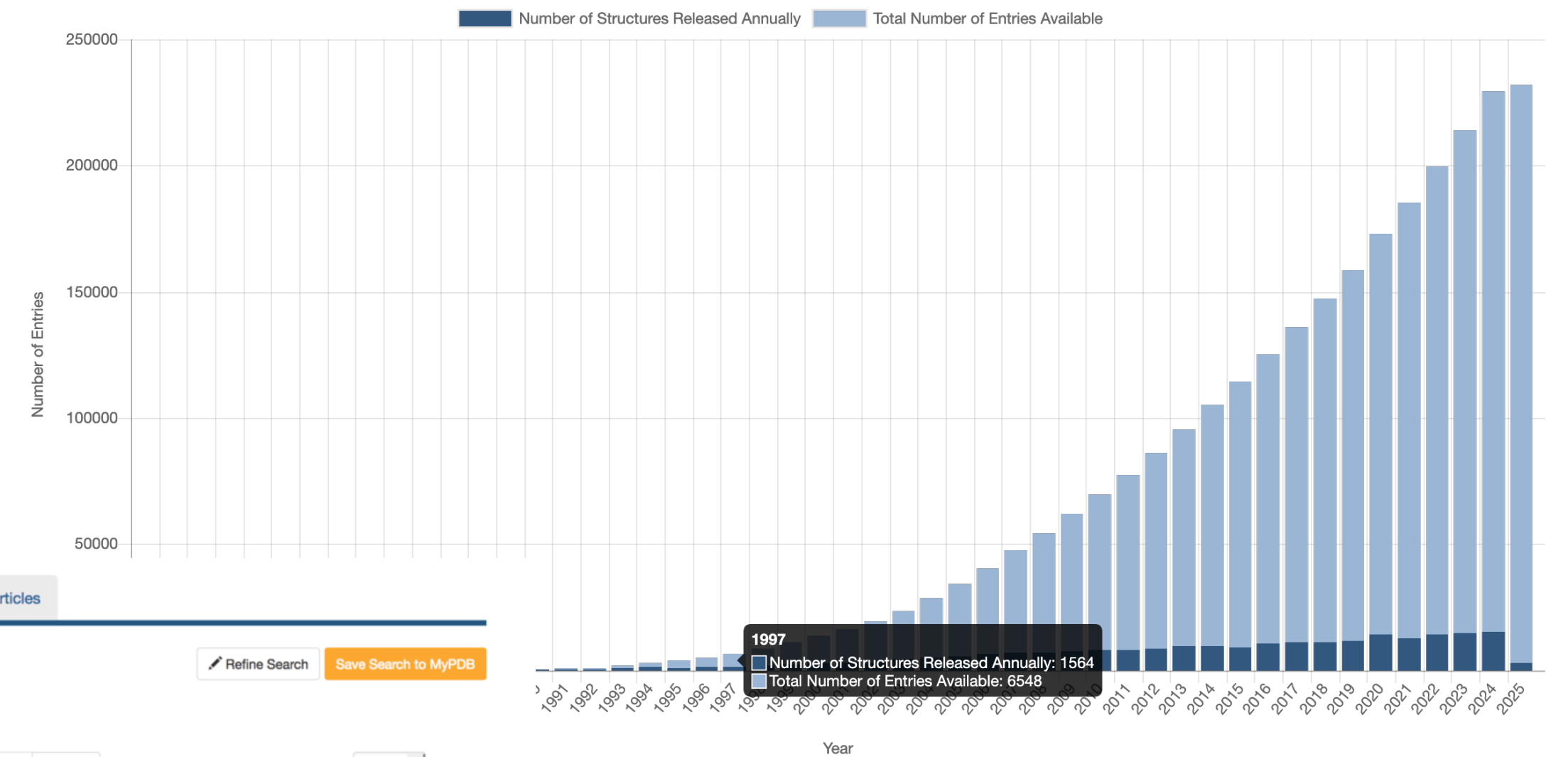
Structure of predicted ancestral pika hemoglobin

Inoguchi, N., Natarajan, c., Storz, J.F., Moriyama, H.

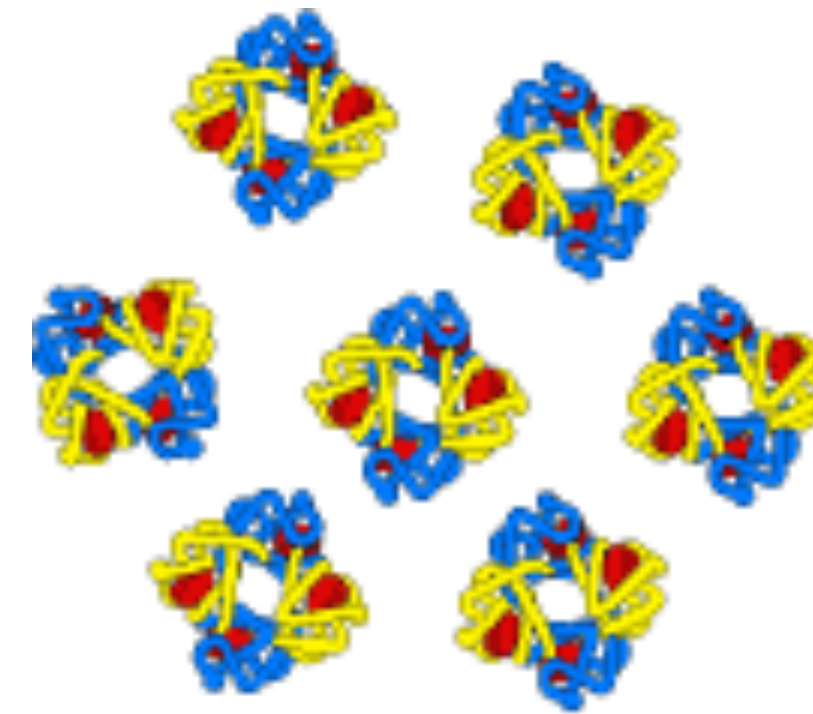
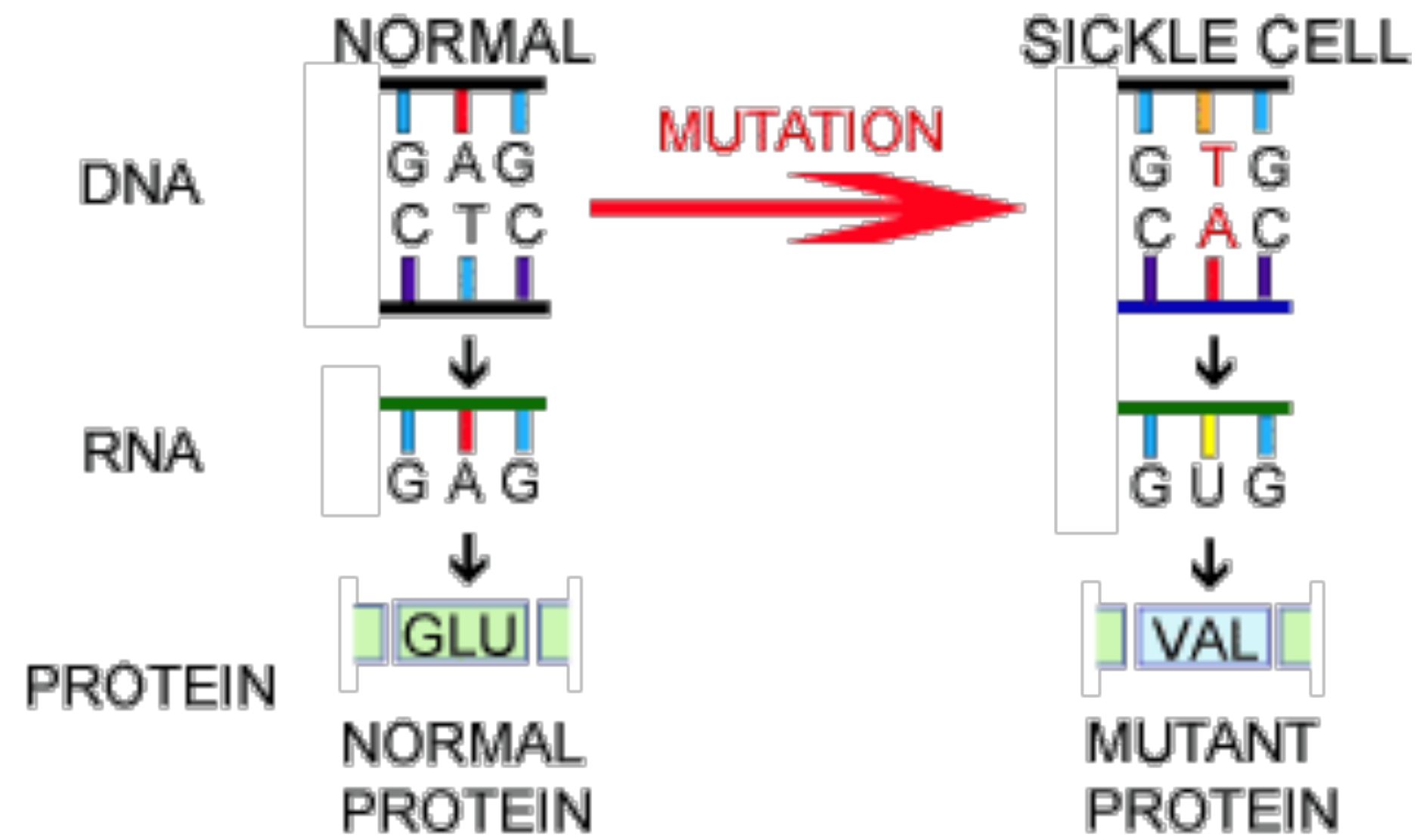
PubMed ID is not available.

Released: 11/30/2016 Method: X-ray Diffraction Resolution: 1.45 Å Residue Count: 287

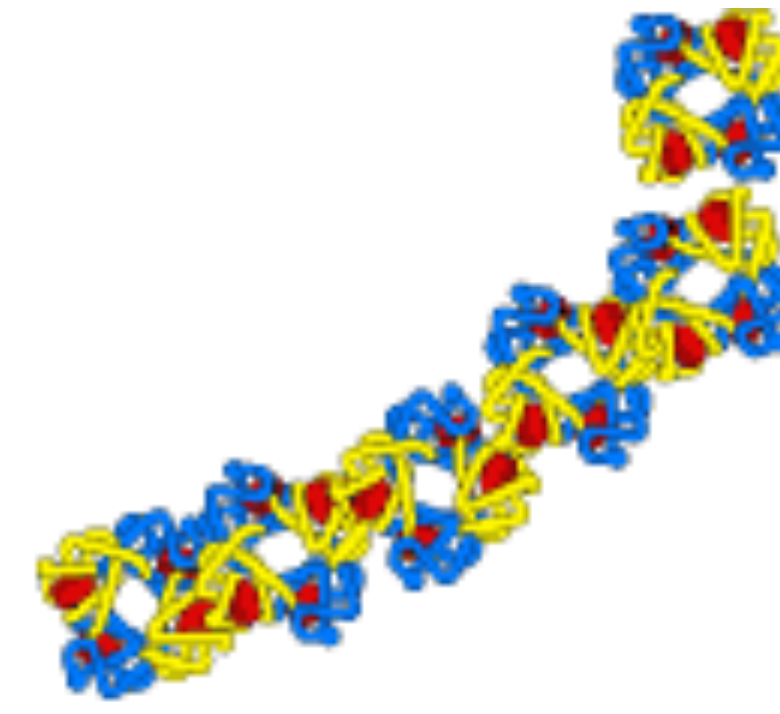
Macromolecule: HBA protein (protein) HBB protein (protein) Unique Ligands: HEM



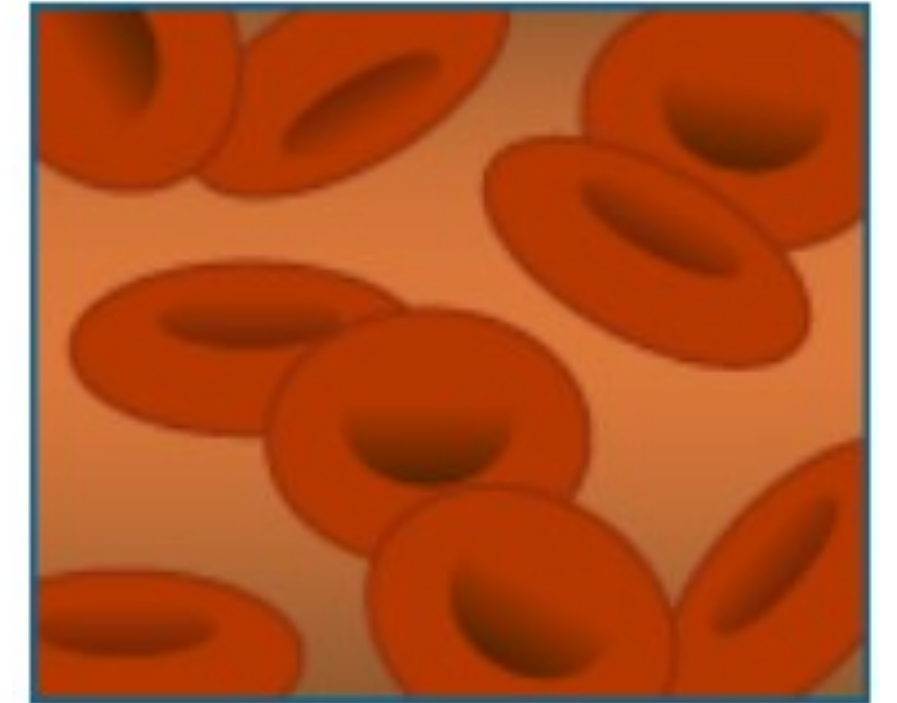
The impact of mutation on structure-function of protein



NORMAL HEMOGLOBIN

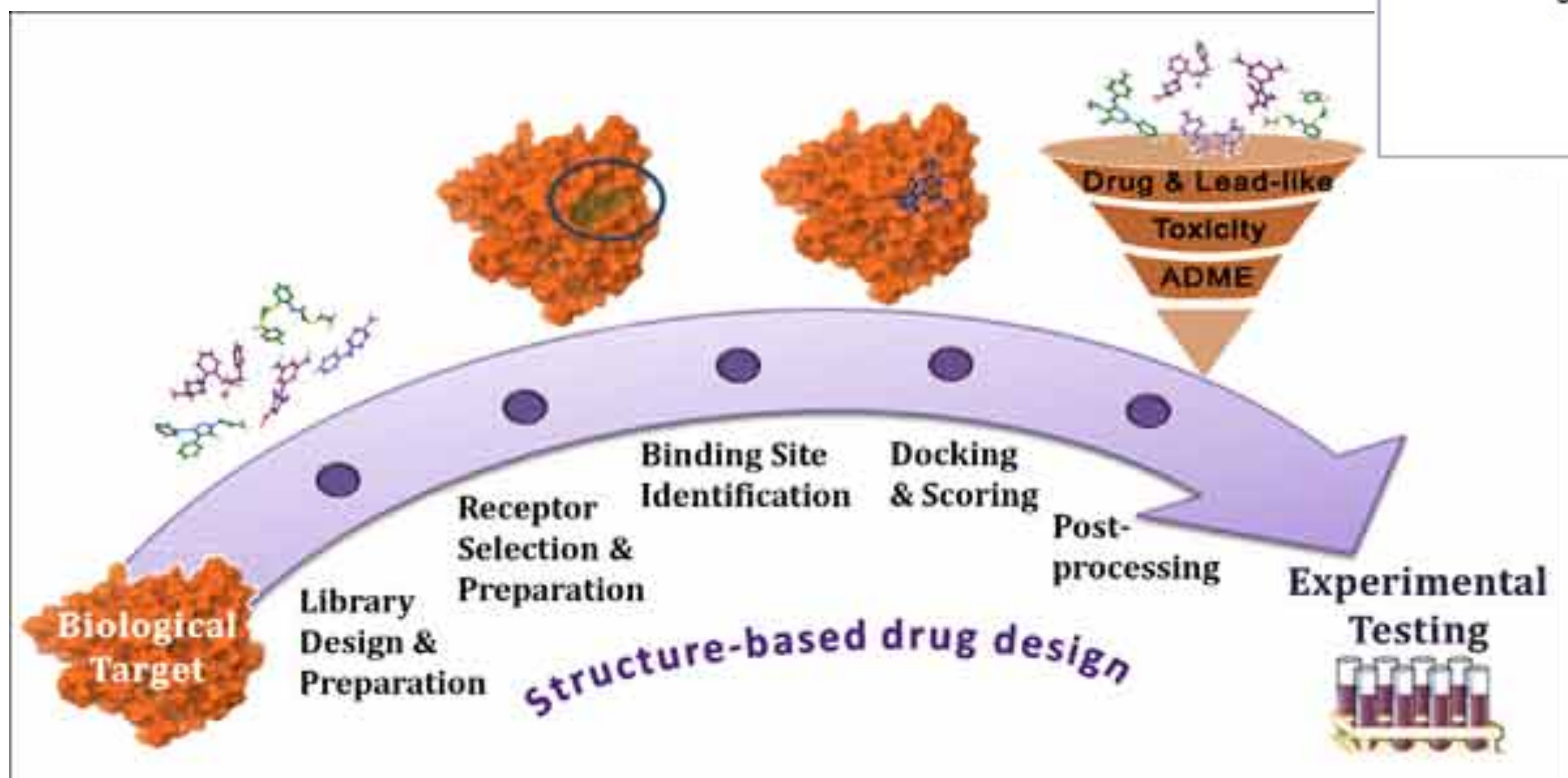
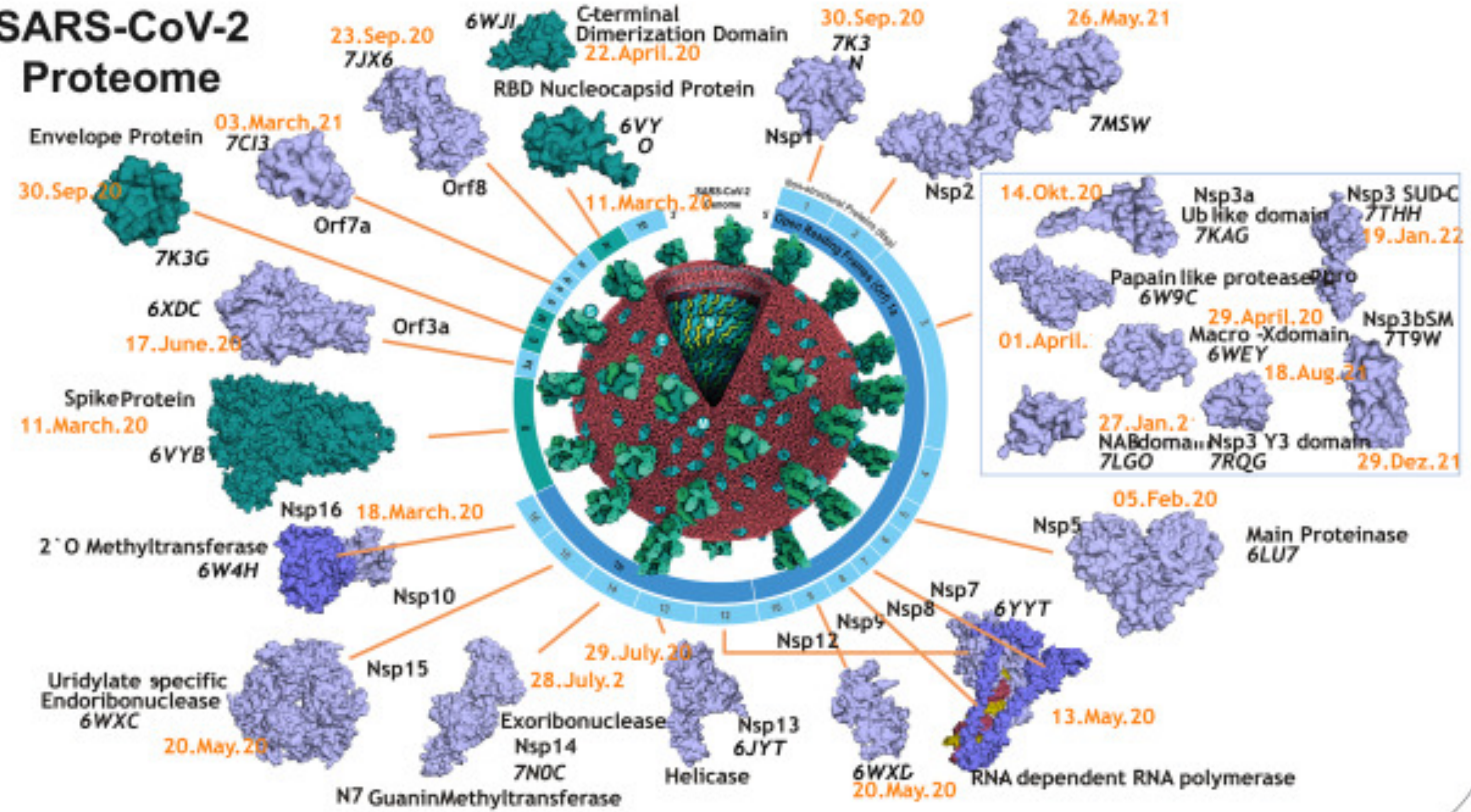


CLUMPED HEMOGLOBIN

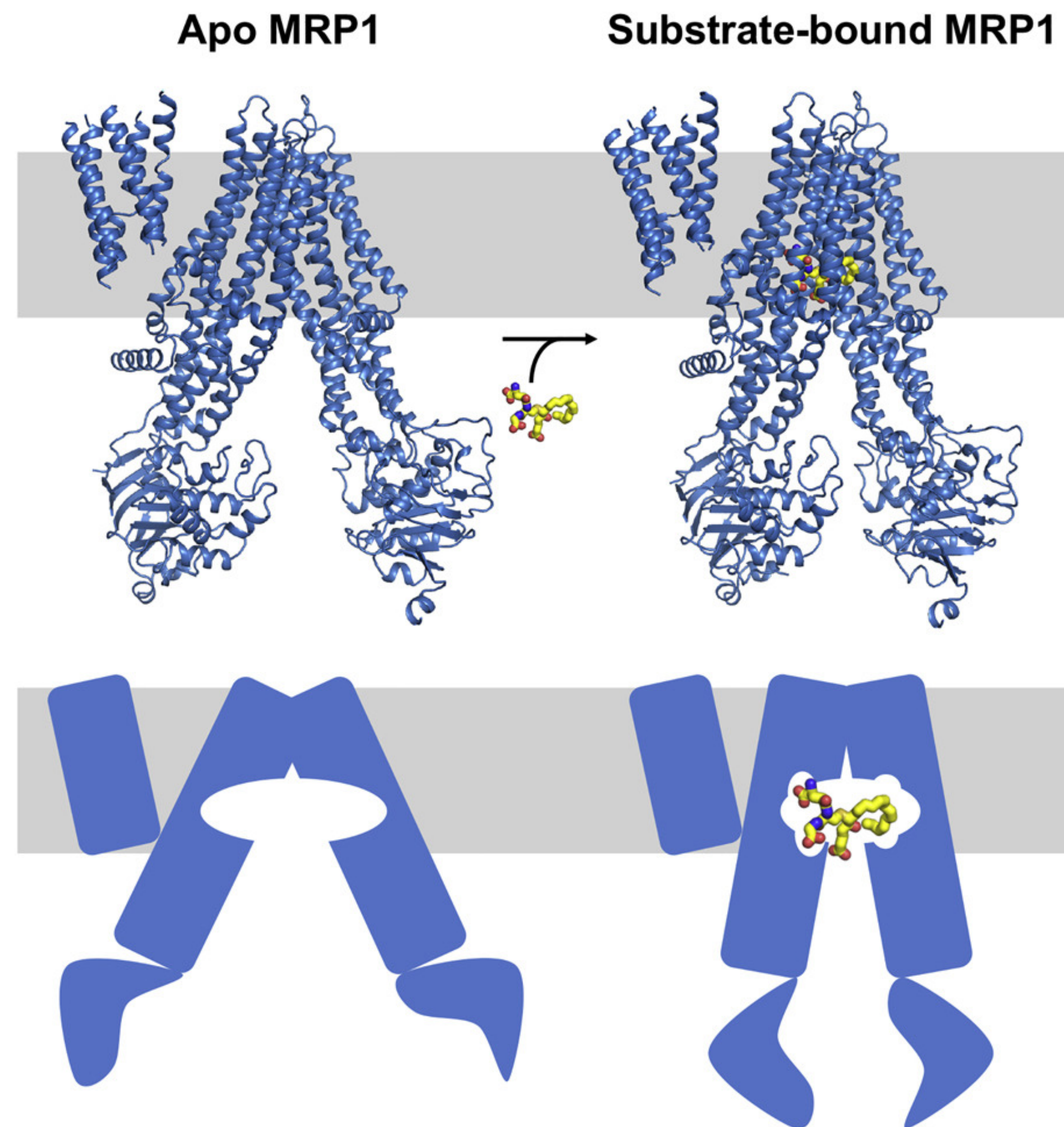


Structure-based drug designing

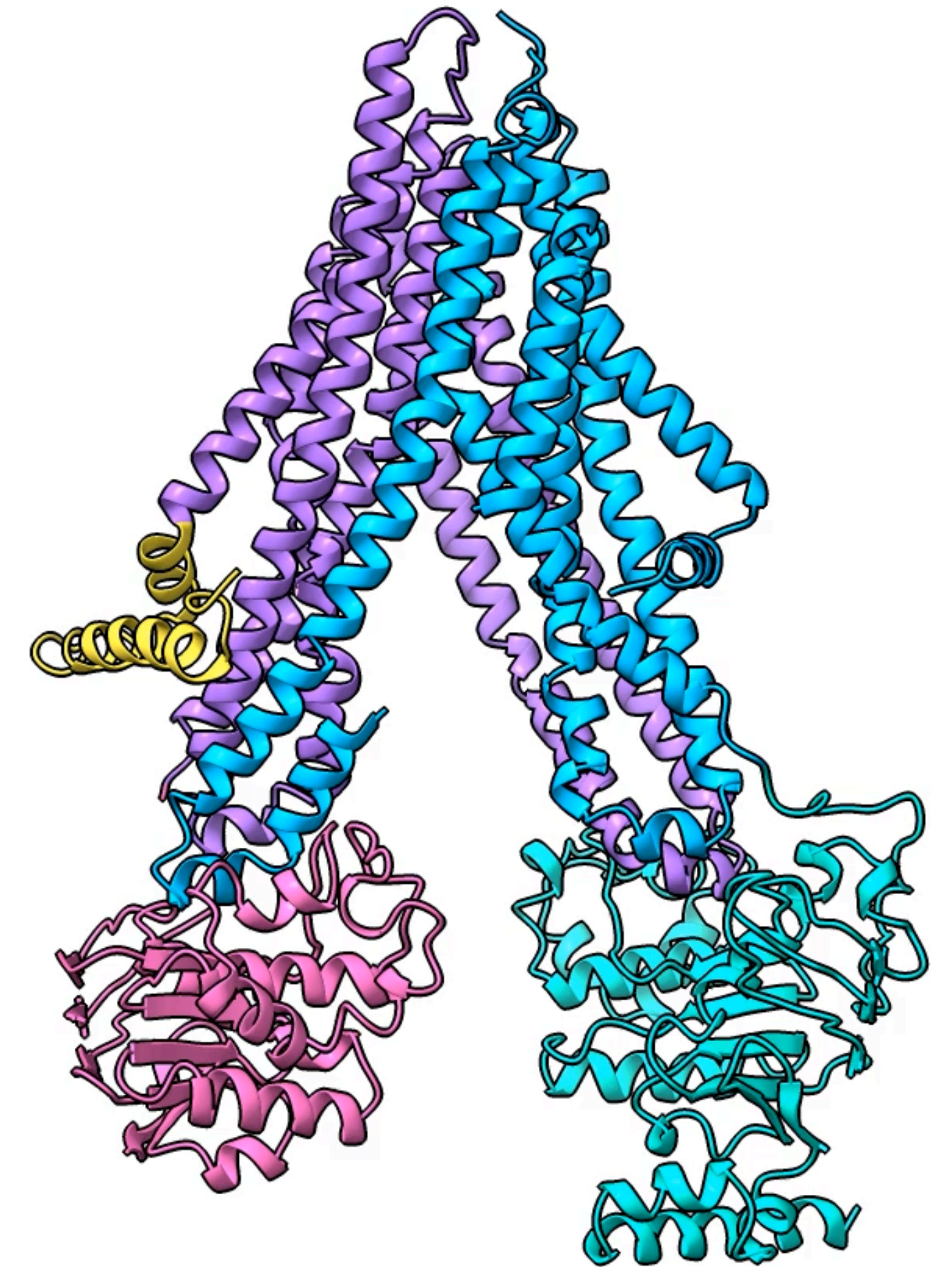
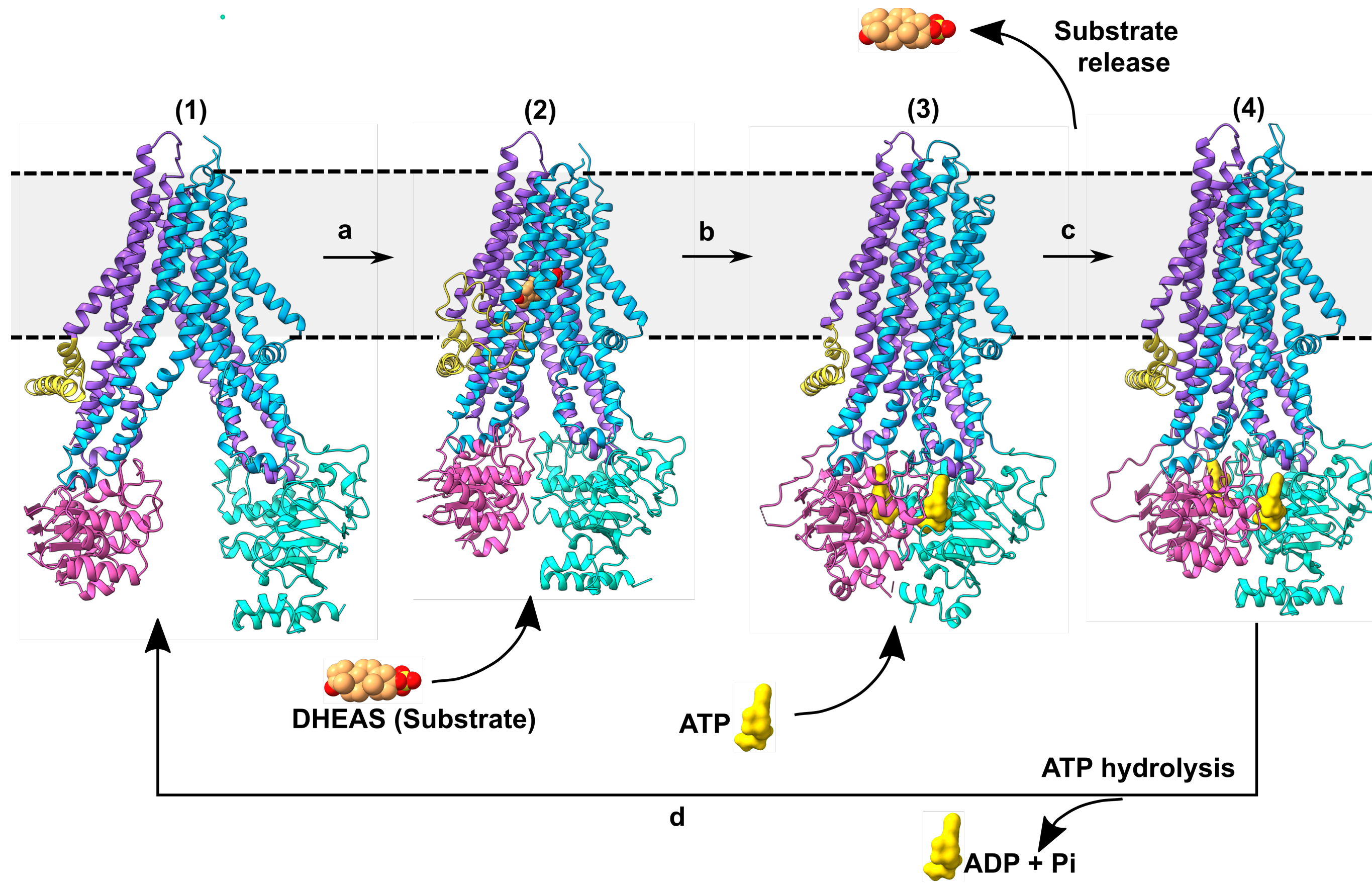
SARS-CoV-2 Proteome



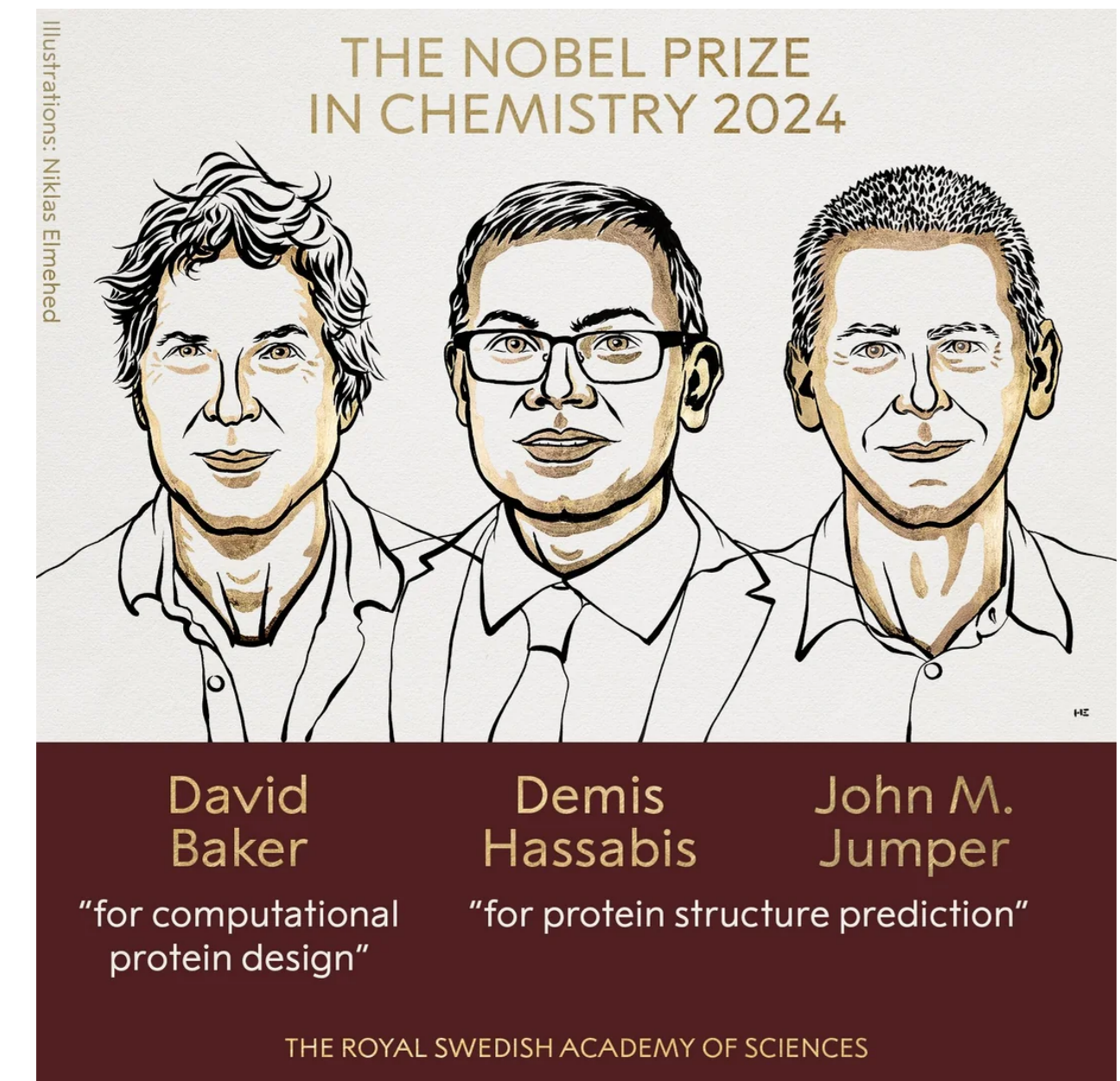
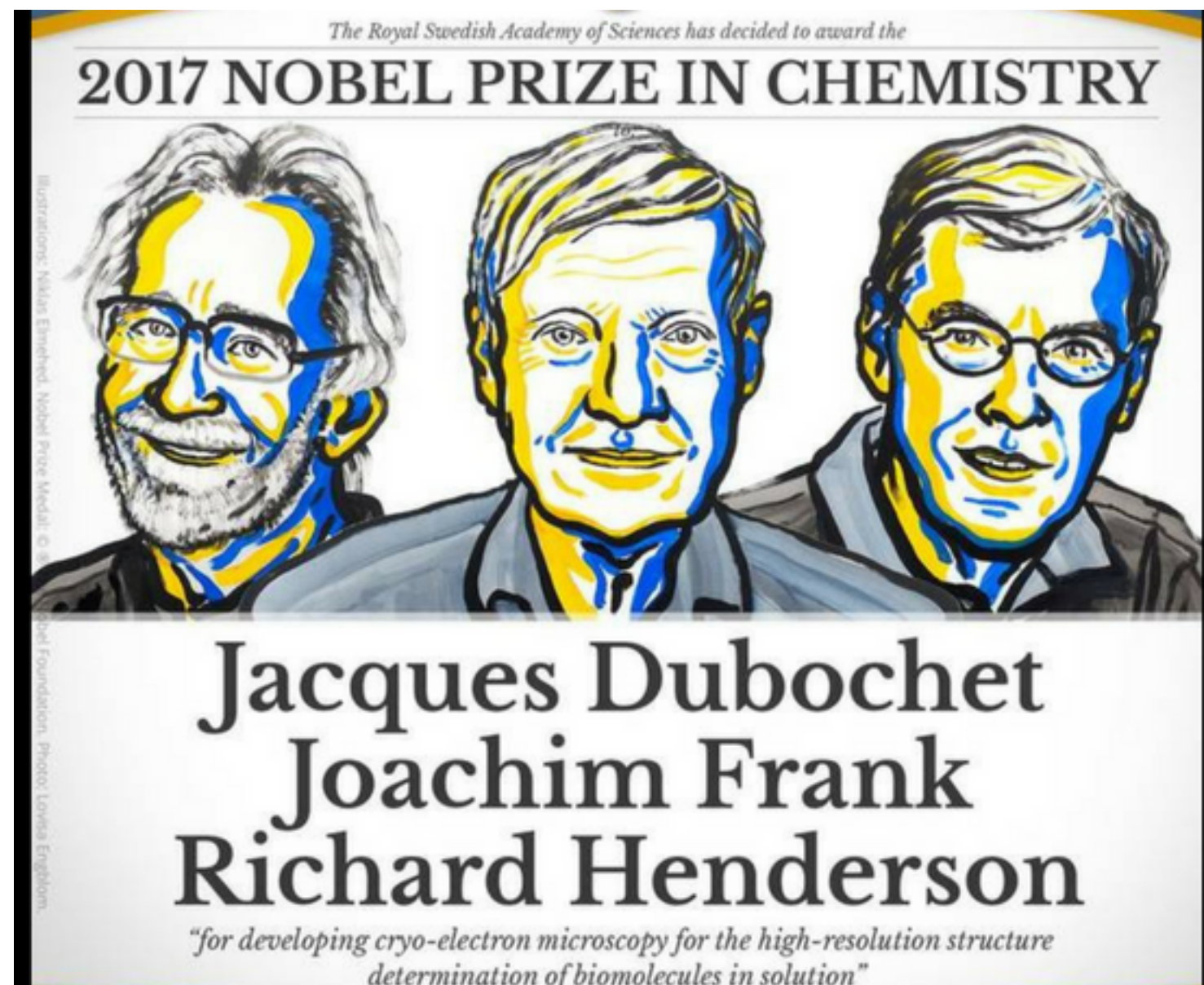
Conformational changes on ligand binding



Structure-functional relationships - catalytic cycle of protein

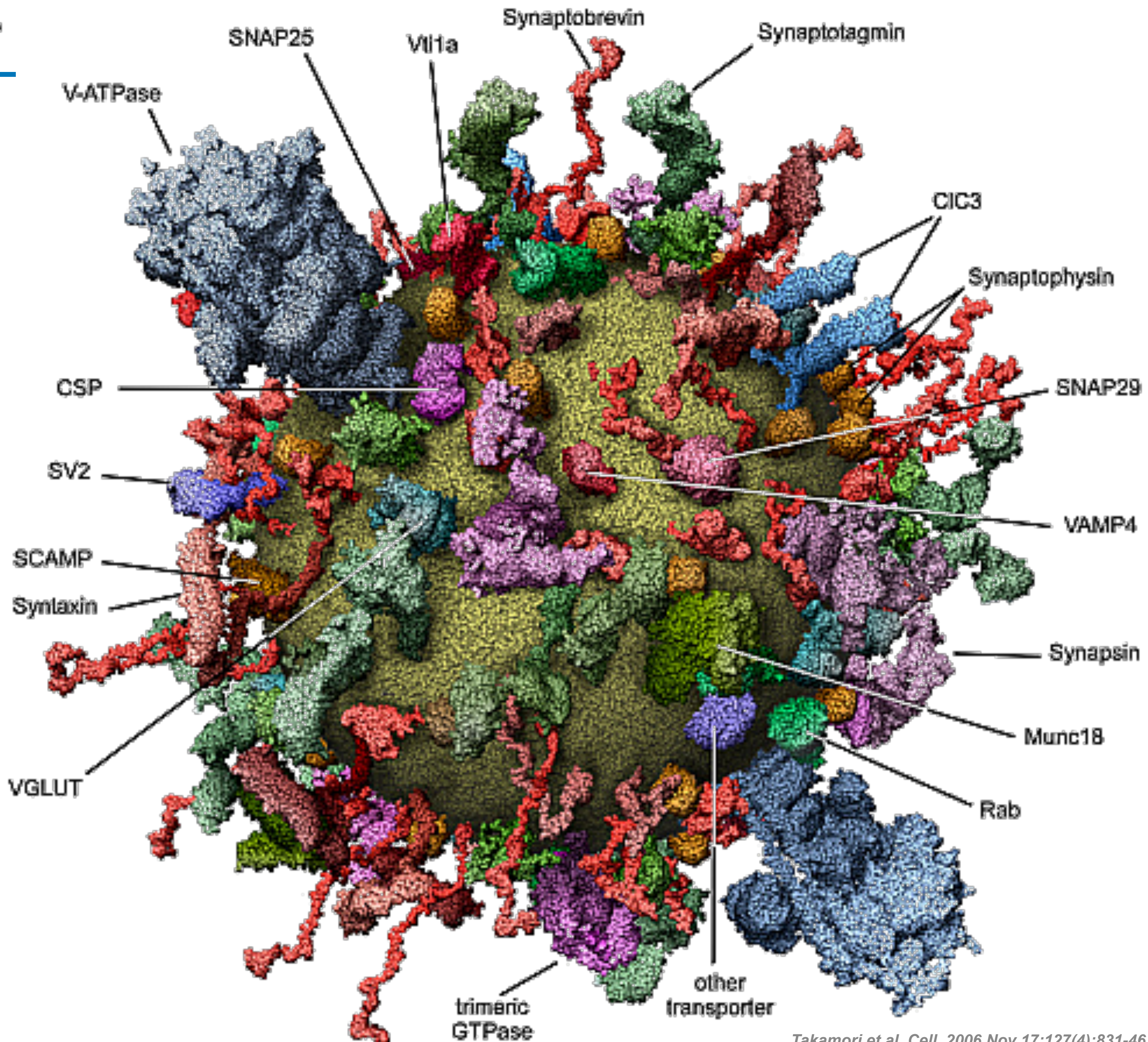
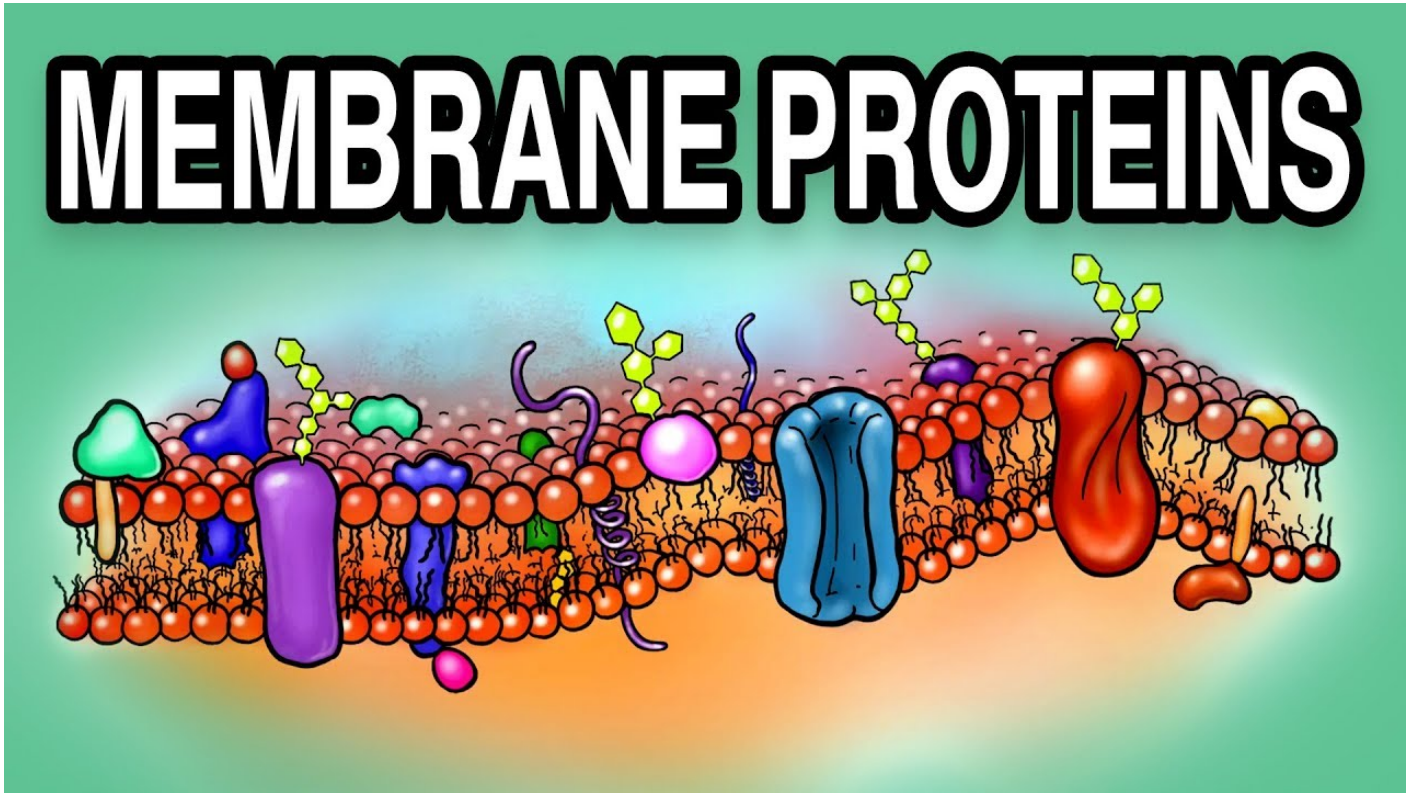


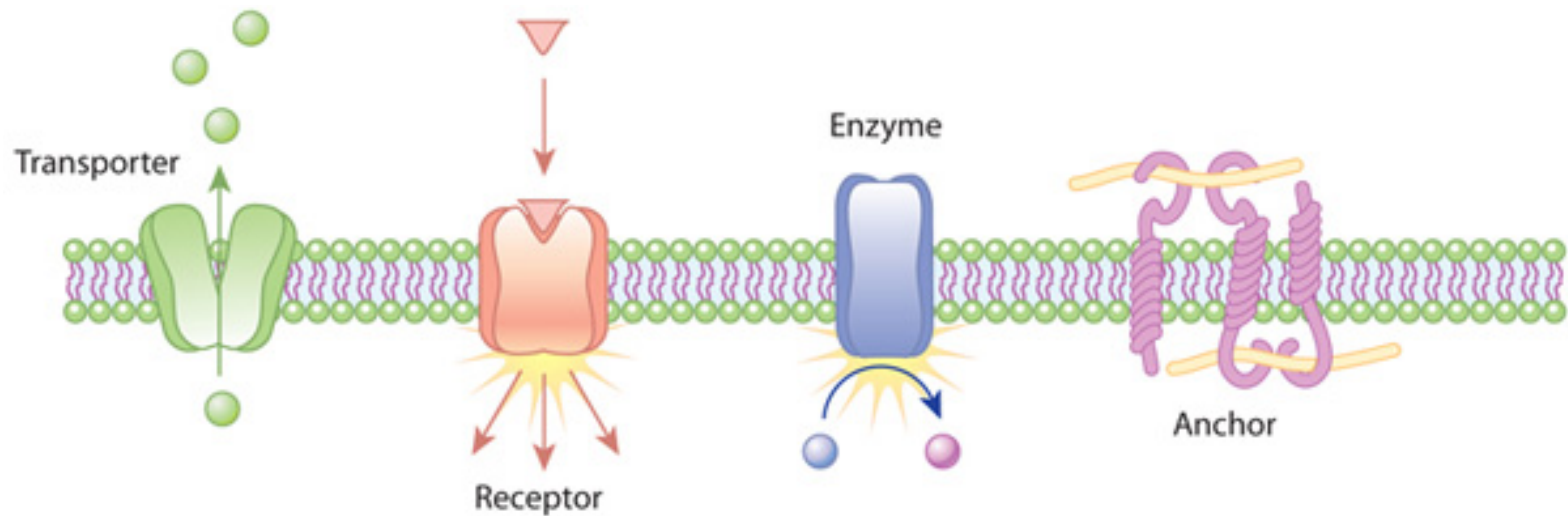
Recent Nobel prizes in Structural Biology



Questions

A special class of proteins - Membrane Proteins





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

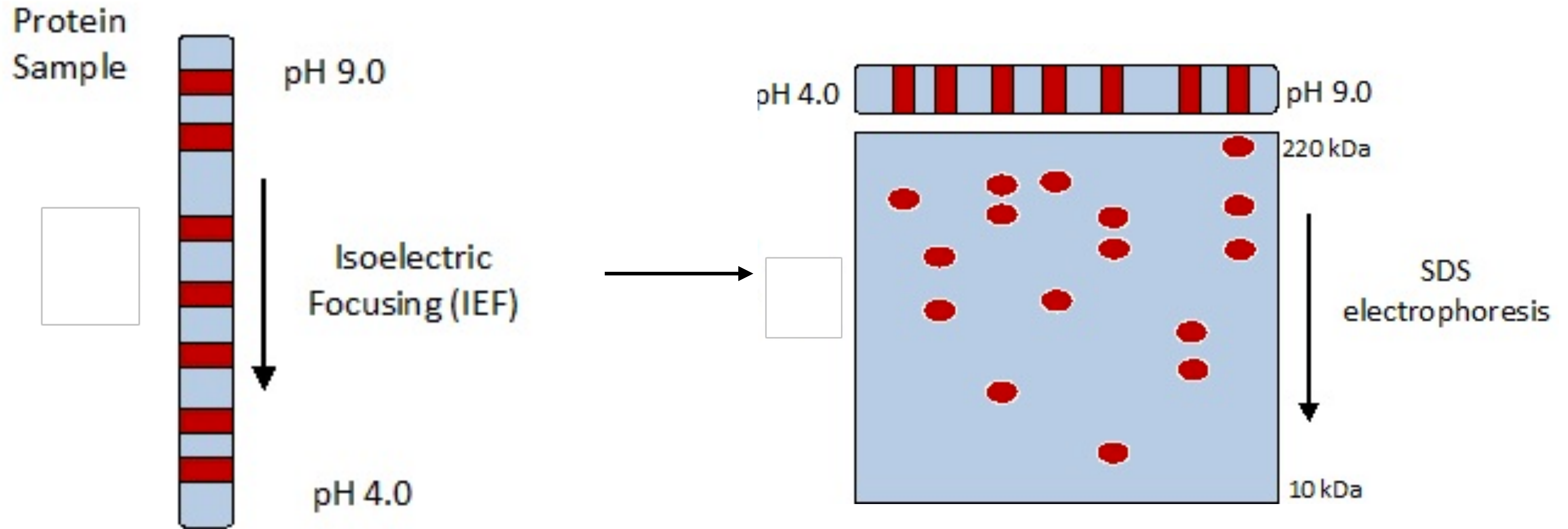
alternate splicing
mRNA editing
alternate promoters

proteolysis
post-translational modifications

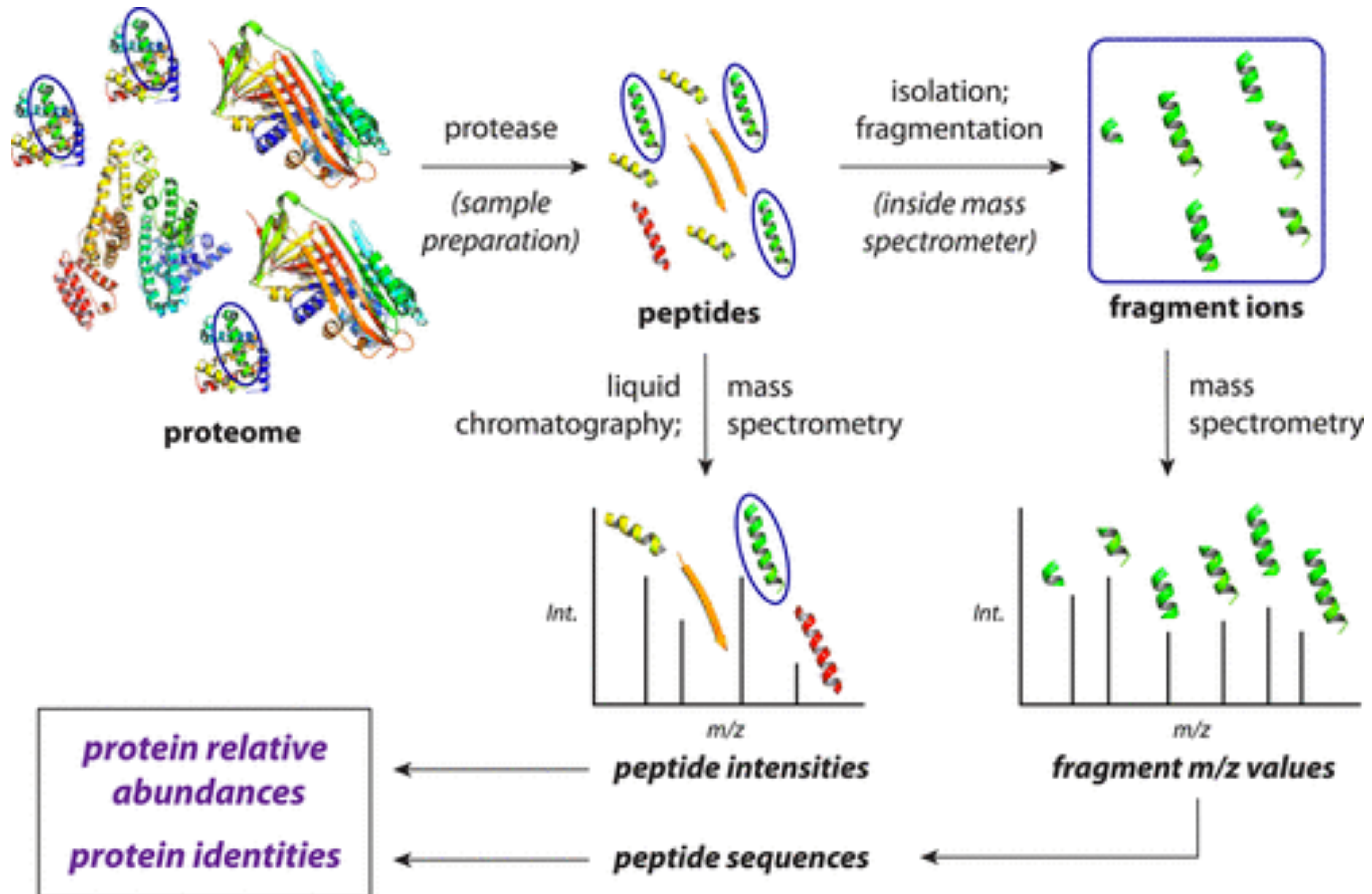
Proteomics can tell a lot of things

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

Old proteomics using 2D Gel Electrophoresis



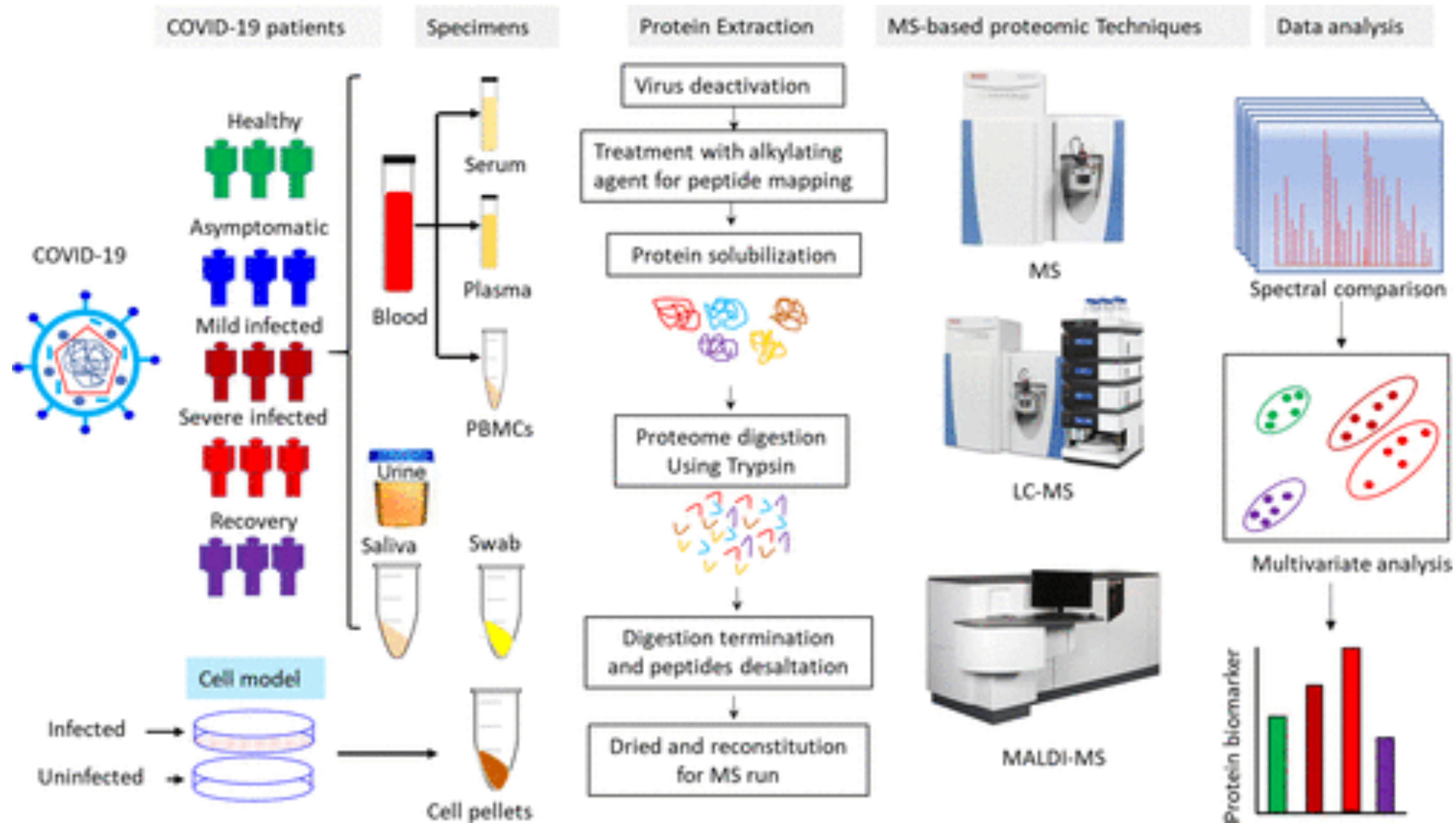
New generation proteomics uses mass spectrometry



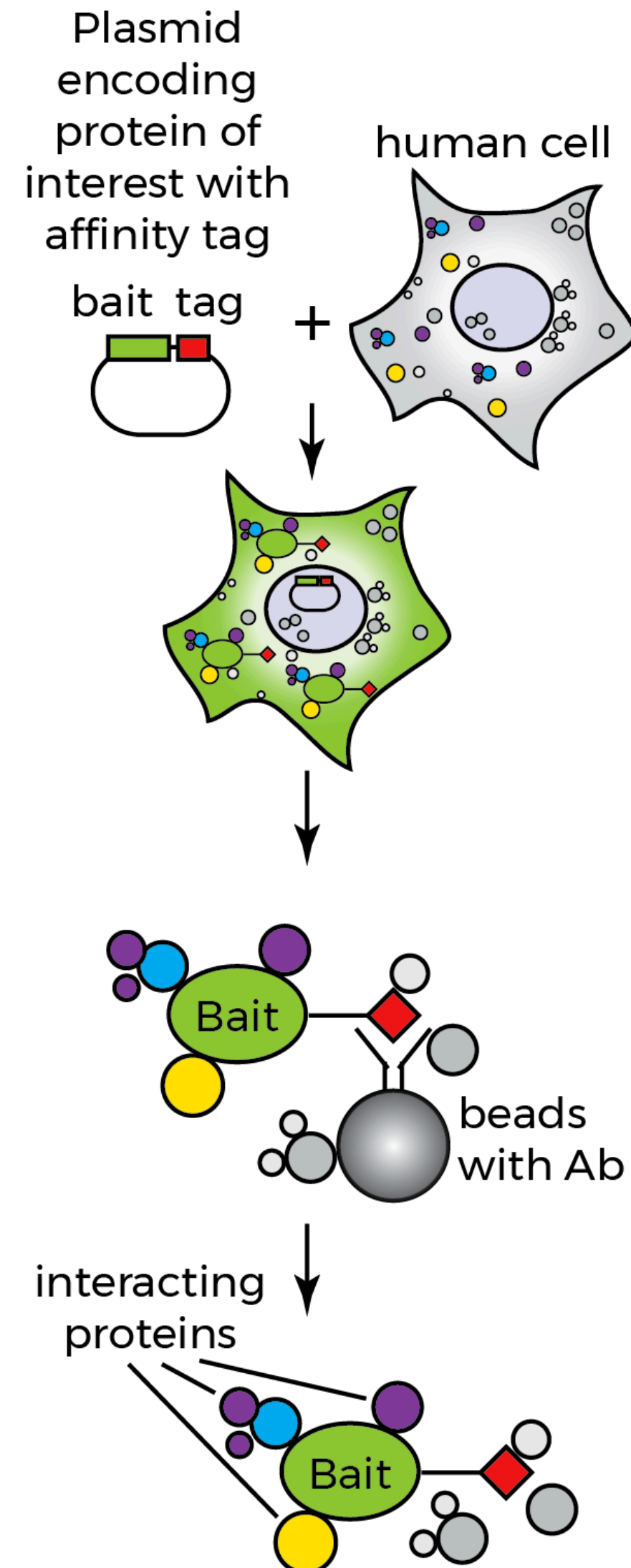
Applications of Proteomics

- 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



Identifying interactions of a favorite protein



Transfect tagged protein of interest

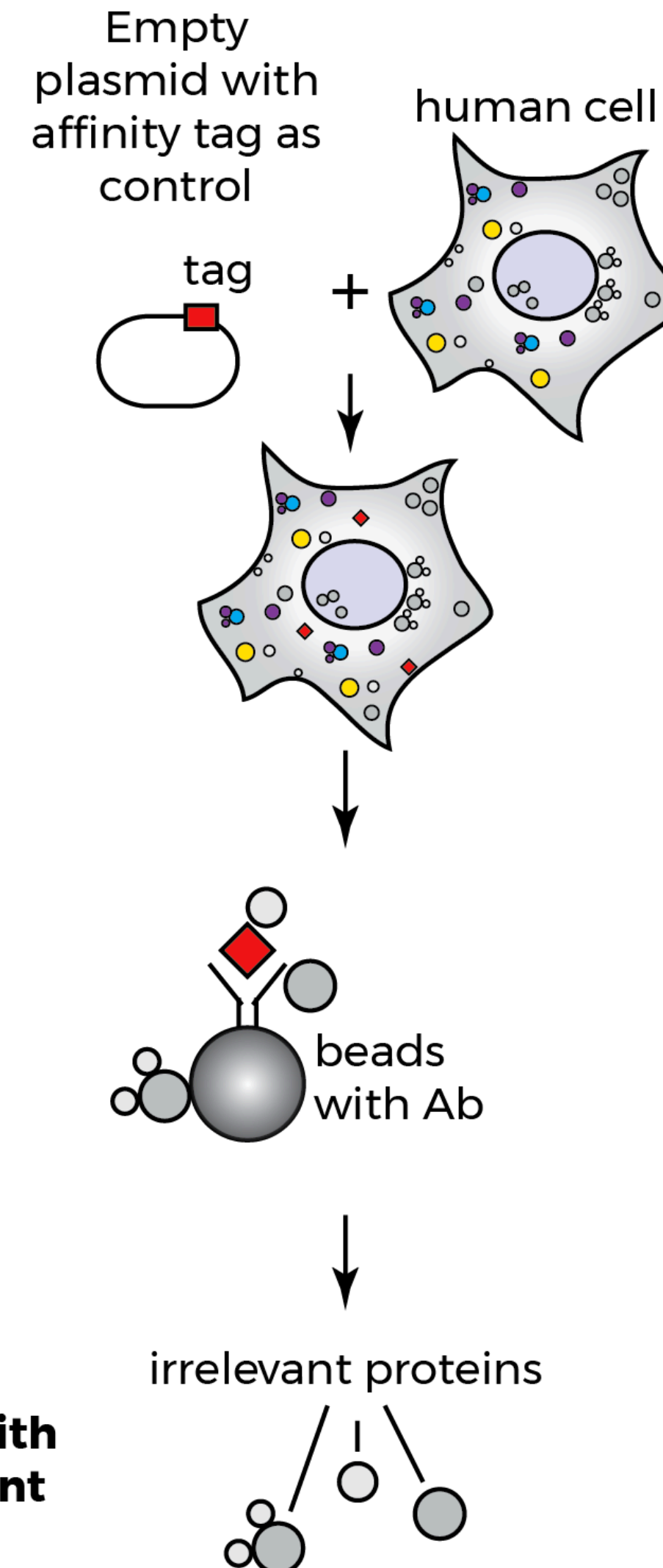
Express protein of interest

Cell lysis

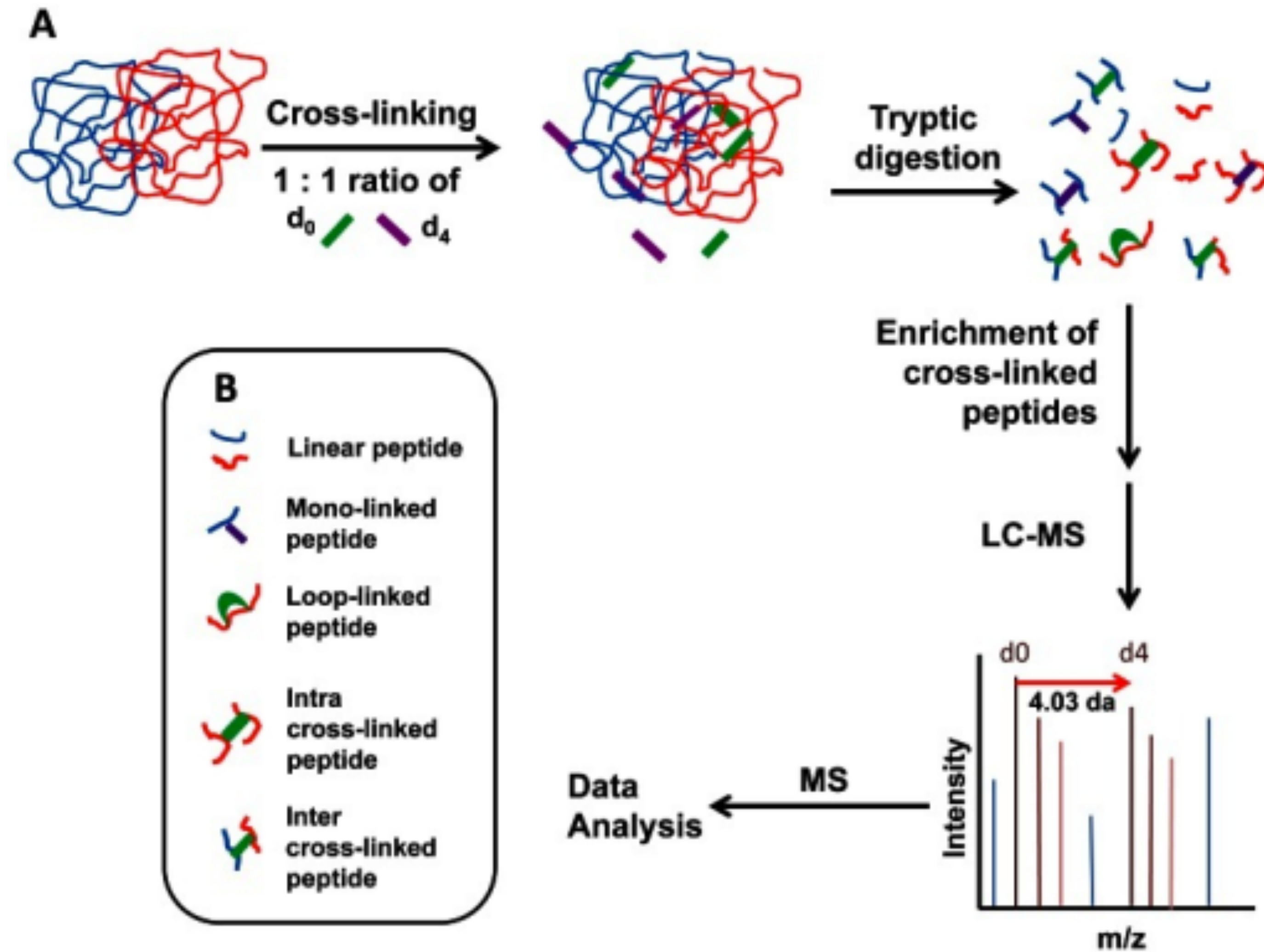
Add beads to capture tag

Elution of bound proteins

Identify proteins with LC-MS measurement



Identification of protein-protein interaction



Questions