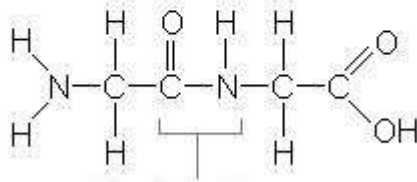
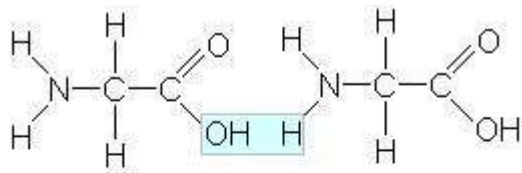


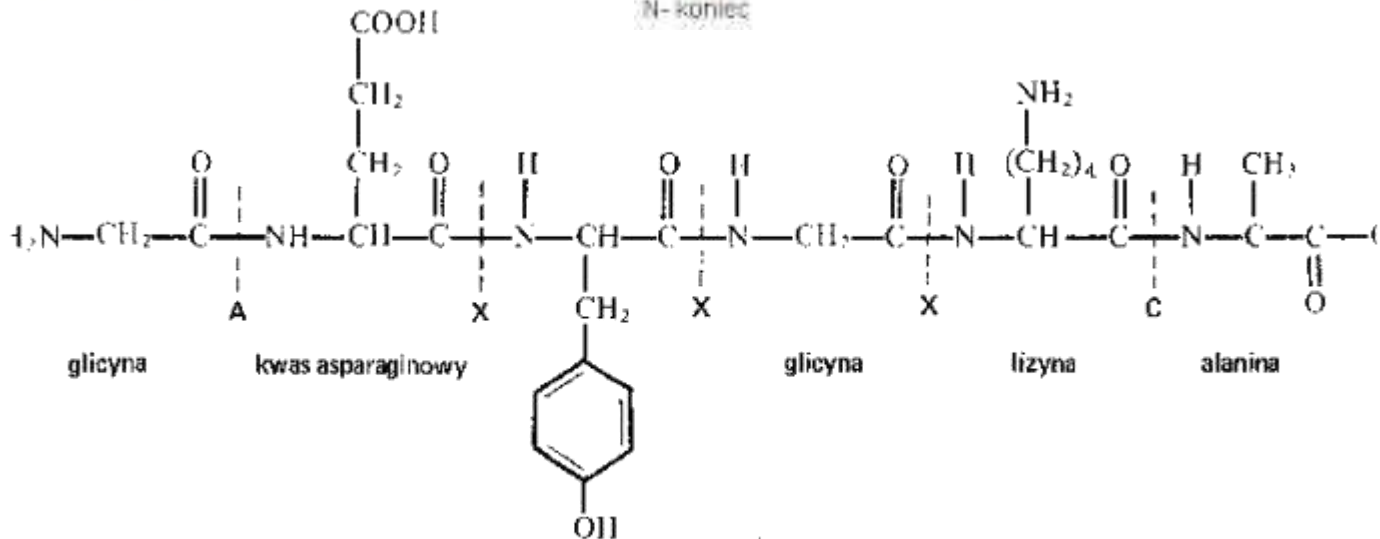
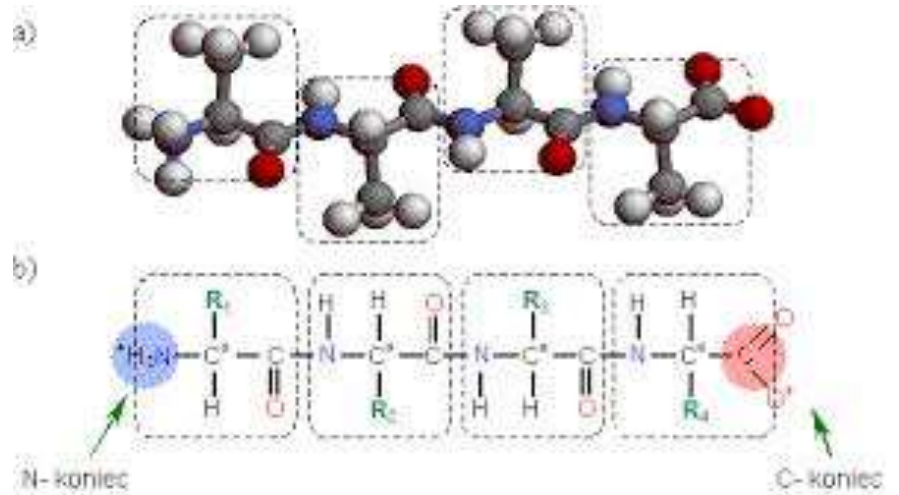
Struktura polimerów i biopolimerów

Niektóre ważne zagadnienia biologii strukturalnej
białek

Łańcuch polipeptydowy



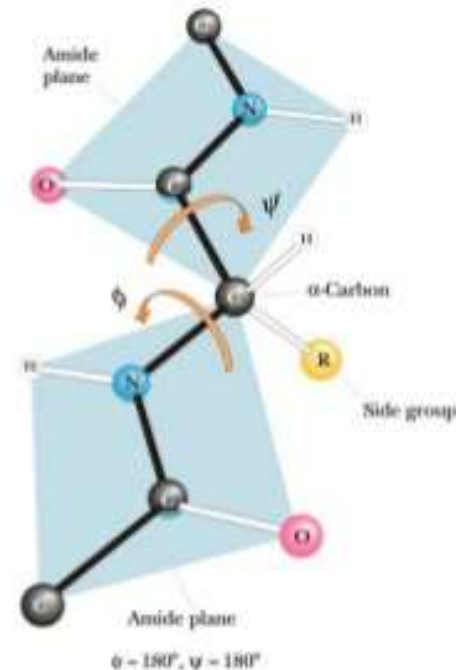
wiązanie peptydowe



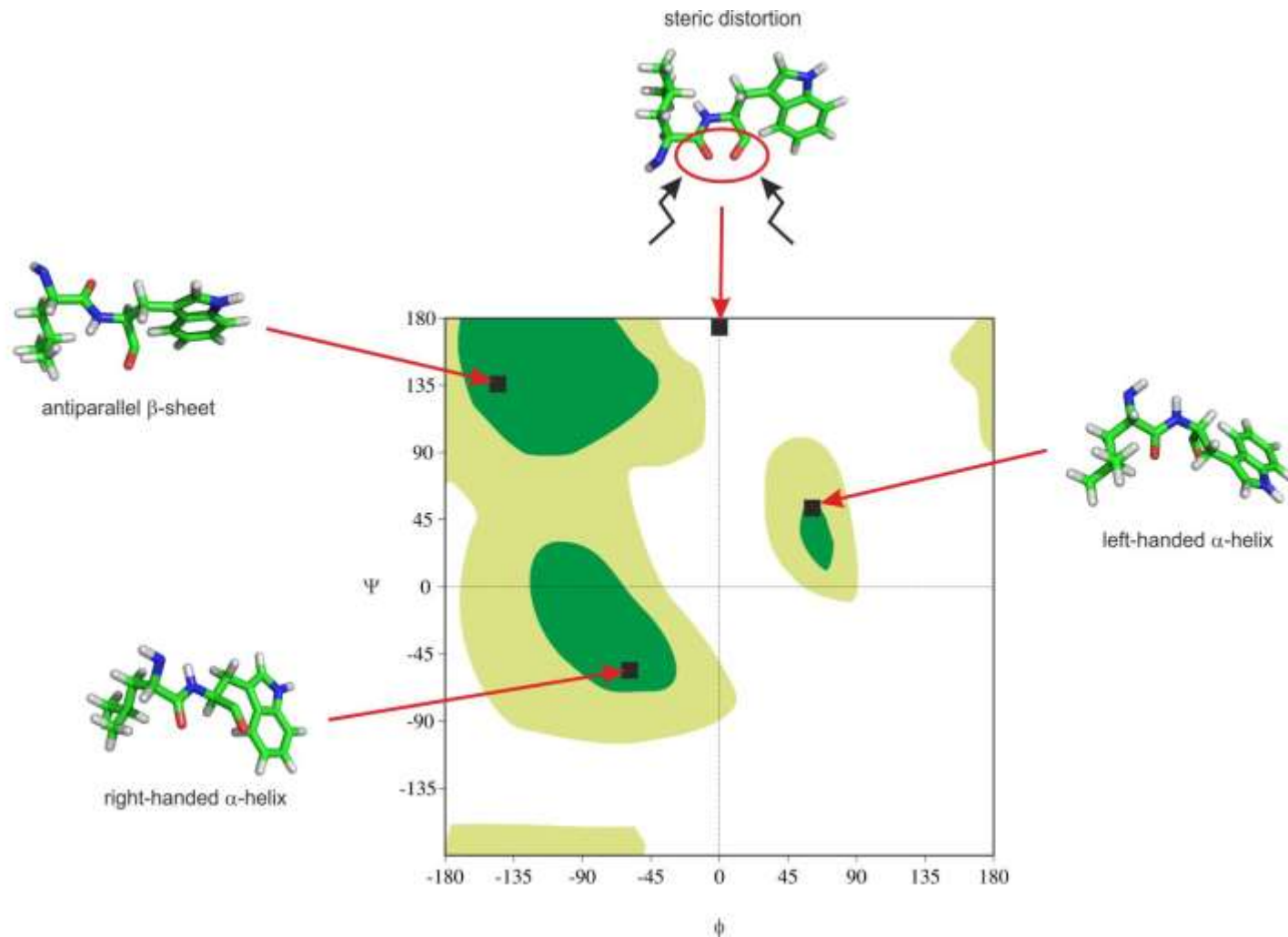
łańcuch polipeptydowy

2° Structure Related to Peptide Backbone

- Double bond nature of peptide bond cause planar geometry
- Free rotation at N - α C and α C - carbonyl C bonds
- Angle about the C(α)-N bond is denoted phi (ϕ)
- Angle about the C(α)-C bond is denoted psi (ψ)
- The entire path of the peptide backbone is known if all phi and psi angles are specified

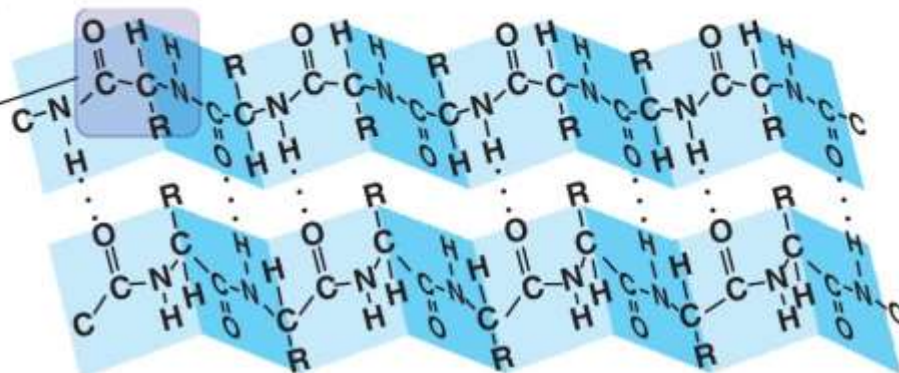


Wykres Ramachandrana

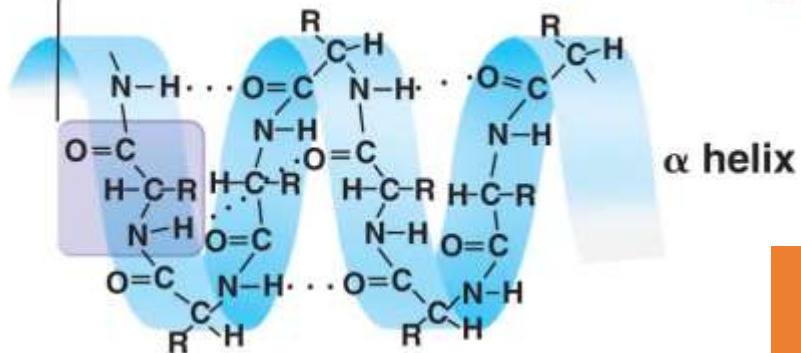


Secondary Structure

β pleated sheet

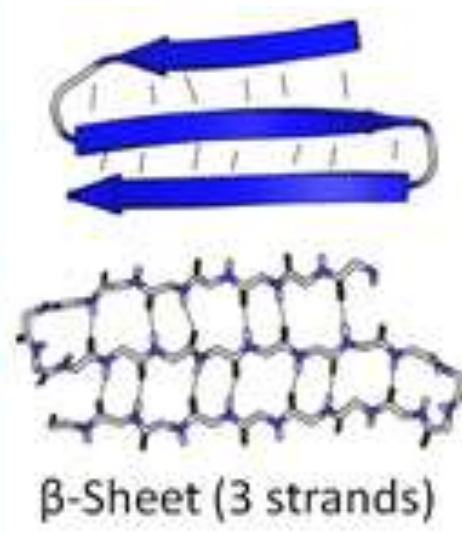


Examples of amino acid subunits



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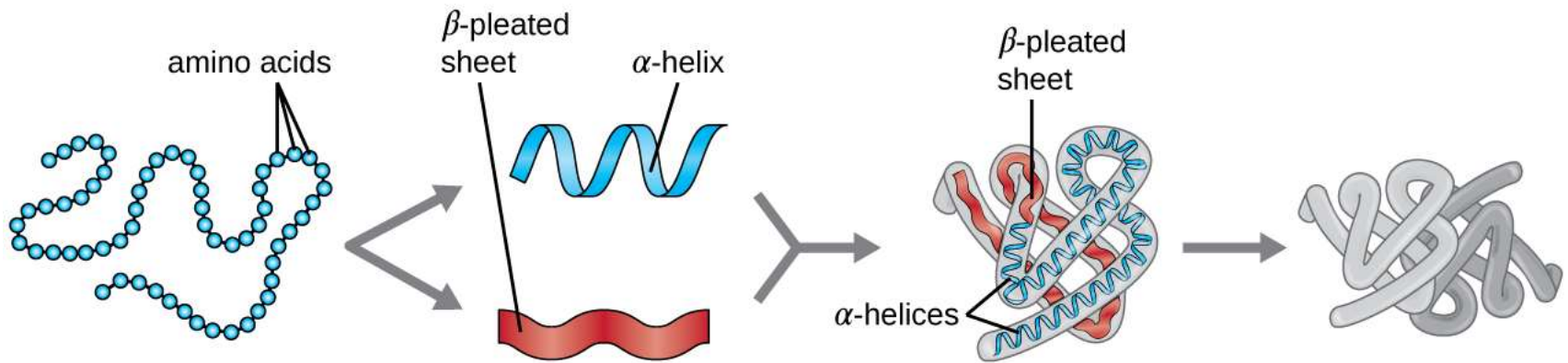
Secondary



β -Sheet (3 strands)

α -helix

Struktura przestrzenna



Primary Protein Structure

Sequence of a chain of amino acids

Secondary Protein Structure

Local folding of the polypeptide chain into helices or sheets

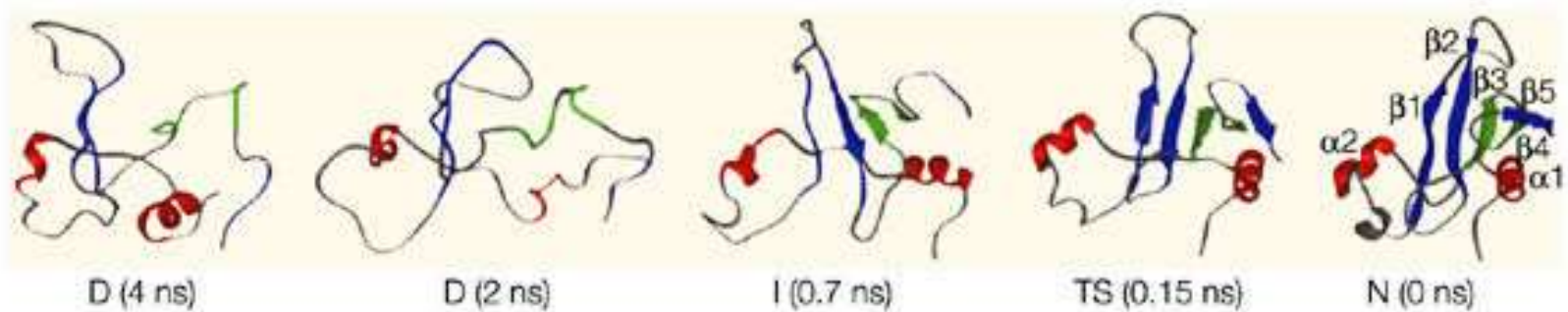
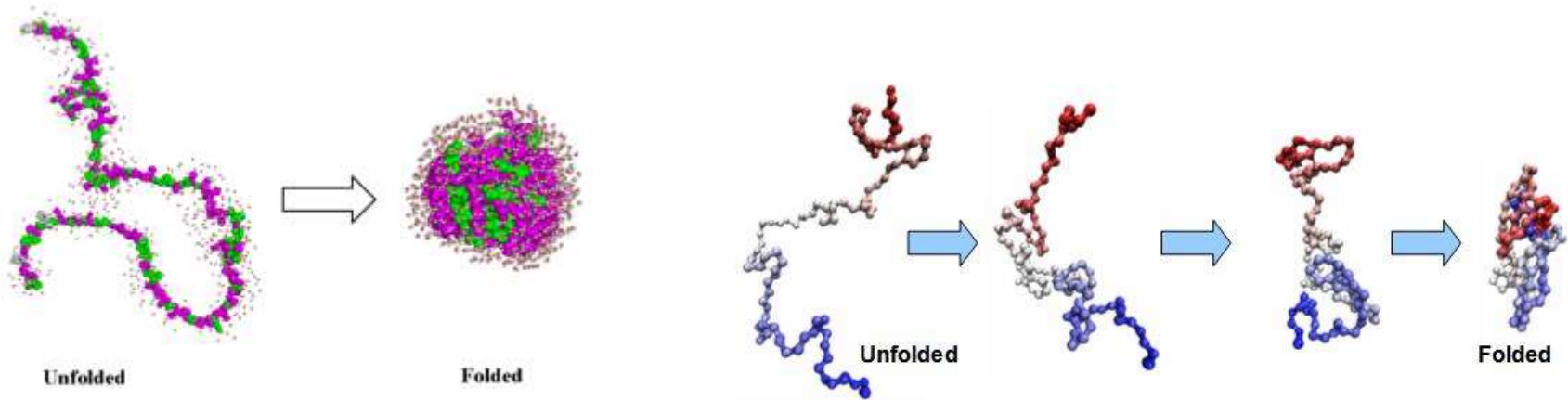
Tertiary Protein Structure

three-dimensional folding pattern of a protein due to side chain interactions

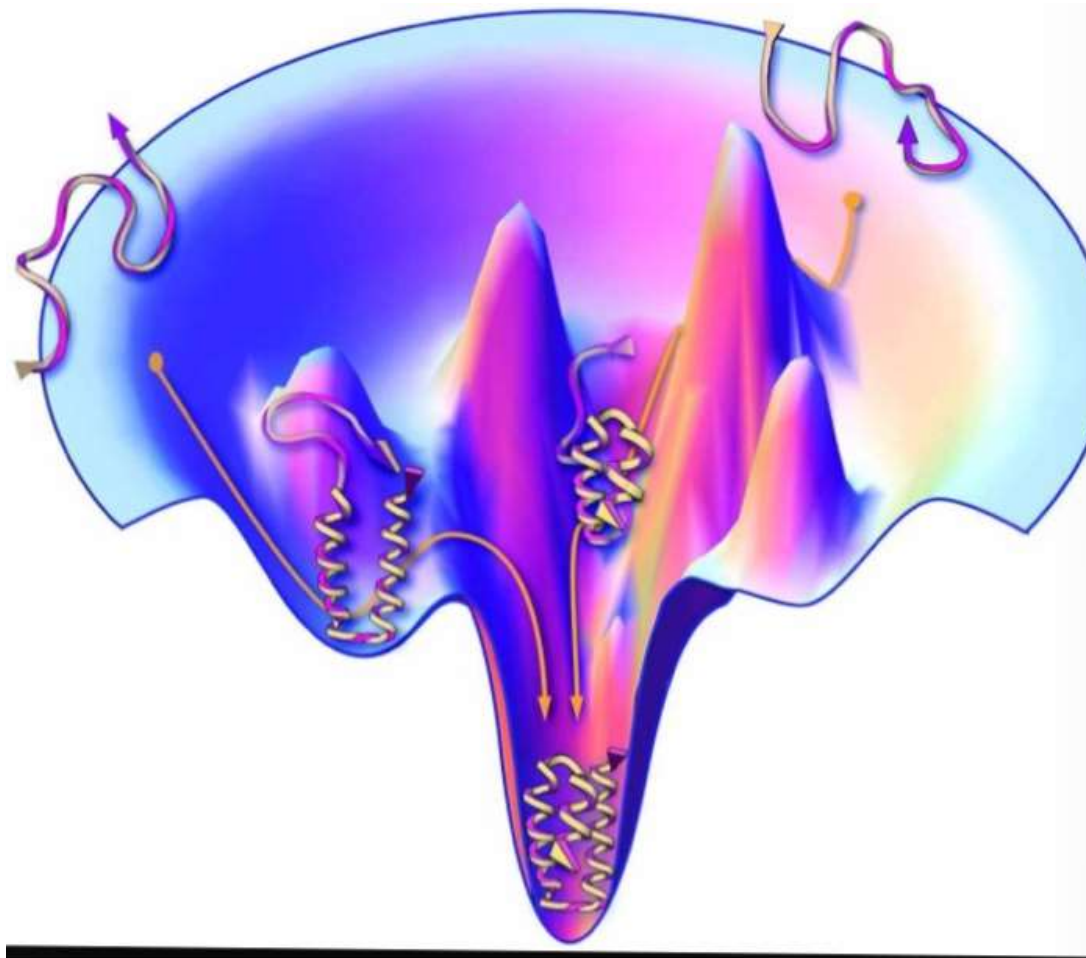
Quaternary Protein Structure

protein consisting of more than one amino acid chain

Łańcuch polipeptydowy – zwijanie struktury (protein folding problem)



Energia i entropia łańcucha białka.
Protein folding funnel (lejek zwijania)



Struktura białek - efekt hydrofobowości

Tertiary Structure and the “Hydrophobic Effect”

What would this protein look like when properly folded?

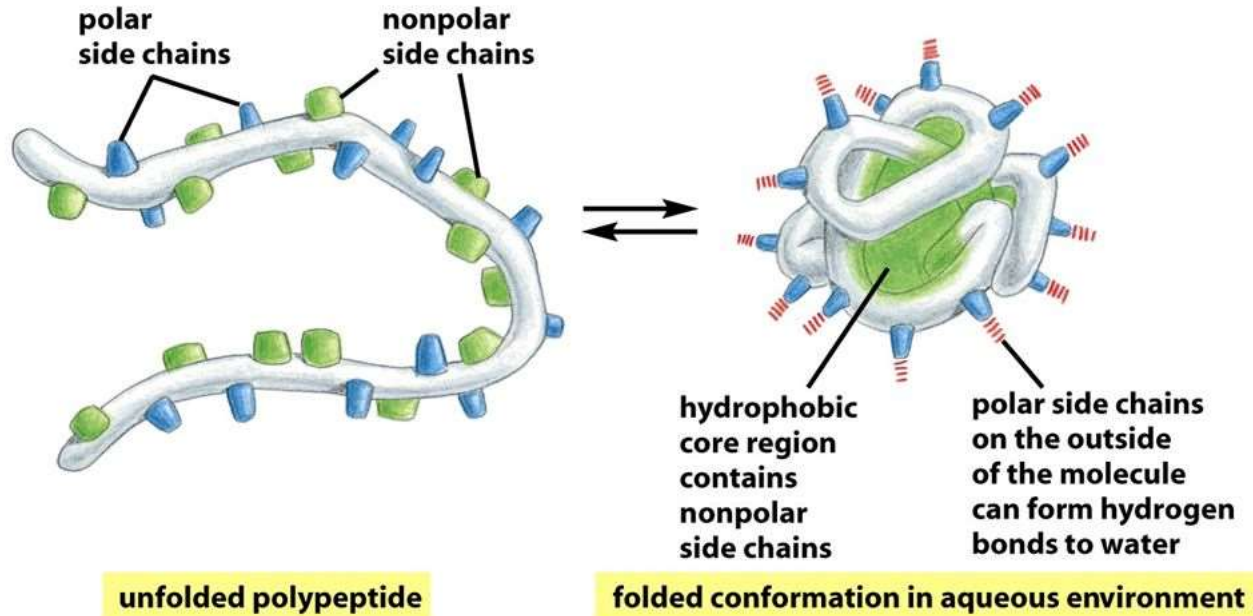
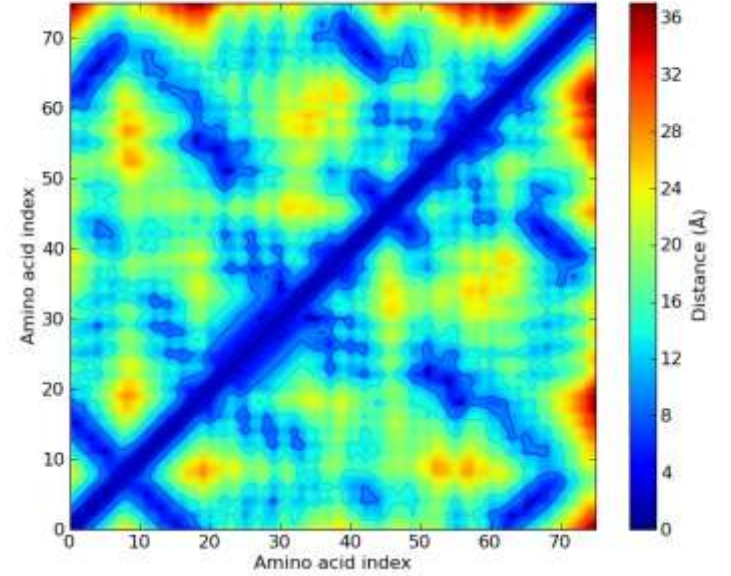
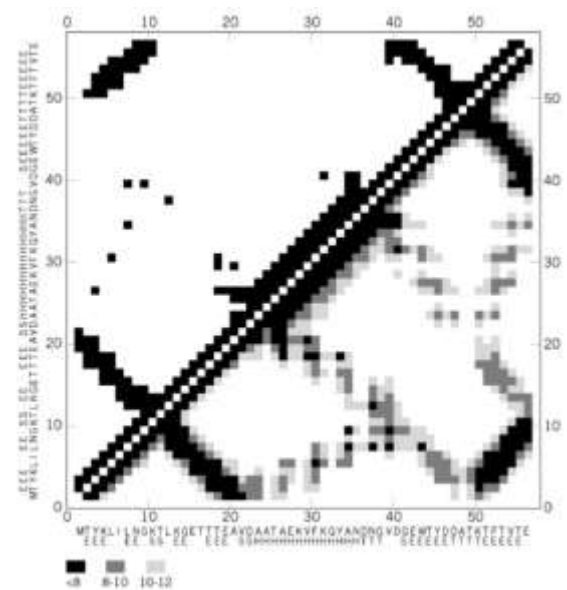
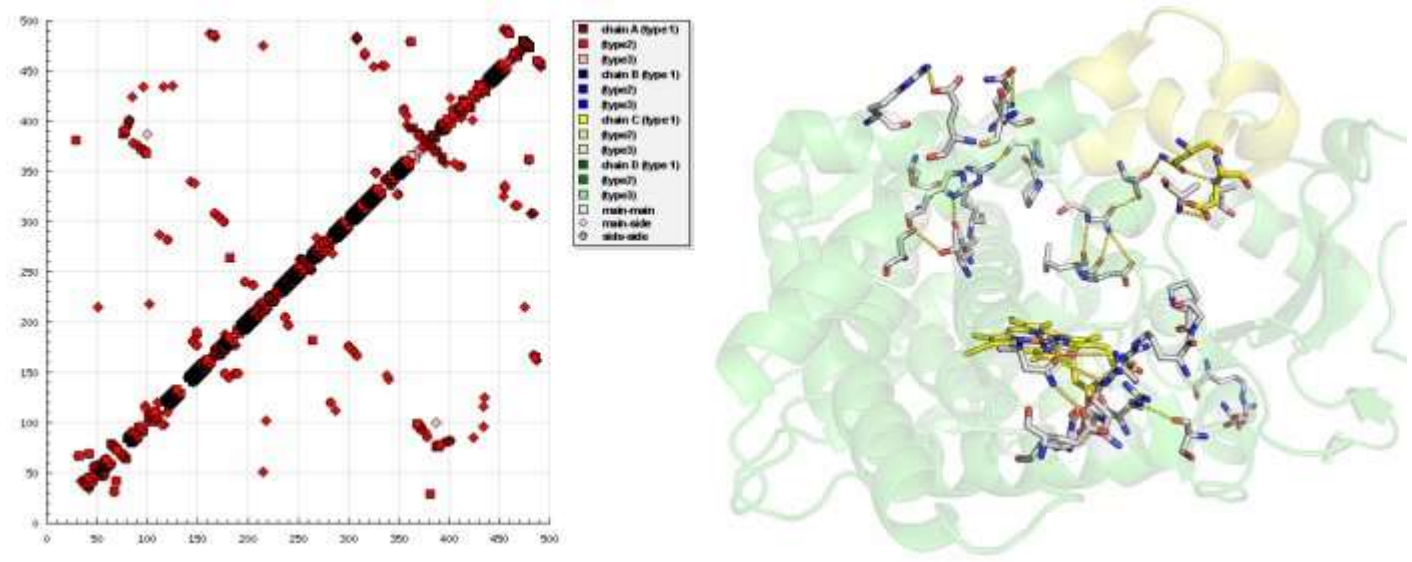
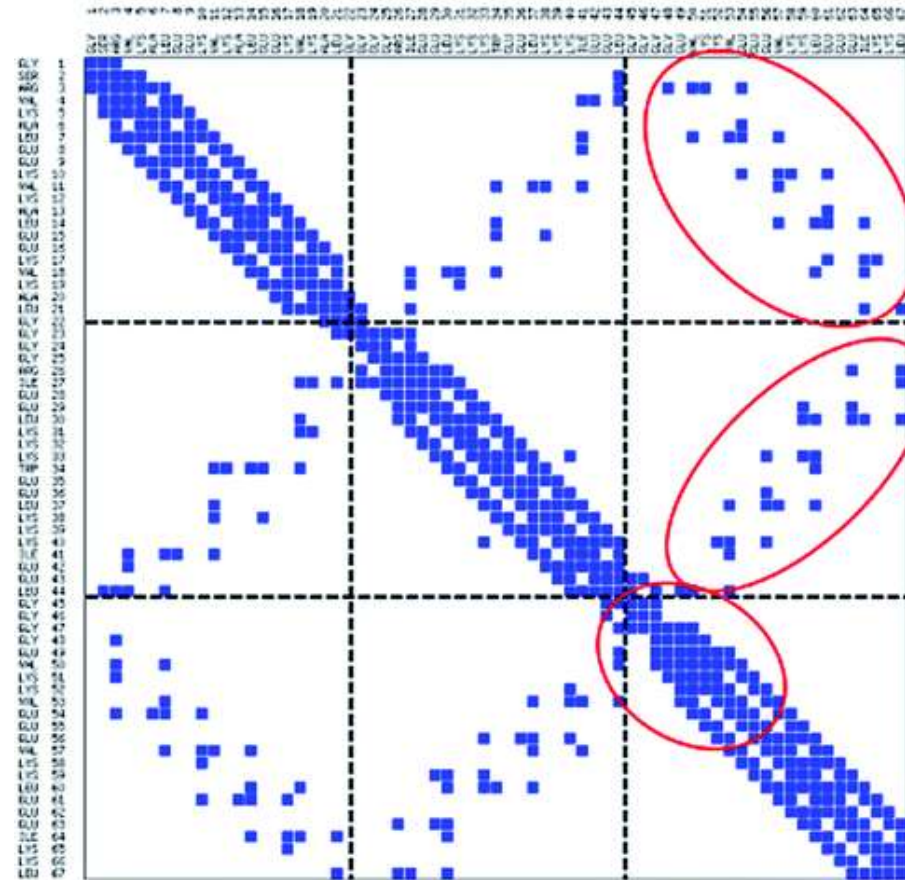


Figure 3-5 *Molecular Biology of the Cell* (© Garland Science 2008)

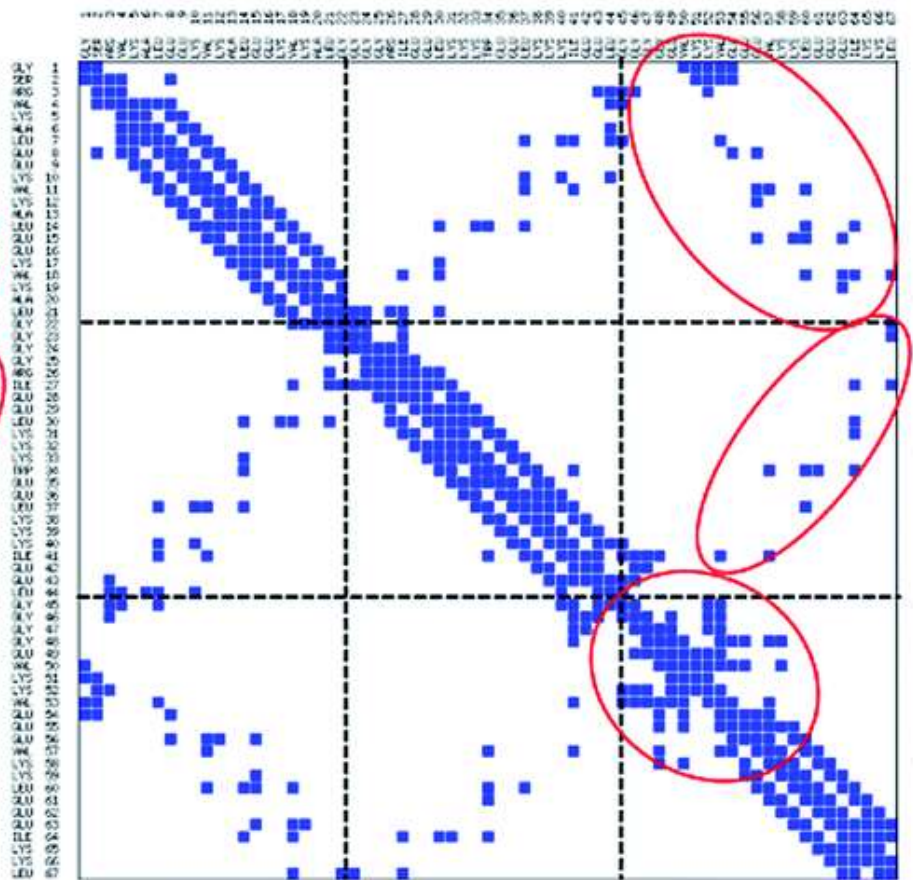
Struktura białek – upakowanie grup bocznych



Struktura białek – upakowanie grup bocznych

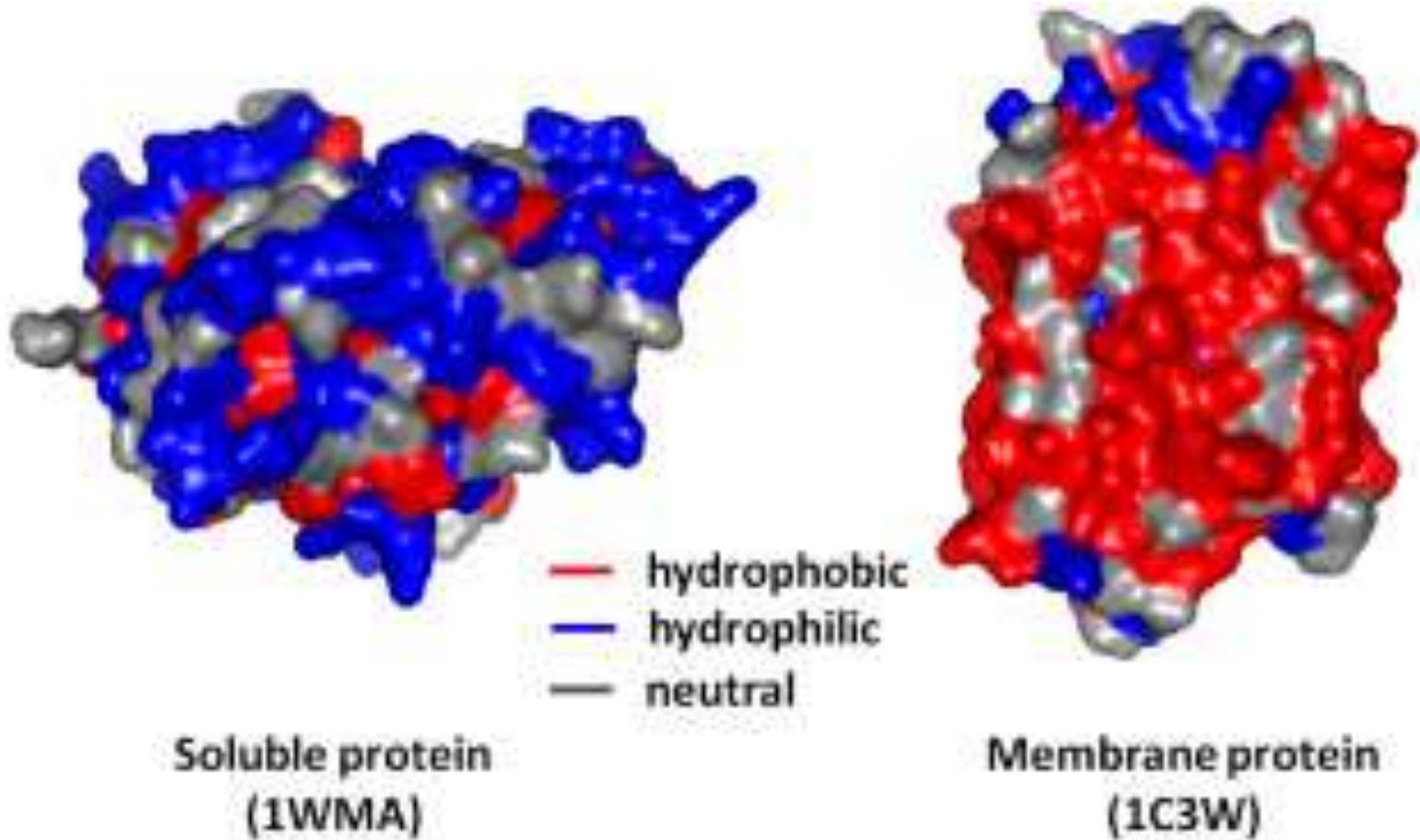


(a) Left-handed Conformation

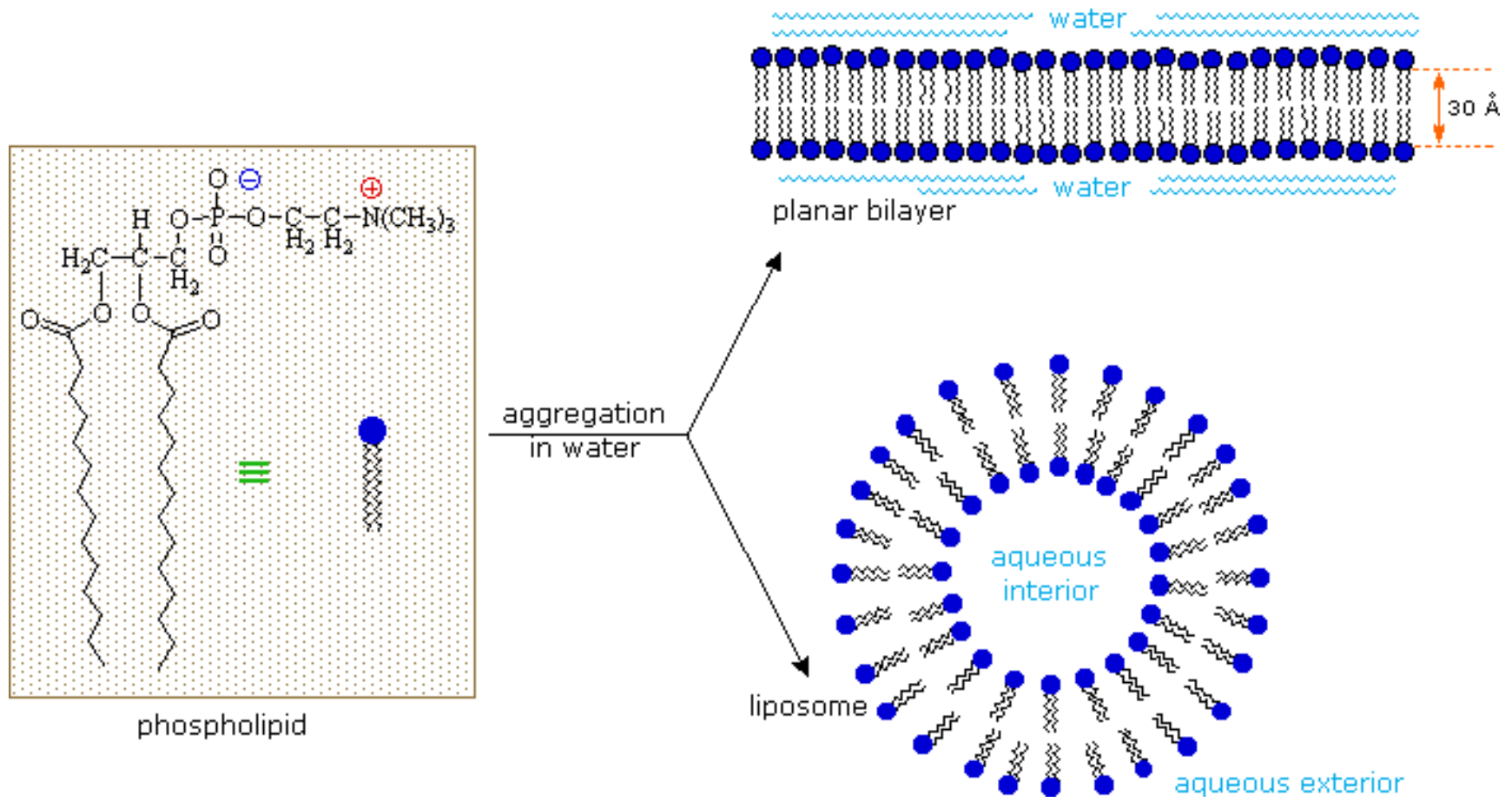


(b) Right-handed Conformation

Struktura białek - efekt hydrofobowości



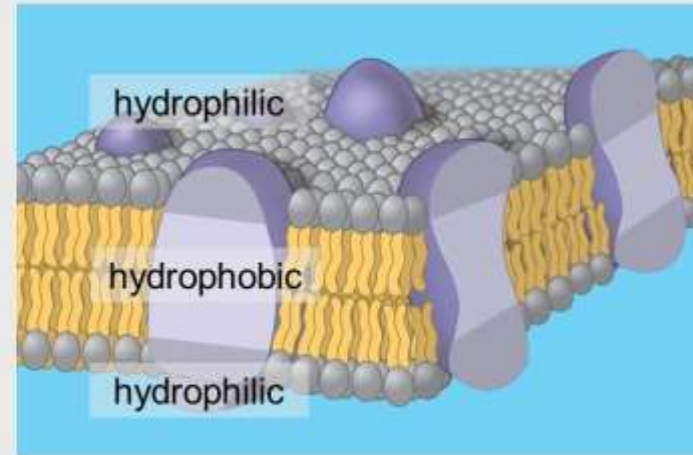
Struktura białek - efekt hydrofobowości membrany



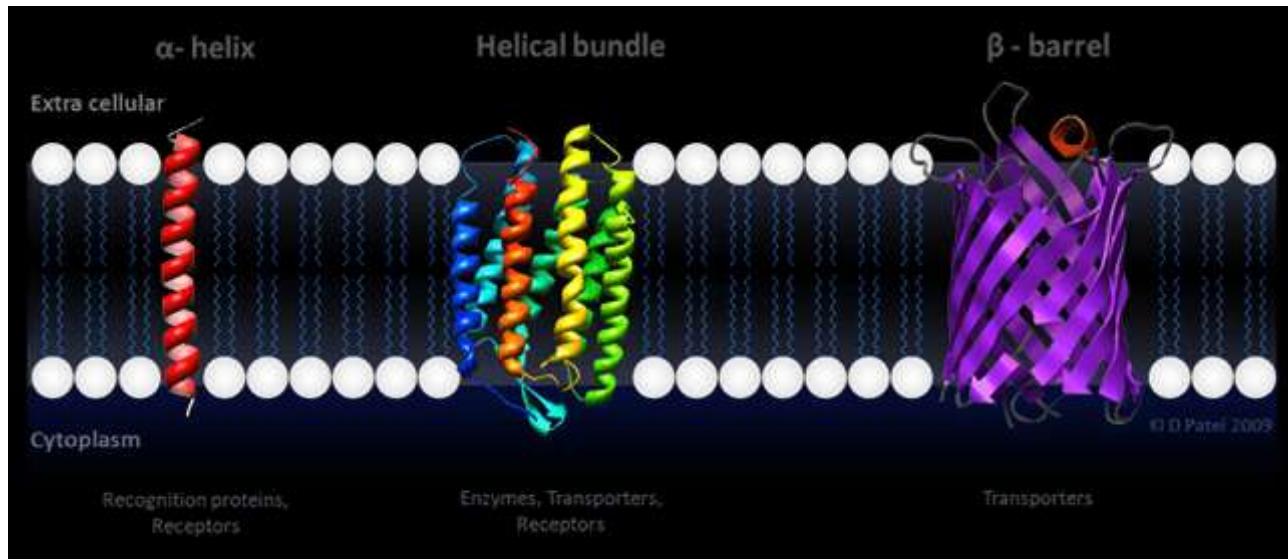
Struktura białek - efekt hydrofobowości membrany

Membrane structure

- cell membrane – amphipathic - hydrophilic & hydrophobic



- membrane proteins that are inserted, also amphipathic



Zwijanie struktury.

Kotranslacyjne czy postranslacyjne ?

5 ribosomes
reading same RNA
sequentially

Growing
polypeptide
chains

Complete
polypeptide

(Initiator
codon)

AUG

5'

UAG

3' mRNA

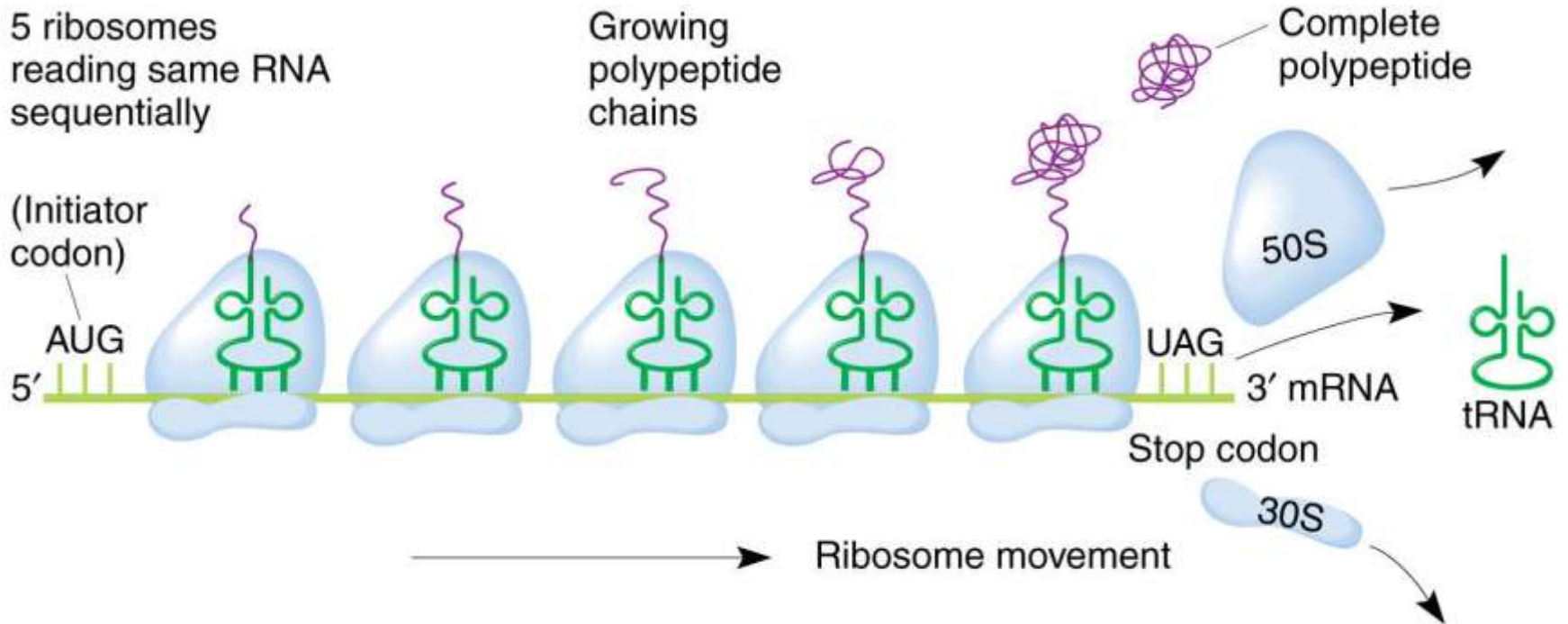
Stop codon

50S

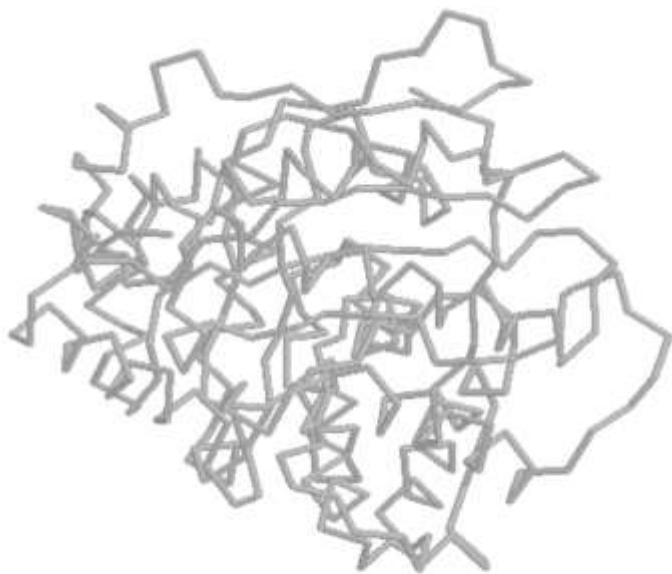
30S

tRNA

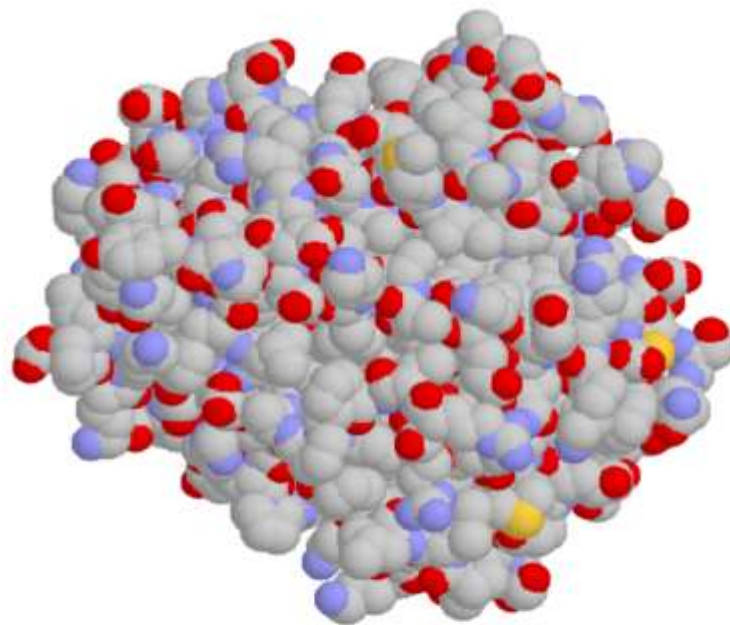
Ribosome movement



Struktura przestrzenna białek (wizualizacja)

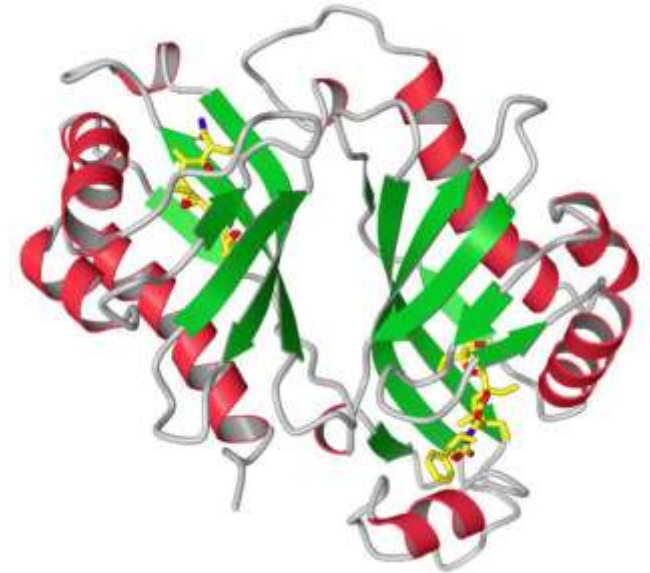
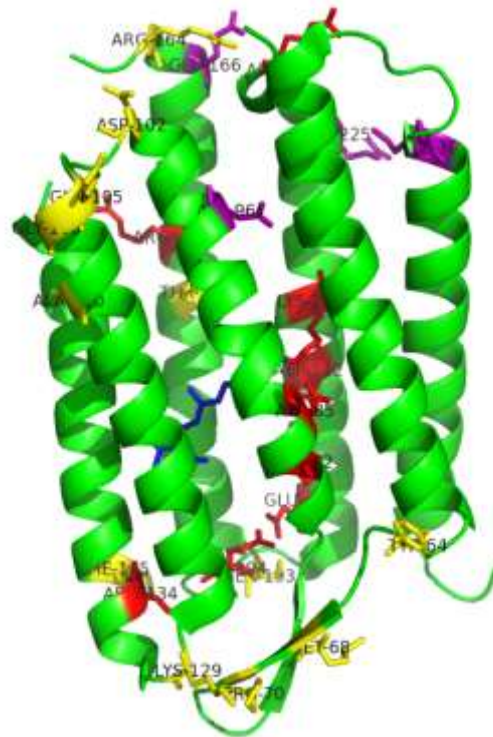
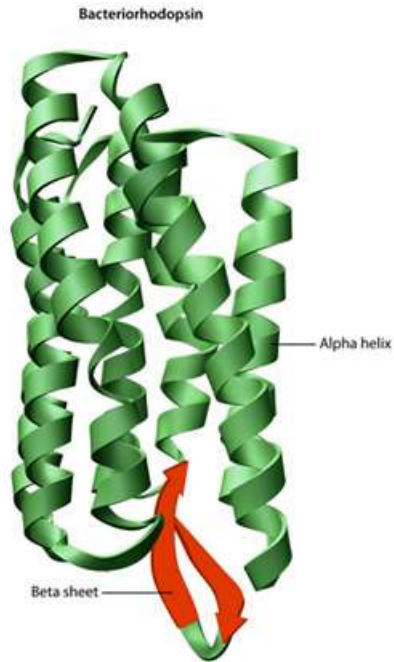


folded protein chain
(main chain view)

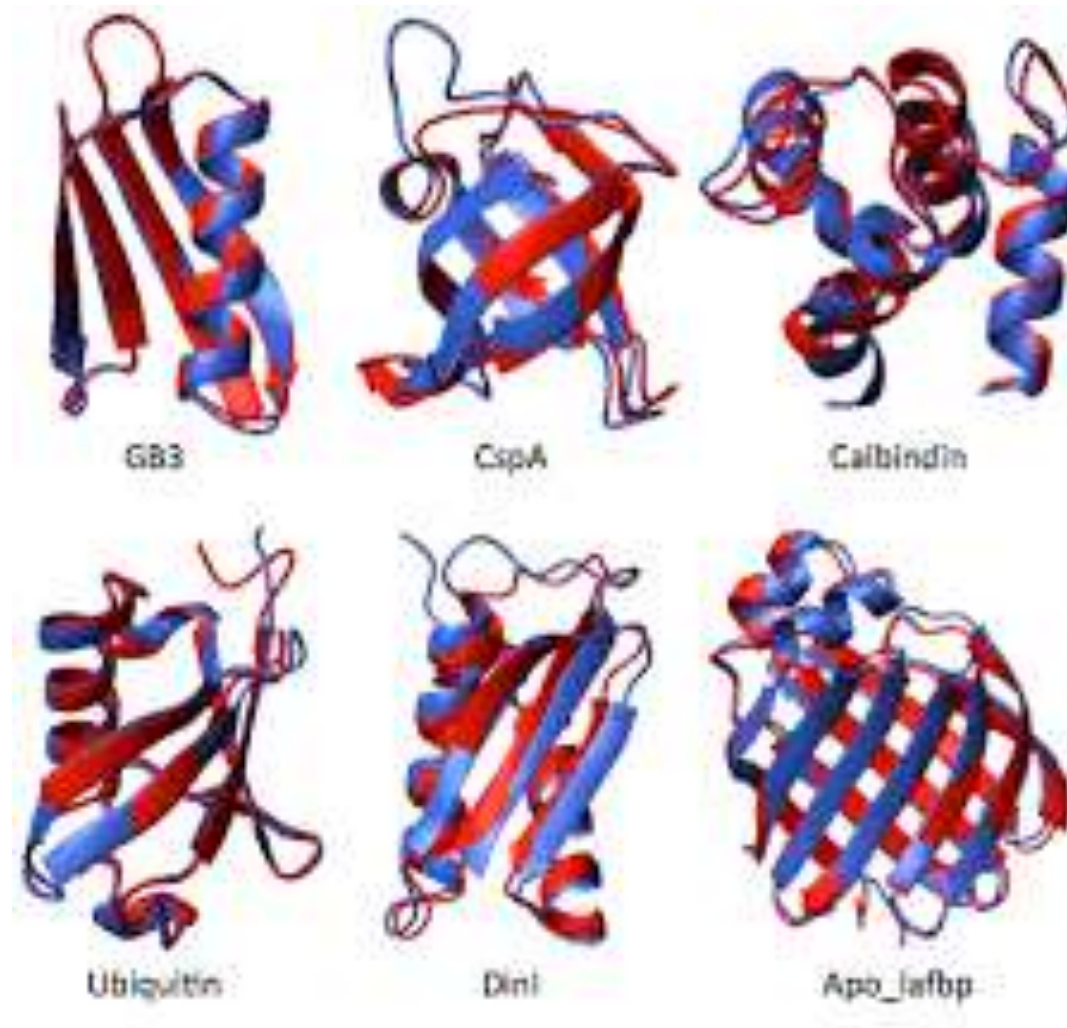


folded protein chain
(‘space-filling’ view)

Struktura przestrzenna białek



Struktura przestrzenna białek



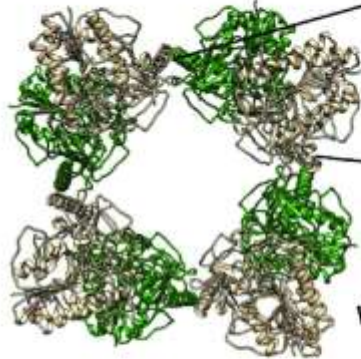
Struktura przestrzenna białek

A. Arylsulfatase A

PDB:1E33

PDB: 1AUK

Mutation:
P428L



WT: Octamer



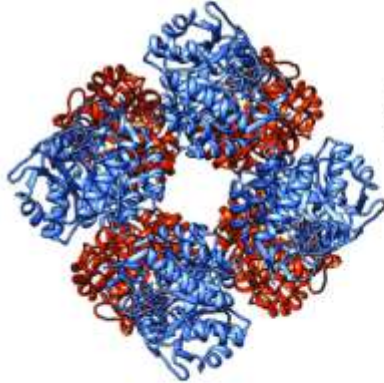
Variant: Dimer

B. Delta-aminolevulinic acid dehydratase

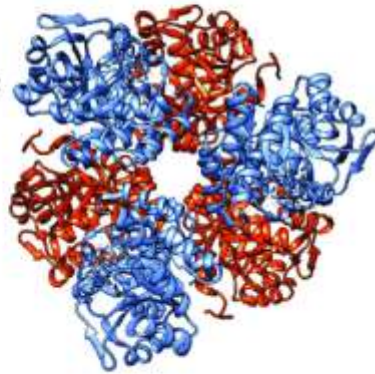
PDB: 1E51

PDB: 1PV8

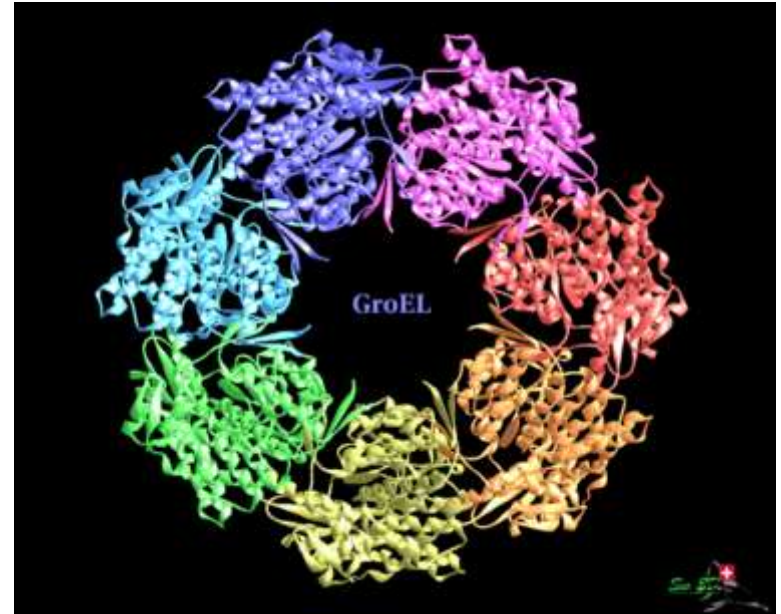
Mutation:
F12L



WT: Octamer
Optimal at pH 7

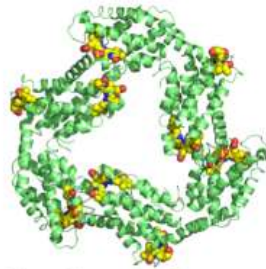


Variant: Hexamer
Optimal at pH 9



GroEL

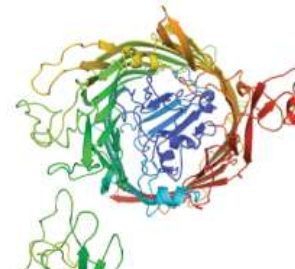
Struktura przestrzenna białek



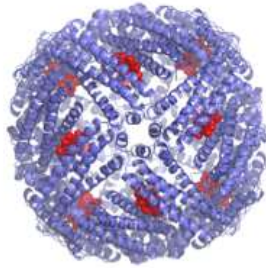
Phycobiliprotein C-Phycocyanin
Richard Cogdell Lab



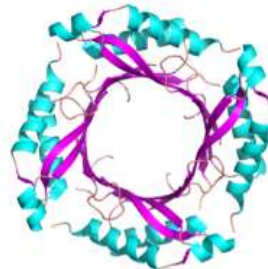
Peroxiredoxin IV
Neil Bulleid Lab



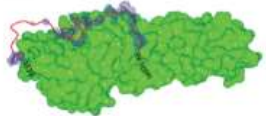
FusA, TonB-dependent outer membrane receptor, Dan Walker Lab



Bacterioferritin, heme binding protein, Richard Cogdell Lab



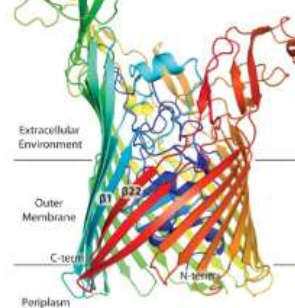
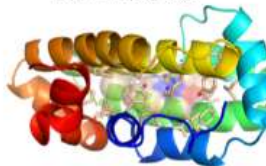
Epimerase FolX, Andy Roe Lab



Bacteriocin Syringacin M
Dan Walker Lab



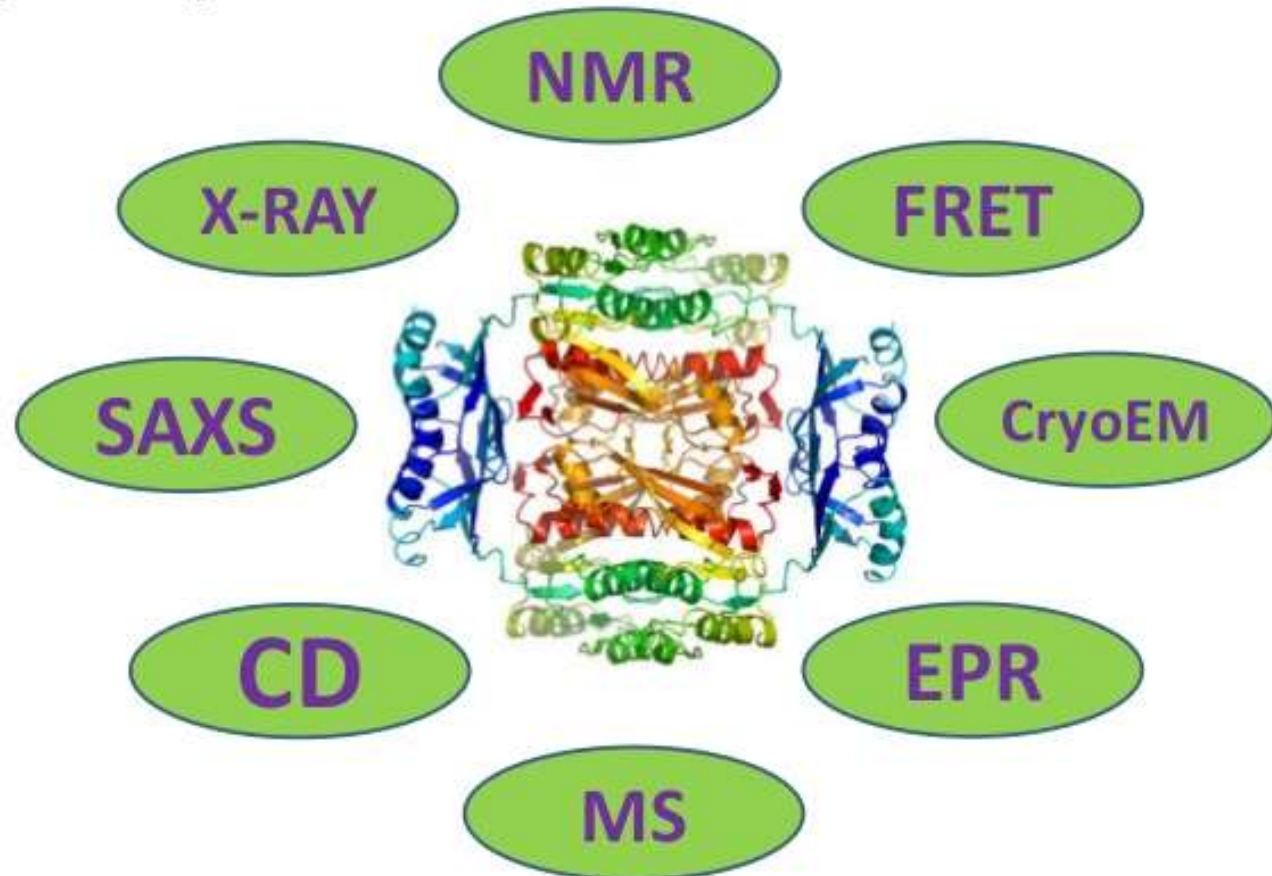
Na-FAR-1, nematode fatty acid binding protein
Brian Smith Lab



FMO, pigment-protein complex
Richard Cogdell Lab

Struktura przestrzenna białek

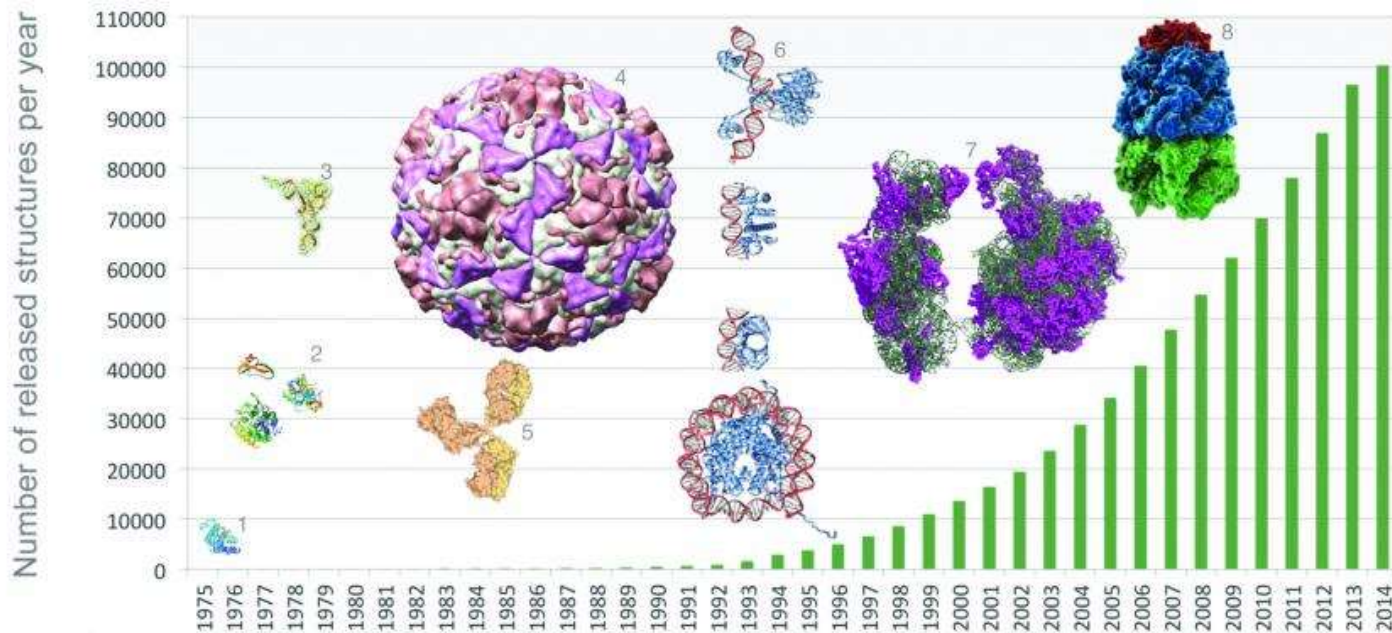
Hybrid protein structure determination



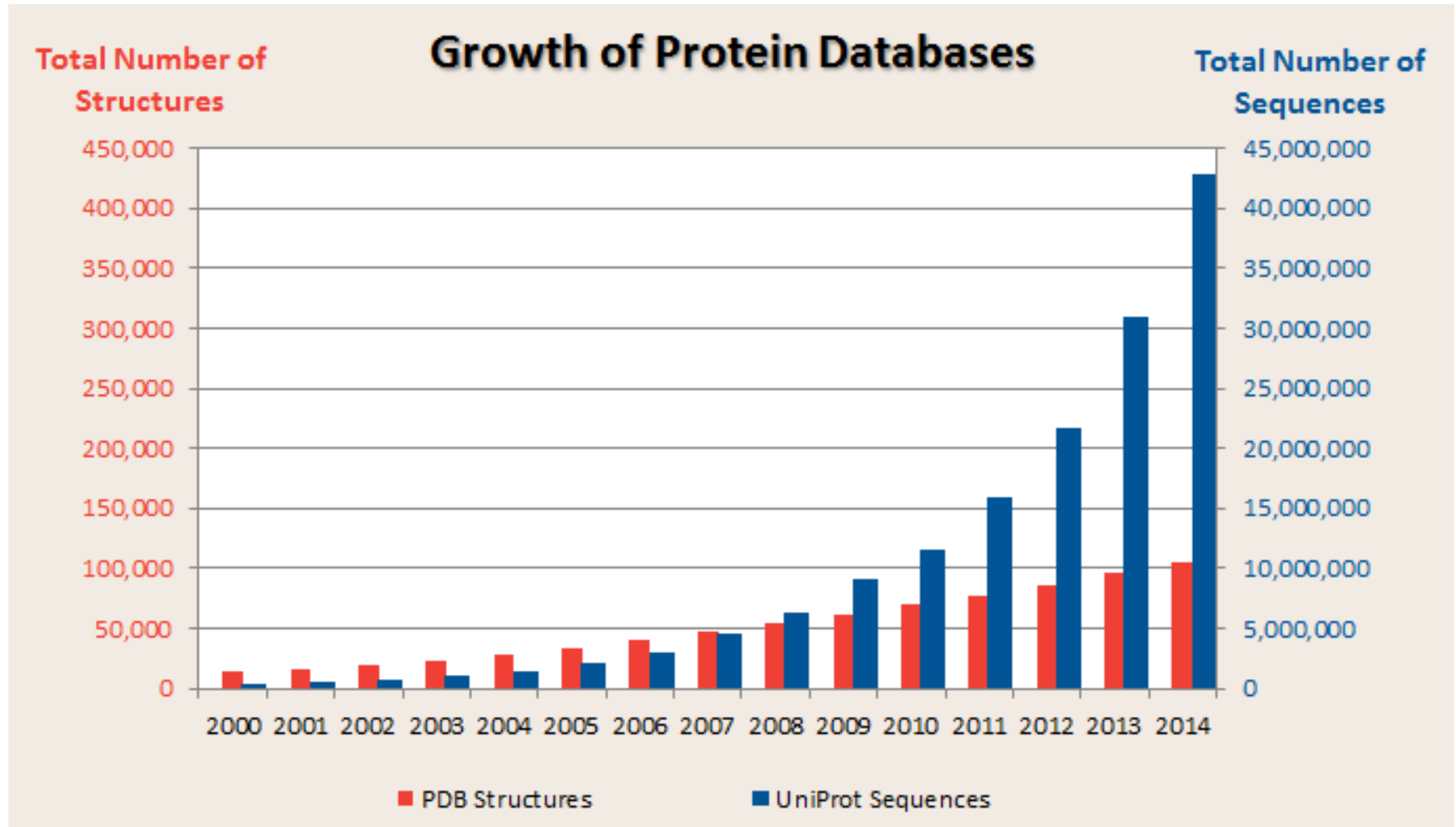
Struktura przestrzenna białek



Research Collaboratory for Structural
Bioinformatics:
Rutgers and UCSD/SDSC

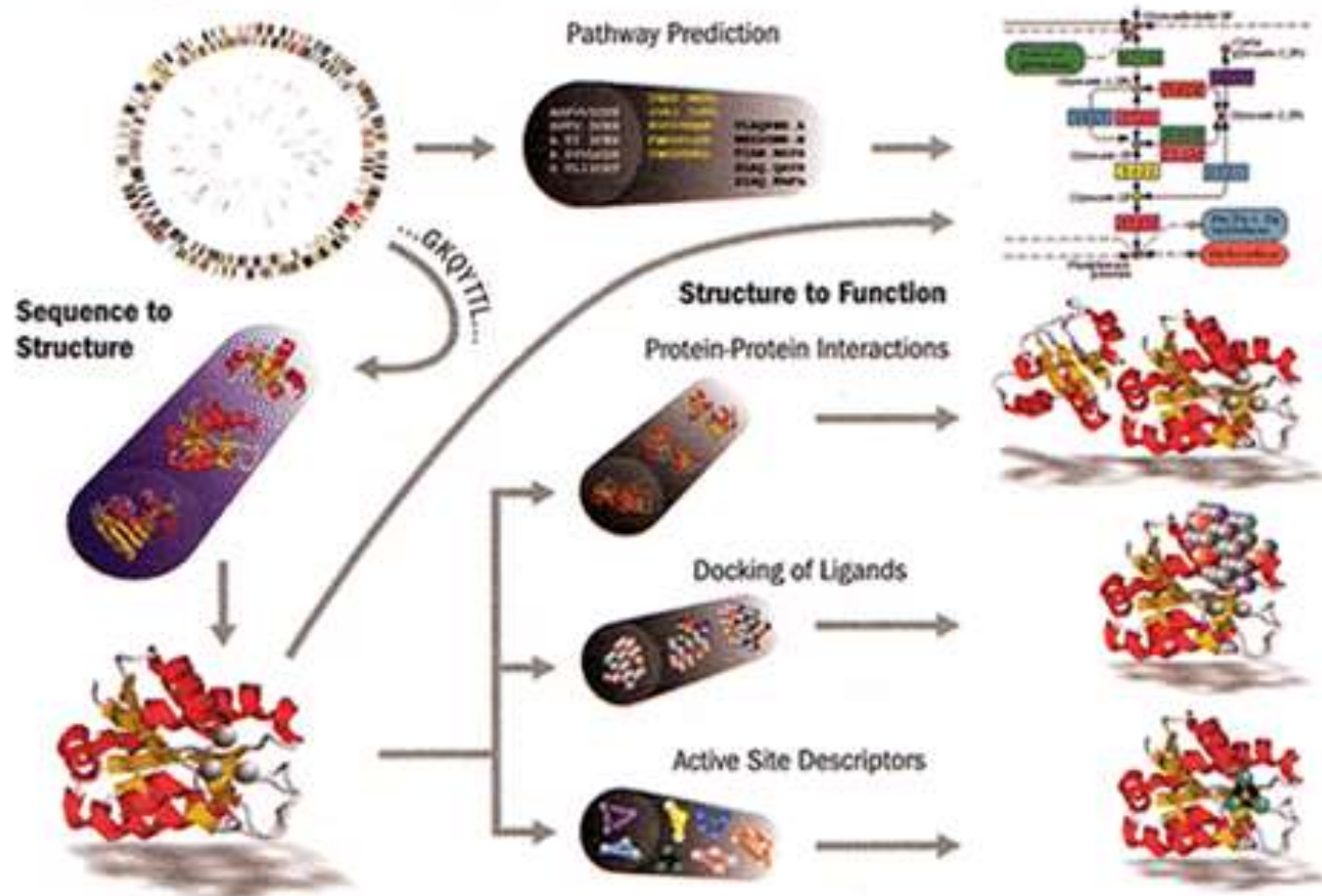


Sekwencja i struktura przestrzenna białek



Genów kodujących białka ma *E. coli* 4000,
drożdże – 6000, a ludzie około 20000

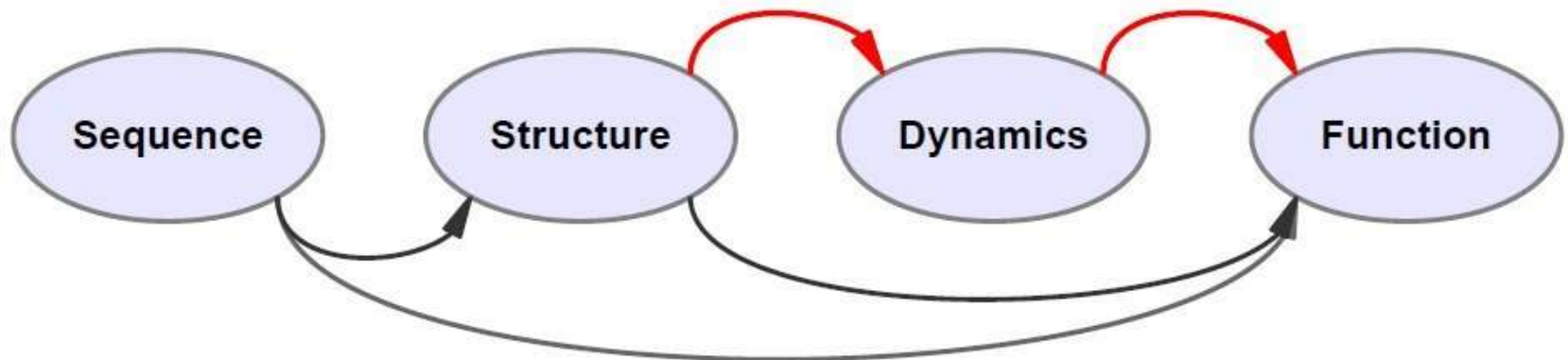
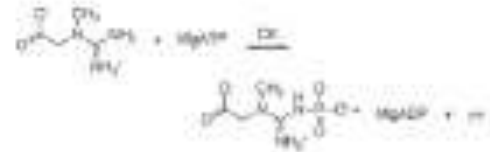
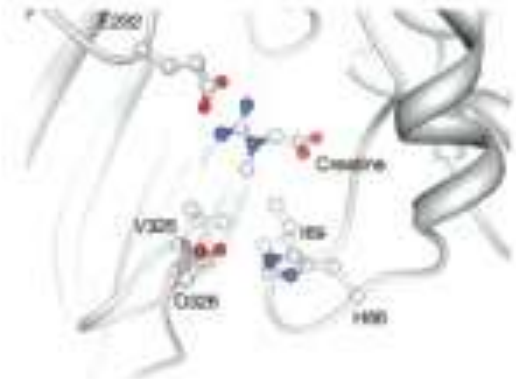
The Sequence-to-Structure-to-Function Paradigm



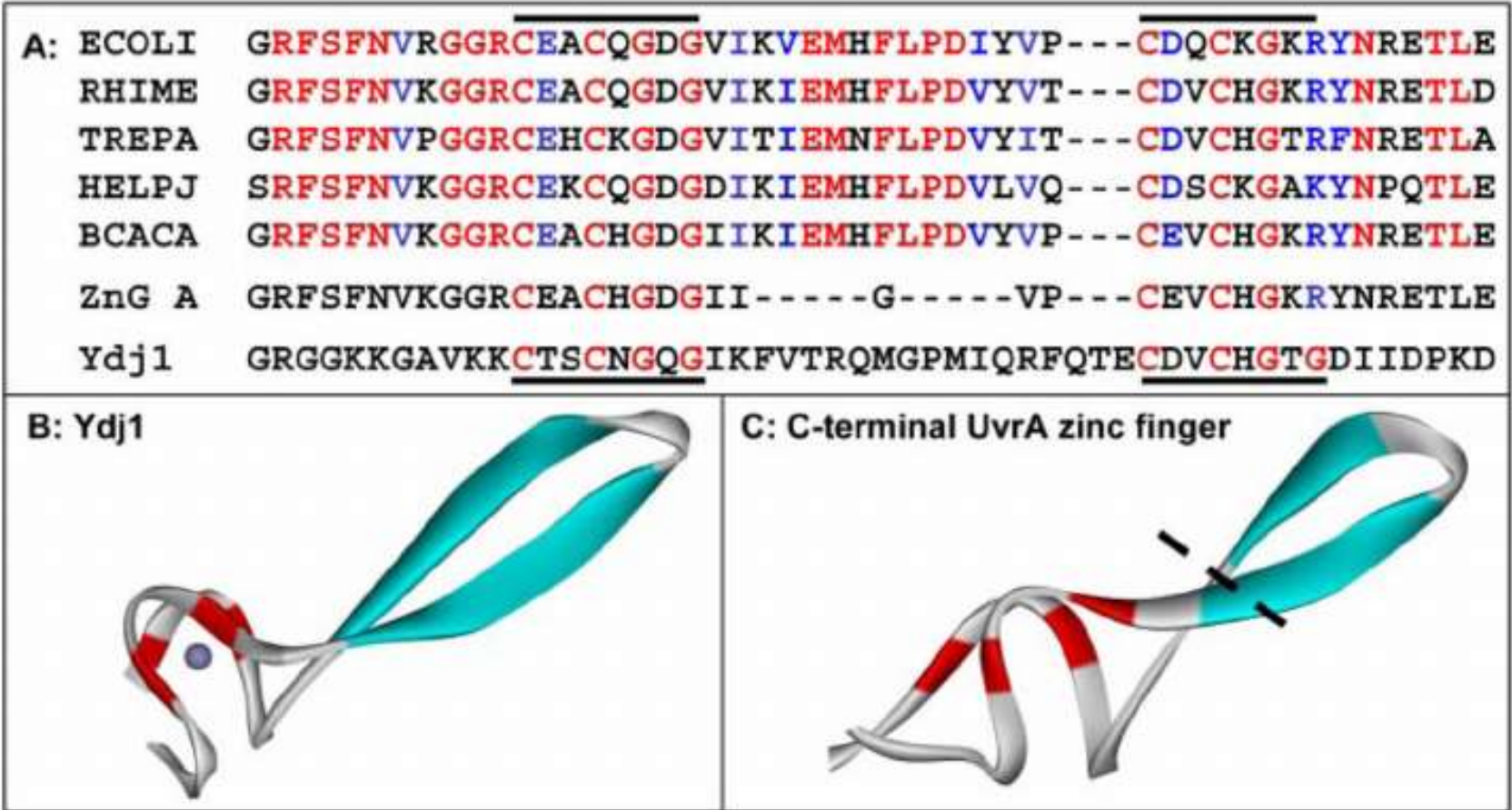
All the potential open reading frames (ORFs) in a protein sequence are threaded through a library of previously solved template protein structures. If a template is found, the structure is scanned for a match to a known active site. Alternatively, ligands can be virtually docked to identify the active site. Threading can also be used to identify potential interacting partners in the genome, or assist ORF pathway assignment.

Sequence → Structure → Function

MPFGNTHNKFKL
NYKPEEEYPDLSK
HNNHMAKVLTL
LYKCLRDKETPSGF
TVDDVIQTGVDNP
GHPFIMTVGCVAG
DEESYEYVFKELFDPI
ISDRHGGYKPTD...





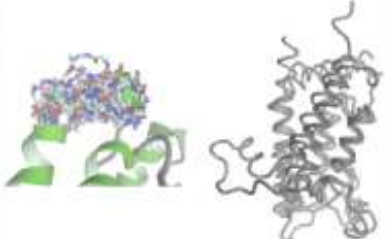
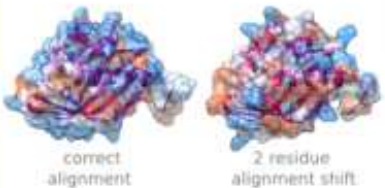

Struktura przestrzenna białek (modelowanie porównawcze)



Comparative Modeling--Basic Protocol

42

1. **Identification** of homologue for target sequence
2. **Alignment** of target sequence to template sequence and structure
3. **Side-chain modeling**, copy the backbone of the template and model the new side chains onto this backbone
4. **Loop modeling**, for insertions and deletions in the alignment
5. **Refinement of model** -- moving template closer to target
6. **Assessment** of (predicted) model quality
7. **Using the model** to explain experiments and guide new ones

Sources of errors			Applications
- experimental errors and uncertainties in X-ray, NMR	1Å 100%		- studying catalytic mechanism / function
- side-chain packing - mis-placed side-chains	1.5Å 95%		- structure-based drug design, ligand docking
- modeling of loop regions (insertions and deletions) - distortions of aligned regions	60%		- structural support for mutagenesis studies - molecular replacement
- alignment errors	3Å 40%		- integrative modeling - modeling into low-resolution density maps
- sub-optimal template selection - model may even have the wrong fold	>3Å <30%		- domain boundaries - identification of structural motives

Struktura przestrzenna białek (modelowanie porównawcze, homology modeling)

Teoretyczne przewidywanie struktury (modelowanie) – Święty Graal (Holy Grail) biologii strukturalnej

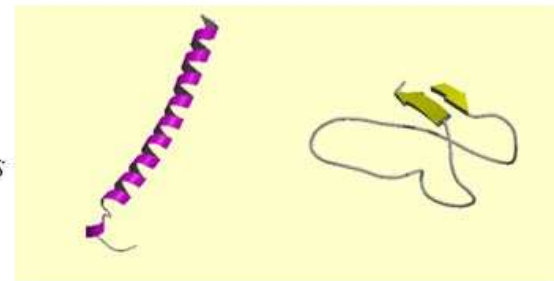
Protein folding problem

PRIMARY STRUCTURE (amino acid sequence)

VHLTPEEKSAVTALWGKVNVDDE
VGGEALGRLLVVYPWTQRFFFE
SFGDLSTPDAVMGNPKVKAHG
KKVLGAFSDGLAHLNLDLGTFA
TLSELHCDKLHVDPENFRLLGN
VLVCVLAHHFGKEFTPPVQAAAY
QKVVAGVANALAHKYH

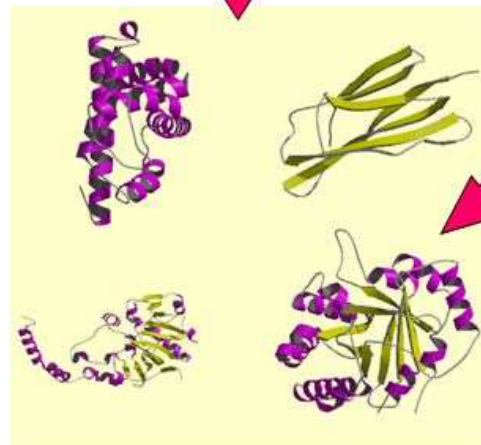
*Each protein sequence
“knows” how to fold into its
tertiary structure. We still do
not understand how and why*

SECONDARY STRUCTURE (helices, strands)



*1-step
process*

*2-step
process*

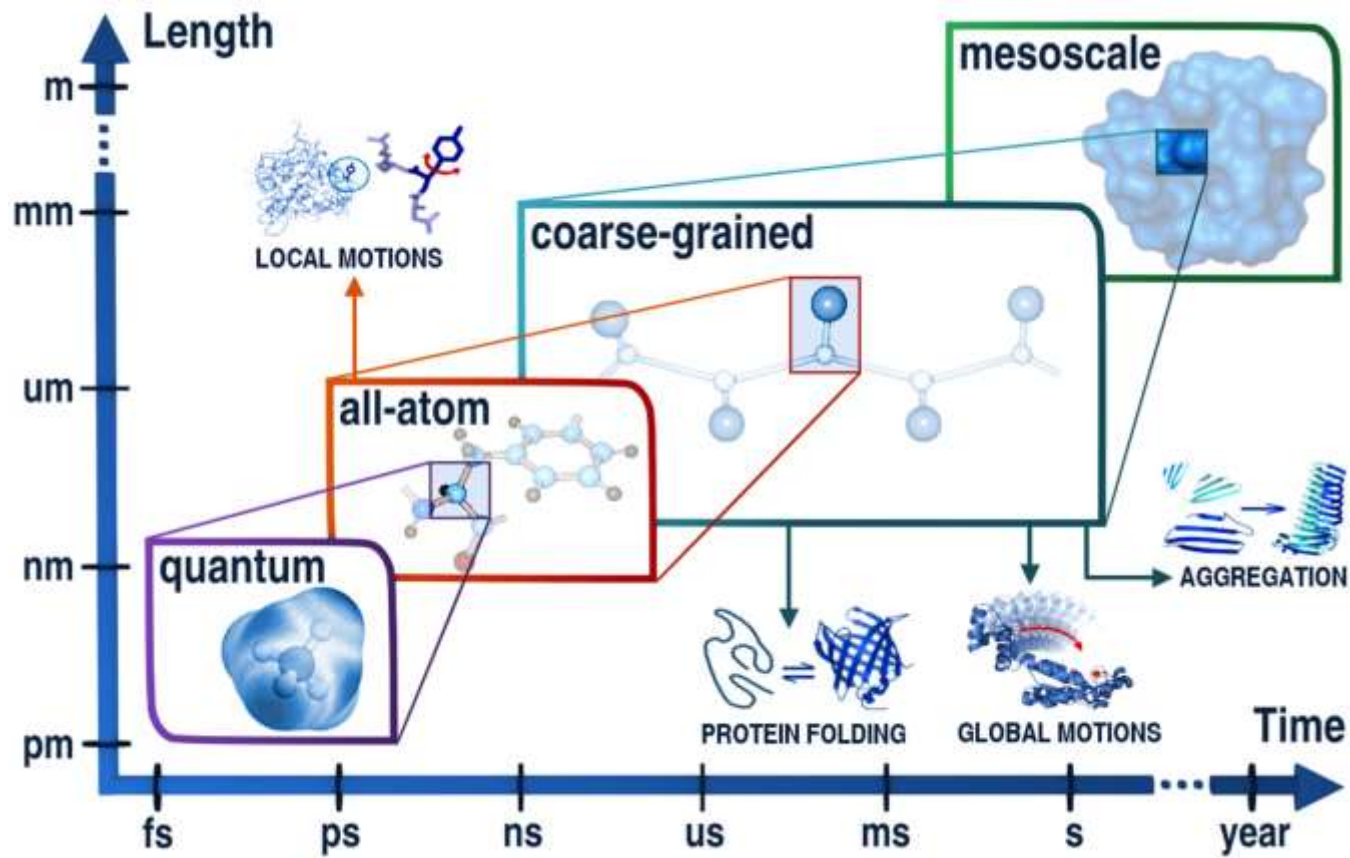


TERTIARY STRUCTURE (fold)

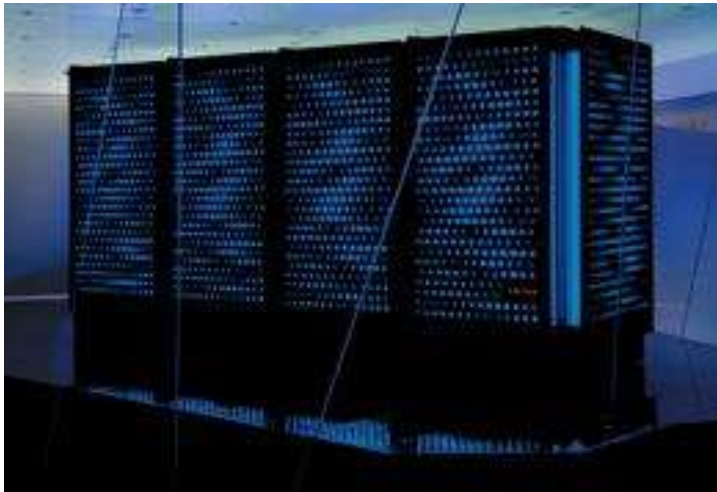
*The 1-step process is based on a
hydrophobic collapse; the 2-step
process, more common in forming
larger proteins, is called the
framework model of folding*



Teoretyczne przewidywanie struktury (modelowanie) – Święty Graal (Holy Grail) biologii strukturalnej



Struktura przestrzenna białek (Dynamika Molekularna)



Anton

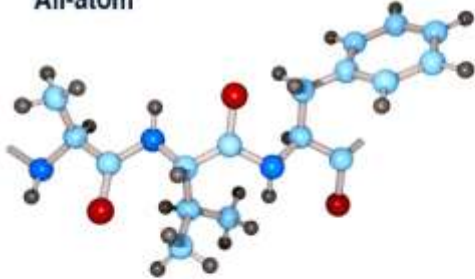
David E. Shaw Research

All-atom MD with explicit water
- milliseconds of folding process
of a small protein.

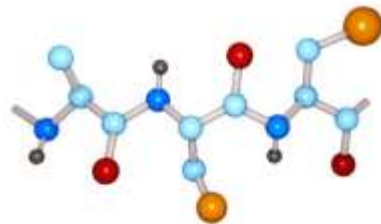
For realistic modeling of larger
biomolecular systems, including
flexible protein-protein docking, **we
need much faster simulations.**

Struktura przestrzenna białek (modelowanie gruboziarniste)

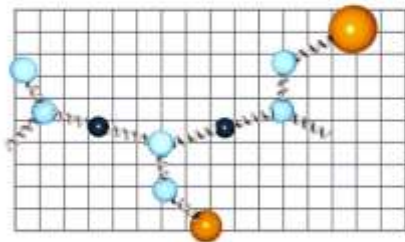
All-atom



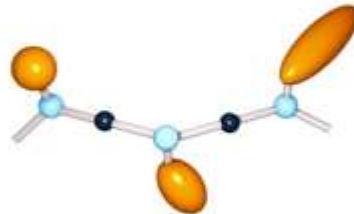
Rosetta CEN



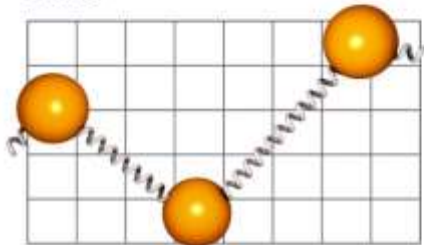
CABS



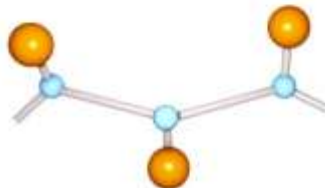
UNRES



SICHO




Levitt-Warshel




Nobelpriset 2013


The Nobel Prize in Chemistry 2013



Martin Karplus
Université de Strasbourg,
France and Harvard
University, Cambridge,
MA, USA



Michael Levitt
Stanford University School of
Medicine, CA, USA



Arieh Warshel
University of Southern
California, Los Angeles, CA,
USA

for "the development of multiscale models for complex chemical systems"