

OV_{OCLEIDIN} ER_{STOGEN} R_{ECEPTOR} VI_{TAMIN-D BINDING PROTEIN} E_{GG} W_{HITE} LYSOZYME

Dr. Zhiyi Wei
SUSTC

Aims

- Master structural features of proteins
 - The relationship between protein sequence and structure
 - Secondary/tertiary/quaternary structures
- Know how to analyze protein structures
 - Architectures
 - Intra/inter-molecular interfaces
 - Protein dynamics
- **Learn to apply structural information to understand protein function**
 - **Structures -> Functions -> Applications (medicine/industry)**

Contents

- Chap 1. From sequence to structure
 - Primary and secondary structure
 - Tertiary structure, domain, and motif
 - Protein folding and flexibility
 - Quaternary structure
- Chap 2. From structure to function
 - Functional sites in protein structures
 - Catalysis
 - Membrane protein
 - Structural proteins
 - Flexibility and protein function
- Chap 3. Control of protein function
 - Environmental control
 - Effector and allostery
 - Protein switches
 - Control by post-translational modification
 - Kinase and signaling regulation
 - Regulation by splicing, proteolysis, and degradation
- Chap 4. Methods and case studies

Experiments

- EXP1. Sequence analysis I
 - Conservation and evolution analysis
 - Secondary structure analysis
- EXP2. Sequence analysis II
 - Functional domain/motif prediction
 - Protein profiling
- EXP3. Structure DIY
 - Manually build hemoglobin β subunit
 - Manually build any protein structure (video record)
- EXP4. Protein databases
 - PDB, understanding coordinates
 - Other structure-based databases
 - Visualizing protein structures using PyMOL
- EXP5. Structure comparison
 - Structural superposition
 - Structural based alignment
- EXP6. Surface analysis
 - Conservation
 - Electrostatics
 - Hydrophobicity
- EXP7. Identification of functional sites
 - Binding site
 - Active site
- EXP8. Membrane protein analysis
 - Transmembrane region prediction
 - Structural analysis
- EXP9. Interaction analysis I
 - Protein-protein interaction
- EXP10. Interaction analysis II
 - Protein-ligand interaction
- EXP11. Protein structure prediction
 - Homology modeling
 - Other modeling methods
- EXP12. Structural quality check

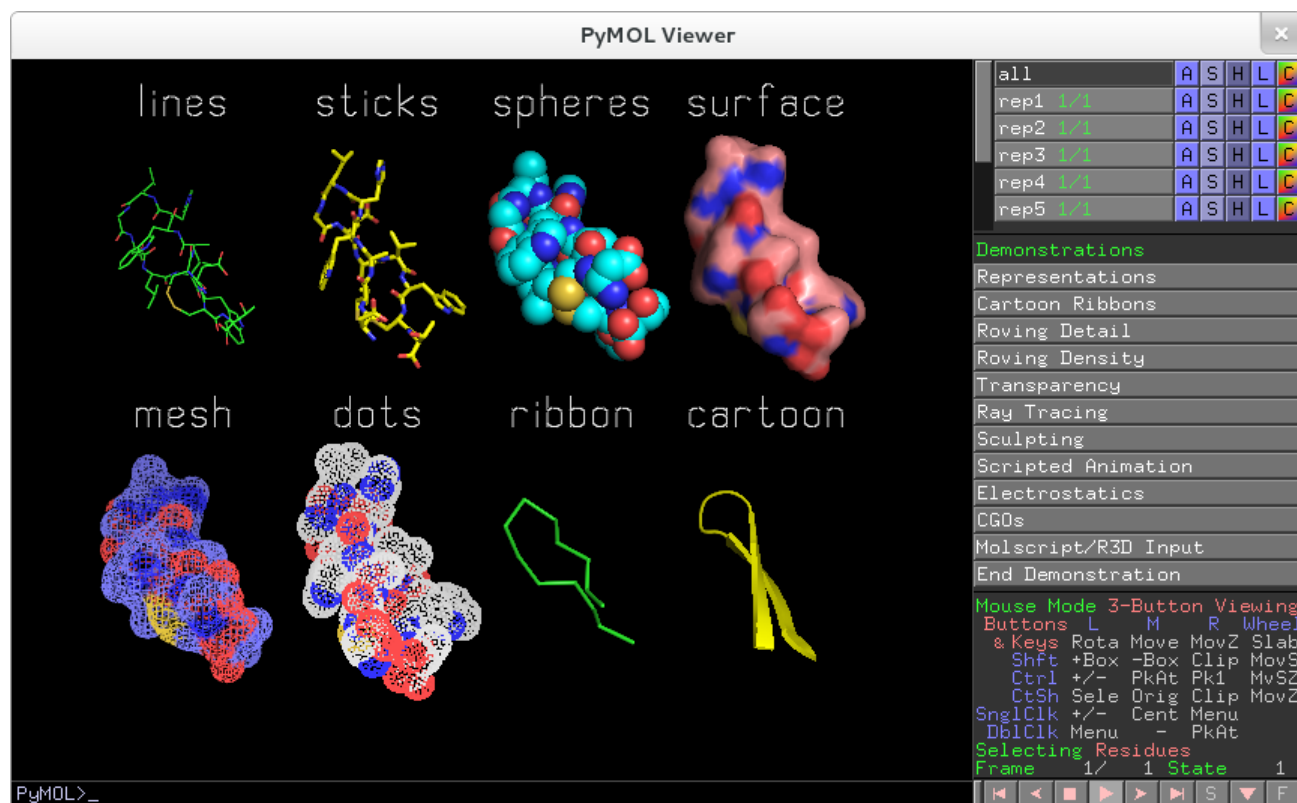
Requirements

- Assessment
 - Experiments: 30%
 - Journal club: 20%
 - Project: 20%
 - Final exam: 30%
- Experimental requirements
 - RM201 (Computer Room), Teaching building 2
 - Attendance
 - Duration: 1-3 hrs
 - Software: PyMOL
- Presentation requirements
 - Journal club
 - One presentation
 - Duration: 15-min talk + 5-min discussion
 - Prepare figures or movies by PyMOL
- Project requirements
 - A proper-formatted article
 - A final presentation: 30-min talk + 5-min discussion

Final Project

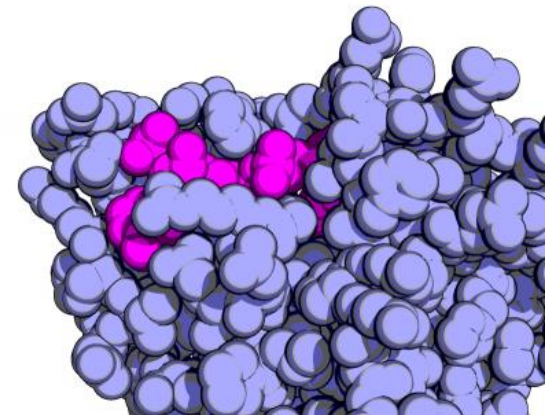
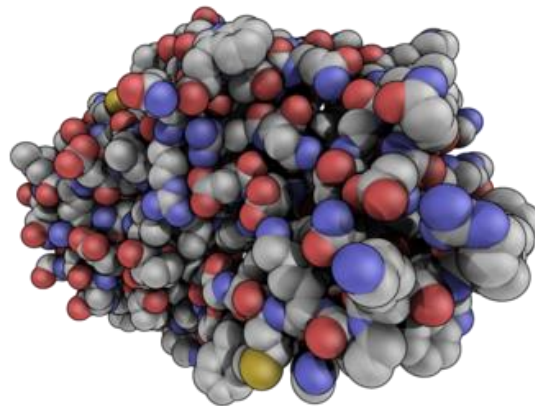
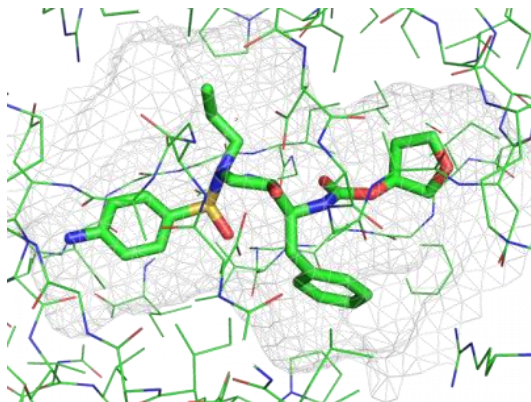
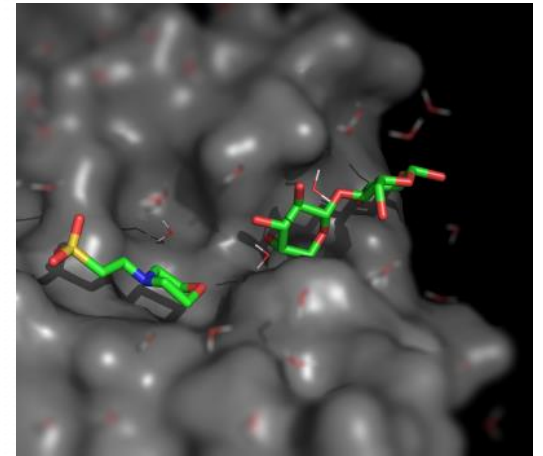
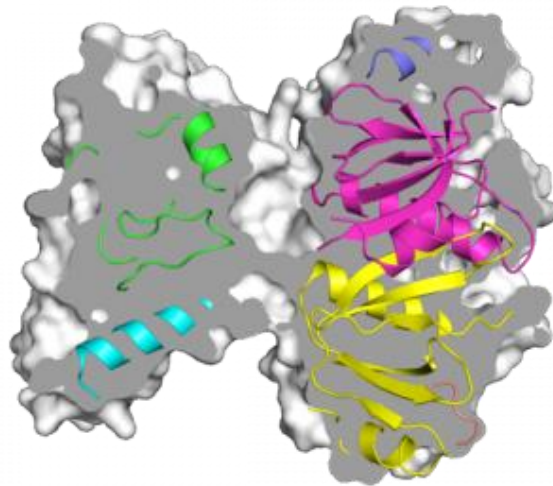
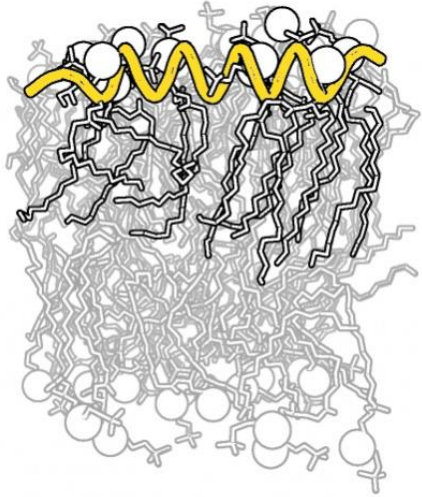
- Title: Structure based functional implications of XXX domain
- Article format
 - Introduction
 - Why do you select this domain?
 - Structural analysis
 - Figures
 - Functional implications
 - Figures
 - Conclusions
 - What do you learn in this case study?
 - References
 - All citations should be academic articles
 - NOT from baidu or wikipedia
- Wikipedia* (not required)
 - Create a new article or improve an existing article
- Presentation
 - Include a movie showing the structural analysis

PyMOL



You can learn everything about PyMOL from www.pymolwiki.org

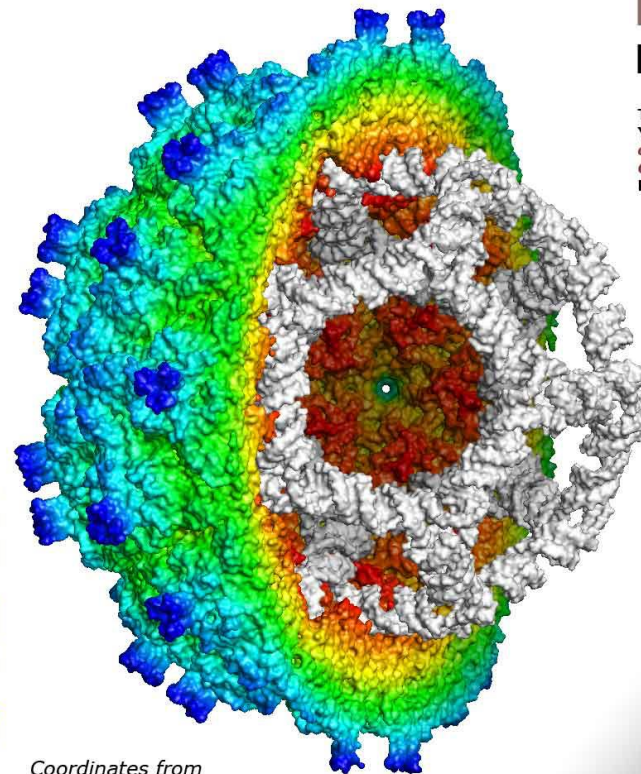
Gallery 1



Gallery 2



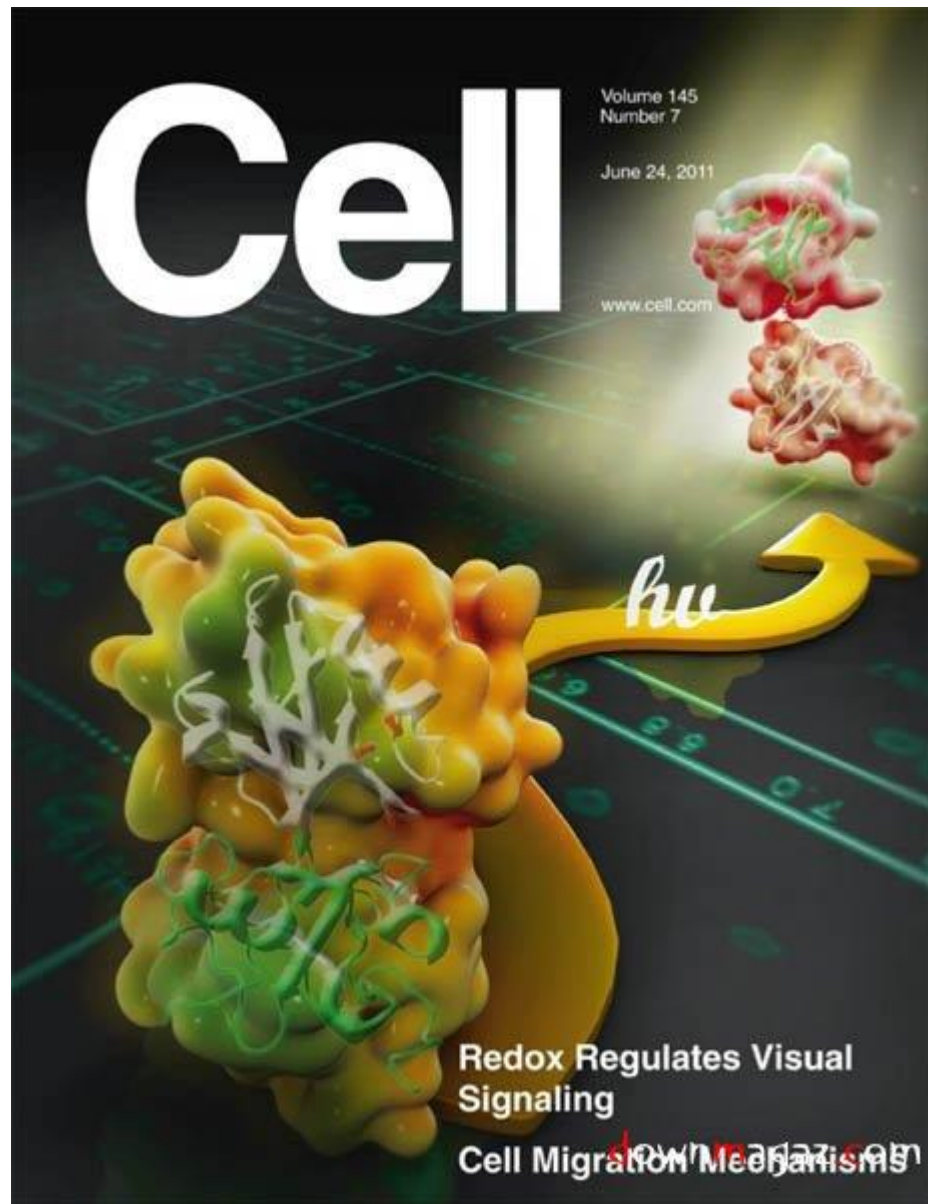
PyMol image by Jean-Yves Sgro © 2005
virology.wisc.edu/virusworld



Coordinates from
PDB: www.rcsb.org
VIPER: viperd.b.scripps.edu

Pariacoto virus PDB_ID: **1F8V**

Tang, L., Johnson, K. N., Ball, L. A., Lin, T., Yeager, M., Johnson, J. E.: *The Structure of Pariacoto Virus Reveals a Dodecahedral Cage of Duplex RNA* Nat.Struct.Biol. 8 pp. 77-83 (2001)



Protein Data Bank (www.pdb.org)

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RCSB PDB An Information Portal to 115306 Biological Macromolecular Structures

Search by PDB ID, author, macromolecule, sequence, or ligands **Go**

Advanced Search | Browse by Annotations | Search History (2) | Previous Results (896)

PDB-101 EMDatabank Structural Biology Knowledgebase

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Welcome

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A Structural View of Biology

This resource is powered by the Protein Data Bank archive—information about the 3D shapes of proteins, nucleic acids, and complex assemblies that helps students and researchers understand all aspects of biomedicine and agriculture, from protein synthesis to health and disease.

As a member of the wwPDB, the RCSB PDB curates and annotates PDB data.

The RCSB PDB builds upon the data by creating tools and resources for research and education in molecular biology, structural biology, computational biology, and beyond.

Take an Interactive Tour of the PDB

BEGIN EXPLORING

January Molecule of the Month

Enterobactin and Iron

Siderocalin

Latest Entries

As of Tuesday, Jan 19

4V1H [PDB Entry](#)

Crystal structure of a mycobacterial ATP synthase rotor ring in complex with Iodo-Bedaquiline

View in 3D

New Features

October 2015 Release

Redesigned Structure Summary Page
New Organization. Improved Layout. Clean. Usable. Simple.

Improved Literature Tab

Better Support for Mobile Browsing

Redesigned Ligand Summary Page

September 2015 Release

Validation Track on Protein Feature View
Mapping validation annotations to sequence

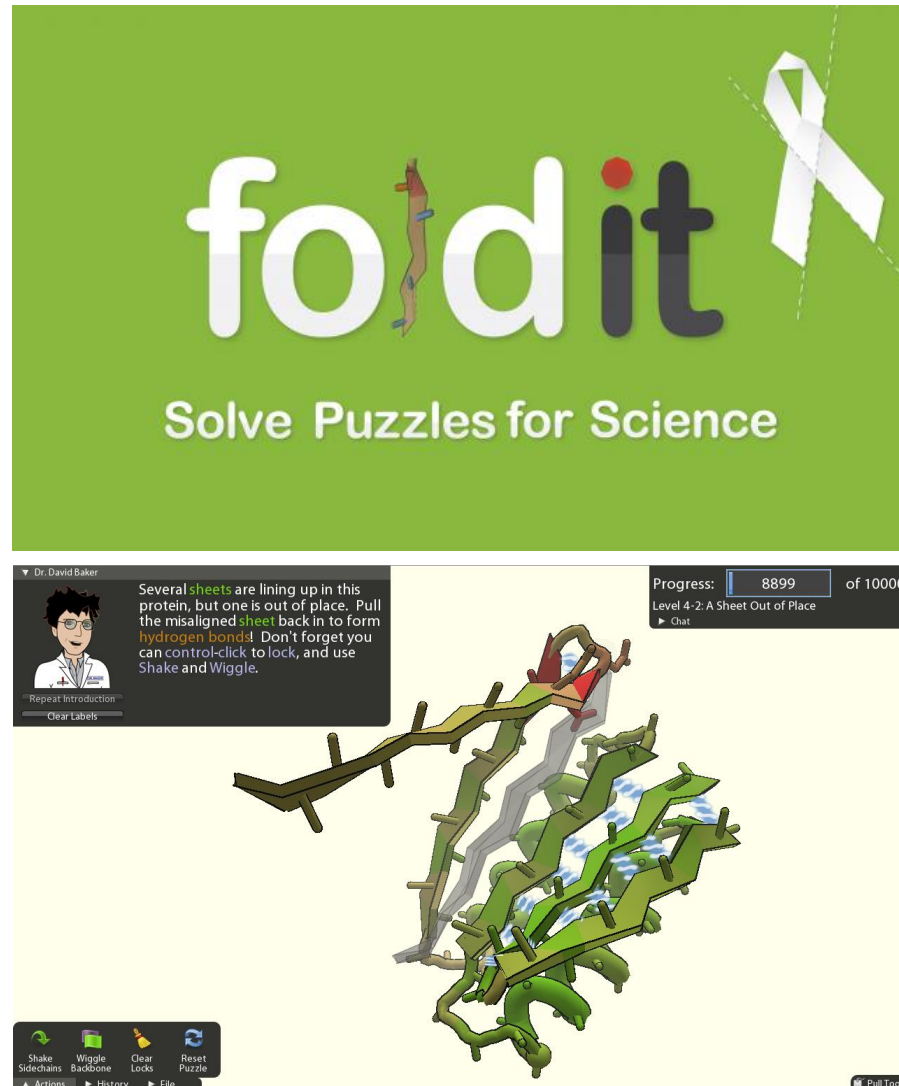
News

Publications

Winter Newsletter Published
Read about 2015 statistics and highlights, the new wwPDB Deposition Tool, RCSB PDB's 2016 protein-drug calendar, and more. The Education Corner describes Using 815,527 Crystal Structures to Teach Chemistry: The Cambridge Structural Database. » 01/19/16

wwPDB Deposition & Annotation System Now Available for NMR and 3DEM Structures
» 01/11/16
Time-stamped Copies of the PDB Archive » 01/06/16

Bonus 1: Play Game (up to 5 points)

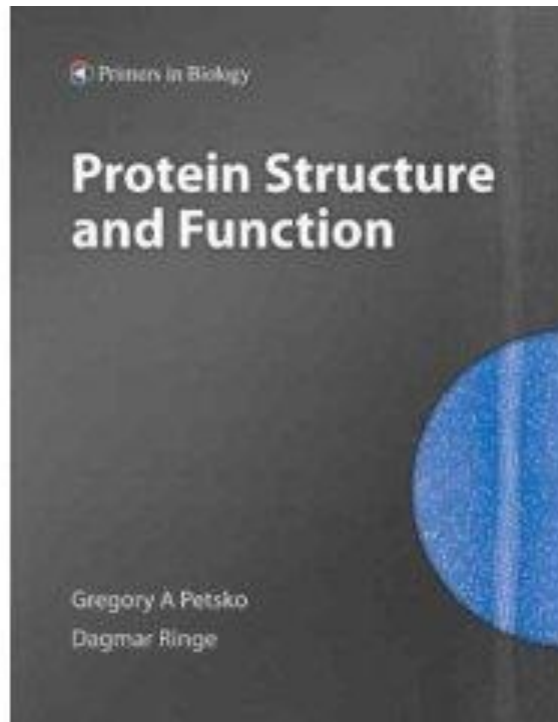


Bonus 2: Find Error (up to 5 points)

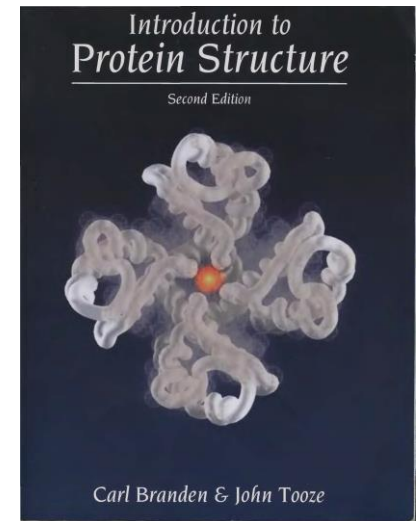
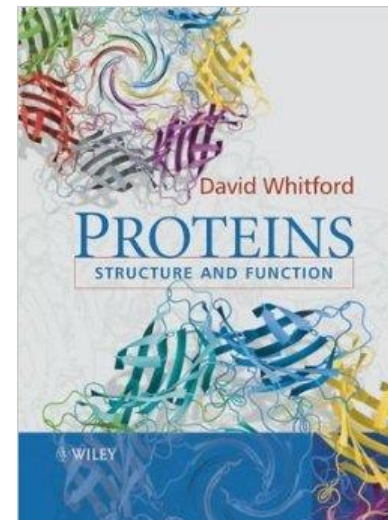
- Find any errors in the teaching material including,
 - Textbook
 - PPT slides
 - Journal club papers
- Find one error get one point!

Readings

Textbook



Reference book



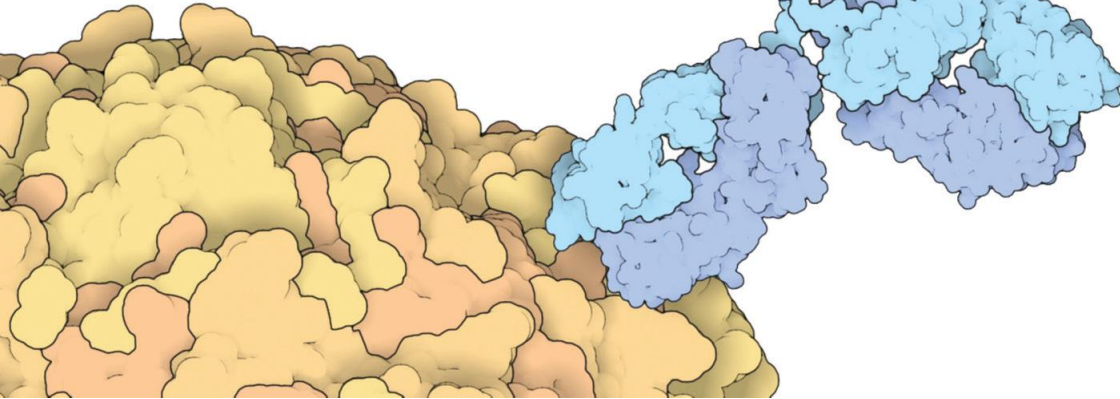
Other Resource

- Internet
 - PDB
 - Google
 - WikiBooks
 - YouTube
- Journals
 - *Current Opinion in Structural Biology*
 - *Annual Review of Biochemistry*
 - *Nature Structural and Molecular Biology*
 - *Structure*
 - *Nature/Cell/Science*

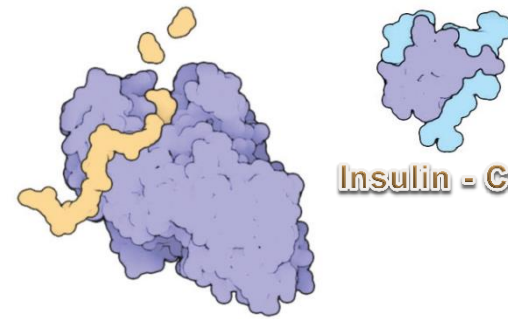
Proteins: the most versatile macromolecules of the cell

- Protein function
 - *Molecular level*: the biochemical function of the protein molecule in isolation
 - *Molecular/Cellular level*: the cellular function that the protein performs as part of an assemblage or complex with other molecules
 - *Cellular/Organism level*: the phenotype that the protein produces in the cell or organism
- Biochemical functions
 - Protein-protein, protein-DNA/RNA, or protein-ligand interactions (binding)
 - Catalysis
 - Molecular switches
 - Structural components
- The function of every protein depends on its 3D structure.

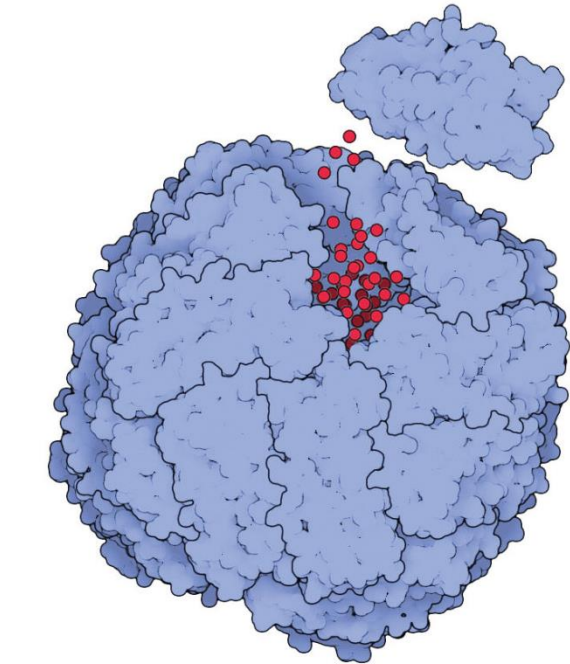
Antibody - Defense



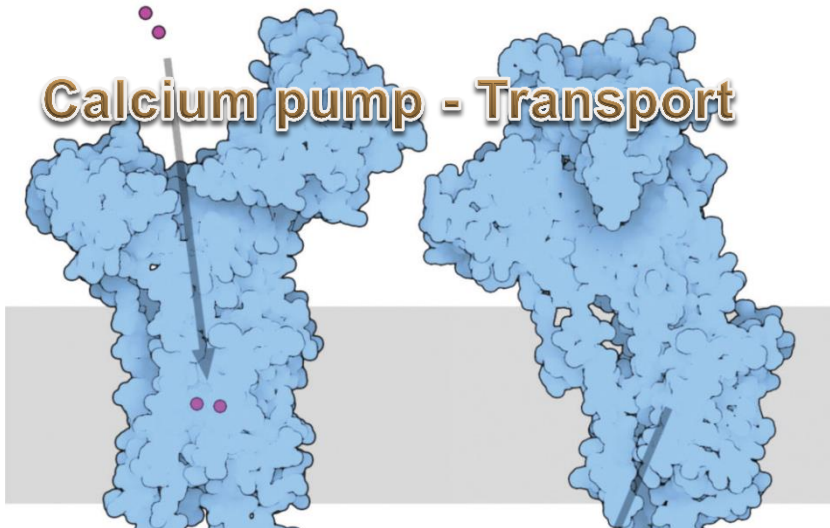
Insulin - Communication



Amylase - Enzyme



Calcium pump - Transport



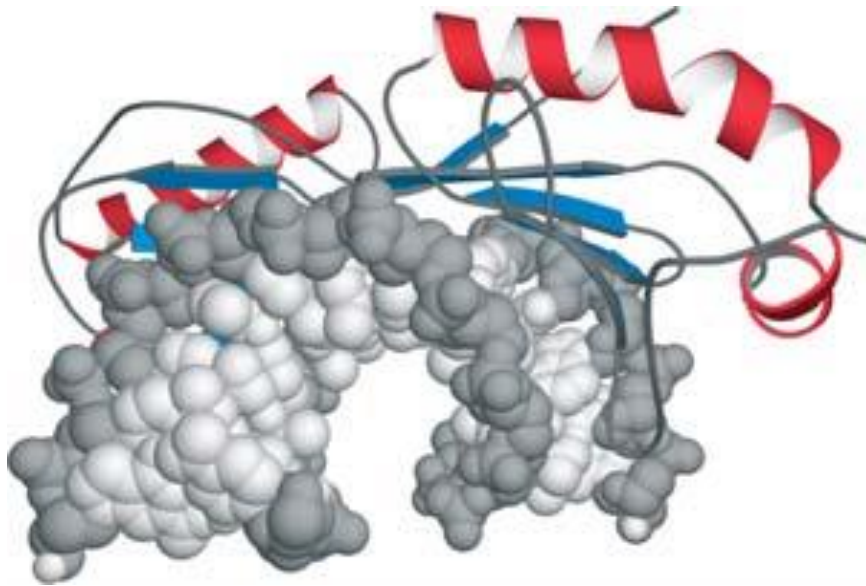
Ferritin - Storage

Collagen - Structure



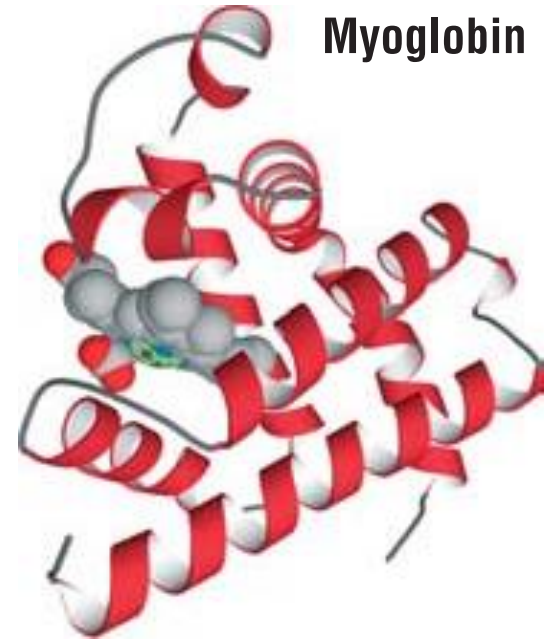
Binding

TATA binding protein



The TATA binding protein binds a specific DNA sequence and serves as the platform for a complex that initiates transcription of genetic information. (PDB **1TGH**)

Myoglobin



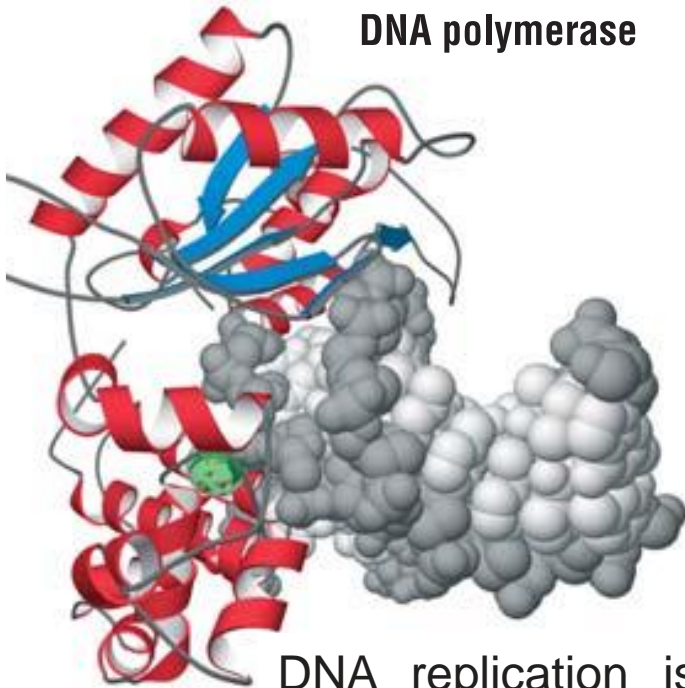
Myoglobin binds a molecule of oxygen reversibly to the iron atom in its heme group. It stores oxygen for use in muscle tissues. (PDB **1A6K**)

Structural features contribute to the binding specificity

- Shape complementarity
- Polar interactions
 - Hydrogen bonding
 - Charge-charge interactions
- Hydrophobic interactions

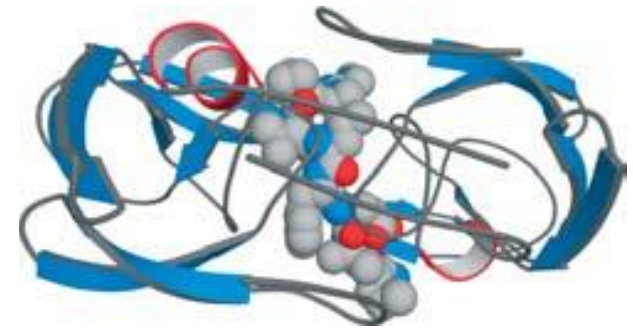
Catalysis

DNA polymerase



DNA replication is catalyzed by a specific polymerase that copies the genetic material and edits the product for errors in the copy. (PDB **1PBX**)

HIV protease



Replication of the AIDS virus HIV depends on the action of a protein-cleaving enzyme called HIV protease. This enzyme is the target for protease-inhibitor drugs. (PDB **1A8K**)

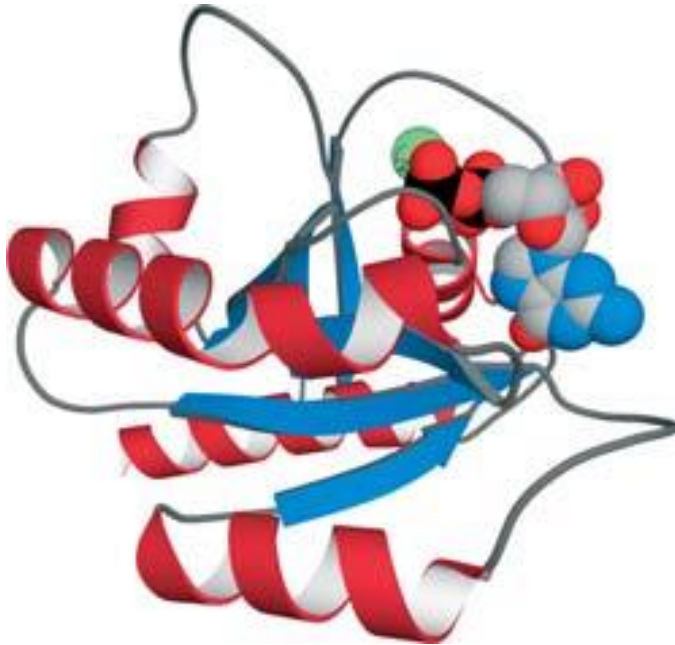
Structural features contribute to the enzymatic catalysis

- Holding reacting groups together in an orientation favorable for reaction
 - proximity
- Binding the transition state of the reaction more tightly than ground state complexes
 - transition state stabilization
- Acid-base catalysis
- ...

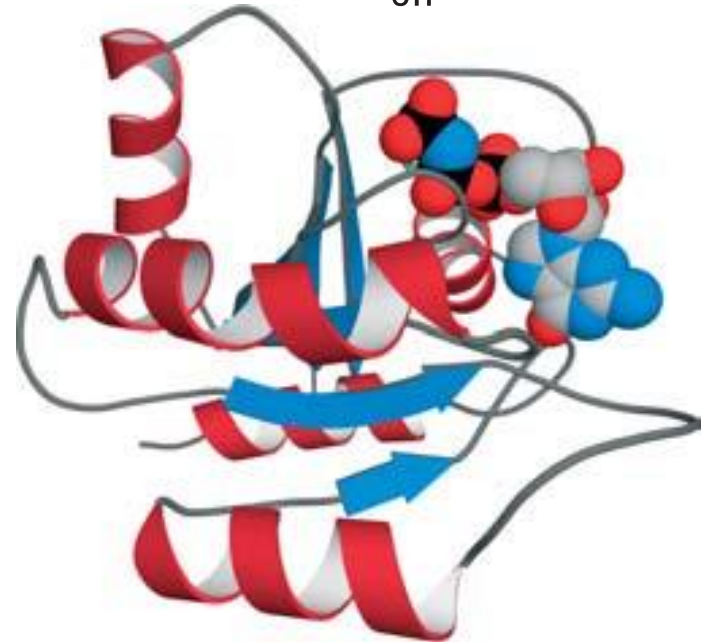
Switching

Ras

"off"



"on"



The GDP-bound ("off"; PDB **1PLL**) state of Ras differs significantly from the GTP-bound ("on"; PDB **121P**) state. This difference causes the two states to be recognized by different proteins in signal transduction pathways.

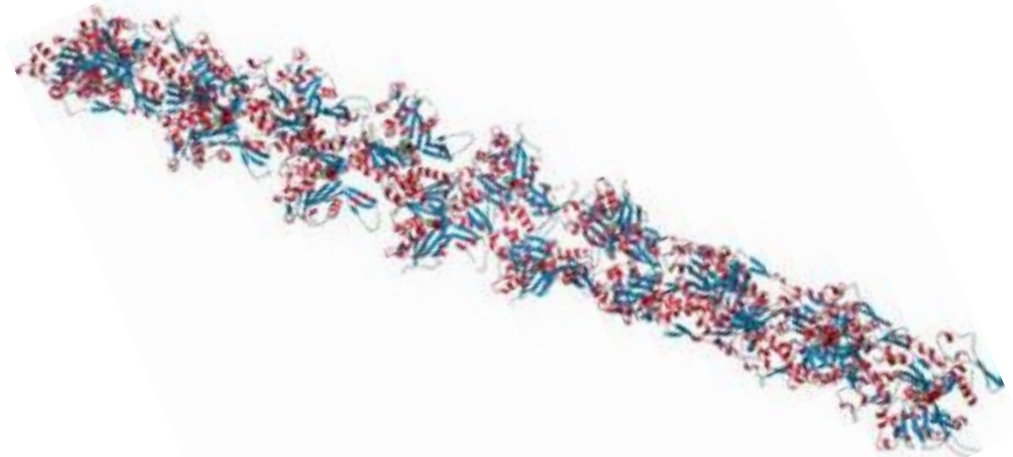
Structural Proteins

Silk



Silk derives its strength and flexibility from its structure: a giant stack of antiparallel β -sheets. Its strength comes from the covalent and H-bonds within each sheet; the flexibility from the van der Waals interactions that hold the sheets together. (PDB **1SLK**)

F-actin



Actin fibers are important for muscle contraction and for the cytoskeleton. They are helical assemblies of actin and actin-associated proteins. (PDB **4A7N**)