Structural Biology (LIBS364)

Rm 535
Monday 14:00 – 15:15
Wednesday 14:00 – 15:15

Prof. Hyun Kyu Song
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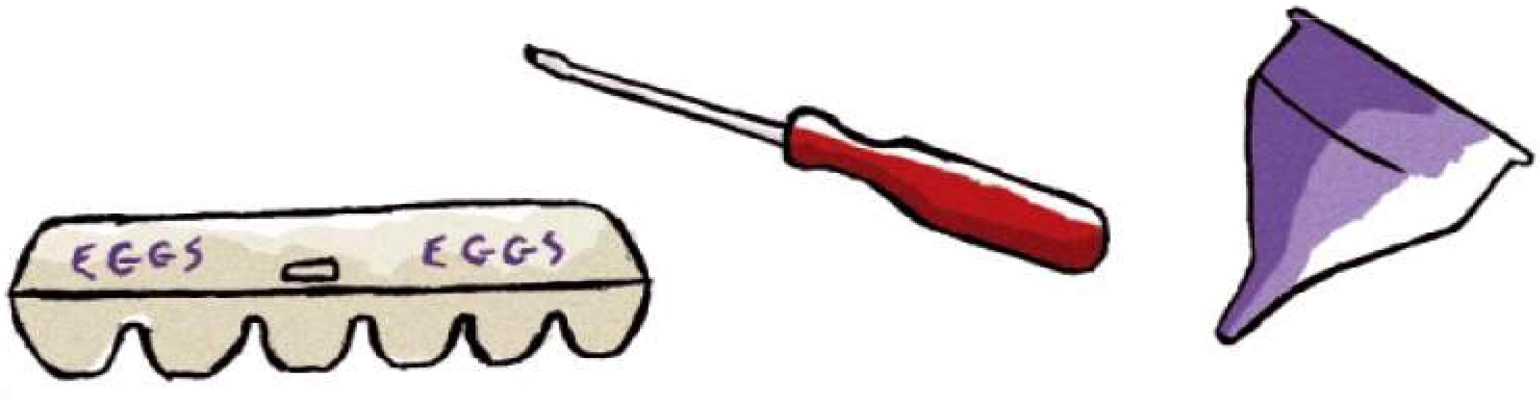
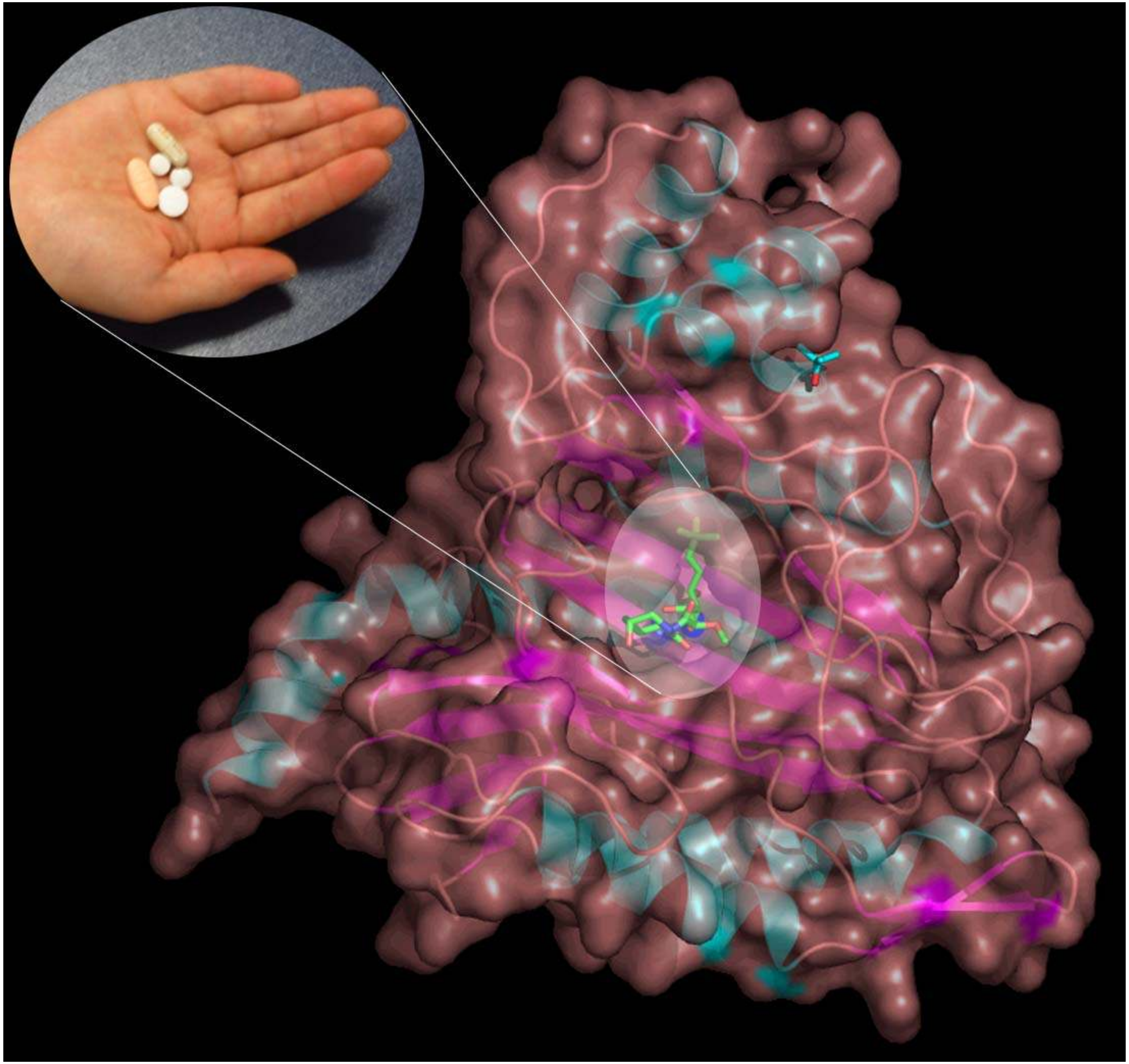
"If biology were a car, structural biologists would be looking under the bonnet to find out how the engine works."

"Put more prosaically, structural biology aims to understand how biology works at the molecular level."

Ad Bax & Dennis A. Torchia, Nature (Feb. 8th 2007)



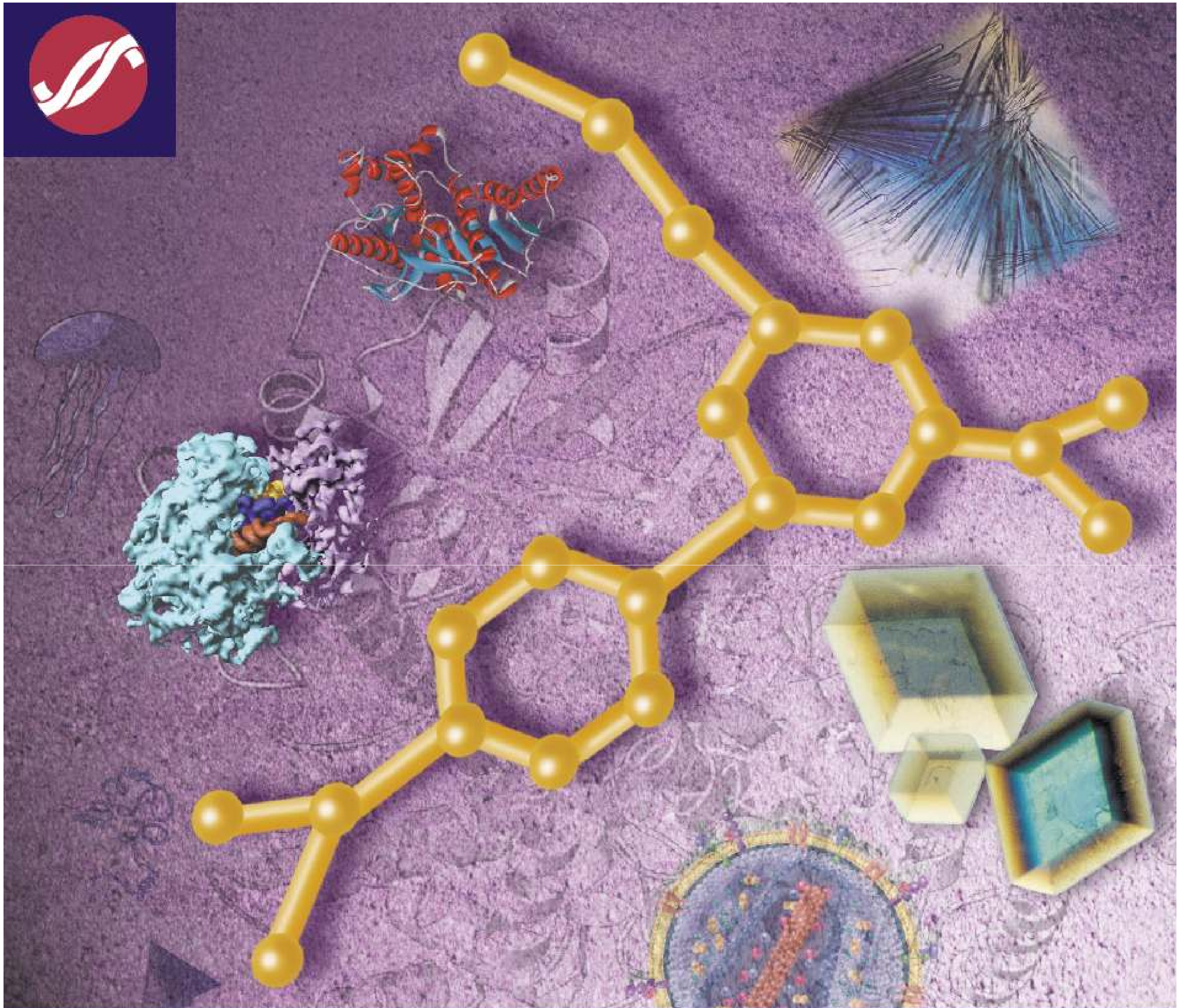
Proteins, like many everyday objects, are shaped to get their job done. The long neck of a screwdriver allows you to tighten screws in holes or pry open lids. The depressions in an egg carton are designed to cradle eggs so they won't break. A funnel's wide brim and narrow neck enable the transfer of liquids into a container with a small opening. The shape of a protein—although much more complicated than the shape of a common object—teaches us about that protein's role in the body.



Introduction to Protein Structure

Second Edition

Carl Branden & John Tooze



The Structures of Life

National Institutes of Health
National Institute of General Medical Sciences

1. The building blocks
2. Motifs of protein structures
3. Alpha-domain structure
4. Alpha/beta structures
5. Beta structures
6. Folding and flexibility
7. DNA structures
8. DNA recognition in prokaryotes by helix-turn-helix motifs
9. DNA recognition by eukaryotic transcription factors
10. Specific transcription factors belong to a few families
11. An examples of enzyme catalysis: Serine proteinases
12. Membrane proteins
13. Signal transduction
14. Fibrous proteins
15. Recognition of foreign molecules by the immune system
16. The structure of spherical viruses
17. Prediction, engineering, and design of protein structures
18. Determination of protein structures

	Chapters	Monday	Wednesday
1 week (8/31-9/4)	Intro, 1	Introduction	The building blocks
2 week (9/7-11)	2, 3	Motifs of protein structures	Alpha-domain structure
3 week (9/14-18)	4, 5	Alpha/beta structures	Beta structures
4 week (9/21-25)	6, 7	Folding and flexibility	DNA structures
5 week (9/28-10/2)	8, 9	DNA recognition in prokaryotes by helix-turn-helix motifs	DNA recognition by eukaryotic transcription factors
6 week (10/5-19)	10		Specific transcription factors belong to a few families
7 week (10/12-16)	11	An examples of enzyme catalysis: Serine proteinases	An examples of enzyme catalysis: Serine proteinases
8 week (10/19-23)			10/21 – Mid-term Exam
9 week (10/26-30)	12	Membrane proteins	Membrane proteins
10 week (11/2-6)	13, 14	**Signal transduction**	**Signal transduction**
11 week (11/9-13)	15	**Fibrous proteins**	Recognition of foreign molecules by the immune system
12 week (11/16-20)	16	The structure of spherical viruses	The structure of spherical viruses
13 week (11/23-27)	17	Prediction, engineering, and design of protein structures	Prediction, engineering, and design of protein structures
14 week (11/30-12/4)	18	Determination of protein structures	Determination of protein structures
15 week (12/7-11)			12/9 – Final Exam

- Prof. Michael J. Eck, MD/PhD
- Department of Biological Chemistry & Molecular Pharmacology, Harvard Medical School
- Department of Cancer Biology, Dana-Farber Cancer Institute
- E-mail: eck@red.dfci.harvard.edu Web: http://red.dfci.harvard.edu

Lecture : Class materials (pdf file - EKU site)

- Reports (The Structures of Life; Due date 11/18)
  "Pdf file already uploaded"

- Hand out "conclusion" in each chapter (Should be hand writing)

- Examination (Mid-term: 10/21; Final: 12/9)

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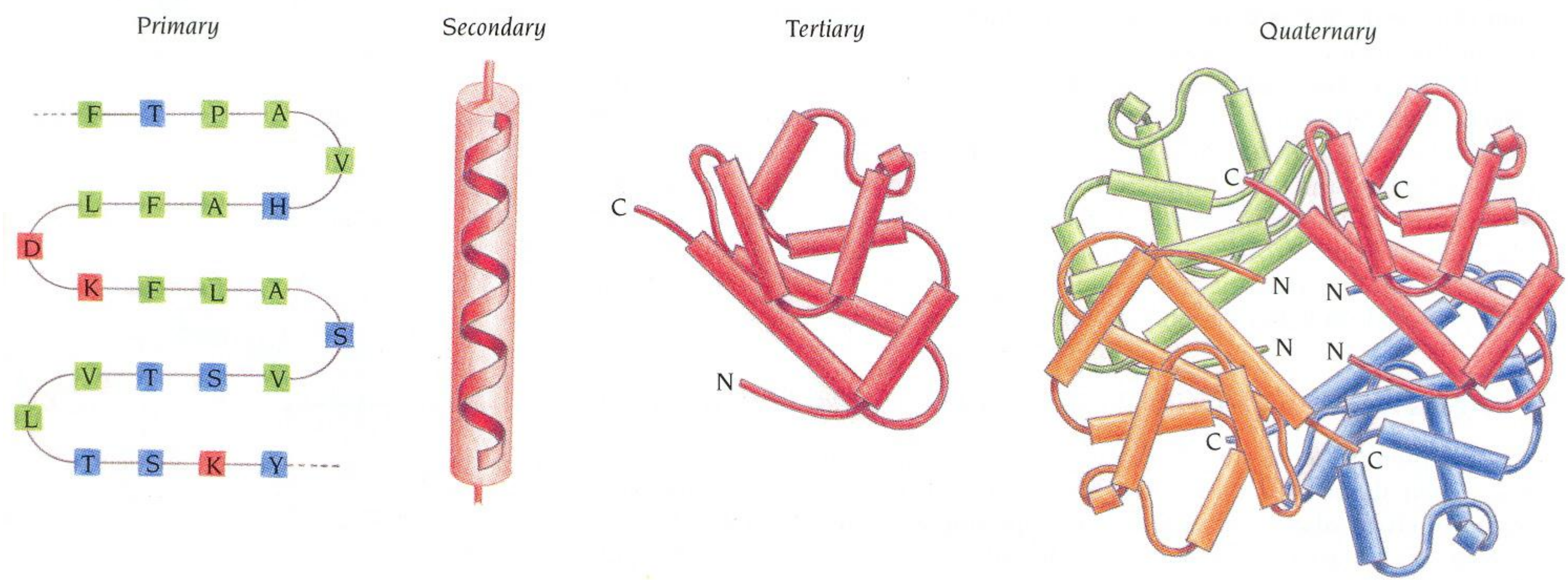
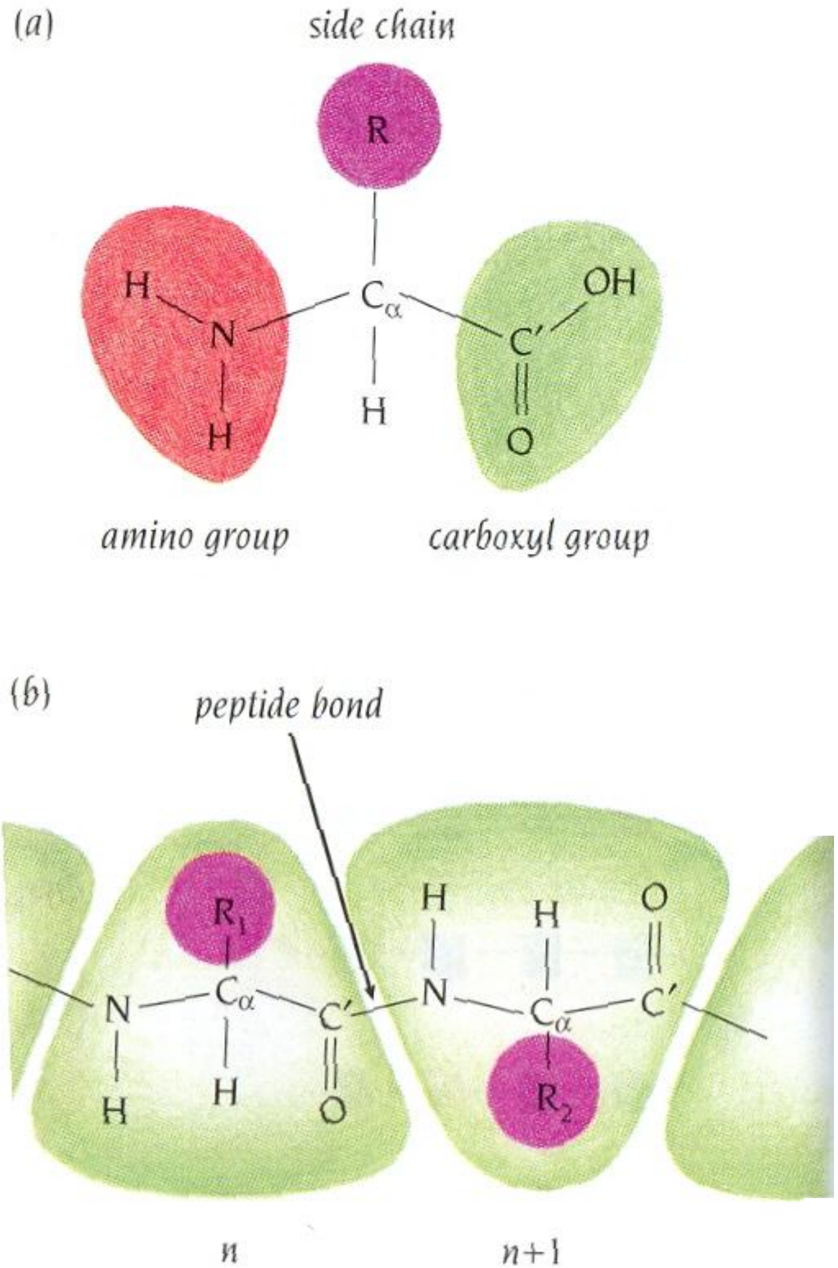
Part 1. Basic Structural Principles

1. The building blocks
2. Motifs of protein structures
3. Alpha-domain structure
4. Alpha/beta structures
5. Beta structures
6. Folding and flexibility
7. DNA structures

Chapter 1. The building blocks



Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.3.



Proteins are polypeptide chains

Successful polypeptide bonds: main chain or backbone

Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.4.

All amino acids in protein have the “L-form”

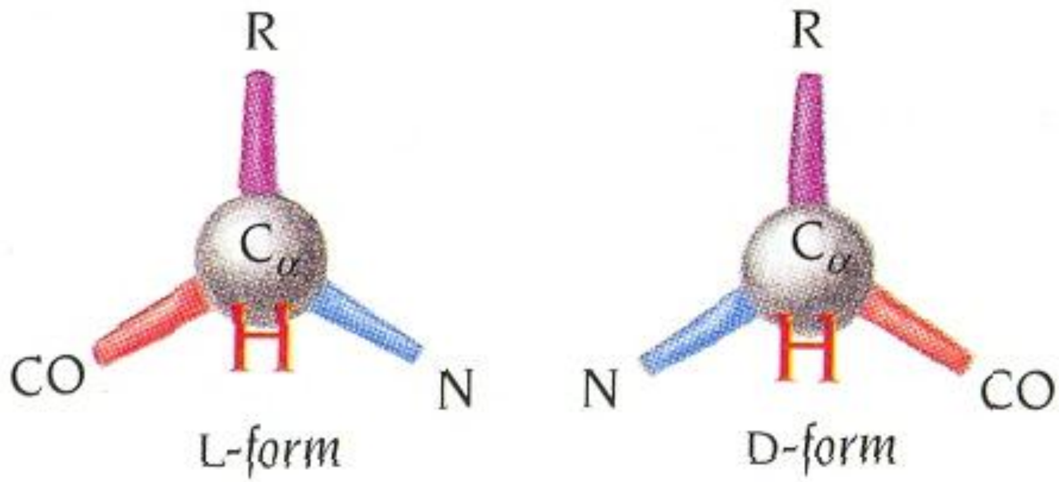


Figure 1.3 The “handedness” of amino acids. Looking down the H–C_α bond from the hydrogen atom, the L-form has CO, R, and N substituents from C_α going in a clockwise direction. There is a mnemonic to remember this; for the L-form the groups read CORN in clockwise direction.

Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.5.

Cysteines can form disulfide bridges

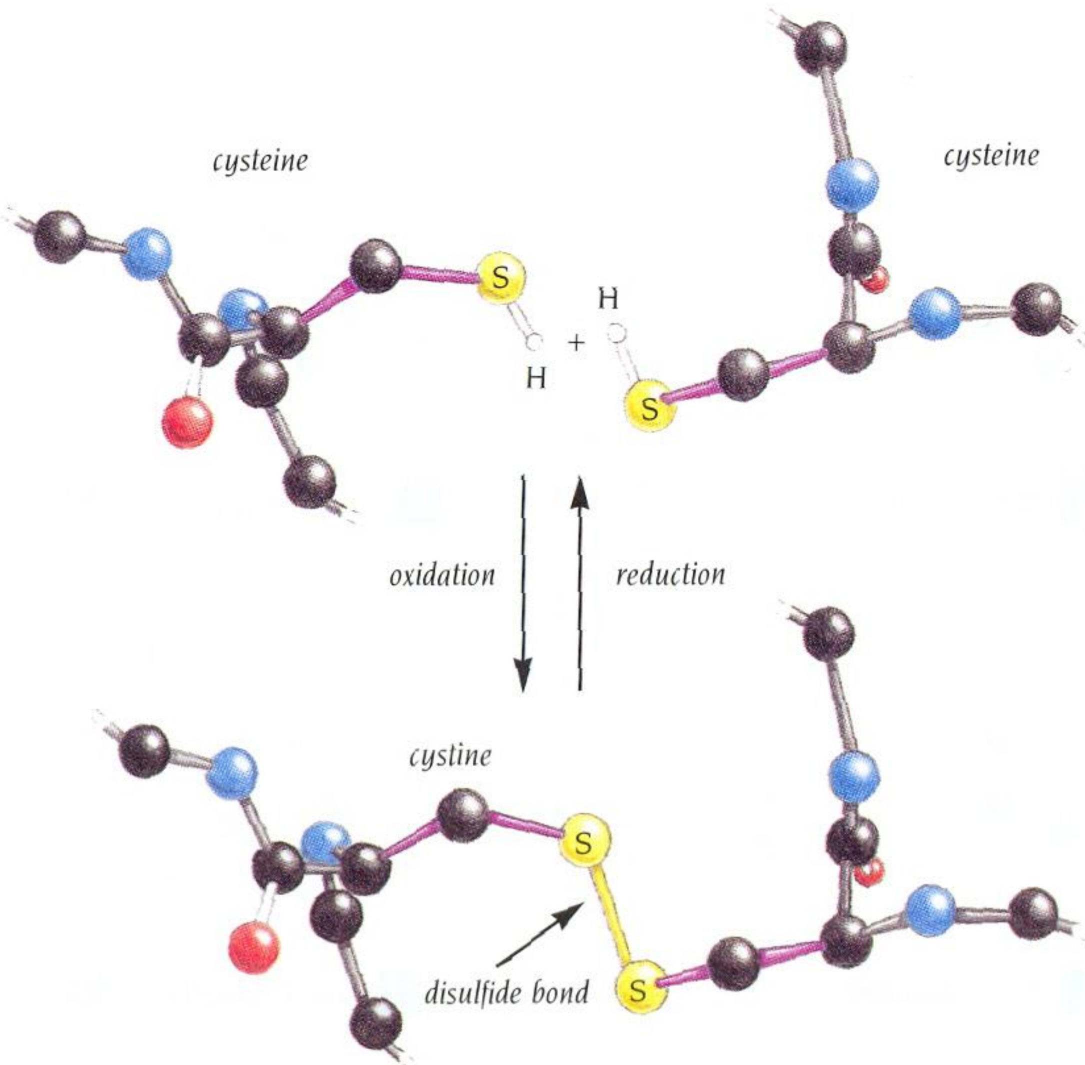


Figure 1.4 The disulfide is usually the end product of air oxidation according to the following schematic reaction scheme:

$$2\ \text{–}CH_2SH + \tfrac{1}{2}\,O_2 \rightleftharpoons \text{–}CH_2\text{–}S\text{–}S\text{–}CH_2 + H_2O$$

Disulfide bonds form between the side chains of two cysteine residues. Two SH groups from cysteine residues, which may be in different parts of the amino acid sequence but adjacent in the three-dimensional structure, are oxidized to form one S–S (disulfide) group.

Branden & Tooze (1998), Introduction to protein structure, 2^{nd} ed., p.5.

Peptide units are building blocks of protein structures

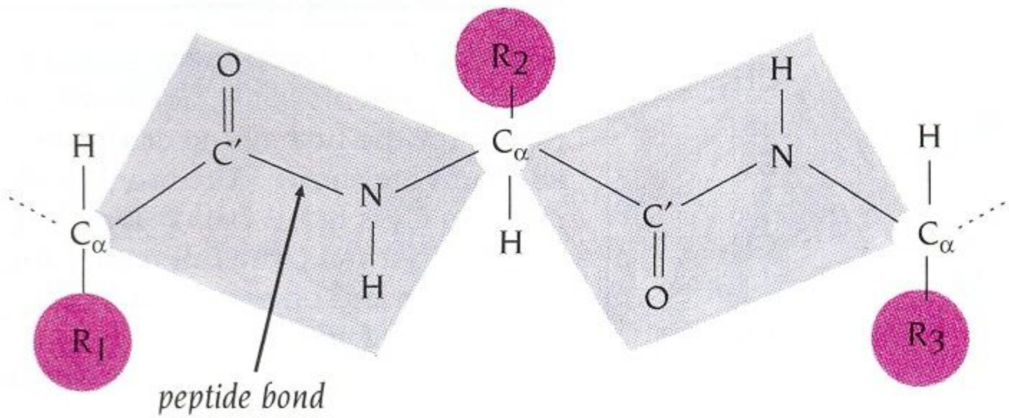
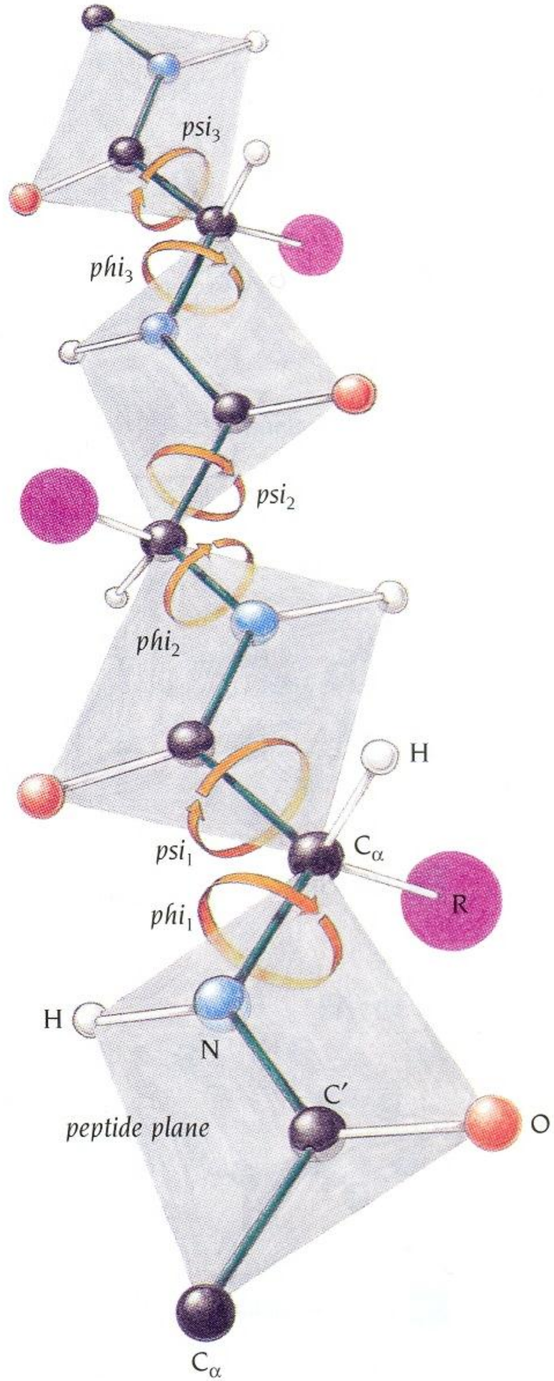


Figure 1.5 Part of a polypeptide chain that is divided into peptide units, represented as blocks in the diagram. Each peptide unit contains the C_α atom and the C′=O group of residue *n* as well as the NH group and the C_α atom of residue $n + 1$. Each such unit is a planar, rigid group with known bond distances and bond angles. R_1, R_2, and R_3 are the side chains attached to the C_α atoms that link the peptide units in the polypeptide chain. The peptide group is planar because the additional electron pair of the C=O bond is delocalized over the peptide group such that rotation around the C–N bond is prevented by an energy barrier.

Branden & Tooze (1998), Introduction to protein structure, 2^{nd} ed., p.8.



The only degrees of freedom:
N-Cα bond: phi (φ)
Cα -C’ bond: psi (ψ)
rotation angle

Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.8.

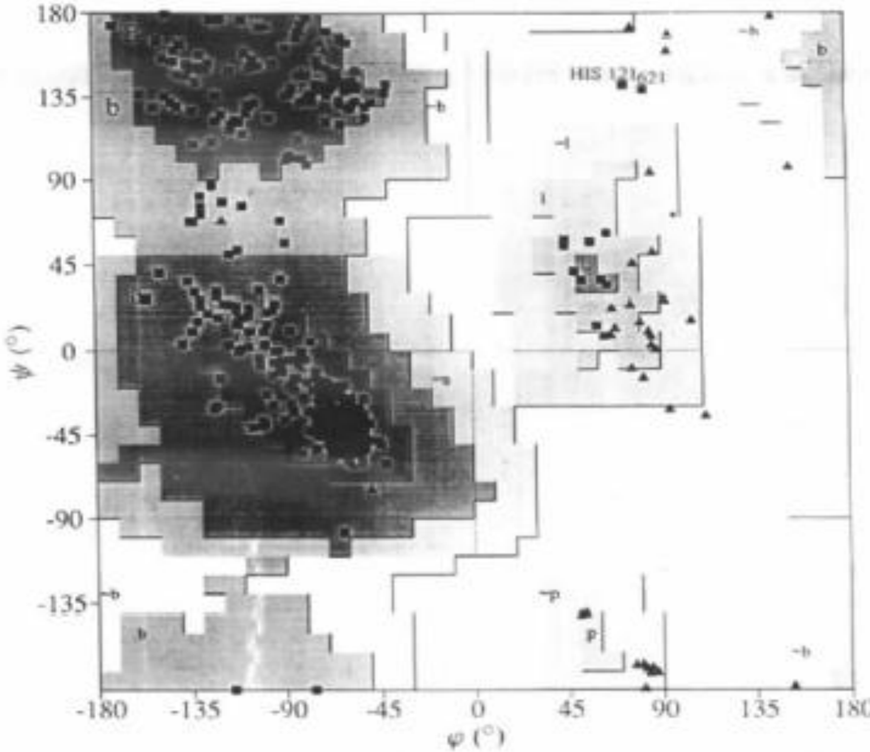


Fig. 2. Ramachandran plot for barley chitinase, created by *PROCHECK* (Laskowski *et al.*, 1993). Glycine and proline residues are denoted by triangles and all other residues by squares. The two labeled residues in the disallowed region are His121 in molecule 1 and His621 in molecule 2. The different regions defined by borderlines are labeled as: A, B, L, most favored; a, b, l, p, allowed; and ~a, ~b, ~l, ~p, generously allowed.

Glycine residues can adopt many different conformations

Song and Suh (1996) Acta Crystallogr. D56, 289-298.

Certain side-chain conformations are energetically favorable: Rotamer

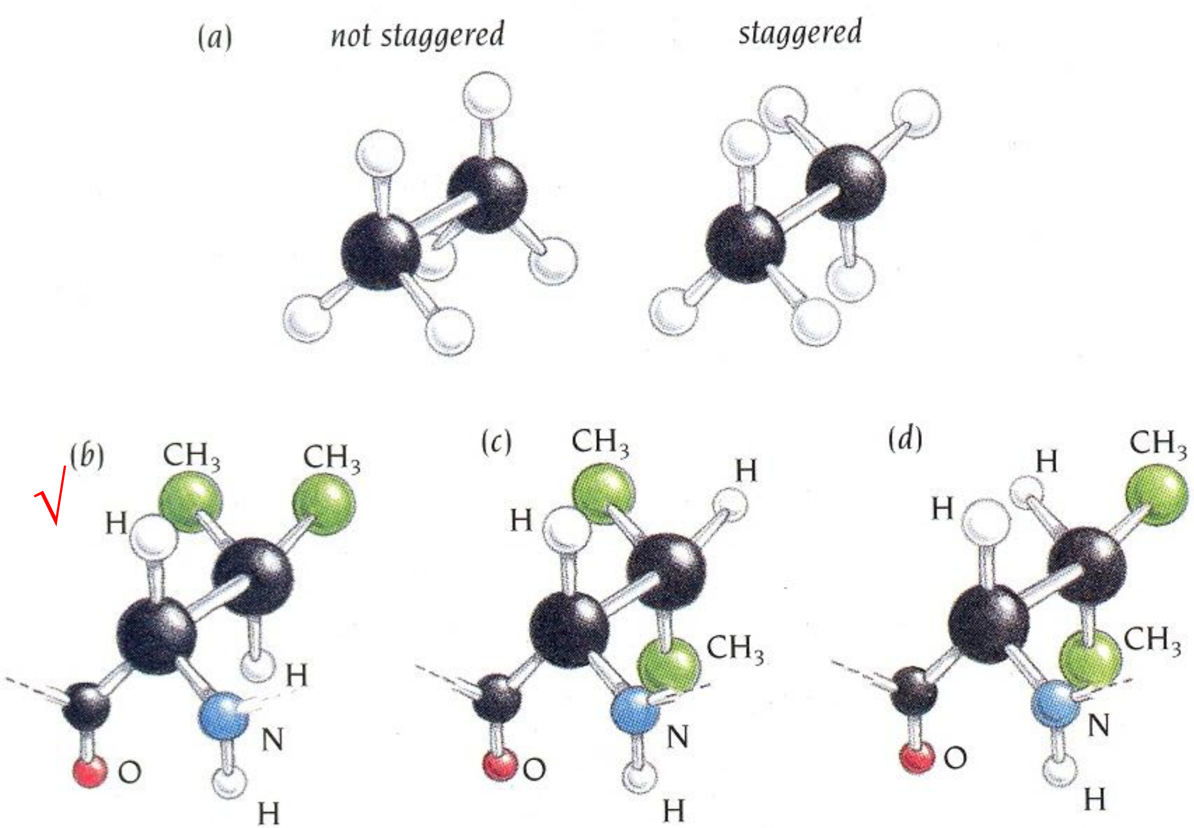


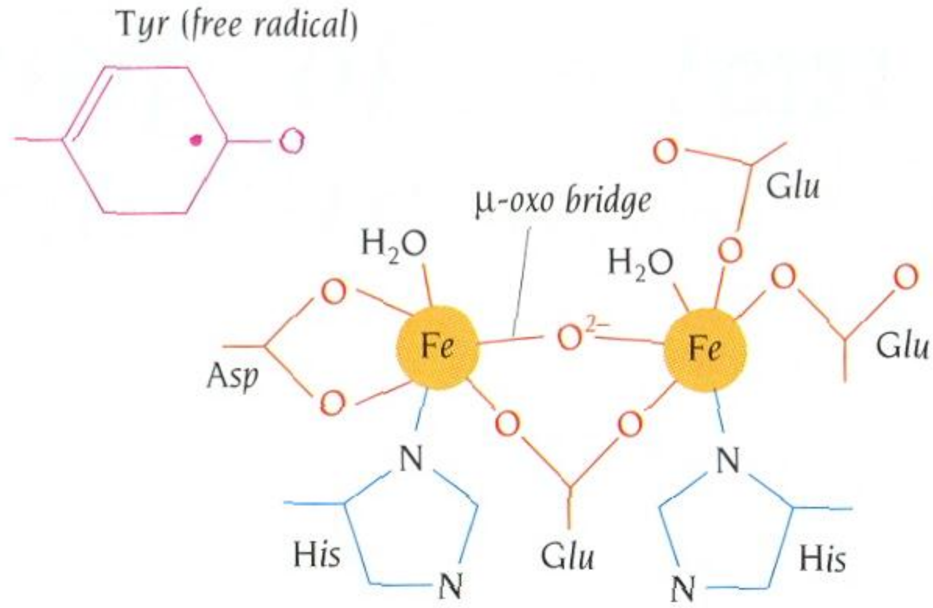
Figure 1.8 The staggered conformations are the most energetically favored conformations of two tetrahedrally coordinated carbon atoms. (a) A view along the C–C bond in ethane (CH_3CH_3) showing how the two carbon atoms can rotate so that their hydrogen atoms are either not staggered (aligned) or staggered. Three indistinguishable staggered conformations are obtained by a rotation of 120° around the C–C bond. (b–d) Similar views as in (a) of valine. The three staggered conformations are different for valine because the three groups attached to C_β are different. The first staggered conformation (b) is less crowded and energetically most favored because the two methyl groups bound to C_β are both close to the small H atom bound to C_α.

Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.10.

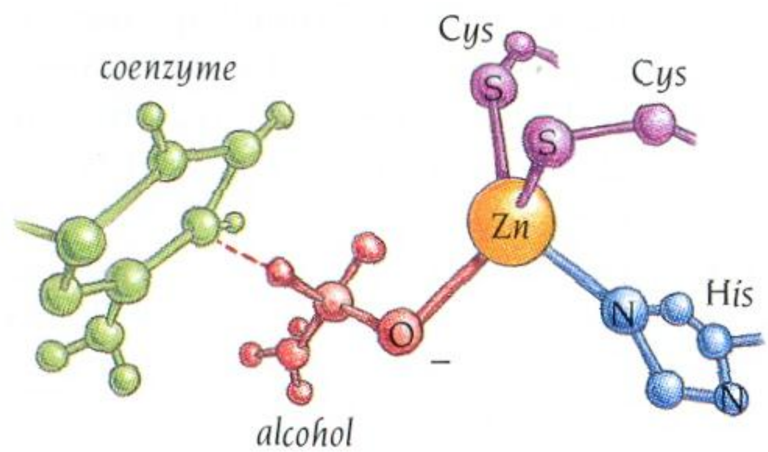
Many proteins contain intrinsic metal atoms

- Excellent ligands: His, Cys, Asp, Glu, H_2O
- Common metals: iron, zinc, magnesium, calcium

(a) Redox center of ribonucleotide reductase



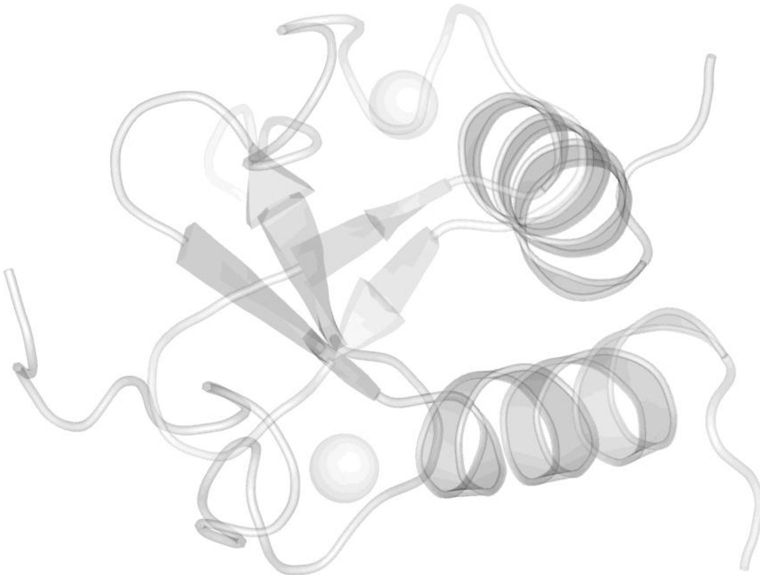
(b) Alcohol dehydrogenase



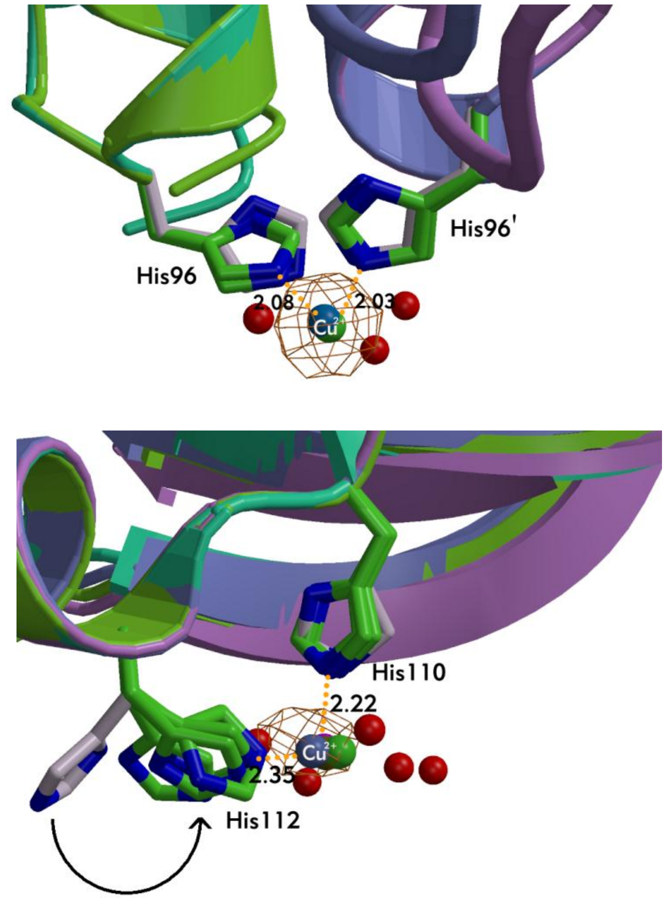
Branden & Tooze (1998), Introduction to protein structure, 2nd ed., p.11.

Many proteins contain intrinsic metal atoms

C4-type zinc finger of ClpX



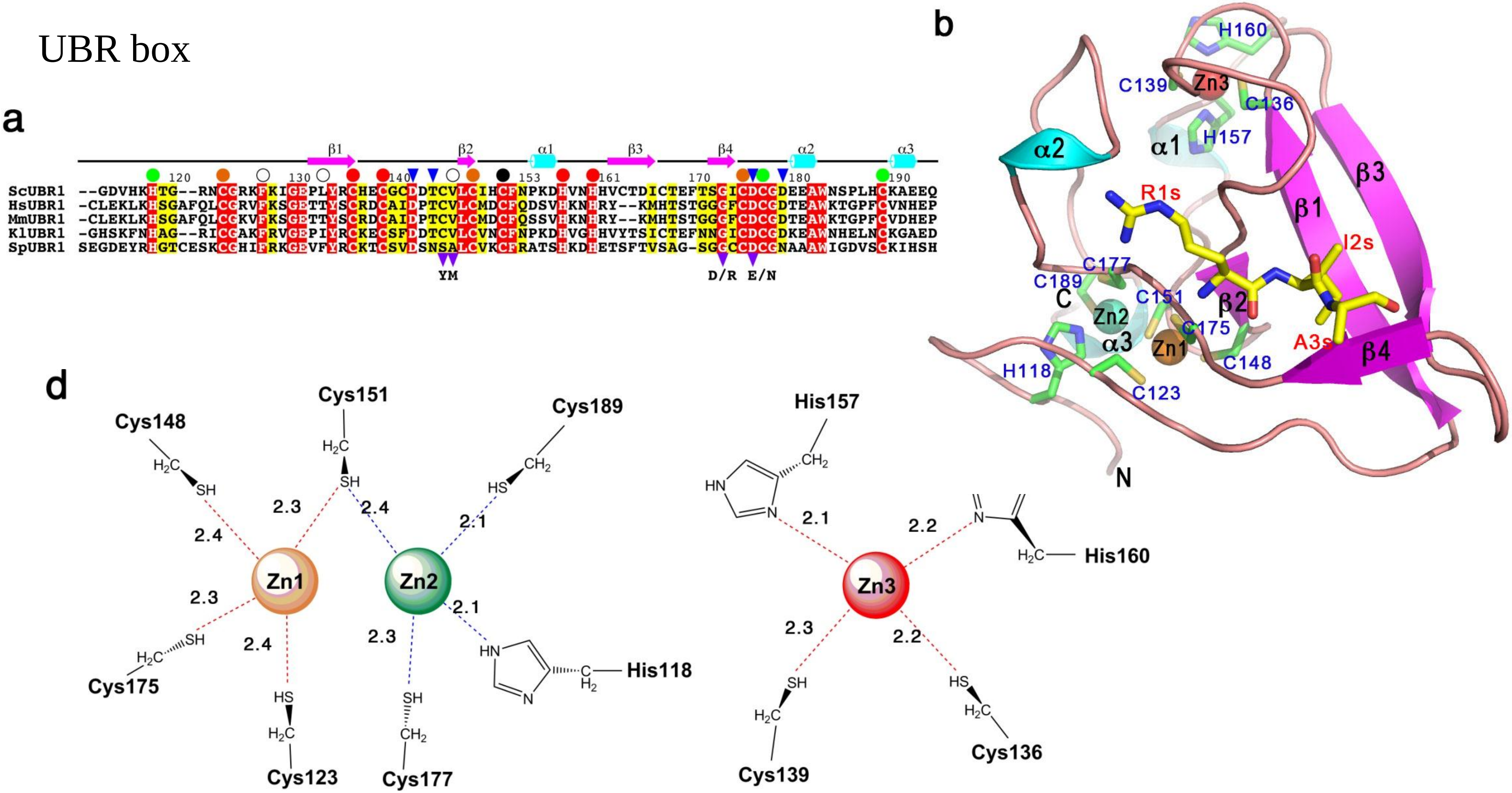
Nickel binding sites of UreE



Song et al. (2001) J. Biol. Chem. 276, 49359-49364

Many proteins contain intrinsic metal atoms

UBR box



Choi et al, unpublished results