Lecture 10 (10/4/17)

• Reading: Ch4; 125, 132-136 (structure determination)
  Ch4; 12-130 (Collagen)
• Problems: Ch4 (text); 10, 15
  (may add some more on website)

NEXT

• Reading: Ch4; 125, 138-141, 141-142
• Problems: Ch4 (text); 7, 9, 11
  Ch4 (study guide); 1, 2

OUTLINE

I. Protein Structure
   A. Tertiary
      1. Depiction; the Protein Database
      2. Examples of Types
      3. Domains
      4. Intrinsically unstructured
      5. Energetics
   B. Quaternary
      1. Nomenclature
      2. Energetics
Tertiary Structure

Bovine Carboxypeptidase A

Based on an X-ray structure by William Lipscomb, Harvard University.
PDBid 3CPA.

Carboxypeptidase A
PDBid 3CPA
Protein Structure-Tertiary

Picturing protein structure

(a) Space-fill
(b) Backbone trace
(c) Ribbon

Triose-phosphate Isomerase (TIM)

Protein Structure-Tertiary

Picturing protein structure

(a) Ribbon
(b) Surface contour
(c) Ribbon with side-chains
(d) Space-filling

Sperm-whale Myoglobin (Mb)
Protein Structure-Tertiary
Protein Classification:
\(\alpha, \beta, \text{or } \alpha/\beta\)

- Cytochrome b562 PDBid 256B
- Human immunoglobulin fragment PDBid 7FAB
- Dogfish lactate dehydrogenase PDBid 6LDH

Protein Structure-Tertiary
Protein Classification:
\(\alpha\)

- Cytochrome b562 PDBid 256B
- Growth hormone
Protein Structure-Tertiary
Protein Classification: α

Human immunoglobulin fragment
PDBid 7FAB

Protein Structure-Tertiary
Protein Classification: β

α1-Antitrypsin
Insecticyanin
Protein Structure-Tertiary
Protein Classification: \( \alpha/\beta \)

Can you find the “Rossmann Fold?”

Protein Structure-Tertiary
Protein Classification: \( \alpha/\beta \)

Can you find the “Rossmann Fold?”
Protein Structure-Tertiary
Protein Topology: 8-Stranded β Barrels

Human retinol binding protein
PDBid 1RBP

Peptide-N4-(N-acetyl-β-D-glucosaminyl) asparagine amidase
PDBid 1PNG

Triose phosphate isomerase
PDBid 1TIM

β-meander
Peptide-N\textsuperscript{4}-(N-acetyl-\textbeta-D-glucosaminyl) asparagine amidase
PDBid 1PNG

Protein Structure-Tertiary
Protein Topology: 8-Stranded \beta Barrels

Greek key
(4-5-6-7)

Trisose phosphate isomerase
PDBid 1TIM

Protein Structure-Tertiary
Protein Topology: 8-Stranded \beta Barrels

\alpha/\beta-barrel
Protein Structure-Tertiary
Protein Topology: 8-Stranded β Barrels

Protein Structure-Tertiary
Protein Domains

**Domains:**
Separate folded structures with hinge all with one polypeptide chain
Protein Structure-Tertiary
Protein Domains

Dogfish lactate dehydrogenase
PDBid 6LDH

α/β-saddle
&
Rossmann Fold (β-α-β-α-β)

Protein Structure-Tertiary
Protein Domains

2-Domain Protein: GAPDH
Glyceraldehyde-3-phosphate dehydrogenase
PDBid 1GD1

α/β-saddle
&
Rossmann Fold (β-α-β-α-β)

Based on an X-ray structure by Alan Winocor, Imperial College, London, U.K. PDBid 1GD1
Unstructured domains:
Part of primary structure without any defined conformation, changeable, dynamic, several possible structures depending on binding partners in cells
Protein Structure-Tertiary

Intrinsically Disordered
Proteins: p53

Figure 9.22
Protein Structure-Tertiary

**Intrinsically Disordered Proteins: CREB**

- Hydropbobic effect
- Hydrogen bonds
- Salt bridges
- Dispersion forces
- Disulfide bonds

**CREB (cAMP response element-binding protein)**

**Kinase-inducible domain of CREB**

PDBid **1KDX**
Hydrophobic effect drives protein folding

<table>
<thead>
<tr>
<th>TABLE 4-3</th>
<th>Hydrophobicity Scales</th>
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<tbody>
<tr>
<td>Residue</td>
<td>Scale A</td>
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<tr>
<td></td>
<td>Scale B</td>
</tr>
<tr>
<td>Phe</td>
<td>2.7</td>
</tr>
<tr>
<td>Met</td>
<td>1.9</td>
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<tr>
<td>Ile</td>
<td>4.5</td>
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<tr>
<td>Leu</td>
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<td>Val</td>
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<tr>
<td>Cys</td>
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<td>Trp</td>
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<tr>
<td>Ala</td>
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<td>Arg</td>
<td>4.3</td>
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</tbody>
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Hydrophobic effect drives protein folding.
Problem

Which residue would be more likely to be ____?
1. On a protein’s surface: Trp or Gln
2. In the protein interior: Ser or Val
3. In the middle of an alpha-helix: Gly or Leu
4. In a beta-sheet: His or Pro

Quaternary Structure
Multiple subunits held together by primarily non-covalent interactions

Nomenclature:
- homo vs. hetero
- subunits indicated with Greek letters ($\alpha$ (1st), $\beta$ (2nd), $\gamma$ (3rd), etc.)

Protein Structure-Quaternary

Same weak interactions determine 4° structure

- Hydrophobic effect
- Hydrogen bonds
- Salt bridges
- Dispersion forces
Protein Structure-Quaternary

4° structure held together with side-chain interactions

Sum of weak interactions

- Hydrophobic effect
- Hydrogen bonds
- Salt bridges
- Dispersion forces

Intermolecular salt bridges formed by conserved, charged residues stabilize HY2-Fd interaction. HY2-bound substrate and the iron-sulfur cluster on AtFd2 are shown in stick representation. Important charged residues in AtFd2-HY2 bonding interface are viewed from the top of Fd side of the docking complex. Residues identified in this study are shown in stick representation with blue (HY2) and brown (AtFd2) carbon atoms. Red circles indicate the salt bridges in between two proteins.

Protein Structure-Summary