Protein structure

Quaternary structure
Protein-Protein Interactions and Quaternary Structure

- Proteins form networks and form larger complexes
- Proteins interact via:
  - Motifs (short, usually secondary structure)
  - Domains (larger, usually tertiary structure)
- Interactions can be transient (temporary) or stable (permanent)
- Proteins interact with each other using the same forces / attractions / bonds that drive tertiary structure formation
- Examples of interactions:
  - Conformational changes to create a site of interaction
  - Some proteins act as “scaffold” for others to bind onto
  - Proteins can compete for binding sites
  - Proteins can have prosthetic groups
Protein-Protein Interactions and Quaternary Structure

- Proteins form networks and form larger complexes
  - monomer, dimer, trimer, ..., oligomer, polymer
  - homomeric (all subunits are the same) or heteromeric (different)

- e.g. Haemoglobin:
  - 2x alpha globin
  - 2x beta globin
  - 4x haem group
  - a heterotetramer
  - or a dimer of two heterodimers?

chapter 4, page 64-65
Microtubule structure

β-tubulin

α-tubulin

tubulin heterodimer (= microtubule subunit)

protofilament

plus end

minus end

lumen

microtubule

Figure 16-11 Molecular Biology of the Cell (© Garland Science 2008)

chapter 8, page 138
Actin filament formation

- Turning a globular protein into a fibrous protein

Figure 16-12  *Molecular Biology of the Cell*  
(© Garland Science 2008)
Conformational changes to create a new site of interaction

- PKR is a kinase that is activated when double stranded RNA is present in the cell, which is usually a sign of viral infection.

- dsRNA binding to PKR changes its conformation, enabling PKR dimerisation, which activates this kinase.

- Activated PKR then phosphorylates a substrate which switches off general translation, inhibiting the ability of the virus to replicate.
Some proteins act as a “scaffold” for others to bind onto.
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Some proteins act as a “scaffold” for others to bind onto

- 48S preinitiation complex formation and mRNA circularisation
- eIF4G acts as a “scaffold” for assembly of 48S complex

chapter 25
page 400-402
Unwanted Protein-protein Interactions

- A motif/domain recognition can be “blind” to the structure of the rest of the protein, implying that the protein-protein interaction is not (sufficiently) specific.

- Antibodies that are meant to recognise foreign antigens can instead cause autoimmune diseases when they interact with native proteins:
  - Multiple Sclerosis, Crohn’s, Lupus, Type 1 Diabetes, …
Proteins can have prosthetic groups

- Proteins can be modified post-translationally at single amino acid side chains (e.g. glycosylation, phosphorylation)
- Other groups can be attached to multiple sites in a protein (e.g. a haem group)

<table>
<thead>
<tr>
<th>Class</th>
<th>Prosthetic Group</th>
<th>Example</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycoprotein</td>
<td>Saccharide</td>
<td>Immunoglobulin</td>
<td>antibody</td>
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<td></td>
<td>Interferon</td>
<td>antiviral agent</td>
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<td>Haemoprotein</td>
<td>haem (heme)</td>
<td>haemoglobin</td>
<td>O₂ carrier in blood</td>
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<td></td>
<td>myoglobin</td>
<td>O₂ carrier in muscle</td>
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<tr>
<td>Lipoprotein</td>
<td>lipid</td>
<td>low- and high-density lipoprotein</td>
<td>lipid carriers</td>
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<td>(LDL, HDL)</td>
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<td>Metalloprotein</td>
<td>metal ion</td>
<td>Calmodulin</td>
<td>Ca²⁺ carrier</td>
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<td>Ferritin</td>
<td>Fe²⁺ storage</td>
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<td>Carboxypeptidase</td>
<td>Zn²⁺ used in digestion</td>
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<tr>
<td>Nucleoprotein</td>
<td>Nucleic acid</td>
<td>small nuclear ribonucleoprotein</td>
<td>RNA splicing</td>
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<td>(snRNP)</td>
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</table>
Summary

**Primary**
- Different types of R-group (in specific sequence)

**Secondary**
- Interactions between polypeptide backbone atoms
- Stable local structures: α-helices, β-sheets
- Hydrogen bonds only

**Tertiary**
- Interactions between R-groups
- Weak = hydrogen bonds, hydrophobic interactions
- Stronger = electrostatic, covalent (disulphide bridges)

**Quaternary**
- Multiple proteins interact in many different ways
- Same types of bonds/forces as in tertiary structures