Learning Outcomes

- Introduction to protein:
  - types
  - composition and synthesis
  - levels of structure
    - primary
    - secondary
    - tertiary
    - quaternary

- The lectures are only the start - further reading:
  - Lodish – Molecular Cell Biology
  - Miesfeld & McEvoy – Biochemistry
  - Berg (Stryer) – Biochemistry
  - Alberts – Molecular Biology of the Cell
  - Older editions are available online (NCBI Bookshelf)

Amount of protein in a human?

### Body Composition

<table>
<thead>
<tr>
<th>Body Component</th>
<th>Average Weight (kg)</th>
<th>Percentage of Total Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>12</td>
<td>20%</td>
</tr>
<tr>
<td>Water</td>
<td>42</td>
<td>60%</td>
</tr>
<tr>
<td>Fat</td>
<td>12</td>
<td>20%</td>
</tr>
<tr>
<td>Glucose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg, Cl, Fe, Zn, Cu</td>
<td></td>
<td></td>
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### Nutritional Value

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Amount (g)</th>
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<tr>
<td>Protein</td>
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<td>2077</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>4.4</td>
<td>186.4</td>
</tr>
<tr>
<td>Fat</td>
<td>12</td>
<td>2077</td>
</tr>
<tr>
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<td>42</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>12</td>
<td>0</td>
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### Cross Section of Muscle Fiber

- X 10
- X 100

- Myosin (thick) filaments
- Actin (thin) filaments
- Fibel
- Whole muscle
- Cross section

### Whole Muscle

- X 10
- X 100
- X 1000 (≈ 10^3 X 100)
- Fiber
- Myosin (thick) filaments
- Actin (thin) filaments

### Fiber

- X 200
- X 20,000 (≈ 20^4 X 100)
- Cross section
- Whole muscle
- Myosin (thick) filaments
- Actin (thin) filaments

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OPSINS

A. Light receptors and their absorption spectrum.

1. Blue cones (450 nm)
2. Green cones (530 nm)
3. Red cones (630 nm)

B. Wavelength (nm)
Protein classes

- **Fibrous** – Insoluble, used for structures, to give strength or to make protective layers
  - Silk – web
  - Coatings – secretory granules or seeds, viruses
  - Intracellular cytoskeleton, extracellular matrix

- **Globular** – soluble, usually offer dynamic functions
  - Enzymes – biological catalysts
  - Transport proteins
  - Hormones
  - “Defence”
  - Toxins
  - In membranes

How can proteins have such diversity?

Polyethylene (polythene)

One repeating subunit = boring, unreactive
20 different subunits = many possible combinations...

Amino Acids – basic structure

- Amine
- Central (α) carbon
- Carboxylic Acid
- Variable R group (polarity and charge)
Amino Acids – Zwitterionic form
(in physiological solution - neutral pH)

Protonation

\[ ^{+}\text{H}_3\text{N} \quad \text{Ca} \quad \text{C} \quad \text{O} \quad \text{O}^{-} \]

Deprotonation

R-groups

20 different side chains are used in proteins – easier to only consider side chains:

LIFE has L- amino acids

Amino Acids – chirality
(stereoisomers/optical isomers)

Groups surround the Ca in a tetrahedral shape

R-groups

- 20 different side chains are used in proteins – easier to only consider side chains:

L- Alanine

d- Alanine
R-groups

- 20 different side chains are used in proteins – easier to only consider side chains:

- Then the simplest (smallest) amino acids are:
  - Glycine, Gly, G
  - Alanine, Ala, A
  - Which are also NON-POLAR (also termed HYDROPHOBIC)
  - NB: Trivial name, Symbol, Single letter symbol

More Non-Polar R-groups

- Breakdown products include Hydrogen Sulphide...
  - Cysteine, Cys, C

More Non-Polar R-groups

- Methionine, Met, M
More Non-Polar R-groups

- Cysteine, Cys, C
- Phenylalanine, Phe, F
- Methionine, Met, M
- Tryptophan, Trp, W

More nonpolar R-groups

- Branched chain (aliphatic)
  - Valine, Val, V
  - Leucine, Leu, L
  - Isoleucine, Ile, I

Protein cocktail is 'elixir of life'

A cocktail of amino acids - the building blocks of proteins - is the latest contender in the age-old search for the elixir of life.

Scientists gave mice drinking water laced with three amino acids. They said the rodents lived significantly longer than other mice fed a normal diet.

The research, reported in a scientific journal, has yet to be verified in people.

The study leader said a large patient trial was needed to provide evidence to convince doctors.

In experiments, middle-aged healthy mice were given drinking water containing the amino acids leucine, iso-leucine and valine.

Dr Eva Hörler, of the University of Mainz, and colleagues, said it increased the average lifespan of the mice by 12% and boosted their fitness and co-ordination.

They wrote in their paper, published in Cell Metabolism: "Our study offers a rationale for deeply exploring the role of amino acids in prevention and control of age-related disorders in humans."

"I always take a protein shake before training and a shake, consisting of whey and amino-acids including leucine plus a carbohydrate e.g. banana or bread, after..."
More nonpolar R-groups

- Branched chain (aliphatic)...

Valine, Val, V  Leucine, Leu, L  Isoleucine, Ile, I

More nonpolar R-groups

- Branched chain (aliphatic)...

Valine, Val, V  Leucine, Leu, L  Isoleucine, Ile, I

- ... and an unusual cyclic amino acid

Uncharged polar R-groups

Serine, Ser, S  Threonine, Thr, T  Tyrosine, Tyr, Y

Asparagine, Asn, N  Glutamine, Gln, Q

Acidic (negatively charged) polar R-groups

- Similarly structured (and therefore similarly named) to Asn and Gln

Aspartic acid, Asp, D  Glutamic acid, Glu, E

- The carboxylate (COO\(^{-}\) group) provides the negative charge as it is deprotonated in solution

- NB, the alternative names Aspartate and Glutamate are sometimes used for these amino acids
**Not just for making proteins**

- Glutamate (E), Aspartate (D) and Glycine (G) are **neurotransmitters**
- Tryptophan (W) is a precursor for **melatonin** and **serotonin**
- Tyrosine (Y) is a precursor for **noradrenalin** and **adrenalin**
- Cysteine (C), Glycine (G) and Glutamate (E) make **glutathione** (important antioxidant)
- Aspartate (D)/Phenylalanine (F) dipeptide (plus methyl group) = **aspartame** artificial sweetener

**Summary table**

<table>
<thead>
<tr>
<th>AMINO ACID</th>
<th>SIDE CHAIN</th>
<th>AMINO ACID</th>
<th>SIDE CHAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspartic acid</td>
<td>Asp</td>
<td>negative</td>
<td>Alanine</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>Glu</td>
<td>negative</td>
<td>Glycine</td>
</tr>
<tr>
<td>Arginine</td>
<td>Arg</td>
<td>positive</td>
<td>Valine</td>
</tr>
<tr>
<td>Lysine</td>
<td>Lys</td>
<td>positive</td>
<td>Leucine</td>
</tr>
<tr>
<td>Histidine</td>
<td>His</td>
<td>positive</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>Asparagine</td>
<td>Asn</td>
<td>uncharged polar</td>
<td>Proline</td>
</tr>
<tr>
<td>Glutamine</td>
<td>Gin</td>
<td>uncharged polar</td>
<td>Phenylalanine</td>
</tr>
<tr>
<td>Serine</td>
<td>Ser</td>
<td>uncharged polar</td>
<td>Methionine</td>
</tr>
<tr>
<td>Threonine</td>
<td>Thr</td>
<td>uncharged polar</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>Tyr</td>
<td>uncharged polar</td>
<td>Cysteine</td>
</tr>
</tbody>
</table>

**Polar amino acids**

**Nonpolar amino acids**

- You may see different textbooks with different classifications (e.g. Miesfeld & McEvoy – Biochemistry!) or further subgroupings
- Cys is sometimes classed as polar (hydrophilic) because it is a weak acid
Names to letters

Table 4.3 THE DAY Hoff SINGLE-LETTER AMINO ACID CODE

<table>
<thead>
<tr>
<th>Amino acid (in protein)</th>
<th>Three letter abbreviation</th>
<th>Single-letter abbreviation</th>
<th>Membrane for single-letter abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine</td>
<td>Gly</td>
<td>G</td>
<td>Glycine</td>
</tr>
<tr>
<td>Alanine</td>
<td>Ala</td>
<td>A</td>
<td>Alanine</td>
</tr>
<tr>
<td>Valine</td>
<td>Val</td>
<td>V</td>
<td>Valine</td>
</tr>
<tr>
<td>Leucine</td>
<td>Leu</td>
<td>L</td>
<td>Leucine</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Ile</td>
<td>I</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>Proline</td>
<td>Pro</td>
<td>P</td>
<td>Proline</td>
</tr>
<tr>
<td>Methionine</td>
<td>Met</td>
<td>M</td>
<td>Methionine</td>
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<tr>
<td>Phenylalanine</td>
<td>Phe</td>
<td>F</td>
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<tr>
<td>Tyrosine</td>
<td>Tyr</td>
<td>Y</td>
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<td>Tryptophan</td>
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<td>W</td>
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6 have a unique first letter – CHIMSV
5 were assigned their first letter as they are more abundant – AGLPY
4 are phonetic(ish)
- aRginine
- Fenylalanine
- tYrosine
- tWyptophan

Last 5 are more random
- asparDic acid
- asparagiNe
- gluE (or glutamEek acid)
- Q-tamine
- Lysine is K

Structural features to codes

- If given a structure – look at the R group
- If you’re ON pole position you like being hydroPHILIC
- COO– – being GluED to revising is negative so listen and
- NH+ – HRK the positive sign
- Other hydrophilic amino acids STYNQ
- OH – STYle is OH so important
- Amides are a (C=O) – they’re Not Quite the acids with similar names N
- If you’re scared you’re not getting ON (pretty much just C and H) – it’s hydroPHOBIC
- Branch out (aliphatic) and you’ll be LiVing longer
- but C Me about sulphur and your
- GAPs in knowledge can be filled, and before you know it
- PheW – you can remember all 20

Joining amino acids together

A condensation reaction occurs to join the Carboxyl group of one amino acid to the Amino group of the next
During translation of an mRNA, ribosomes provide the site for the condensation reaction (next lecture)
The peptide bond is not easily broken
Requires a protease or extreme conditions

Polypeptides have a sequence of residues
The sequence is always described N to C
To estimate the molecular mass (in Daltons, Da) of a protein multiply no. of residues by 110 (approx Mr of aa residue)
eg 400 amino acid residues ~44,000 Da (44 kDa)
Recap

- 20 kinds of amino acids used in protein synthesis
- Amino acids are also precursors to other useful molecules
- Always the L-stereoisomer (except Glycine)
- Classed according to R-group
- Non-polar
- Polar (acidic, basic, uncharged)
- Amino acids join together via peptide bonds to form polypeptide chains
- Peptide bond formation is a condensation reaction (leaves a “residue”)
- The linear sequence of the protein is “read” N–C terminal
- This is also termed the primary structure

**Primary**  |  **Secondary**  |  **Tertiary**  |  **Quaternary**
---|---|---|---
(Sequence)  | (Local)  | (whole protein)  | (Different proteins)