COURSE TITLE: Biomolecules and Microbial Metabolism

Course Code: 24MICCC2

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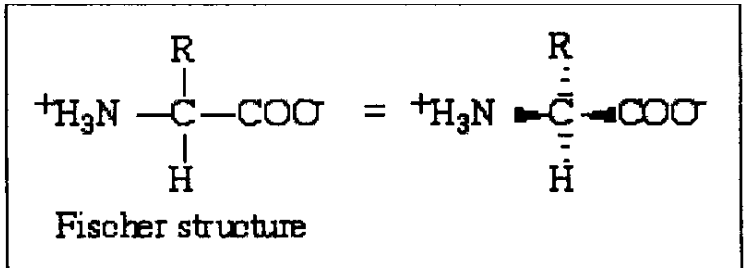
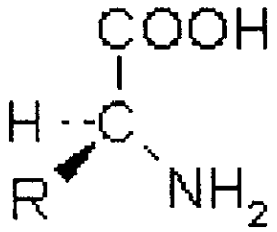
Nomenclature and Classification, structure and Biological Functions of Amino Acids

- The amino acids - building blocks for proteins - nearly all proteins studied are made from the twenty "standard" amino acids.
- Other amino acids are also found in proteins, but most arise by modification from the twenty after they have been incorporated in the protein.
- All are standard amino acids (except for proline, an imino acid). That is they have an amino group to the carboxyl group (they are 2-amino acids).
- At neutral pH (pH =7) both the acid and amine groups will be ionized to give the so-called zwitterion form. There is no pH at which the amino acid structure will have no ionized groups

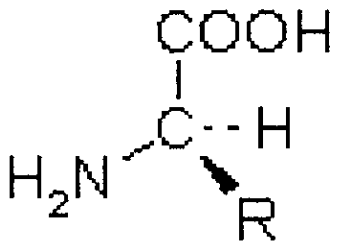


Chemistry of Amino Acids

AAs are the building blocks of proteins. They all have the basic structure shown below:



L-amino acid
CO-R-N goes anticlockwise



D-amino acid
CO-R-N goes clockwise

AAs are chiral: only the L form is found in proteins, although the D form of alanine is an important component of bacterial CWs.

All AAs are chiral except glycine. The *L/D* descriptor is an old fashioned version of the *S/R* descriptor, and almost all AAs are the (S)-isomer because the R group (not to be confused with an (R) descriptor!).

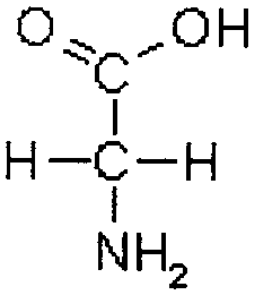
Only cysteine is an exception to this rule, because its R side group is $-CH_2SH$, which has higher priority than COOH.

The *L/D* descriptors come from the **'CO-R-N' law**: if you place the H behind the chiral centre, and count round from the COOH group, to the R group, to the NH_2 group, this goes **anticlockwise**, and for similar reason to the R/S descriptor, this means it's the L isomer. The D-isomer goes **clockwise**.

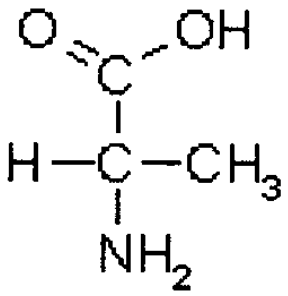
- Glycine is a very unique amino acid in that in contains a H as its side chain (rather than a C as is the case in all other amino acids).
- There are 20 (or so) amino acids, which we will discuss in groups based on their chemical properties.

The hydrophobic amino acids are-

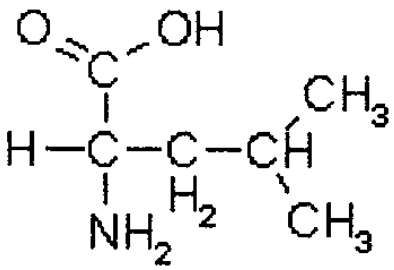
• **Aliphatic**: glycine (Gly, G), alanine (Ala, A), leucine (Leu, L), isoleucine (lle, I), valine (Val, V).



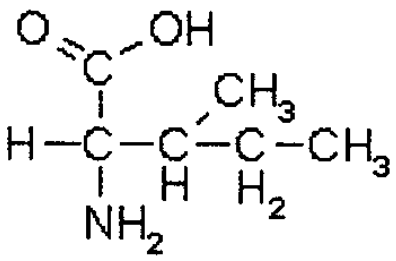
Glycine



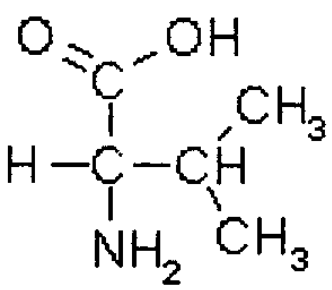
Alanine



Leucine

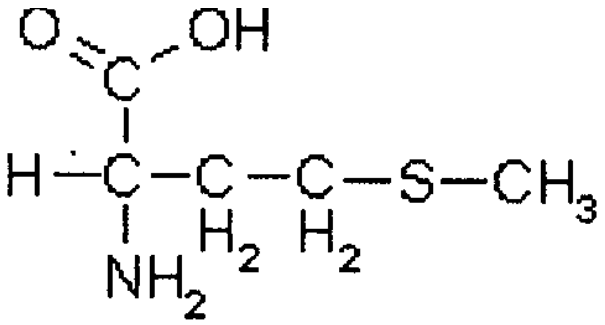


Isoleucine



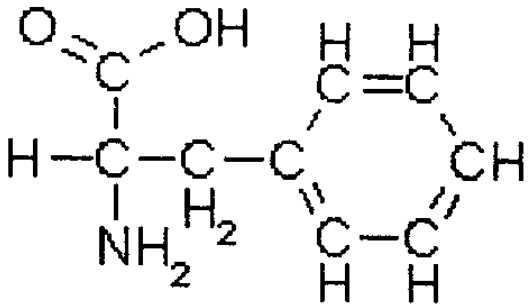
Valine

- **Sulphur containing**: methionine (Met, M

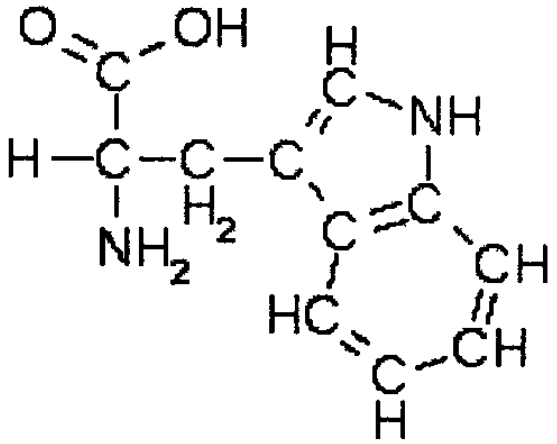


Methionine

Aromatic: phenylalanine (Phe, F), tryptophan (Trp, W).

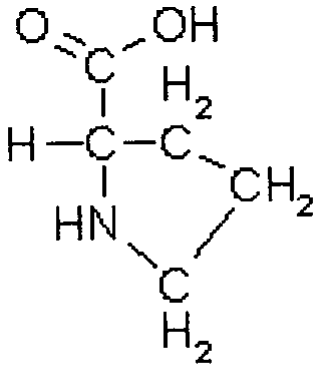


Phenylalanine



Tryptophan

Cyclic imine: proline (Pro, P). Imino acid is any molecule that contains both imine (>C=NH) and carboxyl (-C(=O)-OH) functional groups.



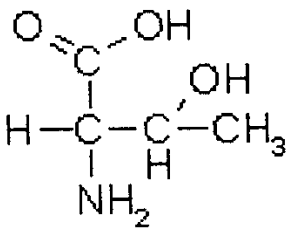
Proline

•Proline has an unusual imine ring structure (a secondary amine), where the terminal amine groups is actually incorporated into the side chain. This causes changes to the secondary structure of a protein.

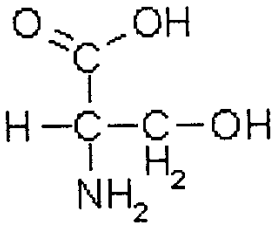
•Hydrophobic residues are often found in membrane bound proteins, and the aromatic ones contribute to protein absorbance at 280 nm, which is an important method of protein quantification.

•**Alanine is the 'don't care' amino acid**, often appearing where nothing interesting is happening!

- **The polar amino acids** are those that are not charged at physiological pH, but which are nevertheless quite polar due to their alcohol or amide groups.
- **Alcohols**: threonine (Thr, T), serine (Ser, S).

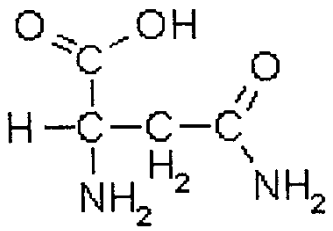


Threonine

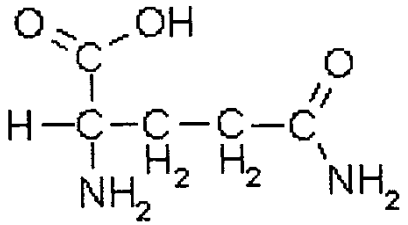


Serine

Amides : asparagine (Asn, N), glutamine (GIn, Q).

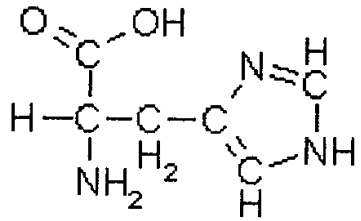


Asparagine



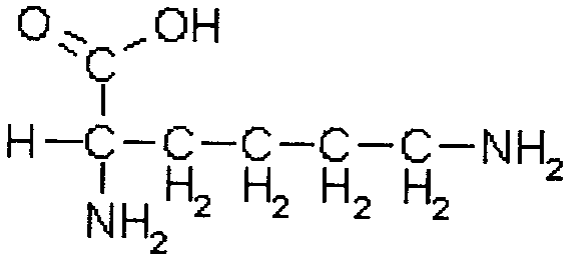
Glutamine

- **The basic amino acids** are those that can accept protons. The pKa refers to the dissociation of the proton from a **positively charged (protonated) amine group.**
- **Imidazole**: histidine (His, H, pKa of protonated form of the group -C=NH+- = 6.04).



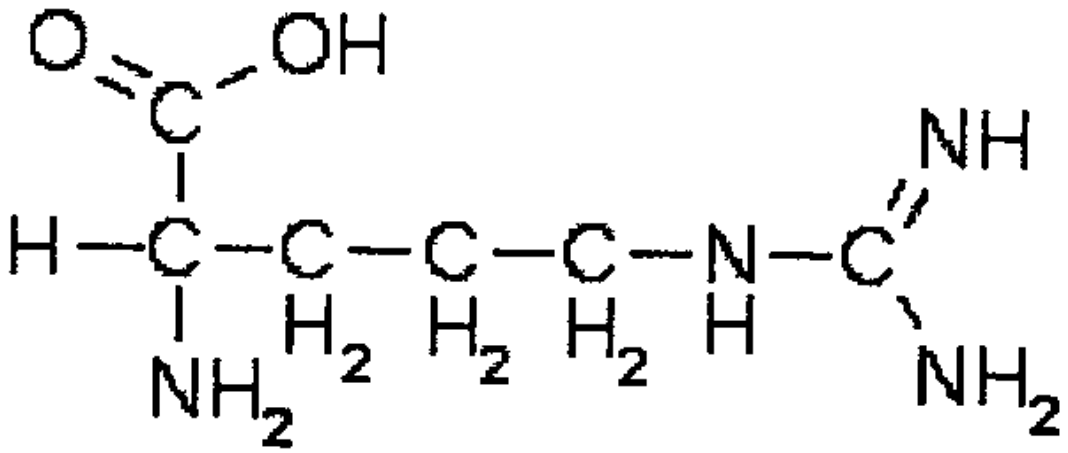
Histidine

- **Amine**: lysine (Lys, K, pKa of protonated form of terminal amine group NH3+ = 10.54).



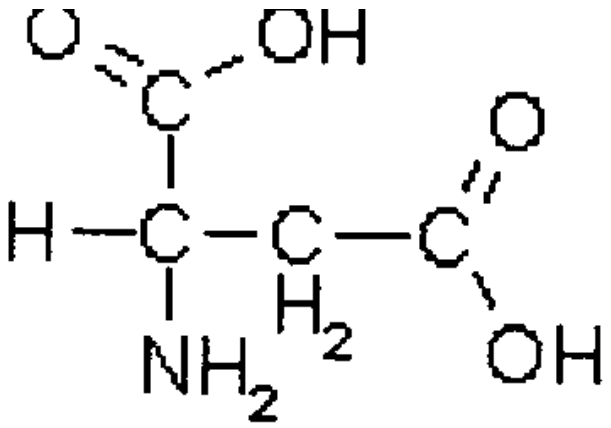
Lysine

- **Guanidinium**: arginine (Arg, R, pKa of protonated form of terminal group -C=NH2+ = 12.48).



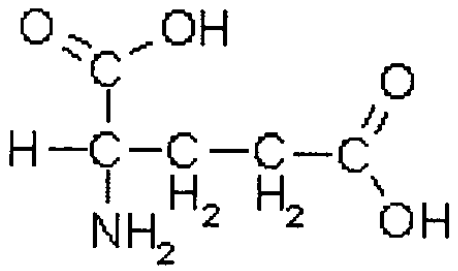
Arginine

- The **acidic amino acids** are carboxylic acids, plus an thiol (cysteine) and a phenol (tyrosine) with dissociable S-H or O-H groups:
- Aspartic acid (Asp, D, pKa of COOH group = 3.90).



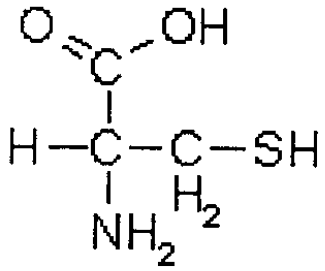
Aspartic acid

- Glutamic acid (Glu, E, pK_a of COOH group = 4.07).



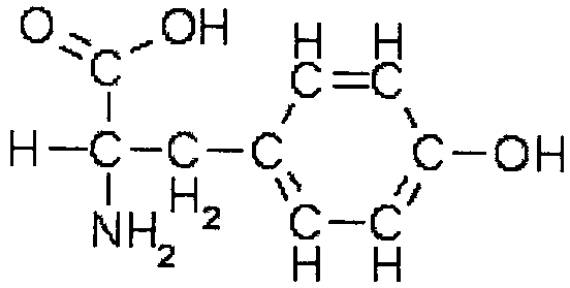
Glutamic acid

- Cysteine (Cys, C, pK_a of SH group = 8.37).



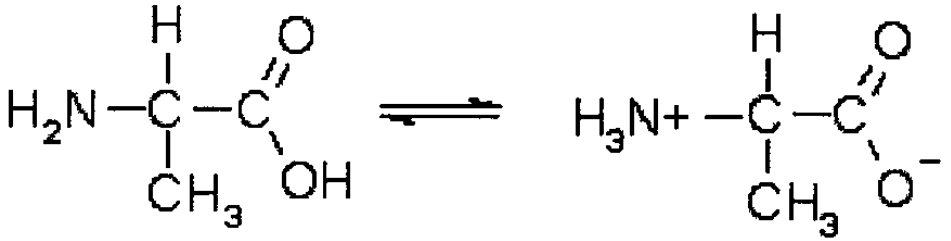
Cysteine

- Phenol: tyrosine (Tyr, Y, pK_a of OH group = 10.46).



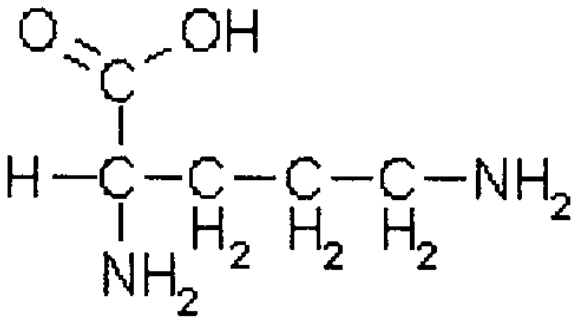
Tyrosine

- The sodium salt of glutamic acid is the flavour enhancer MSG.
- Cysteine is capable of forming a dimer: Cys-SH + Cys-SH = Cys-S-S-Cys. These disulphide bridges (confusingly known as cystine), are responsible for a lot of protein tertiary structures.
- The charged (acidic/basic) and polar amino acids are often involved in catalysis, forming covalent products with substrates.
- The terminal COOH and NH_2 groups on an amino acid (and on larger peptides and proteins) may also be charged, as have their own pKa's.
  - NH3+ has pKa of c. 9.5
  - caOH has pKa of c. 2.5
- At physiological pH, amino acids and proteins are usually charged at both ends, a *zwitterion (i*s an ion that contains two functional groups).

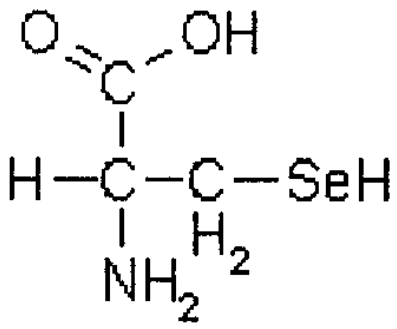


Alanine zwitterion.

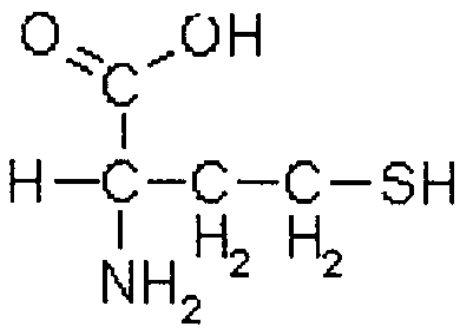
- In addition to the amino acids found in proteins, the cell also contains a number of other amino acids that are not normally found in peptides. This includes ornithine, an important intermediate in the urea cycle, **selenocysteine**, a very rare component of some proteins and **homocysteine**, an important intermediate in sulphur metabolism.



Ornithine

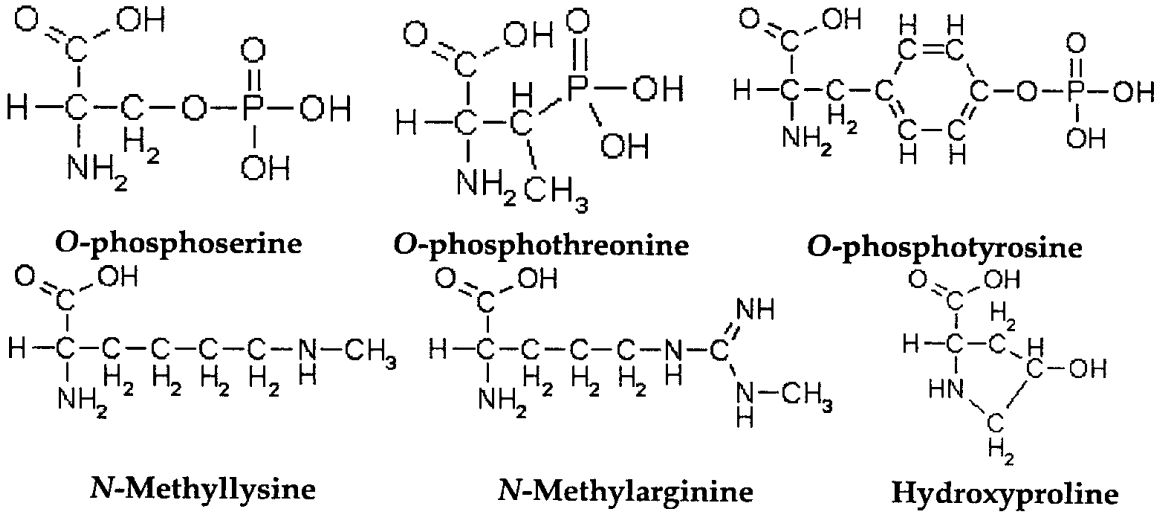


Selenocysteine

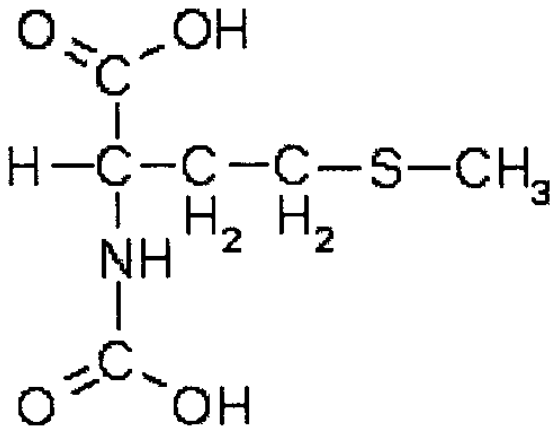


Homocysteine

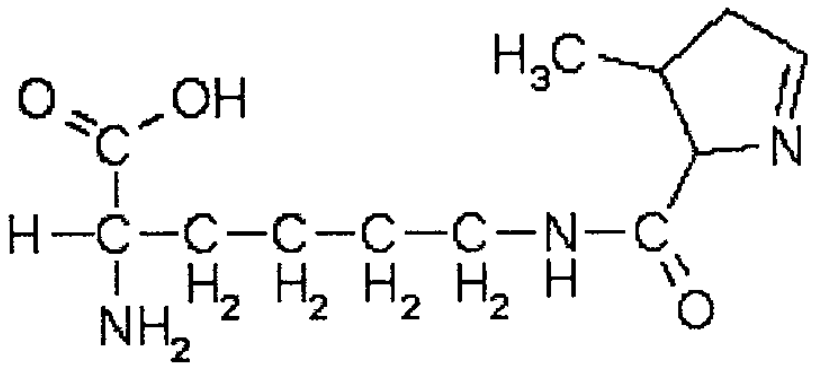
- In addition to this, many amino acids in proteins are modified after translation to incorporate phosphate groups, extra hydrogen, *etc.*
- These modified amino acid residues include the **phosphorylated alcohol amino acids (Ser, Thr, Tyr),** which are **phosphorylated by kinase enzymes**. This is a common strategy for protein regulation.
- The **histone proteins**, which regulate DNA packaging in the nucleus are themselves regulated by methylation of their arginine and lysine residues, and the characteristic triple helical structure of **collagen** is caused by its possession of many **glycine** and **hydroxyproline** (a post-translational modification of **proline**) residues.



- One final interesting amino acid modification is that found in the methanogenic Archaea. These 'bacteria' interpret the amber stop codon as the amino acid **methylpyrrolysine**, making this the **22nd** genetically encoded amino acid (the **21st being** the **N-formyl methionine** that eukaryotes use to start translating all their proteins).



***N*-formyl methionine**



Methylpyrrolysine

- All amino acids share two chemically functional groups, the **carboxyl group and the amino group**. Thus, they will share the chemical reactions of these groups familiar from organic chemistry.
- Many of these reactions are exploited in the laboratory **manipulation of amino acids, peptides, and proteins**. Note that these reactions are also common to the side chains of asp, glu (-COOH), and lys (NH_2).
- Another side-chain with important chemistry is cys (-SH).
- Biologically the most important reactions are those required for protein formation, particularly the peptide bond.