**AMINO ACIDS I**

- All 20 amino acids in pure form are white, crystalline, high-melting solids
- Amino acids act as: enzymes (catalysts), metabolic intermediates, carriers of energy and waste products and hormones.
- Amino acids are the building blocks of proteins
- Proteins are the most abundant macromolecules in living cells. May be 0.1 million different proteins in humans. Play pivotal role in almost every biological process.
- Generally, proteins composed of the 20 naturally occurring amino acids
- Only one way to link amino acids together – peptide bond
- Protein structure and function defined by sequence and type of the amino acids
- Proteins display great diversity in function and structure

- **DEFINITION:**
  
  Any organic molecule with at least one CARBOXYL group (organic acid) and at least one AMINO group (organic base)

**GENERAL STRUCTURE OF THE 20 AMINO ACIDS:**

![GENERAL STRUCTURE OF THE 20 AMINO ACIDS](Figure 3-1 Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons)

At physiological pH zwitterions – positive molecule. Dependent example:
STEREOCHEMISTRY OF AMINO ACIDS:

- Stereochemistry imparts certain characteristics to a compound.
  - Every compound has a mirror image
  - Sometimes mirror images of a molecule are superimposable in space with the original object and some are not
  - NON-superimposable mirror images = CHIRAL
    - Have no plane of symmetry
    - General rule: Carbon atom with 4 DIFFERENT atoms or groups bonded to it is chiral.
    - Other Chiral examples:
      - Hand or foot
      - Right hand is a mirror image of your left hand – note how they cannot be superimposed
  - Superimposable mirror images = ACHIRAL
    - Achiral examples:
      - Two plain coffee mugs
      - You can turn the mirror image of the plain mug in space to make it superimposable.

- Each amino acid (like your hand) also has a mirror image.

These images are NOT superimposable; No matter how you turn the mirror image in space you won’t regain the original. Note no plane of symmetry.
These are called ENANTIOMERS = non-superimposable mirror images
- Most amino acids (except glycine) have four different groups attached to the a-carbon and therefore are **chiral or have a chiral center**.
- For glycine, R is hydrogen. Therefore, the mirror images ARE superimposable and NOT chiral. A plane of symmetry exists.
- **Each amino acid except glycine has 2 ENANTIOMERS**
- The enantiomers are classified based on the ability to rotate polarized light – termed optically active.
  - Rotate light in either (+) or (-) direction
  - Called **D or L enantiomers** (again non-superimposable mirror images)
  - Both D and L amino acids exist in nature but **only L amino acids are used as building blocks for proteins**.
  - D-amino acids are found in a few rare bacteria in the cell walls.

**EXAMPLE 1:**
- Part of aging process may include the isomerization of the amino acid **aspartic acid (aspartate)** from L → D in proteins in teeth and eyes.
- Isomerized proteins are less biologically active
- Scientists are identifying the enzymes that change D back to L to try and slow the aging process.

**EXAMPLE 2: Isomer Isolation Leads Researchers To More Effective Psychiatric Drugs**
In an effort to increase effectiveness and reduce dosing, side effects, and potential drug interactions, pharmacologists are isolating and purifying specific forms of psychiatric drugs.

Mirror image (or racemic) isomers are labeled as "right handed" (termed "R-" or dex-) or "left handed" (termed "S-" or "levo-"). Because the different isomers are difficult to separate, the FDA allows drug companies to include both in medicines, as long as the less-functional isomer is not harmful.

**Lexapro animation:** [http://www.lexapro.com/english/about_lexapro/isomer_animation.aspx](http://www.lexapro.com/english/about_lexapro/isomer_animation.aspx)
**Successes:**

- **Dexmethylphenidate** (Focalin) (Treatment of ADHD)
- **Citalopram** (Celexa) (SSRI; Treatment of depression)
  - S-citalopram under the generic name of escitalopram
  - Escitalopram is nearly four times more potent as an SSRI than the mixture present in the parent compound citalopram
  - Escitalopram has better side-effect and drug-interaction profiles.

**Failure:**

- **Prozac** = R is the more effective enantiomer. S is thought to be potentially dangerous.

Isolating R-fluoxetine could yield a more effective drug with fewer side effects.

However, late in 2000, Eli Lilly and Company halted development of the R-isomer of fluoxetine (Prozac) after Stage III clinical trials revealed unexpected cardiac side effects (*Psychiatric News*, December 1, 2000). The company had hoped that R-fluoxetine would replace fluoxetine, which was facing imminent expiration of its patent protection.

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**CLASSIFICATION AND CHEMICAL CHARACTERISTICS OF EACH AMINO ACID:**

- The “R” group side chains on amino acids are VERY important.
  - Determine the properties of the amino acid itself
  - Determine the properties of the proteins that contain those amino acids; Dictate what a protein can and cannot do and how it folds.
  - Important to remember that biomolecules have three dimensions. It’s this feature that dictates which reactions can take place in a cell.

- All 20 amino acids have both three letter and one letter abbreviations (Table 3.1)

  - **Table 3.1**
    | Name          | One-Letter Abbreviation | Three-Letter Abbreviation |
    |---------------|-------------------------|---------------------------|
    | Glycine       | G                       | Gly                       |
    | Alanine       | A                       | Ala                       |
    | Valine        | V                       | Val                       |
    | Leucine       | L                       | Leu                       |
    | Isoleucine    | I                       | Ile                       |
    | Methionine    | M                       | Met                       |
    | Phenylalanine | F                       | Phe                       |
    | Proline       | P                       | Pro                       |
    | Serine        | S                       | Ser                       |
    | Threonine     | T                       | Thr                       |
    | Cysteine      | C                       | Cys                       |
    | Asparagine    | N                       | Asn                       |
    | Glutamine     | Q                       | Gln                       |
    | Tyrosine      | Y                       | Tyr                       |
    | Tryptophan    | W                       | Trp                       |
    | Aspartate     | D                       | Asp                       |
    | Glutamate     | E                       | Glu                       |
    | Histidine     | H                       | His                       |
    | Lysine        | K                       | Lys                       |
    | Arginine      | R                       | Arg                       |

*Table 3-1 Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons*
- You are responsible for knowing the three letter and one letter codes and well as the structures of all 20 amino acids. (Table 3.1)
- **Groups classified by different properties**
  - I: Non-polar side chains (hydrophobic)
  - II: Polar, uncharged side chains
  - III: Acidic side chains
  - IV: Basic side chains
- We’ll use the groupings in Table 3.5

**GROUP I: NON-POLAR (HYDROPHOBIC) SIDE CHAINS**
- Side chains of Group I aa’s are mainly hydrocarbons – very unreactive amino acids
- 2 subgroups: Aliphatic hydrocarbons & Aromatic hydrocarbons (have benzene rings)
- These amino acids will tend to be buried (away from water) in 3-D structure of proteins
- Non-polar character

1) **ALIPHATIC HYDROCARBONS**
   a. **Glycine (G, Gly)**
      - i. R group is hydrogen
      - ii. Found in flexible parts of proteins
      - iii. Not chiral
      - iv. Can be modified by addition of a fatty acid (myristate – 14 Carbon)
   b. **Alanine (A, Ala)**
      - i. The model amino acid
      - ii. R group is –CH₃ (methyl group)
   c. **Valine (V, Val)**
   Leucine (L, Leu)
   Isoleucine (I, Ile)
      - Extended aliphatic chains
      - Can be branched
d. Methionine (M, Met)
   i. Contains sulfur
   ii. Can interact and bind with metal ions
   iii. Often found in metalloproteins

e. Proline (P, Pro)
   i. Only imino acid
   ii. Affects protein folding
   iii. Often found at bends in protein 3-D structures
   iv. Hydroxylation of proline important for the structure of collagen

2) AROMATIC HYDROCARBONS

a. Phenylalanine (F, Phe) and Tryptophan (W, Trp)
   i. Fluorescent
   ii. UV absorbing at 250-300 nm – can be useful to identify proteins in a mixture
   iii. Tryptophan is converted to serotonin (5-hydroxytryptamine)
      • Serotonin has a sedative effect – gives a pleasant feeling
      • Very low levels of serotonin associated with depression
      • Extremely high levels produce a manic state