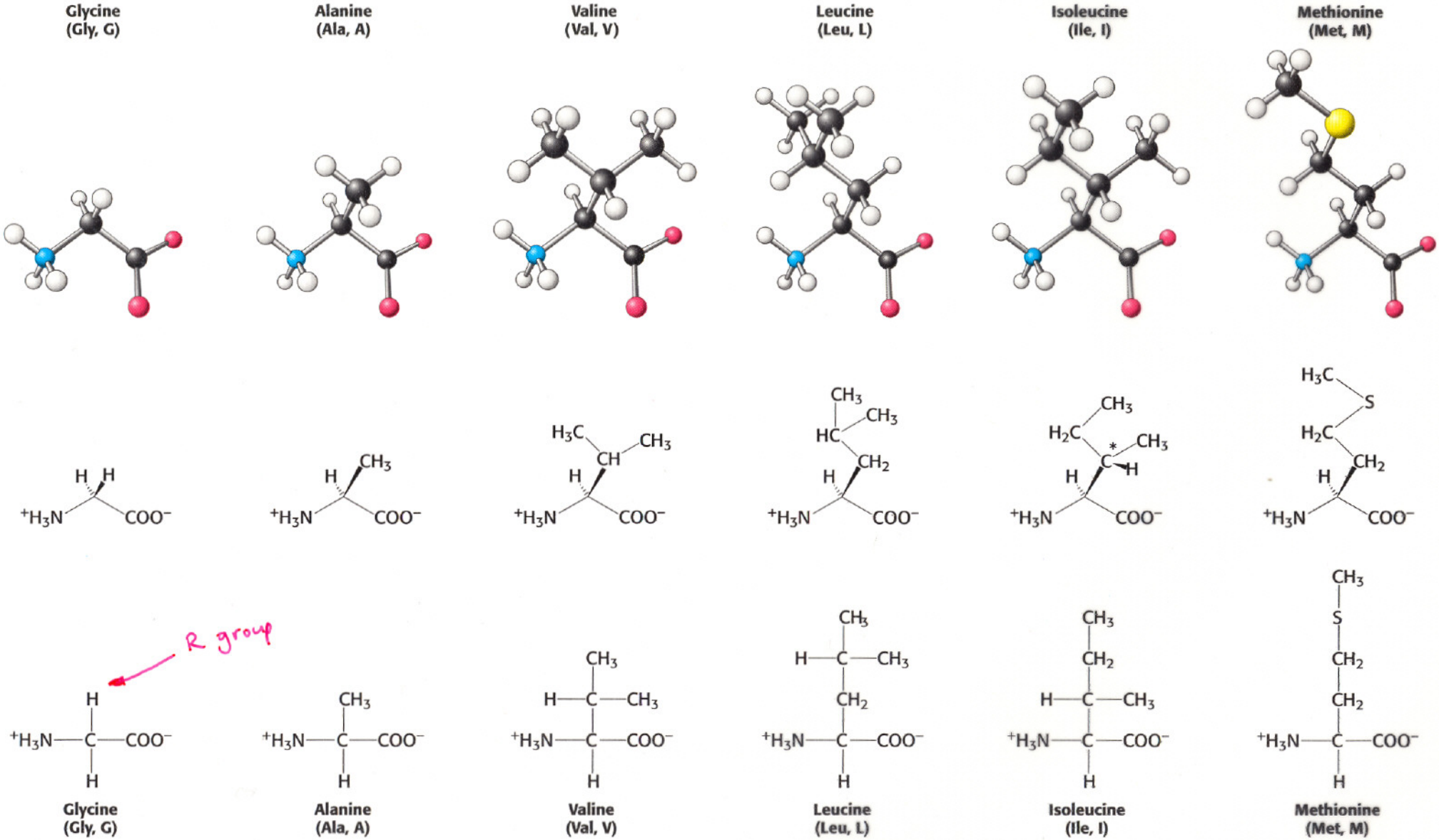


Figure 3-7, 3-8
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

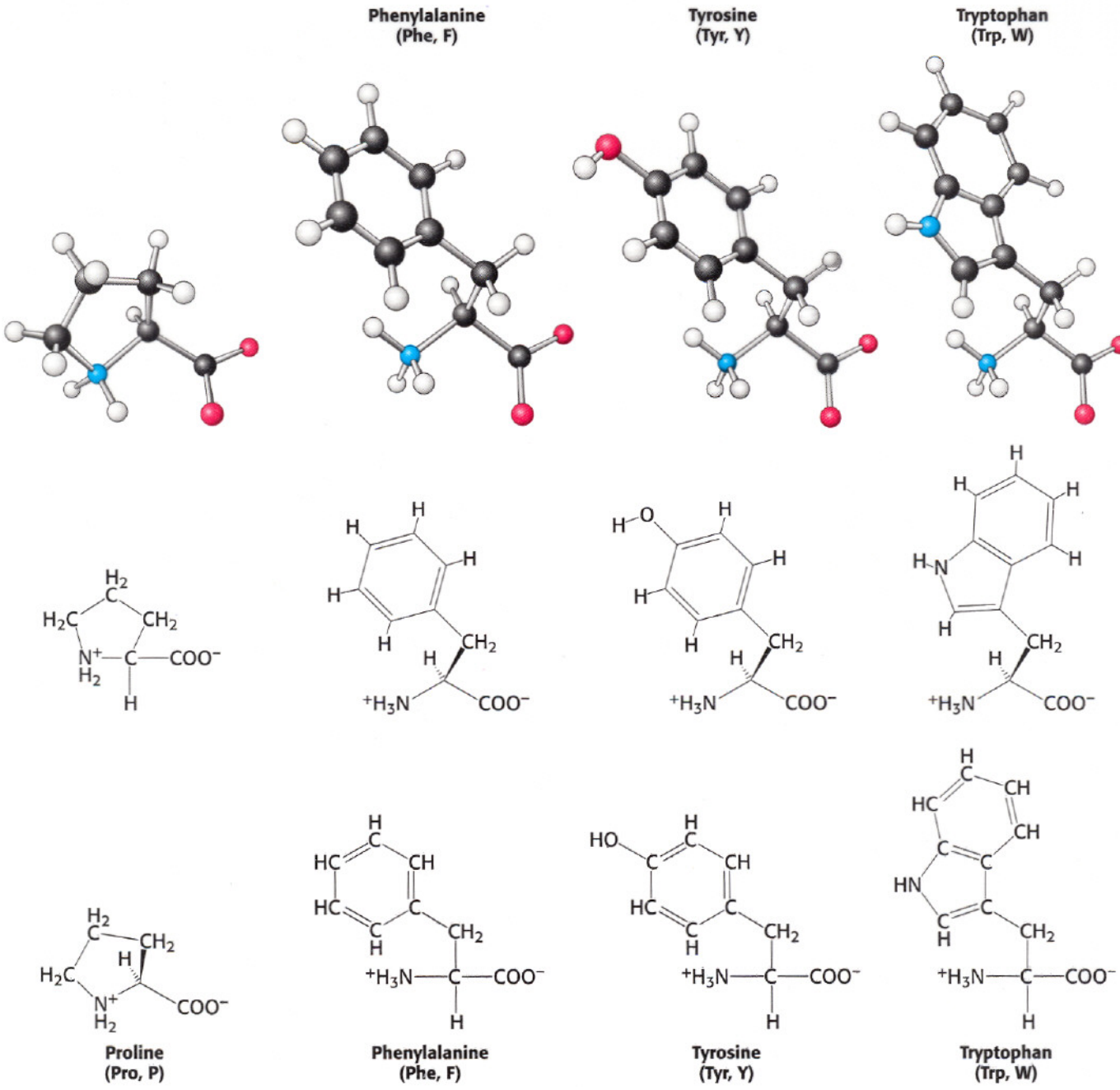
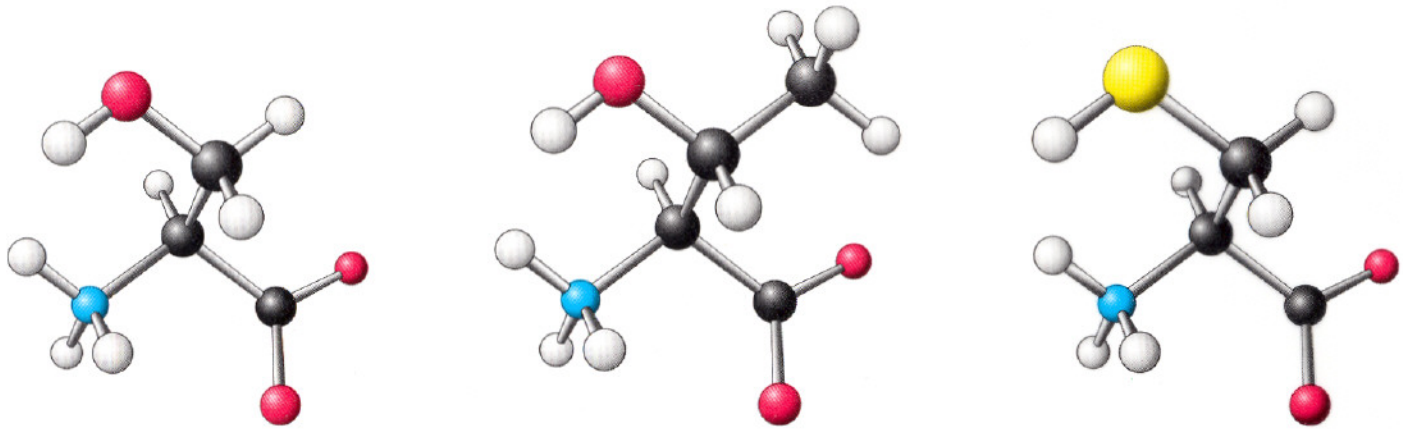
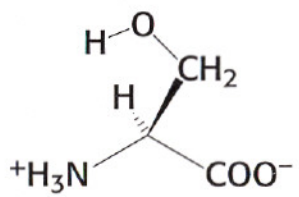


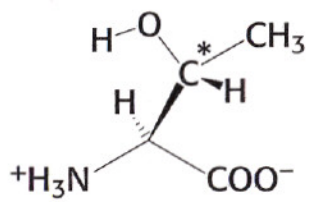
Figure 3-9, 3-10
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

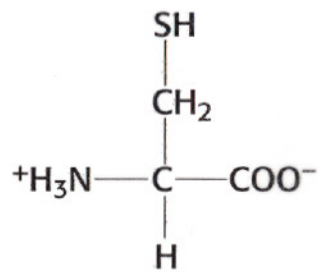
Serine
(Ser, S)

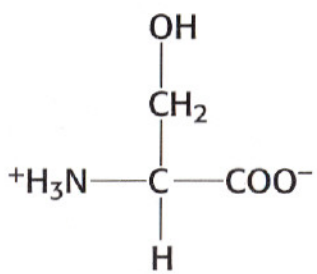
Threonine
(Thr, T)

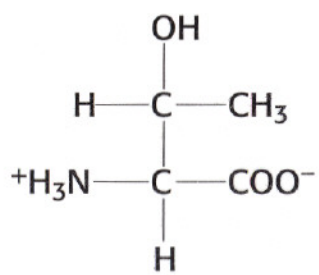


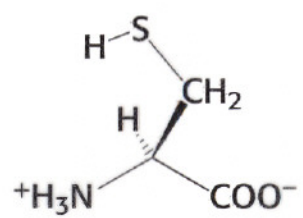












Serine
(Ser, S)

Threonine
(Thr, T)

Cysteine
(Cys, C)

Figure 3-12, 3-13
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

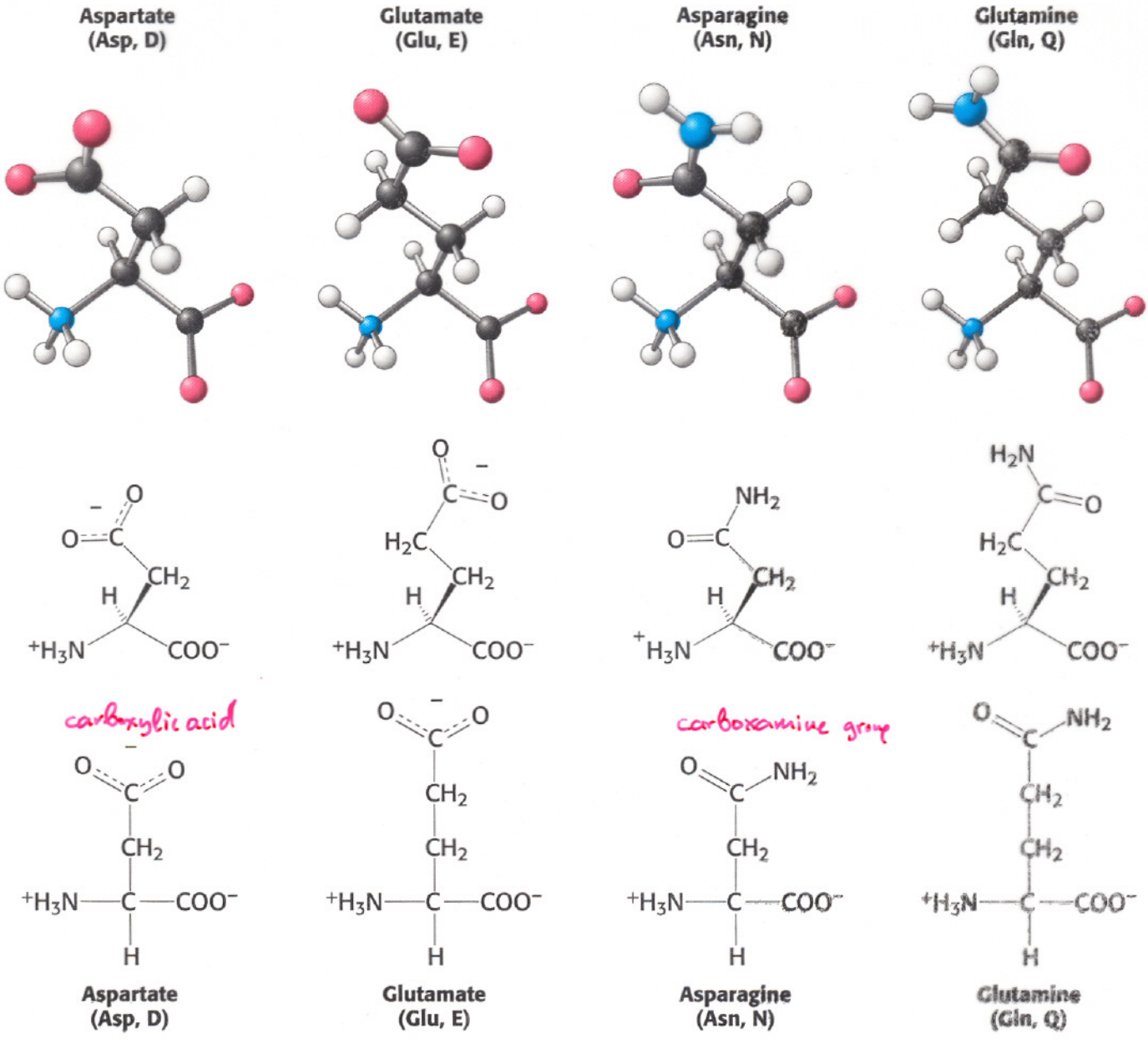
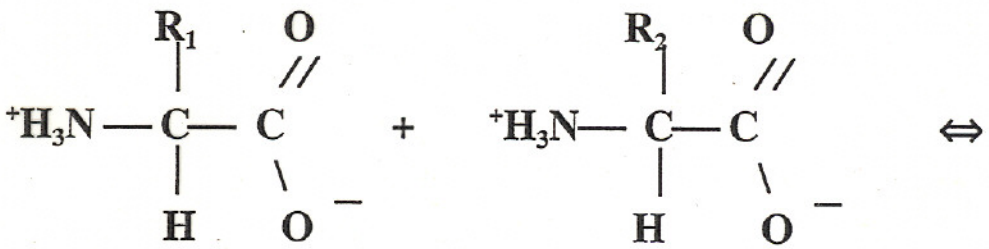
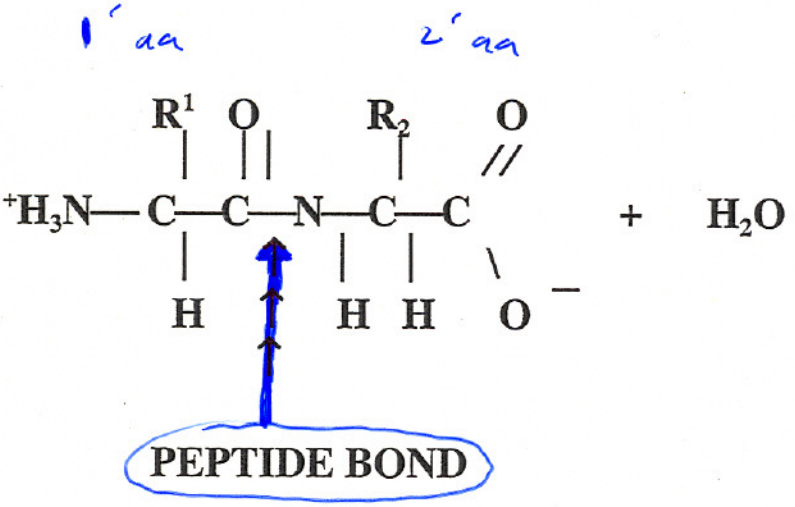


Figure 3-16
Stryer, Tymoczko, & Berg, BIOCHEMISTRY, Fifth Edition.

AMINO ACIDS ARE LINKED BY PEPTIDE BONDS TO FORM POLYPEPTIDE CHAINS

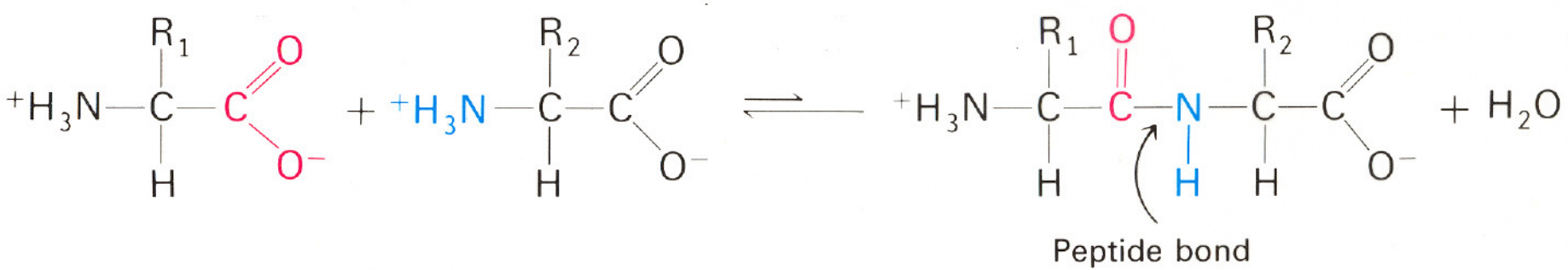
- In proteins, the a-carboxyl group of one amino acid is joined to the a-amino group of another amino acid by a peptide bond

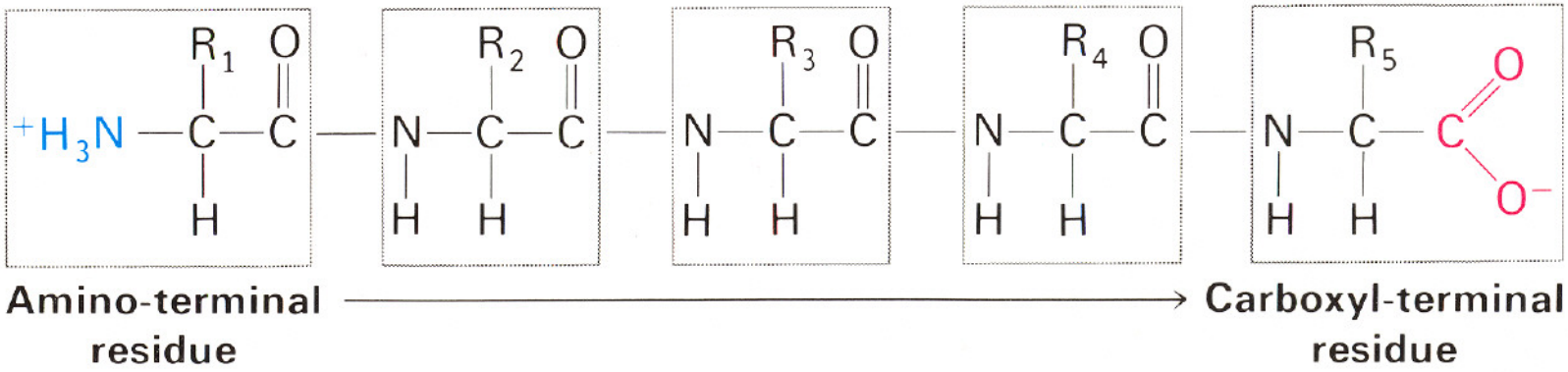




- Many amino acids joined by peptide bonds form a POLYPEPTIDE CHAIN

- RESIDUE: An amino acid unit in a polypeptide





Figures 2-20 and 2-21, page 24

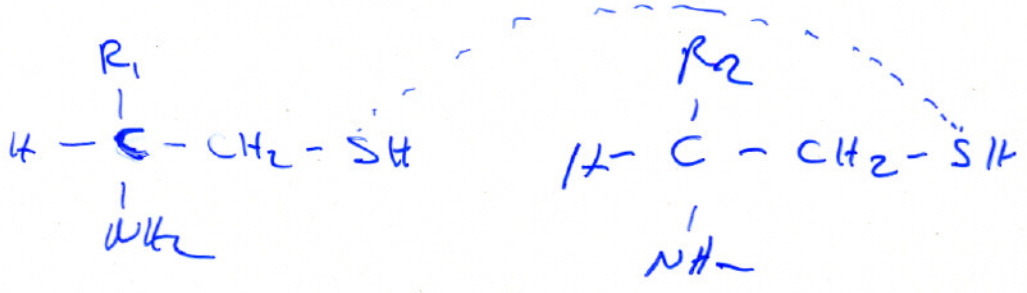
- **A POLYPEPTIDE CHAIN HAS DIRECTION: The amino end is taken to be the beginning of a polypeptide chain and the carboxyl end the end**

NH_2 – Ala — Gly — Trp – COOH NH_2 – Trp — Gly — Ala – COOH

- **The overall molecular weight (MW) of an amino acid is 110**
  - **Molecular weight of a protein = # aa residues x 110**
  - **Mass of a protein. Unit: Dalton (d) or Kilodalton (kd)**
    - **DALTON: A unit of mass very nearly equal to that of a hydrogen bond atom.**

- **Some proteins contain disulfide bonds.**
  - **DISULFIDE BONDS (or BRIDGE, — S — S —): A convalent bond formed from the sulfhydryl groups (— SH) of two cysteine residues of a polypeptide chain**

- **Intracellular proteins usually lack disulfide bonds, whereas extracellular proteins contain several.**



PROTEINS HAVE UNIQUE AMINO ACID SEQUENCES THAT ARE SPECIFIED BY GENES.

In 1953, Fredrick Sanger determined the amino acid sequence of insulin, a protein hormone, showing for the first time that a protein has a precisely defined amino acid sequence.

Insulin consists only of L amino acids in peptide bonds between α- amino and α- carboxyl groups.

THE COMPLETE SEQUENCES OF MORE THAN 10,0000 PROTEINS ARE NOW KNOWN.

Other studies conducted in the late 1950s and early 1960s revealed that the amino acid sequences of proteins are genetically determined (amino acid sequences in proteins are determined by nucleotide sequences in DNA)

Amino acid sequences in proteins are important for many reasons:

1. **Knowledge of the sequence of a protein is very helpful, indeed usually essential, in elucidating its mechanism of action**

2. **Analyses of relations between amino acid sequences and three- dimensional structures of proteins are uncovering the rules that govern the folding of polypeptide chains**

3. **Alternations in amino acid sequence can produce abnormal function and disease (e.g. sickle cell anemia, cystic fibrosis)**

4. **The sequence of a protein reveals much about its evolutionary history. Molecular events in evolution can be traced from amino acid sequences.**

THE PEPTIDE UNIT IS RIGID AND PLANAR

- **Amino acid sequences are important because they specify the conformation of proteins**

- **Proteins function arises from conformation, which is the three- dimensional arrangement of atoms in a structure**

- **The peptide unit is rigid and planar. The bond between the carbonyl carbon atom and the nitrogen atom of the peptide unit is not free to rotate because this link has a double bond character**

- **Proteins can fold in many different ways due to the freedom of rotation on either side of the peptide unit**

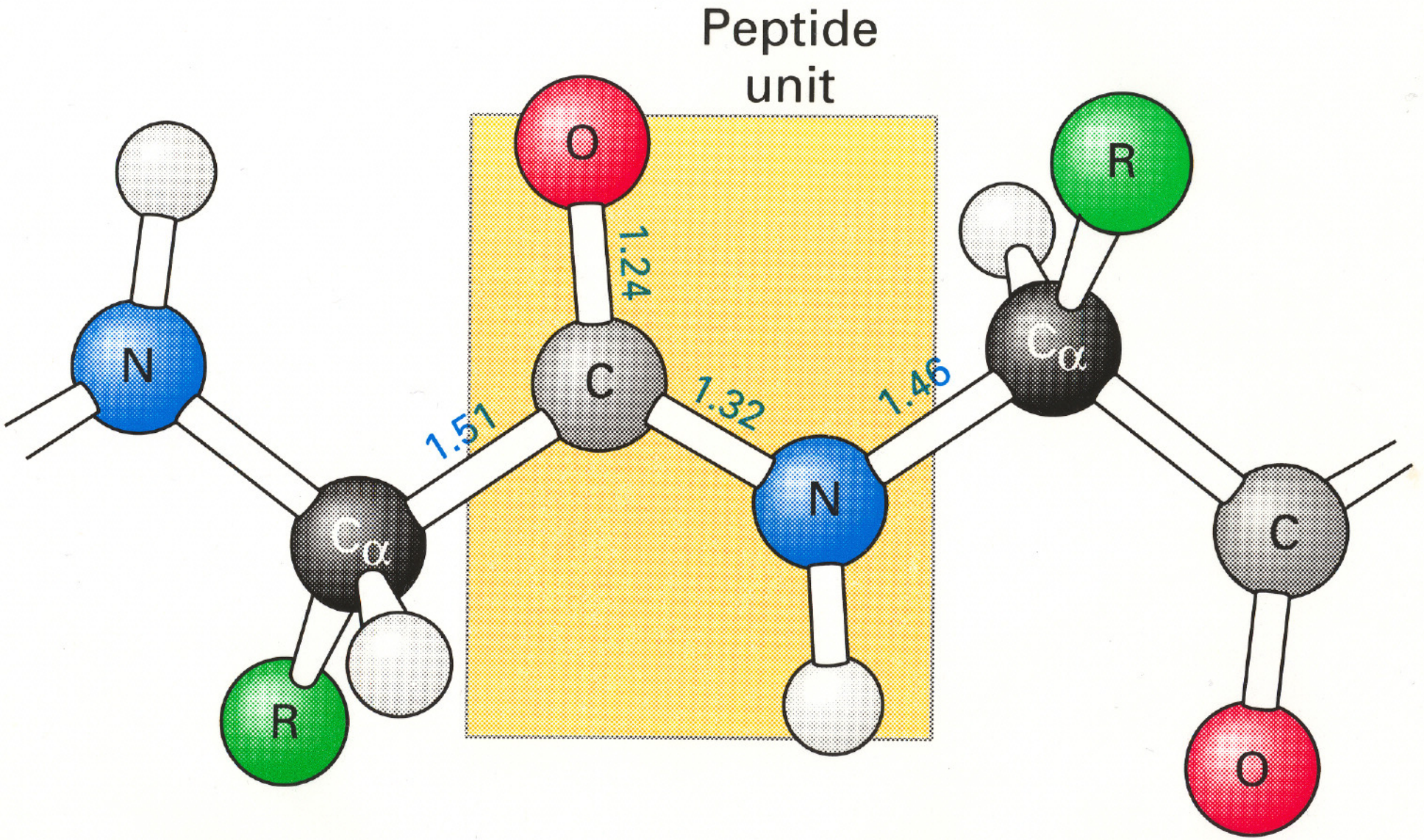


Figure 2-28, page 27

Figure 2-30, page 28

THERE ARE FOUR BASIC LEVELS OF STRUCTURE IN PROTEIN ARCHITECTURE

Four levels of structure are frequently cited in discussions of protein architecture:

1. **Primary structure is the amino acid sequence**

2. **Secondary structure refers to the spanial arrangement of amino acid residues that are near on another in the linear sequence. The α-helix and β strand are elements of secondary structure**

3. **Tertiary structure refers to the spatial arrangement of amino acid residues that are far apart in the linear sequence and to the pattern of the disulfide bonds**

4. **Quaternary structure, (only for proteins containing more than one polypeptide chain, subunits) refers to the spatial arrangement of subunits and the nature of their contacts**

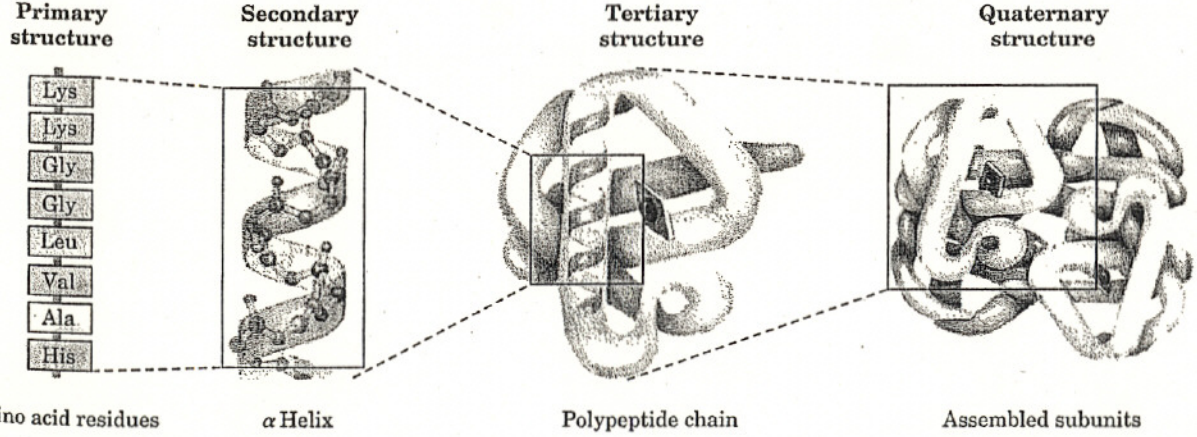
Studies of protein conformation, function, and evolution have revealed the importance of two other levels of organization:

1. **Supersecondary structure, which refers to cluster of secondary structure (e.g. βαβ motif)**

2. **Domains which refer to compact regions that my be joined by a flexible segment of polypeptide chain, like pearls on a string (100-400 amino acid residues)**

figure 5–16

Levels of structure in proteins. The *primary structure* consists of a sequence of amino acids linked together by peptide bonds and includes any disulfide bonds. The resulting polypeptide can be coiled into units of *secondary structure,* such as an α helix. The helix is a part of the *tertiary structure* of the folded polypeptide, which is itself one of the subunits that make up the *quaternary structure* of the multisubunit protein, in this case hemoglobin.



Chapter 1 / Handout 1

BIOCHEMICAL CONNECTIONS

The Second Law and Living Organisms

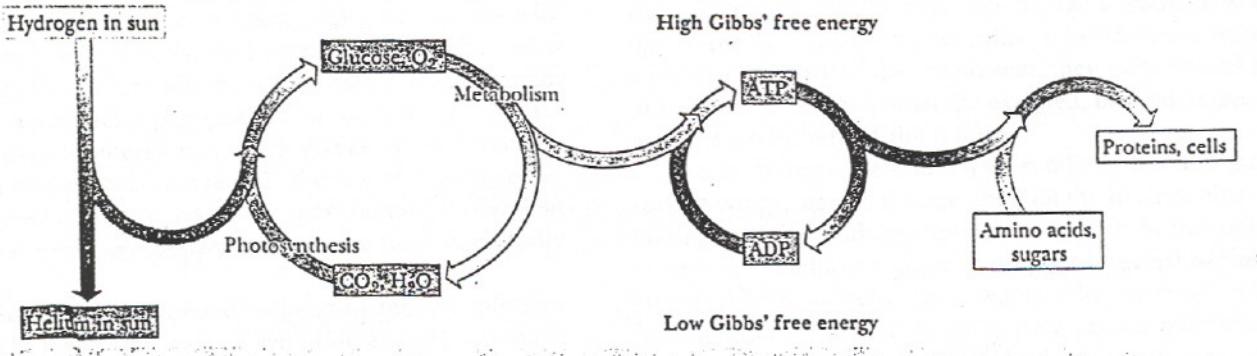
Gibbs' free energy, ΔG, is perhaps the most suitable way to measure energy changes in living systems because it measures *the energy available to do work at constant temperature and pressure,* which describes the living state. Even cold-blooded organisms are at constant temperature and pressure at any given point in time; any temperature and pressure changes are slow enough not to affect measurements of ΔG.

SPONTANEITY AND REVERSIBILITY The concept of spontaneity can be confusing, but it merely means that a reaction can occur without added energy. This is similar to water held behind a dam at the top of a hill, which has the potential energy to flow downhill, but it will not do so unless someone opens the dam. Because water only flows downhill, that is the direction with a negative value of the free energy change ($-\Delta G$); pumping water uphill is nonspontaneous (requires energy) and has a positive value of the free energy change ($+\Delta G$). If the free energy change is only 1 kcal mol^{-1} (about 4 kJ mol^{-1}) in either direction, then the reaction is considered to be freely reversible. The reaction can readily go in either direction. If one adds reactants or removes products, the reaction shifts to the right; if one removes reactants or adds products, the reaction shifts to the left. This is a key aspect of a number of metabolic pathways; many reactions in the middle of the pathway are likely to be freely reversible. This means that the same enzymes can be used whether the pathway is in the process of breaking down a substance or of forming the substance. In reversible metabolic pathways, it is often just the reactions at the ends that are irreversible, and these reactions can be turned on or off to turn the whole pathway on or off or even to reverse it.

DRIVING ENDERGONIC REACTIONS Reactions can sometimes be coupled together. This occurs when the phosphorylation of glucose is coupled to the hydrolysis of one phosphate group of ATP. Of course, there are not really two reactions going on, the enzyme merely transfers the phosphate from the ATP directly to the glucose (see Section 12.10). We can think of the phosphorylation of glucose and the hydrolysis of ATP as two parts of the same reaction. We can then add them together to determine the overall energy change and make sure that overall it is exergonic.

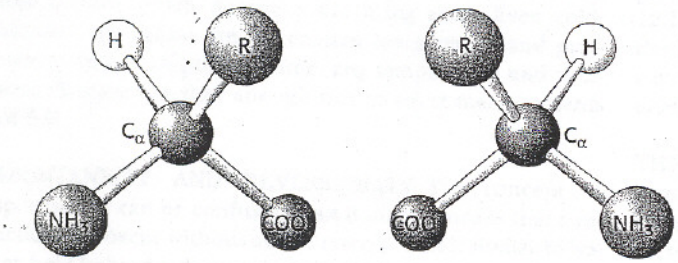
THE SECOND LAW AND EVOLUTION According to the second law, the universe is constantly becoming more random. This statement is consistent with the fact that the universe continues to expand rapidly. Many who oppose the teaching of evolution frequently argue that life violates the second law, since staying alive requires that the body *not* become random; it takes energy to maintain the ordered state. This is not a valid argument because the energy necessary to maintain the order of a human body comes at the expense of making the universe become more random. We see this every day, as we burn fuels to have the energy to run machines to plow fields and plant and harvest crops, as well as to cook or prepare our food so that we can eat.

Some have extended this second law argument to contend that life could never have arisen from inert materials, but experiments like the Urey experiment (Section 1.2) have resulted in the synthesis of amino acids and other biomolecules. Other scientists have also been able to get these monomers, either amino acids or nucleotides, to combine spontaneously into relatively large polymers. These reactions certainly require energy, but they do so at the expense of a more random overall universe.



The synthesis of glucose and other sugars in plants, the production of ATP from ADP, and the elaboration of proteins and other biological molecules are all processes in which the Gibbs' free energy of the system must increase. They occur only through coupling to other processes in which the Gibb's free energy decreases by an even larger amount. There is a local decrease in entropy at the expense of higher entropy of the universe.

CHAPTER 3 / Handout 1



L isomer D isomer

FIGURE 3.4 The L and D isomers of amino acids. R refers to the side chain. The L and D isomers are mirror images of each other.

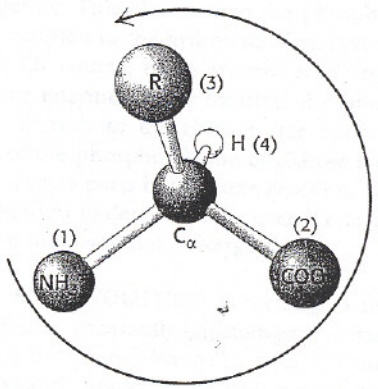


FIGURE 3.5 Only L amino acids are found in proteins. Almost all L amino acids have an *S* absolute configuration (from the Latin *sinister* meaning "left"). The counterclockwise direction of the arrow from highest- to lowest-priority substituents indicates that the chiral center is of the *S* configuration.

BIOCHEMISTRY IN CONTEXT

Why Are Proteins Made of 20 L-Amino Acids?

The almost exclusive use of L-amino acids rather than D-amino acids in proteins prompts the question, Why did nature "choose" L-amino acids over D-amino acids? And why just 20 amino acids and none of the dozens of others that might have been incorporated into proteins?

There are no compelling chemical or physical reasons why L-amino acids should be favored over D-amino acids. The D and L forms of amino acids are equally stable, and a protein made of D-amino acids is physically identical in all other respects to its L counterpart. A quick glance at the hundreds of known amino acids reveals that the few that are used to build proteins do not represent the most naturally abundant or the most easily synthesized or even the most chemically versatile.

The reasons for the limited makeup of modern proteins lie buried in the earliest days of evolution and are accessible only through inference. The first amino acids that appeared on earth were probably racemic mixtures, because they were generated by purely chemical events. It is possible that some early forms of life used D-amino acids but were overtaken by more efficient life forms that, by chance, used L-amino acids. Other chance occurrences decreed that 20 particular amino acids take their places as the raw materials for building proteins. The specificity (and stereospecificity) of present-day biological processes is so complete that investigators in the early twentieth century were able to take advantage of biology to purify certain D-amino acids: When animals were fed a racemic mixture of the amino acid, they metabolized the L but not the D isomer so that the excreted, unused amino acid was almost entirely of the D form.

Just as humans are unlikely to suddenly develop gills or sprout wings, useful though they might be, proteins containing D-amino acids are unlikely to appear. At this point in evolution, L-amino acids are so deeply enmeshed in the biochemical fabric of cells that D-amino acids, however worthy from a strictly chemical point of view, cannot participate in any of the processes that have evolved along with the L-amino acids. In essence, modern proteins are made of 20 L-amino acids because there is no longer any alternative.