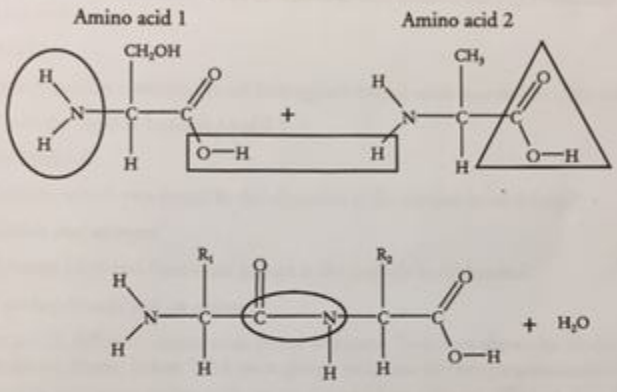
# Protein Structure

What are the levels of protein structure and what role do functional groups play?

## Why?

Proteins accomplish many cellular tasks such as facilitating chemical reactions, providing structure, and carrying information from one cell to another. How a protein chain coils up and folds determines its three-dimensional shape. Its shape will, in turn, determine how it interacts with other molecules and thus performs its function in the cell.

## Model 1 – Formation of a Peptide Bond




Dipeptide

1. Examine the amino acids in Model 1.
   a. Circle an amine group in the diagram.

      *See Model 1.*

   b. Draw a triangle around a carboxylic acid (carboxyl) group.

      *See Model 1.*

2. How are the amino acids similar to one another?

   *Answers will vary, but should include that each amino acid contains a central carbon atom attached to an amine group, a carboxyl group, and a hydrogen atom.*

3. How are the amino acids different from one another?

   *Answers will vary, but should focus on the difference between the R groups in the two amino acids ($-CH_2OH$ and $-CH_3$).*

4. How many amino acids are involved in the reaction to make a dipeptide?

   *Two.*

5. In Model 1 the original amino acids are combined through a **condensation reaction** to make the dipeptide.

   *a.* What does $R_1$ represent in the dipeptide?

   $-CH_2OH$

   *b.* What does $R_2$ represent in the dipeptide?

   $-CH_3$

6. Put a box around the atoms in the amino acids that become the $H_2O$ molecule produced by the reaction in Model 1.

   *See Model 1.*

7. A peptide bond is a covalent bond linking two amino acids together in a peptide.

   *a.* Circle the peptide bond in Model 1.

   *See Model 1.*

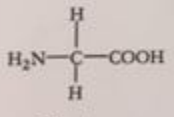
   *b.* Between which two atoms in the dipeptide is the peptide bond located?

   *Carbon and nitrogen.*

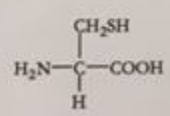
   *c.* Between what two functional groups is the peptide bond located?

   *A carboxylic acid and an amine.*

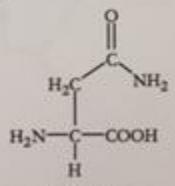
8. There are 22 different amino acids found in nature. Two were shown in Model 1. Additional examples are shown below. With your group, write one or two grammatically correct sentences to describe how these amino acids are similar and how they are different. Use the terms R-group, amine group, and carboxyl group in your description.



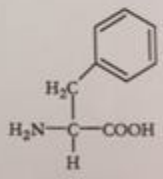
Glycine
(Gly)



Cysteine
(Cys)



Asparagine
(Asn)



Phenylalanine
(Phe)

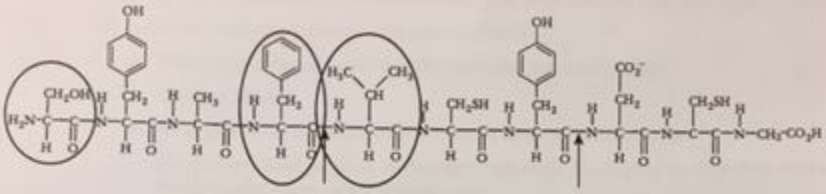
*Amino acids have a central carbon with a hydrogen, amine, carboxyl group, and R-group attached. The R-group varies from one amino acid to another.*

## Model 2 – Protein Structure (Part A)

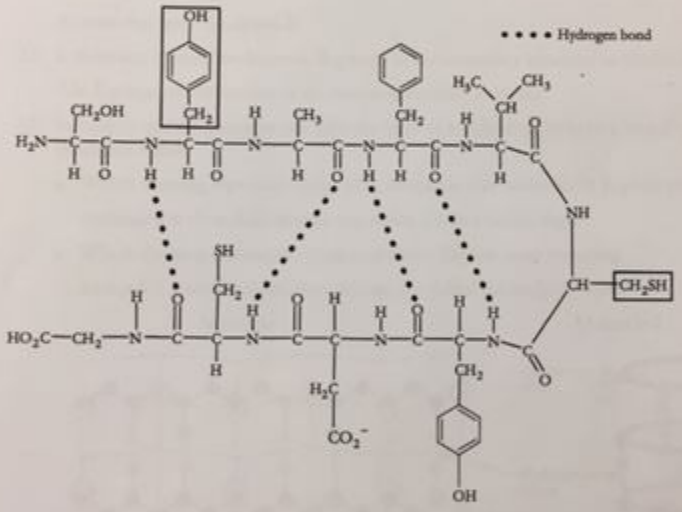
### Primary Structure

Amino acid sequence: Ser – Tyr – Ala – Phe – Val – Cys – Tyr – Asp – Cys – Gly

Peptide structure:



### Secondary Structure




9. Locate the **primary structure** of the polypeptide in Model 2.

   *a.* Draw an arrow to two different peptide bonds in the diagram.

   *See Model 2.*

   *b.* Circle three separate amino acids that were joined together to make the polypeptide.

   *See Model 2.*

10. The first five amino acids in this **polypeptide** are serine, tyrosine, alanine, phenylalanine, and valine, in that order (Ser-Tyr-Ala-Phe-Val). If the amino acids were changed or rearranged (i.e., to Val-Phe-Ala-Ser-Tyr), the polypeptide would have a different name and identity. With your group, use this information to write a definition of the primary structure of a protein.

*The primary structure of a protein is the sequence of the amino acids that make up the protein chain.*

11. Locate the **secondary protein structure** in Model 2.

*a.* What types of bonds are holding the secondary structure in place?

*Hydrogen bonds.*

*b.* What groups on the amino acids are always involved in these bonds?

*The hydrogen bond goes from the hydrogen atom in the N—H group in the peptide bond to the double-bonded oxygen in the carboxyl group.*

12. Draw a rectangle around two different R-groups on the amino acids in the secondary structure in Model 2.

*Answers may vary. See Model 2.*

13. Is there any interaction between R-groups in the secondary structure in Model 2?

*The R-groups do not interact in the secondary structure as shown.*

14. Secondary protein structure can take the form of an alpha(α)-helix or a beta(β)-pleated sheet, as illustrated below.

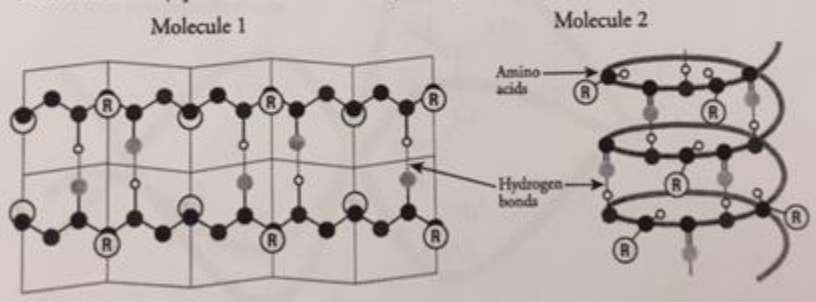
*a.* Which drawing represents an α-helix, Molecule 1 or Molecule 2? Explain your reasoning.

*Molecule 2 is the α-helix because it is coiled, i.e. in a helical shape.*

*b.* Which drawing represents a β-pleated sheet? Explain your reasoning.

*Molecule 1 is the β-pleated sheet, because it is folded (pleated) like a fan.*

Molecule 1 Molecule 2




15. With your group, write a grammatically correct sentence that summarizes how the secondary protein structure is formed from the primary structure.

*The secondary structure is formed by hydrogen bonds holding two different parts of the primary structure together into a folded or coiled molecule.*

16. Examine the **tertiary structure** in Model 3 and note the interactions that hold this level of structure in place.

    *a.* Four types of bonds or interactions are shown. Label them with the following terms.

    Disulfide bridge — Hydrogen bond

    Hydrophobic interactions — Ionic bond

    *See Model 3.*

    *b.* Describe the part of the amino acid that participates in these interactions.

    *The bonds or interactions are between R-groups.*

    *c.* How does your answer in part *b* differ from the bonds that stabilize the secondary structure?

    *Bonds that determine secondary structure occur between the oxygen and hydrogen atoms of the carboxyl and amine groups respectively, not the R-groups.*

17. What type of functional groups or atoms would need to be present in the R-groups for hydrogen bonding to occur between two amino acids in a protein chain?

    *The R-groups would need to contain alcohols (O–H), acids (COOH) or amines ($NH_2$)—polar groups that would contain either oxygen or hydrogen on the end of a polar bond.*

18. What type of functional groups or atoms would need to be present in the R-groups for hydrophobic interactions to occur between two amino acids in a protein chain?

    *The R-groups would need to be nonpolar, containing only hydrocarbon chains or rings.*

19. How many polypeptide chains are shown in the tertiary protein structure in Model 3?

    *One.*

20. Many proteins, but not all, have a fourth level of structure termed **quaternary structure**.

    *a.* How many polypeptide chains are shown in the quaternary structure of the protein in Model 3?

    *Three.*

    *b.* What types of bonds and interactions hold the quaternary structure in place?

    *Disulfide bridges, ionic bonds, hydrophobic interactions, and hydrogen bonds.*

21. With your group, using grammatically correct sentences, define the following.

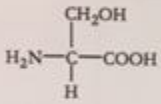
*a.* Tertiary protein structure.

*Tertiary structure is formed by further folding of the amino acid chain (beyond secondary structure), and is held together by various types of bonds between R-groups.*

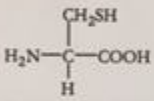
*b.* Quaternary protein structure.

*Quaternary structure is formed when two or more polypeptide chains that make up a protein associate with one another and are held together by bonds between their R-groups.*

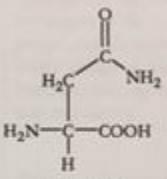
22. Imagine a protein chain that includes the following amino acids among several others.



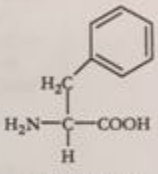
Serine



Cysteine



Asparagine



Phenylalanine

*a.* Which of the amino acids could form a hydrogen bond with another amino acid in the chain to stabilize the secondary structure of a β-pleated sheet?

*All of the amino acids can participate in hydrogen bonding to stabilize secondary structure.*

*b.* Which of the amino acids could form disulfide bonds with another amino acid in the chain to stabilize the tertiary structure of the protein?

*Cysteine.*

*c.* Which of the amino acids could participate in hydrophobic interactions with another amino acid in the chain to stabilize the tertiary structure of the protein?

*Phenylalanine.*

*d.* What types of bonds or interactions could asparagine form with another amino acid in the chain in order to form a quaternary structure with another protein chain?

*Hydrogen bonds.*

23. Fill in the following chart using what you've learned from Models 1–3.

| Structure | Bond(s) or interactions holding the structure together | Short description | Number of polypeptide chains involved |
|---|---|---|---|
| Primary | *Peptide (covalent) bonds.* | *The sequence of amino acids.* | 1 |
| Secondary | *Hydrogen bonds.* | *Hydrogen bonds form between the oxygen of the carboxyl groups and the hydrogen of the amine groups in the carbon backbone causing helix formation or pleating.* | 1 |
| Tertiary | *Hydrogen bonds, ionic bonds, disulfide bridges, and hydrophobic interactions.* | *R-group side chains of different amino acids interact to further fold the protein.* | 1 |
| Quaternary | *Hydrogen bonds, ionic bonds, disulfide bridges, and hydrophobic interactions.* | *Bonds form between individual polypeptide chains.* | 2 or more |


## Read This!

Heating and changing pH levels are two ways to disrupt the shape of a protein. High temperatures or pH levels that vary from the natural environment of the protein will break hydrogen bonds, ionic bonds, disulfide bridges, and hydrophobic interactions. Covalent bonds will usually remain undisturbed. This process of destroying the shape of a protein is called **denaturing**.

24. Which of the four levels of protein structure is maintained after denaturing? Explain your answer.

*Primary structure is the only level of structure that is maintained, as only peptide bonds are retained.*

25. Proteins carry out a variety of functions, and their function is critically dependent upon their structure and shape. Enzymes are proteins. What would happen to the structure and function of an enzyme that was exposed to heat or a drastic change in pH?

*The heat or pH change would disrupt the shape of the enzyme and prevent it from working properly.*

26. When people get their hair chemically straightened, one chemical is put on the hair to break the disulfide bonds that give the hair strands their shape (curled) and a second chemical is used to reform the disulfide bonds to hold the hair in a new position (straight).

   *a.* What level(s) of protein structure is/are affected by these processes?

   *The tertiary and quaternary structures of the proteins would be affected.*

   *b.* Why doesn't the hair stay straight forever after this treatment?

   *The treatment only affects the protein, not the underlying gene, so as new hair grows it retains the curly characteristics coded for in the DNA.*

## Extension Questions

27. If a mutation in the DNA of an organism results in the replacement of an amino acid containing a polar R-group with another amino acid containing a nonpolar R-group, how might the structure of the protein be affected? Address the impact on all levels of the protein structure in your answer.

*Except for the substitution of one amino acid for another, the primary structure will not be affected. The secondary structure also will not be significantly affected, since R-groups are not involved in the maintenance of secondary structure. The tertiary and quaternary structures will be affected because those levels of structure are due to side chain interactions.*

28. Egg whites are primarily composed of the protein albumin. One familiar example of the denaturing of proteins is the difference between the albumin structure in a raw egg versus a cooked egg. Using what you know about the levels of structure in proteins, propose an explanation of changes in albumin (and other proteins) that occur during cooking.

*Denaturing egg proteins during cooking changes the secondary, tertiary, and quaternary structures. It would not change the primary structure (amino acid sequence) of the protein.*

29. Predict what would happen to the egg white if a raw egg were placed in vinegar. Explain your thinking.

*The pH change caused by the acid in the vinegar would denature the protein by affecting the bonds that determine the protein's secondary, tertiary, and quaternary structures. It would not change the primary structure of the protein.*