

## Linear Amino Acid Sequence Folds into Secondary Structures

The linear amino acid sequence defines the primary structure of a protein. Regions of the linear polypeptide chain fold into the stable alpha-helix and beta-sheet structures to form the protein secondary structure.

### Alpha Helix and Beta Sheet Construction Kit Content



11 Alpha Helix backbone pieces

10 Beta Sheet backbone pieces (each has a green A on the alpha carbon)

12 Hydrogen bonds

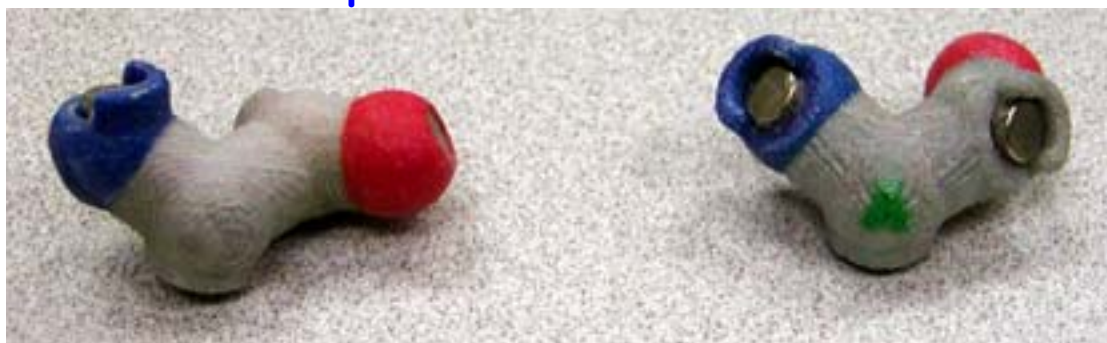
23 Sidechains

1 each of:	arginine	glutamine	lysine	threonine
	asparagine	glycine	methionine	tyrosine
	aspartic acid	histidine	phenylalanine	tryptophan
	cysteine	isoleucine		

2 each of:	alanine	leucine	valine
	glutamic acid	serine	

**\*\*Please note that there is not a model for proline.**

## The Structure of Amino Acid Backbones in an Alpha Helix and Beta Sheet



This kit contains two types of backbone pieces. One type will construct an alpha helix and one will construct a beta sheet. The beta sheet backbone pieces have a green “A” on the alpha-carbon (the “A” symbolizes “anti-parallel”). Each backbone piece has a nitrogen atom (blue), an alpha carbon (gray), a carbonyl carbon (gray) and a carbonyl oxygen (red).

### Activity

1. Examine each type of backbone piece. What are the similarities and differences between the two backbone pieces?

*The backbone pieces are identical in atom composition, but the phi/psi angles are different. The phi angle refers to the bond angle between the nitrogen and alpha-carbon and the psi angle refers to the bond angle between the alpha-carbon and the carbonyl-carbon. In order to adopt the different configurations needed to make an alpha helix or a beta sheet, the phi/psi angles will be different. In the construction kit, the backbone pieces have been designed with fixed angles to construct either an alpha helix or a beta sheet.*

2. Compare your amino acid made from MolyMod® components to the backbone pieces of the construction kits. These are two representations of an amino acid. What are the similarities and differences between the MolyMod® amino acid and the construction kit backbone piece?

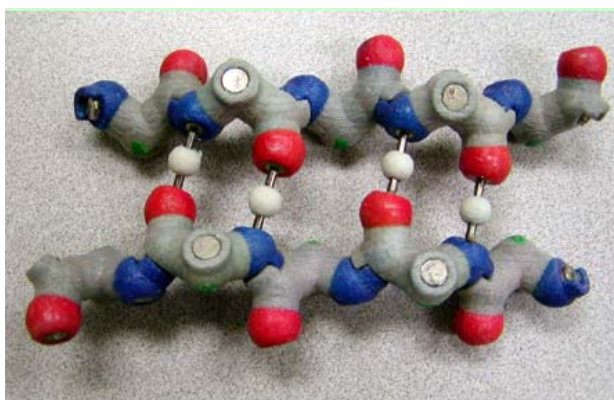
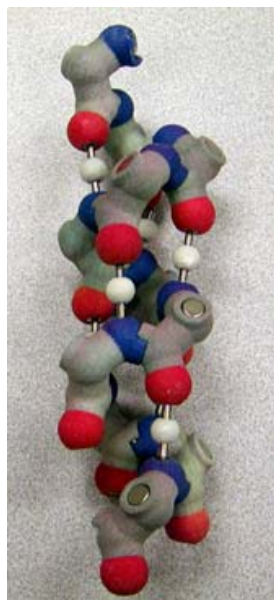
*The main difference is that the bond rotation capacity is not the same in the MolyMod® representation compared to the amino acid construction kits. In the MolyMod® amino acid, there is free rotation between each atom. As mentioned above, the phi/psi angles of the individual amino acids are fixed in the construction kits to allow for construction of either an alpha helix or a beta sheet.*

*The peptide bond more closely resembles a double bond than a single bond. There is a shorter distance between the nitrogen and the carbon than is typically seen in a single bond. There is no rotation around the peptide bond, in contrast to the bond between the nitrogen and alpha-carbon. In the construction kit, the peptide bond is represented by a magnet connecting the nitrogen to the carbonyl carbon.*

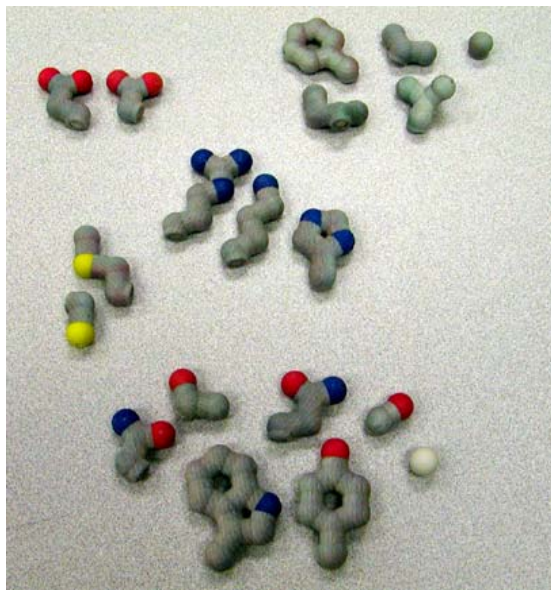
## Building Secondary Structures

### Activity

1. Build an alpha helix using 10 backbone pieces. Build a beta sheet (5 amino acids per beta strand).
  - a. How are these secondary structures the same?
  - b. How are these secondary structures different?
2. Add the hydrogen bonds between an oxygen and a nitrogen.
  - a. What effect does the addition of the hydrogen bonds have on the structure of these secondary structures?
  - b. Why does a hydrogen bond have to be between an oxygen and a nitrogen?
3. Measure the length of the alpha helix and the beta sheet.
  - a. Which is longer?
  - b. Shorter?
  - c. Why?
  - d. What implications does this have on protein folding?



## Amino Acid Sidechains have Different Chemical Characteristics



There are 20 amino acids that are the building blocks of all protein structures within our cells. Each amino acid has same backbone ( $\text{NH}_2\text{-CHR-COOH}$ ). It is the R group that makes the amino acids different from one another.

1. Organize the 19 amino acid sidechains into groups.
  - a. What groupings do you have? Justify your groupings.

*There are several different ways to categorize the amino acids. We typically use the following:*

*Hydrophobic(Non Polar): Alanine, Valine, Leucine, Isoleucine, Phenylalanine*

*Hydrophilic (Polar): Glutamine, Asparagine, Serine, Threonine, Glycine, Tryptophan, Tyrosine*

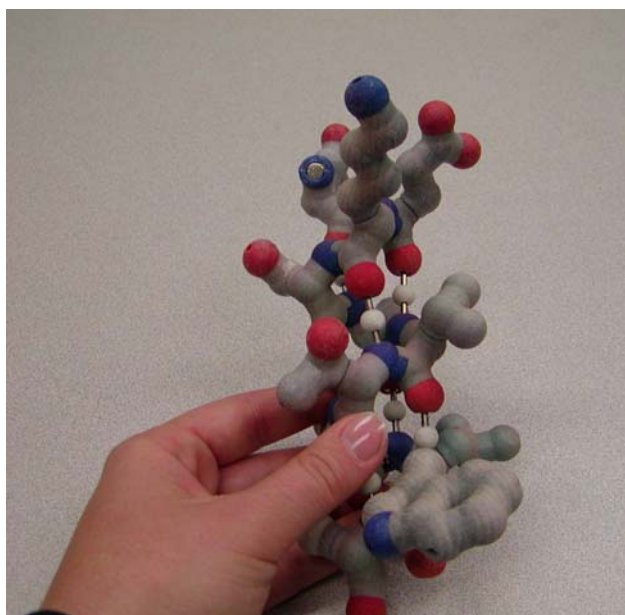
*Positively Charged: Lysine, Arginine, Histidine*

*Negatively Charged: Glutamic Acid, Aspartic Acid*

*Sulfur-Containing Group: Cysteine, Methionine*

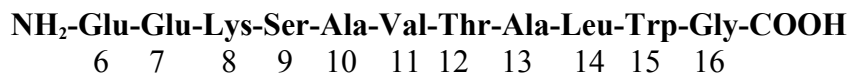
2. Bonus Question: Why is proline not included in the kit?  
*Due to proline's cyclical nature (the R group bonds to the backbone)*

## Modeling Helix A of Beta-Globin



### Activity

1. Using the sidechains provided, construct helix A (residues 6-16) from beta-globin, a subunit of hemoglobin.



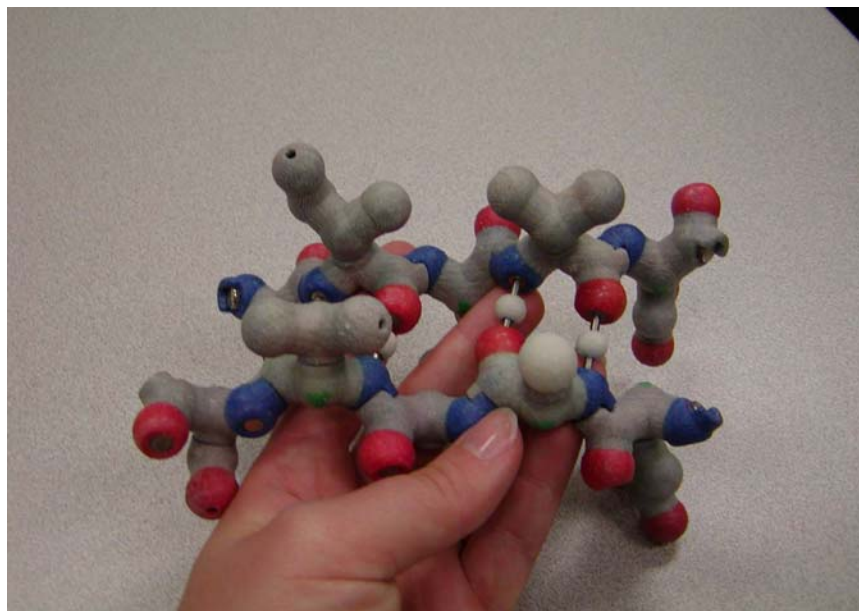
2. One of the major driving forces of protein folding is the interaction of the amino acids with the environment. Examine the helix you just built. Can you determine what effect water has on the folding of these amino acids?

3. Sickle Cell Anemia is caused by a single mutation in the beta-globin gene. Amino acid #7 (glutamate) is replaced with another amino acid (valine). This mutation leads to deformed red blood cells, resulting in anemia. Using your construction Kit, replace the glutamate at position 7 with a valine. What effect does this mutation have on the structural properties of the helix?

**\*\*Possible misconceptions to be aware of when using working with these models:**

Amino acids are not assembled by backbone pieces first and followed by the addition of the sidechains. Physiologically, amino acids are constructed as one unit, which are then linked together during translation to form peptide bonds. The sidechains are separate in this kit to allow for exploration of the different structures of sidechains and to allow for just peptide backbones.

## Modeling a Beta Sheet of Green Fluorescent Protein



### Activity

1. Using the sidechains provided, construct a beta sheet with the following sequence:



What differences do you see on one side of the beta sheet versus the other? What implications does this have on the spatial arrangement of this sheet with the environment? *One of the sides of the beta sheet is predominantly not charged (gray amino acid sidechains) and the other side is mostly charged (red and blue in the amino acid sidechains). This would suggest that the hydrophobic (non-charged) side of the beta sheet might be facing inside the GFP protein barrel and the charged side of the beta sheet is on the outside of the GFP.*

### **\*\*Possible misconceptions to be aware of when using working with these models:**

Amino acids are not assembled by backbone pieces first and followed by the addition of the sidechains. Physiologically, amino acids are constructed as one unit, which are then linked together during translation to form peptide bonds. The sidechains are separate in this kit to allow for exploration of the different structures of sidechains and to allow for just peptide backbones.