



## Overall Student Learning Objective: What Dictates How a Protein Will Fold?

- Proteins are made up of amino acids.
- Different R groups (or sidechains) have unique chemical properties.
- There are two types of protein secondary structure, alpha helices and beta sheets.
- Secondary structures stabilize the tertiary structure of the protein.
- Proteins fold following basic laws of chemistry including:
  - The cysteine amino acids can form disulfide bonds.
  - Acidic and basic amino acids can form salt bridges, or electrostatic interactions.
  - The hydrophobic sidechains are buried in the interior of a globular protein.
  - The hydrophilic sidechains are usually exposed on the surface of a globular protein.

★ We recommend showing the students a 3D model of a protein to begin the activity.

## Sidechain Properties

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Sort the side chains and place them in the appropriate place on the circular amino acid pie chart. You may use the Amino Acid Sidechain Chart to help you sort.

- Notice that some of the side chains have a **YELLOW** band around the bottom. These side chains are **hydrophobic** and DO NOT LIKE water.
- Notice that some of the side chains have a **WHITE** band around the bottom. These side chains are **hydrophilic** and DO LIKE water.
- Notice that some side chains have a **RED** band around the bottom. These side chains are **acids** and carry a negative charge.
- Notice that some side chains have a **BLUE** band around the bottom. These side chains are **bases** and carry a positive charge.
- Notice that some side chains have a **GREEN** band around the bottom. These side chains are **cysteines** and form a disulfide bond between each other (they like to pair together).

1. What pattern can you observe in the structure of the hydrophobic sidechains as compared to the hydrophilic sidechains?

## Folding a Protein

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### Modeling the Primary Structure

- Pick the two cysteine side chains (**green**).
- Pick the two acidic side chains (**red**).
- Pick the two basic side chains (**blue**).
- Pick any three hydrophilic amino acids (**white**).
- Pick any six hydrophobic amino acids (**yellow**).
- **Randomly** distribute them on the TOOBER. (If you space them about three inches apart, you will get an even distribution).

The sequence of amino acids in a protein (from N-terminus to C-terminus) is called its primary structure.

### Modeling the Tertiary Structure

Fold your Protein According to these Chemical Principals:

- The cysteine amino acids can form disulfide bonds.
- Acidic and basic amino acids can form salt bridges, or electrostatic interactions.
- The hydrophobic sidechains are buried in the interior of a globular protein.
- The hydrophilic sidechains are usually exposed on the surface of a globular protein.

The final folded, 3D shape of your protein is called its tertiary structure.

2. Are all of the proteins folded the same way?

3. Why or why not?

4. How many different sequences of amino acids could be generated in your protein if there were an unlimited number of amino acids available for each of the 15 positions?

A protein's shape (structure) determines the function. Changing an amino acid sidechain could alter the protein's shape and thus its function could be impaired.

Change one of the sidechains in your sequence.

5. How might your protein be affected by a change in the sidechain?

### **Modeling the Secondary Structure**

- Unfold your protein and remove the amino acid sidechains.
- Use the toober to fold the backbone of a protein. Incorporate a three-stranded beta sheet and two alpha helices in your structure.
- Shake the protein noting that the protein maintains its basic shape.
- Create an active site on the surface of your protein by adding three amino acid sidechains – a serine, a histidine and a glutamic acid.
- The three amino acid sidechains that make up your protein's active site may bind with a substance.
- Now, unwind your folded protein keeping the amino acids in their original position.

6. Where are the amino acids positioned on the protein backbone relative to each other?

Fold the protein again making the active site but this time **do not** incorporate any alpha helices or beta sheets into the structure. Shake the protein you have just folded.

7. What happened to the shape of the protein when you shook the protein without the alpha helices and beta sheets incorporated into the overall structure?

8. Why are alpha helices and beta sheets important in protein structure?

The secondary structure of a protein consists of alpha helices and/or beta sheets. Proteins can be described as a series of alpha helices and beta sheets, joined by loops of less regular protein structure.