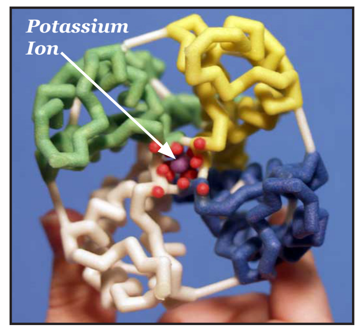
Student Handout 1

Amino Acids - Building Blocks of Proteins

Introduction

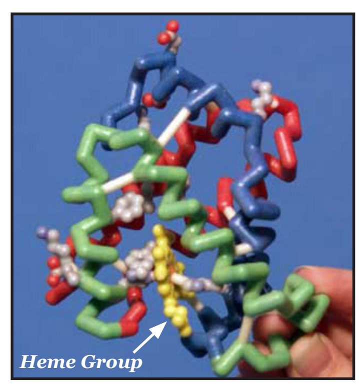
Proteins are more than an important part of your diet. Proteins are complex molecular machines that are involved in nearly all of your cellular functions. Each protein has a specific shape **(structure)** that enables it to carry out its specific job **(function)**.

A **core idea** in the life sciences is that ***there is a fundamental relationship between a biological structure and the function it must perform.*** At the macro level, Darwin recognized that the structure of a finch's beak was related to the food it ate. This fundamental structure-function relationship is also true at all levels below the macro level, including proteins and other structures at the molecular level. *For two examples of proteins and their functions, see the photos and cutlines at the right.*



The potassium channel (above) spans cell membranes and regulates the passage of potassium ions in and out of cells. It folds into a "pore" for the potassium ion to pass through.

The β-globin protein (below) transports oxygen in blood. It accomplishes this with the heme group (yellow structure in photo) in which an iron atom binds to O2. Other proteins perform other functions.



In this activity, you will explore the structure of proteins and the chemical interactions that drive each protein to fold into its specific structure, as noted below.

- Each protein is made of a specific sequence of **amino acids**. There are 20 amino acids found in proteins.
- Each amino acid consists of two parts — a **backbone** and a **side chain**. The backbone is the same in all 20 amino acids and the side chain is different in each one.
- Each side chain consists of a unique combination of atoms which determines its 3D shape and its chemical properties.
- Based on the atoms in each amino acid side chain, it could be ***hydrophobic, hydrophilic, acidic (negatively charged), or basic (positively charged)***.
- When different amino acids join together to make a protein, the unique properties of each amino acid determine how the protein folds into its final 3D shape. The shape of the protein makes it possible to perform a specific function in our cells.

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Chemical Properties Circle & Amino Acid Chart

Hydrophobic and Hydrophilic Properties

What do you think hydrophobic means? Separate the word 'hydrophobic' into its two parts — hydro and phobic. Hydro means water and phobia means fear or dislike, so hydrophobic side chains don't like water. Hydrophobic side chains are also referred to as non-polar side chains.

Now can you guess what hydrophilic means? Philic means likes or attracted to, so hydrophilic side chains like water. Hydrophilic side chains are also referred to as polar side chains.

Acidic (Negatively Charged) and Basic (Positively Charged) Properties

Can you think of acids you have around your house? Lemon and fruit juices, vinegar and phosphoric acid (in dark sodas) are common household acids. Acids taste sour and are typically liquids.

Can you think of bases you have around your house? Tums®, baking soda, drain cleaner and soap are common bases. Bases taste bitter and can be a liquid or solid.

What happens when you mix lemon juice or vinegar with baking soda? They neutralize each other, in a bubbling chemical reaction.

Preparation

The activities described in this handout primarily focus on amino acid side chains. They will help you understand how the unique properties of each side chain contribute to the structure and function of a protein.

First look at the components in your Amino Acid Starter Kit©. Make sure your 1-group set has:

1. 1 **Chemical Properties Circle**
2. 1 Laminated **Amino Acid Side Chain Chart**
3. 1-Meter **Mini Toober**
4. 1 Set of **Red and Blue Endcaps**
5. 22 Clear **Bumpers**
6. 22 **Amino Acid Side Chains**
   - -1 each of the 20 amino acids
   - -1 additional cysteine and
   - -1 additional histidine
7. 22 Plastic **Clips**
   - -8 yellow
   - -8 white
   - -2 blue
   - -2 red
   - -2 green
8. 6 **Hydrogen Bond Connectors**

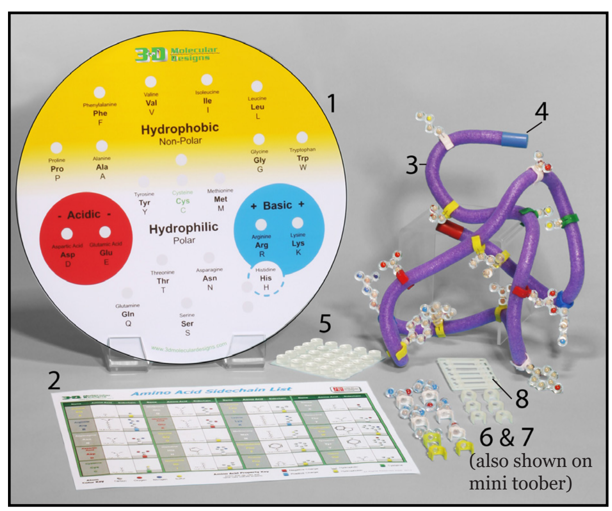


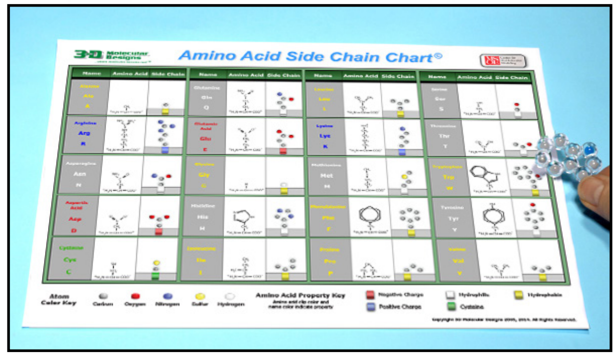
Photo shows a 1-Group Amino Acid Starter Kit.

Chemical Properties Circle (continued)

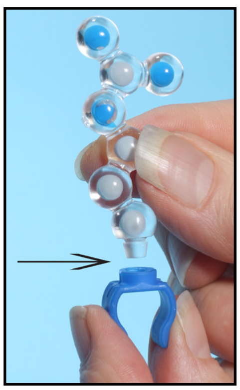
The colored areas on the Chemical Properties Circle, the color coding on the Amino Acid Side Chain Chart, the key below and the colored clips show the chemical properties of side chains.

KEY

Hydrophobic Side Chains are **Yellow**
Hydrophilic Side Chains are **White**
Acidic Side Chains are **Red**
Basic Side Chains are **Blue**
Cysteine Side Chains are **Green**



Amino Acid Side Chain Chart



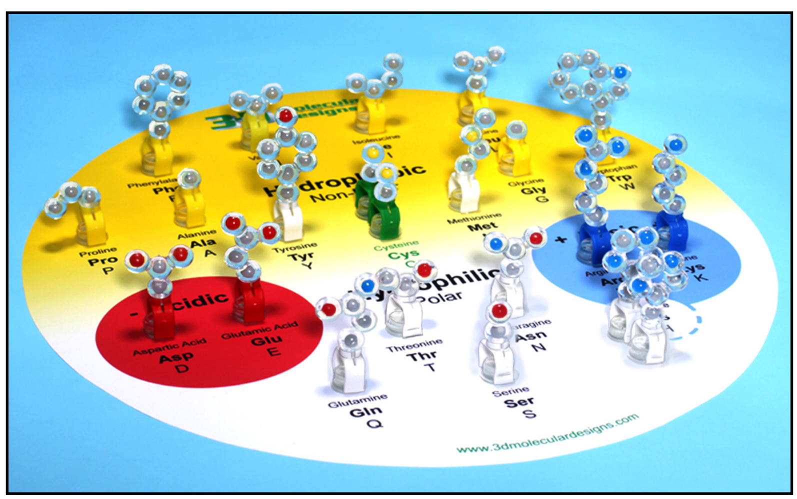
Insert side chain into clip.

Directions

Select any side chain and a colored clip that corresponds to the property of the side chain. Insert the side chain into the clip.

Place each amino acid side chain attached to its clip on the bumper near its name and abbreviations. You will need to consult the Amino Acid Side Chain Chart in your kit to find the name of each side chain, so you can position it correctly on the circle.

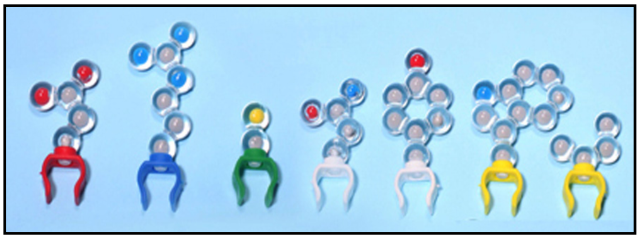
Place clip (with side chain attached) onto the bumper.



Chemical Properties Circle with side chains and clips

Chemical Properties Circle (continued)

After each side chain has been correctly positioned on the circle, look at the colored spheres in each side chain. Scientists established a CPK coloring scheme (see chart below) to make it easier to identify specific atoms in models of molecular structures.



KEY

Carbon is **Gray**
Oxygen is **Red**
Nitrogen is **Blue**
Hydrogen is **White**
Sulfur is **Yellow**

Did you notice similarities of patterns in each group of side chains? Describe your observations.

- Hydrophobic side chains primarily contain ____________________ atoms.
- Acidic side chains contain two ______________________ atoms. This is called a carboxylic acid functional group.
- Basic side chains contain ______________________ atoms. This is called an amino functional group.
- Hydrophilic side chains have various combinations of

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- An exception to the above observation is:

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- **Optional Activity** - Amino Acids Jmol (See *3dmoleculardesigns.com/Teacher-Resources/Amino-Acid-Starter-Kit/Jmols-and-Tutorials.htm.)*

Folding a 15-Amino Acid Protein

Once you have explored the chemical properties and atomic composition of each side chain, think about how proteins spontaneously fold into their 3D shapes.

Predict what causes proteins to fold into their 3D shapes.

- Which side chains might position themselves on the interior of a protein, where they are shielded from water?

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- From your experience with static electricity, which side chains might be attracted to each other?

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- Would the final shape of a protein be a high energy state or a low energy state for all of the atoms in the structure?

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Why?

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1. Unwind the 1-meter mini toober (foam-covered wire) that is in your kit. Place a blue endcap on one end and the red endcap on the other end. The blue endcap represents the N-terminus (the beginning) of the protein and the red endcap represents the C-terminus (the end) of the protein (see photo on next page).

2. Choose 15 side chains from the chemical properties circle as indicated in the chart shown right.

   Mix the side chains together and place them (in any order you choose) on your mini toober.

KEY

6 Hydrophobic side chains
2 **Acidic** side chains
2 **Basic** side chains
2 **Cysteine** side chains
3 **Hydrophilic** side chains

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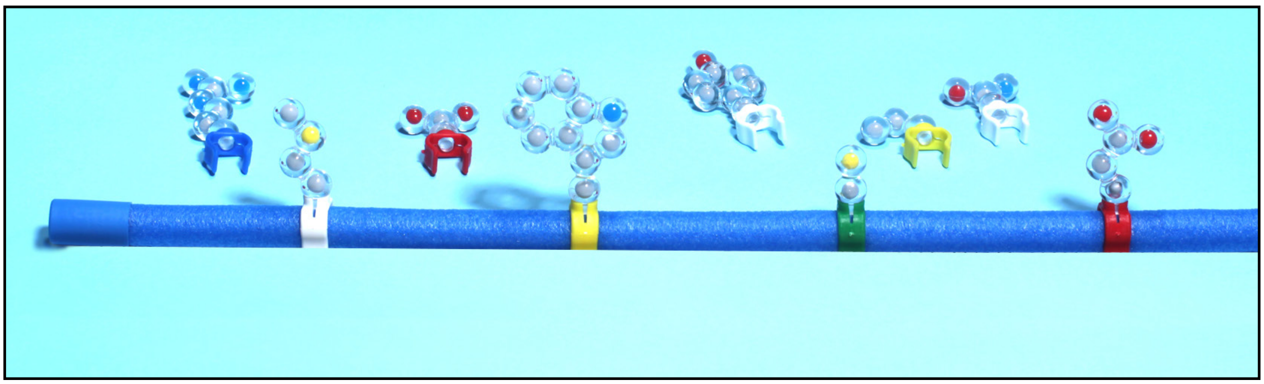
Folding a 15-Amino Acid Protein (continued)

3. You may want to use a ruler to place your side chains on you mini toober.

   Beginning at the N-terminus of your mini toober, measure about 6 centimeters from the end of your mini toober and slide the first colored clip with its side chain onto the mini toober. (See photo.) Place the rest of the clips 6 centimeters apart until all are attached to the mini toober.



- This drawing represents the backbone section of an amino acid. What do you think the clips represent?

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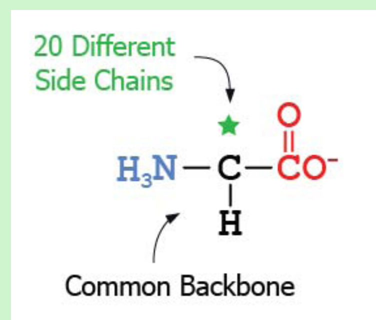
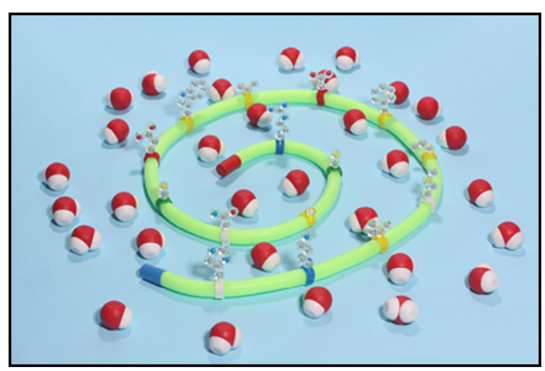


The *sequence* of amino acid side chains that you determined when placing them on the mini toober is called the **primary structure** of your protein. As a general rule the final shape of a protein is determined by its **primary structure**. Remember that protein folding happens in the watery environment of the cell.



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Folding a 15-Amino Acid Protein (continued)

4. Now you can begin to fold your 15-amino acid protein according to the chemical properties of its side chains. Remember all of these chemical properties affect the protein at the same time.

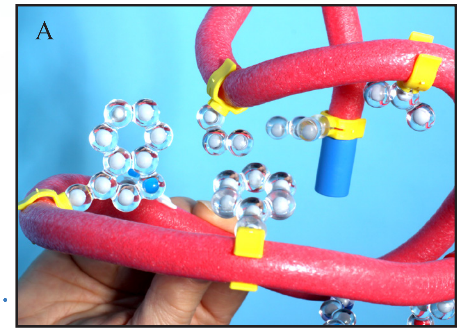

Photo A — Hydrophobic Side Chains
Start by folding your protein so that all of the hydrophobic (non-polar) side chains are buried on the inside of your protein, where they will be hidden from polar water molecules.

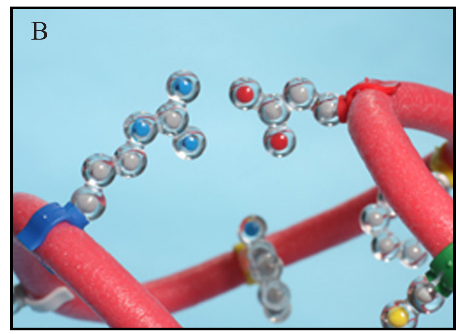

Photo B — Acidic & Basic Side Chains
Fold your protein so the acidic and basic **(charged)** side chains are on the outside surface of the protein. Place one negative (acidic) side chain with one positive (basic) side chain so that they come within one inch of each other and neutralize each other. This positive-negative pairing helps stabilize your protein.

Note: As you continue to fold your protein and apply each new property listed below, you will probably find that some of the side chains you previously positioned are no longer in place. For example, when you paired a negatively charged side chain with a positively charged one, some of the hydrophobic side chains probably moved to the outer surface of your protein. Continue to fold until the hydrophobic ones are buried on the inside again. Find a shape in which all the properties apply ***simultaneously***.

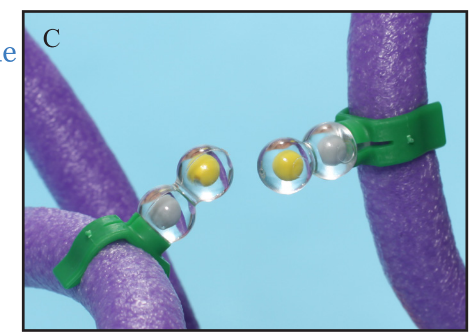

Photo C — Cysteine Side Chains
Fold your protein so that the two cysteine side chains are positioned opposite each other on the inside of the protein where they can form a covalent-disulfide bond that helps stabilize your protein.

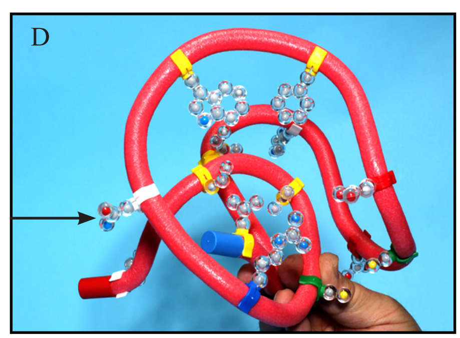

Photo D — Hydrophilic Side Chains
Continue to fold you protein making sure that your hydrophilic (polar) side chains are also on the outside surface of your protein where they can hydrogen bond with water.

The final shape of your protein when it is folded is called the **tertiary structure.**

15-Amino Acid Protein Questions

• What happened as you continued to fold your protein and applied each new chemical property to your protein?

• Were you able to fold your protein so that all of the chemical properties were in effect at the same time?

• If not, do you have any ideas why you weren't able to fold your protein in a way that allowed all of the chemical properties to be in effect simultaneously?

• Did your protein look like the proteins other students folded?______________________
Explain.

• How many different proteins, 15 amino acid long, could you make given an unlimited number of each of the 20 amino acids?

• Most real proteins are actually in the range of 300 amino acids long. How many different possible proteins, 300 amino acids in length, could exist?

15-Amino Acid Protein Questions (continued)

• Research how many different proteins are found in the human body. Hint: how many different genes are there in the human genome*?

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• Assuming that all human proteins are 300 amino acids long, what fraction of the total number of possible different proteins is found in the human body?

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• Why do you think there are fewer actual proteins than possible ones?

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* Completed in 2003, the Human Genome Project (HGP) was a 13-year project coordinated by the U.S. Department of Energy and the National Institutes of Health. During the early years of the HGP, the Wellcome Trust (U.K.) became a major partner; additional contributions came from Japan, France, Germany, China, and others.

Project goals were to:

• Identify all of the approximately 20,000-25,000 genes in human DNA,
• Determine the sequences of the 3 billion chemical base pairs that make up human DNA,
• Store this information in databases,
• Improve tools for data analysis,
• Transfer related technologies to the private sector, and
• Address the ethical, legal, and social issues (ELSI) that may arise from the project.**

*** U.S. Department of Energy Genome Programs website http://ornl.gov/sci/techresources/Human_Genome/home.shtml*

• **Optional Discussion:** Genes can code for multiple proteins through the process of alternative splicing.

15-Amino Acid Protein Questions (continued)

Record the sequence of amino acids in your protein, starting with the N-terminus (blue endcap). Use the single letter abbreviation for each amino acid (Methionine = M).

This is the **primary structure** of your protein.

In the space below, sketch the **tertiary structure** of your protein.

Discussion

Proteins perform critical functions in all our cells. Without proteins, life wouldn't exist. With your group or class, can you think of some of some specific proteins and describe what function they perform? *Proteins are involved in your metabolism, cell structure, immune system, DNA expression, protein folding, transport, movement, communication and storing energy.*

- **Optional Jmol Activity**
  - Basic Priciples of Chemistry that Drive Protein Folding Part 1 Jmol
  - Basic Priciples of Chemistry that Drive Protein Folding Part 2 Jmol

  (See *3dmoleculardesigns.com/Teacher-Resources/Amino-Acid-Starter-Kit/Jmols-and-Tutorials.htm*.)

The next student handout provides folding activities and information that will help you understand the **secondary structure** of proteins.