

Key for Student Handout 1

Amino Acids - Building Blocks of Proteins

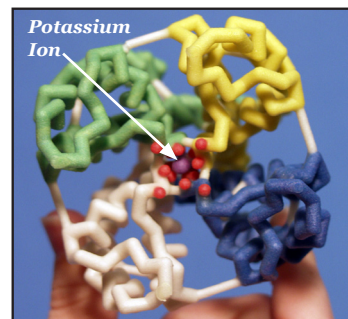
Introduction

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.*

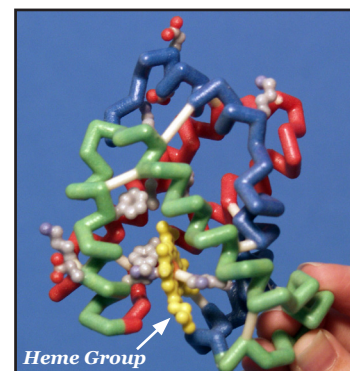
In this activity, you will explore the structure of proteins and the chemical interactions that drive each protein to fold into its specific structure, as noted below.

- 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 **sidechain**. The backbone is the same in all 20 amino acids and the sidechain is different in each one.
- Each sidechain consists of a unique combination of atoms which determines its 3D shape and its chemical properties.
- Based on the atoms in each amino acid sidechain, 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.



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 O_2 . Other proteins perform other functions.





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 sidechains don't like water. Hydrophobic sidechains are also referred to as non-polar sidechains.

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

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 sidechains. They will help you understand how the unique properties of each sidechain 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 **Chemical Properties Circle**
- 1 Laminated **Amino Acid Sidechain List**
- 4' **Mini-Toober**
- 1 Set of **Red and Blue Endcaps**
- 22 Clear **Bumpers**
- 22 **Amino Acid Sidechains**
 - 1 each of the 20 Amino Acids
 - 1 additional cysteine and
 - 1 additional histidine
- 22 Plastic **Clips**
 - 8 yellow
 - 8 white
 - 2 blue
 - 2 red
 - 2 green
- 6 **Hydrogen Bond Connectors**

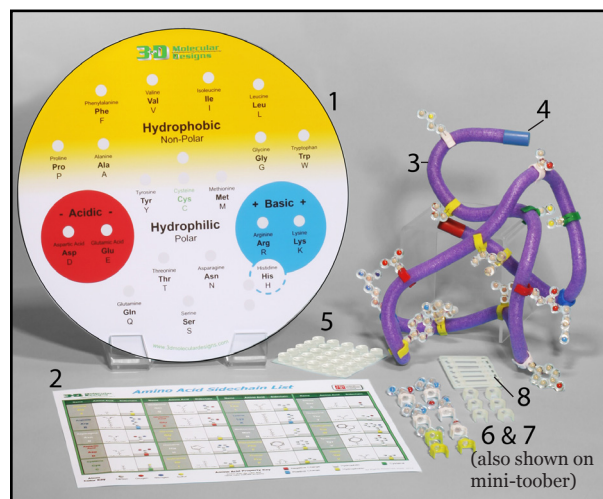


Photo shows a 1-Group Amino Acid Starter Kit.

Chemical Properties Circle (continued)

The colored areas on the Chemical Properties Circle, the color coding on the Amino Acid Sidechain List, the key below and the colored clips show the chemical properties of sidechains.

KEY

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

Amino Acid Sidechain List

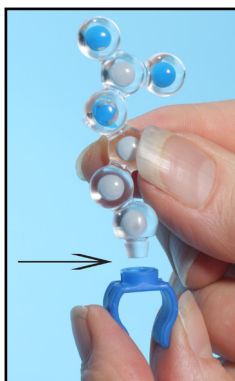
Name	Abbreviation	Sidechain	Color	Property
Alanine	Ala	-CH ₃	White	Hydrophilic
Arginine	Arg	-CH ₂ -NHC(=NH) ₂ ⁺	Blue	Basic
Asparagine	Asn	-CH ₂ -CONH ₂	White	Hydrophilic
Aspartic Acid	Asp	-CH ₂ -COO ⁻	Red	Acidic
Cysteine	Cys	-CH ₂ -SH	Green	Cysteine
Glutamine	Gln	-CH ₂ -CH ₂ -CONH ₂	White	Hydrophilic
Glutamic Acid	Glu	-CH ₂ -CH ₂ -COO ⁻	Red	Acidic
Glycine	Gly	-H	White	Hydrophilic
Histidine	His	-CH ₂ -4-imidazolyl	Blue	Basic
Isoleucine	Ile	-CH(CH ₃)-CH ₂ -CH ₃	Yellow	Hydrophobic
Leucine	Leu	-CH ₂ -CH(CH ₃)-CH ₂ -CH ₃	Yellow	Hydrophobic
Lysine	Lys	-CH ₂ -CH ₂ -CH ₂ -NHC(=NH) ₂ ⁺	Blue	Basic
Methionine	Met	-CH ₂ -CH ₂ -SCH ₃	Yellow	Hydrophobic
Phenylalanine	Phe	-CH ₂ -CH ₂ -C ₆ H ₅	Yellow	Hydrophobic
Proline	Pro	-5-membered ring with N	White	Hydrophilic
Serine	Ser	-CH ₂ -OH	White	Hydrophilic
Threonine	Thr	-CH(CH ₃)-OH	White	Hydrophilic
Tryptophan	Trp	-CH ₂ -indol-3-yl	Yellow	Hydrophobic
Tyrosine	Tyr	-CH ₂ -C ₆ H ₄ -OH	White	Hydrophilic

Amino Acid Sidechain List.

Directions

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

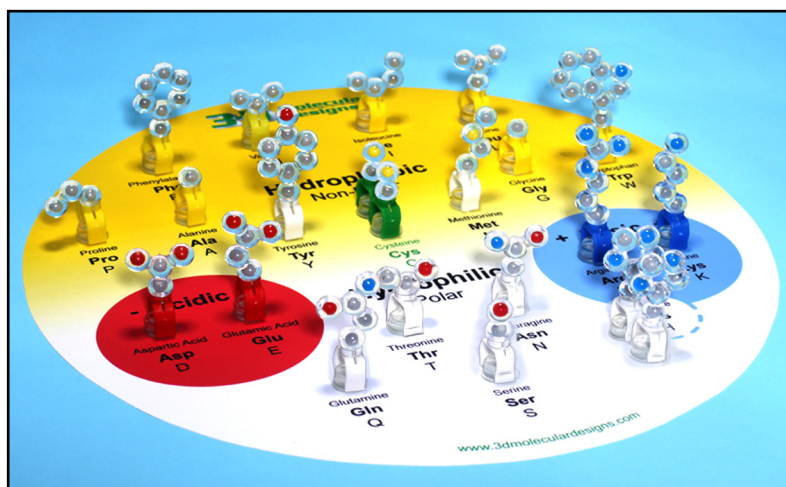
Place each amino acid sidechain attached to its clip on the bumper near its name and abbreviations. You will need to consult the Amino Acid Sidechain List in your kit to find the name of each sidechain, so you can position it correctly on the circle.



Insert sidechain into clip.



Place clip (with sidechain attached) onto the bumper.

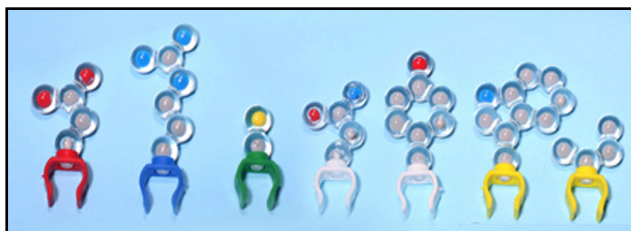


Chemical Properties Circle with sidechains and clips.



Chemical Properties Circle (continued)

After each sidechain has been correctly positioned on the circle, look at the colored spheres in each sidechain. 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 sidechains? Describe Your Observations.

- Hydrophobic sidechains primarily contain _____ carbon _____ atoms.
- Acidic sidechains contain two _____ oxygen _____ atoms. This is called a carboxylic acid functional group.
- Basic sidechains contain _____ one or two nitrogen _____ atoms. This is called an amino functional group.
- Hydrophilic sidechains have various combinations of _____ oxygen, nitrogen and sulfur and carbon atoms. _____
- An exception to the above observation is:
 _____ Tryptophan - a hydrophobic amino acid that contains a nitrogen atom. _____

• **Optional Activity** - Amino Acids Jmol (see AASK Lessons on website)



Folding a 15-Amino Acid Protein

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

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

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

The hydrophobic amino acids - tryptophan, leucine, isoleucine, valine, proline, alanine and glycine.

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

The basic amino acids (+ charge) and the acidic amino acids (- charge).

- 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?

A low energy state.

Why?

A low energy state is more stable than a high energy state.

1. Unwind the 4-foot mini-toober (foam-covered wire) that is in your kit. Place a blue end cap on one end and the red end cap on the other end. The blue end cap represents the N-terminus (the beginning) of the protein and the red end cap represents the C-terminus (the end) of the protein (see photo on next page).
2. Choose 15 sidechains from the chemical properties circle as indicated in the chart below.

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

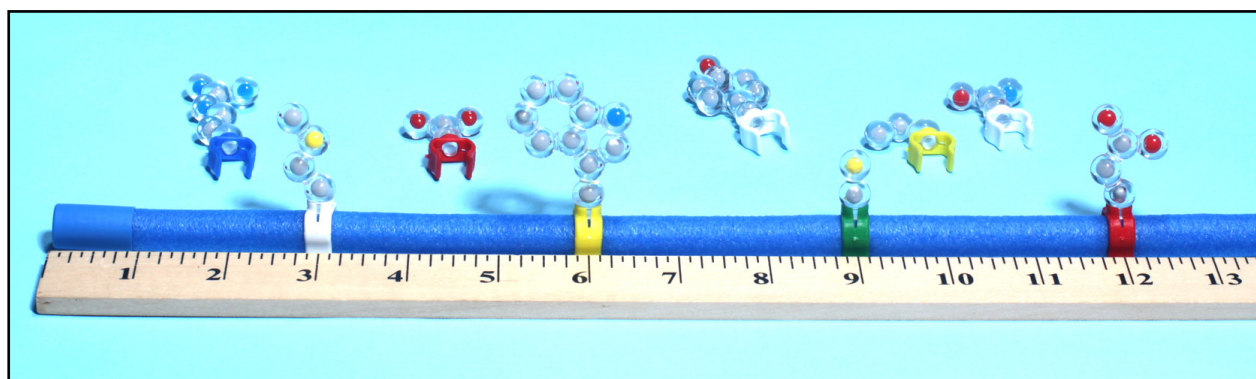
KEY

- 6 **Hydrophobic** sidechains
- 2 **Acidic** sidechains
- 2 **Basic** sidechains
- 2 **Cysteine** sidechains
- 3 **Hydrophilic** sidechains

Folding a 15-Amino Acid Protein (continued)

- You may want to use a ruler to place your sidechains on you mini-toober.

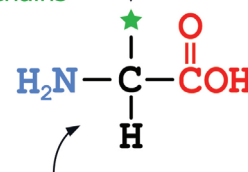
Beginning at the N-terminus of your mini-toober, measure about three inches from the end of your mini-toober and slide the first colored clip with its sidechain onto the mini-toober. (See photo.) Place the rest of the clips three inches apart on your mini-toober until all are attached to the mini-toober.



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

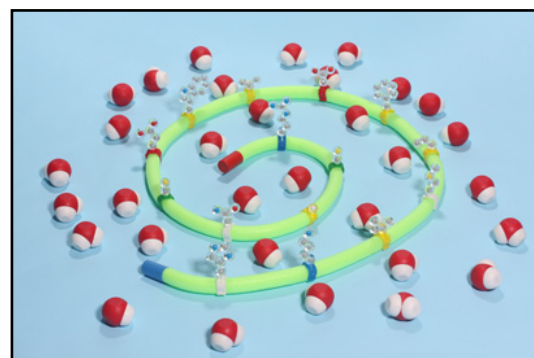
The alpha-carbon, because this is the atom that the sidechains are bonded to.

20 Different Sidechains



Common Backbone

The *sequence* of amino acid sidechains 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.



Folding a 15-Amino Acid Protein (continued)

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

Photo A — Hydrophobic Sidechains

Start by folding your protein so that all of the hydrophobic (non-polar) sidechains are buried on the inside of your protein, where they will be hidden from polar water molecules.

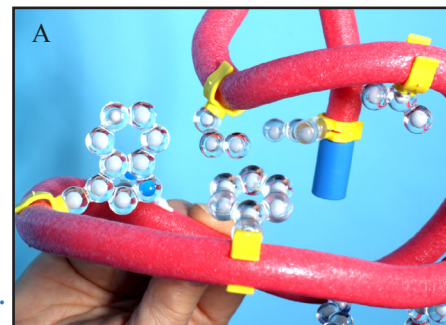
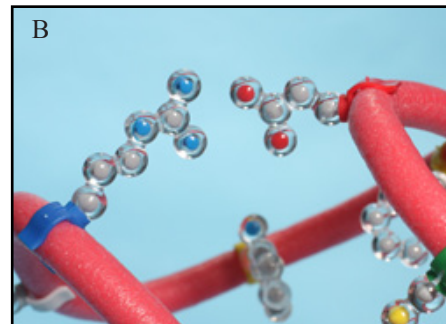


Photo B — Acidic & Basic Sidechains

Fold your protein so the acidic and basic (**charged**) sidechains are on the outside surface of the protein. Place one negative (acidic) sidechain with one positive (basic) sidechain 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 sidechains you previously positioned are no longer in place. For example, when you paired a negatively charged sidechain with a positively charged one, some of the hydrophobic sidechains 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 Sidechains

Fold your protein so that the two cysteine sidechains are positioned opposite each other on the inside of the protein where they can form a covalent-disulfide bond that helps stabilize your protein.

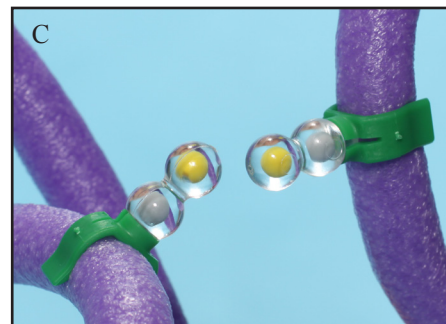
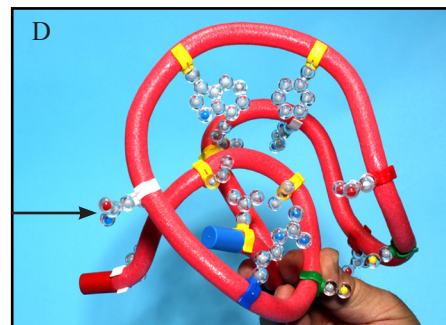


Photo D — Hydrophilic Sidechains

Continue to fold you protein making sure that your hydrophilic (polar) sidechains 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?

It became more compact and more complicated.

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

Yes. (Note to teachers: some students may answer "No".)

- 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?

Some sequences simply do not allow for a single shape that simultaneously satisfies all the principles of chemistry that drive protein folding.

- Did your protein look like the proteins other students folded? No
Explain.

Because everyone had a different sequence of amino acids.

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

$$20^{15} = 3.28 \times 10^{19}$$

- 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?

$$20^{300} = 2 \times 10^{390}$$



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*?

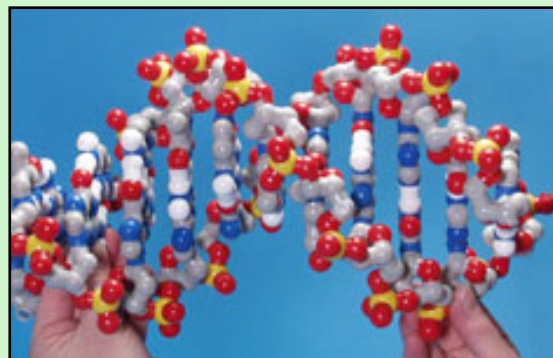
25,000 or 2.5×10^4

- 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?

1×10^{-386} = miniscule!

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

Because only a relatively small number of amino acid sequences can adopt a stable shape that simultaneously satisfies all of the principles of chemistry.



* 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)

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Record the sequence of amino acids in your protein, starting with the N-terminus (blue end cap). 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 Principles of Chemistry that Drive Protein Folding Part 1 Jmol
 - Basic Principles of Chemistry that Drive Protein Folding Part 2 Jmol
- (See AASK Lessons on website.)

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