Teaching DNA, Proteins, and Protein Synthesis with the MIT Edgerton Center Models and Curriculum

PART 1: Proteins

Preface for Teachers

- Please read the document “Teaching Essentials” as your initial guide. [https://edgerton.mit.edu/sites/default/files/media/EssentialsFinal4-25-17.pdf](https://edgerton.mit.edu/sites/default/files/media/EssentialsFinal4-25-17.pdf)

- This PPT is designed to serve as a classroom presentation for Protein Booklet 1. The slides include links to Edgerton videos for each activity. Notes for guiding the class are in blue at the top of the page. Most slides are pages from the booklet.

- **Note:** this PPT is not a substitute for students having booklets. This PPT helps to keep the class on the same page during explanations. Teams will need their own booklets however when working on the activities.
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PART 1: Proteins

Protein Booklet 1— including a Teacher Guide Commentary

January 9, 2018
Teacher holds the chain, shows that it is flexible, and pulls off one or two individual amino acids. Teacher will connect each student’s observation on the model to a real protein feature (or not!).

**Activity to Introduce Proteins**

Students do not need prior knowledge to participate

“Tell me some things you notice about this model…
And I’ll explain how this is like a real protein.”
1. Proteins are made from subunits, **amino acids**, that are joined end to end.

2. Proteins are flexible chains that fold up into different shapes to do work.

3. Amino acids are not all the same. There are 4 different kinds (modeled here by 4 colors).

4. Amino acids have different shapes.
Play Video: “Introduction to Proteins”
https://www.youtube.com/watch?v=EdZET1Tt9Hc

This ~3 minute video can be shown before or after the lesson.
Protein
Booklet 1:
Introduction to Structure and Function

Models and lessons created by Kathleen M. Vander.
Graphics by Amanda Mayer.
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edgerton.mit.edu/dna-proteins-sets
Using Your Booklet and Kit

BOOKLET INSTRUCTIONS:

**Q:** = Helpful Questions (answers on Page 30)
**Bold type** = required actions
**Underlined** = new vocabulary

1. Open the kit. Check the number and location of all amino acids using the inside label shown on the right.

2. Check the small pieces in the bottom right section:
   - 4 gray cylinders (phosphates)
   - 3 yellow tubes (disulfide bonds)
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2. Check the small pieces in the bottom right section:
   - 4 gray cylinders (phosphates)
   - 3 yellow tubes (disulfide bonds)
Instruct students to...
- Pick out any amino acid from the kit.
- Hold it up by the amino end and then by the acid end.
- Recognize what makes one amino acid different from another: the side chain.

Introducing the Amino Acids

Proteins are the molecules that do most of the work inside the cell. Amino acids are the building blocks of proteins. An amino acid is a small molecule with different groups of atoms. Let’s look at the structure of an amino acid.

1. Look at the chemical diagram below the photo. The diagram shows the atoms in a methionine.

Q: Name the different kinds of atoms you see in the diagram.

2. Find a methionine, or Met, in your kit. Hold it in your hand. Use the photo to identify the 3 parts of every amino acid:

- amino group (black block)
- acid group (gray cylinder with knob)
- side chain (colorful shape with abbreviation)

All amino acids have the same amino part and acid part. The side chains of amino acids are what make them different. Let’s look at all the different side chains.
Colors of side chains represent different properties.

Ask. What do yellow side chains represent?

Side chains also have different shapes. Explore this together.

Find and name the amino acids on this page. Then find it in the kit:
- the smallest yellow?
- the largest yellow?
- the yellow that cannot spin?
What do green, pink, and blue side chains represent?

Find and name the amino acids with these side chains on the page. Then find it in the kit.

- the smallest green?
- the largest pink?
- the blue with a bulky shape? (ring structure)
Each student designs their own protein. Do not to build this one!

Building a Protein Chain

A protein is a chain of amino acids joined together. The order of the amino acids in the chain is very important. The order determines the protein’s shape and the work it can do.

1. Choose 4 different amino acids from your kit. Connect them into a short protein chain. The photo shown below is just one example.

2. Look at the two ends of your protein. Find the end with the free amino group (black) and the end with the free acid group (gray).

3. Arrange your protein with the free amino end (black) to the left as shown in the photo.

The amino acid with the free amino end is given the #1. It is the beginning of the protein chain.

Q: Which amino acid is #3 in the photo? Is it polar, acidic, basic, or hydrophobic?

Now look around. Did you make the same protein as someone else? Which amino acid is the first amino acid in the chain?
Review this Big IDEA: The same amino acids in a different order are a different protein!

Video of demonstration next

4. Take apart your protein chain. Build a protein chain with the SAME amino acids in a different order. Again, the photo shows only one example.

You have created a NEW protein!

The order of the amino acids in a protein is very important. A different order creates a different protein. The new protein may have a different final shape and do a completely different job.

Let's see how many different proteins we can make with only 4 amino acids.

There are 20 amino acids to choose from. Any of the 20 amino acids can be in the 4 positions, so we multiply:

Any of 20 amino acids x Any of 20 amino acids x Any of 20 amino acids x Any of 20 amino acids = 160,000

There are 160,000 different ways to make a protein chain that is 4 amino acids long! Most proteins are hundreds of amino acids long so our cells can build an amazing number of unique proteins.

Q: How can you take the same amino acids and make a new protein?
Play Video: “In-Class Demo”

https://www.youtube.com/watch?v=YVse15pdsrA

Important idea: amino acids in a different order = new protein!
DNA in the cell carries the instructions for the order of the amino acids.
PART II: FOLDING PROTEINS

Protein Shapes and Sizes

There are millions of protein molecules inside each cell. Proteins are found in the cytoplasm, the nucleus, and the cell membrane. Proteins have many different jobs in the cell. To do their jobs, protein chains must be folded into specific shapes.

1. Find the single cell in the diagram below.
2. Find the folded protein chain.
3. Find the single amino acid in the chain.

Q: Does the folded protein chain have 2 ends?

Images from the Protein Data Bank: http://www.rcsb.org/
Proteins chains fold into different shapes to work. Let’s try it!

Folding Proteins in Water

Proteins must always fold into the same shape to do their job correctly. One of the rules for folding proteins is based on how the amino acids will behave in water. Hydrophobic amino acids will avoid water molecules. Hydrophilic amino acids will be attracted to water molecules. Let’s practice folding a protein with this rule!

1. Build the protein chain below with the 12 amino acids shown. Keep the amino end [black] to the left as you build.

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
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<th>5</th>
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<th>10</th>
<th>11</th>
<th>12</th>
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</thead>
<tbody>
<tr>
<td>Asn</td>
<td>Val</td>
<td>Met</td>
<td>Ile</td>
<td>His</td>
<td>Ser</td>
<td>Thr</td>
<td>Glu</td>
<td>Val</td>
<td>Trp</td>
<td>Met</td>
<td>Val</td>
</tr>
</tbody>
</table>

On the models, every black amino end has a small hole or eye on one side, and a groove on the other side.

2. Turn all the amino ends so the eyes show, as seen in the photo. Turning the ends helps the model to fold.

Now imagine this protein is surrounded by water molecules. What would happen?

3. Make a guess and gently fold the chain into a shape using the rules above.
Remember to check that the eyes are showing before folding!

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**Note:** One potential answer is shown on the next slide.
There are many correct answers/possibilities!
Protein Folding Video on next slide

The photo shows only one shape the protein could be folded into. Any protein shape that passes the checks below is correct.

4. Check the hydrophobic amino acids in your folded protein.
   • The 2 patches of hydrophobic (yellow) amino acids should be next to each other, near the center of your folded protein.
   • All yellow side chains should be pointing in, away from the water molecules.

5. Move the hydrophobic amino acids if needed.

6. Check the hydrophilic amino acids in your folded protein.
   • The patch of hydrophilic (pink, green, and blue) amino acids should be on the outside.
   • Asn, the first amino acid, should also be on the outside.
   • All pink, green, and blue side chains should be pointing out, toward the water molecules.

7. Move the hydrophilic amino acids if needed.

Real proteins always fold into an exact, repeatable shape. There are variations in this example because we only used one of the folding rules.

Q: How do hydrophobic amino acids behave in water?
Play Video: “Protein Folding in Water”

https://www.youtube.com/watch?v=ICVKtA8a60A
PART III: CHANNEL PROTEINS

Proteins in the Cell Membrane

Some proteins are important because they form cell structures. For example, proteins are needed to make pores in the cell membrane. These channel proteins control the movement of molecules into and out of the cell. Channel proteins have 4 chains that work together to create the pore. Let’s look at a channel protein to see how it fits into the cell membrane and does its job.

1. Find the channel protein in the single cell below.
2. Find the 4 protein chains and the pore.
3. Find the hydrophobic middle of the membrane.
4. Find the molecule going through the pore.

Q: Is the channel protein mostly surrounded by hydrophobic or hydrophilic molecules?
Play Video: “Introduction to Channel Proteins”

https://www.youtube.com/watch?v=5_ZhO1dUzZo
PART III: CHANNEL PROTEINS

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2. Find the 4 protein chains and the pore.
3. Find the hydrophobic middle of the membrane.
4. Find the molecule going through the pore.

Q: Is the channel protein mostly surrounded by hydrophobic or hydrophilic molecules?
Building a Channel Protein

A channel protein needs 4 chains. Let’s build 1 alpha and 1 beta chain.

1. Build the alpha chain first as shown. Keep the amino end (black) to the left.

2. Prepare to fold the chain into a helix. Flip the side chains to be pointing down. Turn the amino ends so all the eyes are showing.

3. Fold the Met upwards as shown.
7. Build the beta chain next. Keep the amino end (black) to the left.

8. Prepare to fold the chain into a helix. Flip the side chains to be pointing down. Turn the amino ends so all the eyes are showing.

9. Fold the Met upwards as shown.
Place your team’s alpha and beta protein chains into the membrane.

Placing Proteins in the Membrane

Let’s assemble a channel protein!

1. Find the cell membrane mat.

2. Fold up the 2 short sides of the mat to create a 3D model of the membrane.

3. Place the alpha and beta chain models you built onto the cell membrane mat as shown in the photo.

In the real protein, the helices are longer. It takes 9 or 10 full turns to go through the membrane (see the diagram on page 19).

Also in the real protein, the helix is coiled tighter. There is no empty space in the center of the helix as seen in the model.
Are the hydrophobic amino acids where they would like to be? The chains on the left side are cards. Use the cards only if a mat needs more chains.*

Now that you have built 2 of the chains, we can use protein cards for the other 2 chains.

3. Find and place the alpha and beta protein cards onto the cell membrane mat as shown in the photo.

You now have a model of a channel protein! But is it correct?

Remember, the protein chains interact mostly with the hydrophobic parts of the membrane (see the diagram on page 19).

Q: Are the hydrophobic amino acids placed where they would like to be?

4. Rotate your protein chains if needed, so the hydrophobic amino acids are in the correct position.

* No cards are needed if 2 teams build 1 mat together. Two teams have the right number of chains.
One side of the helix is hydrophobic and fits into cell membrane. The other side is hydrophilic, helping to move charged molecules/ions through the pore opening.

The photo on page 25 is incorrect! The photo on this page (page 26) is correct.

The hydrophobic membrane surrounds the protein chains, not water! Therefore, the hydrophobic side chains will be pointed towards the outside, not the inside.

5. Check all the protein chains on your mat. The hydrophobic amino acids should be next to the membrane as shown in the photo.

Notice the hydrophilic side chains now point towards the pore. This is how the 4 chains create an opening through the cell membrane.

The channel protein now controls which molecules can get in and out of the cell through the pore.
The order of the amino acids is critical for protein function.

Patterns in Protein Chains

Remember, the order of amino acids is very important. The order determines the shape and job of the protein.

1. Unfold your alpha chain as shown below. Look at the pattern of amino acids.

The amino acid pattern is: 2 hydrophobic -- 2 hydrophilic -- 2 hydrophobic. This pattern makes one side of the helix hydrophobic and one side hydrophilic.

Q: Would the next 2 amino acids in the chain be hydrophilic or hydrophobic?

Now let’s see what happens if we change the pattern of amino acids.
Cystic fibrosis as an example of a genetic disease

Changes in the order of amino acids can cause a protein to be non-functional, or unable to do its job. This can lead to diseases. Let’s see what happens if we change our channel protein.

2. Remove the Arg and replace it with Val. Look at the new pattern.

This chain has a different pattern of hydrophobic and hydrophilic amino acids. When the chain folds into a helix, the hydrophilic side is too short to create a working pore.

Cystic fibrosis is a disease caused by a non-functional channel protein. People with cystic fibrosis have difficulty keeping the correct balance of salt and water molecules in their cells. This disease can be life-threatening. A person with this disease has a problem in their DNA. The DNA instructions for the channel protein are not correct.

To see how DNA directs the production of channel proteins, use DNA/RNA Booklet 1.
## Check Your Understanding

To summarize what you’ve learned, answer the questions below. To see the information again, go to the pages listed.

<table>
<thead>
<tr>
<th>Question</th>
<th>Page(s)</th>
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</thead>
<tbody>
<tr>
<td>1. Why are protein molecules important in the cell?</td>
<td>Page 3 and 10</td>
</tr>
<tr>
<td>2. What are the building blocks of proteins? What 3 parts do they have?</td>
<td>Page 3</td>
</tr>
<tr>
<td>3. Which part of an amino acid makes it unique?</td>
<td>Page 3 and 4</td>
</tr>
<tr>
<td>4. Why is the order of amino acids important?</td>
<td>Page 8 and 9</td>
</tr>
<tr>
<td>5. How many different amino acids are there?</td>
<td>Page 9</td>
</tr>
<tr>
<td>6. Why is the shape of a protein important?</td>
<td>Page 10 and 11</td>
</tr>
<tr>
<td>9. What is the job of a channel protein?</td>
<td>Page 19 and 28</td>
</tr>
<tr>
<td>10. What pattern of amino acids in a chain creates a functional channel protein?</td>
<td>Page 27 and 28</td>
</tr>
<tr>
<td>11. What causes the disease cystic fibrosis?</td>
<td>Page 28</td>
</tr>
</tbody>
</table>
Answers to Helpful Questions

The following are the answers to the questions in the text.

Page 3: The atoms in the chemical diagram are hydrogen (H), oxygen (O), carbon (C), and nitrogen (N).
Page 6: Yellow side chains are hydrophobic. Pink, green, and blue side chains are hydrophilic.
Page 8: The amino acid in position #3 is Tyr or tyrosine. It is a polar amino acid.
Page 9: Different proteins are created by changing the order of the amino acids and/or the length of the protein.
Page 10: Yes, the folded protein has 2 ends. One is near the middle and one is near the outside.
Page 11: Hydrophobic amino acids avoid being near water.
Page 15: Disulfide bonds are created between 2 Cys or cysteine amino acids.
Page 19: The channel protein is mostly surrounded by hydrophobic molecules.
Page 25: No, the hydrophobic amino acids should be placed with their side chains facing the hydrophobic membrane.
Page 27: The next 2 amino acids in the chain would be hydrophilic.
Review of Protein Structure
You have already experienced all four levels of protein structure!

1) **Primary** structure— the order of the amino acids in the chain.
2) **Secondary** structure— the folding of the chains into a helix or a pleated sheet. These structures are held together by hydrogen bonds.
3) **Tertiary** structure— the folding of the chains regulated by the interactions of the hydrophobic and hydrophilic side-chains.
4) **Quaternary** structure-- protein chains interact with other chains and work together. An example is the channel protein. It takes 4 protein chains to create a pore in the cell membrane.
End of Protein Booklet 1 PPT