Will You Be My Val-enzyme?

Rebecca Bernstein | Fall ‘23

Field(s) of Interest: Biology, Chemistry

Brief Overview:
Mentees will learn about how enzymes carry out essential functions in the human body. They will explore the role of catalysts as well as the structure, function, and properties of enzymes.

Agenda:

- Introduction (5 min)
- Module 1: Not Just a Couch Potato (10-15 min)
- Module 2: Who Has an Active (BEAM) Site? (20-30 min)
- Module 3: No Inhibitions! (15-25 min)
- Conclusion (5 min)

Main Teaching Goals/Key Terms:	**Mentor Development Goals:**
➔ Enzyme ➔ Catalyst ➔ Decomposition reaction ➔ Active site ➔ Substrate ➔ Enzyme-substrate complex ➔ Induced fit model ➔ Inhibitor ➔ Competitive inhibition	● **Connect to the demos** ● **Visualization** ● **Classroom management** ● **Adapt**

Mentor Development Notes

Ekansh and Angela

Teaching

When connecting to demos, and to concepts that are particularly difficult, always keep in mind to emphasize the hands-on activities and general ideas. It's not important that students learn about the specific concept, more that they are able to understand the general nature of the lesson. Don't become discouraged if some of the concepts don't seem to be sticking!

Classroom Management

In the third module, people might get rowdy with running around and exertion. Make sure that you have a plan to reign the class back in if they get too rowdy, like switching to the musical chairs activity! For the second module, make sure that people are using their Play-Doh appropriately and not making a mess in the classroom by giving a finite amount of Play-Doh to each mentee.

A Possible Difficult Situation

For the Third module, it might be difficult to get kids to pair up with inhibitors, because the word could have a negative connotation. If you think this might happen, try using an abbreviation like "I's" for the group, so the demo can proceed more smoothly

Connecting to the Bigger Picture

Connect the lesson to potential career goals, such as being a nutritionist, biochemist, or pharmacist! Talk about how enzymes help with digestion, liver function (connecting back to the liver lesson!) and more.

Background for Mentors

Module 1

- Decomposition reaction
- Catalyst
- Enzyme
- Activation energy

Many chemical reactions occur in the human body every day that are essential for us to live. One such reaction, a **decomposition reaction**, occurs when one compound breaks down into simpler components. Decomposition reactions are especially prevalent in digestion, where large molecules that we ingest are broken down into simpler components that can be used to harvest energy, and in toxin removal, where toxic compounds are broken down into non-toxic components that will not harm the body. One specific decomposition reaction that occurs in many living organisms, including humans, is the decomposition of **hydrogen peroxide**, in which the toxic hydrogen peroxide breaks down into water and oxygen.

A **catalyst** is a substance that increases the rate of a chemical reaction without undergoing a chemical change itself. It lowers the **activation energy**, the minimum amount of energy that must be supplied to a chemical reaction for it to proceed. A catalyst may provide an alternate reaction pathway, bring molecules together so that they are optimally oriented, facilitate the breaking and/or formation of chemical bonds, etc.

An **enzyme** is a type of protein found in living organisms that acts as a catalyst for specific chemical reactions. For example, for the decomposition of hydrogen peroxide, an enzyme known as **catalase** is essential for increasing the rate of the chemical reaction. Without catalase, the reaction is so slow that there are virtually no observable changes. Thus, enzymes are vital in the human body, as they are the driving force behind many chemical reactions that are essential for us to live.

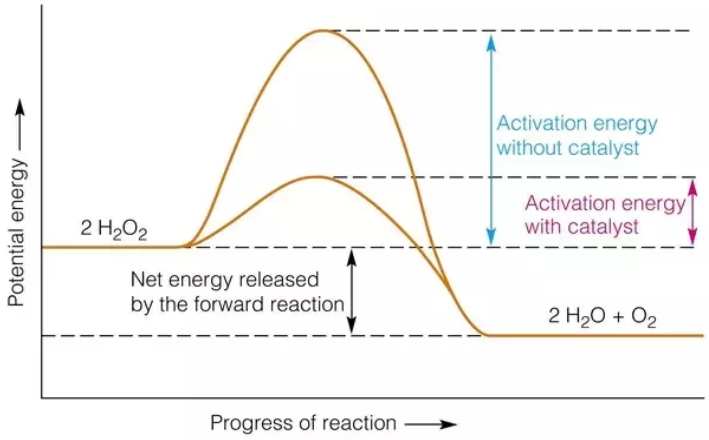

Figure 1: Energy diagram for hydrogen peroxide decomposition with and without catalase

Module 2

- Active site
- Substrate
- Enzyme-substrate complex
- Induced-fit model

An enzyme functions by binding to a specific molecule known as a **substrate**. Each enzyme has a pocket known as an **active site** that determines its specificity for a specific substrate. The substrate forms a strong interaction with the active site of its compatible enzyme. An enzyme may have multiple active sites that each have their own specificity.

When an enzyme is bound to a substrate, it forms a temporary molecule known as an **enzyme-substrate complex**. An enzyme-substrate complex offers an alternative transition state that requires less activation energy than that of the corresponding uncatalyzed reaction. After the substrate(s) are converted into products, the enzyme-substrate complex becomes the **enzyme-product complex**, and then the products are released from the active site.

The earliest model to explain substrate recognition in enzymes is known as the **lock-and-key model**, and it suggests that an enzyme's active site exactly fits the shape of a specific substrate. However, this model was found to be too simple and does not explain how the enzyme-substrate complex is stabilized in the transition state. The **induced-fit model** suggests that when an enzyme's active site binds to a substrate, this binding triggers a change in the enzyme's 3D shape. Often, this conformational change allows the active site and substrate to fit more snugly. The induced-fit model best explains how the enzyme-substrate complex is the most ideal chemical environment for a reaction to occur.

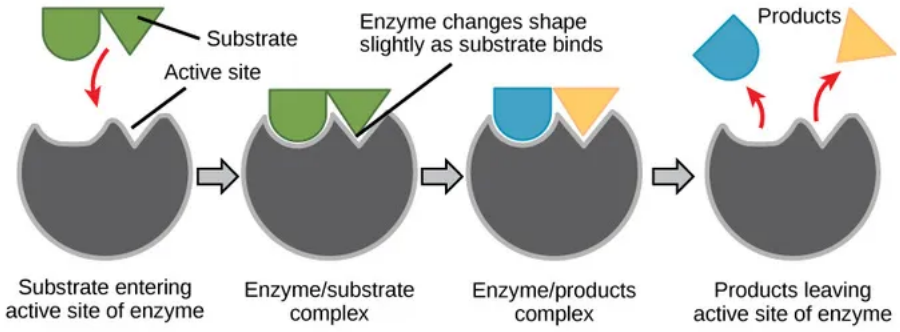

Figure 1: Induced-fit model of enzymes

Module 3

- Inhibitor
- Competitive inhibition
- Uncompetitive inhibition

A molecule known as an **inhibitor** is able to bind to an enzyme and hinder its functionality, slowing the ability of a substrate to react. Inhibitors are important because they regulate enzyme activity, and are also essential in drug development. **Enzyme-inhibiting drugs** are designed to target specific enzymes to disrupt pathways involved in diseases.

There are three main types of inhibition. First, when an inhibitor has a similar structure to that of a specific substrate, it can occupy the active site of that substrate. In this case, the inhibitor and substrate compete to bind to the active site on an enzyme in a process known as **competitive inhibition**.

Additionally, inhibitors can bind to an alternate active site on an enzyme, inducing a conformational change in the enzyme so that the substrate's active site is altered and can no longer bind to the substrate. This process is another type of inhibition known as **non-competitive inhibition**.

The final type of inhibition is known as **uncompetitive inhibition**. In uncompetitive inhibition, an inhibitor binds to an already bound enzyme-substrate complex. However, the presence of this uncompetitive inhibitor affects the ability of the enzyme to function, even though the substrate is already bound, and prevents further catalysis of the chemical reaction.

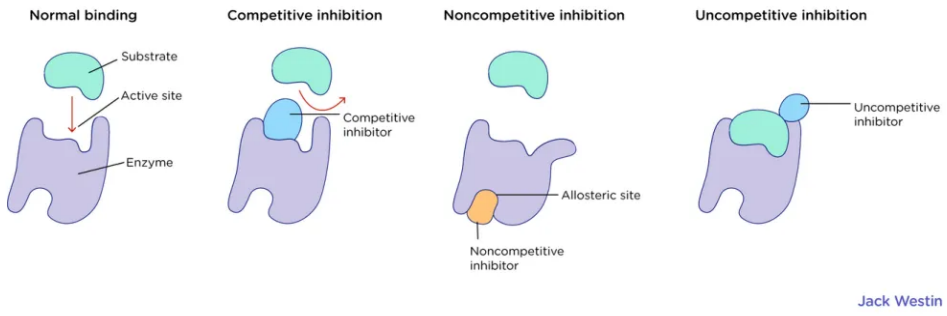

Figure 1: Enzyme inhibition (competitive vs noncompetitive vs uncompetitive)

Introduction

Enzymes are very important in everyday life, especially biology, where enzymes carry out most of our bodily functions. This lesson introduces mentees to the fascinating world of how our bodies work on a microscopic level and the underlying mechanisms that keep living things functioning.

Concepts to Introduce

- Introduce the basic idea of a chemical reaction and give examples
  - Can keep this simple (eg. a chemical reaction is when something turns into something else)
  - A simple example could be burning wood
- Introduce the basic idea of an enzyme
  - Can compare an enzyme to a “helper” or “friend” that helps you do different tasks
- Give some examples of functions that enzymes carry out in the body (eg. digestion)

Questions to Pique Interest

- Can anyone think of an important job that your body does?
  - How do you think your body does this job?
- Can anyone think of an example of a chemical reaction?
  - What about an example of a chemical reaction that occurs in your body?
- Why do you think chemical reactions occur in your body?

Scientists, Current and Past Events

- Scientists are making new enzyme discoveries all the time that allow them to create better therapeutics, because blocking or enhancing the activity of certain enzymes can disrupt diseases. Currently, a lot of enzyme research is focused on treating COVID-19, as illustrated by these two articles.
  - https://news.osu.edu/blocking-enzyme-could-hold-the-key-to-preventing-treating-severe-covid-19/#:~:text=Blocking%20an%20immune%20response%2Drelated,new%20research%20in%20mice%20suggests.
  - https://www.scientificamerican.com/article/lab-made-enzymes-could-chop-up-the-virus-that-causes-covid/

Careers and Applications

- Biochemists make new discoveries that involve enzymes
- Pharmacologists study enzyme-drug interactions
- Chemical engineers design and optimize processes that involve enzymes
- Nutritionists study how enzymes play a role in nutrient absorption

Module 1: Not Just a Couch Potato

This module will explore the role of catalysts in living organisms. This activity will be done in small groups, in which mentees will observe a catalyzed decomposition reaction that is important in biology. Mentees should understand that this reaction only proceeds due to the presence of the enzyme catalase in the potato.

Teaching Goals

1. **Decomposition reaction:** A chemical reaction in which a compound breaks down into simpler components.
2. **Catalyst:** A substance that increases the rate of a chemical reaction without undergoing a chemical change itself.
3. **Enzyme:** A protein that functions as a biological catalyst.
4. **Activation energy:** The minimum amount of energy that must be supplied for a chemical reaction to proceed. A catalyst lowers the activation energy of a reaction.

MD Goals

- **Connect to the demo:** Some of the teaching goals for this module are pretty complicated! Use the demo to your advantage and connect the goals to the potato method.

Materials

- Small, whole potato
- Knife
- 2 plastic cups per group
- 50 mL hydrogen peroxide per group

Different Methods for Teaching

1. **Decomposition reaction:** Have mentees think about how the body might get rid of toxic chemicals. You can also relate this back to the toxicology lesson. It might be useful to draw out a decomposition reaction with shapes (eg. ꝏ→o+o).
2. **Enzyme:** Give some real-world examples of enzymes, such as digestive enzymes that break down food.
3. **Catalyst:** This is a more challenging teaching goal, so for younger sites, you can simplify this by saying that a catalyst is something that allows a chemical reaction to occur. For more advanced sites, you can explain that a catalyst speeds up a chemical reaction so that it is perceivable to human eyes, as we can see in the potato catalase reaction.

Procedure

1. Cut up the potato into small chunks using the knife.
2. Fill the bottom of one cup with hydrogen peroxide and the other cup with water.
3. Place most of the potato chunks in the filled cup of hydrogen peroxide and have the mentees observe the reaction. They should see a lot of bubbles!
4. Place one or two potato chunks in the filled cup of water to show substrate specificity. There should be no reaction!

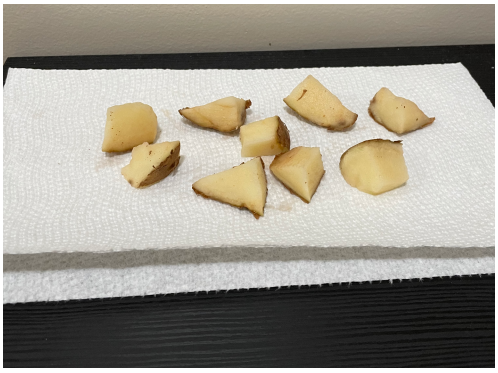

Figure 1: *Size of potato slices*

Figure 1: *Catalase enzyme reaction*

Classroom Notes

Mentors should handle cutting up the potato. When cutting the potato, the more surface area of the potato that is exposed, the more bubbles that will be produced, so placing smaller potato pieces (but more of them) into the solution will yield better results.

Conclusion

Ask the mentees what caused the bubbles to appear. Explain that these bubbles are the result of the decomposition of hydrogen peroxide and that the potato contained an enzyme (catalase) that sped up this chemical reaction.

Module 2: Who has an active (BEAM) site?

This module will explore the structure and function of enzymes. This activity is a build, in which mentees will build a model of an enzyme and use it to observe how an enzyme works as well as some of the properties of enzymes.

Teaching Goals

1. **Substrate:** The specific molecule that an enzyme acts upon.
2. **Active site:** A pocket on an enzyme that fits a specific substrate and binds to it.
3. **Enzyme-substrate complex:** The complex formed when a substrate binds to its compatible enzyme's active site.
4. **Induced-fit model:** When an enzyme's active site binds to a substrate, this binding triggers a change in the enzyme's 3D shape, allowing for a better fit between the substrate and enzyme.

MD Goals

- **Visualization:** Use images, models, and other types of pictorial representations to help connect complicated ideas to tangible things. Even if you don't have a whiteboard available to use, even acting it out could help demystify the topic. (ex: induced fit model is like opening your arms out for a hug, you don't close your arms until you're close to the other person. This could be demonstrated in site)

Materials

- 1 container of Play-Doh per student
- Assortment of small, hard shapes; 1 shape per student

Different Methods for Teaching

1. **Enzyme-substrate complex:** A good analogy is placing two puzzle pieces together. It might be useful to show an enzyme binding a substrate with your hands (place fist of one hand inside another cupped hand). It also may be useful to draw a diagram on the board of an enzyme binding a substrate.
2. **Substrate:** You can connect this back to the first module by explaining that the hydrogen peroxide was a substrate.
3. **Induced-fit model:** A good analogy is hugging someone: when you hug someone, you pull them closer to you so that you "fit" together better. You can think about an enzyme and substrate as "hugging" each other!
4. For this module, the mentees should learn how enzymes work, mainly through the

activity. Especially for younger sites, it is not important for the mentees to learn the names of all of the components and the definition of the teaching goals.

Procedure

1. Hand out a container of Play-Doh to each mentee.
2. Assign one shape to each mentee. Have mentors hold up the shape to show the relative size, but do not hand out the shape yet.
3. Have mentees build an enzyme with their Play-Doh. Ensure that they build a pocket into the Play-Doh that generally fits their assigned shape. The fit does not have to be perfect!
4. Hand each mentee their assigned shape and have them place it into the pocket that they built.
5. Have each mentee squish the Play-Doh around the shape so that the shape fits more snugly into the pocket.

Figure 1: *Example of Play-Doh enzyme (the purple substrate would be replaced with a hard shape and the yellow spheres are unnecessary)*

Classroom Notes

It might be helpful to show the mentees an example model or draw a diagram on the board to make the build activity a little bit more clear!

Conclusion

Conclude by explaining the induced-fit model of an enzyme using the Play-Doh models. Ask the mentees what the difference was before and after they squished the Play-Doh around the shape and explain that there is a better fit after they squished the Play-Doh.

Module 3: No inhibitions!

This module will explore the role of inhibitors in the human body. This activity is a group activity, in which mentees will play the role of enzymes, substrates, and/or inhibitors.

Teaching Goals

1. **Inhibitor:** A molecule that binds to an enzyme and hinders its functionality. Some scientists work to design inhibitors to impede the activity of a specific enzyme, which is used to treat a specific disease.
2. **Competitive inhibitor:** An inhibitor that functions by blocking an enzyme's active site.
3. **Uncompetitive inhibitor:** An inhibitor that functions by binding to an enzyme-substrate complex and preventing the formation of the finished products.

MD Goals

- **Classroom management:** The running enzyme and substrate activity might get rowdy! Make sure that you can keep the classroom still focused on the lesson even though they're having fun. Make sure that all mentees are respecting each others' space in the activity.
- **Adapt**: If you have a rowdier site, you can do the musical chairs activity instead of the tag activity. Make sure to adapt the activity to your site and your own needs!

Materials

- Name tags (2 per mentee)
- Markers
- One rubber dot spot per mentee

Different Methods for Teaching

1. **Inhibitor:** It may be helpful to diagram inhibitors like in Figure 1 of the Module 3 *Background for Mentors*. You can also use the models built in module 2 to show inhibition. For less advanced sites, only show a competitive inhibitor.
2. **Competitive inhibition:** A good analogy for competitive inhibition is a game of soccer - the goalie blocks the ball from going into the goal, just like an inhibitor blocks a substrate from going into the active site of an enzyme.

Procedure

Option 1:

1. Randomly hand out name tags to the mentees, labeled either "enzyme" or "substrate." About

half of the class should be an “enzyme” and the other half should be a “substrate.”

2. For round 1, have mentees spread out around the classroom or outside. Then, when a mentor says “go,” have each mentee try to find a partner with an opposite label and stand together (a “substrate” should find an “enzyme” partner and an “enzyme” should find a “substrate” partner). Partnering represents binding.
3. Ask the mentees to raise their hand if they are a “substrate” and have found a partner. Count the number of “substrates” that were able to find partners.
4. Take back everyone’s name tag and hand out new name tags, this time labeled either “enzyme,” “substrate,” or “inhibitor.” There should be approximately an equal number of “enzymes,” “substrates,” and “inhibitors.”
5. For round 2, repeat step 2, with “inhibitors” partnering with “enzymes” as well as “substrates” partnering with “enzymes.” Not everyone should be able to find a partner.
6. Ask the mentees to raise their hand if they are a “substrate” and have found a partner. Count the number of “substrates” that were able to find partners. There should be less than round 1!
7. For advanced sites, you can add a round where “inhibitors” can only partner with an already formed “enzyme”-“substrate” partnership. This would represent uncompetitive inhibition - only partnerships without a third “inhibitor” partner would still be active!

Option 2 (musical chairs):

1. Have each mentee pick up their chair and place it in a circle OR give each mentee a rubber dot spot and have them place it in a circle in an area with a lot of open space (preferably outside).

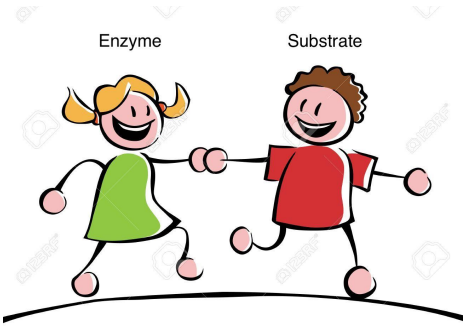

Figure 1: *Option 1 Round 1 - No inhibition*

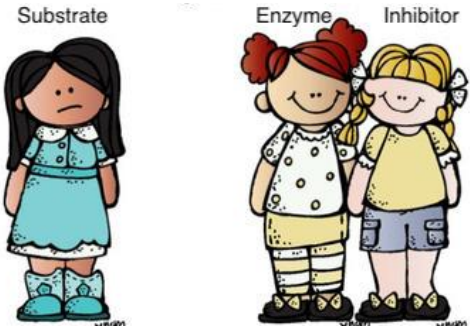

Figure 2: *Option 1 Round 2 - Inhibition*

Figure 3: *Option 2 - Musical chairs set-up*

2. Explain that each chair or dot spot is an enzyme, the mentees are substrates, and the mentors are inhibitors.
3. Play several rounds of musical chairs. For each round, play music while the mentees walk around the circle of chairs/spots. During each round, mentors will remove one or a few chairs/spots from the circle. When the music is stopped, mentees sit down in a chair or on a spot. Mentees who are left standing when all of the chairs/spots are filled are out.

Classroom Notes

For option 1, it might be better to do the activity outside so that the mentees are more spread out and it takes longer to find a partner. If you have a highly energetic group and you think option 2 might be too violent or if you are running low on time, option 1 will probably work better!

Conclusion

For option 1, have the mentees compare the number of “substrates” who found a partner in round 1 vs round 2. Ask them why the number was lower in round 2. Explain how the “inhibitors” blocked the “substrates” from being able to find a partner (bind to an “enzyme”). For option 2, ask the mentees what they noticed was different after each round and explain the connection between musical chairs and competitive inhibition.

References

- https://www.britannica.com/science/enzyme/Factors-affecting-enzyme-activity
- https://www.britannica.com/science/induced-fit-theory

Summary Materials Table

Material	**Amount per Site**	**Expected $$**	**Vendor (or online link)**
Extremely Specific Item Name	1 per student		Amazon