STUDY GUIDE - ***Ch. 8.5 - Regulation of Enzyme Activity Helps Control Metabolism.*** **NAME:** _____

- **PHYSICALLY PRINT OUT this PDF and HANDWRITE (with a black or blue pen) your answers directly on this PDF.** *Typed or digitally-written work is **not** accepted. Do **not** answer questions on separate paper.*
- **Importantly, study guides are NOT GROUP PROJECTS!!!** *You, and you alone, are to answer the questions as you **read** your assigned textbook. You are **not** to share answers with other students. You are **not** to copy any answers from any other source, including the internet.*
- **Get in the habit of writing LEGIBLY, neatly, and in a medium-sized font.** *AP essay readers and I will skip grading anything that cannot be easily read so start perfecting your handwriting, and don't write so large you can't add all the relevant details and key elaborations in the space provided.*
- **SCAN physical documents in color and with good resolution. Then, upload your final work as PDFs to Archie.** *Avoid uploading dark, shaded, washed-out, sideways, or upside-down scans of homework. Keep completed physical study guides organized in your biology binder to use as future study and review tools.*
- **READ FOR UNDERSTANDING and not merely to complete an assignment.** ***First**, read a section quickly to get an overview of the topic covered. Then, read it a **second** time slowly, paraphrasing each paragraph **out loud** and analyzing every figure. Finally, read it a **third** time as you answer the study guide questions if assigned and start building your memory. Try to write answers out in your own words, when possible, and try to purposefully and accurately use all new terminology introduced.*

1. What are the **TWO ways cells control when enzymes are active and thus when a certain chemistry takes place**?

   1.

   2.

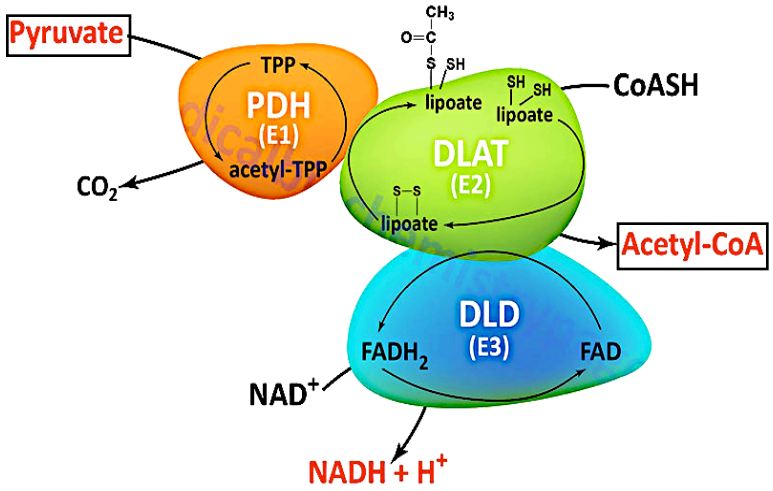
2. What is **allosteric regulation**?

3. **A side-note about multi-enzyme complexes vs multi-site enzymes:**

   Some proteins may be held together into complexes ***(held together in solution or in membranes)*** if the proteins perform related functions. In **multi-enzyme complexes**, multiple enzymes are held together, each enzyme being involved in the catalysis of sequential chemical reactions that all make up one biochemical pathway. These multiple enzymes can be found grouped together in membranes or can be held together in solution by scaffolding proteins.

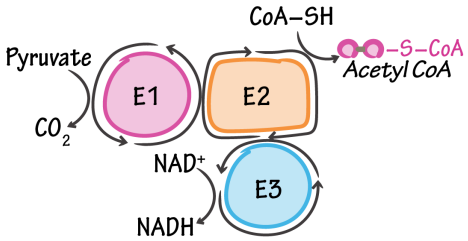
   Below is an example of the biochemical pathway that takes place in the mitochondria in which pyruvate (the precursor of this pathway) is converted into Acetyl-Coa (the final product of this pathway) with the help of three enzymes, each enzyme catalyzing one or more required chemical reactions involved in this biochemical pathway. *(E1 = Enzyme 1; E2 = Enzyme 2; E3 = Enzyme 3).*

Pyruvate Dehydrogenase Complex Enzymes

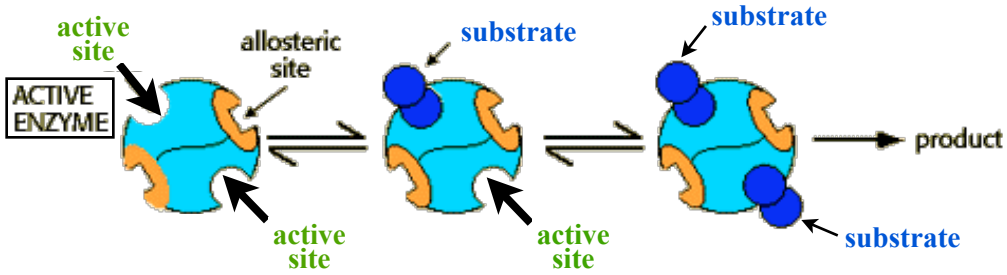


If we consider a metabolic pathway, **the product of one reaction is the substrate for the next enzyme in the pathway.** Direct transfer of a **metabolite (=intermediate)** from one enzyme to another enzyme nearby would avoid dilution of the metabolite in the aqueous environment of the cell and would increase the rate of reaction since the product produced by the first enzyme forms very near the active site of the next enzyme in the biochemical pathway. **Multi-enzyme complexes increase the efficiency of biochemical pathway product formation** since the products released from one enzyme's active site need not diffuse a long distance before encountering the next enzyme's active site in the biochemical pathway, unlike what would have to take place if all the enzymes of a biochemical pathway were floating separately, and father apart, in solution.

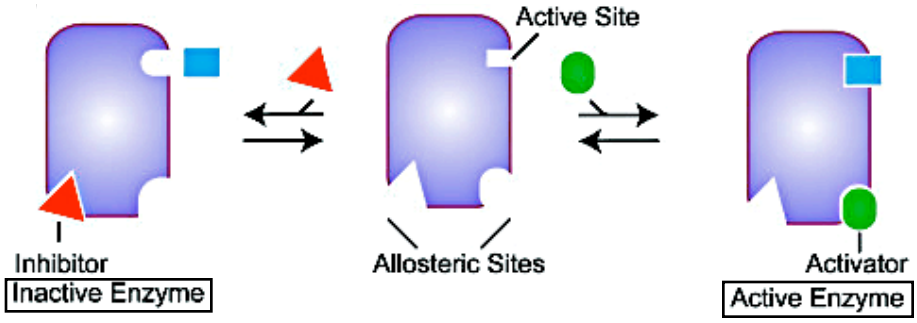
When all enzymes are separately and freely floating around in a solution, **the rate of an enzyme-catalyzed reaction depends on the concentration of the enzyme and substrate**. For an enzyme operating at suboptimal concentrations, the reaction is said to be diffusion-limited, since it depends on the random collision of the enzyme and substrate. However, when enzymes are associated together with other enzymes involved in a particular pathway to form multi-enzyme complexes, the diffusion of the substrate is **not** rate-limiting because the product from with the help of one enzyme are being formed immediately next to the active site of the next enzyme. **Multi-enzyme complexes are, thus, groups of different enzymes held together.**



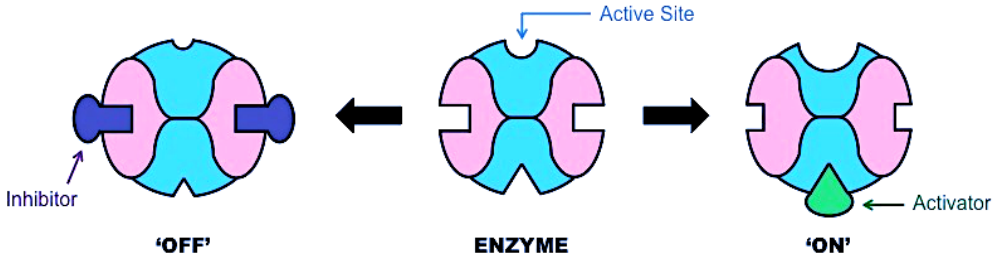
Multi-enzyme complexes, as depicted above, should not be confused with a single enzymes that are themselves made up of multiple subunits (polypeptides), each of which may contain a copy of an active site even. These types of **multi-site enzymes (a.k.a. multi-subunit enzymes)** contain multiple copies of an active site, one active site per enzyme subunit, all subunits being part of ONE enzyme (see image below).



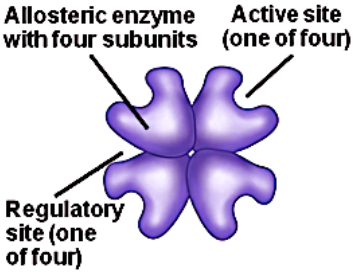
Let's return to the discussion of allosteric regulation, specifically looking at the allosteric regulation of multi-site enzymes. **Enzymes that have one active site may contain multiple allosteric sites where allosteric inhibitors and allosteric activators can bind**.



Multi-site (or multi-subunit) enzymes are composed of multiple polypeptides, **each** of which fold up into subunits that contain an active site, the final enzyme, therefore, having multiple copies of active sites. **This allows for one enzyme to interact with multiple copies of a substrate at once, increasing the rate of product formation.**
(So, some enzymes only have one active site while others have multiple copies of their active site).



Multi-site enzymes may have multiple locations where an allosteric regulator can bind. These enzymes also constantly change between one of two shapes that the entire enzyme (and all its subunits) switches back and forth between: an "on" shape and an "off" shape.

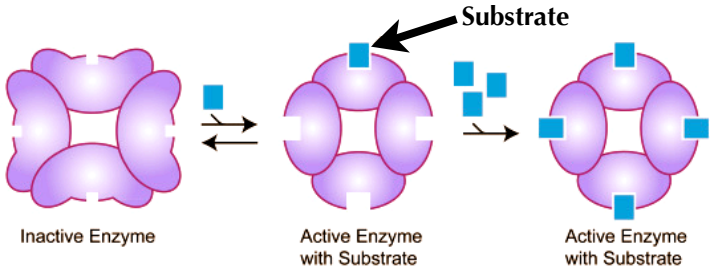


Let's assume there is an enzyme composed of three subunits (three polypeptides), each with a copy of an active site.

a. Describe how an **allosteric activator that binds to an allosteric location on this multi-subunit enzyme can ensure that all three active sites remain active**? *In the box, include a labeled drawing of this multi-submit enzyme bound to the regulator that supports your explanation.*

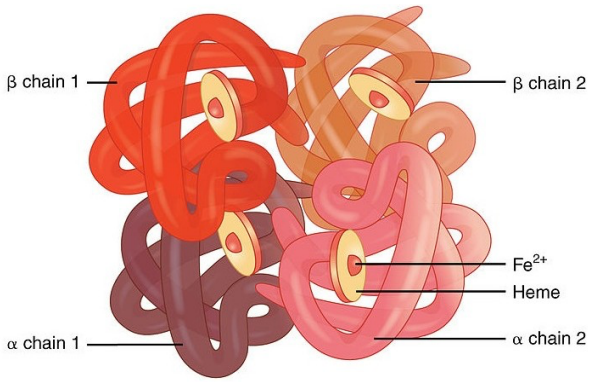
b. Describe how an **allosteric inhibitor that binds to an allosteric location on this multi-subunit enzyme can ensure that all three active sites remain inactive**? *In the box, include a labeled drawing of this multi-submit enzyme bound to the regulator that supports your explanation.*

4. a. With the help of the illustration below and what you have learned from your reading, explain how a **multi-site or multi-subunit enzyme allows for the mechanism of cooperativity** *(a different form of allosteric activation which involves the **effects of a substrate** - instead of an allosteric regulator - on the other multi-submit enzyme active sites).*



b. What is the **benefit of cooperativity** to multi-subunit enzymes?

5. Enzymes are not the only proteins that can show cooperativity, the idea that when one molecule binds to one of the protein's subunits (polypeptides), the other subunits (polypeptides) are affected and when one molecule stops binding to one of the protein's subunits, the other submits are affected as well. Though hemoglobin is **NOT** an enzyme but instead a **transport protein**, **hemoglobin does show cooperativity in binding O_2**. (*To review how oxygen binds to iron atoms in hemoglobin, refer back to your Ch.2 slides)* Explain how hemoglobin works at the gills of the fish where oxygen gas is picked up, and the body tissues of the fish were oxygen gas is released.



6. How does **feedback inhibition (a.k.a. negative feedback regulation) work with regards to the regulation of a biochemical pathway**?

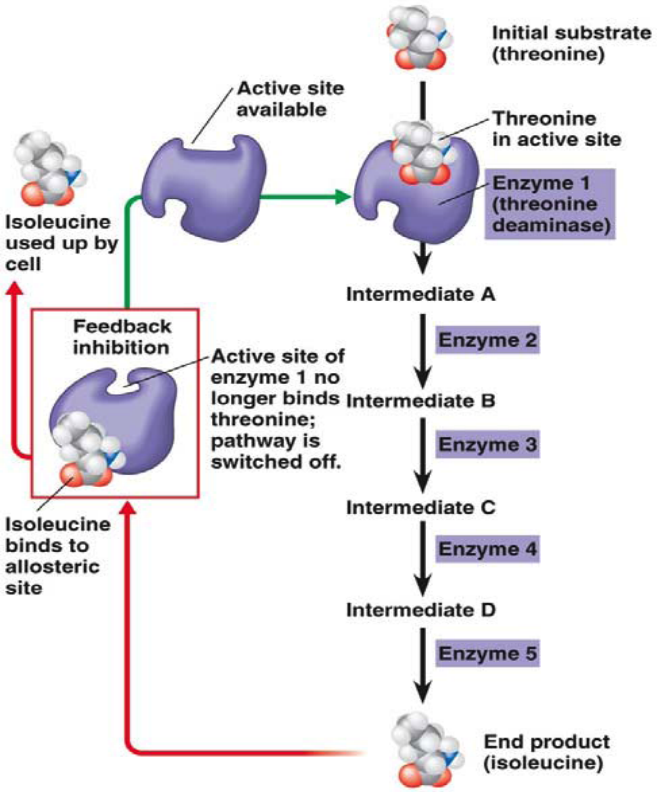
7. a. Study this figure 8.21 in your textbook. What is the **substrate** molecule to initiate this metabolic pathway?

b. What is the **inhibitor** molecule?

c. What **type of inhibitor** is it?

d. When does the inhibitor have the **most significant regulatory effect**?

e. When is **enzyme inhibition overcome**?



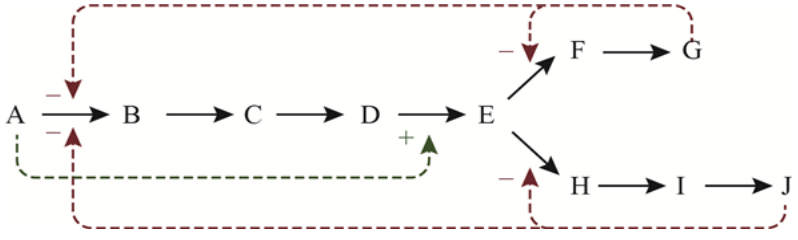
7. Proceed to the TEST YOUR UNDERSTANDING section at the end of the chapter. **Study your chapter sections and all Ch.8 study guides first!** *Then, do your best to try to answer these from memory first in order to test how well you grasped the material before. If you are unsure, return to the relevant section of your chapter and restudy any pertinent material to refresh your memory. (Check your answer by going to the **Ch.8 Test Your Understanding** answers in Appendix A)*

1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____

Drawing models of feedback regulated pathways.

You will be asked and you need to understand how to read models of biological activities that are regulated by positive and negative feedback regulation (feedback activation and feedback inhibition). Below is a model of a biochemical pathway that is under feedback regulation. The **solid arrows** refer to chemical reactions, each one catalyzed by a specific enzyme. A is converted into B by a different enzyme compared to the enzyme that convert B to C. **E is the substrate of two different enzymes**, one which catalyzes a chemical reaction that converts E into F and another enzyme which catalyzes a chemical reaction that converts E into H.

A metabolite is a substance that is part of a chemical reaction, either a reactant or a product. The **dotted arrows** show the regulatory effects certain metabolites in this biochemical pathway have on particular enzymes earlier in the biochemical pathway. So, metabolite G can act as an allosteric inhibitor of the enzyme that coverts E into F **(notice the - sign by the dotted arrow)**. As the concentration of G increases, one would expect less E to be converted into F. Only when the concentration of G drops and there is very little G to inhibit the enzyme it regulates, will E start being converted into F again. Metabolite A, on the other hand, acts as an allosteric activator of the enzyme that converts D into E **(notice the + sign by the dotted arrow)**. When the concentration of A is high, the enzyme it regulates very effectively converts D into E. When the concentration of A drops, however, one would expect D to be converted more slowly into E or not at all.



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Now you give it a try by answering question 7 under the "Test Your Understanding" end of chapter section of your textbook.

7. Drawing of branched biochemical pathway.

a.

b.

c.

d.

9. Labeled Graph:

Proposed Model (**Model = an explanation in words, flow charts, or illustrations of how parts of a system interact to produce results or that allow you to predict outcomes based on a starting set up**)