

Biology 1305

Modern Concepts in Bioscience (ICB Textbook)

Hello and welcome to the weekly resources for BIO-1305 - Biology 1

This week is **Week 11** of class, and typically in this week of the semester, your professors are covering the topics below. If you do not see the topics your particular section of class is learning this week, please take a look at other weekly resources listed on our website for additional topics throughout the semester.

We also invite you to look at the group tutoring chart on our website to see if this course has a group tutoring session offered this semester.

If you have any questions about these study guides, group tutoring sessions, private 30 minute tutoring appointments, the Baylor Tutoring YouTube channel, or any tutoring services we offer, please visit our website www.baylor.edu/tutoring or call our drop in center during open business hours (M-Th 9am-8pm on class days at 254-710-4135).

KEYWORDS: Epinephrine, G-protein, Adenylyl cyclase, c-AMP

TOPIC OF THE WEEK

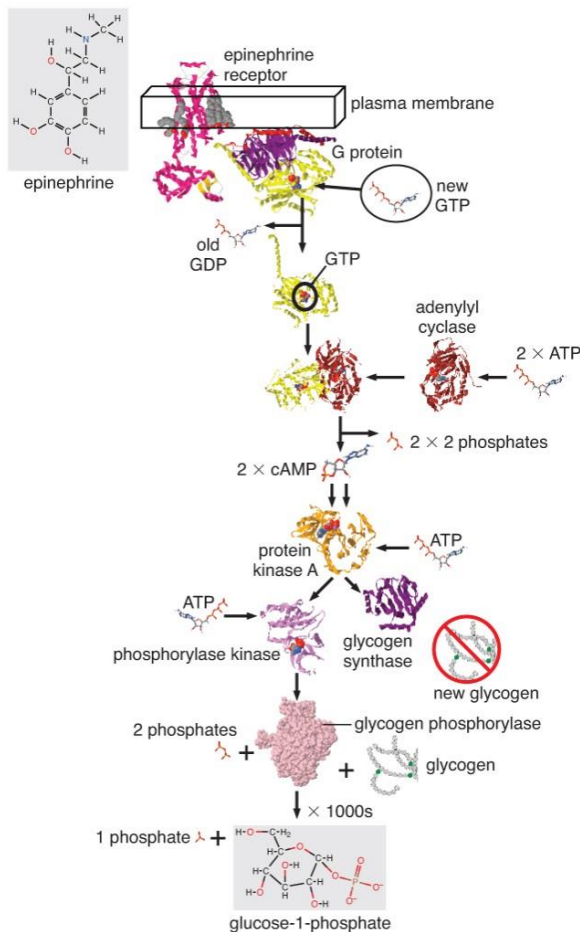
Epinephrine Pathway

As we discussed last week, epinephrine is a hormone which is secreted by your adrenal glands as part of your body's fear response (you may have heard this described as your **fight or flight** response). When your body thinks you are in a dangerous or scary situation, epinephrine is released. The end result of this pathway is that your liver cells will be stimulated to release glucose.

Last week, we looked at the below figure as an overview of the epinephrine signaling pathway. Before we look at some of the evidence that was used to understand this pathway, let's go over its most important steps:

- **Epinephrine** binds to the **receptor**
- The receptor changes shape and interacts with the **G-protein**
- The G protein subunit dissociates and interacts with **adenylyl cyclase**
- Adenylyl cyclase converts ATP into **cyclic AMP**
- cAMP diffuses throughout the cytoplasm until it binds and allosterically activates **protein kinase A**

All diagrams, tables, and external information are property of Integrating Concepts in Biology by Campbell, Heyer and Paradise, unless otherwise specified.



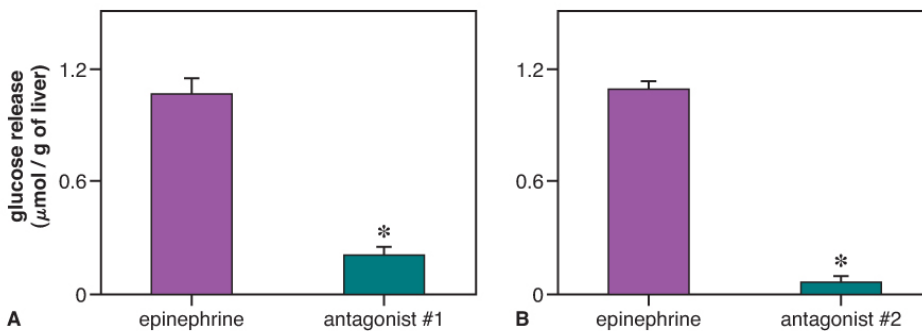
- pKA activates **phosphorylase kinase** and inactivates **glycogen synthase** through **phosphorylation**

- Phosphorylase kinase activates **glycogen phosphorylase**, which removes one glucose from glycogen and adds a phosphate on carbon #1 of glucose to produce a monomer of **glucose-1-phosphate**

- Inactivating glycogen synthase prevents it from synthesizing glycogen from **glucose monomers** (remember that we're trying to release glucose, so we don't want glucose to be stored as glycogen!)

Now that we have looked at the major steps in this pathway, it's time to look at the data!

One of the first experiments studying this pathway was designed by investigators to verify that epinephrine really was the hormone which was responsible for activating the pathway. Investigators isolated a fish liver (which released glucose when stimulated) and injected it with either epinephrine or an epinephrine **antagonist**, and then injected it with epinephrine five minutes later. The below graphs show data for two similar experiments, each with a different antagonist.

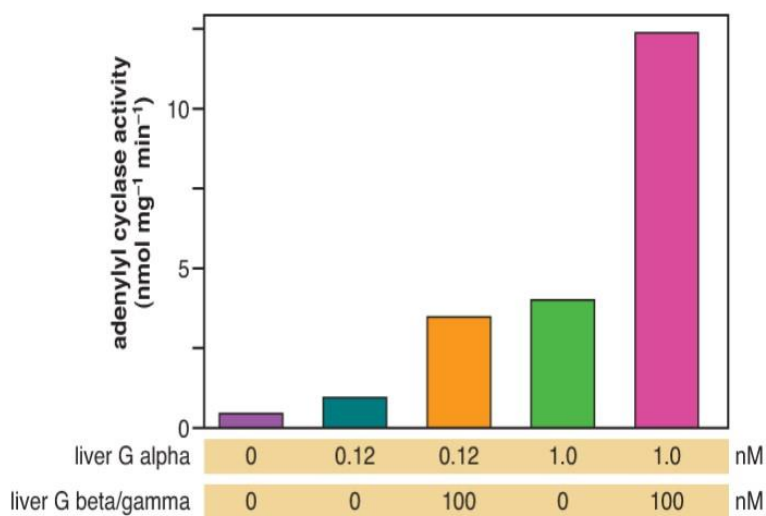


As we can see, when only epinephrine was injected, glucose was quickly released. However, when either antagonist was injected, the epinephrine injected later did not have a strong effect on the release of glucose.

Remember: An antagonist is a molecule that prevents the binding of a ligand to a receptor. In this situation, the antagonist **specifically** blocked the epinephrine receptor and prevented epinephrine from binding when it was injected later.

The results of this experiment allowed investigators to confirm that only epinephrine is responsible for the release of glucose (because the liver was isolated from the body and had no neurological connections).

Next, let's look at a different part of this pathway! As we discussed above, a subunit of the G protein activates **adenylyl cyclase** when it is bound to GTP. Adenylyl cyclase then converts ATP into cAMP. Therefore, **investigators measured adenylyl cyclase activity indirectly based on cAMP produced** with various amounts of subunits of the G-protein.

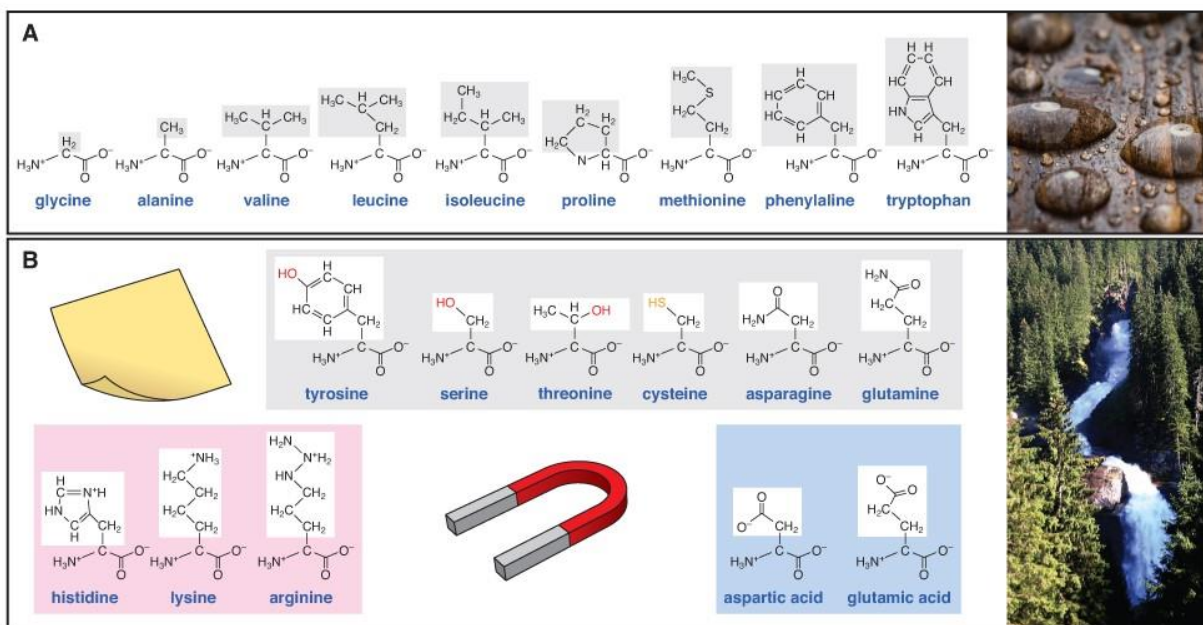


The alpha subunit of the G-protein is responsible for activating adenylyl cyclase, but as we can see from this data, **adenylyl cyclase activity increased when the remaining subunits (beta and gamma) were also included.** This is most likely because **the addition of the β/γ complex allowed α subunits to become reassembled with β/γ , and then reactivated by epinephrine receptors with bound epinephrine.**

The G-protein alpha subunit can repeatedly go through this cycle of being activated by the epinephrine receptor, activating adenylyl cyclase, becoming deactivated and reassembling with the other G-protein subunits, and then being activated again.

HIGHLIGHT #1: Amino Acid Properties

Every amino acid consists of an **amine group** (with a Nitrogen atom), a **carboxyl group** (COOH), and a variable R group, which we call the **side chain**. The side chain is the unique part of an amino acid which determines its properties. **Every amino acid with an N, O, or S atom in its side chain is hydrophilic** because these atoms are electronegative, which means they attract electrons strongly and form polar bonds. Because water is polar, polar molecules are attracted to and are soluble in water. Hydrophobic amino acids are those without any of these electronegative atoms. These molecules tend to avoid water and accumulate in oily pockets, which is a phenomenon known as the **hydrophobic effect**.

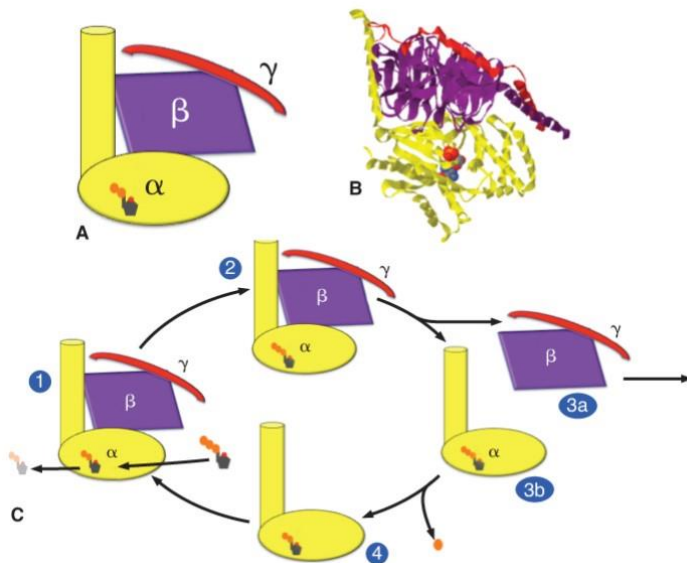


In the above figure, the boxed section of each amino acid is the R group. In order to determine the properties or behavior of an amino acid, look at the atoms in this side chain. A nonpolar side chain will be hydrophobic, and a polar side chain will be hydrophilic.

HIGHLIGHT #2: G-protein Activation Cycle

The below figure depicts the four-step activation cycle of the G-protein. As we saw previously, the G-protein is activated by the epinephrine receptor. When the epinephrine receptor changes its shape, it opens a binding site for the G protein, which binds to the activated receptor. This interaction causes an **allosteric** change in shape in the G protein, which induces it to let go of its bound GDP. Once the α subunit lets go of the old GDP, the G-protein changes shape again, allowing a GTP molecule to bind to the α subunit. When GTP binds, the β and γ subunits let go

of the α subunit, and the α subunit floats into the cytoplasm and eventually activates **adenylyl cyclase**.



After a set amount of time, the GTP is degraded into a GDP and the α subunit is no longer activated. The α subunit bound to GDP will then randomly diffuse in the cytoplasm until it bumps into a β/γ complex to reform the inactivated $\alpha/\beta/\gamma$ G-protein complex. The inactive G-protein can repeat the whole cycle again if the epinephrine receptor is still activated.

Note: An activated epinephrine receptor can activate multiple G proteins. This is an example of amplification, which we discussed last week.

HIGHLIGHT #3: Glucose Production in Muscle Cells

As we discussed previously, glucose is released from liver cells in response to epinephrine. However, because this process takes some time, biochemists wanted to know if the same glucose production pathway takes place in your muscle cells. Although glucose released by the liver eventually makes it to your muscles, it would be helpful if your muscles could also produce some glucose on their own for short term use.

enzyme	liver	skeletal muscle
epinephrine receptor	✓	✓
G protein	✓	✓
adenylyl cyclase	✓	✓
protein kinase A	✓	✓
glycogen synthase	✓	✓
phosphorylase kinase	✓	✓
glycogen synthase	✓	✓

When biochemists compared the enzyme composition of muscle cells and liver cells, the results showed that **both liver cells and muscle cells can rapidly produce glucose in response to fear**. The results in the above table show that the same enzymes and molecules are present in both liver cells and skeletal muscle cells, which are responsible for movement. In muscle cells, the glucose would be consumed right away (muscle cells do not store as many glycogen molecules as liver cells), but by the time muscle cells are depleting their energy reserves, the liver's secreted glucose will reach the muscles and can then be used for energy.

CHECK YOUR LEARNING

(Answers below)

- 1) Why does inactivating glycogen synthase play a role in increasing the release of glucose?
 - 2) Is proline or cysteine more likely to be attracted to water?
 - 3) If a three dimensional protein is in an aqueous solution (contains water), is proline or cysteine more likely to be on the outside of the folded protein?
 - 4) In the epinephrine antagonist experiment, what was injected into the liver which is not written on the graph? When was it injected?
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THINGS YOU MAY STRUGGLE WITH

- Remember that glycogen is a polymer of glucose. Glucose is stored in body tissue as glycogen until the glucose is needed for energy.
- Although only the alpha subunit of the G protein activates adenylyl cyclase, more cAMP is produced when all subunits of the G protein are included. This effect is most likely because the G protein is able to reassemble with the other subunits into a deactivated complex once its GTP is degraded into a GDP, which means it can then be activated and activate adenylyl cyclase again. If the other subunits are not present, this process cannot be repeated
- Remember: two cAMP molecules are required in order to activate one pKA molecule
- Make sure you can identify how each step of the pathway is reset; as a general rule, if an interaction is allosteric, the activating molecule will eventually float away, which will return the shape of the target molecule back to its original shape. If a molecule is

activated or inactivated by a **kinase**, a **phosphatase** needs to remove the covalently-bound phosphate group from the target molecule in order to reverse the effect of the kinase

ANSWERS

- 1) Inactivating glycogen synthase stops it from forming glycogen. When the cell is trying to release glucose, formation of glycogen from glucose monomers opposes this goal. Instead, the cell wants to break down glycogen to release glucose.
- 2) Cysteine
- 3) Cysteine
- 4) Epinephrine was injected five minutes after either epinephrine or the antagonist were injected so that the results could be compared

Thanks for checking out these weekly resources! Don't forget to check out our website for group tutoring times, video tutorials and lots of other resources: www.baylor.edu/tutoring! Answers to Check your Learning questions are below!