Biology 1002B Cycle 3: Thermodynamics and Membranes Breakdown

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Introduction

Dear Student,

Thank you for opening this cycle breakdown for Bio 1002B. This resource has been created by the Education Team at WebStraw. The Education Team consists of students that have previously taken and/or students that are currently taking Bio 1002B.

Purpose

This resource focuses on key concepts that are important for students to understand to succeed within this course. This resource was created by students for other students. Our goal is to help students (1) further develop their understanding of course content and (2) achieve greater academic success. (3) Our resource is also open access meaning there are no financial or legal barriers to students who wish to access and use our resource.

Instructions

To maximize the benefits of this resource, we recommend that you read carefully through the cycle breakdown with specific focus on bolded terms and the “Think about it” paragraphs. Then, try applying your knowledge with some of our custom-made questions at the end of this document. Make sure you already have a good understanding of course content before using this resource, as it will not cover all testable content!

Disclaimer

This resource is supplementary to your course content and is not meant to (1) replace any of the resources provided to you by your instructor nor is it meant to (2) be used as a tool to learn the course material from scratch. We assume that students who use this resource will have a basic understanding of the course content. This resource does not contain everything you need to know for your evaluations. Please refer to the course material provided by your instructors if there are any discrepancies between our resource and your course content.

We wish you the best of luck on your exams!

- The WebStraw Team

Note to Instructors:
If this resource has been created for your course and you would like to collaborate with us, please email us at team@webstraw.ca

Energy and Thermodynamics

- With regard to life the concept of: work and breakdown....use of energy brought in from the environment; maintaining low entropy, how the 2nd law applies to living systems , entropy as energy spreading or disorder.
- Definition of free energy and ΔG, spontaneous
- Distinction between thermodynamics and kinetics and factors that influence each.

The **2nd Law of Thermodynamics** is the reason why living systems constantly have to put in **work** to build up biological molecules and maintain **low entropy**. Cells take in molecules such as carbon dioxide and inputs energy to build larger molecules such as glucose. Over time, these molecules break down (increasing entropy) and are released as heat and waste (energy spreading). Remember what Dr Maxwell said in class: Cells are islands of low energy in a sea of disorder, and it's all because of the 2nd Law of Thermodynamics.

To prepare for exam questions that ask about spontaneity of a reaction or what makes it spontaneous, it's handy to know the **Gibbs Free Energy Equation** and what happens to the overall reaction if a variable changes. **Free Energy** is the amount of energy available to do work, and if a reaction is **spontaneous** it means ΔG (change in free energy) is negative.

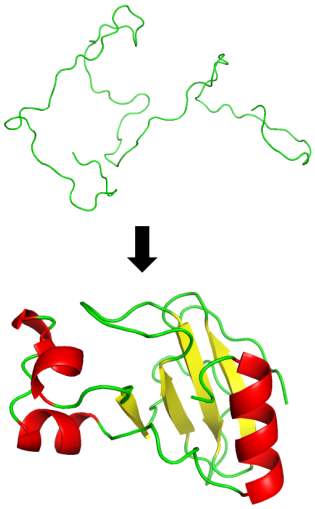
$$\Delta G = \Delta H - T * \Delta S$$

It's important to know that although a **negative ΔH** (meaning the reaction is exothermic) generally means a reaction is spontaneous, that is not always the case as temperature and **change in entropy** also factor into the spontaneity of a reaction. The same can be said for if the reaction is endothermic it is not necessarily always **endergonic**.

A useful distinction to know is the difference between thermodynamics and **kinetics**. Recall that thermodynamics concerns the heat and energy content of the reaction while kinetics is about the speed at which it happens. One concept that often comes up on exams is knowing that the spontaneity of a reaction does not influence the rate, as in a spontaneous reaction could be really slow or fast; we would need more information on the kinetics to know the rate.

Proteins and Enzymes

Proteins and enzymes are arguably some of the most important biological building blocks that are necessary to sustain life on Earth. Let's start by quickly reviewing proteins.



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Protein folding is a **spontaneous process** (-ve ΔG) that involves proteins assembling into their final tertiary and quaternary structures (if applicable). Remember that, even if denatured (by **urea**, for example), some proteins are able to reassemble and continue to function as normal. **This usually tends to hold true as long as their primary sequences are intact (which denaturing does not affect).**

With this in mind however, more complex proteins often require the help of **chaperones** to fully assemble into their functional forms.

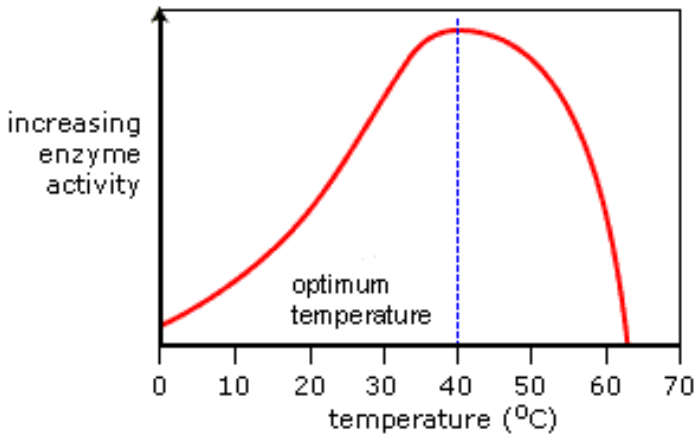
Enzymes are a subset of proteins that **catalyze/speed up reactions**. You've probably been learning about enzymes for many years now, so you should be fairly familiar with them now. Here's a few important caveats and common details that students forget/mix up on tests:

- Enzymes are flexible and change shape when interacting with substrates (**induced fit**)
- BInd substrate through non-covalent forces and destabilizes reactants/stabilizes the transition state
- Can only increase the rate of **endergonic, spontaneous reactions**
- Do not directly supply energy to the reaction
- Lower the **activation energy** of reactions, but **does not affect their overall ΔG** (see picture below). **Enzymes cannot make non-spontaneous reactions spontaneous**

One more important (and super testable!) detail regarding enzymes is understanding how their functionality changes with temperature.

When incubated at low temperatures, enzymes are more rigid and catalyze reactions less efficiently. This rigidity gradually fades as the temperature is raised to the enzyme's optimum. **When incubated at high temperatures,** enzymes quickly begin to denature and lose catalytic efficiency.

With this in mind, the following curve can be deduced. **Notice that the curve is not symmetrical around the optimum.**



A Level Notes

Cystic Fibrosis and The Secretory Pathway

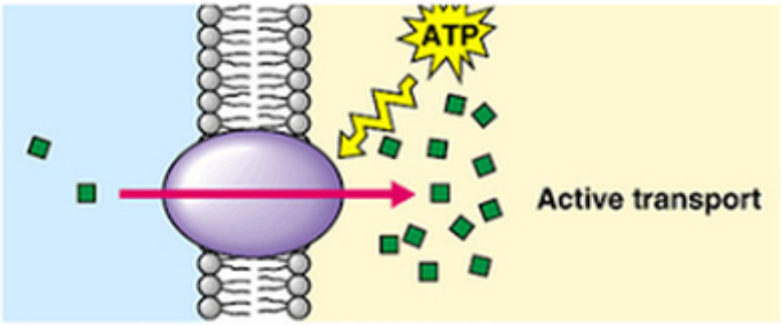
- The secretory pathway (components of it...and what goes through it)
- Linking transport with free energy change....what drives transport
- Basic structure of ABC transporter.
- Cystic fibrosis phenotype.
- Role of chaperone proteins (HSP90) in folding of deltaF508 form and wildtype

Now that we've talked about what proteins do and how they fold, let's get into more specifics on how they get to the folding stage. Proteins that are destined to be secreted out of the cell or to be on the plasma membrane have to go through the **secretory pathway**. Cytosolic ribosomes begin translating the protein until it translates a sequence that produces the **signal peptide**. This is recognized by a **signal recognition protein** (SRP), and translation halts until the ribosome and half-translated peptide/mRNA are brought to the rough ER. Once the ribosome is docked on the ER, the signal peptide is cleaved and translation continues.

Think about it; What mutations or events could occur to components in the secretory pathway that would result in the protein not going where it should be? For example, mutations that destroy the function of the SRP, or a mutation that disrupts the signal peptide sequence could affect the secretory pathway.

An example of a protein that goes through the secretory pathway is the **ABC transporter**; it is a transmembrane protein. This protein is involved in **active transport**. Recall that **simple/facilitated diffusion** don't require ATP; since they transport molecules down a concentration gradient, it is driven by entropy. An ABC transporter drives the transport of molecules UP their concentration gradient. Since this goes against entropy, ATP is required.

It's also important to be familiar with the structure of the ABC transporter. Generally, they have a binding place for ATP and the substrate. It is important that the substrate and substrate binding domain has very high **specificity** so that the transporter doesn't transport the wrong thing.



Plant Life

Let's talk about an example of what happens if something goes wrong in the secretory pathway. Cystic fibrosis is a genetic disorder caused by mutations to the **CFTR protein**. CFTR is a transmembrane protein (like the ABC transporter) that is responsible for pumping chlorine ions into the lumen of the intestine and lungs. By pumping chlorine ions, water follows by osmosis to restore the **ion balance** (this is driven by entropy!). This makes your lungs and intestine moist, which is the optimal condition for them to function in. If CFTR is not present, mucus begins to build up in the lumens and can increase susceptibility to bacterial infections.

The most common mutation in the CFTR gene that causes the disorder is the **ΔF508** mutation. The mutant CFTR can get to the rough ER and finish translating, but

afterwards it is unable to fold into its correct conformation. The rough ER has chaperone proteins such as **HSP 90** that perform quality checks on newly folded proteins and if it sees a misfolded CFTR, it will tag it for degradation. Therefore, ΔF508 CFTR will never make it out of the rough ER and to the plasma membrane.

Fatty Acids and Membrane Biology

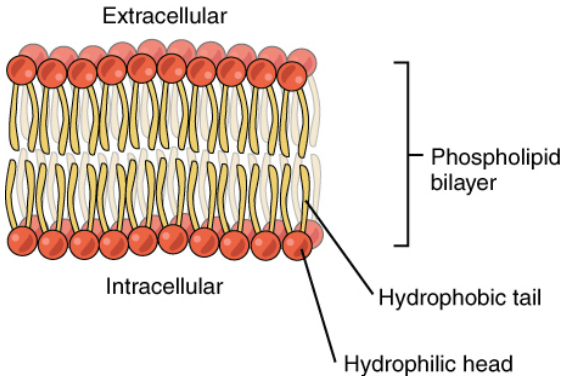
The last topic we need to cover is membrane biology. Most of this should be pretty straight forward review from high school, but the challenge is to make sure you really understand/remember things properly!

Recall that fatty acids are long hydrocarbon chains with a carboxyl group on one end. These fatty acids are very **hydrophobic** (meaning they do not interact with water), and are very useful in both our metabolism and membrane structure.

Fatty acids are a key component of **phospholipids**, which are essentially two fatty acid chains attached to a glycerol molecule, which is joined to a phosphate group. Don't worry too much about the specifics of the molecule itself, as first year bio focuses more on its physical properties and usefulness in the membrane.

Phospholipids compose most of a cell's plasma membrane, along with other fatty acids and proteins embedded throughout. This is called the **Fluid Mosaic Model.**

Why are phospholipids used? Well, phospholipids are **amphipathic**, which means part of the molecule is hydrophobic (the fatty acid tails) while another part is **hydrophilic** (the "phosphate head"). They are positioned tail-to-tail in a **lipid bilayer**, as this promotes favourable interactions between the polar head groups and the surrounding aqueous environments (both inside and outside the cell), while also creating a hydrophobic membrane space for proteins and fatty acids to interact in. This space contains **lipids, glycolipids, transport proteins, sterols, and more.**



Quora

One important caveat to understand is that **the membrane is asymmetrical**. This means that proteins/distinct lipid groups that aren't phospholipids *cannot* flip-flop back and forth between bilayers. The proteins embedded or peripheral to either side of the membrane are also distinct and different (i.e: a protein responsible for cell-cell interaction on the extracellular side of the membrane won't also be on the intracellular side as well. (**Think about it logically!**)

What types of proteins exist in the structure of the membrane? There are two main kinds, **integral/transmembrane** and **peripheral.** Here's a summary of some of their properties:

	Integral Protein (can be transmembrane)	**Peripheral Protein**
Location?	Embedded directly in the membrane. May extend and protrude into the outside or inside of the cell (this is what's referred to as a **transmembrane protein**).	Found on the surface of *either* the outer or inner membrane.
Polarity?	Non-polar and polar regions may exist if protein protrudes into extracellular/intracellular aqueous regions. Often end up having both polar *and* nonpolar regions.	Polar
Interactions with	Covalently bonded within	Held by hydrogen/ionic

Membrane?	the hydrophobic bilayer, or free to move around in the bilayer (will not leave as the environment is hydrophilic).	bonds, does not interact with the hydrophobic region of the bilayer.
Example	Potassium channel transporter (K^+ pumps). Have hydrophobic regions (exterior of ion channel embedded in membrane) and hydrophilic regions (two ends + inside of ion channel	Cytochrome *c* (integral membrane protein in oxidative phosphorylation)

Now that we understand the composition of the plasma membrane a little better, what are some of the things it can do? One of its most quintessential functions is the ability to transport molecules in and out of the cell. As you have learned, this is either through **passive transport** or **active transport.**

For transport, just know which mechanism different types of molecules/structures use.

Passive Diffusion: driven by an increase in entropy of the system. This is just a fancy way of saying that molecules move from areas of high concentration to low concentration, down a gradient.

- **Diffusion** (passive transport through pores in the membrane)
    - Small, non-polar molecules (i.e: O_2)
    - Small polar molecules (i.e: ethanol)
- **Facilitated Diffusion** (passive transport through channel proteins and some carrier proteins)
    - Small ions (i.e: Na^+, K^+, Cl^- through ion channels)
    - Water (through **aquaporins** in **osmosis**)

Active Transport: moving particles against their concentration gradient (an unfavourable decrease in entropy). This requires energy input from the hydrolysis of ATP, or by coupling active transport to the passive transport of another molecule.

- **Active Transporters:** These are usually carrier proteins that undergo conformational changes to facilitate one way transport
    - Proton pumps in the mitochondria during oxidative phosphorylation

- **<u>(Receptor-Assisted) Endocytosis:</u>** plasma membrane of cell pinches off to create a vesicle, engulfing and transporting large molecules into the cell
    - Hydrophobic, large molecules (cholesterol)

The last concept we'll be discussing in this section is the topic of membrane fluidity. Maintaining constant fluidity at various temperature conditions is a key survival adaptation of organisms. This ensures optimal operation/function of the cell. Keep in mind that high temperature increases membrane fluidity, while low temperature reduces it.

There are a few important factors at play when it comes to regulating membrane fluidity.

<u>When the membrane is under high temperature stress:</u>

- Cholesterol inhibits, reducing fluidity **(animals mostly)**
- High proportion of saturated phospholipid tails to allow for closer packing, reducing fluidity

<u>When the membrane is under low temperature stress:</u>

- Cholesterol disrupts fatty acid association in the membrane (**animals mostly**)
- High expression of desaturase enzymes to create more unsaturated, kinked tails, which increases fluidity

Apply Your Knowledge

Consider the following (not multiple choice, these are designed to allow you to think more freely about the testable concepts):

1. Recall that Dr Maxwell said the ΔF508 CFTR is actually functional i.e. it can still pump out chlorine ions. Using your knowledge of the secretory pathway, what would be some theoretical ways to restore chloride ion transport in cystic fibrosis patients?

2. Draw a graph of the overall catalytic cycle in Chlamy as pH goes from 1 to 7. Rationalize what processes are underlying the changes in the catalytic cycle as pH changes.

3. Explain the processes that are happening to a plasma membrane's composition as temperature increases/decreases. Include how cholesterol, desaturases, and saturated/unsaturated fatty acids are affected by the temperature change.

Congratulations for making it through the entire breakdown. Remember to continually reinforce your understanding over as long a period of time as possible in order to maximize your performance. Best of luck in your studies! Here are some links that might interest you.

Want to learn more about WebStraw? Check out our website at www.webstraw.ca