Meiosis & Recombination

[Overview]

The mitotic cell cycle - review

- **Cell cycle:** A period of growth followed by nuclear division and cytokinesis
- **Mitosis** divides replicated DNA equally and precisely
- Replication of DNA for each individual chromosome creates two identical molecules called **sister chromatids**
- **Chromosome segregation:** Equal distribution of daughter chromosomes to each of two cells resulting from cell division (*i.e., separation of the sister chromatids*)

So, cellular reproduction is all about a cell passing its DNA to its offspring, and generating identical clones.

Mitosis provides for growth, cell replacement, and asexual reproduction

- When the cell cycle operates normally, mitosis produces genetically identical cells for:
    - o Growth
    - o Replacement of damaged and lost cells

    *The textbook lists 'reproduction, growth and development, and tissue renewal'

So, note that this is the same genetic material going from the parent cell to the daughter cell

Result of binary fission - prokaryotes

- Cell division yields progeny that are identical to parental cell except for mutations that occur during cellular reproduction
- BUT, at the end, oxygen is <u>NOT</u> the final electron acceptor (a different electronegative molecule is used, instead)

    Z Just remember: anaerobic respiration = no oxygen, so there's no oxygen molecule either!

- **Example:** <u>Sulphate-reducing bacteria</u>

    Sulphate-reducing bacteria are super ancient bacteria that live deep at the bottom of marshes. Instead of having oxygen at the end of their chain, they use a sulphate ion; and so, instead of producing water as a byproduct (from the oxygen), this sulphate ion is reduced and the bacteria produces hydrogen sulphide.

KEY TAKEAWAYS

- Anaerobic & aerobic respiration both go through same processes, BUT anaerobic does <u>NOT</u> use oxygen as its final electron acceptor at end of transport chain

Fermentation is the other method of anaerobic respiration;

Fermentation enables cells to produce ATP without oxygen or an electron transport chain

- Fermentation relies heavily on the fact that glycolysis produces a small amount of ATP
  - The idea here is: keep glycolysis going, & use that small amount of ATP to power one's activity
- Fermentation recycles NADH so it can go back to glycolysis and pick up more electrons; it's all about recycling the electron carrier so the glycolysis doesn't back up and stop
  - Normally in glycolysis, you take a glucose, energize it, follow through the various steps, and then at the end, split it into two pyruvate molecules
    - During this process, you would normally have oxidation of intermediate molecules and generate two NADH molecules (high energy carriers), and with oxygen present, these carriers would then shoot off to the electron transport chain to pass their electrons on.
    - <u>BUT</u> with no oxygen present, the whole chain backs up! The electron carriers have nothing to pass their electrons onto.
  - SO, the whole point of fermentation is to give NADH a molecule to pass its electrons onto, so that it may then be oxidized back into NAD+, which allows it to return to glycolysis and pick up more electrons.
    - In other words, fermentation keeps glycolysis going (and while it is not a lot of ATP being generated, it's enough for some organisms evidently).

There are two types of fermentation that we will focus on: lactic acid fermentation, and alcohol fermentation

<u>Lactic Acid Fermentation</u>:

- Uses pyruvate as the mechanism of recycling: NADH electrons are used to reduce the pyruvate molecule, meaning NADH is again oxidized & can return to glycolysis and pick up more electrons so it can continue to burn sugar.
- When the pyruvate molecule is reduced, it becomes lactate (*lactic acid*)

- Thus, there are certain types of bacteria that, in the absence of oxygen, can ferment instead.
    - ***Side note: our muscle cells can also do this!***
- For bacteria: bacterial lactic acid fermentation has been known about for centuries, & is big in the food production industry.
    - Think milk fermentation, production of cheeses; fermented foods are a modern trend (e.g., Kimchi)

Exertion and energy

When you work your muscles to a point where you create an 'oxygen debt', your muscles will start to ferment & will begin what is essentially lactic acid fermentation

- As this lactate builds up, the blood carries it back to the liver, which then converts it back to pyruvate (by basically just reversing the reaction)
- This pyruvate is then used to produce ATP: after it is converted back, it re-enters oxidation (within the mitochondria of the liver cells), then the citrus cycle, then the electron transporter chain, etc., etc.
- ATP is used to build sugar molecules; this whole process is called GLUCONEOGENESIS
- The sugar molecules are then secreted back into the blood so that they can go back to the muscles, providing the muscles with an ongoing source of energy

So, when you are at the gym, intensely working out, you have aerobic respiration occurring in your liver and your other cells, whilst simultaneously having lactic acid fermentation occurring in your muscles. This system ensures that you can keep producing glucose even when your muscles have run out of it!

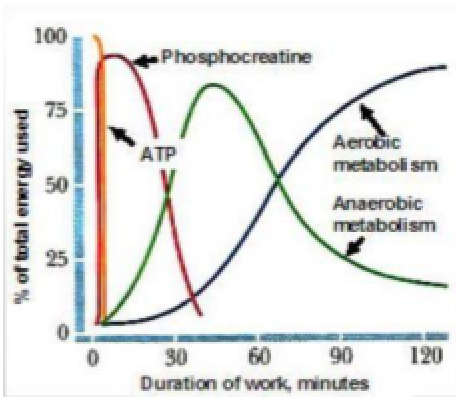
Taking this into consideration, the next question is: how does your body allocate and govern its resources during peak periods of activity? You can't use aerobic respiration all of the time because aerobic respiration is rather 'enzymatically rigorous': it involves a ton of steps [and effort] for your cells, so they won't be running this at peak speed all of the time.

Resting muscles

- Your muscles have lots of oxygen, and are not busy, so they use this downtime to produce a surplus* of ATP, as well as creatine phosphate (which can be used to regenerate ATP) and glycogen.
  ** Note: when we say 'surplus' we're still talking about a relatively small amount; while your muscles can store quite a bit of glycogen, they can't store a lot of ATP or creatine phosphate.*
- So, during rest, you are performing a very, very low level of glycolysis, and activating a very low level of the full aerobic pathway, producing a surplus.

Initial burst of exercise

- It takes a bit of time for the whole aerobic pathway to ramp up and get going, so when you first start exercising, it's all about your surplus of ATP & creatine phosphate, while your body is still operating at a fairly low level of glycolysis and an even lower level for aerobic metabolism. Check out the graph below:



Looking at the graph above, which shows how your energy is spent over a period of exercise, you can see that your ATP and creatine phosphate surpluses (the red and orange lines) are used right away at the beginning of your work out, and are depleted before long (your creatine phosphate storage lasts you a little longer than your ATP).

Moderate activity

As you keep exercising, your demand for ATP increases; by this point, your aerobic metabolism begins to work faster – specifically, glycolysis starts to really pick up (using the glycogen stores).

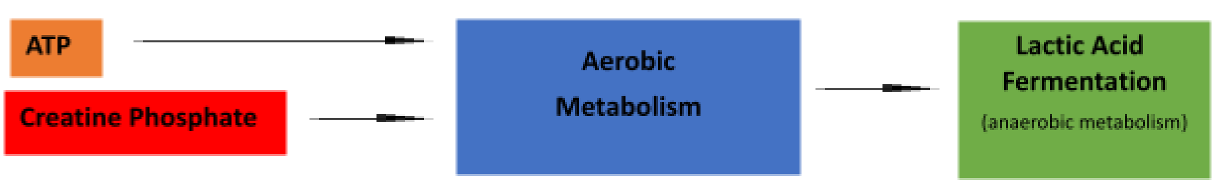
Peak activity

During peak activity, your aerobic metabolism hits its maximum level (which is governed by the availability of oxygen). But what if you keep working out, despite your body hitting this point?

If demand exceeds supply, your muscles will start lactic acid fermentation.

] Fun Fact! The reason you keep breathing heavily after exercising is because of a lactate build-up: Following a heavy work out, there is a bunch of lactate left-over in your muscles and still entering your liver, and you need extra oxygen to turn it back into pyruvate and process it normally (i.e., without lactic acid fermentation).

So, the mechanisms by which you produce energy change throughout a period of activity:



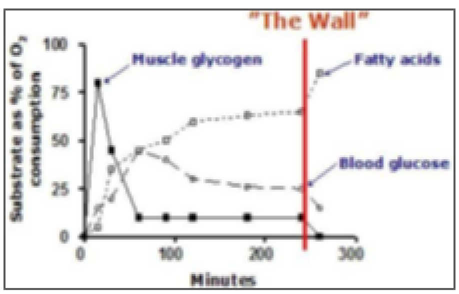
So, we know how the body spends its energy during periods of activity. Let's take a closer look at the actual sources of energy, themselves:

During a workout, the systems that generate the energy are not the only things that change as activity progresses – your body also switches through various fuels. Your muscles, it turns out, burn through their glycogen levels pretty quickly. This creates an interesting problem for your body: It needs to match the demands for ATP 100% to keep your muscles going, but it also needs to match the energy demand coming from the rest of your body—especially, your brain, which requires glucose. Thus, your body must maintain a constant supply of glucose to your brain at all times, must be aware of the energy demands of the rest of the body, AND must now also meet these excessive energy demands within the muscles. How does it manage all of this?!

Well, once it runs out of glycogen (fairly quickly), it initially relies on:

1. The initial rise in blood glucose (coming from the liver); this is via gluconeogenesis: the breakdown of glycogen in the liver & secretion of the glucose into the blood)
2. But soon enough, it switches to the burning of fatty acids; the total amount of material you consume increases as you continue to exercise and burn more; at this point, this becomes your major source of energy, continuing on like this for a long while.

<u>"The Wall"</u>

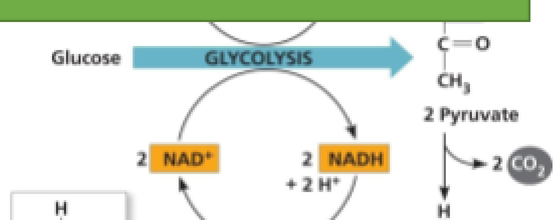


For athletes in high endurance sports, or for individuals who participate in endurance-type activities, such as marathons, they've likely experienced the Wall: the point at which the individual/athlete cannot go on any further, losing the ability to physically move their muscles.

The Wall corresponds to the point at which your liver can no longer match demand, and your blood glucose level starts to drop slightly. This triggers your fatty acid consumption to rise and account for the dip in level; but herein lies the problem: your brain can't run on fatty acids (it needs glucose!). Thus, your cognitive faculties shutdown as your brain is starved of energy, causing one to lose control of their body, and hit the Wall.

KEY TAKEAWAYS

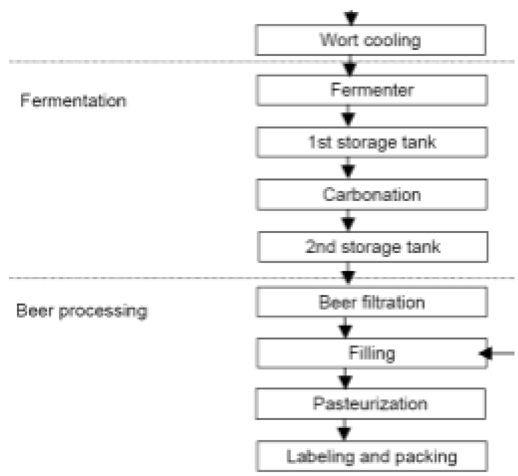
- The Wall: point at which athlete can go no further; corresponds to point at which blood glucose drops
  - Begins burning fatty acids for energy instead, which brain can't use. Brain starved of energy = cognitive shutdown



- Used for centuries, for both baking and winemaking
- Works the **same way**: It offers a mechanism for recycling NADH back into NAD+ so that glycolysis can keep on running
- Certain types of bacteria, as well as yeast (a single-cell eukaryote [fungi]), use this process:
    - First, the pyruvate has a carboxyl group removed, releasing carbon dioxide
    - Then, an intermediate molecule (e.g., acetaldehyde) converts it to ethanol
- So, alcohol fermentation uses the same principle (oxidizing NADH back to NAD+), but differs slightly in that in produces carbon dioxide and alcohol
- The alcohol is actually toxic to the yeast! The yeast has to get it out of the cell, so it excretes the alcohol out, where the alcohol then diffuses away
- To produce wine: trap yeast within a vat of grape/fruit juices. The alcohol that is excreted cannot simply diffuse away, and instead builds up, rising in concentration (alcohol concentration can generally hit ~14% before it becomes too toxic for the yeast, killing it).

Fermentation & the production of beer

- Works the same way for beer
    - To make beer, you give the yeast a form of fermentable sugar as a source of energy (e.g., barley [*most common*], wheat, rye)
    - You mash up the grains, exposing the starches, then mix things together, heat the mixture, etc., performing complex processes to eventually give you wort
    - You let the wort cool down, and allow it to ferment by adding yeast



<u>Lagers vs. Ales</u>

- Lagers use **bottom-fermenting yeasts** (e.g., *saccharomyces pastorianus*) which sink to the bottom of the vat that they're in, and ferment at a relatively low temperature
- Ales use **top-fermenting yeasts** (e.g., *saccharomyces cerevisiae*) which float at the top and ferment at higher temperatures (~20̊, but can be higher)
    - Richer, more complex flavors of ales result from the higher temperature: more aromatic esters are released
- To carbonate drinks, you can force CO2 into the liquid (*artificial carbonation*) or you can add a fresh batch of yeast instead, and it will self-carbonate
- Overall, the yeast is the key player here; and by placing yeast into an environment with no oxygen and with lots of sugar, it utilizes alcohol fermentation to generate its energy

Fermentation & the production of bread

- When baking, you mix yeast into the dough when the dough is in a low oxygen environment. The yeast starts to use alcohol fermentation, producing carbon dioxide and ethanol (as we've seen before)
  - The carbon dioxide bubbles are what cause the bread to rise (the heat causes the alcohol to evaporate, which together cause the CO_2 bubbles that were released to expand)

Fermentation enables cells to produce ATP without oxygen

<u>'The Paradox of Anaerobic Life'</u>

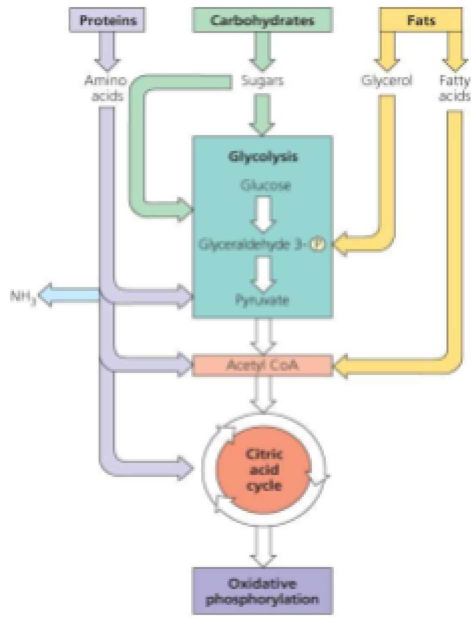
- Despite name, this paradox also pertains to aerobically-respiring organisms as well (like us!)
- Oxygen is potentially toxic: it is very electronegative, and it sits at the end of the electron transport chain, receiving the electrons; the idea is that the oxygen will be reduced to a water molecule, however sometimes things go awry:
  - Sometimes when oxygen is receiving these electrons, it can form a partially reduced form if it doesn't receive all of the electrons it needs to fully reduce
  - In this partially reduced form, oxygen is known as a 'reactive oxygen species' ('ROS')
  - These ROS are a danger to cells because they are extremely electronegative, meaning they will target any organic molecule and strip the electrons away from it, over and over again. This shreds the organic molecule up.
  - The formation of ROS is unavoidable, so how do we fix this?
- Eukaryotes have a special defense called an 'antioxidant defence mechanism'
  - It involves a bunch of 'scavengers' which go around and bind up the ROS, ultimately helping convert them to water
- Obligate anaerobes (e.g., organisms living in stagnant ponds or deep soils to avoid oxygen) do NOT have these defense mechanisms
- Facultative anaerobes (e.g., yeasts, certain bacteria) can switch from fermentation to oxidative phosphorylation, and vice versa – they can use either aerobic or anaerobic respiration to produce ATP
  - They carry out glycolysis, producing pyruvate; if oxygen is present, then the oxygen molecule will be there to carry out the oxidative phosphorylation; if oxygen is MIA, then the organism will flip to fermentation, instead

Glycolysis evolved early in the history of the life on Earth

- Glycolysis is the universal energy-harvesting process of life
- Glycolysis' role in fermentation and respiration dated back 3.5 million years ago, when only prokaryotes existed, and life existed in the absence of oxygen
- The ancient history of glycolysis is supported by its: 1) occurrence in all domains of life, and b) its location (it occurs just in the cytoplasm and doesn't require any complex enzyme reactions or special membrane-bound organelles to carry out the process)

Cells use many kinds of organic molecules as fuel for cellular respiration

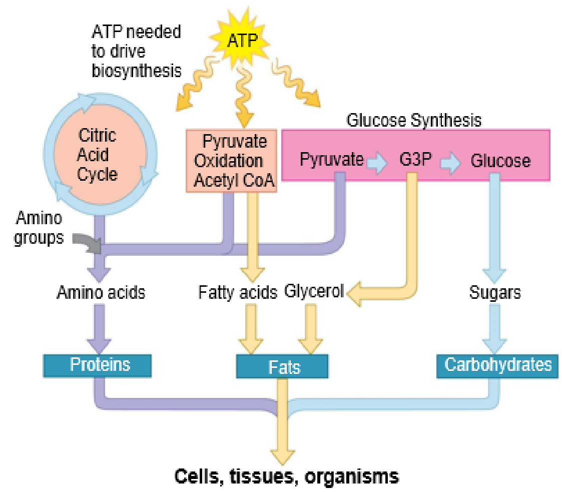
- It's pretty rare to have just pure glucose entering the system
- There are multiple different points of the pathway where different molecules can be fed in to produce one's energy. Looking at the diagram:



  - Carbs don't contain much in the way of glucose, but the simple sugars they provide are broken down into monosaccharides which are fed in right at the start of glycolysis
  - If you eat starch (e.g., from plants), this will be broken down into glucose
  - Glycogen, on the other hand, splits away when it is broken down, becoming gluco-6-phosphate, which is an early intermediate molecule in glycolysis, and thus feeds in near the start as well
  - Carbs can enter at different points depending on the carb in question
  - Fats are a great source of energy. The glycerol group of a fat is broken off as the first step in its processing, which is then sent off and converted to G3P (glyceraldehyde 3-P: the molecule at the end of the energy investment phase of glycolysis) and is then fed in midway through glycolysis
    - The other part of the fat that is left now contains only the nice long hydrocarbon chains, which can be broken into two carbon pieces (in the diagram, they are acetyl groups in the pink) which can then be fed in at the beginning of the citric acid cycle, skipping glycolysis
    - Just like carbs and fats, proteins can also enter at different points:
      - Proteins break down into amino acids; the amino acid group breaks off, and, depending on which amino acid it is, it will either be converted to pyruvate and fed into the pathway at the end of glycolysis (which is then carried on to the next step of oxidation), OR it will be broken down even further into two acetyl groups and fed in at the start of the citric acid cycle
        - Sometimes, they are converted into intermediate molecules within the citric acid cycle
  - Your cells do have a preferred order for consumption (glucose carbs fat proteins)
  - When people climb Mount Everest and return looking emaciated (as if they are wasting away), this is because their glycogen stores are loooooong gone by the time they return, meaning they've burned through all of their fat as well. The last source left to generate

energy is protein. At this point, the body starts to break down muscle mass to generate energy

Food molecules provide raw material for biosynthesis



- The flip side of the pathway for energy is that not everything produced in the pathway is going to be used
- Food molecules provide the raw materials for biosynthesis to build your macromolecules, and they will be fed I and will move through the process
- Many of these intermediate molecules, however, are then pulled out and used for building proteins, fats, and carbs, which together build cells, tissues, and organisms
- Thus, fuel is for more than just food and energy purposes; fuel must be acquired for the purposes of building these macromolecules that are required for your cells to function