



Cellular Respiration

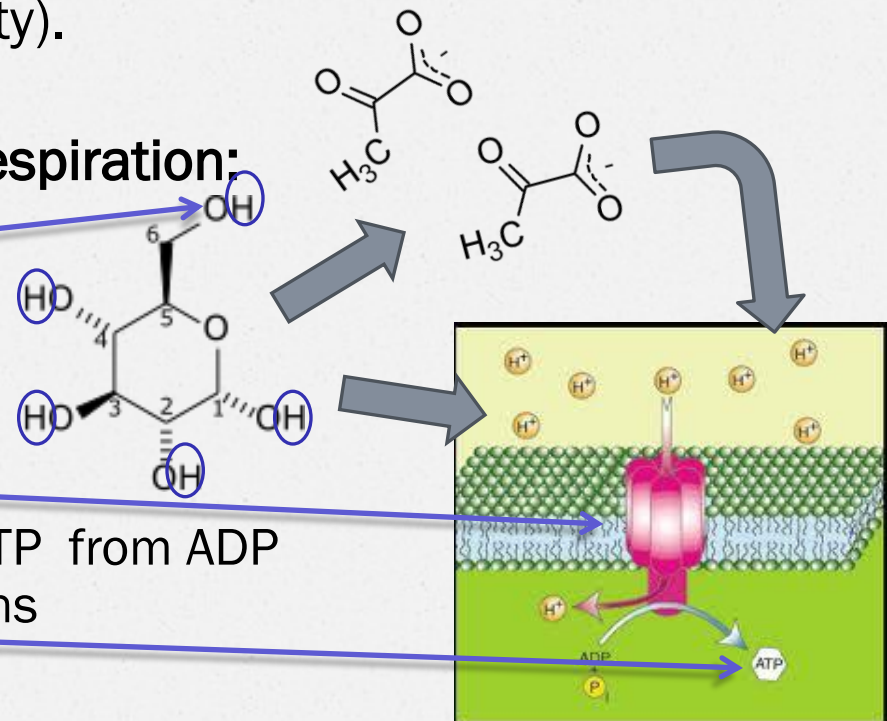
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In a nutshell...

- **Cellular Respiration** is a series of chemical reactions in which **hydrogen atoms** on a **glucose molecule** are removed so that they can be used to turn ATP Synthase proteins and **power the production of ATP** (the source of energy for cellular activity).

- **Key points of Cellular Respiration:**

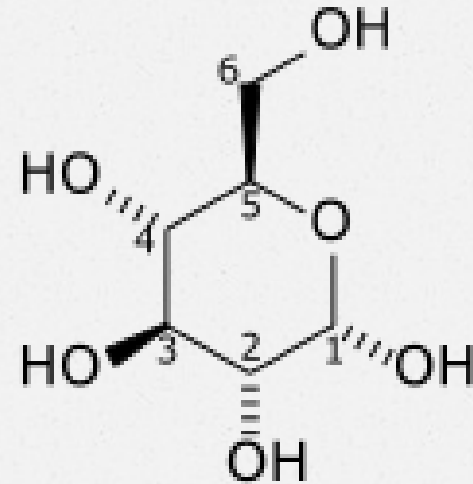
- Hydrogen atoms are removed from glucose
- Those hydrogen atoms are used to turn ATP Synthase
- ATP Synthase makes ATP from ADP and P_i every time it turns



Glucose

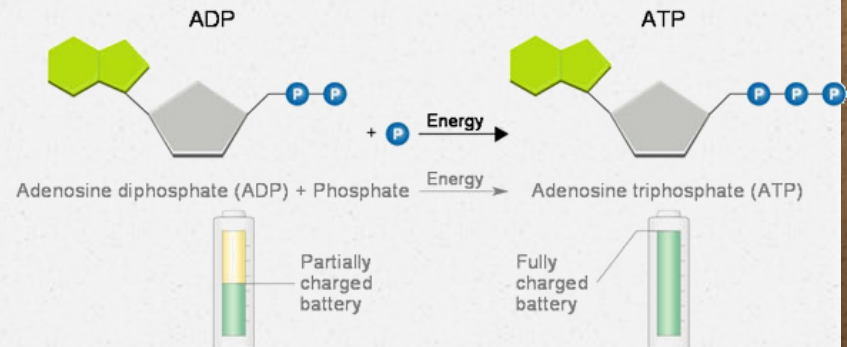
- Glucose is the simplest carbohydrate

- A carbohydrate is an organic molecule that contains carbon, oxygen, and hydrogen (note: carb-o-hhydr-ate).
- Examples include sugars, starches, fibers, and cellulose



- Glucose is **NOT** used to power cellular activities.

- Instead, the hydrogen atoms on glucose are used to power the production of cellular energy
- Glucose is the way in which living organisms get hydrogen into their mitochondria
- Those hydrogen atoms are used to turn ATP Synthase.
- ATP Synthase is the protein that produces ATP
- ATP powers cellular activity



Carbohydrates

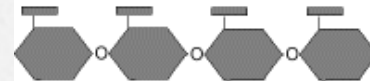
- All carbohydrates are made of chains of glucose.

- The longer the chain of glucose, the more difficult the carbohydrate is to break apart and digest.
- E.g. simple sugars break down easily in our bodies because they are very short chains of glucose
- Fibers break down very slowly because they are very long chains of glucose.

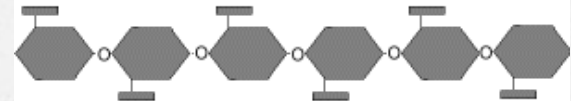
Glucose



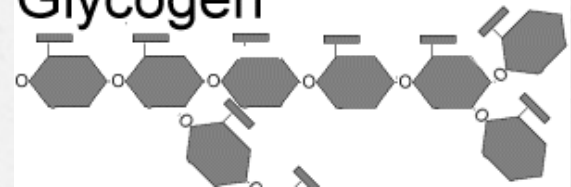
Starch



Cellulose



Glycogen



Source: bioweb.wku.edu

- All carbohydrates must be broken down into individual glucose molecules when we consume them.
- It is necessary to break carbohydrates into individual glucose molecules so that they can be absorbed into the bloodstream
- A starch or fiber would be way too big to be absorbed across the lining of the intestines and through the membrane of a cell.



In the cell...

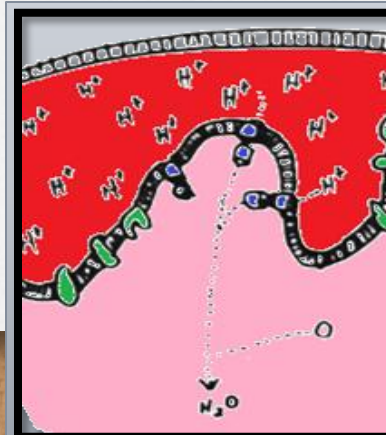
- Once absorbed into the bloodstream, cells absorb the glucose from the blood across their cell membrane and into their cytosol.
 - The breakdown of sugar and the process of cellular respiration begins in the cytosol of a cell.

- When a glucose molecule is absorbed by a cell, it is broken down over a series of steps that each occur in different places. These places include:

- The **cytosol**: the “jelly filling” of the cell that surrounds the organelles
 - Glucose is split in half in the cytosol to form 2 pyruvate molecules.*

- The **matrix of the mitochondria**: this is the innermost middle of the mitochondria

- This is where the pyruvate molecules are completely broken down*

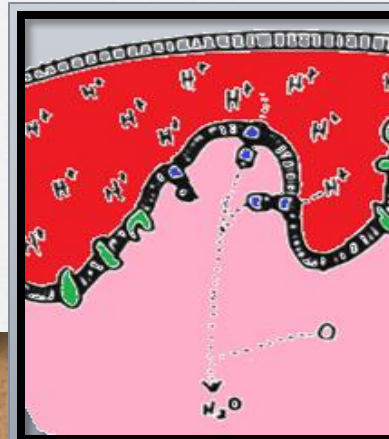
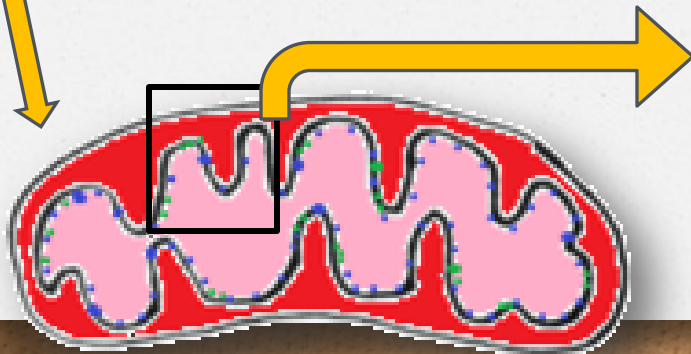


- ← Outer membrane
- ← Intermembrane Space
- ← Inner membrane
- ← Matrix (innermost middle)



Inside the cell (cont.)

- o The intermembrane space of the mitochondria: this is the space between the inner and outer membrane of the mitochondria.
 - o *The hydrogen atoms that were taken from glucose are crammed in here so that they can turn ATP Synthase.*
- o The inner membrane of the mitochondria: this is where we would find ATP Synthase.
 - o *To get out of the intermembrane space, H^+ atoms must pass through ATP Synthase proteins, causing them to turn and make ATP.*



- ← Outer membrane
- ← Intermembrane Space
- ← Inner membrane
- ← Matrix



Mitochondrial Outer
Membrane

Mitochondrial Inner
Membrane

Intermembrane
Space (w/ Hydrogen
atoms)

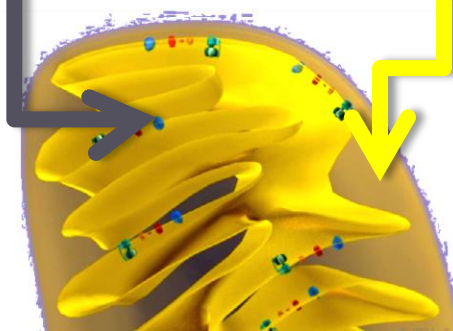
Flowing
Hydrogen

ATP
Synthase

Aden

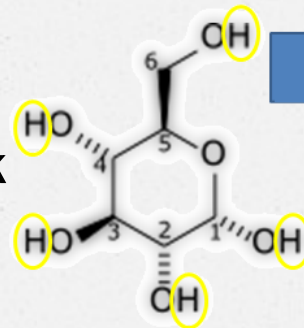
Mitochondrial Matrix
(inside)

As hydrogen moves past ATP Synthase, it causes it to turn. As ATP Synthase turns, it makes ATP from ADP and P_i .

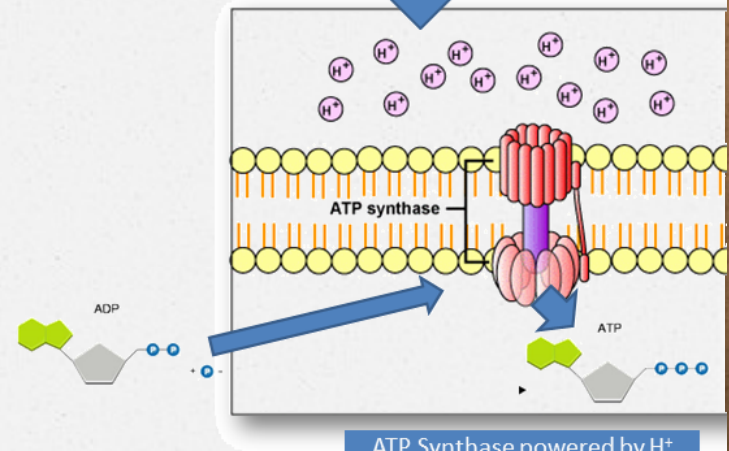


Cellular Respiration

- The main point of cellular respiration is to obtain hydrogen atoms in order to power ATP Synthase.
 - These H^+ atoms primarily come from glucose
 - (although fat and other components of food can be used as a source of hydrogen as well).
- A series of multiple chemical reactions are necessary to break down glucose in order to remove the hydrogen atoms.
 - The process of cellular respiration can be broken into four basic steps
 - Each step consists of multiple chemical reactions



Hydrogen removed through
Cellular Respiration



ATP Synthase powered by H^+
from the glucose molecule.

Source: student.ccbcmd.edu



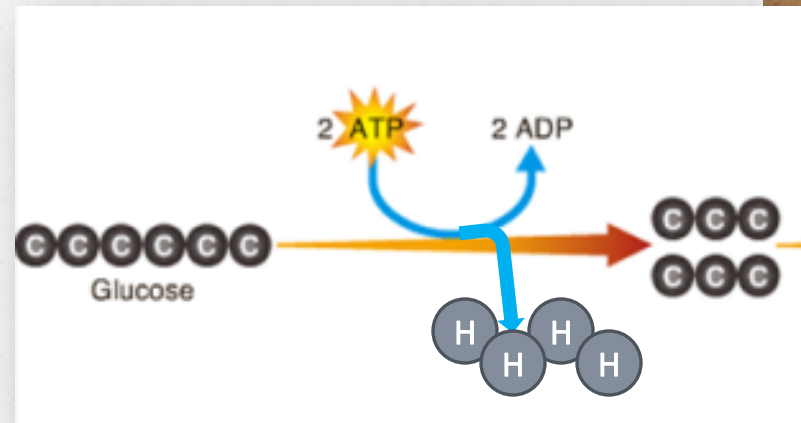
Steps of Cellular Respiration

- o 1. **Glycolysis**: glucose is split in half to become 2 pyruvates. This occurs in the cytosol. Some hydrogen is removed. 2 ATP are used, but 4 are produced via Substrate-level Phosphorylation.
- o 2. **TCA Cycle**: Pyruvates move from the cytosol into the matrix (innermost middle) of the mitochondria. The remaining hydrogen is all removed during the TCA Cycle.
- o 3. **Electron Transport System**: the hydrogen atoms that were removed from glucose are moved into the intermembrane space of the mitochondria.
- o 4. **Oxidative phosphorylation**: the hydrogen is used to turn ATP Synthase so that ATP can be produced from ADP and P_i .



Step 1: Glycolysis

- o Glycolysis: glucose ($C_6H_{12}O_6$) becomes 2 pyruvates ($C_3H_4O_3$) and 4 H^+ atoms
 - o ATP transfers energy on a phosphate to split glucose in half.
 - o Note: only carbons are shown in the image below to simplify it
- o It takes energy to break apart a glucose molecule: 2 ATP molecules to be exact.
 - o However, we do get 4 ATP back eventually
 - o Glycolysis has a final gain of 2 ATP ($-2+4 = +2$)
- o ATP is re-created in Glycolysis using Substrate Level Phosphorylation (next slide)

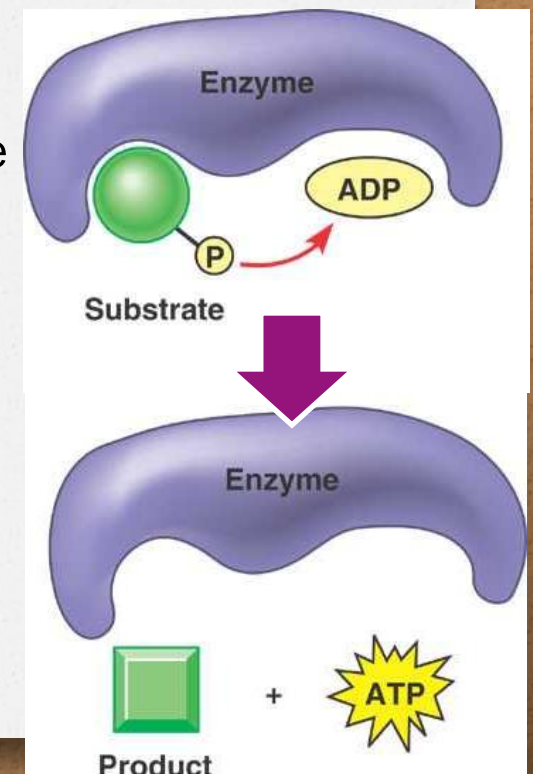


Source: facweb.northseattle.edu



Substrate Level Phosphorylation

- ATP production during Glycolysis is slightly different than in the rest of the stages.
 - Instead of using ATP Synthase to produce ATP, ATP is produced by an “exchange” kind of chemical reaction.
 - Production of ATP using an enzyme reaction to *transfer* a phosphate to ADP is called Substrate Level Phosphorylation.
 - To “phosphorylate” means to add a phosphate
- In glycolysis in the cytosol, an enzyme moves the phosphate from the halved glucose onto the ADP .
 - This is different than what occurs later in the mitochondria, where the phosphate (P_i) must be added by the “turning wheel” of ATP Synthase.



Substrate Level Phosphorylation Animation

Click your mouse to start animations.



Split glucose with
one less P_i

Newly Formed
ATP

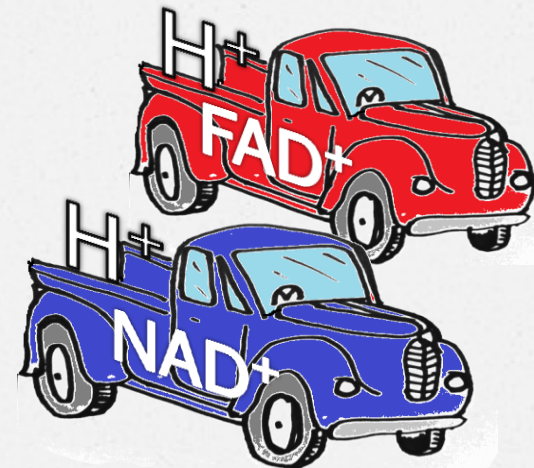
This process will happen once more. Because it happens twice on each half of the original glucose molecule, 4 ATP total are made in this manner (2 ATP per half of glucose).

Note: this all occurs in the cytosol before entering the mitochondria



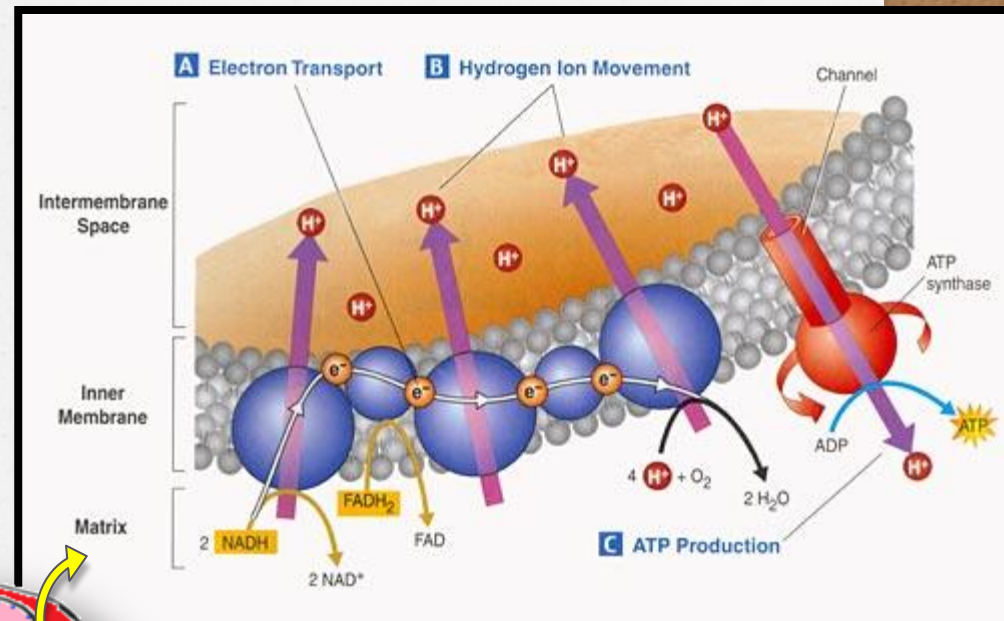
Step 2: TCA Cycle

- **TCA Cycle: The pyruvate molecules get completely broken down.**
 - The 2 pyruvate molecules were formed when glucose was split in half.
 - The 2 pyruvate molecules leave the cytosol and enter the matrix (the innermost middle) of the mitochondria.
- **H^+ atoms are taken off of the disassembled glucose molecule by NAD^+ and FAD^+ at different points of the TCA Cycle.**
 - NAD^+ and FAD^+ are sort of like molecular pickup trucks for hydrogen.
 - When NAD^+ and FAD^+ pick up a hydrogen, they become $NADH$ and $FADH_2$.
- **During glycolysis and the TCA cycle, 6 CO_2 will be produced.**
 - These are made from the six original carbons on glucose ($C_6H_{12}O_6$)



Step 3: The Electron Transport System

- Electron Transport System: H^+ is moved from the matrix to the intermembrane space.
- The inner membrane of the mitochondria has special proteins that get hydrogen from NAD^+ and FAD^+ in the matrix and cram it into the intermembrane space.
- These proteins are powered by electrons taken from the glucose molecule.
- These electrons were removed from glucose during glycolysis and the TCA cycle.*

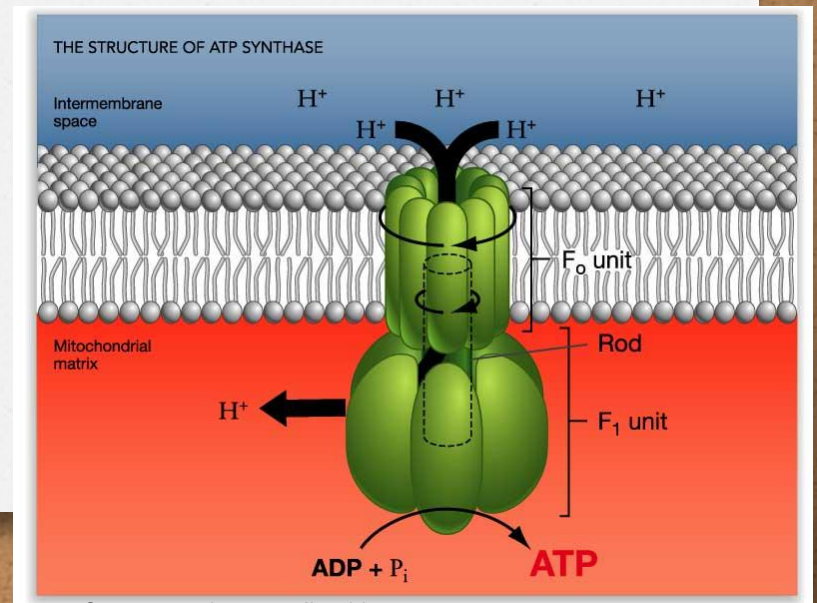


Source: teachersdomain.org

Step 4: Oxidative Phosphorylation

○ Oxidative Phosphorylation: H^+ is used to turn ATP Synthase, powering ATP production

- The H^+ atoms are *crammed* into the intermembrane space – they want to get out!
- The only way out of the intermembrane space is through ATP Synthase (like a revolving door)
- As hydrogen atoms move past ATP Synthase, they turn it, powering the production of ATP from ADP and P_i

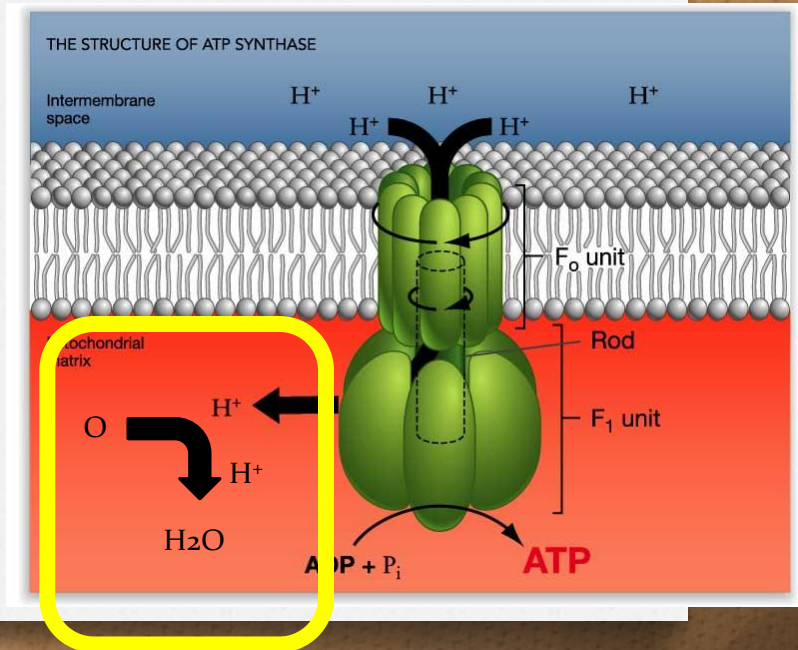


Source: newbotany.mihanblog.com



Step 4: Oxidative Phosphorylation

- “Phosphorylation” means to get a phosphorus atom
 - ADP is *phosphorylated* to become ATP – ADP gains a P_i
 - E.g. “education” is the process of getting educated
 - For every H^+ delivered by NAD^+ and FAD^+ 3 ATPs are created
- After hydrogen atoms move past the ATP Synthase, they enter the matrix.
 - Here, H^+ atoms must be picked up by an oxygen atom.
 - This is the “oxidative” part.
 - When two hydrogen atoms bond to an oxygen atom, they form H_2O (water).



Source: newbotany.mihanblog.com



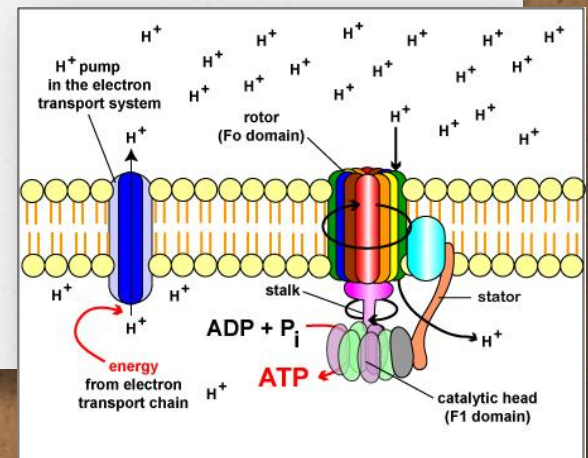
Oxidative Vs. Substrate Level Phosphorylation

- During glycolysis in the cytosol, ATP is formed by Substrate Level Phosphorylation
 - In this case, ATP is created by an enzyme that “transfers” an inorganic phosphate (P_i) from the halved glucose onto ADP.
- In the mitochondria, ATP is formed by oxidative phosphorylation (when ATP Synthase protein powered by the H^+ from glucose makes ATP).
 - In oxidative phosphorylation, H^+ moving through ATP Synthase turns a “wheel” that smashes an inorganic phosphate (P_i) onto an ADP to make ATP.



'Clogged' ATP Synthase

- If hydrogen wasn't removed from the matrix by oxygen, it would "clog" ATP Synthase.
 - This would slow and eventually stop ATP Synthase from turning.
 - If ATP Synthase doesn't turn, ATP isn't produced.
 - If ATP isn't produced, most cells will eventually shut down because they won't have enough ATP to power cellular activity.
 - Exception: cells that can produce ATP by fermentation.
- The lower the concentration of hydrogen in the matrix, the faster ATP Synthase turns and the faster ATP is produced.
 - More oxygen in the matrix means faster H^+ removal
 - This is why you breathe more heavily during exercise than at rest
 - During exercise, you need more oxygen to remove more H^+ to turn ATP Synthase faster to make ATP more quickly
 - In agriculture, plants & animals that can produce more ATP will produce more food.



What if there is no oxygen?

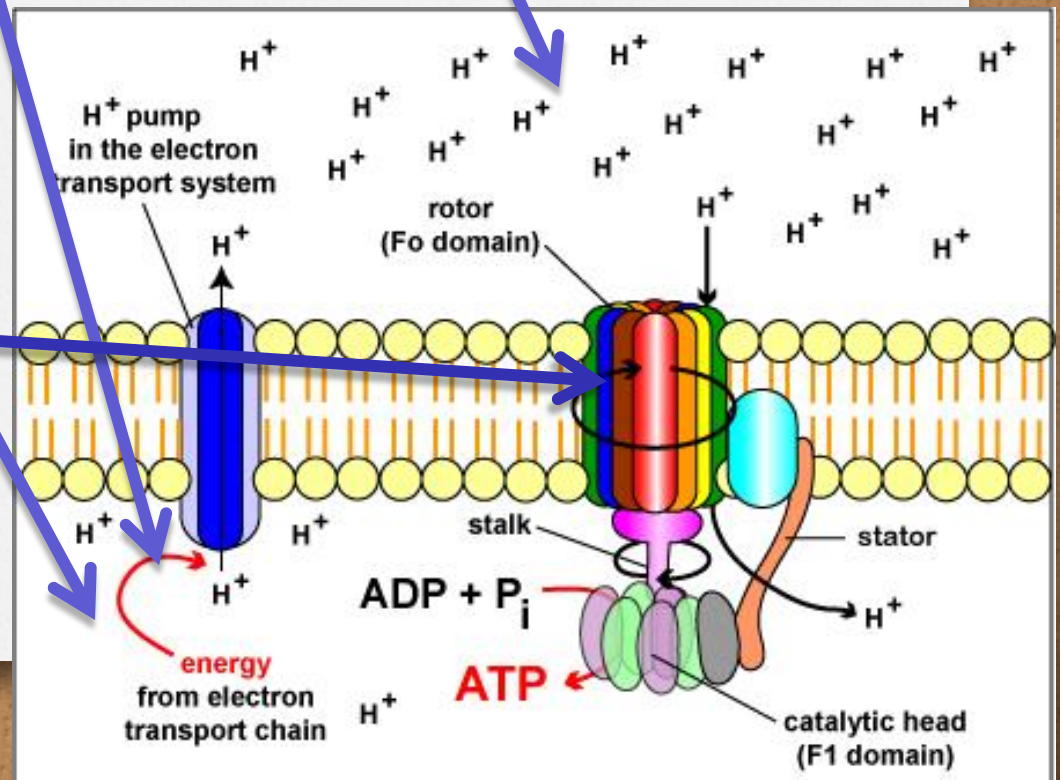
- o As long as there is oxygen present, it will bind to the hydrogen in the matrix (innermost middle) of the mitochondria.
 - o Oxygen will continue to go to the matrix to bind with H^+ to form water and leave the mitochondria.
 - o Oxidative Phosphorylation produces 36-38 ATP.
- o However, if there is no oxygen, Oxidative Phosphorylation cannot occur and ATP cannot be made by ATP Synthase in the mitochondria.
 - o ATP can be made by Substrate-level Phosphorylation in the cytosol.
 - o However, this kind of phosphorylation only produces 2 net ATP.
- o This occurs in humans for short periods when not enough oxygen is available (such as when you are sprinting).
 - o It also occurs in some microorganisms when they ferment.
 - o Fermentation – the breakdown of glucose into ethanol to produce small amounts of ATP in the absence of oxygen.
 - o Energy does remain in the ethanol that is excreted.



In a nutshell...

○ Five ways to maximize Mitochondrial ATP Production
(Note: max ATP = max food production by plants & animals):

1. Maximize H^+ in the intermembrane space
2. Minimize H^+ in the matrix.
3. Maximize O_2 in the matrix
4. Maximize the number of ATP Synthase.
5. Maximize the number of total mitochondria in an organism's cells.



Summary of Cellular Respiration

1. Glucose is consumed, enters the bloodstream, and is absorbed by cells
 - o Glucose is absorbed by cells because higher concentrations are found in the blood than inside the cells.
2. Glucose enters the cytosol of the cell and is broken in half into 2 pyruvates
 - o ATP is produced by substrate-level phosphorylation
3. The pyruvate molecules enter the matrix (innermost middle) of the mitochondria and are broken down in a series of steps so that hydrogen can be removed
 - o *A total of 6 CO₂ molecules are released during cellular respiration (from the original 6 carbons)*



Summary of Cellular Respiration

4. As glucose is broken down completely, NAD^+ and FAD^+ collect hydrogen atoms (like a molecular pickup truck)
5. The hydrogens are brought to the inner membrane of the mitochondria; there they are crammed into the intermembrane space by protein pumps
 - o *The protein pumps are powered by the electrons taken from the glucose molecule.*
6. The hydrogen atoms that are crammed in the intermembrane space want to leave; the only way out is through ATP Synthase.
7. As H^+ atoms move through ATP Synthase, they turn the “revolving door”; when ATP Synthase turns, it makes ATP
 - o *With each H^+ atom, 2-3 ATPs are created from ADP and P_i*



Review Concepts

- Parts of the mitochondria and where each step of respiration occurs in the cytosol/mitochondria.
- Differences and similarities between substrate-level phosphorylation and oxidative phosphorylation.
- Roles of glucose, pyruvate, $\text{NAD}^+/\text{FAD}^+$, the TCA cycle, the Electron Transport System, hydrogen, ATP Synthase, and oxygen.
- 5 ways to increase ATP production
- Summary of the 4 steps of respiration: glycolysis, TCA cycle, Electron Transport System, and Oxidative Phosphorylation.

