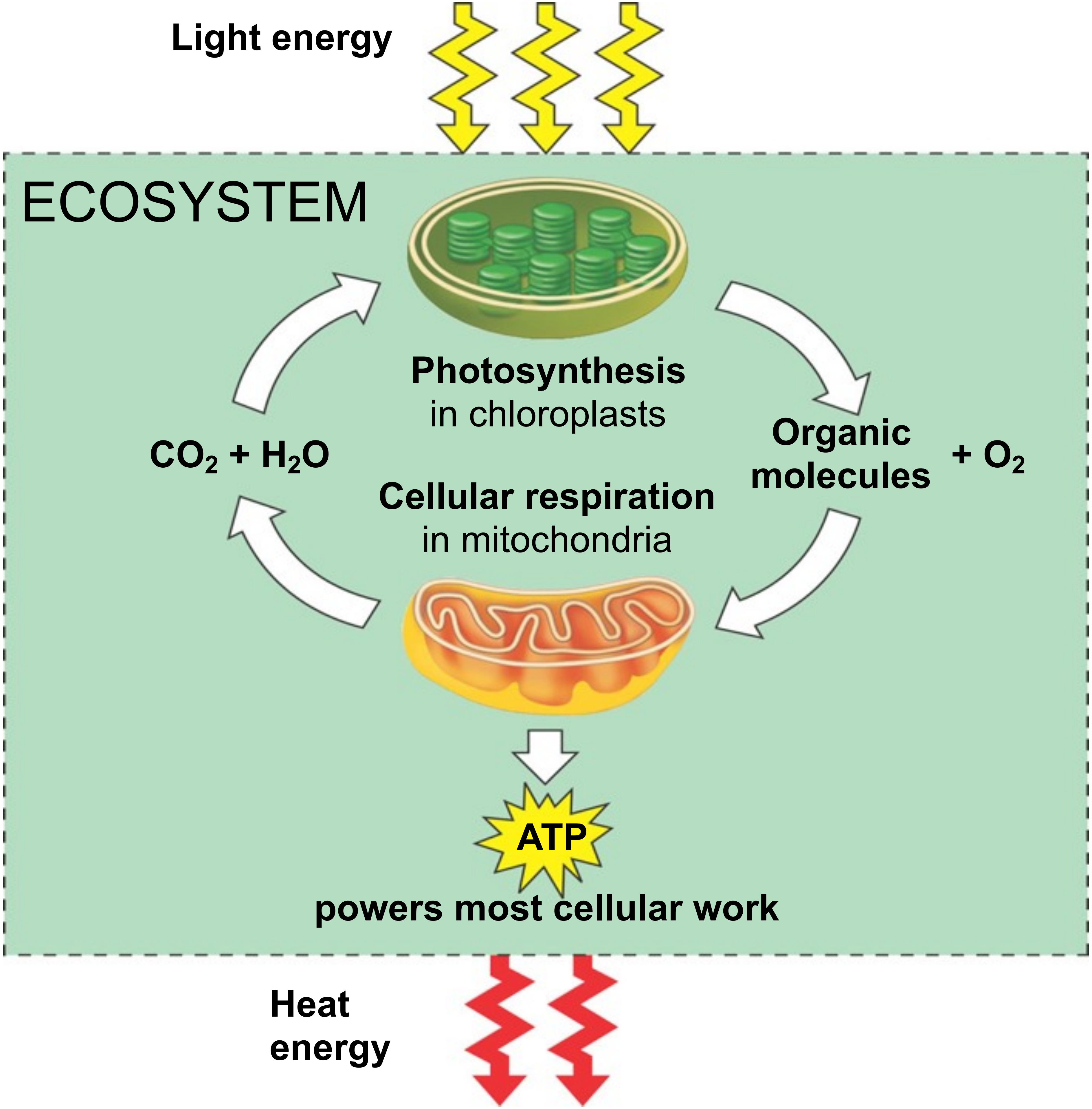
CELL RESPIRATION

PREFACE

- Cellular processes require energy.
- ATP is the cellular energy choice (fuel) that powers cell processes.
- Cell respiration is the process that transfers the chemical bond energy of large organic compounds into the chemical bonds of ATP.
- Photosynthesis builds these large organic molecules using CO2 as building blocks and solar radiation as the energy source.
- The sun is the ultimate source of energy that powers cellular work.


Light energy
ECOSYSTEM
Photosynthesis
in chloroplasts
$CO_2 + H_2O$
Organic
molecules
$+ O_2$
Cellular respiration
in mitochondria
ATP
powers most cellular work
Heat
energy

Cell Respiration

I.

Main Idea: Catabolic (breaking) reactions result in a net release of energy and moving electrons play an important part in this.

Catabolic Pathways in General

- Chemical bonds store potential energy.
- The more bonds, the more potential energy.
  - Larger molecules have more bonds thus more potential energy.
- Breaking these bonds releases the potential energy.
- A cell is able to capture some of this energy and use it ultimately to do work.
- Thermodynamics reminds us that not all the energy can be transferred and thus heat is also liberated in these reactions.

Specific Catabolic Pathways

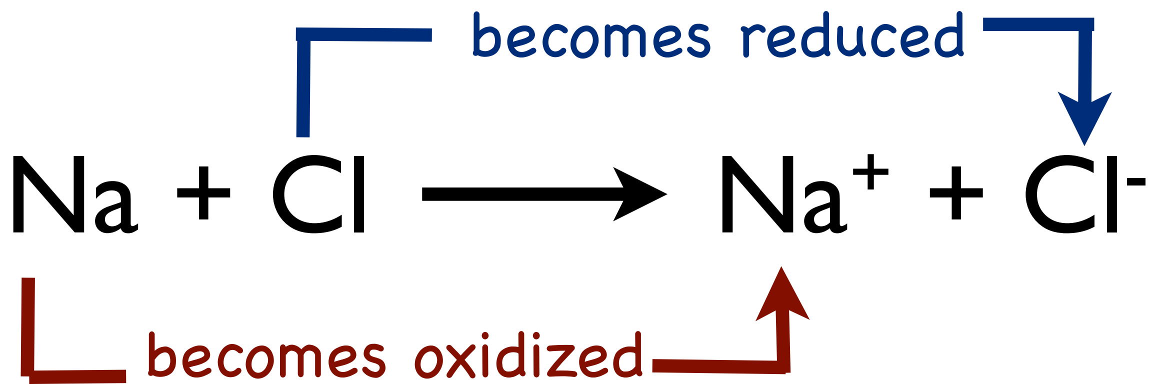
- ***Fermentation***- is the partial degradation of organic molecules and does not require oxygen.
- ***Aerobic Respiration***- involves the degradation of organic molecules and oxygen as a final electron acceptor.
- ***Anaerobic Respiration***- involves the degradation of organic molecules and some other molecule that acts as the final electron acceptor in place of oxygen.
- ***Cellular Respiration***- strictly speaking includes both types of respiration however it is usually synonymous with *aerobic respiration*.

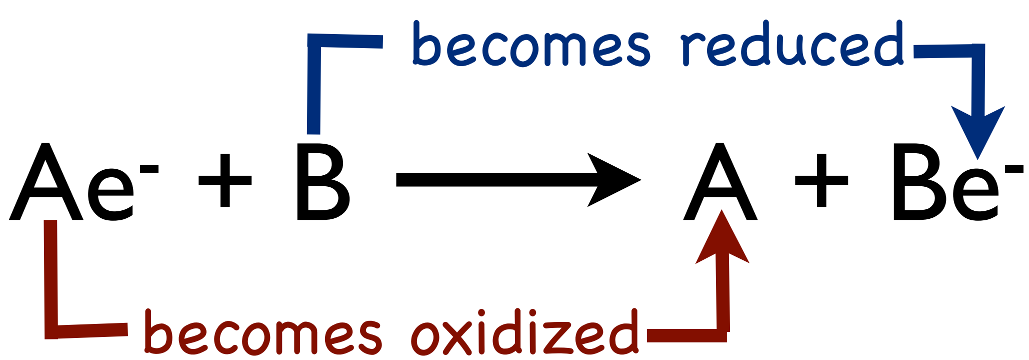
Catabolic Molecules

- The molecules that can be used for fuel are sugars, fats and proteins.
  - *Glucose* is the most common large organic molecule used for fuel and consequently the one addressed in this powerpoint.
- The energy released from the catabolism of glucose is -686 kcal per mole.
- The energy released from glucose far exceeds the required energy need for most cellular work.
- As a result this energy must be transferred to many smaller molecules (ATP) each with potential energy that is more on scale with cellular work

The principle of the "redox reaction"

- Oxidation Reactions- removes electrons from a substance
- Reduction Reactions- adds electrons to a substance





Ae⁻ the "electron donor" is the ***reducing agent***

B the "electron acceptor" is the ***oxidizing agent***

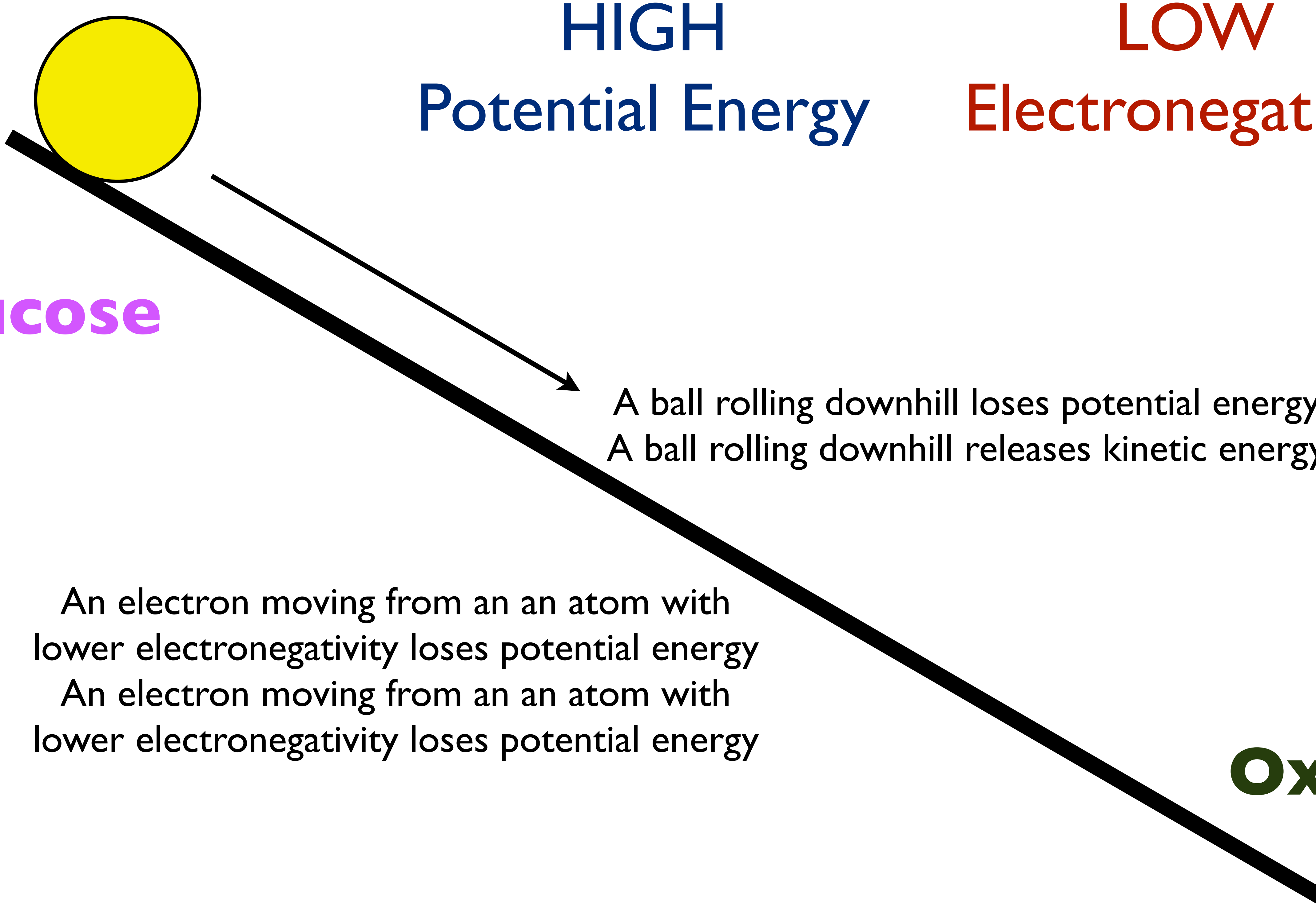
Redox Rxns Release Energy

- Energy is required to pull electrons away from an atom.
- The more electronegative the atom, the more energy is needed to pull away that/those electrons.
  - *recall: electronegativity measures the pull that atom exerts on its electrons*
- An electron(s) loses potential energy if moves from a less electronegative atom to a more electronegative atom.

Recall Redox Analogy

HIGH
Potential Energy

LOW
Electronegativity



Glucose

A ball rolling downhill loses potential energy
A ball rolling downhill releases kinetic energy

An electron moving from an an atom with
lower electronegativity loses potential energy
An electron moving from an an atom with
lower electronegativity loses potential energy

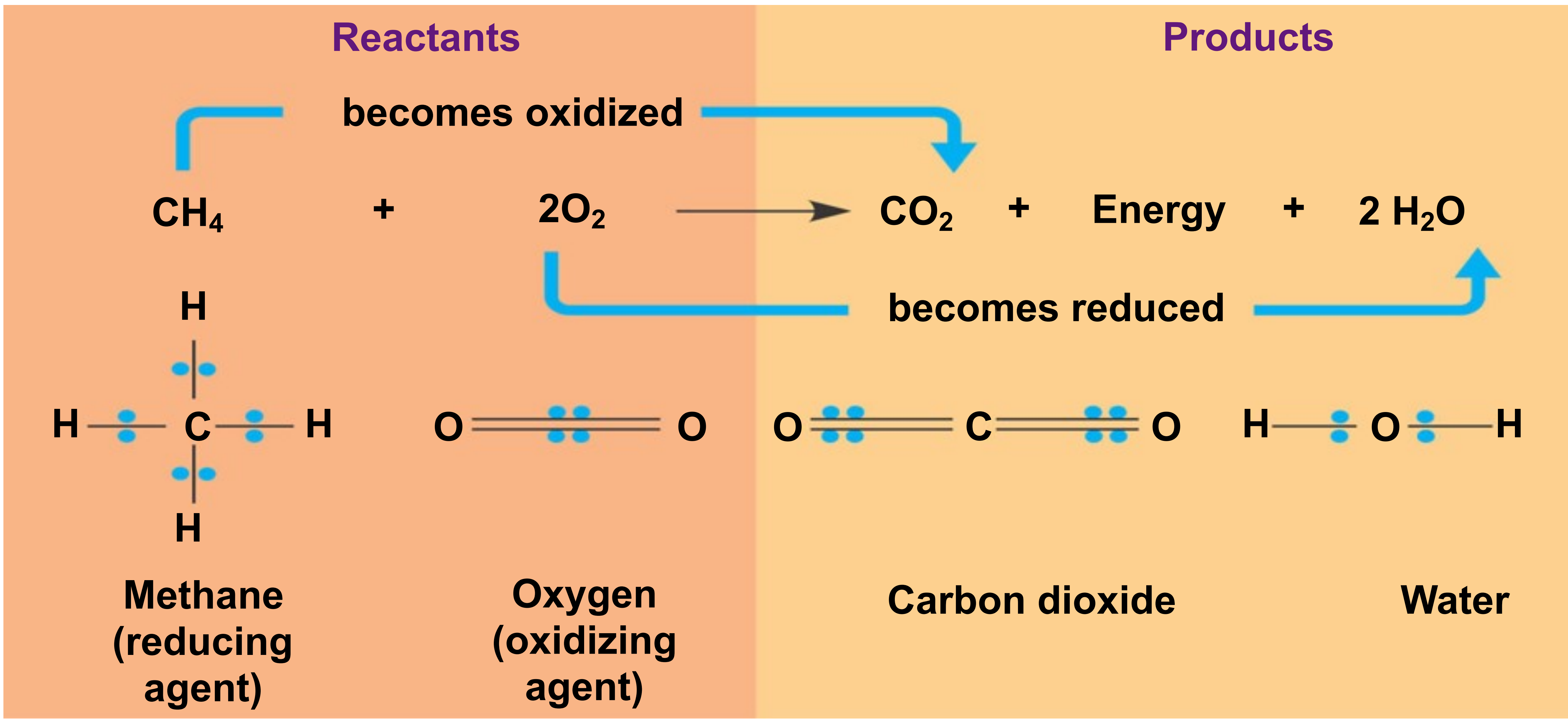
Oxygen

LOW
Potential Energy

HIGH
Electronegativity

Redox Reactions

- Not all redox rxn's involve the complete transfer of electrons.
- Some simply change the degree of electron sharing in covalent bonds.



Cell Respiration is a "redox reaction"

- Recall the following
  - Oxidation Reactions- removes electrons from a substance
    - catabolic / breaking down a substance / releases energy
  - Reduction Reactions- adds electrons to a substance
    - anabolic / building down a substance / requires energy

becomes oxidized

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$$

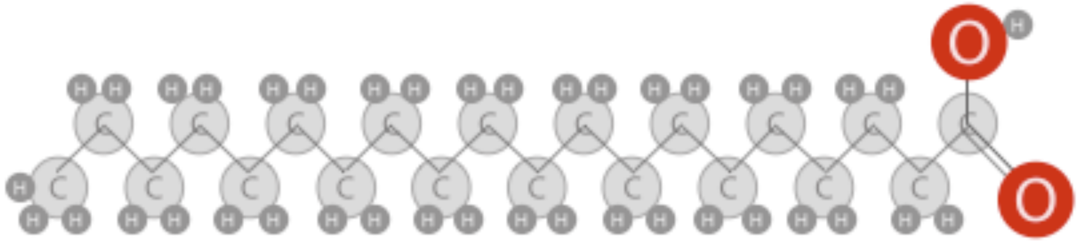
becomes reduced

Cell Respiration is a “redox reaction”

- As electrons make their way to oxygen energy is released.
- The challenge for the cell is two fold:
  - 1. move the electrons to oxygen in the most controlled manner, in order to capture the mazimum energy
  - 2. use this captured energy to do cellular work
- In general molecules with lots of hydrogens make good fuels:
  - they have lots of electrons, each with lots of potential energy

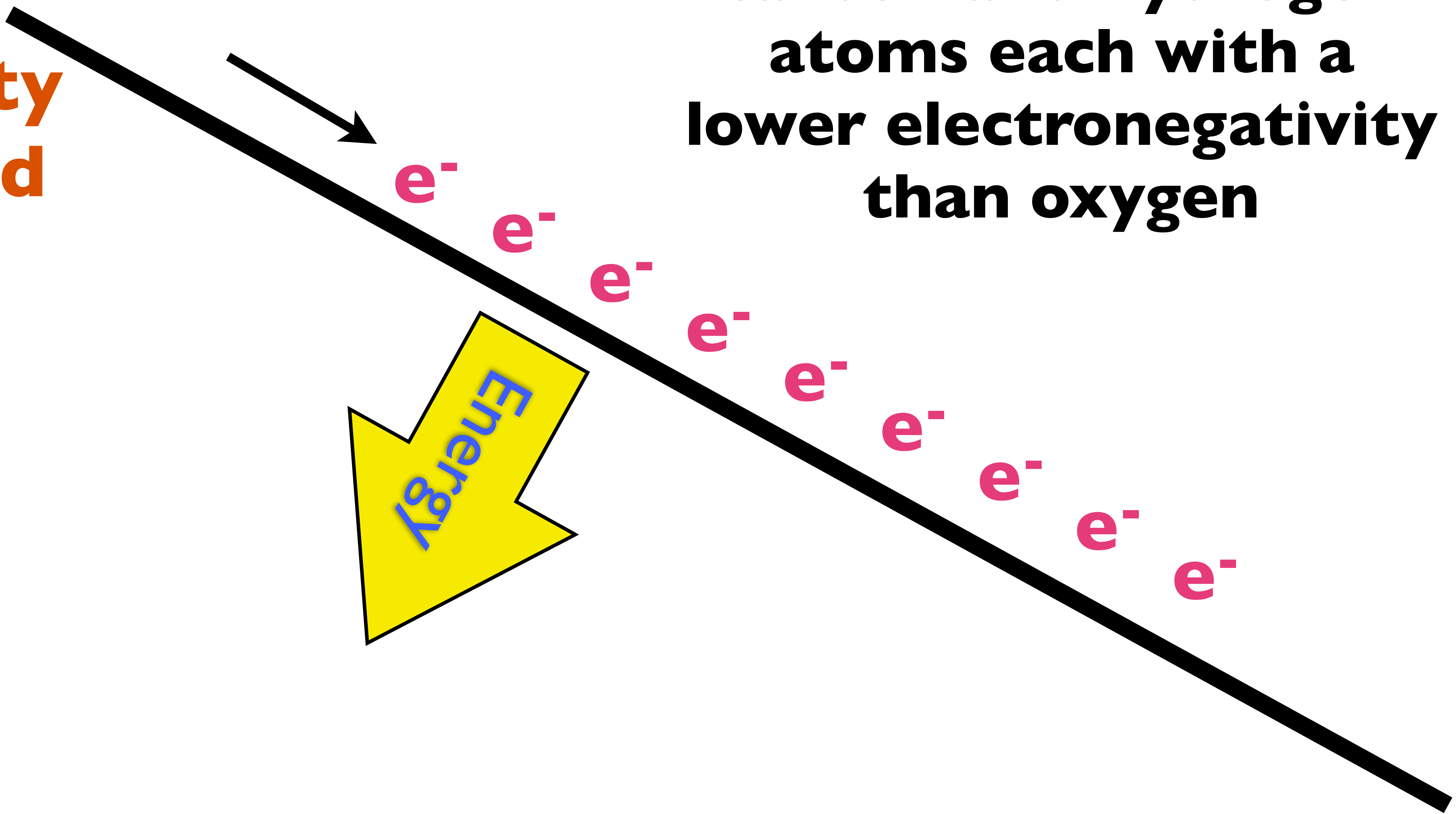
HIGH Potential Energy

Lower Electronegativities



80 Electrons between carbon and hydrogen atoms each with a lower electronegativity than oxygen

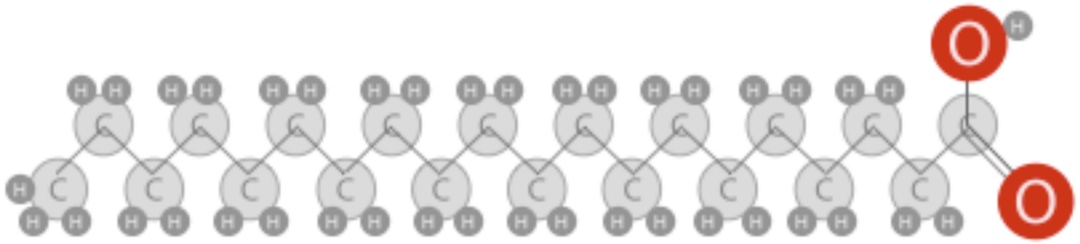
Fatty Acid



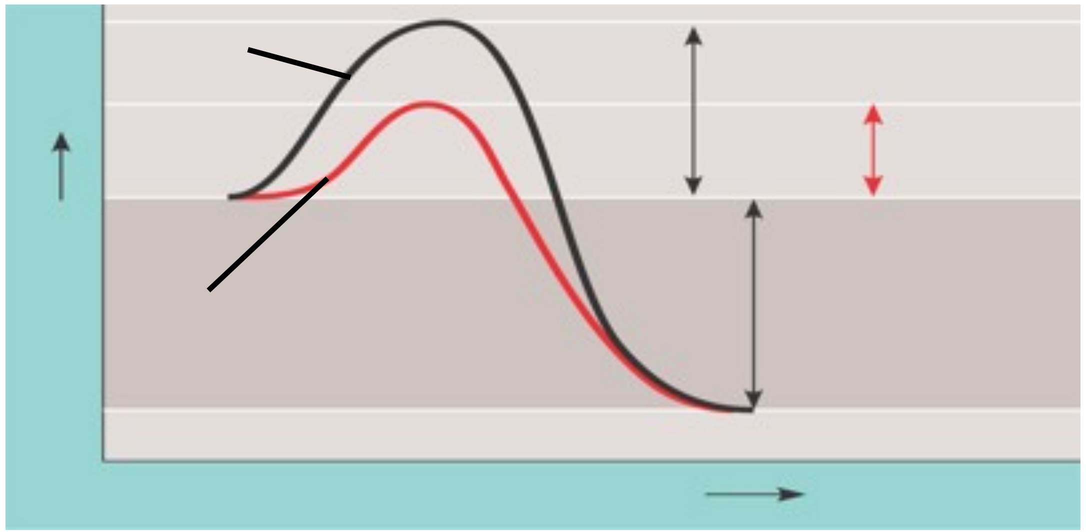
LOW Potential Energy

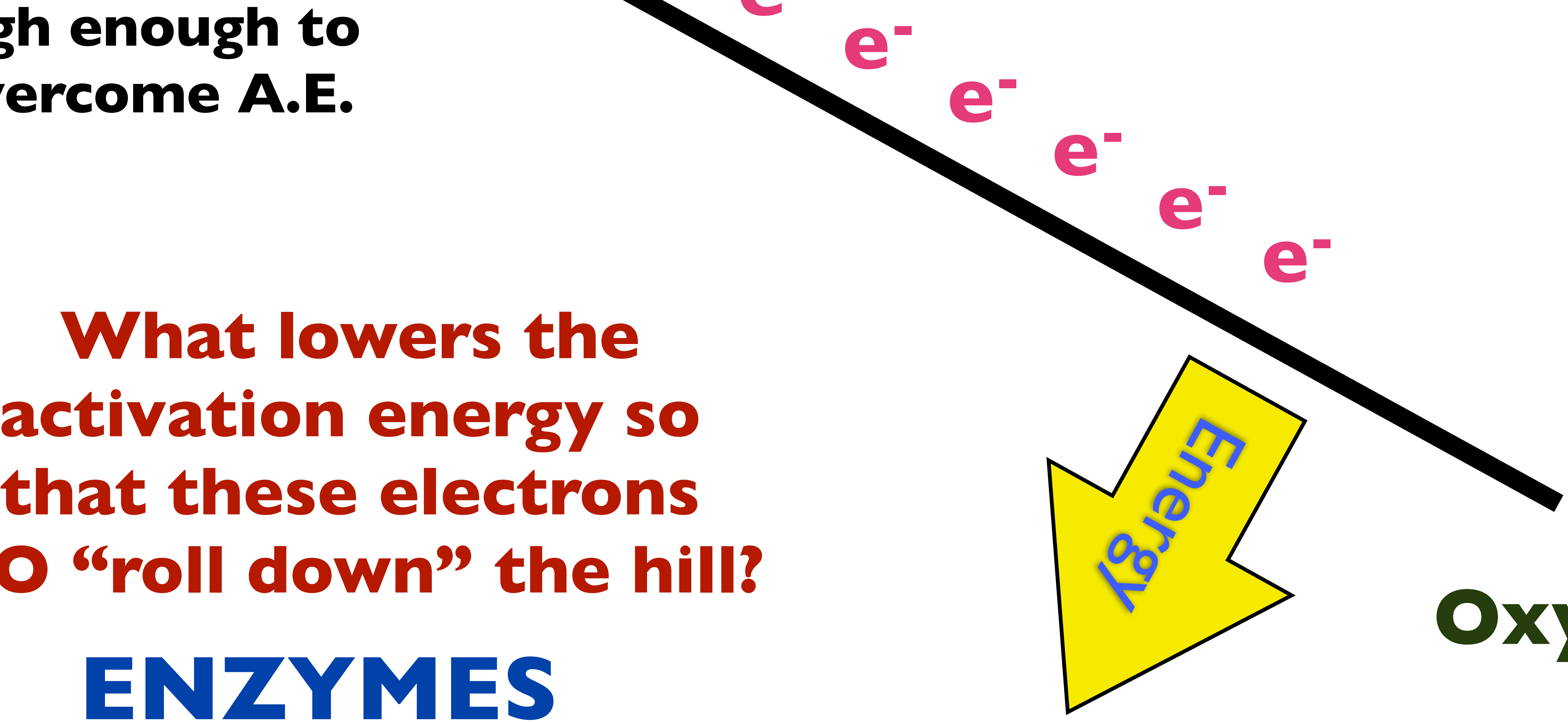
HIGH Electronegativity

Oxygen



The Activation Energy barrier is the only reason why these electrons do not spontaneously "roll down" the hill





Body temp is not high enough to overcome A.E.

What lowers the activation energy so that these electrons DO "roll down" the hill?

ENZYMES

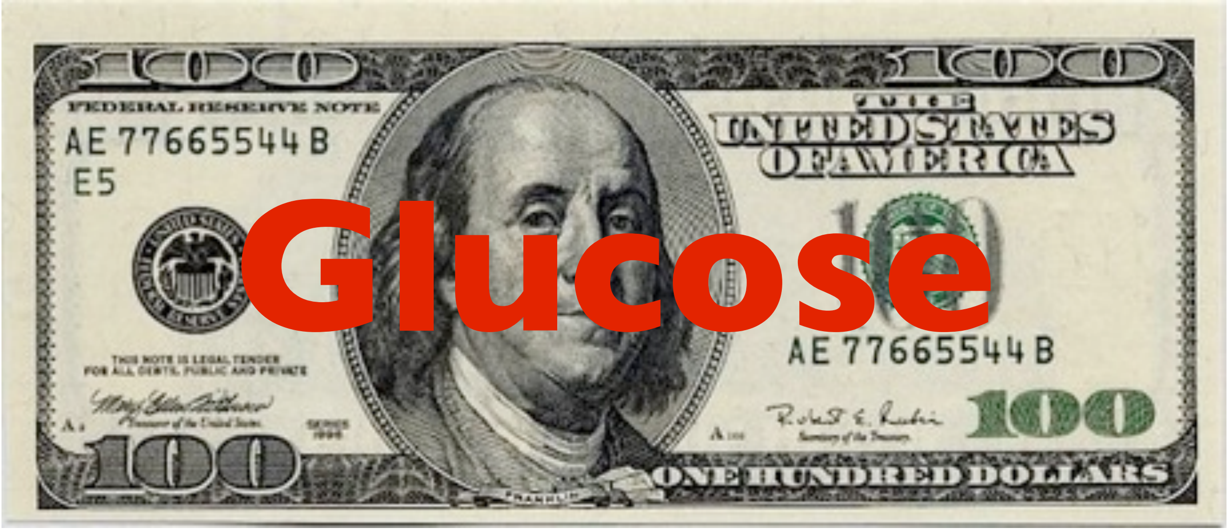
Oxygen

Harvesting Energy from Electrons

- Energy released from a fuel, say gasoline, all at once may be useful in Hollywood movies but is useless for constructive work, like driving the car below.

Harvesting Energy from Electrons

- Like the car...Energy released from glucose, all at once would be destroy the cell or at least be extremely wasteful.



Imagine going to a county fair. To enjoy the fair you decide to bring money, in order to buy food and play games. The cost of food and games are each just a few dollars at most. You bring five 100$ bills to fair, thinking that should be more than enough (each bill would easily cover the cost of food item or game). Not long after you arrive you realize that no vendor has change for a 100$ bill. You have 2 choices: 1. Use a 100$ bill for each purchase, over paying for everything and run out of money fast or 2. do not buy anything. Neither choice is reasonable.

What should you have prior to coming to the fair?

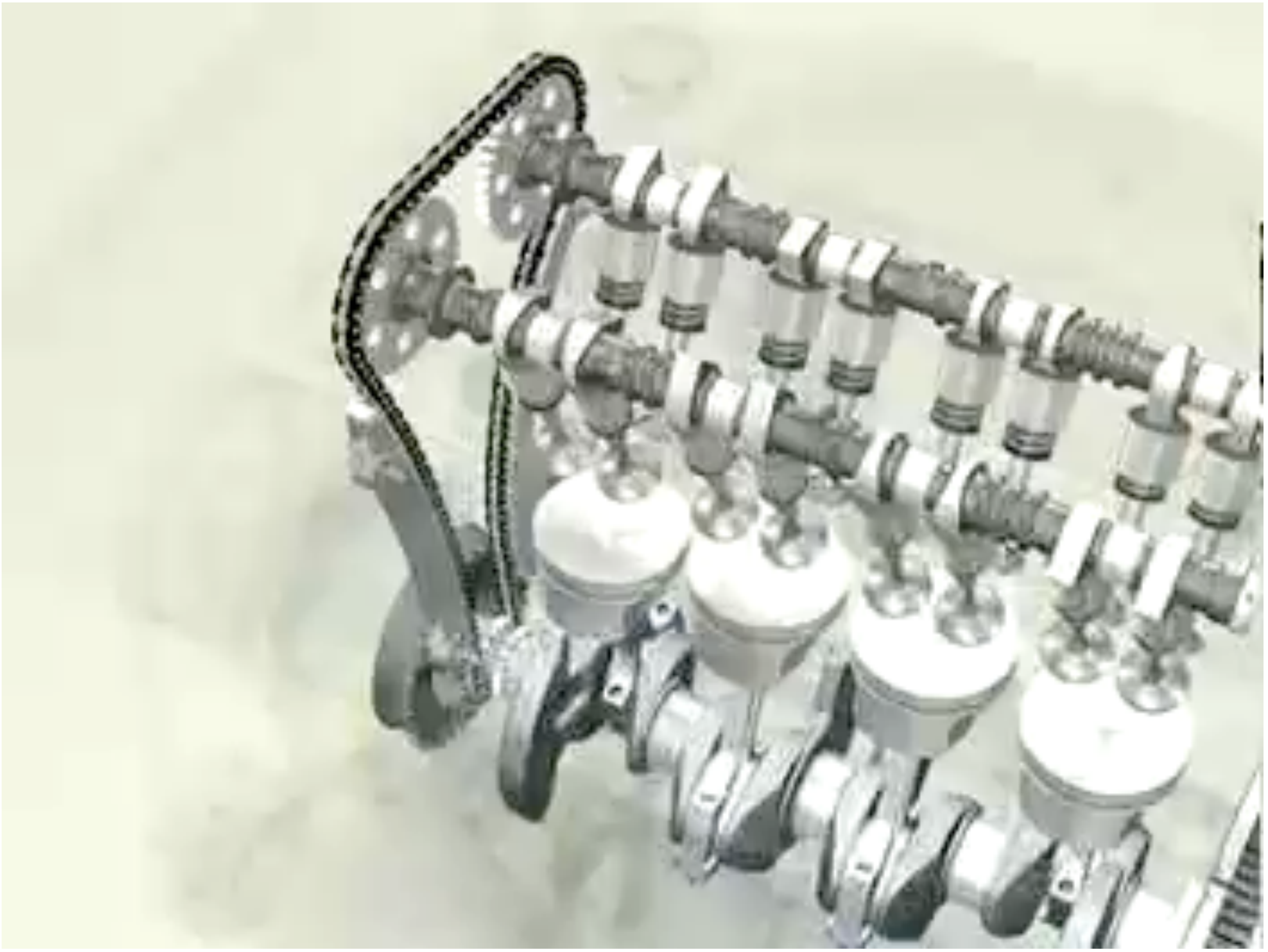
Here is an alternative solution! Take the 100$ bills to the bank. Change the 100$ into smaller currency say 1$ bills. Now your ready to go to the fair.

What does the bank represent in my analogy?

Mitochondria, Cell Respiration

Harvesting Energy from Electrons

- To effectively harvest energy from a fuel to do constructive work you must slowly, in step like fashion extract the energy.



Harvesting Energy from Electrons

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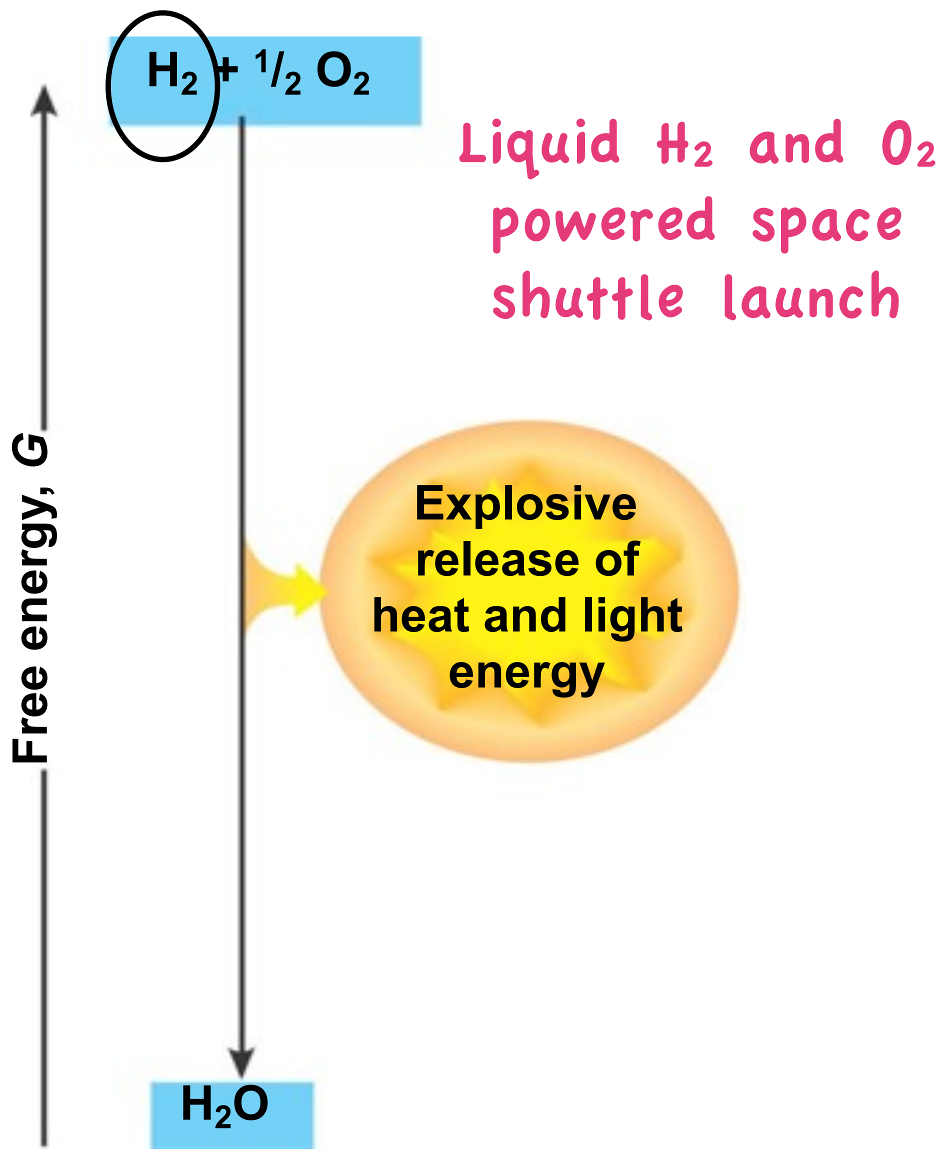
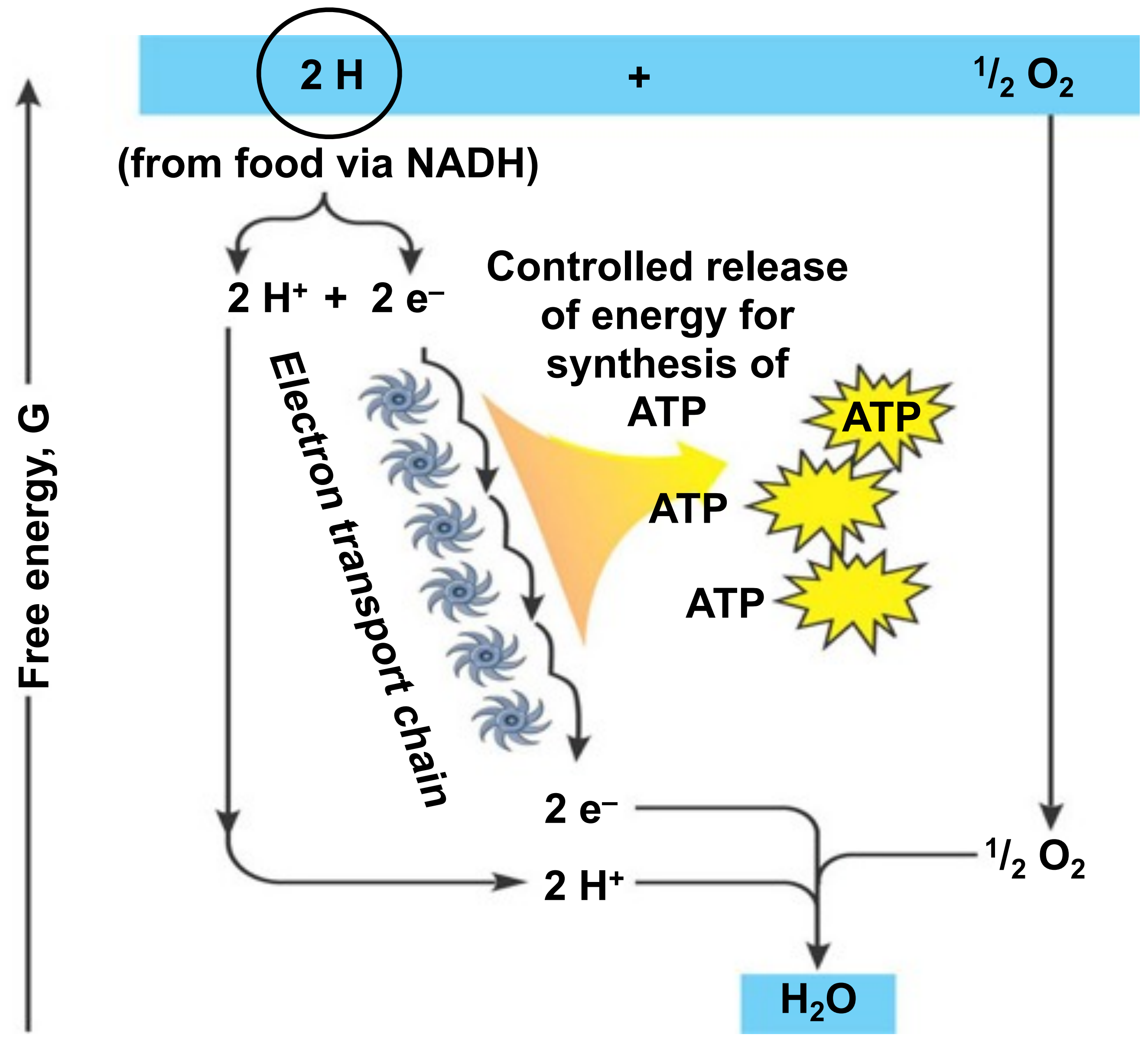


Uncontrolled reaction- (car explosion)

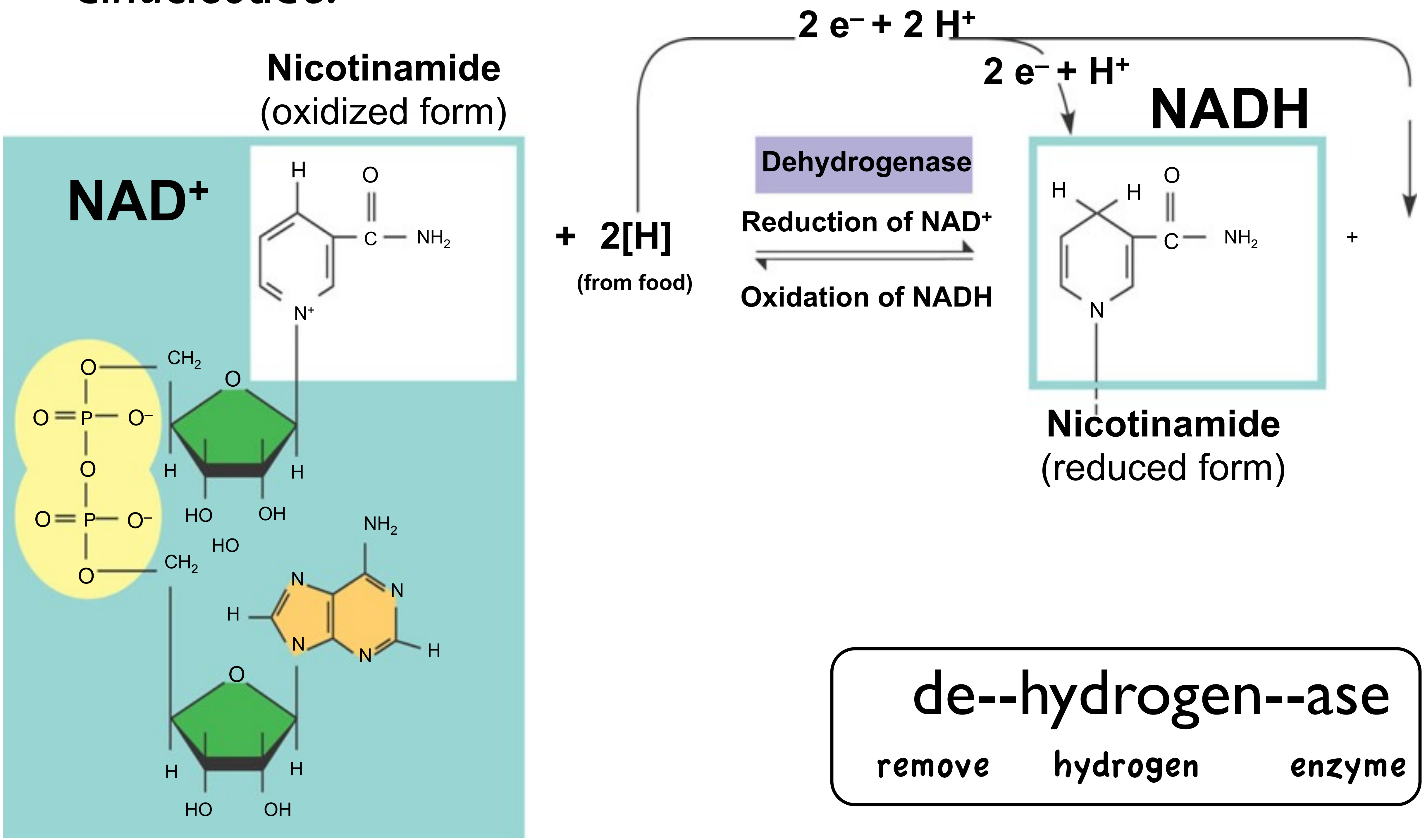
VS.



Cellular respiration- combustion engine

Electron Acceptors & Transport

- The first molecule that usually accepts electrons from organic molecules is a coenzyme called *Nicotinamide adenine dinucleotide*.



de--hydrogen--ase

remove hydrogen enzyme

Electron Acceptors & Transport

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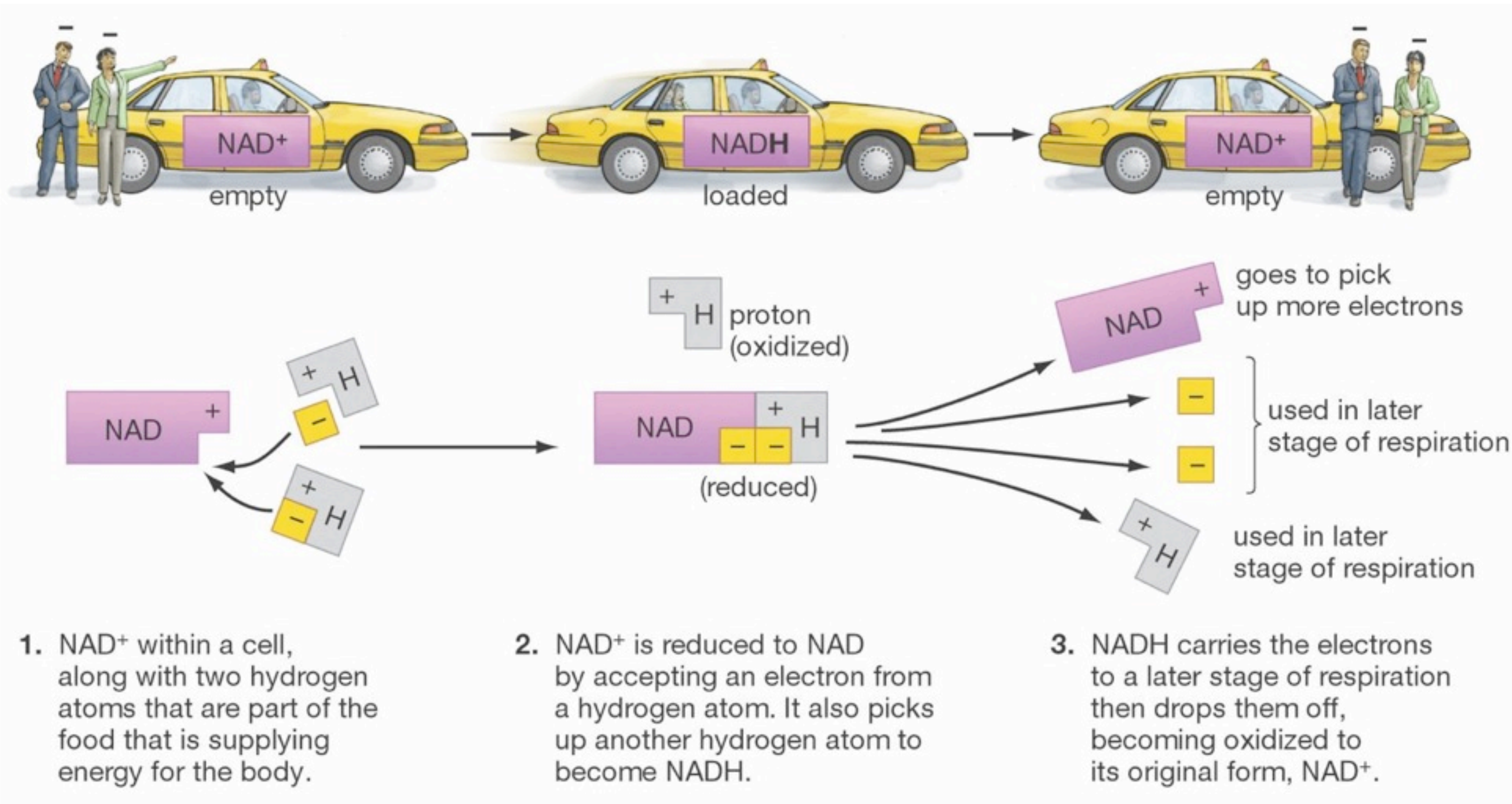
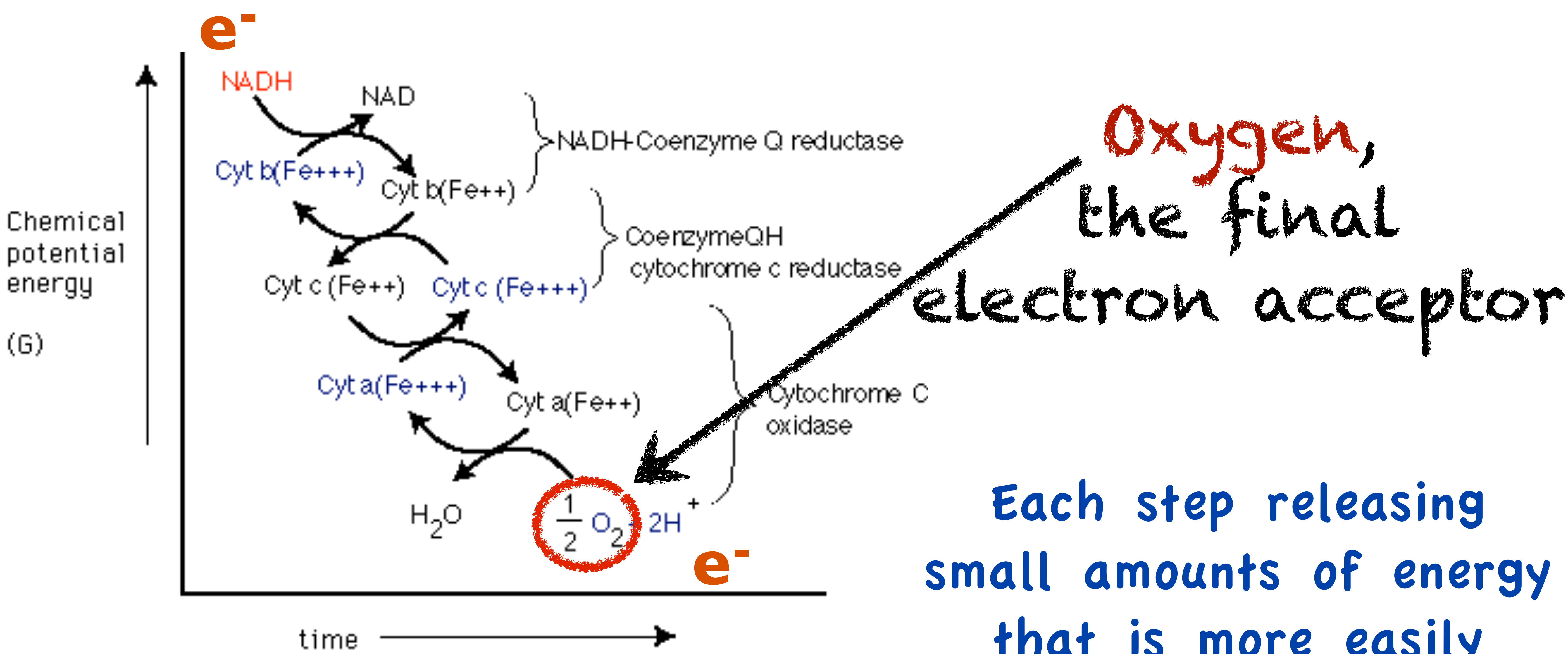


Electron Acceptors & Transport

- The NADH then passes the electrons to another molecule, and so on and so forth.
- Each molecule slightly more electronegative than the prior one

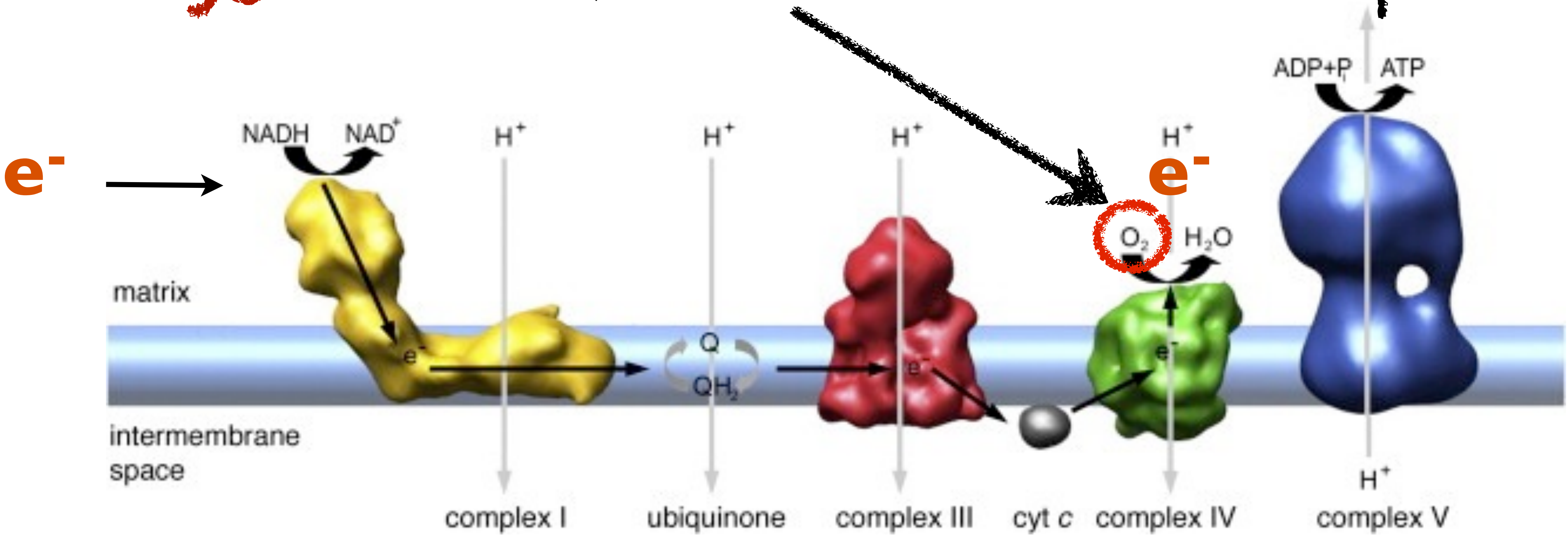


Each step releasing small amounts of energy that is more easily captured by the cell

Electron Acceptors & Transport

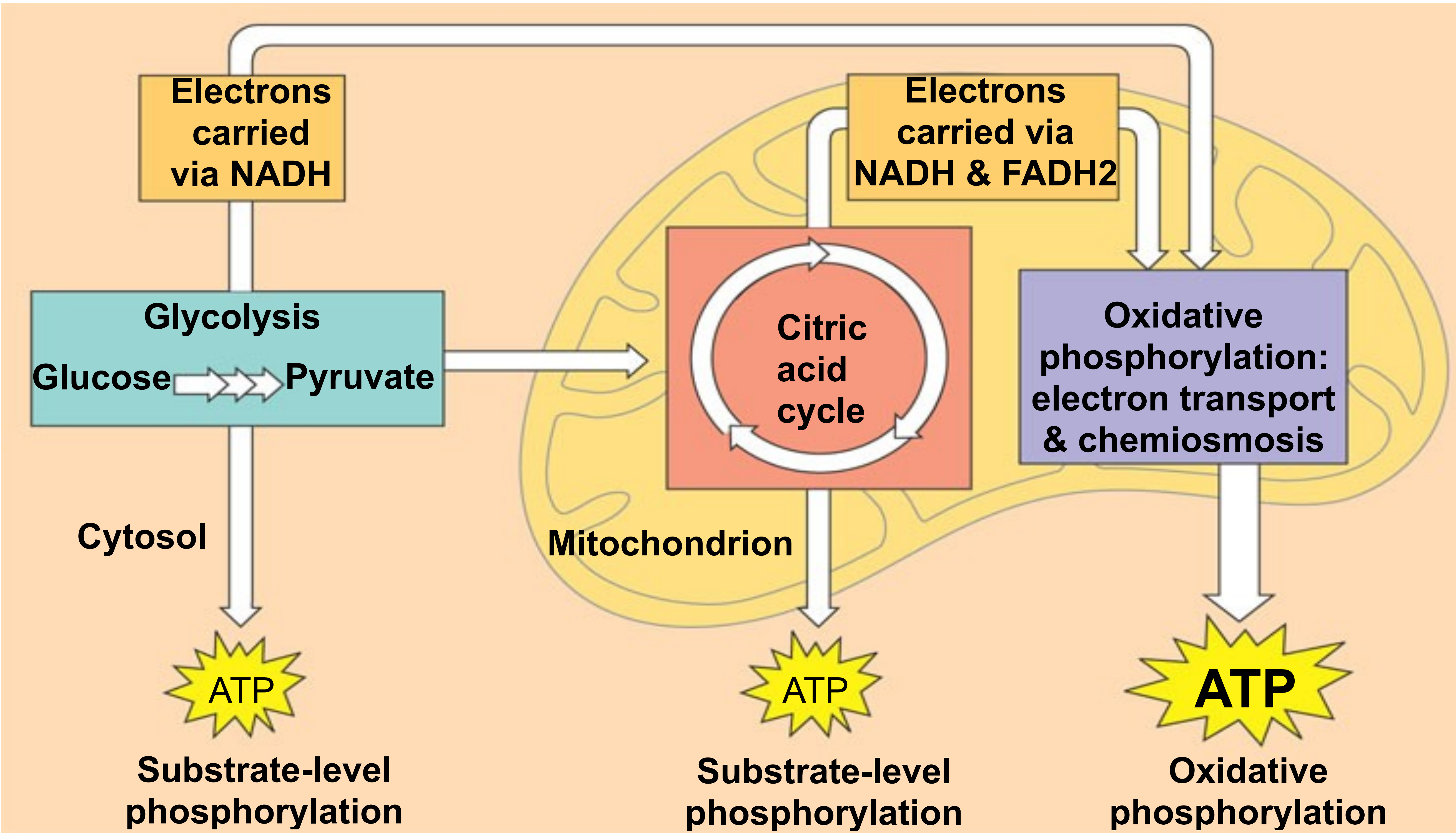
- The *electron transport chain* consists of mainly proteins, embedded into a membrane.
  - *in eukaryote's inner mitochondrial membrane, in eukaryote's thylakoid membranes and prokaryote's plasma membrane*
- The e^- transfer from NADH to O_2 releases -53 kcal/mol of energy.

Oxygen, the final electron acceptor



An Overview of Cellular Respiration

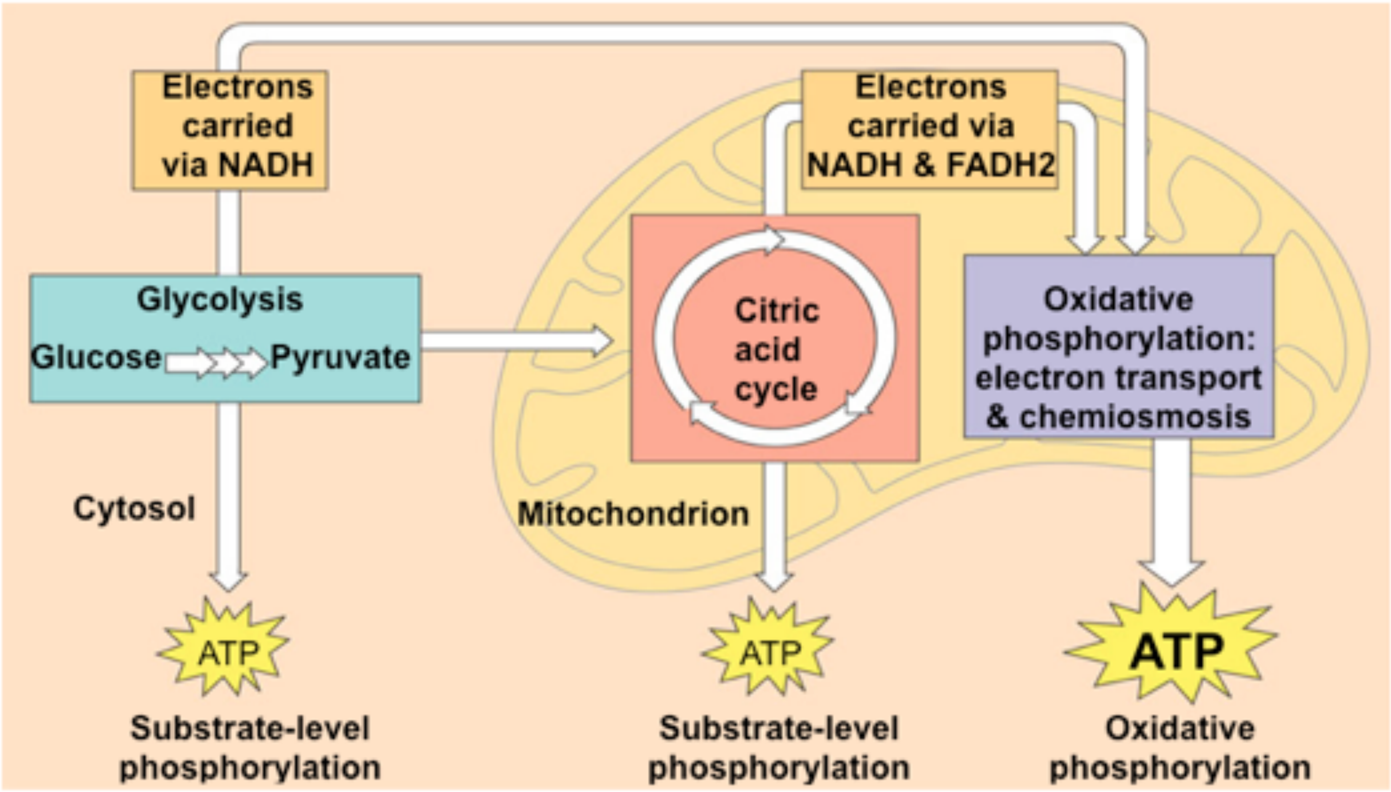
- Focus on the location, the input(s) and the output(s) for each the three stages.



An Overview of Cellular Respiration

Strictly speaking cell respiration only includes steps 2 & 3 however the so many cells use the products of glycolysis to feed the Citric acid cycle, glycolysis is often included loosely in cell respiration

Each ATP has 7.3 kcal/mol of free energy



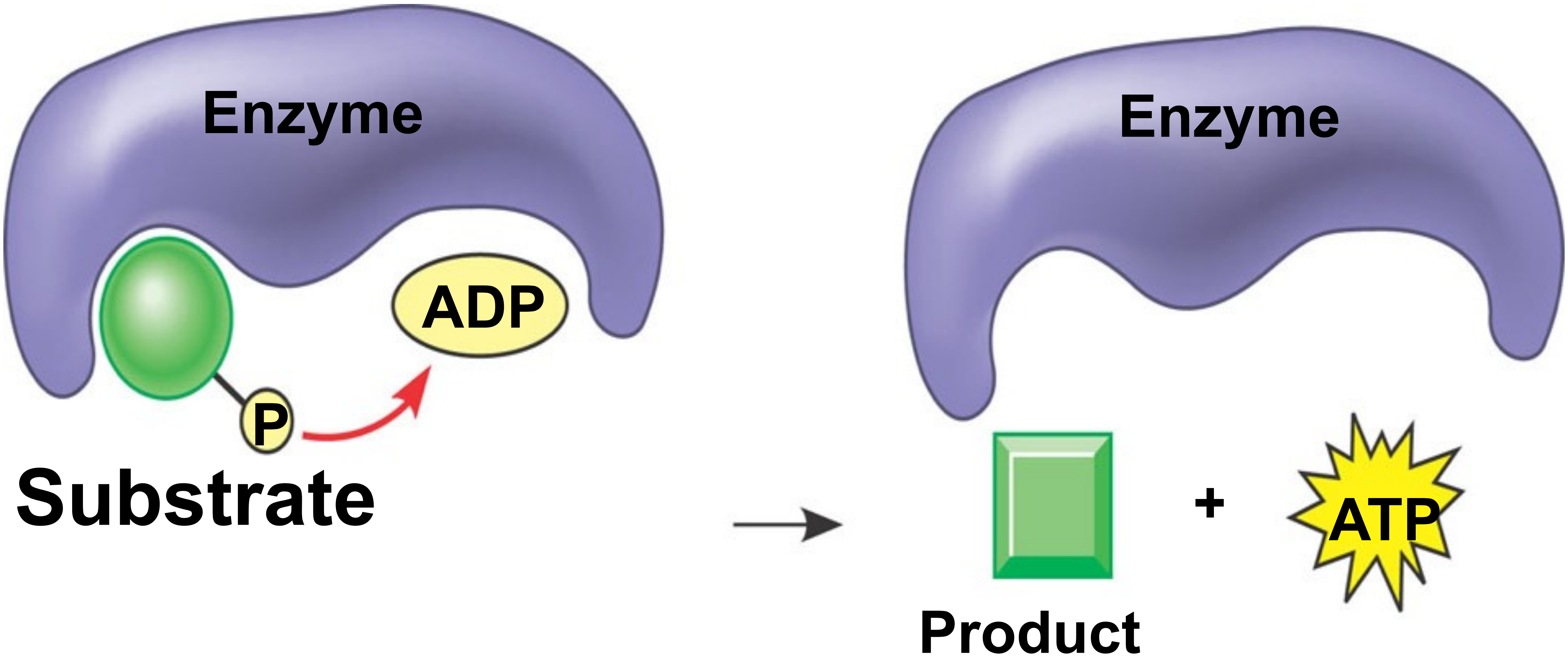
The ETC and chemiosmosis takes place in plasma membrane of bacteria

Accounts for 10% of ATP production

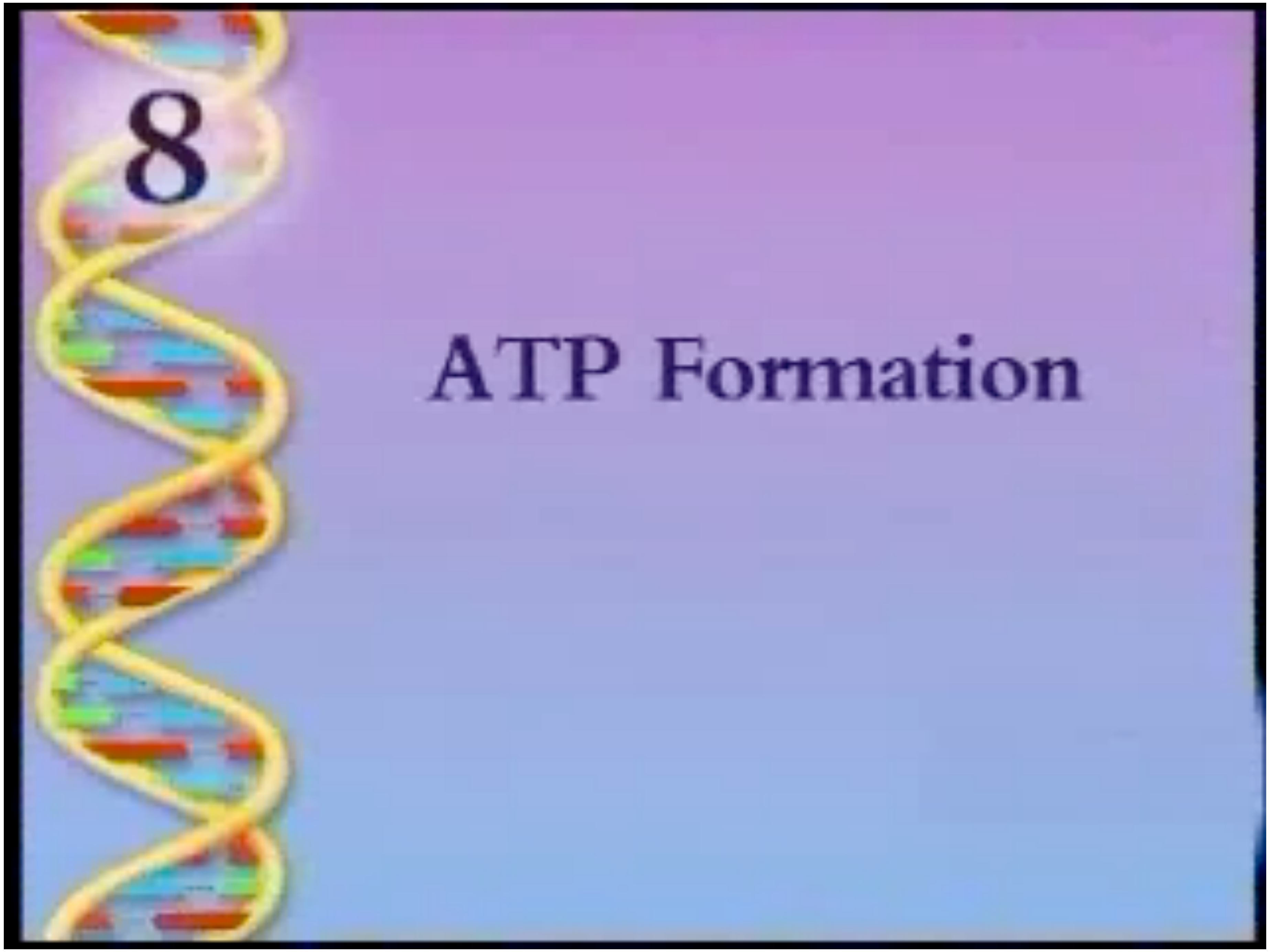
Accounts for 90% of ATP production

ATP Production

- Most ATP is produced via oxidative phosphorylation and these details will be discussed on later slides.
- The remaining ATP is produced via ***substrate level phosphorylation***.
    - This involves moving a phosphate group from one molecule to ADP.



ATP the MOlecule & Its Formation



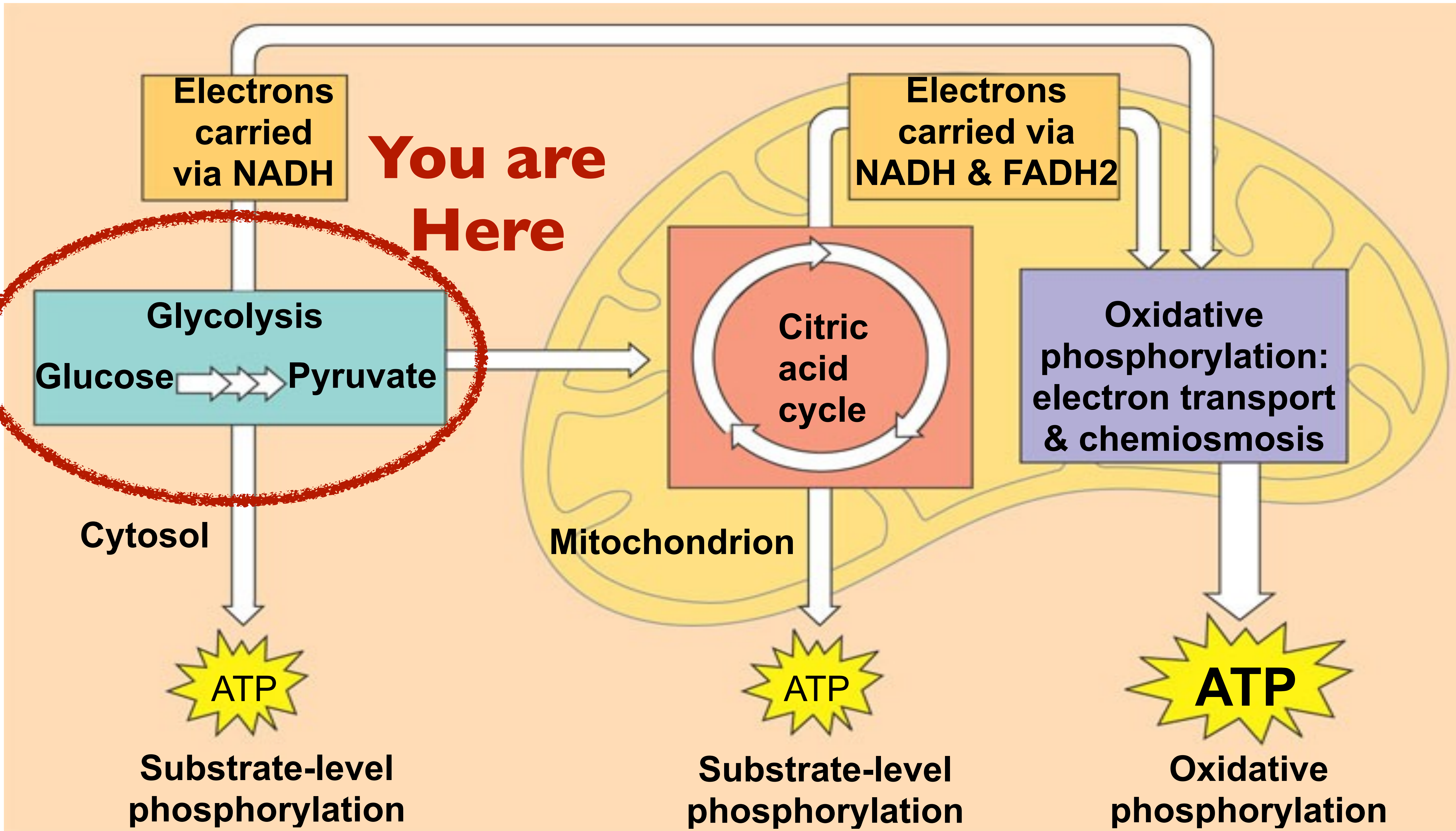
Cell Respiration

II.

Main Idea: The first step in cell respiration (catabolism of glucose) is to simply cut the 6 carbon glucose into two 3 carbon products.

An Overview of Cellular Respiration

- Focus on the location, the input(s) and the output(s) for each the three stages.

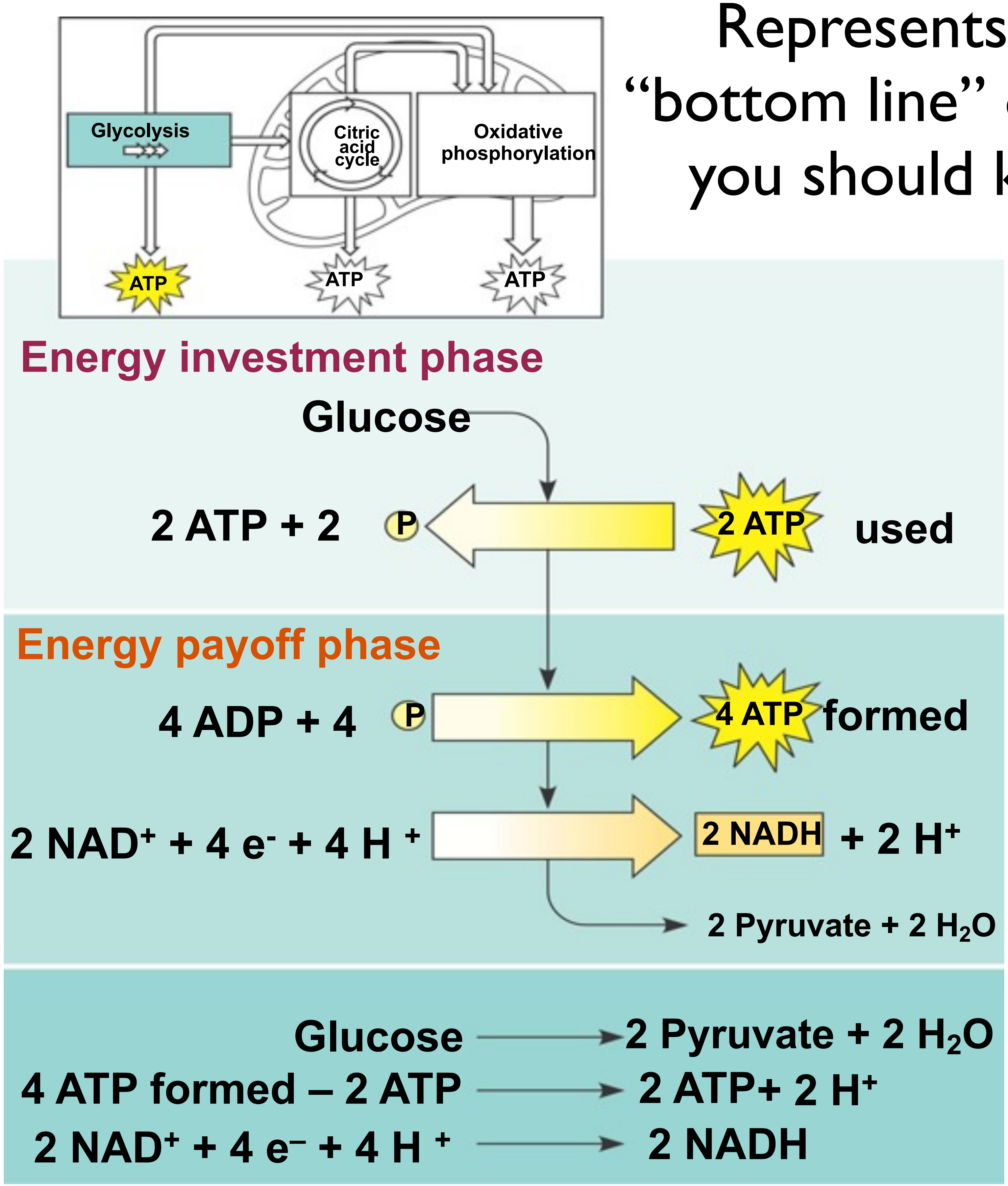


An Overview of Glycolysis

- Glycolysis translated means "sugar splitting".
- Glycolysis occurs in the cytosol
- Glycolysis is a ten step enzymatically driven metabolic pathway
- Glycolysis can be broken into two parts:
  - *the Energy Investment Phase & the Energy Pay-Off Phase*
- Glycolysis both requires ATP and produces ATP
- Glycolysis requires electron acceptors
- Glycolysis does not require oxygen not does it produce carbon dioxide.
- Glycolysis produces 2 pyruvate molecules

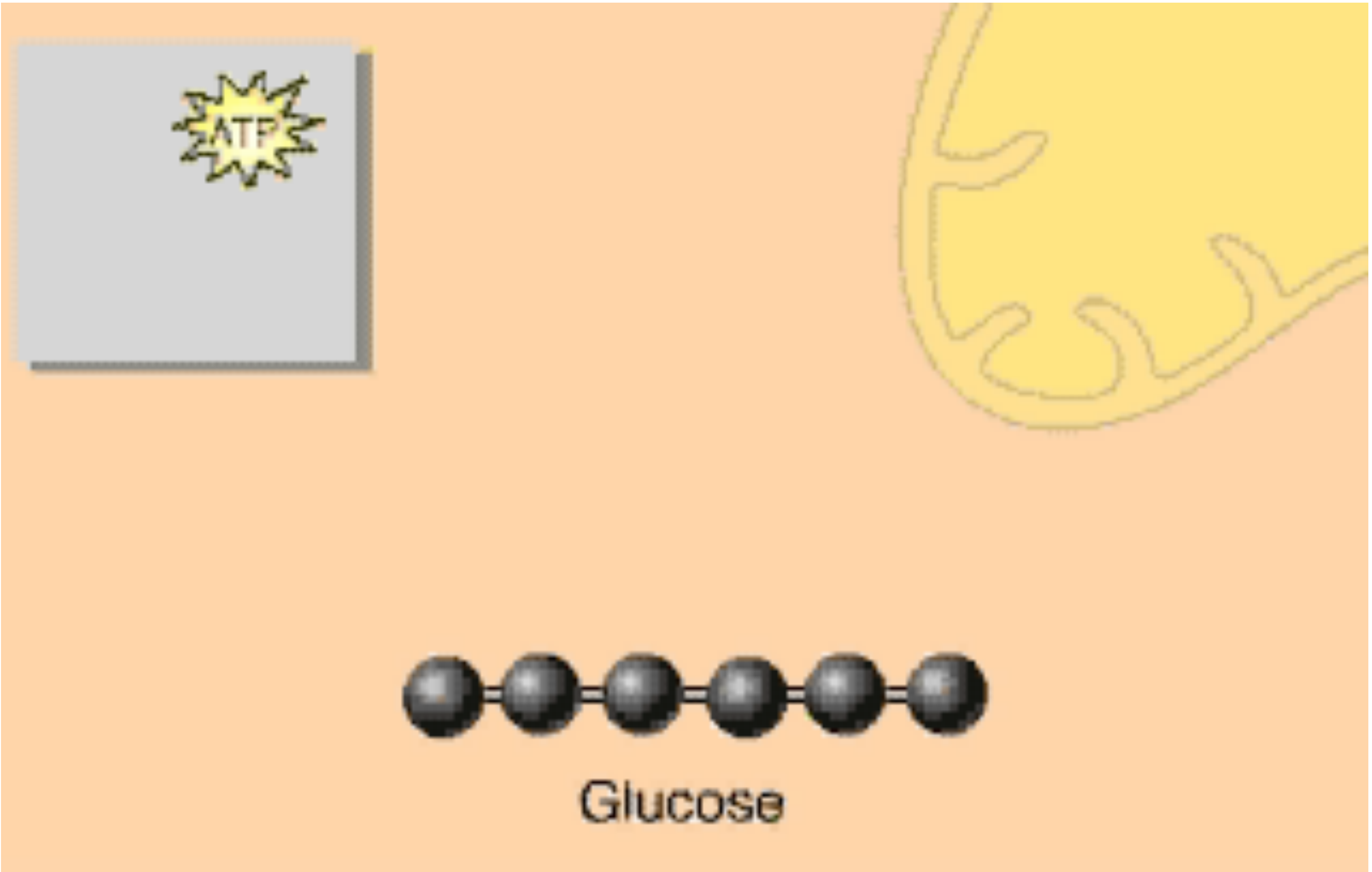
An Overview of Glycolysis

Represents the "bottom line" of what you should know



Glycolysis only extracts 25% of the potential energy, the rest still resides in pyruvate

An Overview of Glycolysis

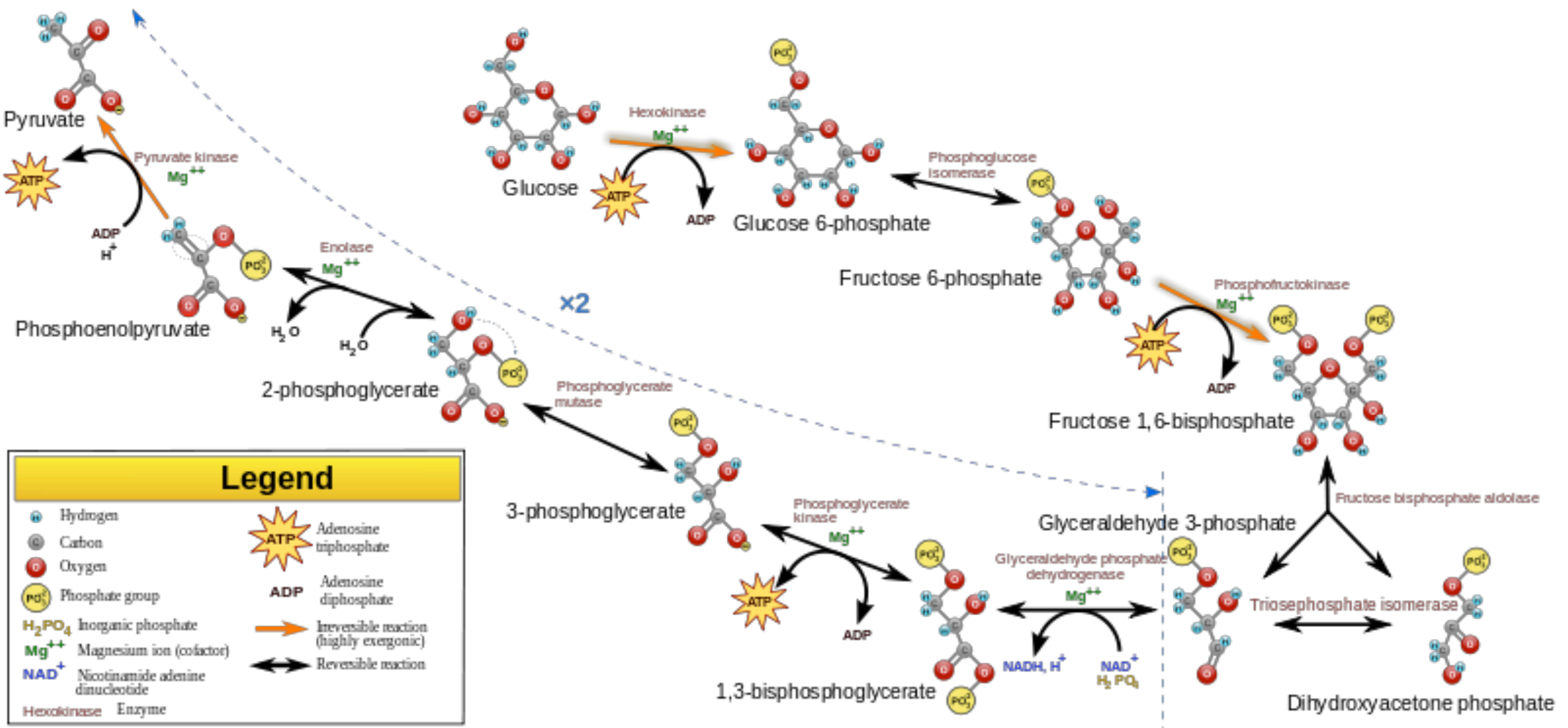


A Closer Look at Glycolysis

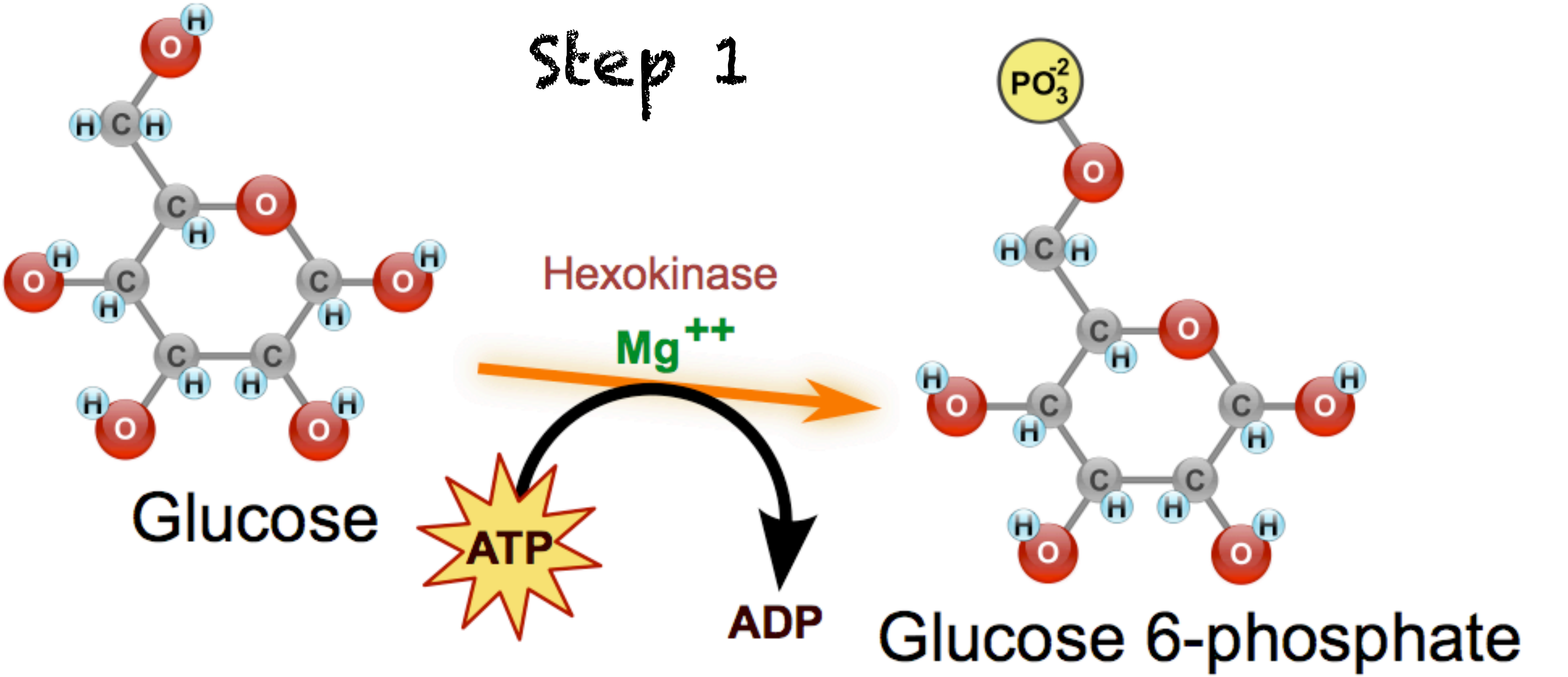
You are not responsible for these details.

Instead let's use to do the following:

1. Suggest enzyme functions based upon their name
2. Explain molecular nomenclature based upon structures
3. Find common pathways, molecules or enzymes from photosynthesis

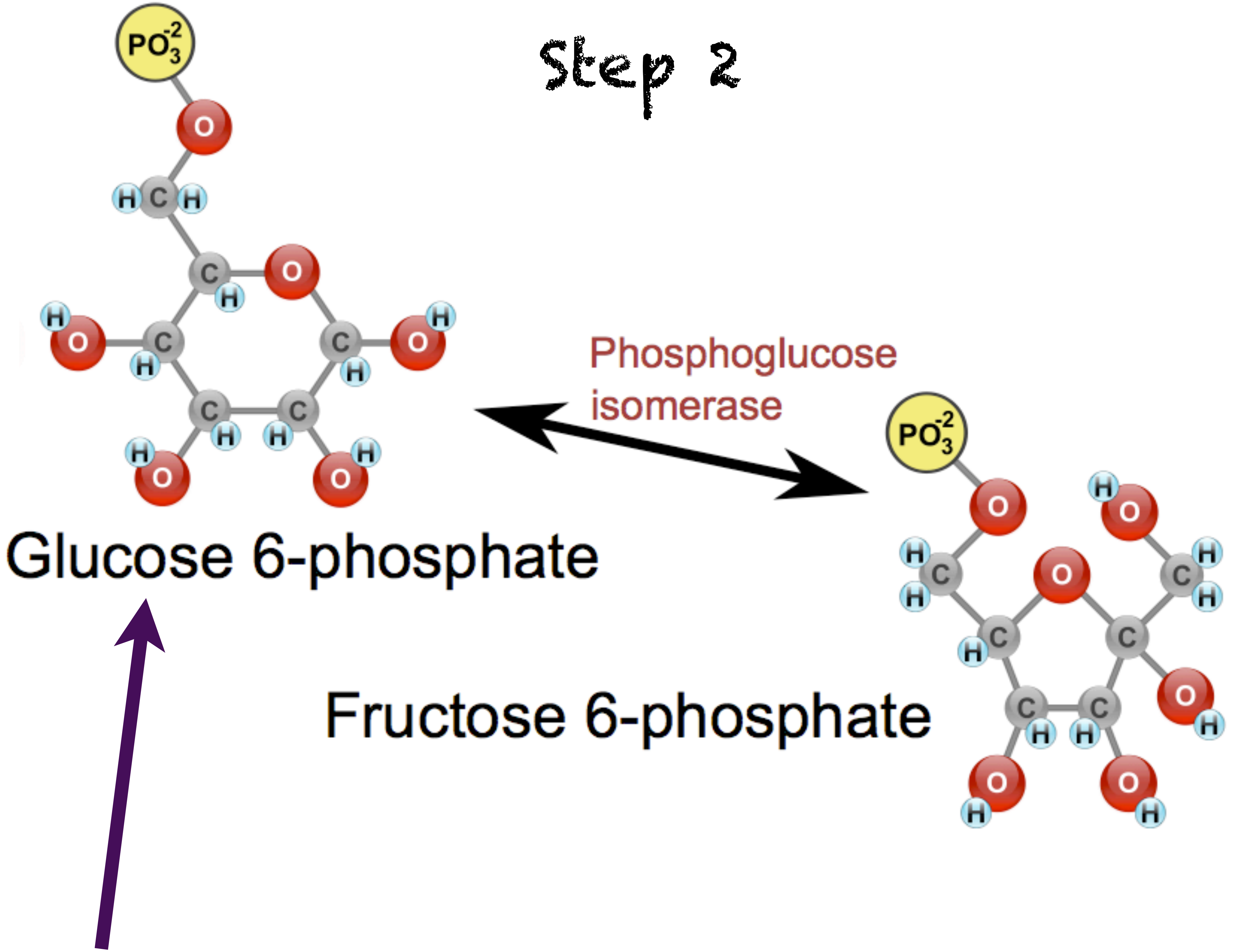


Step 1



What is the function of kinases? Why "hexo"?

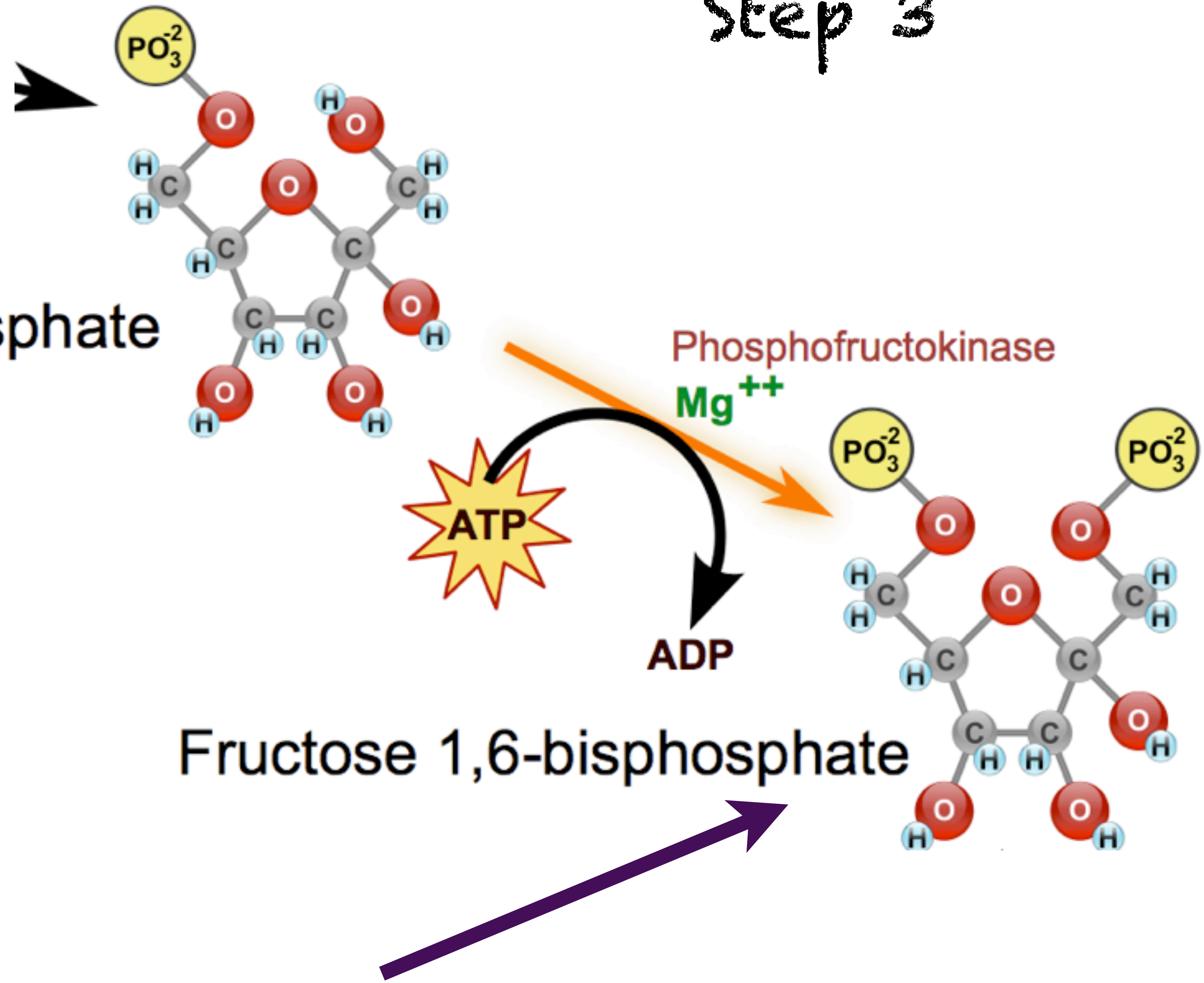
Step 2



Why do you suppose we name it this?

Step 3

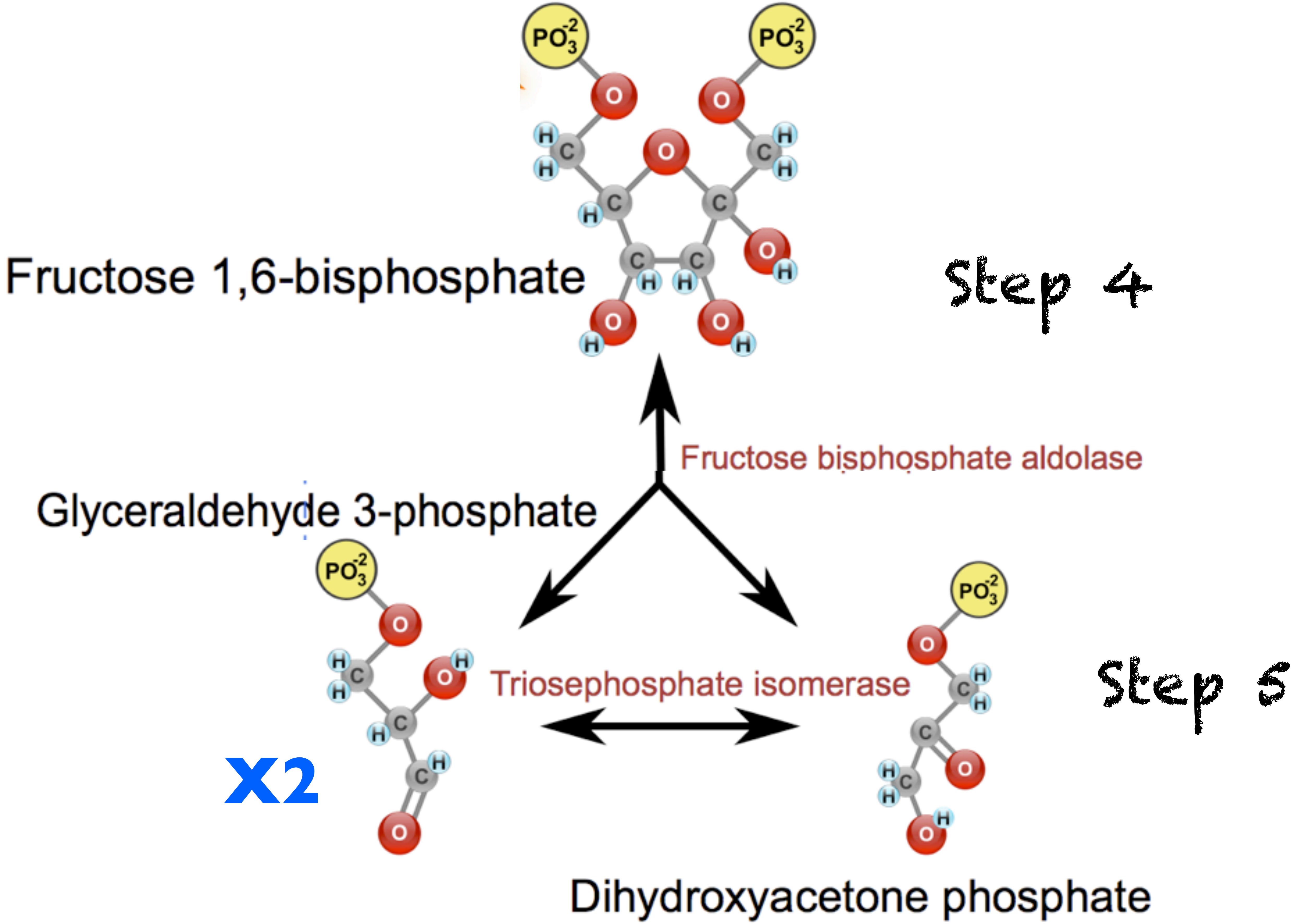
Fructose 6-phosphate



Fructose 1,6-bisphosphate

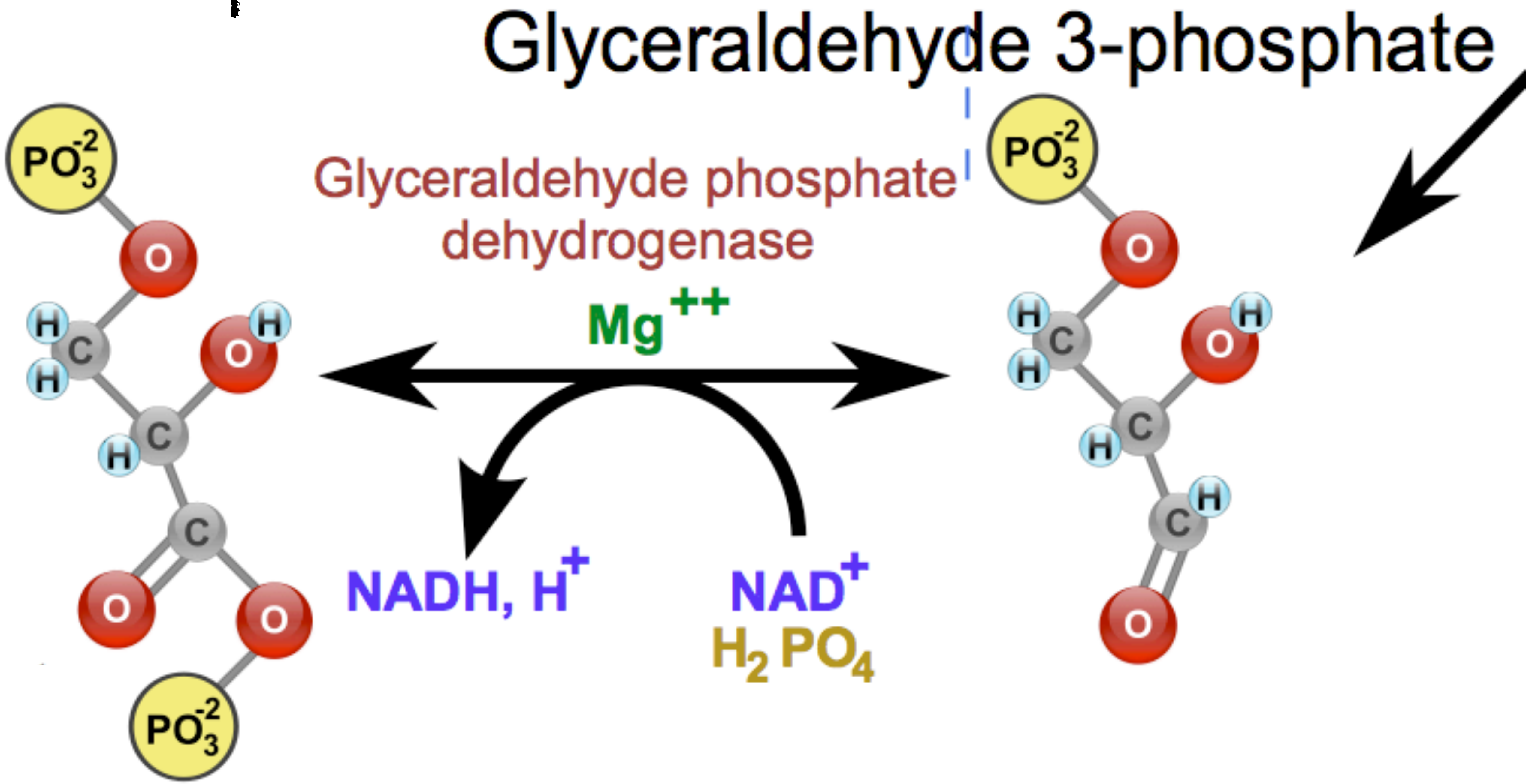
Why do you suppose we name it this?

What is the function of phosphofructokinase?



Have we seen glyceraldehyde 3-phosphate before?

X2 Step 6

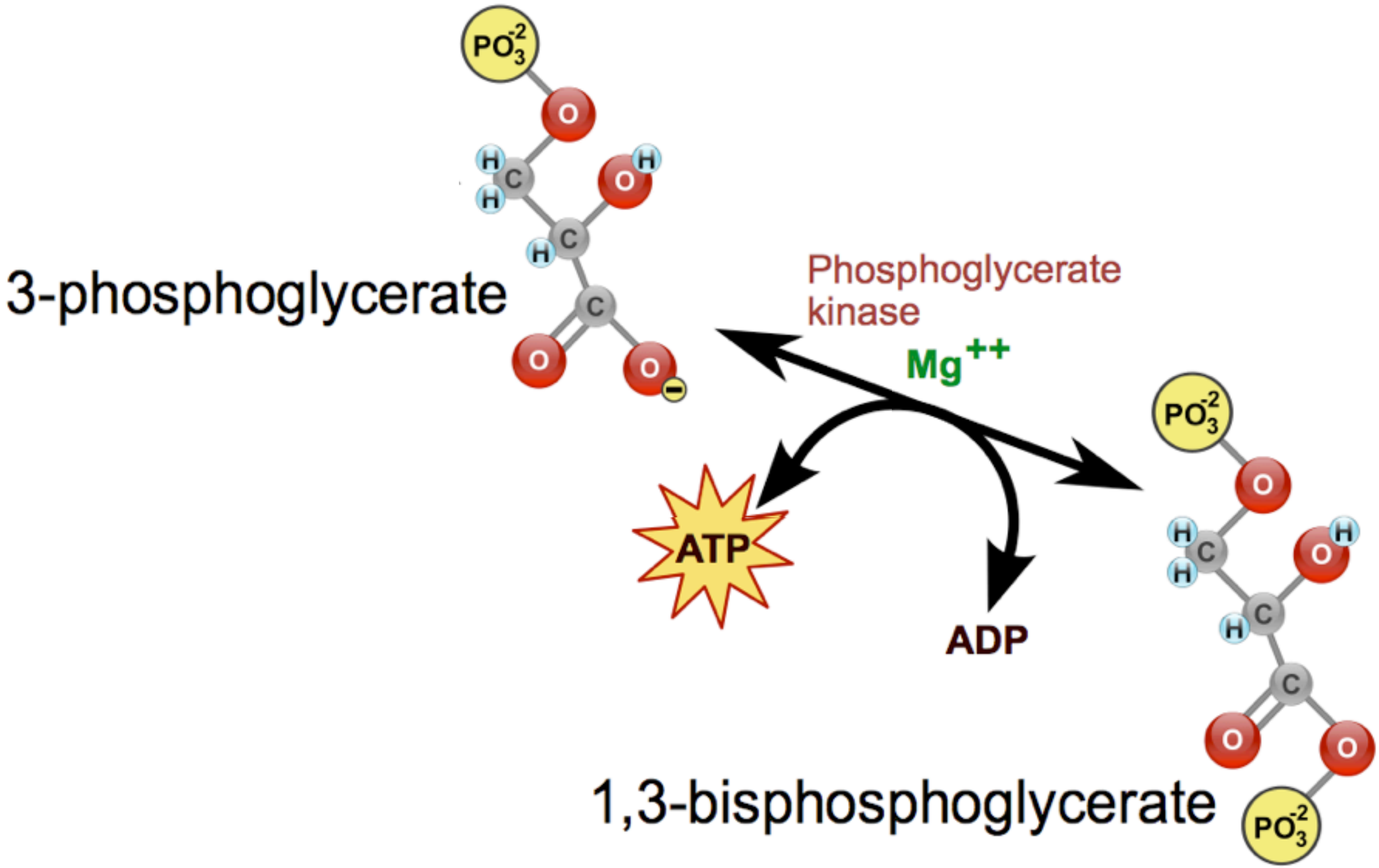


1,3-biphosphoglycerate

What was reduced? Oxidized?

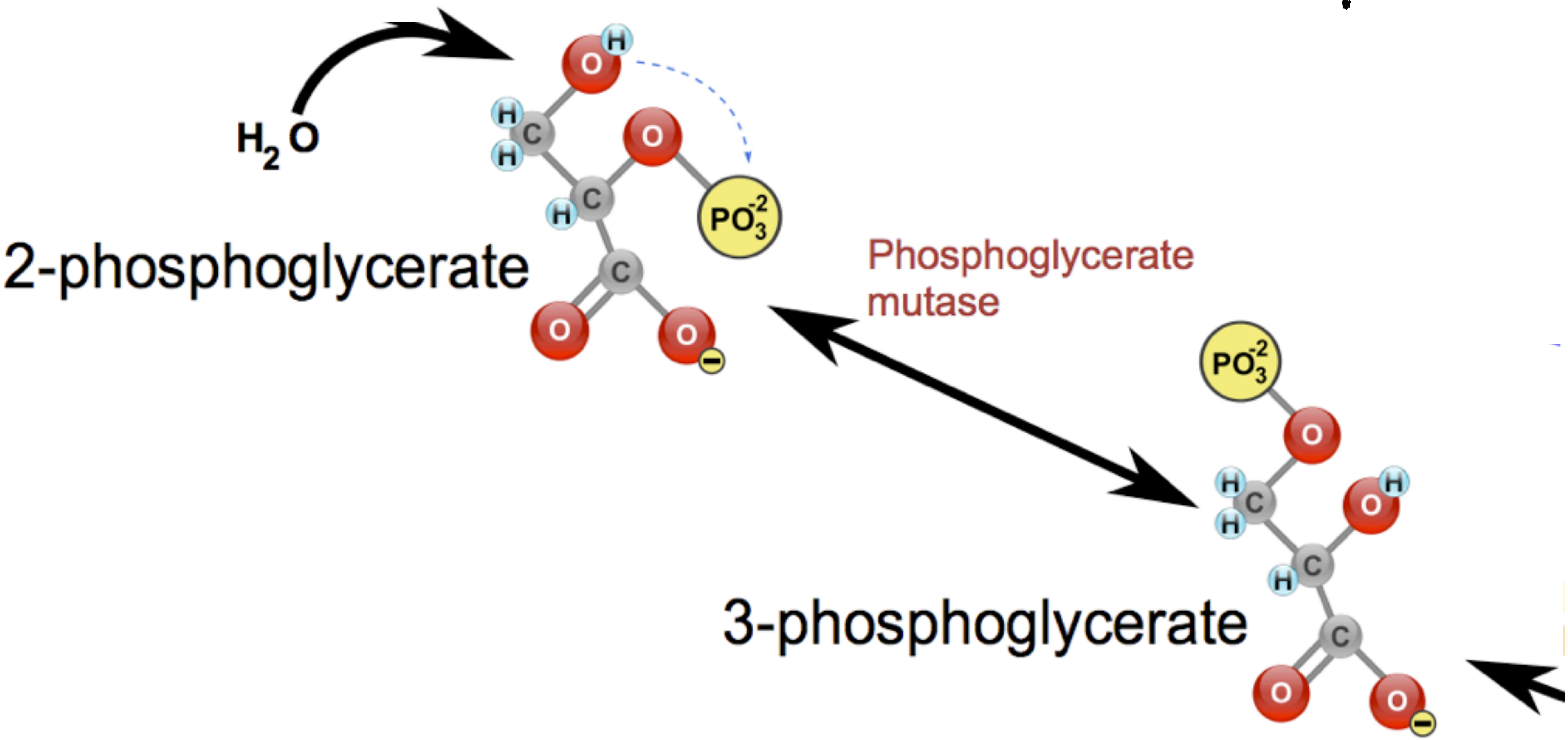
What is the reducing agent? Oxidizing Agent?

X2 Step 7



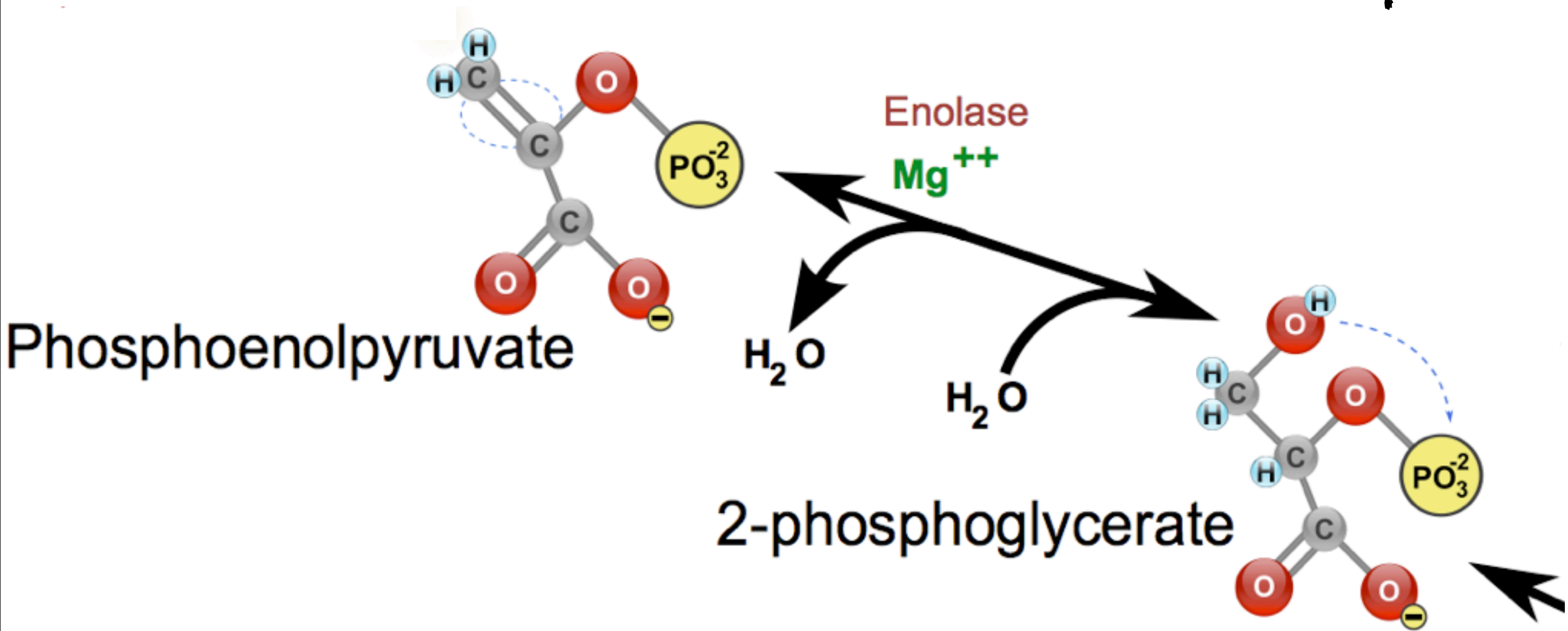
What is the name of the process that produces ATP in this step?

X2 Step 8



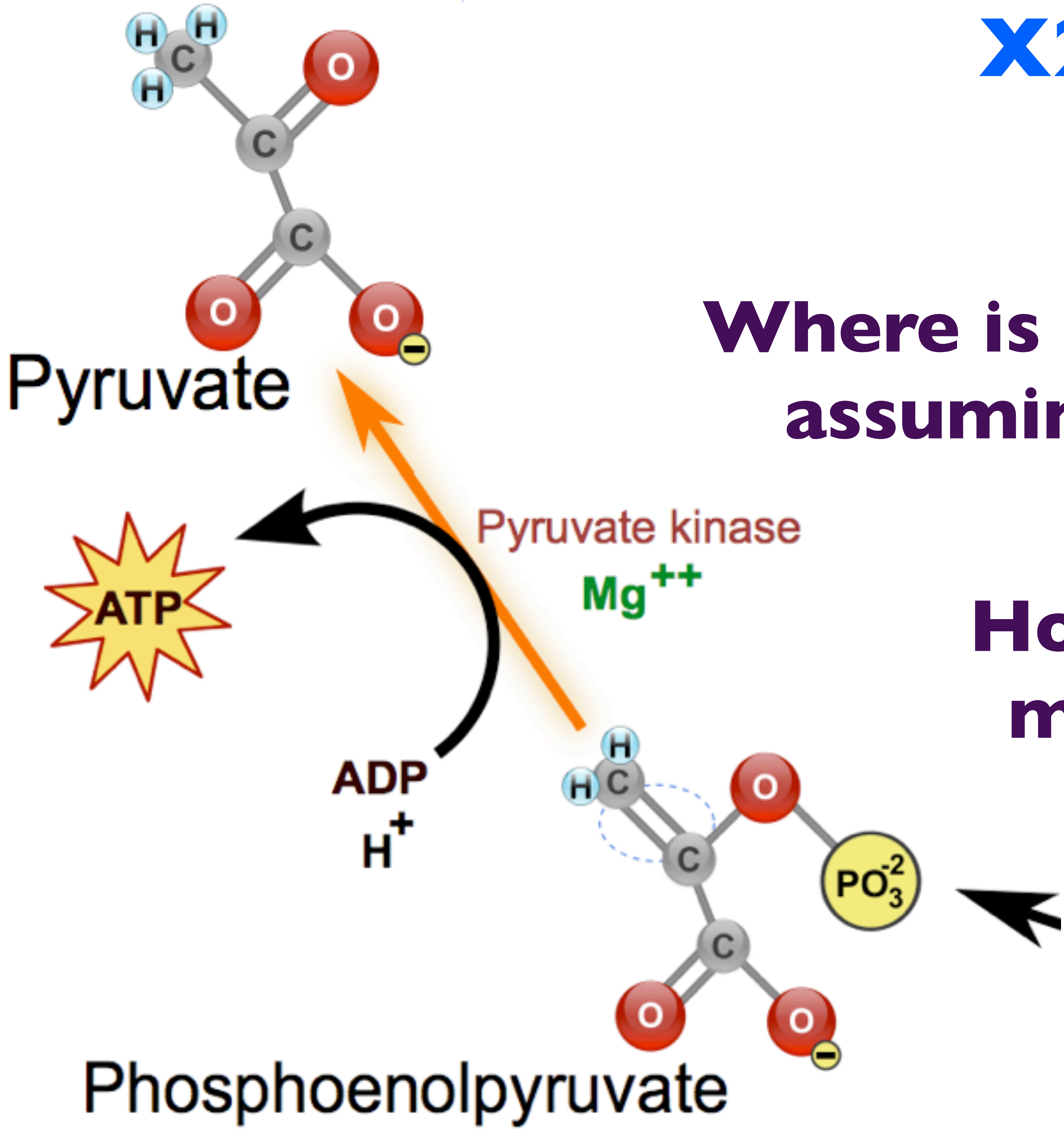
What is the function of mutase?

X2 Step 9



Have we seen phosphoenolpyruvate before?
(aka..."PEP" does that help?)

X2 Step 10



Where is pyruvate going, assuming their is O_2?

How will pyruvate move across the membrane?

Why?

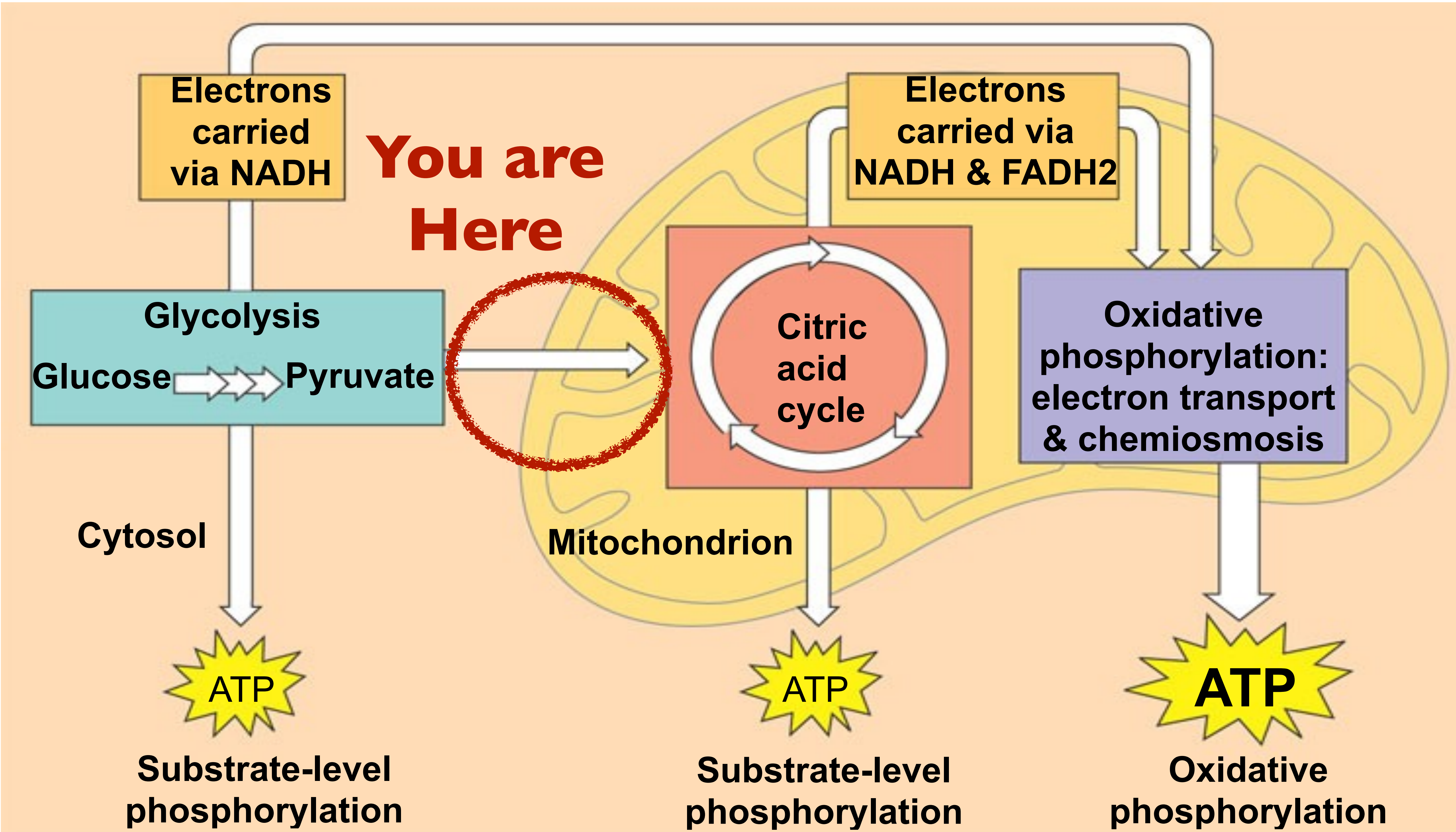
Cell Respiration

III.

Main Idea: Pyruvate must be transported across the outer membrane of the mitochondria and converted to different molecule in order to the enter the next step of cell respiration.

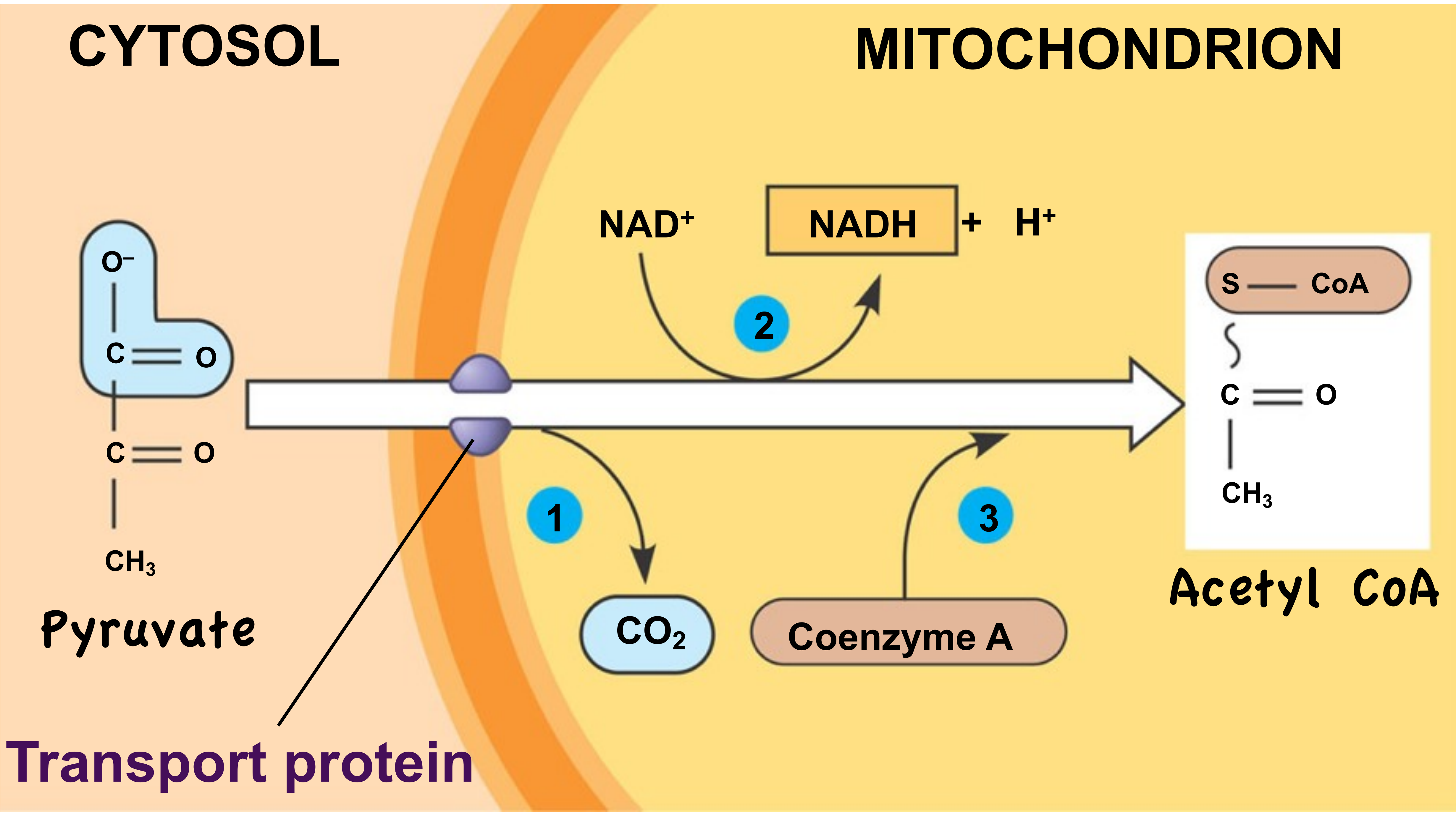
An Overview of Cellular Respiration

- Focus on the location, the input(s) and the output(s) for each the three stages.



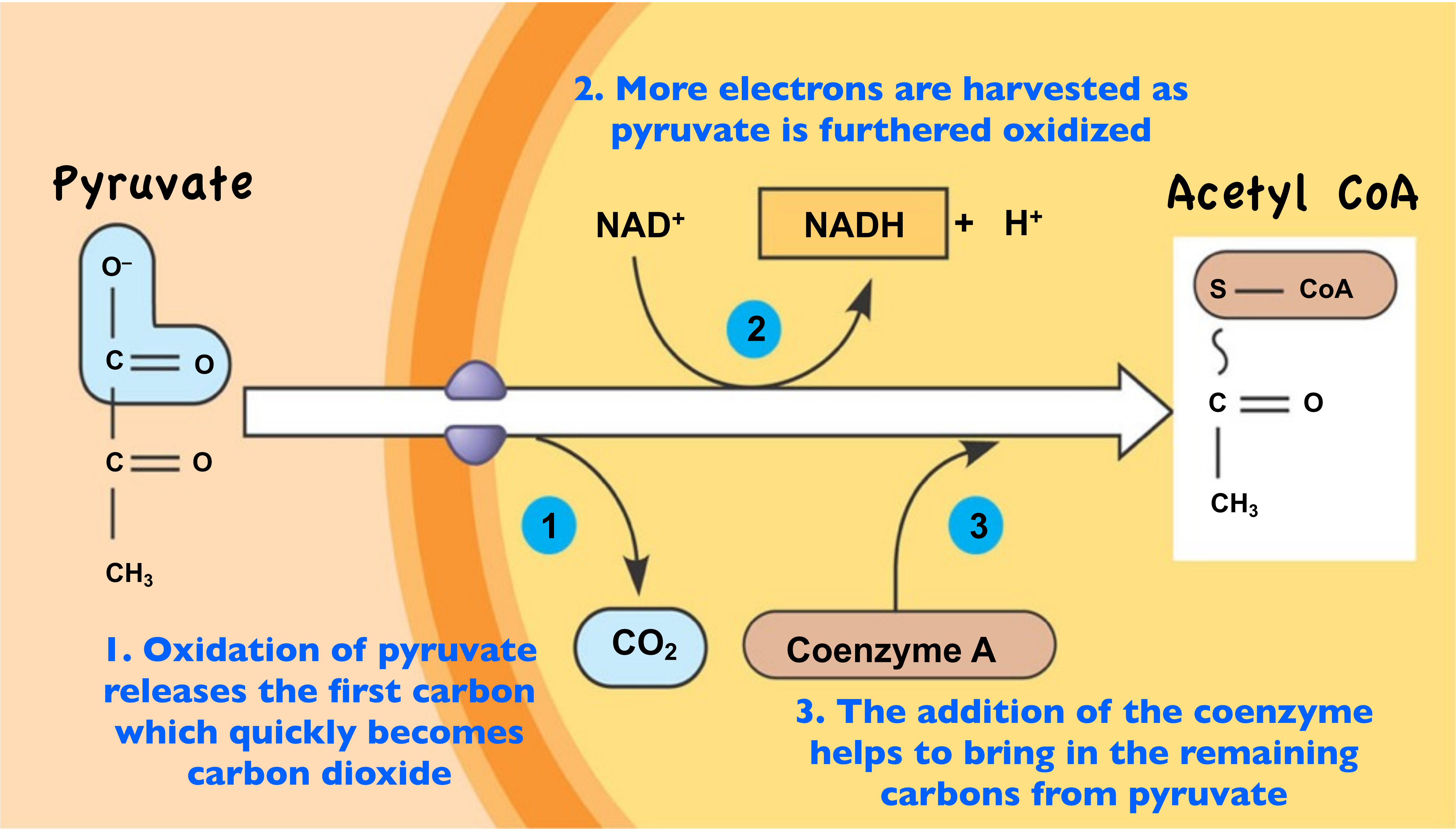
Transport of Pyruvate into Mitochondria

- Pyruvate can not pass freely through the mitochondrial membrane (too large and charged), it must be actively transported across.



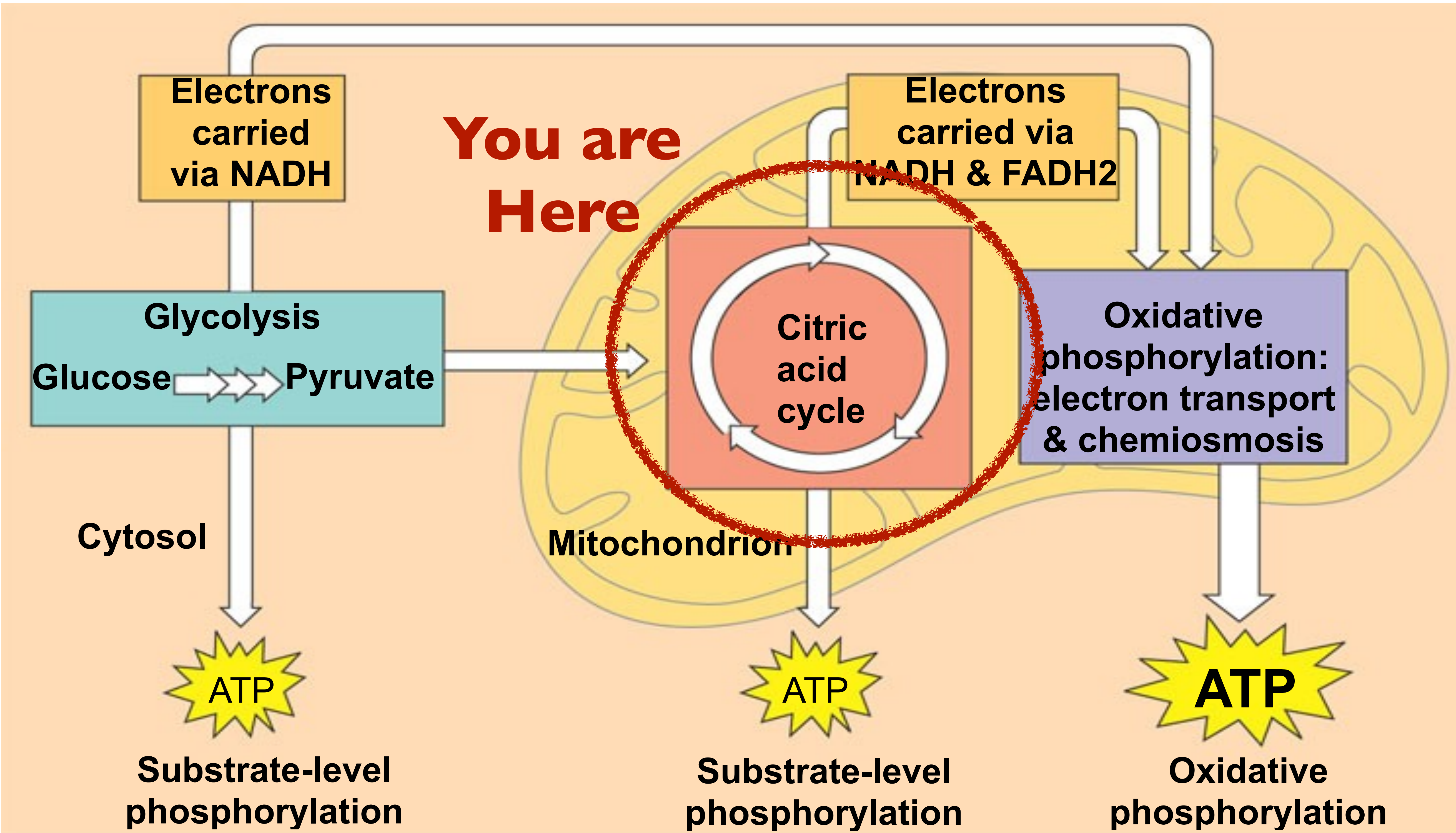
The "Prep Step"

- Pyruvate can not enter the Citric Acid cycle, it must be converted to Acetyl Coenzyme A.



An Overview of Cellular Respiration

- Focus on the location, the input(s) and the output(s) for each the three stages.

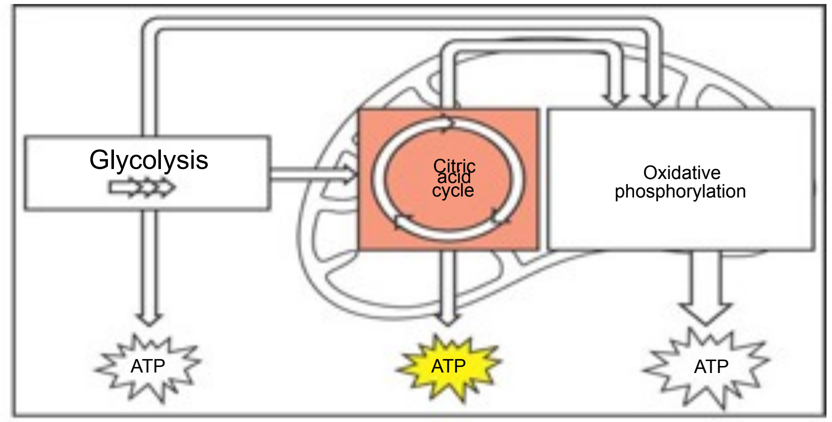


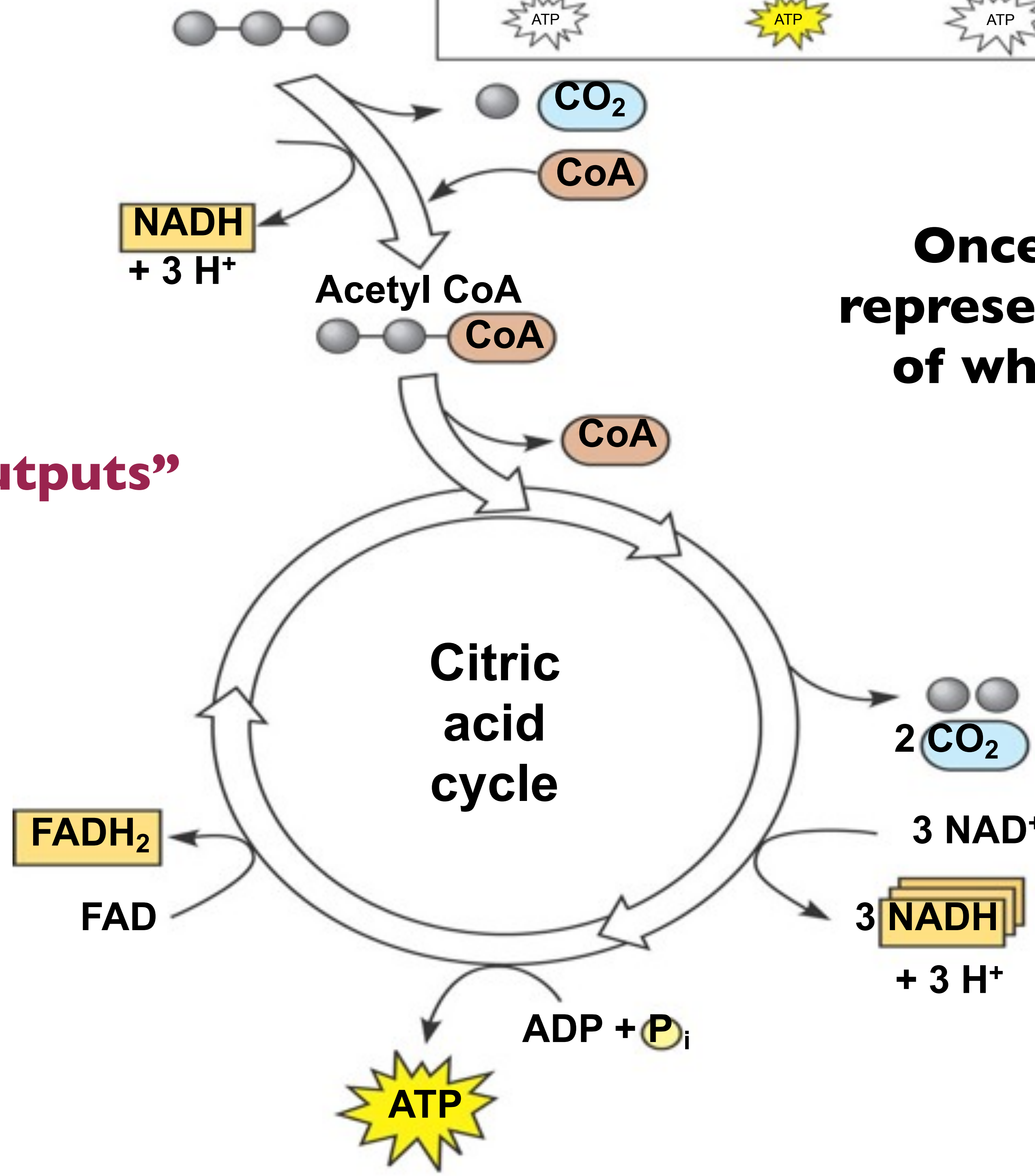
The Citric Acid Cycle or Krebs Cycle

- Harvests the remaining electrons from acetyl CoA (originally from glucose).
- In addition, it generates some more ATP via substrate level phosphorylation.
- Carbon dioxide is released as a waste product.
  - Ultimately each of the six original carbons in glucose will be released as six carbon dioxide molecules.
    - 2 of the 6 in the prep step
    - 4 of the 6 in the citric acid cycle

An Overview of the Citric Acid Cycle

Pyruvate
(from glycolysis,
2 molecules per glucose)



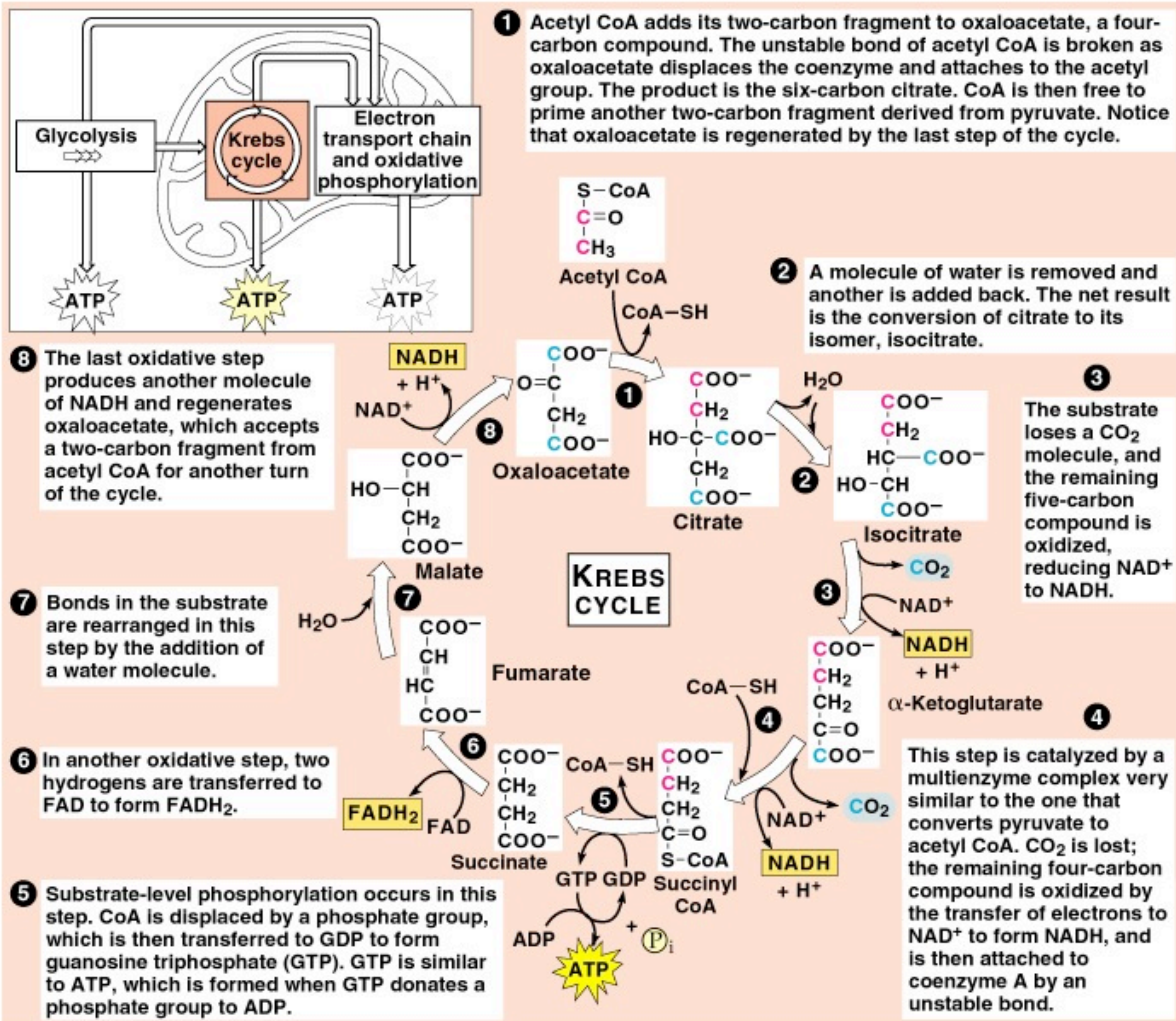


Focus on "inputs" and "outputs"

Once agin the overview represents the "bottom line" of what you should know

PER TURN

A Closer Look at the Citric Acid Cycle

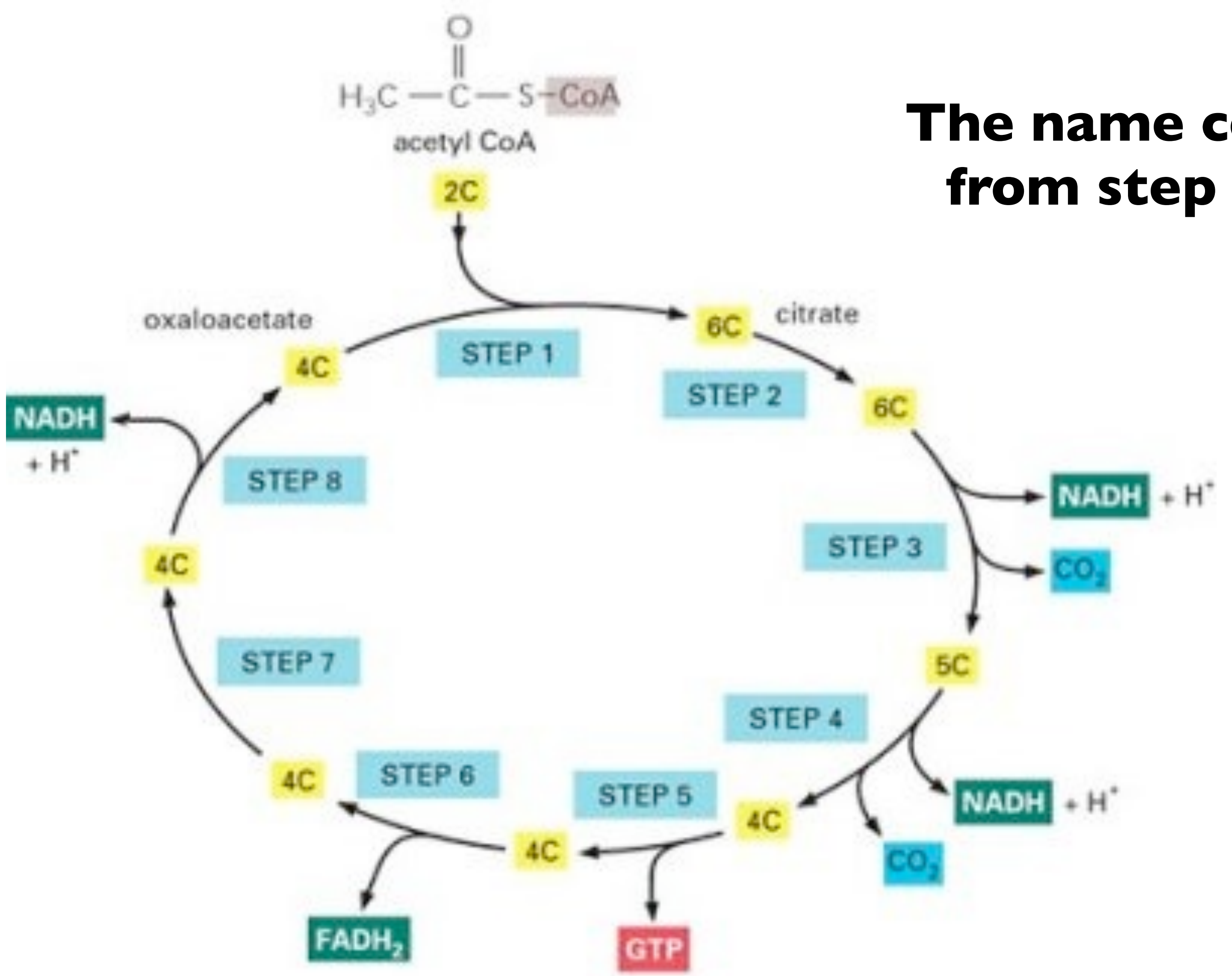


A Closer Look at the Citric Acid Cycle

Count the carbon atoms, notice the loss of carbons with each turn.

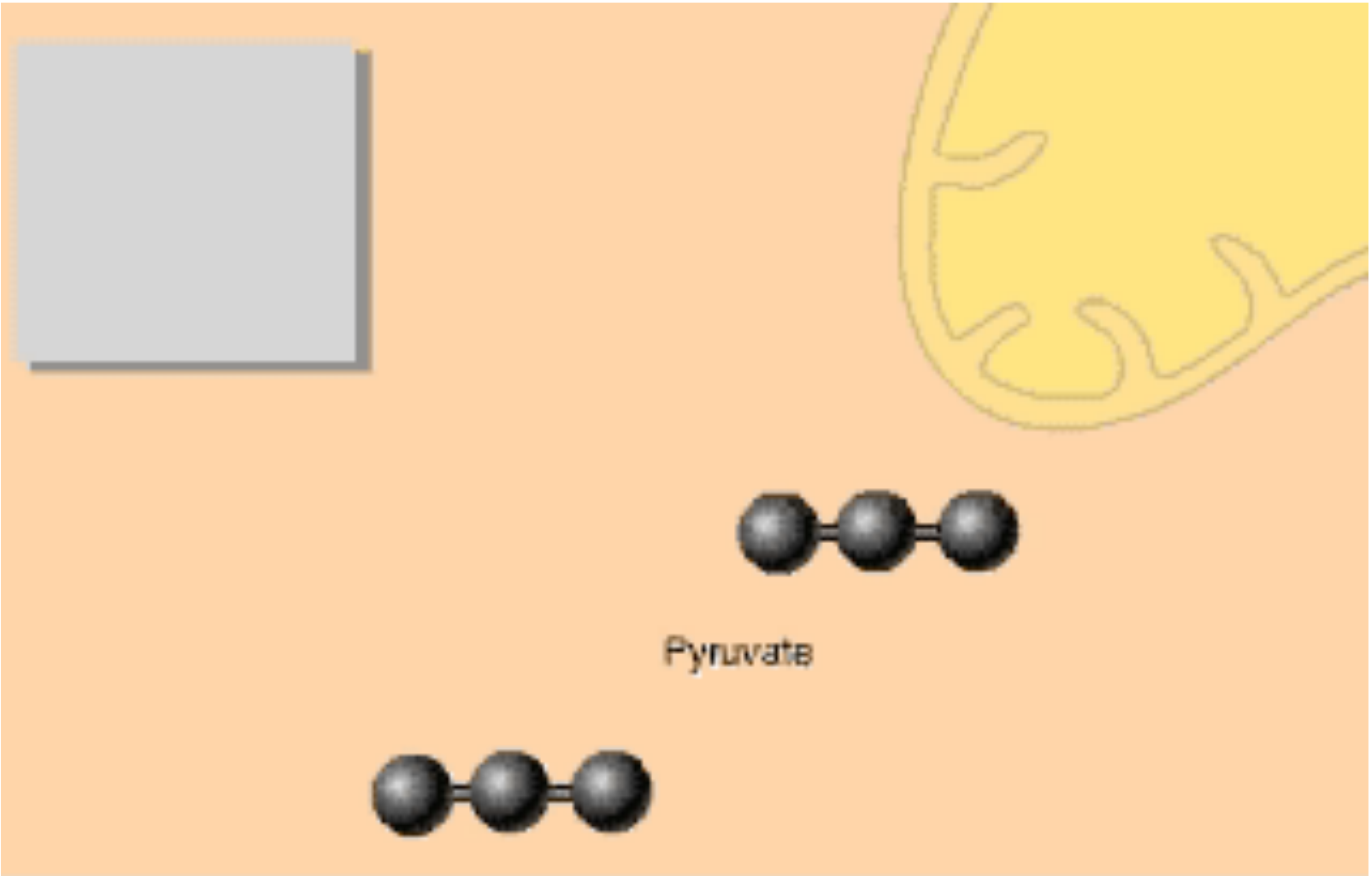
Compare the Krebs Cycle (catabolic) with the Calvin Cycle (anabolic)

The name comes from step one



NET RESULT: ONE TURN OF THE CYCLE PRODUCES THREE NADH, ONE GTP, AND ONE $FADH_2$, AND RELEASES TWO MOLECULES OF CO_2

The Citric Acid Cycle



Cell Respiration

IV.

Main Idea: The electrons harvested in glycolysis and the citric acid cycle are used to power the production of ATP through oxidation phosphorylation.

An Overview of Cellular Respiration

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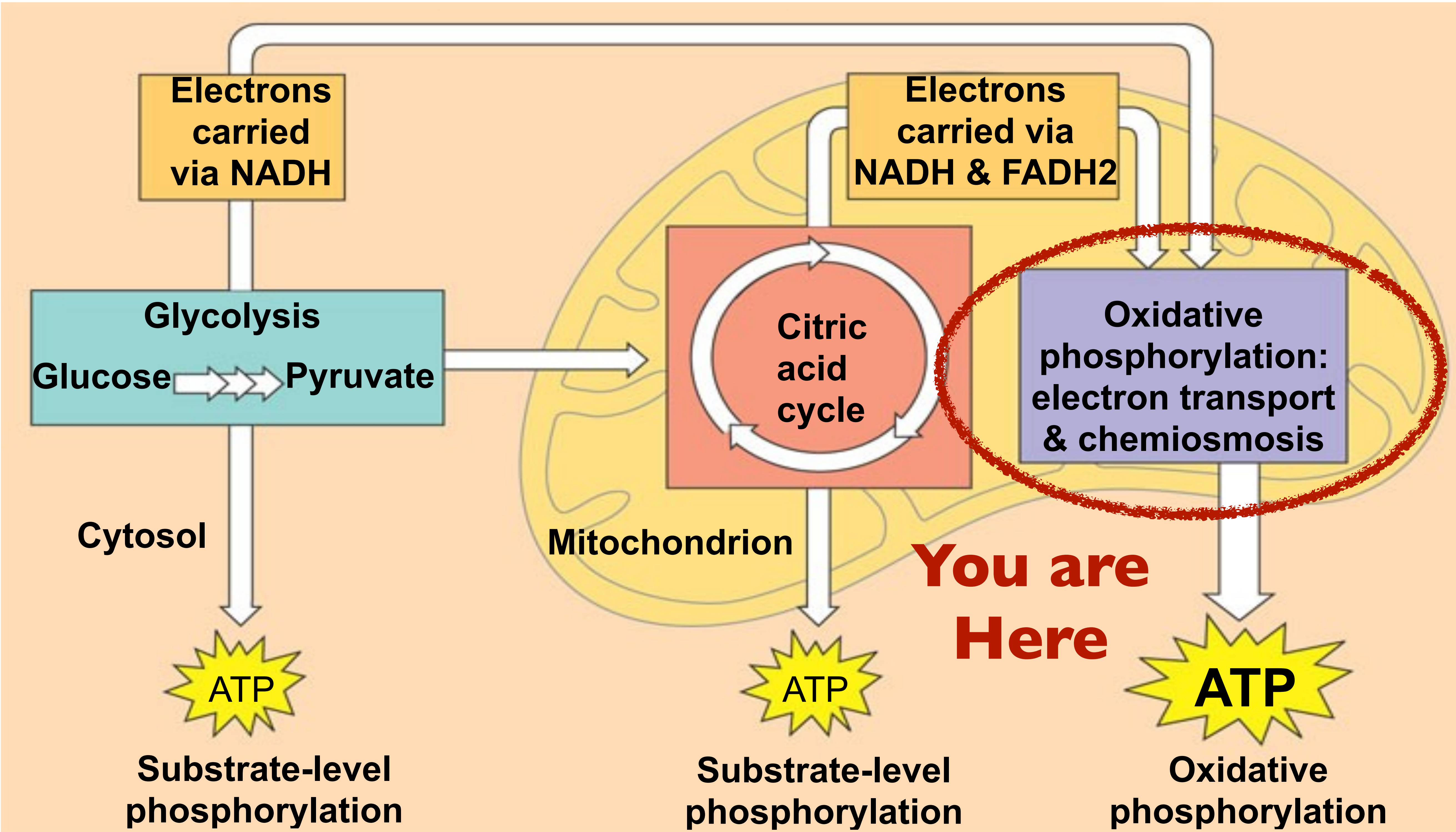
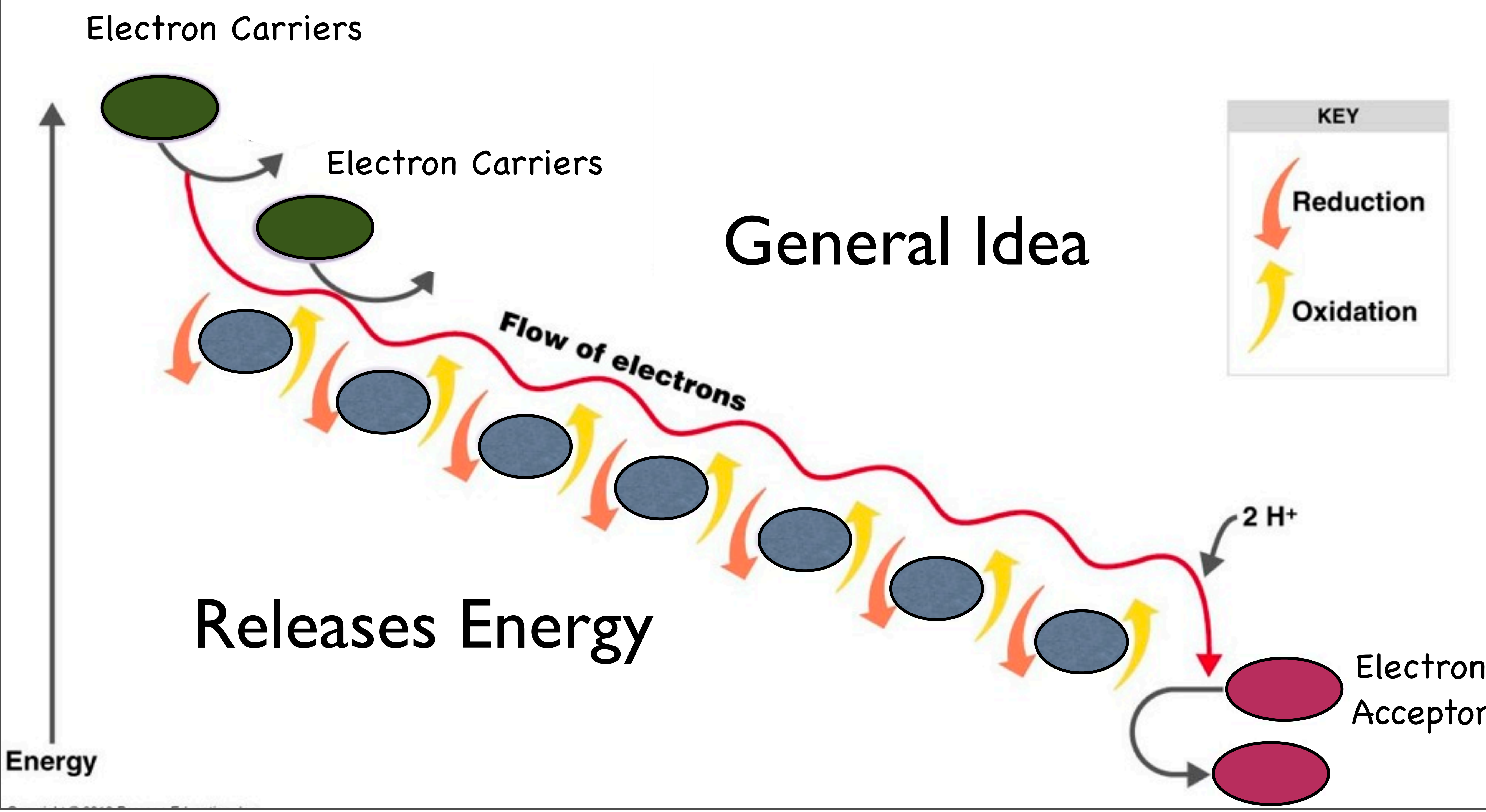


Electron Acceptors & Transport

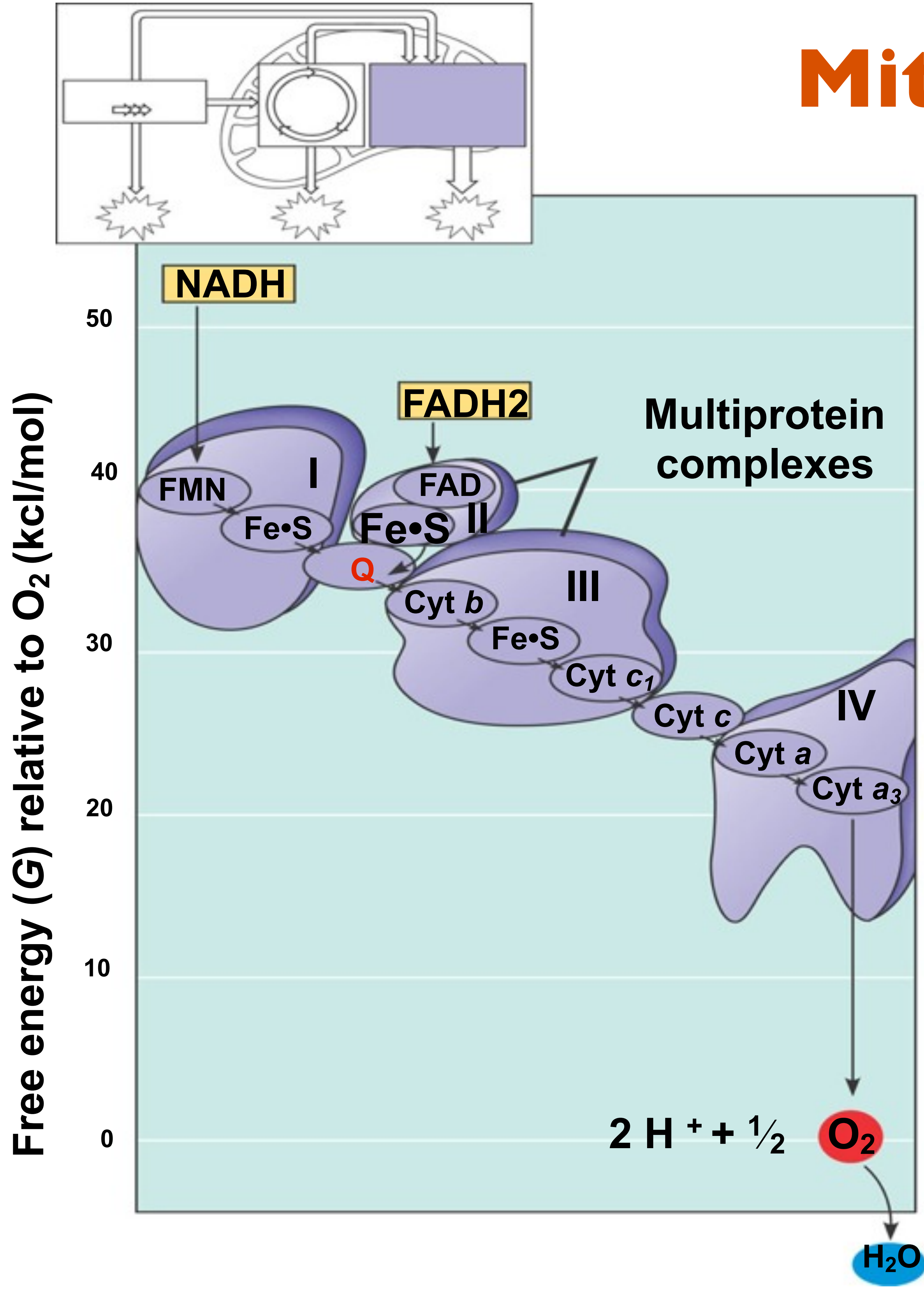
- To get electrons from photosystem II to photosystem I requires an ***electron transport chain***.
- The *electron transport chain* consists of mainly proteins, embedded into a membrane.
    - *in eukaryote's inner mitochondrial membrane, in eukaryote's thylakoid membranes and prokaryote's plasma membrane*
- An electron carrier passes the electrons to another molecule, that is more electronegative, and so on and so forth
    - *Each molecule slightly more electronegative than the prior one*

Electron Acceptors & Transport

REVIEW



Mitochondrial E.T.C.



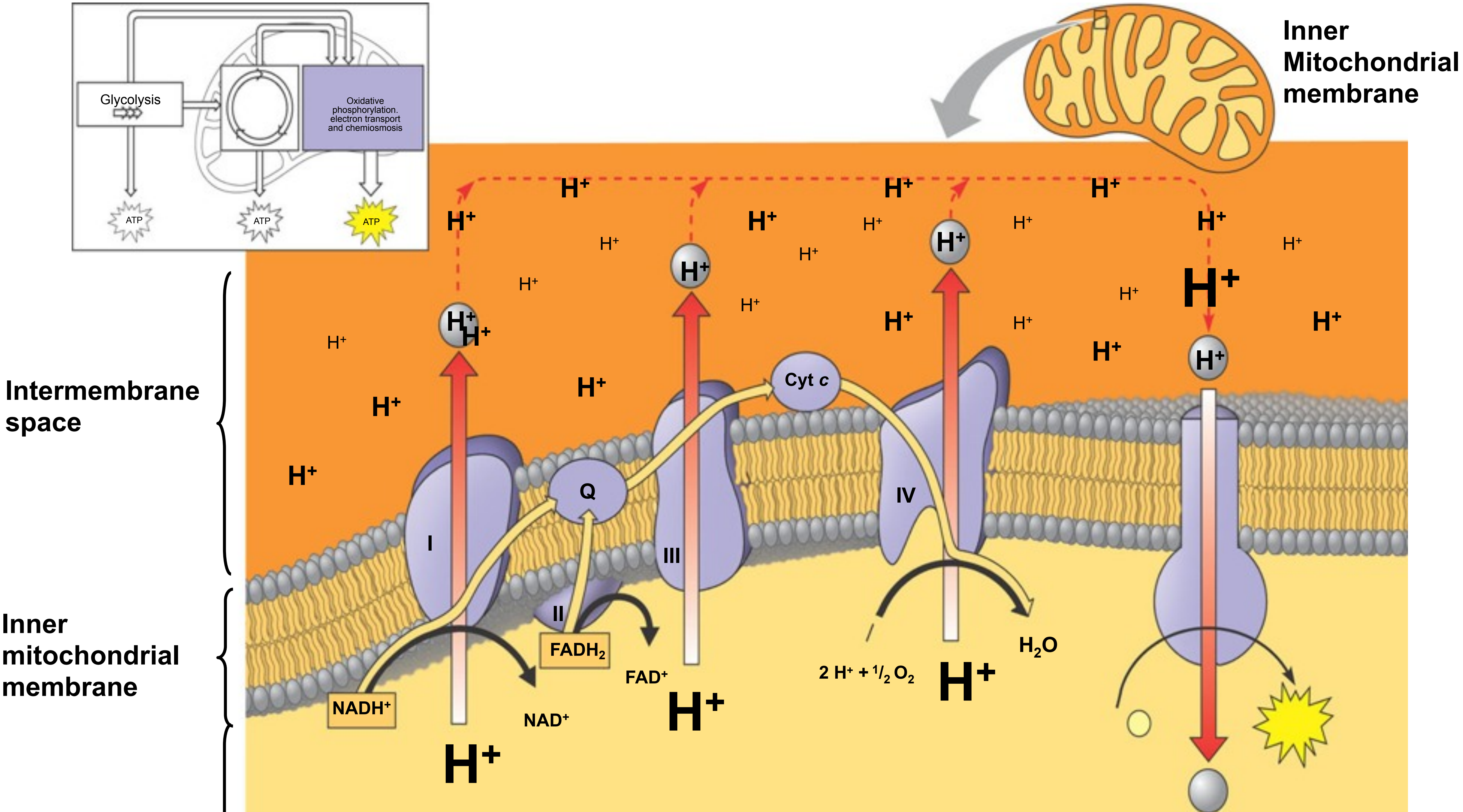
located on the folded inner membrane of the mitochondria

Q is the only non protein, it is called ubiquinone or CoQ often sold as a nutritional supplement

E.T.C. Establishes a H^+ ion Gradient

- The ***electron transport chain*** makes no ATP.
- The e^- transfer releases energy as the electron moves through the chain, this energy is used to pump H^+ ions through a membrane.
    - *This generates a electrochemical gradient with great potential energy*

E.T.C. and Chemiosmosis



Some members of the ETC accept H+ ions along with the electrons, which they then release into the intermembrane space

E.T.C. and Chemiosmosis

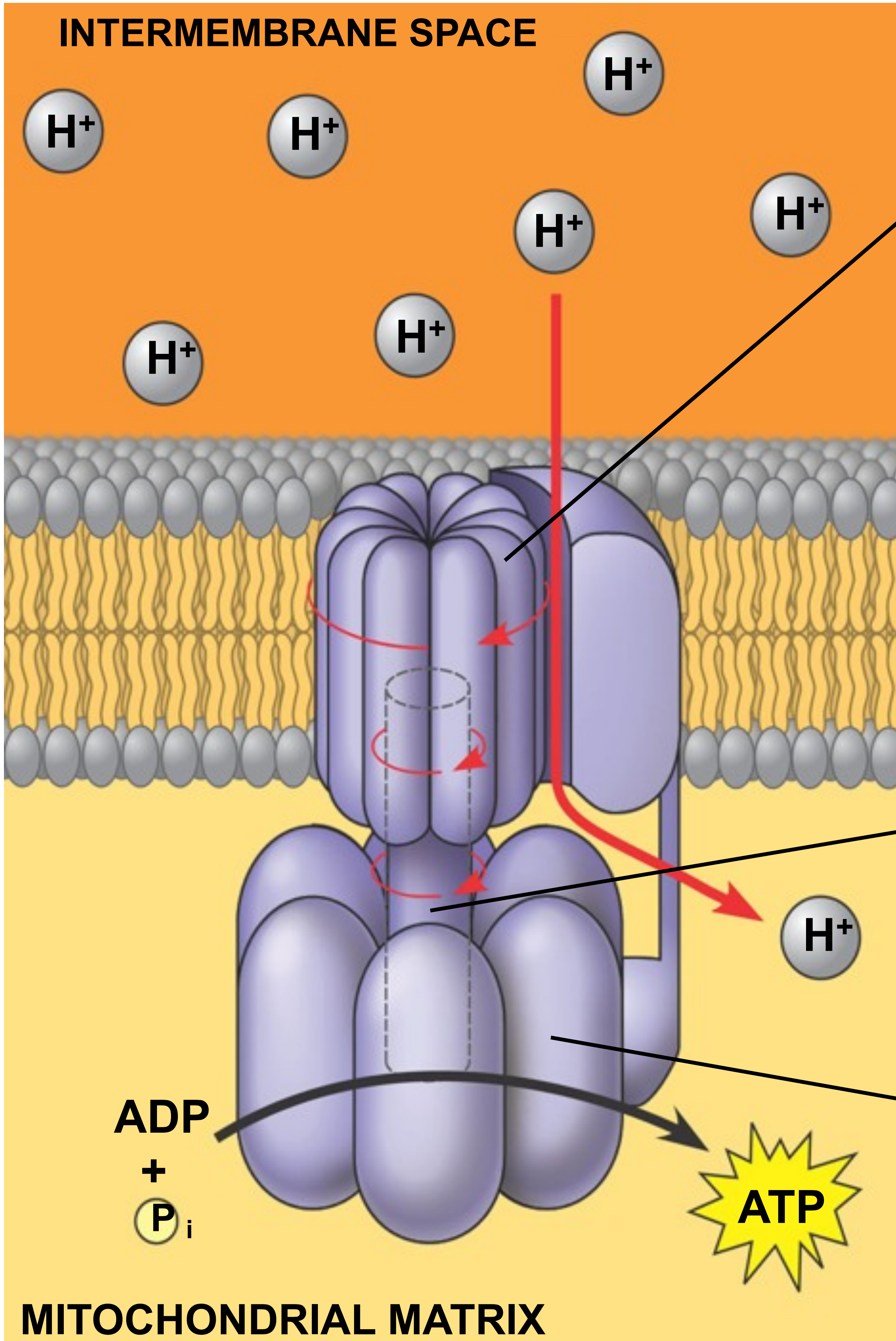
- Stored energy in the form a H^+ ion gradient across a membrane is called the ***proton motive force,*** it is used to produce ATP (or drive other cellular work), which is called ***chemiosmosis***.

- ***Chemiosmosis*** *is an energy coupling mechanism that uses energy stored in in the form of H+ ion gradients across membranes to drive cellular work*

  - *Osmosis is the diffusion of water*

  - *Chemiosmosis is the diffusion of H^+ ions*

- Specifically an enzyme ATP synthase uses the energy to produce ATP from ADP



ATP Synthase

A **rotor** within the membrane spins clockwise when H^+ flows past it down the H^+ gradient.

A **stator** anchored in the membrane holds the knob stationary.

A **rod** (for "stalk") extending into the knob also spins, activating catalytic sites in the knob.

Three catalytic sites in the stationary **knob** join inorganic Phosphate to ADP to make ATP.

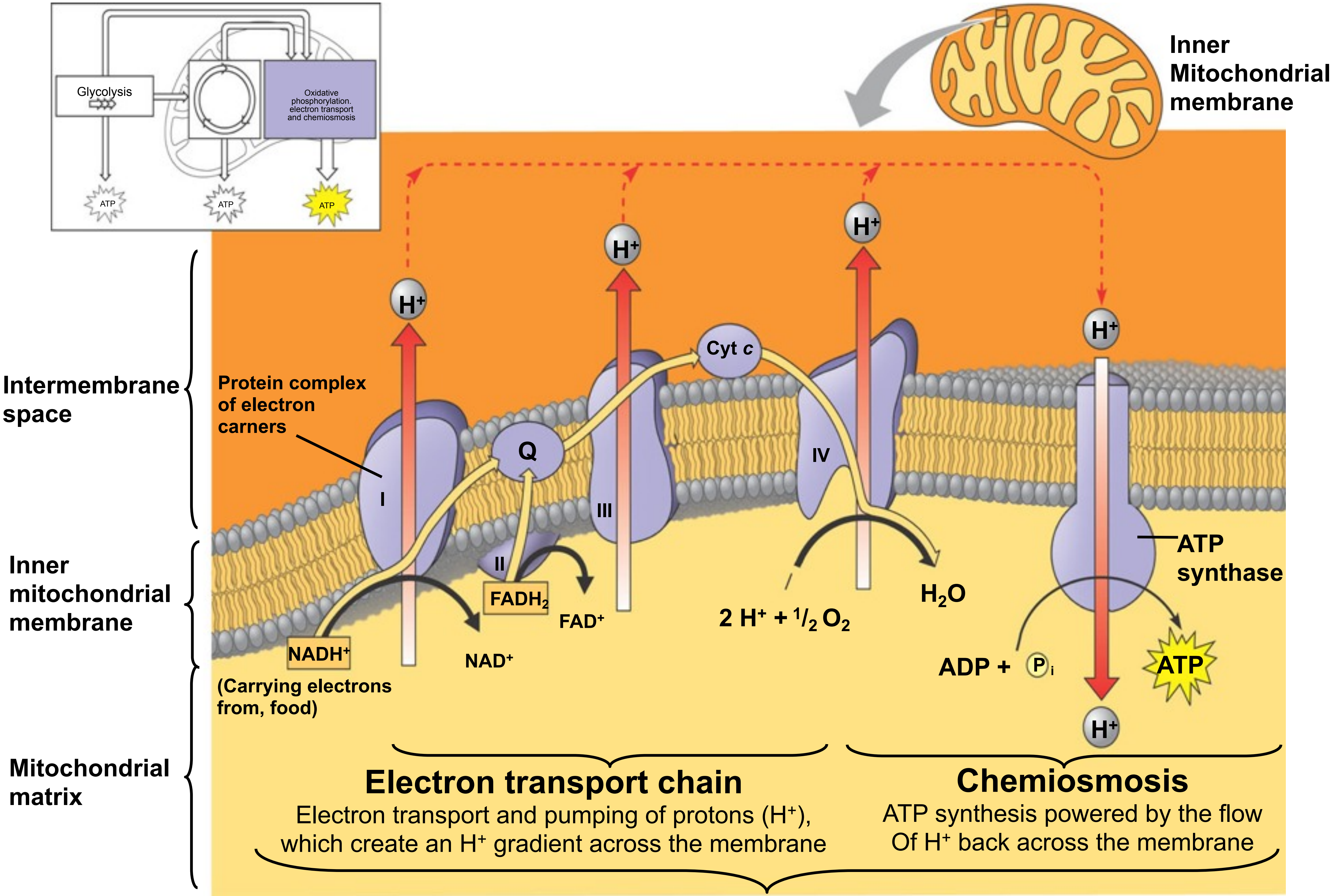
Side Bar: Prokaryotes

Prokaryotes use an ATP synthase to power their flagella...Sense & **Respond**

Prokaryotes use an ATP synthase to pump nutrients in...**Nutrition**

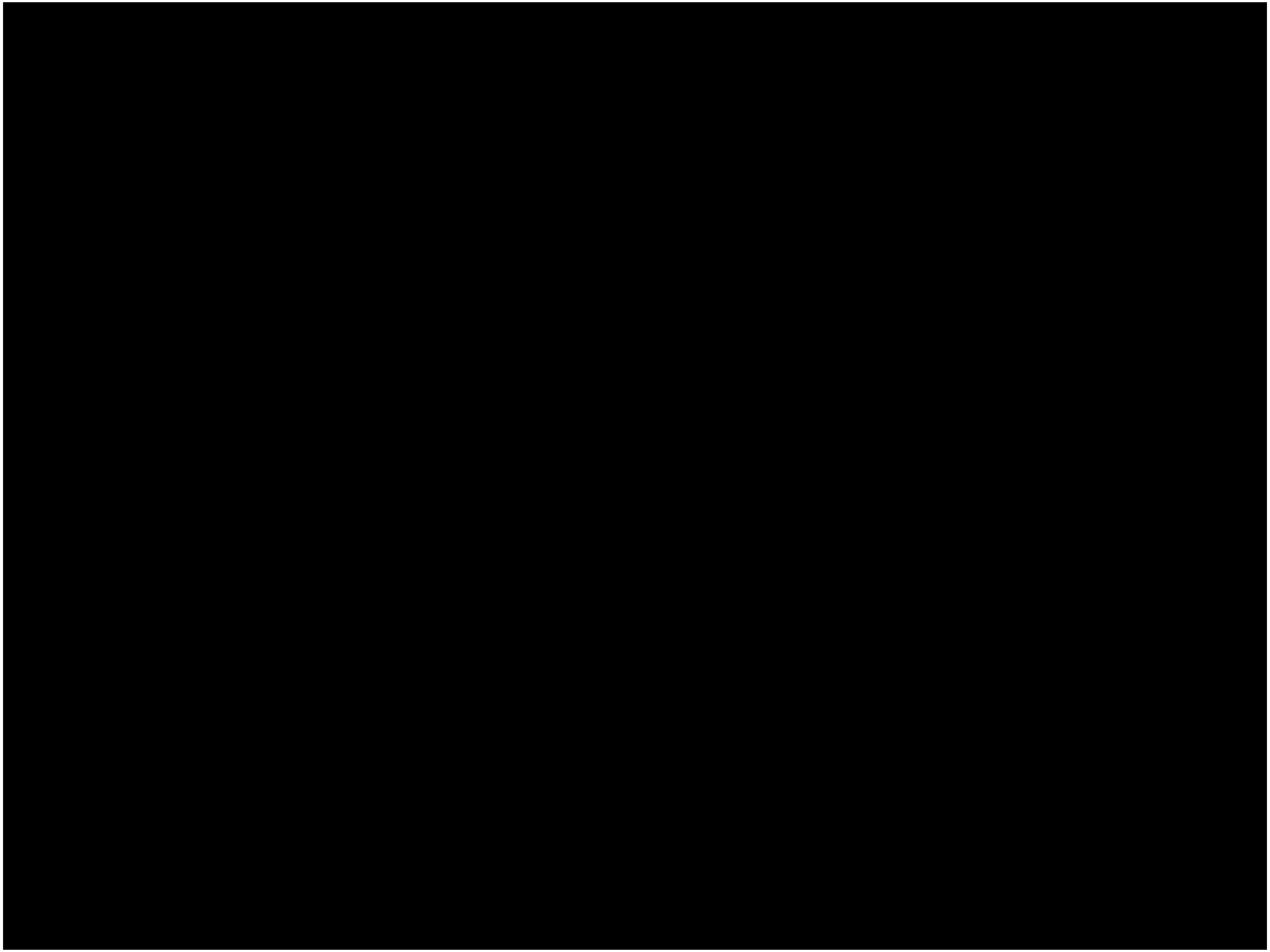
Prokaryotes use an ATP synthase to pump waste...Water & **Waste**

Prokaryotes use an ATP synthase to produce ATP...**Energy**

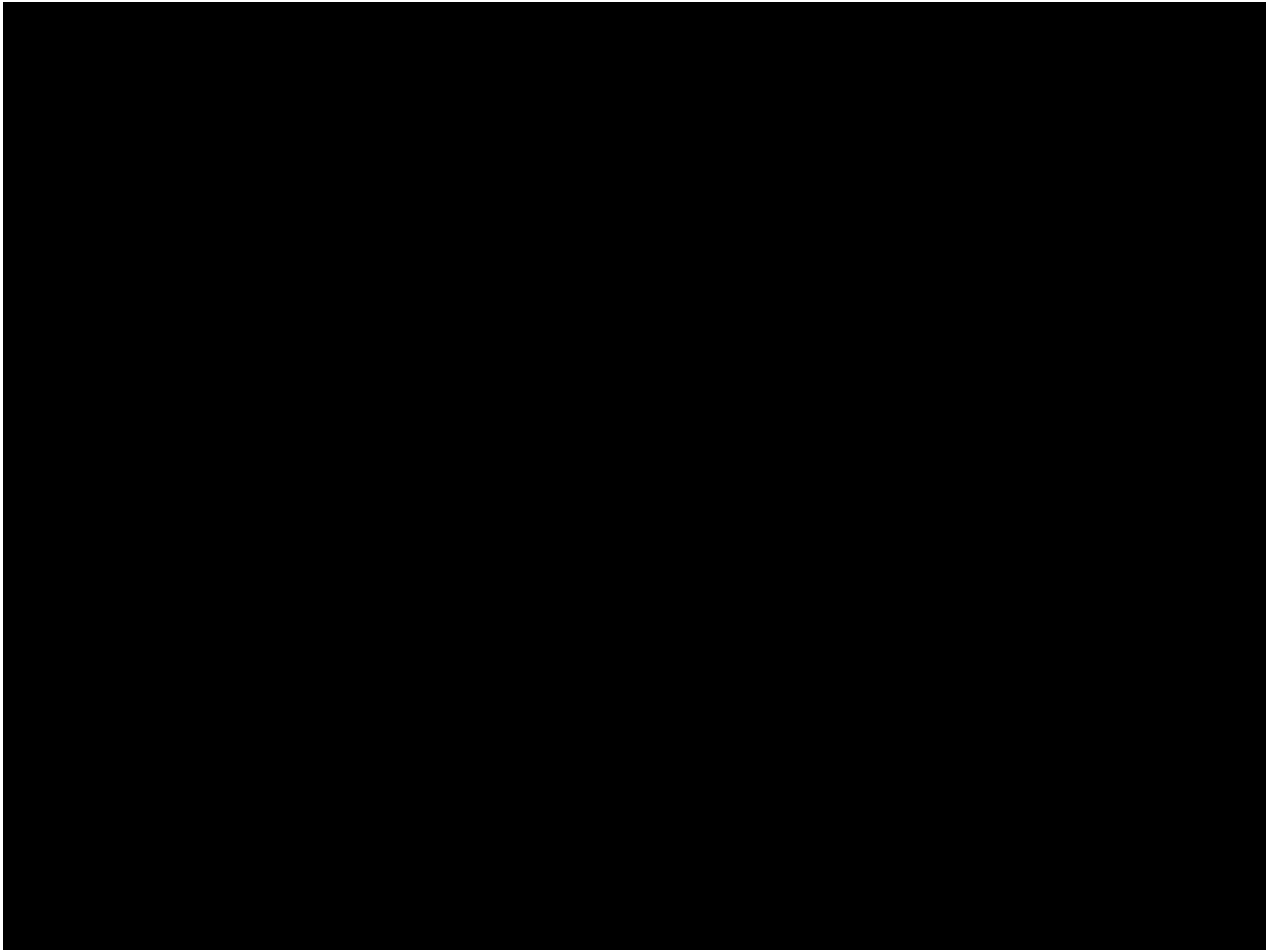


Oxidative Phosphorylation

E.T.C. and Chemiosmosis



ATP Synthase



Chemiosmosis- SIMILARITIES
Chloroplasts vs. Mitochondria

- Both generate ATP
- Both employ an Electron Transport Chain
    - Cytochromes in the E.T.C. are nearly identical
- Both generate a Proton Motive force
- Both use ATP synthase to generate ATP
- Both have chemiosmosis occurring in the inner membrane of the organelle

Chemiosmosis- DIFFERENCES
Chloroplasts vs. Mitochondria

Chloroplasts

photophosphorylation

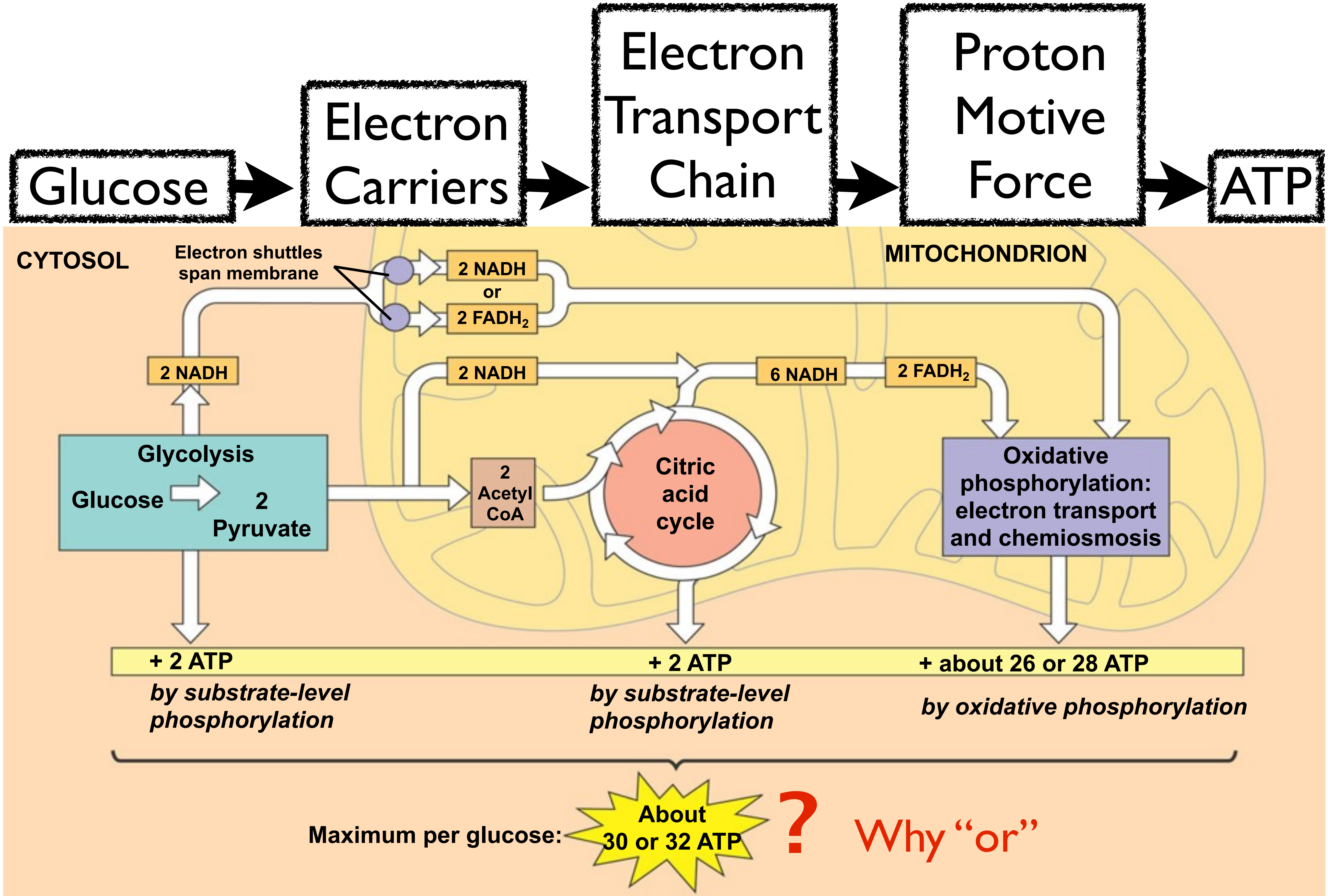
- Electrons come from "water"
- H+ pumped into thylakoid space
- Light energy drives electron flow
- Spatial organization differs

Mitochondria

oxidative phosphorylation

- Electrons come from "food"
- H+ pumped out into intermembrane space
- Chemical energy drives electron flow
- Spatial organization differs

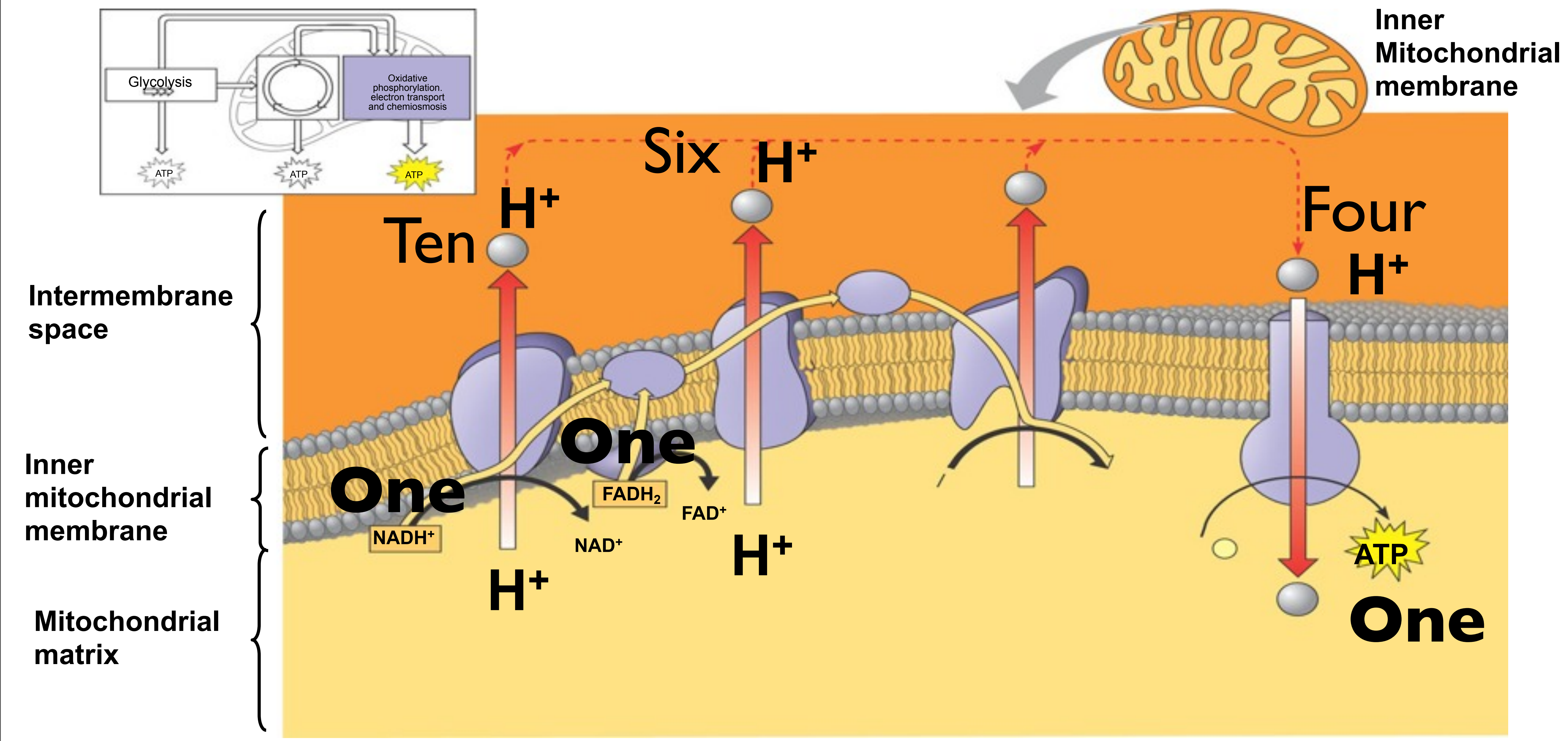
Tracking Energy Flow & ATP Production



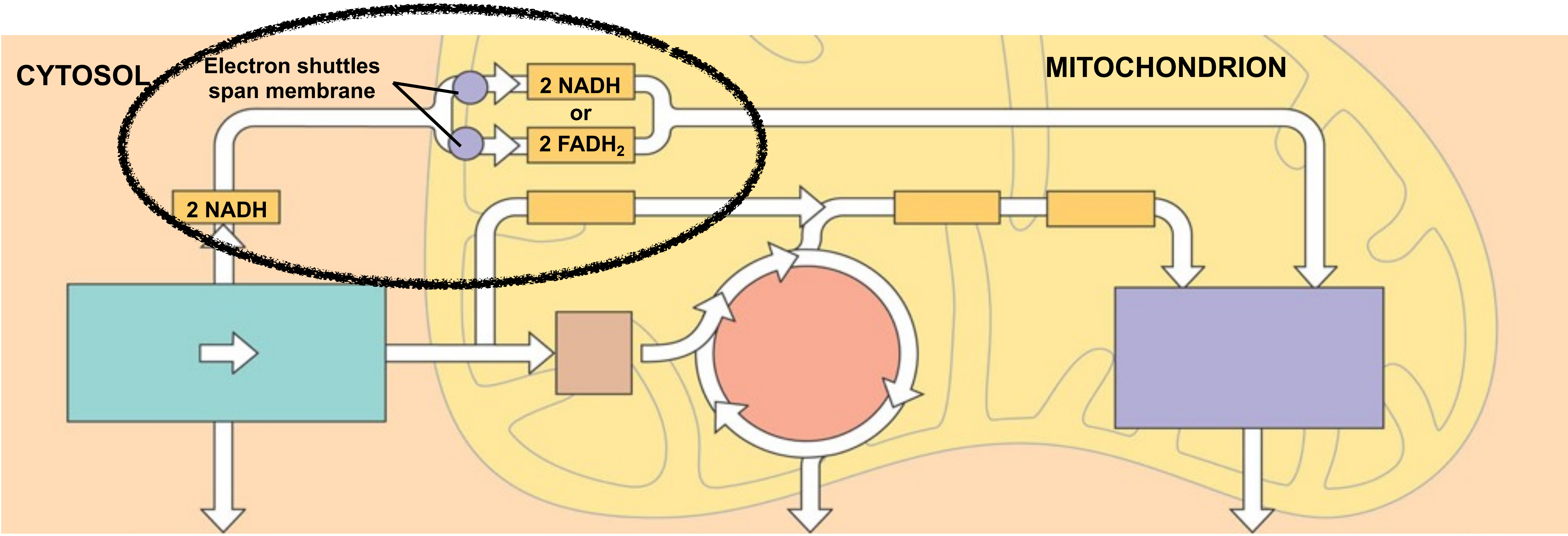
3 Reasons...
Why ATP production is not Exact! #1

- ATP production and Redox Reactions are not directly coupled.

1 NADH yields 2.5 ATP **1 $FADH_2$ yields 1.5 ATP**

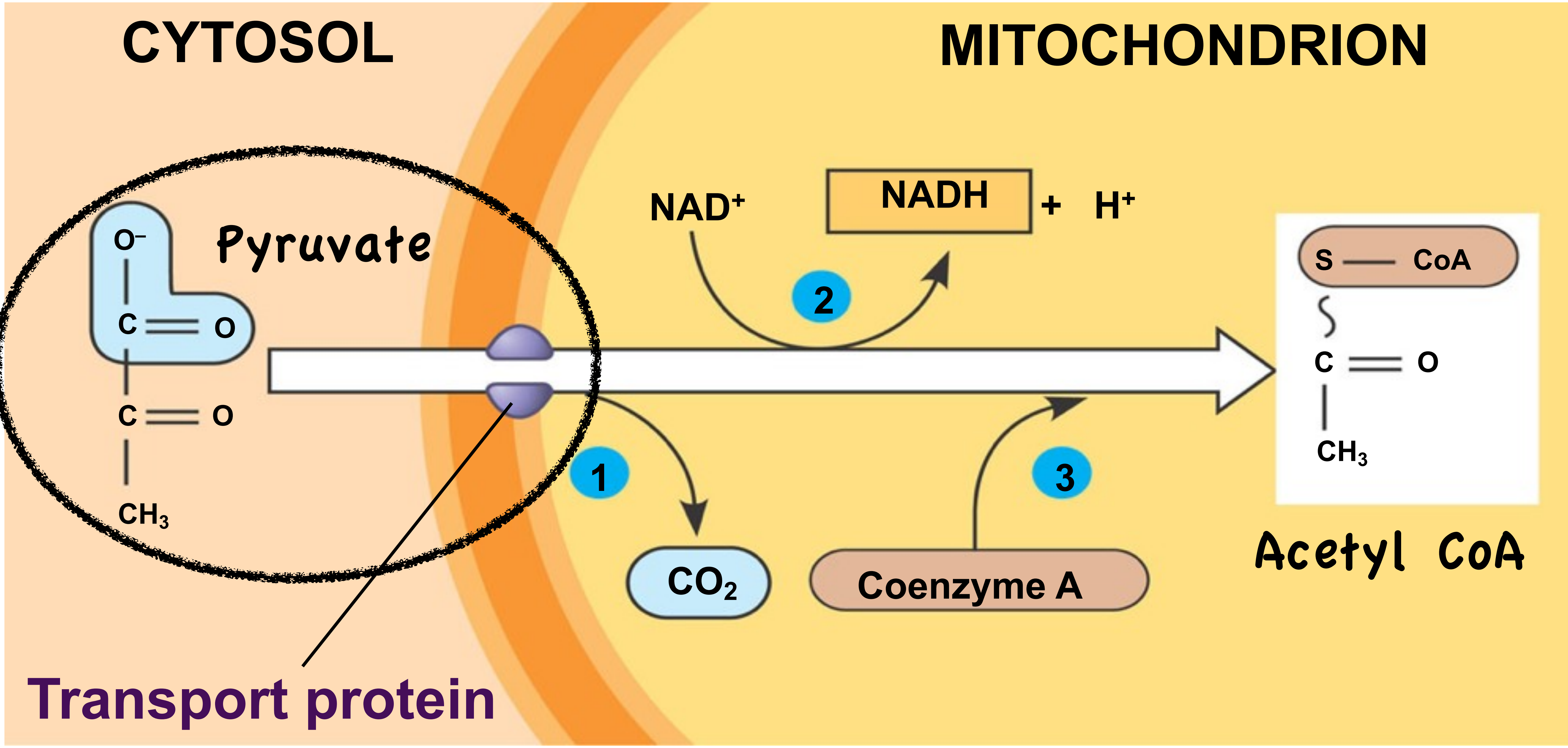


3 Reasons...
Why ATP production is not Exact! #2



- NADH can not pass through the membrane, its electrons must be transferred to another carrier molecule.
- If electrons are transferred to another NADH, then max ATP is made but if passed to $FADH_2$ less ATP will be made

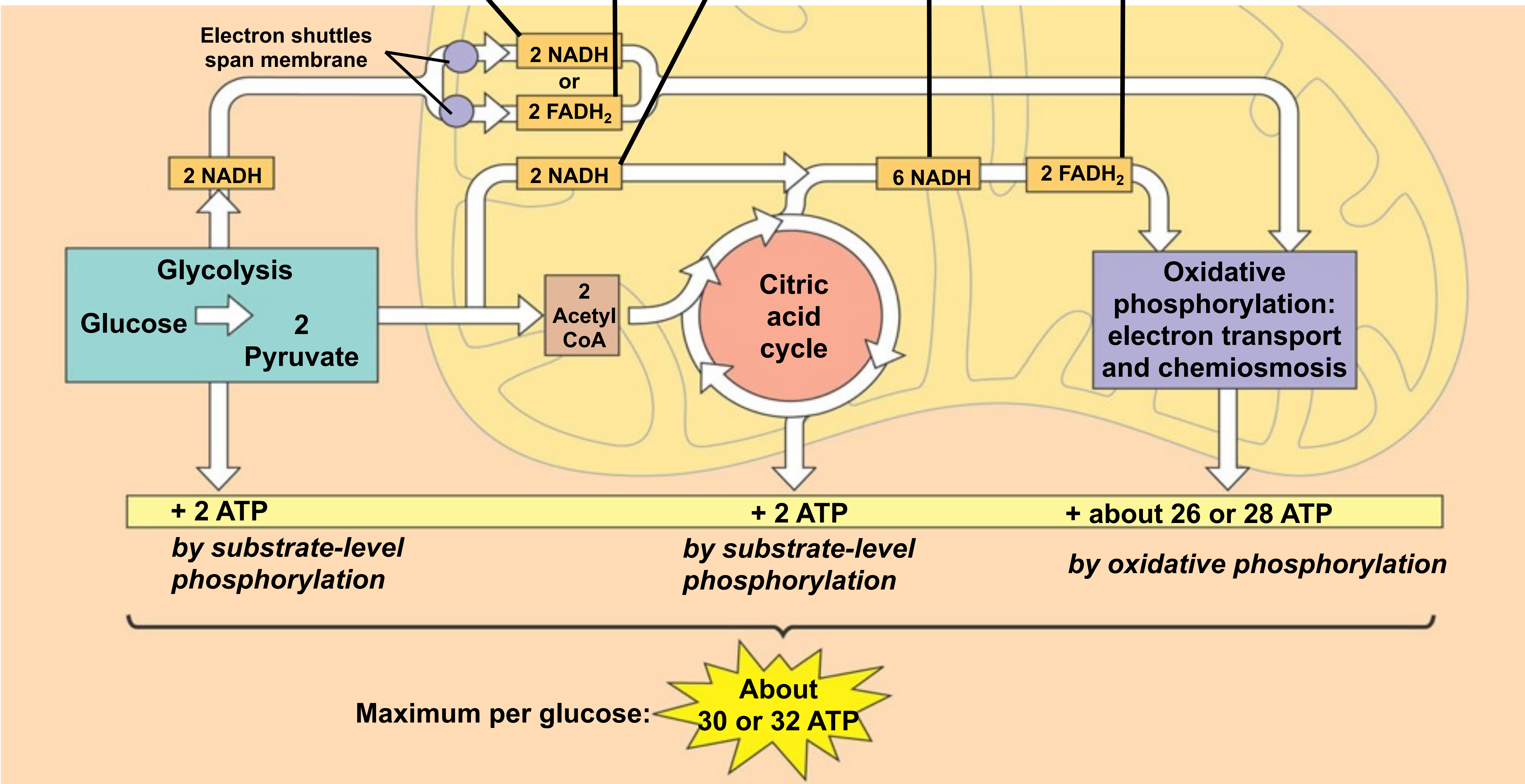
3 Reasons...
Why ATP production is not Exact! #3



- This transport is powered using the same proton motive force that pumps H+ ions across inner membrane, if any of the "PMF" is used here then less ATP is made.

Now...
Can you explain where the "26 or 28" come from?

5 "or" 3 + 5 + 15 + 3 =



Respiration Efficiency

Glucose contains -686 kcal/mol energy

ATP contains -7.3 kcal/mol energy

Max ATP production = 32

$(32)(-7.3) = -233.6$ kcal/mol energy

$-233.6/-686 = 0.34$ or 34% efficiency

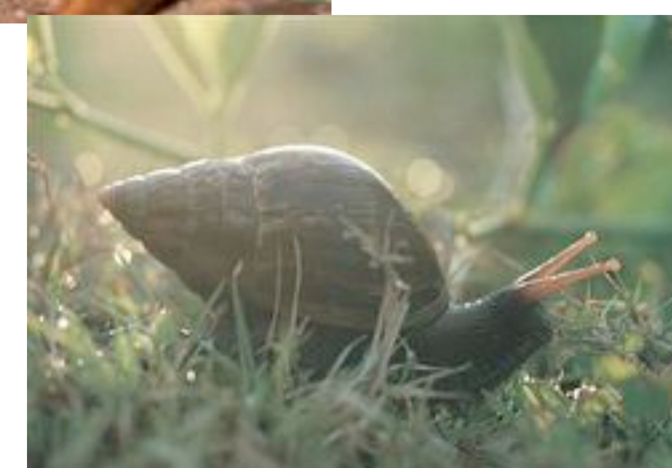
Respiration at 34% is very efficient, most man made machines are far less efficient. Also, the energy lost as heat is used for something useful like maintaining body temperature. In most machines this energy is simply lost to its surroundings

Hibernation & Respiration Efficiency

- There are times when respiration inefficiency is actually favored...during hibernation!






Hibernation & Respiration Efficiency

- A hibernating animal needs to generate heat, without making ATP, throughout the winter
- If hibernating animals continued to use simple cell respiration, it would eventually shut down.
    - ATP would build up in the cells because animal is inactive, as ATP builds a feedback loop would shut down respiration thus stopping ATP production AND HEAT PRODUCTION
- Hibernating animals have brown fat, a cell with many mitochondria that have a unique structure that allows them to carry out respiration without making ATP!

Cell Respiration

V.

Main Idea: There are alternate ways to make ATP that do not require the presence of oxygen.

Fermentation & Anaerobic Respiration

- Aerobic respiration requires oxygen, and with oxygen generates the greatest amount of ATP
- Cells have alternate ways of making ATP when oxygen is not available.
  - Fermentation
  - Anaerobic Respiration
- The distinction between them lies in the presence or absence of electron transport chains.
  - Fermentation- does not have Electron Transport Chains
  - Anaerobic Respiration- has Electron Transport Chains

Anaerobic Respiration

- Anaerobic respiration takes place in bacteria in environments devoid of oxygen.
  - They use Electron Transport Chains
  - They use a Proton Motive Force
  - They use ATP synthase
- The machinery resides in their plasma membrane.
- The final electron acceptor is sulfate ions (SO_4^{2-})
- They produce H_2S instead of H_2O
  - *hence the smell of rotten eggs in mangroves due to* H_2S

Anaerobic Respiration

pics?

Fermentation

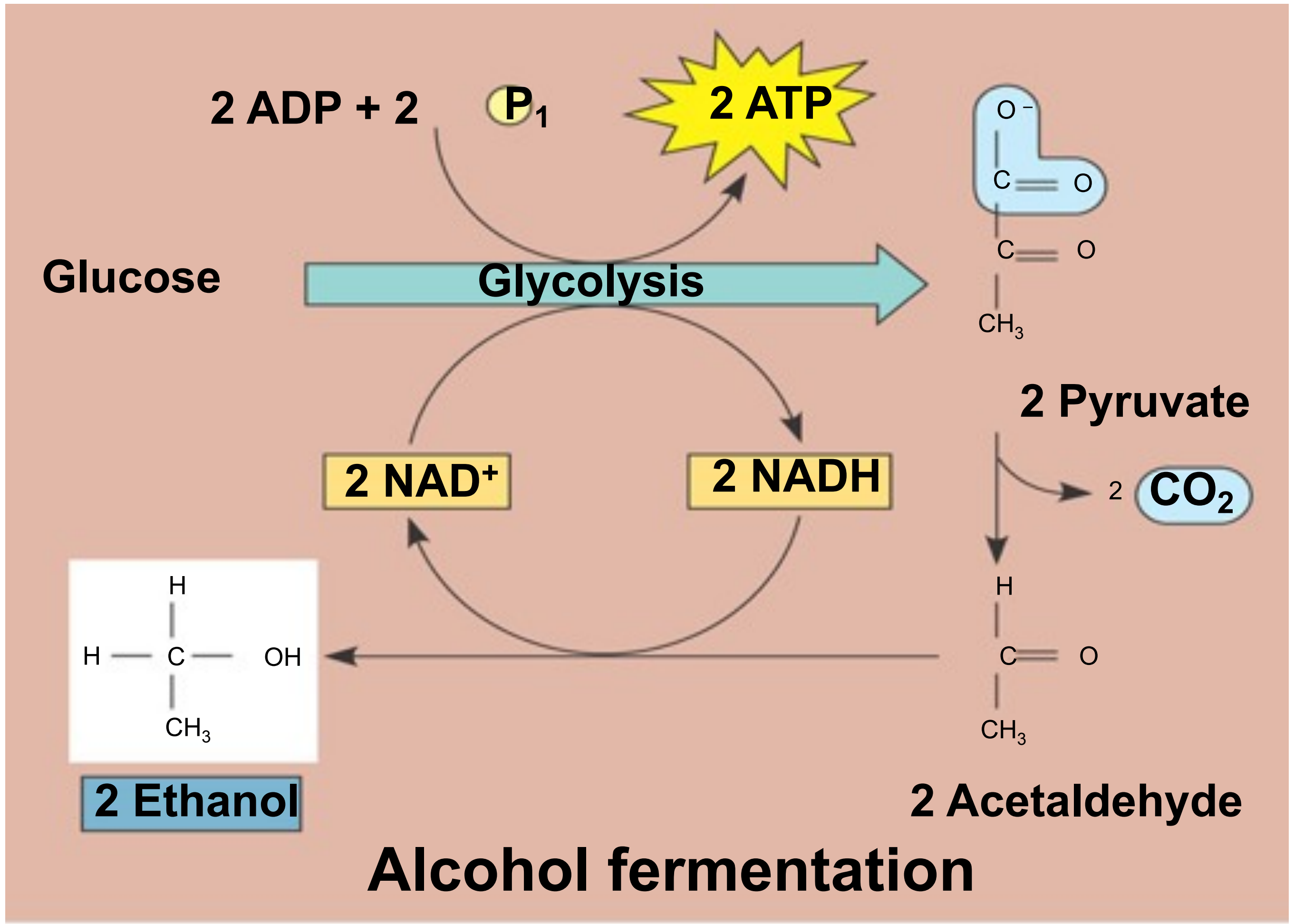
- Fermentation is a mechanism that harvests chemical energy (ATP) without oxygen and without an electron transport chain.
- Glycolysis oxidizes organic compounds with or without oxygen and without an electron transport chain.
- Fermentation is an extension of glycolysis that allows for the continuous production of ATP by substrate level phosphorylation.
  - It does require however a continuous supply of electron carriers (NAD^+)

Fermentation

- A continuous supply of electron carriers (NAD^+) is not a problem when oxygen is present because NADH can pass its electrons into the mitochondria.
- Without oxygen NADH needs to "dump" its electrons somewhere else.
- Fermentation is the extension of glycolysis involves NADH transferring its electrons to pyruvate, so that it is free to oxidize more fuel (glucose).
  - There are two types of Fermentation
    - Lactic Acid Fermentation
    - Alcohol Fermentation

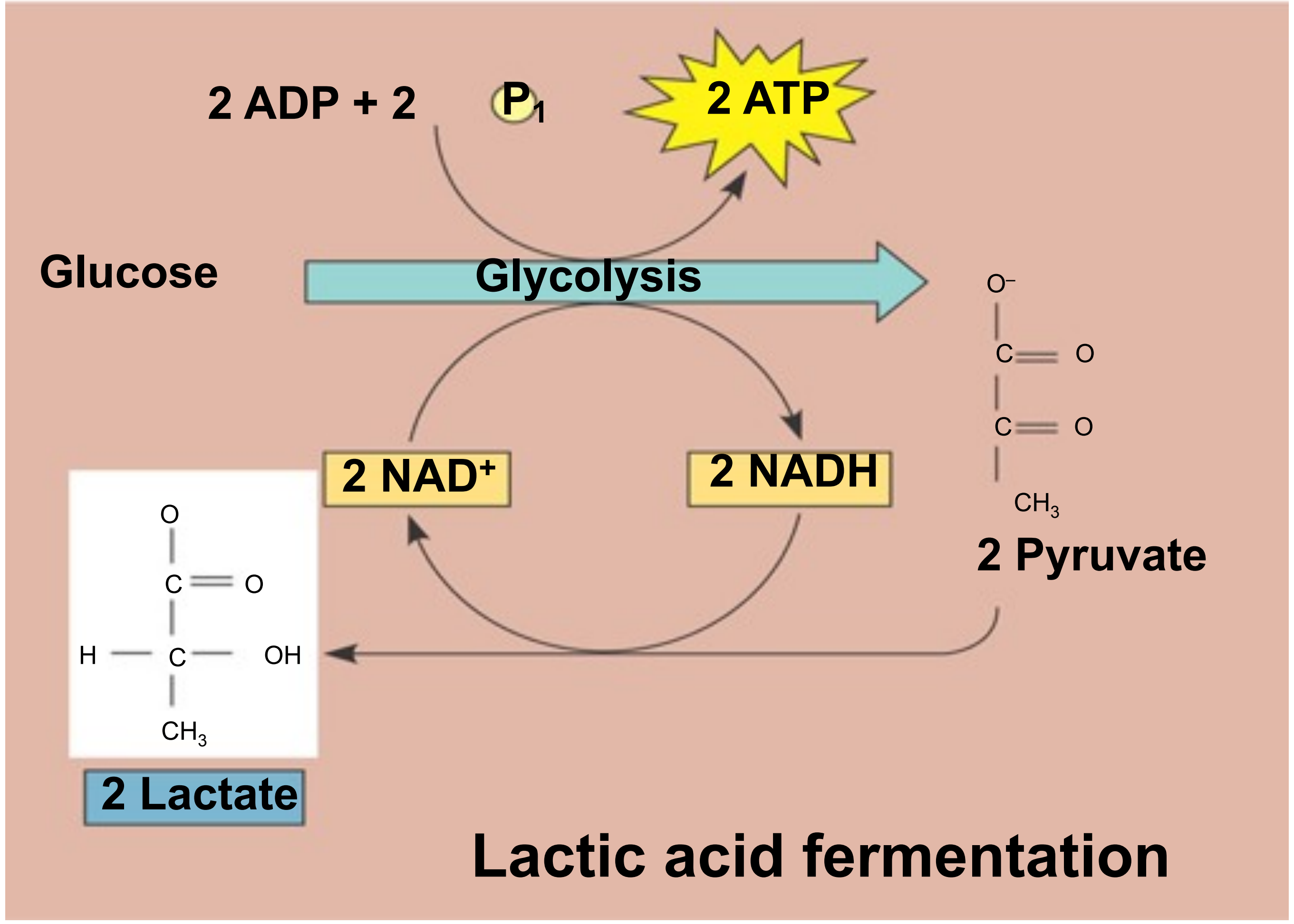
Two Types of Fermentation

Many bacteria and yeasts use this alcohol fermentation in anaerobic conditions, they are used in brewing and baking



Bacteria and fungi that use this lactic fermentation are used in the dairy industry to make cheeses and yogurts

also used by muscle cells but will discuss later



A Summary & Comparisons

- 3 Ways to make ATP
  - Fermentation
  - Anaerobic Respiration
  - Aerobic Respiration

- **Similarities**
  - **All harvest chemical energy from "food"**
  - **All use glycolysis**
  - **All make 2 ATP, via substrate level phosphorylation**
  - **All use NAD^+ as their oxidizing agent**

A Summary & Comparisons

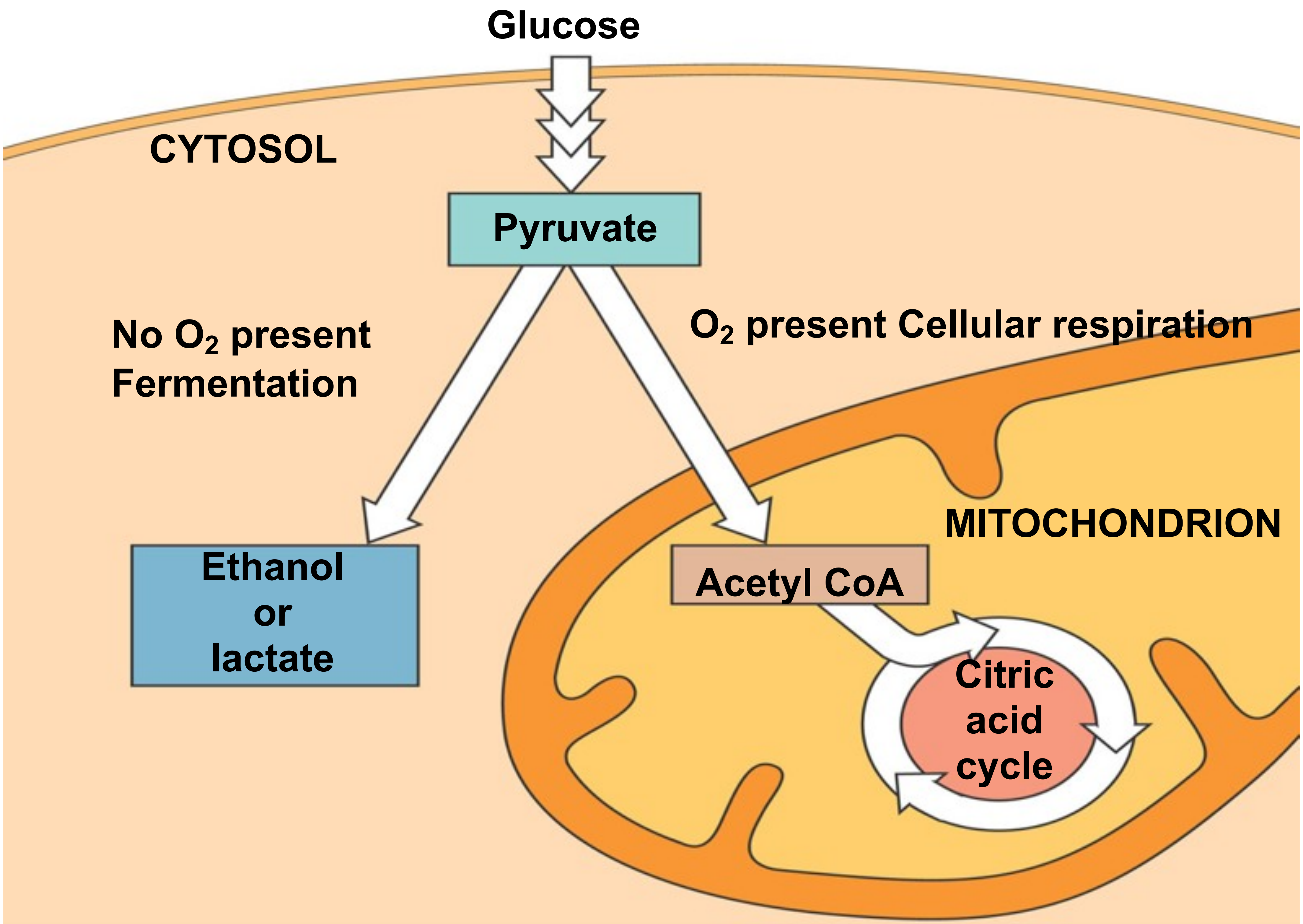
- **<u>Differences</u>**
  - **Mechanism that converts NADH back to NAD^+**
    - Fermentation: electrons passed to organic compound either pyruvate or acetylaldehyde
    - Anaerobic Respiration: electrons passed to E.T.C. and then to electronegative inorganic molecule (H_2S)
    - Aerobic Respiration: electrons passed to E.T.C. and then to electronegative inorganic molecule (O_2)

Diversity in ATP Production

- **Obligate Anaerobes**- organisms/cells use only fermentation or anaerobic respiration
  - ex. clostridium bacteria
- **Obligate Aerobes**- organisms/cells use only aerobic oxidation
  - ex. brain cells
- **Facultative Anaerobes**- organisms/cells use either fermentation or aerobic respiration
  - ex. yeasts

Diversity in ATP Production

- Muscle cells act like **Facultative Anaerobes**



The Evolution of Glycolysis

- Glycolysis is likely the most ancient and most common way to produce ATP.
  - The cytosolic location implies antiquity
  - The fact that no oxygen is required implies antiquity
  - The fact that no membrane is required also implies antiquity
  - And finally that the fact that it is found in virtually every cell also implies antiquity

Cell Respiration

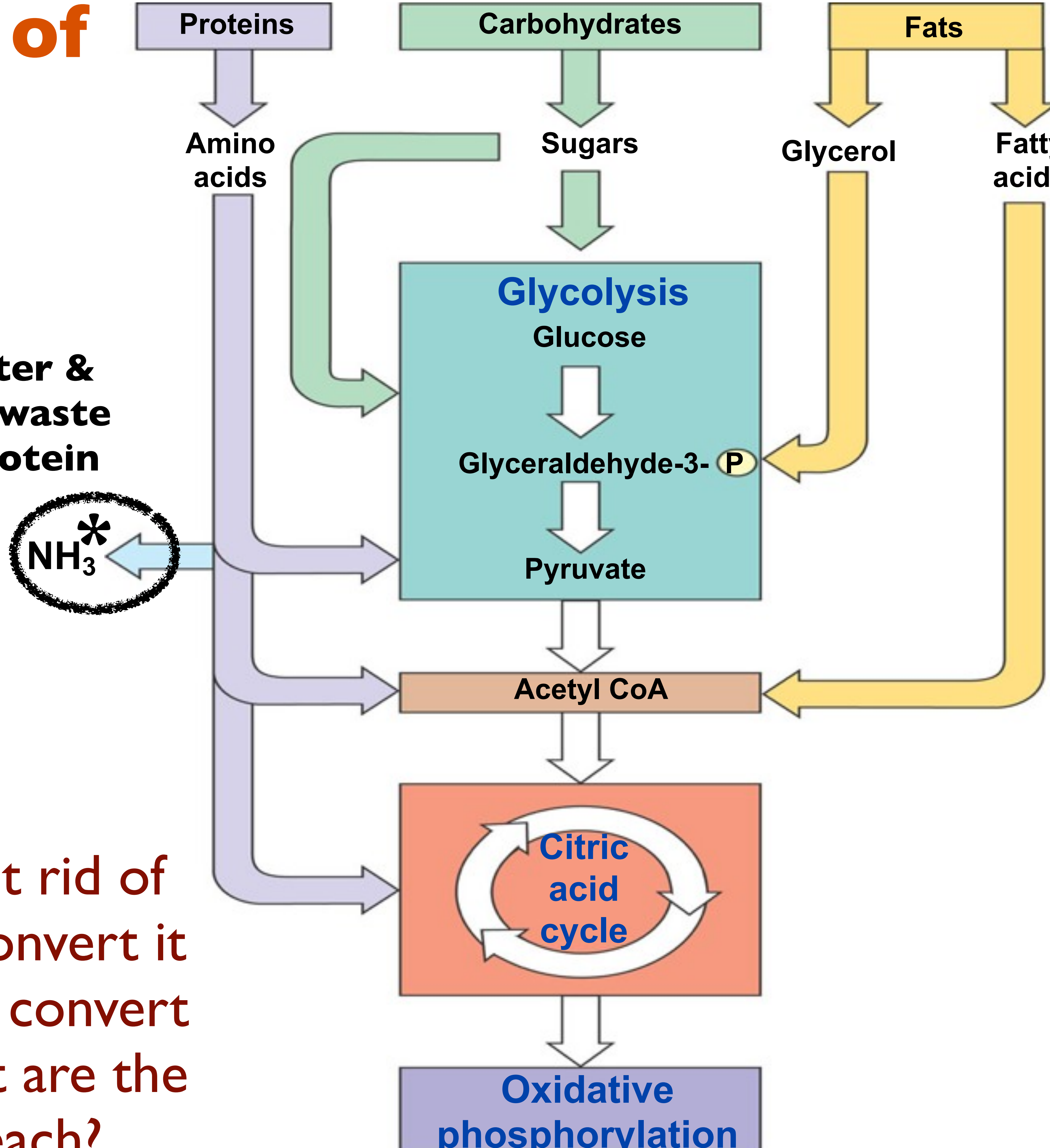
VI.

Main Idea: Metabolic Pathways are diverse and those discussed (glycolysis and the citric acid cycle) are simply intersections for many more catabolic and anabolic pathways.

Versatility of Catabolic Pathways

- Glucose is the standard fuel used when teaching/learning about cellular respiration. Free glucose is however not common in most diets.
- Cells use a variety of other "food fuels" such as fats, proteins and other types of sugars.
- When these other fuels are used they are oxidized into smaller subunits which are then fed into the metabolic pathways of cell respiration at various points along the path.

Versatility of Catabolic Pathways



* Recall in C.C. Water & Waste, Ammonia waste produced from protein catabolism!

Which animals get rid of ammonia, which convert it to uric acid, which convert to uric acid.? What are the trade offs for each?

Versatility of Catabolic Pathways

- Sugars are most commonly used, they are the first fuel of choice by most cells.
- Fats actually have 2X more potential energy per gram than sugars.
  - This makes fats an excellent choice for a storage fuel.
- Proteins can also be used by cells to generate ATP, but this is the cells last choice.
  - Most amino acids are needed for building blocks, not fuel.
  - Furthermore the catabolism of amino acids produces a very toxic by product in ammonia

Versatility of Anabolic Pathways

- Metabolism is both versatile and adaptable.
- Not all food is used for ATP production, cells need the molecules from food to build, grow and repair as well.
  - Intermediates from the citric acid cycle can be used to generate half of all 20 amino acids.
  - Intermediates from glycolysis can be used to generate fats (stored energy for later) when fuel is abundant.
    - This is why eating to much sugar can make you fat.

Whether these food molecules are used for energy or building blocks, the implication is that cells have the ability to decide. This must mean that they can detect the environment and respond accordingly.

Cell Respiration

VII.

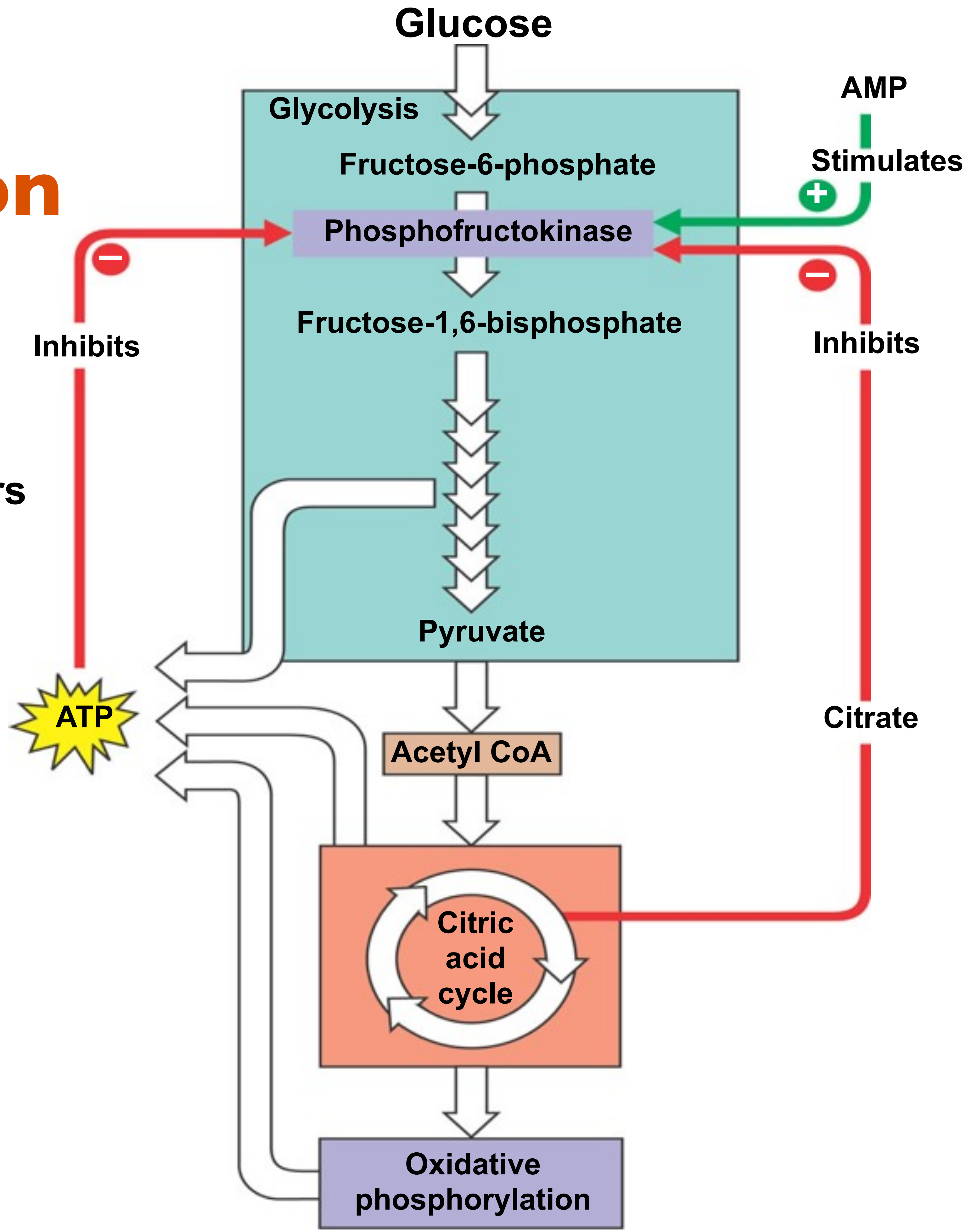
Main Idea: Cells favor efficiency as cellular circumstances change so to must cell respiration.

Regulation of Cell Respiration

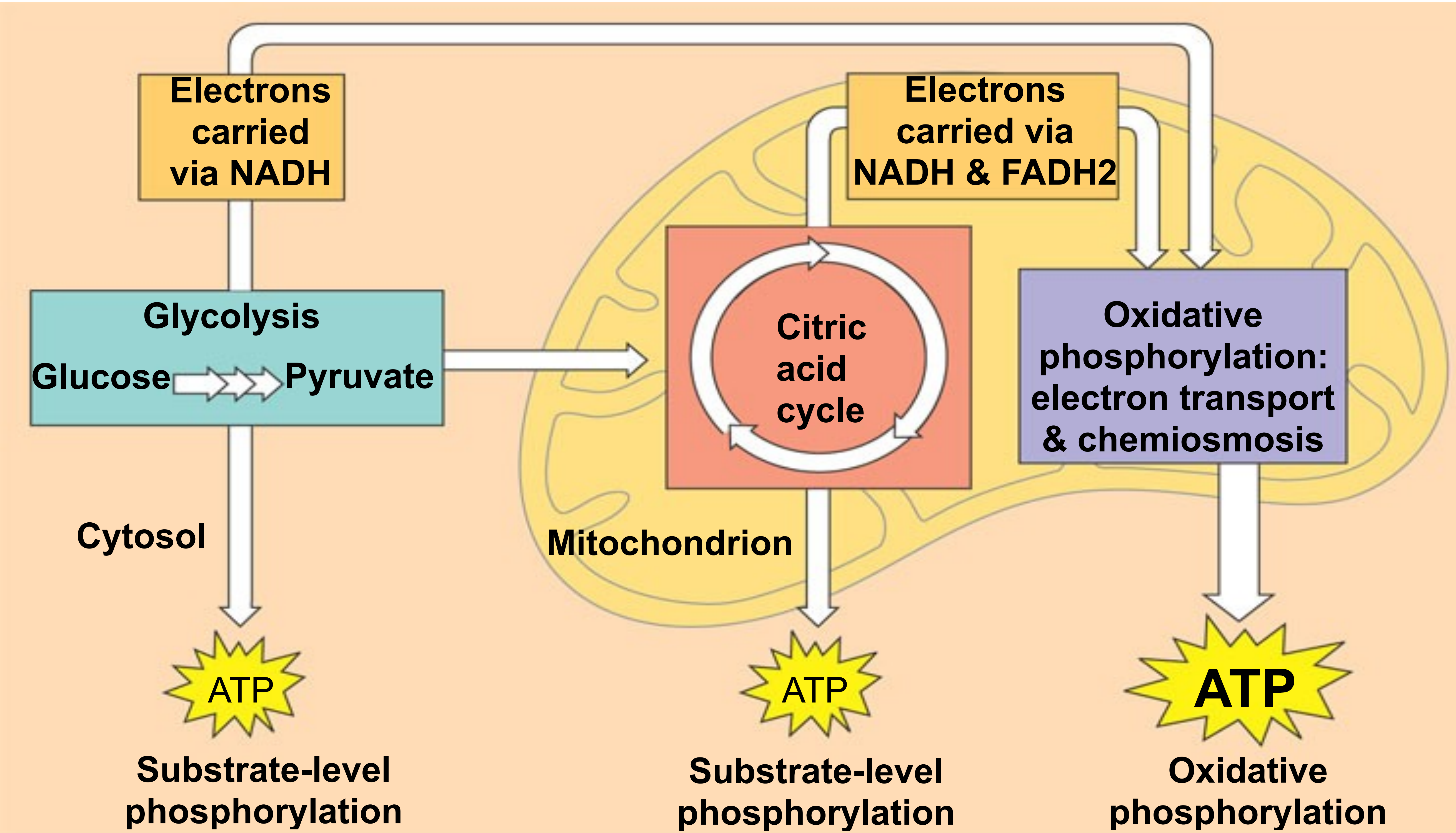
- Supply and Demand regulate metabolic decisions!
- Cells do not want to make more ATP if the demand is not there, likewise it would not want make a particular amino acid if it was already abundant.
- Bottom line cells have adapted mechanisms that allow them to stop, start and divert chemical reactions in metabolic pathways and cycles according to the need.
- The most common mechanism for doing this is **negative feedback inhibition**.
- Cells are thrifty, expedient and responsive.

Regulation of Cell Respiration

Phosphofructokinase is an allosteric enzyme. It has two receptor sites, one for inhibitors and the other for activators.



An Overview of Cellular Respiration



Ecological viewpoint of Cellular Respiration

- Remember Cell Respiration does not make energy it simply releases the energy stored in molecules.
- The SUN is ultimate source of energy!