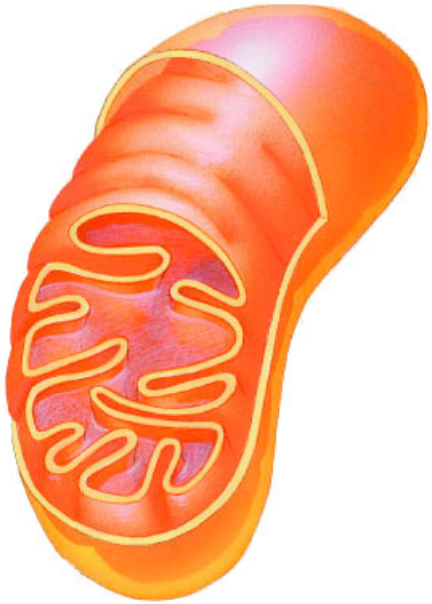
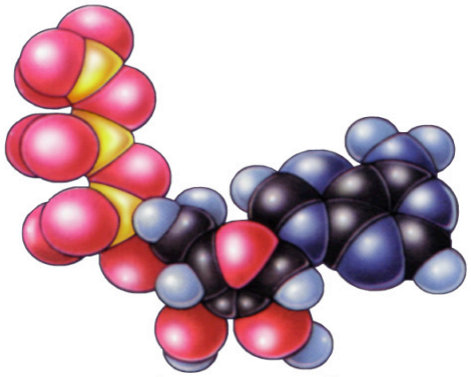
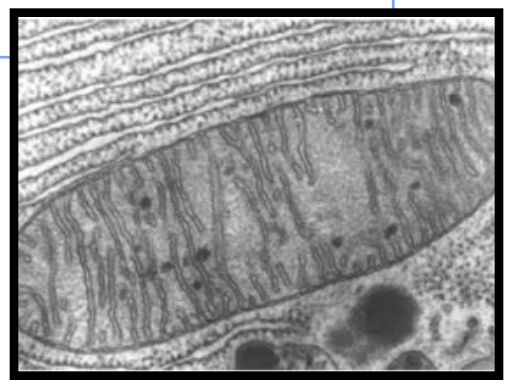


Aerobic Cellular Respiration

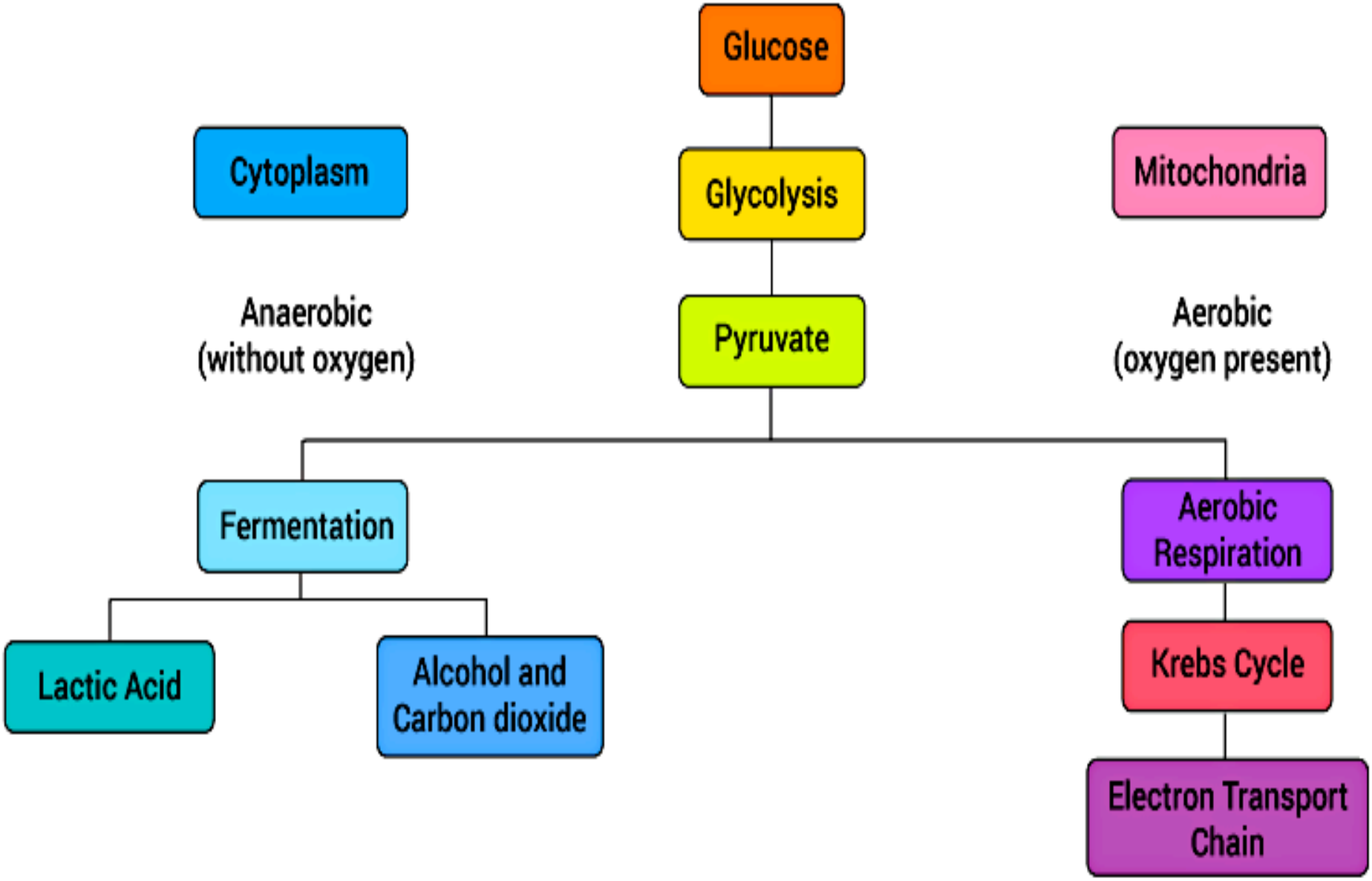
Stage * & 2:

Oxidation of Pyruvate & Citric Acid (Krebs) Cycle



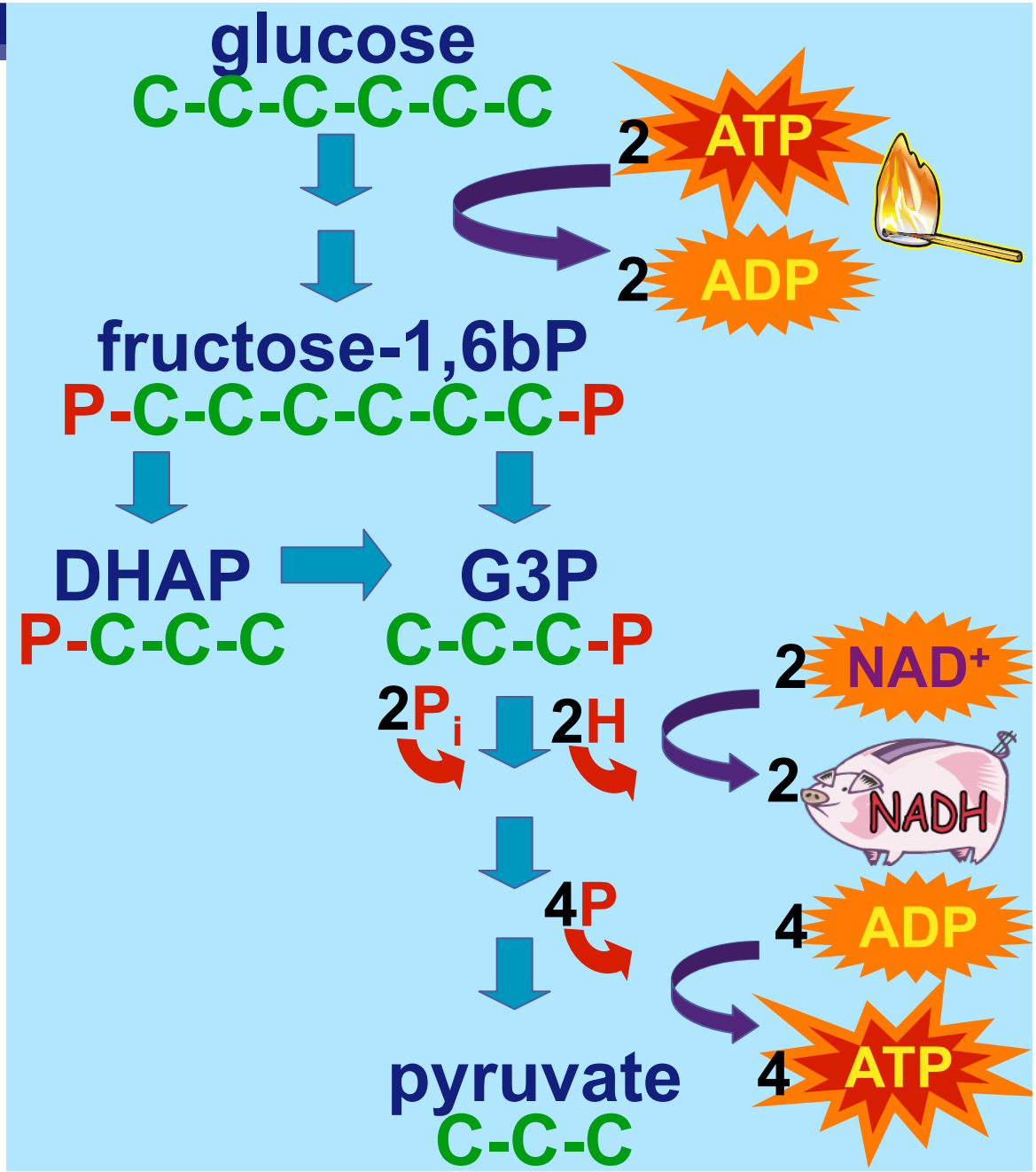


Aerobic Respiration & Fermentation



Summary of Glycolysis

- glucose (6C) converted into 2 pyruvate (3C)
- Final net products: 2 ATP *(source of potential energy)* & 2 NADH *(carrying 4 high energy electrons)*
  - produces: 4 ATP & 2 NADH
  - consumes: 2 ATP



$$Glucose + 2ATP + 2NAD^+ + 4ADP + 2P_i \rightarrow Pyruvate + 4ATP + 2NADH + 2H^+$$

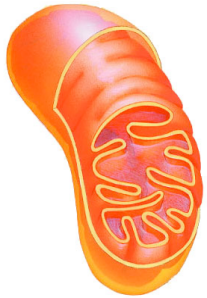
Glycolysis is only the start

- Glycolysis

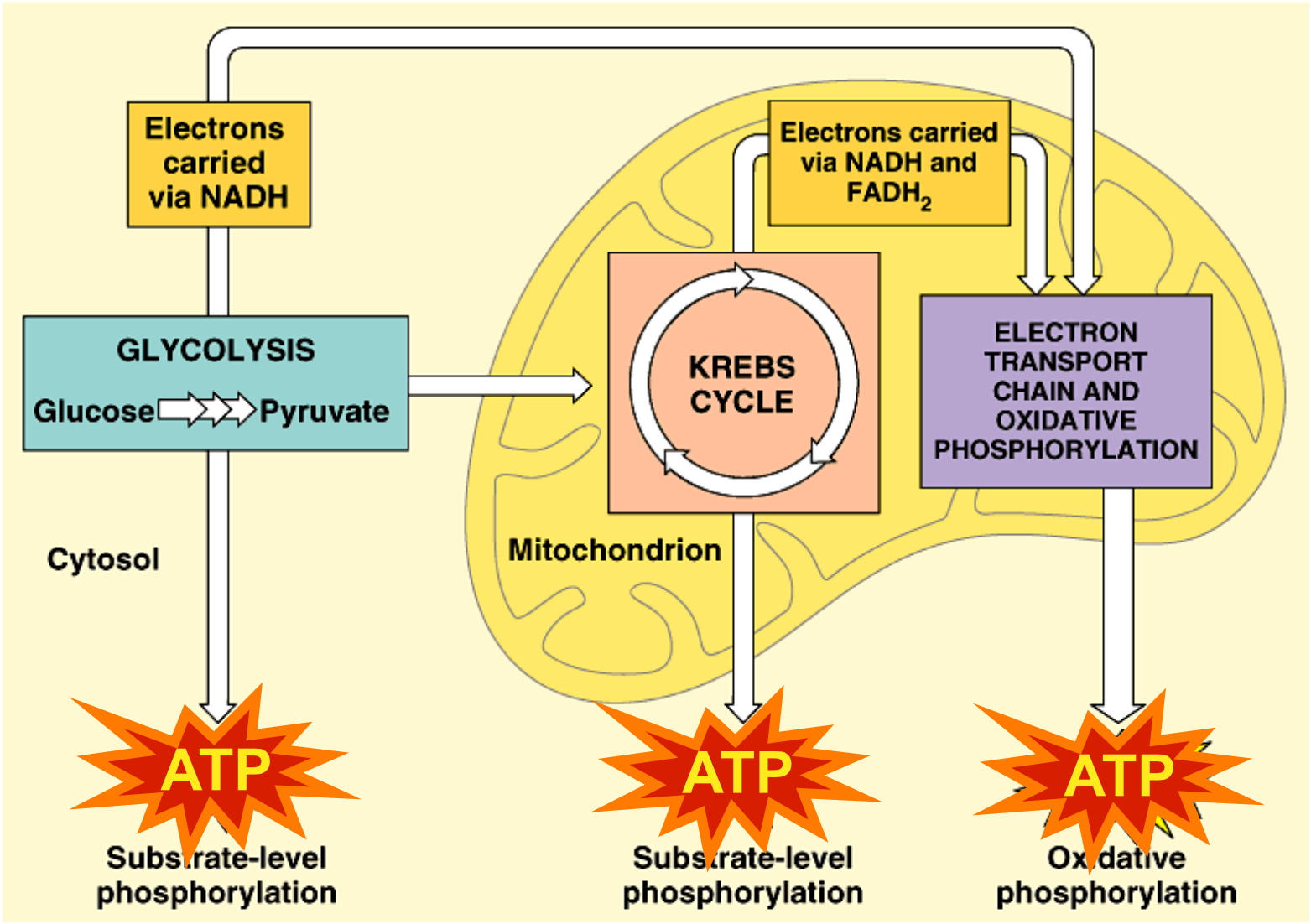
glucose → → → → → pyruvate
6C 2x 3C

- Pyruvate STILL has more ENERGY stored in its bonds!!!
  - 3 more C to strip high energy electrons & energy from (to oxidize)
  - In eukaryotes, if O_2 is available, pyruvate enters MITOCHONDRIA where enzymes of Citric Acid Cycle complete the full oxidation of sugar to CO_2
  - In prokaryotes, full oxidation of pyruvate will occur in the cytoplasm

pyruvate → → → → → → 2 CO_2
3C 1C



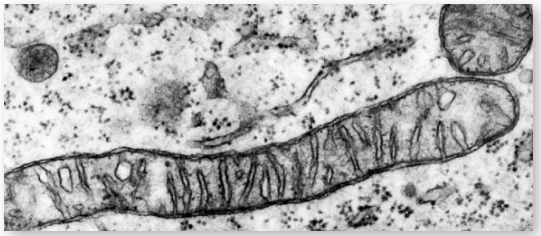
Aerobic Cellular respiration



Mitochondria — Structure

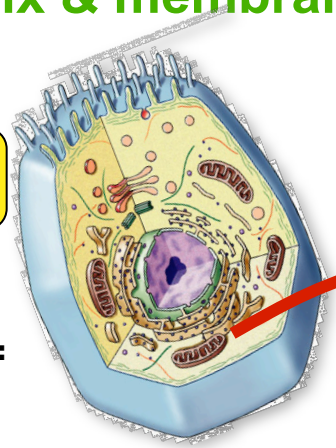
Double-membraned, energy-harvesting organelle

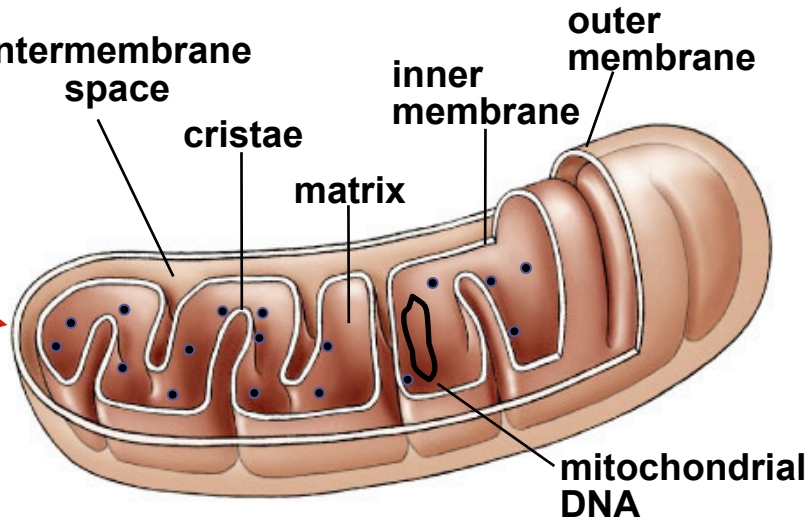
- smooth outer membrane
- highly folded inner membrane
  - Forms folds known as cristae
- intermembrane space
  - fluid-filled space between membranes
- matrix
  - inner fluid-filled space
- Mitochondria have own circular DNA & ribosomes (which look similar to prokaryotic ribosomes in size)
- enzymes
  - free in matrix & membrane-bound



Which cells would have a lot of mitochondria?

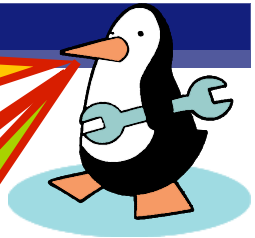
- # correlated with aerobic metabolic activity: More activity = more energy needed = more mitochondria



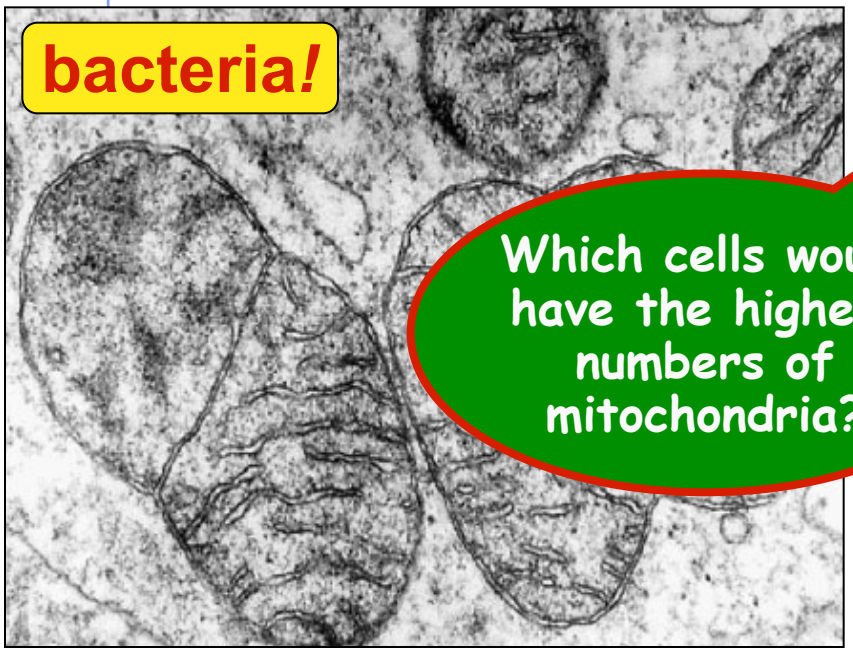


Mitochondria – Function

Ooooh! Form fits function!



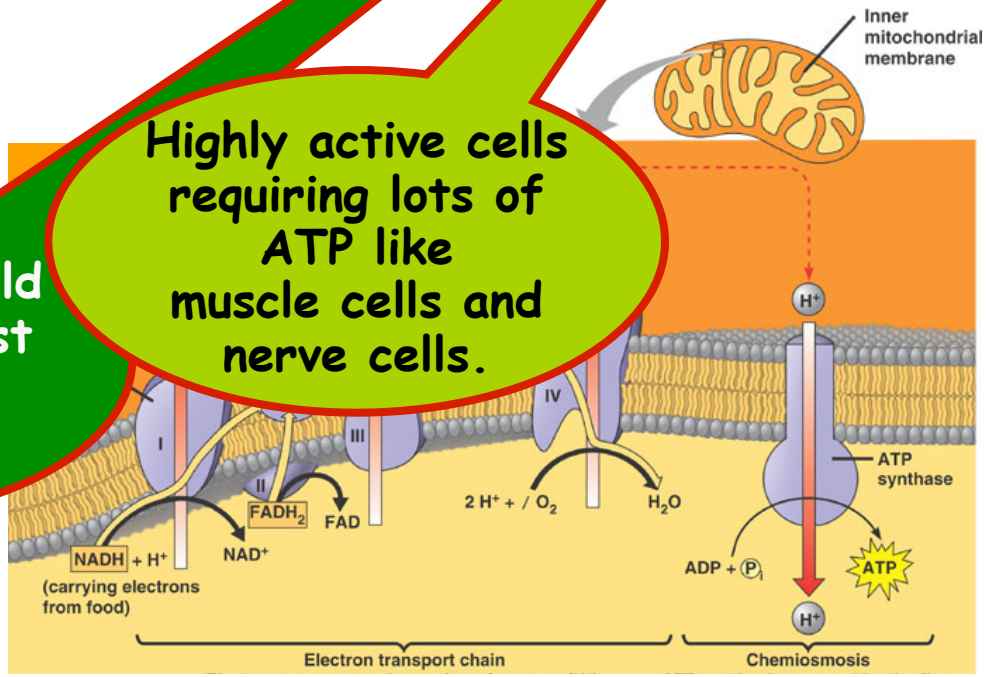
Mitochondria Divide Independently:
Who else divides like that?



Which cells would have the highest numbers of mitochondria?

Membrane-bound proteins:
Enzymes & transferases

Highly active cells requiring lots of ATP like muscle cells and nerve cells.

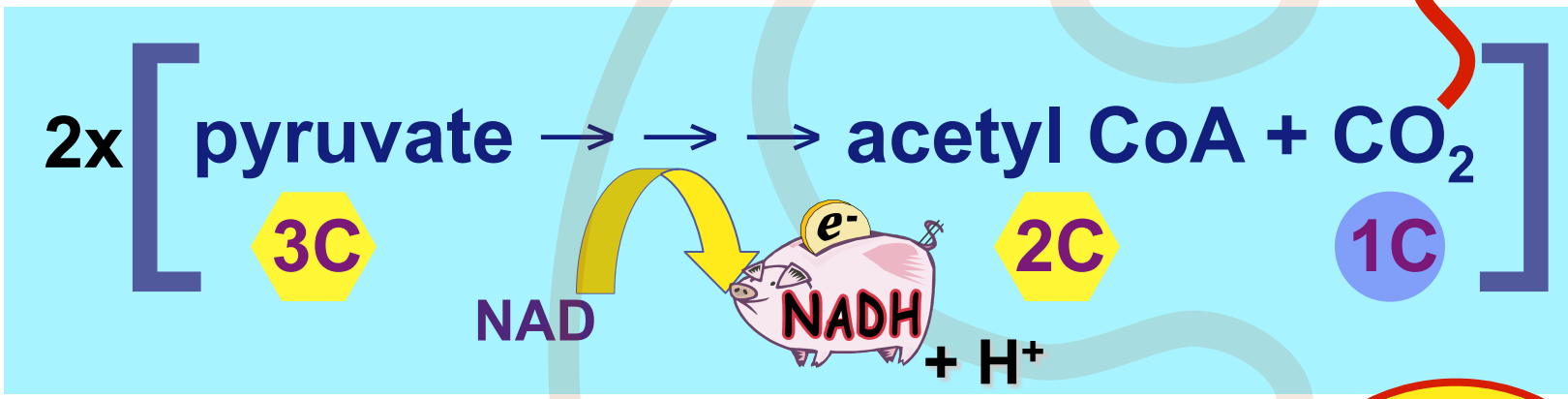


What does this tell us about the evolution of eukaryotes?
Endosymbiosis!

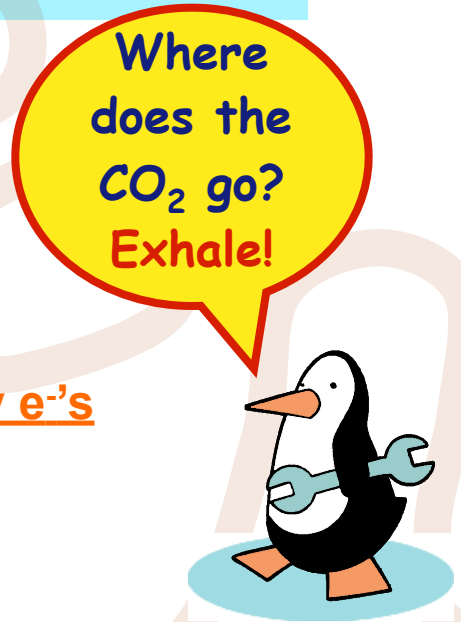
Advantage of highly folded inner membrane?
More surface area for membrane-bound enzymes & proteins that extract energy from high energy electrons.

Oxidation of pyruvate

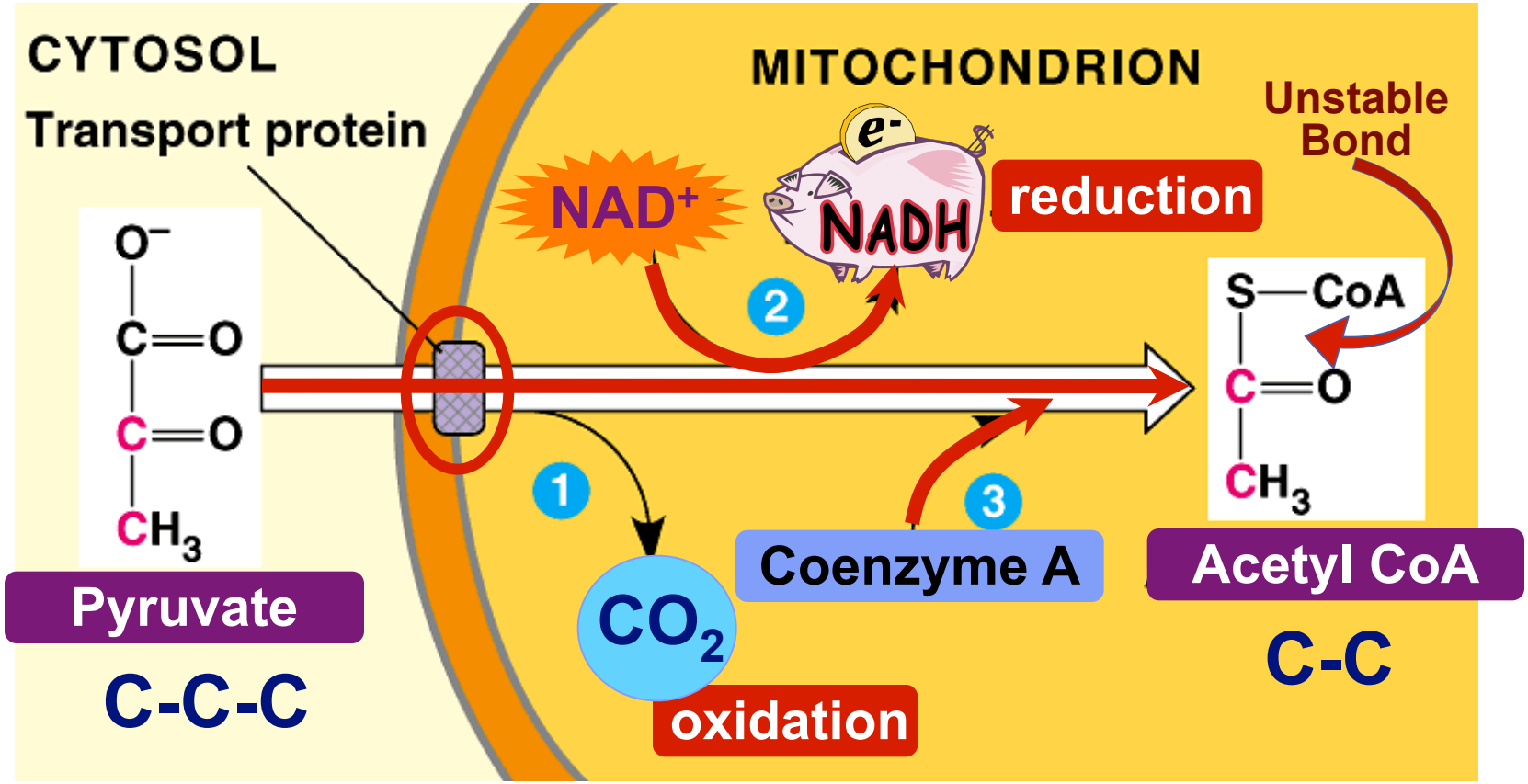
- Pyruvate enters mitochondrial matrix



  - 3 step oxidation process
  - Per GLUCOSE MOLECULE (2 pyruvates):
    - releases 2 CO_2 (count the carbons!)
      - CO_2 = Fully oxidized carbon
    - reduces 2 NAD → 2 NADH (moves high energy e-'s onto two more electron carriers)
    - produces 2 acetyl CoA
- Acetyl CoA enters Krebs cycle



Pyruvate oxidized to Acetyl CoA



2 x [Yield = 2C sugar + NADH (+ H^+) + CO_2]

Krebs cycle

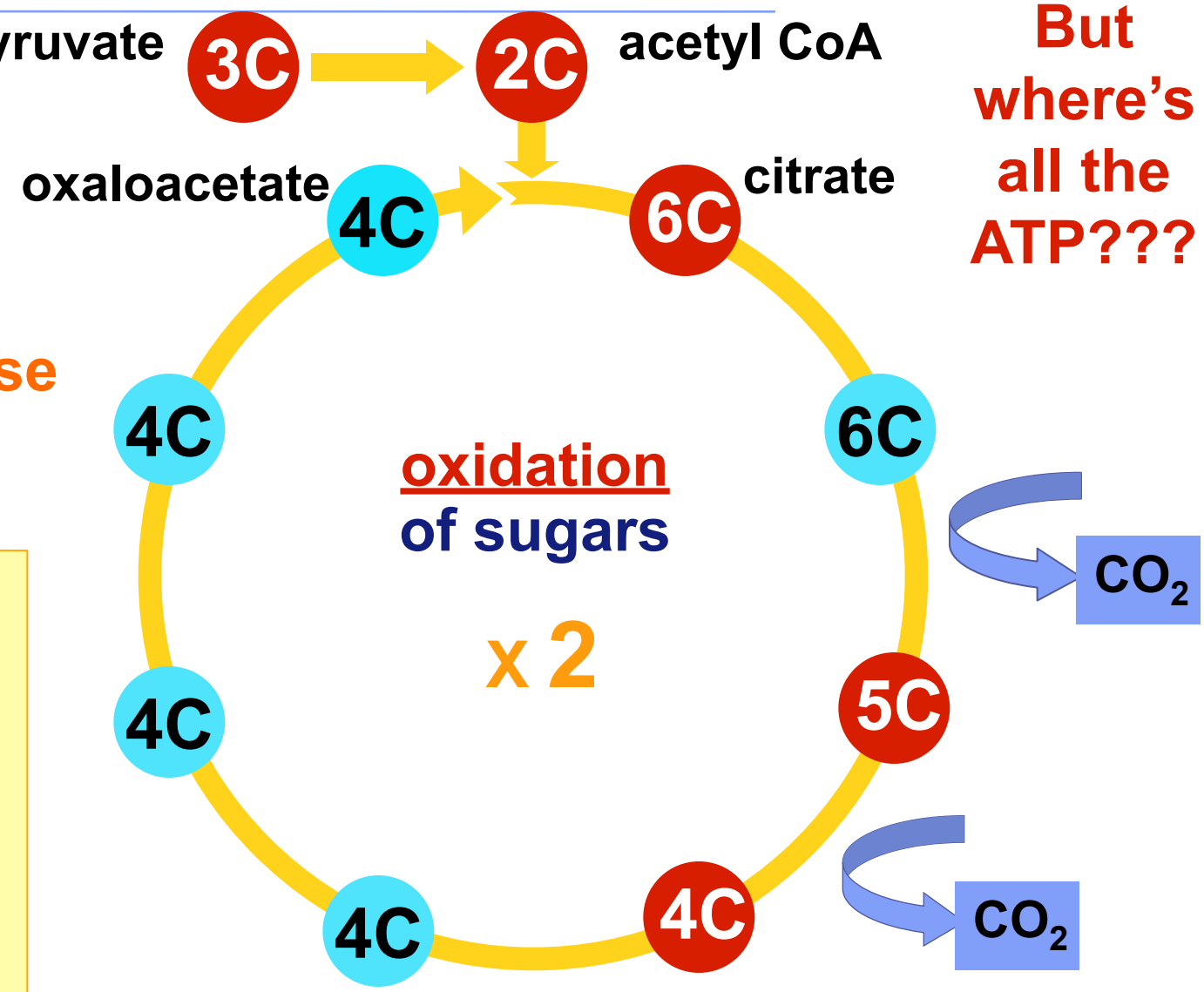
1937 | 1953

Hans Krebs
1900-1981

- **A.k.a. Citric Acid Cycle**
  - **Occurs in mitochondrial matrix**
  - **8 step pathway**
    - **each catalyzed by specific enzyme**
    - **step-wise catabolism of 6C citrate molecule**
- **Evolved after than glycolysis!!!**
  - **does that make evolutionary sense?**
    - **anaerobic bacteria →3.5 billion years ago (glycolysis & fermentation)**
    - **free O_2 → 2.7 billion years ago (cyanobacteria release oxygen via photosynthesis)**
    - **aerobic bacteria → 2.5 billion years (aerobic respiration, using molecular oxygen, O_2)**
    - **aerobic eukaryotes → by 2 billion years ago (aerobic respiration = organelles → mitochondria)**

Citric Acid Cycle: Count the carbons!

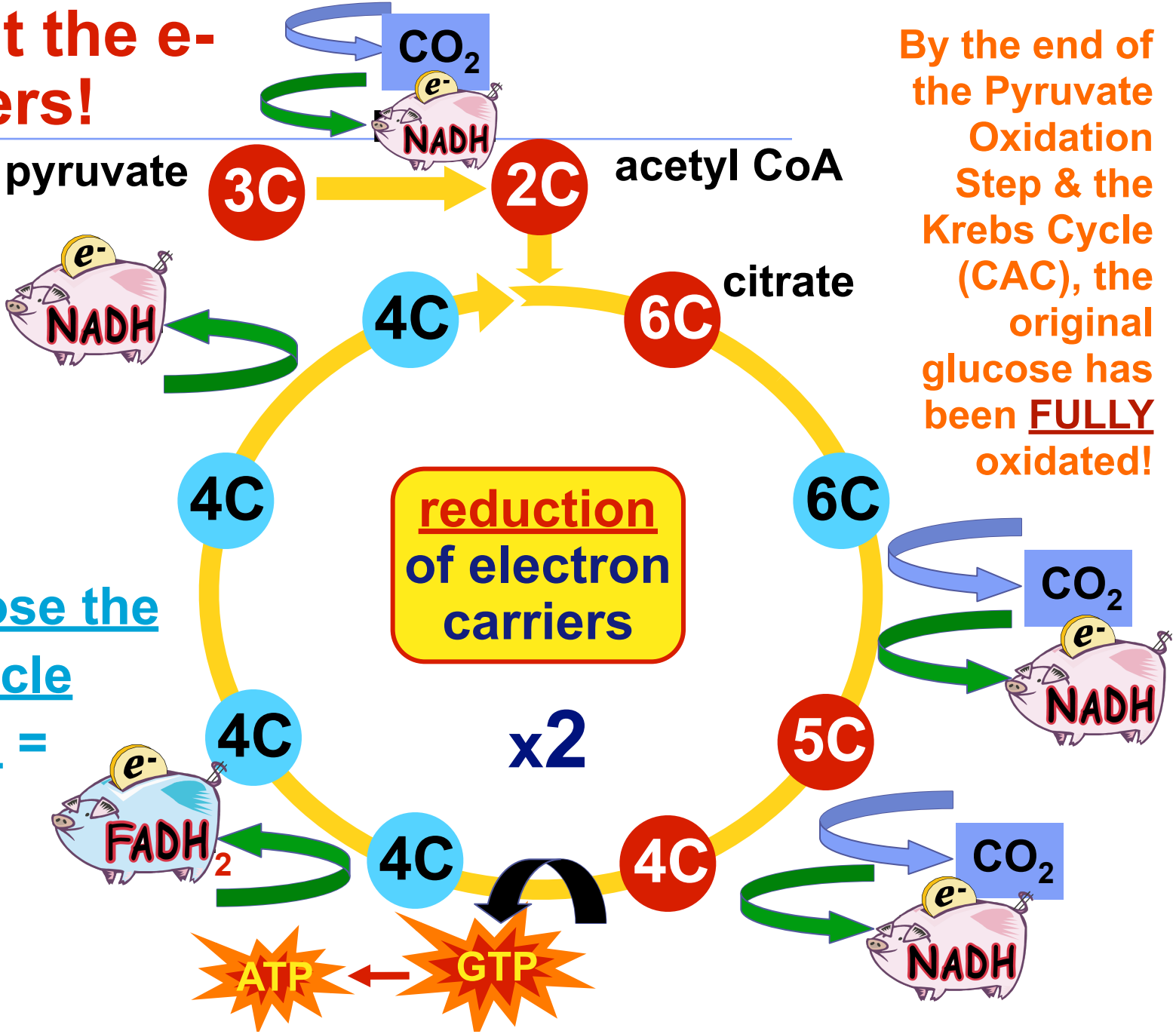
The C.A.C. or Krebs Cycle happens <u>twice</u> for each glucose molecule



But where's all the ATP???

2C compound goes in and two CO_2 molecules were produced. Glucose has now been fully oxidized!

Count the e- carriers!



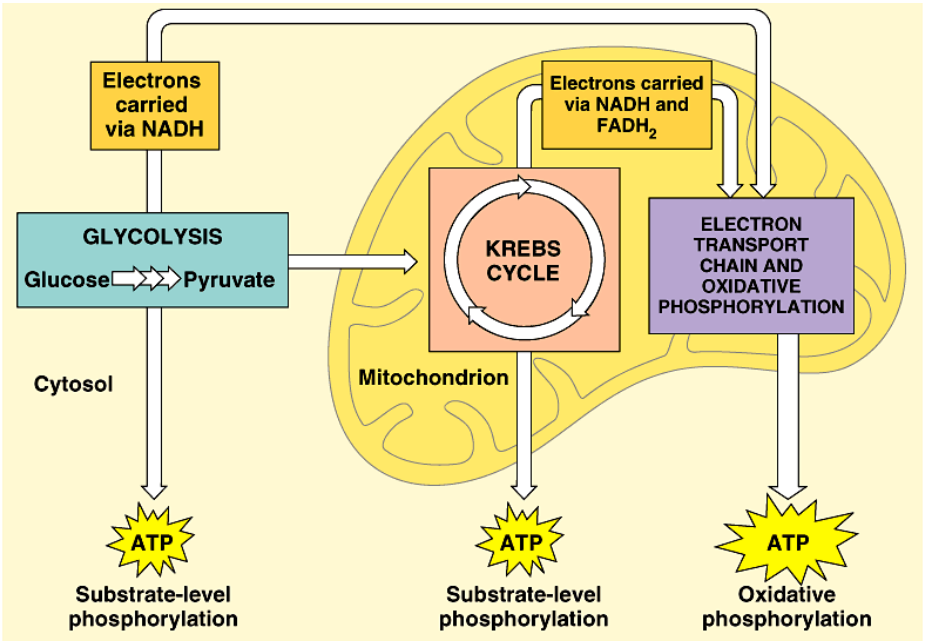
By the end of the Pyruvate Oxidation Step & the Krebs Cycle (CAC), the original glucose has been FULLY oxidated!

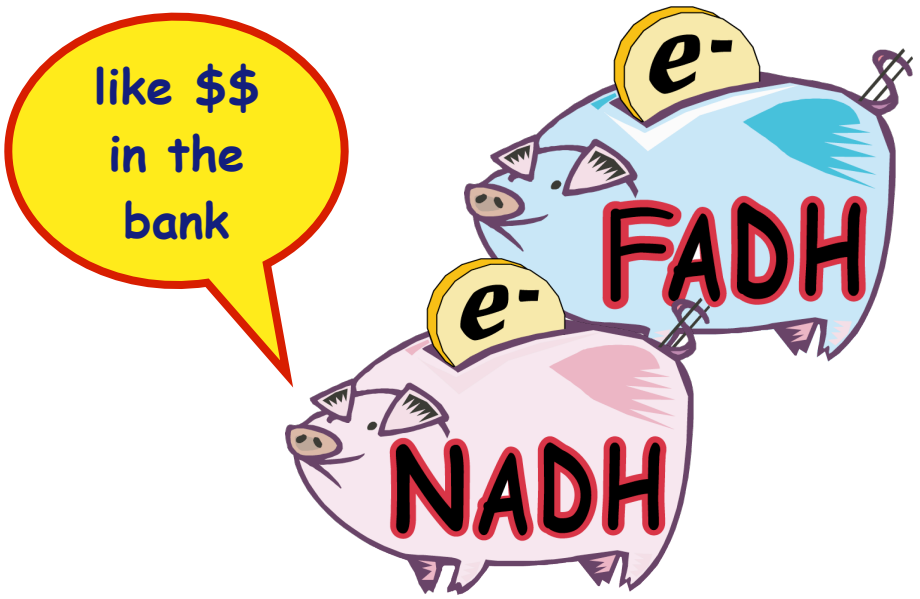
Per glucose the Krebs Cycle results in =

- 6 NADH +
- 2 $FADH_2$
- 4 CO_2
- 2 ATP

Value of Krebs cycle?

- If the yield is only 2 ATP then how was the Krebs cycle an adaptation?
  - Produces valuable reduced electron carriers: NADH & $FADH_2$
    - reduced carriers carry high energy-electrons that will be used in the Electron Transport Chain



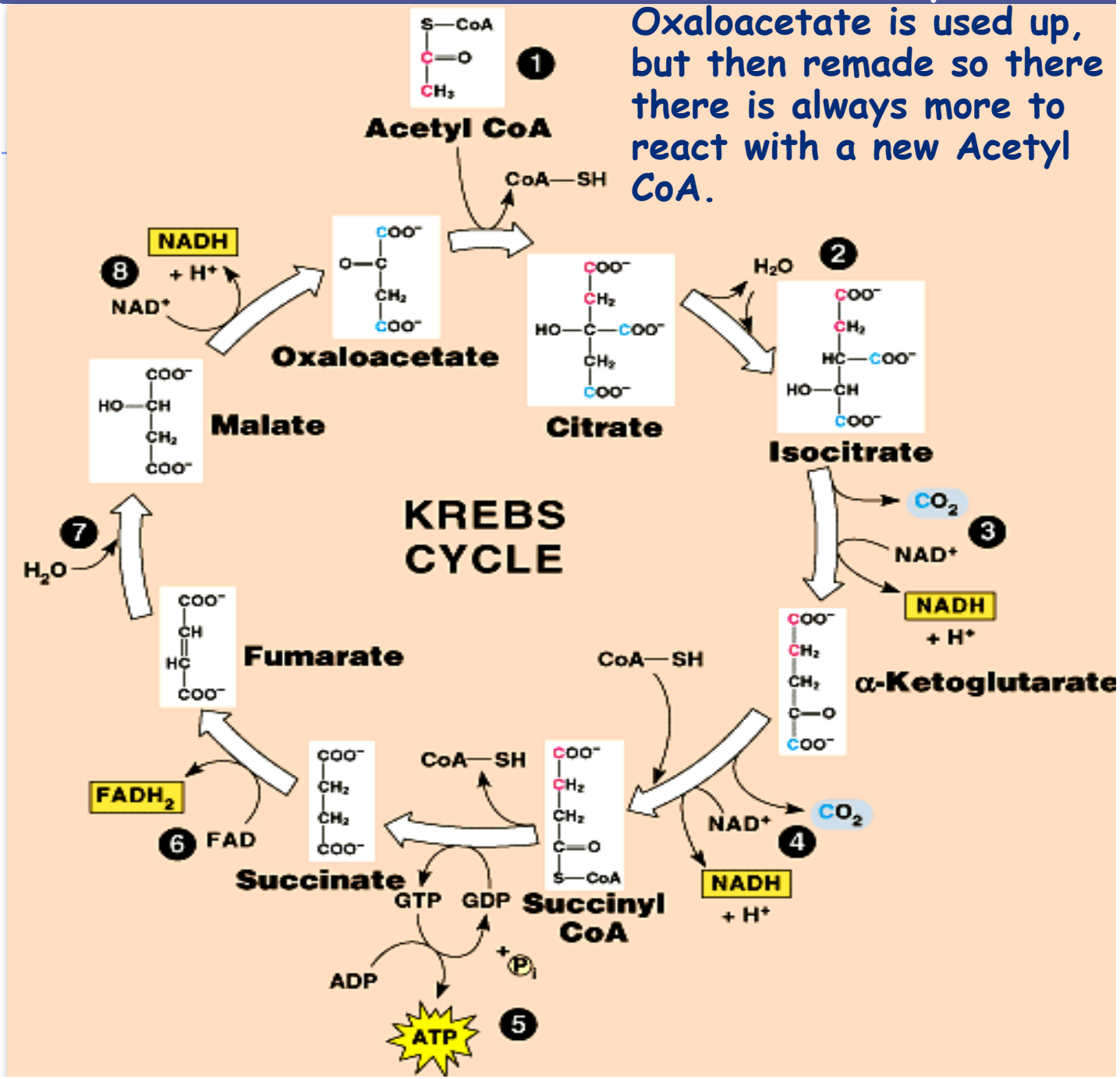


Glycolysis started with a 6-carbon, high-energy-containing glucose.

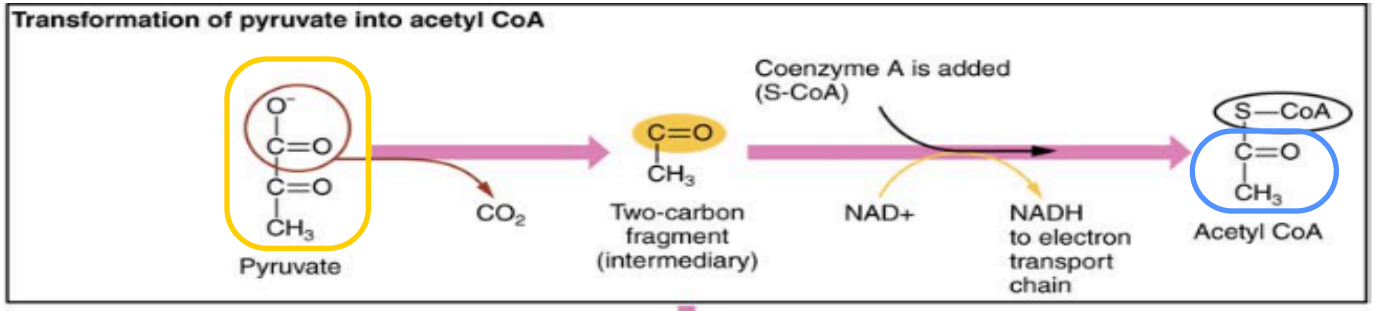
By the end of the Pyruvate Oxidation Step & the Krebs Cycle (CAC), 6 carbons have been lost as CO_2!

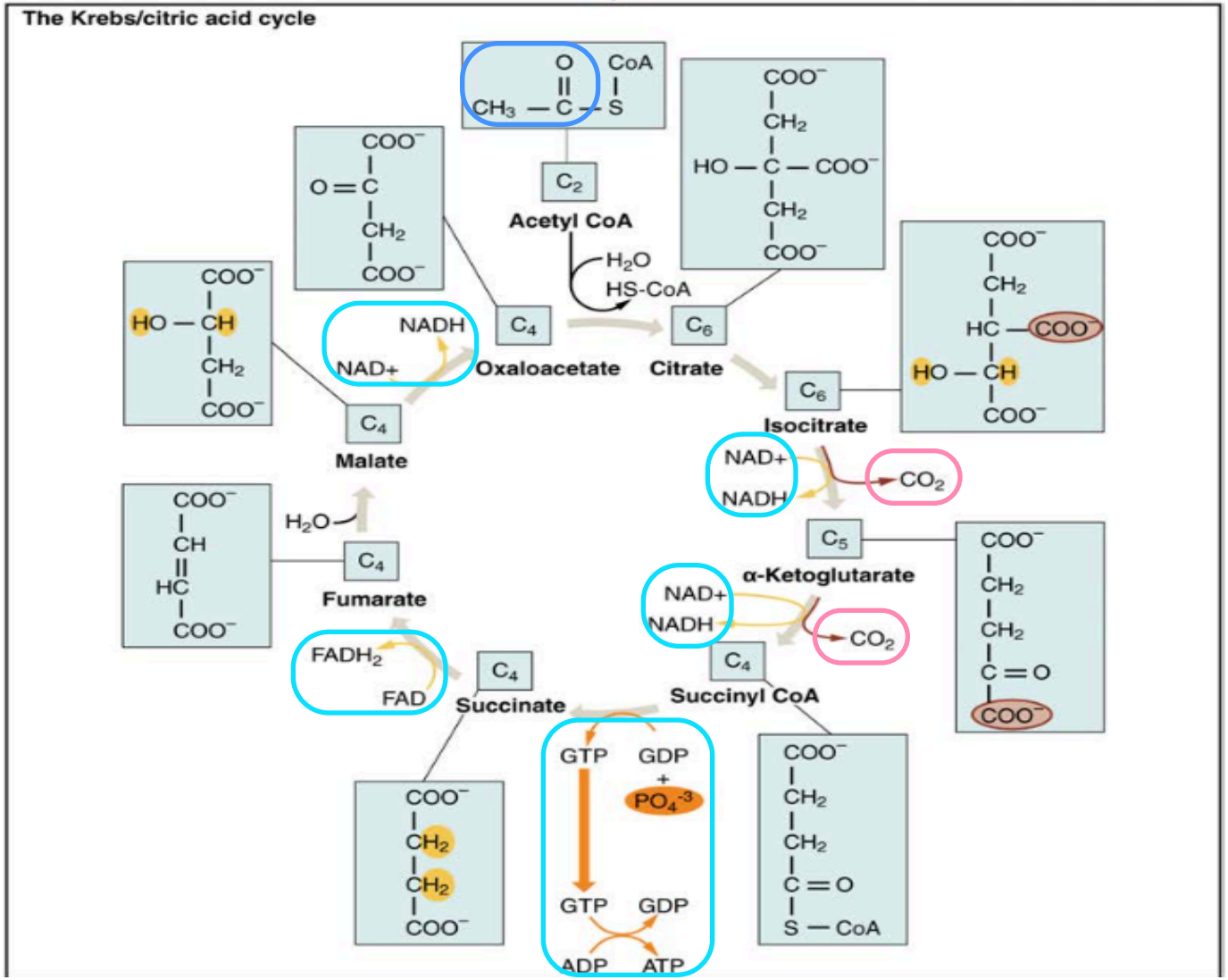
Also, 4 ATPs have been made and numerous high-energy electrons have been collected on electron carriers.

Indeed, It's a cycle! Oxaloacetate is used up, but then remade so there there is always more to react with a new Acetyl CoA.

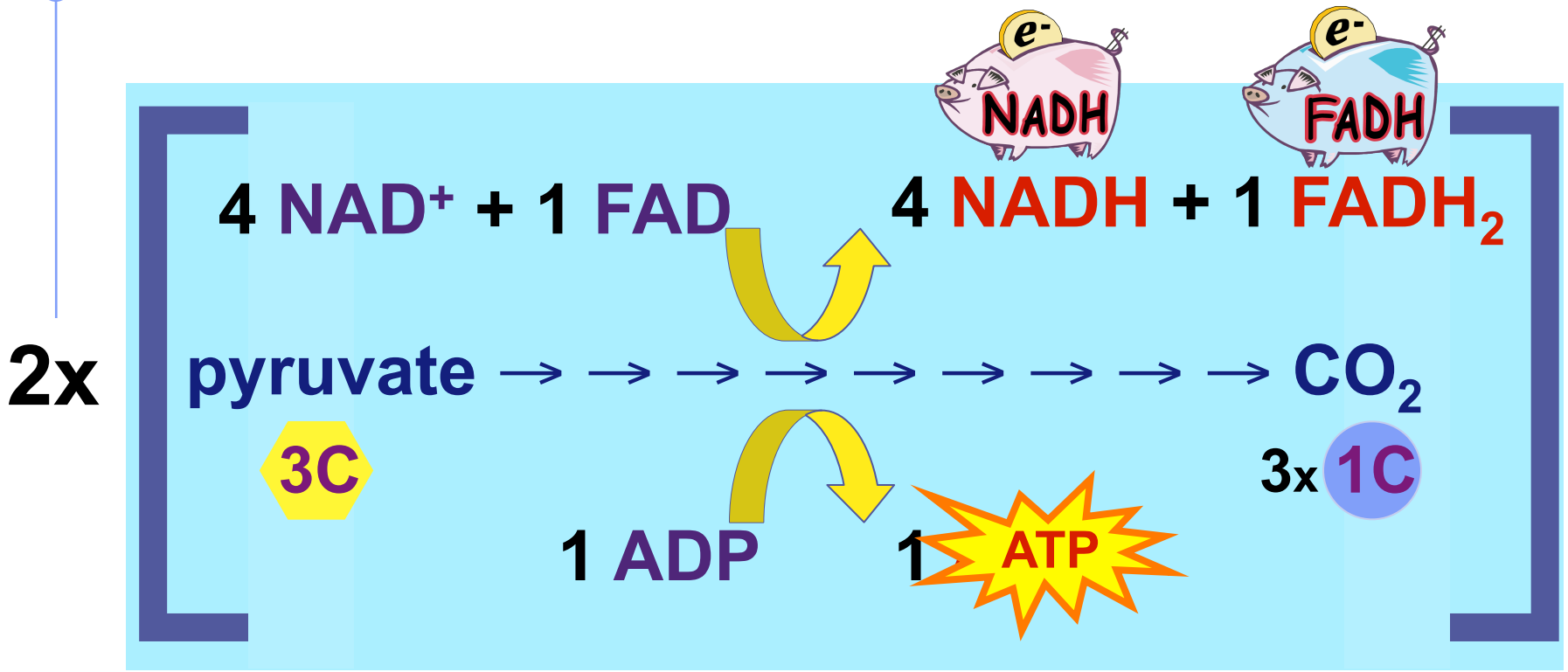


Pyruvate oxidation & Krebs Cycle (C.A.C.) occur in the mitochondrial matrix in eukaryotes.





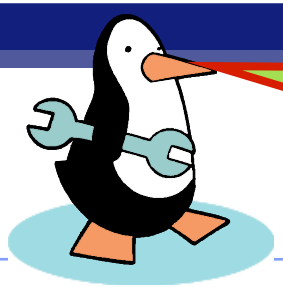
Energy accounting of Pyruvate oxidation & Krebs Cycle combined



Net gain = 2 ATP

= 8 NADH + 2 $FADH_2$ *(all carrying high-energy electrons)*

So far…



What's so important about electron carriers?

So we fully oxidized glucose from glycolysis, through pyruvate oxidation + Krebs Cycle:

$C_6H_{12}O_6$

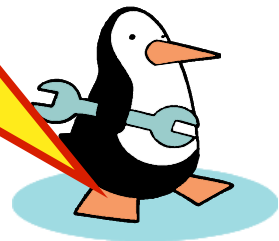
↓

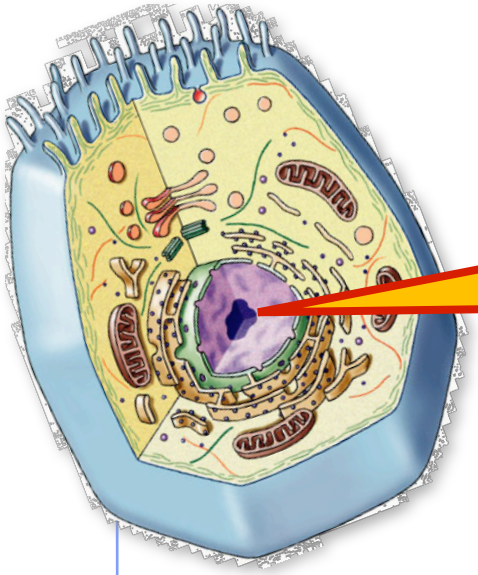
CO_2

Are we done yet?

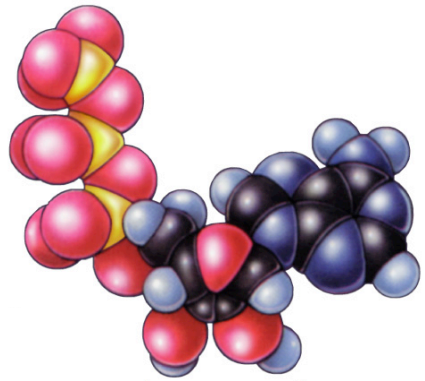
No!
Though we extracted some energy from glucose and used it to make 4ATPs, we can extract more energy from the high-energy electrons collected!

& ended up with 4 ATP (10NADH + 2$FADH_2$)!



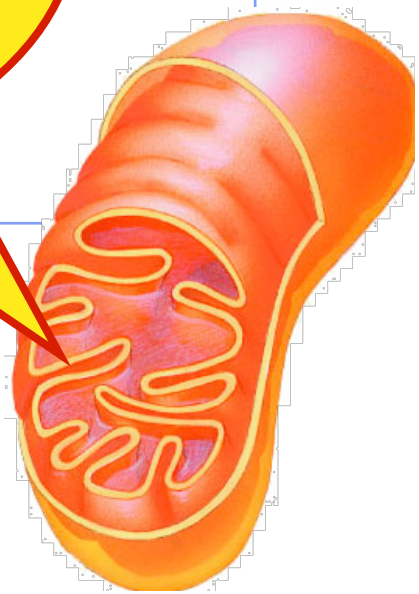


What's the point of this e- transport chain?



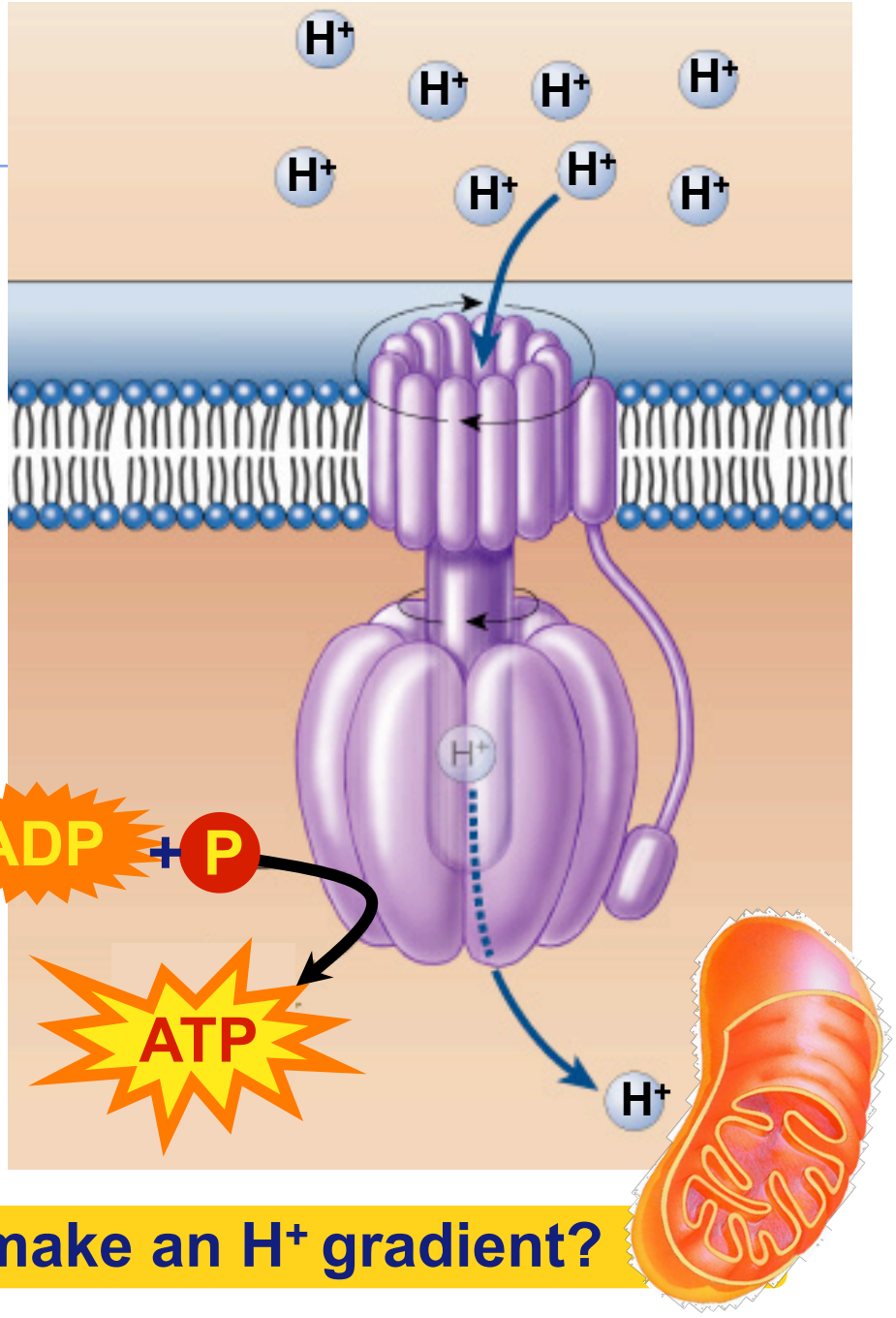
The point is to make some serious ATP!

ATP

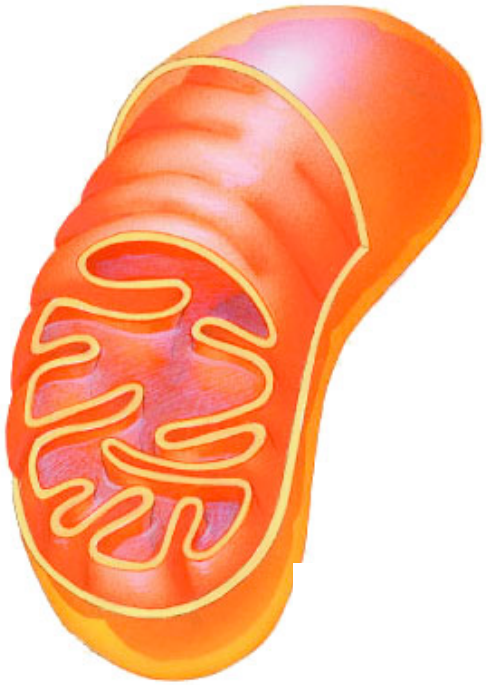


And how do we catalyze ATP Production?

- Use ATP synthase
  - But first we need a H^+ gradient that stores the potential energy *(found in the high-energy electrons taken from glucose)* needed to drive the endergonic reaction of ADP + P_i → ATP
    - Then we allow H+ to flow through ATP synthase
    - This action powers the bonding of Pi to ADP by the enzyme



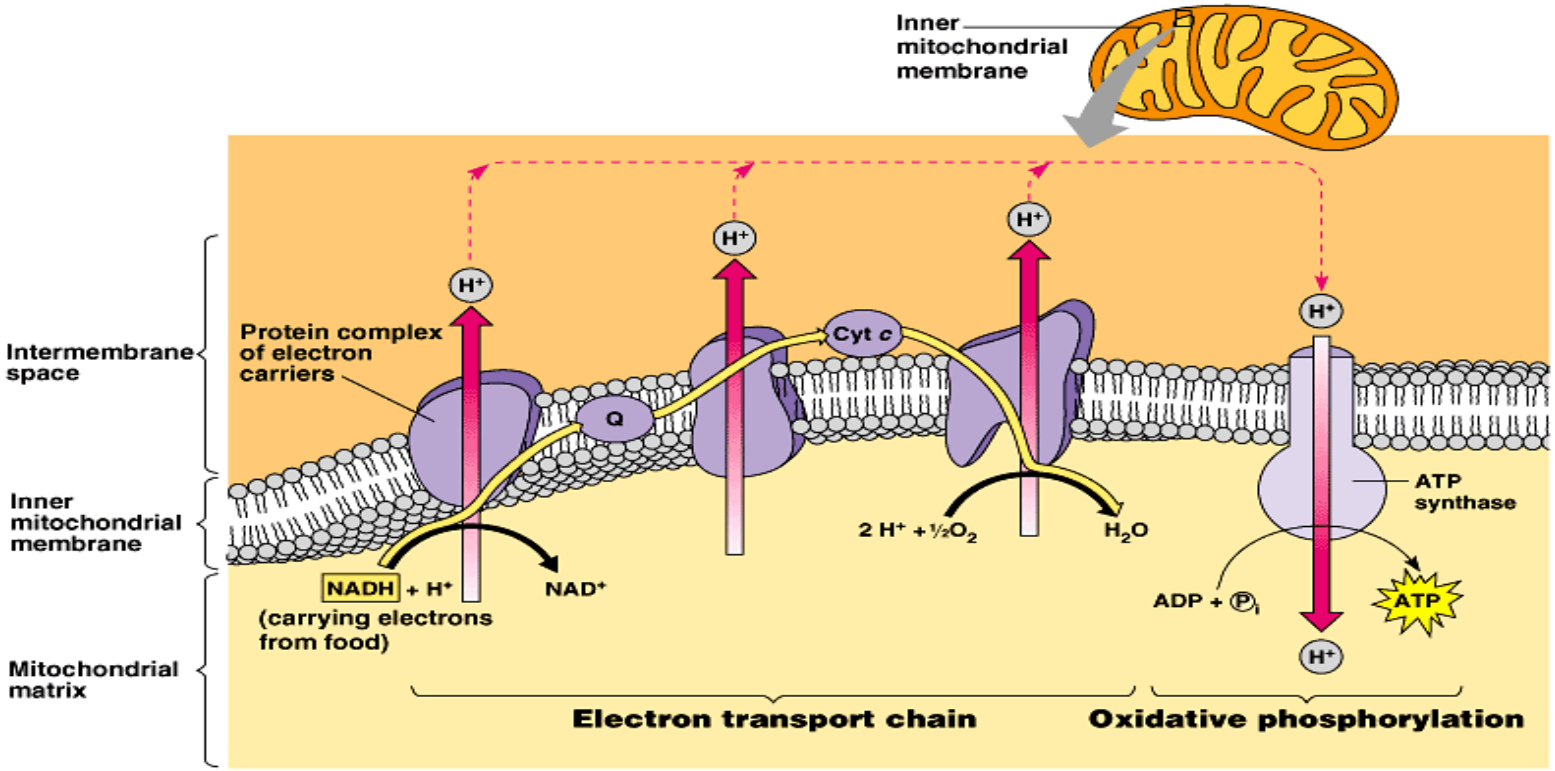
But… How do and why do we make an H^+ gradient?



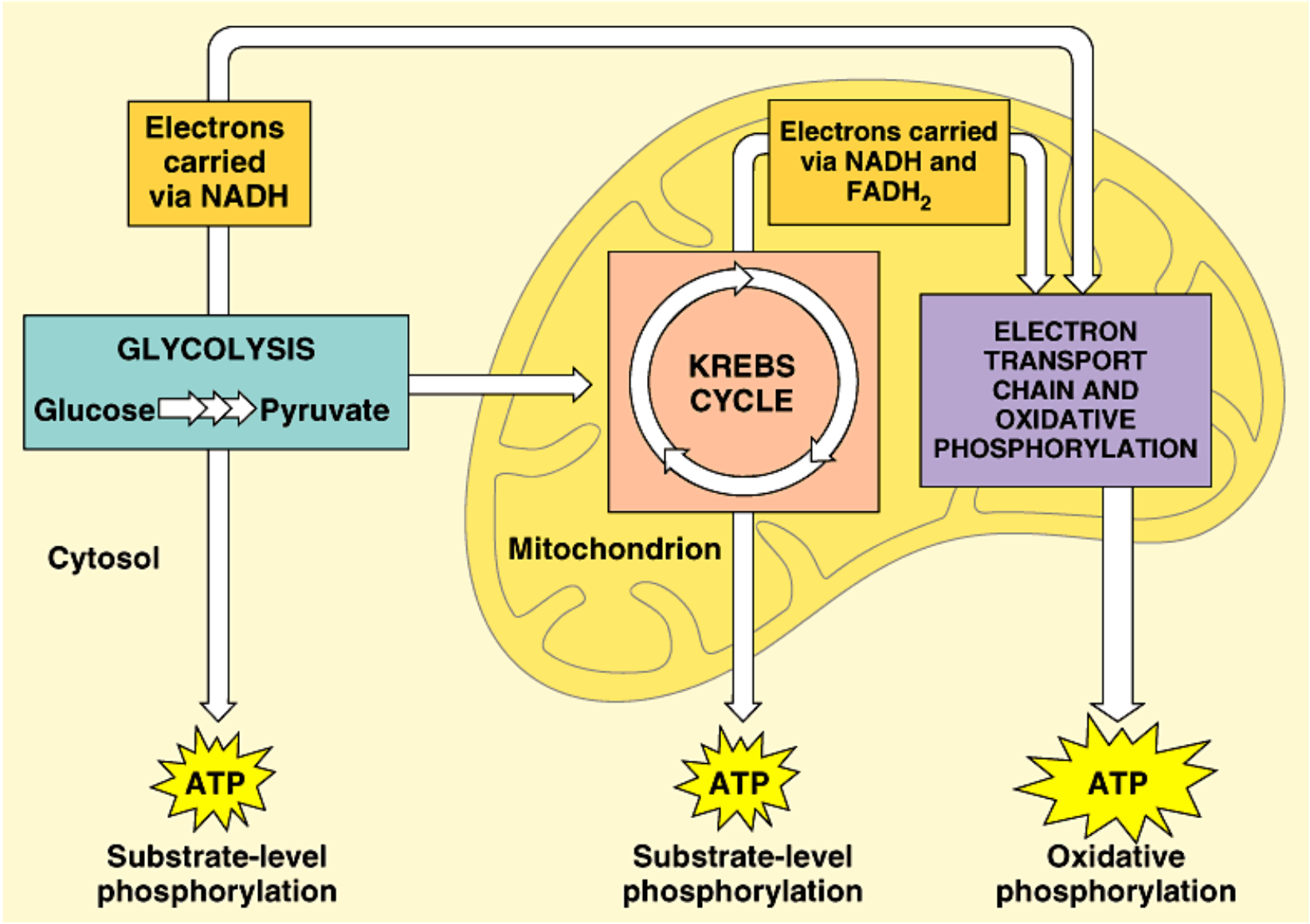
Aerobic Cellular Respiration

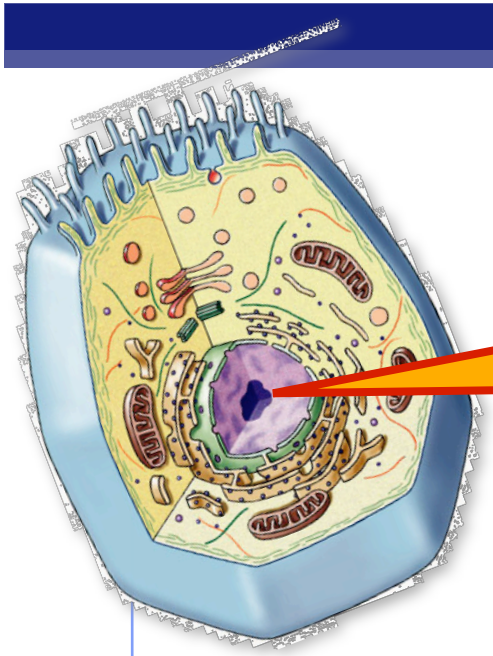
Stage 3:

Electron Transport Chain

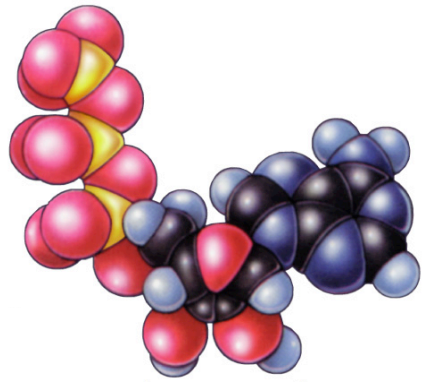


Cellular respiration's 3 main stages



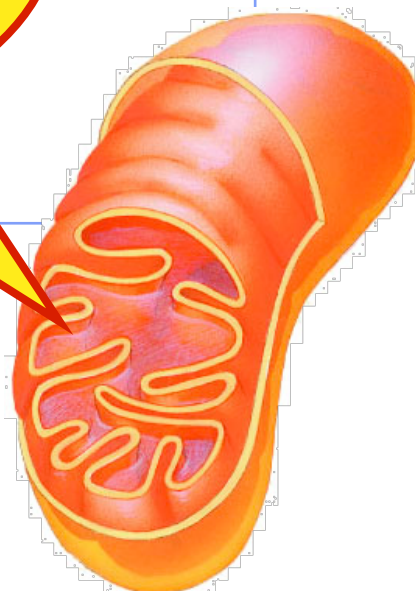


What are we doing?



MAKING ATP! Duh!!!

ATP

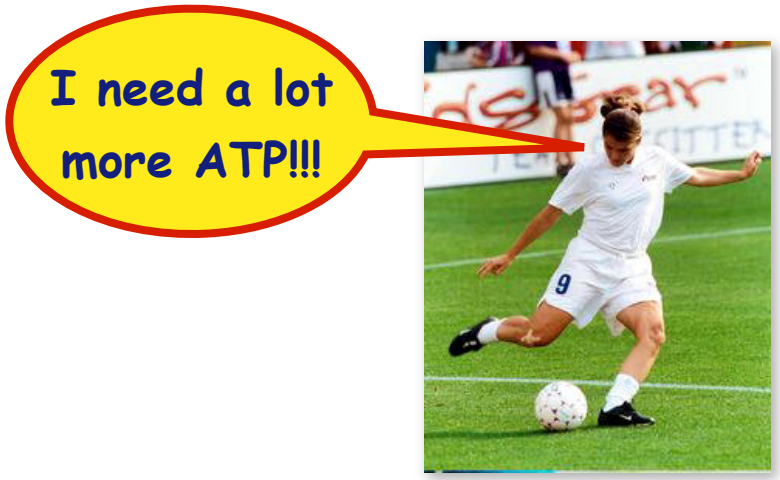


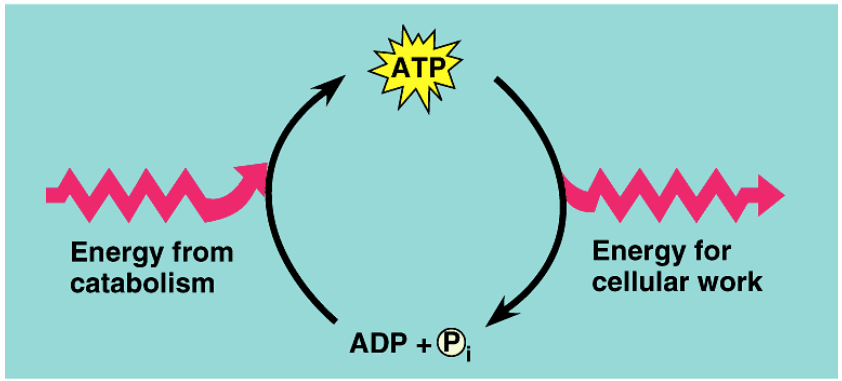
ATP accounting so far for the oxidation of one glucose…

- Glycolysis → net 2 ATP
- Citric Acid's Cycle → 2 ATP
  - Life takes a lot of energy to run, need to extract more energy than 4 ATP per glucose!

There's got to be a better way to make ATP!

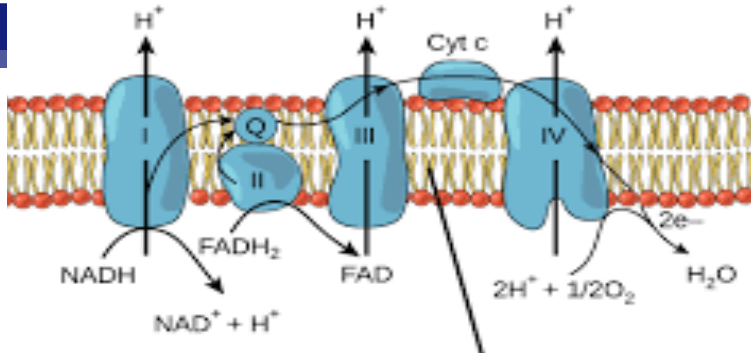
- $NADH + FADH_2$ [not the 4 ATPs made] account for most of the energy extracted from glucose because of the high-energy electrons they are holding on to.





A working muscle recycles over 10 million ATPs per second

Aerobes Making More ATP

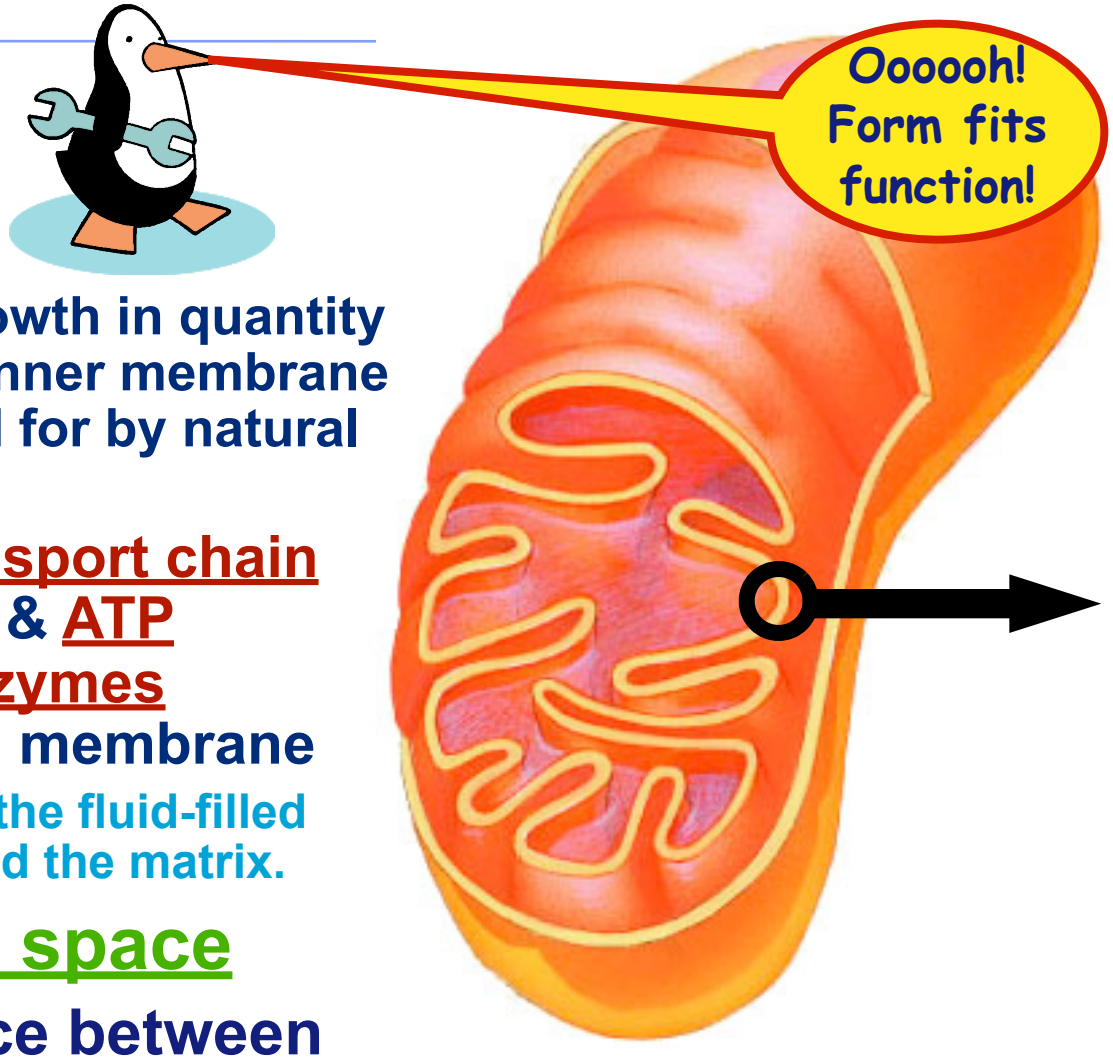


- **Electron Transport Chain**
  - Series of multi-protein complexes built into INNER mitochondrial membrane *(plasma membrane in prokaryotes)*
    - Along the cristae
    - Complexes are make of transport proteins & enzymes & electron carriers & prosthetic groups = *non-protein components essential for the catalytic functions of certain enzymes*
  - the transport of electrons down/through ETC is linked to the pumping of H^+ to create and H^+ gradient
  - ATP Synthase uses the energy stored in the H+ gradient to make ATP
  - ETC & ATP Synthase activity yields 32-34 additional ATP from the original glucose*!*
  - ETC requires O_2 (aerobic respiration)

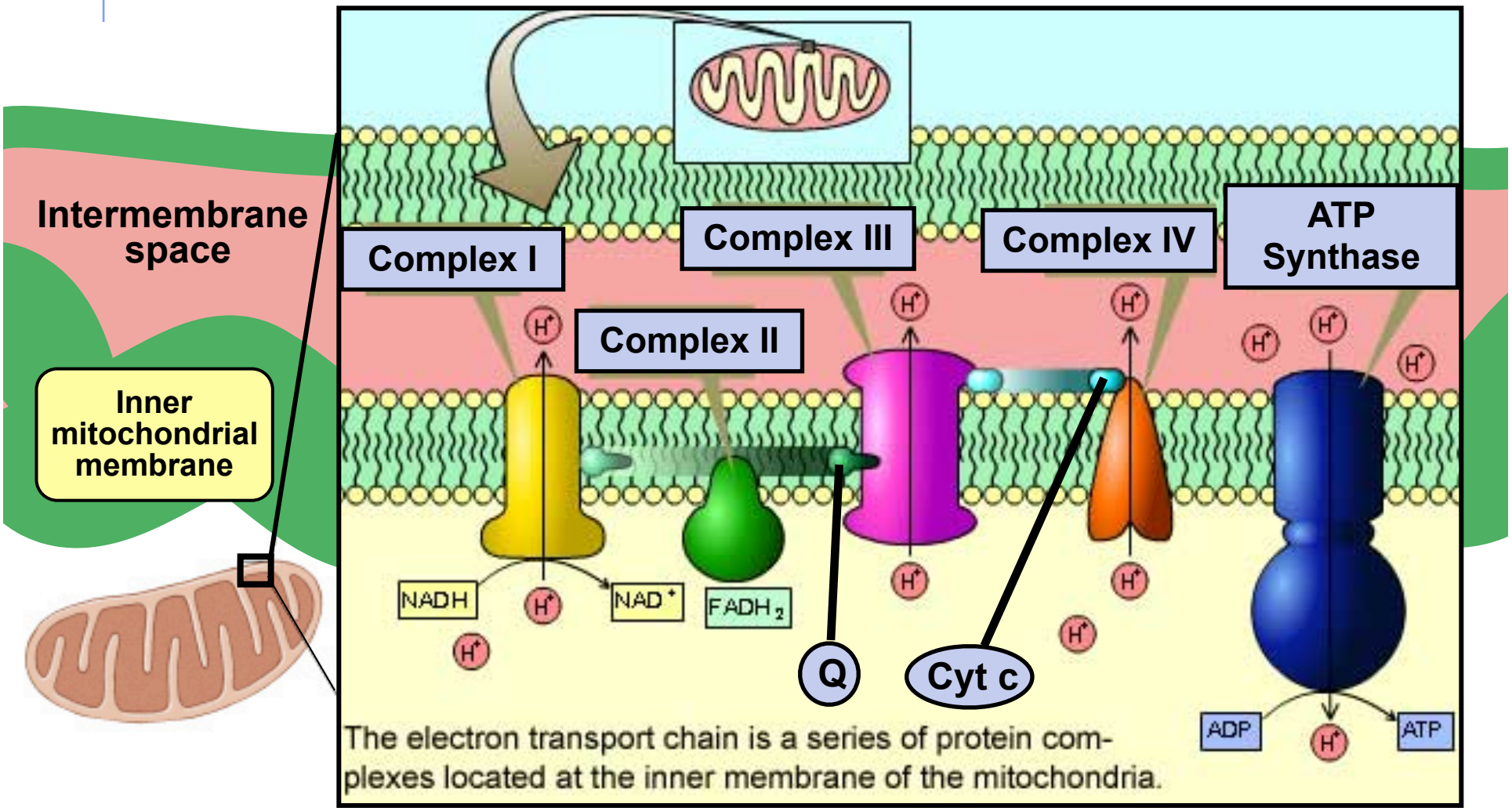
O_2

Mitochondria

- Double membrane
  - outer membrane
  - inner membrane
    - highly folded - growth in quantity (surface area) of inner membrane has been selected for by natural selection
      - Electron transport chain components & ATP Synthase enzymes embedded in membrane
        - Surrounds the fluid-filled center called the matrix.
  - intermembrane space
    - fluid-filled space between membranes



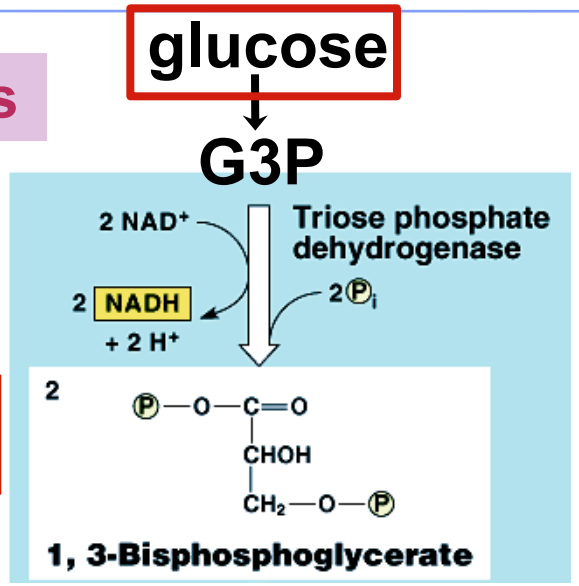
Electron Transport Chain is located in the inner membrane

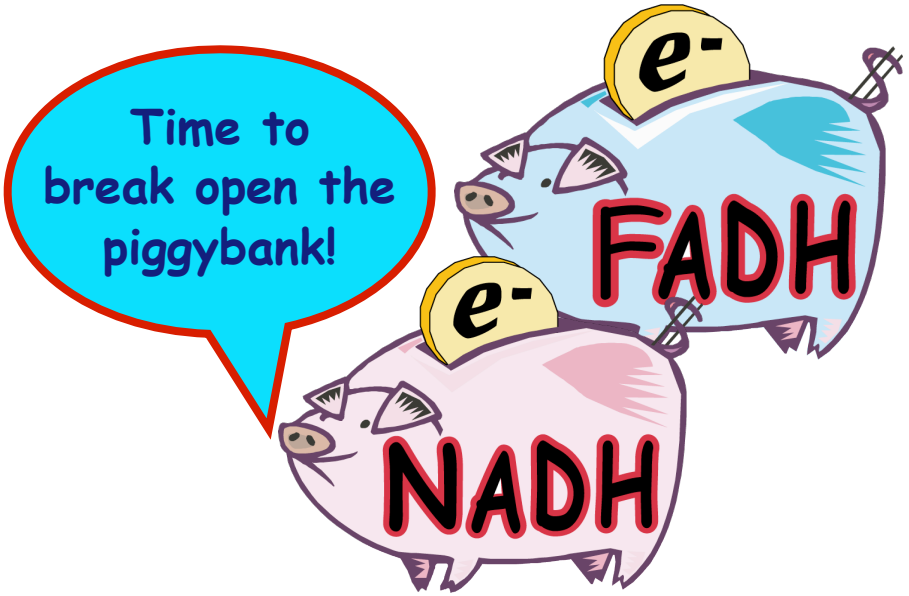


Remember the Electron Carriers? They're still holding almost all the energy extracted from glucose.

Glycolysis

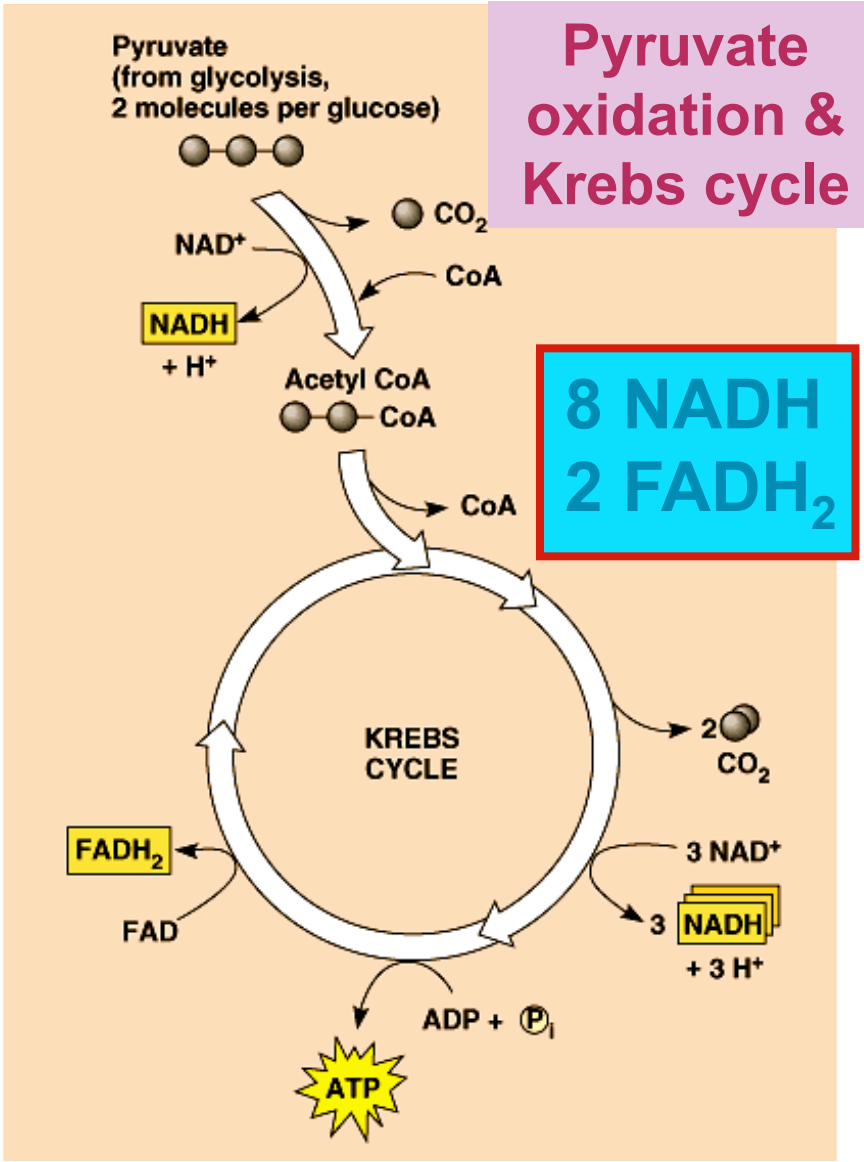
2 NADH



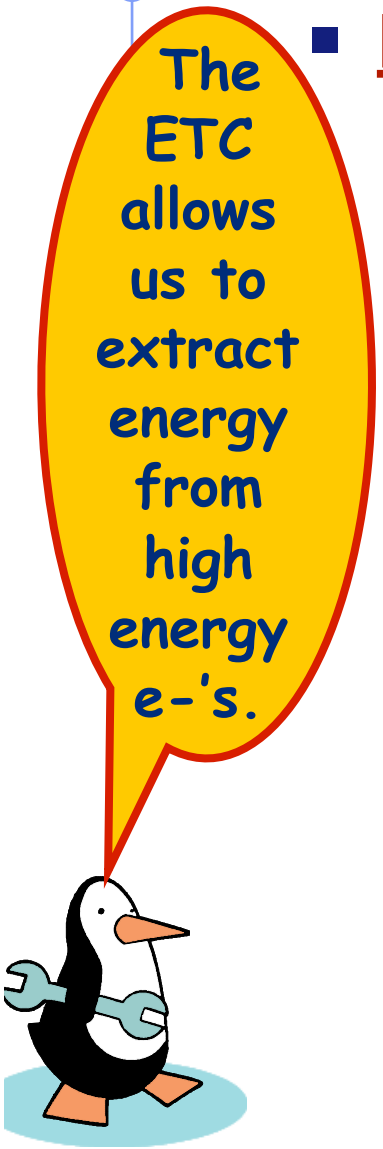


Pyruvate oxidation & Krebs cycle

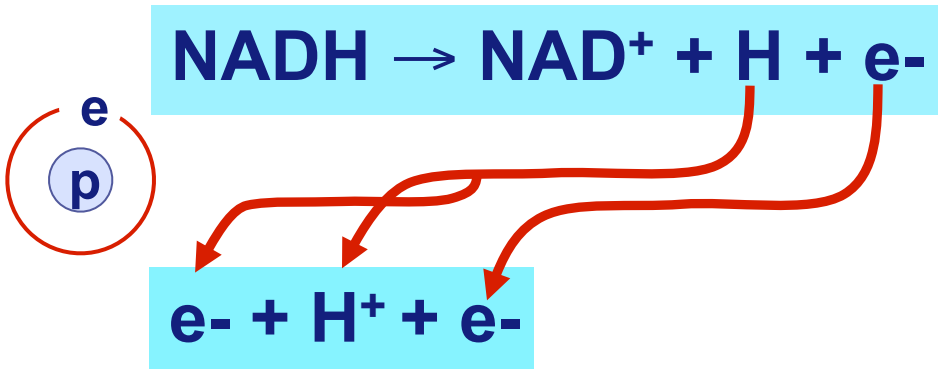
8 NADH
2 $FADH_2$



Stripping H's from Electron Carriers (Oxidizing Carriers)



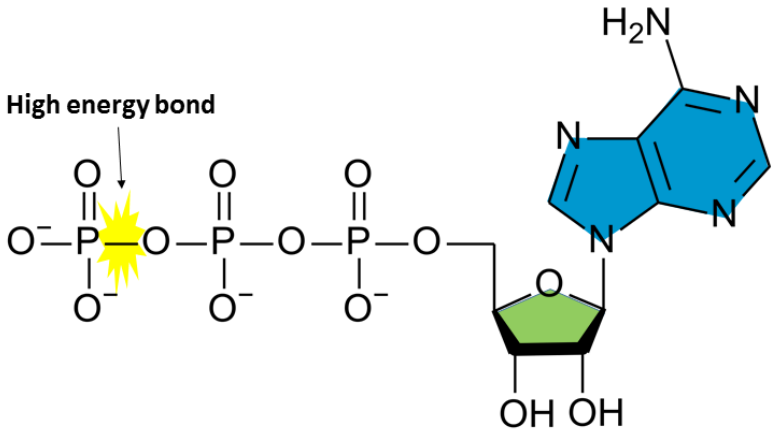
- **Electron carriers pass electrons to the ETC**
  - The H + e- is removed from NADH by an enzyme of an ETC complex



  - The 2 H's are removed from $FADH_2$ by an enzyme of an ETC complex
  - Electrons stripped from H atoms leaving behind H^+ (protons) in the matrix
    - Electrons are passed from one electron carrier to next through the complexes of the ETC

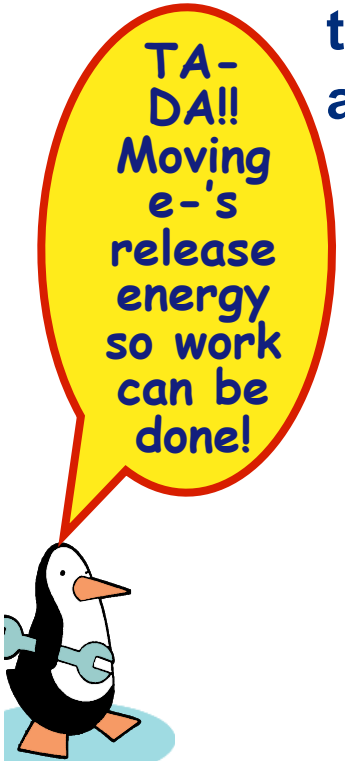
Extracting The Energy from High-Energy Electrons in a Controlled Manner

- As electrons are moved from one Electron Transport Chain Complex to the next, electron carriers in the complexes alternate between reduced and oxidized states as they accept and then donate electrons
  - As electrons move each time to a more electronegative atom as they are moved through one complex and to the next
    - In the process, the electrons slowly loose potential energy!
      - This energy is the energy we want to store on ATP



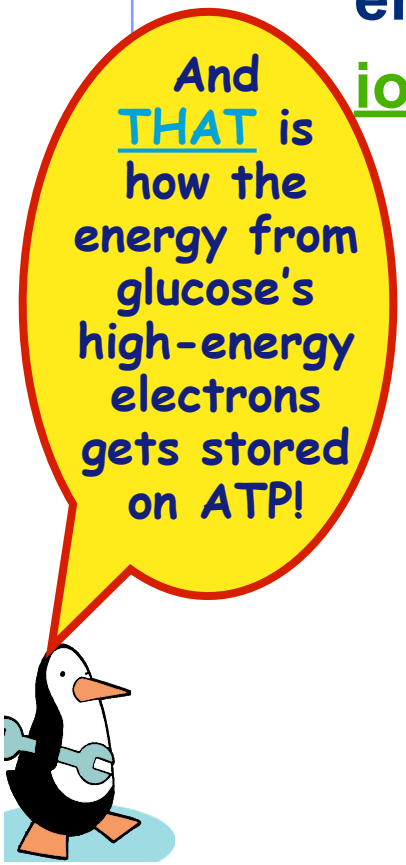
1st Law of Themodynamics:
Energy cannot be created or destroyed

- **The ETC along with ATP synthase, allows the cell to extract the energy of high energy electrons and move that energy over to ATP molecules.**
  - **How do we move this energy?**
    - **The "downhill" flow of electrons [electrons moving through the ETC] provides the energy to do work like pumping H^+s against their concentration gradient.**
      - **Transport proteins [part of Complexes I, II, IV] in the membrane pump H^+ (protons) across inner membrane from the mitochondrial matrix to the intermembrane space using the EXERGONIC flow of electrons through the ETC**
        - **As electrons lose their energy, the energy is used to create a proton gradient across the inner membrane.**



1st Law of Themodynamics:
Energy cannot be created or destroyed

- The creation of a proton gradient across the inner mitochondrial membrane stores potential energy.
  - The potential energy is thus *moved* from the high energy electrons to the high concentration of H^+ ions in the intermembrane space.
    - ATP Synthase will provide a pathway for H^+ ions to diffuse back to the matrix.
    - As the H^+ ions diffuse down their concentration gradient back to the matrix, the potential energy released is used to drive the endergonic creation of ATP from ADP/AMP and P_is.
      - The energy has thus been moved from the H^+ gradient to ATP molecules.



Electron Transport Chains

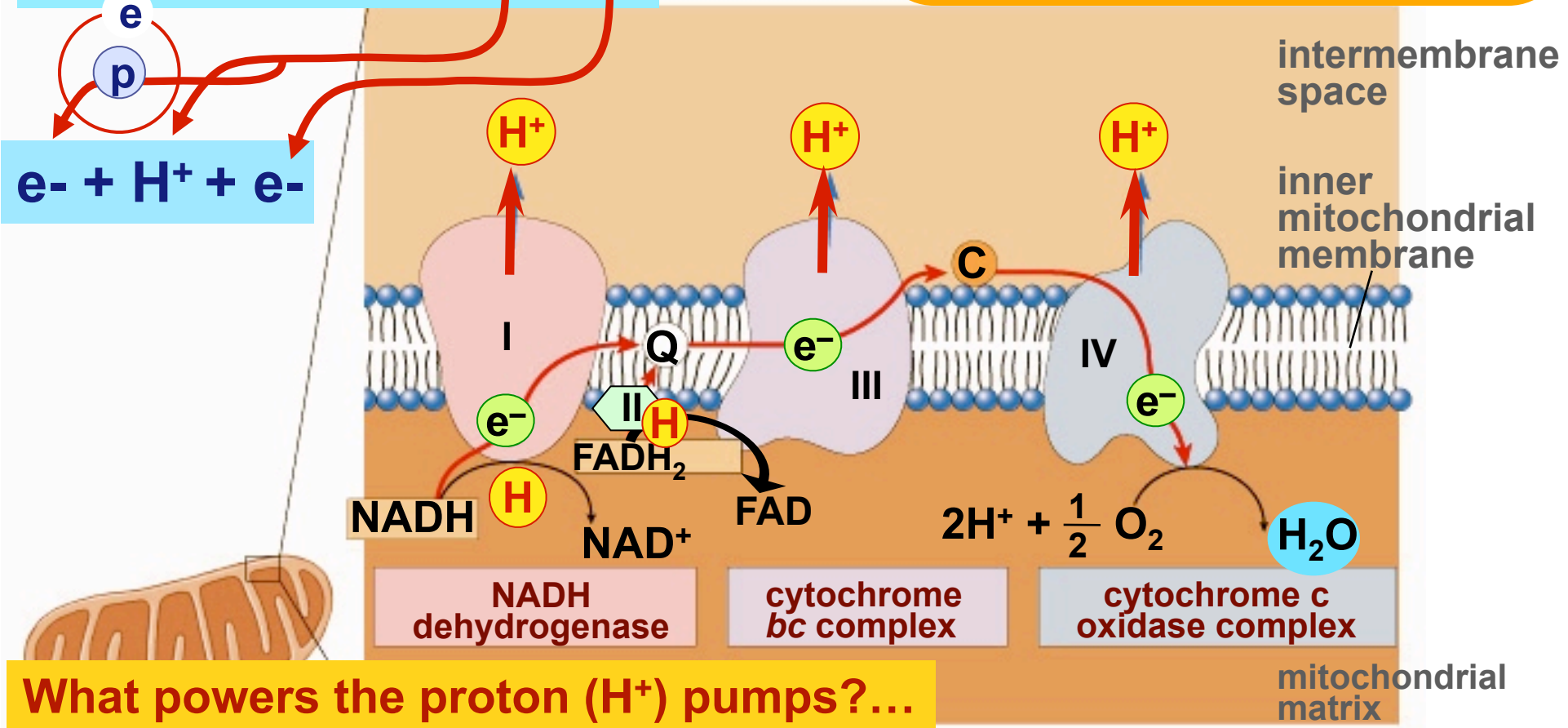
We are building a proton gradient called the PROTON MOTIVE FORCE!!!! *[stored Potential Energy because of the proton gradient created]*

NADH → NAD⁺ + H + e-

e

p

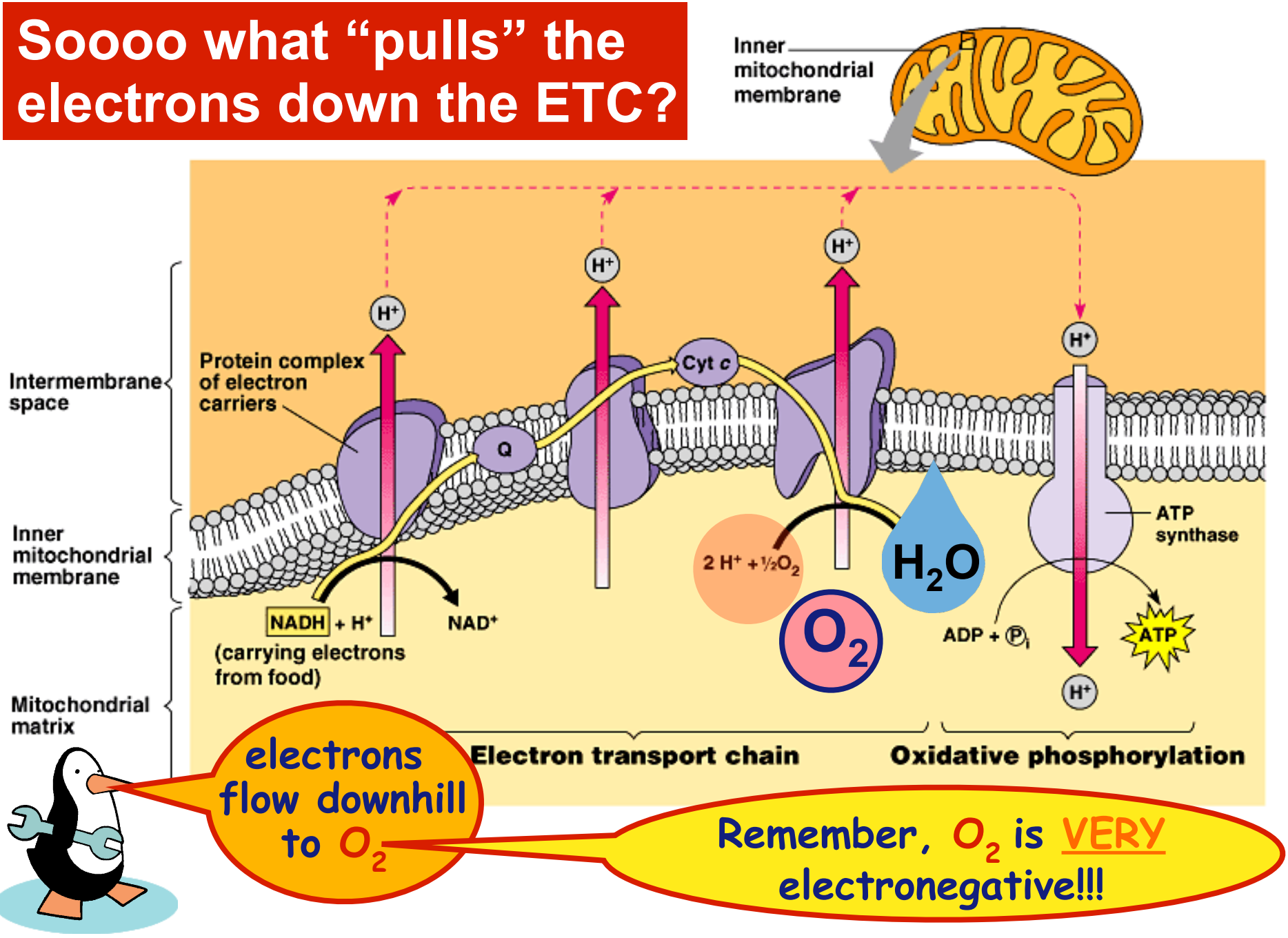
e- + H⁺ + e-



What powers the proton (H⁺) pumps?…

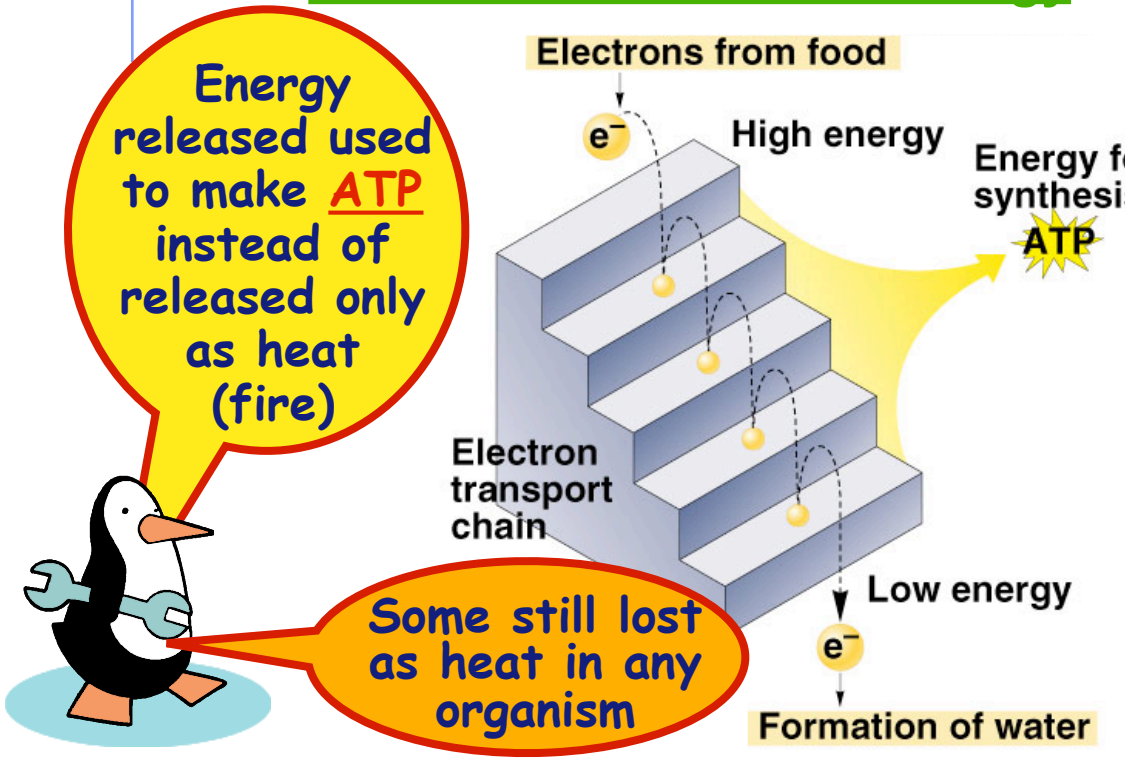
Cannot be ATP. That's what we are trying to make not use up! Soooo..... the flow of electrons powers the H+ pump.

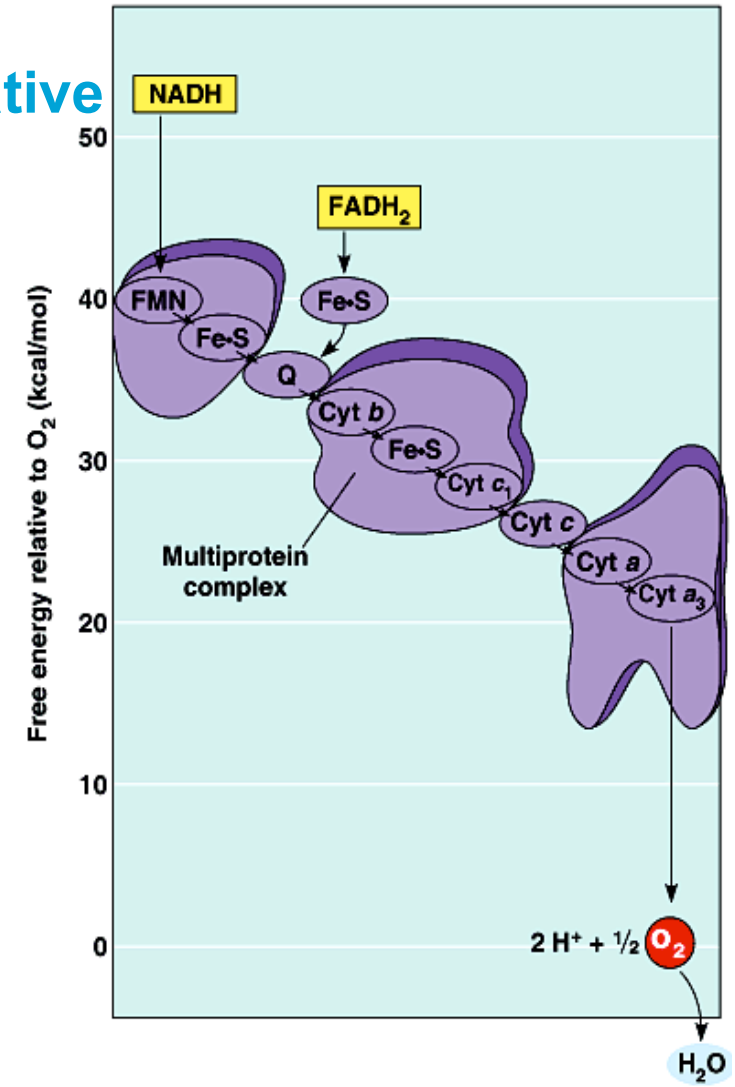
Soooo what "pulls" the electrons down the ETC?



Electrons flow "downhill"

- Electrons move from complex to complex eventually to oxygen
  - each complex is more electronegative than the previous one
  - This is controlled oxidation
    - A controlled release of energy

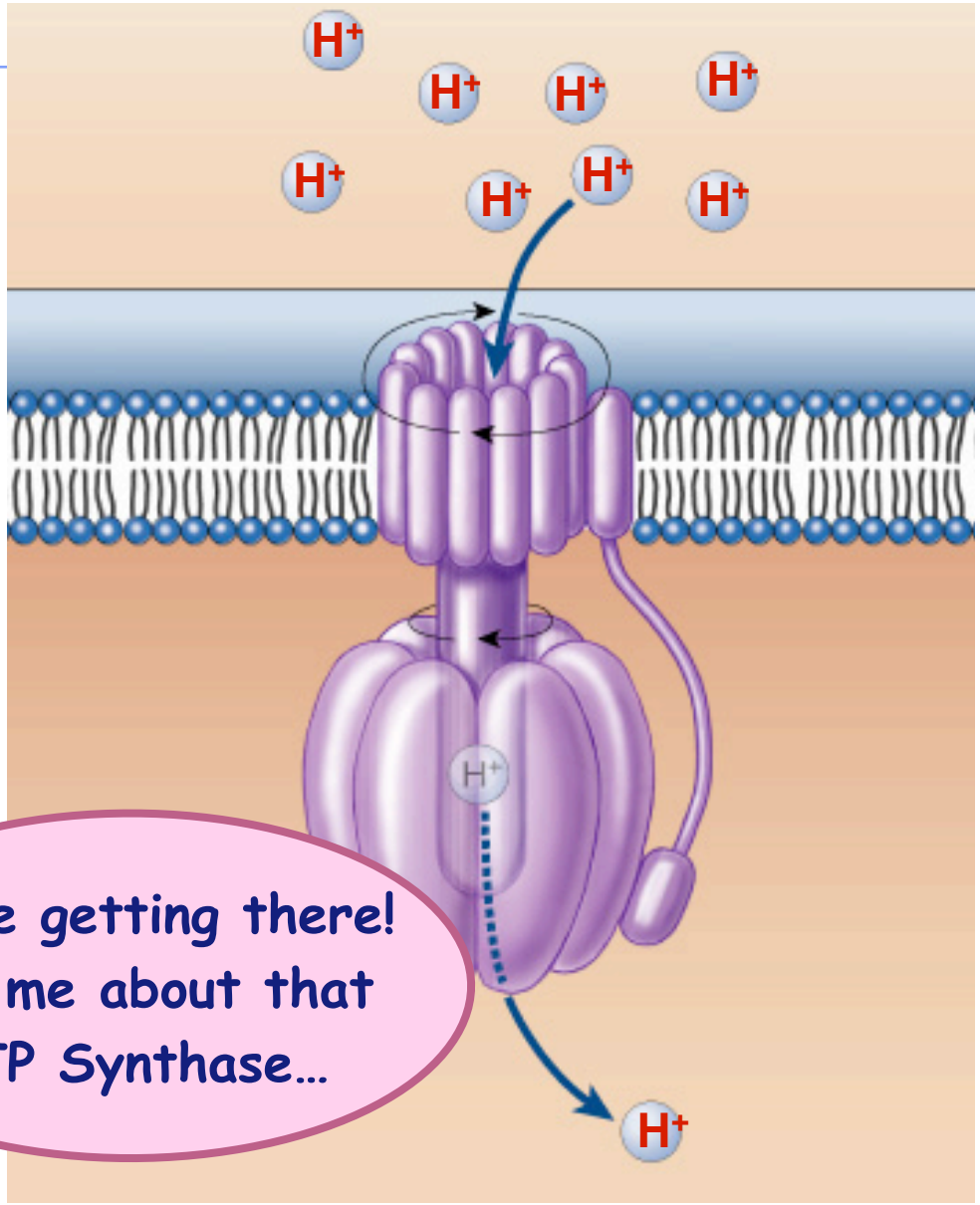


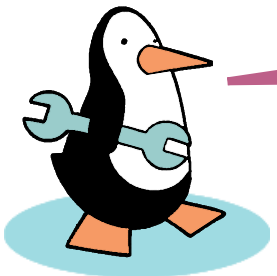


Creating the H^+ gradient

Electro-chemical gradient:
"proton-motive" force

As electrons flow, H+ get pumped from the mitochondrial matrix to the inter-membrane space setting up a Proton-Motive Force (A electro-chemical gradient that stores potential energy that can be used to do work like building ATP)



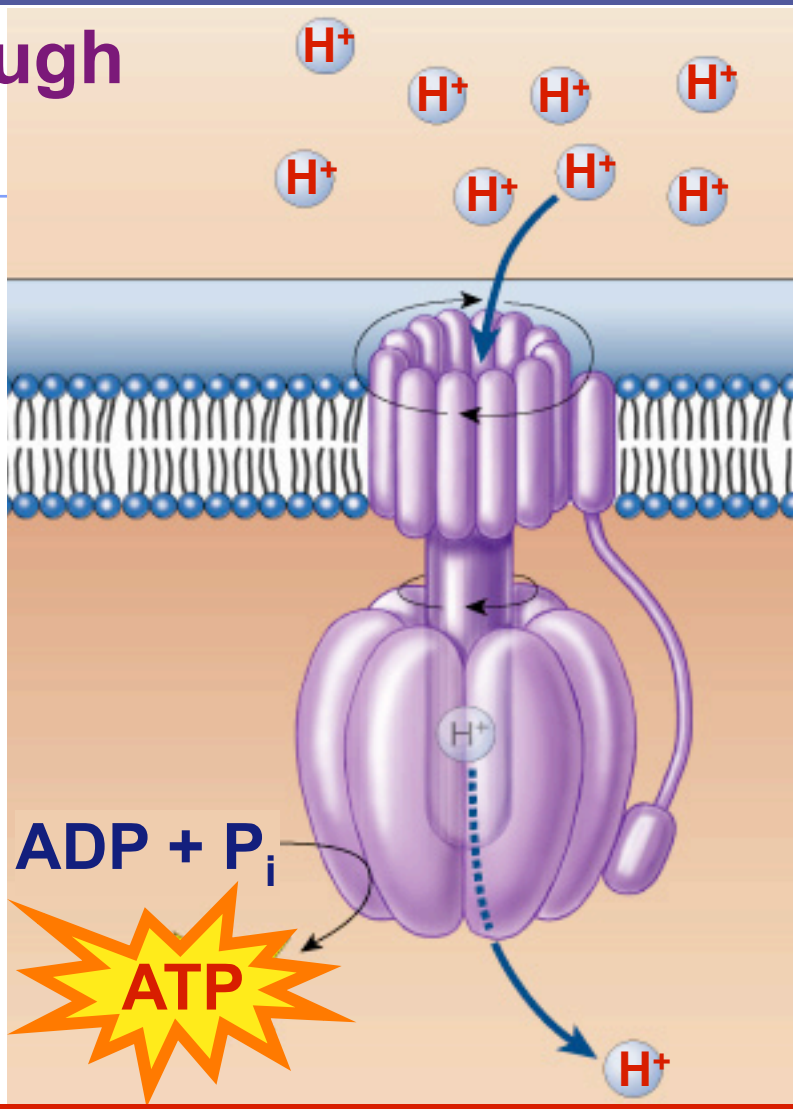


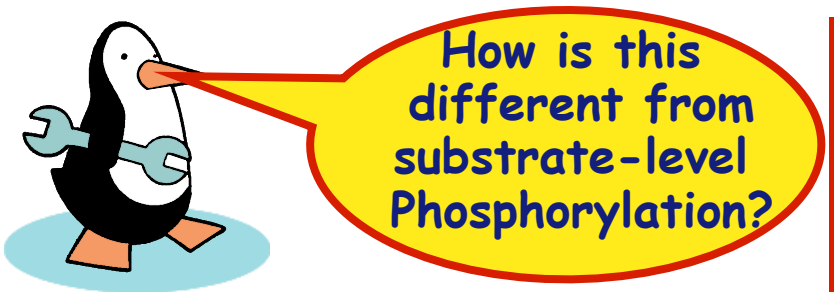
We're getting there! Tell me about that ATP Synthase...

ATP Synthase Builds ATP Through Oxidative Phosphorylation

- Protons want to diffuse down their concentration gradient
- The *ONLY* passage for these protons is through ATP synthase
  - This enzyme catalyzes the synthesis of ATP by allowed INORGANIC phosphates to be added to ADP.

$ADP + P_i \rightarrow ATP$

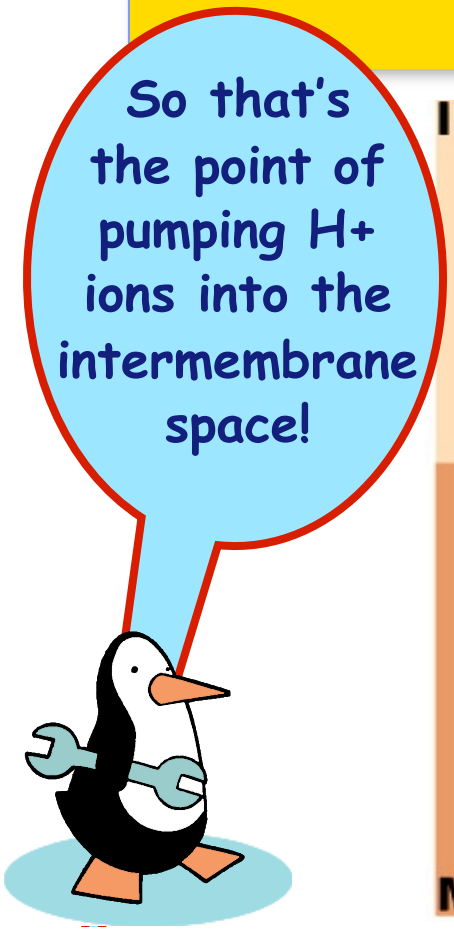


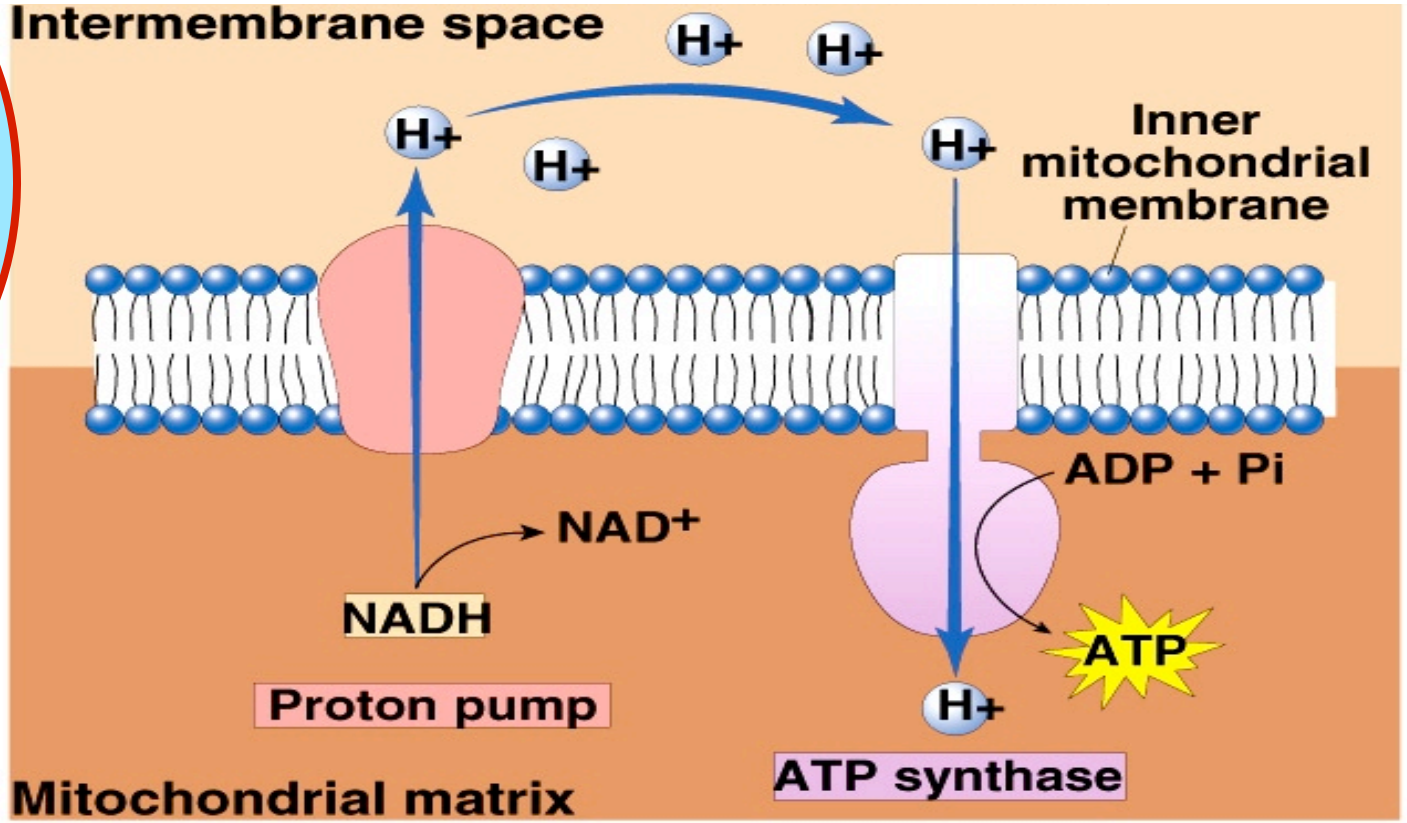


oxidative phosphorylation - ATP synthesis powered by the redox reactions of the ETC

What do we call the diffusing of H+ through ATP Synthase?

Chemiosmosis *[the facilitated diffusion of H^+ ions through ATP Synthase]* **links the Electron Transport Chain to ATP synthesis. It is the diffusion of hydrogen ions across a membrane in order to generate ATP.**

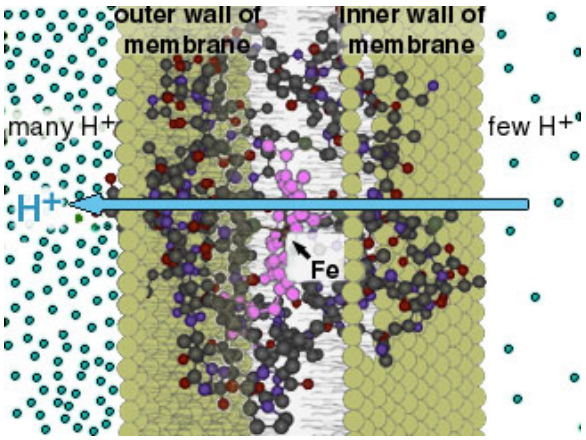




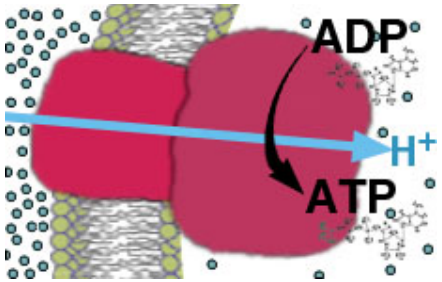
Peter Mitchell

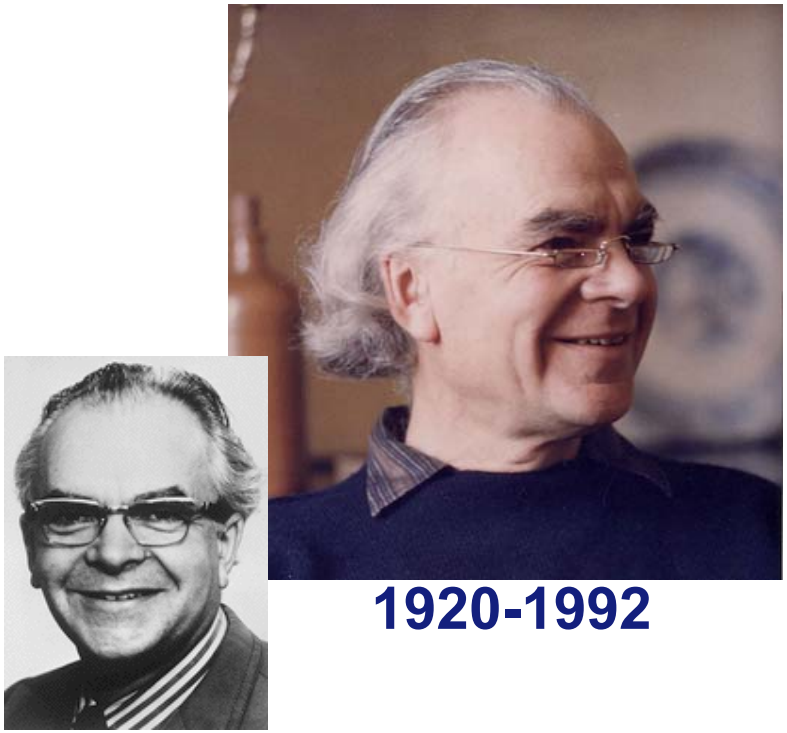
1961 | 1978

- Proposed chemiosmotic hypothesis for ATP production.
  - revolutionary idea at the time

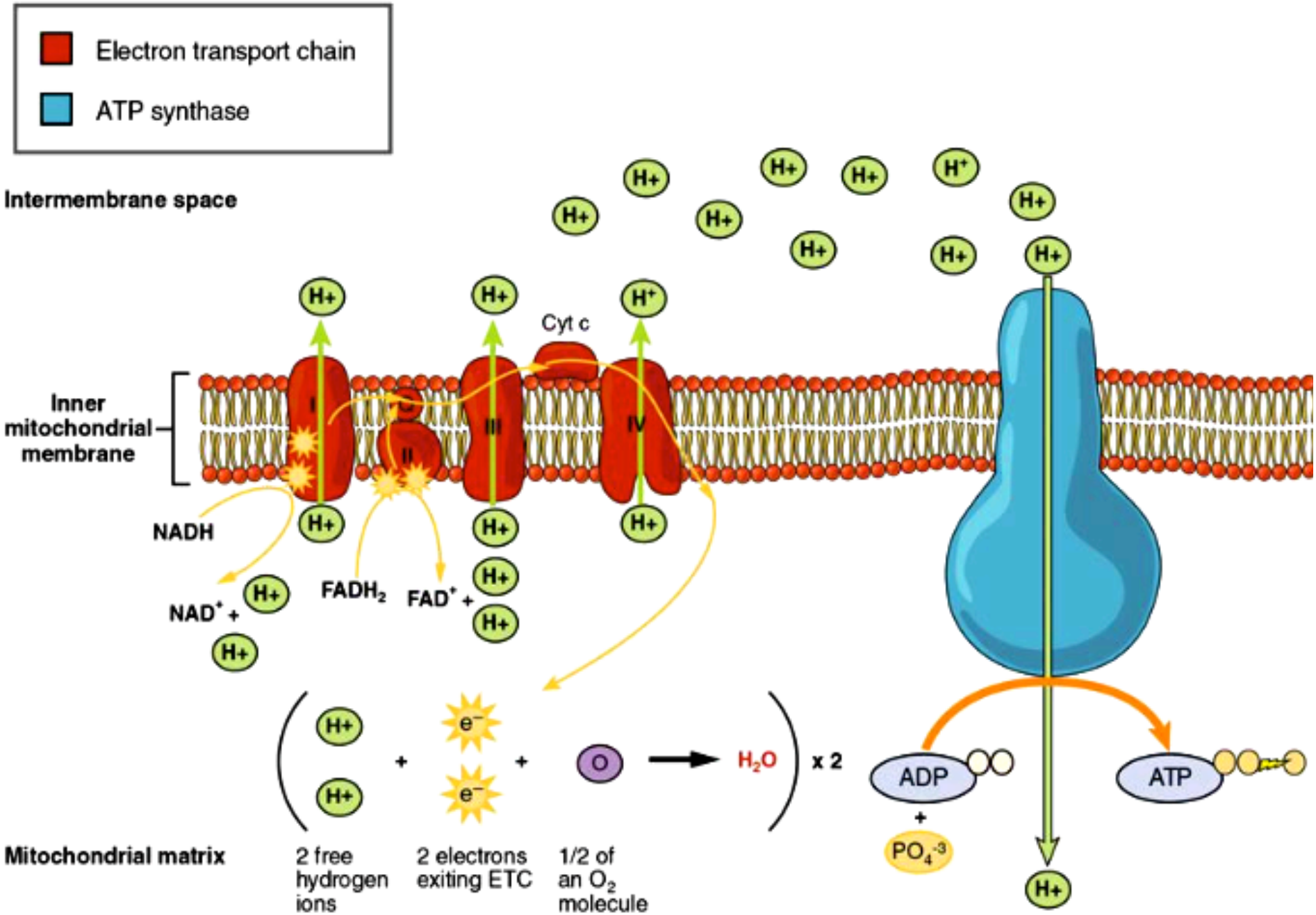


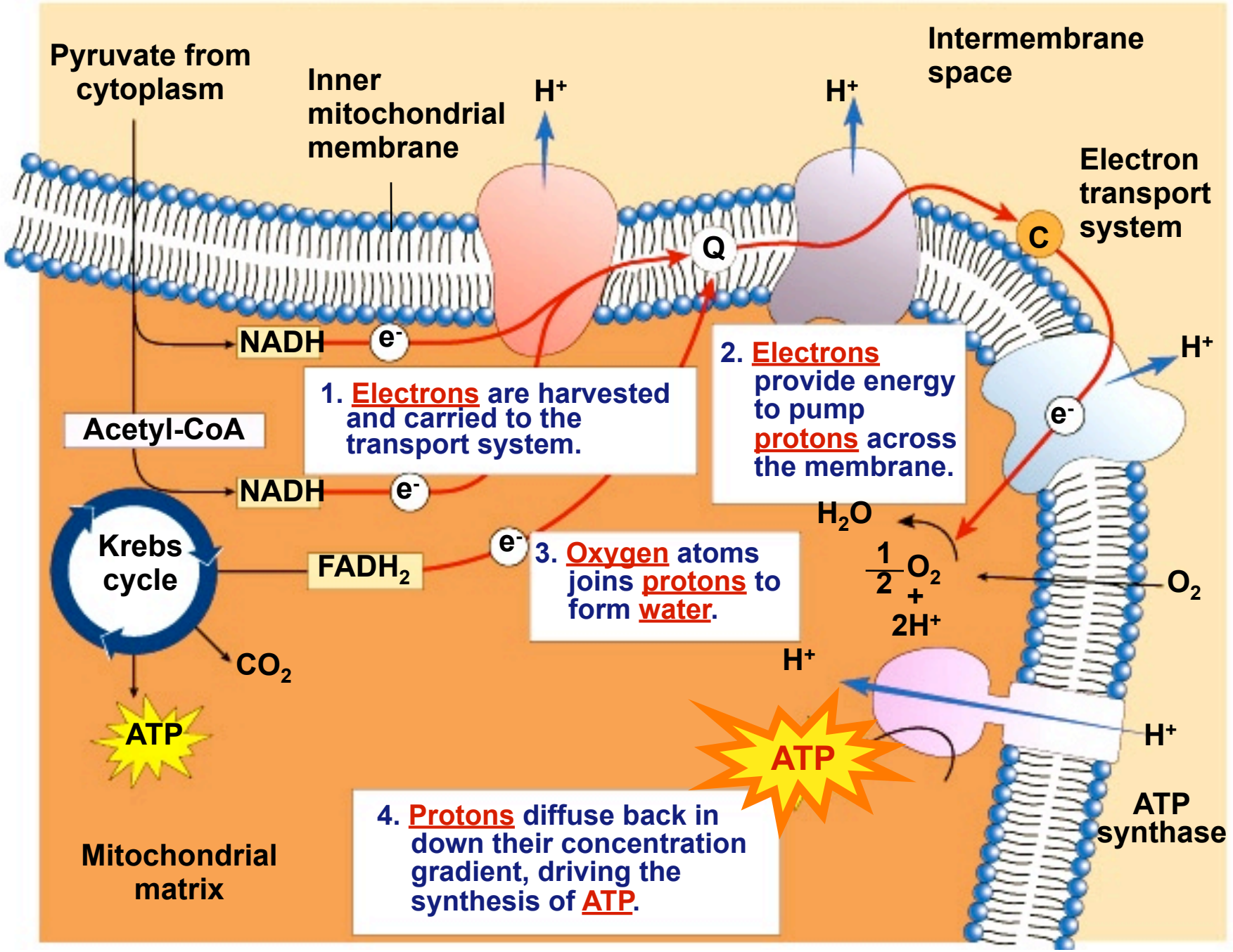
proton motive force





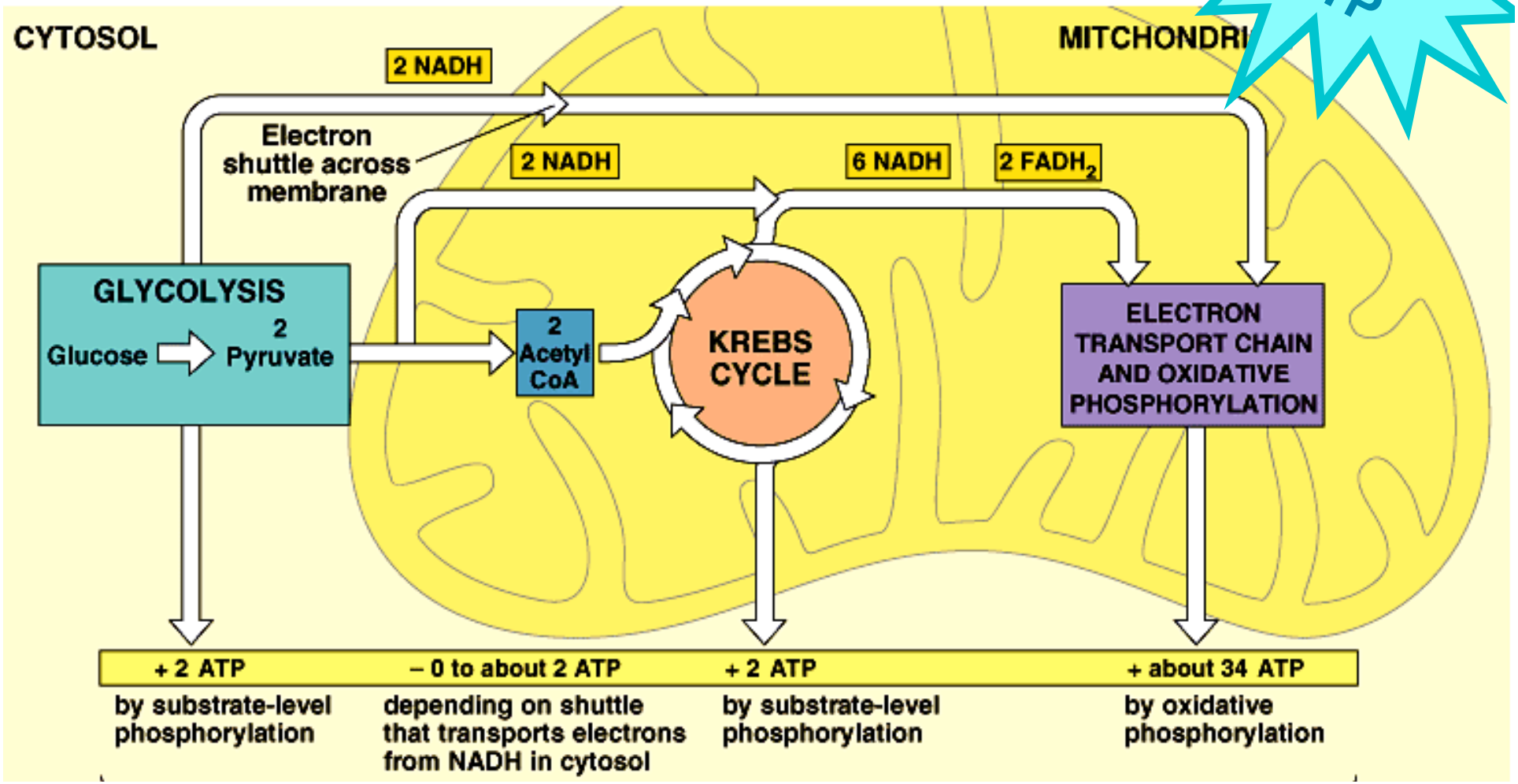
1920-1992


Electron transport chain
ATP synthase
Intermembrane space
Inner mitochondrial membrane
Cyt c
I
II
III
IV
NADH
NAD+ +
FADH2
FAD+ +
H+
e−
O
H2O
x 2
ADP
+
PO4-3
ATP
Mitochondrial matrix
2 free hydrogen ions
2 electrons exiting ETC
1/2 of an O2 molecule


Pyruvate from cytoplasm
Inner mitochondrial membrane
H+
H+
Intermembrane space
Electron transport system
C
Q
NADH
e-
1. Electrons are harvested and carried to the transport system.
2. Electrons provide energy to pump protons across the membrane.
H+
e-
Acetyl-CoA
NADH
e-
H2O
Krebs cycle
e-
FADH2
3. Oxygen atoms joins protons to form water.
1/2 O2 + 2H+
O2
CO2
H+
ATP
ATP
H+
4. Protons diffuse back in down their concentration gradient, driving the synthesis of ATP.
Mitochondrial matrix
ATP synthase

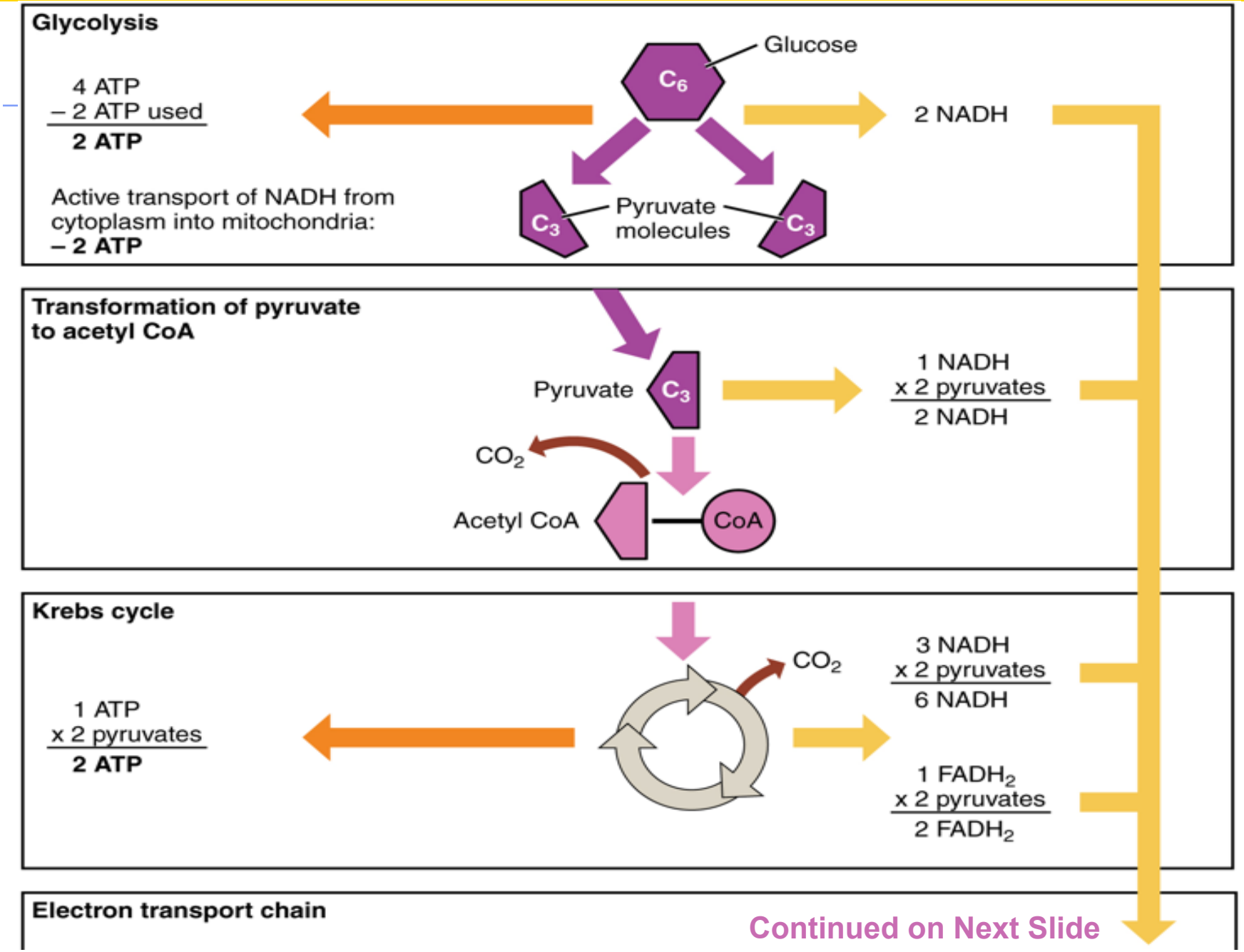
Aerobic Cellular respiration

~36-38 ATP



2 ATP + 2 ATP + ~32-34 ATP

Aerobic Cellular respiration Summary



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Aerobic Cellular respiration Summary

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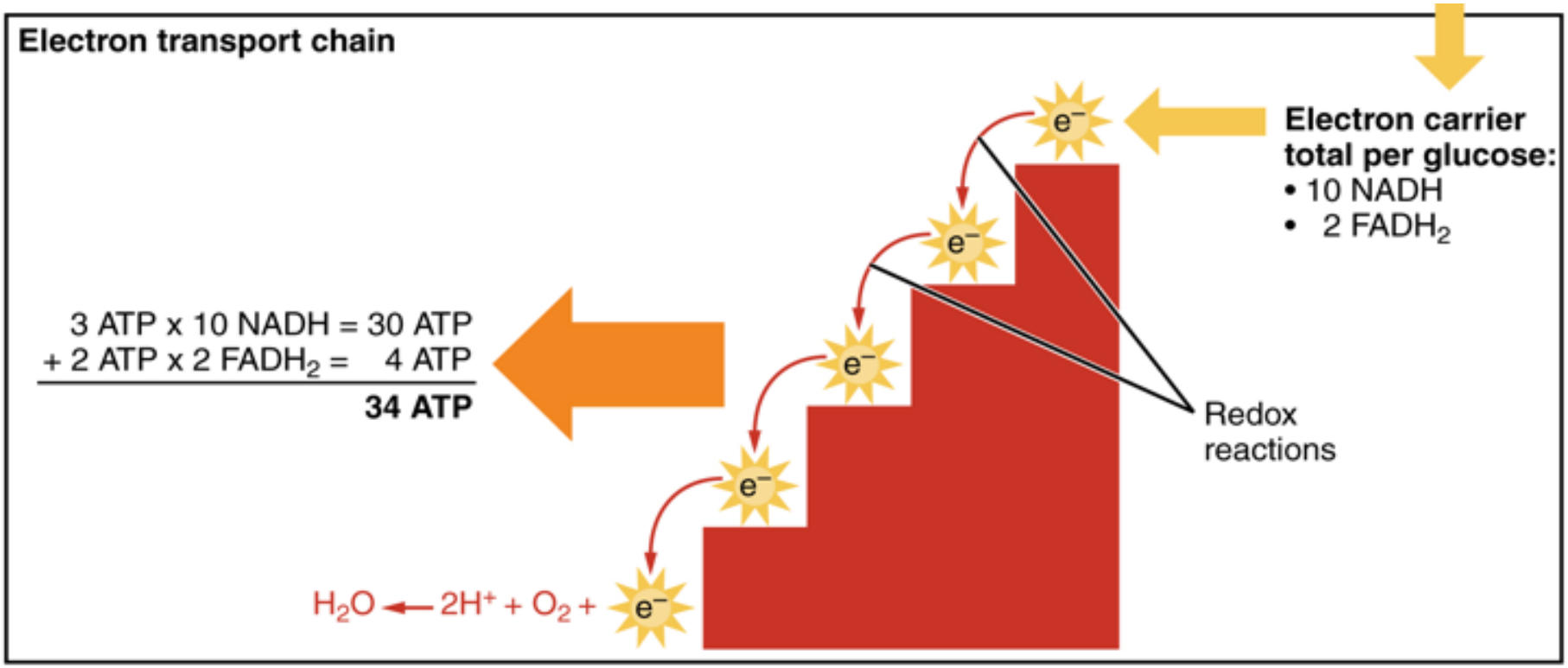


Total ATP produced:

Glycolysis =	2 ATP
NADH transport cost =	–2 ATP
Pyruvate into acetyl CoA =	0 ATP
Krebs cycle =	2 ATP
+ ETC =	34 ATP
	36 ATP per glucose

Summary of cellular respiration

$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$ (+ ~36/8 ATP)

- Where did the glucose come from?
- Where did the O_2 come from?
- Where did the CO_2 come from?
- Where did the CO_2 go?
- Where did the H_2O come from?
- Where did the ATP come from?
- What else is produced that is not listed in this equation?
- Why do we breathe?

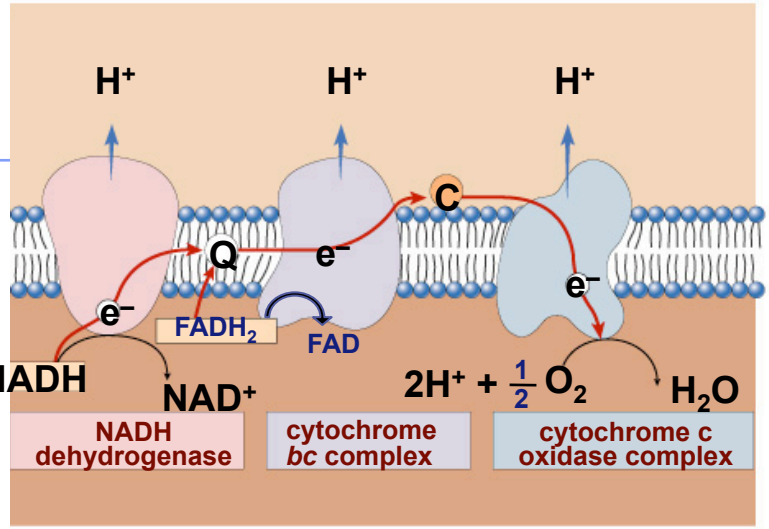
Answer Key

- Where did the glucose come from? Absorbed from diet or made by photosynthesis
- Where did the O_2 come from? From the air
- Where did the CO_2 come from? The oxidation of glucose (and other high-energy organic molecules)
- Where did the CO_2 go? Into the air
- Where did the H_2O come from? The reduction of O at the end of the electron transport chain.
- Where did the ATP come from? The phosphorylation of ADP using the energy extracted from glucose and its high-energy electrons
- What else is produced that is not listed in this equation? Some HEAT
- Why do we breathe? To engage in gas exchange: Bring into the lung space air carrying O_2 so O_2 can diffuse into the blood and bring blood high in CO_2 so CO_2 can diffuse out of the blood and into the lung space to be removed from the body.

Taking it beyond…

- What is the final electron acceptor in Electron Transport Chain?

O_2



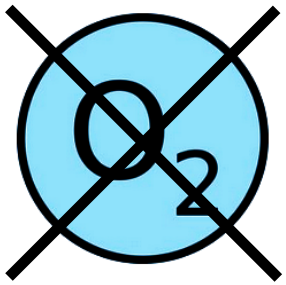
- So what happens if O_2 unavailable?
  - ETC backs up
    - nothing to pull electrons down chain!
    - NADH & $FADH_2$ can't unload their electron cargo so:
      1. ATP production ceases
      2. Krebs Cycle, Oxidation of Pyruvate, Glycolysis stop because they lack oxidized "empty" electron carriers
      3. Cells run out of energy for doing work
      4. And, eventually, yeah, you die*!*

Some organisms can extract energy from organic molecules in the absence of O_2

- **Alternative glucose breakdown pathways (to extract energy for ATP production) occur when aerobic cellular respiration is not possible -** ***when oxygen isn't around to act as an acceptor at the end of the electron transport chain.***
  - **Alternative glucose breakdown pathways in anaerobic environments:**
    1. **Fermentation**
    2. **Anaerobic Respiration**

Some organisms can extract energy from organic molecules in the absence of O_2

- **Fermentation**
  - **Fermentation is an anaerobic (non-oxygen-requiring) pathway for breaking down glucose.**
    - **During fermentation, the only energy extraction pathway is glycolysis with some extra fermentation reactions tacked on at the end.**



Some organisms can extract energy from organic molecules in the absence of O_2

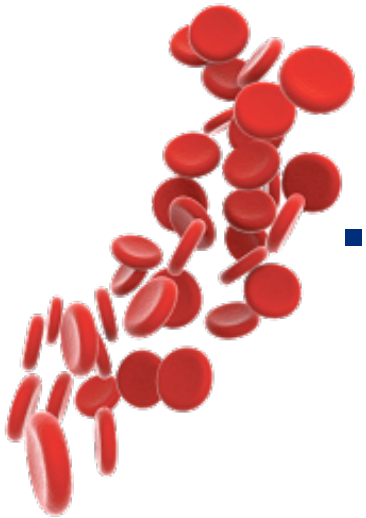
- **Fermentation**
  - Fermentation and cellular respiration begin the same way, with glycolysis.
    - In fermentation, however, the pyruvate made in glycolysis does not continue through oxidation in the citric acid (Krebs) cycle.
    - In fermentation, however, the electron transport chain and ATP Synthase also do not run.

Some organisms can extract energy from organic molecules in the absence of O_2

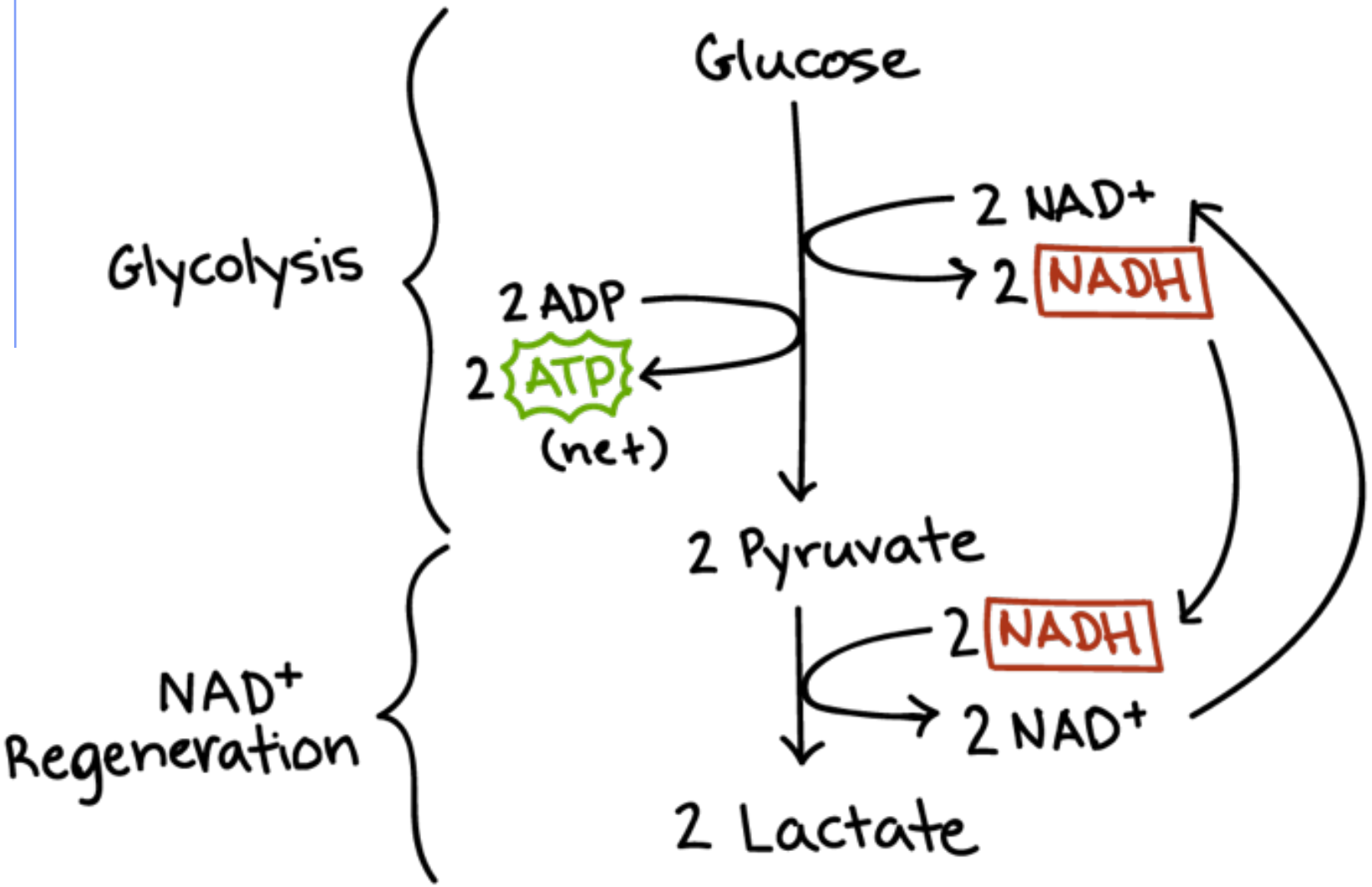
- **Fermentation**
  - **Because the electron transport chain isn't functional, the NADH made in glycolysis cannot drop its electrons off on the electron transport chain to turn back into NAD+**
    - **The purpose of the extra reactions in fermentation, therefore, is to regenerate the electron carrier NAD+ from the NADH produced in glycolysis.**
      - **The extra reactions of fermentation let NADH drop its electrons off onto an organic molecule (such as pyruvate, the end product of glycolysis).**
        - **By re-oxidizing NADH into NAD+, glycolysis is able to keep running and 2 ATP per glucose can keep forming.**

The Two Forms of Fermentation

- **Lactic Acid Fermentation**
  - At the end of glycolysis, NADH transfers its electrons directly to pyruvate, which is converted into lactate (ionized lactic acid) as waste product.
    - The bacteria that make yogurt carry out lactic acid fermentation
    - Skeletal muscle cells can carry out lactic acid fermentation too, in addition to aerobic respiration, when oxygen levels are too low as is the case during heavy exercise.
    - Red blood cells in your body carry out lactic acid fermentation too since they are animal cells that interestingly lack mitochondria (so they don't use up the O_2 gas they are carrying on the hemoglobin) and thus can't perform aerobic cellular respiration!



Lactic Acid Fermentation

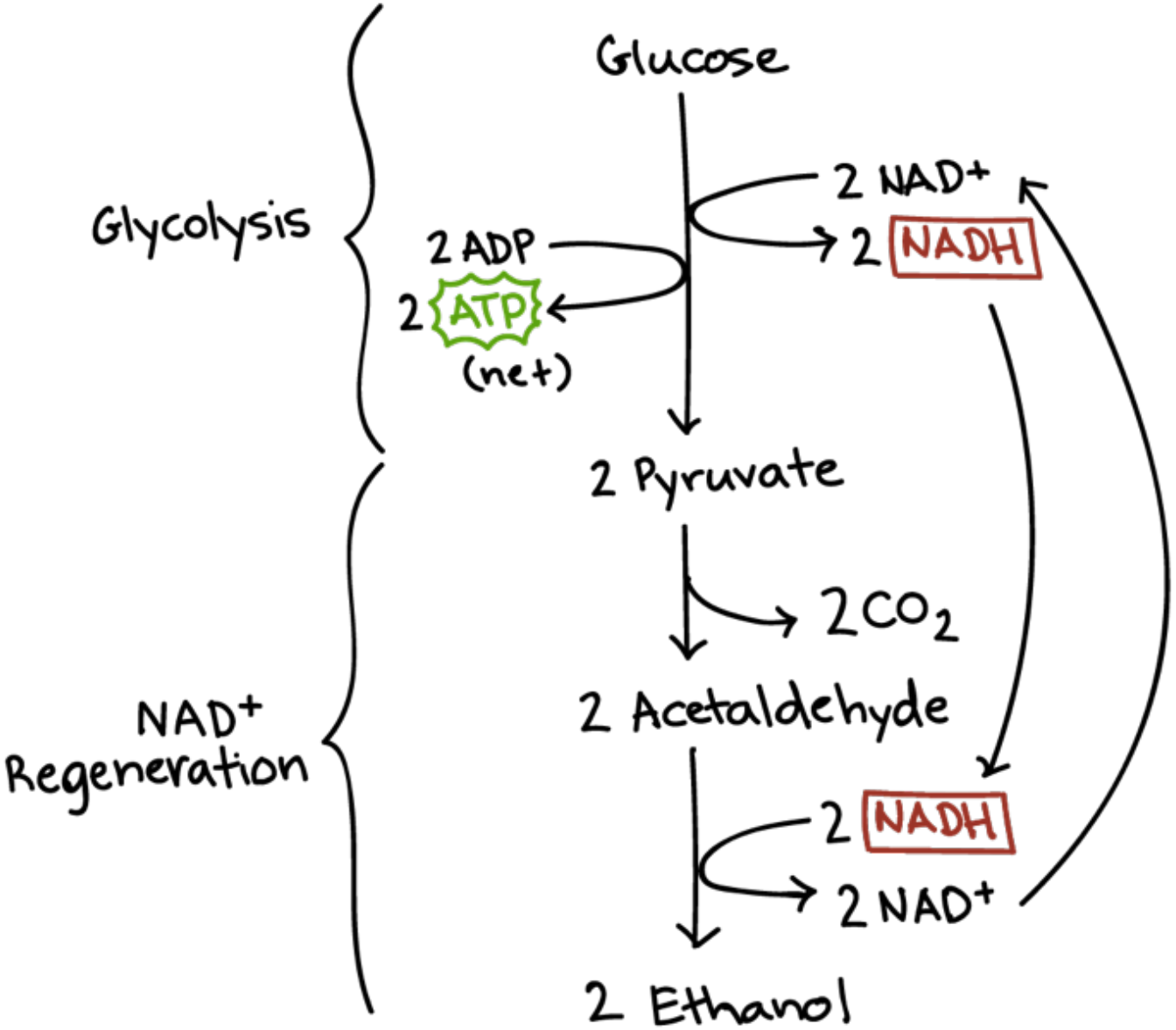


The Two Forms of Fermentation

Alcohol (Ethanol) Fermentation

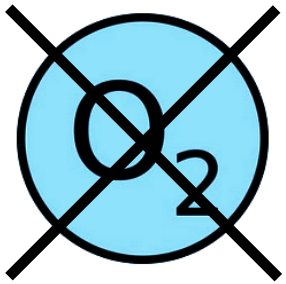
- At the end of glycolysis, NADH transfers its electrons to a derivative of pyruvate, producing ethanol and CO_2
  - Going from pyruvate to ethanol is a two-step process.
    1. In the first step, a carboxyl group is removed from pyruvate and released in as CO_2, producing a two-carbon molecule called acetaldehyde.
    2. In the second step, NADH passes its electrons to acetaldehyde, regenerating NAD+ and forming ethanol.
- Yeast produce the ethanol (& CO_2) found in alcoholic drinks like beer and wine.
  - However, alcohol is toxic to yeasts in large quantities (just as it is to humans), which puts an upper limit on the percentage alcohol in these drinks.

Alcohol Fermentation



Some organisms can extract energy from organic molecules in the absence of O_2

- **Anaerobic Cellular Respiration**
  - **Fermentation is a widespread pathway, but it is not the only way to get energy from high-energy organic molecules like glucose ("fuels") anaerobically** ***(in the absence of oxygen).***
    - **Some organisms use all the "machinery" of aerobic cellular respiration, but use an inorganic molecule other than O_2 as a final electron acceptor (such as sulfate) at the end of their electron transport chain.**
      - **This process, called anaerobic cellular respiration, and is performed by some bacteria and archaea.**



Some organisms can extract energy from organic molecules in the absence of O_2

- **Anaerobic Cellular Respiration**
  - **Anaerobic respiration is similar to aerobic respiration in that electrons extracted from a high-energy organic "fuel" molecules (like glucose) are passed through an electron transport chain to extract the potential energy used to synthesize ATP using ATP Synthase.**
    - **Some organisms use sulfate (SO_4^{2-}) as the final electron acceptor (instead of O_2) at the end to the transport chain, while others use nitrate (NO_3^-)**

Some organisms can extract energy from organic molecules in the absence of O_2

- **Anaerobic Cellular Respiration**
  - **Some prokaryotes—bacteria and archaea - that live in low-oxygen environments rely on anaerobic respiration to break down fuels.**
    - **For Ex: Some archaea called methanogens can use CO_2 as a terminal electron acceptor, producing methane (CH_4) as a by-product.**

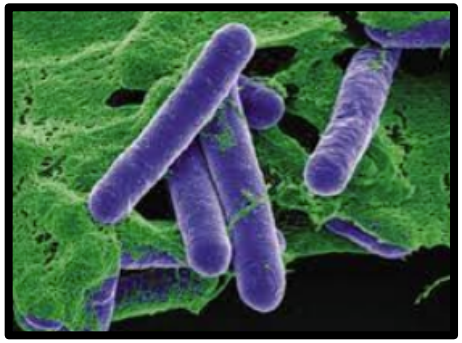
      - **Methanogens are found in soil and in the digestive systems of ruminants, a group of animals including cows and sheep.**
    - **For Ex: Sulfate-reducing bacteria and some Archaea use sulfate as a terminal electron acceptor, producing hydrogen sulfide (H_2S) as a byproduct.**

Facultative and Obligate Anaerobes

- **Many bacteria and archaea are facultative anaerobes, meaning they can switch between aerobic respiration and anaerobic pathways (fermentation or anaerobic respiration) depending on the availability of oxygen.**
  - **This allows these prokaryotes to make more ATP with the energy of glucose molecules when O_2 is present - *since aerobic respiration makes more ATP than anaerobic pathways* - while also making some ATP in order to stay alive when O_2 is scarce.**

Facultative and Obligate Anaerobes

- Other bacteria and archaea are obligate anaerobes, meaning they can live and grow only in the absence of oxygen. Oxygen is toxic to these microorganisms and injures or kills them on exposure.
  - For instance, the Clostridium bacteria that are responsible for botulism (a form of food poisoning) are obligate anaerobes
    - Recently, some multicellular animals have even been discovered in deep-sea sediments where no oxygen gas exists.

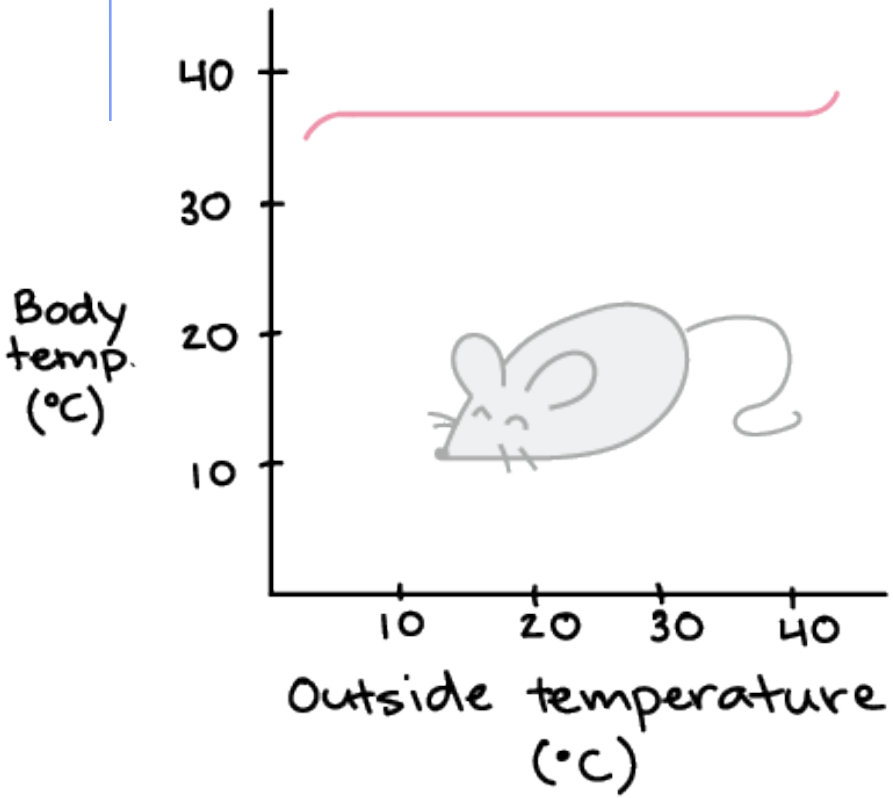


Thermoregulation

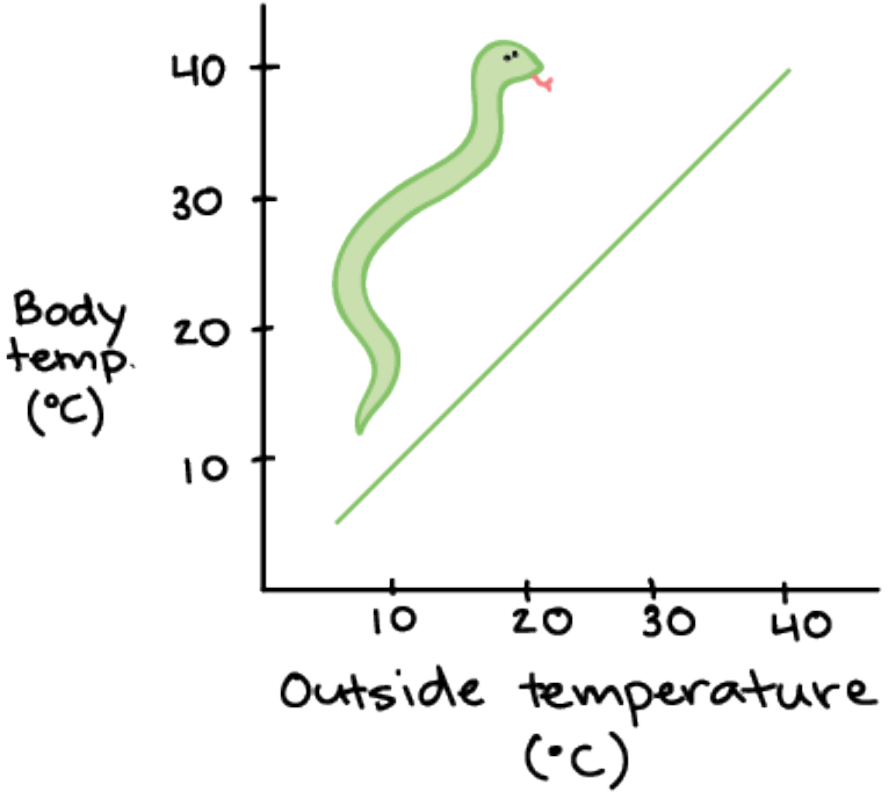
- Thermoregulation (controlling internal body temperature) in organisms runs along a spectrum from endothermy to ectothermy.
  - An ectotherm (like a reptile/amphibian) relies primarily on its external environment to regulate the temperature of its body.
    - Ectotherms use external sources of temperature to regulate their internal body temperatures.
  - An endotherm (like mammals/birds) is able to regulate their body temperatures by releasing extra energy in the form of heat (thermal energy) within the body as needed to maintain a steady body temperature.
    - Endotherms release most of their thermal energy through metabolic processes (cell respiration chemistry), using the heat to maintain a constant internal body temperature

Endytherms vs. Ectotherms

ENDOTHERMS
like the mouse generate metabolic heat to maintain internal temperature



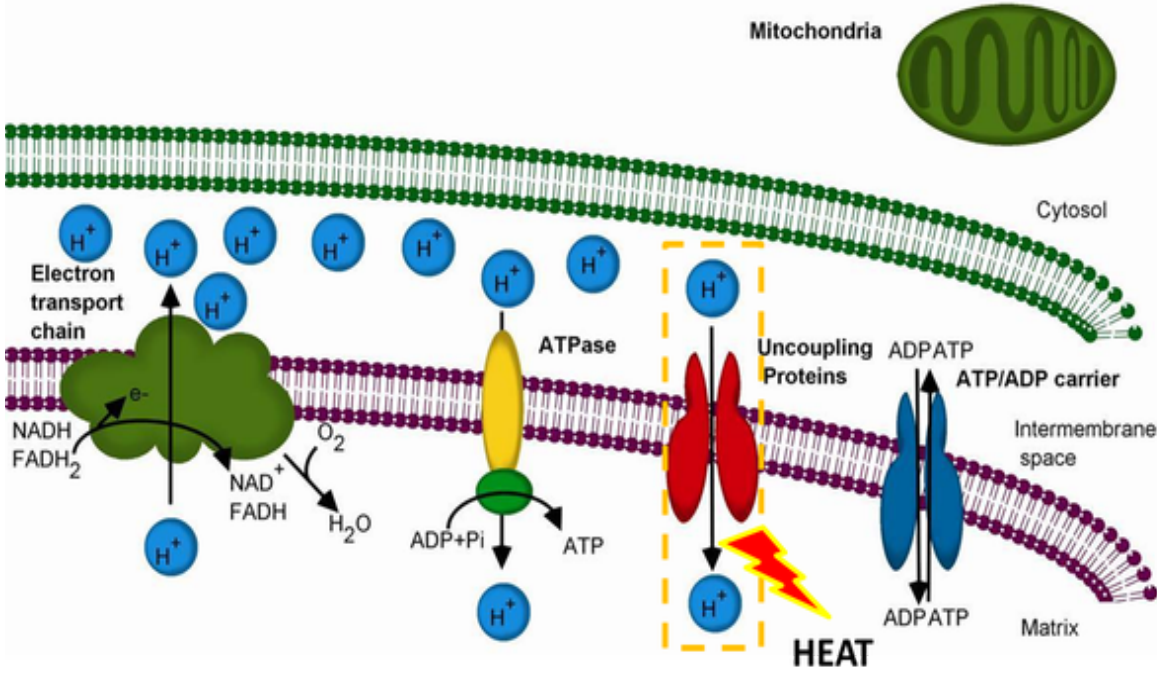
ECTOTHERMS
like the snake have a body temperature that changes with the temperature of the environment



Thermogenesis in Endotherm

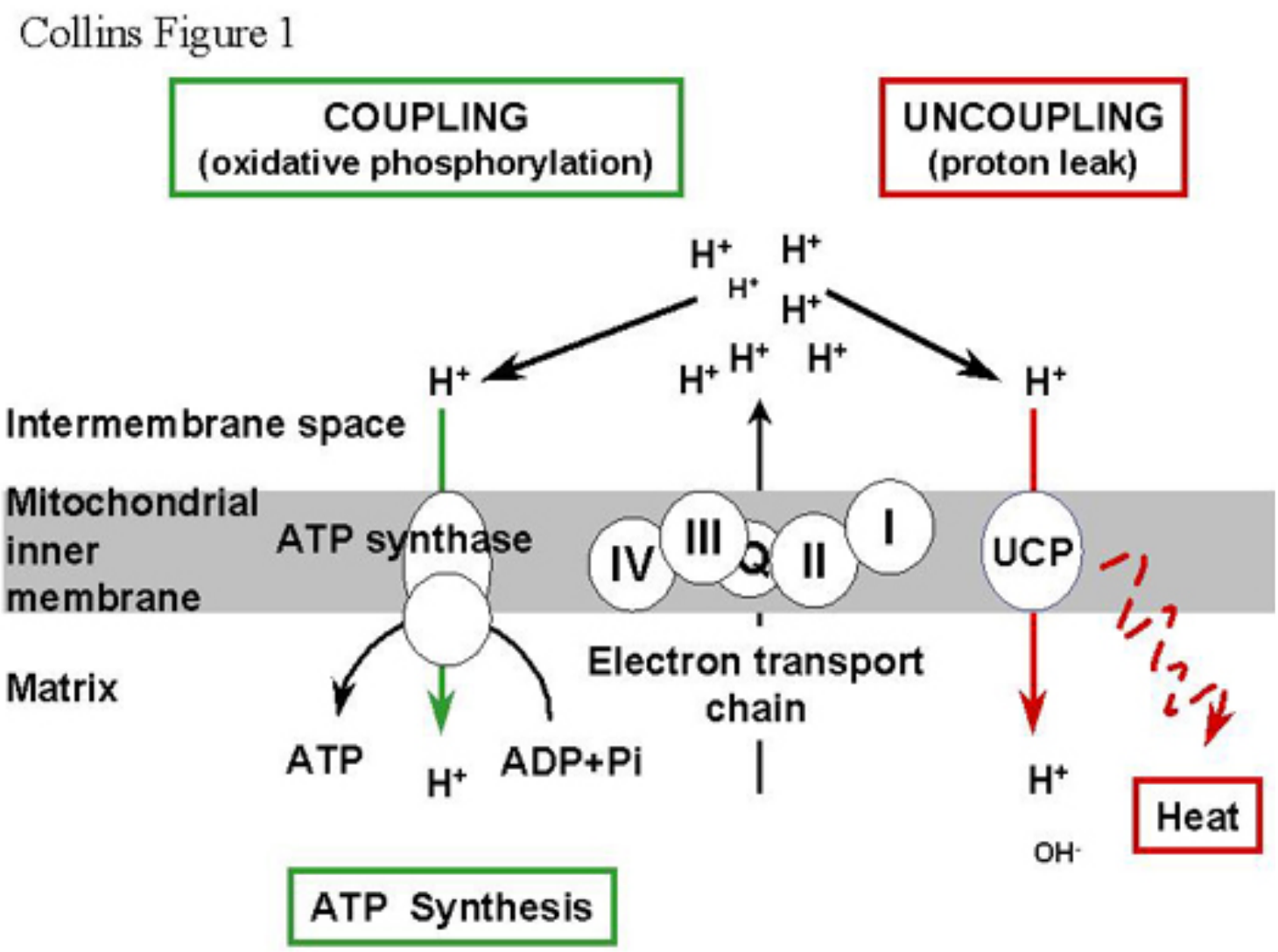
- **Endotherms use uncoupling proteins (UCP) located in the a mitochondrial inner membrane**
  - **Uncoupling proteins (UCPs) dissipate (erase) the proton gradient by allowing protons to diffuse back down their concentration gradient, releasing the stored potentially energy of the proton gradient as <u>heat</u>.**
    - **They are a regulated proton channel/transporter.**

- **The energy lost when the proton gradient is destroyed is <u>NOT</u> used to do cellular work.**
  - **Instead, the potential energy is lost as thermal energy: <u>HEAT</u> is generated!!!**



Thermogenesis in Endotherm

When protons diffuse back into the matrix through the Uncoupling Protein, potential energy is released from the proton gradient as HEAT instead of the potential energy being used to make ATP from ADP and Pi as happens when protons diffuse through ATP Synthase.

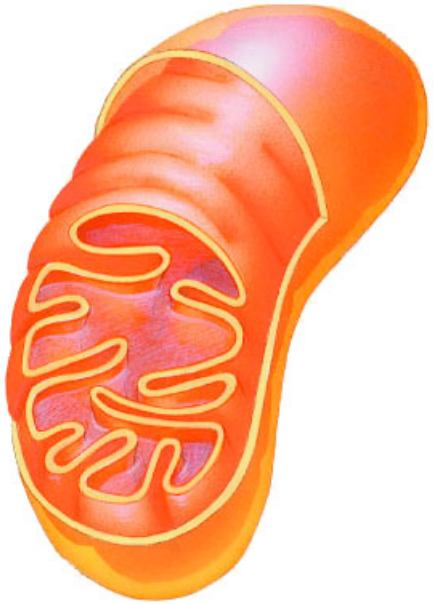


Thermogenesis in Endotherm

- Uncoupling proteins help endotherms ("warm blooded animals") maintain a steady internal body temperature
  - They use the energy extracted from high-energy organic molecules like glucose to generate heat
- Hibernating bears drop their metabolic rates during winter, but maintain a steady body temperature.
  - Hibernation (when a bear does not wake or forage - search/hunt for and ingest nutrients and water) is an adaptation for surviving winter time when food and liquid water are scarce and energy for those activities is not easily found
    - The uncoupling protein allows a bear to release the energy stored in fat molecules made during the Summer & Fall in order to generate heat (for thermogenesis) instead of for the producing ATP alone.

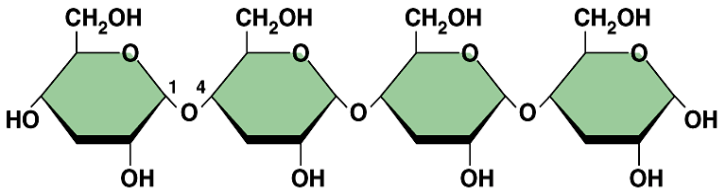
Thermogenesis in Endotherm

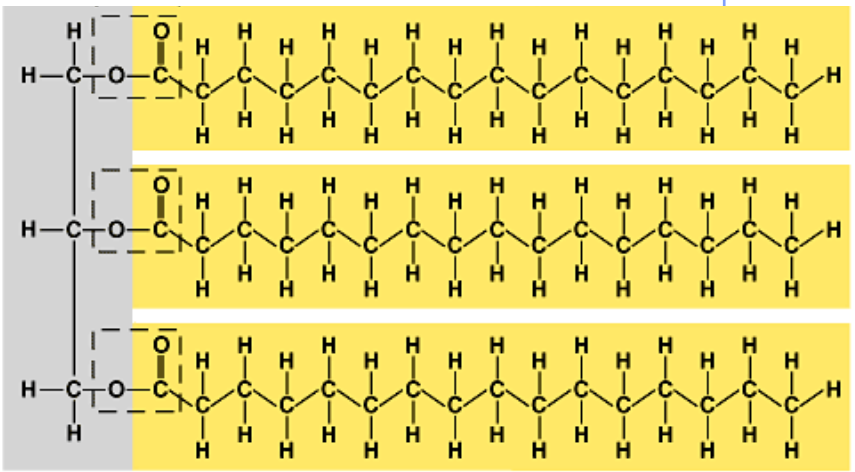
- **Even some ectotherms use uncoupling proteins for special purposes, maximizing their biological fitness.**
  - **Eastern skunk cabbage keeps the temperature of its spikes as much as 20°C higher than the environment**
    - **At warmer temperatures, odor molecules evaporate faster into the air, allowing the flower to attract insects better**
      - **Acting as pollinators, the insects accidentally carry the pollen (within which the sperm cells are made) from one plant flower to another (where the egg is kept), increasing the reproductive success of this species of plant.**



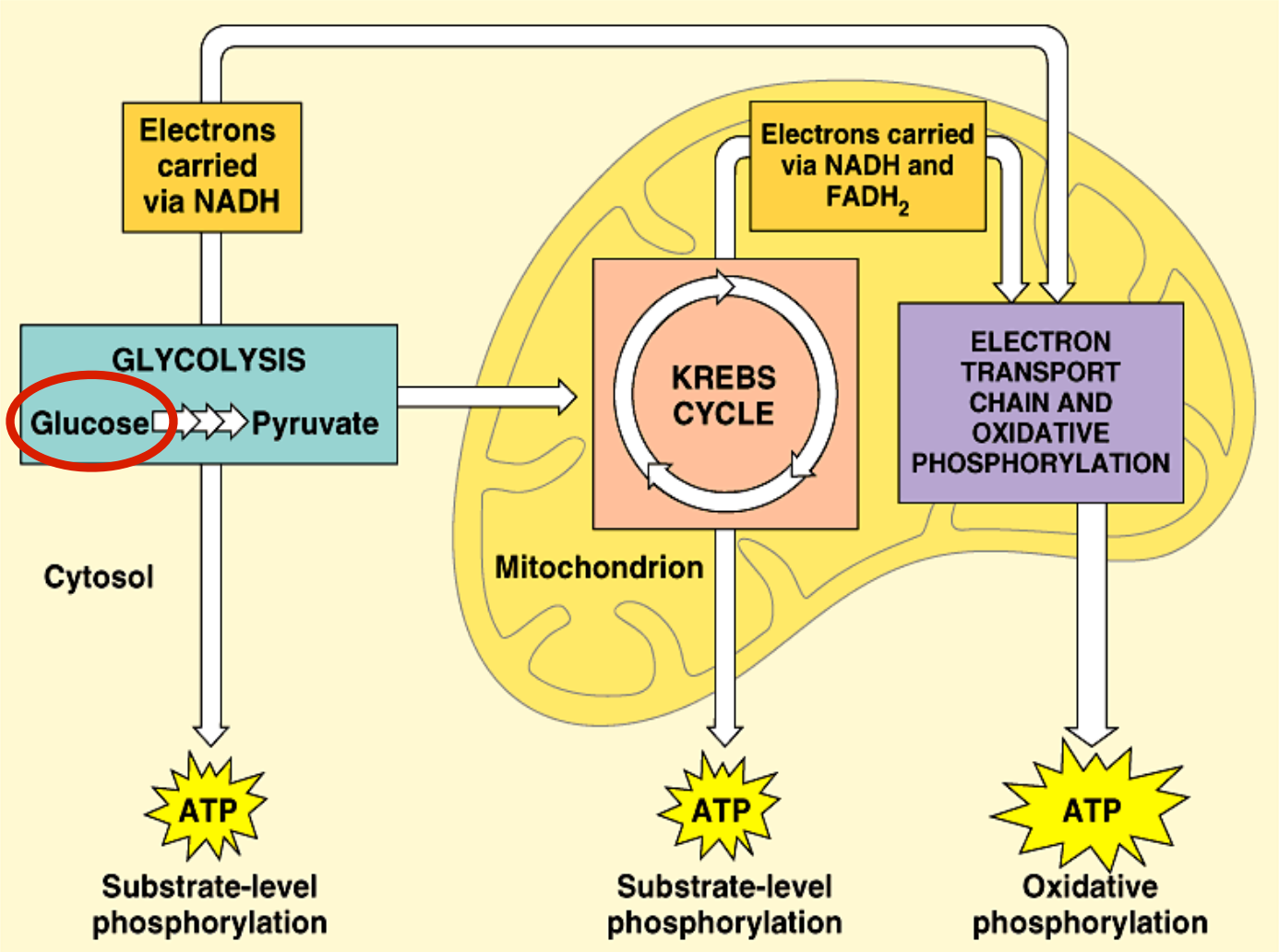
Cellular Respiration

Other Metabolites &
Control of Respiration





Cellular respiration Can use More than Only Glucose



Carbohydrate, fats, & proteins can ALL be used as fuel for cellular respiration!

Monomers of these enter glycolysis OR the citric acid cycle at various points.

Beyond glucose: Other carbohydrates

- **Glycolysis accepts a wide range of carbohydrate fuels.**
  - Polysaccharides can be broken down into their individual glucose monomers
  - Monosaccharides can often be converted to glucose or one of glycolysis' intermediates

polysaccharides → → → glucose
hydrolysis

- ex. starch, glycogen

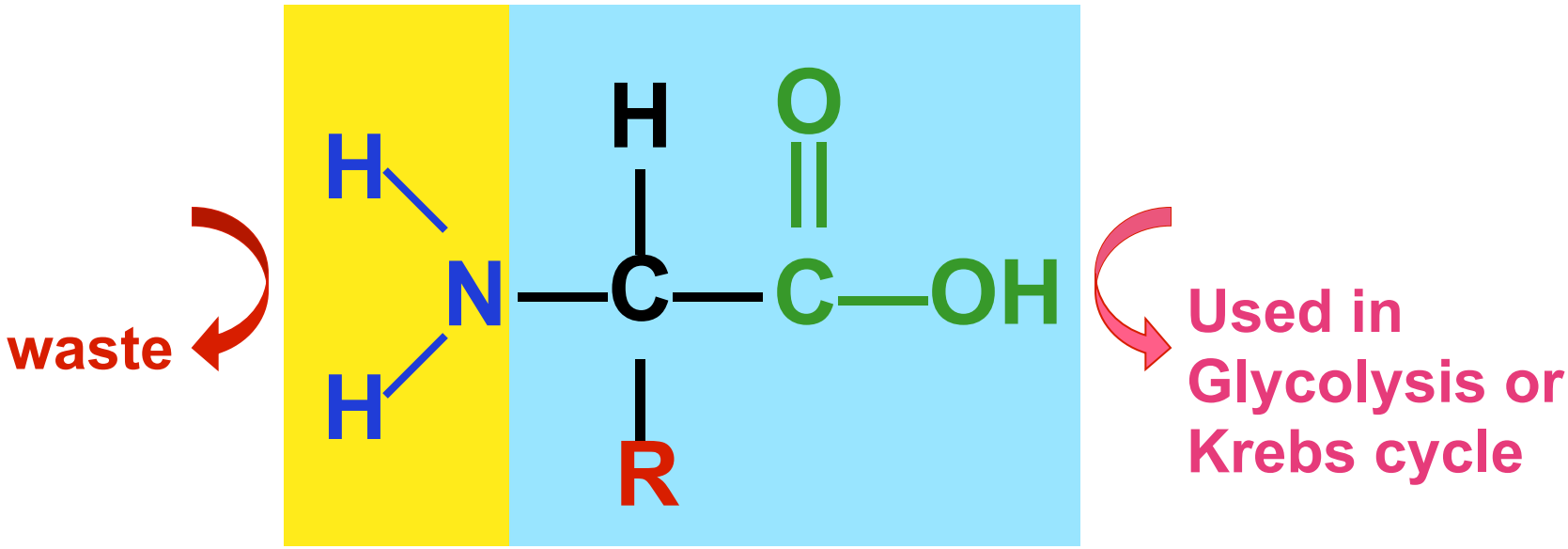
other 6C sugars → → → glucose
modified

- ex. galactose, fructose

GLYCOLYSIS

Beyond glucose: Proteins

proteins → → → → → amino acids
hydrolysis



amino group = During deamination, the amino group is removed, becoming a waste product, transported out of the cell and excreted from the animal body as ammonia, urea, or uric acid

2C sugar skeleton = Enzymes change the 2C portion of the amino acid into intermediates of glycolysis or Krebs cycle (enter at different stages)

Beyond glucose: Fats

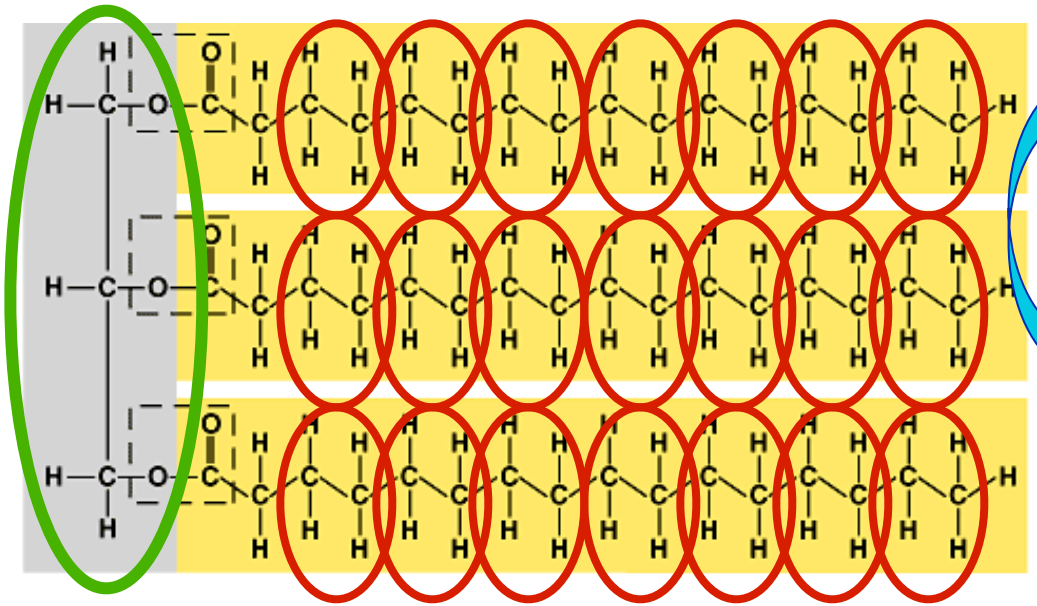
fats → → → → → glycerol + fatty acids
hydrolysis

glycerol (3C) → → G3P → → glycolysis

fatty acids → 2C acetyl groups → acetyl coA → Krebs cycle

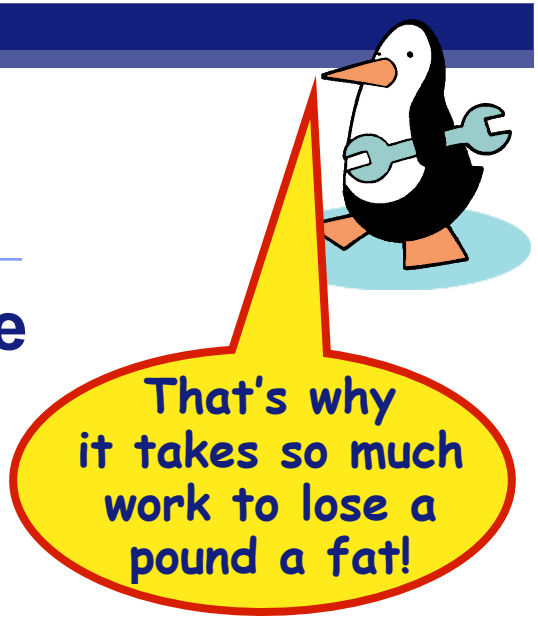
3C glycerol

Enters glycolysis as G3P (glycolysis intermediate)



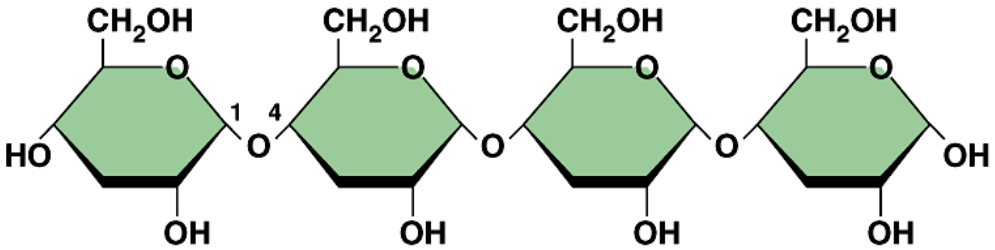
Fatty acids undergo Beta Oxidation, which converts them into 2C fragments and reduces $NADH$ & $FADH_2$ carrying e-'s for the ETC. 2C-molecules enter the Krebs Cycle as acetyl CoA

Carbohydrates vs. Fats

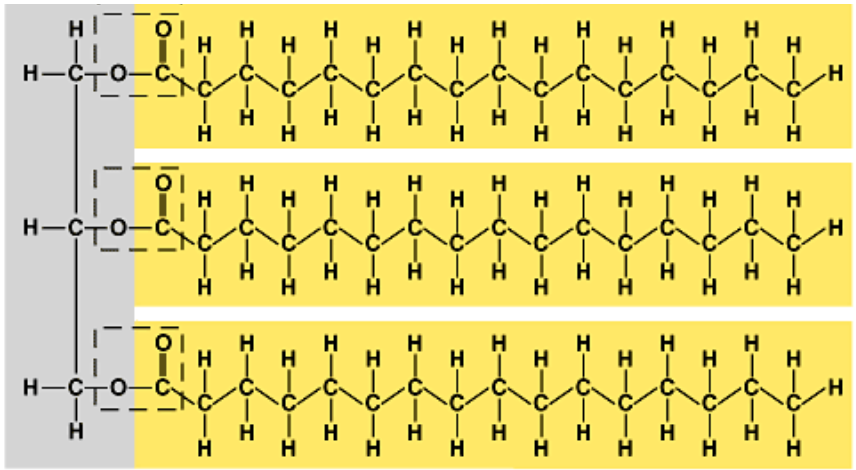


- Fat generates 2x ATP vs. carbohydrate
  - more C in a gram of fat
    - more energy releasing C-H bonds
  - more O in gram of carbohydrate
    - so carbohydrate (with C-O & H-O bonds) are already partly oxidized - *contain fewer high-energy e-'s*
    - less energy available

carbohydrate



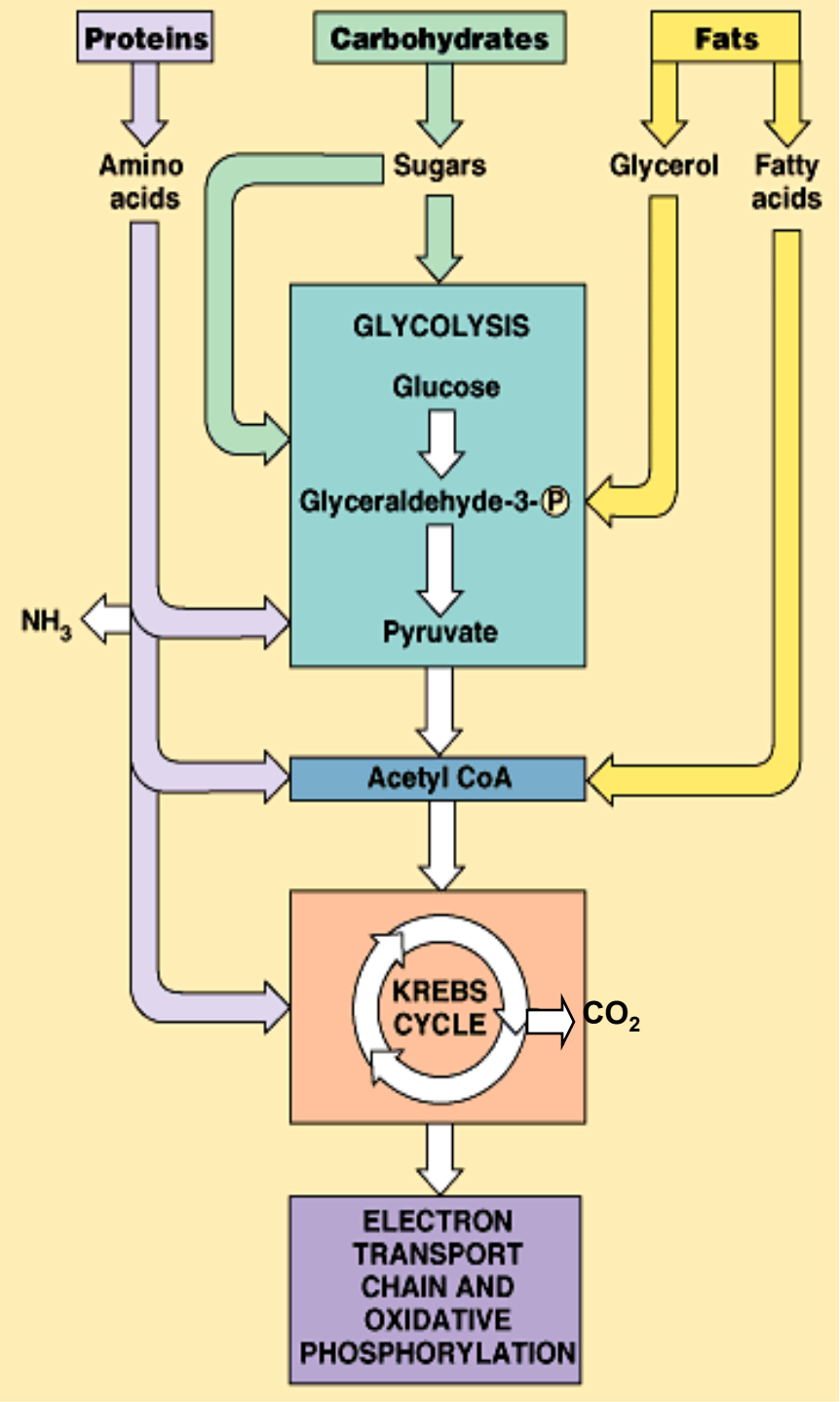
fat



Metabolism

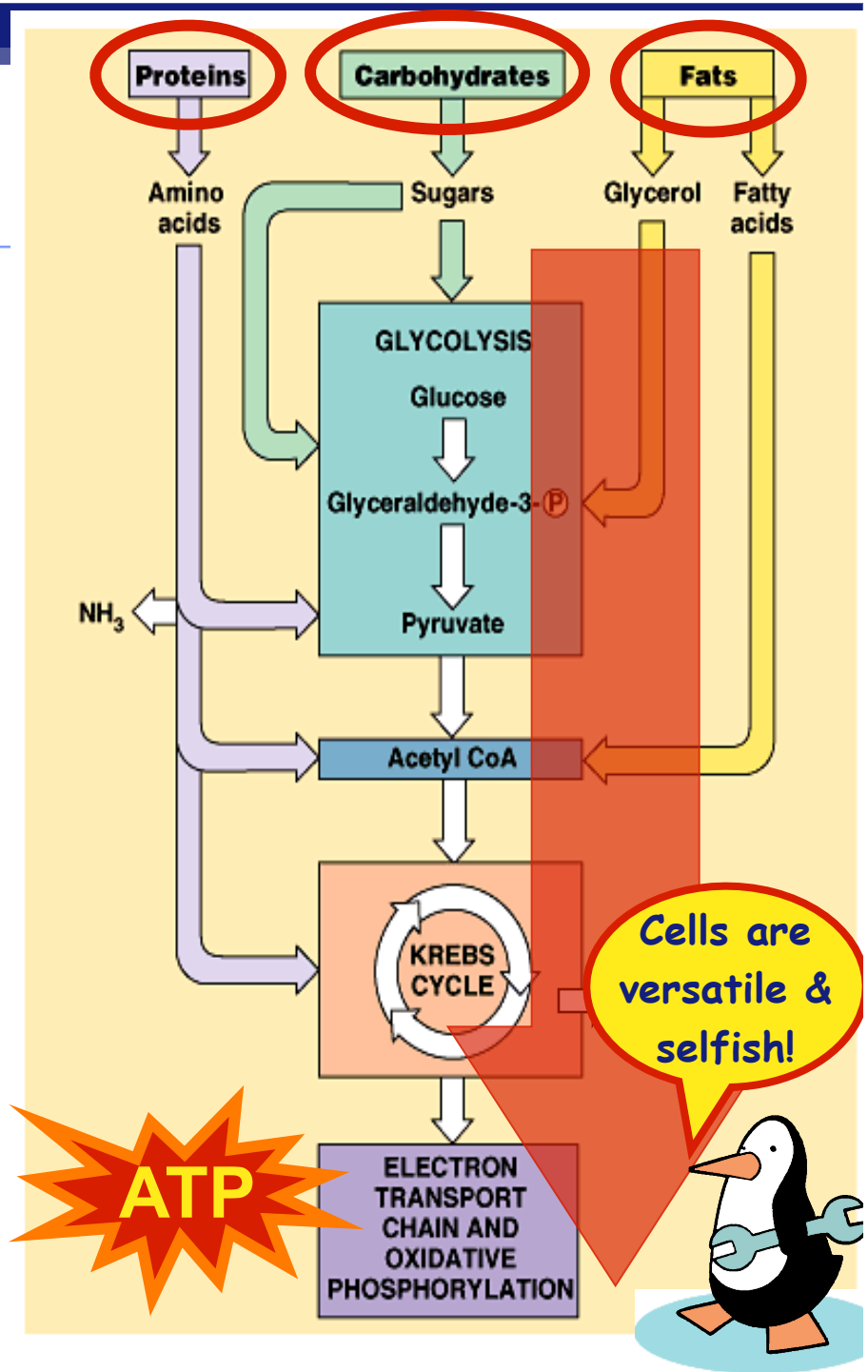
Coordination of chemical processes across organism must occur:

- **DIGESTION**
  - catabolism occurs when organism needs energy or needs raw materials
- **BIOSYNTHESIS**
  - anabolism occurs when organism has enough energy & a large supply of raw materials
- **REGULATION BY ENZYMES**
  - feedback mechanisms
    - raw materials (reactants) stimulate more production
    - products inhibit further production



Metabolism

- **Digestion**
  - digestion of carbohydrates, fats & proteins
    - enter cellular respiration pathway at different points
    - all catabolized (broken down) through same pathways of cellular respiration
  - Cells extracts energy from every available source!

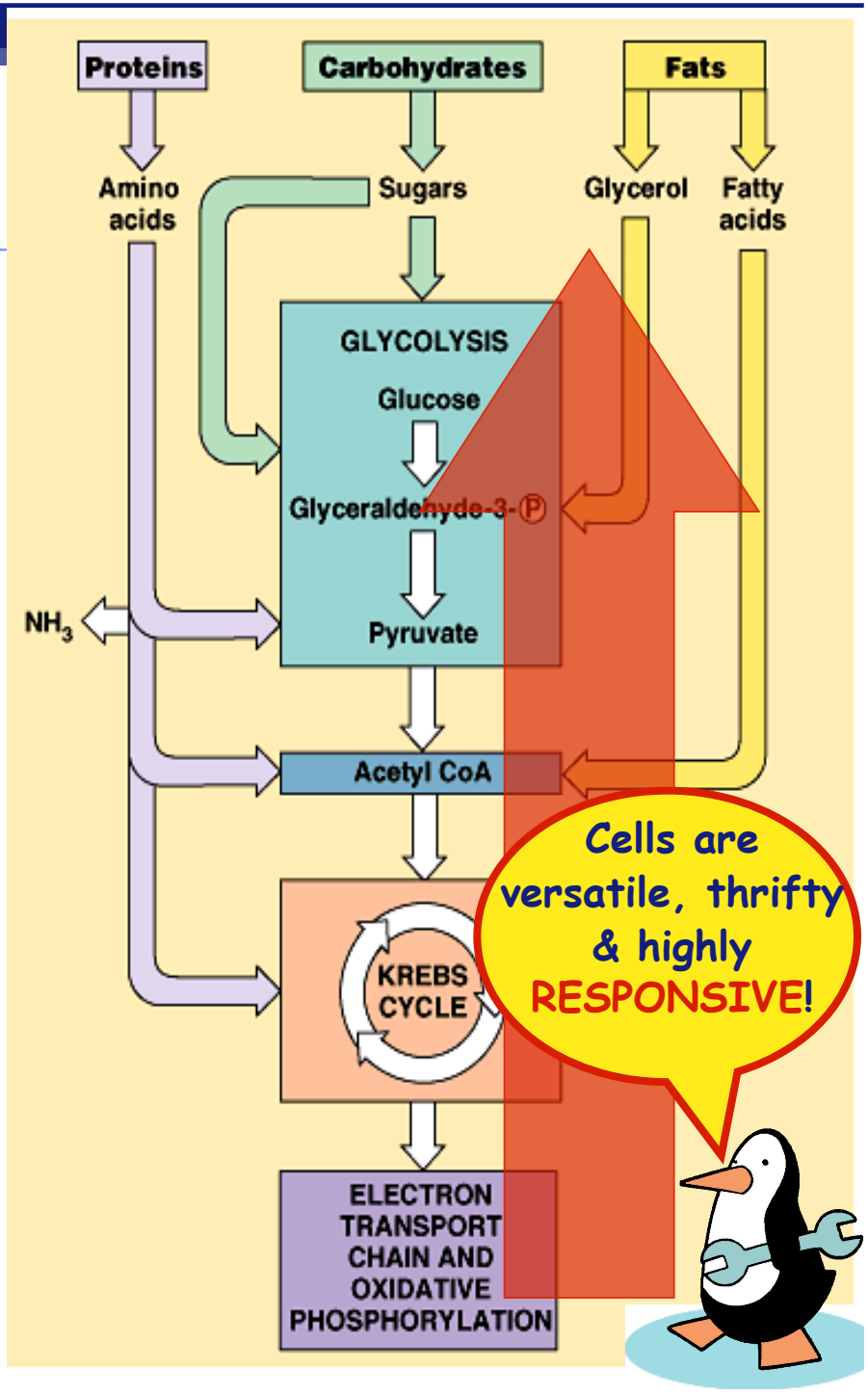


Metabolism

- **Synthesis**
  - Got enough energy (ATP)?

    Let's build stuff then instead of catabolizing organic molecules to build ATP*!*
    - cells can use the intermediates of glycolysis & the Krebs cycle in other biochemical pathways to synthesize other types of organic molecules

pyruvate	→ →	glucose
Krebs cycle intermediaries	→ →	amino acids
acetyl CoA	→ →	fatty acids



It gets complicated:

Glycolysis & the Krebs cycle function as metabolic interchanges that enable cells to convert one kind of molecule to another as needed.

Ex: A human cell can synthesize about half the 20 different amino acids by modifying compounds from the Krebs cycle. These are essential to your body but not essential in your diet.

Ex: Excess carbohydrates & proteins can be converted by putting them into the cellular respiration Glycolysis and/ or Krebs Cycle pathways into intermediates that can be used to build fat molecules (to store in fat cell). This is a way of storing energy long term and in an efficient way.

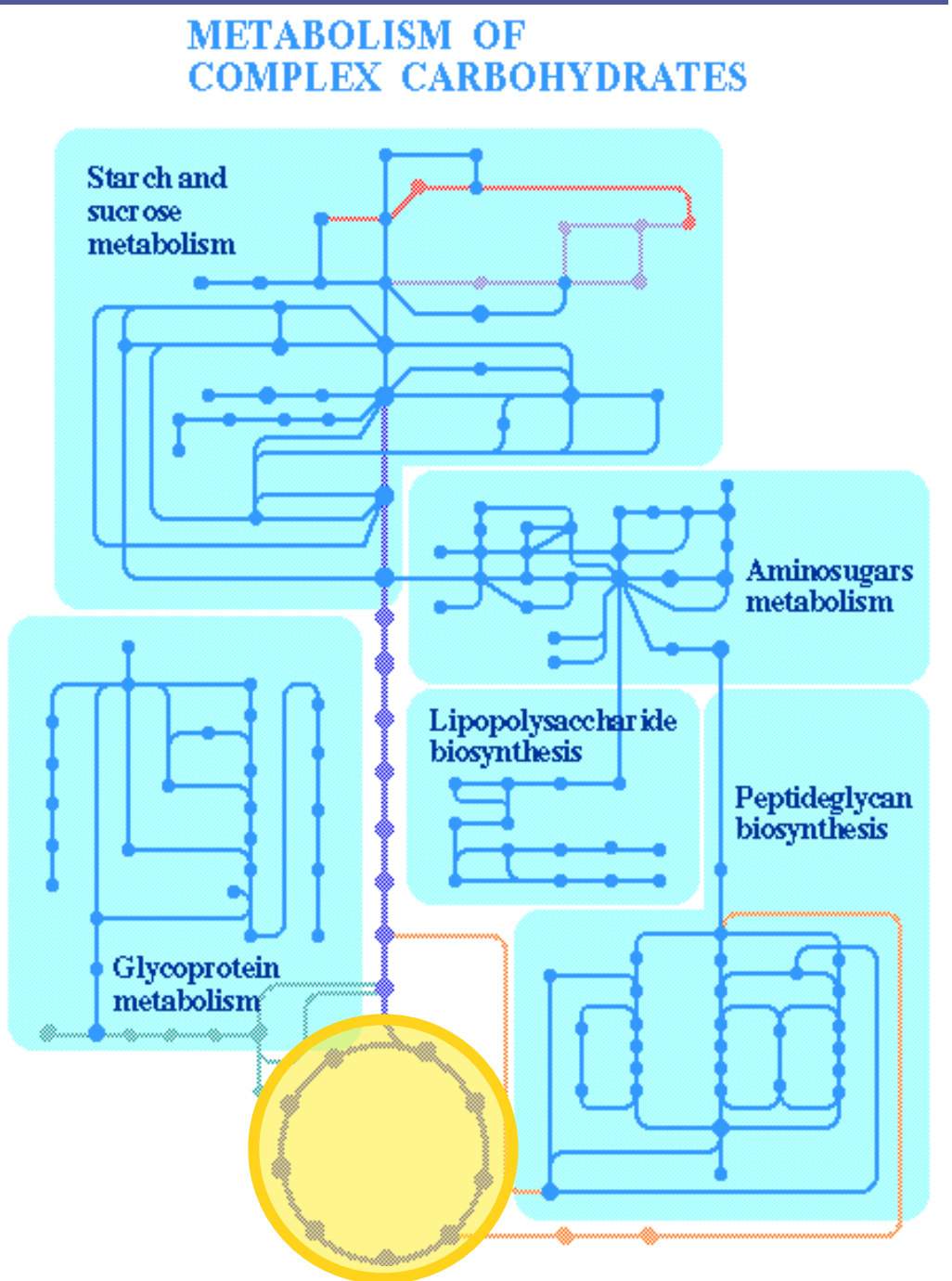
- **You can make fat from eating too much sugars and carbohydrates!!**

Carbohydrate Metabolism

The many stops on the Carbohydrate Line

from Krebs cycle back through glycolysis

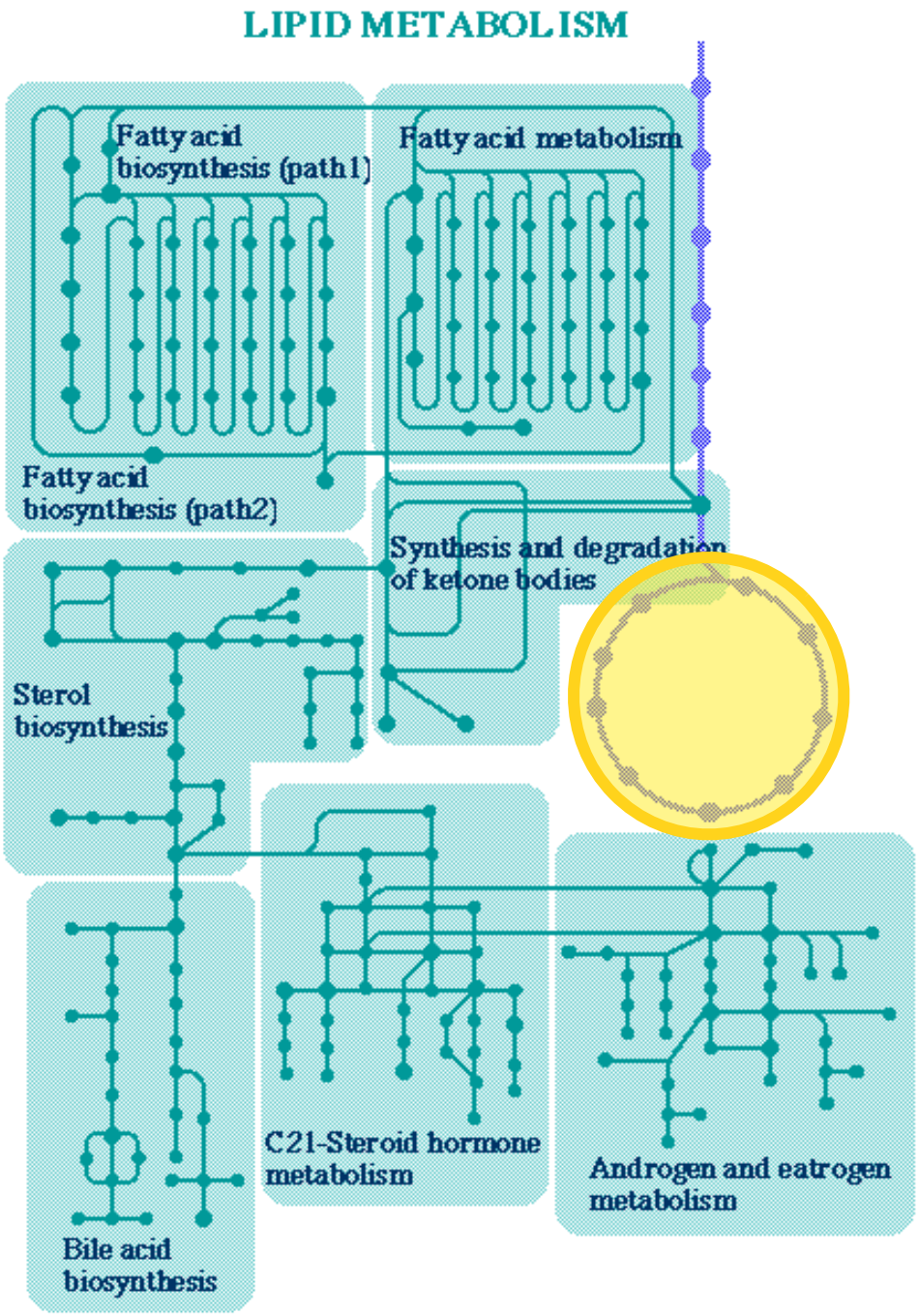
"gluconeogenesis" =
running glycolysis in reverse to build glucose



Lipid Metabolism

The many stops on the Lipid Line

from Krebs cycle intermediates & acetyl CoA to a variety of lipid synthesis pathways

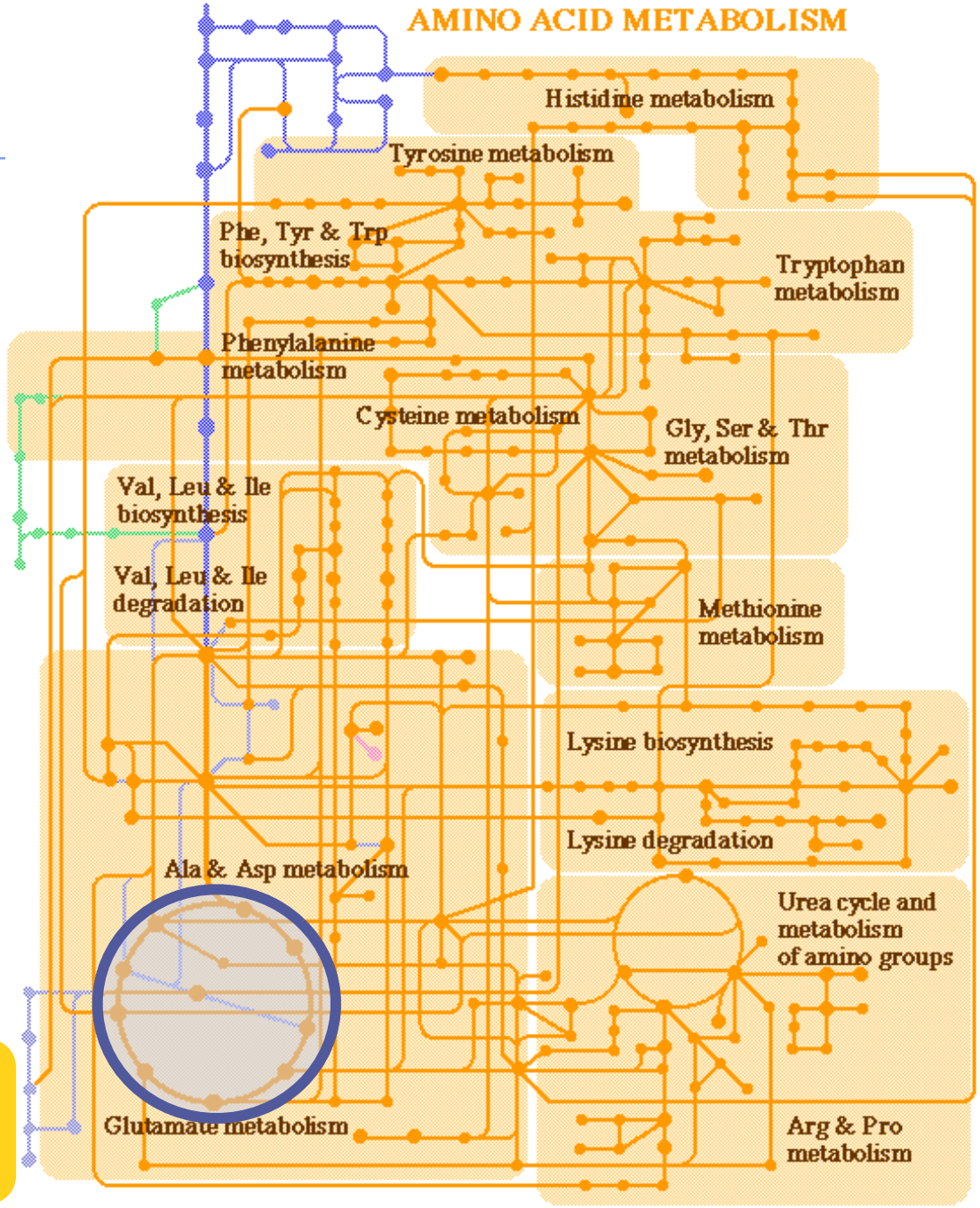


Amino Acid Metabolism

The many stops on the Amino Acid Line

from Krebs cycle & glycolysis to an array of amino acid synthesis pathways

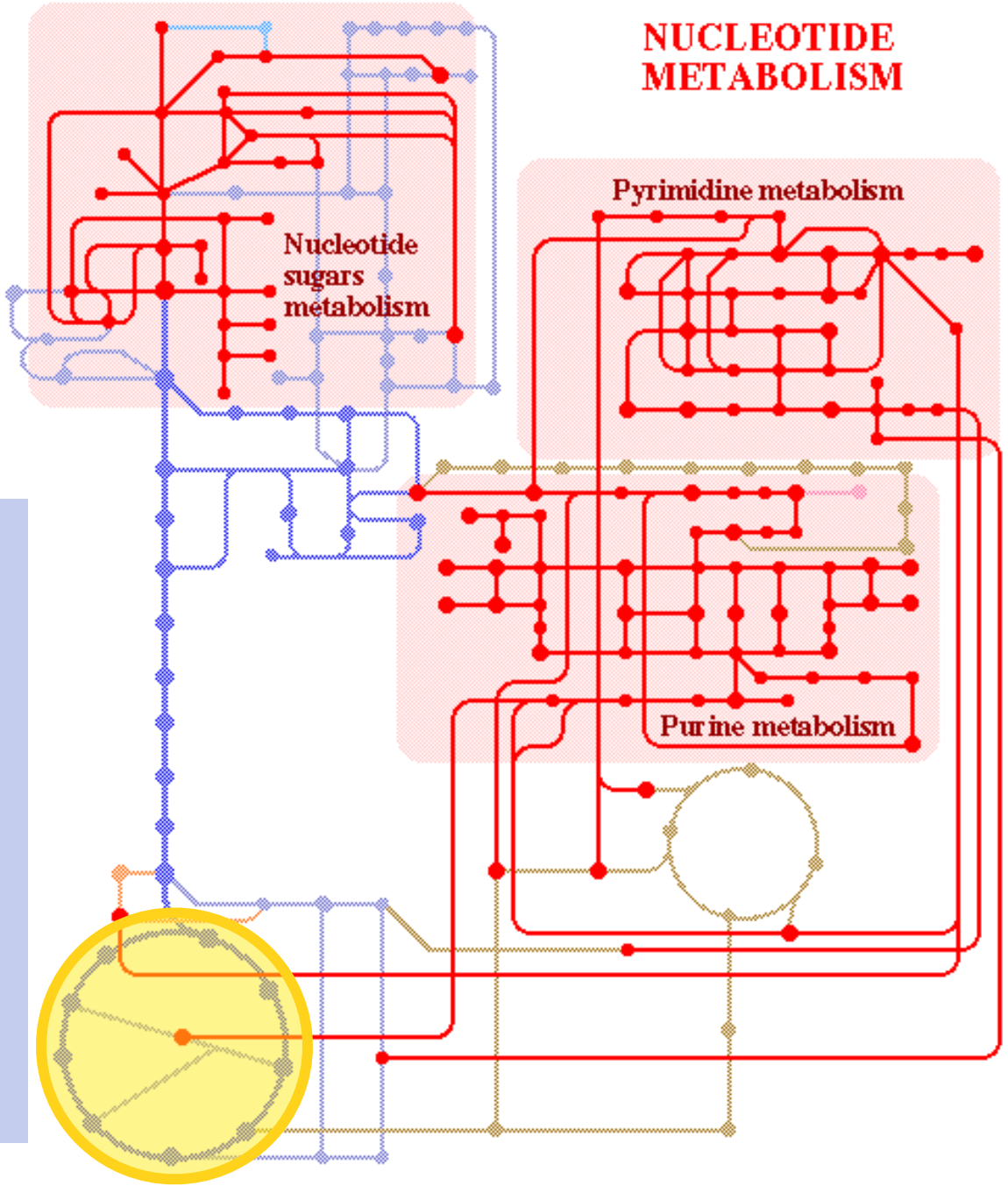
8/9 essential amino acids
11/12 synthesized a.a.'s



Nucleotide Metabolism

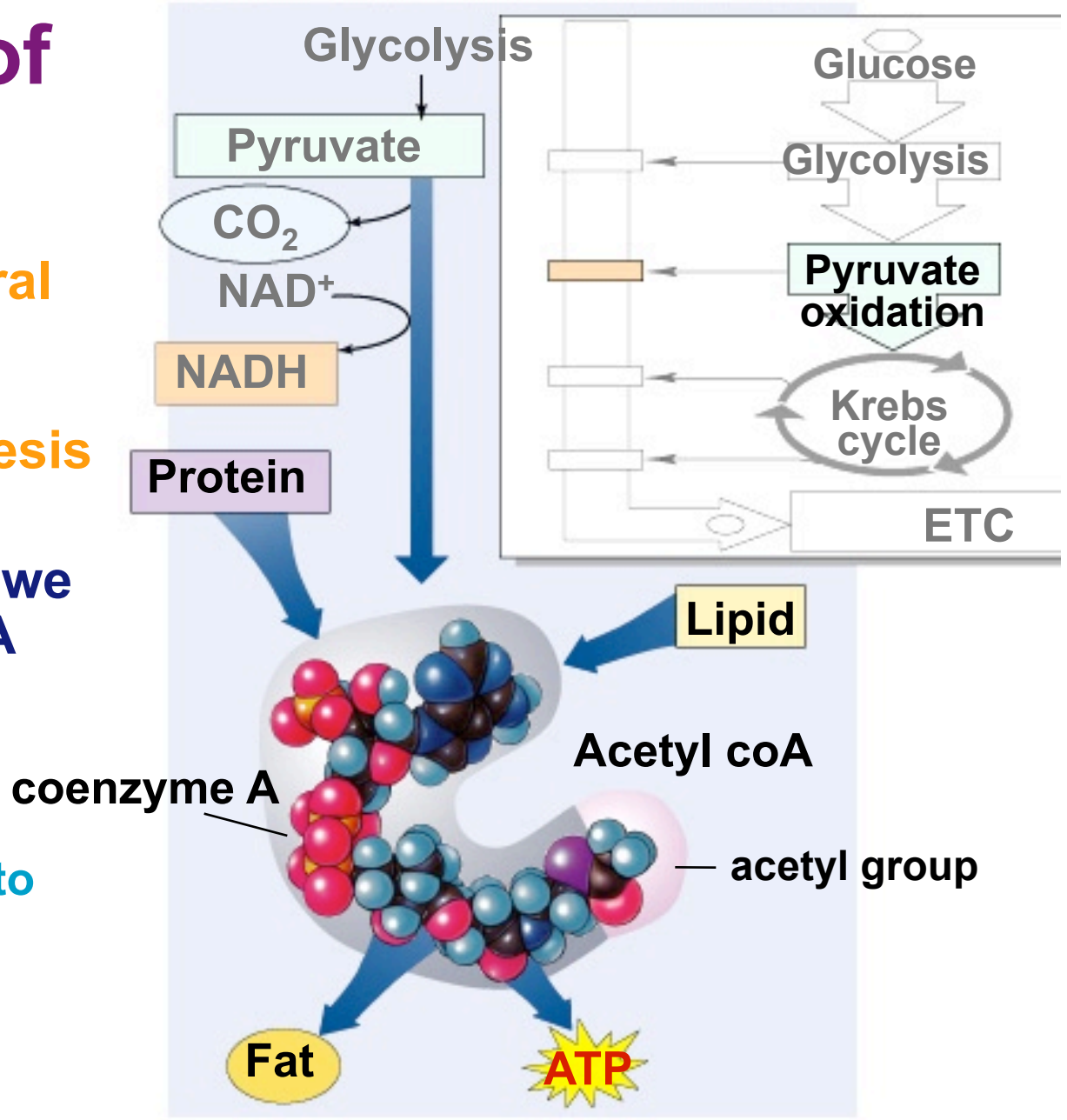
The many stops on the ATCG Line

- sugar from glycolysis
- phosphate & Nitrogenous base made from Krebs cycle intermediaries



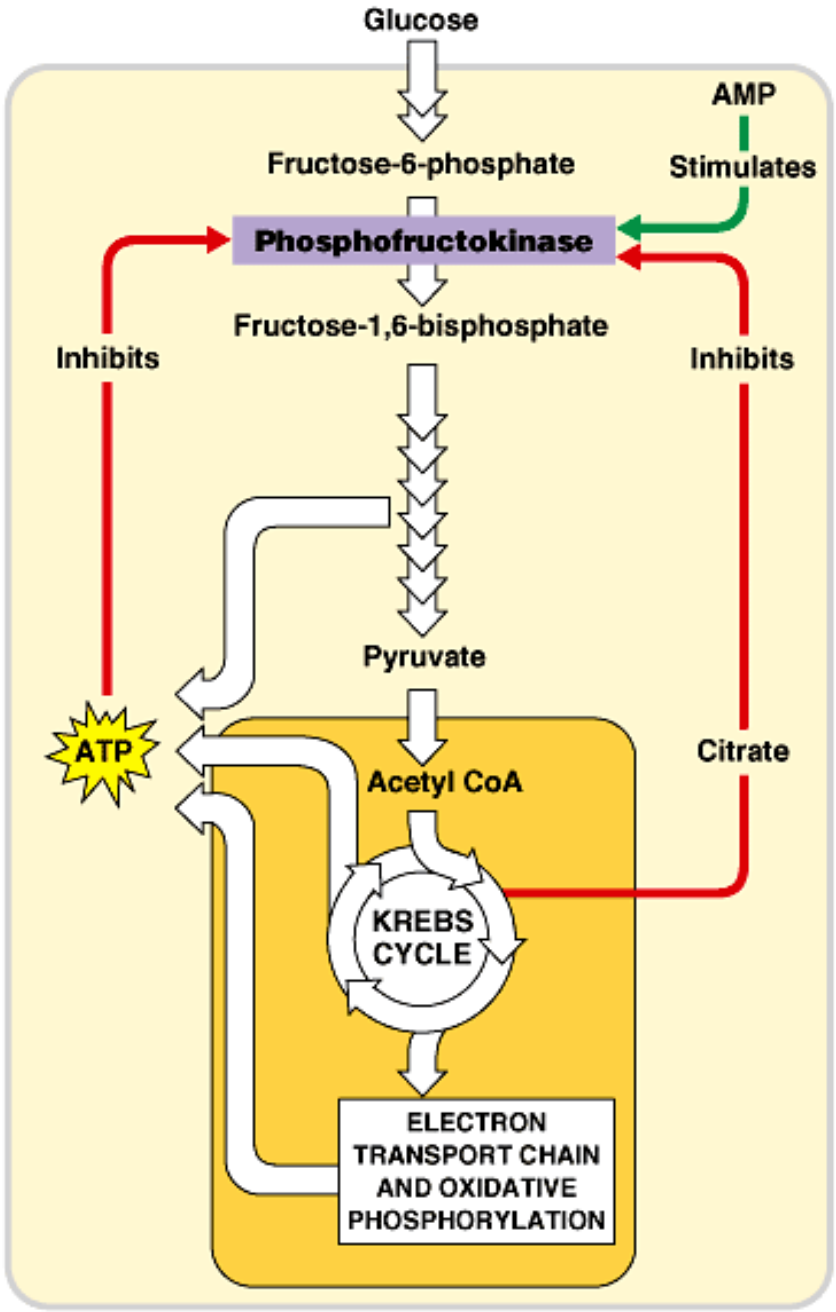
Central Role of Acetyl CoA

- Acetyl CoA is central to both energy production & biomolecule synthesis
- Depending on organism's needs, we can use Acetyl CoA to…
  - build ATP
    - To carry energy immediate use to do work with
  - build fats
    - To store energy long term



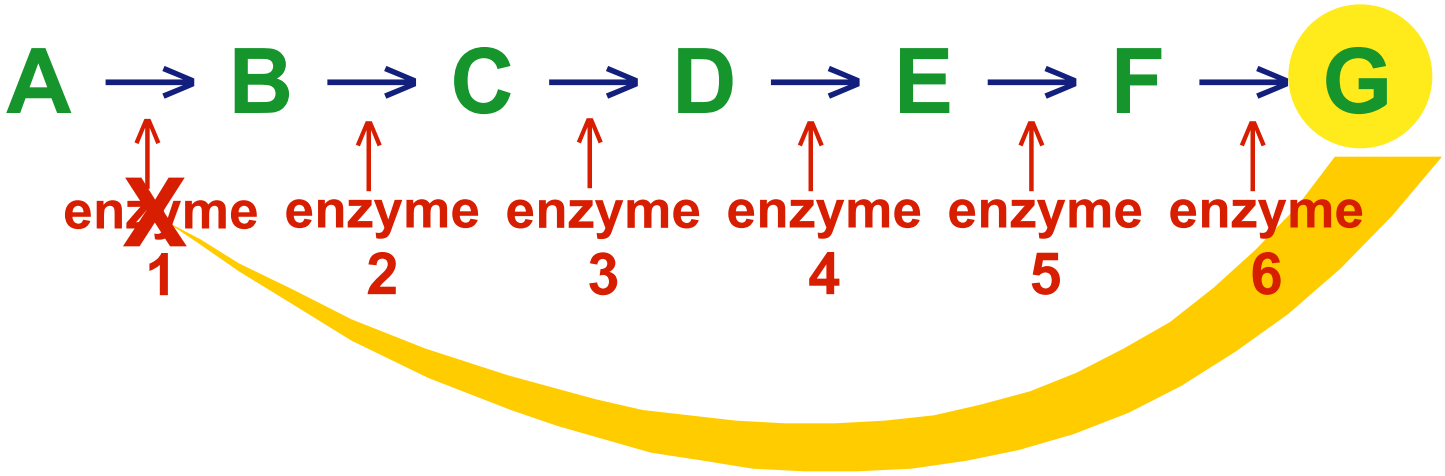
Control of Respiration

Feedback Control



Feedback Inhibition is used to regulate the rates of glycolysis

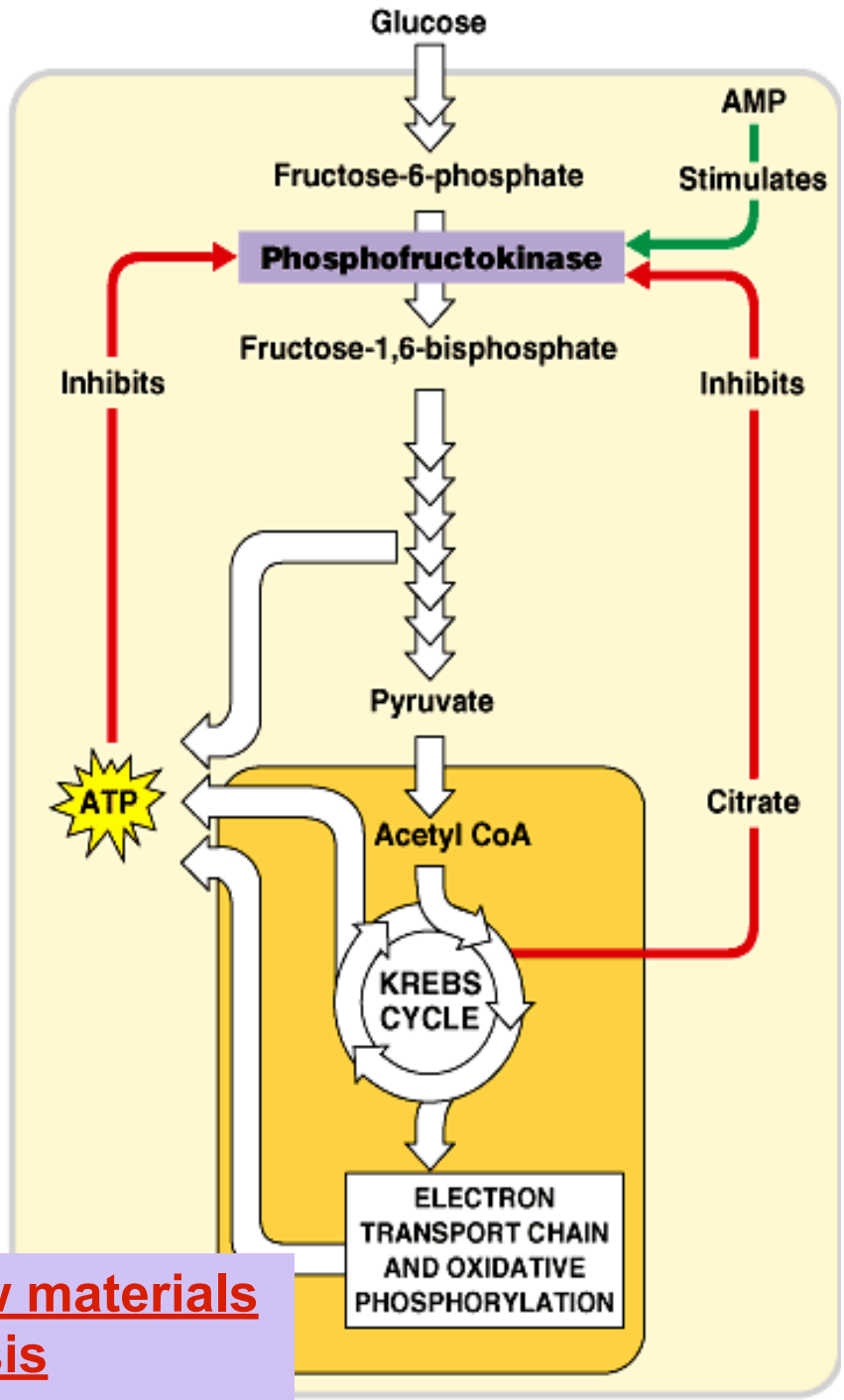
- **Regulation & coordination of production**
  - final product is inhibitor of earlier step in pathway
    - It is the allosteric inhibitor of an earlier enzyme in its own biochemical pathway
  - no unnecessary accumulation of product will thus occur
    - Production of product is self-limiting



G is an allosteric inhibitor of enzyme 1

Key point of control: Phosphofructokinase (ENZYME)

- This is an allosterically regulated enzyme of glycolysis
  - Why here? The chemical reaction catalyzed represents the "can't turn back" step before the splitting glucose occurs.
    - This key enzyme controls the commitment step of glycolysis right before glucose is cleaved into 2 3C sugars

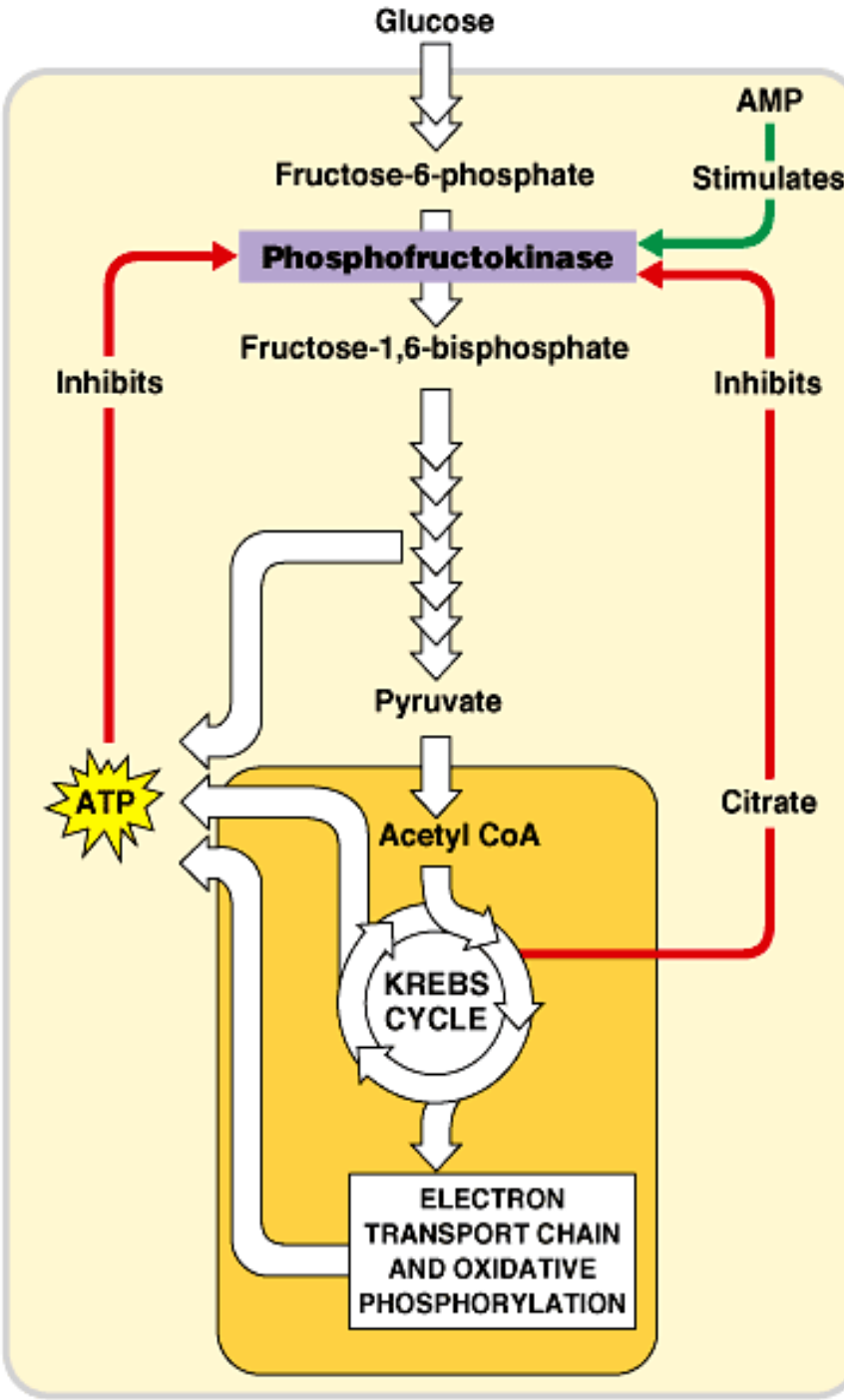


Why is this regulation important?

Life is a balancing act: Availability of raw materials vs. energy demands vs. need for synthesis

Key point of control: Phosphofructokinase (ENZYME)

- Allosteric regulation of PFK allows us to only run glycolysis when needed.
  - AMP & ADP stimulate PFK
  - ATP inhibits PFK
  - Citrate inhibits PFK
    - Citrate, the first product of the Krebs cycle.
    - Too much citrate accumulation in the mitochondria and cytoplasm means that Krebs cycle is backing up.



Basic principles of supply & demand regulate metabolic economy

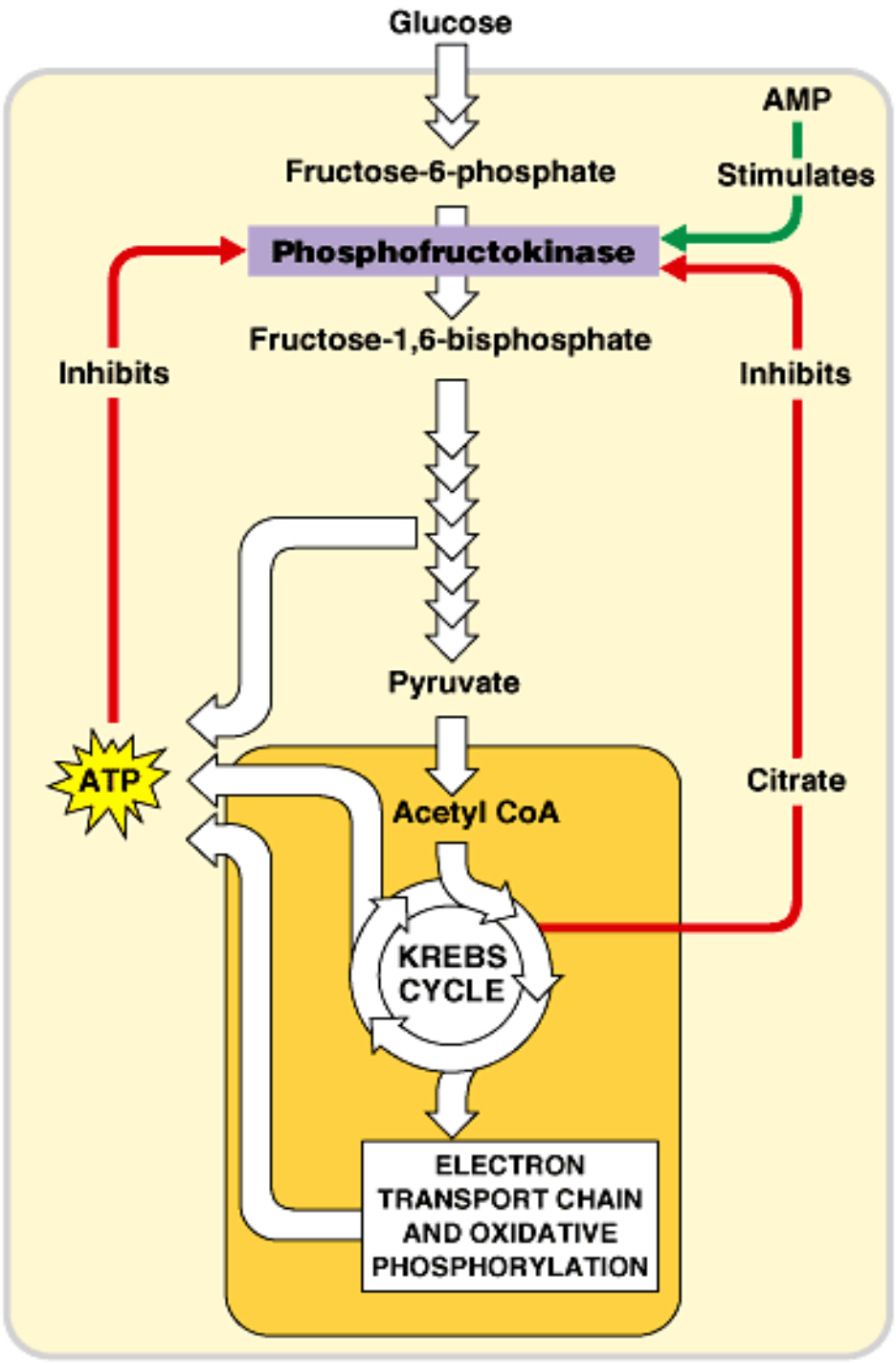
- **Raw material and products become feedback regulators**
  - they control enzymes at strategic points in glycolysis & Krebs cycle
    - levels of AMP, ADP, ATP
      - Regulate final products & raw materials of cell. resp.
    - levels of intermediates compounds in pathways
      - regulate earlier steps in cell. resp. pathways
    - levels of other biomolecules in the cell/body
      - regulates rate of siphoning off of cell respiration intermediates to other synthesis pathways

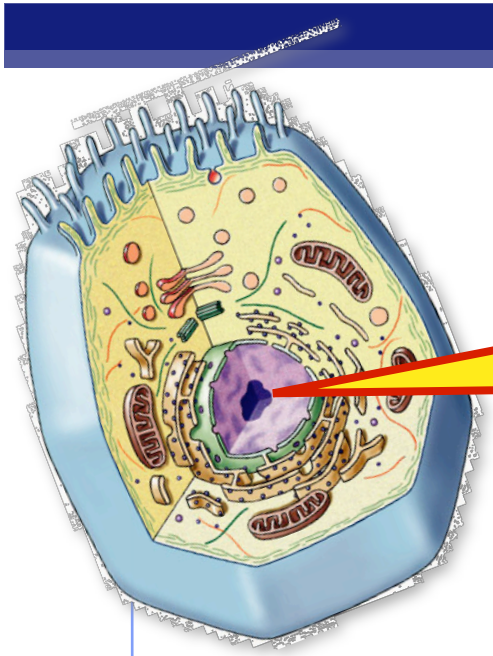
EX: When there is an excess of an amino acid in the cell, feedback inhibition prevents diversion of more intermediary molecules from the Krebs cycle to the synthesis pathway of that amino acid.

Ex: If intermediaries from the Krebs cycle are diverted to other uses (e.g., amino acid synthesis), glycolysis speeds up to replace these molecules.

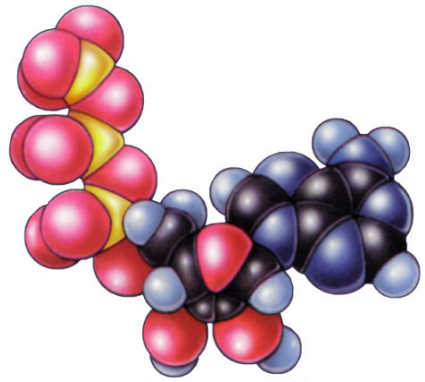
It's a Balancing Act

- Balancing synthesis with availability of both energy & raw materials is essential for survival!
  - do it well & you survive longer
  - you survive longer & you have more offspring
  - you have more offspring & you get to "take over the world" :)



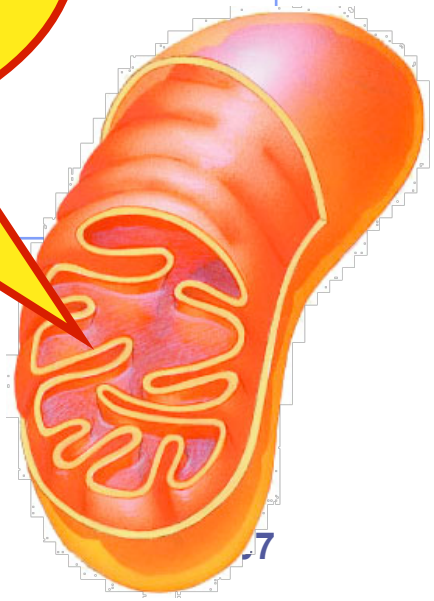


What's the point?



The point is to make ATP!

ATP



Got the energy…

Ask Questions*!!*