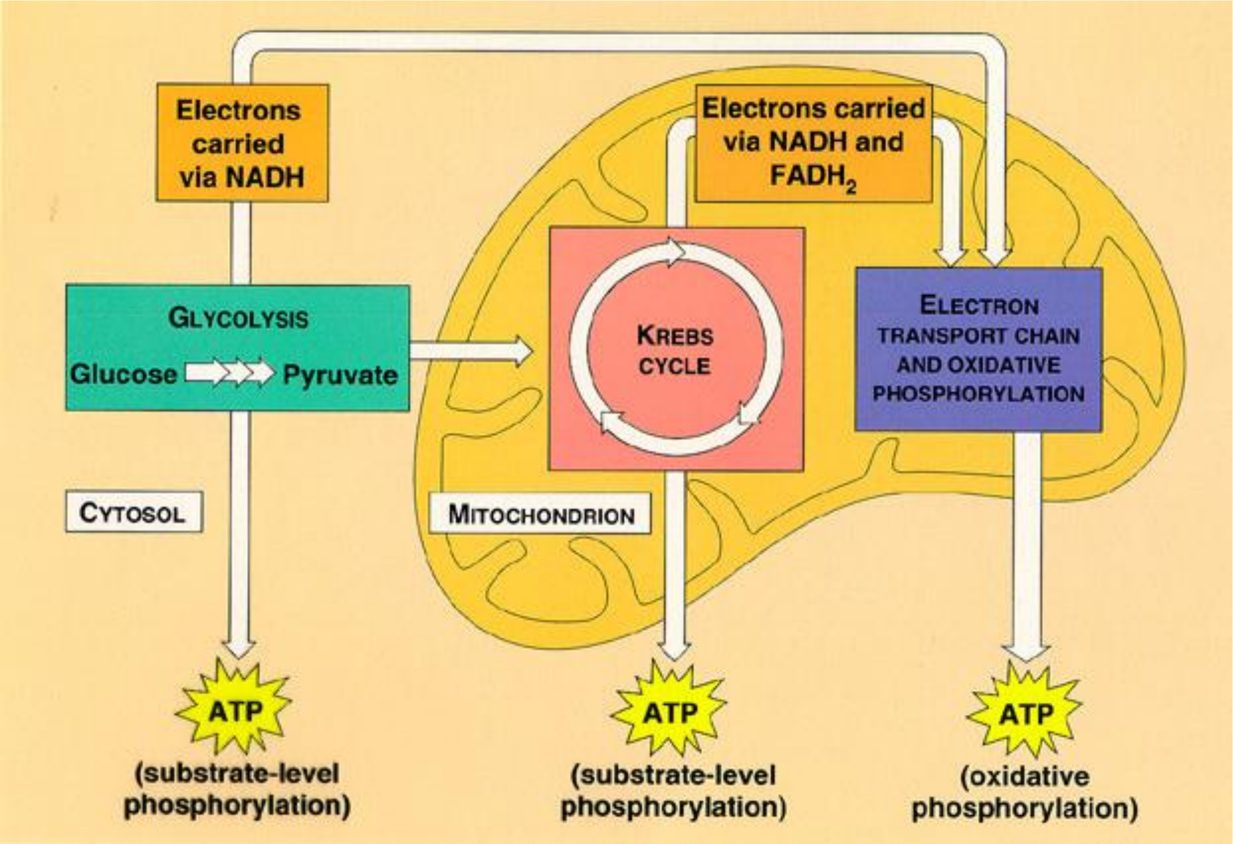
Chapter 07

Cellular Respiration

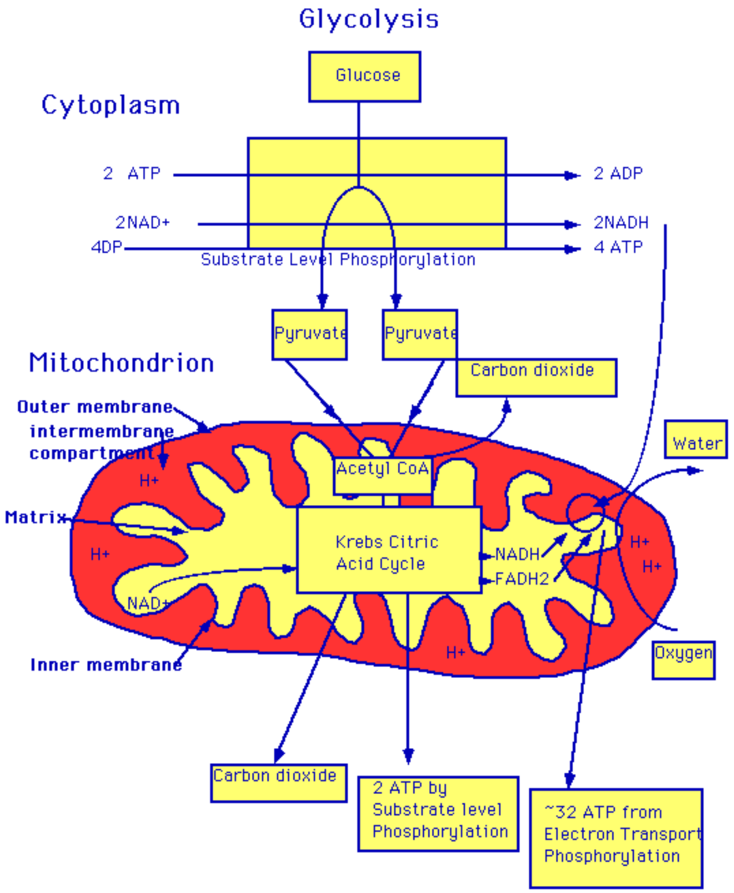


http://www.mobento.com/video/DiyoEA5Mc

Important study hints

- Draw out processes on paper and label structures and steps

- Keep working on those flash cards!

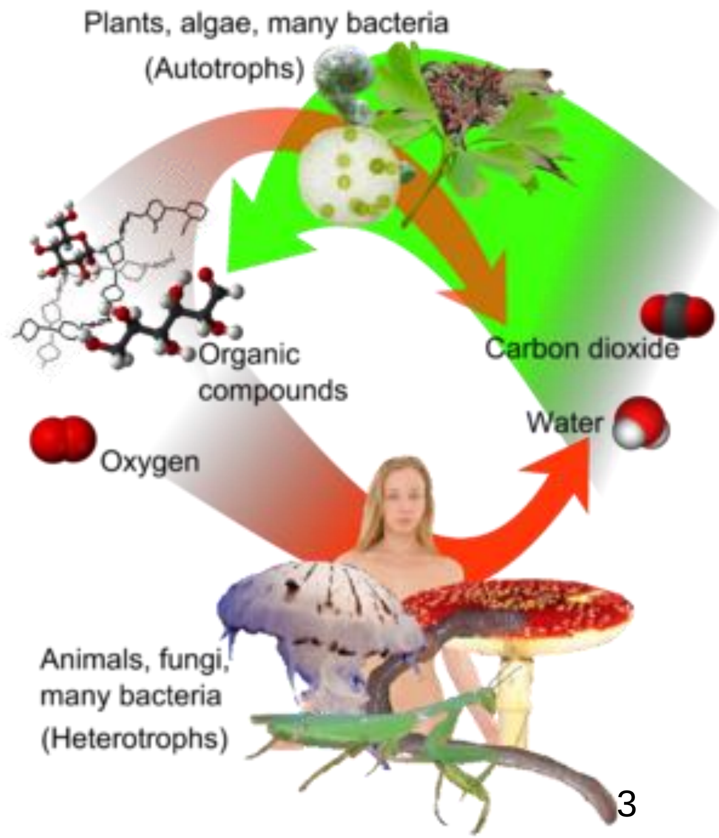


http://getyournotes.blogspot.com/2012/01/cellular-respiration-aerobic-and.html

Respiration

- Organisms can be classified based on how they obtain energy:
  - **Autotrophs**
    - Able to produce their own organic molecules through photosynthesis
  - **Heterotrophs**
    - Live on organic compounds produced by other organisms

- All organisms use cellular respiration to extract energy from organic molecules

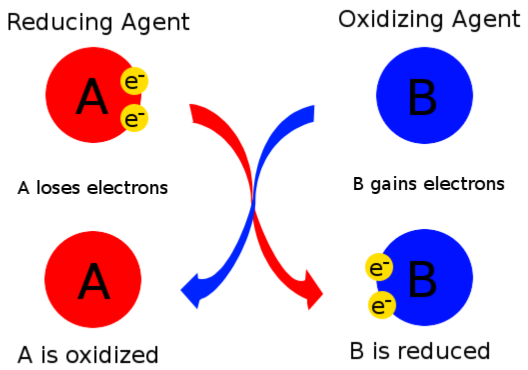


http://en.wikipedia.org/wiki/Heterotroph http://chemwiki.ucdavis.edu/Analytical_Chemistry/Electrochemistry/Redox_Chemistry/Oxidizing_and_Reducing_Agents

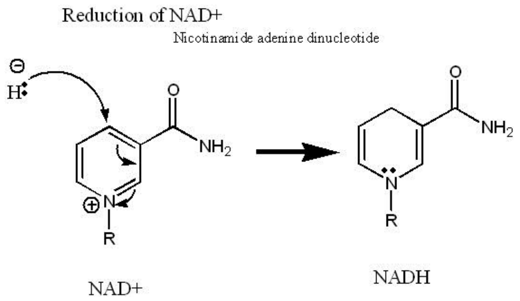
Cellular respiration

OILRIG

- Cellular respiration is a series of reactions…
  - **Oxidation** – loss of electrons
  - **Reduction** – gain of electron

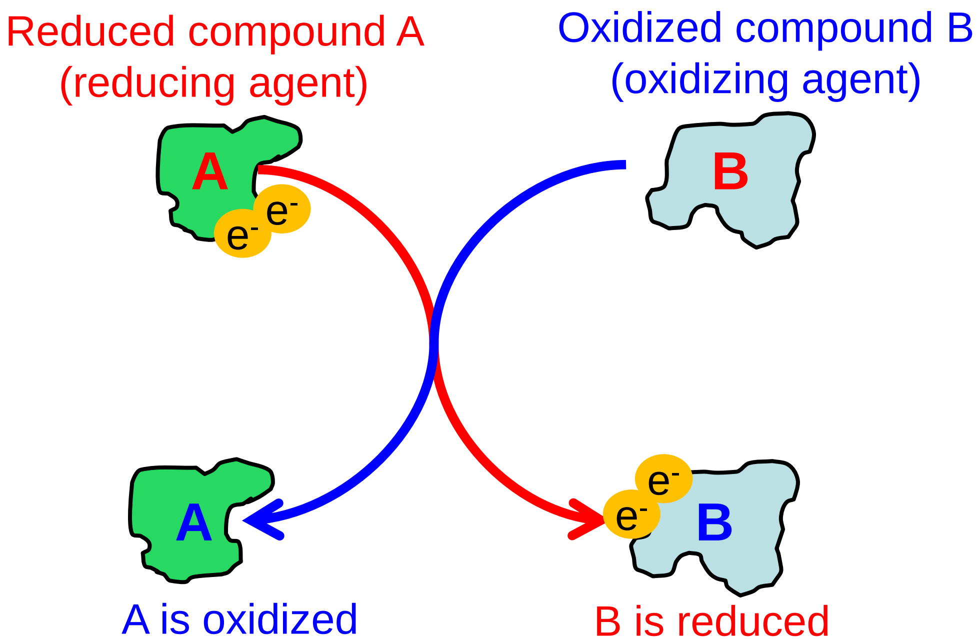


  - **Dehydrogenation** – lost electrons are accompanied by protons
    - A hydrogen atom is lost (1 electron, 1 proton)



Redox

- During redox reactions, electrons carry energy from one molecule to another
  - Redox reactions are often coupled with an electron carrier (NAD^+)

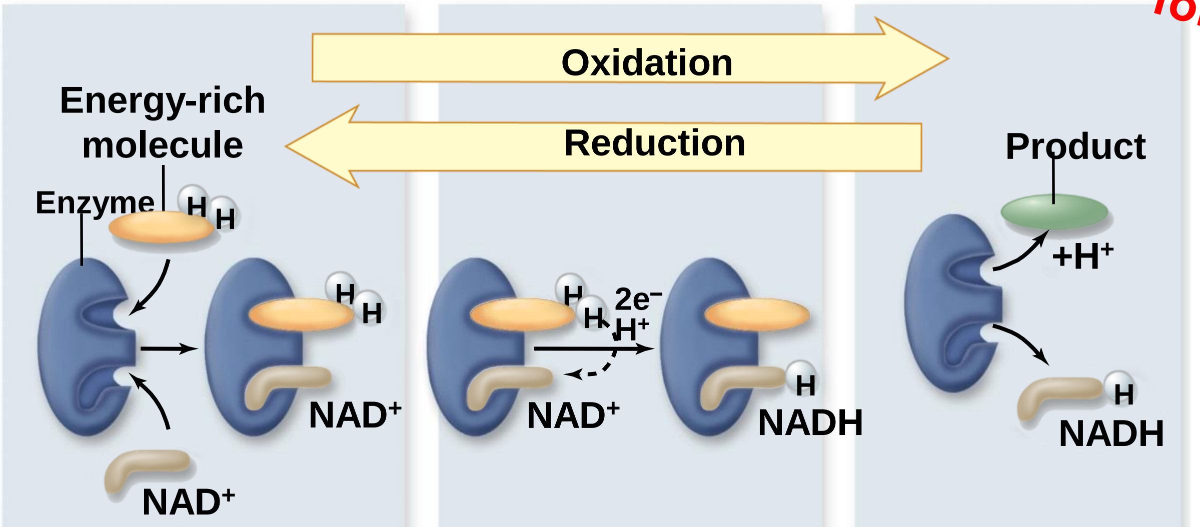


Redox

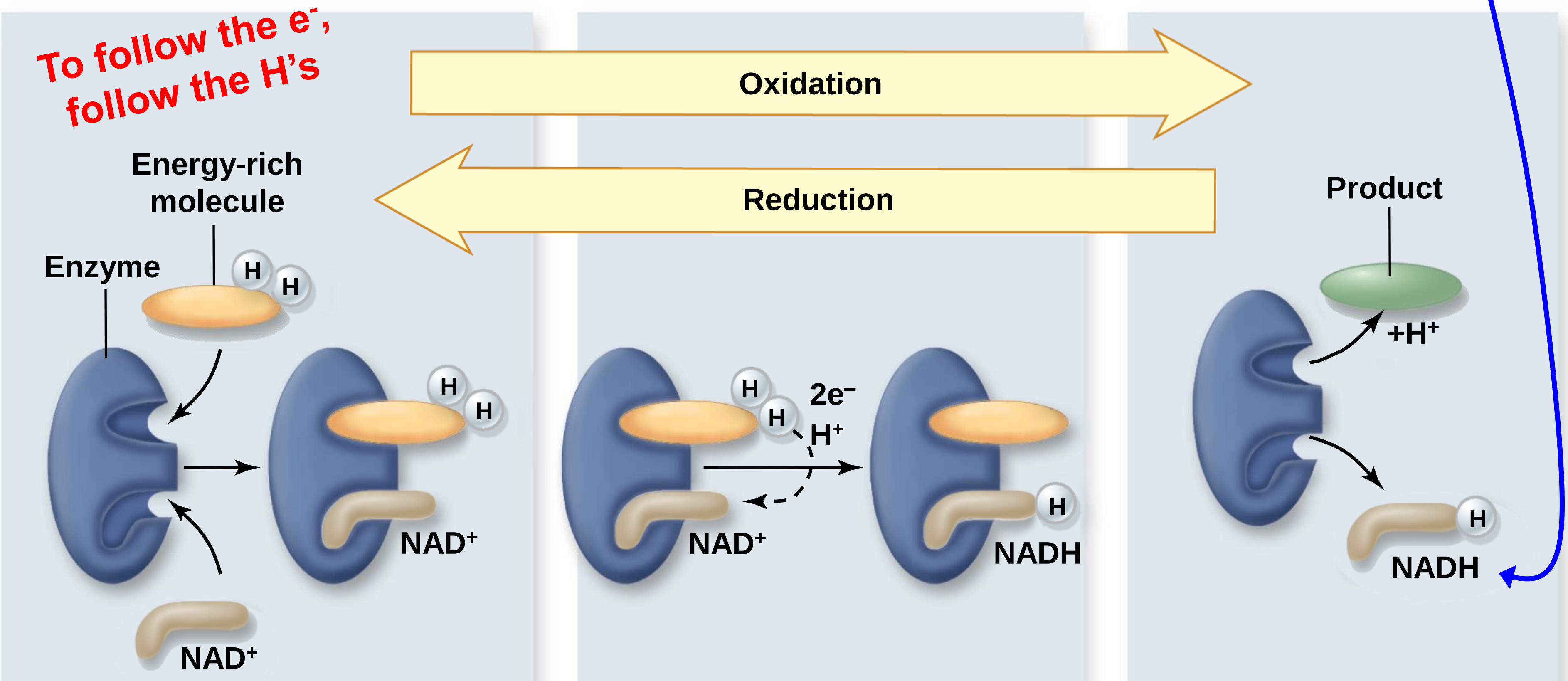
- Nicotinamide adenosine dinucleotide (**NAD^+**)
  - An electron carrier
  - NAD^+ accepts 2 electrons and 1 proton from another molecule to become NADH
  - Reaction is reversible

To follow the e^-, follow the H's

As energy-rich molecule is oxidized, NAD^+ is reduced to NADH



Note change from textbook



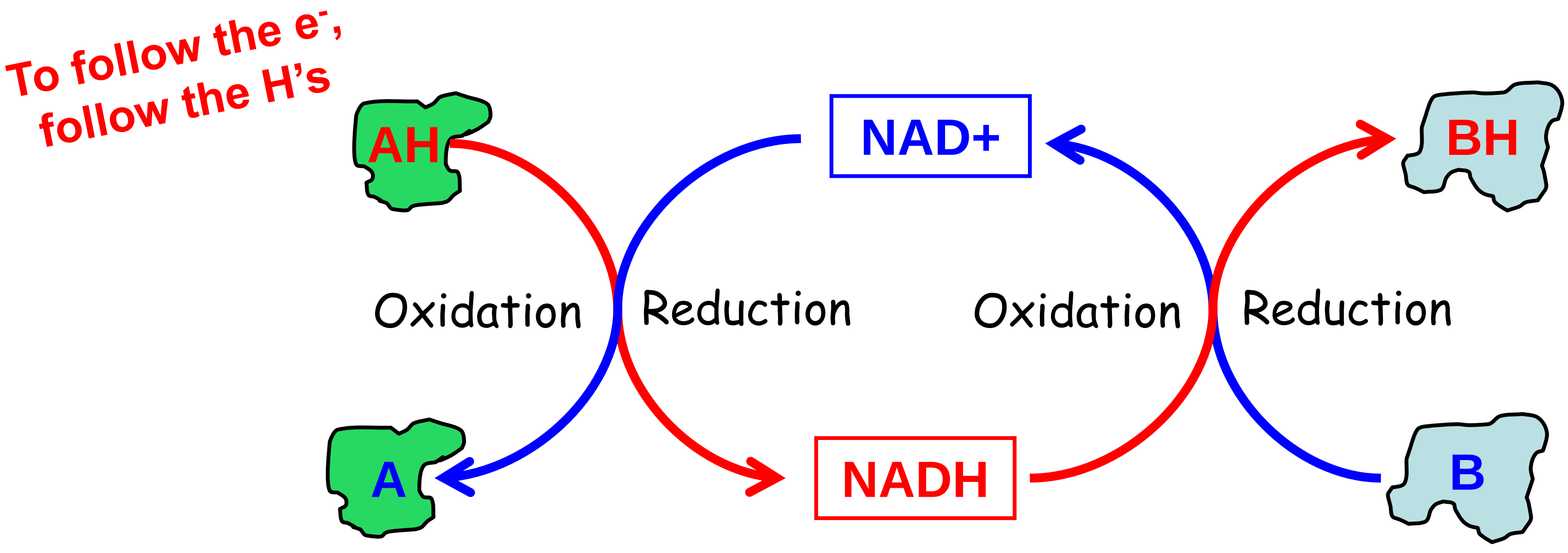
1. Enzymes that use NAD^+ as a cofactor for oxidation reactions bind NAD^+ and the substrate.

2. In an oxidation–reduction reaction, 2 electrons and a proton are transferred to NAD^+, forming NADH. A second proton is donated to the solution.

3. NADH diffuses away and can then donate electrons to other molecules.

As energy-rich molecule is oxidized, NAD^+ is reduced to NADH

- In overall cellular energy harvest
  - Dozens of redox reactions take place
  - Number of electron acceptors, including NAD^+
- In the end, high-energy electrons from initial chemical bonds have lost much of their energy
  - Electrons are transferred to a final electron acceptor



Types of Cellular Respiration

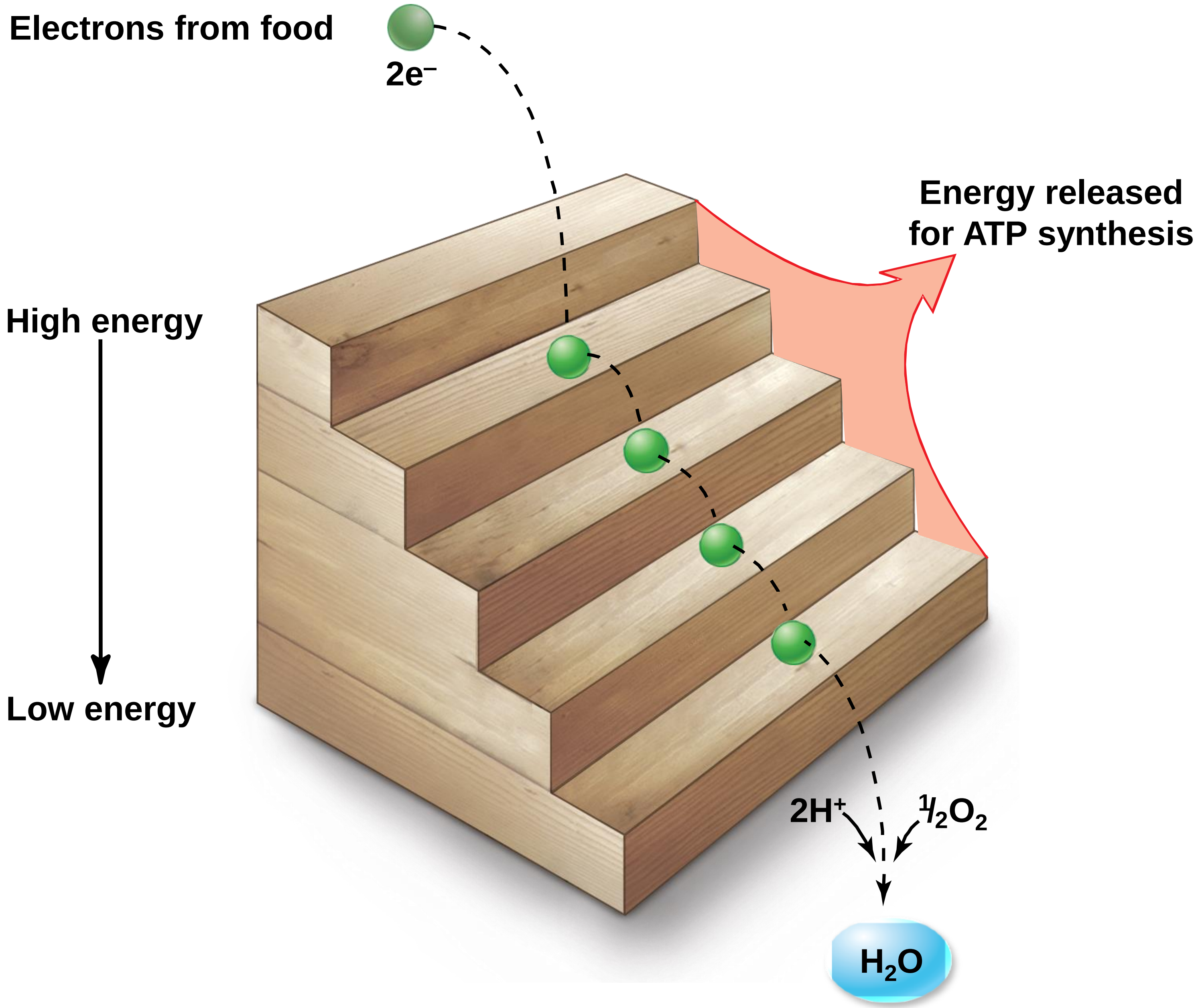
- **Aerobic respiration**
  - Final electron receptor is oxygen (O_2)
- **Anaerobic respiration**
  - Final electron acceptor is an inorganic molecule (not O_2)
- **Fermentation**
  - Final electron acceptor is an organic molecule, such as lactic acid or ethanol

Aerobic respiration

To follow the e⁻, follow the H's

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

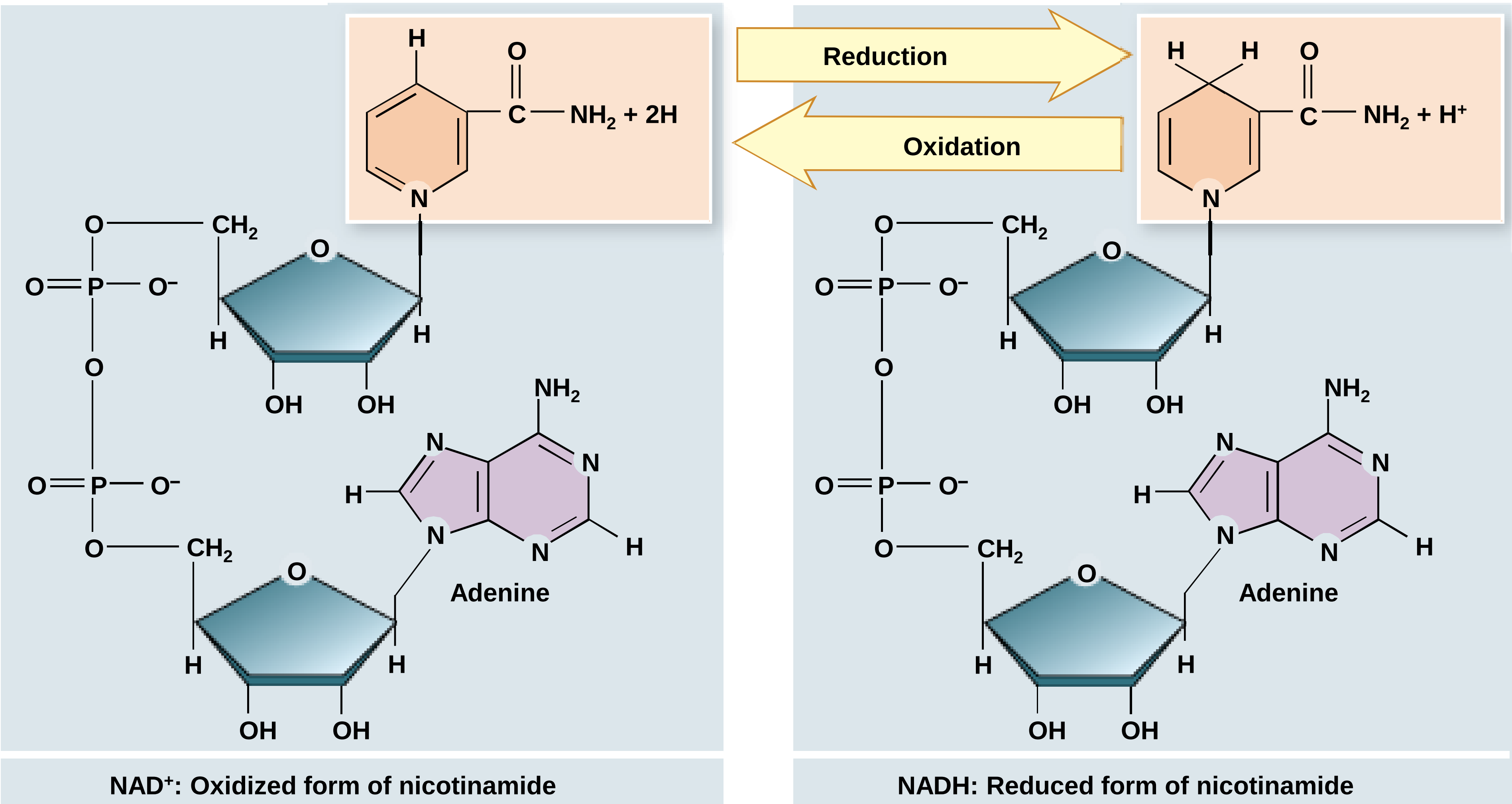
- Free energy = – 686 kcal/mol of glucose
  - Free energy can be even higher than this in a cell
  - This large amount of energy must be released in small steps rather than all at once.
  - $C_6H_{12}O_6$ *(general form for 6 carbon sugar such as glucose)*


Electrons from food
2e⁻
Energy released
for ATP synthesis
High energy
Low energy
2H⁺
½O₂
H₂O

Electron carriers

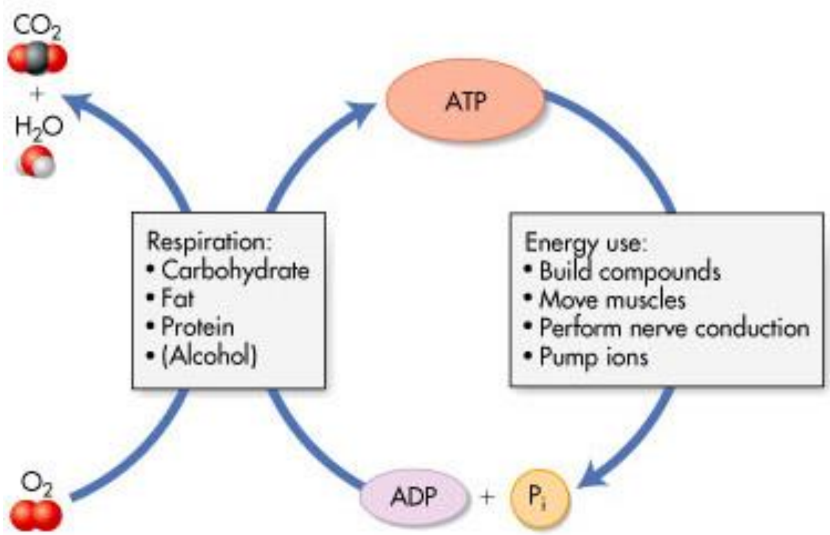
- Many types of carriers used
  - Soluble, membrane-bound, move within membrane
- All carriers can be easily oxidized and reduced
  - Some carry just electrons, some electrons and protons
  - NAD^+ acquires 2 electrons and a proton to become NADH

To follow the e⁻, follow the H's



ATP

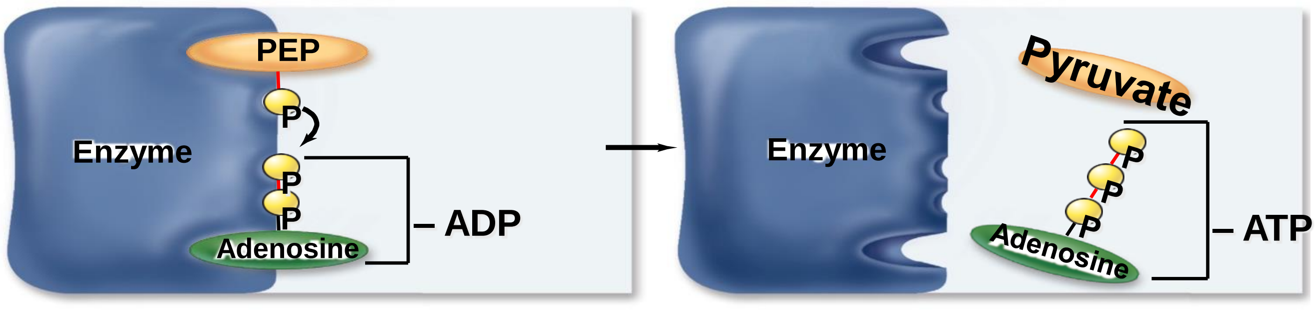
- Cells use ATP to drive endergonic reactions
  - ΔG (free energy) = –7.3 kcal/mol
  - *Compare with ΔG* from complete combustion of glucose = *–686 kcal/mol*



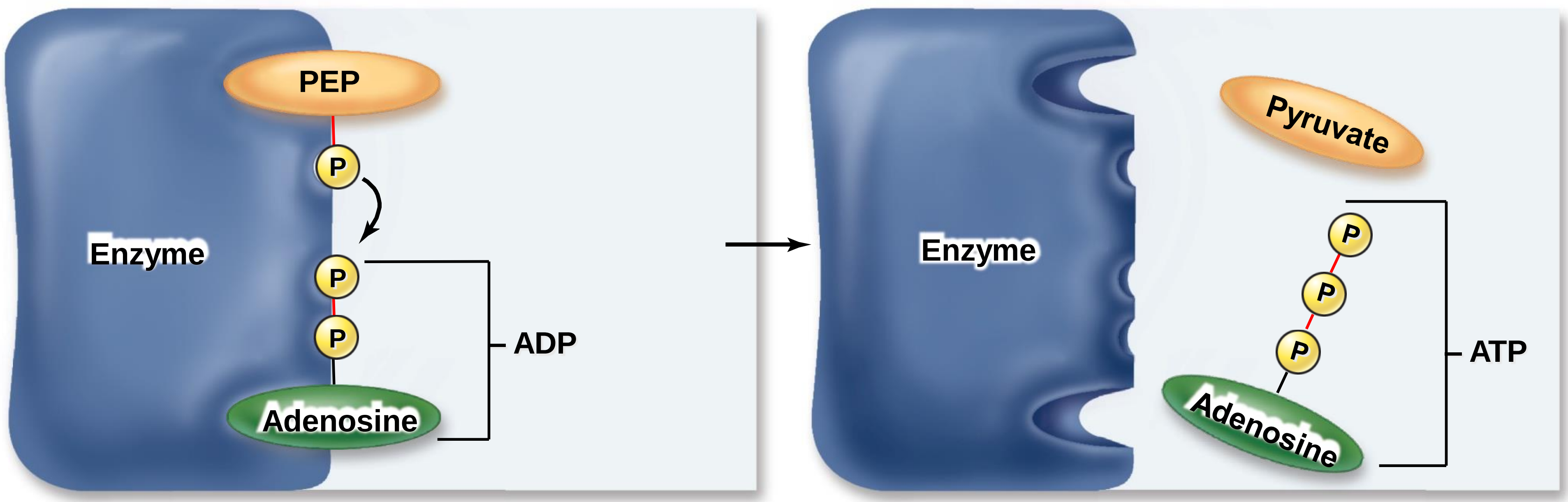
Cellular reactions can't use all the energy of glucose breakdown at once, so cells must use stepwise breakdown and intermediaries such as ATP

http://fgamedia.org/faculty/cholcroft/Bio45/miscellaneous_web_pages/Lectures/Metabolism/Metabolism_Intro.html

- 2 mechanisms for ATP synthesis
  1. **Substrate-level phosphorylation**
     - Transfer phosphate group directly from substrate molecule to ADP
     - During glycolysis and Krebs cycle



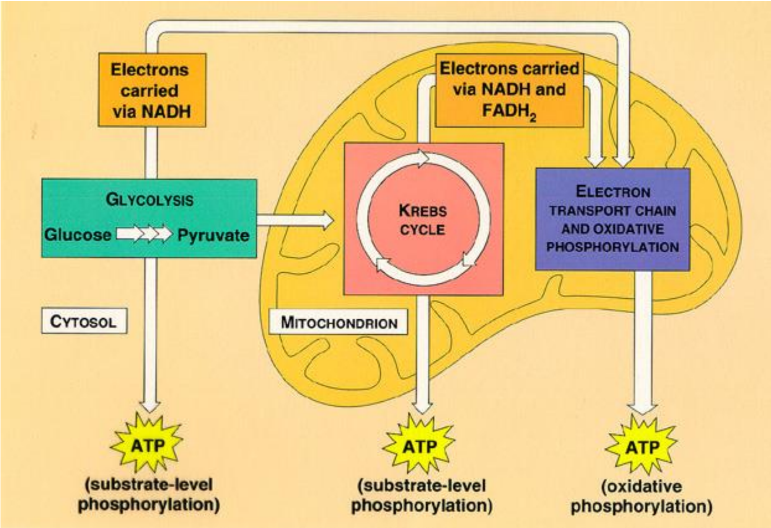
  2. **Oxidative phosphorylation**
     - ATP synthase uses energy from a proton gradient in the electron transport chain


PEP
P
Enzyme
P
P
ADP
Adenosine
Enzyme
Pyruvate
P
P
P
ATP
Adenosine

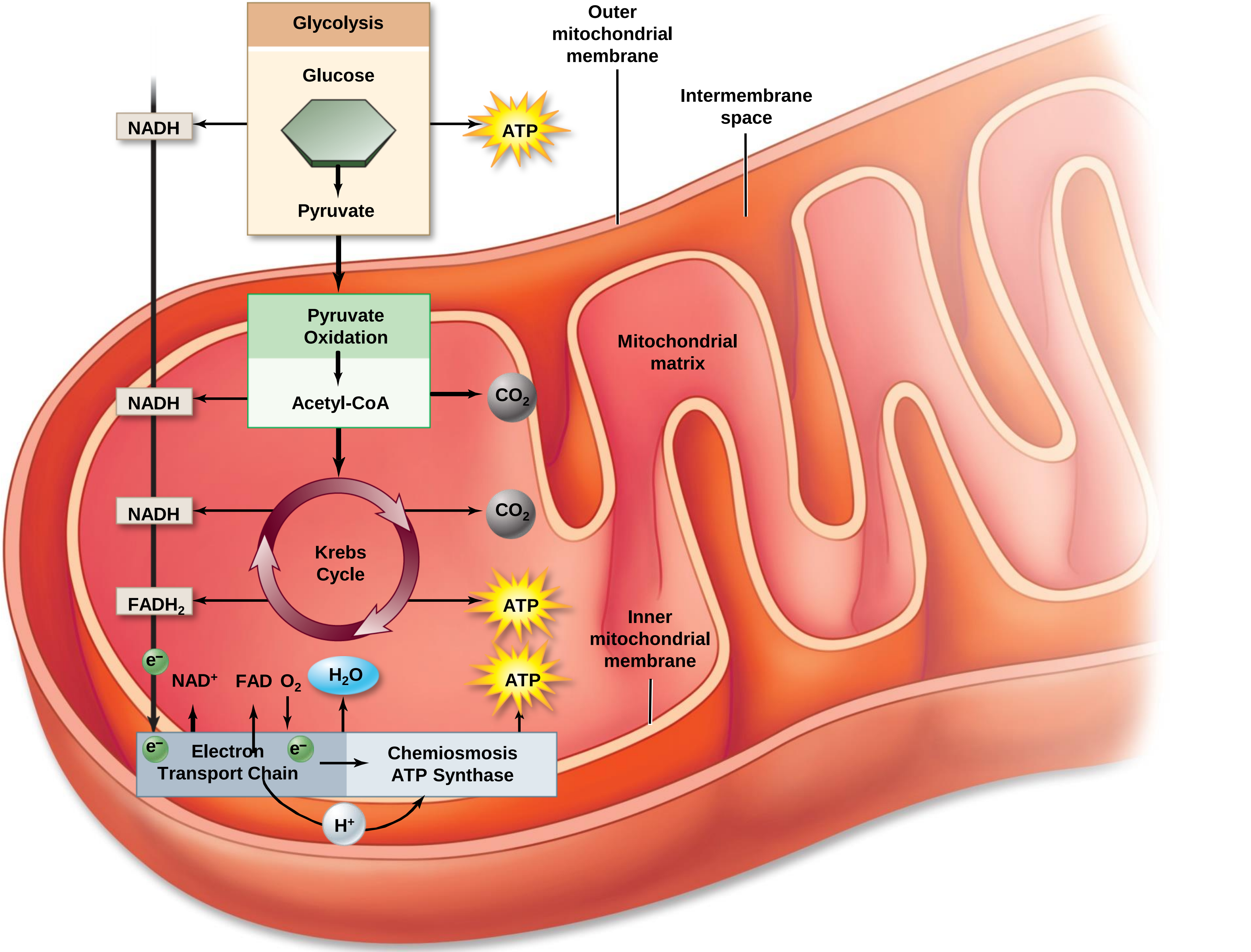
Oxidation of Glucose

The complete oxidation of glucose proceeds in stages:

1. **Glycolysis**
2. **Pyruvate oxidation**
3. **Krebs cycle**
4. **Electron transport chain** & **chemiosmosis**

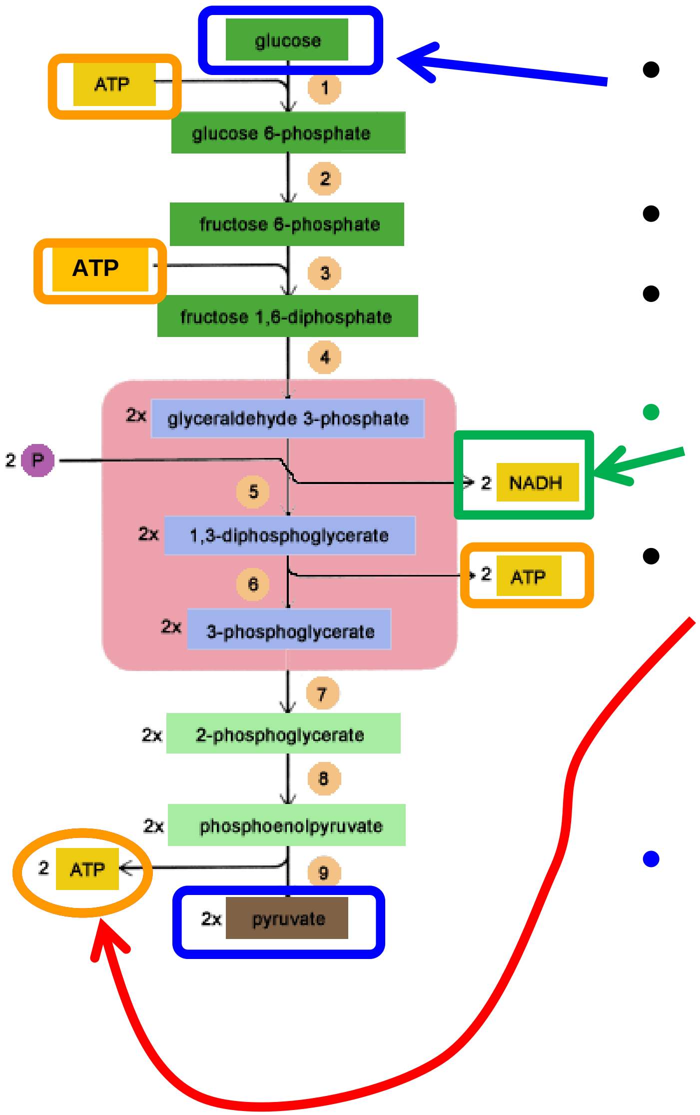


http://www.mobento.com/video/DiyoEA5Mc

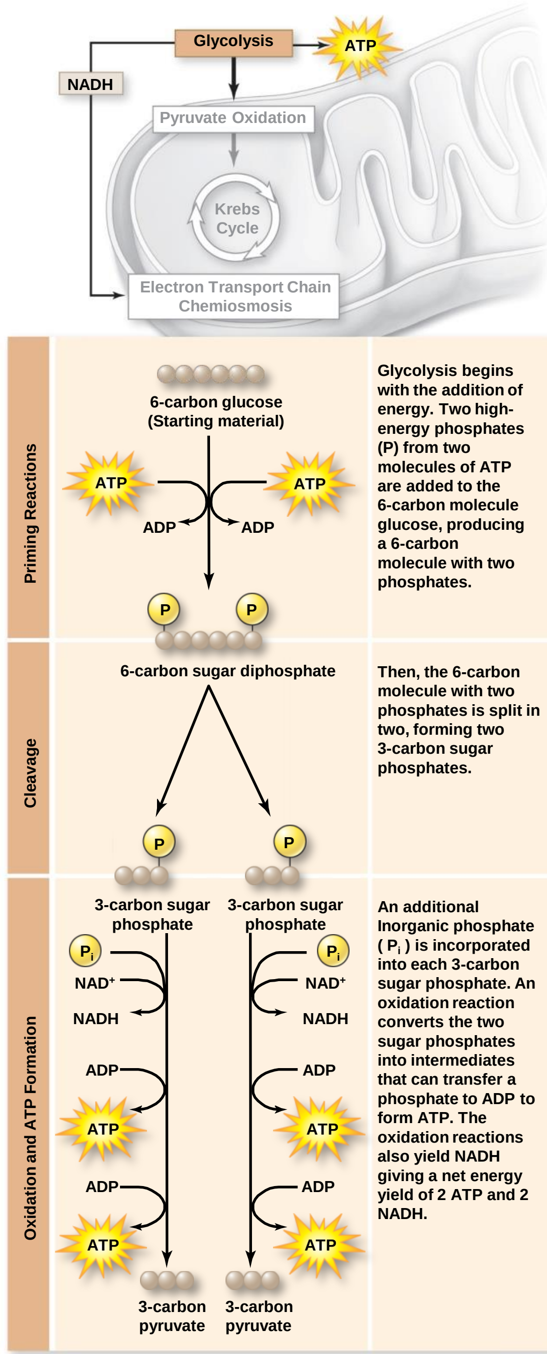


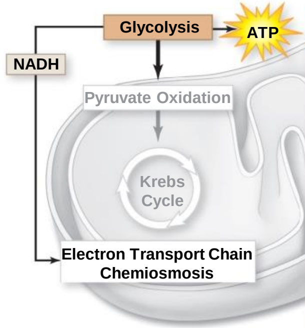
Glycolysis
Glucose
Pyruvate
NADH
ATP
Outer mitochondrial membrane
Intermembrane space
Pyruvate Oxidation
Acetyl-CoA
NADH
CO_2
Mitochondrial matrix
NADH
Krebs Cycle
CO_2
$FADH_2$
ATP
e^-
NAD^+
FAD
O_2
H_2O
ATP
Inner mitochondrial membrane
e^-
Electron Transport Chain
e^-
Chemiosmosis ATP Synthase
H^+

Glycolysis



- Converts 1 glucose (6 carbons) to 2 pyruvate (3 carbons)
- 10-step biochemical pathway
- Occurs in the cytoplasm
- 2 NADH produced by the reduction of NAD^+
- Net production of 2 ATP molecules by **substrate-level phosphorylation**
  - (uses 2 ATPs and produces 4 total = 2 net ATPs)
- Fun fact
  - *Only process that occurs in red blood cells since they do not have mitochondria!*


Glycolysis
ATP
NADH
Pyruvate Oxidation
Krebs Cycle
Electron Transport Chain Chemiosmosis
Priming Reactions
6-carbon glucose (Starting material)
ATP
ATP
ADP
ADP
P
P
Glycolysis begins with the addition of energy. Two high-energy phosphates (P) from two molecules of ATP are added to the 6-carbon molecule glucose, producing a 6-carbon molecule with two phosphates.
Cleavage
6-carbon sugar diphosphate
P
P
Then, the 6-carbon molecule with two phosphates is split in two, forming two 3-carbon sugar phosphates.
Oxidation and ATP Formation
3-carbon sugar phosphate
3-carbon sugar phosphate
P_i
P_i
NAD^+
NAD^+
NADH
NADH
ADP
ADP
ATP
ATP
ADP
ADP
ATP
ATP
3-carbon pyruvate
3-carbon pyruvate
An additional Inorganic phosphate (P_i) is incorporated into each 3-carbon sugar phosphate. An oxidation reaction converts the two sugar phosphates into intermediates that can transfer a phosphate to ADP to form ATP. The oxidation reactions also yield NADH giving a net energy yield of 2 ATP and 2 NADH.



1. Phosphorylation of glucose by ATP.

2–3. Rearrangement, followed by a second ATP phosphorylation.

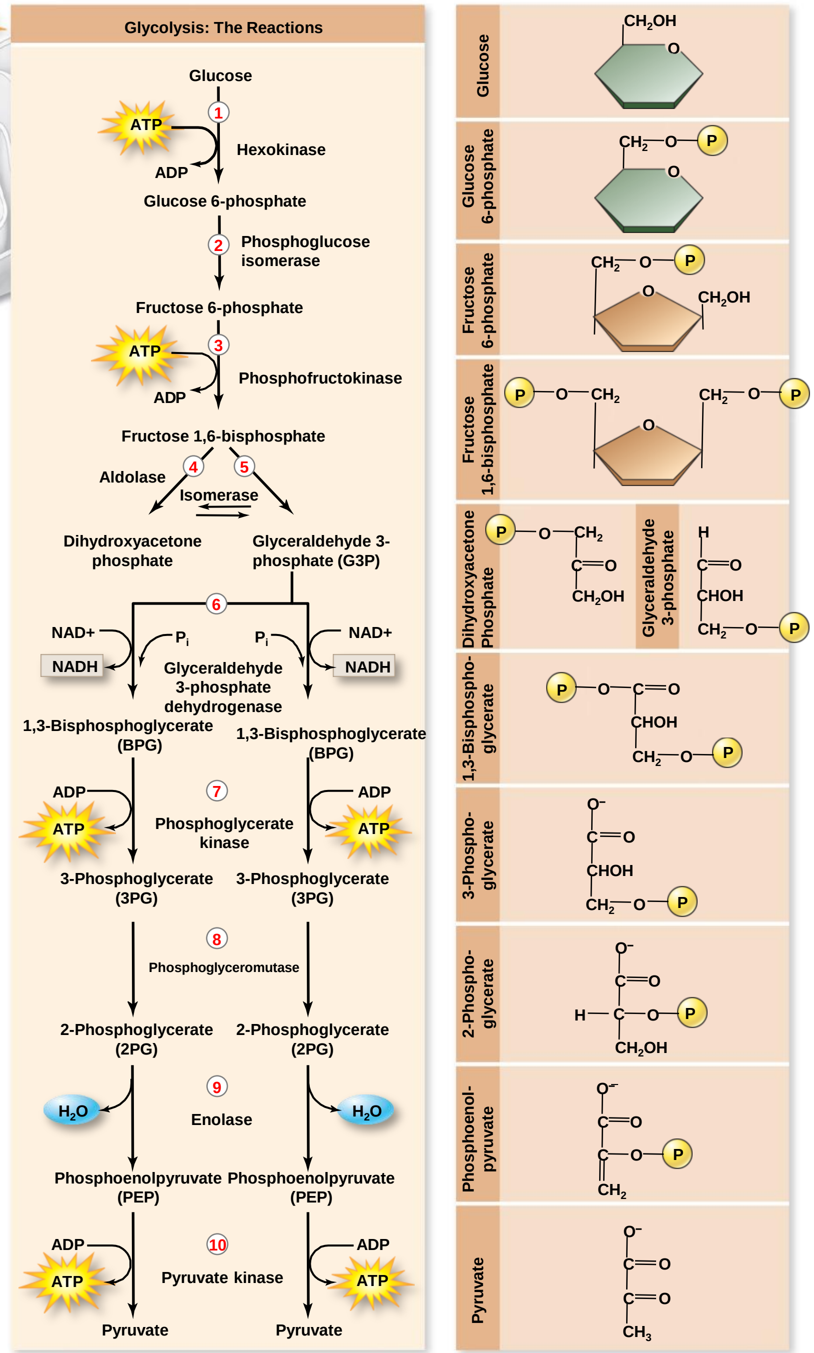
4–5. The 6-carbon molecule is split into two 3-carbon molecules—one G3P, another that is converted into G3P in another reaction.

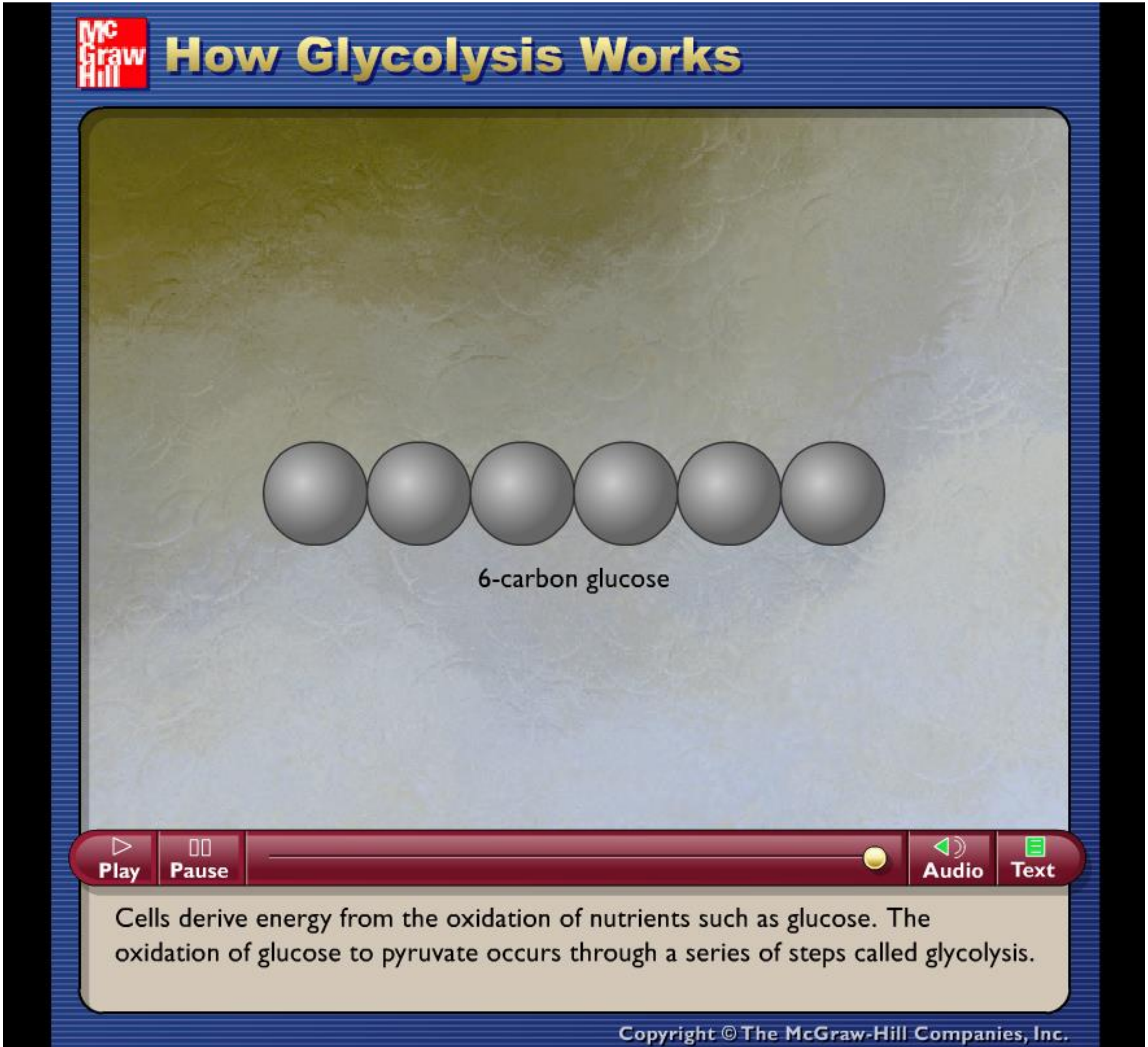
6. Oxidation followed by phosphorylation produces two NADH molecules and two molecules of BPG, each with one high-energy phosphate bond.

7. Removal of high-energy phosphate by two ADP molecules produces two ATP molecules and leaves two 3PG molecules.

8–9. Removal of water yields two PEP molecules, each with a high-energy phosphate bond.

10. Removal of high-energy phosphate by two ADP molecules produces two ATP molecules and two pyruvate molecules.




How Glycolysis Works
6-carbon glucose
Play
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Cells derive energy from the oxidation of nutrients such as glucose. The oxidation of glucose to pyruvate occurs through a series of steps called glycolysis.
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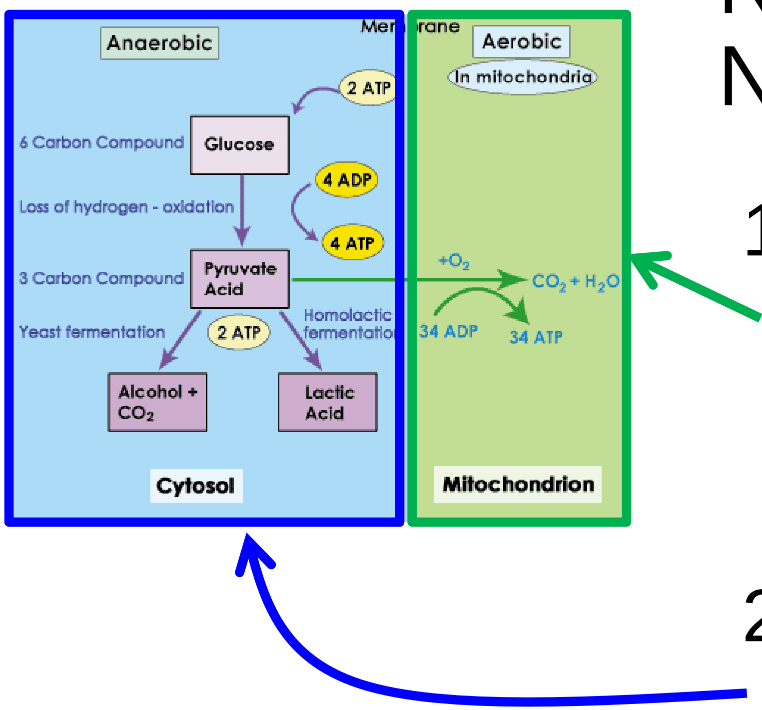
NADH must be recycled



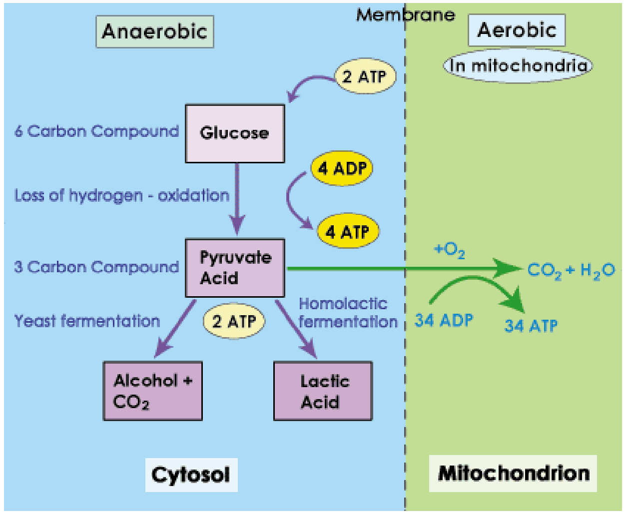
- For glycolysis to continue, NADH must be recycled to NAD^+ by either:

1. **Aerobic respiration**
   - **Oxygen** is available as the *final electron acceptor*
   - Produces significantly more ATP
2. **Fermentation**
   - Occurs when oxygen is not available
   - Organic molecule is the final electron acceptor

http://getyournotes.blogspot.com/2012/01/cellular-respiration-aerobic-and.html

Fate of pyruvate

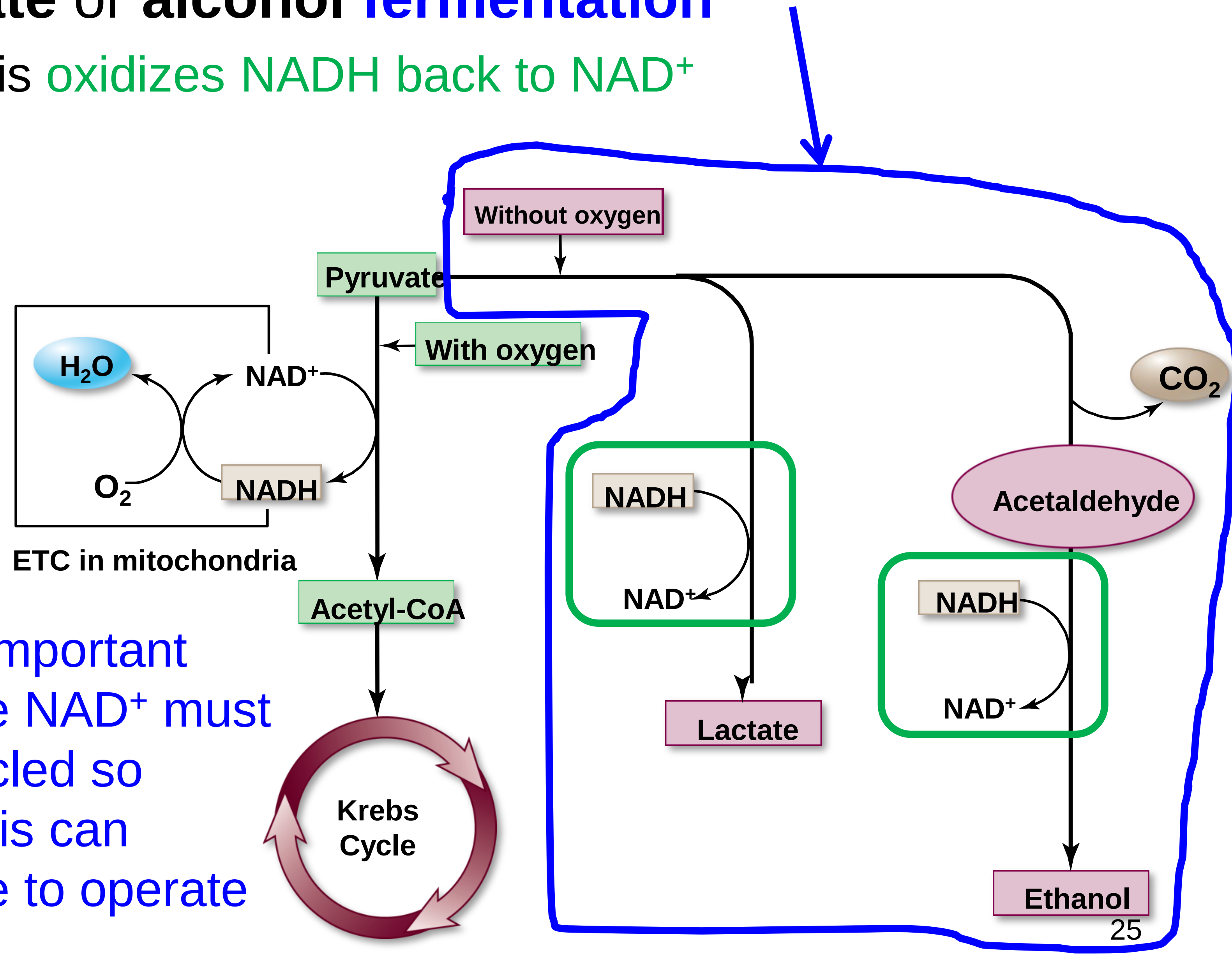
- Depends on oxygen availability
  - When oxygen is present, pyruvate is oxidized to acetyl-CoA which enters the Krebs cycle
    - Aerobic respiration
  - Without oxygen, pyruvate is reduced in order to oxidize NADH back to NAD^+
    - Fermentation



http://getyournotes.blogspot.com/2012/01/cellular-respiration-aerobic-and.html

– Without oxygen, pyruvate is reduced by **lactate** or **alcohol** **fermentation**

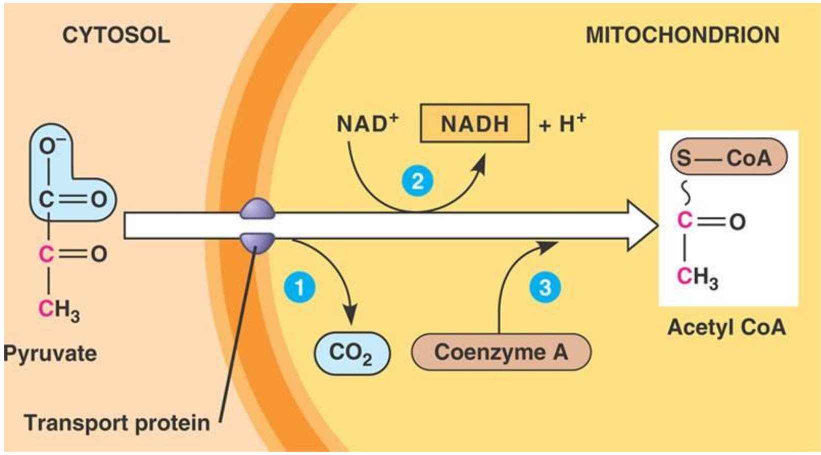
- This oxidizes NADH back to NAD^+



- This is important because NAD^+ must be recycled so glycolysis can continue to operate

Pyruvate Oxidation

- In the presence of oxygen, pyruvate is oxidized
  - Occurs in the mitochondria in eukaryotes
    - multienzyme complex called pyruvate dehydrogenase catalyzes the reaction
  - Occurs at the plasma membrane in prokaryotes

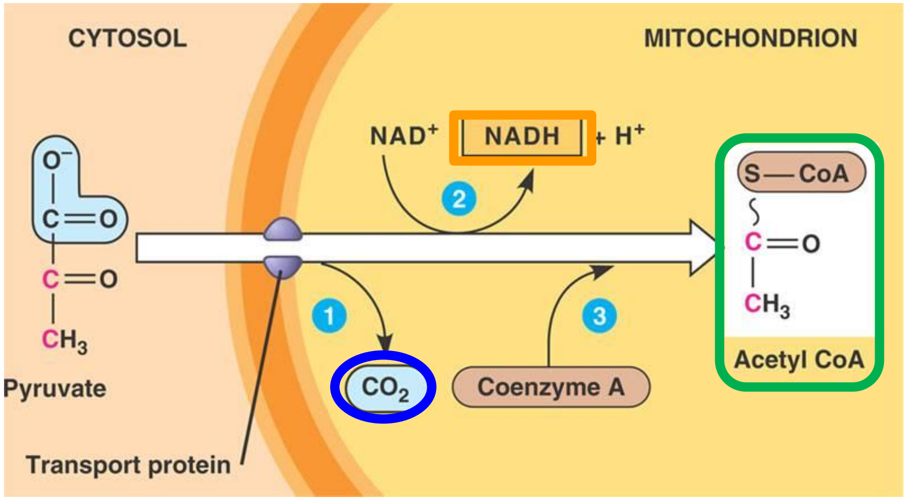


http://schoolworkhelper.net/cellular-respiration-glycolysis-pyruvate-kerbs-etc/

Products of pyruvate oxidation

- For each 3-carbon pyruvate molecule:
  - 1 **CO_2**
    - Decarboxylation by pyruvate dehydrogenase
  - 1 NADH
  - 1 Acetyl-CoA which consists of 2 carbons from pyruvate attached to coenzyme A
    - Acetyl-CoA proceeds to the Krebs cycle

***Double each of these products per glucose molecule



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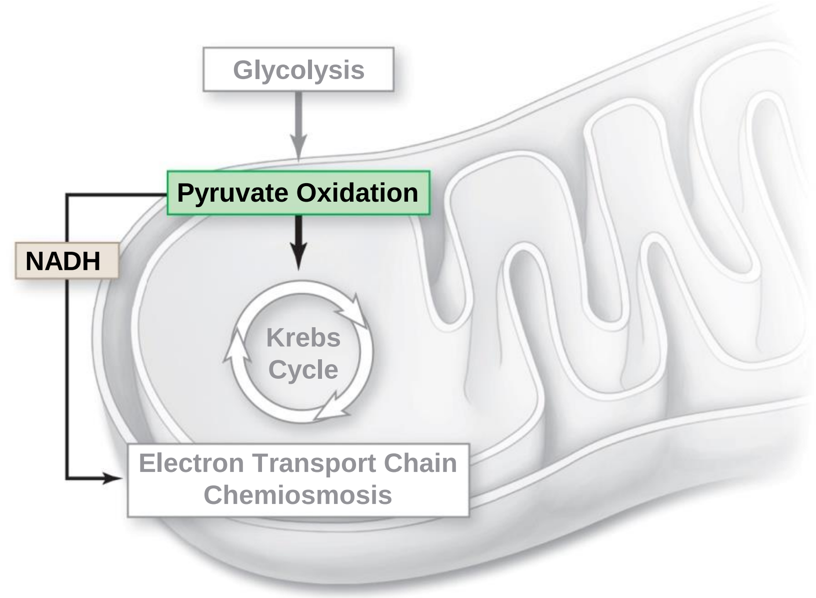
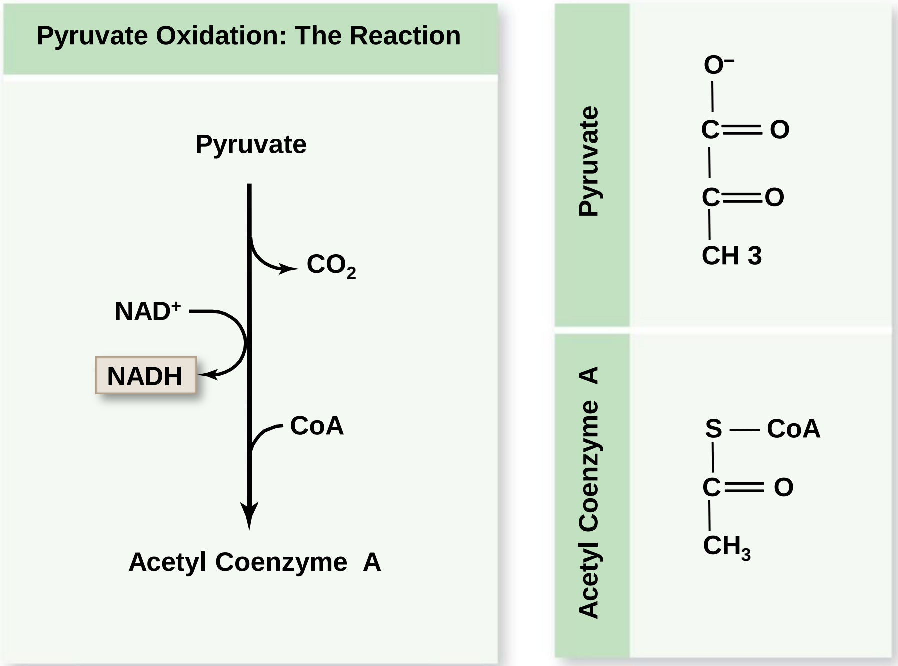


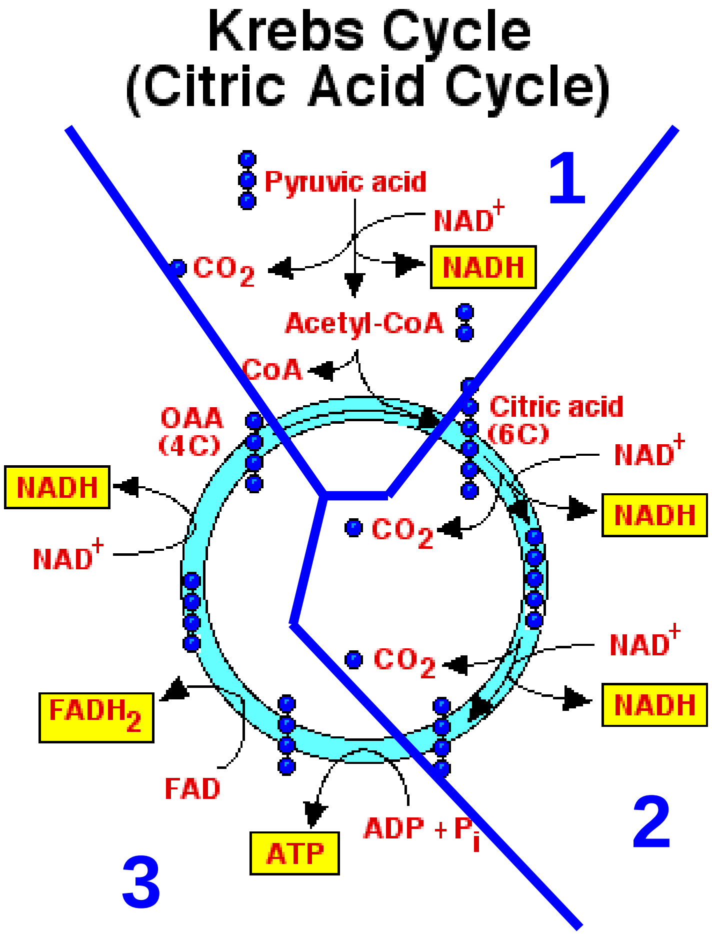
Per glucose molecule =

- 2 CO_2
- 2 NADHs
- 2 Acetyl CoA

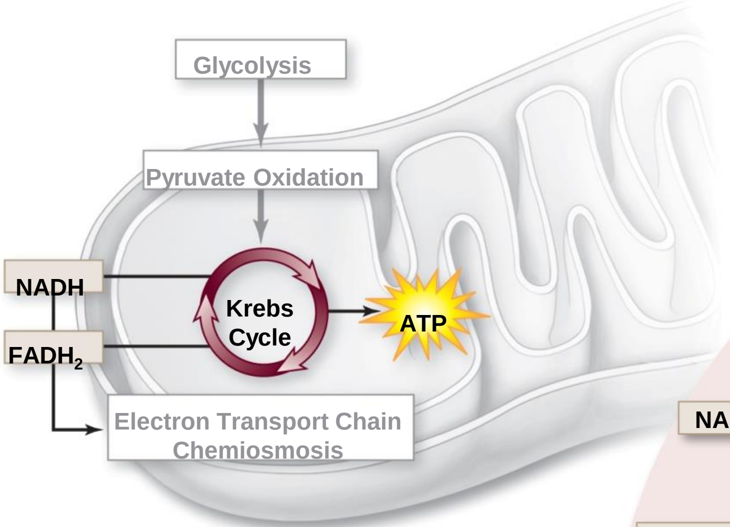


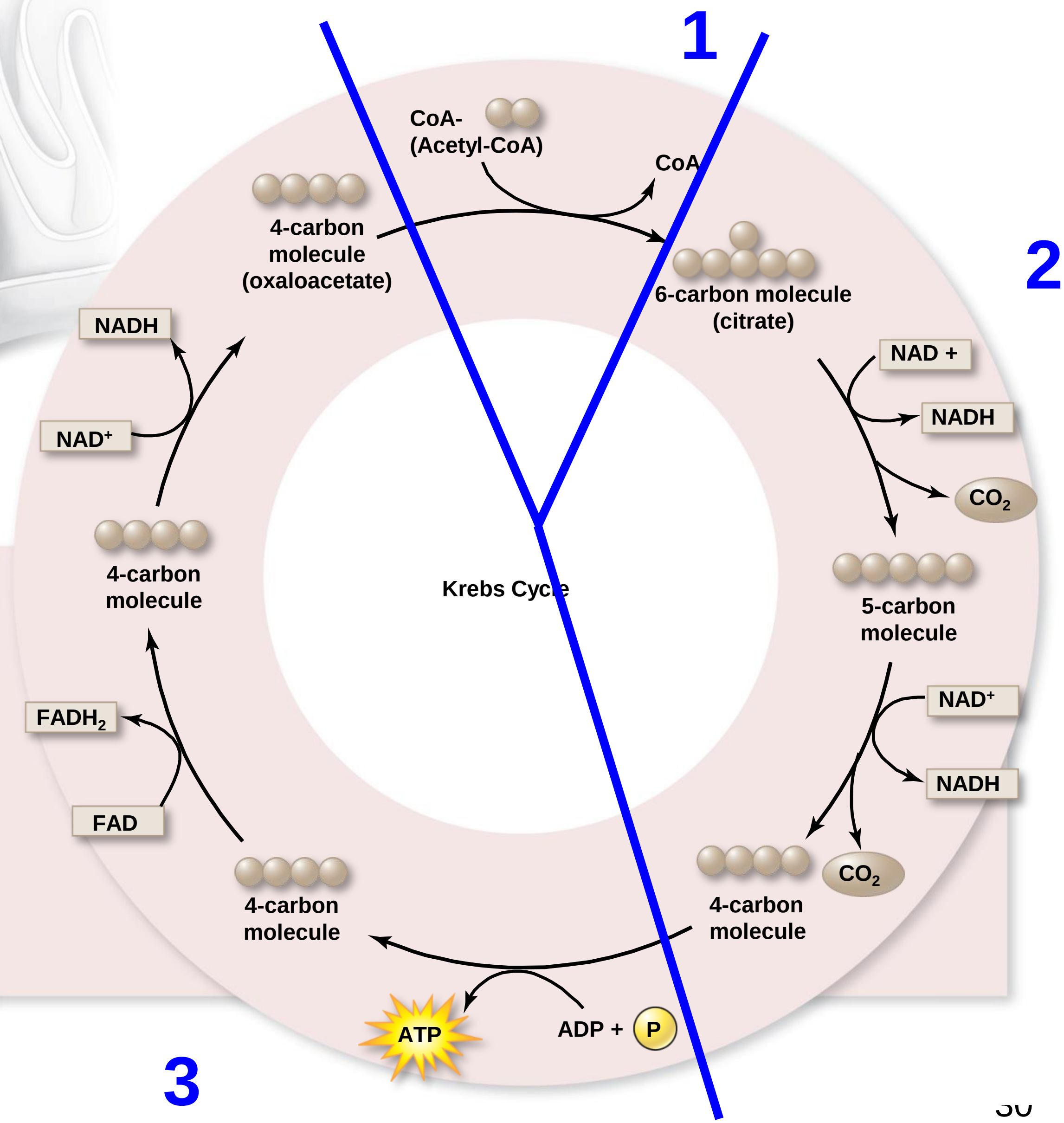
Krebs Cycle

- Oxidizes the acetyl group from pyruvate
- Occurs in the matrix of the mitochondria
- Biochemical pathway of 9 steps in three segments
  1. Acetyl-CoA + oxaloacetate → citrate
  2. Citrate rearrangement and decarboxylation
  3. Regeneration of oxaloacetate



http://drchadedwards.com/244/energy-production-through-the-krebs-cycle/

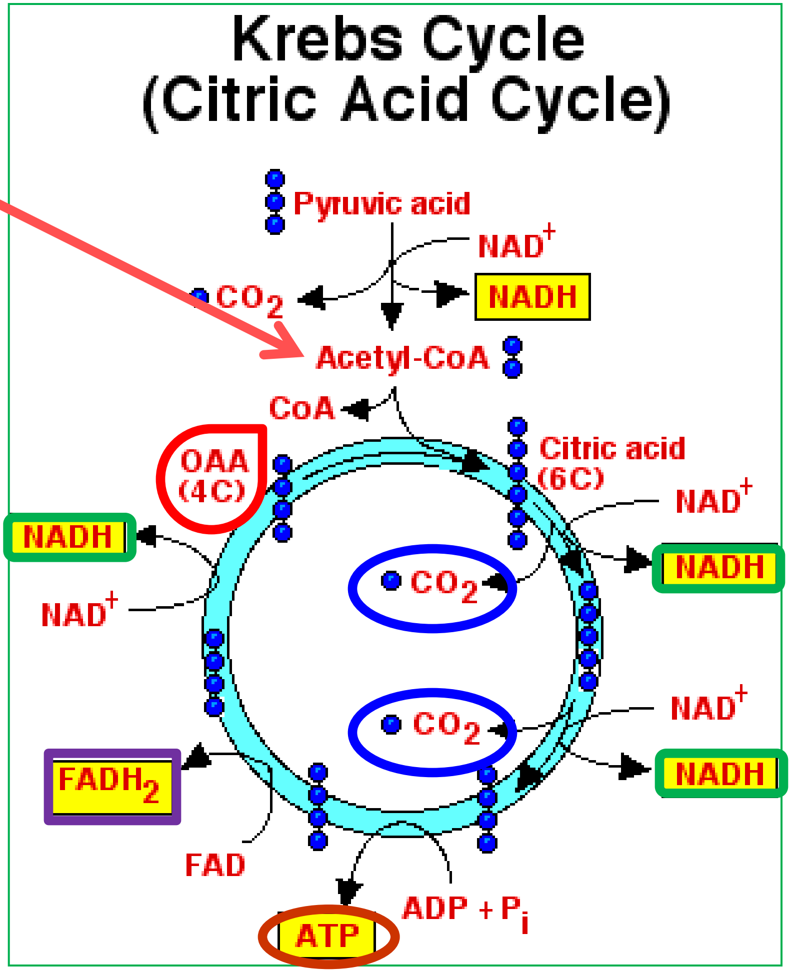




Pyruvate from glycolysis is oxidized Krebs Cycle into an acetyl group that feeds into the Krebs cycle. The 2-C acetyl group combines with 4-C oxaloacetate to produce the 6-C compound citrate (thus this is also called the citric acid cycle). Oxidation reactions are combined with two decarboxylations to produce NADH, CO_2, and a new 4-carbon molecule. Two additional oxidations generate another NADH and an FADH$_2$ and regenerate the original 4-C oxaloacetate.

Krebs Cycle

- For each Acetyl-CoA entering:
  - Release 2 molecules of **CO_2**
  - Reduce 3 NAD^+ to 3 **NADH**
  - Reduce 1 FAD (electron carrier) to **$FADH_2$**
  - Produce 1 **ATP**
  - Regenerate oxaloacetate



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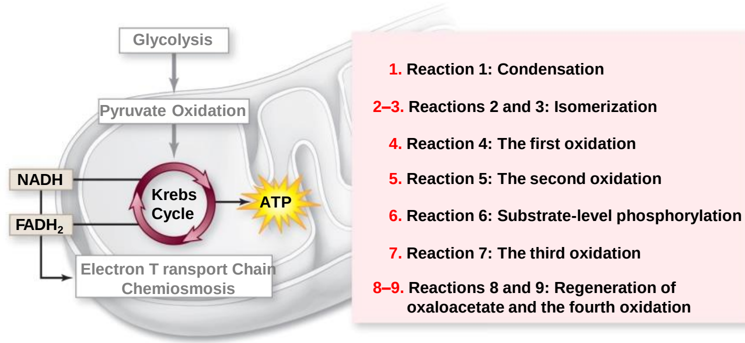
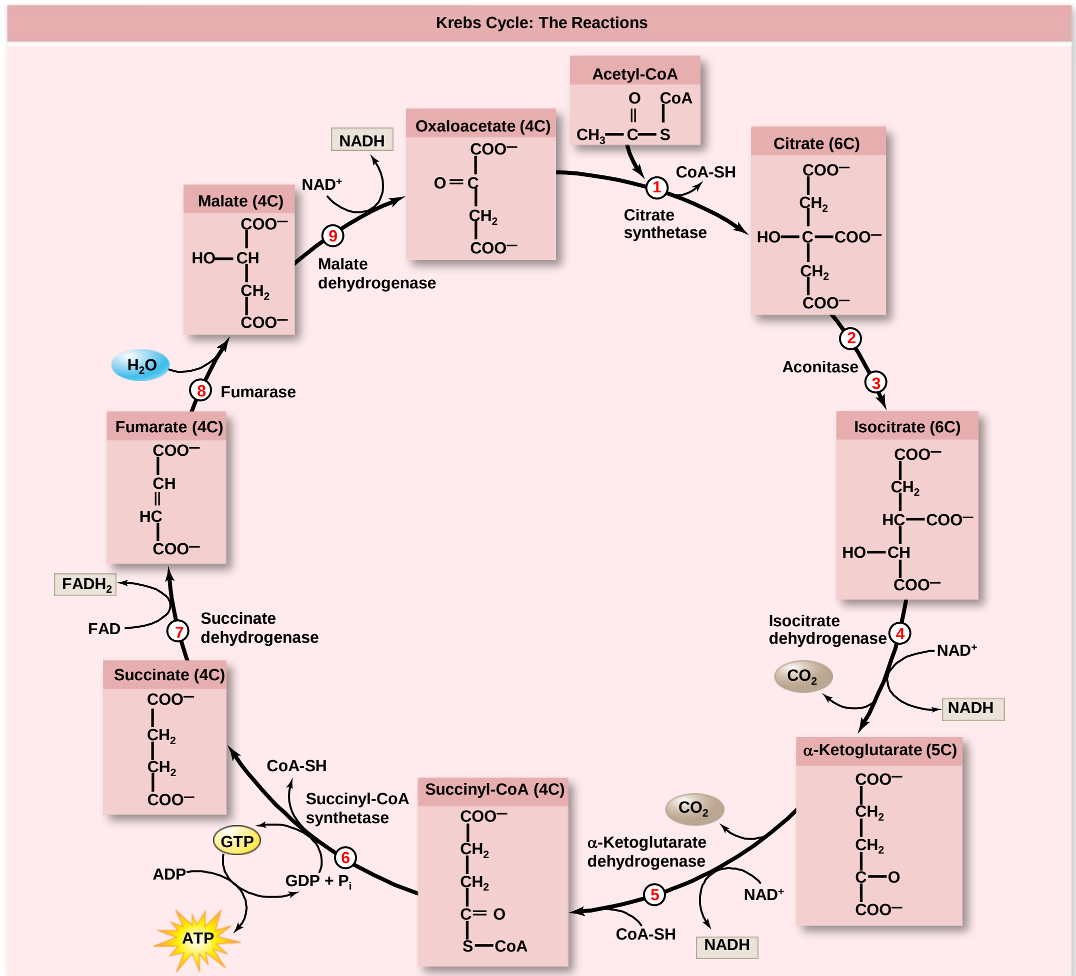




Per glucose molecule, the Krebs cycle produces…

- 4 CO_2
- 6 NADHs
- 2 $FADH_2$
- 2 ATP

At this point

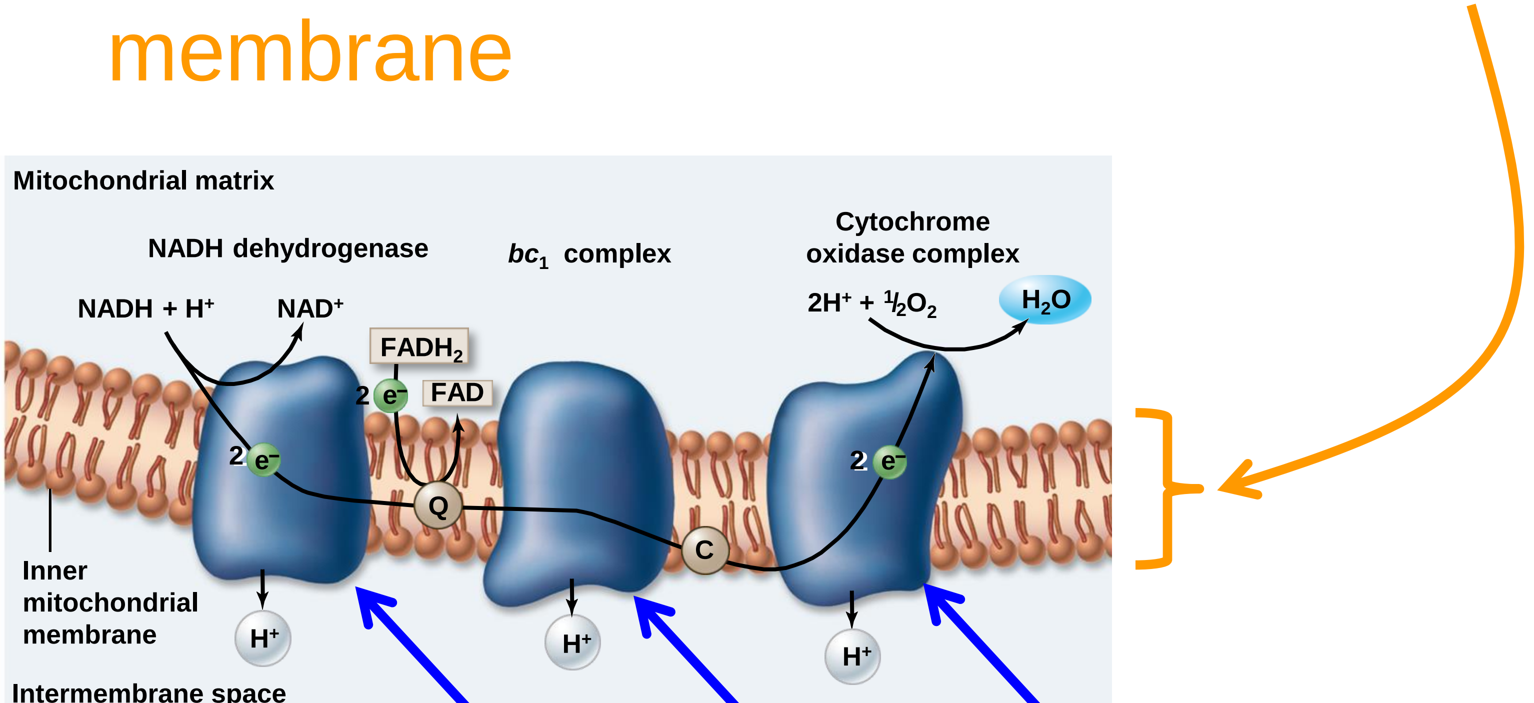
- Glucose has been oxidized to:
  - 6 CO_2 (byproduct of aerobic respiration)
  - 4 ATP
  - 10 NADH
  - 2 $FADH_2$

These two types of electron carriers proceed to the electron transport chain

- Electron transfer has released 53 kcal/mol of energy by gradual energy extraction
- Energy will be put to use to manufacture ATP in ETC

Electron Transport Chain (ETC)

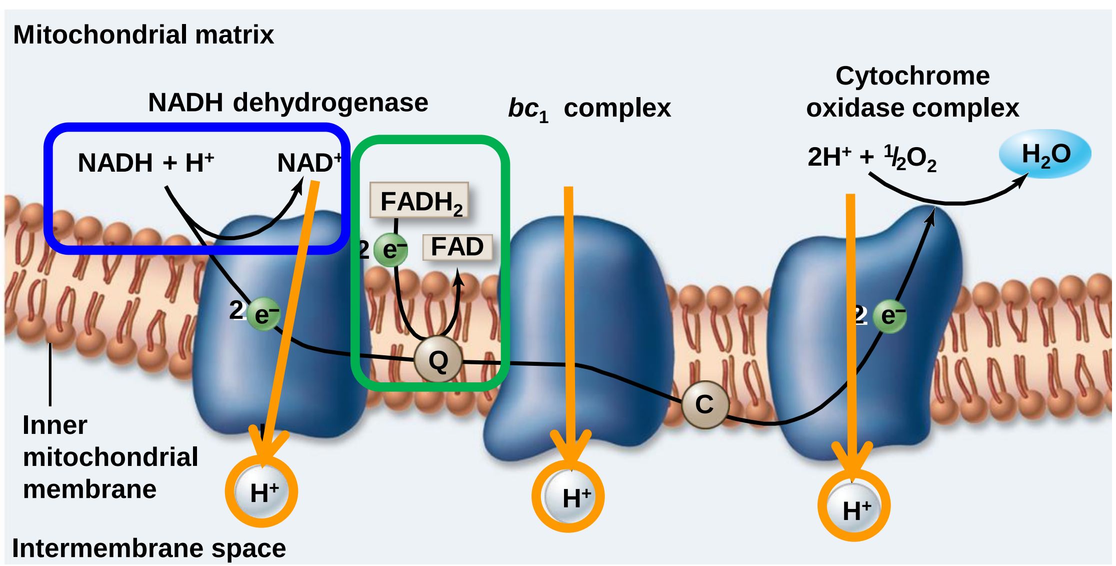
- ETC is a series of membrane-bound electron carriers
- Embedded in the inner mitochondrial membrane



***a*. The electron transport chain**

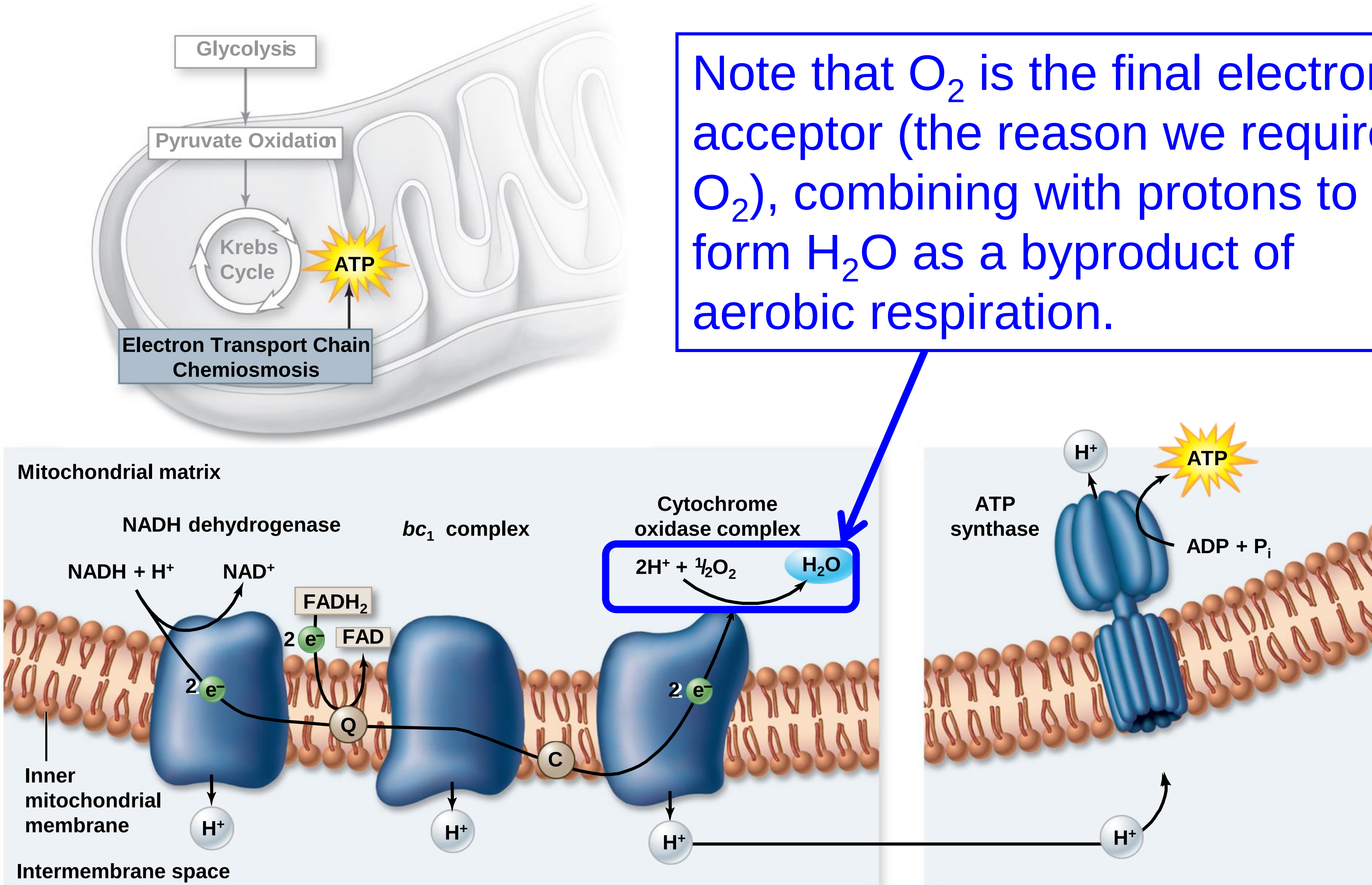
Electron Transport Chain (ETC)

- Electrons from **NADH** and **$FADH_2$** are transferred to complexes of the ETC
- Each complex…
  - A proton pump creating proton gradient
  - Transfers electrons to next carrier



a. **The electron transport chain**

Note that O_2 is the final electron acceptor (the reason we require O_2), combining with protons to form H_2O as a byproduct of aerobic respiration.

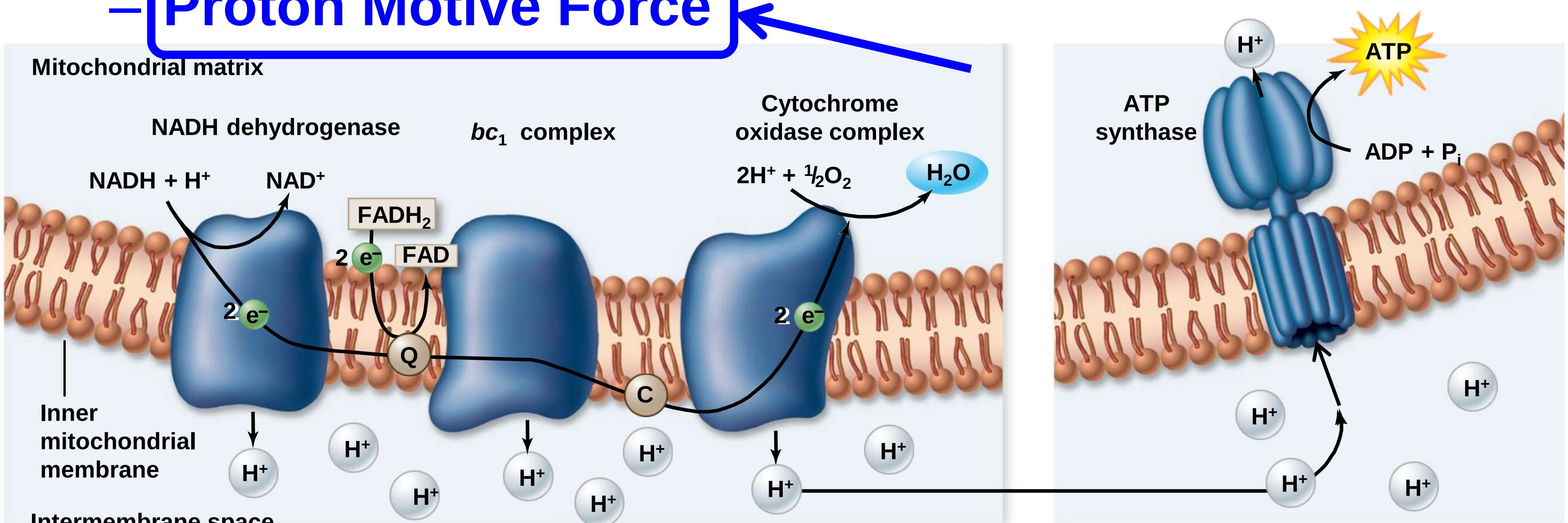


a. The electron transport chain

b. Chemiosmosis

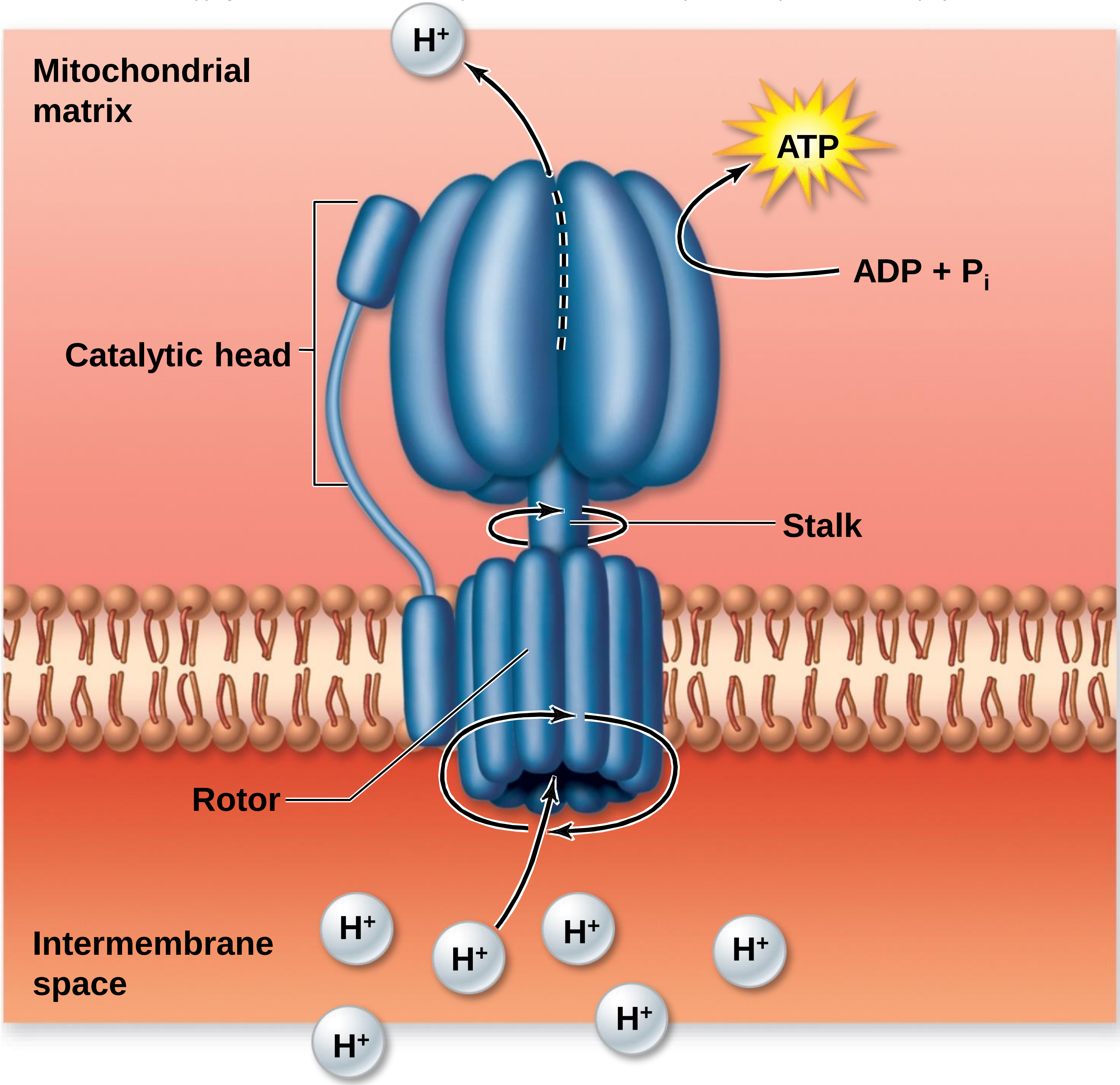
Chemiosmosis

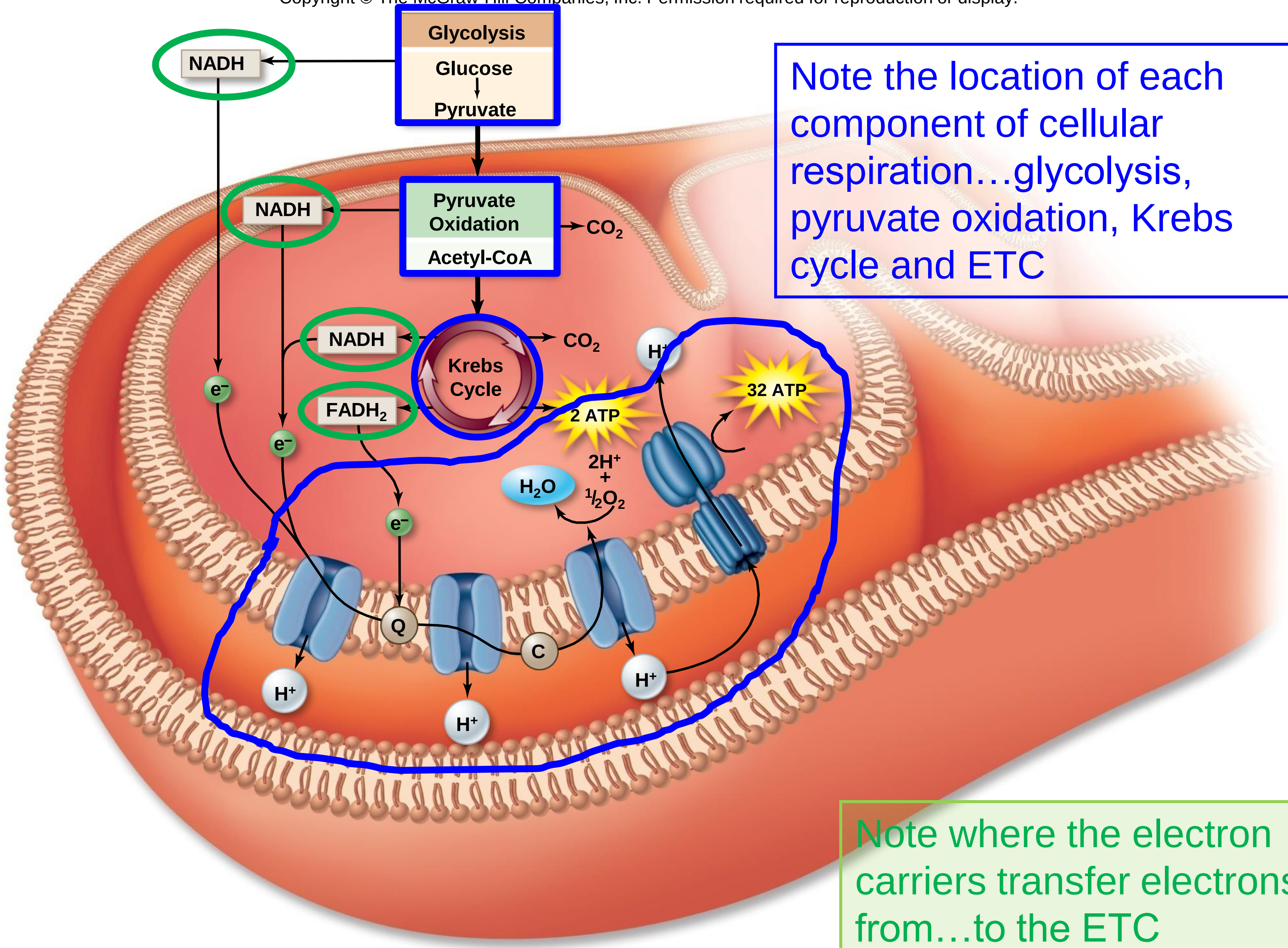
- Accumulation of protons (H^+) in **intermembrane space** drives protons into the matrix via diffusion
- Membrane relatively impermeable to ions
- Most H^+ can only reenter matrix via **ATP synthase**
  - Uses energy of gradient to make ATP from ADP + P_i
  - Proton Motive Force



a. The electron transport chain

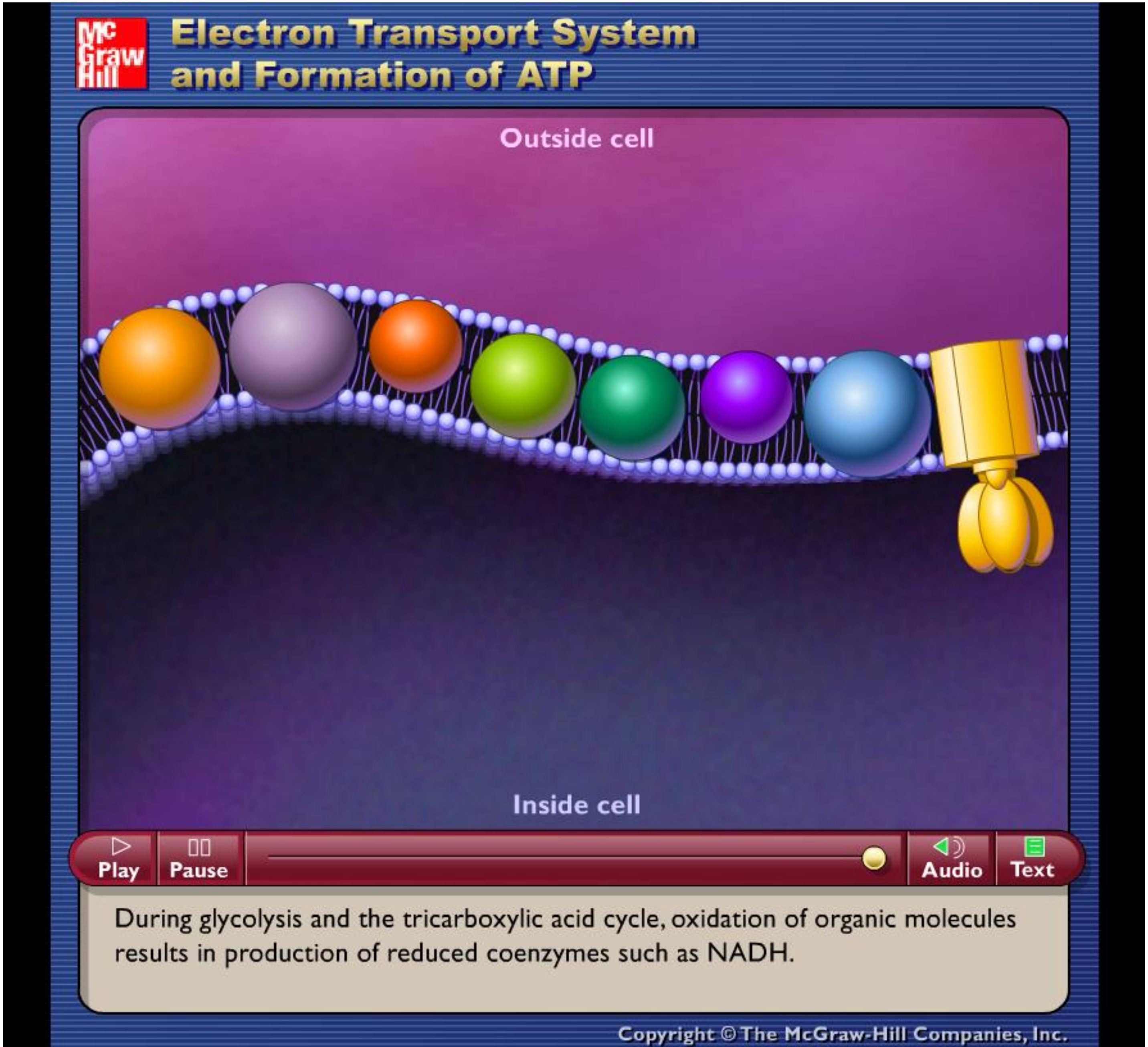
b. Chemiosmosis


H+
Mitochondrial matrix
ATP
ADP + Pi
Catalytic head
Stalk
Rotor
Intermembrane space
H+
H+
H+
H+
H+
H+



Note the location of each component of cellular respiration…glycolysis, pyruvate oxidation, Krebs cycle and ETC

Note where the electron carriers transfer electrons from…to the ETC


McGraw Hill
Electron Transport System and Formation of ATP
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During glycolysis and the tricarboxylic acid cycle, oxidation of organic molecules results in production of reduced coenzymes such as NADH.
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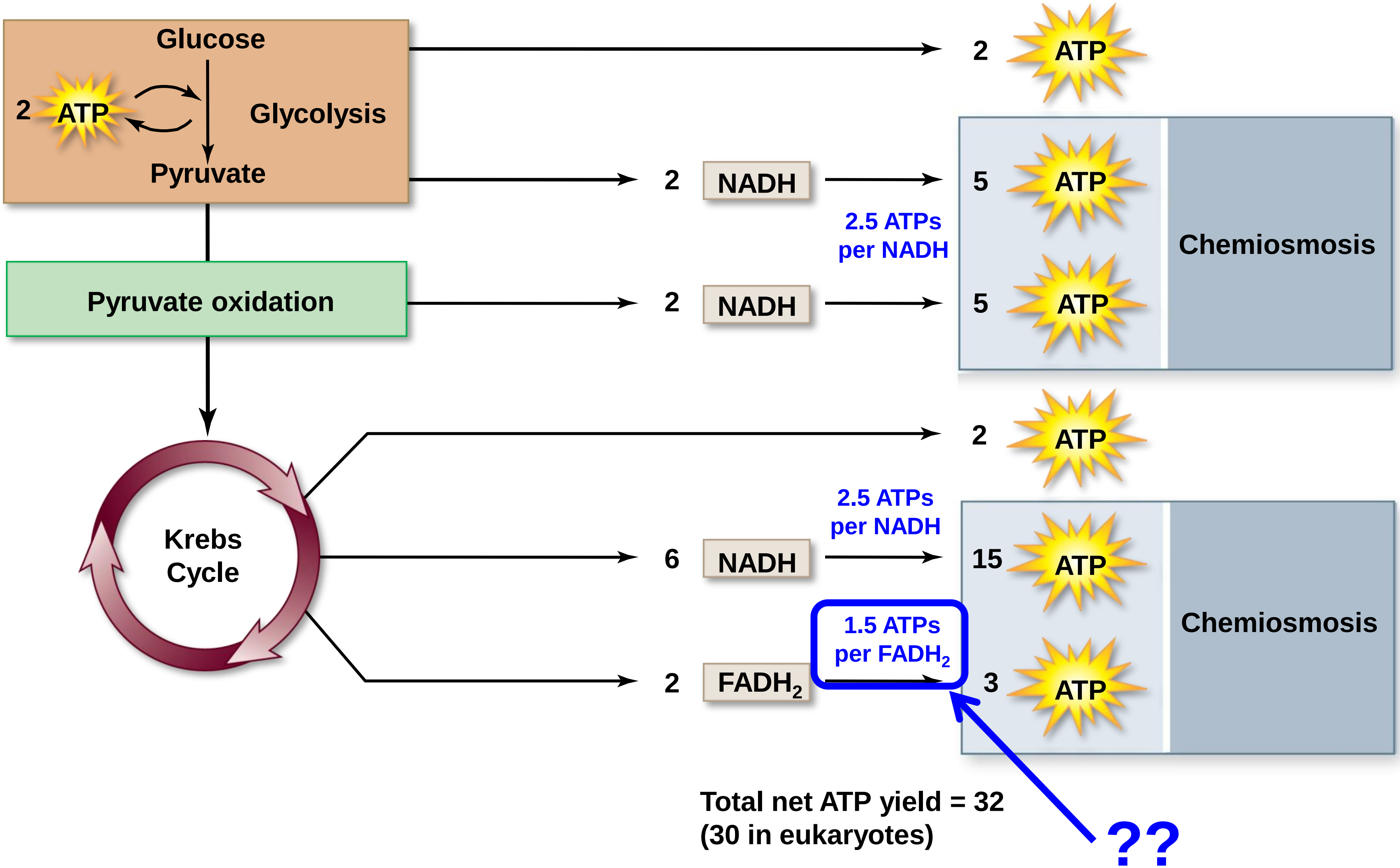
Energy Yield of Respiration

- Theoretical energy yield (these values vary from book to book)
  - 38 ATP per glucose for bacteria
  - 36 ATP per glucose for eukaryotes

Really Important!!

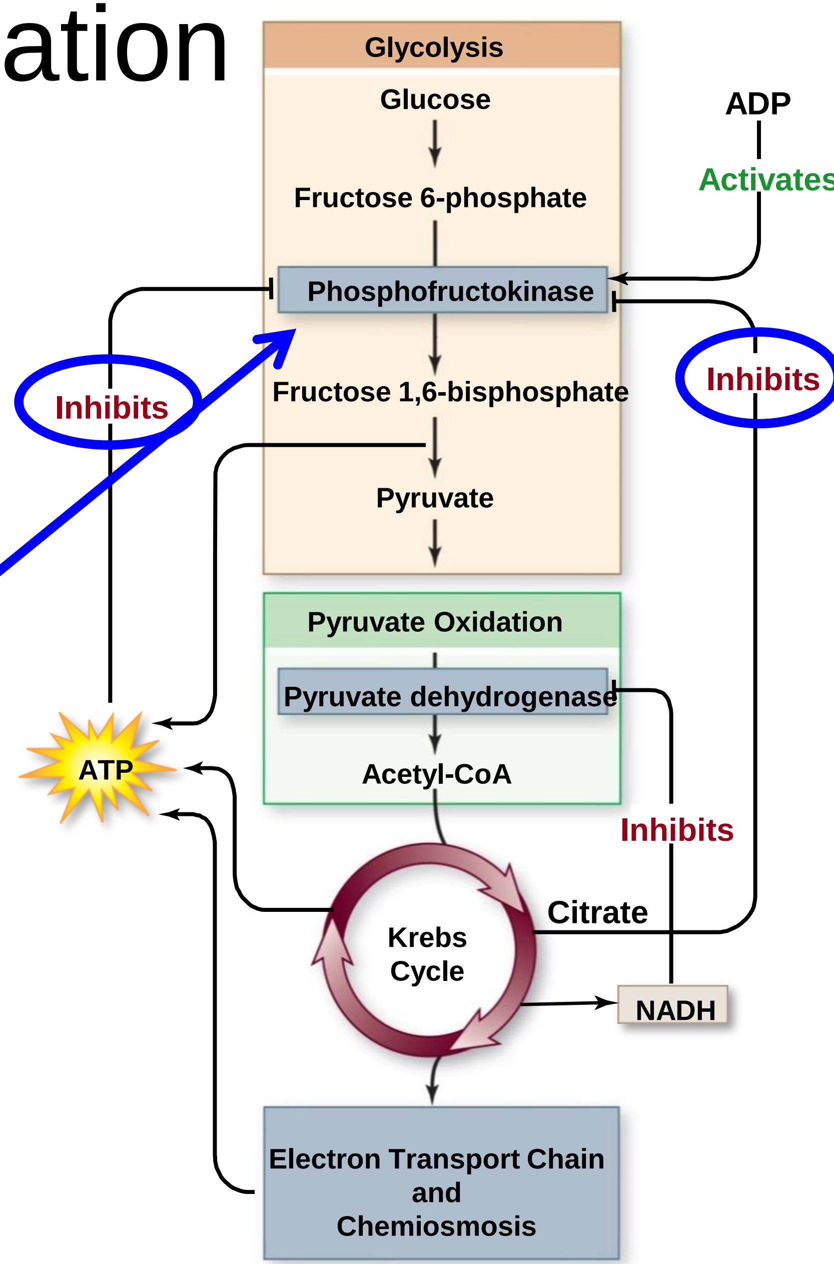
- Actual energy yield
  - 30 ATP per glucose for eukaryotes
  - Reduced yield is due to…
    - "Leaky" inner membrane
    - Use of the proton gradient for purposes other than ATP synthesis



Total net ATP yield = 32
(30 in eukaryotes)

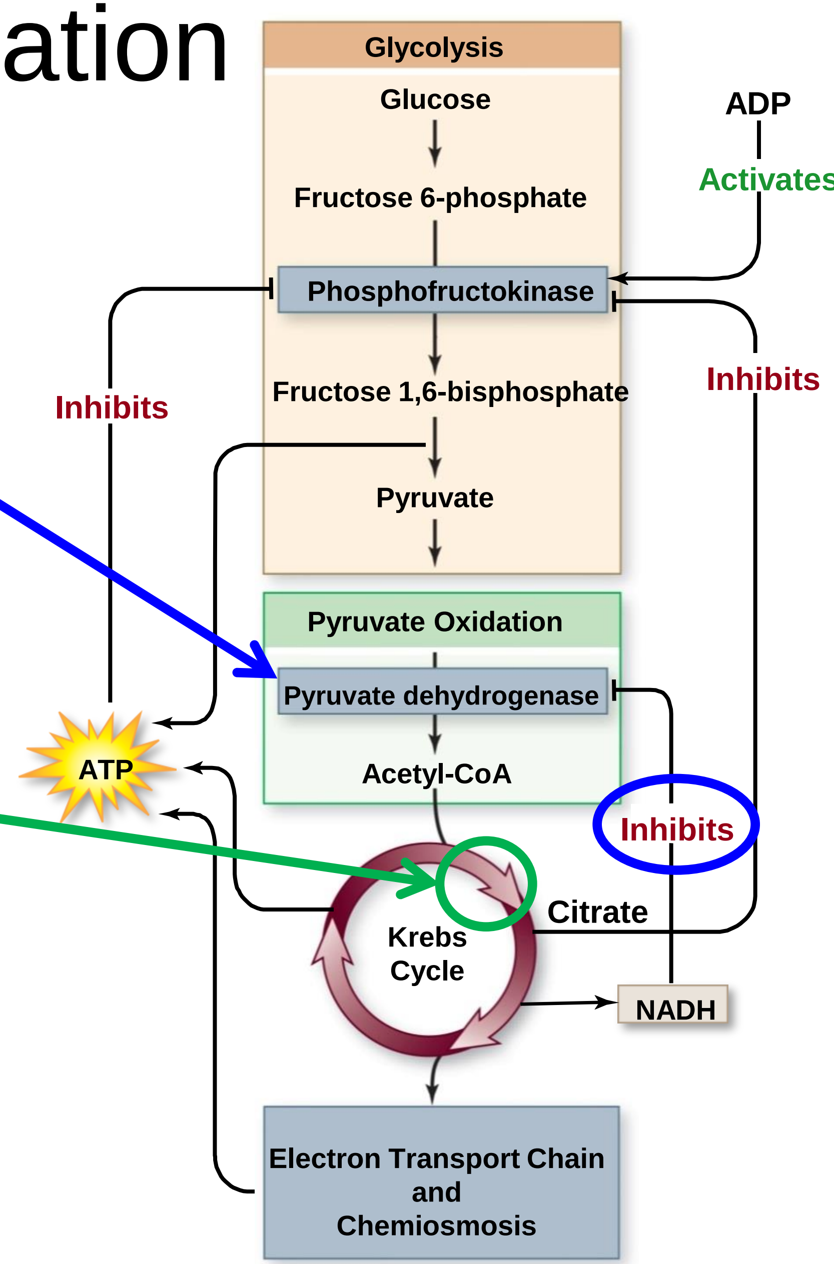
Regulation of Respiration

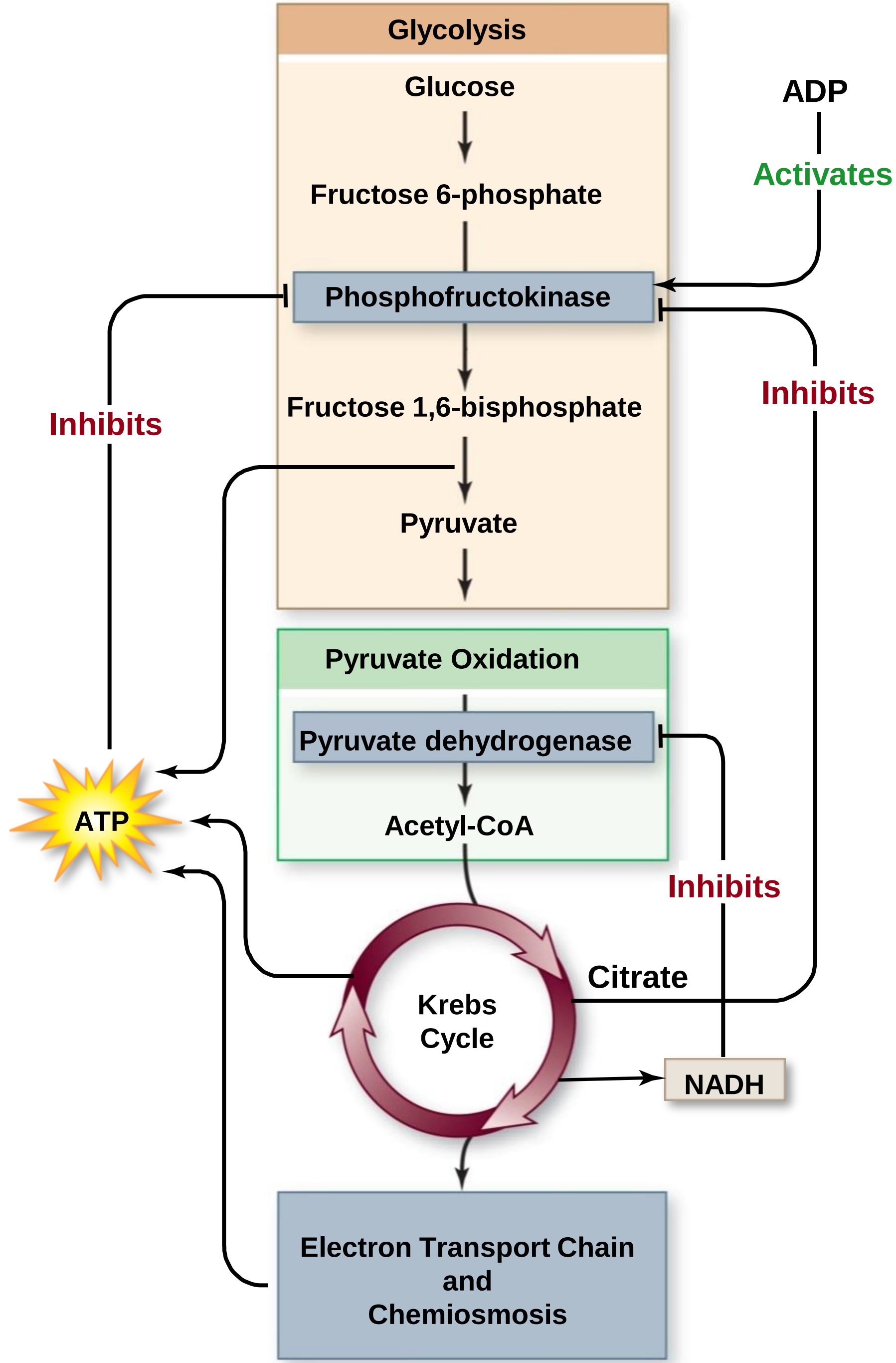
- Examples of *negative* feedback inhibition
- Two key control points
  1. In glycolysis
     - **Phosphofructokinase** is allosterically inhibited by ATP and/or citrate



Regulation of Respiration

- Two key control points
  2. In pyruvate oxidation
     - Pyruvate dehydrogenase inhibited by high levels of NADH
     - Citrate synthetase inhibited by high levels of ATP




Glycolysis
Glucose
Fructose 6-phosphate
Phosphofructokinase
Fructose 1,6-bisphosphate
Pyruvate
ADP
Activates
Inhibits
Inhibits
Pyruvate Oxidation
Pyruvate dehydrogenase
Acetyl-CoA
Inhibits
ATP
Citrate
Krebs
Cycle
NADH
Electron Transport Chain
and
Chemiosmosis

Oxidation Without O_2

1. **Anaerobic respiration**
   – Use of inorganic molecules (other than O_2) as final electron acceptor
   – Many prokaryotes use sulfur, nitrate, carbon dioxide or even inorganic metals

2. **Fermentation**
   – Use of organic molecules as final electron acceptor

Anaerobic respiration

- Methanogens
  - CO_2 is reduced to CH_4 (methane)
  - Found in diverse organisms including cows
- Sulfur bacteria
  - Inorganic sulphate (SO_4) is reduced to hydrogen sulfide (H_2S)
  - Early sulfate reducers set the stage for evolution of photosynthesis

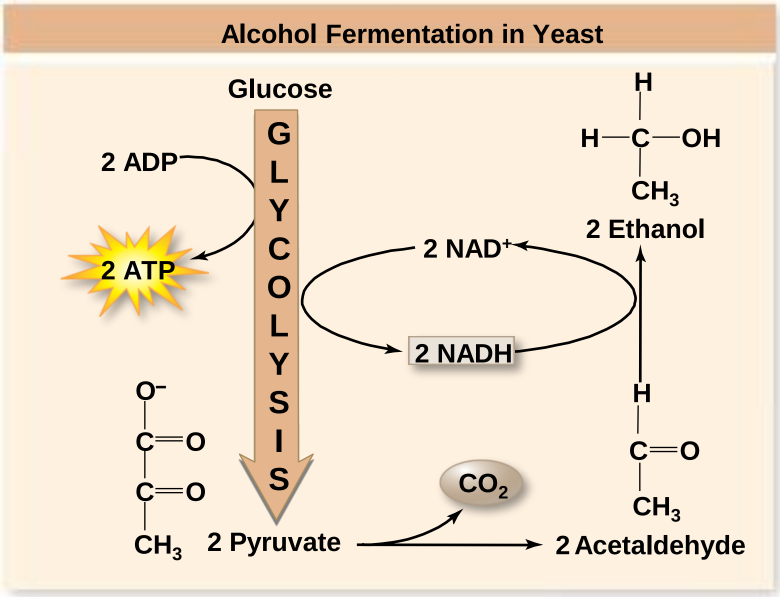
a. ***b.***

a: © Wolfgang Baumeister/Photo Researchers, Inc.; b: NPS Photo

Fermentation

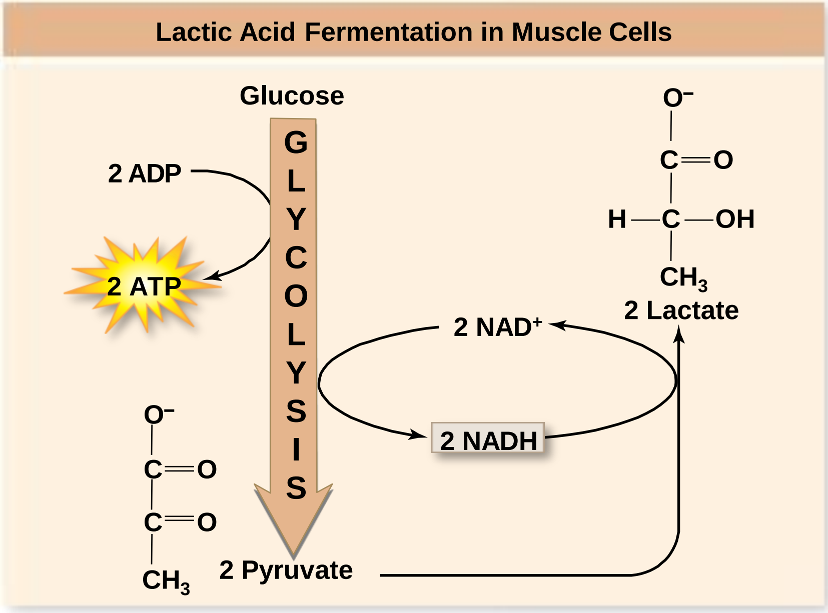
- Reduces organic molecules in order to *<u>regenerate NAD⁺</u>* to supply glycolysis allowing it to continue, even in absence of O_2

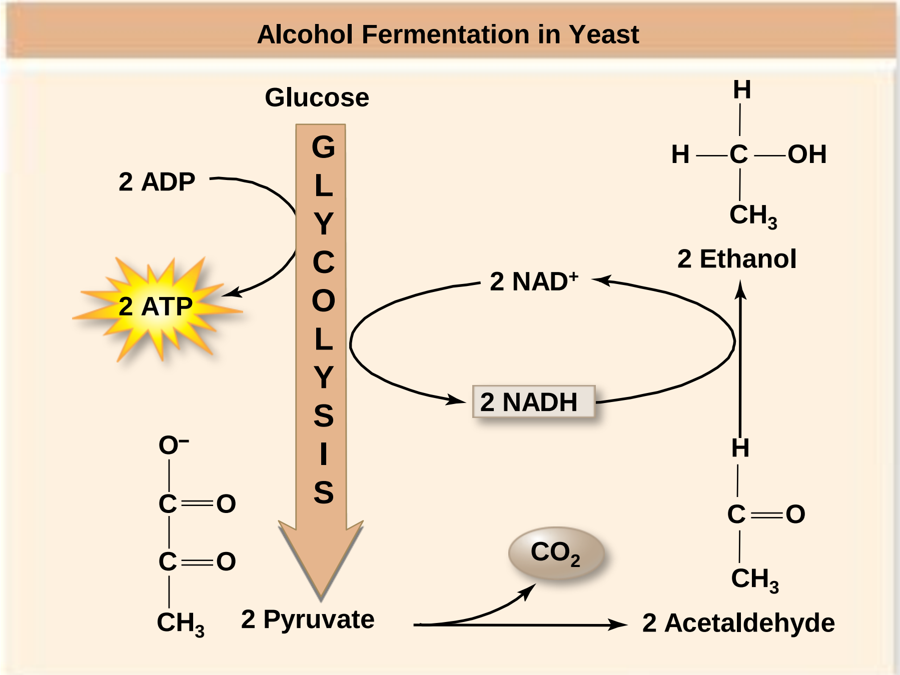
1. **Ethanol fermentation** occurs in yeast
   - CO_2, ethanol, and NAD^+ are produced

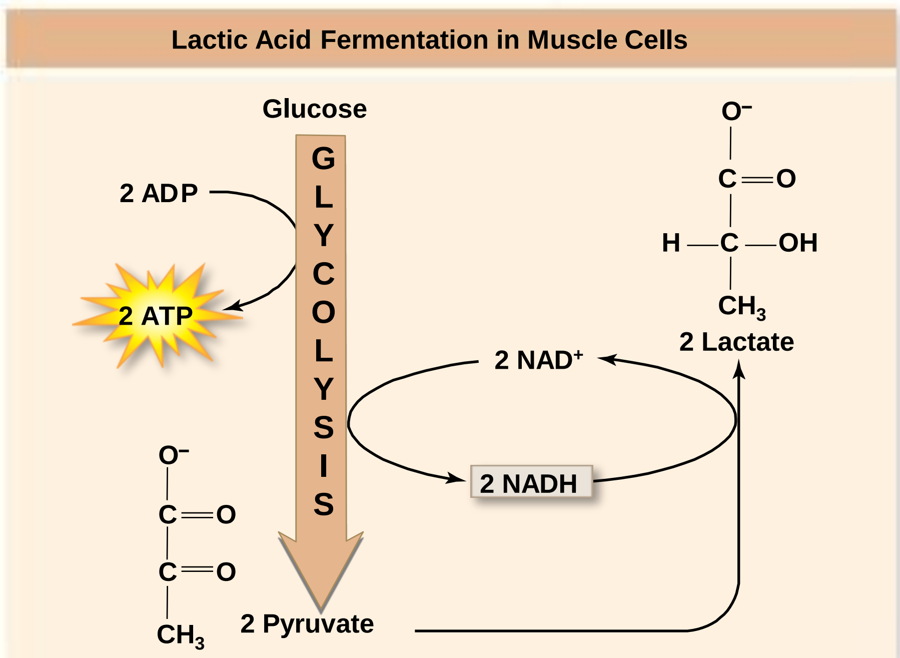


Fermentation

2. **Lactic acid fermentation**
   - Electrons are transferred from NADH to pyruvate to produce lactic acid
   - Occurs in animal cells (*especially muscles, such as during sprinting)*

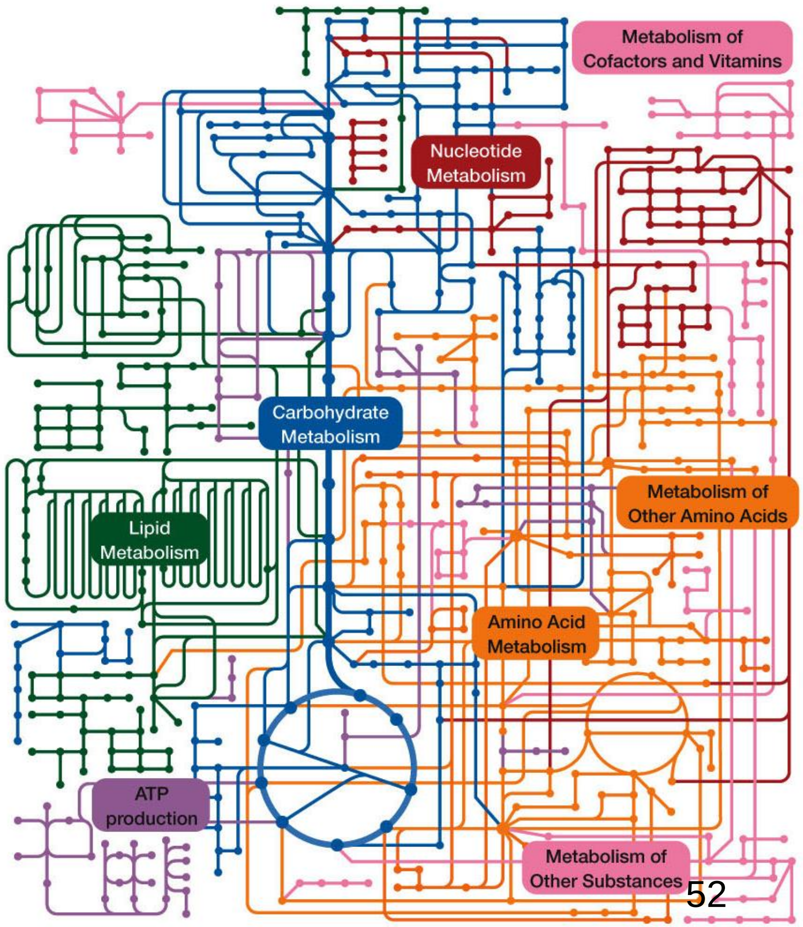



Alcohol Fermentation in Yeast
Glucose
GLYCOLYSIS
2 ADP
2 ATP
2 NAD+
2 NADH
2 Ethanol
CO2
2 Pyruvate
2 Acetaldehyde


Lactic Acid Fermentation in Muscle Cells
Glucose
GLYCOLYSIS
2 ADP
2 ATP
2 NAD+
2 NADH
2 Lactate
2 Pyruvate

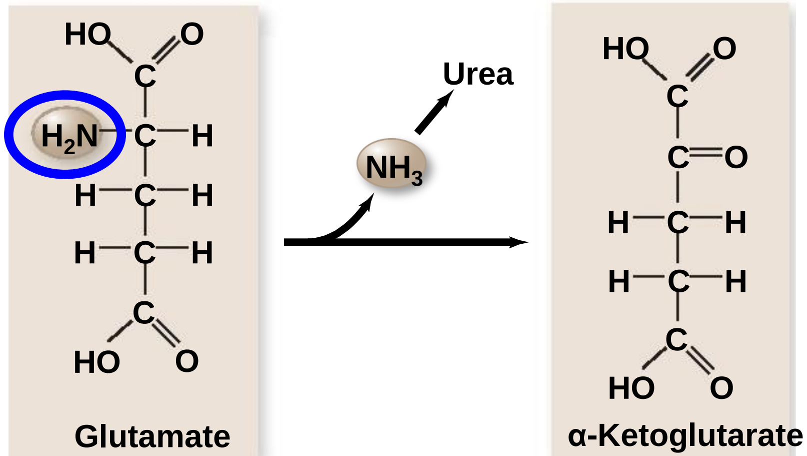
Anabolic and Catabolism Pathways

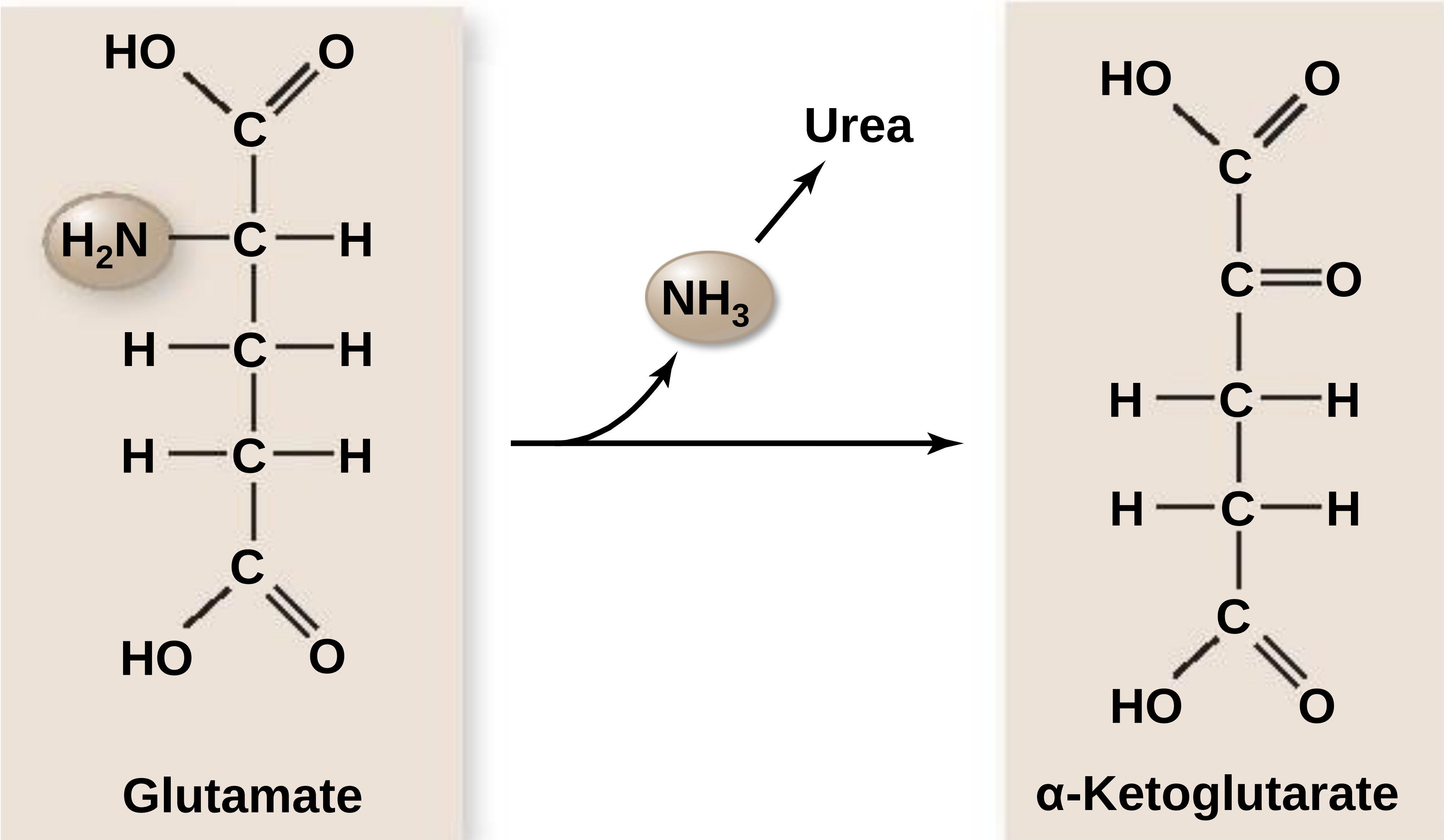
- Metabolic pathways are linked to reversible pathways of cellular respiration
  - Large molecules broken down and rearranged – **catabolic pathways**
  - Most larger molecules needed by the cell are produced – **anabolic pathways**



Example of Catabolism of Protein

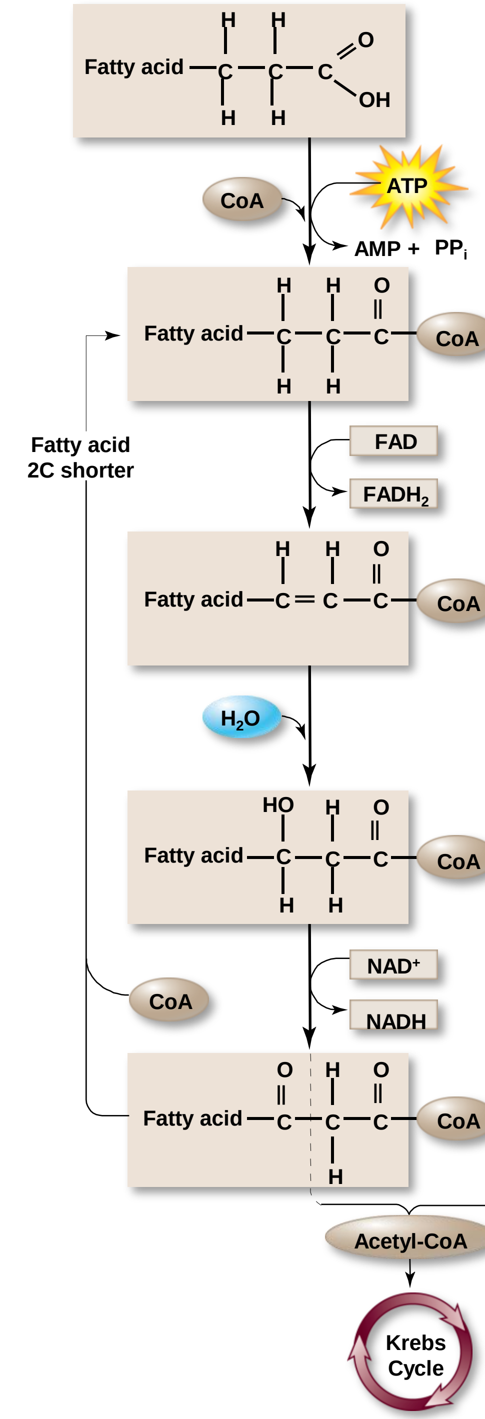
- Amino acids undergo deamination to remove the amino group (-NH_2)
- Remainder of the amino acid is converted to a molecule that enters glycolysis or the Krebs cycle
  - Alanine is converted to pyruvate
  - Aspartate is converted to oxaloacetate

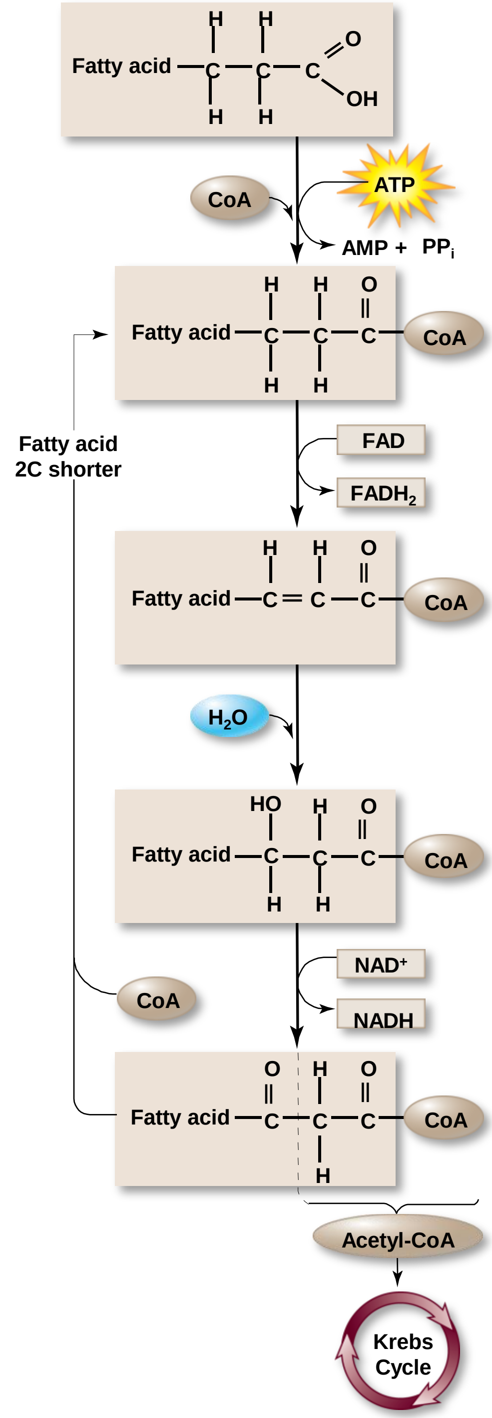


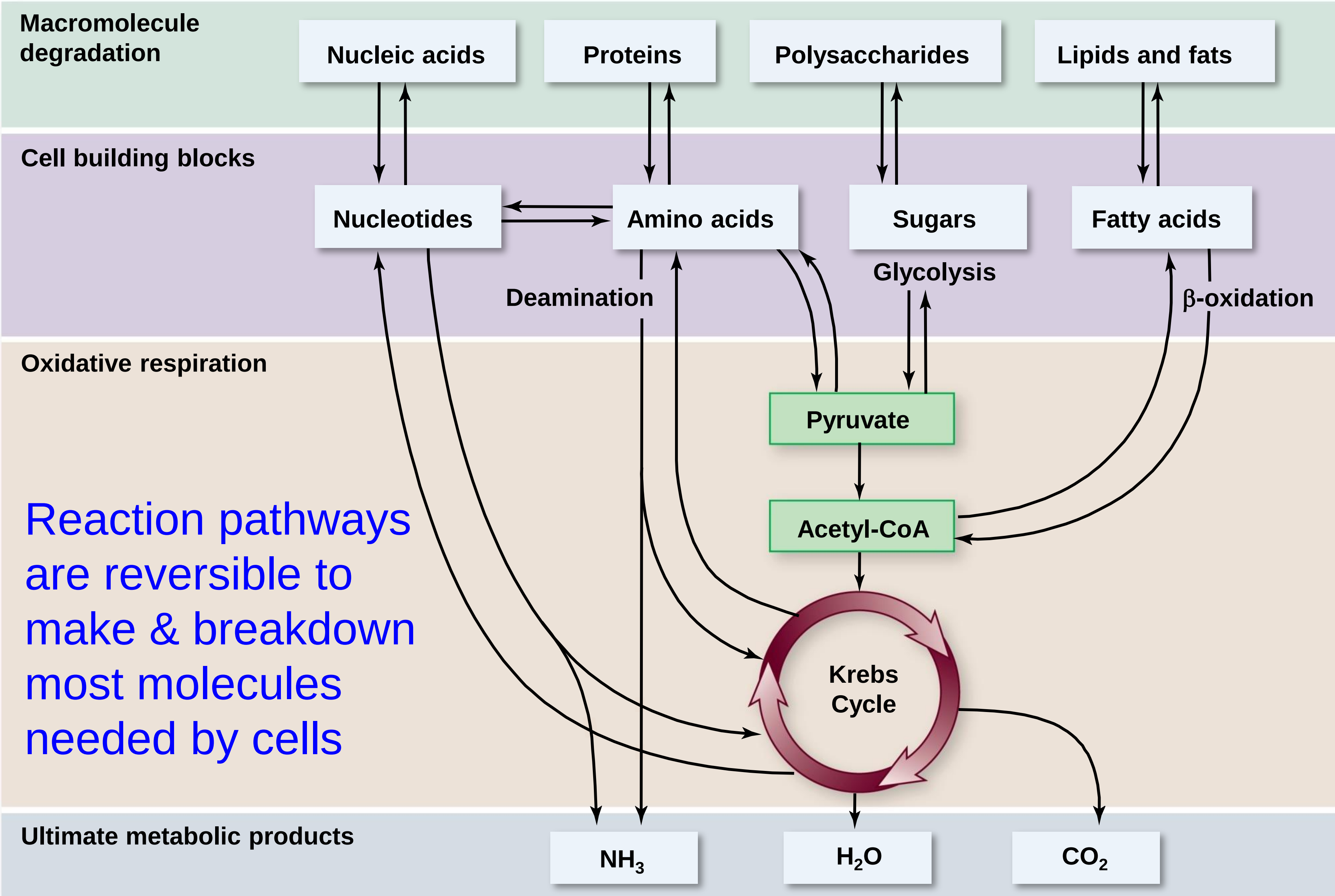

HO
O
C
H_2N
C
H
H
C
H
H
C
H
C
HO
O
Glutamate
Urea
NH_3
HO
O
C
C
O
H
C
H
H
C
H
C
HO
O
α-Ketoglutarate

Catabolism of Fat

- Fats are broken down to fatty acids and glycerol
  - Fatty acids are converted to 2-C acetyl groups by β-oxidation
  - Oxygen-dependent process
- The respiration of a 6-carbon fatty acid yields 20% more energy than 6-carbon glucose
- Runs in reverse to produce fats




Fatty acid
CoA
ATP
AMP + PPi
Fatty acid
CoA
FAD
FADH2
Fatty acid 2C shorter
Fatty acid
CoA
H2O
Fatty acid
CoA
NAD+
NADH
CoA
Fatty acid
CoA
Acetyl-CoA
Krebs Cycle



Reaction pathways are reversible to make & breakdown most molecules needed by cells

Evolution of Metabolism

- Hypothetical timeline
  1. Ability to store chemical energy in ATP
  2. Evolution of glycolysis
     - Pathway found in all living organisms
  3. Anaerobic photosynthesis (using H_2S)
  4. Use of H_2O in photosynthesis (not H_2S)
     - Begins permanent change in Earth's atmosphere about 2.4 Bya
  5. Evolution of nitrogen fixation
  6. Aerobic respiration evolved most recently