General Biology 1
BIO1101
Syllabus & Textbook: http://goo.gl/rvgdrH

Lecturer: Michael Gotesman, PhD
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Letter Grade	Numerical Ranges
A	93-100
A-	90-92.9
B+	87-89.9
B	83-86.9
B-	80-82.9
C+	77-79.9
C	70-76.9
D	60-69.9
F	59.9 and below

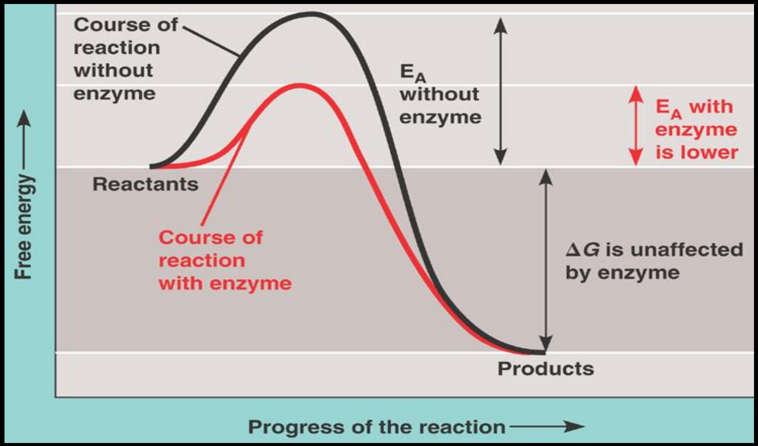
OER
Lecture: https://openlab.citytech.cuny.edu/bio-oer/page/2/
Lab: https://openlab.citytech.cuny.edu/bio-oer/

Grade Breakdown:
Exams (4): 20% Each
Quizzes: 20% Average

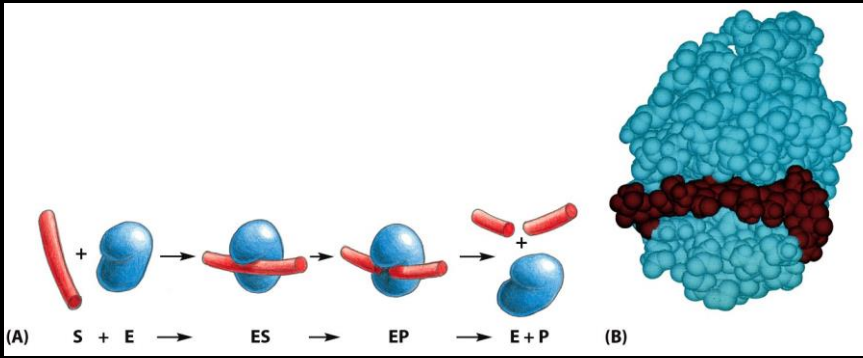
Recap: Lecture 15

A. Enzymes are Organic Catalysts

1) Lower the E_a (Activation energy) of reaction
2) They participate in Metabolic reactions



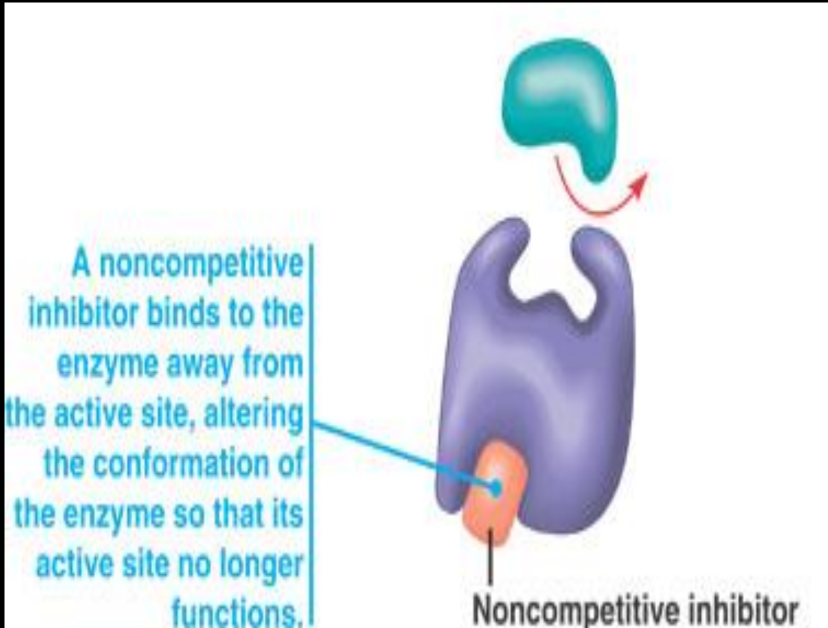
B. 4 Steps in reaction:



What's an active site?

C. Factors that effect Enzyme Activity

1) Temperature
2) pH
3) Substrate concentration



D. Enzyme Control

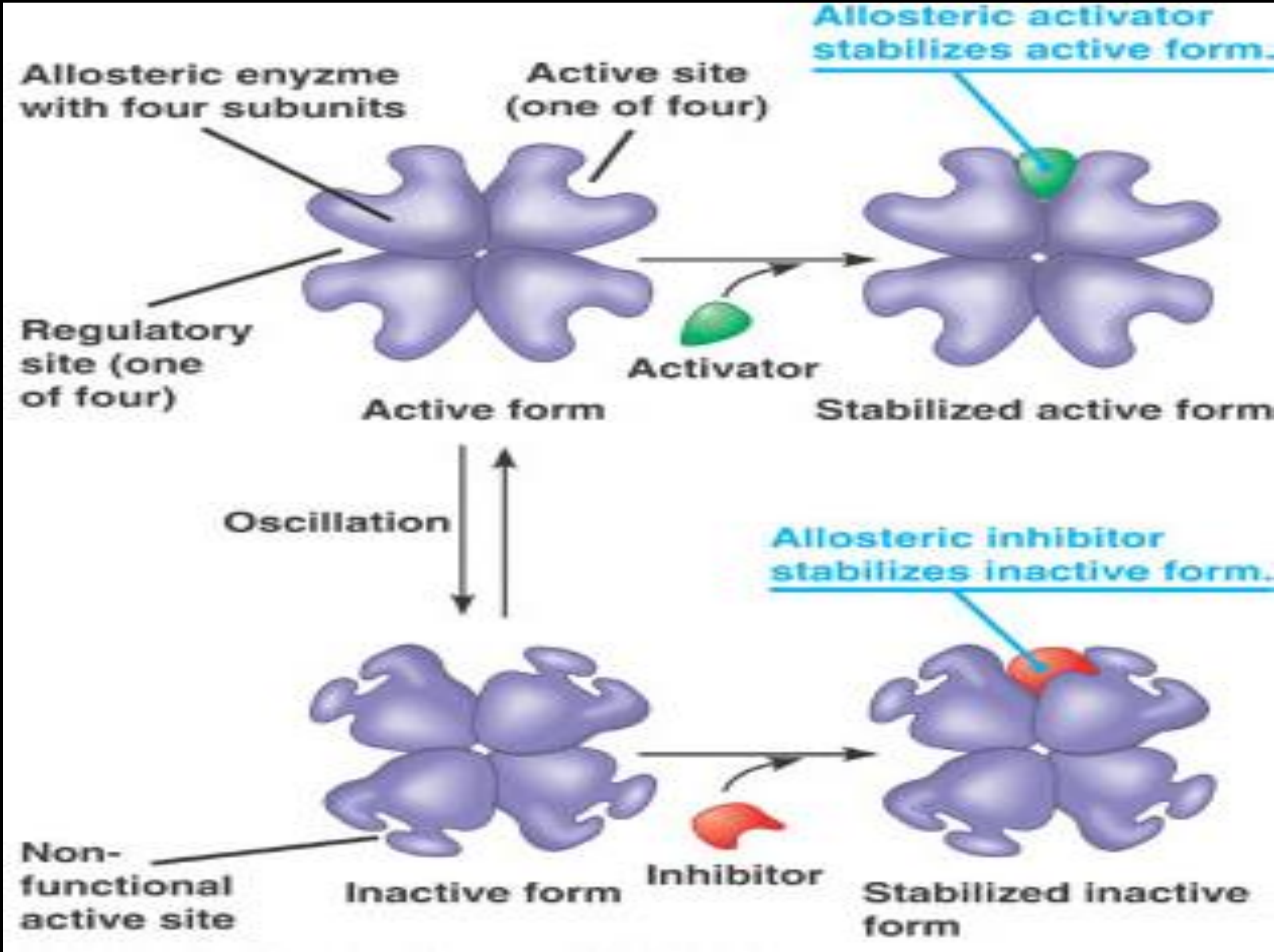
A) Activation/Inhibition
B) Direct/Indirect (Allosteric)

Metabolic Control

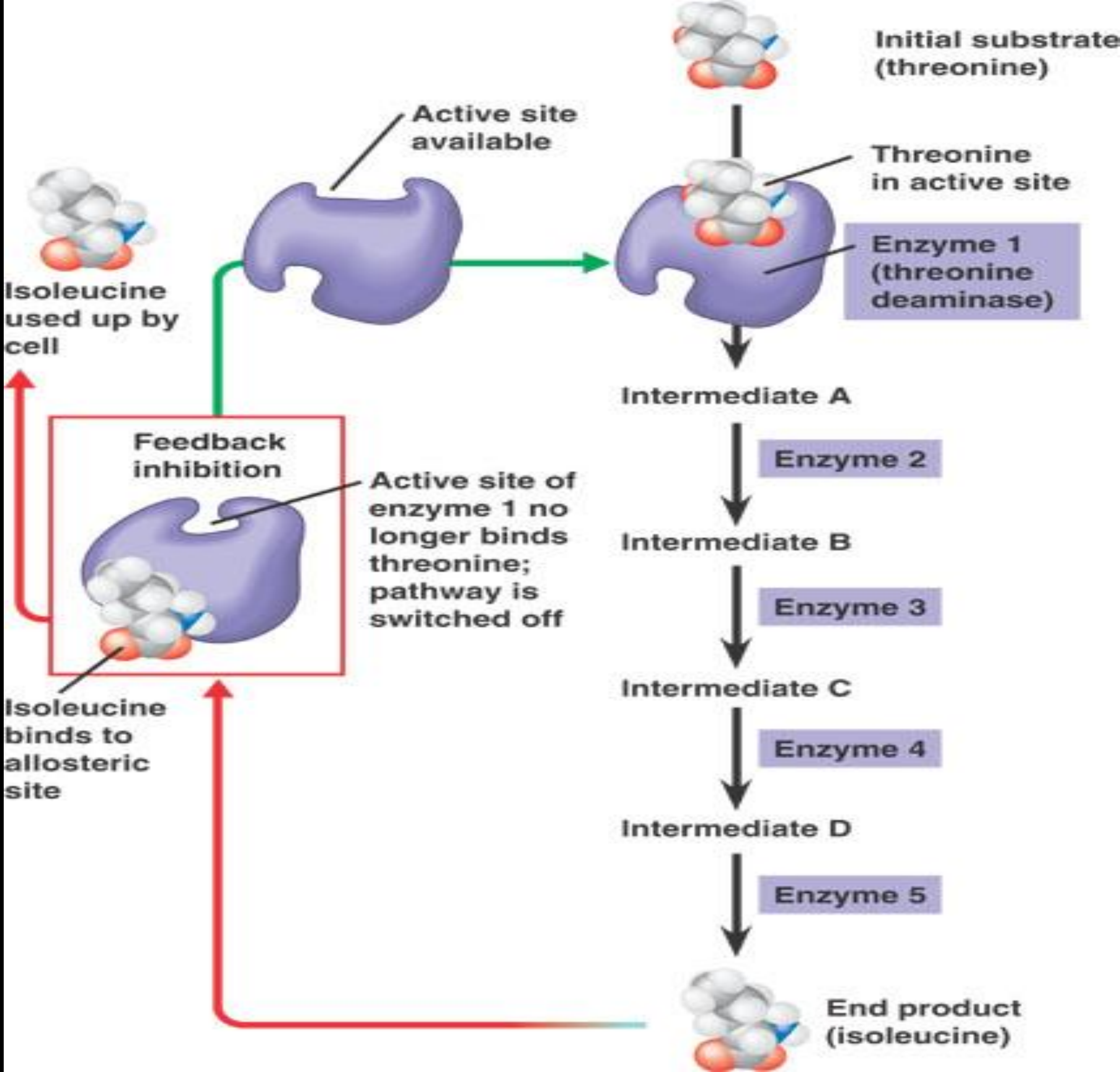
- Not all metabolic pathways are “turned on” all the time.
- Enzyme pathways are “regulated” (ON or OFF as needed)
  - Sometimes, enzyme are only MADE when needed
  - More often… they are controlled by **allosteric regulation**
    - Can be positive or negative
- **Feedback Inhibition** is the most common
  - This is when the final product of a pathway (in high concentration) inhibits the enzymes of that pathway

Allosteric regulation:

Lactate dehydrogenase is composed of four subunits (tetramer).



Feedback inhibition



Irreversible Inhibition

- Materials that irreversibly inhibit an enzyme are known as poisons
- Cyanides inhibit enzymes resulting in all ATP production
- Penicillin inhibits an enzyme unique to certain bacteria
- Heavy metals irreversibly bind with many enzymes
- Nerve gas irreversibly inhibits enzymes required by nervous system

Name: Quiz 6 10/25/17

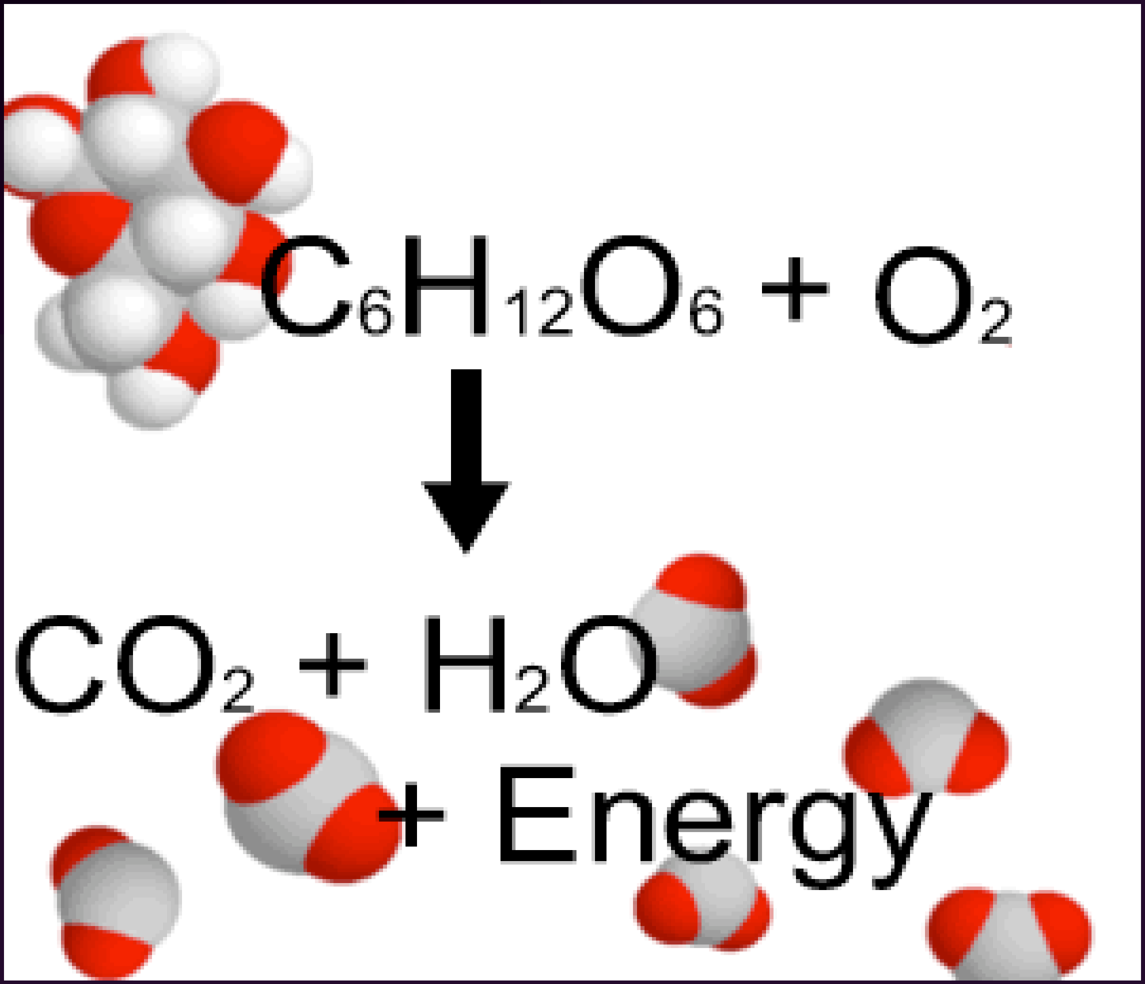
Q1 (10 points): True or False, All the Energy of the universe is constant?
Q2 (10 points): True or False, There's a tendency for Entropy to decrease during reactions?
Q3 (10 points): True or False, When the ΔG change in Gibb's is positive, the reaction will be spontaneous (occur on its own)?

Q4 (20 points): Explain the difference between Endergonic and Exergonic?
(Fill in the blank) In an endergonic rxn…. In an exergonic….

Q5 (20 points): Explain the difference between Anabolic and Catabolic?
(Fill in the blank) Anabolic rxn…. In an catabolic….

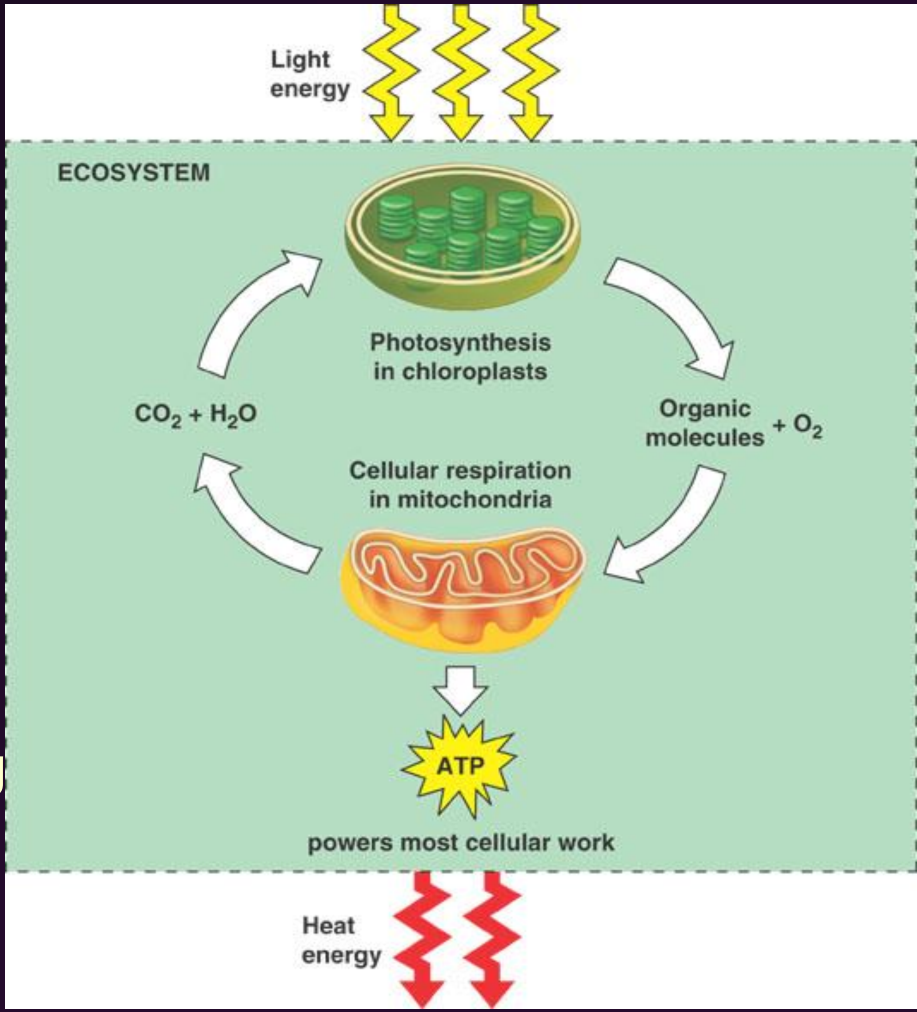
Q6 (10 points): What is the currency of the cell?
Q7 (10 points): What do we call an organic catalyst made of protein?
Q8 (10 points): What is meant by the terms: product & substrate?

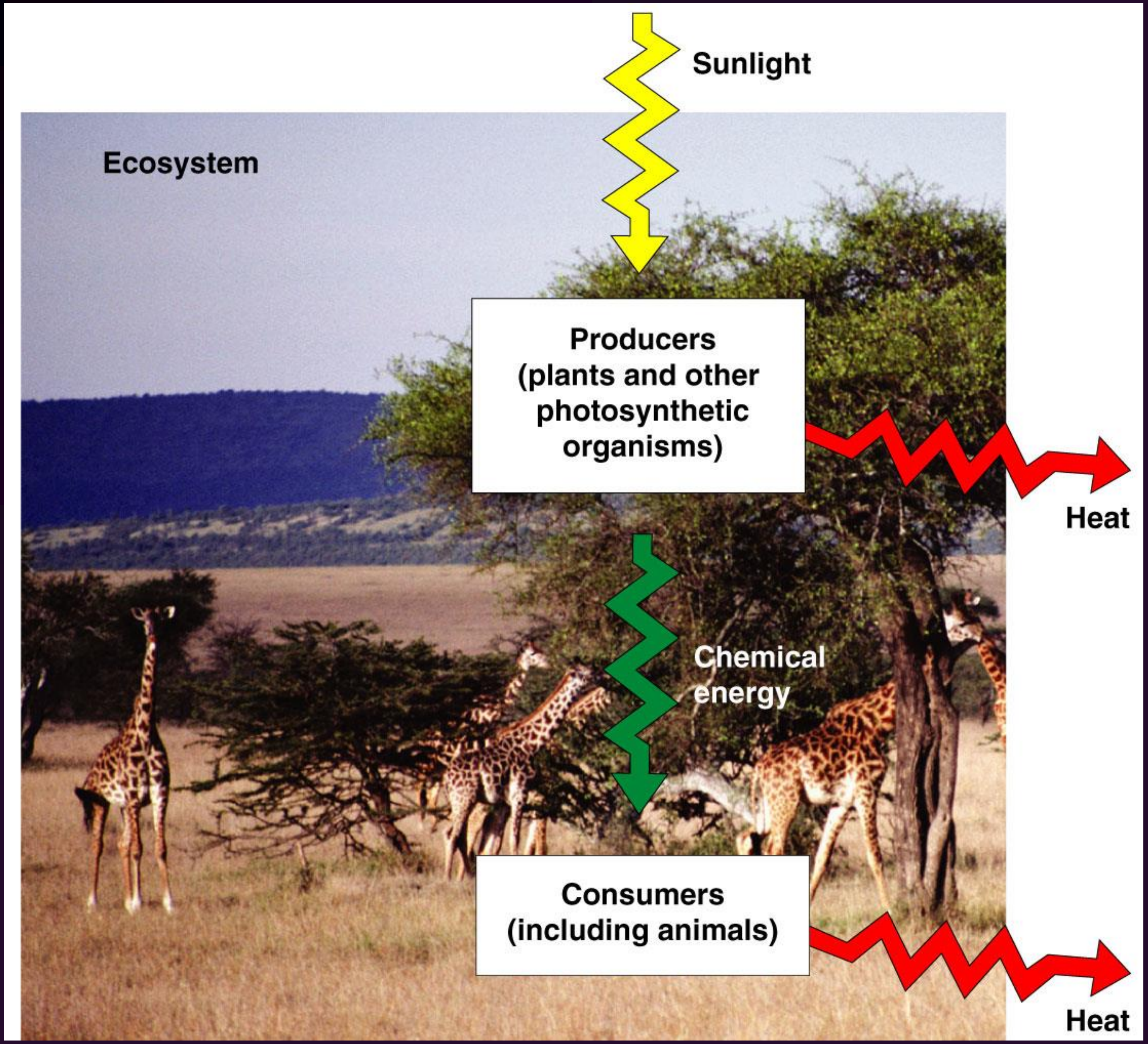
Cellular Respiration



Review of Energy Flow

- E comes to earth from the sun:
- Solar E converted to chemical E by photosynthesis (chloroplasts)
  - Glucose
- Cells harvest Chemical E by Respiration (mitochondria)
  - ATP
- The E of ATP powers cellular “work”
  - Most E is actually lost as heat along the way!




Sunlight
Ecosystem
Producers
(plants and other
photosynthetic
organisms)
Heat
Chemical
energy
Consumers
(including animals)
Heat

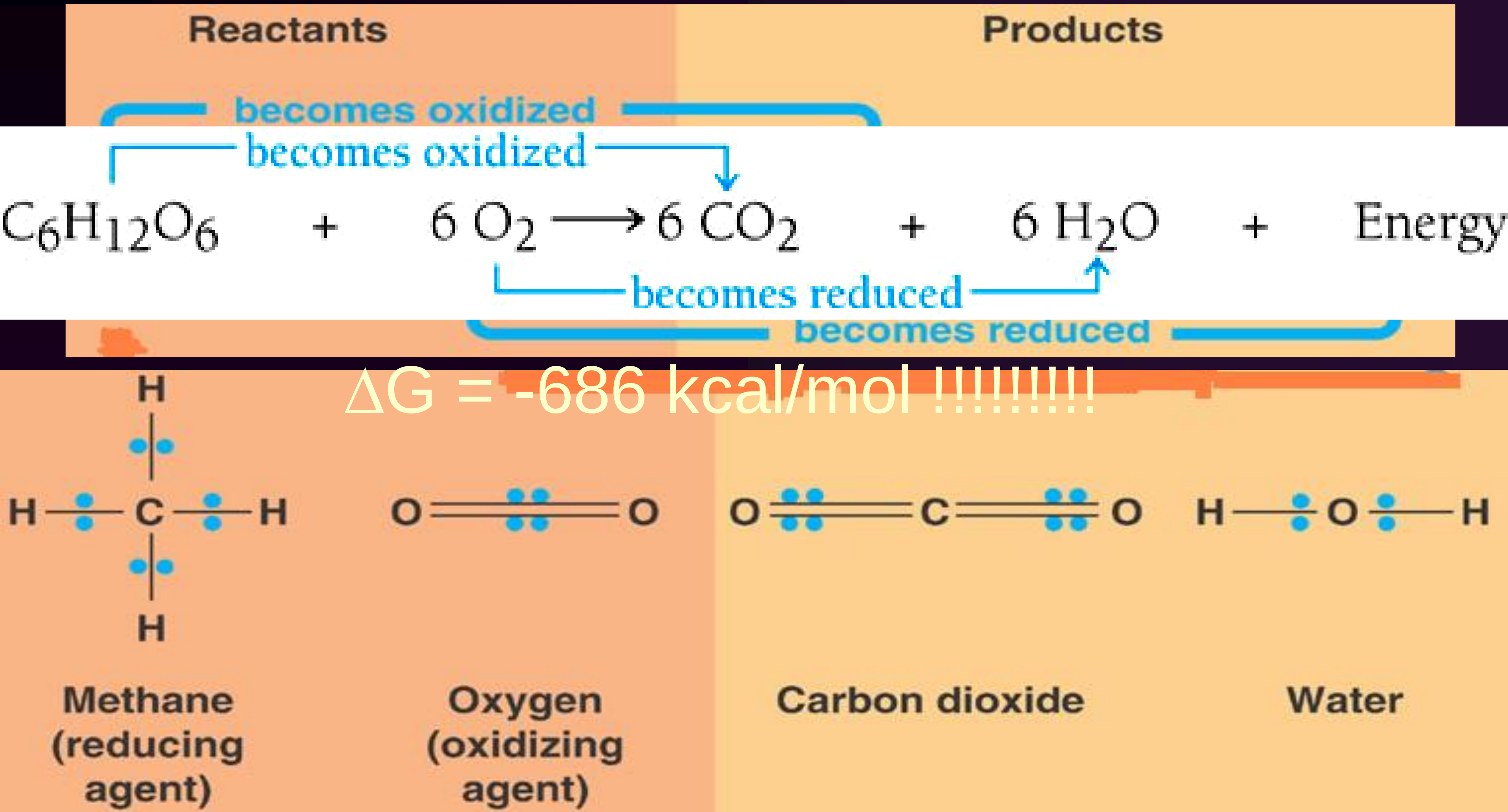
Oxidation-Reduction

- Oxidation-reduction (redox) reactions:
  - Electrons pass from one molecule to another
    - The molecule that loses an electron is oxidized
    - The molecule that gains an electron is reduced
  - Both take place at same time
  - One molecule accepts the electron given up by the other

Oxidation / Reduction (redox)

- **Oxidation** = loss of electrons
- **Reduction** = gain of electrons
    - *Tip – think "reduction" of charge number*
- This is why they always occur together (redox)
- Other rules of Redox
    - Gain of O = oxidation, loss of O = reduction
    - Gain of [H^-] = reduction, loss of [H^-] = oxidation
        - *Tip – the "H" always goes with the e^-'s*
        - *This is because, in redox, the e^-'s are passed as a hydride ion (H^-)*

Examples



$\Delta G = -686$ kcal/mol !!!!!!!!!

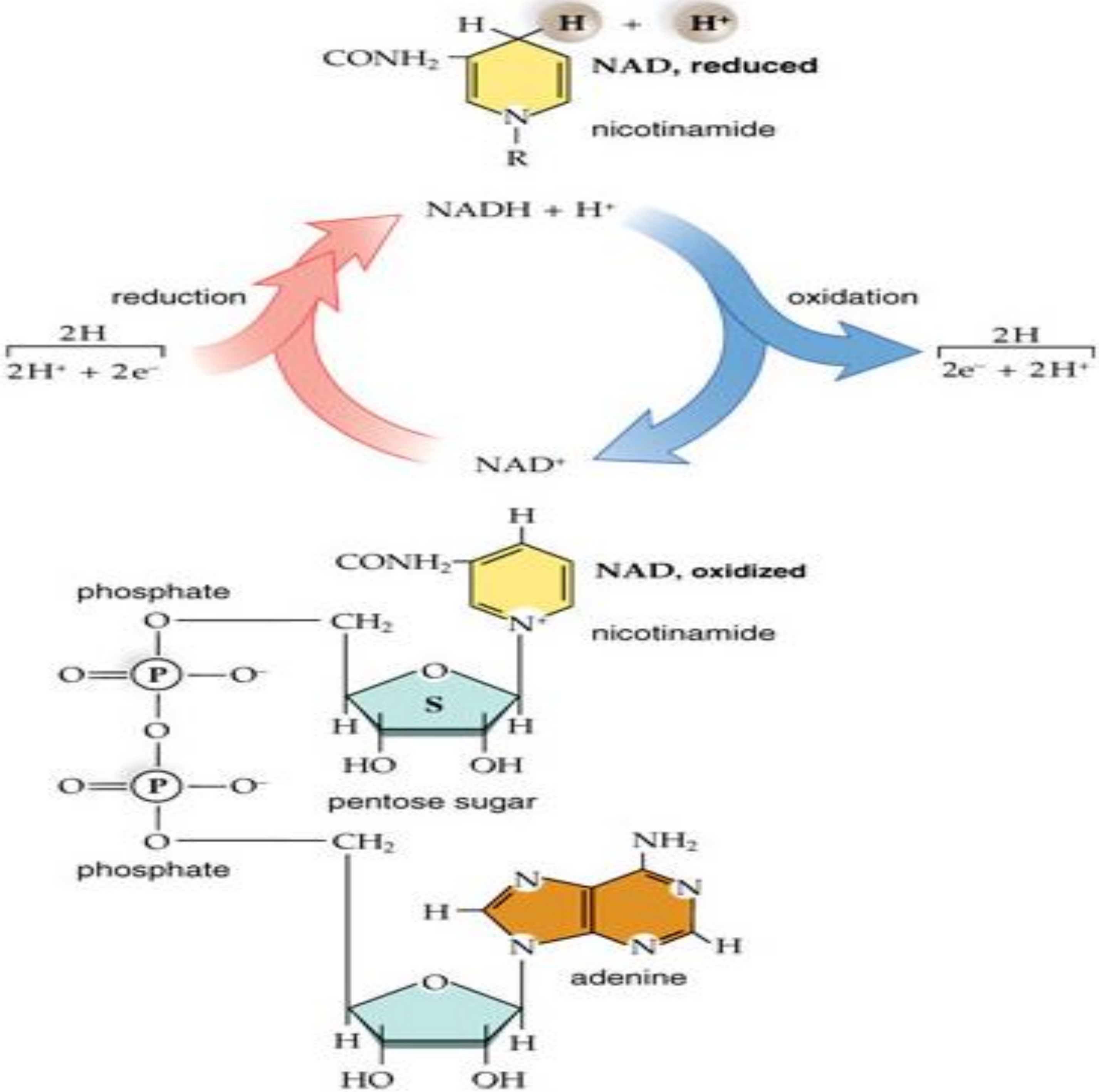
Respiration is catabolism

- There are 2 catabolic pathways for sugars:
  - **Fermentation** – **anaerobic** (no O_2 required), only partial degradation, much less E harvested
  - **Cellular Respiration** – **aerobic** (O_2 required), COMPLETE oxidation of all carbons to CO_2
    - Much more E is harvested
- The catabolic reactions of life involve the transfer of high-energy electrons. Thus, these are called Oxidation/Reduction reactions

NAD^+ and FAD

- NAD^+ (nicotinamide adenine dinucleotide)
  - Called a coenzyme of oxidation-reduction it can
    - Oxidize a metabolite by accepting electrons
    - Reduce a metabolite by giving up electrons
  - $NAD^+ + H^- \rightarrow NADH$
  - Each NAD^+ molecule used over and over again
- FAD (flavin adenine dinucleotide)
  - Also a coenzyme of oxidation-reduction
  - Sometimes used instead of NAD^+
  - Accepts two electrons and two hydrogen ions (H^+) to become $FADH_2$

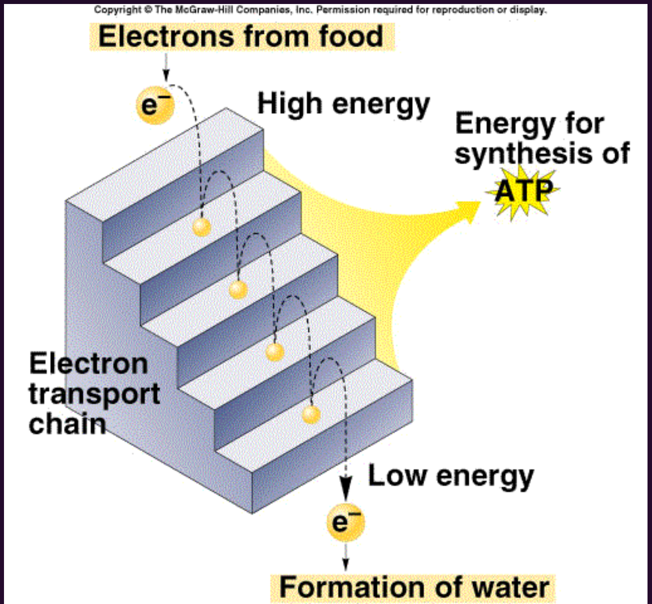
NAD$^+$ Cycle



H
H
+
H+
CONH2
NAD, reduced
N
nicotinamide
R
NADH + H+
reduction
oxidation
2H
2H+ + 2e−
2H
2e− + 2H+
NAD+
H
CONH2
NAD, oxidized
phosphate
O
CH2
N+
nicotinamide
O
P
O−
S
H
H
HO
OH
pentose sugar
phosphate
NH2
N
N
H
N
N
H
adenine
O
H
H
HO
OH

Cellular Respiration

- A cellular process that requires oxygen and gives off carbon dioxide
- Usually involves breakdown of glucose to carbon dioxide and water
  - Oxidation-reduction enzymes include NAD^+ and FAD as coenzymes
- Energy extracted from glucose:
  - Released step-wise
  - Allows ATP to be produced efficiently



The energy of electrons

- e^-' s that are in C-H bonds are shared equally (nonpolar bond)
  - Thus, the e^- in C-H are considered "high energy"
- Explanation….
- Pulling e- from a MORE electronegative and giving to a LESS electronegative atom would require E. (Splitting H_2O)
  - This is what photosynthesis does!
- So, passing e- from a LESS electronegative atom to a MORE electronegative atom RELEASES E
- Remember that the H goes with the e^- (as H^-)

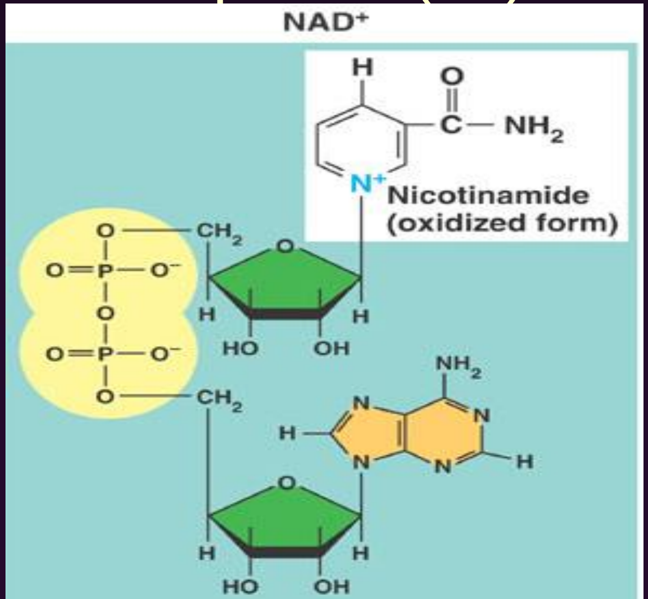
becomes oxidized

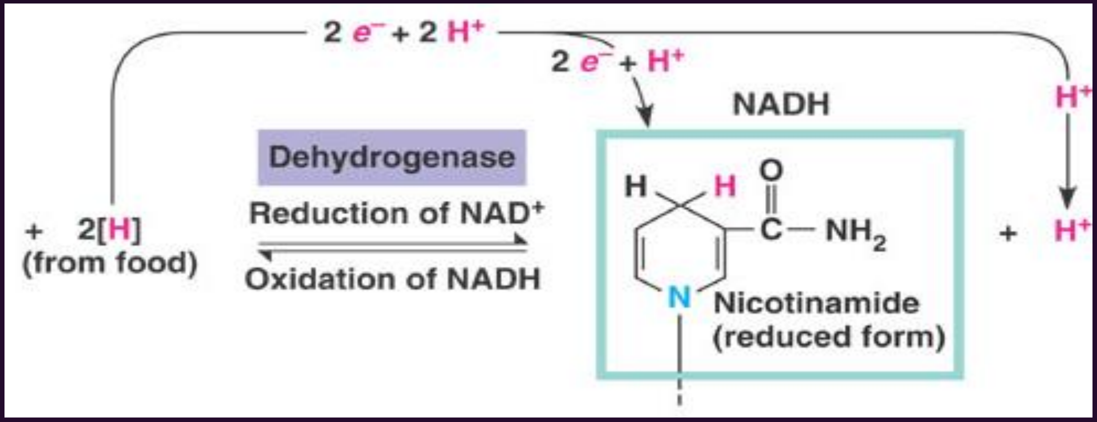
$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + \text{Energy}$$

becomes reduced

e⁻' s are passed in small steps

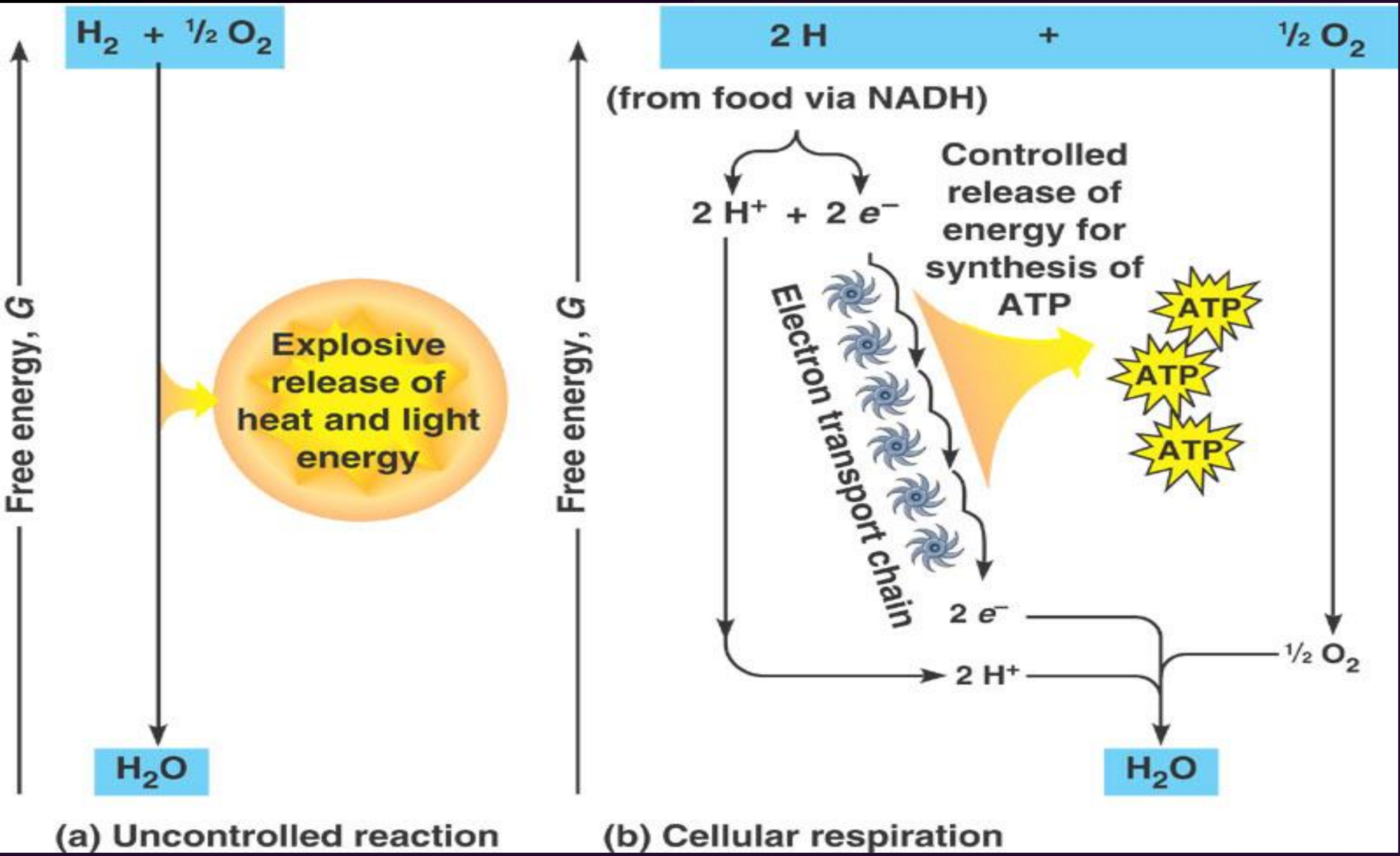
- In order to be best harvested, the E from glucose must be released in small steps
- e^-'s are taken from glucose and passed to the e^- carrier, NAD+
  - NAD^+ is a co-enzyme, also a nucleotide!
- As glucose is oxidized, NAD^+ is reduced to NADH and holds the high-energy electrons for later steps (ATP production)
- The transfer is conducted by a **dehydrogenase** enzyme
- A lone proton (H^+) is also lost from glucose.





The fate of electrons

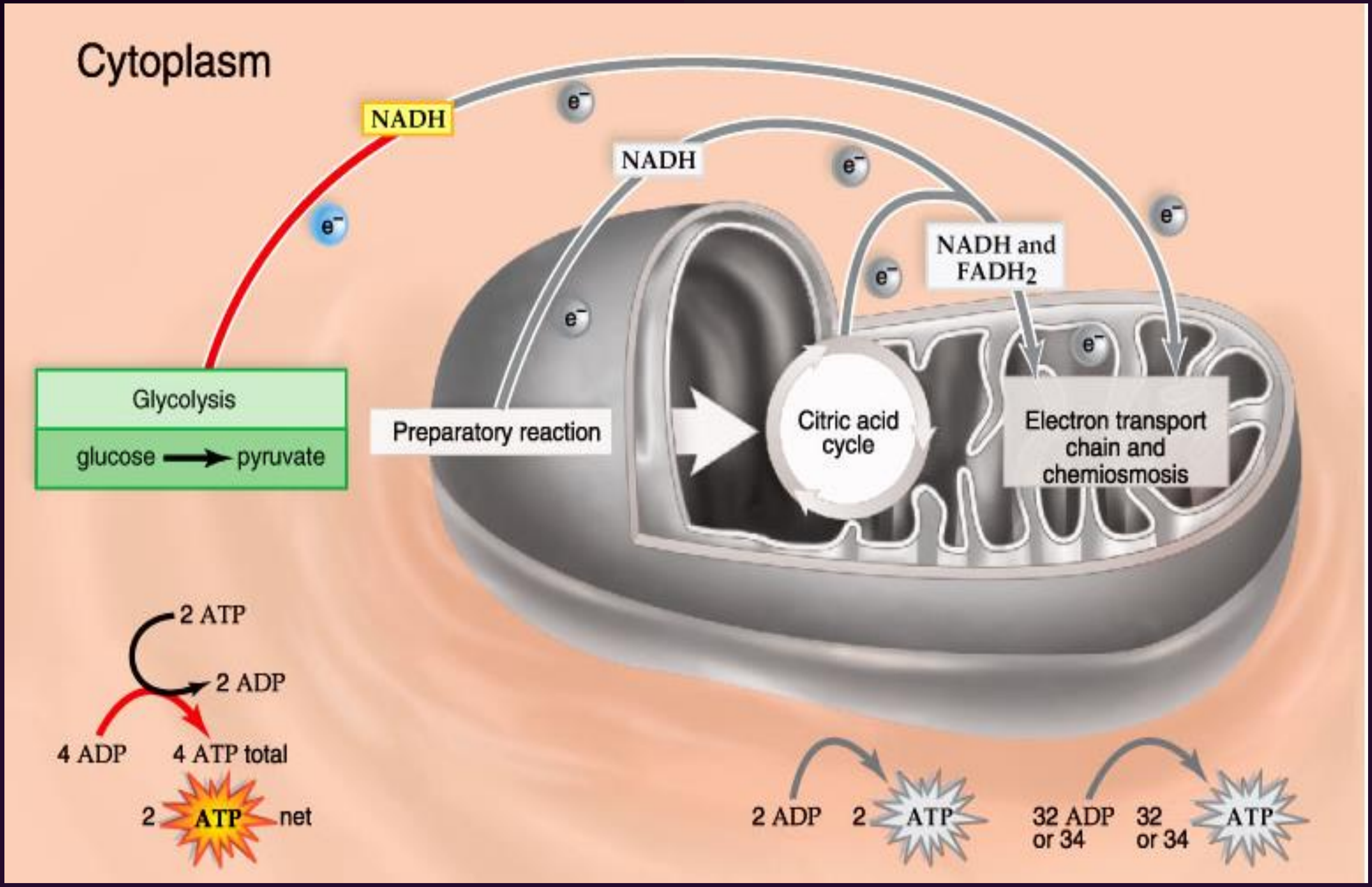
- The "high-energy" e^-'s that are taken from glucose are first passed to NAD+ to form NADH
  - Very little loss of E for this step
- Then, they are passed to the **electron transport chain** on the inner membrane of the mitochondria
- The e^- transport chain, in many steps, gradually harnesses the E for ATP production
- The e^-'s are eventually passed to O_2 and H_2O is formed!



https://www.nasa.gov/topics/technology/hydrogen/hydrogen_fuel_of_choice.html

The Three Major Steps of Respiration that produce ATP

- Glycolysis -- Cytoplasm
- Krebs Cycle – Mitochondria
- Electron Transport Chain -- Mitochondria



The Four Phases of Respiration

1- Glycolysis

- Initial oxidation (breakdown) of 1 glucose into 2 pyruvate molecules
- Occurs in cytoplasm
- Does NOT require oxygen! (anaerobic)
- ATP is formed
- Pyruvate transferred into Mitochondria

2 - Transition reaction (Preparatory stage)

- Occurs in Mitochondria
- Both pyruvates are oxidized
- Electron energy is stored in NADH
- Two carbons are released as CO_2
- No ATP is formed

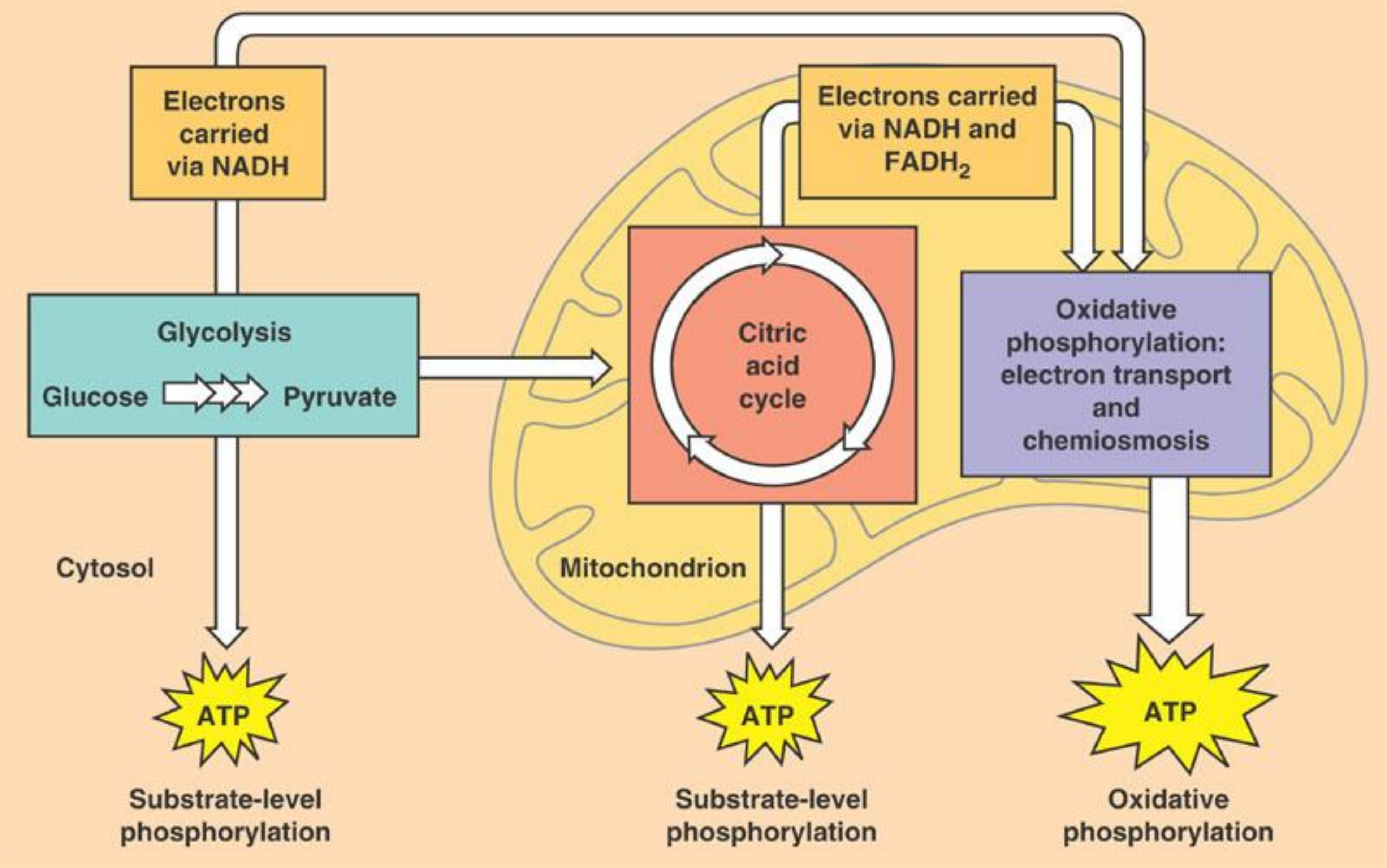
The Four Phases of Respiration

3 - <u>Citric acid cycle</u>

- Aka "Krebs cycle" and "TCA cycle" tricarboxylic acid
- completes oxidation of pyruvate
- <u>Occurs in matrix of mitochondria</u>
- Electron energy is stored in NADH and $FADH_2$
- ATP is formed
- Four carbons are released as CO_2

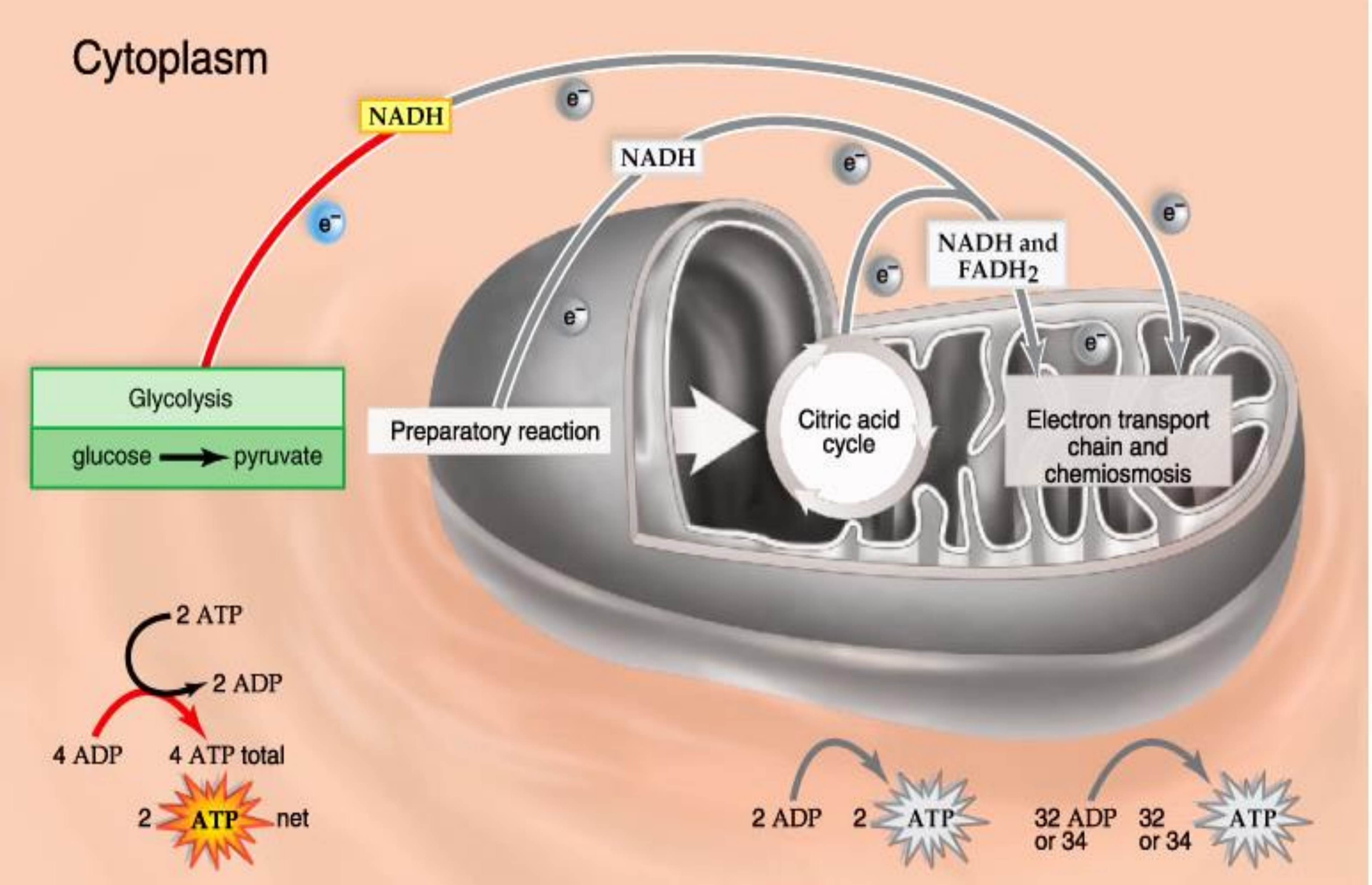
4- <u>Oxidative phosphorylation</u> (OxPhos) -- ETC

- Uses high-energy e^-' s to generate ATP
- Extracts energy from NADH & $FADH_2$
- Produces 32 or 34 molecules of ATP
- Occurs in the Cristae of Mitochondria
- 1) ETC = e^- transport chain uses the energy from the e^-' s
- 2) <u>**chemiosmosis**</u> (makes the ATP)



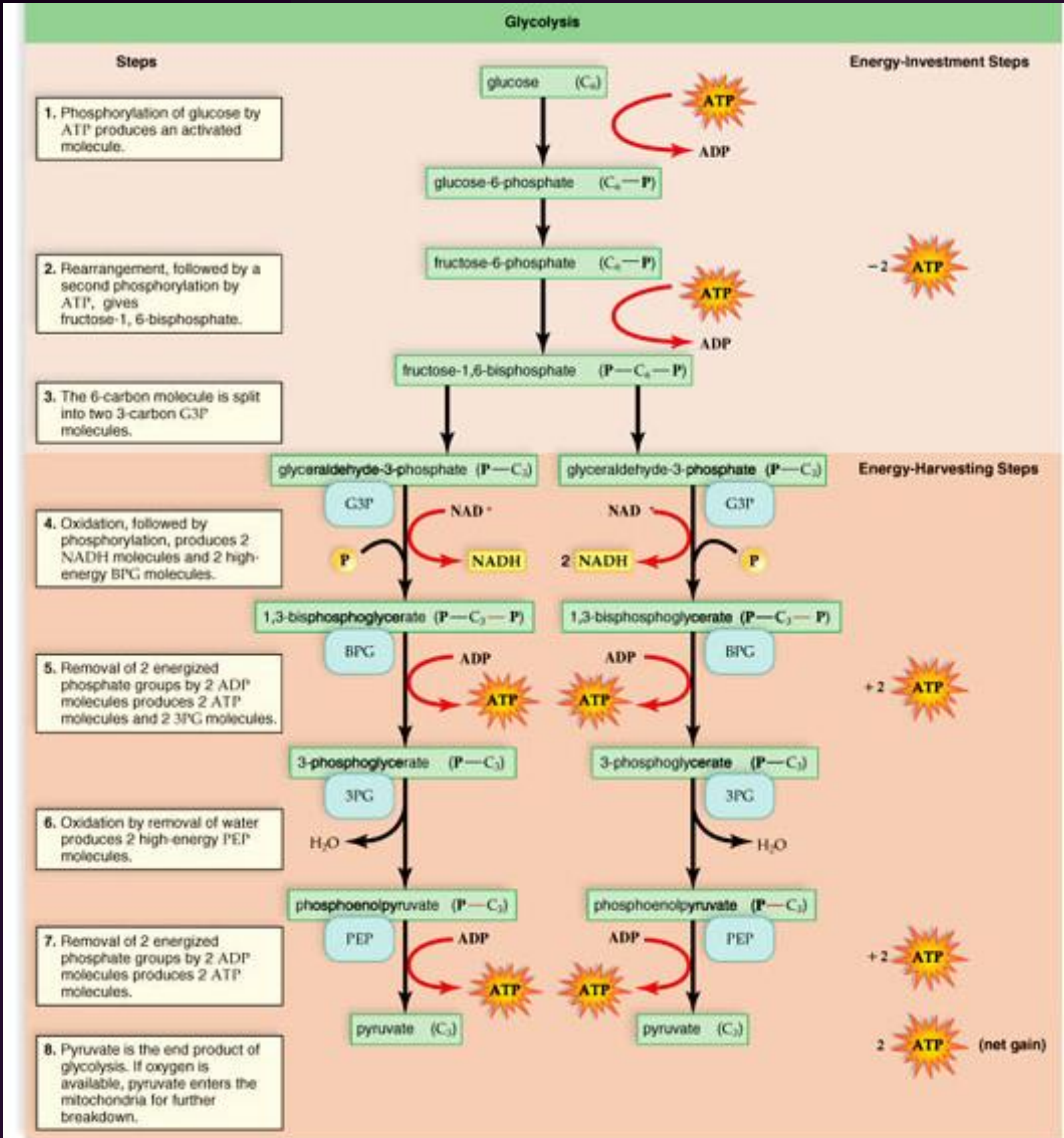
Electrons carried via NADH
Electrons carried via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
Cytosol
Mitochondrion
ATP
ATP
ATP
Substrate-level phosphorylation
Substrate-level phosphorylation
Oxidative phosphorylation

Glycolysis



Cytoplasm
NADH
e⁻
NADH
e⁻
e⁻
e⁻
NADH and FADH2
e⁻
e⁻
e⁻
Glycolysis
glucose → pyruvate
Preparatory reaction
Citric acid cycle
Electron transport chain and chemiosmosis
2 ATP
2 ADP
4 ADP
4 ATP total
2 ATP net
2 ADP
2 ATP
32 ADP or 34
32 or 34 ATP

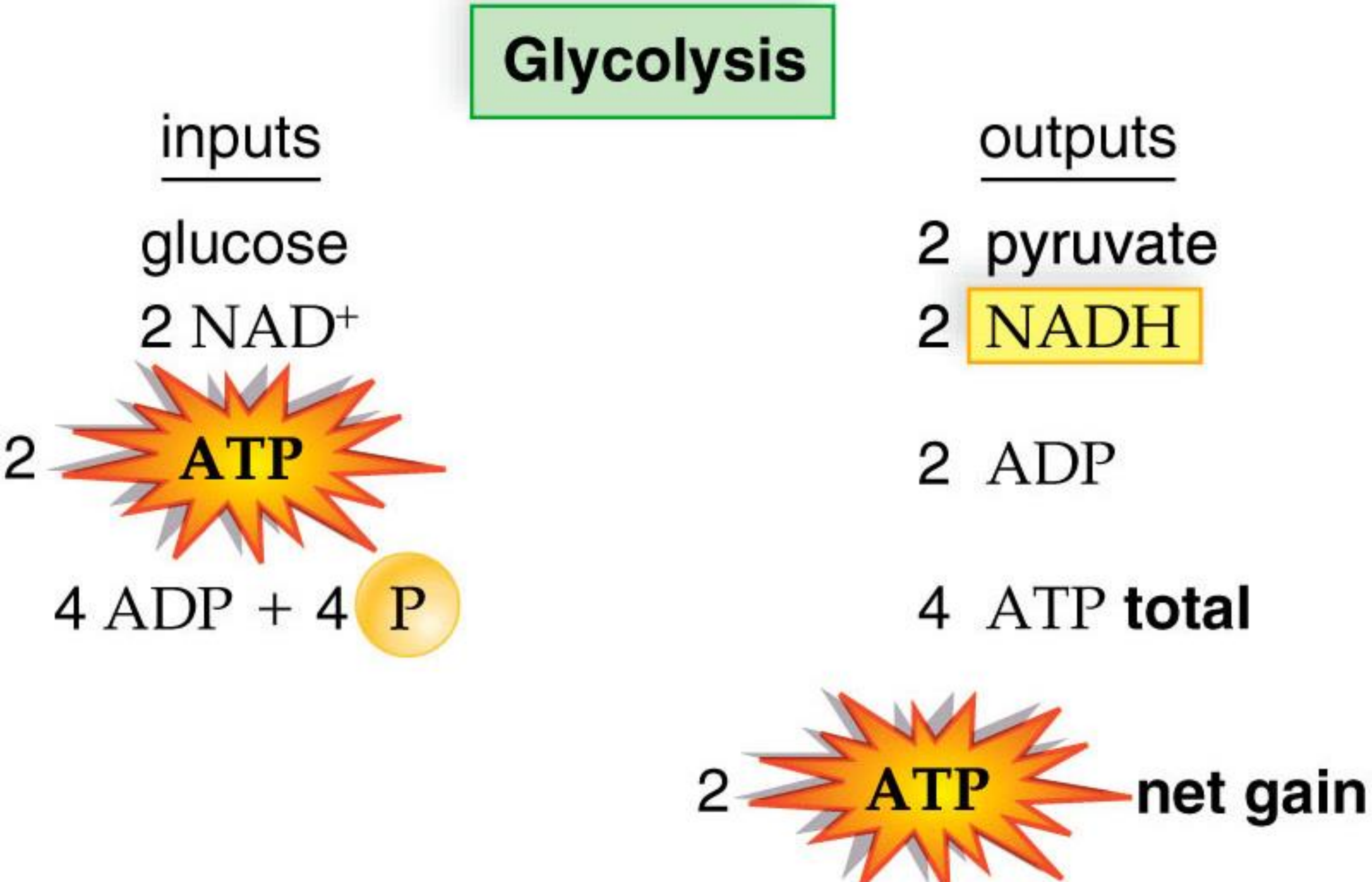
Glycolysis


Glycolysis
Steps
Energy-Investment Steps
glucose (C6)
ATP
ADP
glucose-6-phosphate (C6—P)
fructose-6-phosphate (C6—P)
−2 ATP
ATP
ADP
fructose-1,6-bisphosphate (P—C6—P)
1. Phosphorylation of glucose by ATP produces an activated molecule.
2. Rearrangement, followed by a second phosphorylation by ATP, gives fructose-1, 6-bisphosphate.
3. The 6-carbon molecule is split into two 3-carbon G3P molecules.
glyceraldehyde-3-phosphate (P—C3)
glyceraldehyde-3-phosphate (P—C3)
Energy-Harvesting Steps
G3P
NAD+
NADH
2 NADH
P
4. Oxidation, followed by phosphorylation, produces 2 NADH molecules and 2 high-energy BPG molecules.
1,3-bisphosphoglycerate (P—C3—P)
1,3-bisphosphoglycerate (P—C3—P)
BPG
ADP
ATP
+2 ATP
5. Removal of 2 energized phosphate groups by 2 ADP molecules produces 2 ATP molecules and 2 3PG molecules.
3-phosphoglycerate (P—C3)
3-phosphoglycerate (P—C3)
3PG
H2O
6. Oxidation by removal of water produces 2 high-energy PEP molecules.
phosphoenolpyruvate (P—C3)
phosphoenolpyruvate (P—C3)
PEP
ADP
ATP
+2 ATP
7. Removal of 2 energized phosphate groups by 2 ADP molecules produces 2 ATP molecules.
pyruvate (C3)
pyruvate (C3)
2 ATP (net gain)
8. Pyruvate is the end product of glycolysis. If oxygen is available, pyruvate enters the mitochondria for further breakdown.

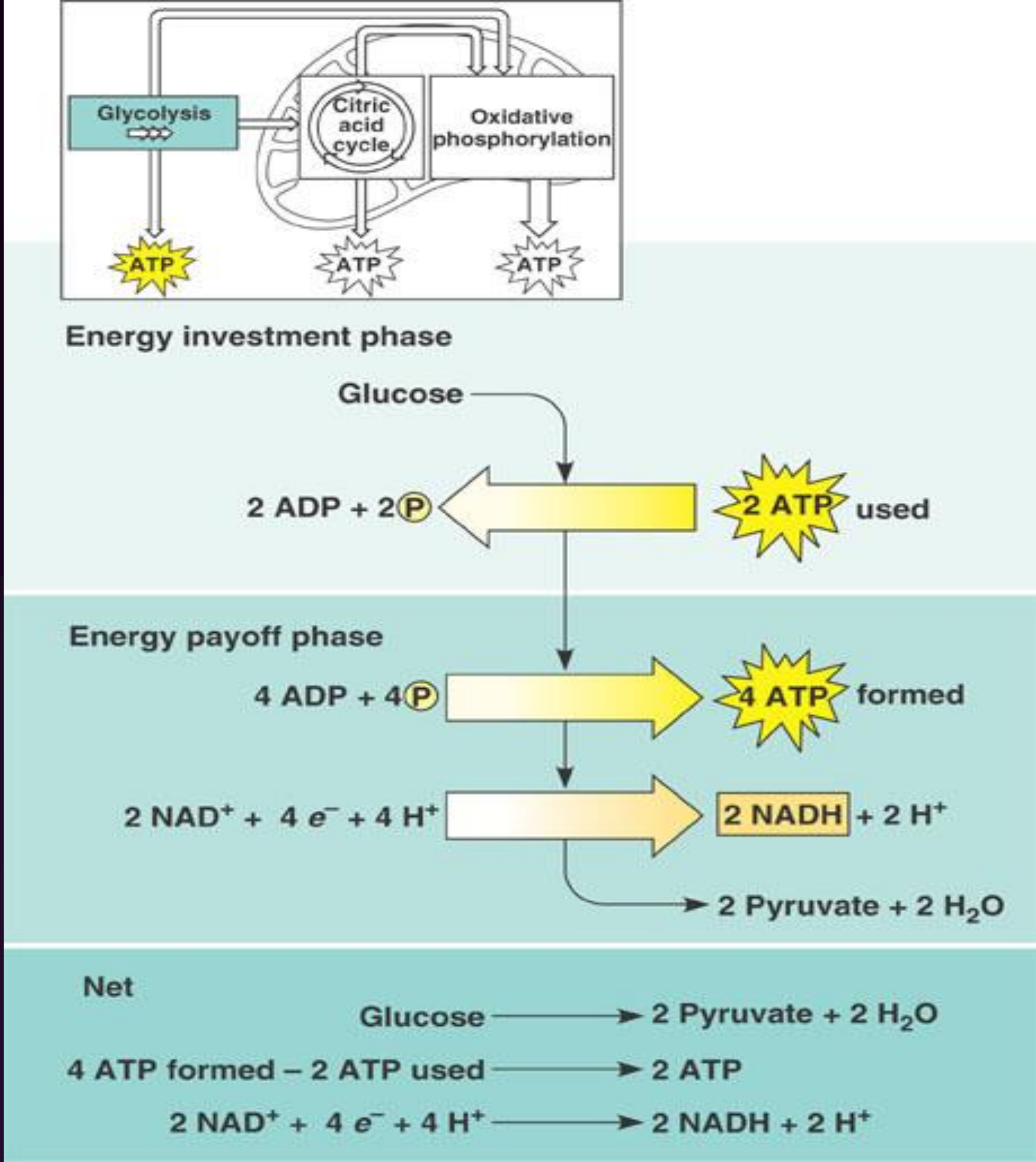
Glycolysis Summary

- Begin with ONE glucose molecule:
  - That's 6 carbons!
- Gets phosphorylated on BOTH ends
  - This costs two ATPs
- Gets chopped in half (so two 3-C molecules)
- Both "halves" are converted to pyruvate (3 C's)
  - Along the way:
  - 1 NADH generated per "half" (so 2 total)
  - 1 water " " " (" 2 ")
  - 2 ATPs " " " (" 4 ")
    - But remember, it took 2 to get started, so net of 2 ATP!
- Note... No O_2 required, no CO_2 created, occurs in cytoplasm.

Glycolysis: The Balance Sheet

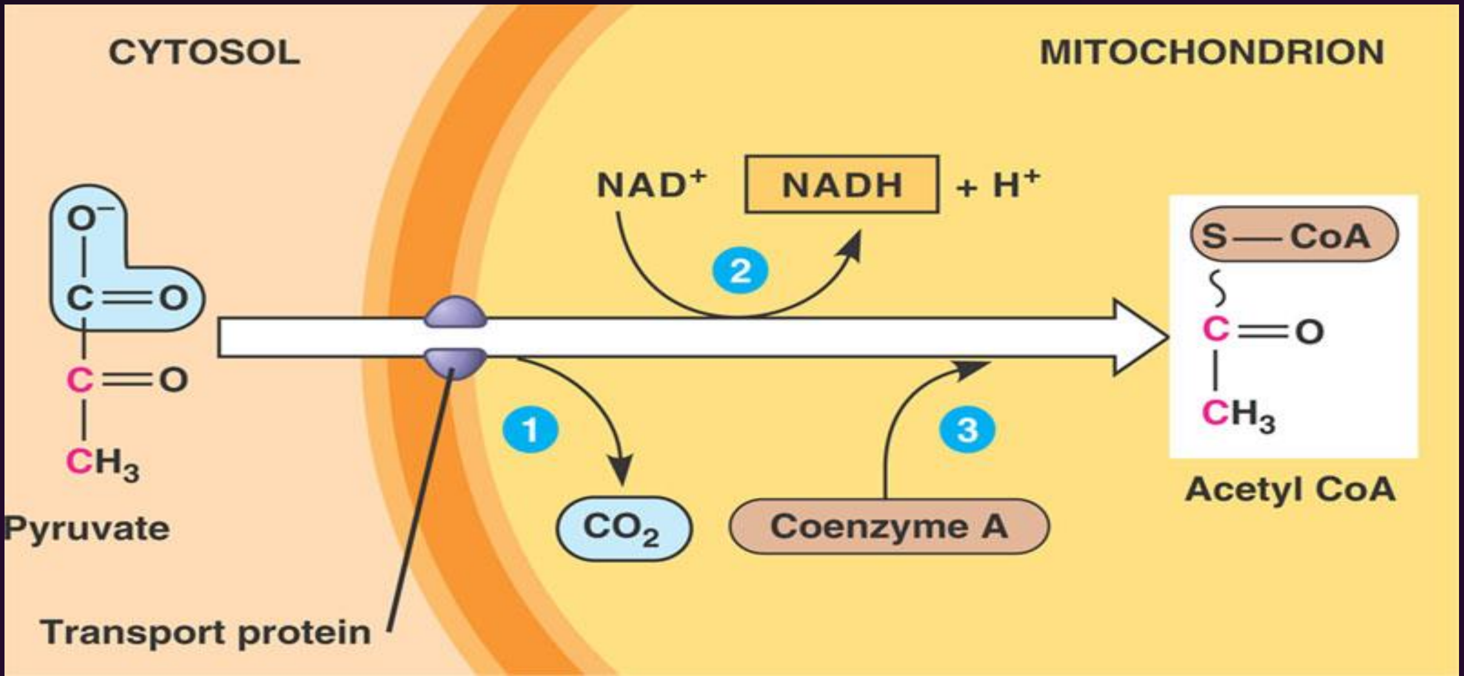


After glycolysis, only about ¼ of the E of glucose is harvested, most remains in the pyruvates!

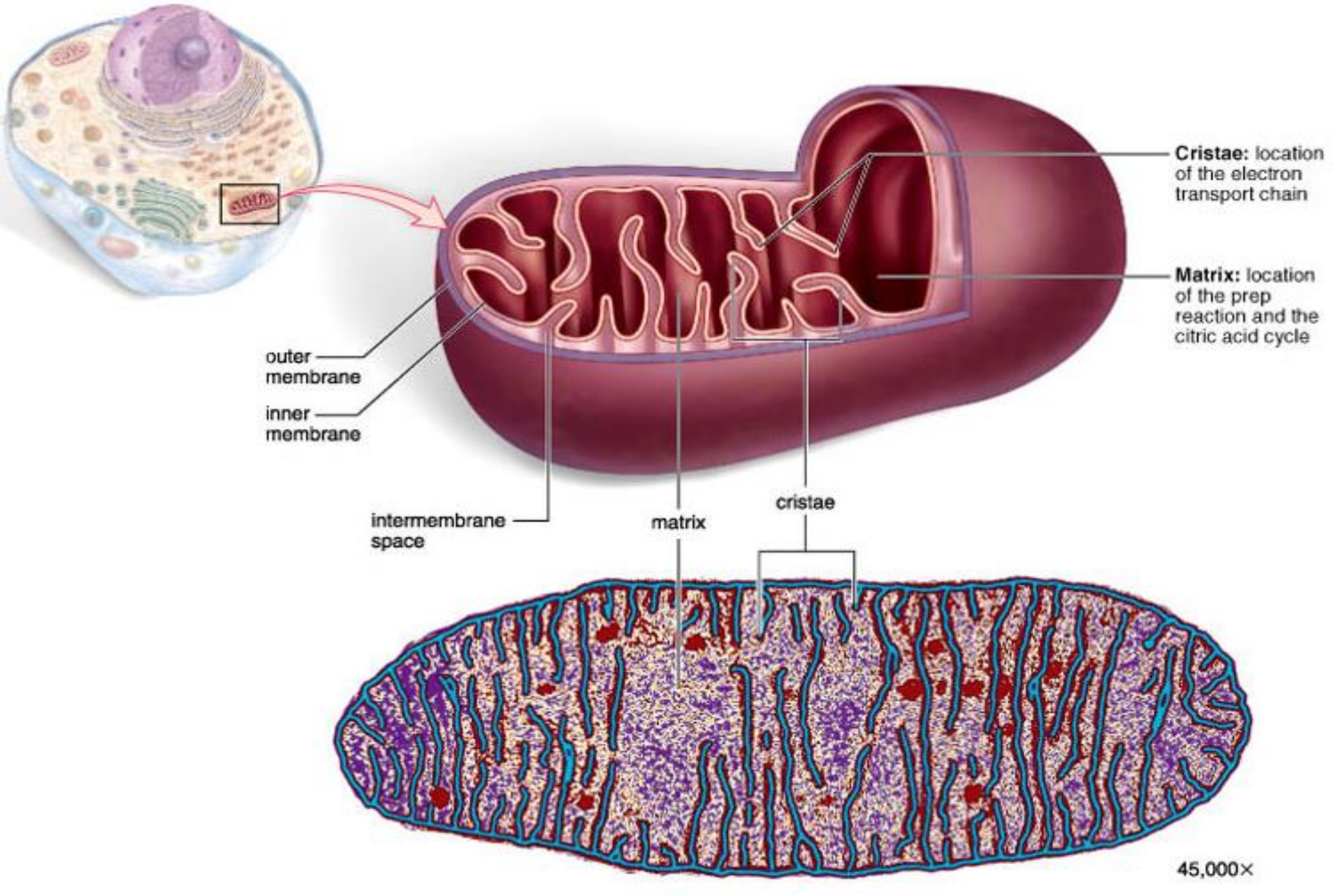


The Preparatory phase (Mitochondria)

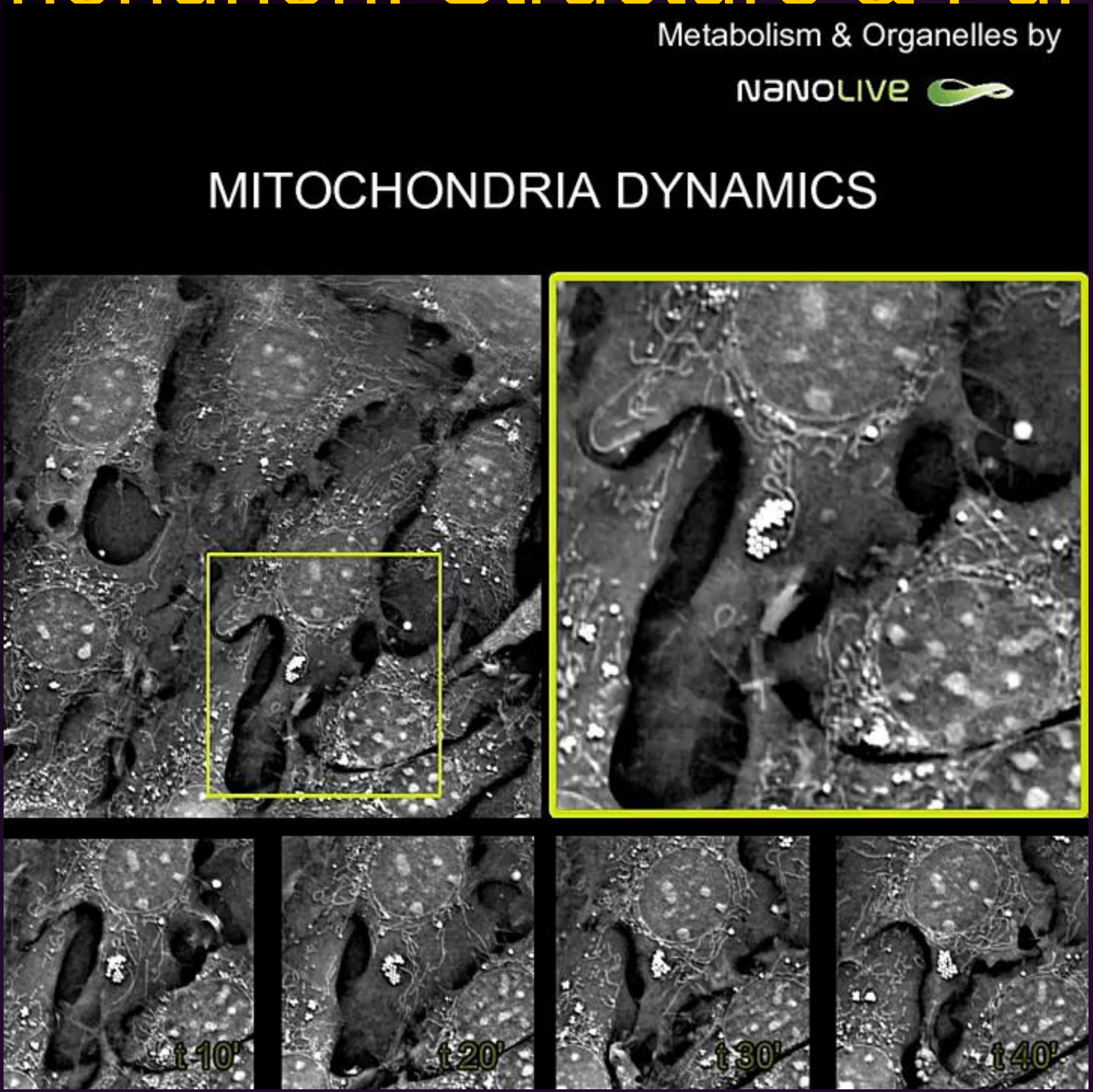
- After glycolysis but before Krebs
- The pyruvates are transported into the matrix of the mitochondria
- 2 of the C's from pyruvate are attached to CoA to form Acetyl-CoA
- 1 C released as CO_2 & 1 NADH generated / pyruvate



Mitochondrion: Structure & Function



Mitochondrion: Structure & Function



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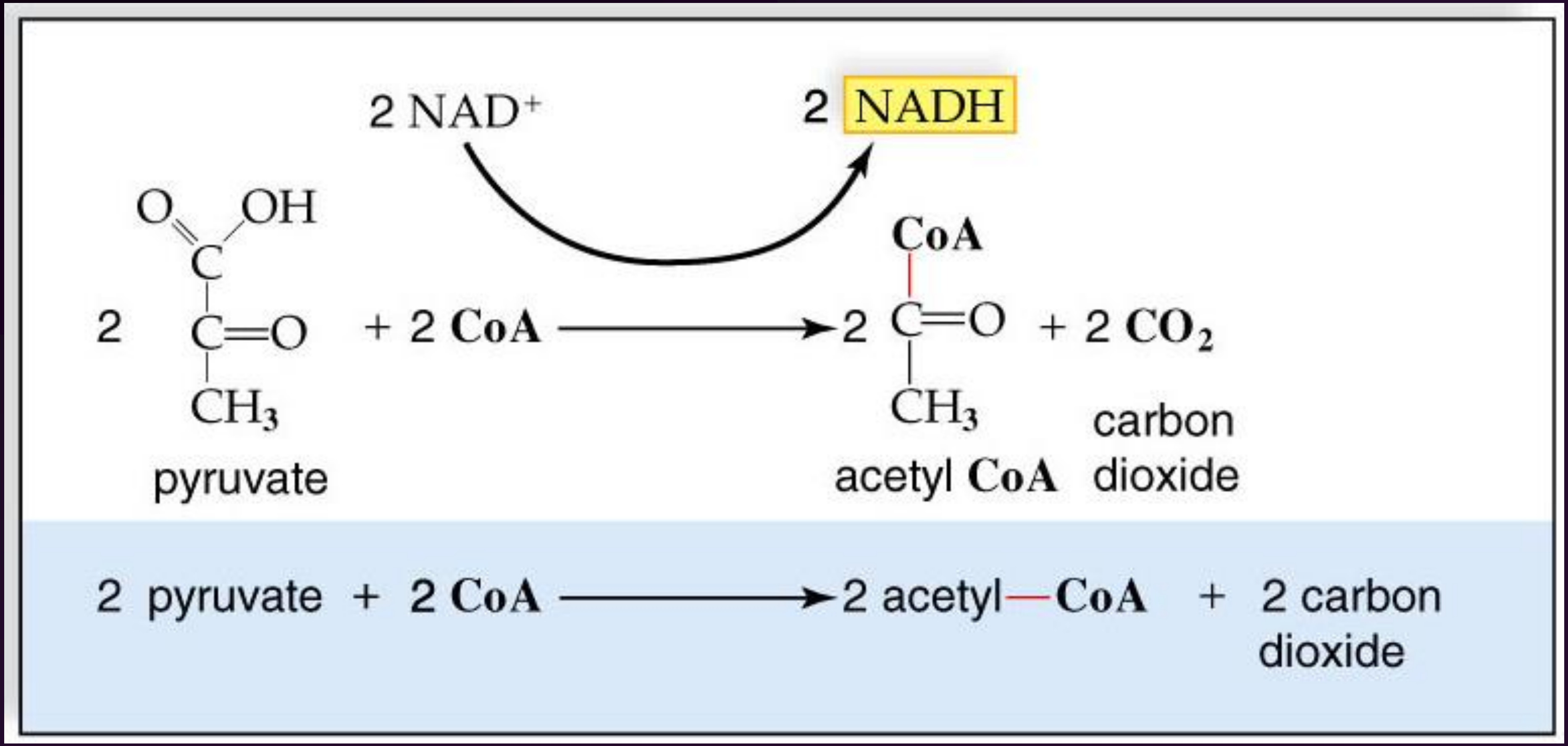
Preparatory Reaction



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OER
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Lab: https://openlab.citytech.cuny.edu/bio-oer/

Grade Breakdown:
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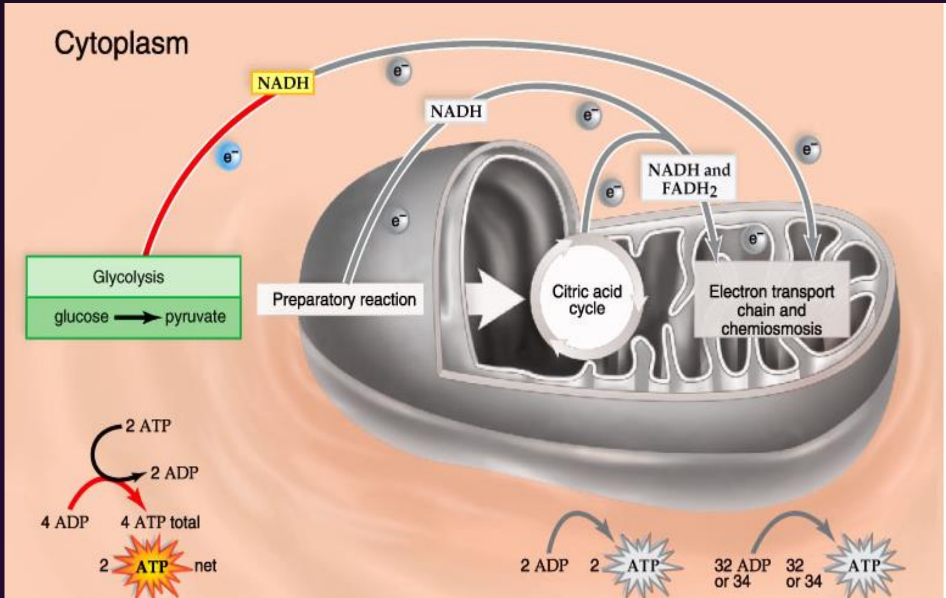
Quizzes: 20% Average

Recap: Meeting 16

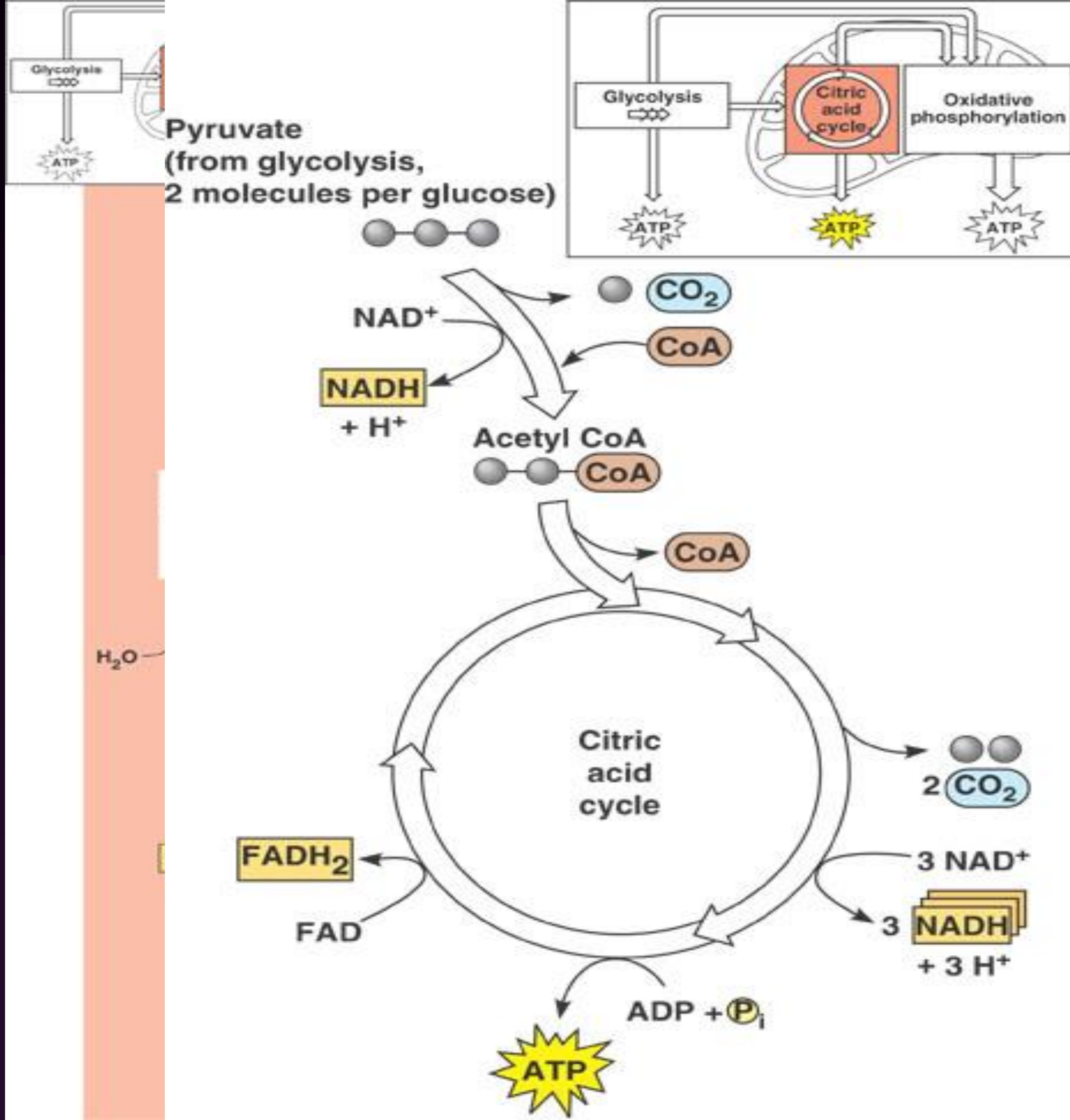
A. Catabolic Pathways:
1) Fermentation (anaerobic) without O_2
2) Cellular Respiration (aerobic) with O_2
   - A) Glycolysis -- Cytoplasm
   - B) Krebs Cycle (TCA) – Mitochondria
   - C) Electron Transport Chain -- Mitochondria

B. Oxidation/Reduction – Transfer of electrons
1) Cellular Respiration: NAD^+/NADH + FAD/$FADH_2$ (e^-) Carriers
2) Glycolysis: $C_6H_{12}O_6$ + 2ATP → 2 Pyruvate (3C) + 4 ATP
3) Preparatory step (mitochondria): Pyruvate (3C) → acetyl (2C)-CoA + NADH + CO_2

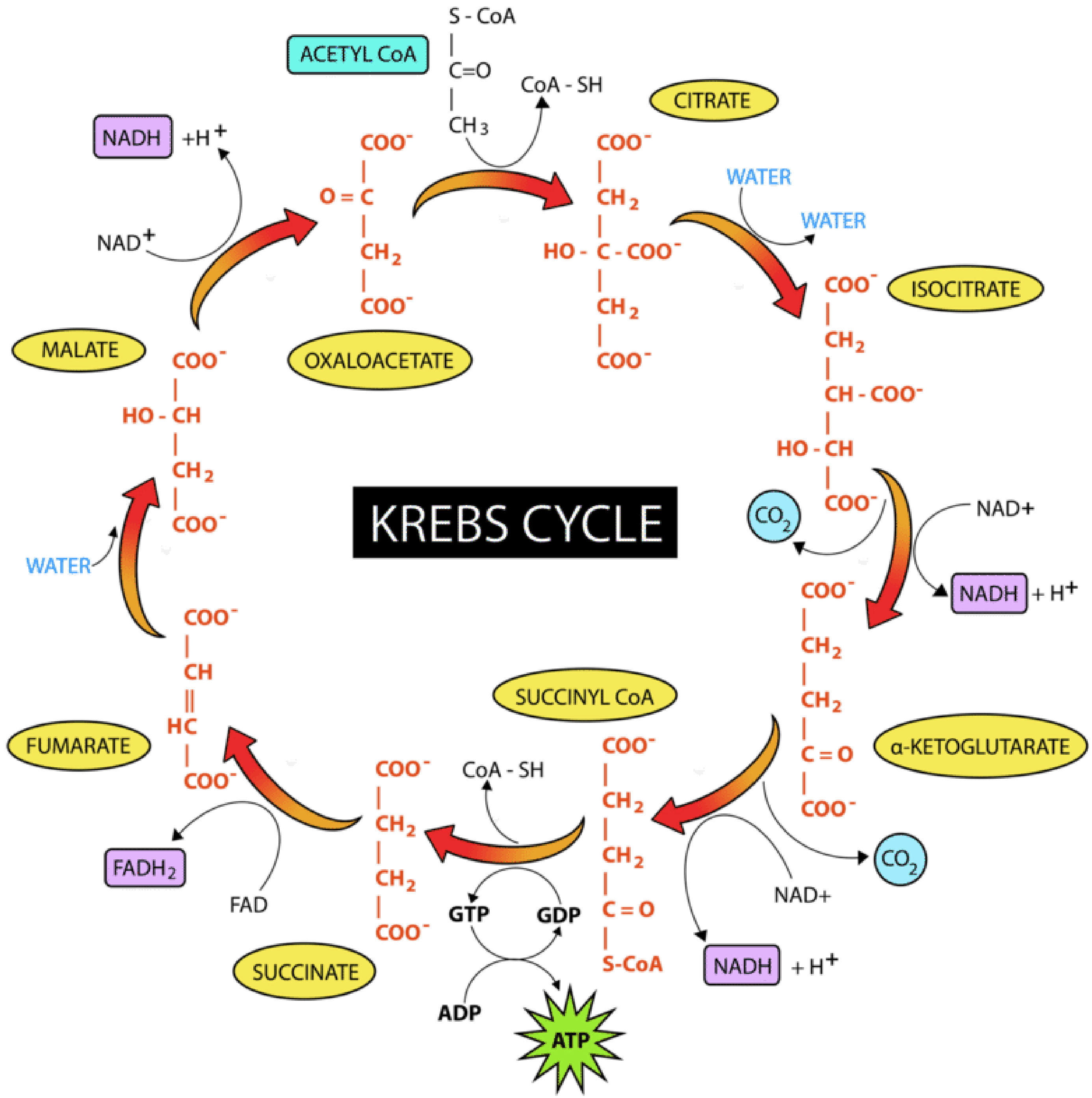


Citric Acid Cycle

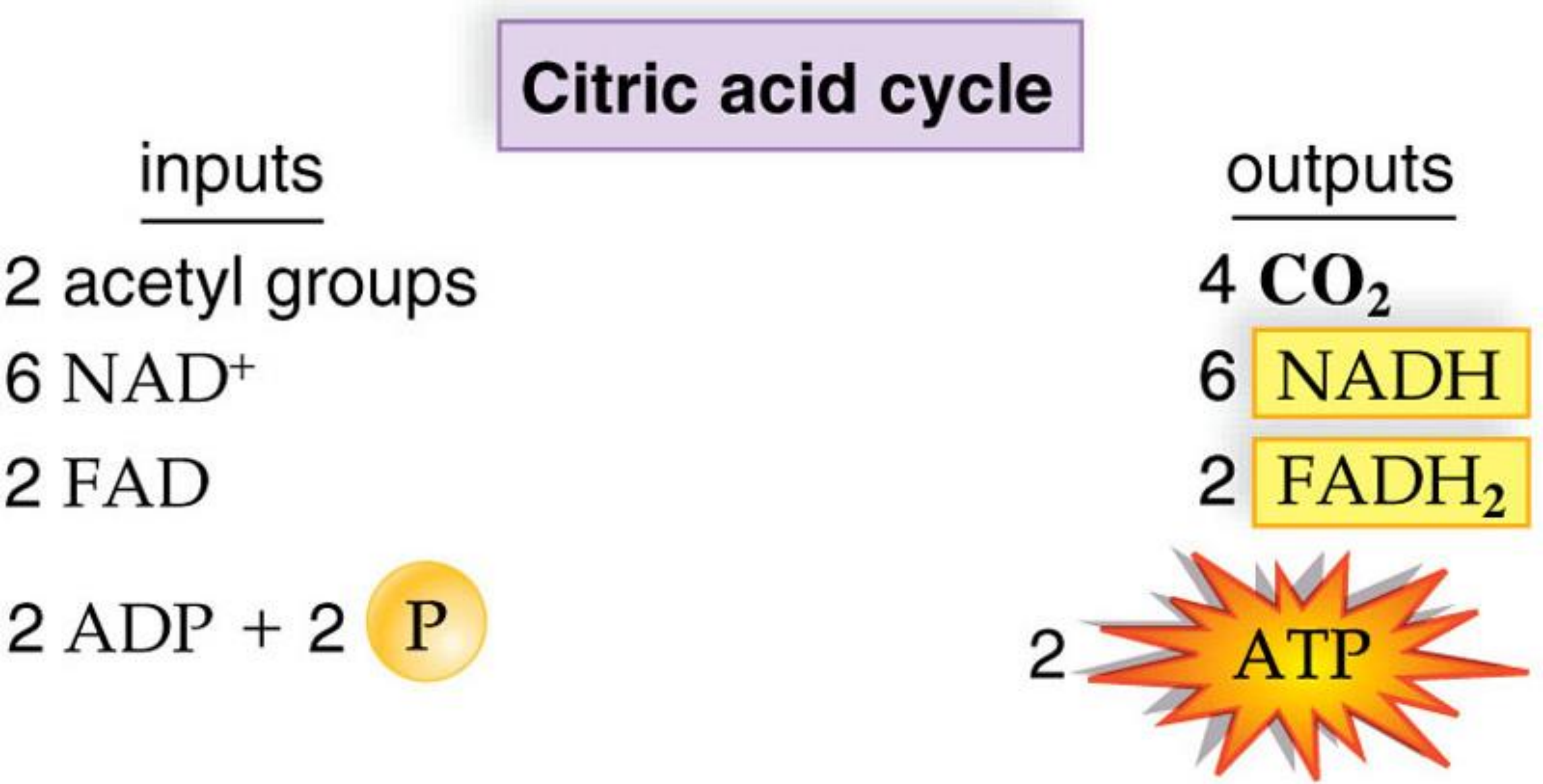
- Acetyl-CoA (2 C' s) enters the Krebs by joining with the 4-Carbon molecule Oxaloacetate
  - So now back to a 6-Carbon molecule
- As the cycle "turns"
  - Two Carbons are completely oxidized to CO_2 and released
    - The remaining 4-Carbon molecule is transformed back into oxaloacetate, to start the cycle over with another acetyl-CoA
  - Generated: 3 NADH, 1 $FADH_2$, 1 ATP, 2 CO_2
- Because glucose yields TWO pyruvates, you get TWO turns of the cycle per glucose!



Glycolysis
Citric acid cycle
Oxidative phosphorylation
ATP
ATP
ATP
Pyruvate
(from glycolysis,
2 molecules per glucose)
CO2
NAD+
CoA
NADH
+ H+
Acetyl CoA
CoA
CoA
Citric acid cycle
2 CO2
3 NAD+
FADH2
FAD
3 NADH
+ 3 H+
ADP + Pi
ATP
H2O

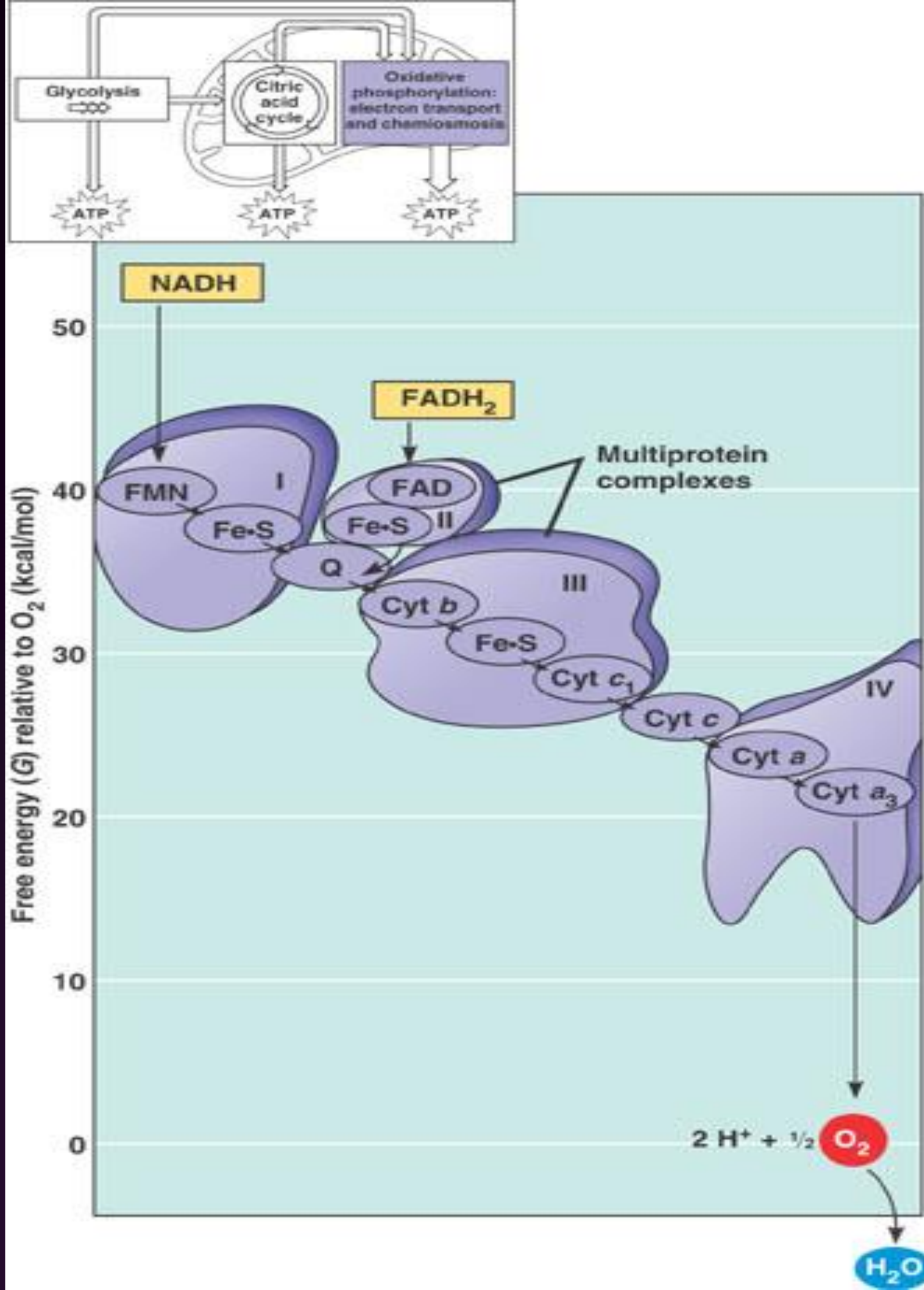

KREBS CYCLE
ACETYL CoA
S - CoA
C=O
CH_3
CoA - SH
CITRATE
OXALOACETATE
ISOCITRATE
α-KETOGLUTARATE
SUCCINYL CoA
SUCCINATE
FUMARATE
MALATE
WATER
WATER
WATER
NAD+
NADH
+H+
CO_2
NAD+
NADH
+ H+
CO_2
NAD+
NADH
+ H+
CoA - SH
GTP
GDP
ADP
ATP
FAD
$FADH_2$
COO^-
O = C
CH_2
HO - C - COO^-
CH - COO^-
HO - CH
C = O
S-CoA
CH
HC

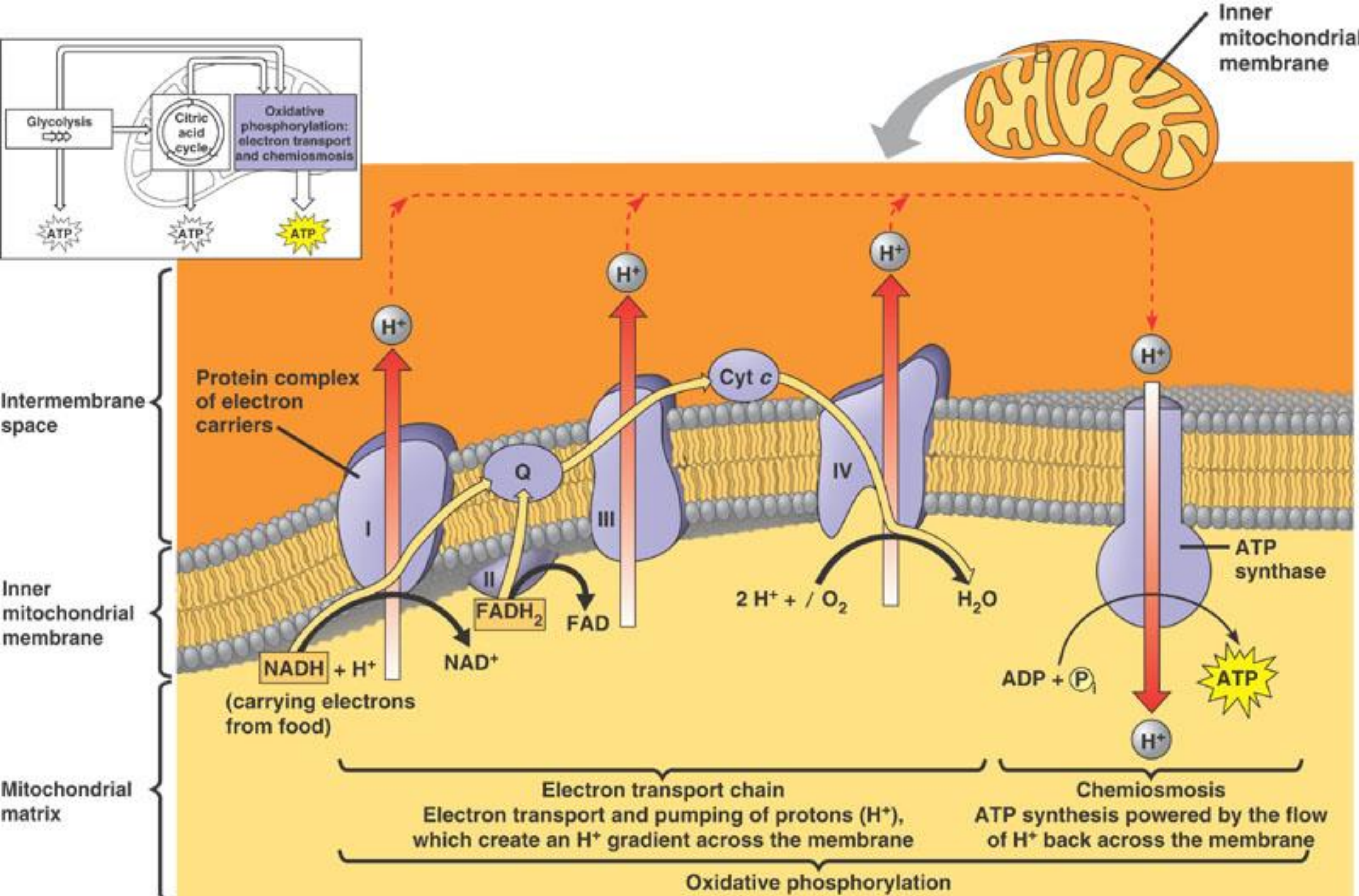
Citric Acid Cycle: Balance Sheet



Oxidative Phosphorylation

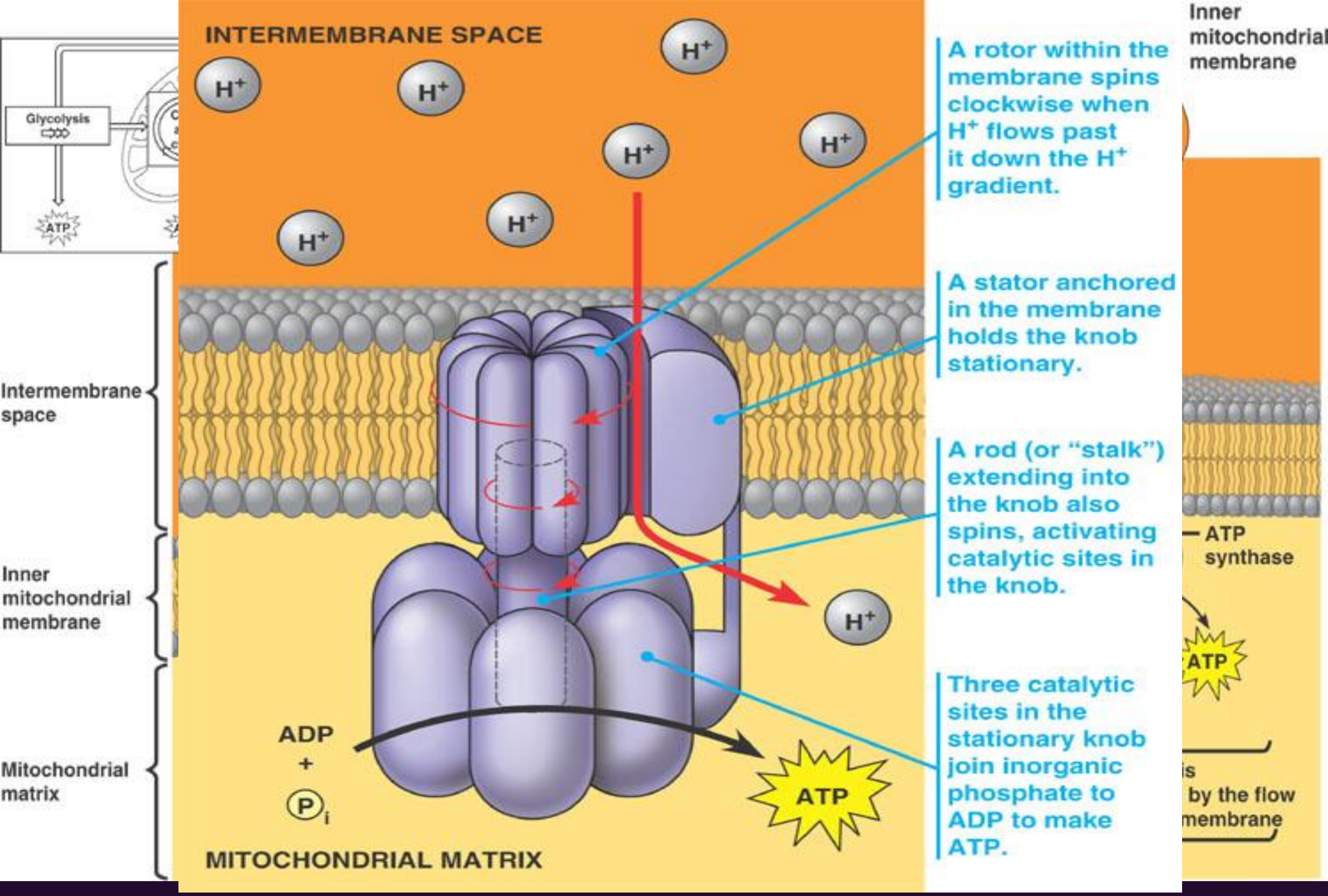
- So far… in glycolysis, prep, and Krebs, only a little ATP has been produced, but A LOT of NADH (and some $FADH_2$).
- NADH (and $FADH_2$) are carriers of high-energy e^-' s.
    - Remember, e^-' s are passed as H^-
- OxPhos is how the energy is finally harvested and ATP is generated.
- In the matrix of the mito, NADH (and $FADH_2$) pass their high-E e^-' s to the e^- transport chain (ETC, proteins and cytochromes)
    - The ETC is embedded in INNER MEMBRANE (Cristae) of the mito for eukaryotes! (PM for Prokaryotes)


Glycolysis
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
ATP
ATP
ATP
NADH
FADH2
Multiprotein complexes
FMN
I
Fe•S
FAD
Fe•S
II
Q
III
Cyt b
Fe•S
Cyt c1
Cyt c
IV
Cyt a
Cyt a3
2 H+ + ½ O2
H2O
Free energy (G) relative to O2 (kcal/mol)
50
40
30
20
10
0

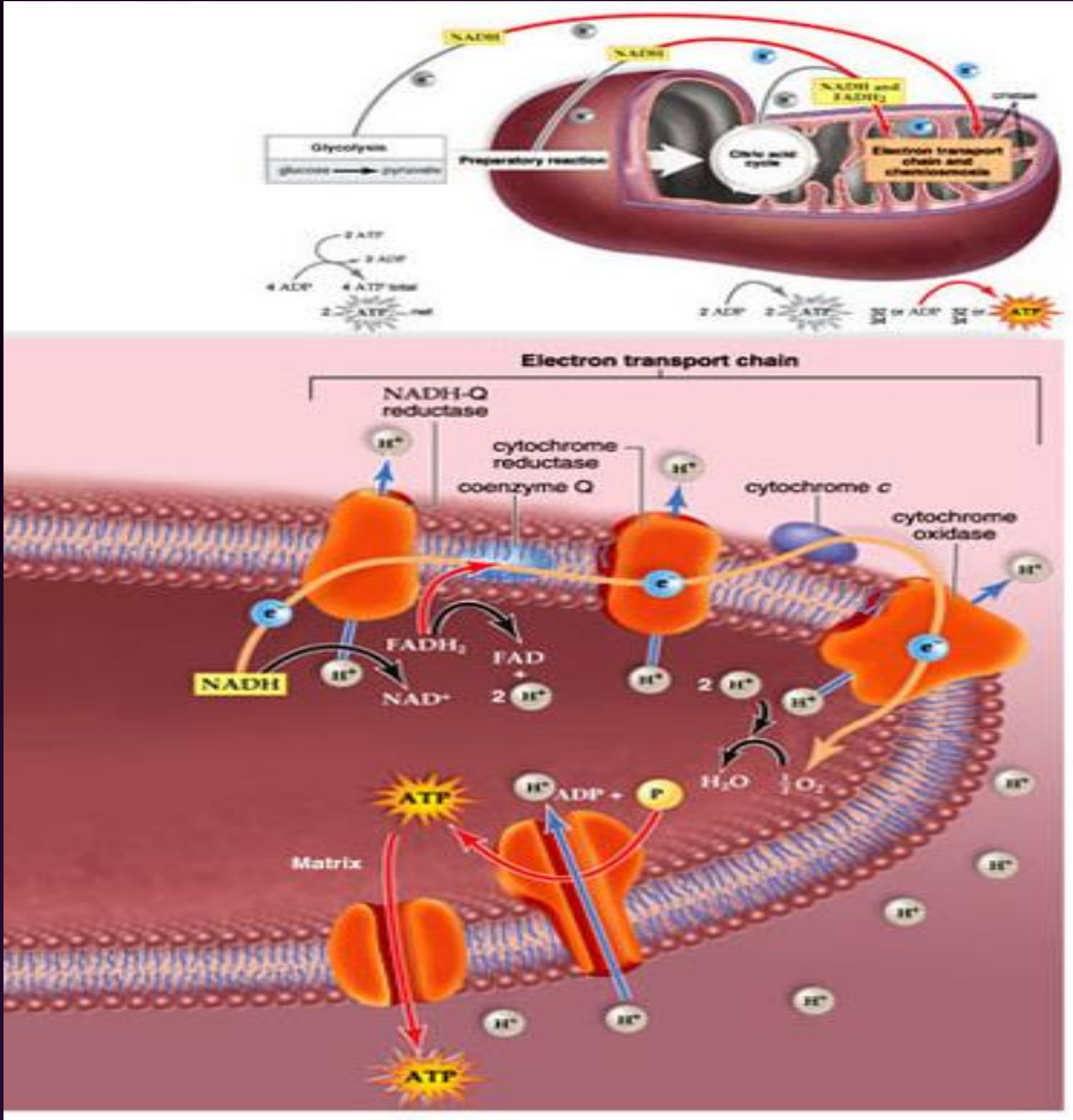

Inner mitochondrial membrane
Glycolysis
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
ATP
ATP
ATP
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
Protein complex of electron carriers
I
II
III
IV
Q
Cyt c
H^+
H^+
H^+
H^+
H^+
NADH + H^+
(carrying electrons from food)
NAD^+
$FADH_2$
FAD
2 H^+ + / O_2
H_2O
ATP synthase
ADP + Ⓟi
ATP
Electron transport chain
Electron transport and pumping of protons (H^+), which create an H^+ gradient across the membrane
Chemiosmosis
ATP synthesis powered by the flow of H^+ back across the membrane
Oxidative phosphorylation

(Oxidative Phosphorylation, con't)

- The ETC then passes the e^-'s along, using the E of the e^-'s to pump H^+ out of the matrix into the inter-membrane space.
- This is creates a **proton gradient** across the inner membrane
- Lastly, protons are allowed to flow back through the inner membrane, but only through a membrane channel (and enzyme) called **ATP synthase**
- ATP synthase is like a turbine! As protons flow through it (DOWN their concentration gradient), it turns a crank that generates ATP. This is called **chemiosmosis**.
- At the end of the ETC, the e-'s (no longer high E) are passed to O_2 to form H_2O. (This is b/c the e^-'s are always passed as H^-.)


INTERMEMBRANE SPACE
H+
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 (or "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.
ADP
+
P i
ATP
MITOCHONDRIAL MATRIX
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
Glycolysis
Inner mitochondrial membrane
ATP synthase
by the flow
membrane

Organization of Cristae

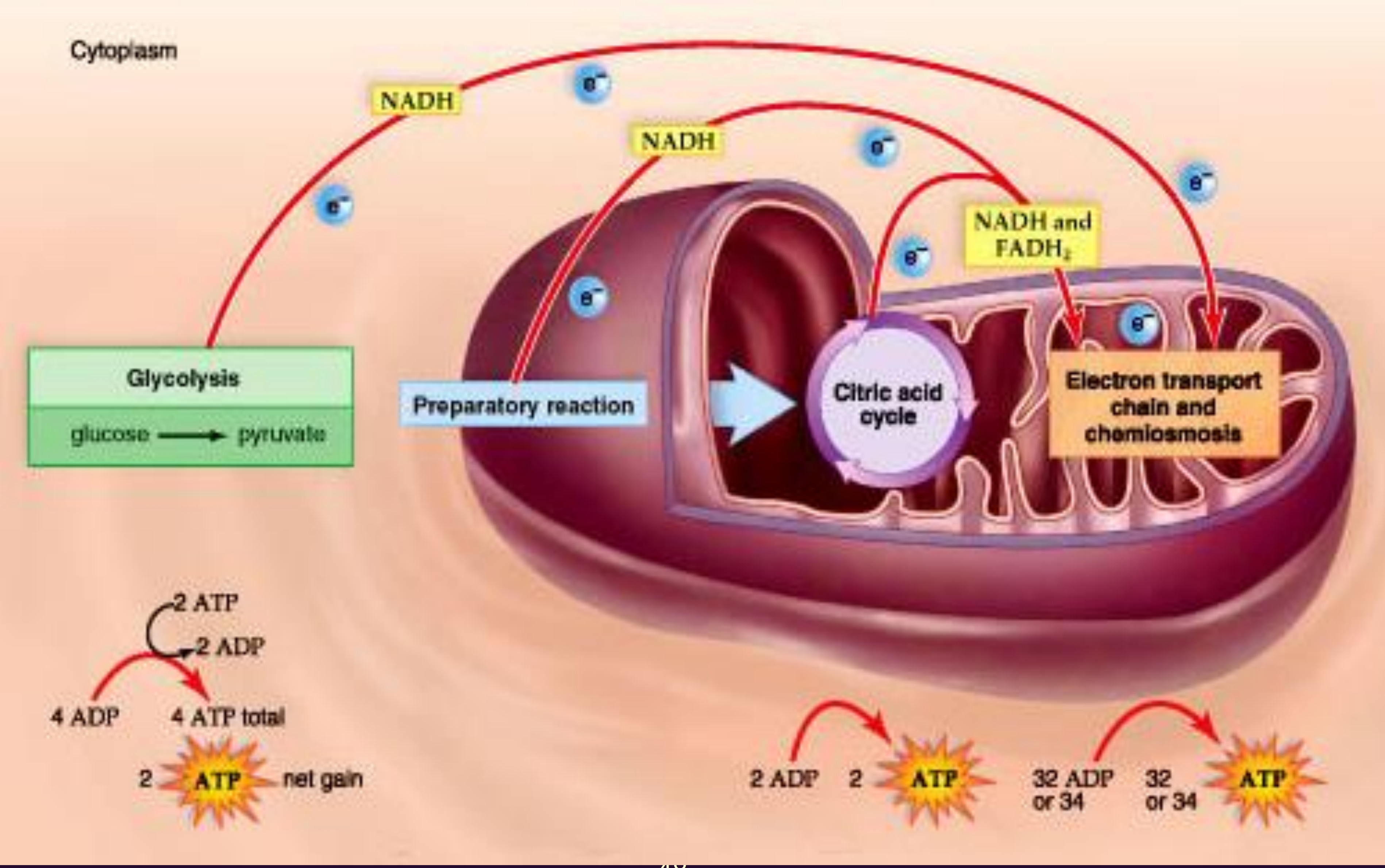


So, why is O_2 so important?

- …because it is the final acceptor of e^-' s
- (This creates a water molecule)
- If there is no oxygen around:
  - The ETC cannot pass e^-' s, so stops!
  - No ETC = No H^+ pumping
  - No H^+ gradient, ATP synthase stops. (no chemiosmosis)
- When ETC stops:
  - NADH (and $FADH_2$) cannot pass e^-' s to it.
  - NADH builds up (no NAD^+ and FAD)
  - So Krebs stops too!

- Summary: No O_2 = no flow of e^-' s and everything stops!

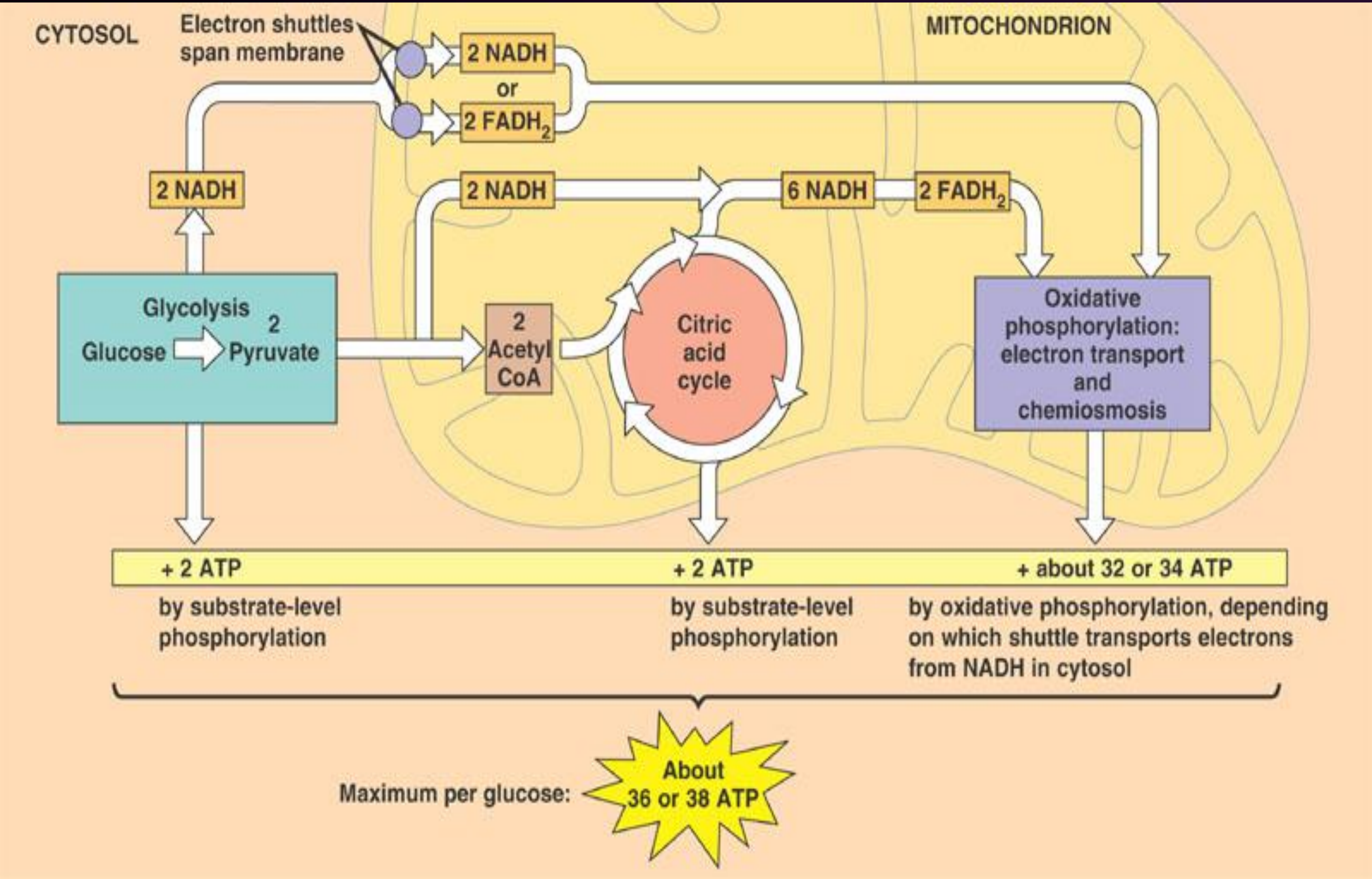
Glucose Breakdown: Overview of 4 Phases



Final Summary

	Glycolysis	Prep	Krebs	OxPhos
Where?	Cytoplasm	Mitochondria	Mitochondria (Matrix)	Mitochondria (Cristae)
What goes in	1 glucose 2 ATP 2 NAD^+	2 pyruvate 2 NAD^+ 2 CoA	2 Acetyl-CoA 6 NAD^+ 2 $FADH^+$	10 NADH 2 $FADH_2$ 6 O_2
What comes out	2 pyruvate 4 ATP 2 NADH	2 Acetyl-CoA 2 NADH 2 CO_2	4 CO_2 6 NADH 2 $FADH_2$ 2 ATP	6 H_2O 32-34 ATP (10 NAD^+) (2 $FADH^+$)

Final Summary



The Hydrolysis of ATP…

- …is very EXERGONIC (ΔG = -7.3 kcal/mol)
- …is easy to couple to other things!
- …involves water!
- The crowding of negative charges is like a "loaded spring"
- Cellular respiration has overall VERY negative ΔG
  - Makes LOTS of ATP, drives all cellular work!

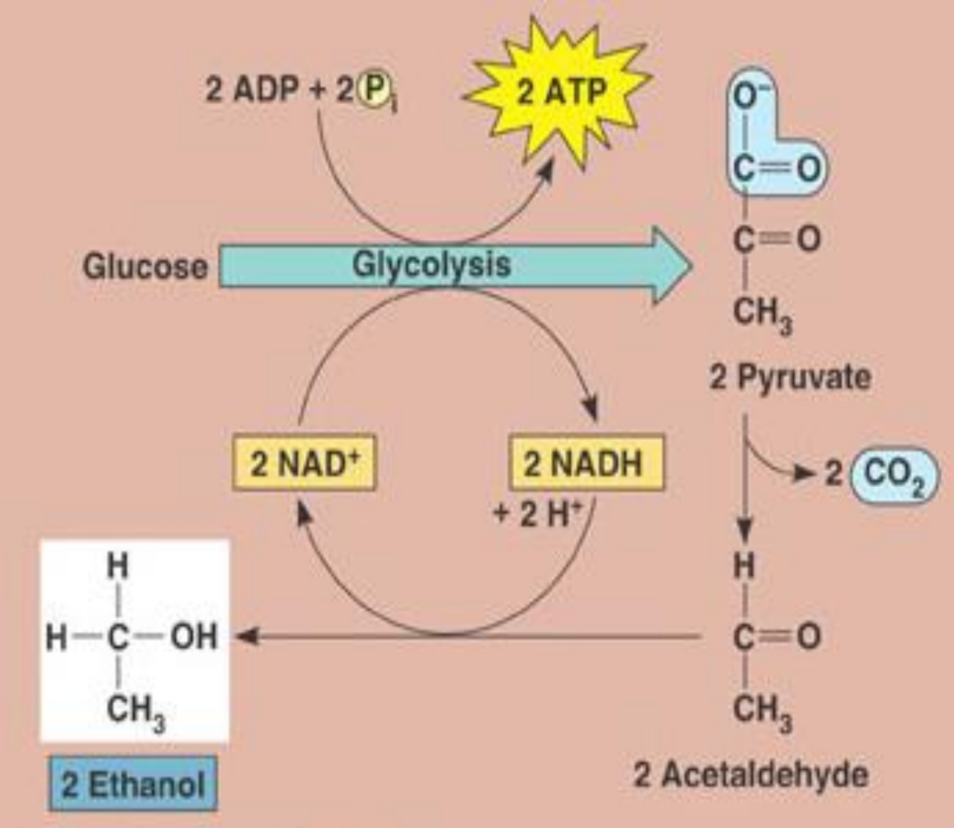
ΔG = -7.3 kcal/mol ~ 507 g (ATP) – 38 ATP per molecule of sugar
ΔG = -686 kcal/mol ~ 180g ($C_6H_{12}O_6$)

Which is more Exergonic?

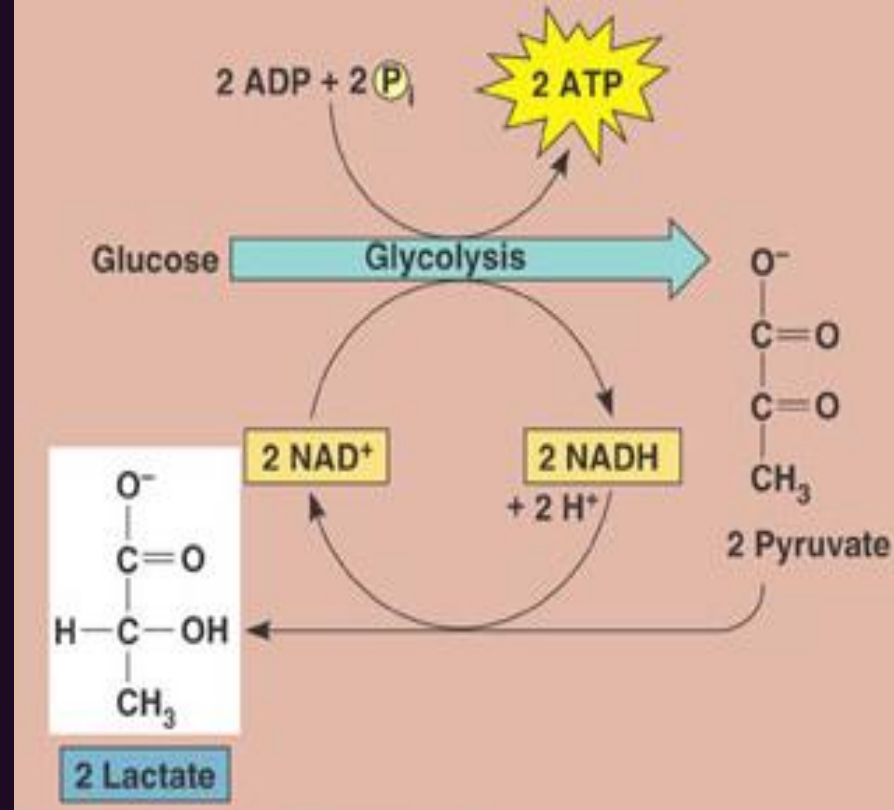
Where does the "lost" energy go?

Anaerobic Respiration = **Fermentation**

- When there is no O_2 around, cells can still use glycolysis to generate SOME ATP from glucose
- But, to keep glycolysis going, you must find a way to re-generate NAD^+
  - Remember, O_2 is the final acceptor of e^-' s, so everything backs up w/o it.
- The answer is Fermentation. This occurs in cytoplasm.
- Two Types (both re-generate NAD^+)
  - Alcoholic fermentation – converts pyruvate to ethanol and CO2 (yeast)
  - Lactic acid fermentation - " " lactic acid (animals)

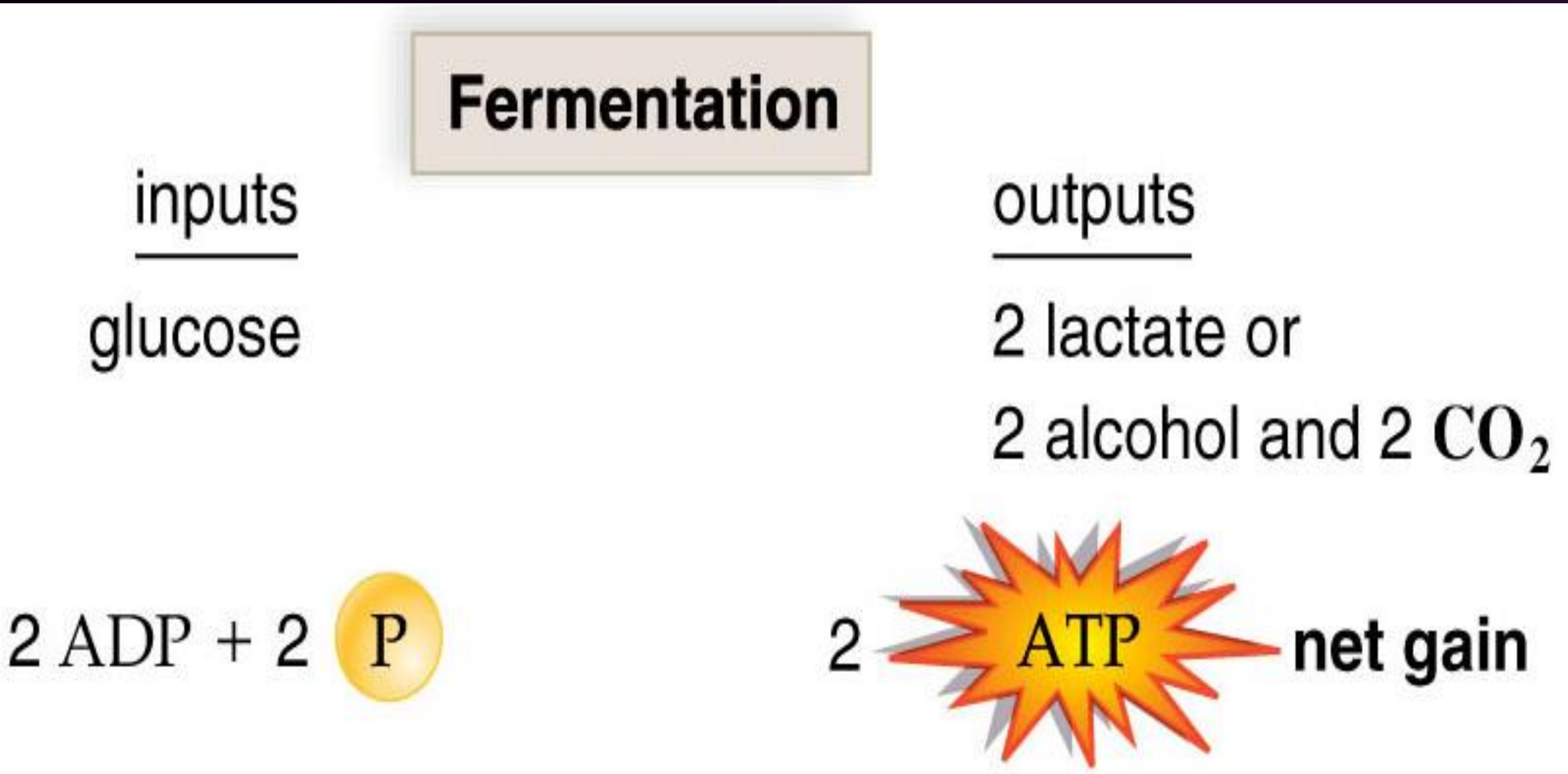


(a) Alcohol fermentation



(b) Lactic acid fermentation

Efficiency of Fermentation



Fermentation (2)

- Pyruvate reduced by NADH to:
  - Lactate
    - Animals & some bacteria
    - Cheese & yogurt; sauerkraut
  - Ethanol & carbon dioxide
    - Yeasts
    - Bread and alcoholic beverages

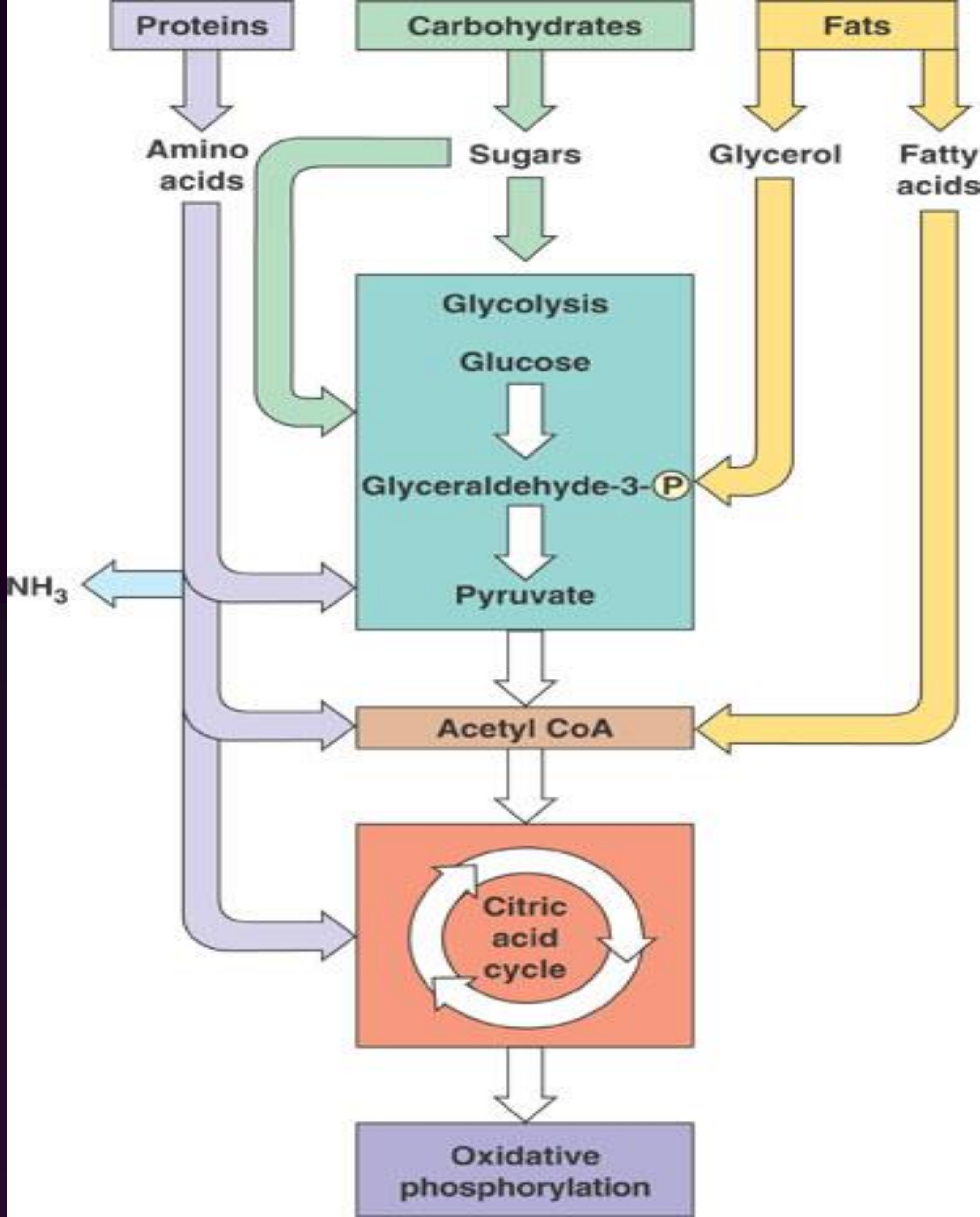
- Allows glycolysis to proceed faster than O_2 can be obtained
  - Anaerobic exercise
  - Lactic acid accumulates
  - Causes cramping and oxygen debt

- When O_2 restored, lactate broken down to acetyl-CoA and metabolized

Metabolic pool: The Versatility of Catabolism

- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of carbohydrates
- Proteins must be digested to amino acids; amino groups can feed glycolysis or the citric acid cycle
- Fats are digested to glycerol (used in glycolysis) and fatty acids (used in generating acetyl CoA)
- An oxidized gram of fat produces more than twice as much ATP as an oxidized gram of carbohydrate

Not just glucose!



Metabolic Pool: **Anabolism**

- All metabolic reactions part of metabolic pool
- Intermediates from respiratory pathways can be used for anabolism
- Anabolism (build-up side of metabolism):
  - Carbs:
    - Start with acetyl-CoA
    - Basically reverses glycolysis (but different pathway)
  - Fats
    - G3P converted to glycerol
    - Acetyls connected in pairs to form fatty acids

Metabolic Pool: **Anabolism** (2)

- Anabolism (cont.):
  - Proteins:
    - Made up of combinations of 20 different amino acids
    - Some amino acids (11) can be synthesized from respiratory intermediates
      - organic acids in citric acid cycle can make amino acids
      - Add NH_2 – transamination
    - However, other amino acids (9) cannot be synthesized by humans
      - Essential amino acids
      - Must be present in diet or die

The Metabolic Pool Concept