

Lecture Series 12

Cellular Pathways That
Harvest Chemical Energy

Cellular Pathways That Harvest Chemical Energy

A. Obtaining Energy and Electrons from Glucose

B. An Overview: Releasing Energy from Glucose

C. Glycolysis: From Glucose to Pyruvate

D. Pyruvate Oxidation

E. The Citric Acid Cycle

Cellular Pathways That Harvest Chemical Energy

F. The Respiratory Chain: Electrons, Proton Pumping, and ATP

G. Fermentation: ATP from Glucose, without O₂

H. Contrasting Energy Yields

I. Metabolic Pathways

J. Regulating Energy Pathways

Cellular Pathways In General

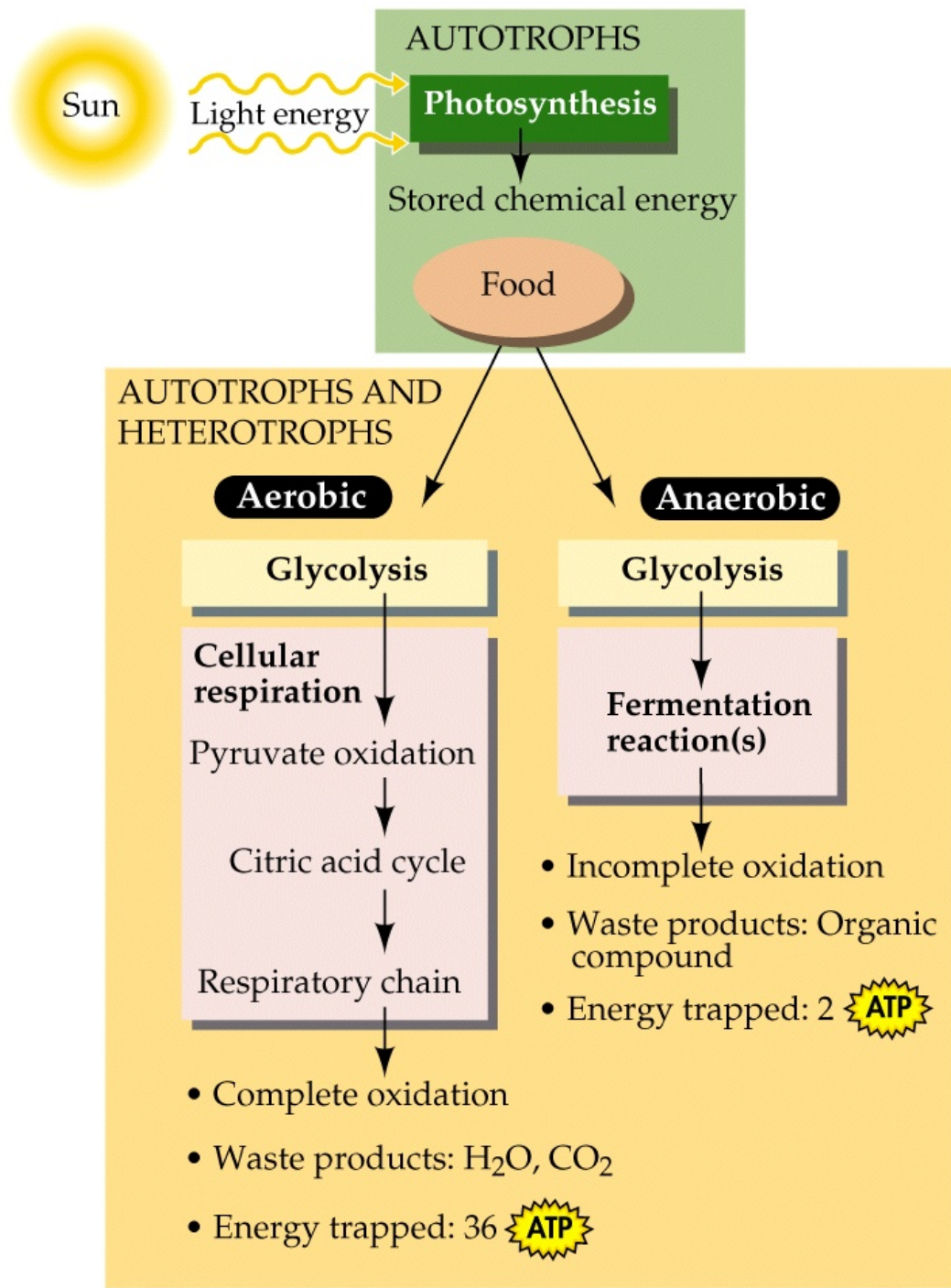
- Metabolic pathways occur in small steps, each catalyzed by a specific enzyme.
- Metabolic pathways are often compartmentalized and are highly regulated.

A. Obtaining Energy and Electrons from Glucose

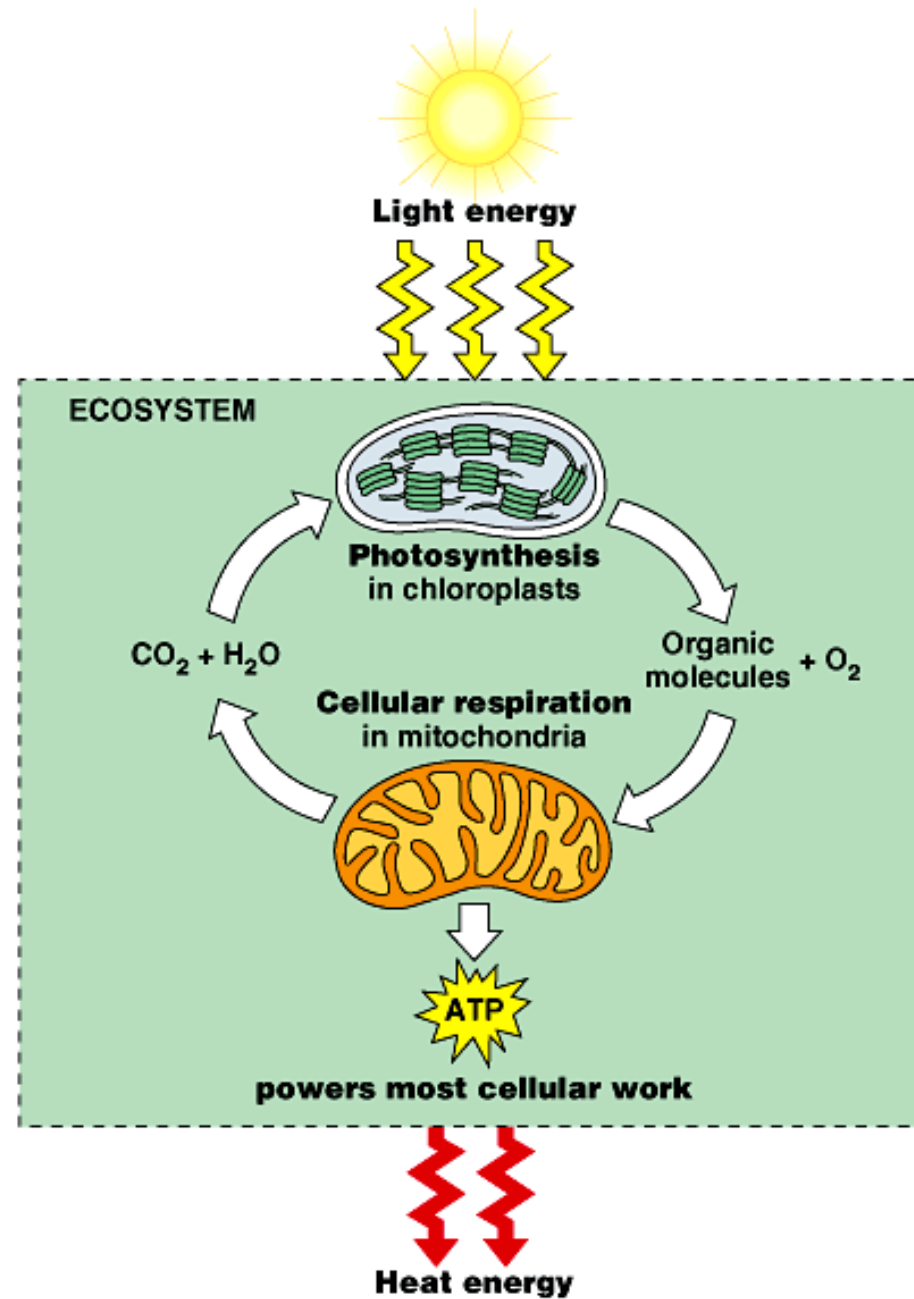
- When glucose burns, energy is released as heat and light:



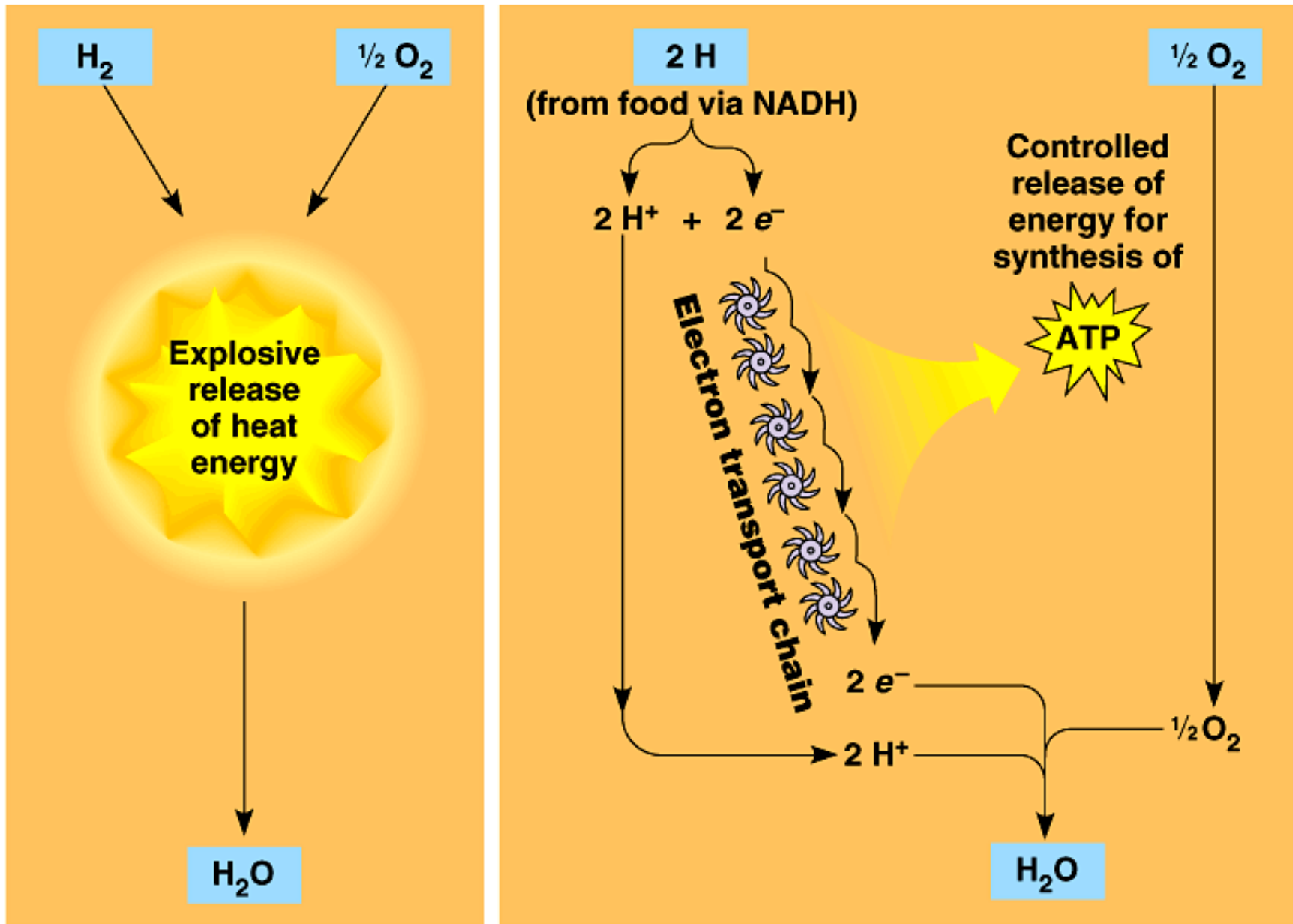
- The same equation applies to the metabolism of glucose by cells, but the reaction is accomplished in many separate steps so that the energy can be captured as ATP with minimal loss as heat.



Energy flow and chemical recycling in ecosystems



An introduction to electron transport chains



(a) Uncontrolled reaction

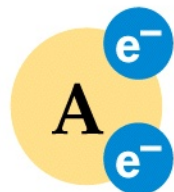
(b) Cellular respiration

A. Obtaining Energy and Electrons from Glucose

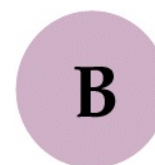
- As a material is oxidized, the electrons it loses transfer to another material, which is thereby reduced.
- Such redox reactions transfer a lot of energy. Much of the energy liberated by the oxidation of the reducing agent is captured in the reduction of the oxidizing agent.

Redox Rxns: Transfer Electrons and Energy

Reduced
compound A
(reducing
agent)



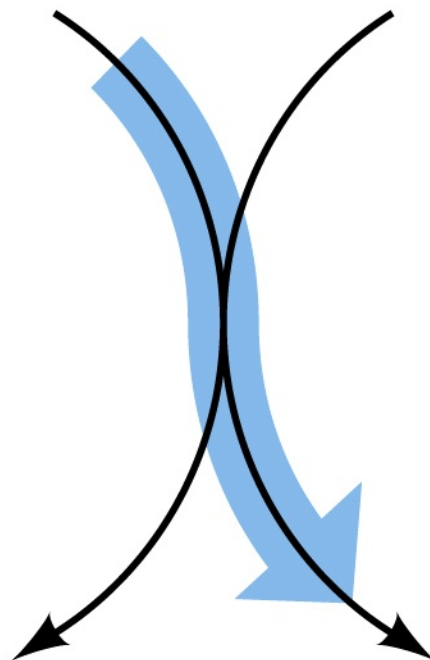
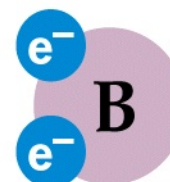
Oxidized
compound B
(oxidizing
agent)



Oxidized
compound A



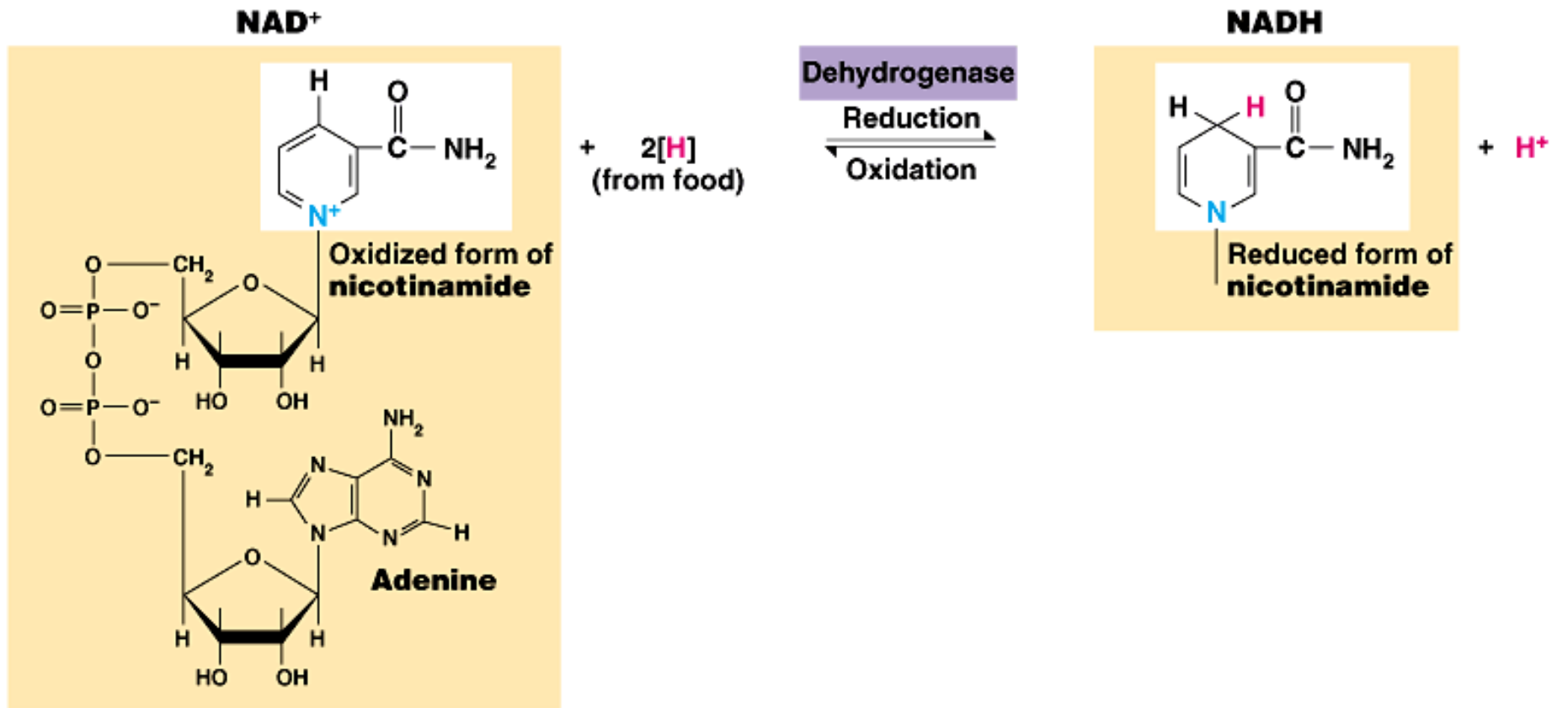
Reduced
compound B



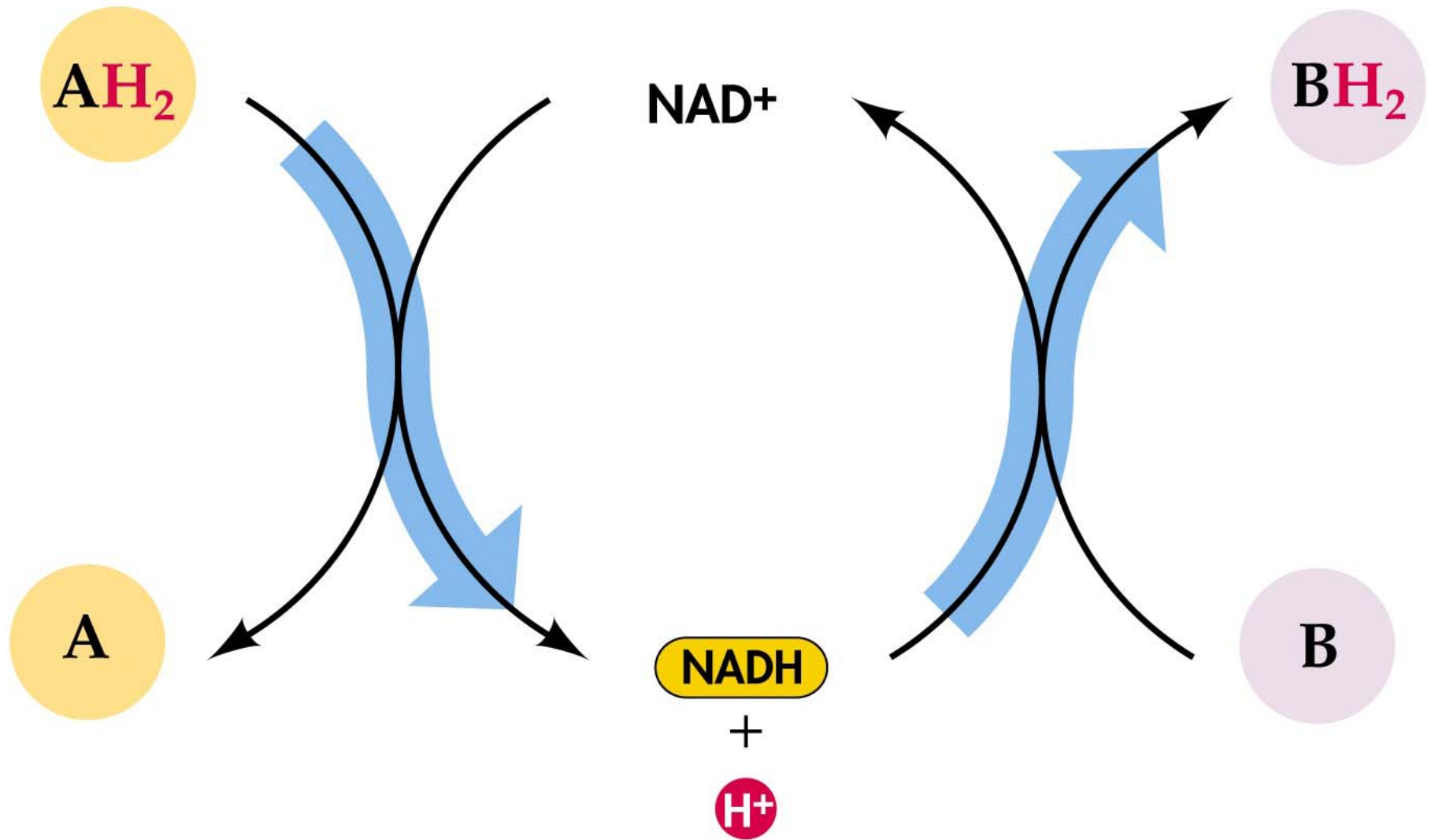
A. Obtaining Energy and Electrons from Glucose

- The coenzyme NAD is a key electron carrier in biological redox reactions.
- It exists in two forms, one oxidized (NAD^+) and the other reduced ($\text{NADH} + \text{H}^+$).

NAD⁺ as an electron shuttle



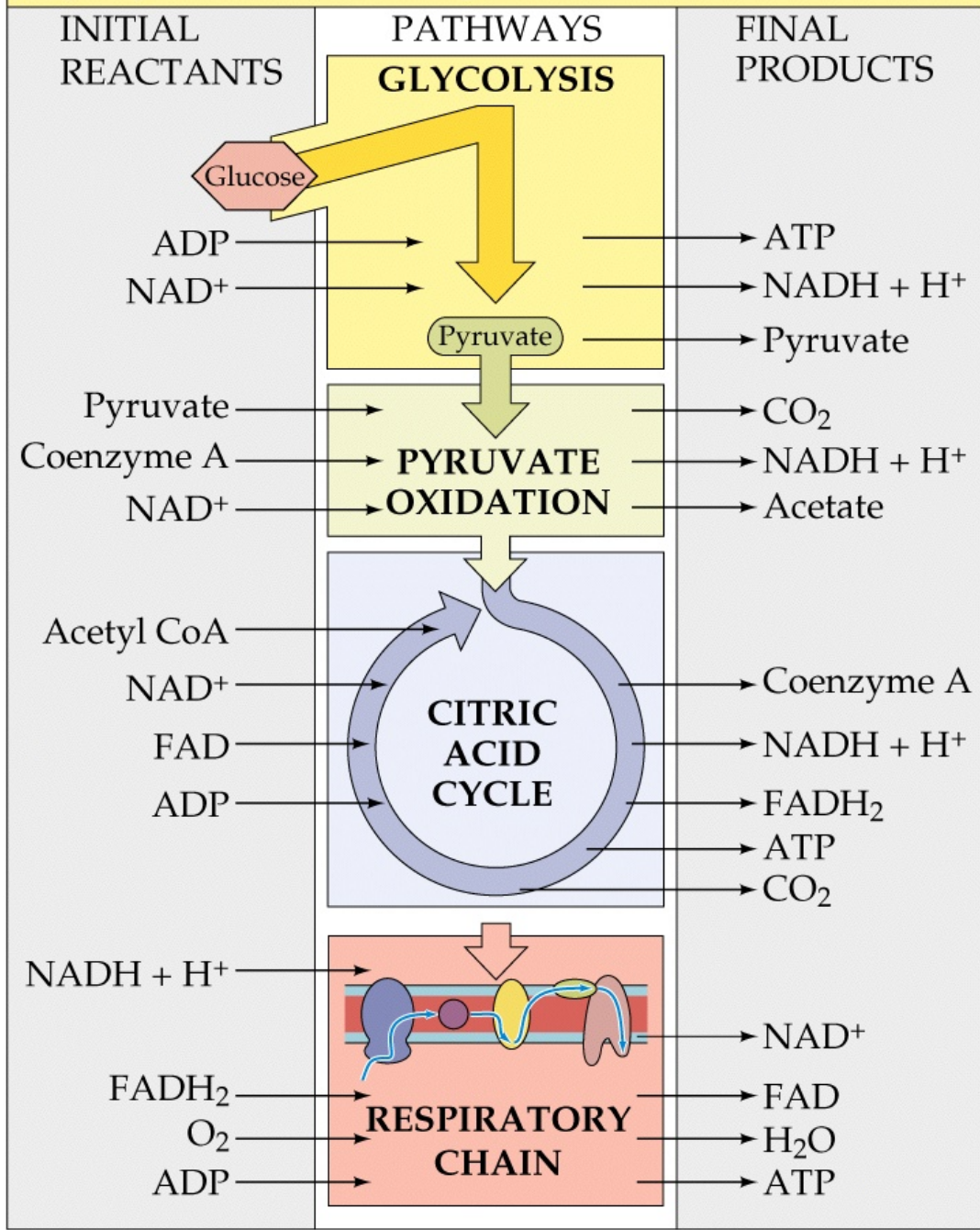
NAD as an Electron Carrier and Redox Couple



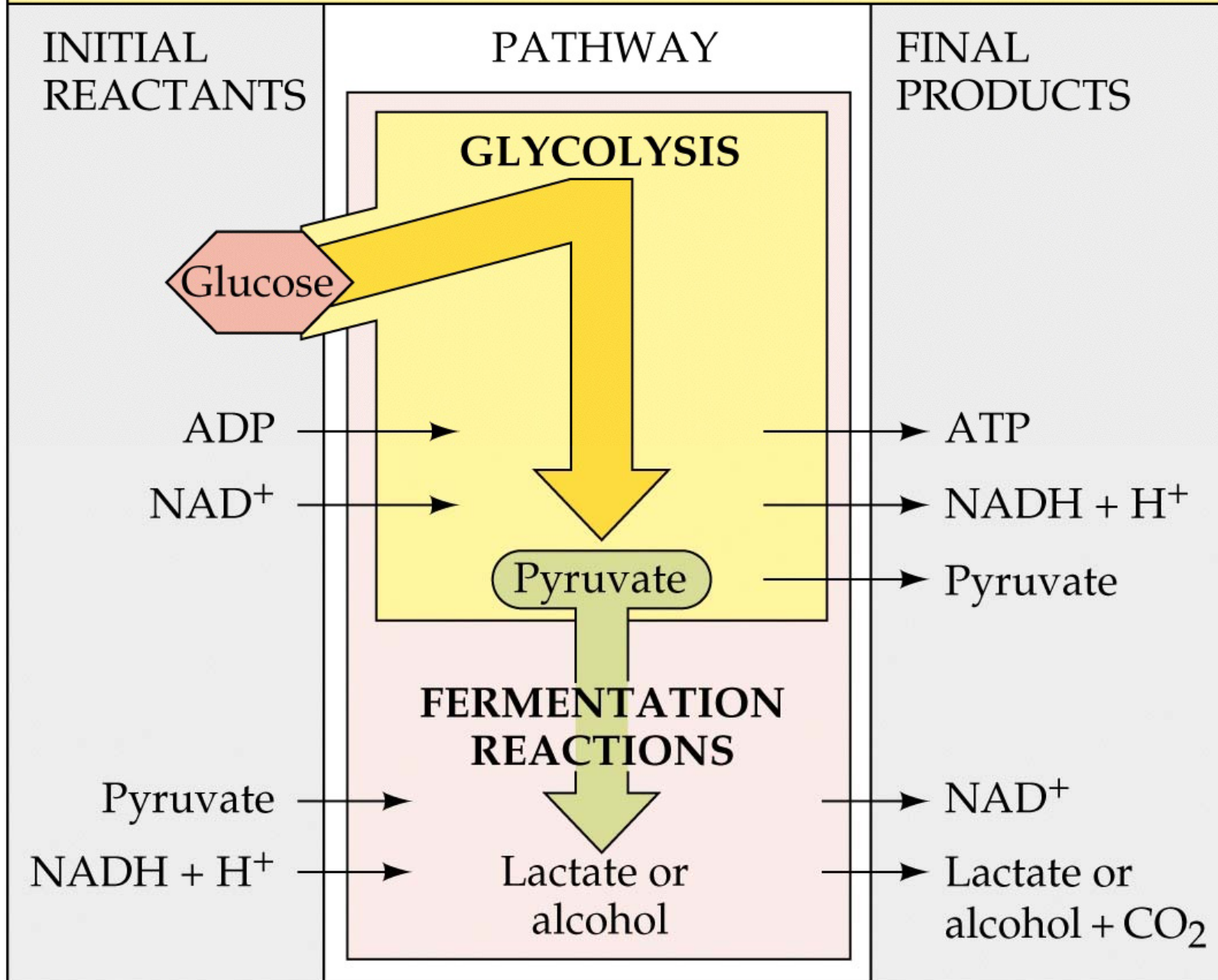
B. An Overview: Releasing Energy from Glucose

- Glycolysis operates in the presence or absence of O_2 .
- Under aerobic conditions, cellular respiration continues the breakdown process.

Glycolysis and cellular respiration



Glycolysis and fermentation reactions



B. An Overview: Releasing Energy from Glucose

- Pyruvate oxidation and the citric acid cycle produce CO_2 and hydrogen atoms carried by NADH and FADH_2 .
- The respiratory chain combines the hydrogens with O_2 , releasing enough energy for additional ATP synthesis.

B. An Overview: Releasing Energy from Glucose

- In some cells under anaerobic conditions, pyruvate can be reduced by NADH to form lactate and regenerate the NAD needed to sustain glycolysis.
- This is called a fermentation.

B. An Overview: Releasing Energy from Glucose

- In eukaryotes, glycolysis and fermentation occur in the cytoplasm outside of the mitochondria; pyruvate oxidation, the citric acid cycle, and the respiratory chain operate in association with mitochondria.
- In prokaryotes, glycolysis, fermentation, and the citric acid cycle take place in the cytoplasm; and pyruvate oxidation and the respiratory chain operate in association with the plasma membrane.

7.1 Cellular Locations for Energy Pathways in Eukaryotes and Prokaryotes

EUKARYOTES

External to mitochondrion

Glycolysis

Fermentation

Inside mitochondrion

Inner membrane

Pyruvate oxidation

Respiratory chain

Matrix

Citric acid cycle

PROKARYOTES

In cytoplasm

Glycolysis

Fermentation

Citric acid cycle

On inner face of plasma membrane

Pyruvate oxidation

Respiratory chain

C. Glycolysis: From Glucose to Pyruvate

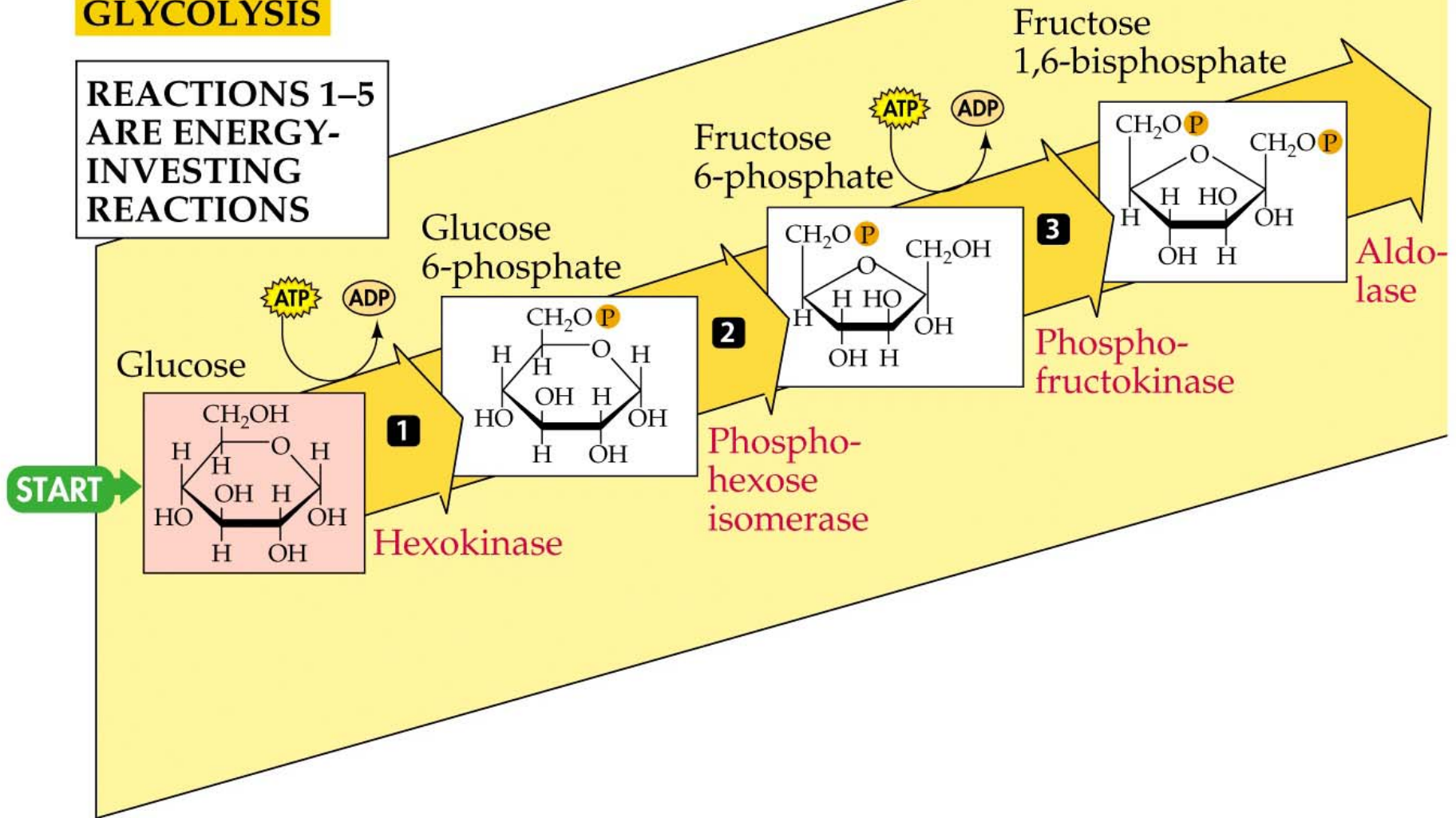
- Glycolysis is a pathway of ten enzyme-catalyzed reactions located in the cytoplasm.
- It provides starting materials for both cellular respiration and fermentation.

C. Glycolysis: From Glucose to Pyruvate

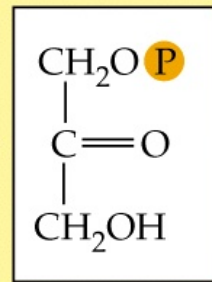
- The energy-investing reactions of glycolysis use two ATPs per glucose molecule and eventually yield two glyceraldehyde 3-phosphate molecules.
- In the energy-harvesting reactions, two NADH molecules are produced, and four ATP molecules are generated by substrate-level phosphorylation.
- Two pyruvates are produced for each glucose molecule.

GLYCOLYSIS

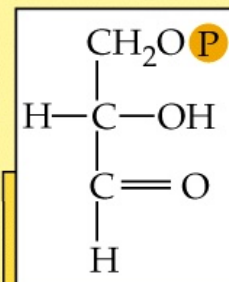
REACTIONS 1-5
ARE ENERGY-
INVESTING
REACTIONS



4 Dihydroxyacetone phosphate



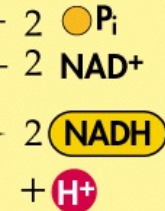
5 Glyceraldehyde 3-phosphate



4,5

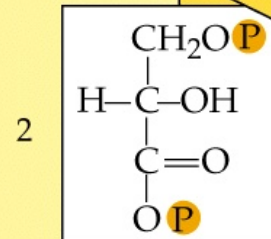
Isomerase

Triose phosphate dehydrogenase



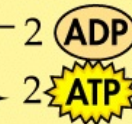
REACTIONS 6, 7,
AND 10 ARE
ENERGY-
HARVESTING
REACTIONS

6

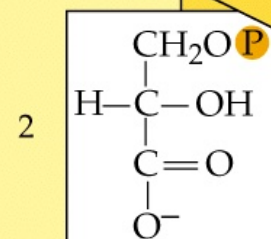


1,3-Bisphosphoglycerate

Phosphoglycerate kinase



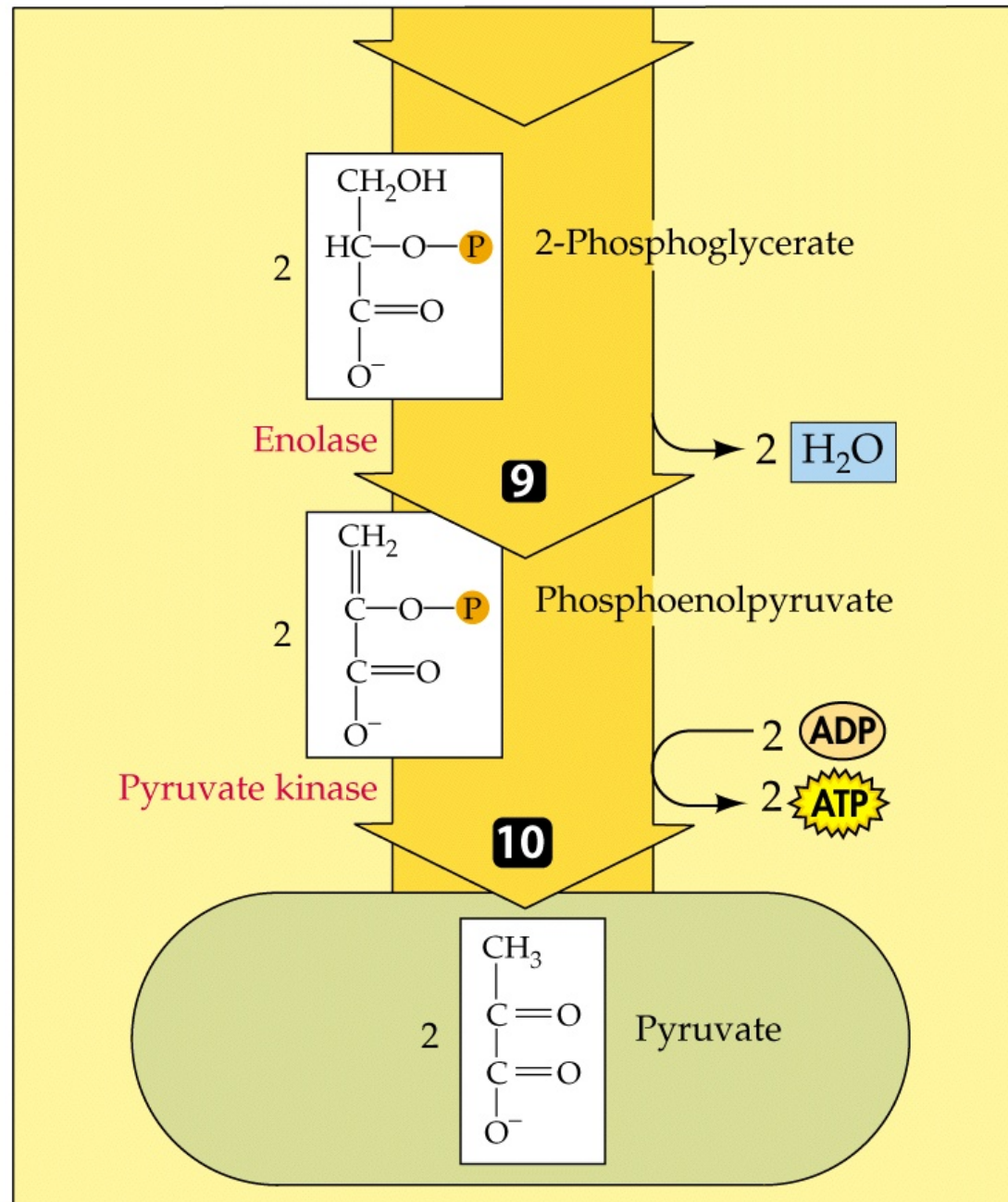
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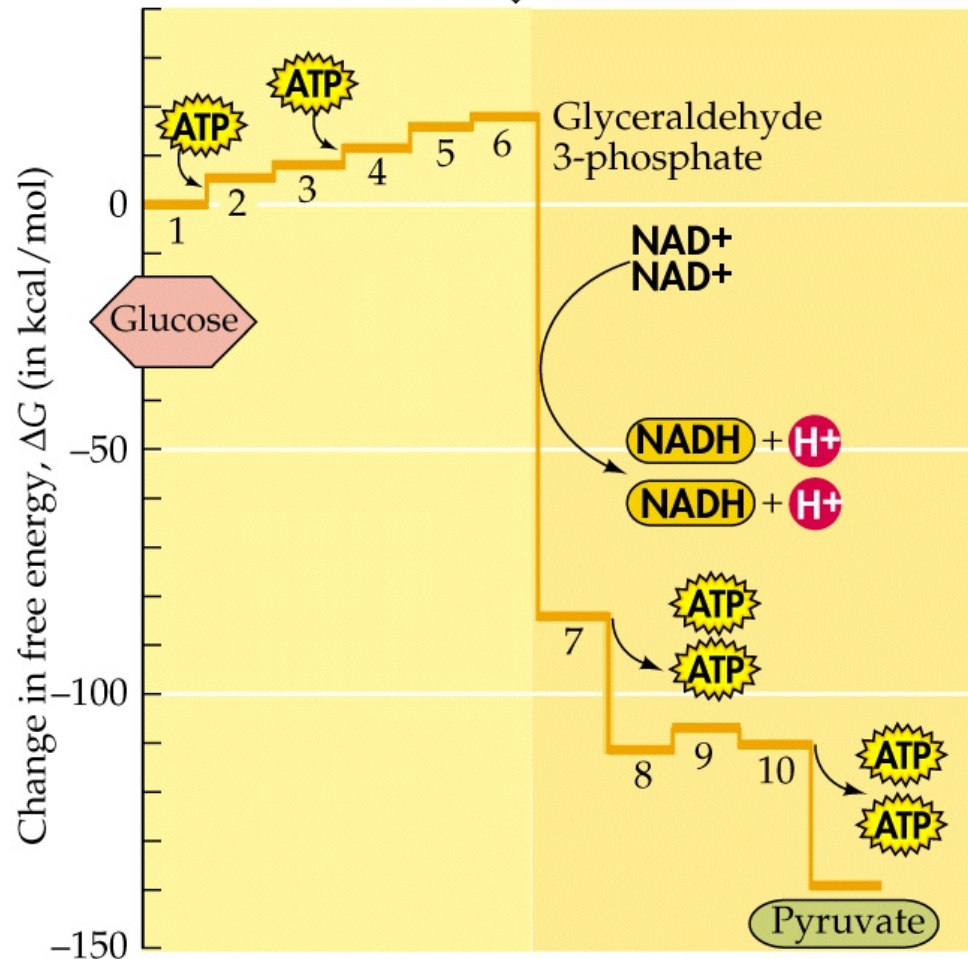
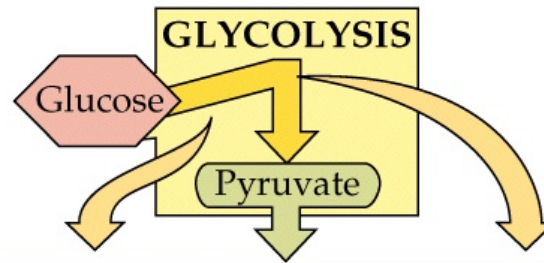
3-Phosphoglycerate

Phosphoglyceromutase

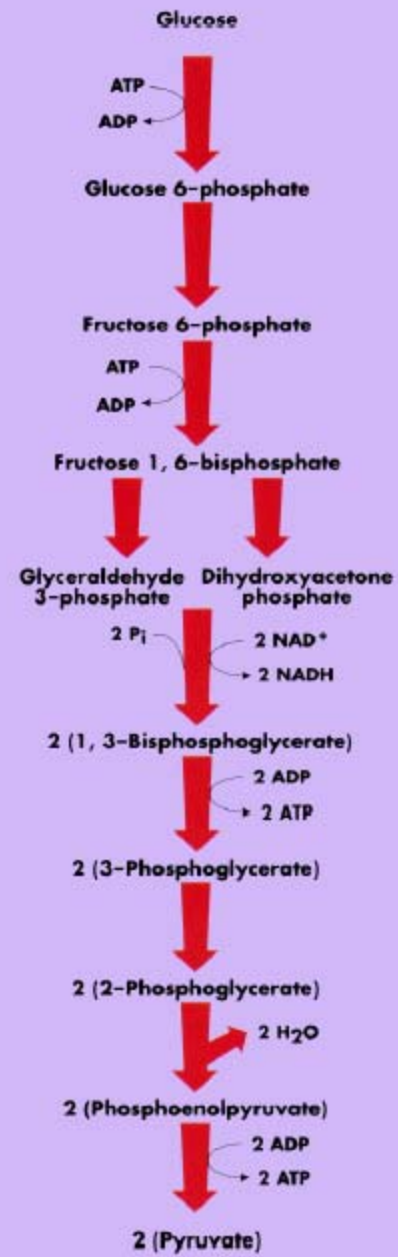
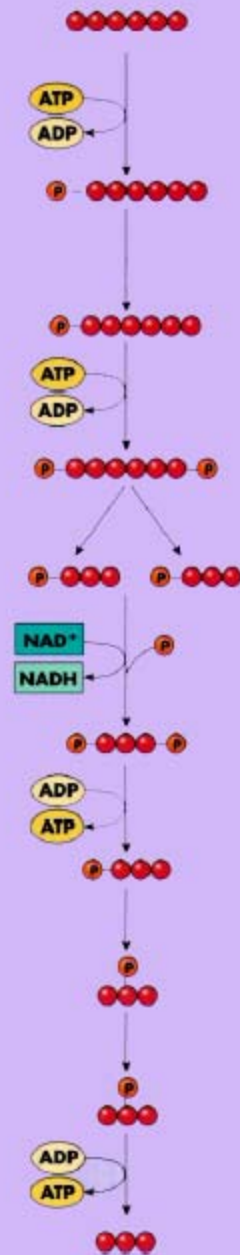
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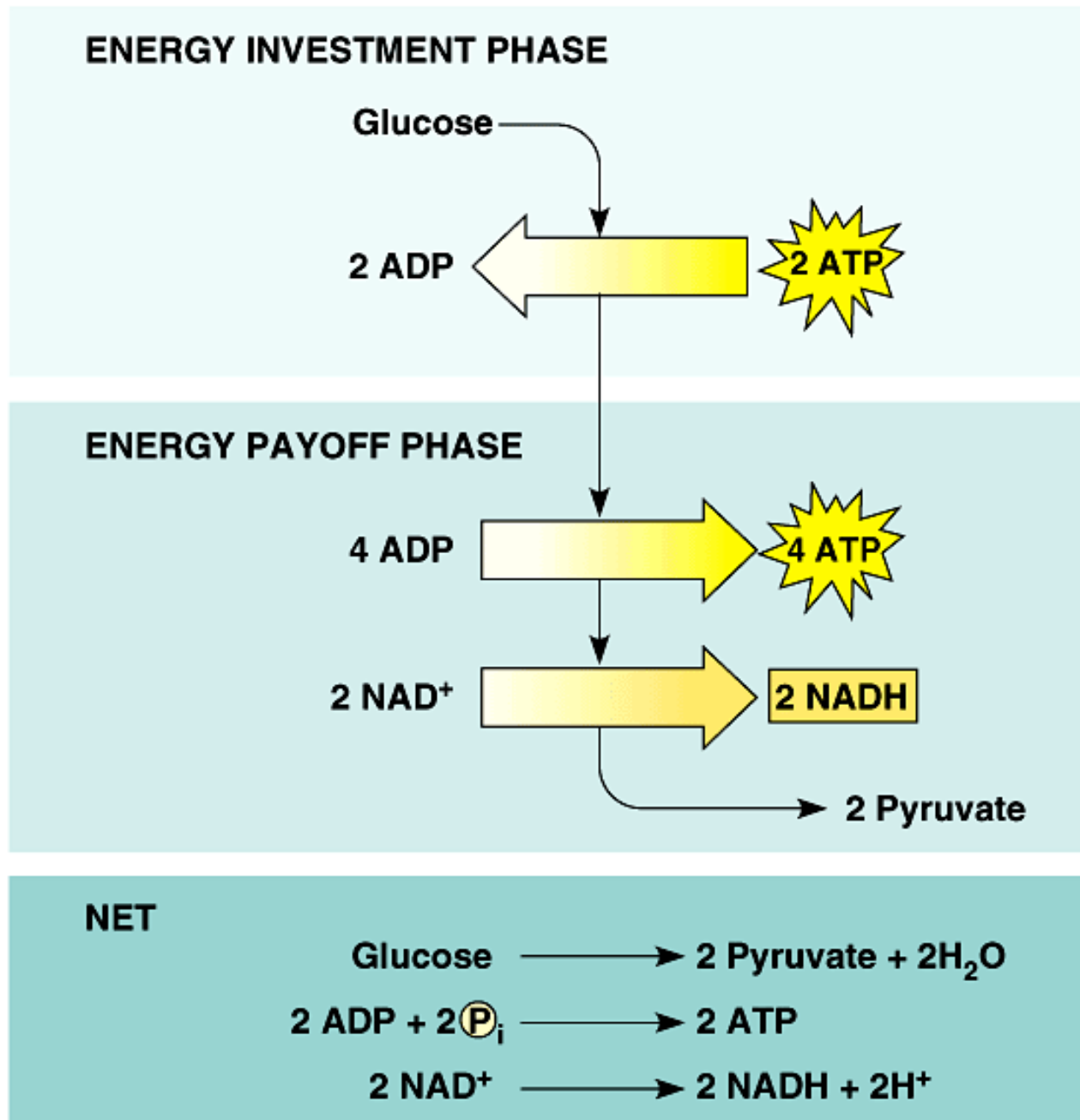
Glycolysis nets two molecules of ATP and two molecules of the electron carrier NADH. Two molecules of pyruvate are produced.



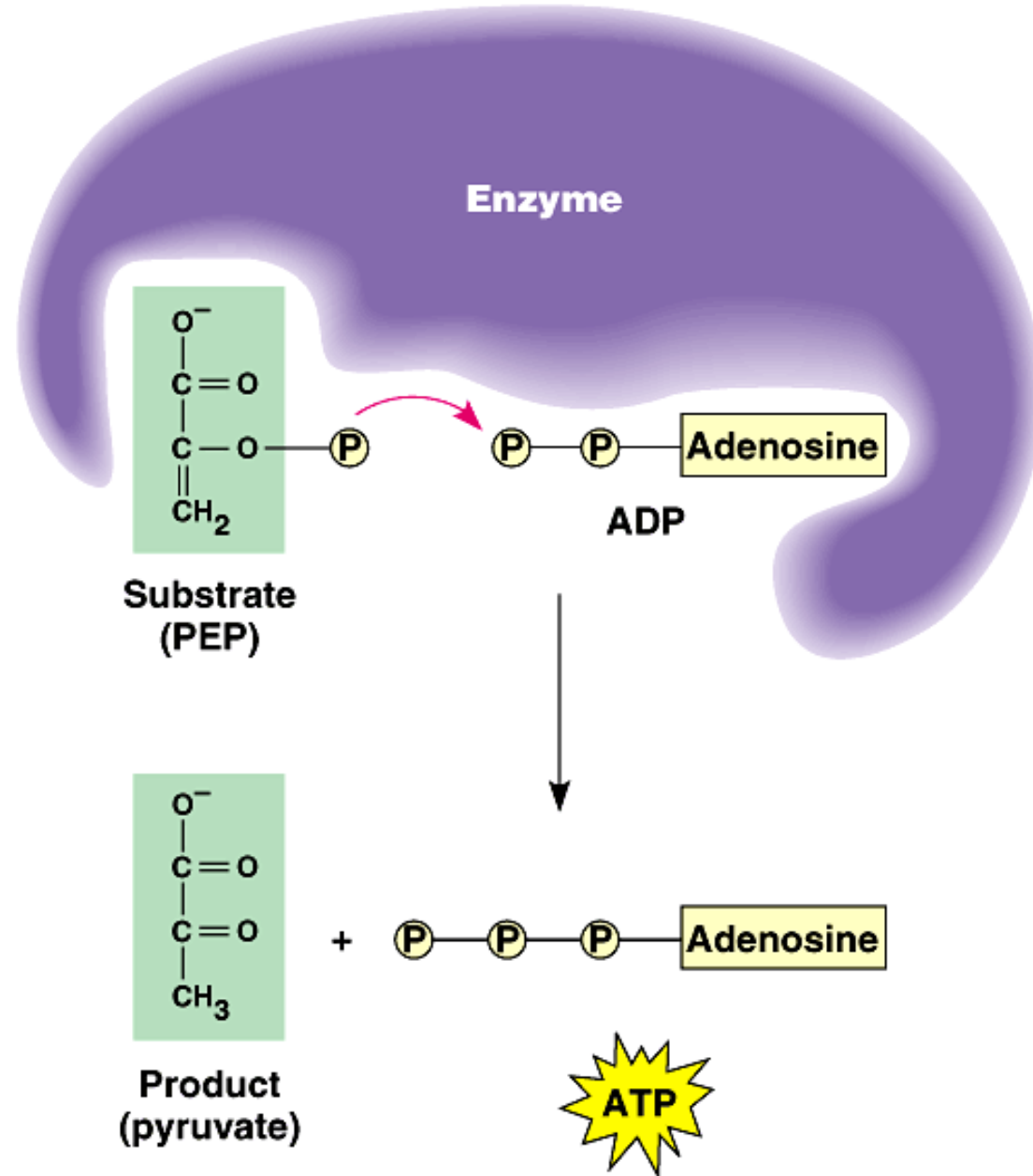
For each glucose:
 2 Pyruvate
 2 $\text{NADH} + 2 \text{H}^+$
 2 ATP are produced.



The energy input and output of glycolysis



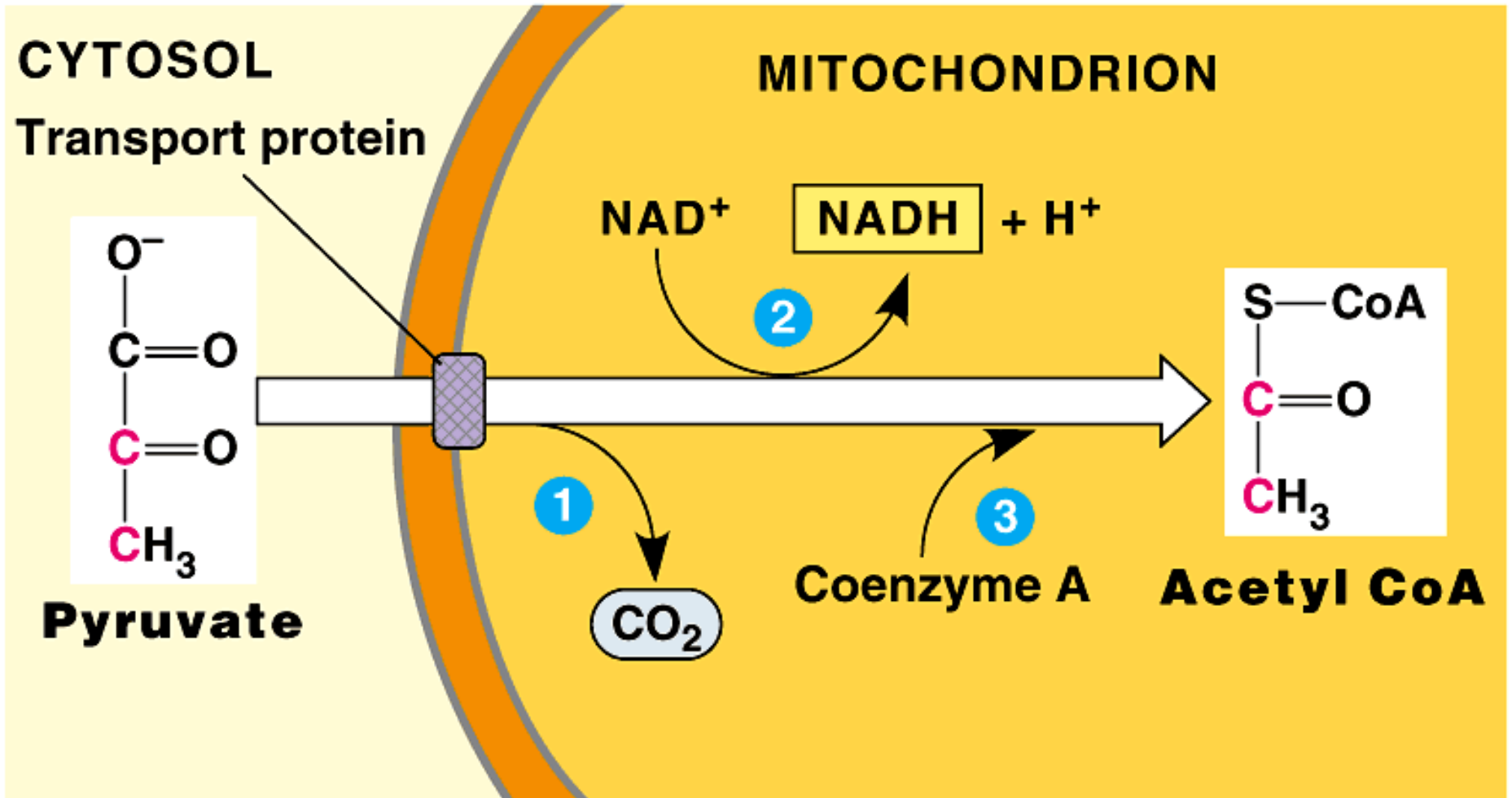
Substrate-level phosphorylation

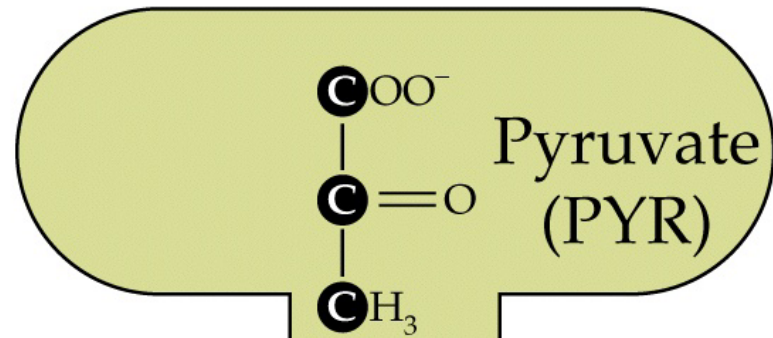


D. Pyruvate Oxidation

- The pyruvate dehydrogenase complex catalyzes three reactions:
- (1) Pyruvate is oxidized to the acetyl group, releasing one CO_2 molecule and energy;
- (2) some of this energy is captured when NAD^+ is reduced to $\text{NADH} + \text{H}^+$; and
- (3) the remaining energy is captured when the acetyl group combines with coenzyme A, yielding acetyl CoA.

Conversion of pyruvate to acetyl CoA, the junction between glycolysis and the Krebs aka Citric Acid Cycle



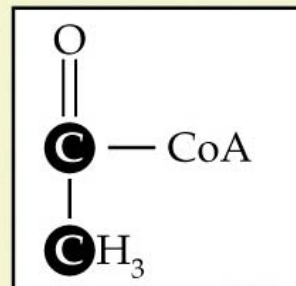


NAD⁺

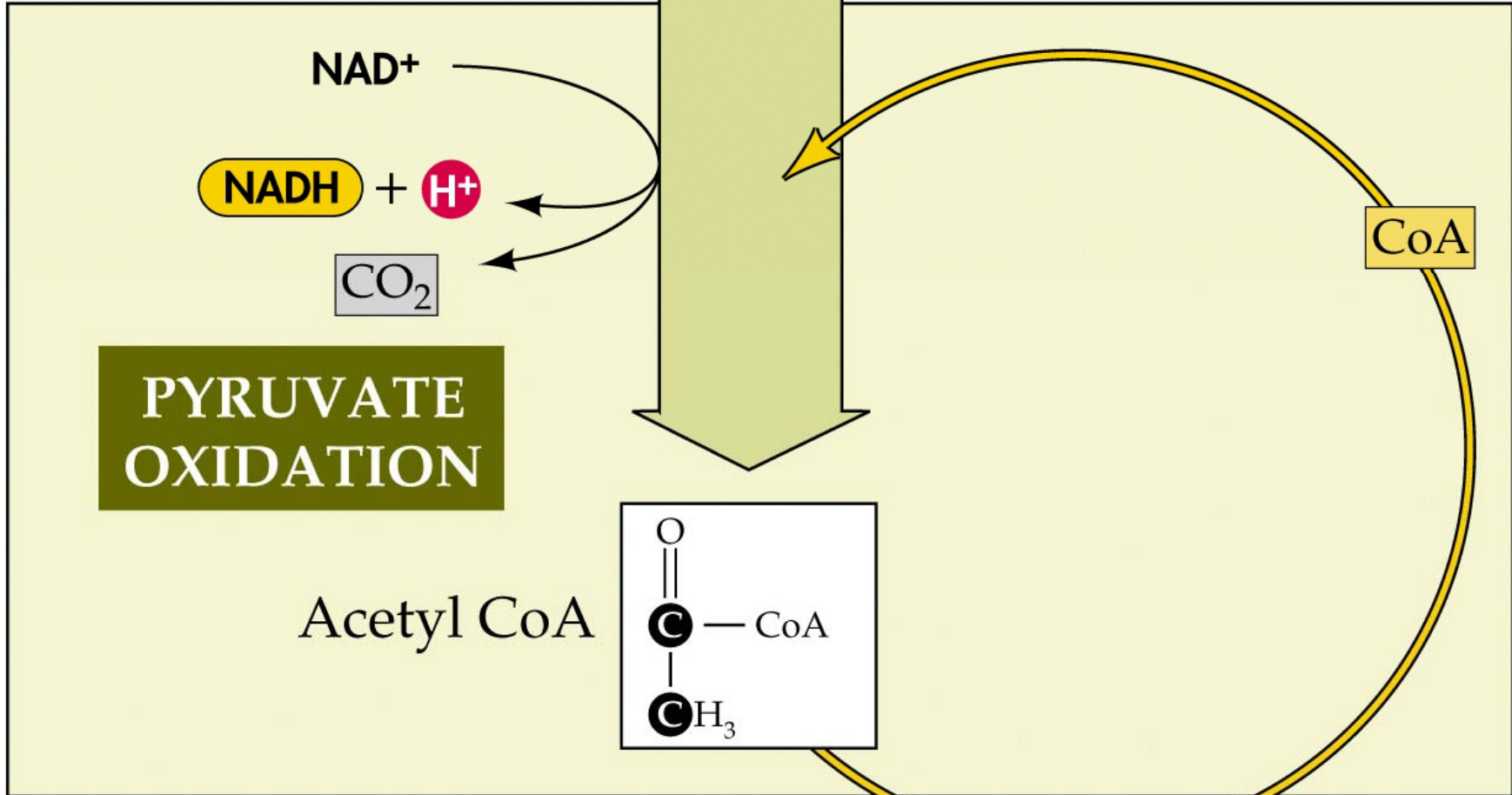


**PYRUVATE
OXIDATION**

Acetyl CoA

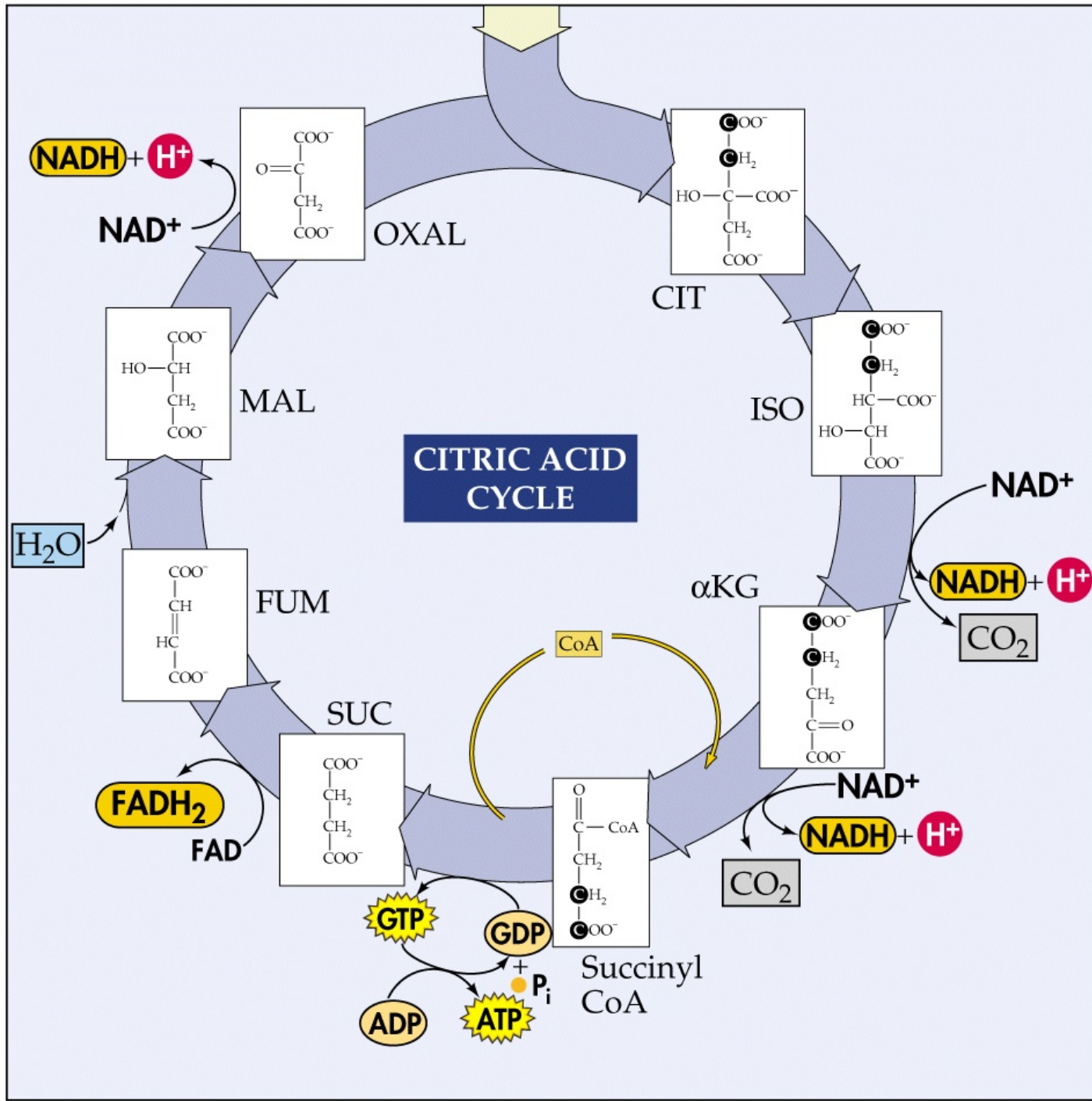


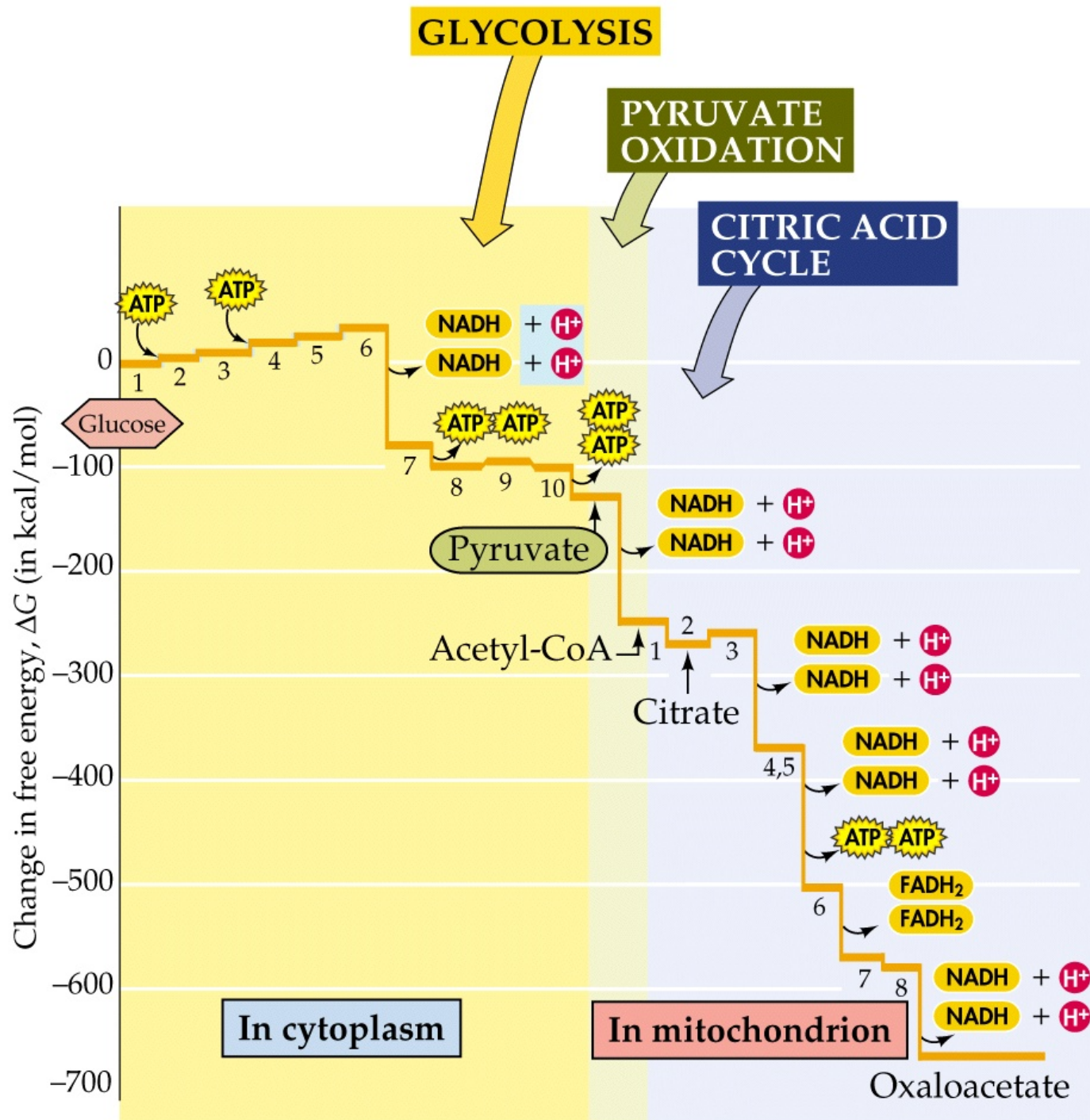
CoA

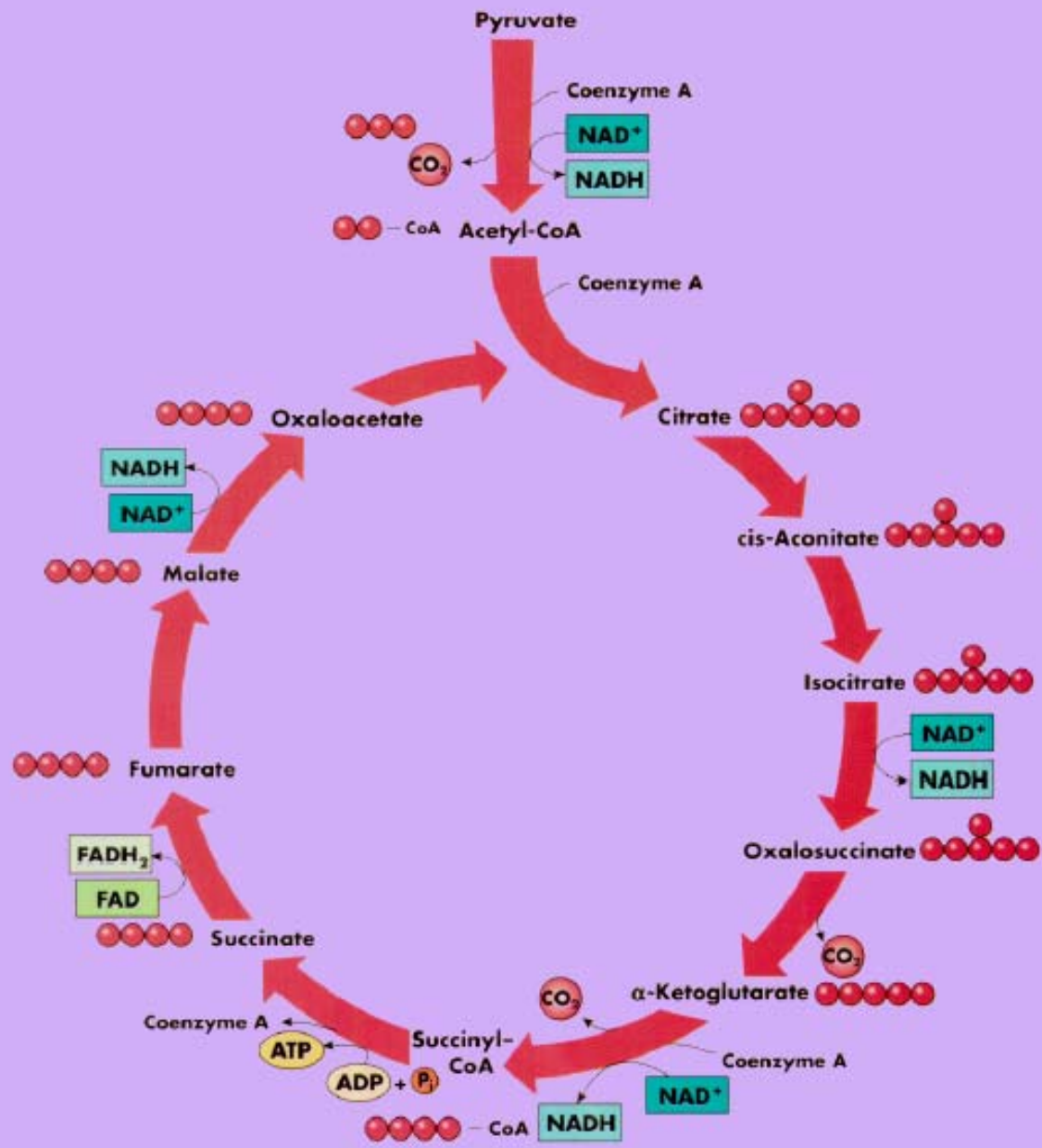


E. The Citric Acid Cycle

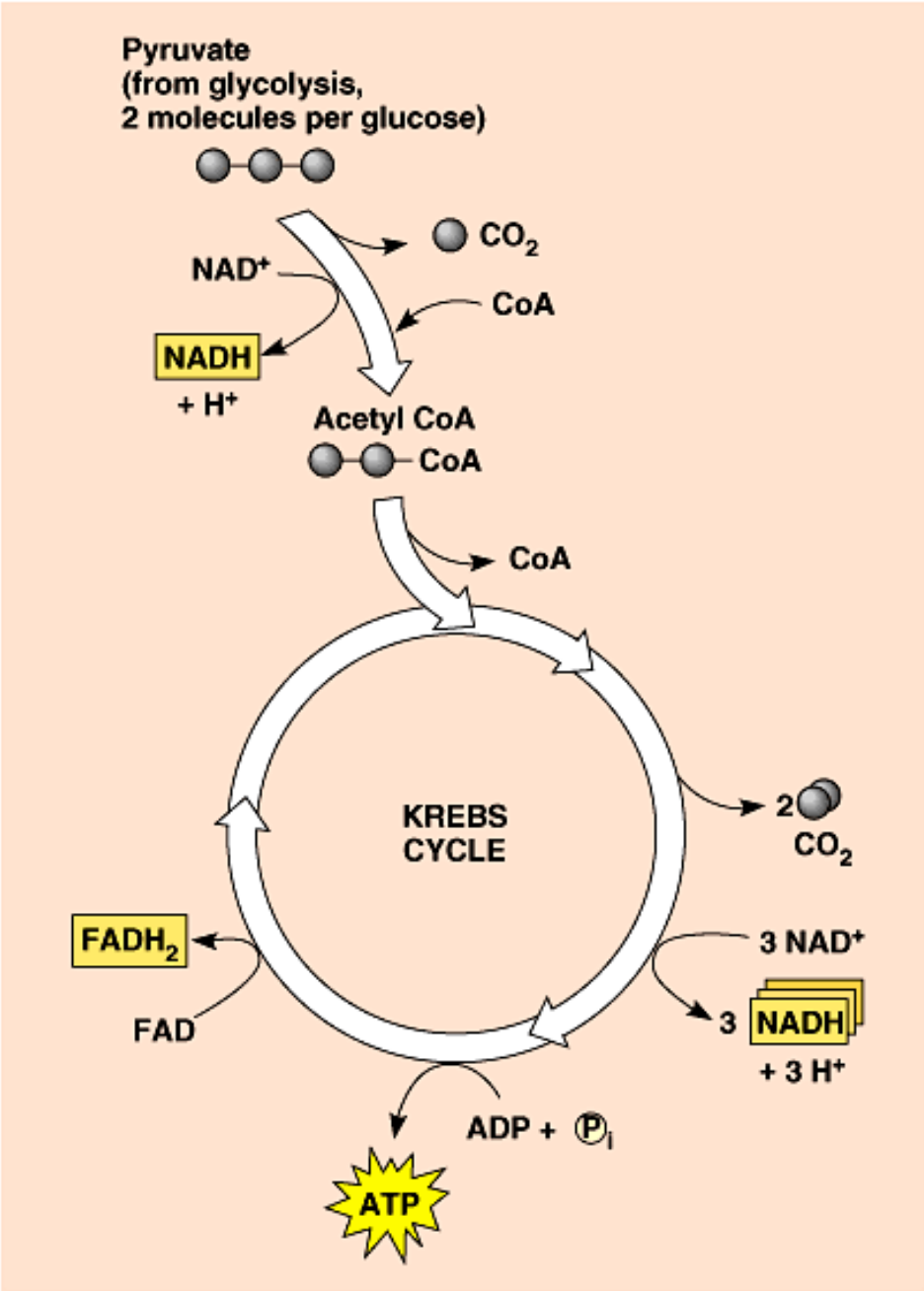
- The energy in acetyl CoA drives the reaction of acetate with oxaloacetate to produce citrate.
- The citric acid cycle is a series of reactions in which citrate is oxidized and oxaloacetate regenerated.
- It produces two CO_2 , one FADH_2 , three NADH , and one ATP for each acetyl CoA.







A summary of the Krebs cycle



F. The Respiratory Chain: Electrons, Proton Pumping, and ATP

- NADH + H⁺ and FADH₂ from glycolysis, pyruvate oxidation, and the citric acid cycle are oxidized by the respiratory chain, regenerating NAD⁺ and FAD.
- Most of the enzymes and other electron carriers of the chain are part of the inner mitochondrial membrane.
- O₂ is the final acceptor of electrons and protons, forming H₂O.

The Oxidation of $\text{NADH} + \text{H}^+$

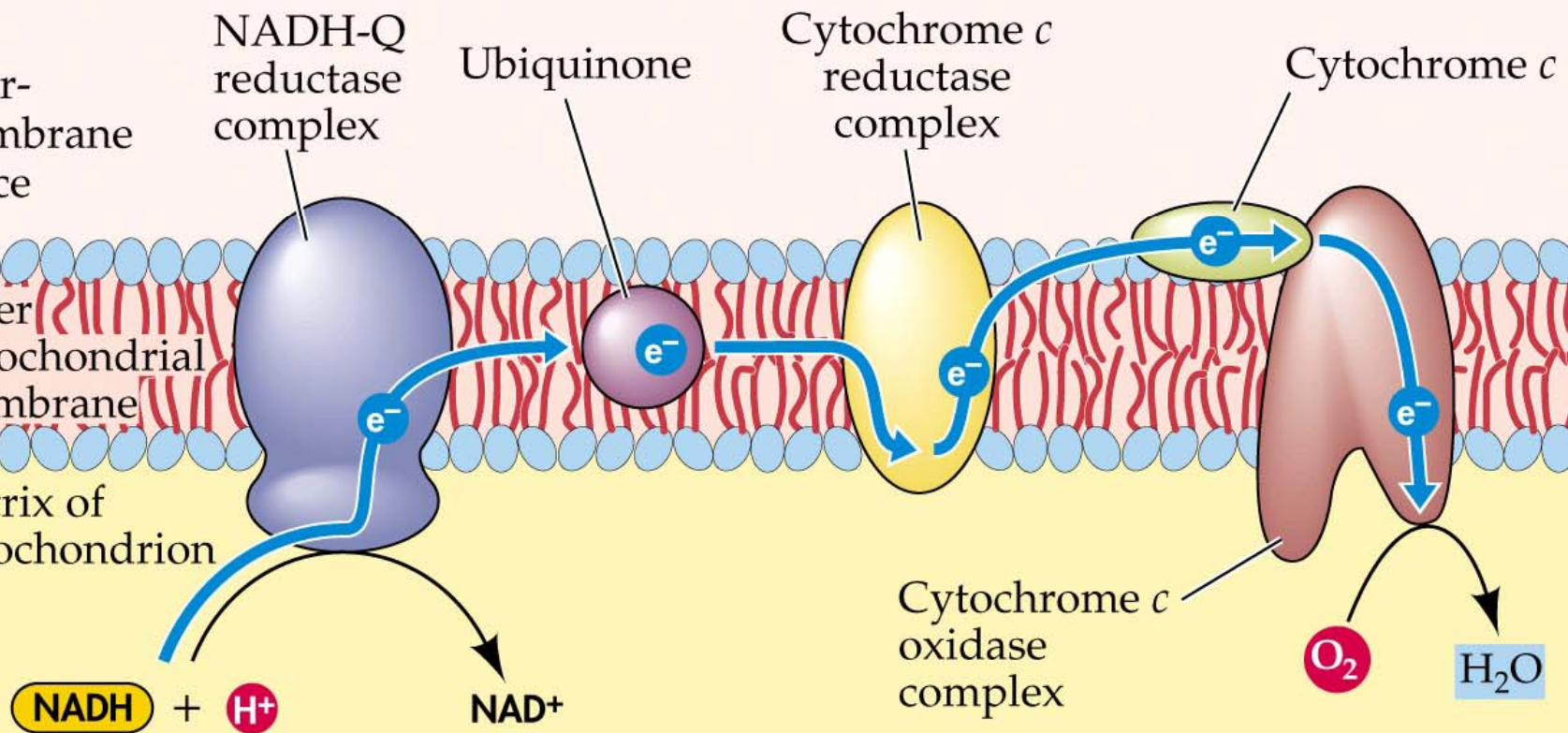
Cytosol

Outer mitochondrial membrane

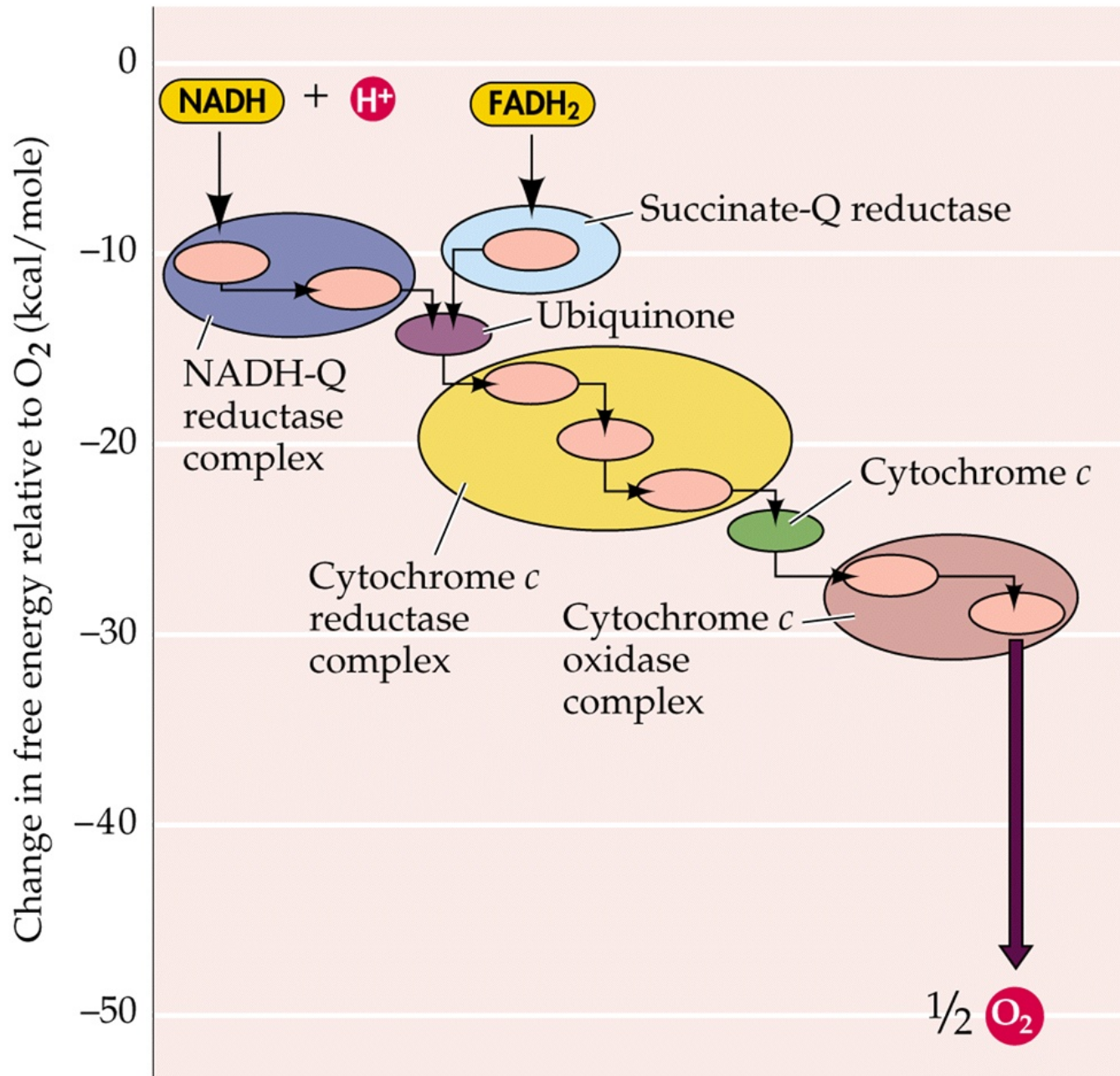
Inter-membrane space

Inner mitochondrial membrane

Matrix of mitochondrion



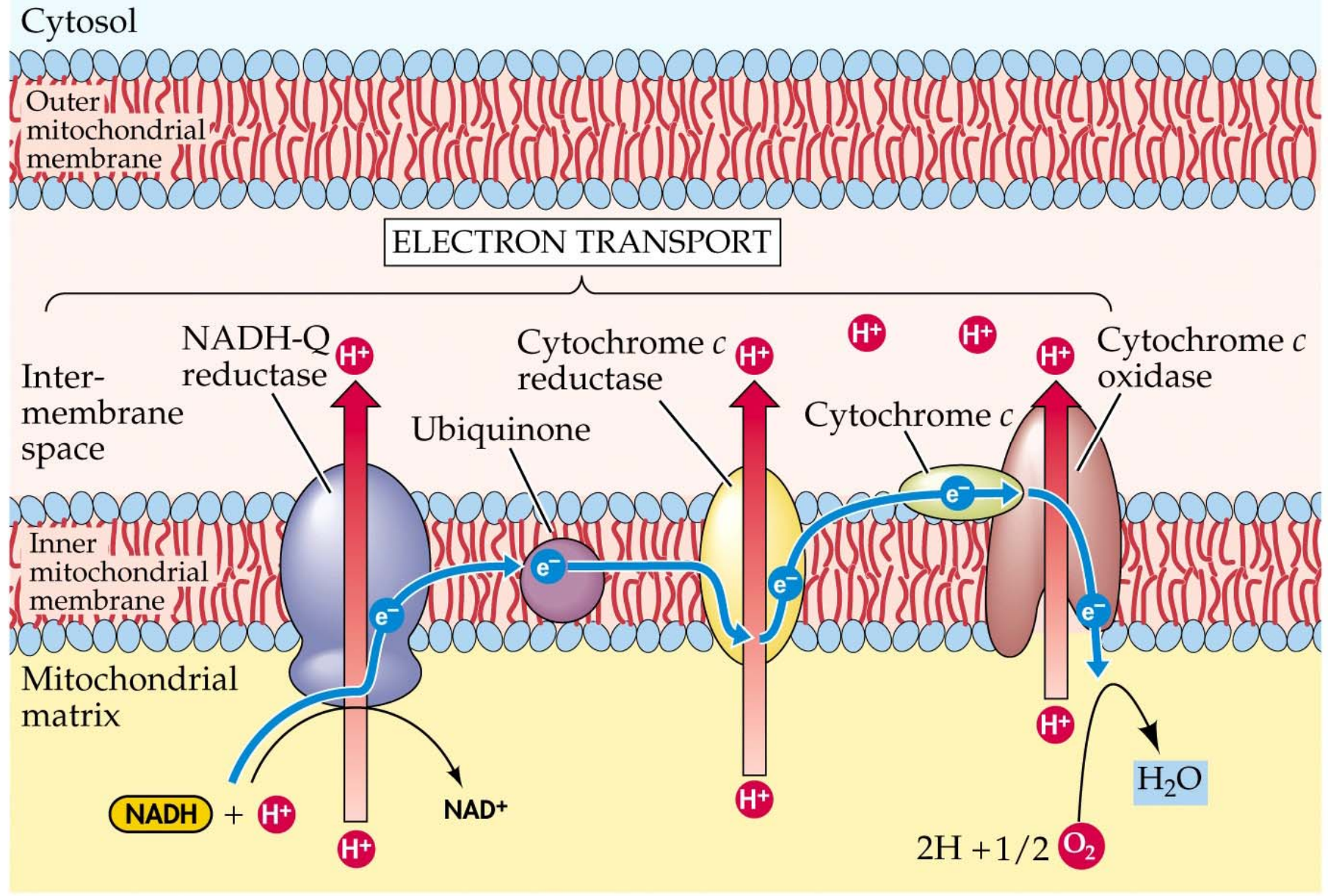
The Complete Respiratory Chain



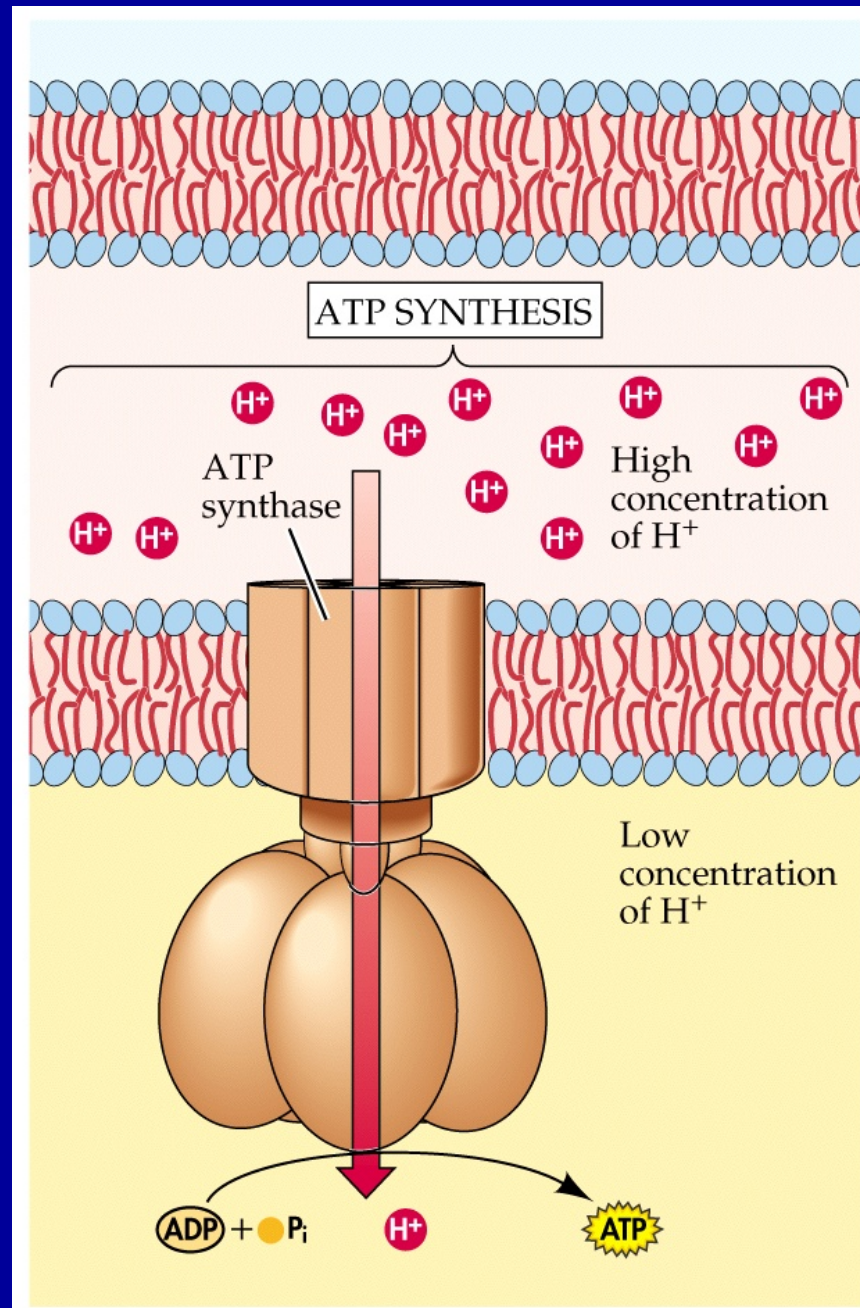
F. The Respiratory Chain: Electrons, Proton Pumping, and ATP

- The chemiosmotic mechanism couples proton transport to oxidative phosphorylation.
- As the electrons move along the respiratory chain, they lose energy, captured by proton pumps that actively transport H^+ out of the mitochondrial matrix, establishing a gradient of proton concentration and electric charge—the proton-motive force or PMF.

The Chemiosmotic Mechanism Produces ATP



The Chemiosmotic Mechanism Produces ATP



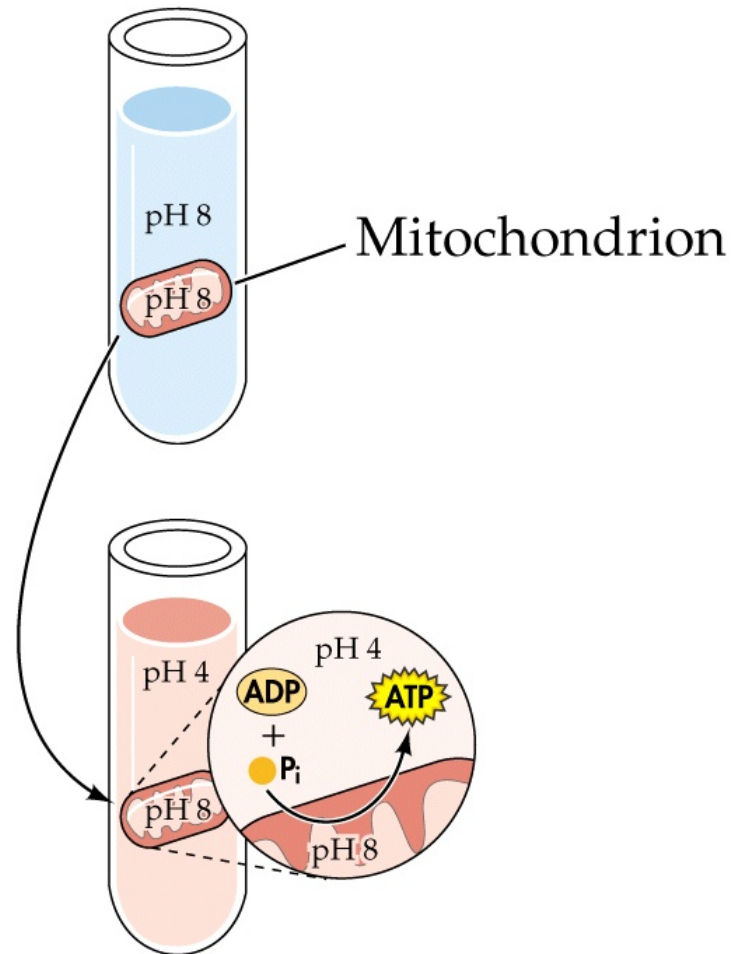
“OxPhos”
ATP
synthesis

F. The Respiratory Chain: Electrons, Proton Pumping, and ATP

- The proton-motive force causes protons to diffuse back into the mitochondrial interior through the membrane channel protein ATP synthase, which couples that diffusion to the production of ATP.
- Several key experiments demonstrate that it is chemiosmosis that produces ATP.

EXPERIMENT 1

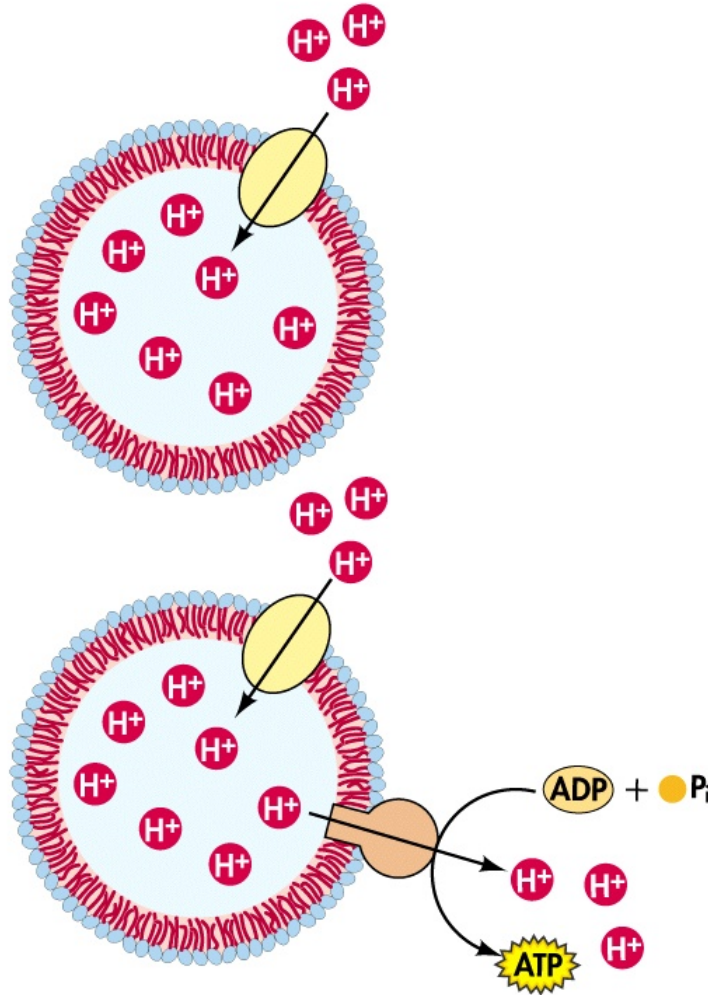
Question: Can an H^+ gradient drive ATP synthesis by isolated mitochondria?



Conclusion: In the absence of electron transport, an artificial H^+ gradient is sufficient for ATP synthesis by mitochondria.

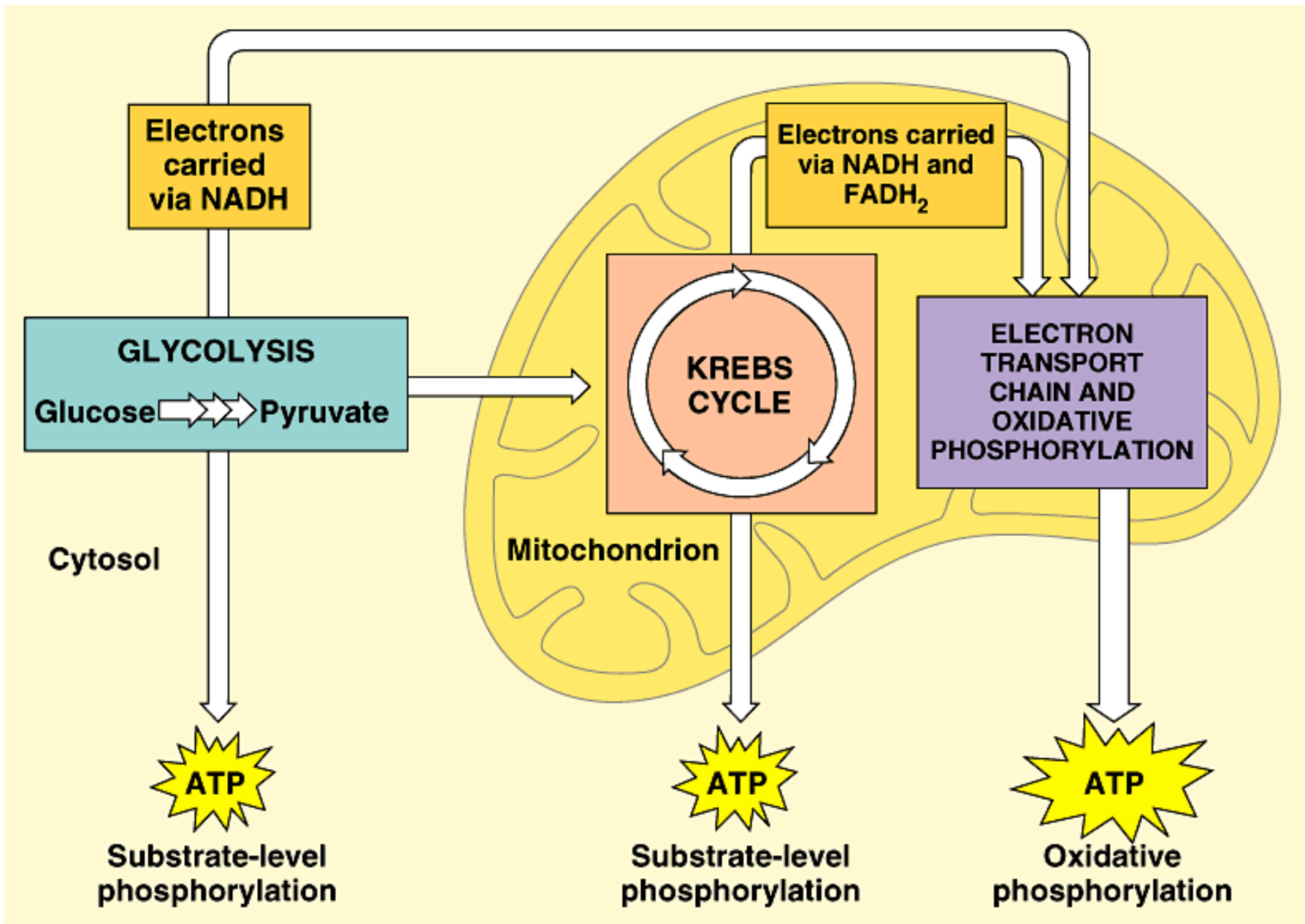
EXPERIMENT 2

Question: What is the role of H^+ pumps in ATP synthesis?



Conclusion: If an H^+ gradient is created by directional pumping, a second pump, acting as an H^+ channel, is necessary for ATP synthesis.

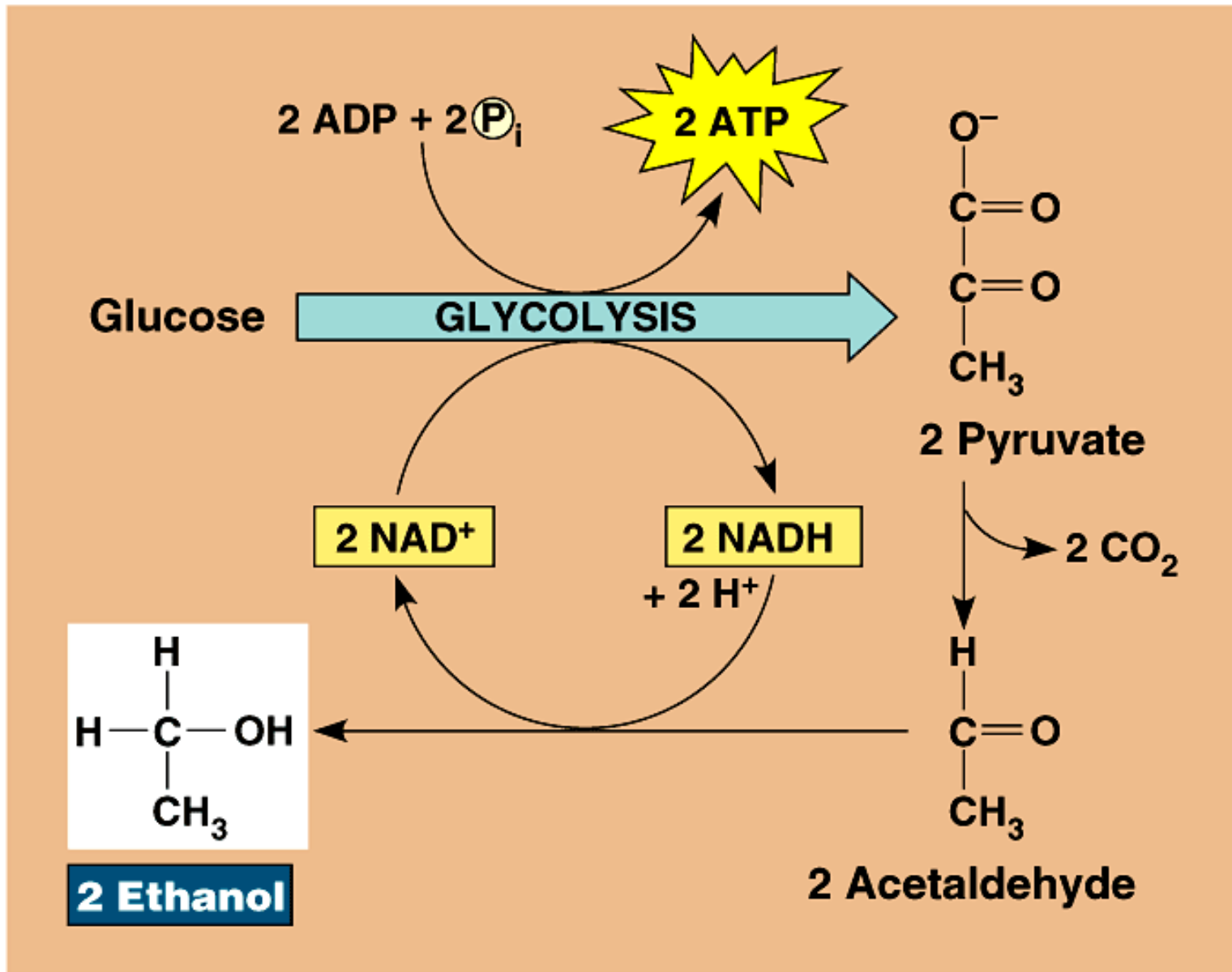
An overview of cellular respiration



G. Fermentation: ATP from Glucose, without O₂

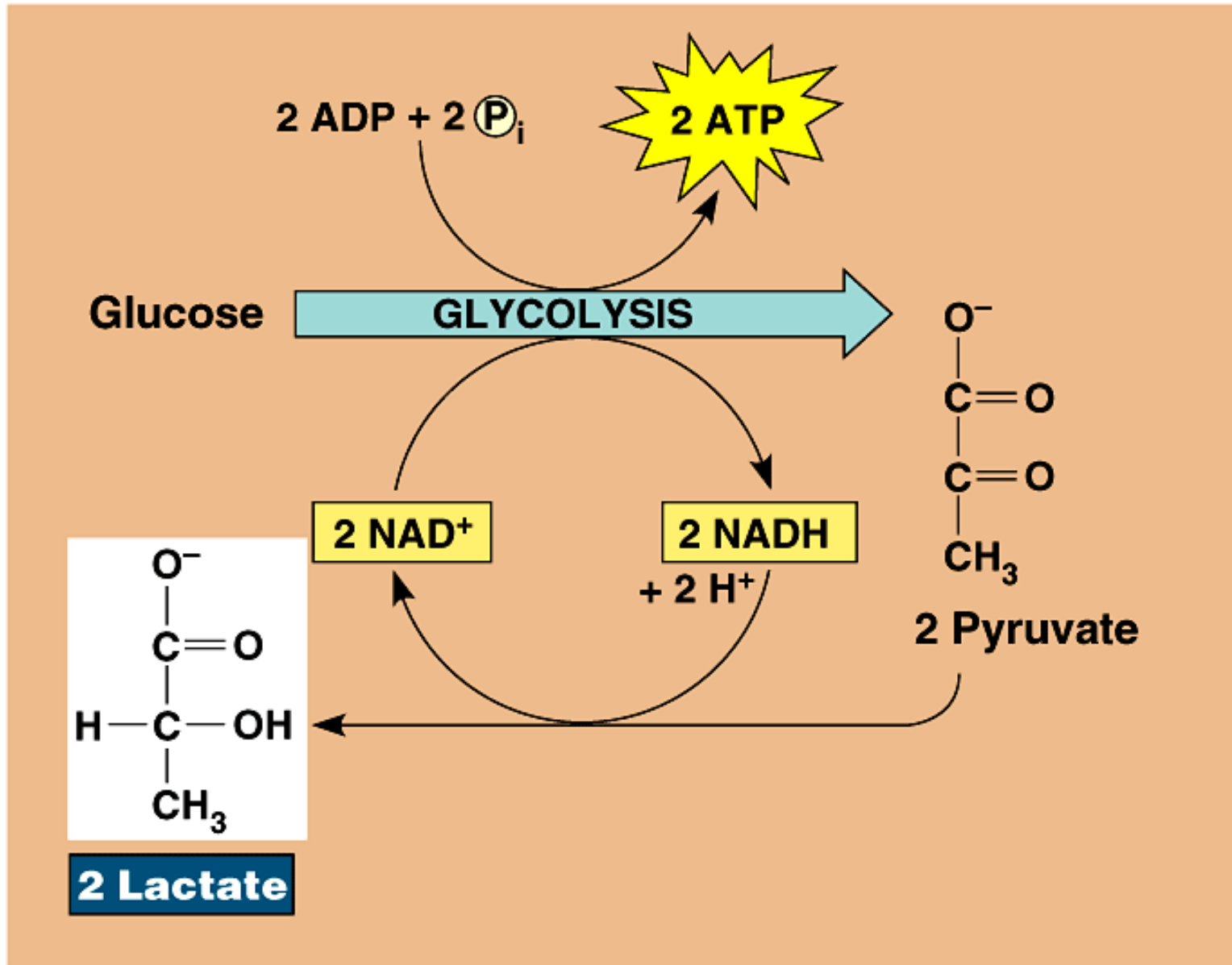
- Many organisms and some cells live without O₂, deriving energy from glycolysis and fermentation.
- Together, these pathways partly oxidize glucose and generate energy-containing products.
- Fermentation reactions anaerobically oxidize the NADH + H⁺ produced in glycolysis.

Fermentation



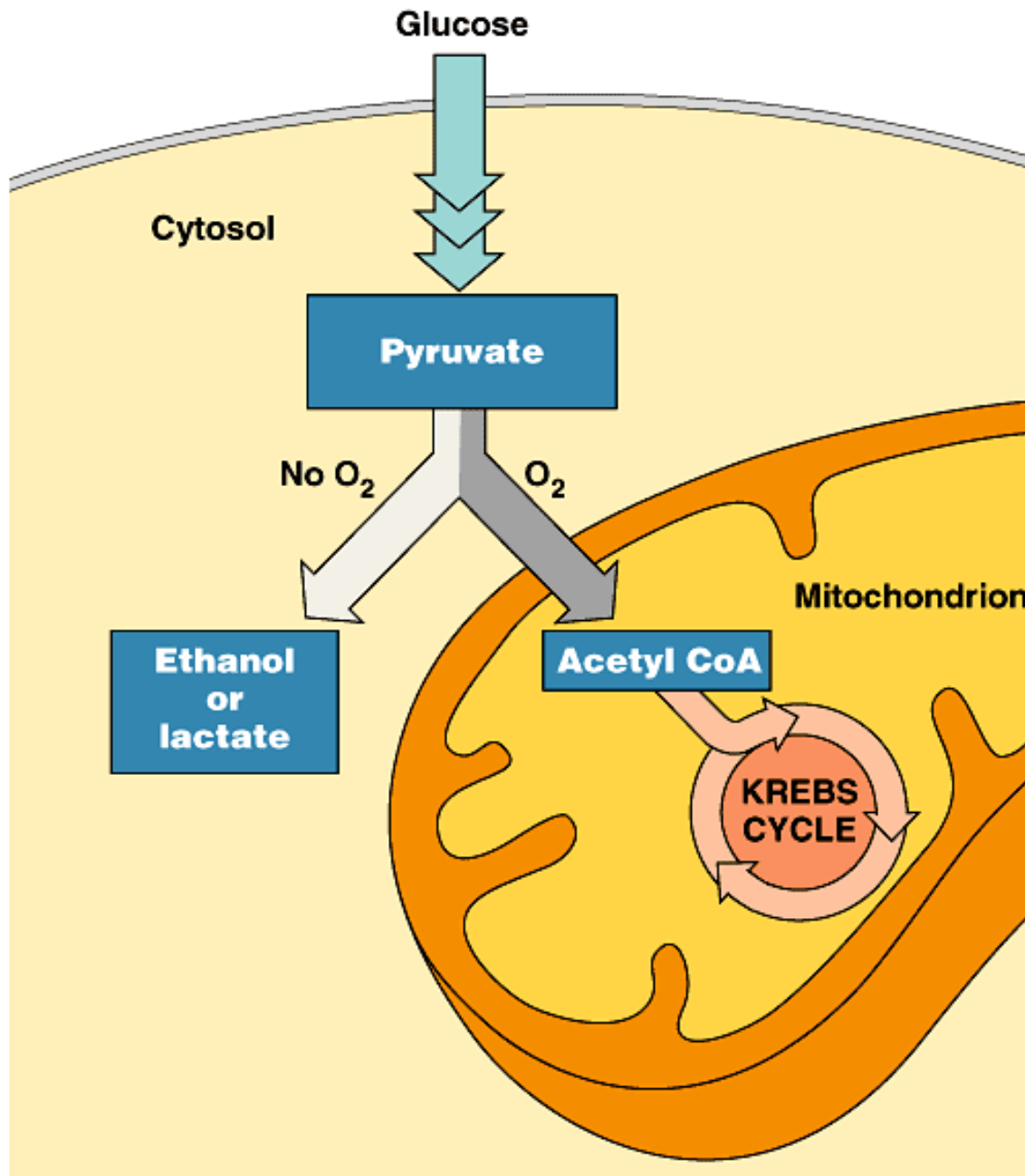
(a) Alcohol fermentation

Fermentation



(b) Lactic acid fermentation

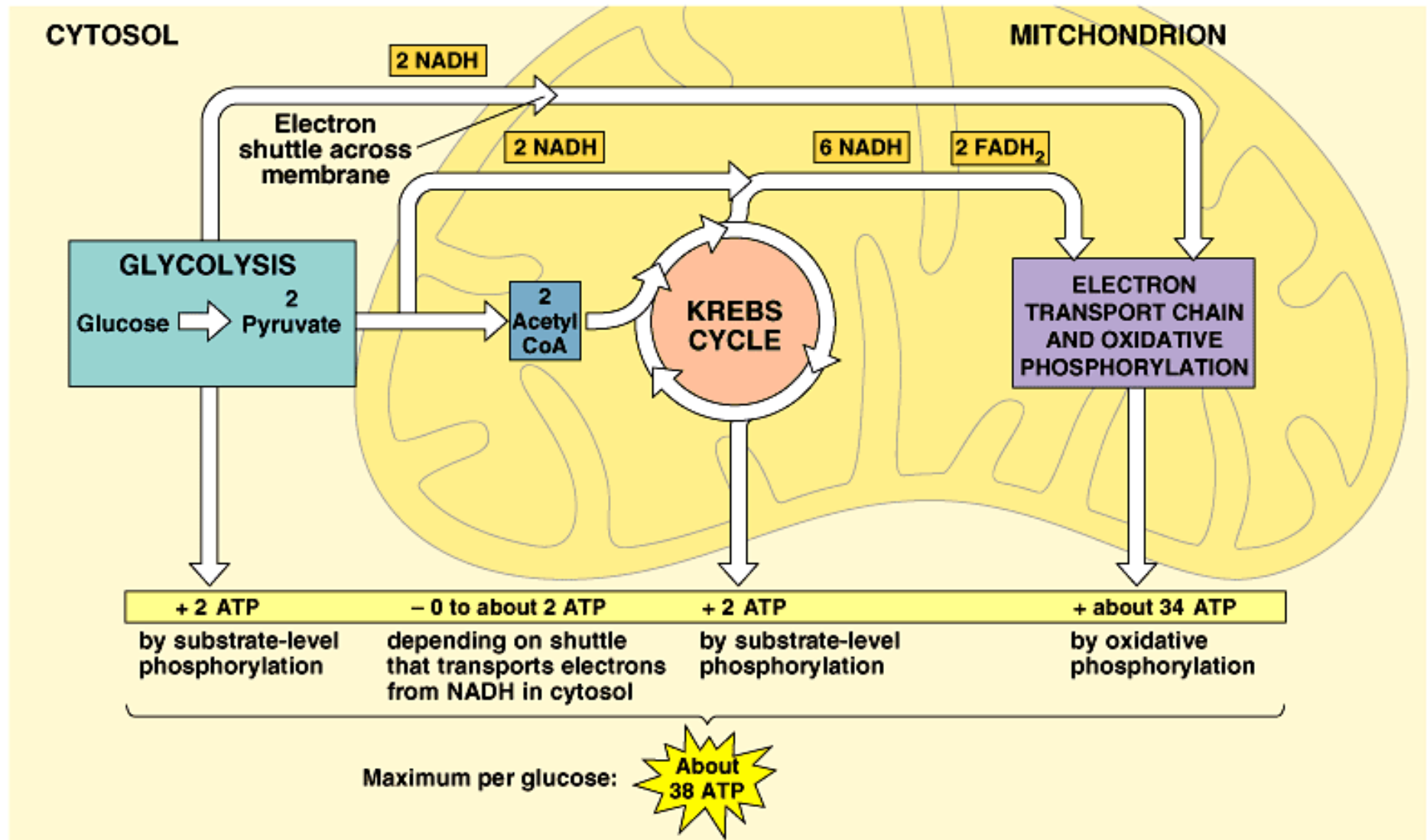
Pyruvate as a key juncture in catabolism



H. Contrasting Energy Yields

- For each molecule of glucose used, fermentation yields 2 molecules of ATP.
- In contrast, glycolysis operating with pyruvate oxidation, the citric acid cycle, and the respiratory chain yields up to 36 or 38.

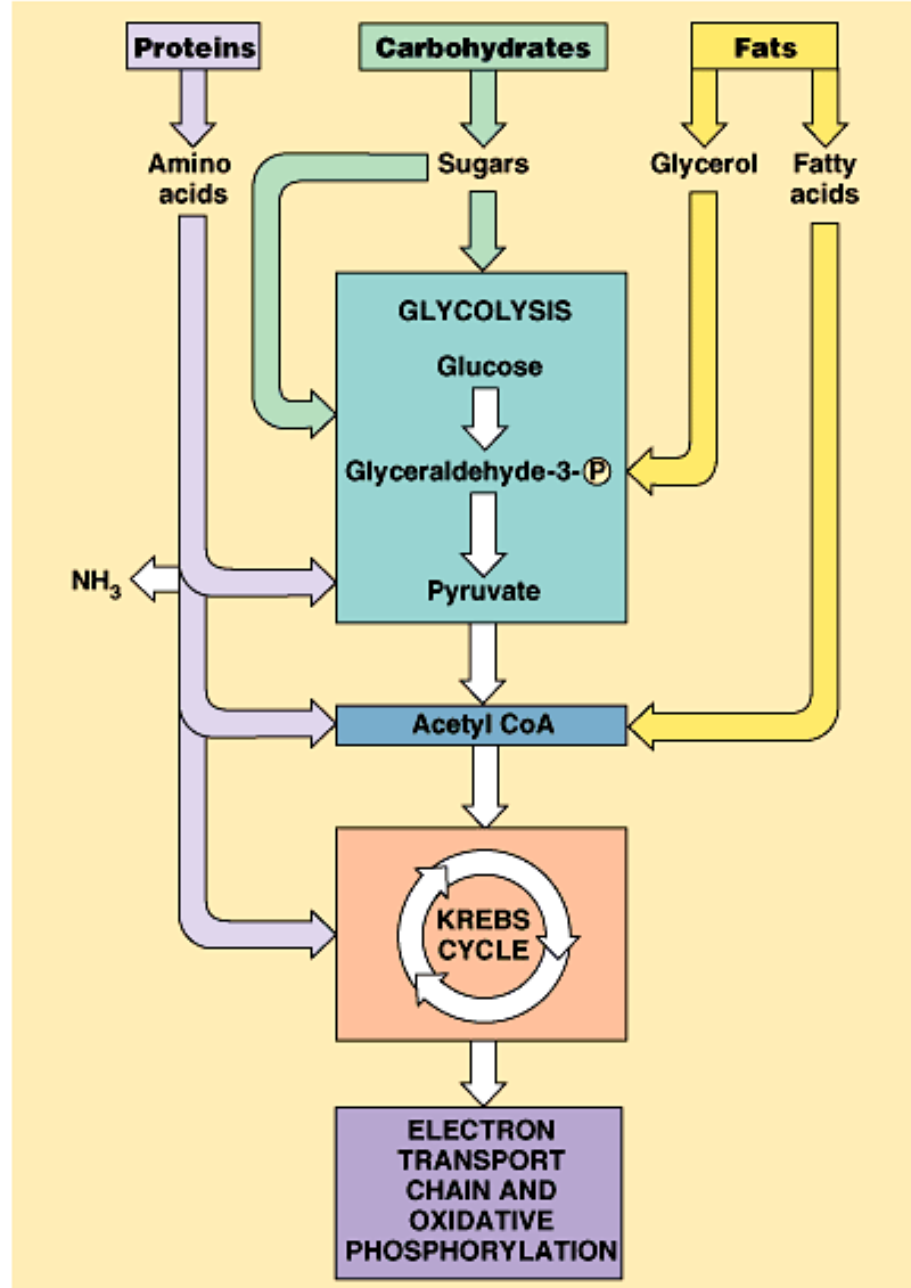
Review: How each molecule of glucose yields many ATP molecules during cellular respiration



I. Metabolic Pathways

- Catabolic pathways feed into the respiratory pathways.
- Polysaccharides are broken down into glucose, which enters glycolysis.
- Glycerol from fats also enters glycolysis, and acetyl CoA from fatty acid degradation enters the citric acid cycle.
- Proteins enter glycolysis and the citric acid cycle via amino acids.

The catabolism of various food molecules



I. Metabolic Pathways

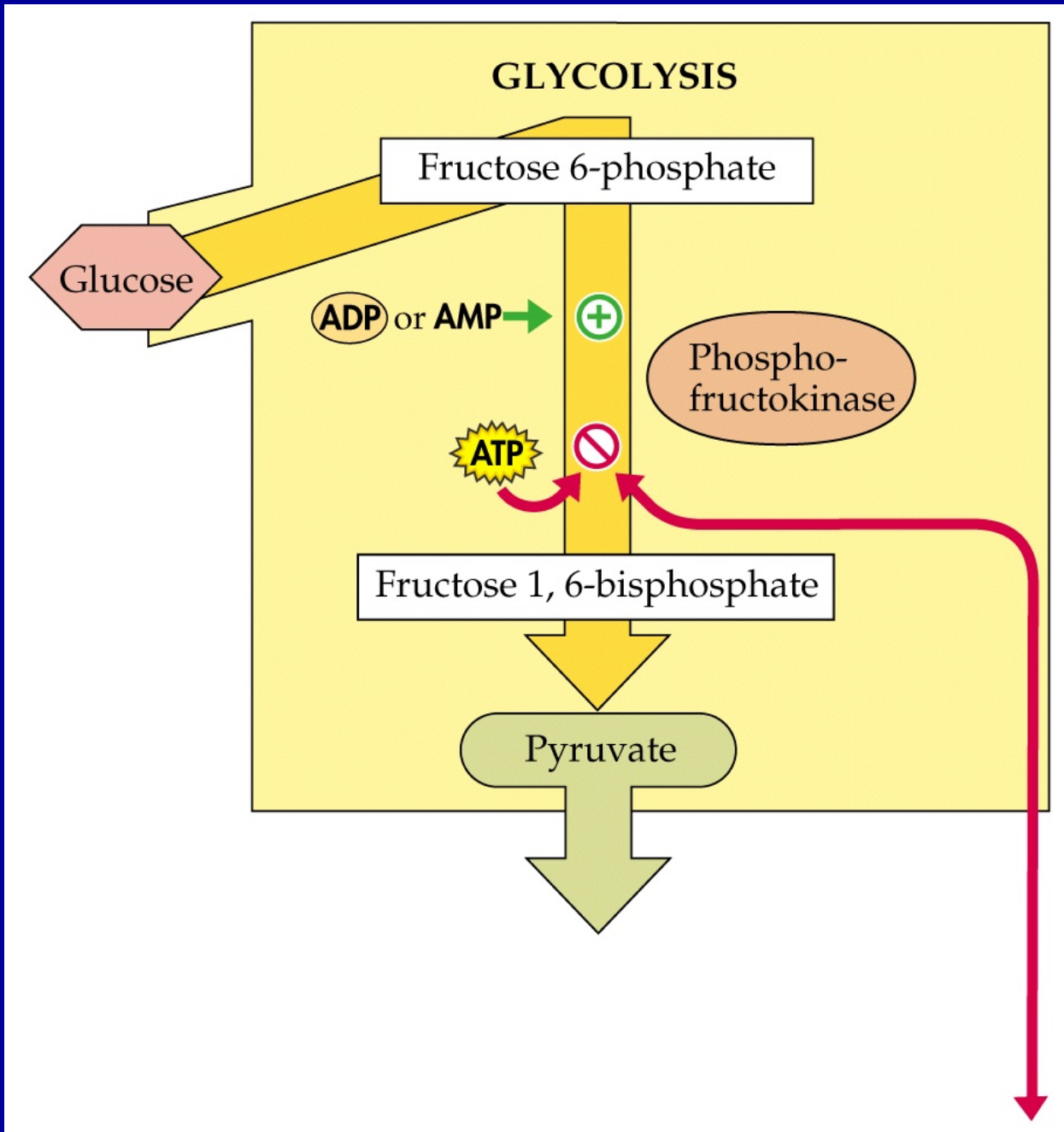
- Anabolic pathways use intermediate components of respiratory metabolism to synthesize fats, amino acids, and other essential building blocks for cellular structure and function.

J. Regulating Energy Pathways

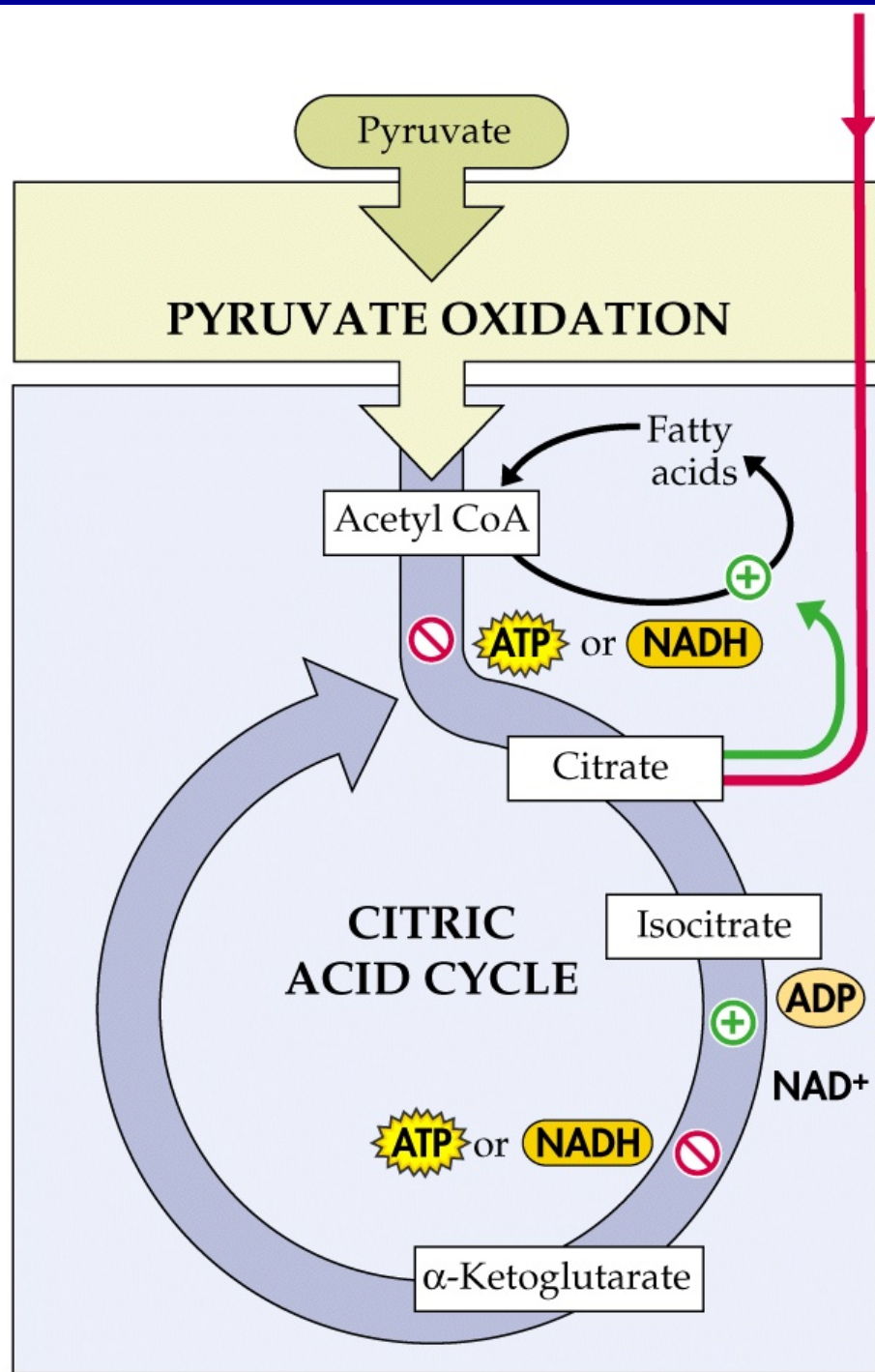
- The rates of glycolysis and the citric acid cycle are increased or decreased by the actions of ATP, ADP, NAD^+ , or $\text{NADH} + \text{H}^+$ on allosteric enzymes.
- Evolution has led to metabolic efficiency.

J. Regulating Energy Pathways

- Inhibition of the glycolytic enzyme phosphofructokinase by abundant ATP from oxidative phosphorylation slows glycolysis. ADP activates this enzyme, speeding up glycolysis.
- The citric acid cycle enzyme isocitrate dehydrogenase is inhibited by ATP and NADH and activated by ADP and NAD⁺.
- Citrate also inhibits PFK.



Citrate



Isocitrate DH