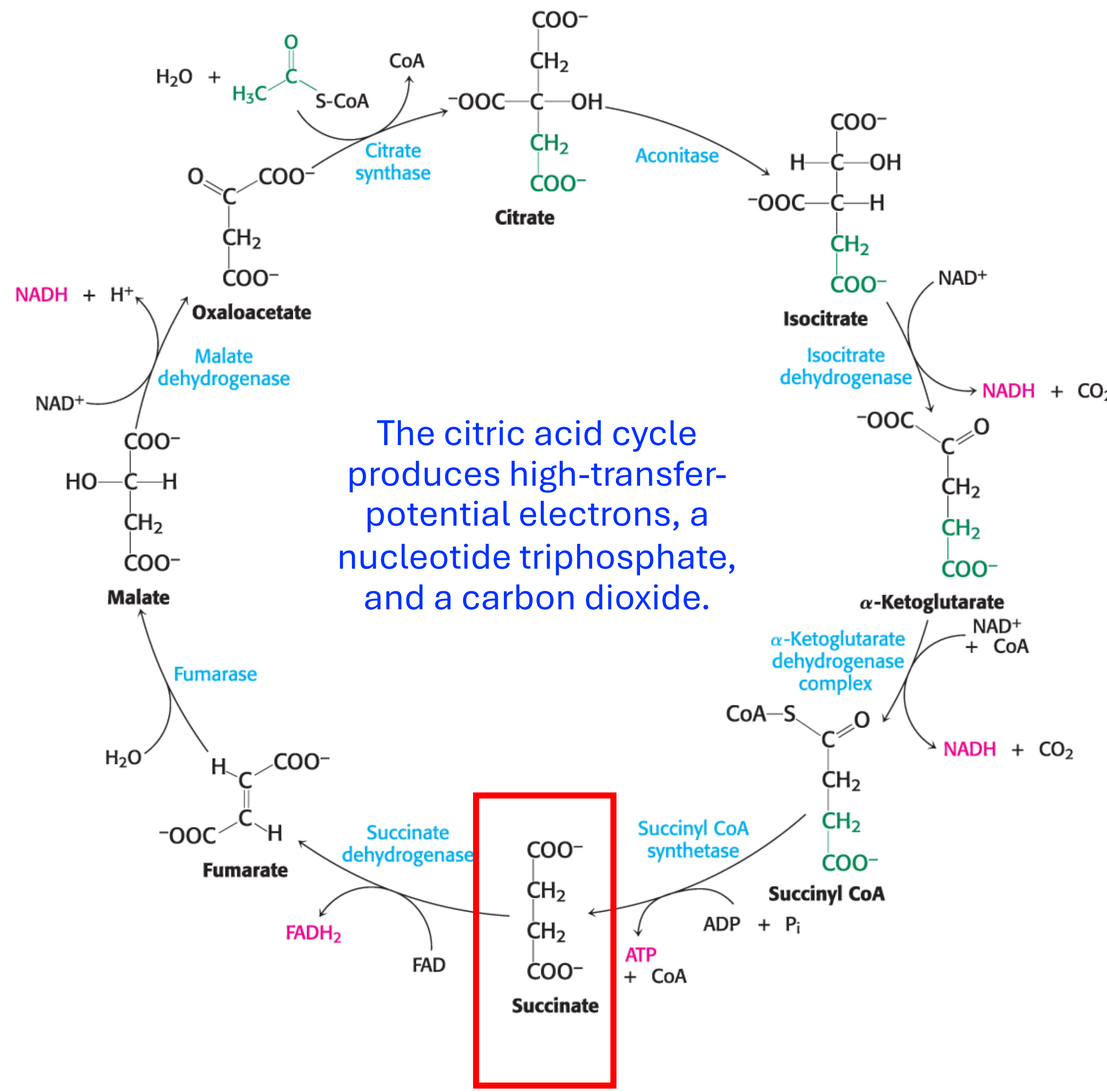
The Citric Acid Cycle

- All enzymes of the citric acid cycle form a supramolecular complex (physically associated structure).
- This close enzyme arrangement increases efficiency of the cycle.
- **Substrate channeling** : reaction products move directly between active sites via connecting channels.
- TCA demonstrates that enzymes organized into supramolecular structures for functional advantage.

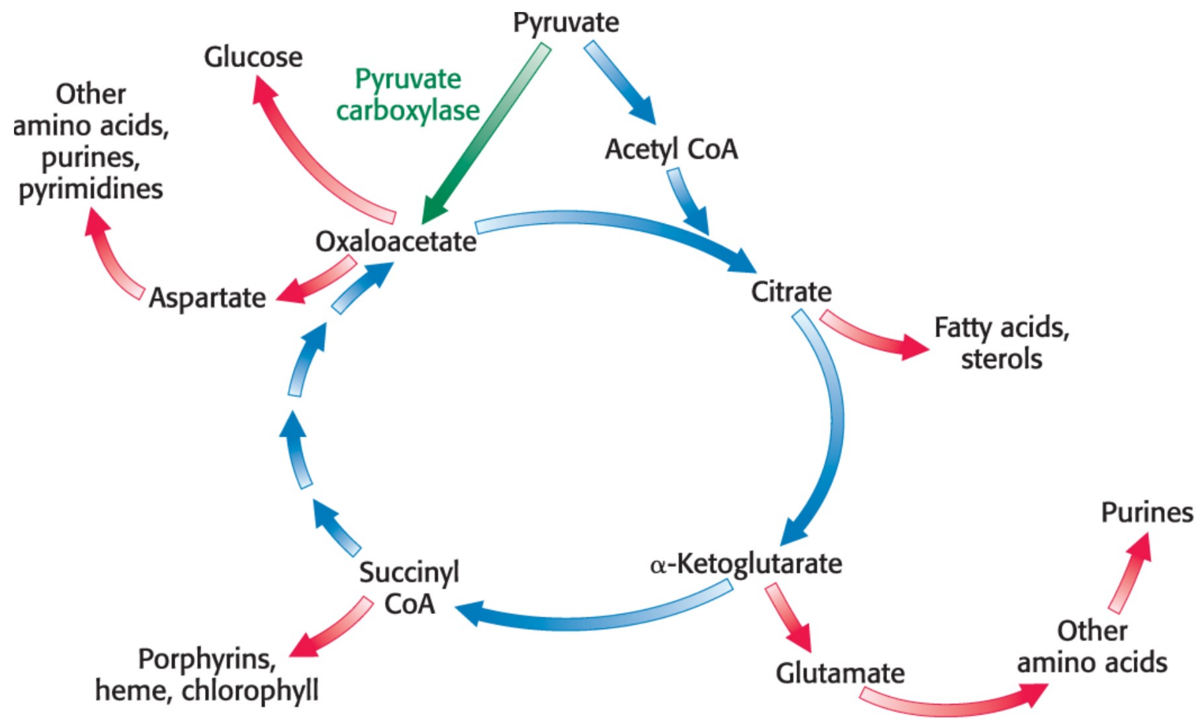


$$\text{Acetyl CoA} + 3\ \text{NAD}^+ + \text{FAD} + \text{ADP} + \text{P}_i + 2\ \text{H}_2\text{O} \rightarrow$$

$$2\ \text{CO}_2 + 3\ \text{NADH} + \text{FADH}_2 + \text{ATP} + 2\ \text{H}^+ + \text{CoA}$$

The Citric Acid Cycle Is a Source of Biosynthetic Precursors

- **The citric acid cycle must be capable of being rapidly replenished.**
- Because the citric acid cycle provides precursors for biosynthesis, reactions to replenish the cycle components are required if the energy status of the cells changes.
- These replenishing reactions are called anaplerotic reactions.
- A prominent anapleurotic reaction is catalyzed by pyruvate carboxylase. Recall that this reaction is also used in gluconeogenesis and is dependent on the presence of acetyl CoA.



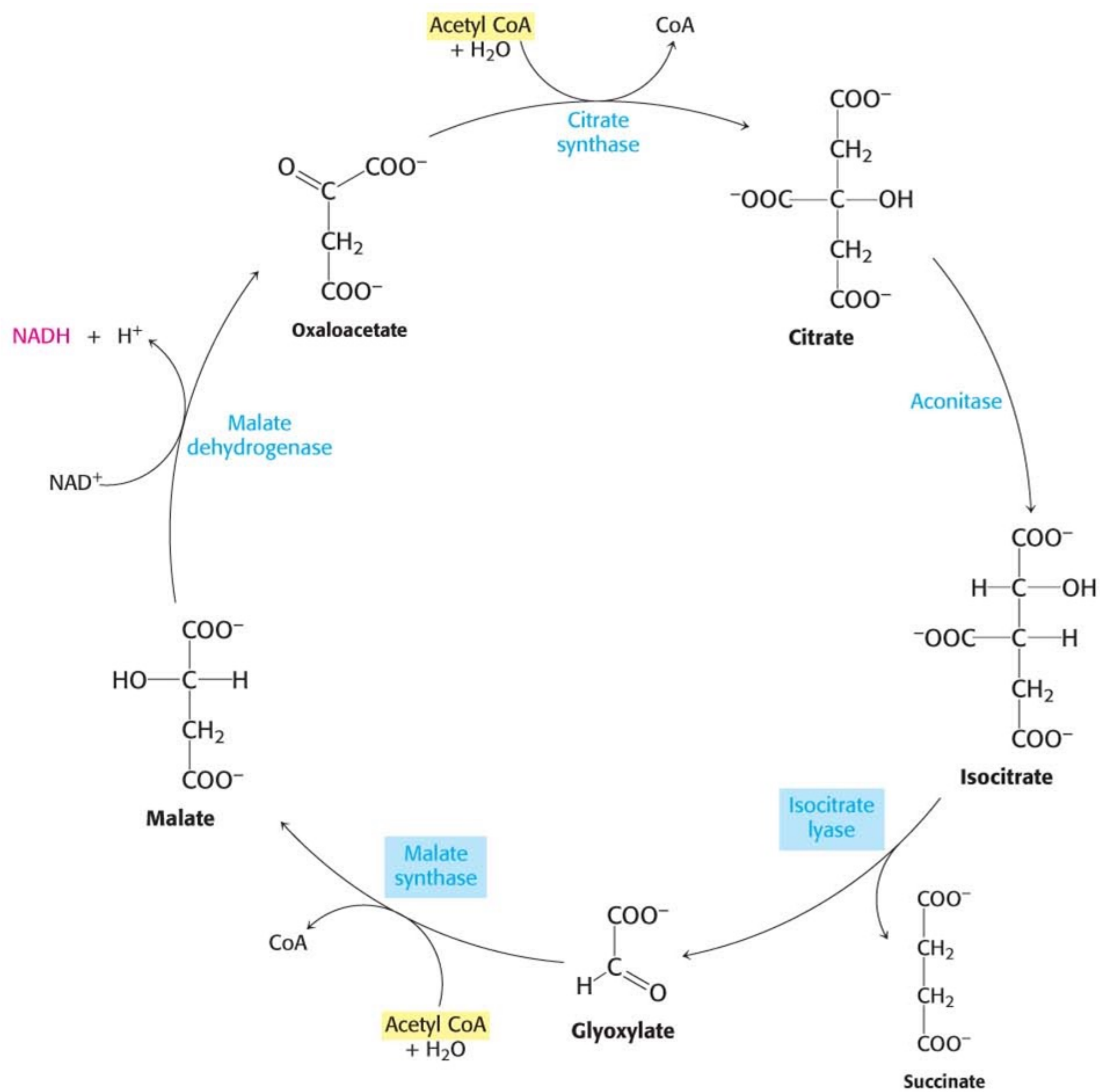
The Metabolic Hub of the Cell

The Glyoxylate Cycle Enables Plants and Bacteria to Convert Fats into Carbohydrates

- The glyoxylate cycle is similar to the citric acid cycle but bypasses the two decarboxylation steps, allowing the synthesis of carbohydrates from fats.

- Succinate can be converted into oxaloacetate and then into glucose.

- The glyoxylate cycle is prominent in oil-rich seeds such as sunflower seeds.



Quick Quiz 5

The sum reaction of the glyoxylate pathway shows that carbon enters the cycle from _________ and leaves as ________________.

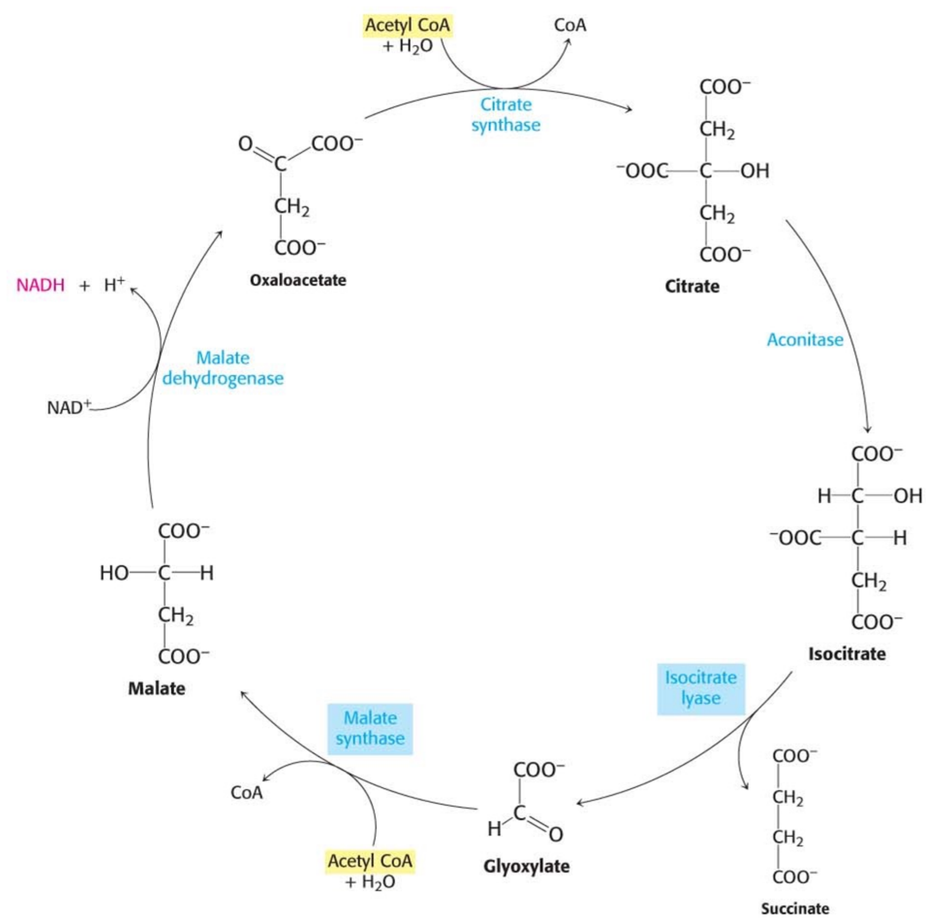
A. acetyl CoA; succinate

B. acetyl CoA; CO_2

C. acetyl CoA; isocitrate

D. succinate; acetyl CoA

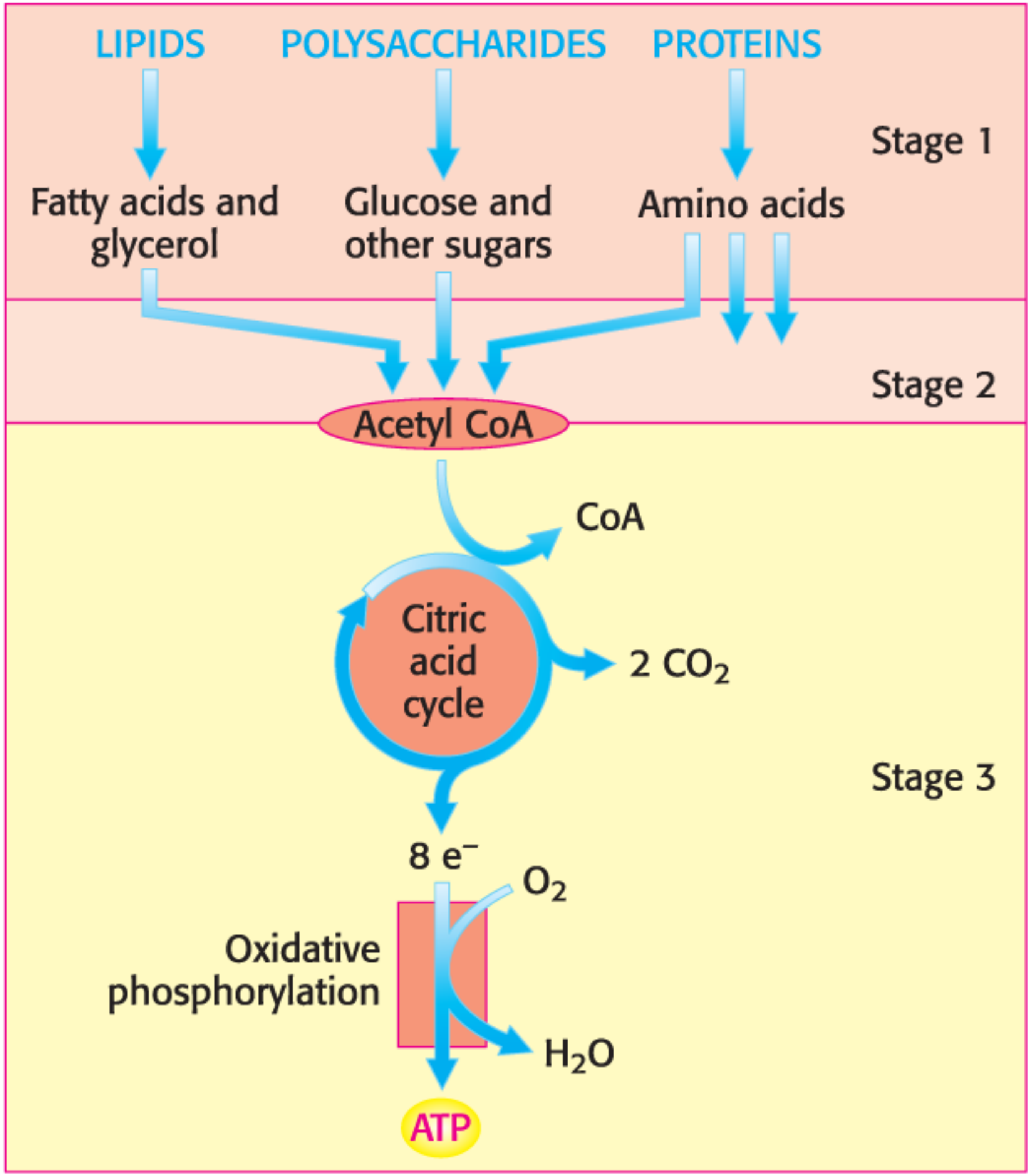
E. oxaloacetate; citrate.

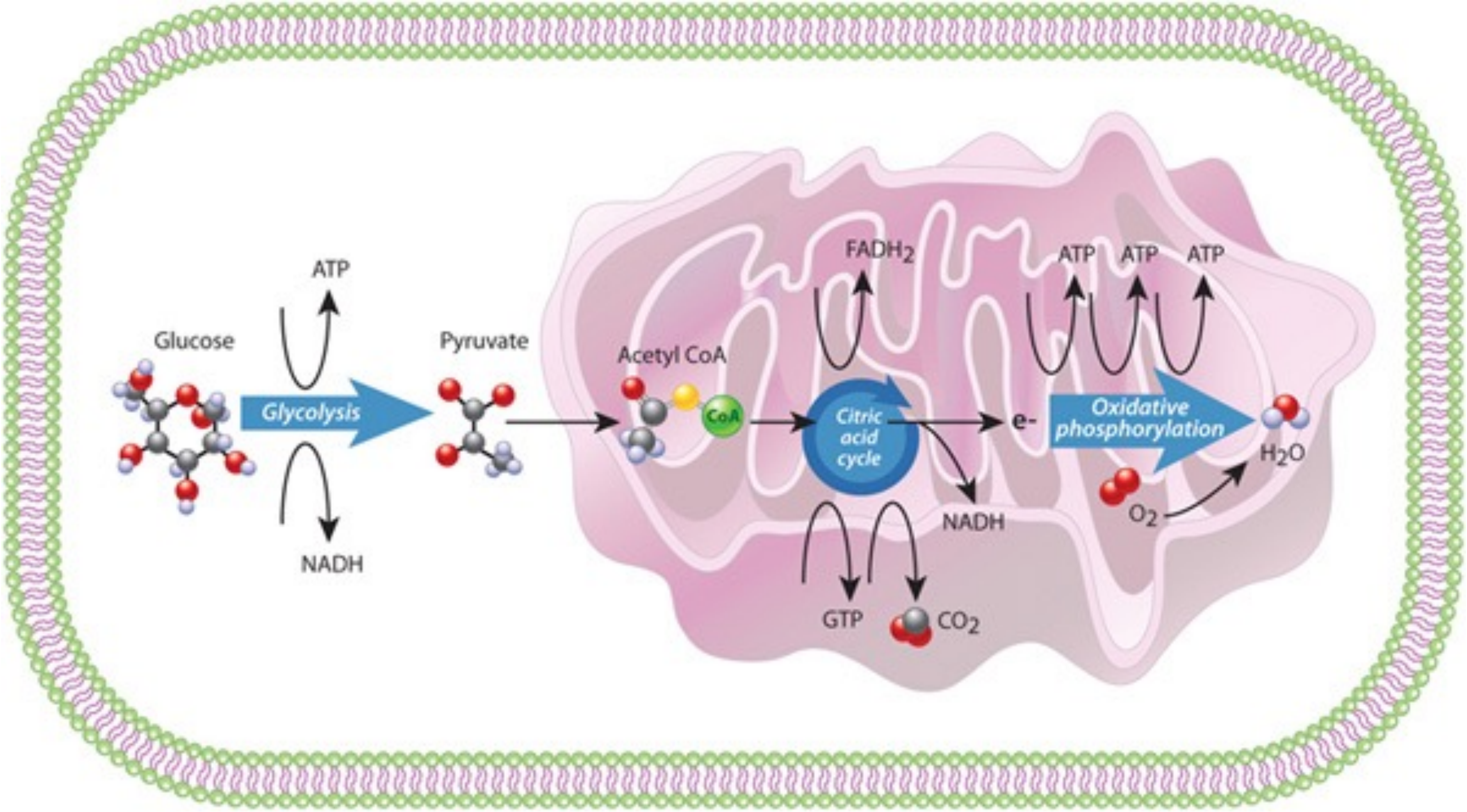


Answer:

A

Stages of Catabolism

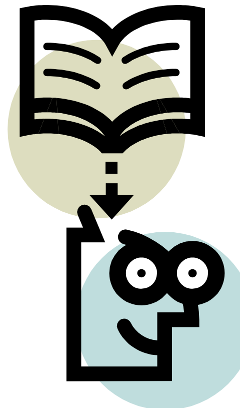




Lecture 11

Oxidative Phosphorylation

Oxidative Phosphorylation



Lecture Outline:

- Oxidative Phosphorylation in Eukaryotes Takes Place in Mitochondria
- Oxidative Phosphorylation Depends on Electron Transfer
- The Respiratory Chain Consists of Proton Pumps and a Physical Link to the Citric Acid Cycle
- Shuttles Allow Movement Across Mitochondrial Membranes
- Cellular Respiration is Regulated by the Need for ATP

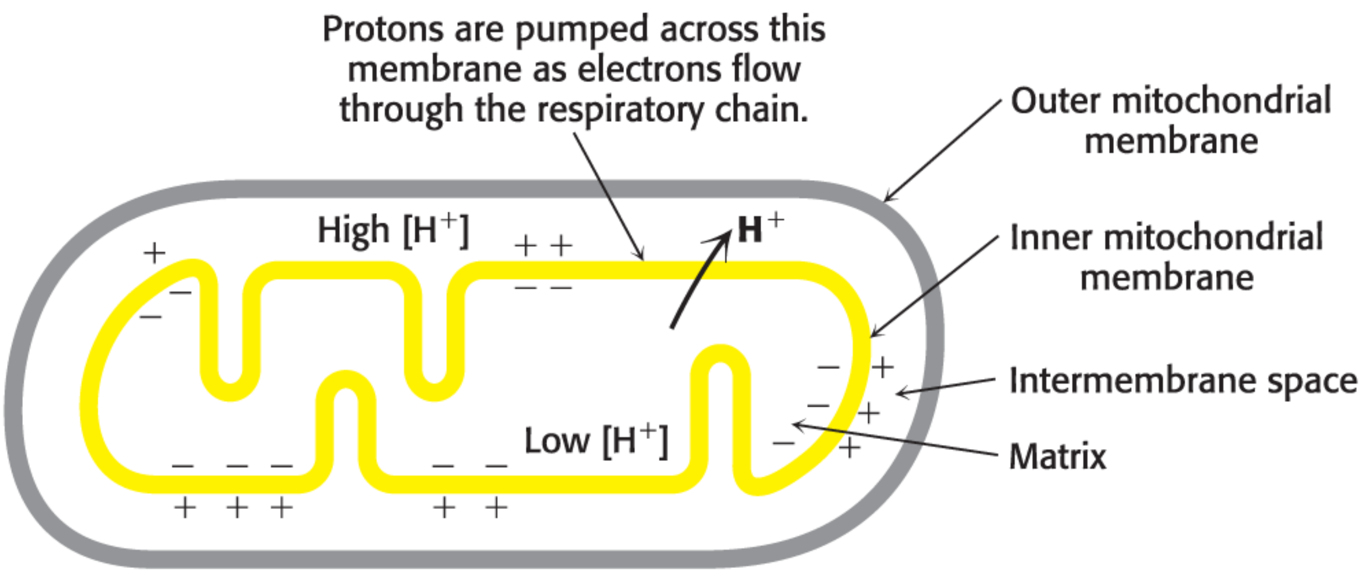
Readings:

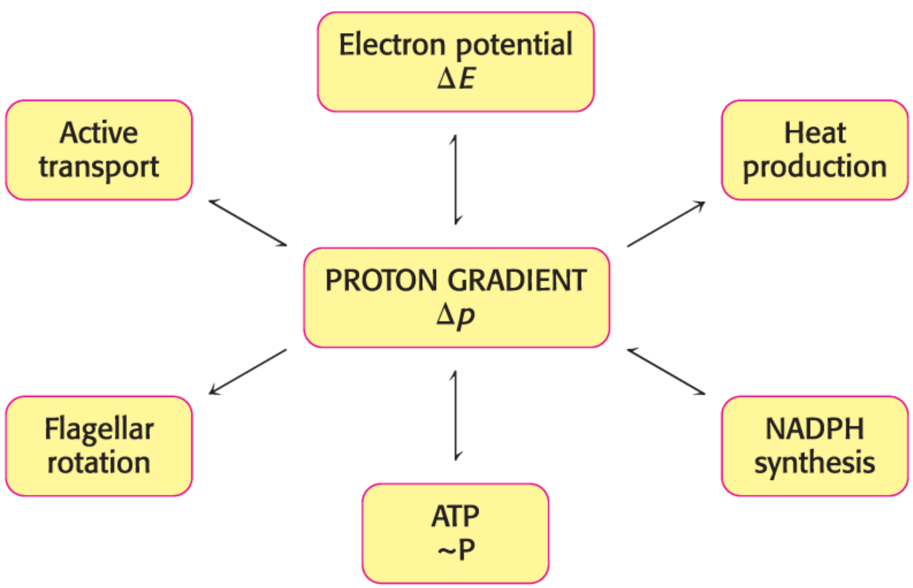
Tymochko, Berg, Stryer, Biochemistry, 2nd Edition, Ch. 20, 21, pp. 349 – 385

3rd E 3

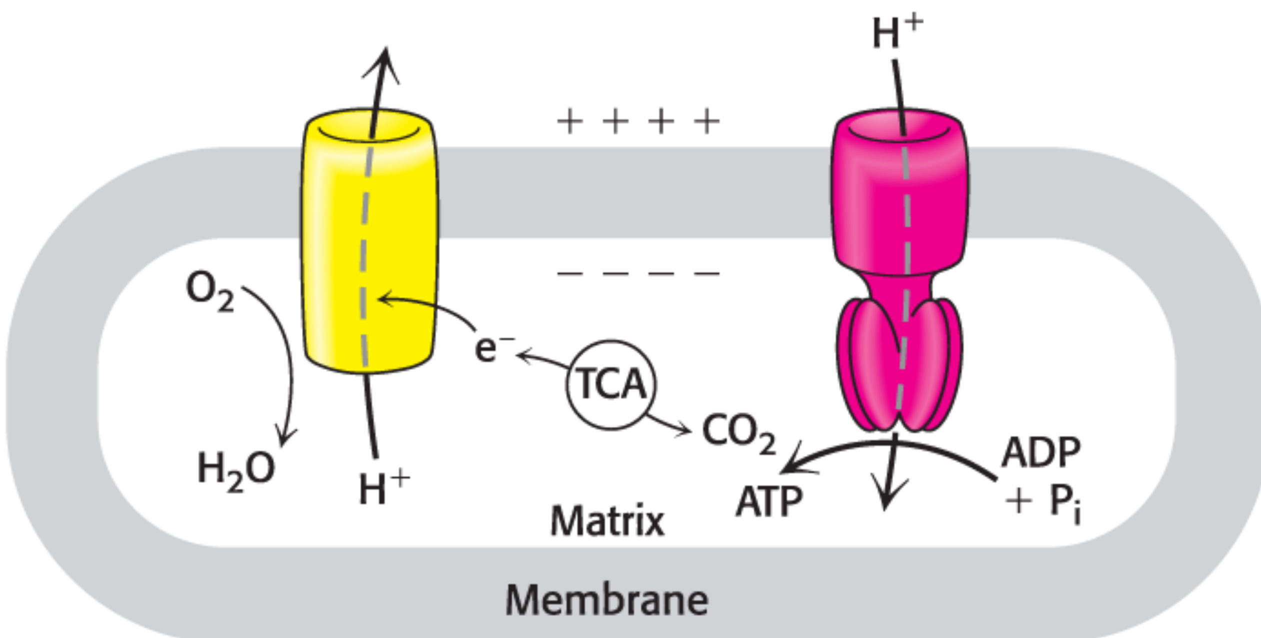
4 -437

The Cell's Microscopic Power Plant



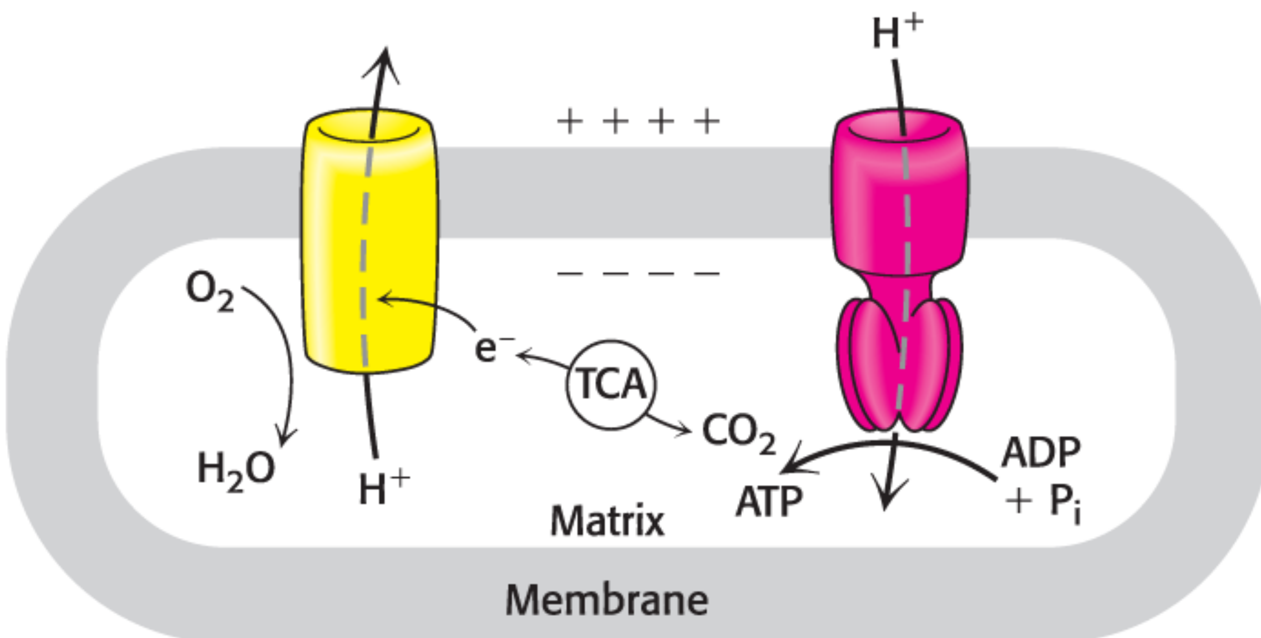


Powering the Cell One Electron at a Time



- Oxidative phosphorylation captures the energy of high-energy electrons to synthesize ATP.
- The flow of electrons from NADH and $FADH_2$ to O_2 occurs in the electron-transport chain or respiratory chain.
- This exergonic set of oxidation-reduction reactions generates a proton gradient.
- The proton gradient is used to power the synthesis of ATP.
- Collectively, the citric acid cycle and oxidative phosphorylation are called **cellular respiration** or simply **respiration**.

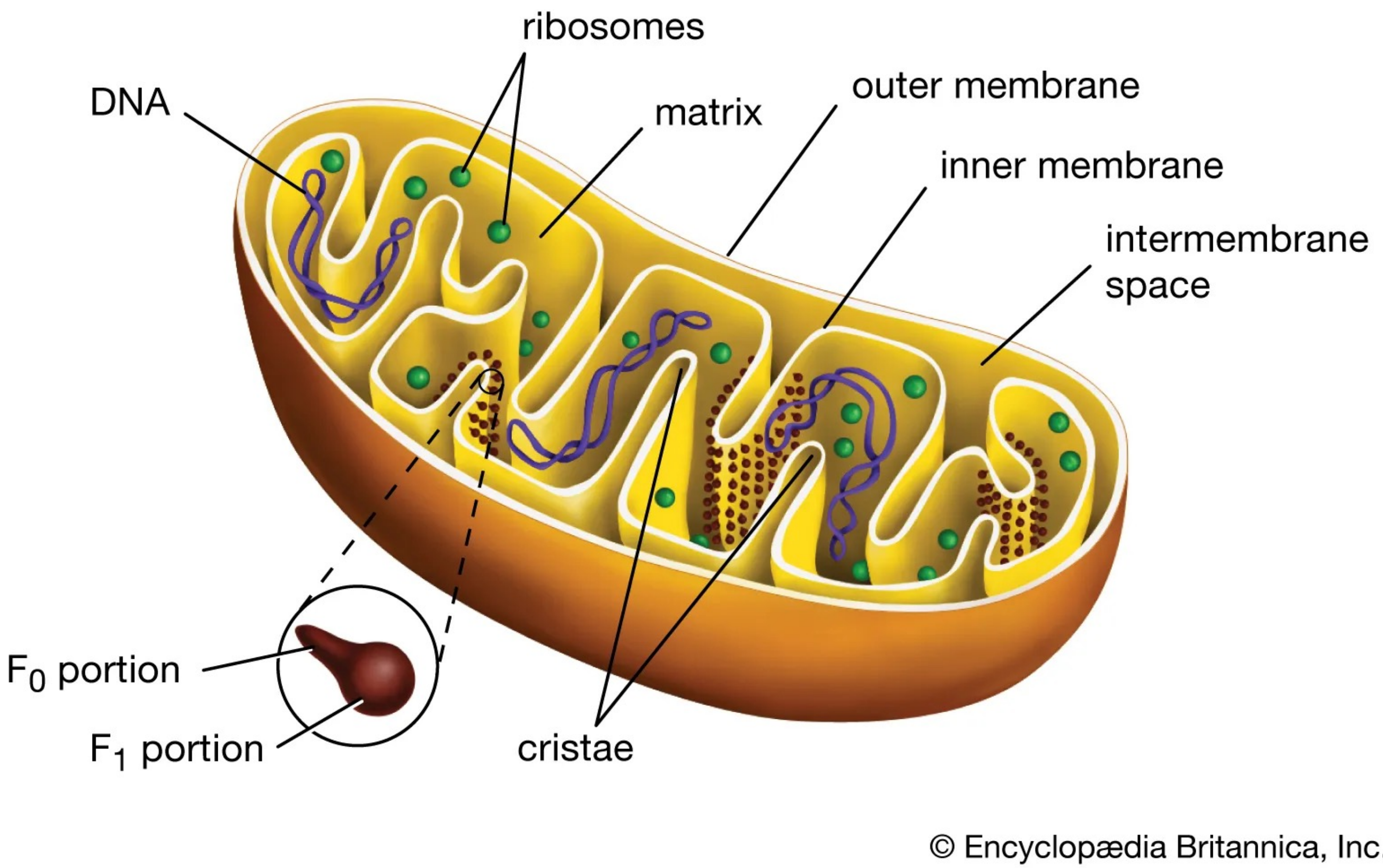
Powering the Cell One Electron at a Time



Where do electrons come from?

- NADH and FADH2 carry high-energy electrons.
- These are produced in:
  - Glycolysis
  - Pyruvate oxidation
  - Citric acid cycle

The Cell's Microscopic Power Plant



- The electron-transport chain and ATP synthesis occur in the mitochondria.
- Recall that the citric acid cycle occurs in the mitochondrial matrix.
- Sequence data suggest that all mitochondria are descendants of an ancestor of *Rickettsia prowazekii*, which was engulfed by another cell.

Oxidative Phosphorylation Depends on Electron Transfer

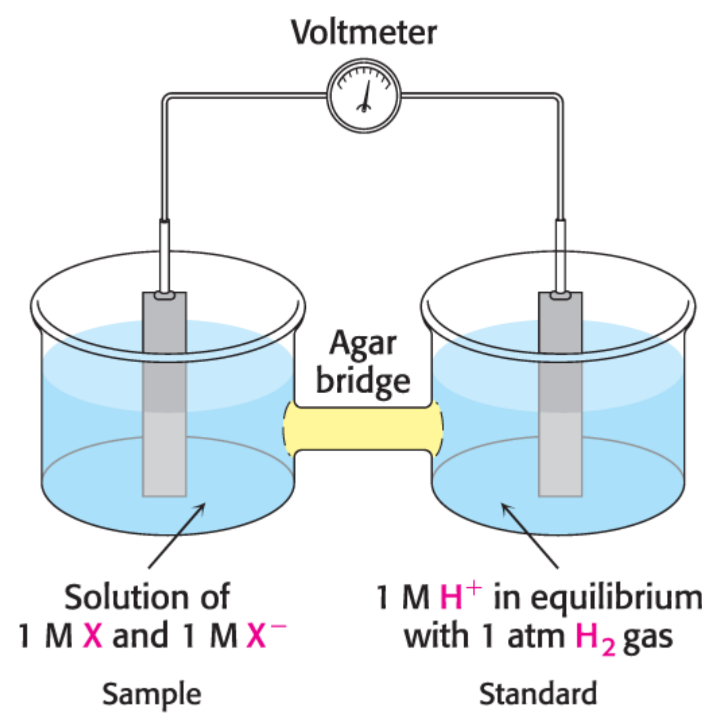
- The electron-transport chain is a series of coupled redox reactions that transfer electrons from NADH and $FADH_2$ to oxygen.
- The reduction potential E_0', or redox potential, is a measure of a molecule's tendency to donate or accept electrons.
- A strong reducing agent readily donates electrons and has a negative E_0'.
- A strong oxidizing agent readily accepts electrons and has a positive E_0'.
- The standard free-energy change is related to the change in reduction potential.

$$\Delta G^{\circ\,\prime} = -nF\Delta E_0'$$

where n is the number of electrons transferred and F is the Faraday constant

($96.48\ \mathrm{kJ\ mol^{-1}\ V^{-1}}$, or $23.06\ \mathrm{kcal\ mol^{-1} V^{-1}}$)

- [Cellular Respiration (Electron Transport Chain)]



Oxidative Phosphorylation Depends on Electron Transfer

Electron flow through the electron-transport chain creates a proton gradient.

➢ Energy is released when high-energy electrons are transferred to oxygen:

$$\frac{1}{2}\,O_2 + 2\,H^+ + 2\,e^- \rightarrow H_2O \quad E_0' = +0.82\ V$$

$$NAD^+ + H^+ + 2\,e^- \rightarrow NADH \quad E_0' = -0.32\ V$$

$$\frac{1}{2}\,O_2 + NADH + H^+ \rightarrow H_2O + NAD^+ \quad \Delta E_0' = 1.14\ V$$

$$\Delta G^{\circ\prime} = -nF\Delta E_0'$$

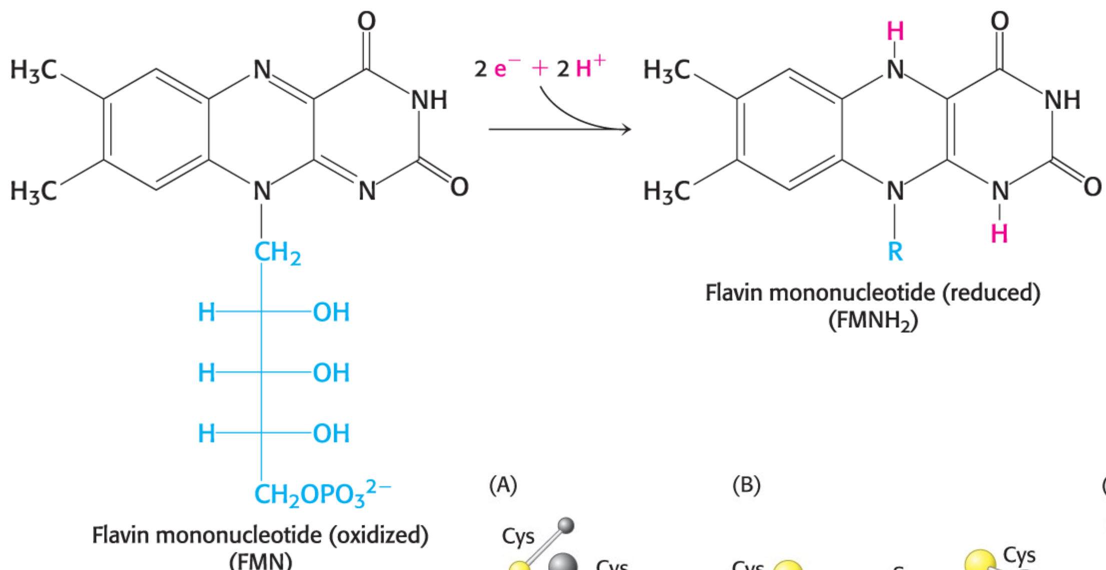
$$\begin{aligned}\Delta G^{\circ\prime} &= (-2 \times 96.48\ \text{kJ mol}^{-1}\,\text{V}^{-1} \times 0.82\ \text{V}) + (-2 \times 96.48\ \text{kJ mol}^{-1}\,\text{V}^{-1} \times 0.32\ \text{V}) \\ &= -158.2\ \text{kJ mol}^{-1} + (-61.7\ \text{kJ mol}^{-1}) \\ &= -220\ \text{kJ mol}^{-1}\end{aligned}$$

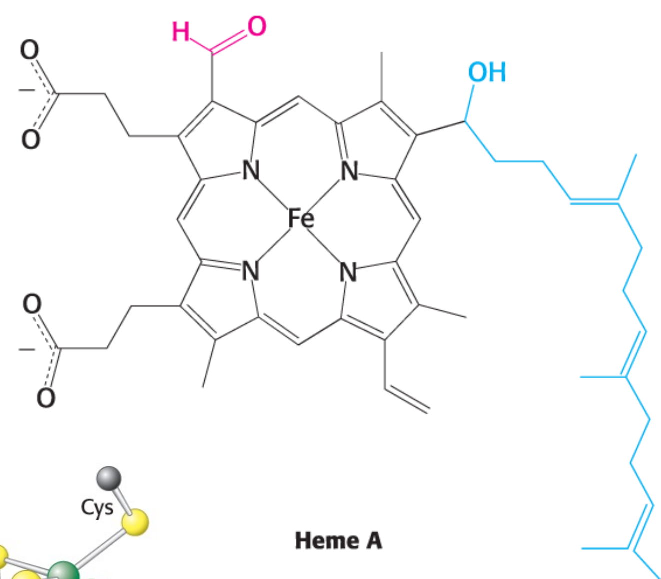
➢ **The energy is used to establish a proton gradient!**

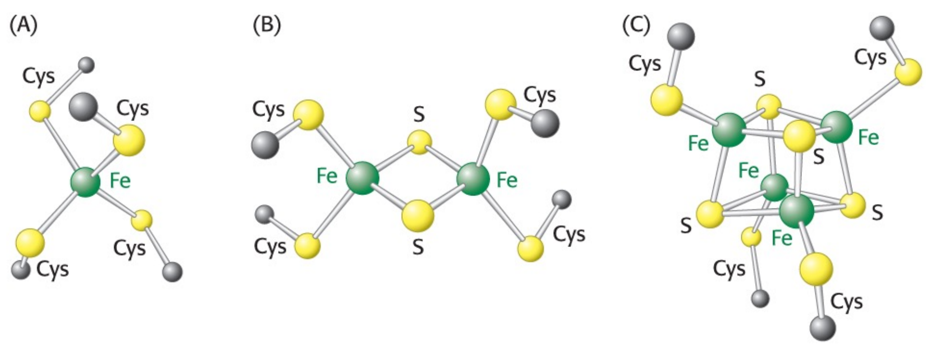
Oxidative Phosphorylation Depends on Electron Transfer

The electron-transport chain is a series of coupled oxidation-reduction reactions.

- The electron-transport chain is composed of four large protein complexes.
- The electrons donated by NADH and $FADH_2$ are passed to electron carriers in the protein complexes.
- The carriers include flavin mononucleotide (FMN), iron associated with sulfur in proteins (iron-sulfur proteins), iron incorporated into hemes that are embedded in proteins called cytochromes, and a mobile electron carrier called coenzyme Q (Q).

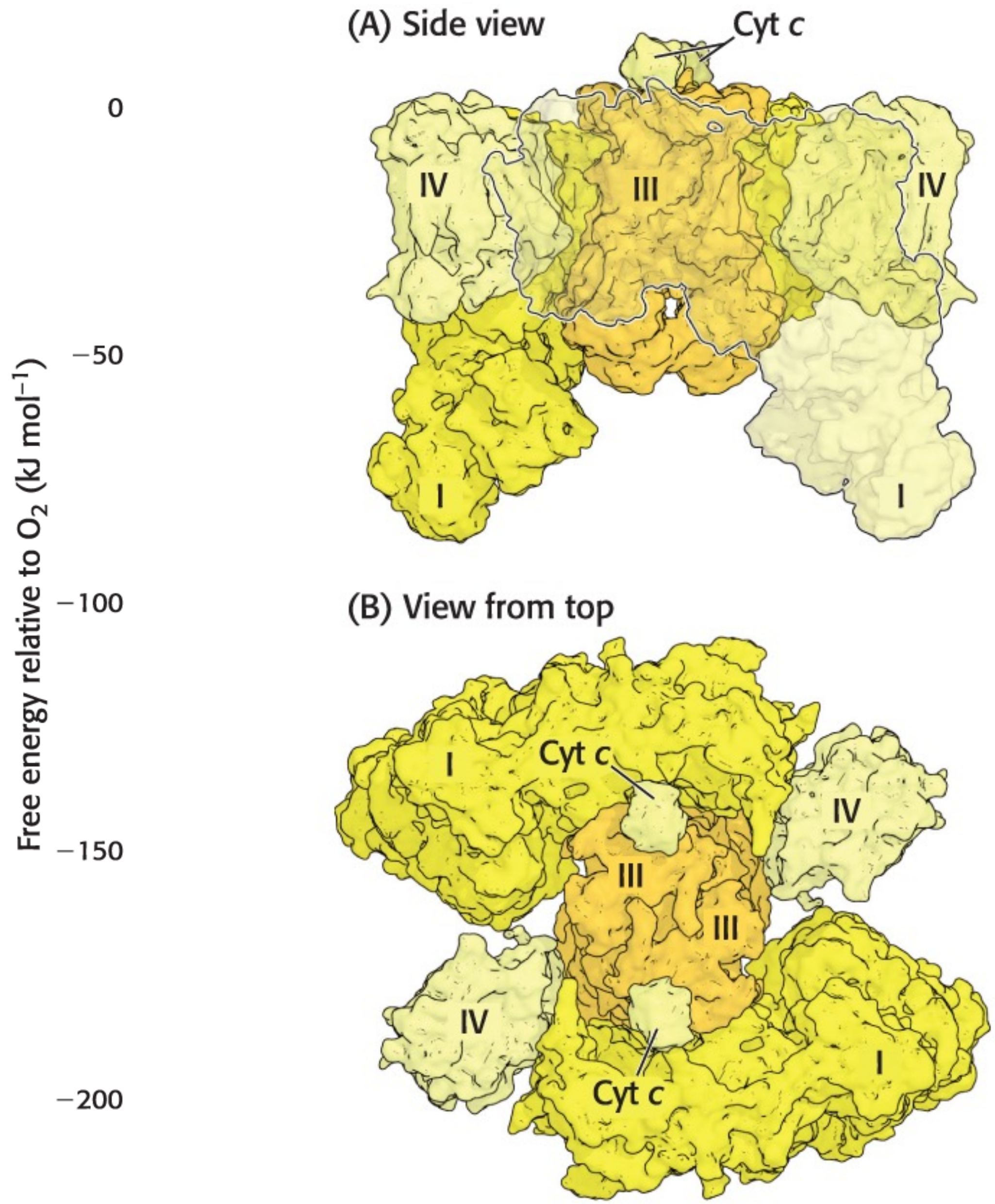






Components of the Electron-Transport Chain (ETC)

- ➢ Electrons flow down an energy gradient from NADH to O_2.
- ➢ The flow is catalyzed by four protein complexes.
- ➢ Iron is a component of all of the complexes as well as ***Q.***

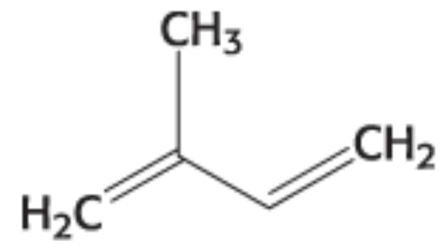


Why bother?

- ➢ "Without the electron transport chain, you wouldn't last more than a few minutes."
- ➢ The ETC is essential for aerobic life.
- ➢ This is where most of your ATP comes from!

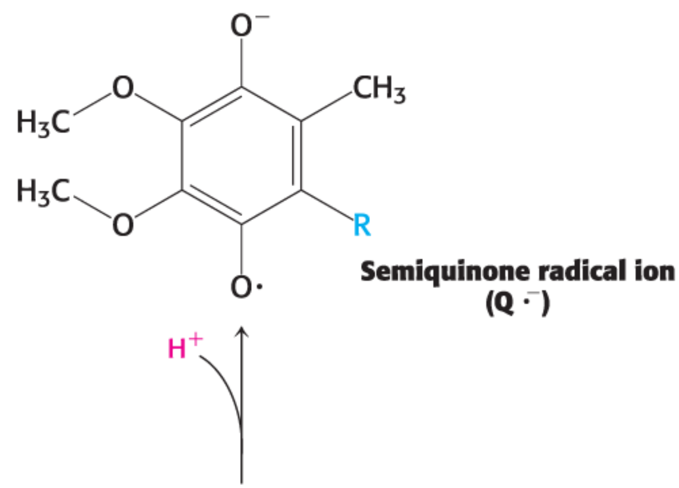
Oxidative Phosphorylation Depends on Electron Transfer

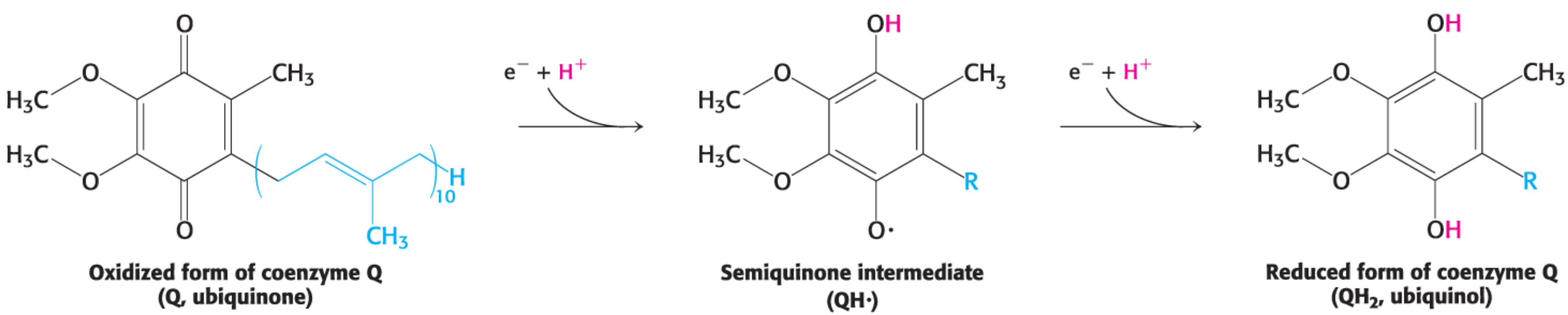
- Coenzyme Q is derived from isoprene.
- Coenzyme Q binds protons (QH_2) as well as electrons, and can exist in several oxidation states.
- Oxidized and reduced Q are present in the inner mitochondrial membrane in what is called the Q pool.



Isoprene

For quinones ➝ electron transfer happens together with proton binding or release ➝ combined action is important for moving protons across membranes





Quick Quiz 2

Consider a substance that can exist in an oxidized form X and a reduced form X–. Such a pair is called ____________.

A. a redox couple
B. a reduction couple
C. an X:X– couple
D. a half-cell
E. an electron-transfer potential

The Respiratory Chain Consists of Proton Pumps and a Physical Link to the Citric Acid Cycle

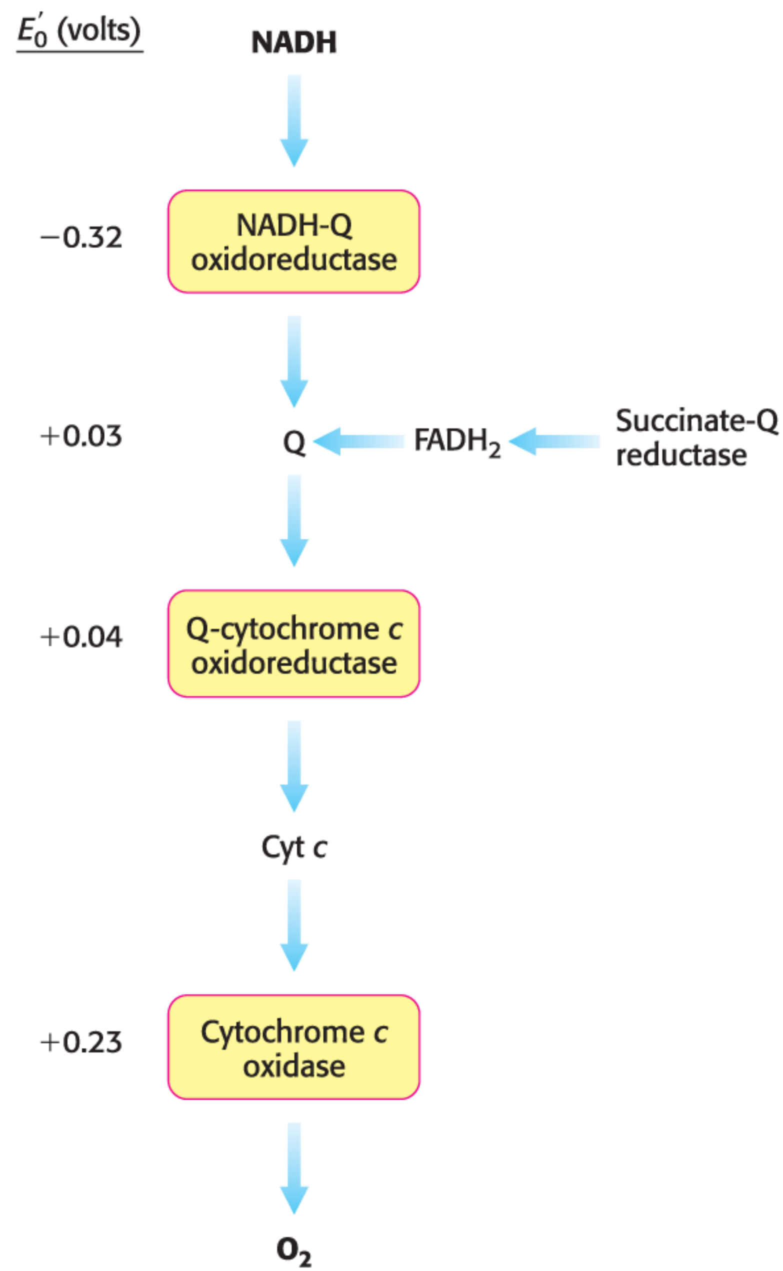
- Electrons flow from NADH to O_2 through three large protein complexes embedded in the inner mitochondria membrane.
- These complexes pump protons out of the mitochondria, generating a proton gradient.
- The complexes are:

NADH-Q oxidoreductase (Complex I)

Q-cytochrome c oxidoreductase (Complex III)

Cytochrome c oxidase (Complex IV)

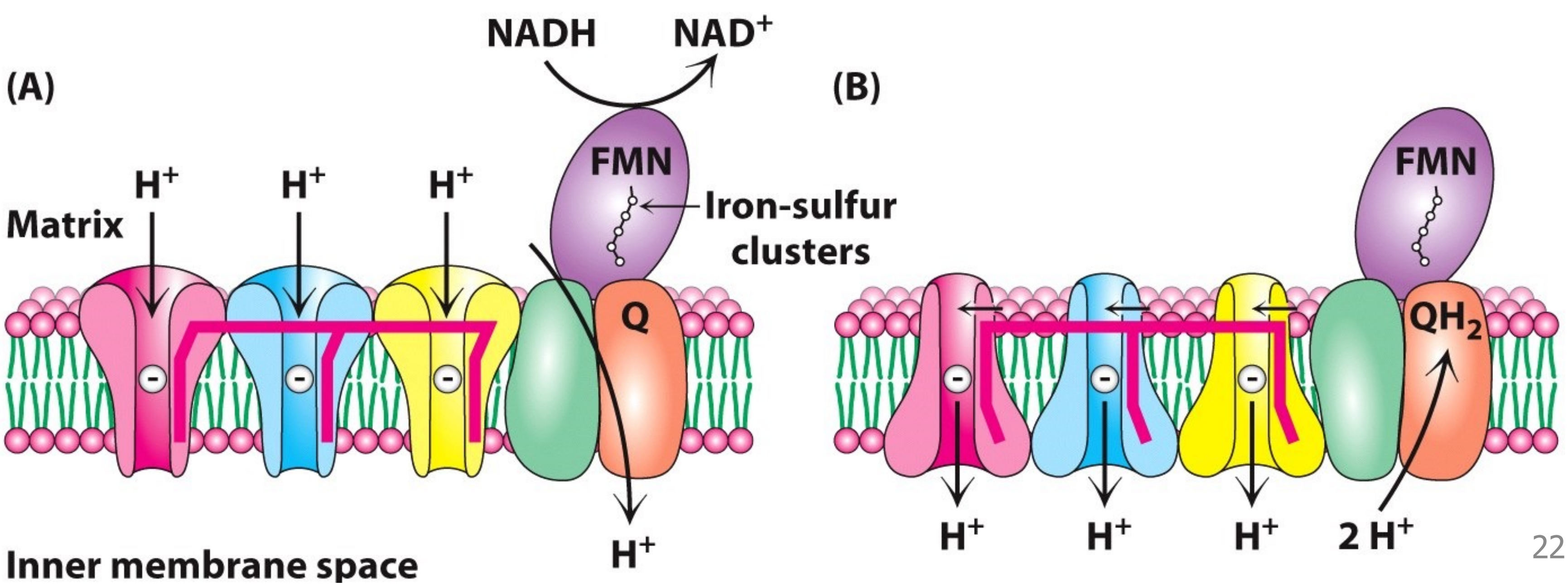
- An additional complex, **succinate Q-reductase (Complex II)**, delivers electrons from $FADH_2$ to Complex III.
- Succinate-Q reductase is not a proton pump.



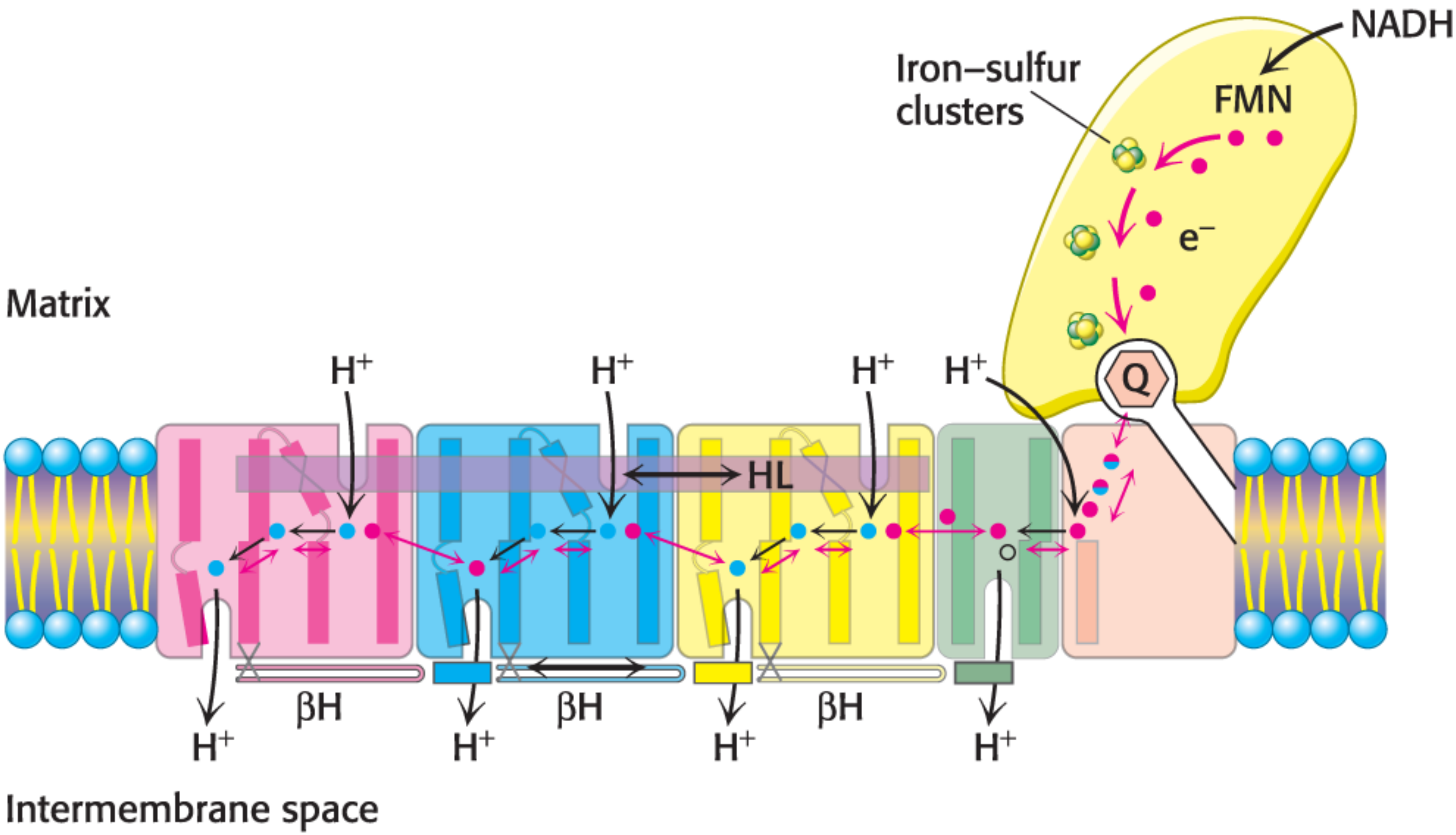
The Respiratory Chain Consists of Proton Pumps and a Physical Link to the Citric Acid Cycle

- Electron flow within the complexes in the inner-mitochondrial membrane generate a proton gradient.
- These complexes appear to be associated with one another in what is called the ***respirasome***.
- The electrons from NADH are passed along to Q to form QH_2 by Complex I. QH_2 leaves the enzyme for the Q pool in the hydrophobic interior of the inner-mitochondrial membrane.
- Four protons are simultaneously pumped out of the mitochondria by Complex I.

$$\mathrm{NADH} + \mathrm{Q} + 5\,\mathrm{H}^+_{\text{matrix}} \longrightarrow \mathrm{NAD}^+ + \mathrm{QH}_2 + 4\,\mathrm{H}^+_{\text{inner membrane space}}$$



Coupled electron-proton transfer reactions through NADH-Q



The Electron Transport Chain