

Chemiosmotic Theory

Peter Mitchell (1961) | Nobel Prize in Chemistry, 1978 | 5-Mark Answer

Statement: ATP synthesis in mitochondria (and chloroplasts) is driven by an electrochemical proton (H^+) gradient across a membrane, generated by the electron transport chain. The energy stored in this gradient — the **proton-motive force** — is used by ATP synthase to phosphorylate ADP to ATP.

Chemiosmotic Theory — Coupling of Electron Transport to ATP Synthesis

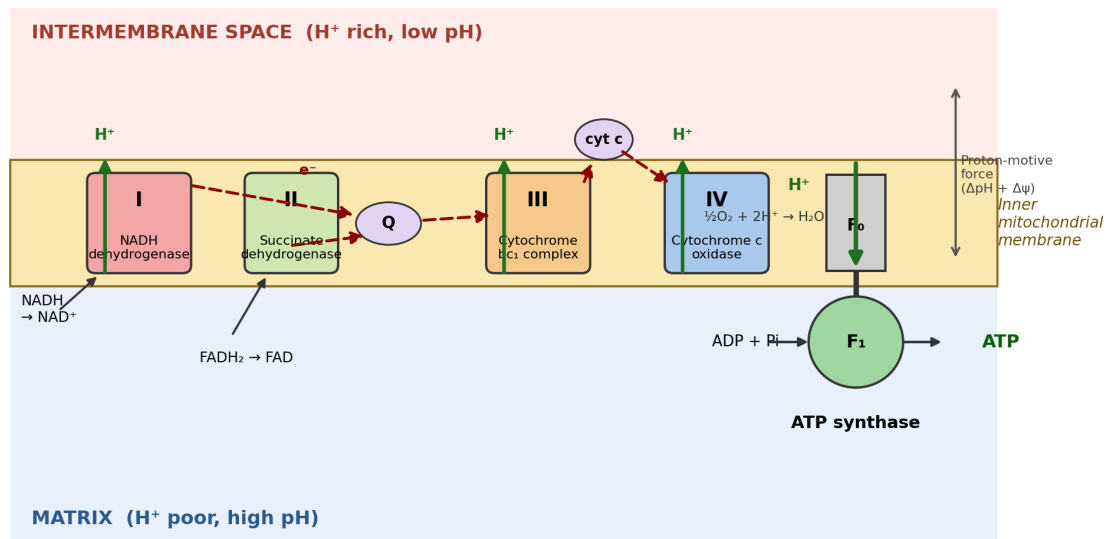


Fig: Chemiosmotic coupling across the inner mitochondrial membrane

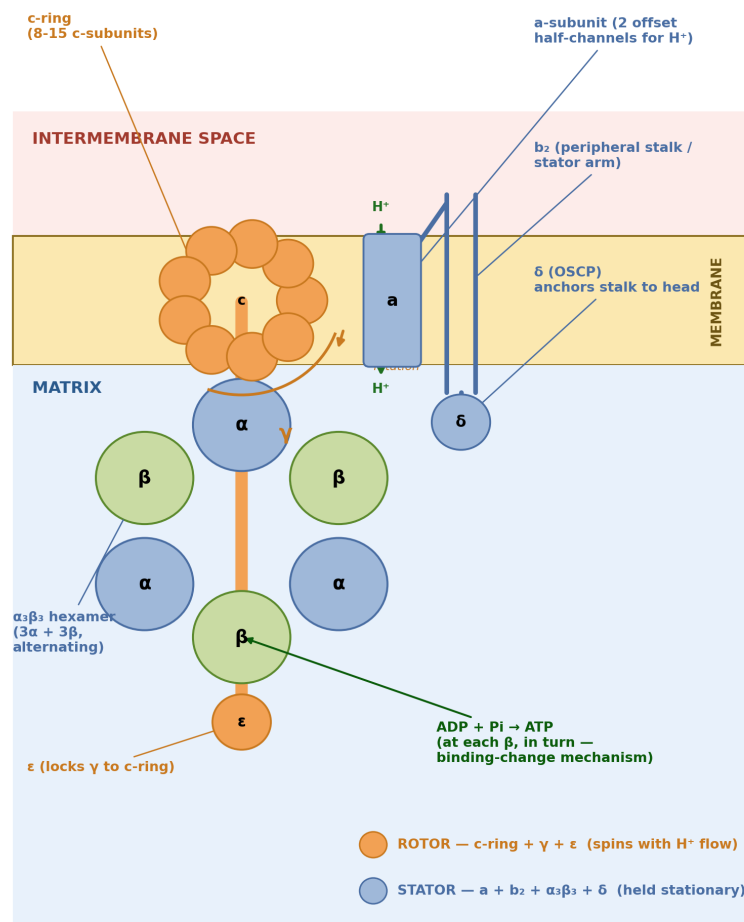
Mechanism — Key Points

- **1. Electron transport chain (ETC):** NADH and $FADH_2$, produced in glycolysis, the link reaction and the Krebs cycle, donate electrons to Complex I / Complex II. Electrons pass sequentially through Complex I $\rightarrow$ ubiquinone (Q) $\rightarrow$ Complex III $\rightarrow$ cytochrome c $\rightarrow$ Complex IV, finally reducing O_2 to H_2O .
- **2. Proton pumping:** The energy released as electrons move through Complexes I, III and IV is used to actively pump H^+ ions from the matrix into the intermembrane space, against their concentration gradient.
- **3. Proton-motive force (PMF):** Pumping makes the intermembrane space H^+ -rich/acidic and the matrix H^+ -poor/alkaline. This electrochemical gradient (a pH difference plus a membrane potential) is the proton-motive force — a store of potential energy, analogous to water held behind a dam.
- **4. Chemiosmosis through ATP synthase:** The inner membrane is impermeable to H^+ except through the F_0 channel of ATP synthase. Protons flow back down their gradient into the matrix through F_0 , and this flow drives rotation of the F_1 head.
- **5. ATP synthesis (coupling):** Rotation of F_1 causes conformational changes in its catalytic sites that bind ADP + P_i and condense them into ATP. Because ATP synthesis is mechanically coupled to proton flow (not directly to electron transport), the process is called **chemiosmotic coupling**.

Significance: The chemiosmotic theory explains how the redox energy of respiratory electron carriers is converted into the chemical energy of ATP without any high-energy phosphorylated intermediate — resolving a major problem in bioenergetics and underpinning oxidative phosphorylation and photophosphorylation alike.

Structure of the F_0 - F_1 Particle (ATP Synthase)

The molecular motor that couples H^+ flow to ATP synthesis



F_0 — membrane sector (proton channel)

- **a-subunit:** single copy; provides two offset half-channels through which H^+ enters from the intermembrane space and exits into the matrix, without crossing the membrane fully.
- **b_2 -subunit:** two copies forming the peripheral stalk (“stator arm”) that clamps the a-subunit to the top of the F_1 head via subunit δ , holding the $\alpha_3\beta_3$ hexamer still while the rotor turns inside it.
- **c-ring:** 8–15 c-subunits arranged in a ring; each H^+ passing through the a-subunit half-channel binds a c-subunit and drives stepwise rotation of the entire ring.

F_1 — headpiece (catalytic sector, in the matrix)

- **$\alpha_3\beta_3$ hexamer:** 3 α (structural, non-catalytic) and 3 β (catalytic) subunits alternate around a central cavity; each β subunit binds ADP + Pi and condenses them to ATP as it is squeezed by the rotating γ shaft.
- **γ -subunit:** a long coiled-coil shaft fixed to the c-ring; it passes through the centre of the $\alpha_3\beta_3$ hexamer and rotates with the c-ring, forcing each β subunit through open $\rightarrow$ loose $\rightarrow$ tight conformations (binding-change mechanism).
- **ϵ -subunit:** attached at the base of γ , locking it to the c-ring so the two rotate as a single rotor.

Rotor vs stator: c-ring + γ + ϵ form the **rotor**, which spins as H^+ flows down its gradient. a-subunit + b_2 + δ + the $\alpha_3\beta_3$ hexamer form the **stator**, which stays fixed and provides the catalytic sites acted upon by the turning γ shaft — this is why the enzyme is often called a “rotary motor.”