

Biological Oxidation

How the cell cashes in the electrons harvested from food — redox couples, the mitochondrial electron transport chain, chemiosmosis, and the drugs and toxins that jam or short-circuit the machinery.

[SLP vs OxPhos](#)[Redox Potential](#)[ETC Complexes](#)[Chemiosmosis](#)[ATP Synthase](#)[Inhibitors & Uncouplers](#)[SLP vs OxPhos](#)[Redox Potential](#)[ETC Components](#)[Mechanism](#)[P/O Ratio](#)[1](#)

1 Substrate-Level vs. Oxidative Phosphorylation

Two routes to the same product — ATP

Every ATP the cell makes comes from one of two fundamentally different mechanisms — a direct chemical handoff, or a current of electrons harnessed across a membrane.

Basis	Substrate-Level Phosphorylation	Oxidative Phosphorylation
Site	Cytoplasm (glycolysis) & mitochondrial matrix (TCA cycle)	Inner mitochondrial membrane

O ₂ required?	No — can occur anaerobically	Yes — O ₂ is the final electron acceptor
Mechanism	Direct transfer of a phosphate group from a high-energy intermediate to ADP	Electron flow down the ETC builds a proton gradient that drives ATP synthase
Key enzyme	Substrate-specific kinase	ATP synthase (Complex V)
Contribution/glucose	Minor — 4 ATP gross (2 net)	Major — ~26–28 ATP

The two SLP reactions



Glycolysis, step 7



TCA cycle, step 5

these are direct, one-step, enzyme-catalysed transfers — no O₂, no membrane

2 Redox Potential & Redox Couples

The thermodynamic currency behind electron flow

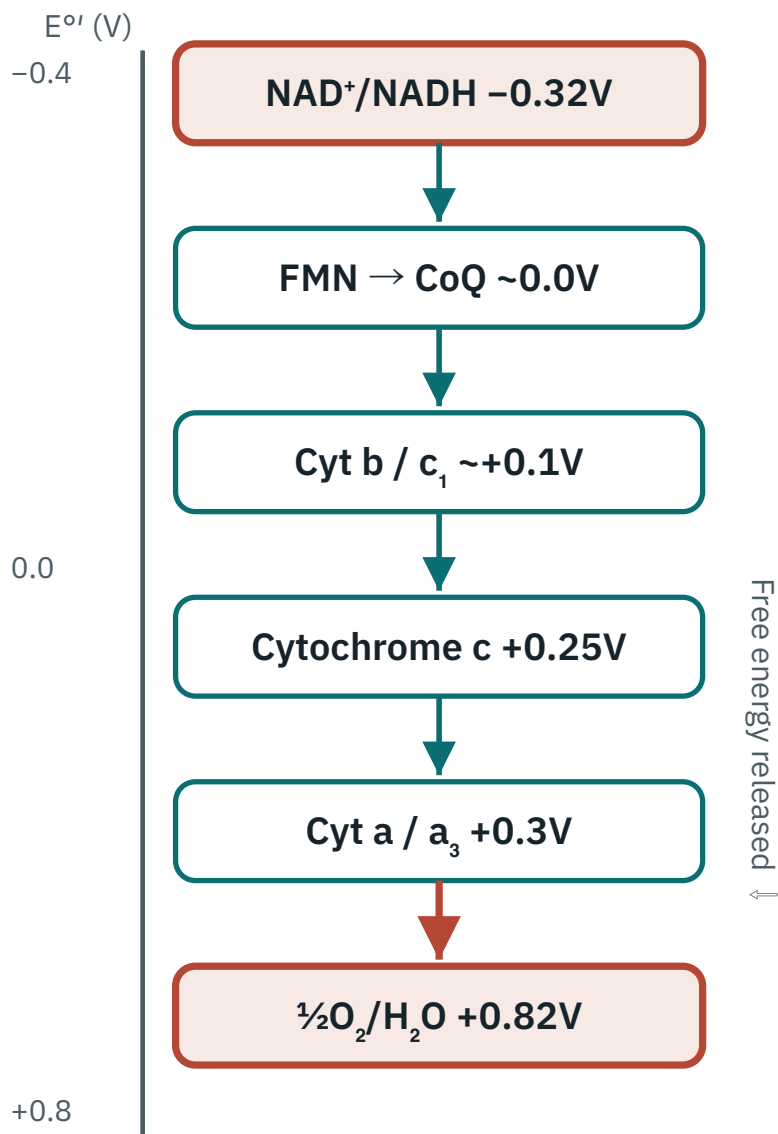
A **redox couple** is an oxidised/reduced pair of the same substance (e.g. NAD⁺/NADH) that can accept or donate electrons. Its **standard redox potential (E°)** — measured in volts against the hydrogen electrode, at pH 7 — quantifies its affinity for electrons.

- More **negative** E° → stronger tendency to *donate* electrons (good reducing

agent)

- More **positive** $E^{\circ'}$ $\rightarrow$ stronger tendency to *accept* electrons (good oxidising agent)
- Electrons flow spontaneously from a couple of lower $E^{\circ'}$ to one of higher $E^{\circ'}$
- $\Delta G^{\circ'} = -nF\Delta E^{\circ'}$ — n = electrons transferred, F = Faraday constant (23.06 kcal·V⁻¹·mol⁻¹). A positive $\Delta E^{\circ'}$ gives a negative $\Delta G^{\circ'}$: spontaneous, energy-releasing electron flow

The redox tower – electrons "fall" from NADH to O₂



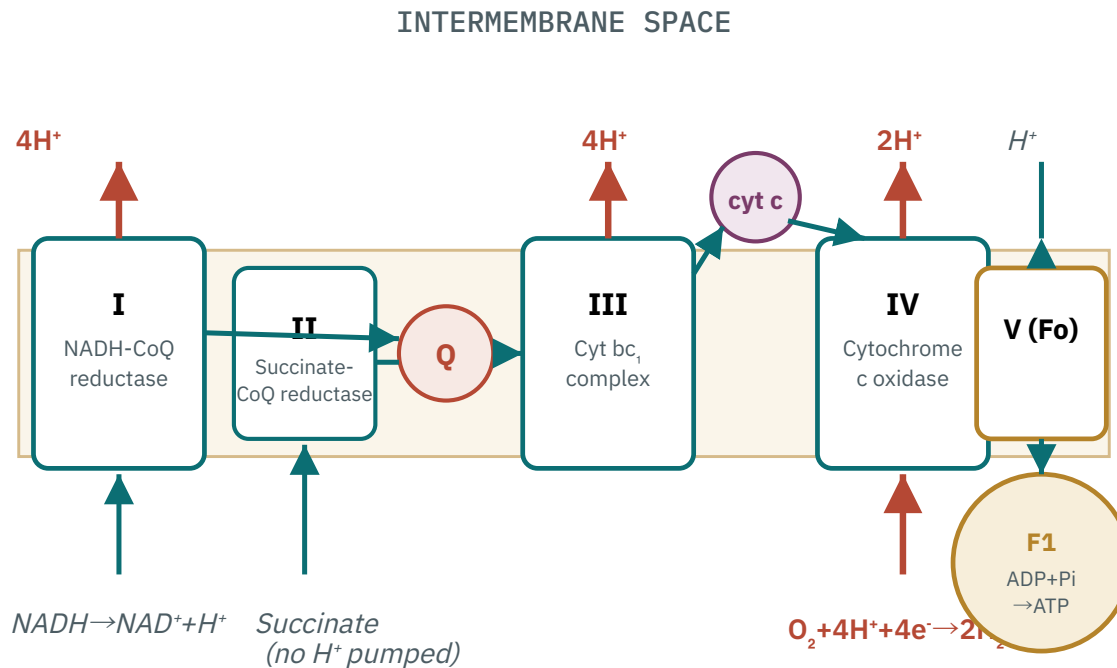
Values are representative standard potentials — the ordering, not the decimals, is what matters for exams.

3 Mitochondrial Electron Transport Chain

Inner mitochondrial membrane · four fixed complexes + two mobile carriers

Electrons stripped from NADH and FADH_2 pass through a sequence of membrane complexes and mobile carriers, losing free energy at each step — energy that Complexes I, III and IV capture as a proton gradient.

Electron flow across the inner membrane



COMPONENT SUMMARY

- I — FMN + Fe-S clusters · pumps $4H^+$
- II — FAD + Fe-S · part of TCA cycle · pumps none
- III — Cyt b, c_1 , Rieske Fe-S · pumps $4H^+$ (Q cycle)
- IV — Cyt a, a_3 , Cu $_A$ /Cu $_B$ · pumps $2H^+$ · reduces O_2
- CoQ & Cyt c — small, mobile, lipid- / water-soluble carriers
- V — ATP synthase, Fo (channel) + F1 (catalytic head)

4 Mechanism of Electron Transport & ATP Synthesis

Chemiosmotic theory (Peter Mitchell) & the binding-change mechanism (Paul Boyer)

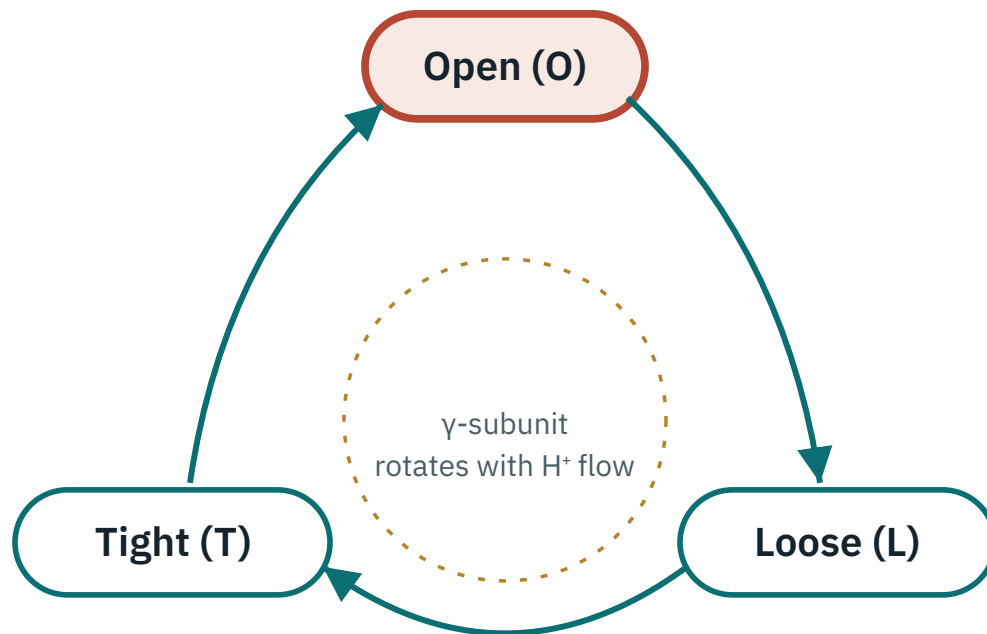
As electrons descend the ETC, Complexes I, III and IV pump protons from the

matrix into the intermembrane space, building an electrochemical gradient — the **proton-motive force ($\text{pmf} = \Delta\Psi + \Delta\text{pH}$)** — which is then spent to make ATP.

CHEMIOSMOTIC COUPLING, IN ONE LINE

Electron transport is *vectorial* (directional across a membrane); the resulting H^+ gradient is potential energy; ATP synthase is the turbine that converts it back into the chemical energy of ATP. No membrane integrity $\rightarrow$ no coupling, even if the ETC itself runs freely.

ATP synthase – the binding-change mechanism



O — releases ATP, awaits substrate
L — binds $\text{ADP} + \text{P}_i$ loosely
T — catalyses ATP formation (tight fit)

- H^+ flow through the F_0 c-ring rotates the central γ -stalk, cycling each of the three F_1 β -subunits through $\text{O} \rightarrow \text{L} \rightarrow \text{T}$ conformations
- $\sim 3 \text{ H}^+$ drive synthesis of 1 ATP at F_1 ; ~ 1 more H^+ is spent transporting P_i and exchanging ADP/ATP across the membrane (adenine nucleotide translocase) — so $\sim 4 \text{ H}^+$ are charged per ATP exported to the cytosol

5 Oxidative Phosphorylation — Yield & Control

P/O ratio and respiratory (acceptor) control

Electron entry point	H ⁺ pumped	P/O ratio
NADH → Complex I	4 + 4 + 2 = 10 H ⁺	≈ 2.5 (classically taught as 3)
FADH ₂ → Complex II	4 + 2 = 6 H ⁺	≈ 1.5 (classically taught as 2)

P/O ratio = ATP synthesised per pair of electrons per oxygen atom reduced. FADH₂ enters at CoQ, bypassing Complex I entirely — so it yields fewer protons pumped, and less ATP, than NADH.

RESPIRATORY (ACCEPTOR) CONTROL

Electron transport is tightly coupled to ADP availability. **State 3** (ADP abundant) — rapid respiration, high O₂ consumption. **State 4** (ADP depleted, mostly ATP) — respiration slows sharply. This is why resting muscle, with plenty of ATP and little ADP, consumes far less O₂ than exercising muscle.

SHUTTLE SYSTEMS FOR CYTOSOLIC NADH

NADH made in glycolysis cannot cross the inner mitochondrial membrane directly. The **malate–aspartate shuttle** (liver, heart, kidney) delivers electrons to Complex I (full ~2.5 ATP/NADH). The **glycerol-3-phosphate shuttle** (skeletal muscle, brain) delivers them to CoQ instead (only ~1.5 ATP/NADH) — a tissue-specific difference worth remembering.

6 Inhibitors & Uncouplers

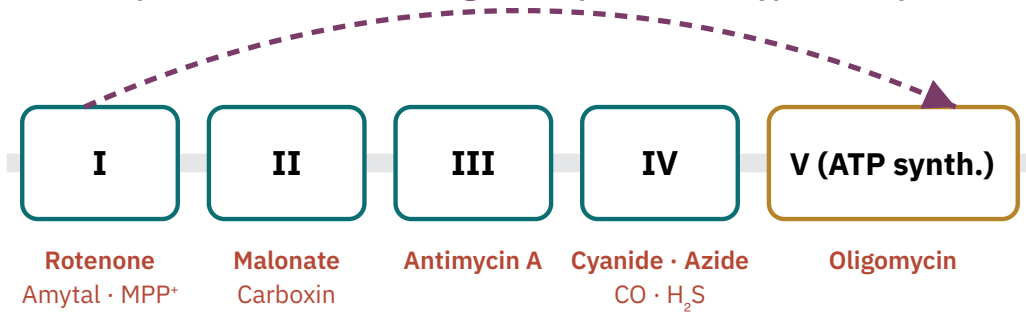
Where the chain can be blocked — and where it can be short-circuited

Two very different pharmacological strategies hit the same pathway: **inhibitors** block a specific complex and halt both electron flow and ATP synthesis; **uncouplers** leave electron flow running (even accelerating it) while destroying the

proton gradient, so no ATP is made — the energy is released as heat instead.

Site of action along the chain

Uncouplers (DNP, FCCP, thermogenin) — proton leak, bypass Complex V



UNCOUPLER EFFECT

O₂ consumption ↑↑ (uncontrolled) · ATP synthesis ↓↓ · Heat ↑↑
Physiological example: thermogenin (UCP1) in brown fat

Agent type	O ₂ consumption	ATP synthesis	Heat
ETC inhibitor (e.g. cyanide)	↓↓	↓↓	↓
Uncoupler (e.g. DNP)	↑↑ (uncontrolled)	↓↓	↑↑
ATP synthase inhibitor (oligomycin)	↓↓ (gradient backs up)	↓↓	↓

CLINICAL CORRELATIONS

Cyanide poisoning is treated with amyl/sodium nitrite (induces methaemoglobin, which traps CN⁻) followed by sodium thiosulfate (rhodanese converts it to renally-excreted thiocyanate). 2,4-Dinitrophenol was once marketed as a weight-loss aid — uncontrolled uncoupling caused fatal hyperthermia and it was banned. Complex I mutations underlie Leber's hereditary optic neuropathy (LHON).

7 Exam Corner

Practice question set — end-semester format

B.Sc. Biochemistry — End-Semester Examination

Paper: Biological Oxidation

Full Marks: 30

Time: 1.5 Hrs

GROUP A — LONG ANSWER (ANSWER ANY TWO)

1. Describe the components of the mitochondrial electron transport chain and explain, with a labelled diagram, how electron flow is coupled to ATP synthesis according to the chemiosmotic theory. **10**
2. Define redox potential. Arrange the redox couples of the electron transport chain in order of increasing E° and derive the relationship between ΔG° and ΔE° . **10**
3. Discuss the site and mechanism of action of electron transport chain inhibitors and uncouplers, clearly distinguishing their effects on oxygen consumption, ATP synthesis, and heat production. **10**

GROUP B — SHORT NOTES (ANSWER ANY TWO)

- a. Substrate-level phosphorylation, with two examples **5**
- b. ATP synthase — structure and the binding-change mechanism **5**
- c. P/O ratio and respiratory control **5**