Electron Transport Chain

-Dr. Ekta Khare
Department of Microbiology
Institute of Biosciences & Biotechnology,
CSJM University, Kanpur

Electron Transport Chain

- Only the equivalent of four ATP molecules is directly synthesized when one glucose is oxidized to six CO_2 molecules by way of glycolysis and the TCA cycle.
- Most ATP generated comes from the oxidation of NADH and $FADH_2$ in the electron transport chain.
- The mitochondrial electron transport chain is composed of a series of electron carriers that operate together to transfer electrons from donors, like NADH and $FADH_2$, to acceptors, such as O_2.
- The electrons flow from carriers with more negative reduction potentials to those with more positive potentials and eventually combine with O_2 and H^+ to form water.

ETC

- The electron transport chain carriers reside within the inner membrane of the mitochondrion or in the bacterial plasma membrane.
- The mitochondrial system is arranged into four complexes of carriers, each capable of transporting electrons part of the way to O_2 (figure 1).
- Coenzyme Q and cytochrome c connect the complexes with each other.
- The process by which energy from electron transport is used to make ATP is called **oxidative phosphorylation.**

Complex I: NADH to Ubiquinone

- The electron carriers of the respiratory chain are organized into membrane-embedded supramolecular complexes that can be physically separated.
- ***Complex I: NADH to Ubiquinone (*NADH:ubiquinone oxidoreductase** or **NADH dehydrogenase), is a large enzyme** composed of 42 different polypeptide chains, including an FMN-containing flavoprotein and at least six ironsulfur centers.
- Complex I catalyzes two simultaneous and obligately coupled processes:
  - the exergonic transfer to ubiquinone of a hydride ion from NADH and a proton from the matrix, expressed by:

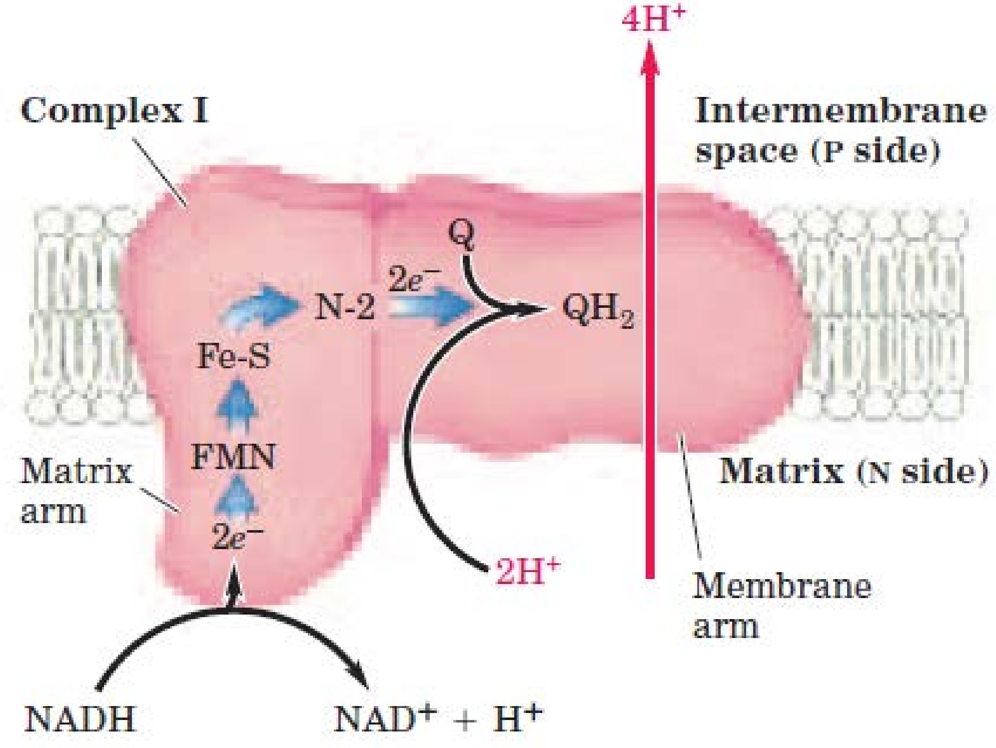
$$NADH + H^+ + Q \longrightarrow NAD^+ + QH_2$$

  - and the endergonic transfer of four protons from the matrix to the intermembrane space.
- The overall reaction is often written with subscripts that indicate the location of the protons: P for the positive side of the inner membrane (the intermembrane space), N for the negative side (the matrix):

$$NADH + 5H^+_N + Q \longrightarrow NAD^+ + QH_2 + 4H^+_P$$

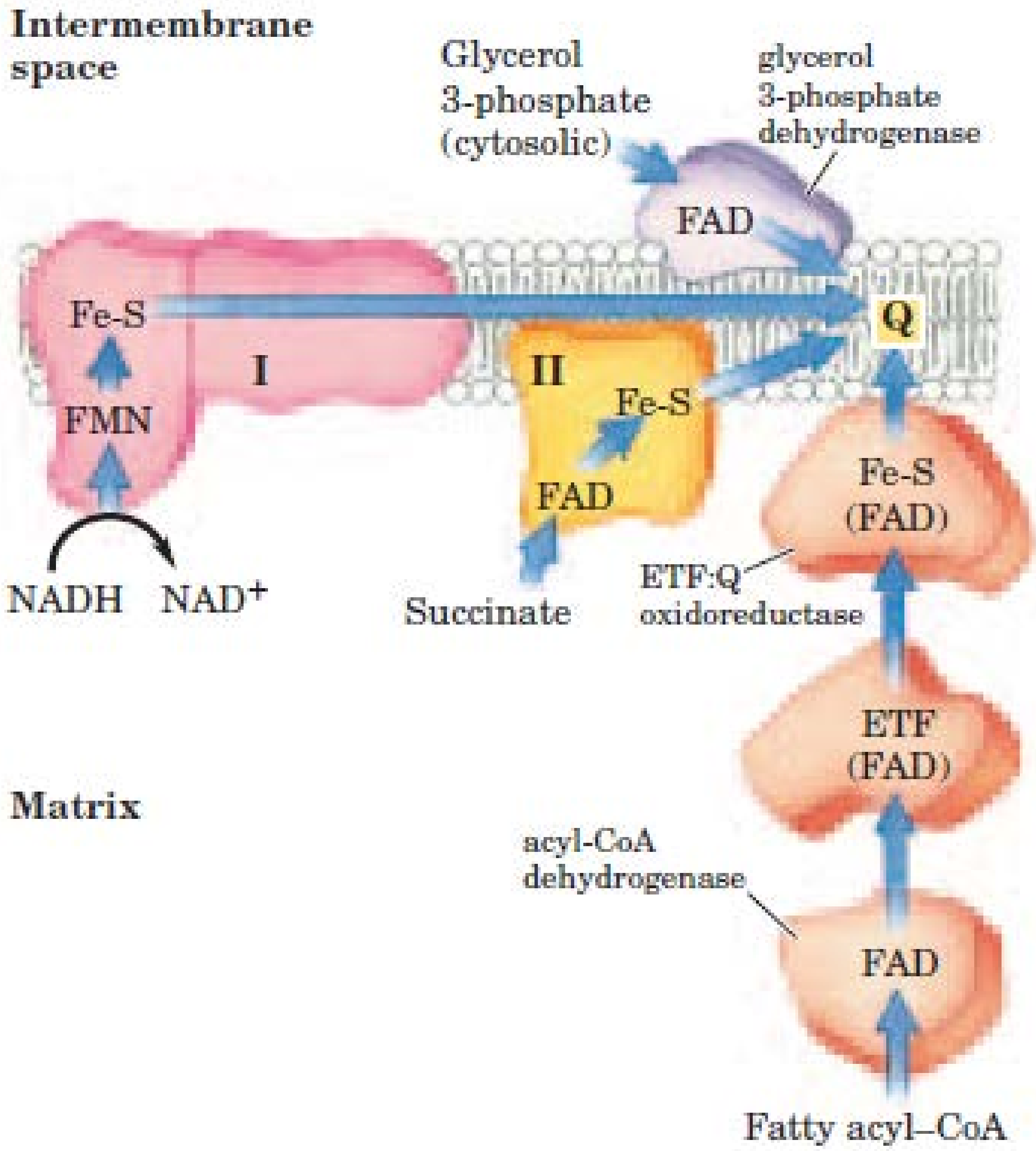
- Ubiquinol (QH_2, the fully reduced form;diffuses in the inner mitochondrial membrane from Complex I to Complex III, where it is oxidized to Q in a process that also involves the outward movement of H^+.

Complex I: NADH to Ubiquinone



Complex II: Succinate to Ubiquinon

- Complex II or succinate dehydrogenase, the only membrane-bound enzyme in the citric acid cycle.
- Complex II, contains five prosthetic groups of two types and four different protein subunits.
- Subunits C and D are integral membrane proteins; they contain a heme group, heme *b, and a binding site for ubiquinone, the* final electron acceptor in the reaction catalyzed by Complex II.
- Subunits A and B extend into the matrix (or the cytosol of a bacterium); they contain three 2Fe-2S centers, bound FAD, and a binding site for the substrate, succinate.
- The path of electron transfer is from the succinate-binding site to FAD, then through the Fe-S centers to the Q-binding site.
- This contribute to the pool of reduced ubiquinone. QH_2 from all these reactions is reoxidized by Complex III.


Intermembrane space
Glycerol 3-phosphate (cytosolic)
glycerol 3-phosphate dehydrogenase
FAD
Q
Fe-S
I
FMN
NADH
NAD+
II
Fe-S
FAD
Succinate
Fe-S (FAD)
ETF:Q oxidoreductase
ETF (FAD)
Matrix
acyl-CoA dehydrogenase
FAD
Fatty acyl–CoA

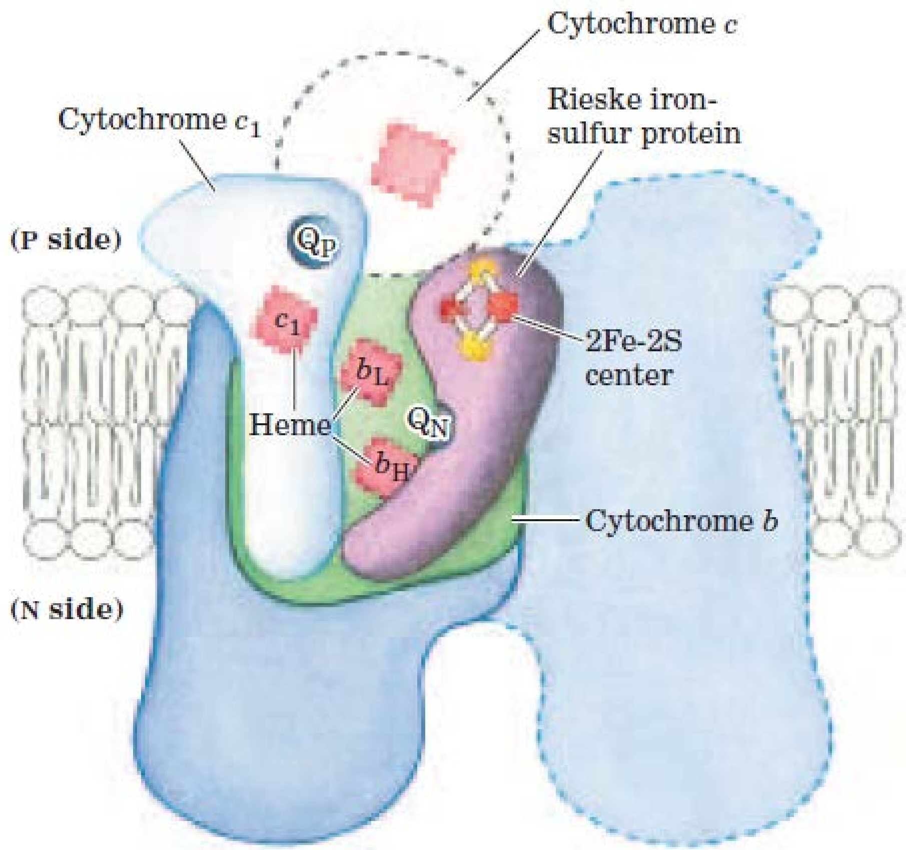
Complex III: Ubiquinone to Cytochrome c

- **Cytochrome *bc1 complex or ubiquinone:cytochrome c oxidoreductase,*** couples the transfer of electrons from ubiquinol (QH_2) to cytochrome *c with the vectorial* transport of protons from the matrix to the intermembrane space.
- The complex is a dimer of identical monomers, each with 11 different subunits.
- **Structure of a monomer consist of the functional core of three subunits (Fig. 2):**
  - cytochrome *b with its two hemes (bH and bL);*
  - the Rieske iron-sulfur protein with its 2Fe-2S centers;
  - and cytochrome *c1 with its heme*
- Cytochrome *c1* and the Rieske iron-sulfur protein project from the P surface and can interact with cytochrome *c* in the intermembrane space.
- The complex has two distinct binding sites for ubiquinone, Q_N and Q_P.
- Based on the structure of Complex III and detailed biochemical studies of the redox reactions, a reasonable model has been proposed for the passage of electrons and protons through the complex.

$$QH_2 + 2\ \text{cyt}\ c_1(\text{oxidized}) + 2H^+_N \longrightarrow Q + 2\ \text{cyt}\ c_1(\text{reduced}) + 4H^+_P$$

- Cytochrome *c is a soluble protein of* the intermembrane space.
- After its single heme accepts an electron from Complex III, cytochrome *c moves to* Complex IV to donate the electron to a binuclear copper center.

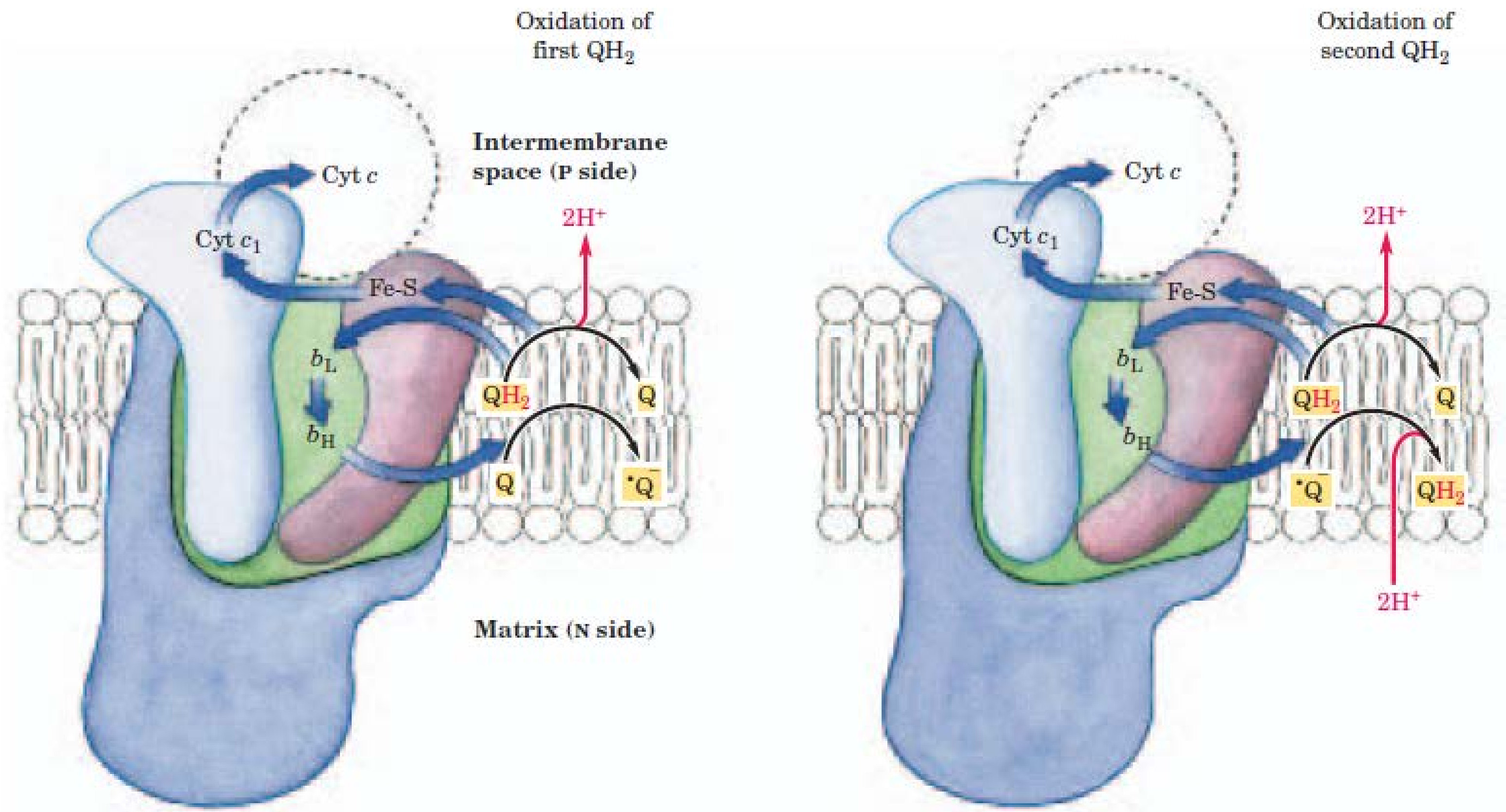
Cytochrome *bc1 complex*



Q-Cycle

- The path of electrons through Complex III is shown by blue arrows (Figure 3).
- On the P side of the membrane, two molecules of QH_2 are oxidized to Q near the P side, releasing two protons per Q (four protons in all) into the intermembrane space.
- Each QH_2 donates one electron (via the Rieske Fe-S center) to cytochrome *c1,* and one electron (via cytochrome b) to a molecule of Q near the N side, reducing it in two steps to QH_2.
- This reduction also uses two protons per Q, which are taken up from the matrix.

Q-Cycle



QH_2 + cyt c_1 (oxidized) $\longrightarrow$
$^{\bullet}Q^-$ + $2H_P^+$ + cyt c_1 (reduced)

QH_2 + $^{\bullet}Q^-$ + $2H_N^+$ + cyt c_1 (oxidized) $\longrightarrow$
QH_2 + $2H_P^+$ + Q + cyt c_1 (reduced)

Net equation:

QH_2 + 2 cyt c_1 (oxidized) + $2H_N^+$ $\longrightarrow$ Q + 2 cyt c_1 (reduced) + $4H_P^+$

Complex IV: Cytochrome c to O_2

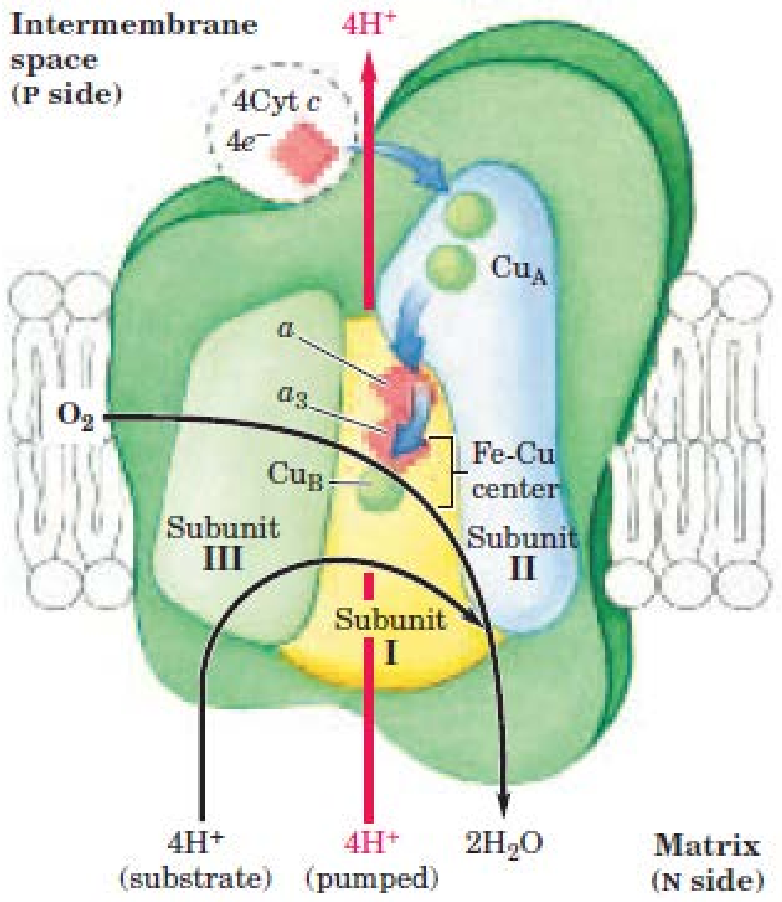
- **Complex IV, also called cytochrome oxidase**, carries electrons from cytochrome *c* to molecular oxygen, reducing it to H_2O.
- Complex IV is a large enzyme (13 subunits; Mr 204,000) of the inner mitochondrial membrane.
- Bacteria contain a form that is much simpler, with only three or four subunits, but still capable of catalyzing both electron transfer and proton pumping.
- Comparison of the mitochondrial and bacterial complexes suggests that three subunits are critical to the function.
- Mitochondrial subunit II contains two Cu ions complexed with the OSH groups of two Cys residues in a binuclear center.
- Subunit I contains two heme groups, designated *a* and *a3*, and another copper ion (Cu_B).
- Heme *a3* and Cu_B form a second binuclear center that accepts electrons from heme *a* and transfers them to O_2 bound to heme *a3*.

Complex IV: Cytochrome c to O_2

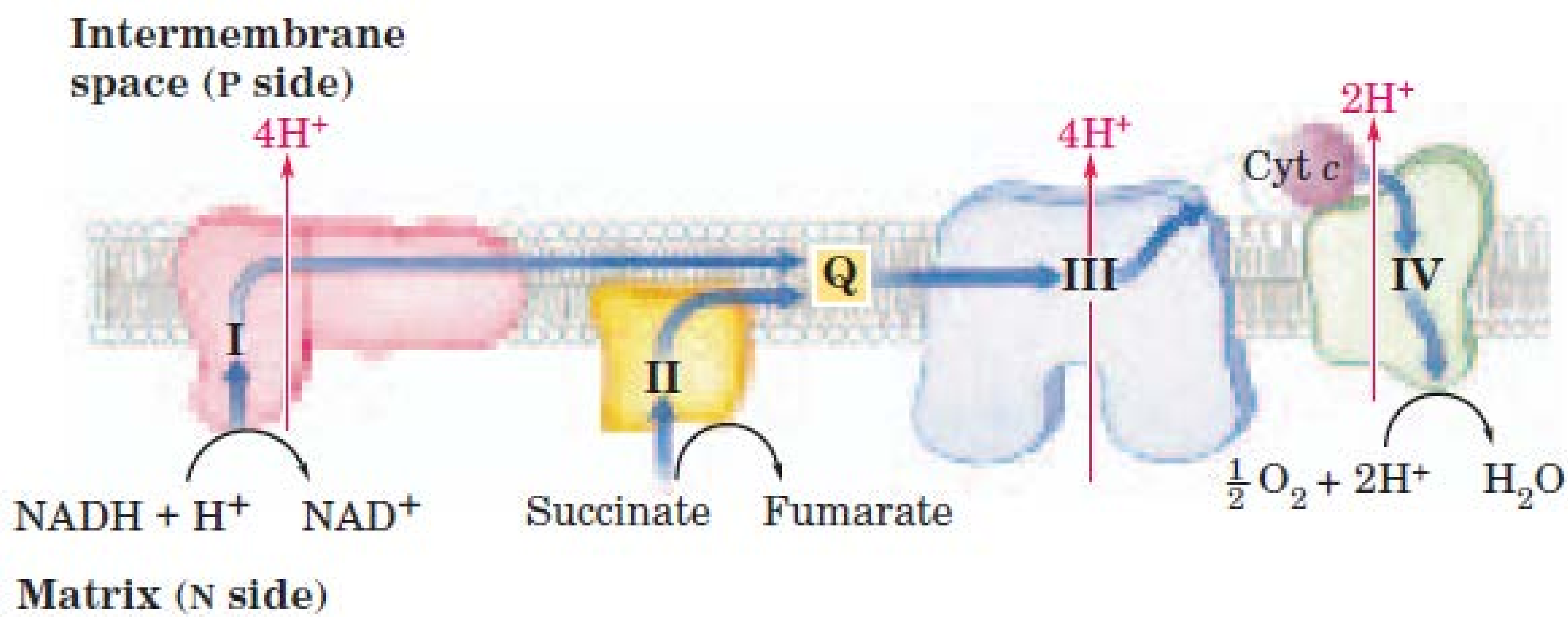
- Electron transfer through Complex IV is from cytochrome *c* to the *CuA* center, to heme *a,* to the heme *a3–CuB* center, and finally to O_2 (Fig. 4).
- For every four electrons passing through this complex, the enzyme consumes four "substrate" H from the matrix (N side) in converting O_2 to $2H_2O$.
- It also uses the energy of this redox reaction to pump one proton outward into the intermembrane space (P side) for each electron that passes through, adding to the electrochemical potential produced by redox-driven proton transport through Complexes I and III.
- The overall reaction catalyzed by Complex IV is:

$$4 \text{ Cyt } c \text{ (reduced)} + 8H^+_N + O_2 \longrightarrow 4 \text{ cyt } c \text{ (oxidized)} + 4H^+_P + 2H_2O$$

Complex IV: Cytochrome c to O_2



Summary of the flow of electrons and protons through the four complexes of the respiratory chain



Questions

- What are the different components of various complexes involve in eukaryotic respiratory electron transport chain?
- Write a short note on Q-cycle.
- Write an essay on respiratory electron transport system of eucaryotes.
- Explain respiratory electron transport process of bacteria.
  - *E. coli*
  - *Paracoccus denitrificans*
- What do you mean by oxidative phosphorylation? What are the steps of oxidative synthesis?
- Explain chemiosmotic model of ATP synthesis.
- Explain structure of ATP synthase.
- Explain binding change mechanism of ATP synthesis given by Paul D. Boyer.
- Differentiate between oxidative and substrate level phosphorylation.
- What is Pasteur effect? Briefly discuss.