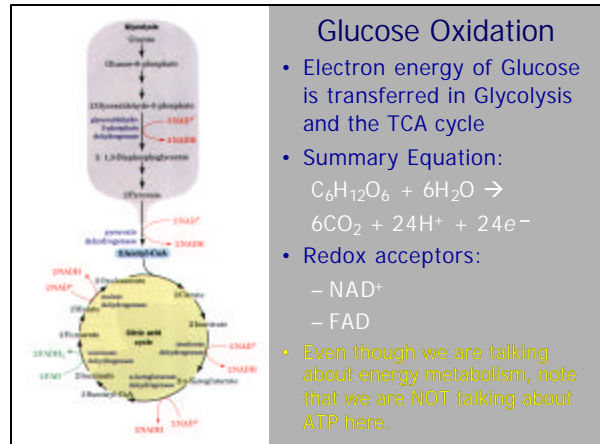


10: Mitochondrial ETS

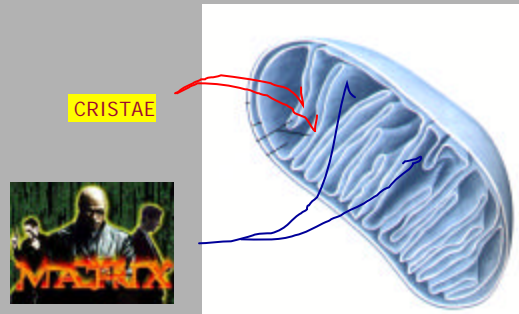


Electron Transport System

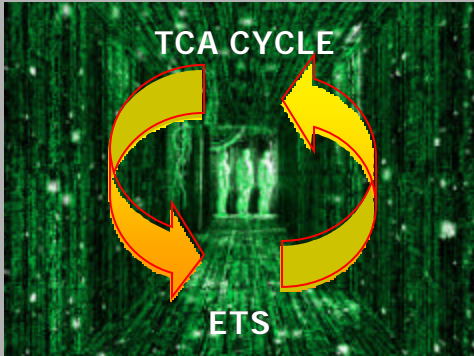


- 24 e⁻ will be passed from NADH, FADH₂
- System of linked electron carriers
- 10 redox centers in 4 enzyme complexes
- Coupled with H⁺ translocation to establish a chemiosmotic gradient for ATP synthesis
- Eventually, O₂ is reduced to 2H₂O

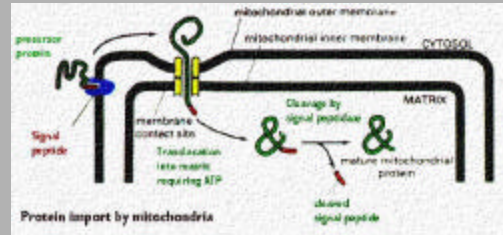
Membrane Structure



Welcome to the MATRIX

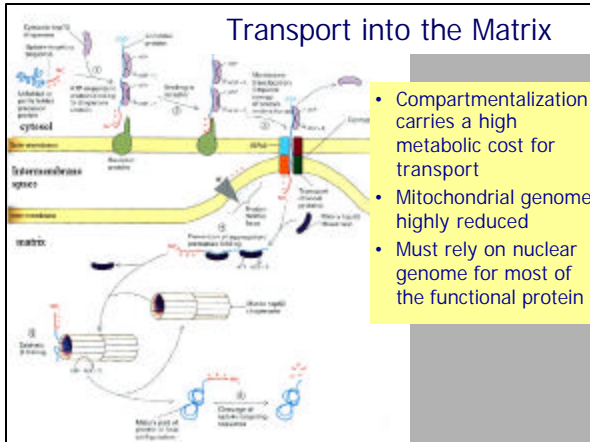


Mitochondrial Matrix



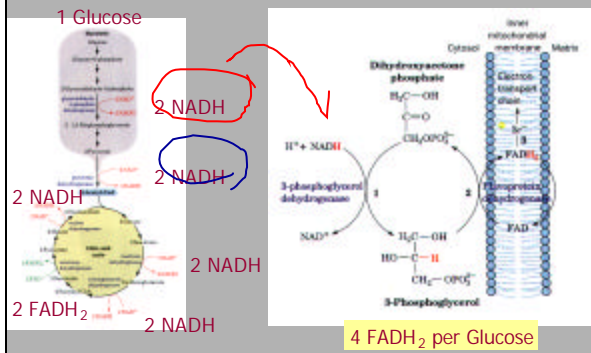
- High compartmentalization: concentration and coordination"
- The inner cristae (membranes) are 75% protein
- This membrane is freely permeable only to O_2 , CO_2 and H_2O . . . all other transport is tightly regulated
- Generates a unique ionic environment inside the matrix (chemiosmotic gradients).

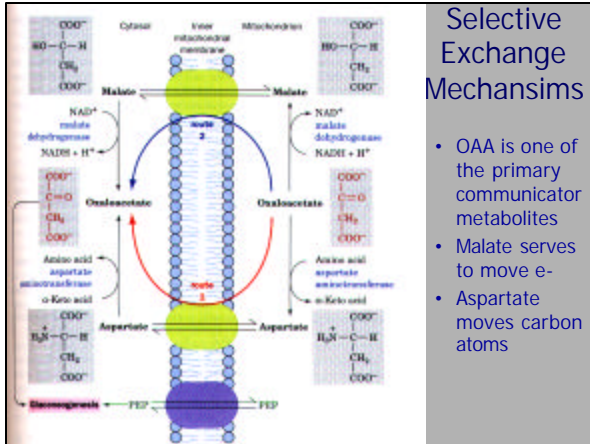
Transport into the Matrix



- Compartmentalization carries a high metabolic cost for transport
- Mitochondrial genome highly reduced
- Must rely on nuclear genome for most of the functional protein

NADH: Transport from cytosol





Selective Exchange Mechanisms

- OAA is one of the primary communicator metabolites
- Malate serves to move e-
- Aspartate moves carbon atoms

NADH oxidation

$$\text{NAD}^+ + \text{H}^+ + 2 e^- \rightleftharpoons \text{NADH} \quad \Delta \mathcal{E}^{o'} = -0.315 \text{ V}$$

$$\frac{1}{2} \text{O}_2 + 2 \text{H}^+ + 2 e^- \rightleftharpoons \text{H}_2\text{O} \quad \Delta \mathcal{E}^{o'} = 0.815 \text{ V}$$

- O_2 has a greater standard reduction potential than NAD^+ , so in this redox coupling, O_2 is the acceptor and NADH is the donor.
 - Total $\Delta E^{o'} = +1.130 \text{ V}$
- The standard free energy change:
 - $\Delta G^{o'} = -218 \text{ kJ mol}^{-1}$
 - which requires the transfer of 2 mol e^-
- Electrons are sequential passed between 4 protein complexes to harness the full chemical potential of this change in free energy state

Sequential e^- transfers

- ATP synthesis is not directly coupled to the cytochromes
- H^+ translocation at the cytochromes generates the chemiosmotic gradient necessary for ADP phosphorylation

Complex I

- $\text{NADH} + \text{CoQ} \rightarrow \text{NAD}^+ + \text{CoQ-H}_2$
 - $\Delta E^{o'} = 0.36 \text{ V}$
 - $\Delta G^{o'} = -69.5 \text{ kJ mol}^{-1}$
- Largest protein complex in inner membrane
 - 43 polypeptides
 - 850 kD
- Coenzyme:
 - FMN: flavin mononucleotide
 - Coenzyme-Q
 - Iron-Sulfur proteins (4Fe-4S)

FMN & CoQ

Flavin mononucleotide (FMN) oxidized or quinone form

FMN^{•-} radical or semiquinone form

FMN_H (reduced or hydroquinone form)

Ubiquinone (CoQ) oxidized or quinone form

Ubiquinone radical (semiquinone form)

Ubiquinol (reduced or hydroquinone form)

- Each cofactor can have 3 oxidation states
- They are capable of accepting 1 OR 2 electrons
- NADH can only pass e-pairs (2)
- THUS, FMN and CoQ serve as the intermediate for paired electron transfers from NADH and single electron transfers to the cytochrome system

Intermediate between FMN and CoQ

- Fe-S proteins
- Ferredoxin
- Capable of single e-transfers
- H⁺ pumping mechanism is not understood, but probably involves conformational changes associated with Fe-S redox

Component	E ^{o'} (V)
NADH	-0.315
Complex I (NADH-CoQ reductase; 850 kD, 43 subunits):	
FMN	?
(Fe-S)N-1a	-0.380
(Fe-S)N-1b	-0.250
(Fe-S)N-2	-0.030
(Fe-S)N-3,4	-0.245
(Fe-S)N-5,6	-0.270

NADH → FMN → 6: Fe-S → CoQ

Complex I Transfers

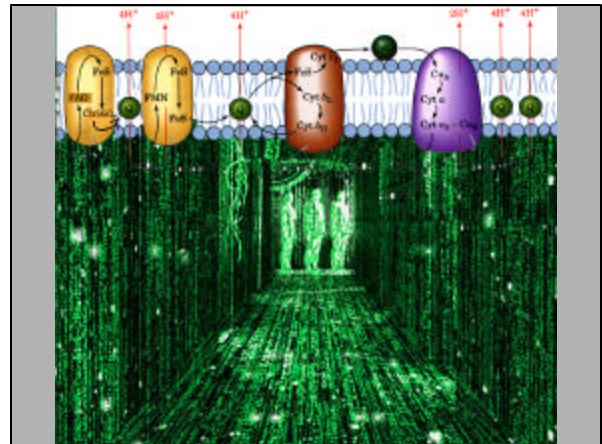
Complex II

- Contains Succinate Dehydrogenase as a component
- Functions to pass electrons from succinate to CoQ
- Transfer:
 - FADH₂
 - 4Fe-4S crystal
 - two 2Fe-2S crystal
 - Cytochrome b₅₆₀
 - CoQ

Complex II Integration

Complex II

- ΔG of e⁻ transfer is insufficient for H⁺ translocation
 - No ATP synthesis as a direct result of the transfer
- Electrons passed to CoQ
- CoQ is diffusive within the inner membrane
- Which side is the MATRIX?



Complex II Reduction Potentials

Component	E° (V)
Succinate	0.031
Complex II (succinate–CoQ reductase; 127 kD, 5 subunits):	
FAD	-0.040
(Fe-S)S-1	-0.030
(Fe-S)S-2	-0.245
(Fe-S)S-3	0.060
Cytochrome b_{560}	-0.080

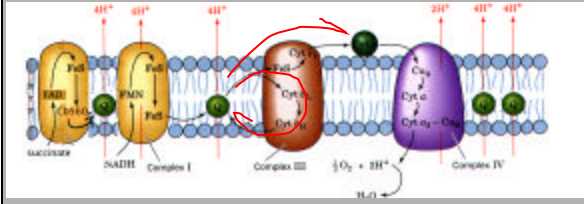
- E° of CoQ = -0.045
- $\Delta E^\circ = E^\circ$ (CoQ) – E° (succinate)
- $\Delta G^\circ = -2.70 \text{ kJ mol}^{-1}$

Complex III

- Receives electron pairs from CoQH₂
- 1 electron can be passed to each cytochrome
- Electron flow has two transfer paths:
 - Fe-S to Cyt c1
 - Cyt b back to CoQ
- “Q-Cycle”

Note: model shows one of two subunits (dimer)

Complex III Transfers

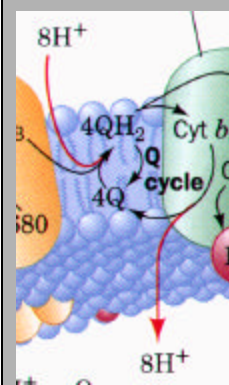


Complex III Reduction Potentials

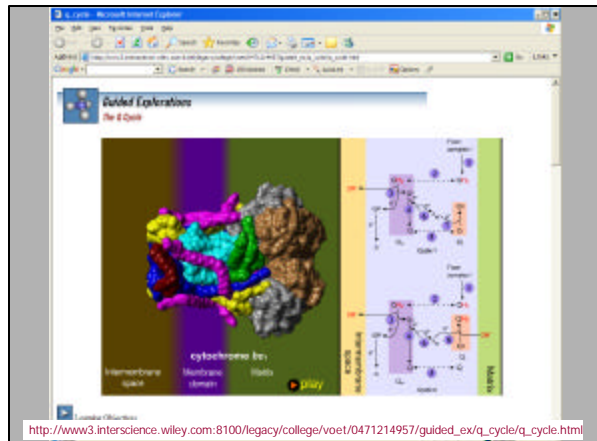
Coenzyme Q	0.045
Complex III (CoQ-cytochrome <i>c</i> reductase; 248 kD, 11 subunits):	
Cytochrome <i>b</i> ₁₁ (<i>b</i> ₅₆₂)	0.030
Cytochrome <i>b</i> _L (<i>b</i> ₅₆₆)	-0.030
(Fe-S)	0.280
Cytochrome <i>c</i> ₁	0.215
Cytochrome <i>c</i>	0.235

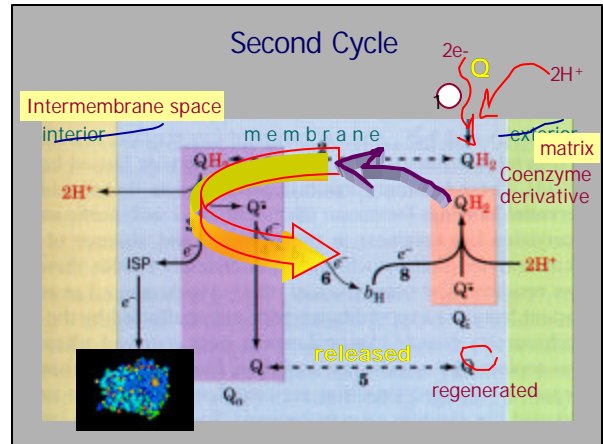
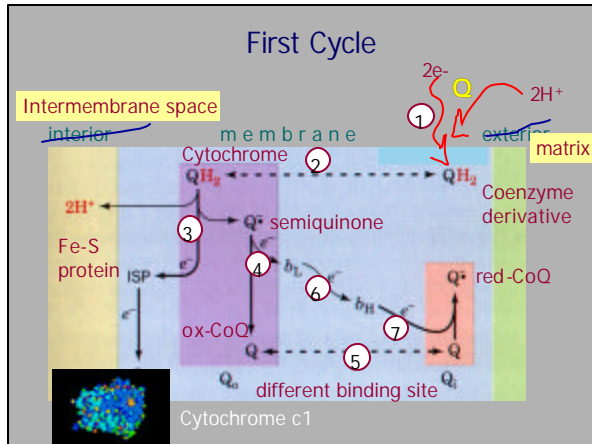
- $\Delta E^\sigma = E^\sigma (\text{Cyto } c) - E^\sigma (\text{CoQ})$
- $\Delta G^\sigma = -36.66 \text{ kJ mol}^{-1}$
- Enough free energy change for proton translocation and ATP synthesis

Q-cycle



- Quinones are diffusively distributed throughout the interior hydrophilic domain of the chloroplast membranes
- Redox cycle with no net chemical change, but chemical work results in the movement of 8 protons (per cycle) from 'exterior' to 'interior'.
- Q_BH₂ in PSII coordinates the 'pick-up' of H⁺ from the ext.; Cyt b coordinates the delivery of H⁺ into the int.





Net cycle activity

- 1: $Q_{\alpha} + 2e^{-} + 2H^{+}_{ext} + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{-} + 2H^{+}_{int}$
- 2: $Q_{\beta} + 2e^{-} + 2H^{+}_{ext} + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{2-} + 2H^{+}_{int} + Q_{\beta}$
- 2b: $Q_{\alpha}^{2-} + 2H^{+}_{ext} \rightarrow Q_{\alpha}H_2$
- 2c: $Q_{\alpha}H_2 + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{-} + 2H^{+}_{int}$

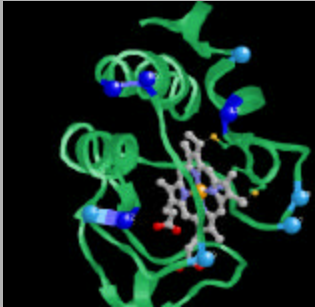
Net cycle balance

- 1: $Q_{\alpha} + 2e^{-} + 2H^{+}_{ext} + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{-} + 2H^{+}_{int}$
- 2: $Q_{\beta} + 2e^{-} + 2H^{+}_{ext} + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{2-} + 2H^{+}_{int} + Q_{\beta}$
- 2b: $Q_{\alpha}^{2-} + 2H^{+}_{ext} \rightarrow Q_{\alpha}H_2$
- 2c: $Q_{\alpha}H_2 + Fe^{3+} \rightarrow Fe^{2+} + Q_{\alpha}^{-} + 2H^{+}_{int}$

~~$Q_{\alpha} + 4e^{-} + 6H^{+}_{ext} + 3Fe^{3+} \rightarrow 3Fe^{2+} + Q_{\alpha}^{-} + 6H^{+}_{int}$~~

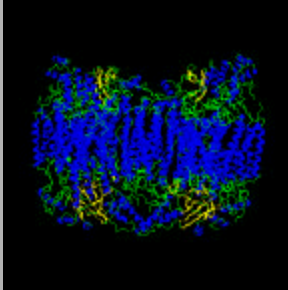
Complex IV

Cytochrome c



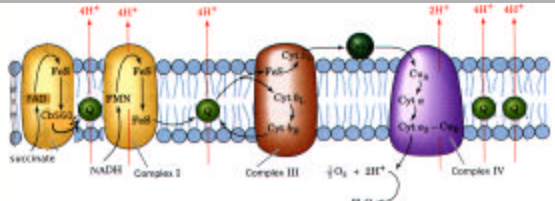
- Soluble & diffusive in intermembrane space

Complex IV



- Cytochrome c oxidase
- COX: mitochondrial prot.

Complex IV Transfers

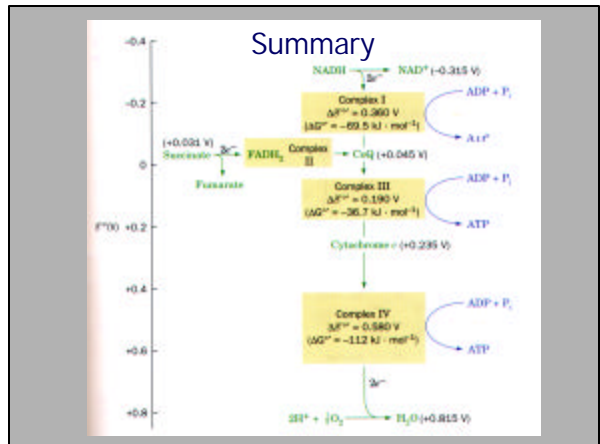
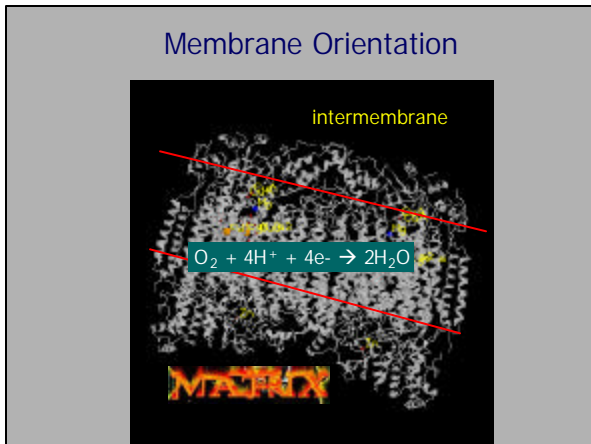
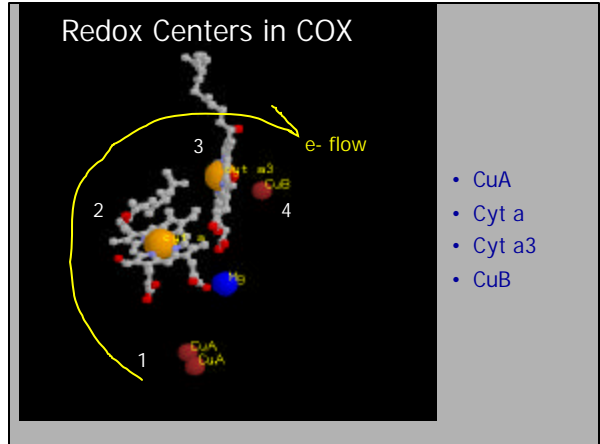
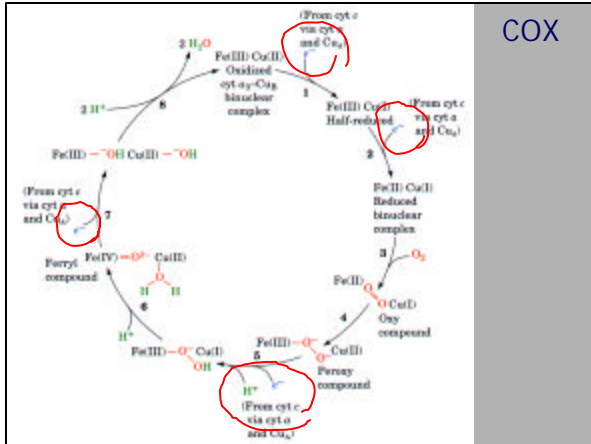


- $Cu_A \rightarrow Cyt\ a \rightarrow Cyt\ a_3 \sim\sim\sim Cu_B \rightarrow O_2$

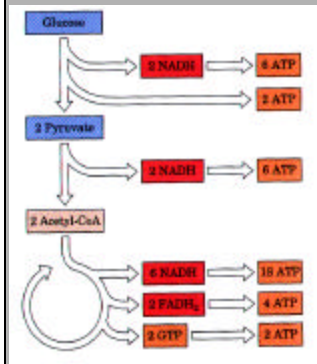
Complex IV Transfers

Cytochrome c	0.235
Complex IV (cytochrome c oxidase; ~200 kD, 6–13 subunits):	
Cytochrome a	0.210
Cu _A center	0.245
Cu _B	0.340
Cytochrome a ₃	0.385
O ₂	0.815

- $Cu_A \rightarrow Cyt\ a \rightarrow Cyt\ a_3 \sim\sim\sim Cu_B \rightarrow O_2$
- $\Delta G^\circ = -112\text{ kJ mol}^{-1}$



Energy Balance



- For 1 Glucose:
- Total Yield:
 - 38 ATP equivalents