BIOLOGIC OXIDATION & OXIDATIVE PHOSPHORYLATION

Kuntarti

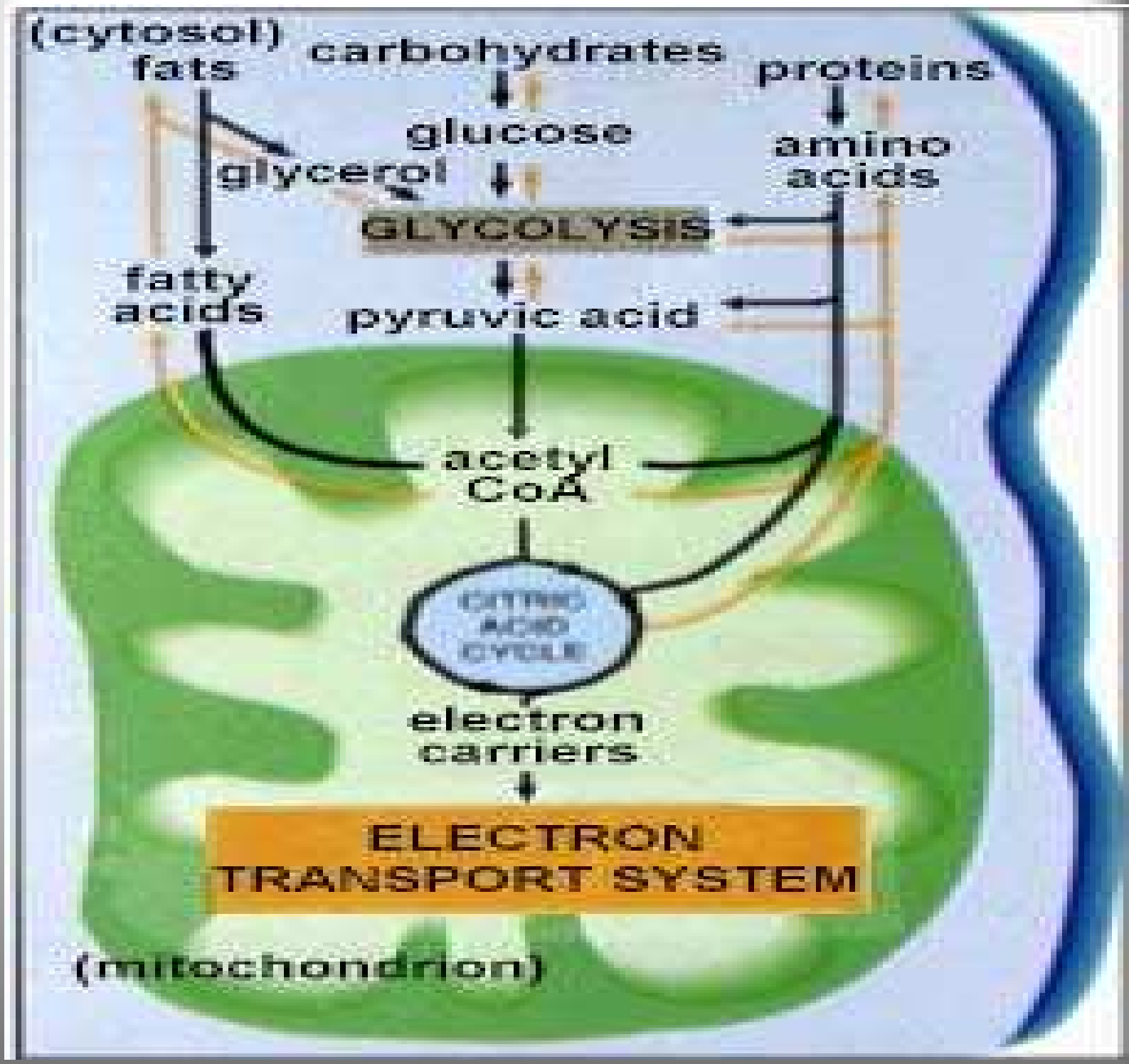
Biologic oxidation

- Are central to respiration & energy conservation in cells
- Energy is extracted from metabolic fuels by a series of oxidations, in which pairs of electrons are transferred from the fuel, through e series of ELECTRON CARRIERS, to oxygen
- An important concept underlying of the nature of biologic oxidation ➔ oxidation-reduction
- Oxidation : the removal of electrons
  Reduction : the gain of electrons

  $$Fe^{2+} \rightarrow Fe^{3+} + e^{-}$$
- Respiration in living organism → **use of oxygen** ➔ the process by which cells derive energy in the form ATP from the controlled reaction of hydrogen with oxygen to form water
- Free energy changes (ΔG) ➔ an oxidation-reduction/ redox potential

Metabolic Source of Energy

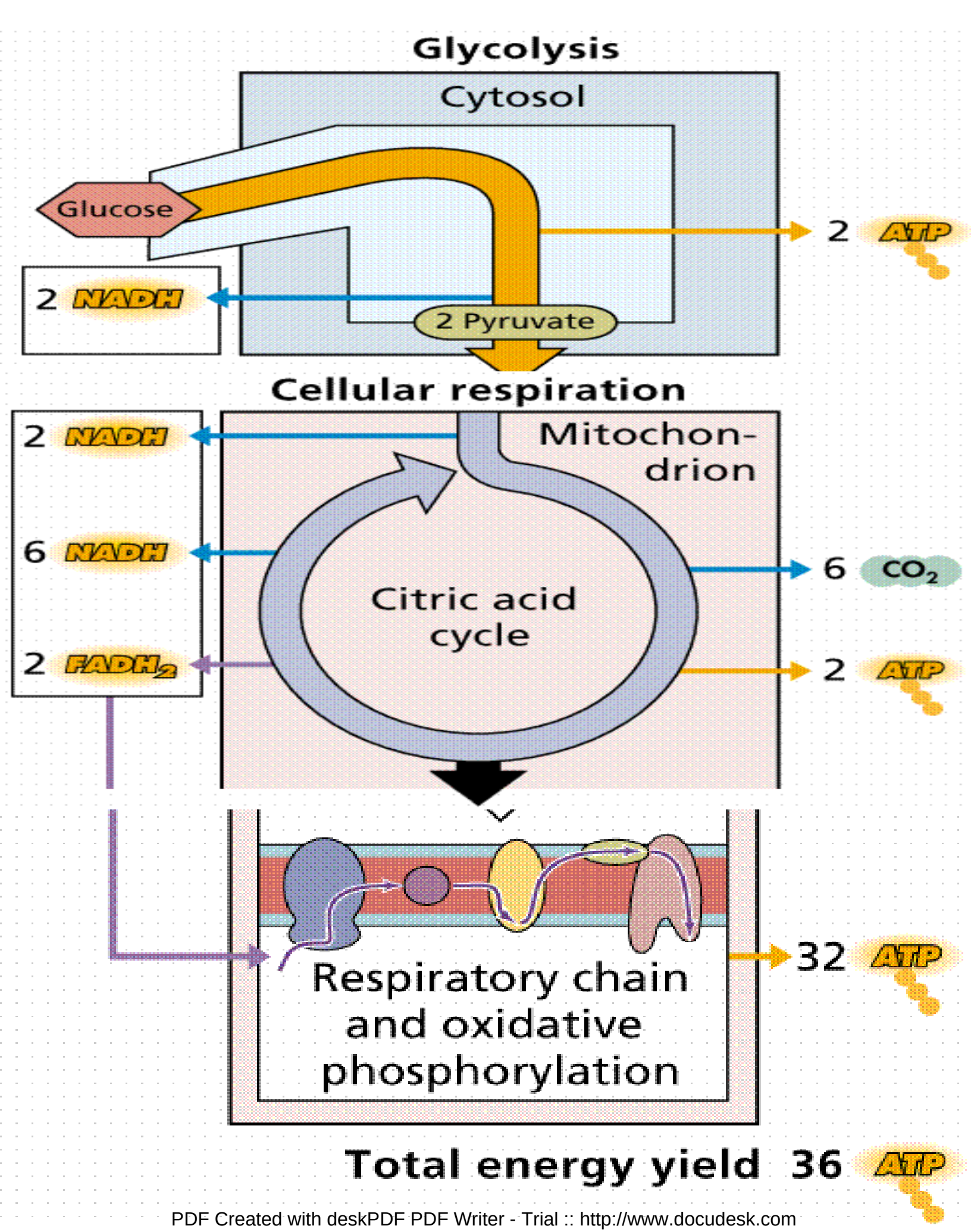
- 1st stage: macromolecule (P, L, CH) → amino acids, glucose, fatty acids (the building blocks)
- 2nd stage: the oxidized building blocks → acetyl Co-A
- 3rd stage: oxidation of acetyl Co-A by Tricarboxylic acid cycle (TCA) → O2
- 4th stage: transfer of electron pairs in Acetyl Co-A to electron carriers (NAD+[oxidized Nicotinamide Adenine Dinucleotide] & FAD [Flavin Adenine Dinucleotide]) → NADH & FADH2 by oxidative phosphorylation ➔ ATP



- http://www.biosci.uga.edu/almanac/bio_104/notes/jun4.html

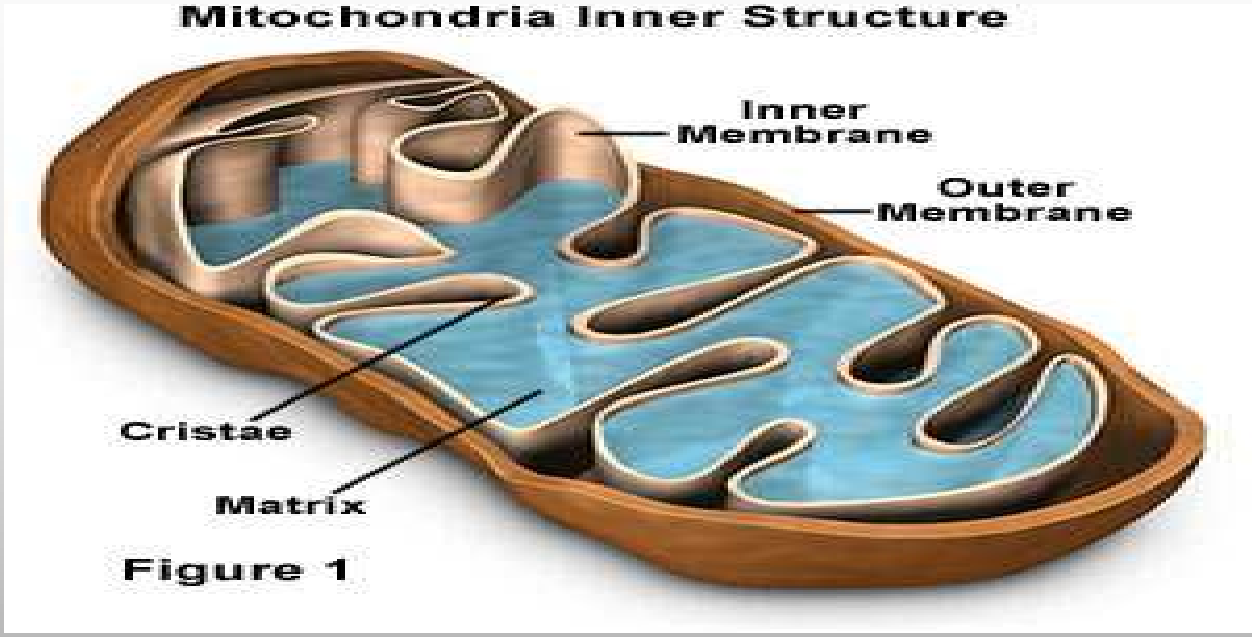
Major Electron Carriers in Metabolism

- The oxidation of metabolic fuels involves a large number of dehydrogenases, which require COENZYME that acts as ELECTRON CARRIERS.
- The most important COENZYMES:
  1. NAD+ → in the mitochondria
  2. FAD & FMN (Flavin Mononucleotide)
     → in the mitochondria & peroxisomes
  3. NADPH → in the cytoplasm of cells, is formed in the pentose phosphate pathways



Mitochondrial Respiration Chain

- Mitochondrial compartments



- Embedded in the inner membrane are proteins and complexes of molecules that are involved in the process called electron transport.

The Electron Transport System (ETS)

- ETS is the major consumer of oxygen in the cell.
- ETS accepts energy from carriers in the matrix and stores it to a form that can be used to phosphorylate ADP.
- The energy released by oxidation of NADH & FADH2 is coupled with the phosphorylation of ADP to ATP by ATP synthase.
- Components of ETS
  * 4 protein-lipid complexes
  * 2 mobile component

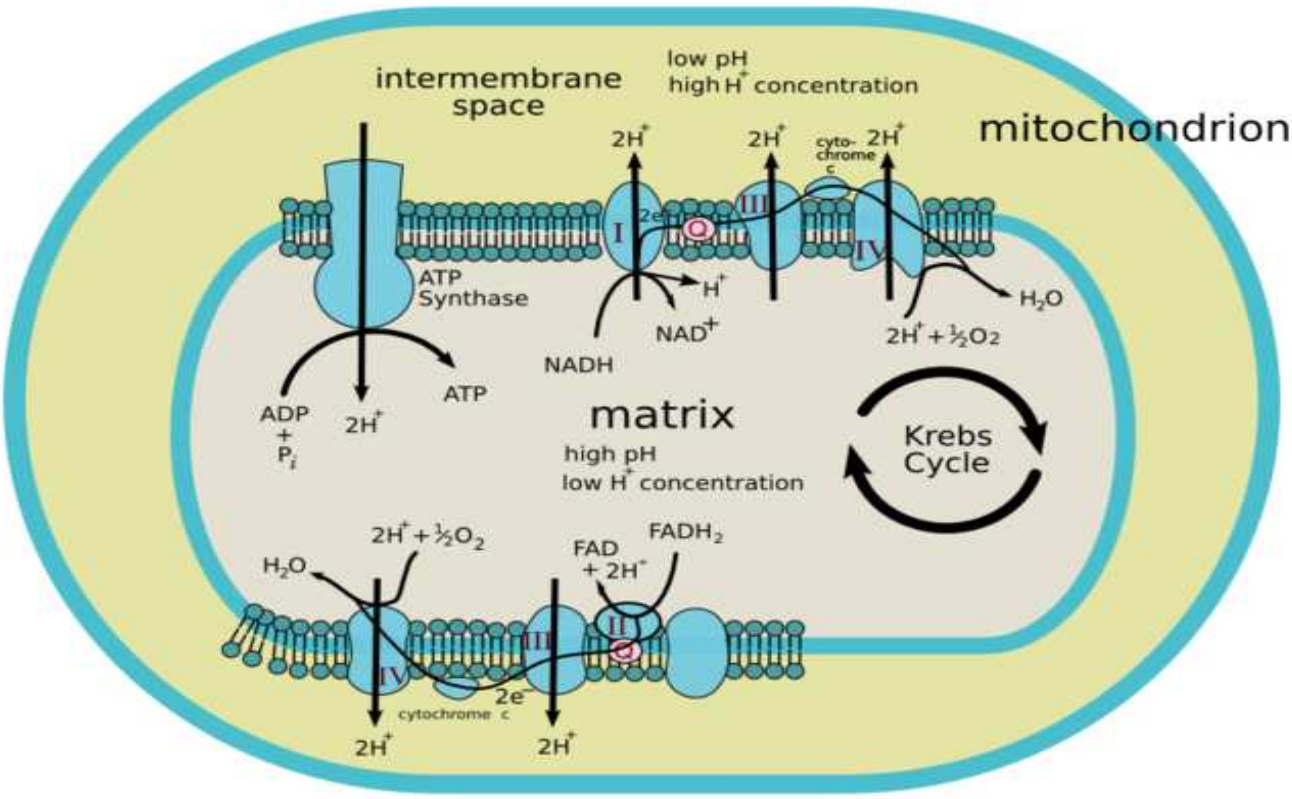
Components of ETS

- 4 protein-lipid complexes:
  Complex I: NADH-CoQ reductase/ NADH dehydrogenase
  Complex II: Succinate dehydrogenase/ Succinate-CoQ reductase
  Complex III: CoQH2-cytochrome-c reductase/ Ubiquinol cytochrome reductase
  Complex IV: Cytochrome-c oxidase
- 2 mobile components (electron carriers):
  - Coenzym-Q (CoQ) = ubiquinon
  - Cytochrome C

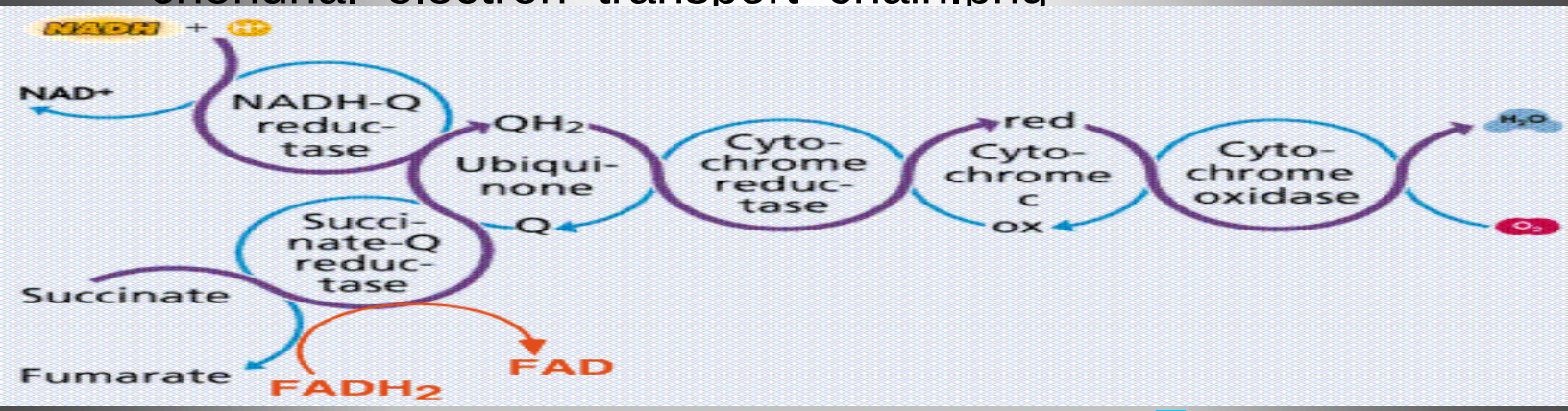
Electron Carriers

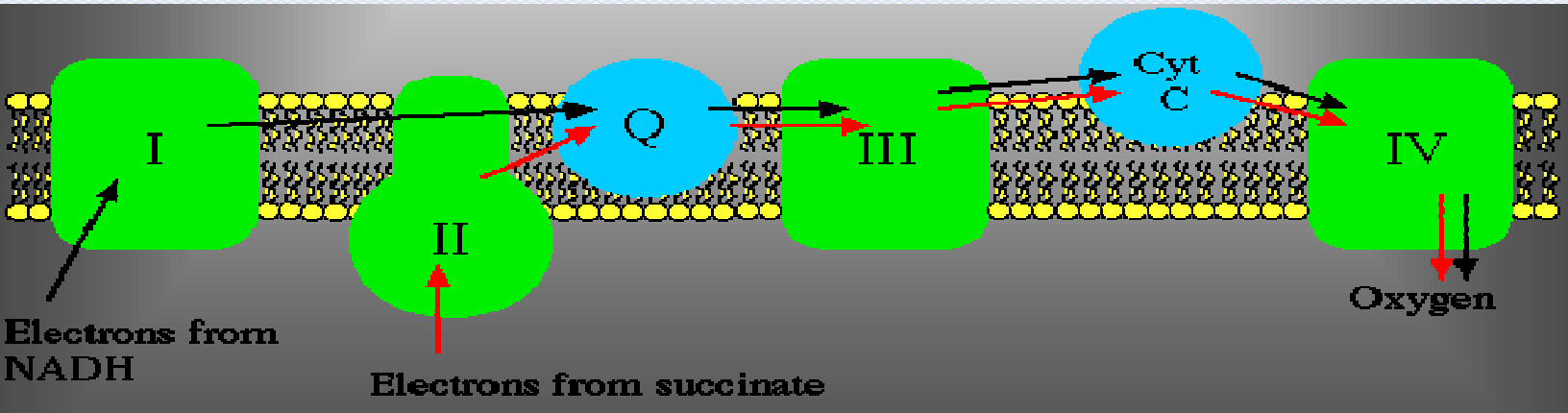
The ETS consists of 4 classes of cofactors that acts as electron carriers:

1. Flavin nucleotides
   FMN is a cofactor for complex I
   FAD is cofactor for complex II
2. Coenzyme Q (CoQ) = ubiquinone
   is a small lipophilic cofactor for complex III; has ability to accept electrons from a variety of reactions that produce FADH2
3. Iron-sulfur centers participate in one electron transfer reaction are associated with complex I, II, & III
4. Heme, the prosthetic group of the cytochrome, has a central iron atom. In the myoglobin & hemoglobin, the heme iron must be in the ferrous (Fe2+) state to be active
   Classification of cytochromes (a,b,c) found inm ETS is based on slight structural differences in the heme of these proteins.

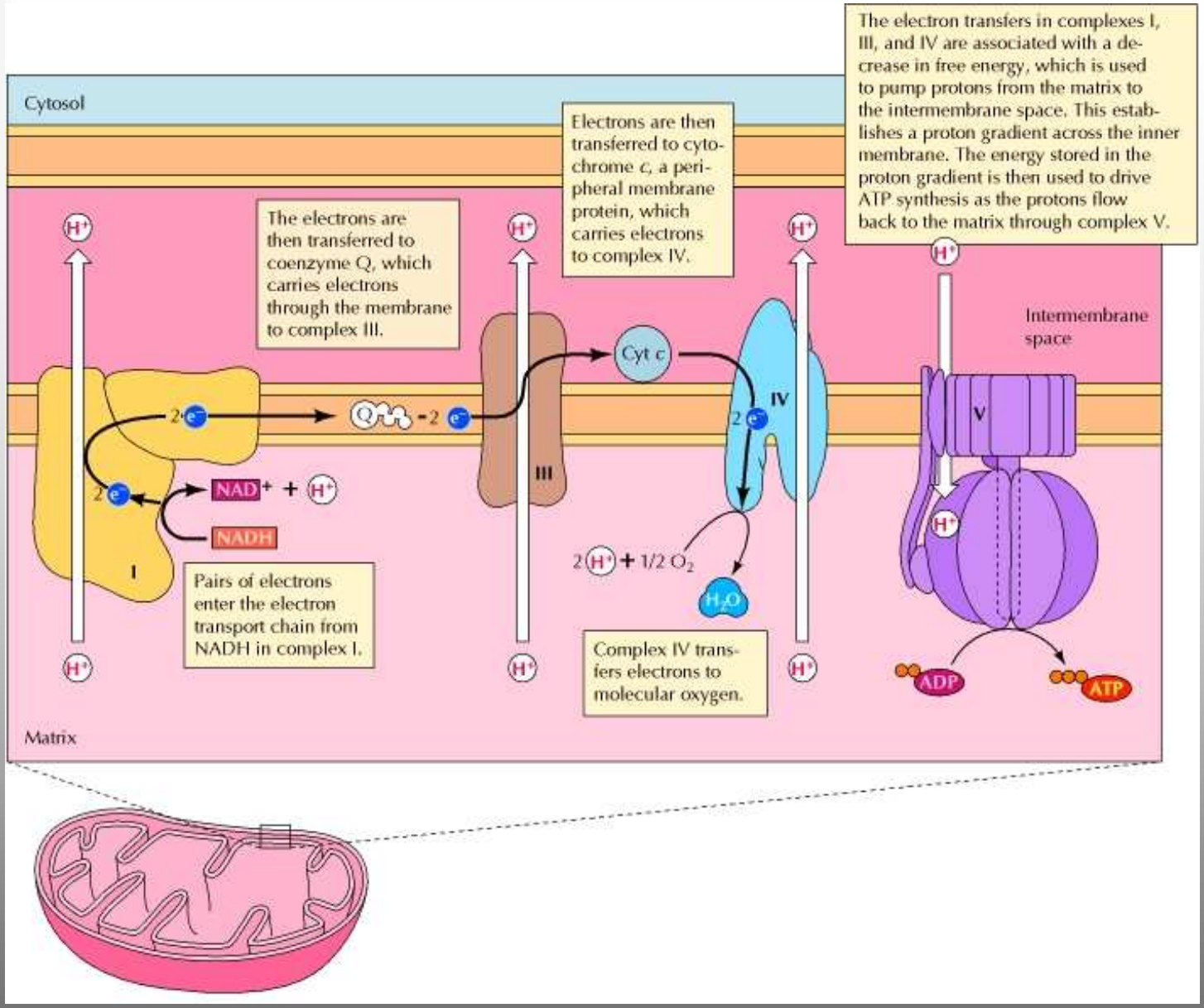


- http://upload.wikimedia.org/wikipedia/commons/7/7d/Mitochondrial_electron_transport_chain.png



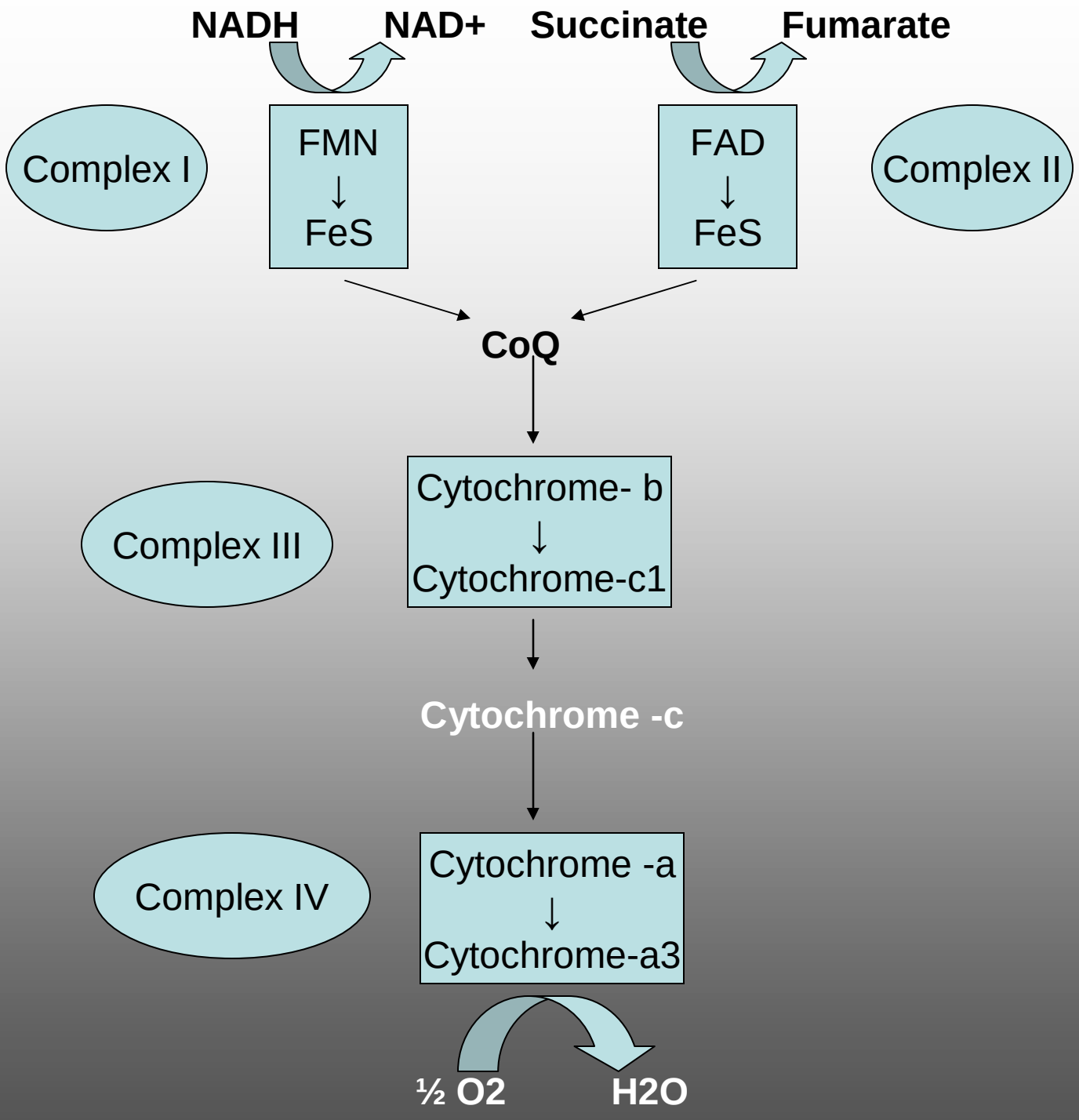


Pathways of Electron Transport



Cooper, GM (2000). *The Cell: a molecular approach*. 2nd ed. Washington: ASM Press.

Pathways of Electron Transport



Energy release

- Energy released by oxidation of NADH & FADH2 ≈ the transfer electrons from NADH & FADH2 to oxygen

  NADH $\Delta G^{\circ\prime} = -52.6$ kcal/mol

  FADH2 $\Delta G^{\circ\prime} = -40.5$ kcal/mol

- Energy required for the synthesis of ATP from ADP & Pi is 7.3 kcal/mol

Coupling of Oxidation & Phosphorylation

- How the energy released by oxidation of NADH & FADH2 is used for mitochondrial ATP synthesis ➔ ***the chemiosmotic theory*** (Peter Mitchell, 1961)
- 2 basic postulates of the chemiosmotic theory:
  1. As electrons flow through the ETS, the energy released is used to create a H+ gradient (protomotive force) across the inner mitochondrial membrane; and
  2. the movement of proton back across the membrane releases energy that can be used to drive the synthesis of ATP

P/O Ratio

- Is the number of inorganic phosphate group (Pi) incorporated into ATP per atom of molecular oxygen consumed (1/2 O2)
- Substrates that are oxidized with the formation of NADH (pyruvate, malate, isocitrate) have P/O = 3
- Substrates that are oxidized with the formation of FADH2 (succinate, α-glycerol phosphate) have P/O = 2

Inhibitors of Mitochondrial ATP synthesis

3 major classes of compounds inhibit oxidative phosphorylation:

1. ***Site-specific inhibitors of electron transports***
   → by decreasing ability of the ETS to establish a H+ gradient
   Complex I: Rotenone, barbiturates
   Complex III: antimycin
   Complex IV: Cyanide, CO, Azide
2. ***Bind to ATP synthase***
   Oligomycin binds to the Fo (component of ATP synthase that spans the IMM forming channel for H+) & inhibits electron transport.
3. ***Uncouplers of Oxidative Phosphorylation***
   Aspirin, dinitrophenol, thermogenin inhibits phosphorylation & increases rate of oxidation → released energy as heat

Mitochondrial Membrane Transport Systems

- “bilipid” IMM is the most permeable for O2, water, NH3, monocarboxilate acid (acetate, aceto-acetate, Gliserol-3P)
- The transport systems that are important for oxidative phosphorylation are:
  1. The shuttle systems
     *α-glycerol phosphate shuttle
     → transfer of electron from cytosol NADH to mitochondrial FADH2, then it’s transported back to the cytosol to complete shuttle

Mitochondrial Membrane Transports Systems

* Malate-Aspartate shuttle
  → effectively transfers electrons from cytosol to mitochondrial NADH

2. Adenine Nucleotide Transports Protein
   → exchanges mitochondrial ATP for cytosol
   ➔ atractyloside, a toxin found in plant inhibits this transport

Regulation of Mitochondrial Pathways

- The major metabolic pathways in mitochondria are fatty acid oxidation, the TCA cycle, & oxidative phosphorylation.
- The rates for these pathways are dependent on the availability of oxygen & ADP ➔ respiratory control
- Anaerobic conditions
  In the absence of adequate supply of oxygen, the rate of oxidative phosphorylation increases → NADH & FADH2 accumulated→ inhibits TCA cycle → anaerobic Glycolysis
- Aerobic conditions
  In the presence of an adequate supply O2, the rate of P/O is dependent on the availability of ADP → ADP >< ATP→ an accumulation of ADP → signal the need of supply O2 →increases the rate of electron transport & ATP synthesis

The End