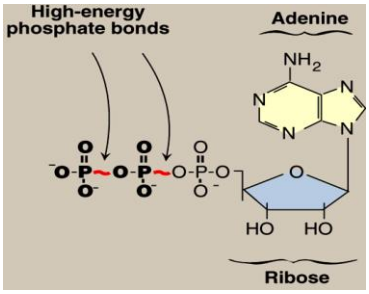
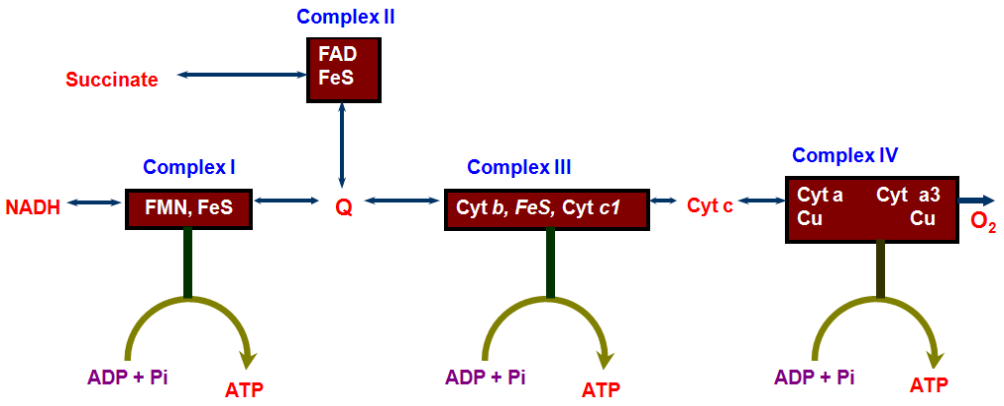
Unit II – Problem 3 – Biochemistry: Respiratory Chain and Oxidative Phosphorylation

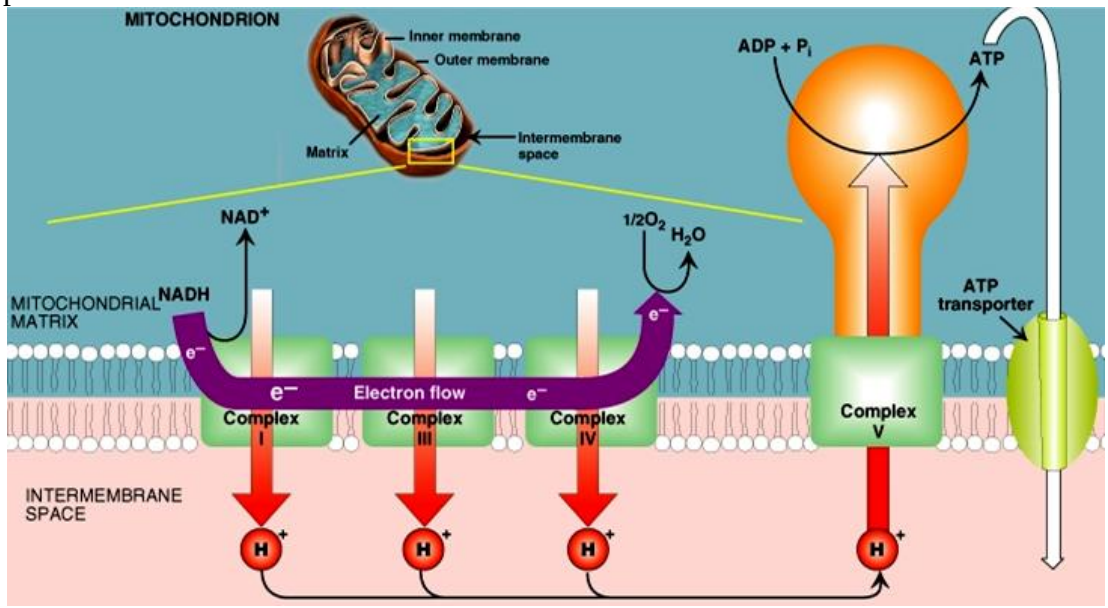
- **Bioenergetics الطاقة الحيوية:**
  - **Definition**: reactions associated with change in free energy (ΔG)
  - Reactions which generate energy are **exergonic (ΔG is negative).**
  - Reactions which consume energy are **endergonic (ΔG is positive).**
- **Adenosine Tri-Phosphate (ATP):**



  - Hydrolysis of one phosphate bond from ATP or ADP (but not from AMP) will release 7.3 kcal/mol.
  - Metabolism of major nutrients transfers electrons to co-enzymes NAD+ and FAD to form energy-rich NADH and $FADH_2$.
  - These are re-oxidized by transfer of electrons to respiratory chain to produce ATP.
- **The mitochondria has:**
  - **Outer membrane.**
  - **Inner membrane:**
    - ✓ Which is folded to form what is known as cristae.
    - ✓ The inner membrane is not permeable to most ions and intermediates (so they must have specific carriers or shuttles in case of transporting NADH generated from glycolysis from the cytosol to mitochondria).
- **What are the characteristics of electron transport chain?**
  - It is a set of specialized electron carriers arranged along the cristae into 4 complexes (I, II, III and IV) followed by ATP-synthase (which is usually considered as complex V).
  - Electron carriers are arranged according to their oxidation potentials.
  - The final acceptor of electron in this chain is oxygen (forming water H_2O).
  - **All electron carriers of the chain are fixed to the inner membrane of mitochondria except:**
    - ✓ Co-enzyme Q (ubiquinone).
    - ✓ Cytochrome C.
      These are non-protein lipid-constituents of the mitochondria.
  - **Cytochromes:**
    - ✓ They are arranged in an increasing redox potential in the chain as: Cyt b, Cyt c_1, Cyt c and Cyt $_{aa3}$
    - ✓ Notice that cytochrome C is the only soluble cytochrome, and with con-enzyme Q are the most mobile components of the chain.
    - ✓ Cytochrome oxidase with Cyt $_{aa3}$ forms the only irreversible reaction in the respiratory chain. This cytochrome has a very high affinity for oxygen and is inhibited by cyanide and carbon monoxide (CO) poisons with fatal consequences.



- **Energy production of the respiratory chain:**
  - NADH oxidized via NAD-linked dehydrogenase will yield 3 ATPs.
  - $FADH_2$ oxidized via FAD-linked dehydrogenase will yield 2 ATPs.
    These reactions are termed oxidative phosphorylation at the respiratory chain level.
- **Mechanism of oxidative phosphorylation:**
  - Respiratory chain complexes (I, II, III and IV) will act as proton (H^+) pumps.
  - This generates electrochemical potential difference across the mitochondrial membrane that stimulates a membrane located ATP-synthase (complex V), which in presence of ADP and Pi will form ATP.



- **Oxidation of extramitochondrial NADH:**
  - **NADH generated in glycolysis cannot penetrate the mitochondrial membrane (because the inner membrane is not permeable for most molecules). Two shuttles are used:**
    - ✓ Glycerophosphate shuttle.
    - ✓ Malate shuttle.
      Note: please try to look for more details about these shuttles.
- **Transport of ATP from the mitochondria to cytosol:**
  - ATP leaves the mitochondria in exchange with ADP + Pi
  - ADP + Pi is converted to ATP via ATP synthase using the energy or translocation of protons through ATP synthase.
- **Inhibitors of respiratory chain:**
  - Carbon monoxide (CO) and cyanide: inhibiting cytochrome oxidase and totally arresting respiration.
  - Uncouplers act via dissociation of oxidation from phosphrylation thus respiration is no longer limited by ADP and Pi concentrations.