**Oxidative Phosphorylation**

**15.1: The Thermodynamics of Oxidation-Reduction Reactions**

* Summarize the thermodynamics of oxidation-reduction reactions.
	+ Use standard reduction potential and concentration to calculate a substance’s tendency to become reduced. (calc. 15.1)
	+ Predict the direction of electron transfer in a mixture of two substances.
	+ Convert the change in reduction potential to the change in free energy for a reaction. (calc. 15.2)

**Reduction Potential: Electron Affinity**

* $E°'$ = standard reduction potential
* Higher $E°'$ = greater tendency to accept electrons (become reduced)

**The Nernst Equation**



*R* = Gas Constant = 8.3145 J  mol-1 K-1

*T* = temperature in Kelvin

*n* = # of electrons transferred (1-2)

*F* = Faraday’s constant = 96,485 J  V-1 K-1

**Free Energy Changes of Electron Transfers**





**15.2: Mitochondrial Electron Transport**

* Map the path of electrons through the redox groups of the electron transport pathway.
	+ Explain why the mitochondrion includes a variety of transport systems.
	+ Identify the sources of electrons for Complexes I, II and IV.
	+ Describe the mechanisms for transporting protons across the mitochondrial membrane.

**NADH Transport: Malate-Aspartate Shuttle**

* NADH cannot cross IM, so reducing equivalents are used to transport conserved energy
* Malate = reducing equivalent
* Cytosolic malate dehydrogenase vs. mitochondrial (citrate transport)

**Citrate Transport**

* ATP-citrate lyase undoes exergonic citrate synthase reaction
* Provides Acetyl-CoA for fatty acid synthesis (cytosolic)
* Pyruvate regenerated by cytosolic malic enzyme
* Citrate and pyruvate can cross the mitochondrial membrane via specific transport proteins.
* Provides acetyl-CoA for lipid synthesis = “acetyl-CoA shuttle”
* Pyruvate is regenerated

**ATP/ADP Transport: Adenine Nucleotide Translocase**

* ATP translocase protein imports ADP and exports ATP
* A symport protein permits simultaneous movement of P*i* and H+

**Complex I: NADH:ubiquinone oxidoreductase/NADH dehydrogenase**

* Transfers 1 pair of electrons from NADH to Q
* Largest protein in ETC (peripheral arm in matrix)
* Electron transport occurs in peripheral arm via prosthetic groups = redox centers
* Electrons travel from lower to higher reduction potentials
* 4 protons transferred from matrix to IM space via proton wire along membrane spanning helices
* Conformational changes in arm transmitted to membrane arm; protons travel via H-bonds (jumping) in protein and water molecules

**Complex III: ubiquinol:cytochrome *c* oxidoreductase/cytochrome *bc*1**

* Integral membrane protein; transfers 2 electrons from QH2 to 2 cytochrome *c* (peripheral)
* Cytochrome heme prosthetic group undergoes reversible single electron reduction (Fe3+/Fe2+)
* Electrons must travel alone, thus they split apart from QH2 in order to transfer via carriers to cytochrome *c1*
* Q cycle: sequential rounds of electron transfer
* Four protons translocated to IM space (two each round)

**The Q Cycle:**

* 2 electron transfer from QH2 to 2 cytochrome *c*
* 4 protons translocated to IM space (2 per QH2 each round)

**Complex IV: Cytochrome *c* Oxidase**

* Reduces O2 to H2O (4 electron transfer)
* Redox centers include heme groups and copper ions (Fe-Cu)
* E- travels from cyt c to Cu redox center, then to heme a group; reduction of O2 occurs in Fe-Cu center of heme)
* Consumes 4 protons from matrix via two proton wires; conformational changes precede proton relay
* Depletion of [proton]matrix and increase proton gradient across IM

**15.3: Chemiosmosis**

* Explain how the protonmotive force links electron transport and ATP synthesis.
	+ Describe the formation of the proton gradient.
	+ Relate the pH difference of the proton gradient to the free energy change. (calc. 15.3)

**15.4: ATP Synthase**

* Describe the structure and operation of ATP synthase.
	+ Recognize the structural components of ATP synthase.
	+ Identify the energy transformations that occur in ATP synthase.
	+ Describe the binding change mechanism.
	+ Explain why P:O ratios are nonintegral.
	+ Explain why oxidative phosphorylation is coupled to electron transport.

**Complex V: ATP Synthase**

* F0: H+ channel
* F1: ATP synthase

**Structure of ATP Synthase**

* F0: 1 alpha, 2 beta, c ring (varies)
* F1: 3 alpha + 3 beta
* Stalk: $γδε$
* Proton transport occurs via *c* ring rotation past *a* subunit
* C unit binds IM space proton, rotation allows release to matrix
* Rotation is driven by H+ gradient (rotation is reversible)

**Proton Transport by ATP Synthase**

* Proton binding by *c* subunit causes rotation away from (anticlockwise) *a* subunit
* Rotation causes release of previously bound proton into matrix

**The Binding Change Mechanism**

* Mechanical energy attaches phosphoryl group to ADP >>> chemical energy
* Rotation causes conformational changes, which alter affinity of $β$ subunits for nucleotides
* 3 different conformations (one each subunit):
* 1: loose: ADP and P*i* bind
* 2: tight: ATP formed (upon conformational shift; mechanical energy)
* 3: open: ATP released
* Cooperativity causes all subunits to change conformation simultaneously
* 1 ATP released per turn