BIOLOGICAL OXIDATION

INTRODUCTION

Cellular Metabolism

- Breakdown of macromolecules to simple subunits
- Breakdown of simple subunits to acetyl CoA (production of little ATP and NADH)
- Complete oxidation of acetyl CoA to H_2O and CO_2 (production of large amounts of ATP and NADH)

Bioenergetics/Biochemical Thermodynamics

Study of energy changes (transfer and utilization) in biochemical reactions

Exergonic Reactions

Energy is released

Endergonic Reactions

Energy is absorbed

Free Energy (ΔG)

Actual energy available for utilization in reactions

Enthalpy (ΔH)

Measure of the change in heat content of the reactants, compared to products

Entropy (ΔS)

- Change in the randomness or disorder of reactants and products
- Maximum value is observed at Equilibrium
- $\Delta G = \Delta H - T\Delta S$
- *T - absolute temperature in Kelvin (K = 273 + °C)*

Standard Free Energy (ΔG°)

Free energy change when the reactants or products are at a concentration of 1 mol/l at pH 7.0

HIGH ENERGY COMPOUNDS

Substances which possess sufficient free energy to liberate at least 7 Cal/mol at pH 7.0

LOW ENERGY COMPOUNDS

Compounds which liberate less than 7.0 Cal/mol

Compounds	*ΔG° (Cal/mol)*
High-energy phosphates	
Phosphoenol pyruvate	–14.8
Carbamoyl phosphate	–12.3
Cyclic AMP	–12.0
1,3-Bisphosphoglycerate	–11.8
Phosphocreatine	–10.3
Acetyl phosphate	–10.3
S-Adenosylmethionine*	–10.0
Pyrophosphate	–8.0
Acetyl CoA**	–7.7
ATP → ADP + Pi	–7.3
Low-energy phosphates	
ADP → AMP + Pi	–6.6
Glucose 1-phosphate	–5.0
Fructose 6-phosphate	–3.8
Glucose 6-phosphate	–3.3
Glycerol 3-phosphate	–2.2

High Energy Bonds

- Consists of acid anhydride bonds (mostly phosphoanhydride bonds)
- Formed by the condensation of two acidic groups or related compounds
- Free energy is liberated when these bonds are hydrolysed

Synthesis of ATP

Oxidative Phosphorylation

Major source of ATP in aerobic organisms

Associated with the mitochondrial electron transport chain

Substrate Level Phoshorylation

ATP are directly synthesized during substrate oxidation in the metabolism

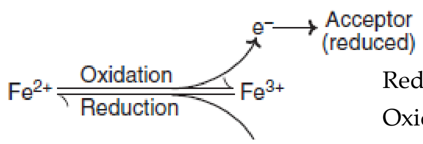
E.g.: phosphoenolpyruvate and 1,3-bisphosphoglycerate (intermediates of glycolysis) and succinyl CoA (of citric acid cycle)

BIOLOGICAL OXIDATION

- Process of transfer of electrons
- **Oxidation:** Removal of electrons
- **Reduction:** gain of electrons
- Oxidation is always accompanied by reduction of an e- acceptor

Redox Reactions

E.g.: Interconversion of ferrous ion (Fe^{2+}) to ferric ion (Fe^{3+})



Reducing agent = e- donating molecule

Oxidizing agent = e- accepting molecule

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Redox Potential/Oxidation Reduction Potential (E°)

- Measure of the tendency of a redox pair to lose or gain electrons
- Free energy change is proportional to the tendency of reactants to donate/accept e^{-s} denoted by E°
- Redox potential (E°) is directly proportional the change in the free energy (ΔG°)
- A reaction with a + ve ΔE° has a – ve ΔG° (exergonic)
- More negative redox potential has greater tendency (of reductant) to lose electrons
- More positive redox potential has a greater tendency (of oxidant) to accept electrons

ENZYMES INVOLVED (OXIDOREDUCTASES)

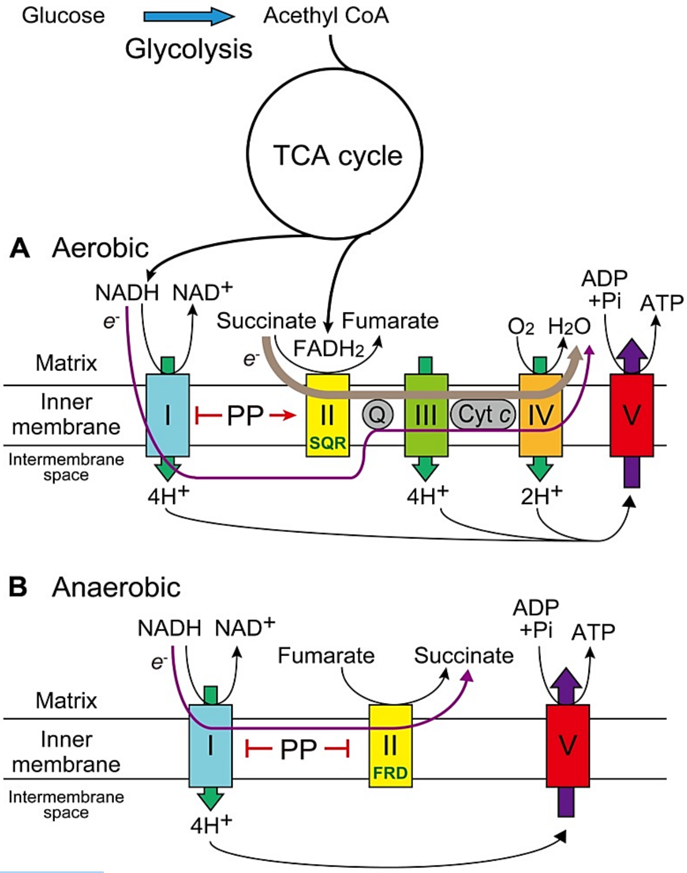
Enzyme	*Features*	*Examples*
Oxidases	• Use O_2 as an electron acceptor • Catalyse the elimination of hydrogen from the substrates which is accepted by oxygen	1. Cytochrome oxidase 2. Tyrosinase 3. Monoamine oxidase 4. L-amino acid oxidase (FMN) 5. Xanthine oxidase (FAD)
Dehydrogenases	• Cannot utilize oxygen as hydrogen acceptor • Catalyse the reversible transfer of hydrogen from one substrate to another	1. NAD+ dependent: Alcohol dehydrogenase, Glycerol 3-phosphate 2. Dehydrogenase 3. NADP+ dependent: HMG CoA reductase, Enoyl reductase 4. FMN dependent: NADH dehydrogenase 5. FAD dependent: Succinate dehydrogenase, Acyl CoA dehydrogenase 6. Cytochromes (except the terminal cytochrome oxidase)
Hydroperoxidases	Hydrogen peroxide is the substrate	1. Peroxidases 2. Catalases
Oxygenases	Catalyses the direct incorporation of oxygen into the substrate molecules	
	Dioxygenases • Incorporate both atoms of oxygen into the substrate	1. Homogentisate oxidase 2. L-tryptophan pyrrolase.
	Monooxygenases • Catalyse the incorporation of one atom of oxygen while the other oxygen atom is reduced to H_2O	1. Cytochrome P_{450} monooxygenase system of microsomes

ELECTRON TRANSPORT CHAIN (ETC)

- Series of membrane-bound electron carriers
- Embedded in mitochondrial inner membrane
- Electrons from NADH and $FADH_2$ are transferred to complexes of ETC
- Each complex transfers the electrons to the next complex in the chain

COMPONENTS/COMPLEXES

Complex	*Co-factors*	*Functions*
Complex I: NADH-CoQ reductase	FMN = 1 Fes = 22 - 24	Proton pump Electron transfer
Complex II: Succinate-CoQ reductase	FAD = 1 Fes = 8	Only Electron transfer No sufficient energy for proton pump function
Complex III: CoQ-cytochrome C reductase	Fes = 2 Cyt-b_{562} Cyt-b_{566} Cyt-C_1	Proton pump Electron transfer
Complex IV: Cytochrome C oxidase	Cyt-a Cyt-a_3 Copper ions	Proton pump Electron transfer



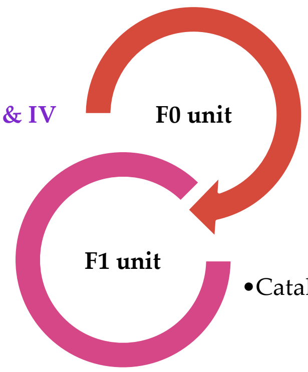
ADP:O / P:O RATIO

- Number of inorganic phosphate molecules utilized for ATP generation for every atom of oxygen consumed
- Represents the number of ATP synthesized per pair of electrons carried through ETC

Molecule	*P:O Ratio*
NADH	2.5
$FADH_2$	1.5

ATP SYNTHASE/ATPase

- Hydrolyse ATP to ADP and Pi
- Sites of ATP synthesis are – **Complexes I, III & IV**
- ATP synthase has 2 units



- Inhibited by oligomycin
- Acts as proton channel

- Catalyzes ATP synthesis

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