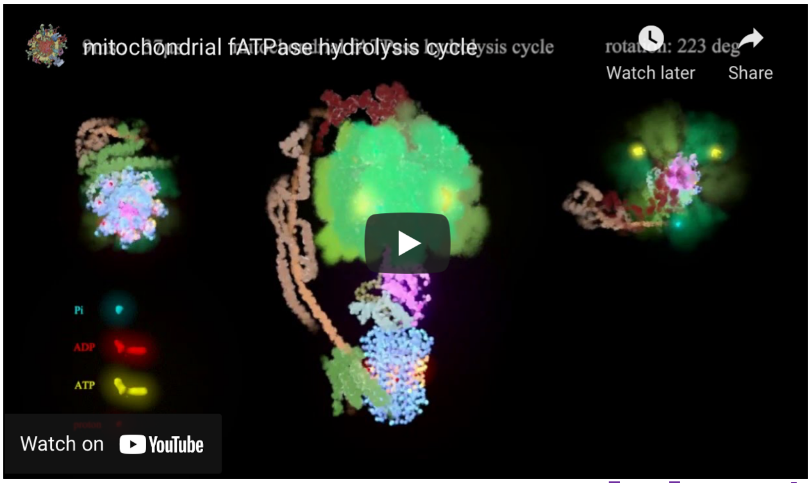
Phosphorylation

The Respiratory Chain and ATP Synthase Produce ATP by a Chemiosmotic Mechanism



Animation of ATP Synthase

(https://www.youtube.com/watch?v=E1qTSwc1o3U)

- Every F_0 turn uses 8-17 H^+
- Every turn gets 3 ATP
- Additional 3 H^+ to transport P_i

BI/CH 422/622

OUTLINE:

Pyruvate
- pyruvate dehydrogenase

Krebs' Cycle
- How did he figure it out?
- Overview
- 8 Steps
- Energetics
- Regulation
- Summary

Oxidative Phosphorylation
- Energetics (–0.16 V needed for making ATP)
- Mitochondria
- Transport (2.4 kcal/mol needed to transport H+ out)
- Electron transport
  - Discovery
  - Four Complexes
    - Complex I: NADH→ $CoQH_2$
    - Complex II: Succinate→ $CoQH_2$
    - Complex III: $CoQH_2$→ Cytochrome C (Fe^{2+})
    - Complex IV: Cytochrome C (Fe^{2+}) → H_2O
- Chemiosmotic theory
  - ATPase
  - Mitchell Hypothesis
  - Binding-Change Model
  - Connection to the proton motive force
- Net ATP production
- Regulation

OUTLINE:

Lipid Degradation (Catabolism)
- FOUR stages in the catabolism of lipids:
  - Mobilization from tissues (mostly adipose)
  - Activation of fatty acids
  - Transport
  - Oxidation

Exam-2 material

Oxidative Phosphorylation

Net Production of ATP via Catabolic Pathways

TABLE 19-5 ATP Yield from Complete Oxidation of Glucose *

Process	Direct product	Final ATP
Glycolysis	2 NADH (cytosolic) 2 ATP	3 or 5[a] 2
Pyruvate oxidation (two per glucose)	2 NADH (mitochondrial matrix)	5
Acetyl-CoA oxidation in citric acid cycle (two per glucose)	6 NADH (mitochondrial matrix) 2 $FADH_2$ 2 GTP	15 3 2
Total yield per glucose		30 or 32

[a]If the malate/aspartate shuttle is used to transfer reducing equivalents into the mitochondrion, yield is 5 ATP. If the glycerol 3-phosphate shuttle is used, the yield is 3 ATP.

- Every F_0 turn uses 8-17 H^+
- Every turn gets 3 ATP
- Additional 3 H^+ to transport P_i

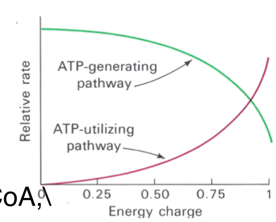
What is the yield for c_{17}?

*
- This Table assumes F_0 is c_9 and uses 9 H^+ per turn
- Additional 3 H^+ to transport P_i needs 12 H^+ per 3 ATP
- This is 4 H^+ per ATP
- NADH pumps10 H^+, so 10/4 = 2.5 ATP/NADH oxidized

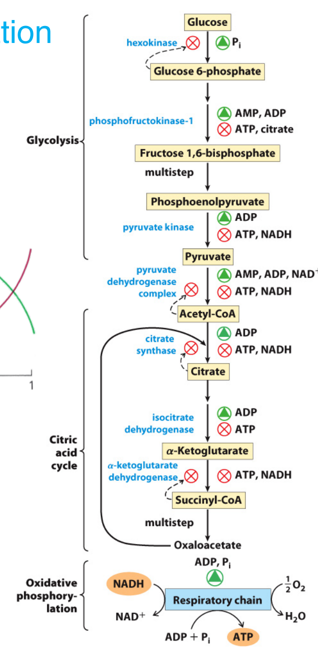
Oxidative Phosphorylation

- Primarily regulated by substrate availability
  - NAD^+ and ADP/P_i
- Inhibition of OxPhos leads to accumulation of NADH.
  - causes feedback inhibition cascade up to PFK-1 in Glycolysis

Local feedback inhibition
  - Succ-CoA, Citrate, Ac-CoA, and Glc6P.
- Inhibitor of F_1 (IF_1)
  - prevents hydrolysis of ATP during low oxygen
  - IF_1 only active at lower pH in matrix, encountered when electron transport is stalled (i.e., low oxygen)



Regulation

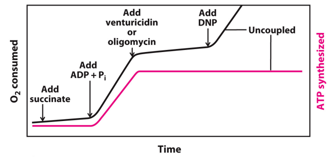


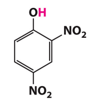
Oxidative Phosphorylation

UNCOUPLING

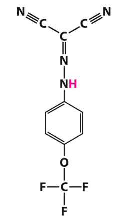
Chemically uncoupling ET and ATP biosynthesis:

Recall:



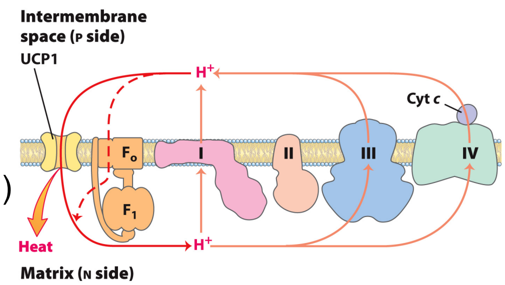


2,4-Dinitrophenol (DNP)



Carbonylcyanide-*p*-trifluoromethoxyphenylhydrazone (FCCP)

- In addition to chemical uncouplers (DNP & FCCP), there are times when uncoupling is needed physiologically
- Uncoupling protein 1 (UCP-1) in babies
- Hibernating animals



Summary:Oxidative Phosphorylation

We learned that:

- the reduced cofactors pass electrons into the electron-transport chain in mitochondria
- stepwise electron transport is accompanied by the directional transport of protons across the membrane against their concentration gradient
- the energy in the electrochemical proton gradient drives synthesis of ATP by coupling the flow of protons via ATP synthase to conformational changes that favor formation of ATP in the active site

End of material for Exam 2

Lipid Degradation