Chapter 10

Chemotrophic Energy Metabolism: Aerobic Respiration
Figure 10-1

1. GLYCOLYSIS

Glucose → Pyruvate

2. PYRUVATE OXIDATION

Pyruvate → Acetyl CoA

3. TCA CYCLE

Acetyl CoA → CO₂

4. ELECTRON TRANSPORT AND PROTON PUMPING

CO₂ → H₂O

5. ATP SYNTHESIS

H₂O → ATP + P

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Figure 10-6

THE TCA CYCLE

Pyruvate → Acetyl CoA → Oxaloacetate → Citrate → Succinate → ATP

Reactions involving NAD⁺ and FAD

NAD⁺ + H⁺ → NADH + H⁺

Energy production through ATP synthesis.
The conversion of pyruvate to acetyl CoA can be summarized as follows:

\[
\text{CoA} - \text{SH} + \text{Pyruvate} \rightarrow \text{CoA} - \text{S} - \text{CH}_3 + \text{CO}_2
\]
Figure 10-7

Pantothenic acid

CH₂
CH₂
H
N
C=O
CH₂
H
C=O
H
C=OH
CH₃
C=CH₃
CH₂
O
O
O
CH₂
O
OH
O
PO₄
O
PO₄
PO₄

Sulphydryl group
Thioester group
Acetyl CoA formation
Acetyl CoA
Acetyl group from pyruvate

Pyrophosphate bridge

Coenzyme A

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Figure 10-8

THE TCA CYCLE

Enzymes That Catalyze These Reactions
PDH: Pyruvate dehydrogenase complex
TCA-1: Citrate synthase
TCA-2: Aconitase
TCA-3: Isocitrate dehydrogenase
TCA-4: α-ketoglutarate dehydrogenase
TCA-5: Succinyl CoA synthetase
TCA-6: Succinate dehydrogenase
TCA-7: Fumarate hydratase
TCA-8: Malate dehydrogenase
Figure 10-9

Riboflavin (oxidized form) + 2 [H] \rightarrow \text{Reduction}\rightarrow \text{Oxidation} \rightarrow \text{Riboflavin (reduced form)}

FAD

Pyrophosphate bridge
Summing Up: The Products of the TCA Cycle Are CO$_2$, ATP, NADH, and FADH$_2$

- The TCA cycle accomplishes the following:

1. Two carbons enter the cycle as acetyl CoA, which joins oxaloacetate to form the six-carbon citrate

2. Decarboxylation occurs at two steps to balance the input of two carbons by releasing two CO$_2$

3. Oxidation occurs at four steps, with NAD$^+$ the electron acceptor in three steps and FAD in one
The Products of the TCA Cycle Are \( \text{CO}_2 \), ATP, NADH, and FADH\(_2\) (continued)

- The TCA cycle accomplishes the following:

  4. ATP is generated at one point, with GTP as an intermediate in the case of animal cells

  5. One turn of the cycle is completed as oxaloacetate, the original 4C acceptor, is regenerated
Regulation of acetyl CoA

- Overall availability of acetyl CoA is determined mainly by the activity of the PDH complex

- PDH is allosterically inhibited by ATP, NADH, and acetyl CoA and high [ATP/ADP] (enzyme: PDH kinase)

- It is activated by AMP, NAD\(^+\), and free CoA and low [ATP/ADP] (enzyme: PDH phosphatase)
Enzymes That Catalyze These Reactions

E₁: PDH phosphatase
E₂: PDH kinase
All other enzymes as in Figure 10-8.
Electron Transport and Coenzyme Oxidation

- Electron transport involves the highly exergonic oxidation of NADH and FADH$_2$ with O$_2$ as the terminal electron acceptor and so accounts for the formation of water

- $\text{NADH} + \text{H}^+ + \frac{1}{2}\text{O}_2 \rightarrow \text{NAD}^+ + \text{H}_2\text{O}$
  $\Delta G^\circ' = -52.4 \text{ kcal/mol}$

- $\text{FADH}_2 + \frac{1}{2}\text{O}_2 \rightarrow \text{FAD} + \text{H}_2\text{O}$
  $\Delta G^\circ' = -45.9 \text{ kcal/mol}$
<table>
<thead>
<tr>
<th>Redox Pair (oxidized form → reduced form)</th>
<th>No. of Electrons</th>
<th>( E'_0 ) (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetate → pyruvate</td>
<td>2</td>
<td>-0.70</td>
</tr>
<tr>
<td>Succinate → α-ketoglutarate</td>
<td>2</td>
<td>-0.67</td>
</tr>
<tr>
<td>Acetate → acetaldehyde</td>
<td>2</td>
<td>-0.60</td>
</tr>
<tr>
<td>3-phosphoglycerate →</td>
<td>2</td>
<td>-0.55</td>
</tr>
<tr>
<td>glyceraldehyde-3-P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-ketoglutarate → isocitrate</td>
<td>2</td>
<td>-0.38</td>
</tr>
<tr>
<td>NAD(^+) → NADH</td>
<td>2</td>
<td>-0.32</td>
</tr>
<tr>
<td>FMN → FMNH(_2)</td>
<td>2</td>
<td>-0.30</td>
</tr>
<tr>
<td>1,3-bisphosphoglycerate →</td>
<td>2</td>
<td>-0.29</td>
</tr>
<tr>
<td>glyceraldehyde-3-P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaldehyde → ethanol</td>
<td>2</td>
<td>-0.20</td>
</tr>
<tr>
<td>Pyruvate → lactate</td>
<td>2</td>
<td>-0.19</td>
</tr>
<tr>
<td>FAD → FADH(_2)</td>
<td>2</td>
<td>-0.18</td>
</tr>
<tr>
<td>Oxaloacetate → malate</td>
<td>2</td>
<td>-0.17</td>
</tr>
<tr>
<td>Fumarate → succinate</td>
<td>2</td>
<td>-0.03</td>
</tr>
<tr>
<td>(2H^+) → H(_2)</td>
<td>2</td>
<td>0.00**</td>
</tr>
<tr>
<td>CoQ → CoQH(_2)</td>
<td>2</td>
<td>+0.04</td>
</tr>
<tr>
<td>Cytochrome (b) (Fe(^{3+}) → Fe(^{2+}))</td>
<td>1</td>
<td>+0.07</td>
</tr>
<tr>
<td>Cytochrome (c) (Fe(^{3+}) → Fe(^{2+}))</td>
<td>1</td>
<td>+0.25</td>
</tr>
<tr>
<td>Cytochrome (a) (Fe(^{3+}) → Fe(^{2+}))</td>
<td>1</td>
<td>+0.29</td>
</tr>
<tr>
<td>Cytochrome (a_1) (Fe(^{3+}) → Fe(^{2+}))</td>
<td>1</td>
<td>+0.55</td>
</tr>
<tr>
<td>Fe(^{3+}) → Fe(^{2+}) (inorganic iron)</td>
<td>1</td>
<td>+0.77</td>
</tr>
<tr>
<td>(\frac{1}{2}O_2) → H(_2)O</td>
<td>2</td>
<td>+0.816</td>
</tr>
</tbody>
</table>

*Each \( \Delta E'_0 \) value is for the following half-reaction, where \( n \) is the number of electrons transferred:

- oxidized \( + nH^+ + ne^- \) → reduced form.

**By definition, this redox pair is the reference point for determining values of all other redox pairs. It requires that [H\(^+\)] = 1.0 M and therefore specifies pH 0.0. At pH 7.0, the value for the 2H\(^+\)/H\(_2\) pair is -0.42 V.
(a) Complex I receives 2 electrons from NADH and passes them to CoQ via FMN and an Fe-S protein. During this process, 4 $H^+$ are pumped out of the matrix by complex I.
Figure 10-16B

(b) Complex III passes electrons from CoQH$_2$ to cytochrome c via cytochromes b and c$_1$ and an Fe-S protein. CoQH$_2$ carries 2 H$^+$ across the inner membrane and 2 more H$^+$ are pumped out of the matrix.
(c) Complex IV receives electrons from cytochrome c and, via cytochrome a and a₃, passes them to molecular oxygen, which is reduced to water as 2 more H⁺ are pumped from the matrix by complex IV.
(d) ATP synthase uses the energy from the proton gradient generated during electron transport to synthesize ATP from ADP and $P_i$. 
Respiratory Control of Electron Transport

• The availability of ADP regulates the rate of oxidative phosphorylation and thus of electron transport

• This is called respiratory control

• Electron transport and ATP generation will be favored when ADP concentration is high and inhibited when ADP concentration is low
The Chemiosmotic Model: The “Missing Link” Is a Proton Gradient

• In 1961 Peter Mitchell proposed the chemiosmotic coupling model

• The essential feature of the model is that the link between electron transport and ATP formation is the electrochemical potential across a membrane

• The electrochemical potential is created by the pumping of protons across a membrane as electrons are transferred through the respiratory complexes
Coenzyme Oxidation Pumps Enough Protons to Form 3 ATP per NADH and 2 ATP per FADH$_2$

- The transfer of two electrons from NADH is accompanied by the pumping of a total of 10 protons (12 if the Q cycle is operating)

- The number of protons required per molecule of ATP is thought to be 3 or 4, with 3 regarded as most likely

- So, about 3 molecules of ATP are synthesized per NADH oxidized
Number of ATP generated is an estimate

- FADH$_2$ donates electrons to **complex II** with higher reduction potential, pumping 6 protons (8 if the Q cycle is operating)

- So about 2 ATP are synthesized per FADH$_2$

- These values are estimates, affected by an organism’s specific ATP synthase and other factor
The Chemiosmotic Model Is Affirmed by an Impressive Array of Evidence

- Since its initial formulation, the chemiosmotic model has become universally accepted as the link between electron transport and ATP synthesis

- Several lines of evidence support the mode
1. Electron Transport Causes Protons to Be Pumped Out of the Mitochondrial Matrix

- Mitchell and Moyle demonstrated experimentally that the flow of electrons through the ETS is accompanied by the unidirectional pumping of protons across the inner mitochondrial membrane.

- One mechanism involves allosteric changes in protein conformation as electrons are transferred, allowing protons to be moved to the outer surface of the membrane.
2. Components of the Electron Transport System Are Asymmetrically Oriented Within the Inner Mitochondrial Membrane

- Electron carriers of the ETS must be asymmetrically oriented in the membrane.
- Otherwise, protons would be pumped randomly in both directions.
- Labeling studies show that some parts of the respiratory complexes face inward, some are transmembrane proteins, others face outward.
3. Membrane Vesicles Containing Complexes I, III, or IV Establish Proton Gradients

- Vesicles can be reconstituted from various components of the ETS

- Vesicles that contain complex I, III, or IV are able to pump protons out of the vesicle, if provided with an appropriate oxidizable substrate
4. Oxidative Phosphorylation Requires a Membrane-Enclosed Compartment

- Without the mitochondrial membrane, the protein gradient that drives ATP synthesis could not be maintained.

- Electron transfer carried out by isolated complex cannot be coupled to ATP synthesis unless the complexes are incorporated into membranes that form enclosed vesicles.
5. Uncoupling Agents Abolish Both the Proton Gradient and ATP Synthesis

- Dinitrophenol (DNP) is known to uncouple ATP synthesis from electron transport
- When membranes are treated with DNP, they allow protons to cross the membrane freely, so that no proton gradient can be formed
- ATP synthesis is abolished as well
6. The Proton Gradient Has Enough Energy to Drive ATP Synthesis

• The electrochemical proton gradient across the membrane involves both a membrane potential and a concentration gradient

• A mitochondrion actively respiring has a membrane potential of about 0.16V (positive on the intermembrane space side) and a pH gradient of about 1.0 (higher on the matrix side)
Proton motive force

- The electrochemical gradient exerts a **proton motive force (pmf)**, that tends to drive protons back down their concentration gradient (back into the matrix)

- $\text{pmf} = V_m + 2.303 \, RT \, \Delta \text{pH}/F$
Proton motive force in a mitochondrion

• In a mitochondrion that is undergoing aerobic respiration, the pmf can be calculated:

\[
\text{pmf} = 0.16 + \left( \frac{2.303(1.987)(37 + 273)(1.0)}{23,062} \right)
\]

\[
= 0.16 + 0.06 = 0.22 \text{ V}
\]

• Note that the membrane potential accounts for more than 70% of the pm
Pmf can be used to calculate $\Delta \ G^o'$

- The pmf can be used to calculate $\Delta \ G^o'$ as follows:

$$\Delta G^o' = -nF(pmfa) = -(23.062)(0.22) = -5.1 \text{ kcal/mol}$$

- $\Delta \ G'$ for phosphorylation of ADP is about 10–14 kcal/mol, so 3 or 4 protons would produce enough free energy to produce ATP
7. Artificial Proton Gradients Are Able to Drive ATP Synthesis in the Absence of Electron Transport

• Direct evidence for the model comes from work using vesicles or mitochondria that are exposed to artificial pH gradients

• When the external proton concentration is increased, ATP is generated in response

• So, ATP can be generated by a proton gradient, even when electron transport is not taking place
ATP Synthesis: Putting It All Together

• Some of the energy of glucose is transferred to reduced coenzymes during glycolysis and the TCA cycle

• This energy is used to generate an electrochemical proton gradient across the inner mitochondrial membrane

• The pmf of that gradient is harnessed to make ATP
F₁ Particles Have ATP Synthase Activity

- Racker and colleagues took intact mitochondria and disrupted the membrane to form small vesicles called *submitochondrial particles*.

- These particles could carry out electron transport and ATP synthesis.

- By mechanical agitation or protease treatment, the F₁ structures were isolated from the membranes.
Figure 10-18A

(a) Intact mitochondrion
Electron transport? Yes
ATP synthesis? Yes

Disruption
Figure 10-18B

(b) Submitochondrial particles
Electron transport? Yes
ATP synthesis? Yes
ATPase activity? No
Figure 10-18C

- Inner mitochondrial membrane
- Outer mitochondrial membrane

(c) Dissociated particles
  - Electron transport? Yes
  - ATP synthesis? No
  - ATPase activity? Yes
Uncoupling synthesis of ATP and electron transport

- $F_1$ particles and membranous vesicles were separated by centrifugation

- The membranes could still carry out electron transport, but could not synthesize ATP

- The isolated $F_1$ particles could synthesize ATP but could not carry out electron transport
Figure 10-18D

(d) Membranous fraction
Electron transport? Yes
ATP synthesis? No
ATPase activity? No
Figure 10-18E

(e) Soluble fraction with $F_1$ spheres
Electron transport? No
ATP synthesis? No
ATPase activity? Yes
Reconnecting synthesis of ATP and electron transport

- Separated $F_1$ particles and membranous vesicles were reconstituted
- The reconstituted structures were capable of both electron transport and ATP synthesis
- The $F_1$ particles were called *coupling factors* and are now known to have ATP synthesizing activity
Figure 10-18E

(e) Soluble fraction with $F_1$ spheres
Electron transport? No
ATP synthesis? No
ATPase activity? Yes
Figure 10-18F

(f) Reconstituted particles
Electron transport? Yes
ATP synthesis? Yes
ATPase activity? No
The $F_o F_1$ Complex: Proton Translocation Through $F_o$ Drives ATP Synthesis by $F_1$

- The $F_1$ complex is not directly membrane-bound, but is attached to the $F_o$ complex that is embedded in the inner membrane.

- $F_o$ acts as a **proton translocator**, the channel through which protons flow across the membrane.
The $F_oF_1$ ATP synthase

- $F_o$ provides a channel for exergonic flow of protons across the membrane
- $F_1$ carries out the ATP synthesis, driven by the energy of the proton gradient
- Together, they form a complete ATP synthase
(a) The $F_o$ static component consists of one $a$ and two $b$ subunits. The $a$ subunit forms the proton channel and is immobilized in the membrane. The $b$ subunits form the peripheral stalk and are attached both to the $a$ subunit and to $F_1$.

(b) The $F_o$ mobile component consists of a ring of 10 $c$ subunits. Only one $c$ subunit can form an ionic bond with the $a$ subunit at a time. For each proton translocated, the ring rotates one-tenth of a turn as the adjacent $c$ subunit in the ring bonds with the $a$ subunit.

(c) The $F_1$ static component consists of the $\delta$ subunit plus a catalytic ring formed by a hexagon of alternating $\alpha$ and $\beta$ subunits. The $\alpha_3\beta_3$ ring is the site of ATP synthesis and is immobilized by the $\delta$ subunit, which connects it to the $b_2$ peripheral stalk of $F_o$.

(d) The $F_1$ mobile component consists of the $\epsilon$ and $\gamma$ subunits, which form the central stalk that is firmly attached to the $c_{10}$ ring of $F_o$. As proton translocation turns the $c_{10}$ ring, the $\gamma$ subunit rotates inside the $\alpha_3\beta_3$ catalytic ring of $F_1$. 
(a) The $F_o$ static component consists of one $a$ and two $b$ subunits. The $a$ subunit forms the proton channel and is immobilized in the membrane. The $b$ subunits form the peripheral stalk and are attached both to the $a$ subunit and to $F_1$. 

INTERMEMBRANE SPACE

H$^+$

ADP + $P_i$ → ATP

MATRX
(b) The $F_0$ mobile component consists of a ring of 10 $c$ subunits. Only one $c$ subunit can form an ionic bond with the $a$ subunit at a time. For each proton translocated, the ring rotates one-tenth of a turn as the adjacent $c$ subunit in the ring bonds with the $a$ subunit.
(c) The F₁ static component consists of the δ subunit plus a catalytic ring formed by a hexagon of alternating α and β subunits. The α₃β₃ ring is the site of ATP synthesis and is immobilized by the δ subunit, which connects it to the b₂ peripheral stalk of F₀.
**Figure 10-19D**

(d) The $F_1$ mobile component consists of the $\epsilon$ and $\gamma$ subunits, which form the central stalk that is firmly attached to the $c_{10}$ ring of $F_0$. As proton translocation turns the $c_{10}$ ring, the $\gamma$ subunit rotates inside the $\alpha_3\beta_3$ catalytic ring of $F_1$. 
Video: Rotation of ATP Synthase
Use windows controls to play
ATP Synthesis by $F_0F_1$ Involves Physical Rotation of the Gamma Subunit

- Paul Boyer proposed the **binding change model** in 1979.

- He proposed that each of the three $\beta$ subunits of the $F_1$ complex progresses through three different conformations.

- Each conformation has distinct affinities for the substrates, ADP and Pi, and the product, ATP.
The three conformations

- Boyer named the conformations

  - L (for loose), which binds ADP and Pi loosely

  - T (for tight), which binds ADP and Pi tightly and catalyzes the formation of ATP

- O (for open), with little affinity for either substrates or product
Rotation of $\alpha$ and $\beta$ with respect to $\gamma$

- Boyer proposed that at any time, each of the active sites is in a different conformation and the hexagonal ring of $\alpha$ and $\beta$ subunits rotates relative to the central stalk containing the $\gamma$ subunit.

- The rotation was thought to be driven by the flow of protons through $F_o$.

- It is now known that it is the $\gamma$ subunit that actually rotates.
The Binding Change Model in Action

• Each $\beta$ subunit passes through the O, L, and T conformations as the $\gamma$ subunit rotates 360 degrees.

• In $F_o$, the 10 $c$ subunits each have an asp residue with an ionic bond to an arg residue on the immobile $a$ subunit.

• When taken up, a proton neutralizes the asp, disrupting the ionic bond, and rotating the $c_{10}$ ring (and attached $\gamma$ subunit) 1/10$^{th}$ turn.
The binding change model (continued)

- As the ring turns, the asp in the adjacent residue loses a proton and forms an ionic bond to arg in the \( a \) subunit

- As 10 protons pass through the membrane via the \( a \) subunit, the ring goes through one complete rotation
Steps of the model

- Step 1a: The $\beta_1$ subunit in the O conformation shifts to the L conformation (loosely binding ADP and $P_i$) when the flow of protons through $F_o$ causes a 120-degree rotation of the $\gamma$ subunit.

- Step 1b: ATP is synthesized by $\beta_3$.

- Step 2a: The $\gamma$ subunit rotates another 120 degrees, inducing $\beta_1$ to shift to the T conformation.
Steps of the model (continued)

• Step 2b: The $\beta_1$ subunit has an increased affinity for ADP and $P_i$, allowing spontaneous formation of ATP

• Step 3a: The $\gamma$ subunit rotates another 120 degrees, inducing $\beta_1$ to shift to the O conformation, releasing ATP

• Following ATP generation by the $\beta_2$ unit (step 3b), the cycle is complete
A 120° rotation of the γ subunit converts the β₁ subunit into its L conformation, causing loose binding of ADP and Pᵢ.

Proton flux through Fₚₗ; γ rotates 120°

3a A third 120° rotation of the γ subunit returns the β₁ subunit to the O conformation and results in release of the newly formed ATP molecule.

Proton flux through Fₚₗ; γ rotates 120°

2b This results in the condensation of ADP and Pᵢ into a molecule of ATP at the β₁ catalytic site.

A second 120° rotation of the γ subunit induces a shift of β₁ to the T conformation, causing tight binding of ADP and Pᵢ to its catalytic site.

3b ATP is then synthesized by the β₂ subunit, completing one full cycle of catalysis.

1b At this point, ATP is synthesized by one of the other subunits (β₃) and released by yet another of the subunits (β₂).
Spontaneous Synthesis of ATP?

- Each of the three steps at which ATP is formed occurs without a direct input of energy.

- However, ATP synthesis is highly endergonic (*in dilute aqueous solution*).

- The catalytic site of a β subunit is such that the charge repulsion between ADP and Pᵢ is minimized, favoring ATP formation with a $\Delta G^o$ close to zero.
Synthesis of ATP without thermodynamic cost?

• ATP synthesis does not proceed without thermodynamic cost

• The needed input of energy occurs elsewhere in the cycle

• Energy comes from the proton gradient generated by electron transport and transmitted through rotation of the $\gamma$ subunit
Synthesis of ATP without thermodynamic cost?

- ATP synthesis does not proceed without thermodynamic cost

- The needed input of energy occurs elsewhere in the cycle

- Energy comes from the proton gradient generated by electron transport and transmitted through rotation of the $\gamma$ subunit
Figure 10-21

\[
\text{ADP} + P_i + H^+ \rightarrow \text{ATP} + H_2O \\
\Delta G^{\circ'} = +7.3 \text{ kcal/mol}
\]

(a) ATP synthesis in dilute aqueous solution

\[
\Delta G^{\circ'} \approx 0 \text{ kcal/mol}
\]

(b) ATP synthesis from protein-bound ADP and \( P_i \)
The Chemiosmotic Model Involves Dynamic Transmembrane Proton Traffic

- There is continuous, dynamic two-way proton traffic across the inner membrane.

- NADH sends 10 protons across via complexes I, III, and IV; FADH$_2$ sends 6 across, via complexes II, III, and IV.

- Assuming that 3 protons must return through F$_{0}$F$_{1}$ per ATP generated, this means 3 ATP per NADH and 2 per FADH$_2$ are generated.
Aerobic Respiration: Summing It All Up

- As carbohydrates and fats are oxidized to generate energy, coenzymes are reduced

- These reduced coenzymes represent a storage form of the energy released during oxidation

- This energy can be used to drive ATP synthesis as the enzymes are reoxidized by the ETS
Summing it all up (continued)

• As electrons are transported from NADH or FADH$_2$ to O$_2$, they pass through respiratory complexes where proton pumping is coupled to electron transport

• The resulting electrochemical gradient exerts a pmf that serves as the driving force for ATP synthesis
The Maximum Yield of Aerobic Respiration Is 38 ATPs per glucose

- The **maximum ATP yield** per glucose under aerobic conditions:

\[ 10\text{NADH} + 10\text{H}^+ + 2\text{FADH}_2 + 6\text{O}_2 + 34\text{ADP} + 34\text{P}_i \rightarrow 10\text{NAD}^+ + 2\text{FAD} + 12\text{H}_2\text{O} + 34\text{ATP} \]

- Including the summary reactions of glycolysis and the TCA cycle to this gives:

\[ \overset{38\text{ADP} + 38\text{P}_i}{\text{C}_6\text{H}_{12}\text{O}_6} \quad \overset{38\text{ATP}}{\rightarrow} \quad 6\text{CO}_2 \quad + \quad 6\text{H}_2\text{O} \]
1. Why Does the Maximum ATP Yield in Eukaryotic Cells Vary Between 36 and 38 ATPs Per Glucose?

- Glycolysis produces two NADH per glucose in the cytosol, and catabolism of pyruvate produces eight more in the mitochondrial matrix.

- NADH in the cytosol cannot enter the matrix to deliver its electrons to complex I.

- Instead, the electrons and H\(^+\) ions are passed inward by an electron shuttle system.
Electron shuttle systems

- There are several electron shuttle systems that differ in the number of ATP molecules formed per NADH molecule oxidized.

- Electron shuttle systems consist of one or more electron carriers that can be reversibly reduced, with transport proteins in the membrane for both reduced and oxidized forms of carrier.
The glycerol phosphate shuttle

- The **glycerol phosphate shuttle** is one type of electron shuttle

- NADH in the cytosol reduces dihydroxyacetone phosphate (DHAP) to glycerol-3-phosphate, which is transported into the mitochondrion

- There it is reoxidized to DHAP using FAD, so the electrons bypass complex I, generating 2 ATP instead of 3
2. Why Is the ATP Yield of Aerobic Respiration Referred to as the “Maximum Theoretical ATP Yield”? 

- Yields of 36 to 38 ATP per glucose are possible, only if the energy of the electrochemical gradient is only used for ATP synthesis.

- This is not realistic, because the pmf of the proton gradient is used for other processes too, as needed by the cell.
Figure 10-24C

(c) Tricarboxylate carrier

Citrate

Isocitrate

Citrate

Isocitrate
Figure 10-24E
Aerobic Respiration Is a Highly Efficient Process

- To determine efficiency of respiration, we need to determine how much of the energy of glucose is preserved in the resulting 36–38 ATP

- $\Delta G^0'$ for glucose $\rightarrow CO_2 + H_2O$ is $-686$ kcal/mol

- ATP hydrolysis under cellular conditions is about $-10$ to $-14$ kcal/mol
Efficiency of aerobic respiration

- For 36–38 ATP, assuming a value of 10 kcal/mol, the energy per mole of glucose is about 360–380 kcal conserved.

- This efficiency of 52–55% is well above that obtainable from the most efficient machines created.