Respiration occurs in three metabolic stages:

1. glycolysis
2. Krebs cycle (aka Citric Acid Cycle)
3. Electron transport chain
**Glycolysis** occurs in the cytoplasm.

- It begins catabolism by breaking glucose into two molecules of pyruvate.

**The Krebs Cycle** occurs in the mitochondrial matrix.

- It degrades pyruvate to carbon dioxide.

- Both of these stages produce NADH which will transfer electrons to the **Electron Transport Chain**.
ELECTRON TRANSPORT CHAIN

the electrons move from molecule to molecule until they combine with oxygen and hydrogen ions to form water.

• As they are passed along the chain, the energy carried by these electrons is stored in the mitochondrion in a form that can be used to synthesize ATP via OXIDATIVE PHOSPHORYLATION.

Who knows what oxidative phosphorylation means?

• Oxidative phosphorylation produces almost 90% of the ATP generated by respiration.
• Some ATP is also generated in glycolysis and the Krebs cycle by **SUBSTRATE-LEVEL PHOSPHORYLATION**.

• Here an enzyme transfers a phosphate group from an organic molecule (the substrate) to ADP, forming ATP.

Fig. 9.7
The steps of Glycolysis

1. glucose, a six carbon-sugar, is split into two three-carbon sugars.

2. These smaller sugars are oxidized and rearranged to form two molecules of pyruvate.
   - Each of the ten steps in glycolysis is catalyzed by a specific enzyme.
   - These steps can be divided into two phases: an energy investment phase and an energy payoff phase.
In the energy investment phase, ATP provides activation energy by phosphorylating glucose.

- This requires 2 ATP per glucose.

In the energy payoff phase, ATP is produced by substrate-level phosphorylation and NAD$^+$ is reduced to NADH.

- 4 ATP (net) and 2 NADH are produced per glucose.
Fig. 9.9a

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Fig. 9.9b
• The net yield from glycolysis is 2 ATP and 2 NADH per glucose.
  
  • No CO₂ is produced during glycolysis.

• Glycolysis occurs whether O₂ is present or not.
  
  • If O₂ is present, pyruvate moves to the Krebs cycle and the energy stored in NADH can be converted to ATP by the electron transport system and oxidative phosphorylation.
The Krebs cycle

- More than three quarters of the original energy in glucose is still present in two molecules of pyruvate.
- If oxygen is present, pyruvate enters the **MITOCHONDRION** where enzymes of the Krebs cycle complete the oxidation of the organic fuel to carbon dioxide.
1. As pyruvate enters the mitochondrion, a multienzyme complex modifies pyruvate to **ACETYL COA** which enters the Krebs cycle in the matrix.

2. A carboxyl group is removed as CO$_2$.

3. A pair of electrons is transferred from the remaining two-carbon fragment to NAD$^+$ to form NADH.
The Krebs cycle is named after Hans Krebs who was largely responsible for elucidating its pathways in the 1930s.

4. acetyl CoA combines with **OXALOACETATE** to form **CITRATE**.

- Ultimately, the oxaloacetate is recycled and the acetate is broken down to CO$_2$.
- Each cycle produces **1 ATP, 3 NADH, and 1 FADH** by substrate-level phosphorylation, per acetyl CoA.
• The Krebs cycle consists of eight steps.
• The conversion of pyruvate and the Krebs cycle produces large quantities of **ELECTRON CARRIERS**.

• So what do you think the major purpose of the Krebs cycle is??

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Fig. 9.12

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The Electron Transport Chain

- Only 4 of 38 ATP ultimately produced by respiration of glucose are derived from substrate-level phosphorylation.
- The vast majority of the ATP comes from the energy in the electrons carried by NADH (and FADH₂).
- The energy in these electrons is used in the electron transport system to power ATP synthesis.
• Thousands of copies of the electron transport chain are found in the extensive surface of the CRISTAE, the inner membrane of the mitochondrion.

• Most components of the chain are proteins that are bound with prosthetic groups that can alternate between reduced and oxidized states as they accept and donate electrons.

• Electrons drop in free energy as they pass down the electron transport chain.
1. Electrons carried by NADH are transferred to the first molecule in the electron transport chain, **FLAVOPROTEIN**.

2. The electrons continue along the chain that includes several **CYTOCHROME** proteins and one lipid carrier.

3. The electrons carried by FADH$_2$ have lower free energy and are added to a later point in the chain.
• Electrons from NADH or FADH$_2$ ultimately pass to **OXYGEN**.

• The electron transport chain generates no ATP directly.

• Its function is to break the large free energy drop from food to oxygen into a series of smaller steps that release energy in manageable amounts.

• The movement of electrons along the electron transport chain does contribute to **CHEMIOSMOSIS** and ATP synthesis.
• A protein complex, **ATP SYNTHASE**, in the cristae actually makes ATP from ADP and P$_i$.

• ATP uses the energy of an existing proton gradient to power ATP synthesis.

  • This proton gradient develops between the intermembrane space and the matrix.
• The proton gradient is produced by the movement of electrons along the electron transport chain.

• Several chain molecules can use the exergonic flow of electrons to pump $H^+$ from the matrix to the intermembrane space.
  • This concentration of $H^+$ is the proton-motive force.
Fig. 9.15
• The ATP synthase molecules are the only place that will allow H\(^+\) to diffuse BACK TO THE MATRIX.

• This exergonic flow of H\(^+\) is used by the enzyme to generate ATP.

• This coupling of the redox reactions of the electron transport chain to ATP synthesis is called CHEMIOSMOSIS.
Chemiosmosis is an energy-coupling mechanism that uses energy stored in the form of an $H^+$ gradient across a membrane to drive cellular work.

- In the mitochondrion, chemiosmosis generates ATP.
- Chemiosmosis in chloroplasts also generates ATP, but light drives the electron flow down an electron transport chain and $H^+$ gradient formation.
- Prokaryotes generate $H^+$ gradients across their plasma membrane.
  - They can use this proton-motive force not only to generate ATP but also to pump nutrients and waste products across the membrane and to rotate their flagella.
In review

• During respiration, most energy flows:
  glucose \rightarrow \text{NADH} \rightarrow \text{electron transport chain} \rightarrow \text{proton-motive force} \rightarrow \text{ATP}.

• Considering the fate of carbon, one six-carbon glucose molecule is oxidized to six CO$_2$ molecules.

• Some ATP is produced by SUBSTRATE-LEVEL PHOSPHORYLATION during glycolysis and the Krebs cycle.

BUT most comes from OXIDATIVE PHOSPHORYLATION.
• Each NADH contributes enough energy to generate a maximum of 3 ATP (rounding up).

• Each FADH$_2$ can be used to generate about 2 ATP.

• Assuming the most energy-efficient shuttle of NADH from glycolysis, a maximum yield of 34 ATP is produced by oxidative phosphorylation.

• This plus the 4 ATP from substrate-level phosphorylation gives a bottom line of 38 ATP.
Fig. 9.16
How efficient is respiration in generating ATP?

- Complete oxidation of glucose releases 686 kcal per mole.
- Formation of each ATP requires at least 7.3 kcal/mole.
- Efficiency of respiration is $7.3 \text{ kcal/mole} \times 38 \frac{\text{ATP}}{\text{glucose}} / 686 \text{ kcal/mole glucose} = 40\%$.
- The other approximately 60% is lost as heat.
- Cellular respiration is remarkably efficient in energy conversion.