

Chapter 10

Cell Respiration

Lecture Presentations by Nicole Tunbridge and Kathleen Fitzpatrick

© 2018 Pearson Education Ltd.

ife Is Work

- Living cells require energy from outside sources to do work
- The work of the cell includes assembling polymers, membrane transport, moving, and reproducing
- Animals can obtain energy to do this work by feeding on other animals or photosynthetic organisms

- Energy flows into an ecosystem as sunlight and leaves as heat
- The chemical elements essential to life are recycled
- Photosynthesis generates O2 and organic molecules, which are used in cellular respiration
- Cells use chemical energy stored in organic molecules to generate ATP, which powers work



oncept 10.1: Catabolic pathways yield energy by oxidizing organic fuels

- Catabolic pathways release stored energy by breaking down complex molecules
- Electron transfer plays a major role in these pathways
- These processes are central to cellular respiration

Ligh E. state in Fuels (such as gucore). lower E. state in waste products (such as H2O; COZ). Some energy can be used to to work the vest is dissipated as heat.

atabolic Pathways and Production of ATP

- The breakdown of organic molecules is exergonic
- Fermentation is a partial degradation of sugars that occurs without O2
- Aerobic respiration consumes organic molecules and O2 and yields ATP > most efficient.
- Anaerobic respiration is similar to aerobic respiration but consumes compounds other than O2

» done by some prokaryotes

- Cellular respiration includes both aerobic and anaerobic respiration but is often used to refer to aerobic respiration
- Although carbohydrates, fats, and proteins are all consumed as fuel, it is helpful to trace cellular respiration with the sugar glucose \rightarrow from break-C6H12O6 + 6 O2 \rightarrow 6 CO2 + 6 H2O + Energy (ATP + heat)

$$\Delta GI = -686 \text{ kcd/mol}$$

of glucose
exergonic
[spontaneous].

edox Reactions: Oxidation and Reduction

- The transfer of electrons during chemical reactions releases energy stored in organic molecules
- This released energy is ultimately used to synthesize ATP

he Principle of Redox

- Chemical reactions that transfer electrons between reactants are called oxidation-reduction reactions, or redox reactions
- In oxidation, a substance loses electrons, or is oxidized
- In reduction, a substance gains electrons, or is reduced (the amount of positive charge is reduced)





- The electron donor is called the reducing agent
- The electron receptor is called the **oxidizing agent**
- Some redox reactions do not transfer electrons but change the electron sharing in covalent bonds
- An example is the reaction between methane and O2

bond is 'unstable" [possesses high potential energy]. due to equal value 's affinity the CfH off. equally is. shaved e is. C & H. [non-polar covalent bond] © 2018 Pearson Education Ltd.



xidation of Organic Fuel Molecules During Cellular Respiration

- During cellular respiration, the fuel (such as glucose) is oxidized, and O2 is reduced
- Organic molecules with an abundance of hydrogen are excellent sources of high-energy electrons
- Energy is released as the electrons associated with hydrogen ions are transferred to oxygen, a lower energy state

C: H BONDS one converted to C=O BONDS





tepwise Energy Harvest via NAD+ and the **Electron Transport Chain**

- In cellular respiration, glucose and other organic molecules are broken down in a series of steps
- Electrons from organic compounds are usually first transferred to NAD+, a coenzyme
- As an electron acceptor, NAD+ functions as an oxidizing agent during cellular respiration
- Each NADH (the reduced form of NAD+) represents stored energy that is tapped to synthesize ATP Nicotinamide adenine dinucleotide oxidized & reduced & wickly cycles between its sell-snited for electron NAD

mansportation.

NADH

© 2018 Pearson Education Ltd.







Figure 10.UN04



The transfer of et's from NADH to Oxygen is exergonic with $\Delta G = -53 \text{ kcol/mol}$.

- NADH passes the electrons to the electron transport chain for each electron acceptor has prefer to granter entry offinity than the preceding doner
 Unlike an uncontrolled reaction, the electron [Les entry].
- Unlike an uncontrolled reaction, the electron Les envy
 transport chain passes electrons in a series of steps
 instead of one explosive reaction
- O2 pulls electrons down the chain in an energyyielding tumble $\int O_2$ is analogous to gravity.
- The energy yielded is used to regenerate ATP



he Stages of Cellular Respiration: A Preview

• Harvesting of energy from glucose has three stages

Glycolysis (breaks down glucose into two molecules of pyruvate)

The **citric acid cycle** (completes the breakdown of glucose)

Oxidative phosphorylation (accounts for most of the ATP synthesis)

Figure 10.UN05

- **1** GLYCOLYSIS (color-coded blue throughout the chapter)
- **2** PYRUVATE OXIDATION and the CITRIC ACID CYCLE
 (color-coded light orange and dark orange)
- 3 OXIDATIVE PHOSPHORYLATION: Electron transport and
 chemiosmosis (color-coded purple)



- The process that generates almost 90% of the ATP is called oxidative phosphorylation because it is powered by redox reactions
- A smaller amount of ATP is formed in glycolysis and the citric acid cycle by substrate-level phosphorylation

Figure 10.7



For each molecule of glucose degraded to CO2 and water by respiration, the cell makes up to 32 molecules of ATP
 30 2 32 Mar in this start.

- We can use money as an analogy for cellular respiration:
 - Glucose is like a larger-denomination bill—it is worth a lot, but it is hard to spend
 - ATP is like a number of smaller-denomination bills of equivalent value—they can be spent more easily
 - Cellular respiration cashes in a large denomination of energy (glucose) for the small change of many molecules of ATP 7-3 kcd/mol

© 2018 Pearson Education Ltd.

oncept 10.2: Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

- Glycolysis occurs in the cytoplasm and has two major phases
 - Energy investment phase $\int 2ATP$
 - Energy payoff phase 3 + 4ATP + 2NADH
- Glycolysis occurs whether or not O2 is present

$$\Delta C = 0$$
, $6 \times 1 = 3 \times 2 \rightarrow pyrmatemoleculesC/ghicose molecules$

© 2018 Pearson Education Ltd.









oncept 10.3: After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

 In the presence of O2, pyruvate enters a mitochondrion (in eukaryotic cells), where the oxidation of glucose is completed

xidation of Pyruvate to Acetyl CoA

- Before the citric acid cycle can begin, pyruvate must be converted to acetyl coenzyme A (acetyl CoA), which links glycolysis to the citric acid cycle
- This step is carried out by a multienzyme complex that catalyzes three reactions

Oxidation of pyruvate and release of CO2

Reduction of NAD+ to NADH

Combination of the remaining two-carbon fragment and coenzyme A to form acetyl CoA


Figure 10.10





- The citric acid cycle has eight steps, each catalyzed by a specific enzyme
- The acetyl group of acetyl CoA joins the cycle by combining with oxaloacetate, forming citrate
- The next seven steps decompose the citrate back to oxaloacetate, making the process a cycle
- The NADH and FADH2 produced by the cycle relay electrons extracted from food to the electron transport chain 3,17 per acetyl-CoA.



Figure 10.11

▼ Figure 10.10 An overview of pyruvate oxidation and the citric acid cycle. The inputs and outputs per pyruvate molecule are shown with a focus on the carbon atoms involved. To calculate on a per-glucose basis, multiply by 2 because each glucose molecule is split during glycolysis into two pyruvate molecules.



Now let's look at the citric acid cycle in more detail. The cycle has eight steps, each catalyzed by a specific enzyme. You can see in **Figure 10.11** that for each turn of the citric acid cycle, two carbons (red) enter in the relatively reduced form of an acetyl group (step **1**), and two different carbons (blue) leave in the completely oxidized form of CO_2 molecules (steps **3** and **4**). The acetyl group of acetyl CoA joins the cycle by combining with the compound oxaloacetate, forming citrate (step **1**). Citrate is the ionized form of citric acid, for which the cycle is named. The next seven steps decompose the citrate back to oxaloacetate. It is this regeneration of oxaloacetate that makes the process a *cycle*.

Referring to Figure 10.11, we can tally the energy-rich molecules produced by the citric acid cycle. For each acetyl group entering the cycle, 3 NAD⁺ are reduced to NADH (steps 3, 4, and 8). In step 6, electrons are transferred not to NAD⁺, but to FAD, which accepts 2 electrons and 2 protons to become FADH₂. In many animal tissue cells, the reaction in step **5** produces a guanosine triphosphate (GTP) molecule by substrate-level phosphorylation. GTP is a molecule similar to ATP in its structure and cellular function. This GTP may be used to make an ATP molecule (as shown) or directly power work in the cell. In the cells of plants, bacteria, and some animal tissues, step 5 forms an ATP molecule directly by substrate-level phosphorylation. The output from step **5** represents the only ATP generated during the citric acid cycle. Recall that each glucose gives rise to two molecules of acetyl CoA that enter the cycle. Because the numbers noted earlier are obtained from a single acetyl group entering the pathway, the total yield per glucose from the citric acid cycle turns out to be doubled, or 6 NADH, 2 FADH₂, and the equivalent of 2 ATP.

Most of the ATP produced by respiration is generated later, from oxidative phosphorylation, when the NADH and FADH₂ produced by the citric acid cycle and earlier steps relay the electrons extracted from food to the electron transport chain. In the process, they supply the necessary energy for the phosphorylation of ADP to ATP. We will explore this process in the next section.

Figure 10.11a





oncept 10.4: During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

- Following glycolysis and the citric acid cycle, NADH and FADH2 account for most of the energy extracted from food $\int (2.5 \times 10 + 1.5 \times 2) = 28$ AT P is exidative
- These two electron carriers donate electrons to the electron transport chain, which powers ATP synthesis via oxidative phosphorylation

he Pathway of Electron Transport

- The electron transport chain is in the inner membrane (cristae) of the mitochondrion
- Most of the chain's components are proteins, which exist in multiprotein complexes = { 1, 11, 111, 112 }

In Prokaryotes

in the plasma

membrane

- Electrons drop in free energy as they go down the chain and are finally passed to O2, forming H2O
- Electron carriers alternate between reduced and oxidized states as they accept and donate electrons
 Multiprotrin complexes are tightly bound to Prosthetic Groups
 nonprotrin components s.a. cofactors & coenzymes.
 which are essential to the cotalytic function of certain enzymes.

- Electrons are transferred from NADH or FADH2 to the electron transport chain
- Electrons are passed through a number of proteins including cytochromes (each with an iron atom) to O2
- The electron transport chain generates no ATP directly
- It breaks the large free-energy drop from food to O2 into smaller steps that release energy in manageable amounts





hemiosmosis: The Energy-Coupling Mechanism

- The energy released as electrons are passed down the electron transport chain is used to pump H+ from the mitochondrial matrix to the intermembrane space
- H+ then moves down its concentration gradient back across the membrane, passing through the protein complex ATP synthase >> which "assembles" ATP

from ADP & (P);

ivorganic prosphate

unlike kinases.

- H+ moves into binding sites on the rotor of ATP synthase, causing it to spin in a way that catalyzes phosphorylation of ADP to ATP
- This is an example of chemiosmosis, the use of energy in a H+ gradient to drive cellular work





- Certain electron carriers in the electron transport chain accept and release H+ along with the electrons
- In this way, the energy stored in a H+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis
- The H+ gradient is referred to as a proton-motive force, emphasizing its capacity to do work

ATP synthese is the smallest molecular rotary motor known in nature.

Figure 10.15a



n Accounting of ATP Production by Cellular Respiration

During cellular respiration, most energy flows in this sequence:

glucose \rightarrow NADH \rightarrow electron transport chain \rightarrow proton-motive force \rightarrow ATP

- About 34% of the energy in a glucose molecule is transferred to ATP during cellular respiration, making about 32 ATP
 See the math of 34% [link left-wise].
- The rest of the energy is lost as heat

Figure 10.16d



Most biochemists now agree on that: 2.5 ATP/NADH, 1.5 ATP/FADHz, 4H⁺/ATP 10 H⁺ 6H⁺ 5 in chemics mosis

 There are three reasons why the number of ATP is not known exactly

Photophosphorylation and the redox reactions are not directly coupled; the ratio of NADH to ATP molecules is not a whole number

ATP yield varies depending on whether electrons are passed to NAD+ or FAD in the mitochondrial matrix e.g.'s Liver & Brain cells. - 1.5 ATP/Glyonlysis MADH
 The proton-motive force is also used to drive other kinds of work such as uptake of pyruvate from the Cytosol.
 if all H⁺ gradient force was used for oxidative phosphorylation, a maximum of (30 or 32) ATP is obtained = 4 + 26 depending on performing on the cytosol.

We can now roughly estimate the efficiency of respiration that is, the percentage of chemical energy in glucose that has been transferred to ATP. Recall that the complete oxidation of a mole of glucose releases 686 kcal of energy under standard conditions ($\Delta G = -686$ kcal/mol). Phosphorylation of ADP to form ATP stores at least 7.3 kcal per mole of ATP. Therefore, the efficiency of respiration is 7.3 kcal per mole of ATP times 32 moles of ATP per mole of glucose divided by 686 kcal per mole of glucose, which equals 0.34. Thus, about 34% of the potential chemical energy in glucose has been transferred to ATP; the actual percentage is bound to vary as ΔG varies under different cellular conditions. Cellular respiration is remarkably efficient in its energy conversion. By comparison, even the most efficient automobile converts only about 25% of the energy stored in gasoline to energy that moves the car.

The rest of the energy stored in glucose is lost as heat. We humans use some of this heat to maintain our relatively high body temperature (37°C), and we dissipate the rest through sweating and other cooling mechanisms.

Surprisingly, perhaps, it may be beneficial under certain conditions to reduce the efficiency of cellular respiration. A remarkable adaptation is shown by hibernating mammals, which overwinter in a state of inactivity and lowered metabolism. Although their internal body temperature is lower than normal, it still must be kept significantly higher than the external air temperature. One type of tissue, called brown fat, is made up of cells packed full of mitochondria. The inner mitochondrial membrane contains a channel protein called the uncoupling protein that allows protons to flow back down their concentration gradient without generating ATP. Activation of these proteins in hibernating mammals results in ongoing oxidation of stored fuel (fats), generating heat without any ATP production. In the absence of such an adaptation, the buildup of ATP would eventually cause cellular respiration to be shut down by regulatory mechanisms that will be discussed later. Brown fat is also used for heat generation in humans. In the Scientific Skills Exercise, you can work with data in a related but different case where a decrease in metabolic efficiency in cells is used to generate heat.

oncept 10.5: Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

- Most cellular respiration depends on electronegative oxygen to pull electrons down the transport chain
- Without oxygen, the electron transport chain will cease to operate
- In that case, glycolysis couples with anaerobic respiration or fermentation to produce ATP

Anaerobic $30^{+6}_{-1} 2^{-1}_{-1} + 42^{-2}_{-2}$ both use e^{-1}_{-1} trans. chain Aerobic $0^{-1}_{-2} + 42^{-2}_{-2}$ aka: respiratory chain

- Anaerobic respiration uses an electron transport chain with a final electron acceptor other than oxygen, for example, <u>sulfate</u>) -> Similar marine bacteria.
- Fermentation uses substrate-level phosphorylation instead of an electron transport chain to generate ATP

ypes of Fermentation $\frac{\pi}{\sqrt{-1}}$

 Fermentation consists of glycolysis plus reactions that regenerate NAD+, which can be reused by glycolysis

2 ATP/ Gilnesse only; by substrate-level phosphorylation.

Two common types are alcohol fermentation and lactic acid fermentation

- In **alcohol fermentation**, pyruvate is converted to The first step releases CO2 from pyruvate
 The second stop press ethanol in two steps

 - The second step produces NAD+ and ethanol -> CH₂CH₂OH
- Alcohol fermentation by yeast is used in brewing, winemaking, and baking



- In **lactic acid fermentation**, pyruvate is reduced by NADH, forming NAD+ and lactate as end products, with no release of CO2 $3C = Pyruvate (\Delta C = 0)$

 Human muscle cells use lactic acid fermentation to generate ATP during strenuous exercise when O2 is scarce



(b) Lactic acid fermentation

What about lactate production in humans? Previously, we thought that human muscle cells only produced lactate when O_2 was in short supply, such as during intense exercise. Research done over the last few decades, though, indicates that the lactate story, in mammals at least, is more complicated. There are two types of skeletal muscle fibers. One (red muscle) preferentially oxidizes glucose completely to CO₂; the other (white muscle) produces significant amounts of lactate from the pyruvate made during glycolysis, even under aerobic conditions, offering fast but energetically inefficient ATP production. The lactate product is then mostly oxidized by red muscle cells in the vicinity, with the remainder exported to liver or kidney cells for glucose formation. Because this lactate production is not anaerobic, but the result of glycolysis in these cells, exercise physiologists prefer not to use the term fermentation.

During strenuous exercise, when carbohydrate catabolism outpaces the supply of O_2 from the blood to the muscle, lactate can't be oxidized to pyruvate. The lactate that accumulates was once thought to cause muscle fatigue during intense exercise and pain a day or so later. However, research suggests that, contrary to popular opinion, lactate production actually improves performance during exercise! Furthermore, within an hour, excess lactate is shuttled to other tissues for oxidation or to the liver and kidneys for production of glucose or its storage molecule, glycogen. (Nextday muscle soreness is more likely caused by trauma to cells in small muscle fibers, which leads to inflammation and pain.)

omparing Fermentation with Anaerobic and **Aerobic Respiration**

- All use glycolysis (net ATP = 2) to oxidize glucose and harvest the chemical energy of food
- In all three, NAD+ is the oxidizing agent that accepts electrons during glycolysis 1 Aerobic Respiration

 - 2 Anaerobic Resp. 3 Fermentation

- The processes have different mechanisms for oxidizing NADH to NAD+:
 - In fermentation, an organic molecule (such as pyruvate or acetaldehyde) acts as a final electron acceptor > lactic acid form.
 - In cellular respiration, electrons are transferred to the electron transport chain finally to O2 or another.
- Cellular respiration produces 32 ATP per glucose molecule; fermentation produces 2 ATP per glucose molecule $(\frac{1}{16}, \frac{1}{15})$ as efficient glucose -ATPuise

D'obligate aerobes": such as vertebrate brain cells which can only carry out <u>aerobic</u> axidation <u>- L pyruvate</u>.

- Obligate anaerobes carry out fermentation or anaerobic respiration and cannot survive in the presence of O2
- Yeast and many bacteria are facultative anaerobes, meaning that they can survive using either fermentation or cellular respiration
- In a facultative anaerobe, pyruvate is a fork in the metabolic road that leads to two alternative catabolic routes }, depending on the presence of O2. faster rate -- > about 16 times faster consumption.



he Evolutionary Significance of Glycolysis

• Glycolysis is an ancient process

Early prokaryotes likely used glycolysis to produce ATP before O2 accumulated in the atmosphere

Used in both cellular respiration and fermentation, it is the most widespread metabolic pathway on Earth

This pathway occurs in the cytosol so does not require the membrane-bound organelles of eukaryotic cells

oncept 10.6: Glycolysis and the citric acid cycle connect to many other metabolic pathways

 Gycolysis and the citric acid cycle are major intersections to various catabolic and anabolic pathways
he Versatility of Catabolism

- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of carbohydrates including starch, glycogen, and several disaccharides

 Proteins that are used for fuel must be digested to amino acids and their amino groups must be removed is deamination process
deamination process
amino groups are excreted as NH3, urea, or other woste products.

An intermediate of Glycolysis) Glyceraldehyde 3-Phosphote G3P Fats are digested to glycerol (used to produce) compounds needed for glycolysis) and fatty acids Fatty acids are broken down by beta oxidation and much ATP as an oxidized gram of carbohydrate [see ch.5] @ S due to the abundancy of (C÷H) High Energy bonds because of the structure of Fatty acid tails.



© 2018 Pearson Education Ltd.

iosynthesis (Anabolic Pathways)

- The body uses small molecules from food to build other their own molecules such as proteins
- These small molecules may come directly from food, from glycolysis, or from the citric acid cycle



egulation of Cellular Respiration via Feedback Mechanisms Ch6: an endproduct inhibits an enzyme that catalyzes an early step of the pathway.

- Feedback inhibition is the most common mechanism for metabolic control
- If ATP concentration begins to drop, respiration speeds up; when there is plenty of ATP, respiration slows down
- Control of catabolism is based mainly on regulating the activity of enzymes at strategic points in the catabolic pathway

Figure 10.20



▼ Figure 10.19 The control of cellular respiration. Allosteric enzymes at certain points in the respiratory pathway respond to inhibitors and activators that help set the pace of glycolysis and the citric acid cycle. Phosphofructokinase, which catalyzes an early step in glycolysis (see Figure 10.8, step ③ and Figure 7.32b), is one such enzyme. It is stimulated by AMP (derived from ADP) but is inhibited by ATP and by citrate. This feedback regulation adjusts the rate of respiration as the cell's catabolic and anabolic demands change.



the substrate passes step (3) it is committed irreversibly to the glycolysis pathway; i.e. phosphofructo kinase inhibition is crucial for resource monagement. Step 3 regulators ie. ATP], inhibits citrate AMP-stimulates regulate the rate of Glycolysis.





Pho sph ofru ctok inas e acti vity



Fructose 6-phosphate concentration



Figure 10.UN18

Jubiquinone "Q"-, hydrophobic Greely moving in **CoO10** the Inner membrane 100 mg DIETARY SUPPLEMENT **30 SOFTGELS**