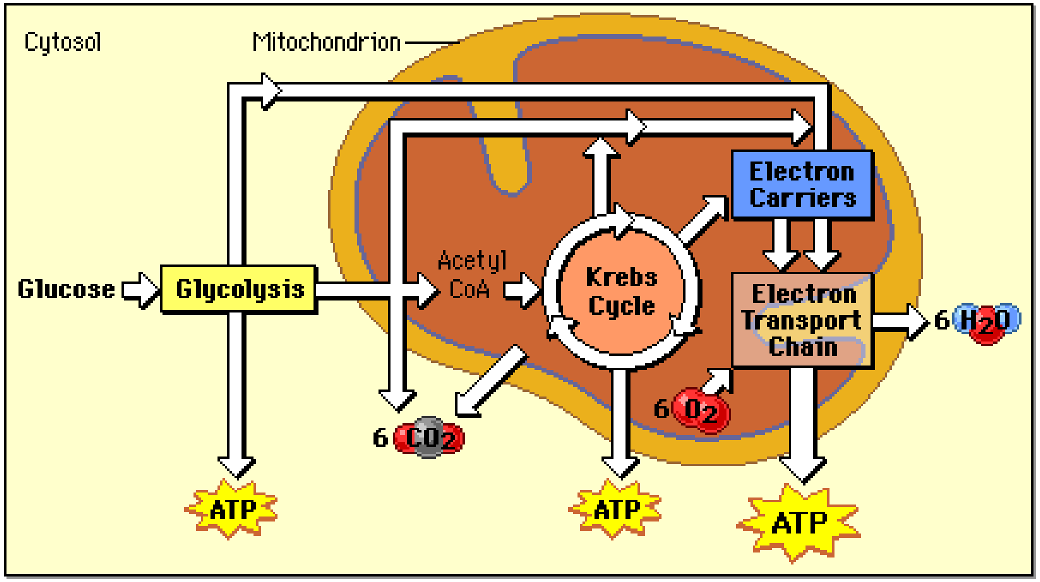
Chapter 9

Cellular Respiration:
Harvesting Chemical Energy

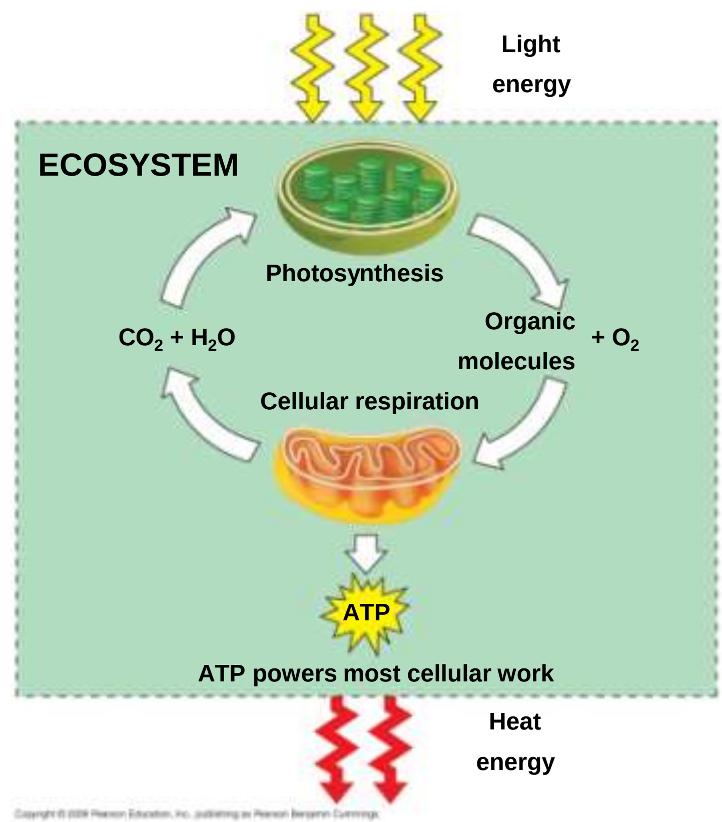


AP Biology

Overview: Life Is Work

- Living cells need energy that they can only get from outside sources
    - Ex) A giant panda gets energy by eating plants
    - Ex) Other animals get energy by feeding on other organisms
  - Ultimately, all the energy stored in organic molecules of food comes from the sun

- Energy flows into the ecosystem as sunlight
    - This energy then leaves in the form of heat
- Chemical elements essential to life are recycled, however:
    - Photosynthesis generates oxygen and organic molecules (glucose)
    - Cell respiration breaks these organic molecules down, generating ATP that drives cellular work
    - Waste products of respiration (CO_2 and water) are then used as raw materials for photosynthesis



Concept 9.1:
Catabolic pathways yield energy by oxidizing organic fuels

Catabolic Pathways Involved in Cellular Respiration

- Metabolic pathways that release stored energy (catabolic pathways) are essential to cellular respiration and related pathways
  - They include:
    - Fermentation
    - Aerobic respiration
    - Anaerobic respiration

Catabolic Pathways and Production of ATP

- Organic compounds contain potential energy due to their arrangement of atoms
  - With the help of enzymes, these organic compounds can be broken down to release this stored energy
- The exergonic breakdown of organic molecules can occur in one of 3 ways:
  - 1) One of these catabolic processes is ***FERMENTATION:***
    - Fermentation is the partial degradation of sugar in the absence of oxygen
  - 2) A more prevalent and efficient catabolic pathway is ***AEROBIC RESPIRATION:***
    - In this pathway, oxygen is consumed along with sugar
      - More energy (in the form of ATP) is produced
    - Most eukaryotic and many prokaryotic organisms use aerobic respiration
  - 3) Some prokaryotes obtain energy without using any oxygen at all, a process called ***ANAEROBIC RESPIRATION***
    - These organisms use substances other than oxygen as reactants
      - Even still, the process is similar

- ***Cellular respiration*** includes both aerobic and anaerobic processes, though it is often used to refer to aerobic respiration
  - It originated as a synonym for aerobic respiration because of the relationship between the 2 processes (both consume O_2 and release CO_2)
- The overall process of aerobic respiration can be summarized as:

  Organic compounds + Oxygen -----> Carbon dioxide + Water + Energy

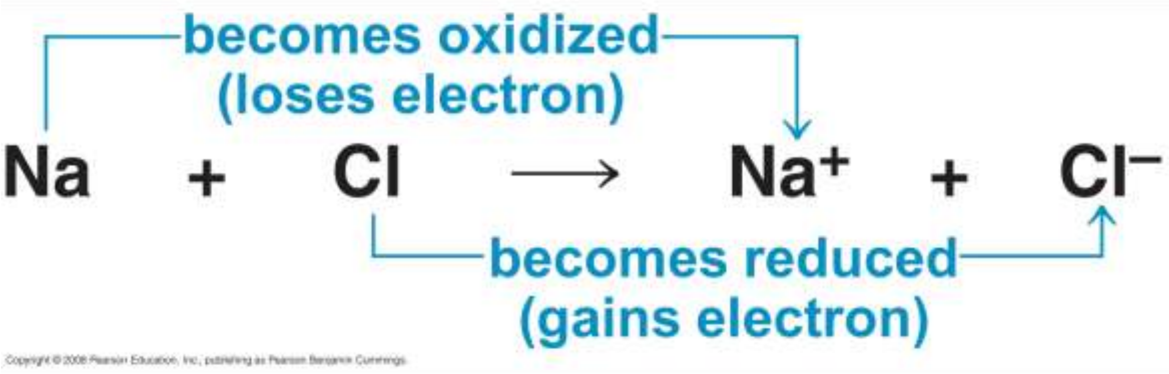
  - Even though carbohydrates, fats, and proteins can all be processed and consumed as fuel, it is helpful to learn the steps of cellular respiration by tracking the breakdown of glucose

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{Energy (ATP + heat)}$$

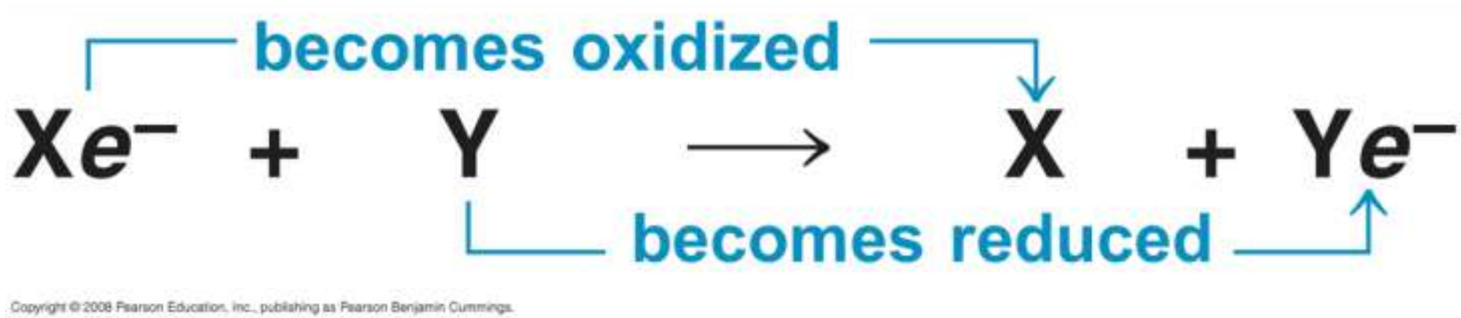
  - Breakdown of glucose is exergonic (ΔG = -686 kcal/mol of glucose decomposed)
    - $-\Delta G$ indicates the reaction is spontaneous and occurs without the input of energy
    - The energy released is used to generate ATP the cell can use for work

Redox Reactions: Oxidation and Reduction

- Catabolic pathways like cellular respiration yield energy through the transfer of electrons during chemical reactions
  - Relocation of electrons releases energy stored in organic molecules
    - This energy is ultimately used to make ATP
  - Chemical reactions that transfer electrons from one reactant to another are called ***OXIDATION-REDUCTION (REDOX) REACTIONS***
    - A reaction in which there is a loss of electrons is called ***OXIDATION***
    - A reaction in which electrons are gained is called ***REDUCTION*** (adding negatively charged electrons REDUCES the amount of positive charge)

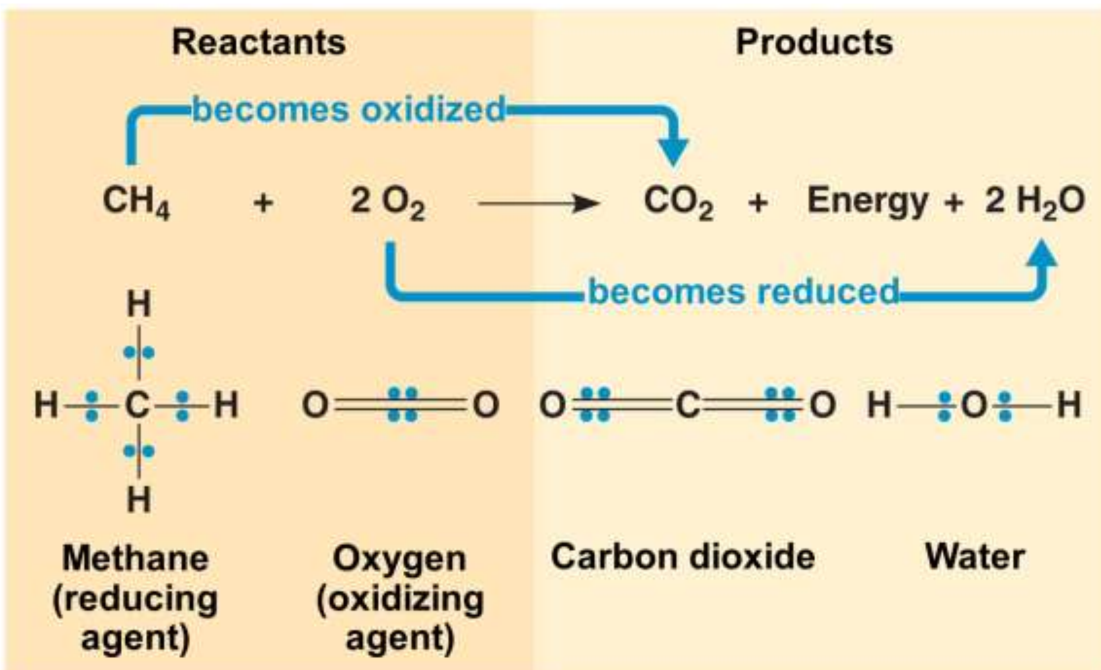


- In a more generalized reaction:

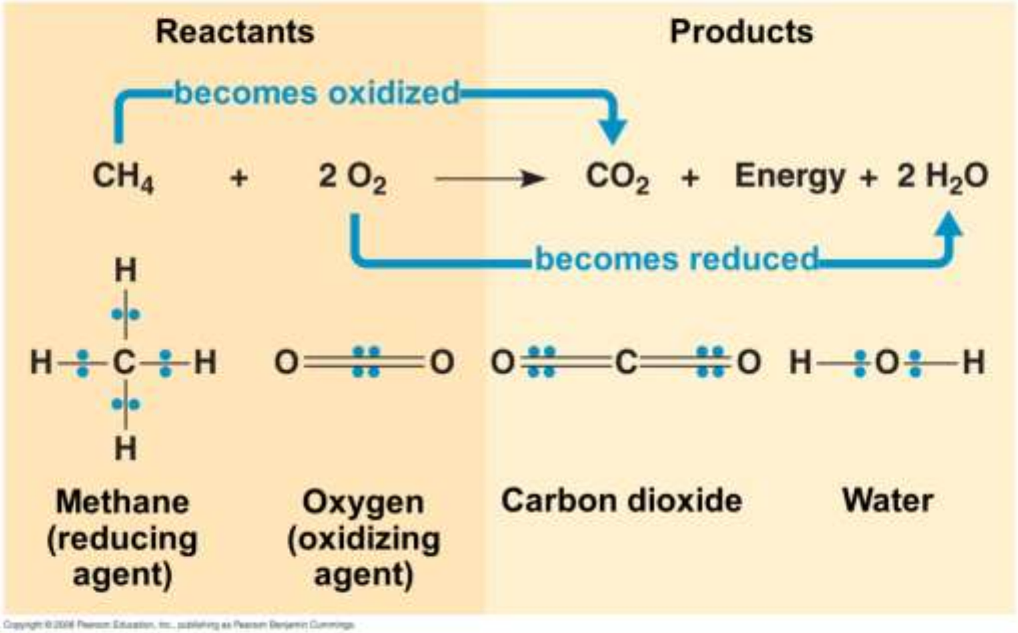


  – Xe = electron donor (loses electrons, becomes oxidized)
    - Called the ***REDUCING AGENT***
  – Y = electron acceptor (gains electrons, becomes reduced)
    - Called the ***OXIDIZING AGENT***
      – Ex) reaction between methane and oxygen

- Because electron transfers require both a donor and acceptor, oxidation and reduction always go together
    - Not all redox reactions, however, involve complete transfer of electrons from one substance to another
  - Some change the degree of electron sharing in covalent bonds
    - Ex) Reaction between methane and oxygen

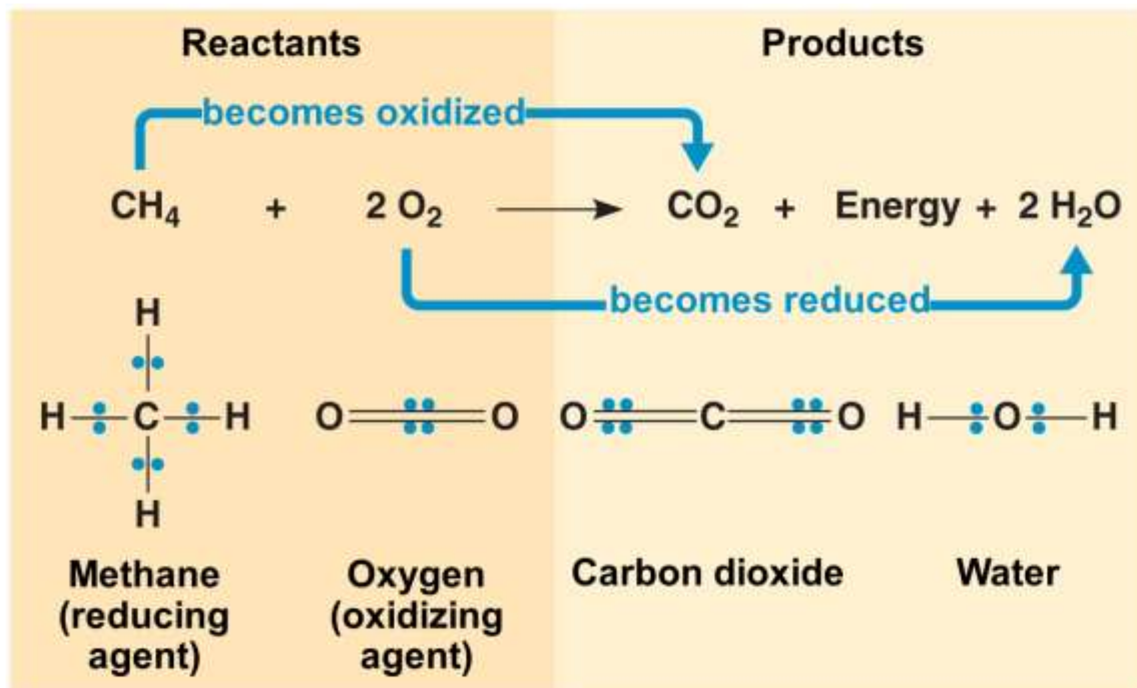


- Covalent electrons in CH_4 are shared nearly equally between its atoms because carbon and hydrogen have about the same affinity for valence electrons (they are about equally electronegative)
  - When CH_4 reacts with O_2, forming CO_2, electrons end up shared less equally between carbon atom and its new covalent partners, the oxygen atoms (oxygen is very electronegative)
    - In effect, the carbon atom has partially "lost" its shared electrons (CH_4 has been oxidized)
  - In the reactant O_2, both oxygens share electrons equally (same electronegativity)
    - When O_2 reacts with CH_4, forming water, electrons of the covalent bond spend more time near oxygen
      - In effect, each oxygen atom has partially "gained" electrons (becomes reduced)



Potential Energy and Oxidation-Reduction

- Energy must be added to pull an electron away from an atom (like pushing a ball uphill)
  - The more electronegative an atom, the stronger its pull on electrons
    - More energy is thus required to take an electron away from it (less energy to keep it there = less potential energy)
  - Electrons lose potential energy when they shift from less electronegative atom to more electronegative atom
    - Like a ball loses potential energy when it rolls downhill



Oxidation of Organic Fuel Molecules During Cellular Respiration

- The combustion of methane is similar to the oxidation-reduction that occurs in cellular respiration:
  - The fuel (glucose) is oxidized (loses electrons)
  - Oxygen is reduced (gains electrons)
  - Electrons lose potential energy along the way
    - This energy is released to form ATP

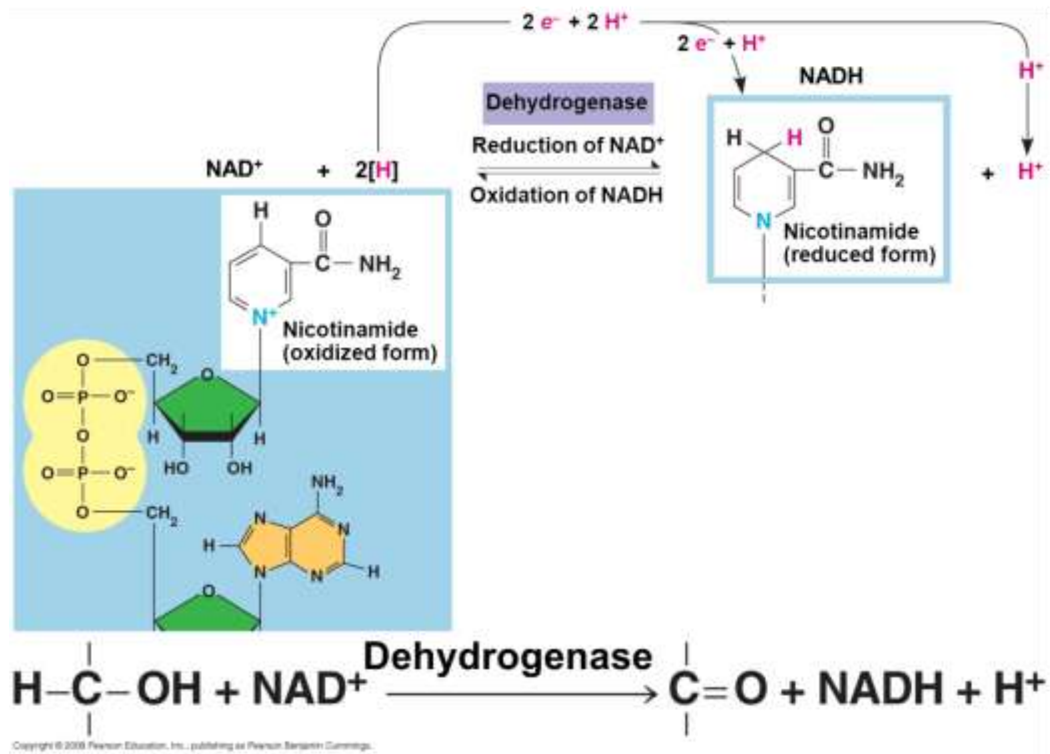
Stepwise Energy Harvest via NAD^+ and the Electron Transport Chain

- If energy is released from fuel all at once, it can't be harnessed for constructive work
    - Ex) If a gas tank explodes, it won't drive the car very far
  - Cell respiration doesn't oxidize glucose in a single step
    - Glucose and its products are broken down in a series of steps
      - At key steps, electrons are stripped from glucose, each traveling with a proton (in the form of a hydrogen atom)

- Hydrogen atoms are not transferred directly to oxygen, however
  - They are usually passed first to an electron carrier
    - The electron carrier in cellular respiration is a coenzyme called NAD+ (nicotinamide adenine dinucleotide – a derivative of the vitamin niacin)
      - By accepting electrons, NAD+ functions as an oxidizing agent
  - Enzymes called dehydrogenases remove a pair of hydrogen atoms (2 electrons, 2 protons) from glucose – OXIDATION
    - Dehydrogenase delivers the 2 electrons and 1 proton to NAD+ (the other proton is released as an H+ ion in the surrounding solution)
      - By receiving 2 negatively charged electrons but only one positively charged proton, the charge on NAD+ is neutralized (becomes NADH) - REDUCTION
  - Electrons lose very little potential energy when they are transferred from glucose to NAD+
    - Therefore, each NADH formed represents stored energy that can be tapped to make ATP when electrons complete their “fall” down an energy gradient from NADH to oxygen

NAD+ as an Electron Shuttle

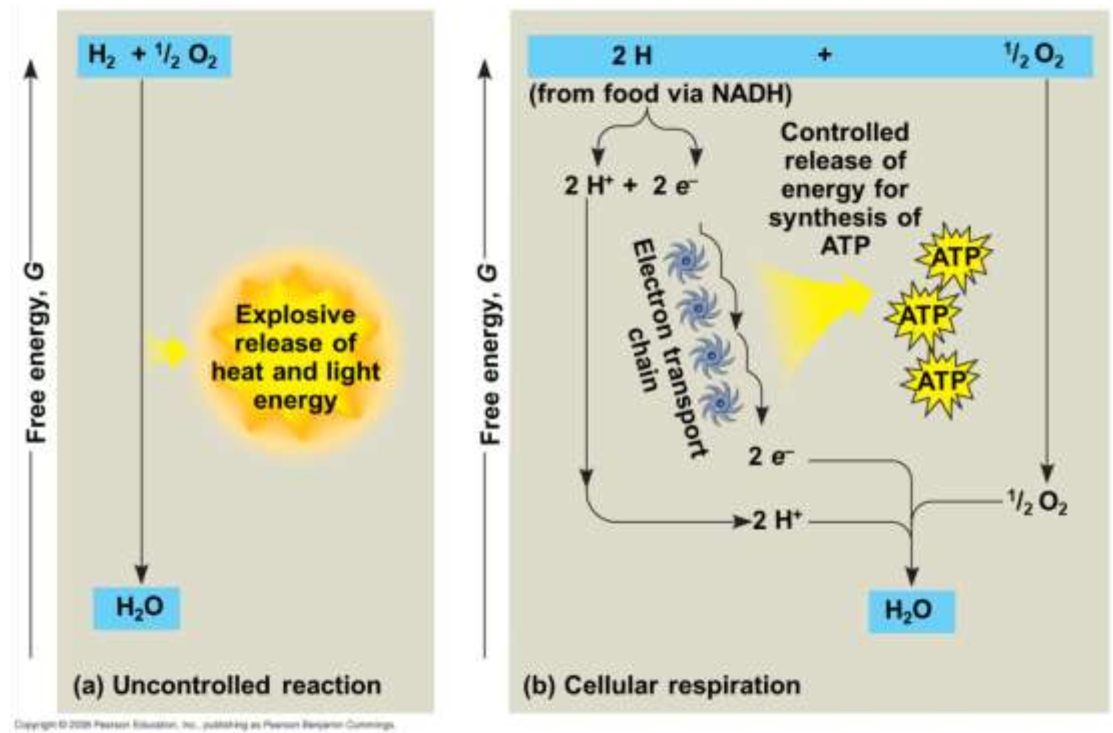
- NAD+ traps electrons from glucose (food)
  - Enzymes called dehydrogenases remove a pair of hydrogen atoms (2 electrons, 2 protons) from glucose
    - The enzymes deliver the 2 electrons (along with one proton) to the coenzyme NAD+, forming NADH
    - The other proton is released as an H+ ion into surrounding solution
- Structure of NAD+
  - Consists of 2 nucleotides joined together at their phosphate groups (shown in yellow)



The Electron Transport Chain

- Respiration uses an E***LECTRON TRANSPORT CHAIN (ETC)*** to break the fall of electrons to oxygen into several energy-releasing steps
    - The ETC is made up of many molecules, mostly proteins, that are built into the inner membranes of mitochondria (eukaryotes) or plasma membranes (prokaryotes)

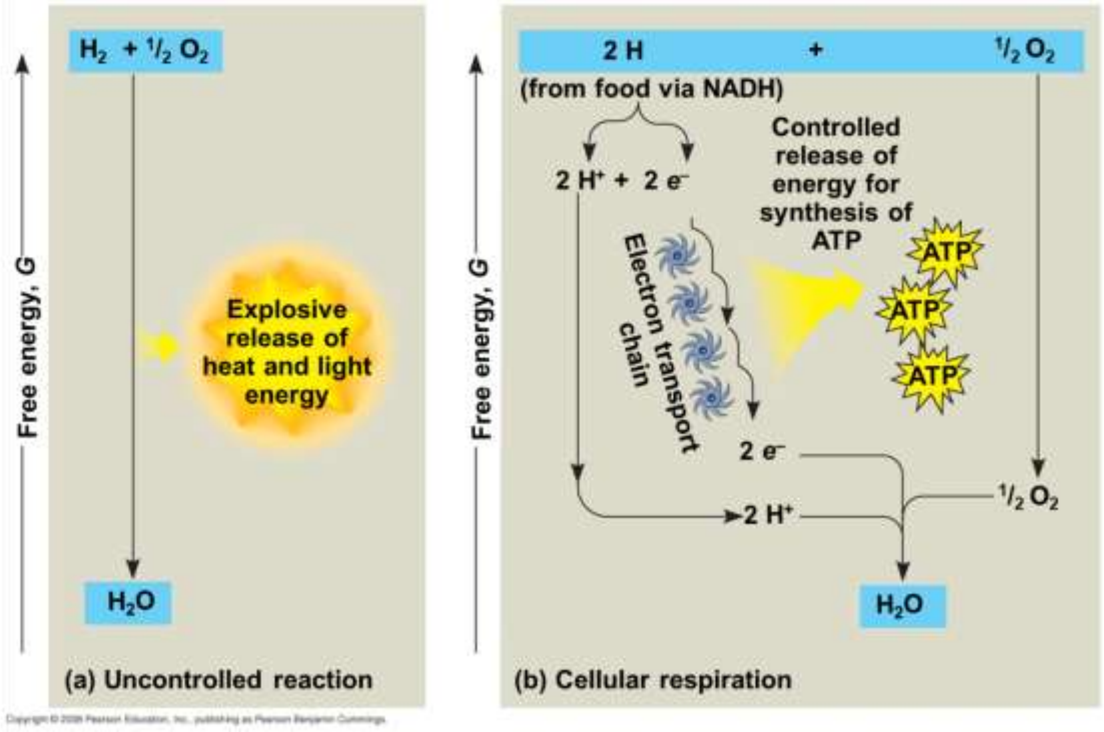
  – Electrons removed from glucose are shuttled by NADH to the top, higher-energy end of the chain



  - Electrons then cascade down the chain from one carrier molecule to the next in a series of redox reactions

The Electron Transport Chain

- Electrons lose a small amount of energy in each step
  - Each redox reaction is exergonic, releasing –53 kcal/mol of energy
- – Each “downhill” carrier is more electronegative than the next, making it capable of oxidizing its “uphill” neighbor (taking away an electron)
  - At the bottom, lower-energy end, oxygen (the most electronegative molecule in the chain) captures these electrons, along with a H+ ion to form water
    - – The energy released is used to regenerate ATP

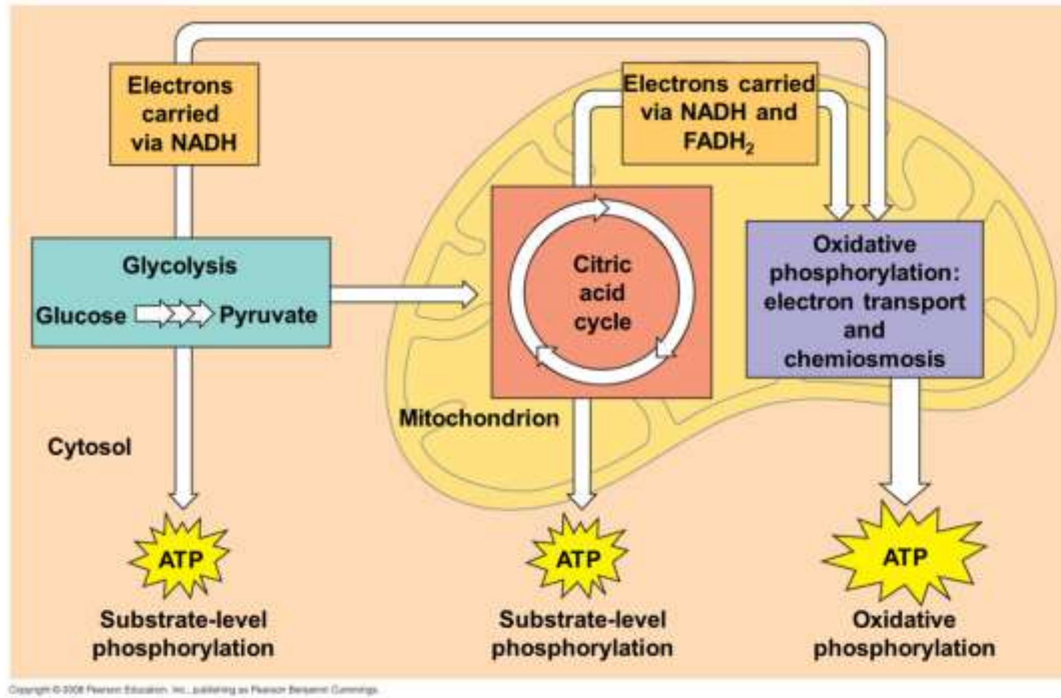


The Stages of Cellular Respiration: A Preview

- Cellular respiration has 3 stages:
  - 1) **Glycolysis:** breaks glucose down into 2 molecules of pyruvate
  - 2) **Citric acid cycle** (or ***Kreb's cycle***): completes the breakdown of glucose, oxidizing a derivative of pyruvate to CO_2
  - 3) **Oxidative phosphorylation:** the ETC accepts electrons from the breakdown products of the first 2 stages
    - It then passes these electrons along until they combine with oxygen and H+ ions at the end of the chain, forming water
    - The stored energy resulting from these electron transfers is used to make ATP

An Overview of Cellular Respiration

- ***Glycolysis:***
  - Each glucose is broken down into 2 pyruvate in the cytosol



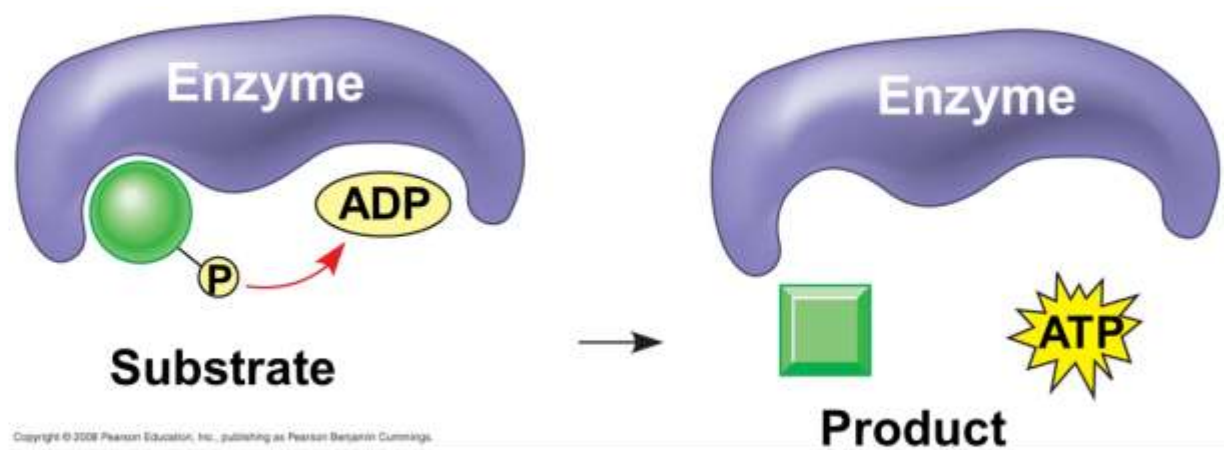
- ***Citric Acid Cycle:***
  - In eukaryotes, pyruvate enters mitchondrion
  - Pyruvate is then oxidized (loses electrons) to CO_2
- ***Electron Transport Chain:***
  - NADH and a similar electron carrier, FADH2, transfer electrons to ETC
    - In eukaryotes, the ETC is built into inner mitochondrial membrane
    - In prokaryotes, ETC is built into plasma membrane
  - During oxidative phosphorylation, ETC converts chemical energy to a form used for ATP synthesis (called chemiosis)

Oxidative Phosphorylation

- The process that generates most of the ATP is called oxidative phosphorylation because it is powered by redox reactions
    - Oxidative phosphorylation accounts for almost 90% of ATP generated by respiration
  - A smaller amount of ATP is formed directly in glycolysis and TCA cycle by a process called ***substrate-level phosphorylation***
    - In this process, an enzyme transfers a phosphate group from a substrate molecule to ADP, rather than adding an inorganic phosphate to ADP (like in oxidative phosphorylation)
      - In this case, the substrate refers to an organic molecule generated as a intermediate during the breakdown of glucose

PLAY

BioFlix: Cellular Respiration



Concept Check 9.1

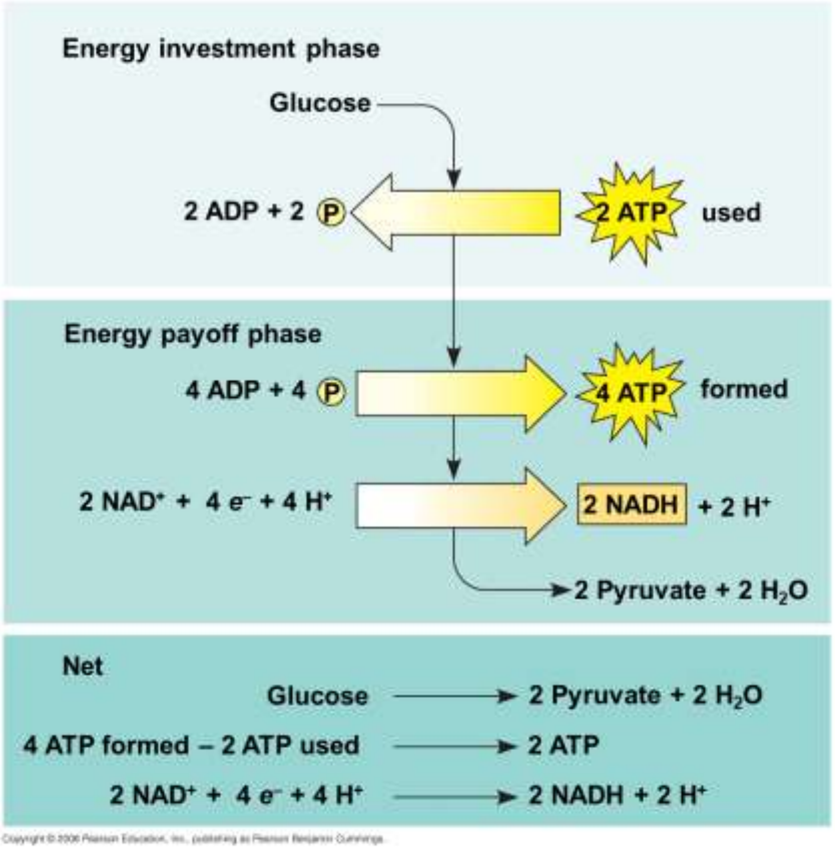
- 1) Compare and contrast aerobic and anaerobic respiration.
- 2) If the following redox reaction occurred, which compound would be oxidized and which reduced?

$$C_4H_6O_5 + NAD^+ \rightarrow C_4H_4O_5 + NADH + H^+$$

Concept 9.2:
Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

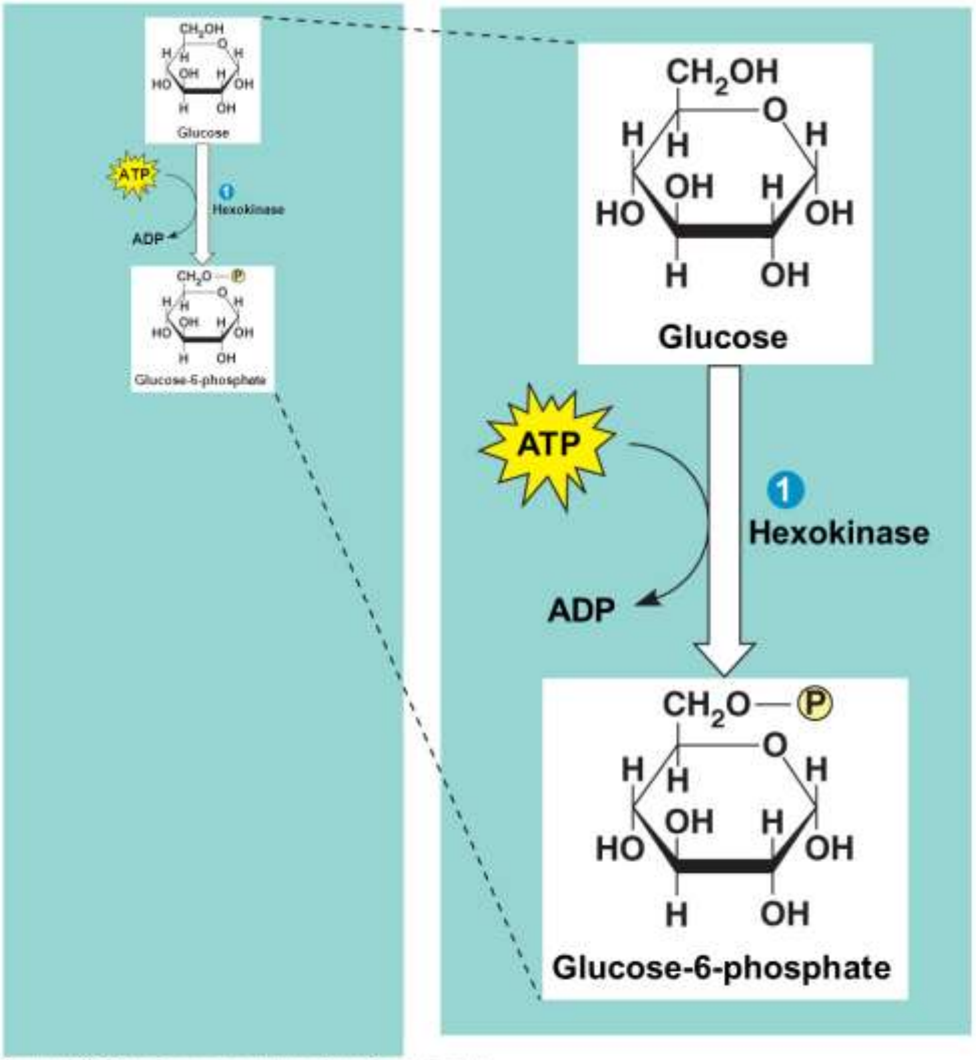
Glycolysis

- Glycolysis means "sugar splitting"
  - The 6-carbon glucose is broken down into two 3-carbon sugars
    - These smaller sugars are oxidized (lose electrons)
    - The remaining atoms are rearranged to form 2 molecules of pyruvate
- Glycolysis can be divided into 2 phases:
  - 1) *Energy investment phase* – cell spends (2 ATP/glucose molecule)
  - 2) *Energy pay-off phase* – ATP used in the 1st part of glycolysis is repaid with interest (4 ATP, NADH)
    - The net energy yield is 2 ATP and 2 NADH per glucose molecule



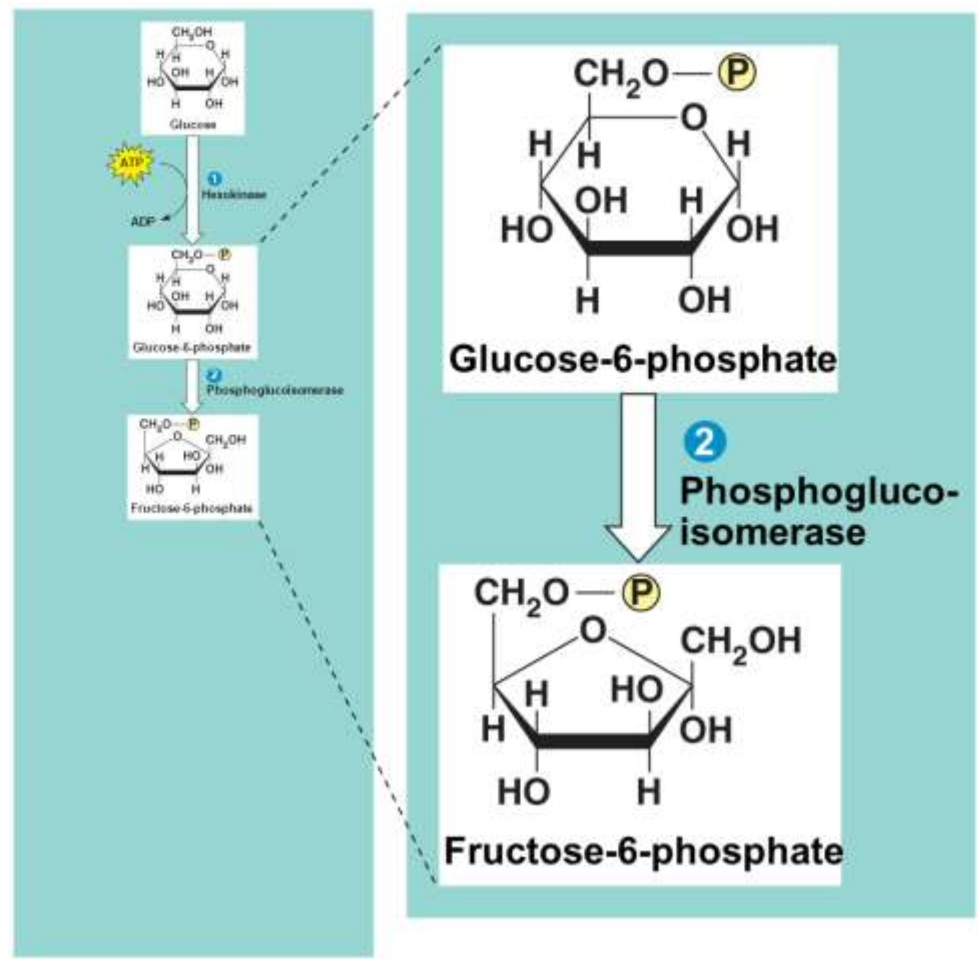
Glycolysis: Step 1

- 1) Glucose enters cell and is phosphorylated by ***hexokinase*** (an enzyme), which transfers a phosphate group from ATP (***1st ATP used)
    - The negative charge of the phosphate group traps the sugar in the cell (membrane impermeable to large ions)
    - Phosphorylation also makes glucose more chemically reactive
  – Phosphorylation forms a molecule called g***lucose-6-phosphate*** (phosphate attached to C6)



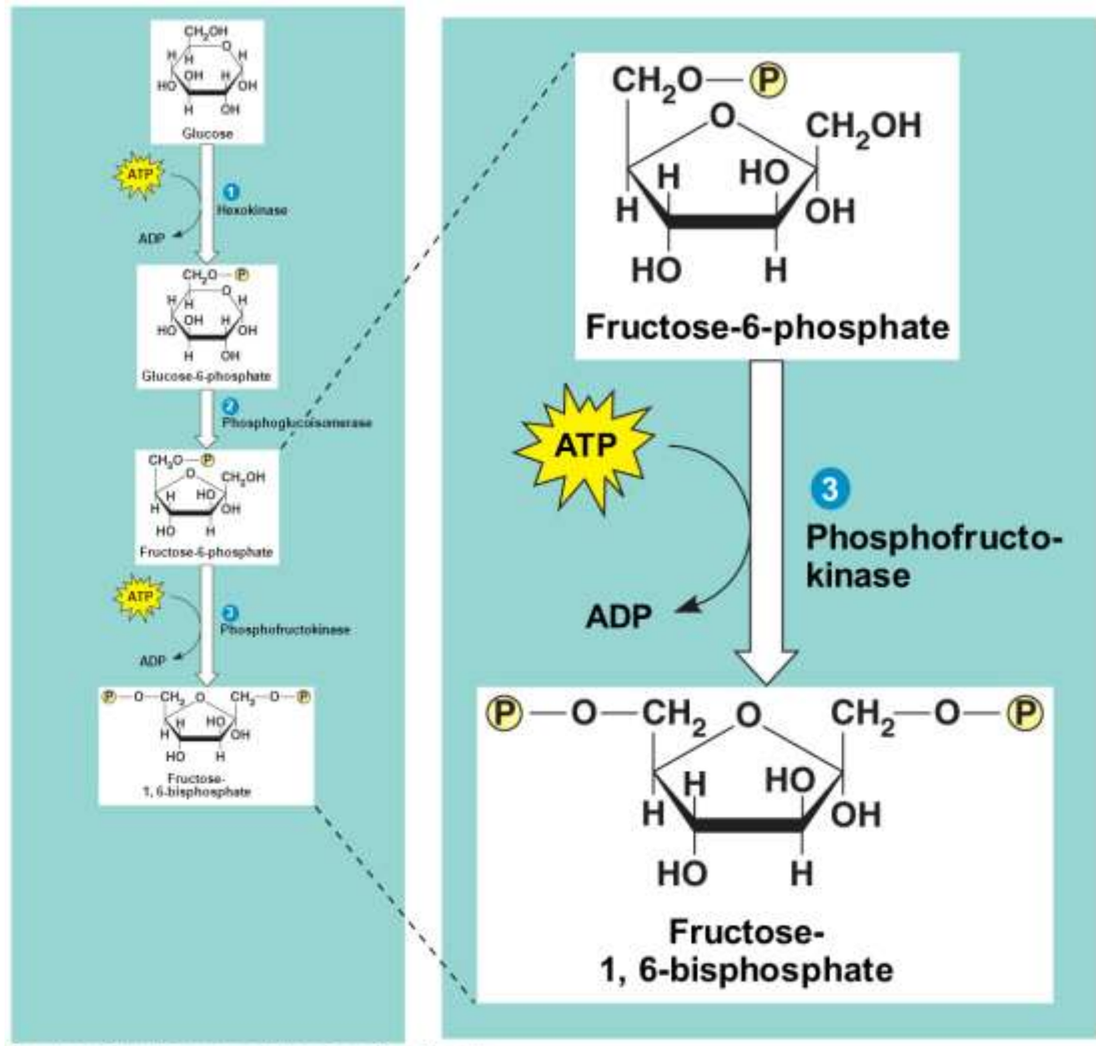
Glycolysis: Step 2

- 2) Glucose-6-phosphate is converted to its isomer, ***fructose-6-phosphate***
  - This conversion is catalyzed by the enzyme ***phosphoglucoisomerase***



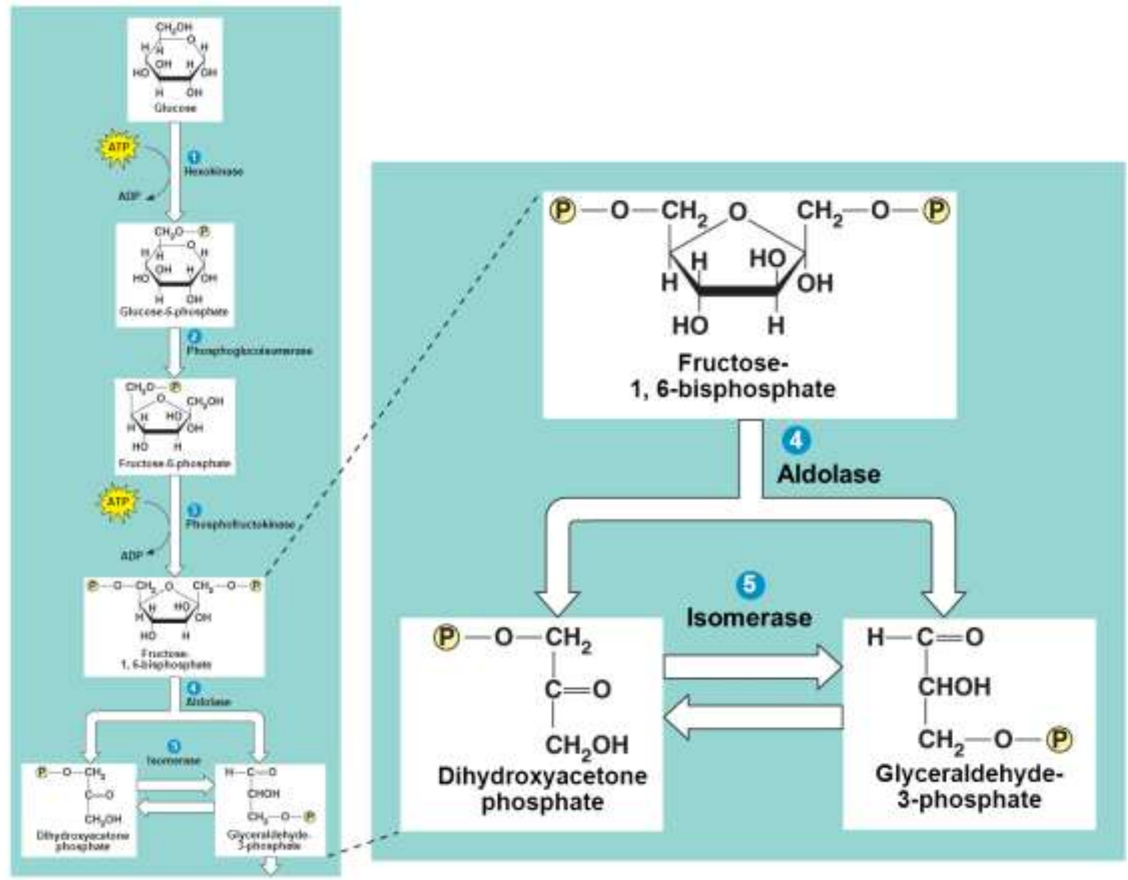
Glycolysis: Step 3

- 3) ***Phosphofructikinase*** transfers another phosphate group from ATP (***2nd ATP used)
  - This forms a molecule called ***fructose-1,6-bisphosphate***
    - This sugar is now ready to be split in half with phosphate groups on opposite ends



Glycolysis: Steps 4 & 5

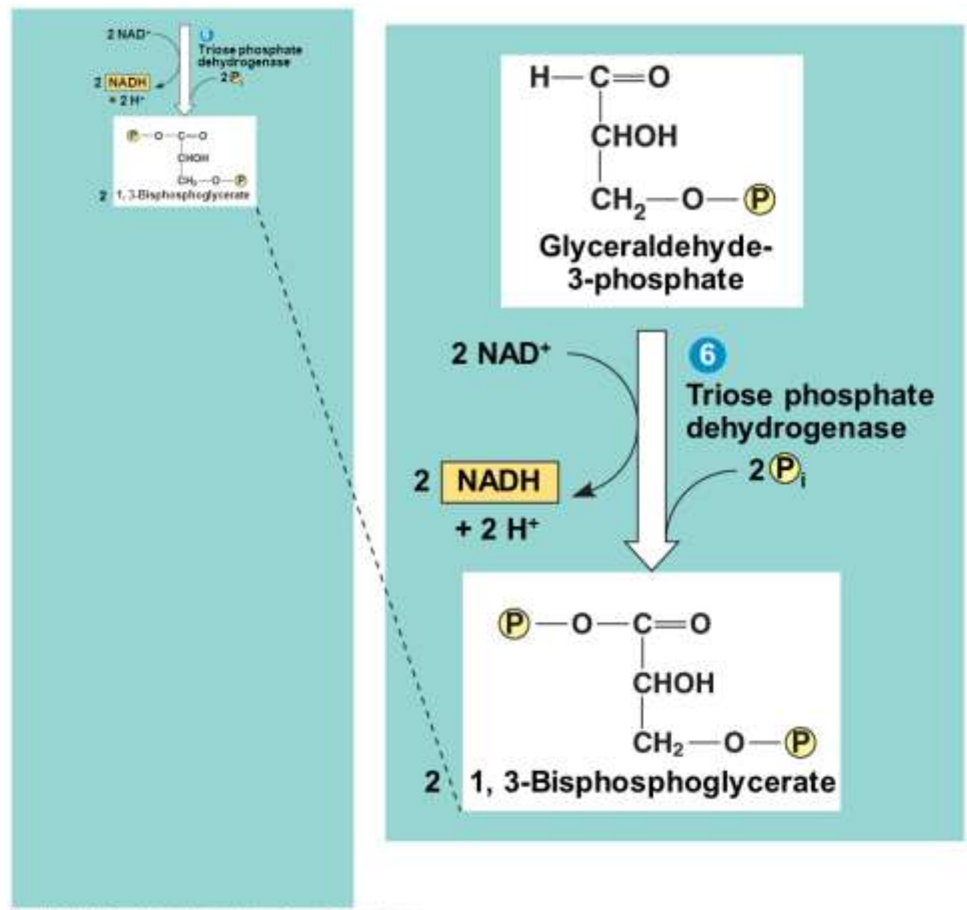
- 4) ***Aldolase*** cleaves fructose-1,6-bisphosphate into two 3-carbon sugars, ***dihydroxyacetone phosphate*** and ***glyceraldehyde-3-phosphate (G3P)***
  - These 3-carbon sugars are isomers of one another
- 5) ***Isomerase*** catalyzes the reversible conversion between these two 3-carbon sugars
  - This reaction never reaches equilibrium because the next reaction in glycolysis uses only G3P
    - This pulls equilibrium in the direction of G3P, which is removed as fast as it is formed



  - The net result is 2 molecules of glyceraldehyde-3-phosphate
    - Both progress through remaining steps of glycolysis

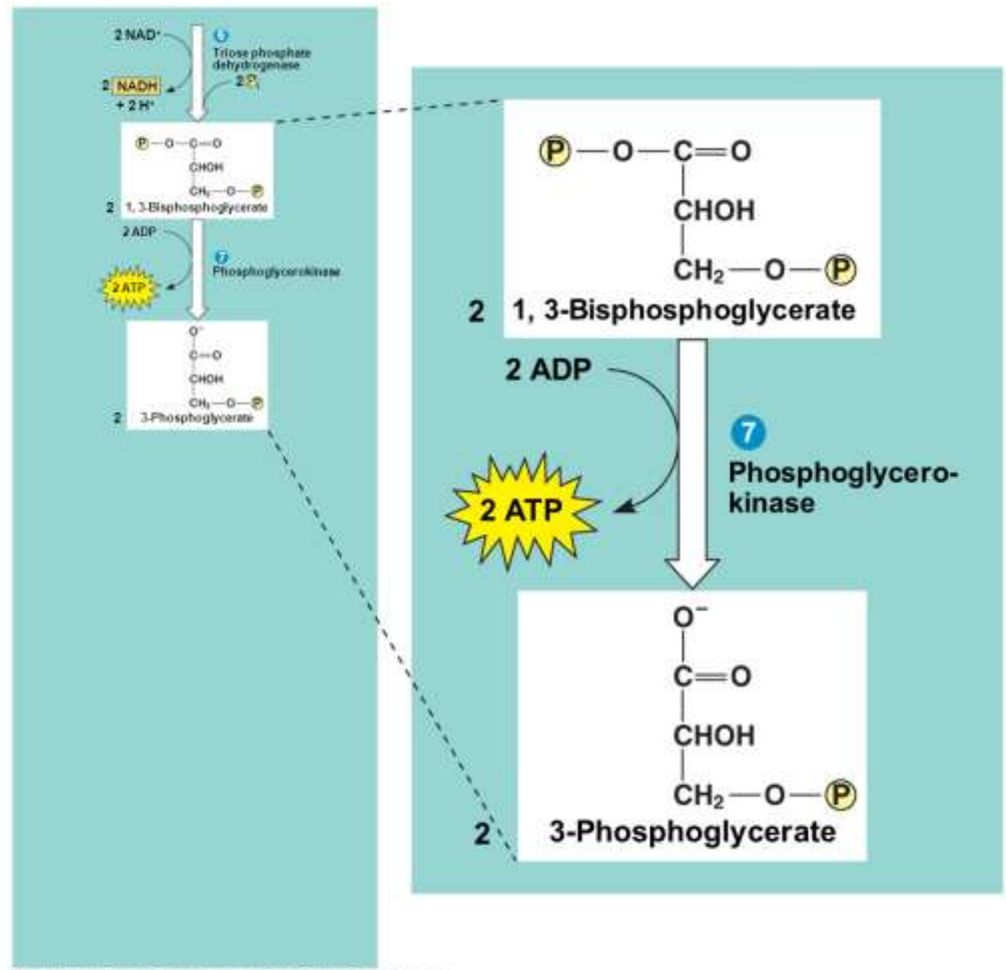
Glycolysis: Step 6

- Step 6 of glycolysis is the beginning of the Energy Payoff Phase:
  - 6) Glyceraldehyde-3-phosphate is oxidized, forming ***1,3-bisphosphoglycerate***
    - 2 electrons and a H+ ion are transferred to NAD+ forming NADH
    - This reaction is very exergonic (releases a lot of energy)
      - The released energy is used to attach a phosphate group to the sugar
      - The source of this phosphate is the pool of inorganic phosphate ions always present in cytosol
    - **Notice there is a coefficient of 2 in all molecules of payoff phase***
      - These steps occur after glucose has been split in 2



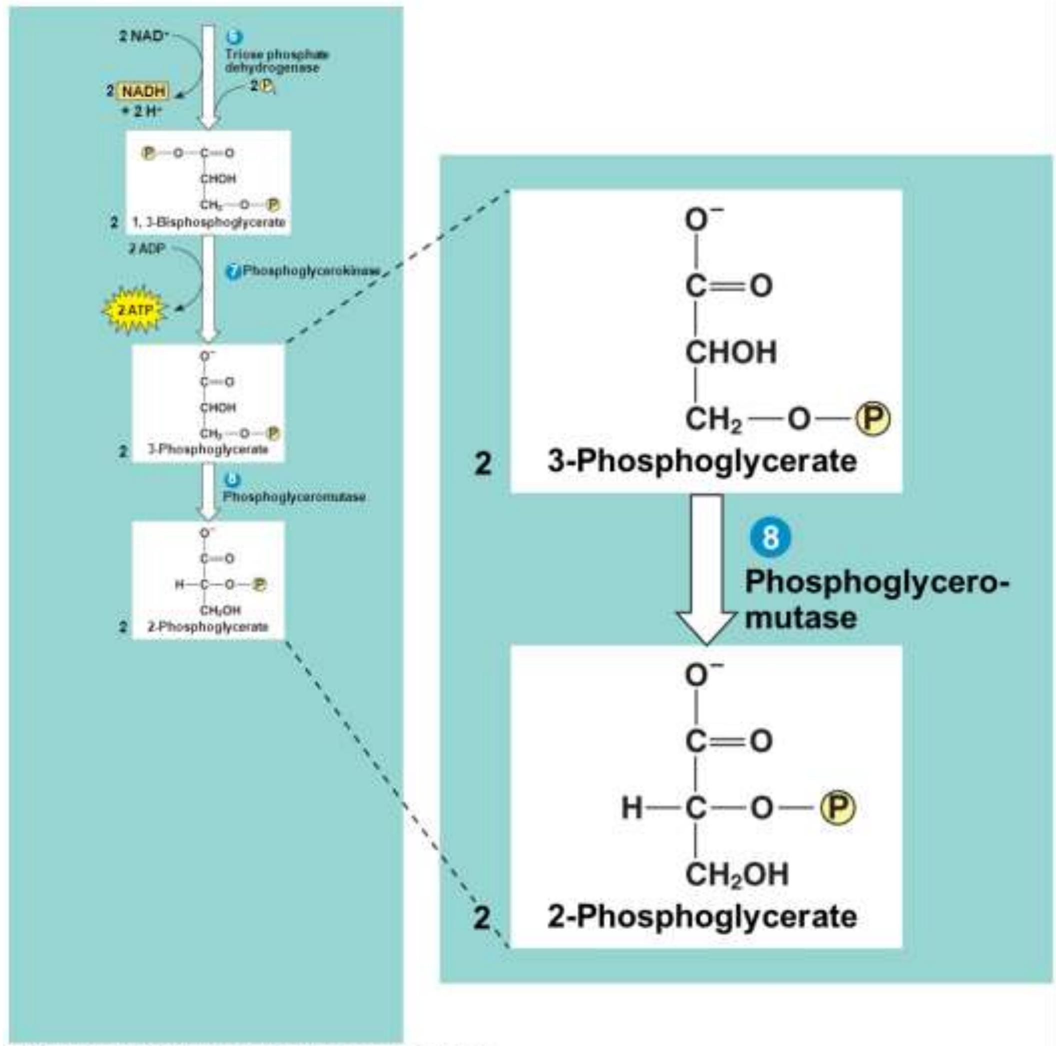
Glycolysis: Step 7

- 7) The phosphate group from the previous step is transferred to ADP, forming an ATP (substrate level phosphorylation)
  - Because there are 2 substrates, 2 total ATP are formed
    - ***Thus, the ATP debt has been repaid***
  - This converts bisphosphoglycerate into ***3-phosphoglycerate***, an organic acid



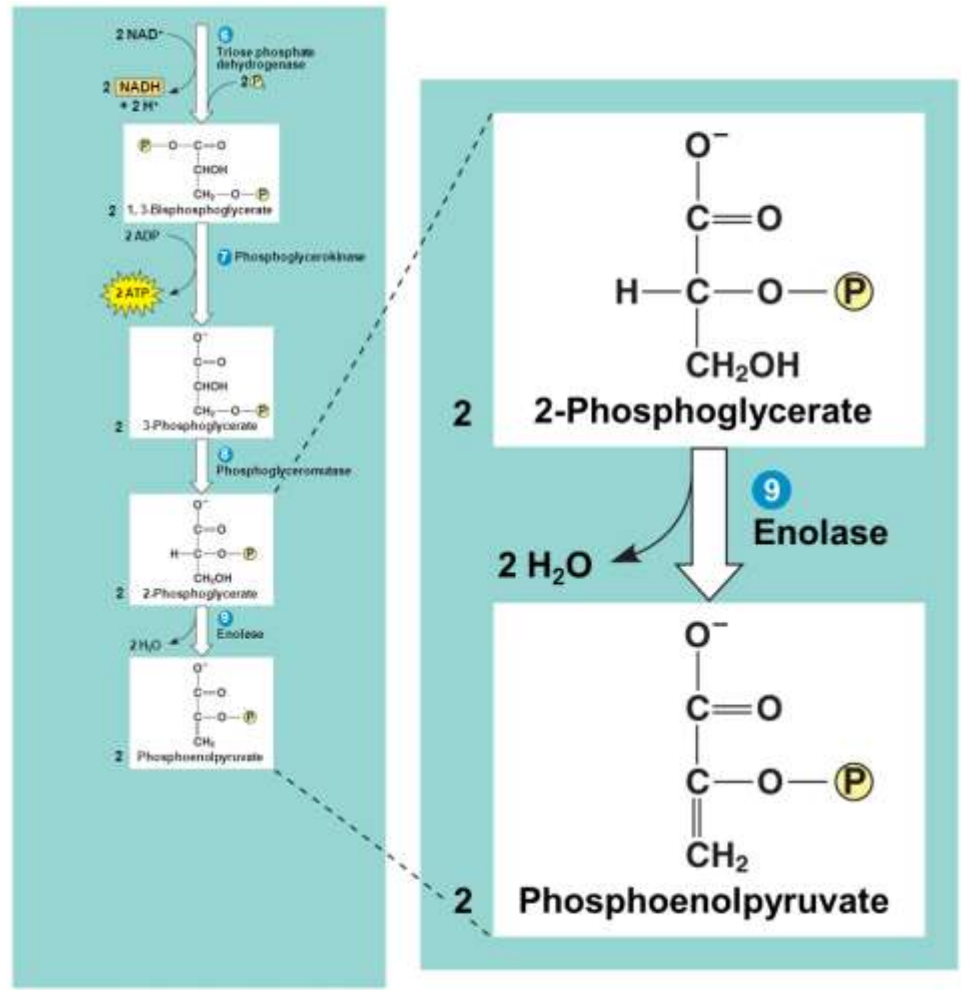
Glycolysis: Step 8

- 8) The remaining phosphate group on 3-phosphoglycerate is relocated by an enzyme called ***phosphoglyceromutase***
  - This forms a molecule called ***2-phosphoglycerate***



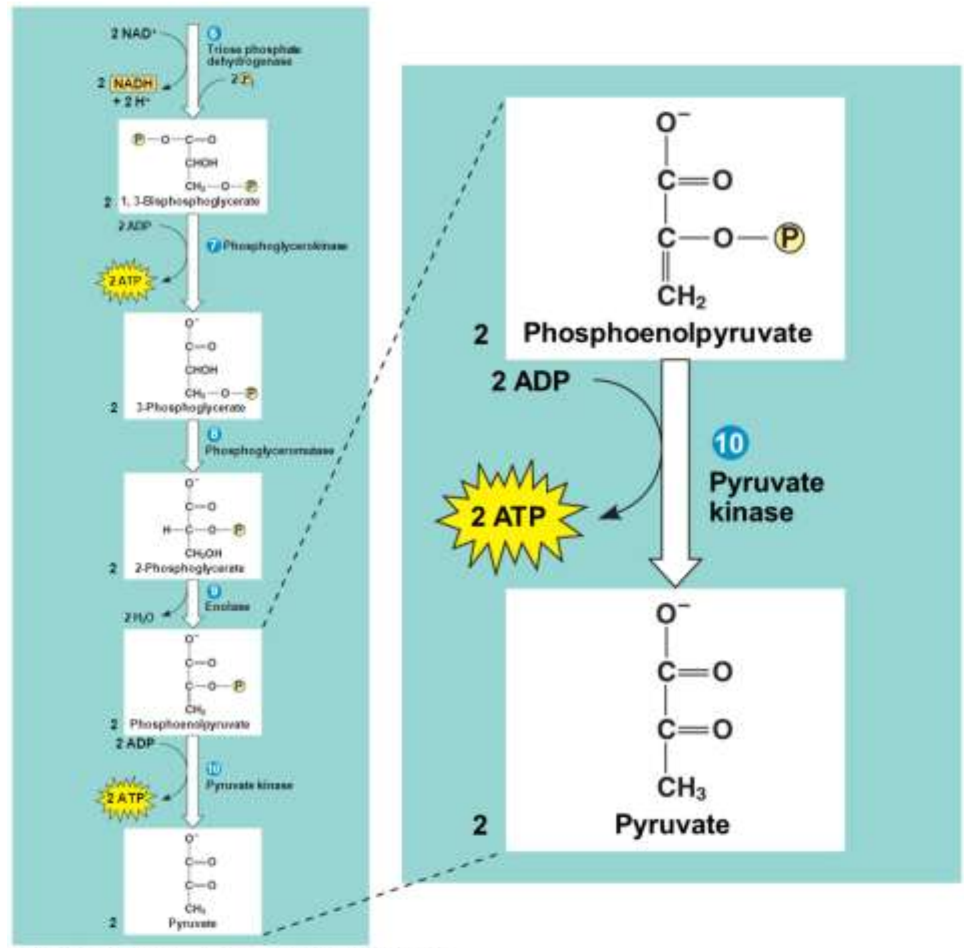
Glycolysis: Step 9

- 9) ***Enolase*** causes a double bond to form by extracting a water molecule
  - This forms ***phosphoenolpyruvate (PEP)***, which is very high in potential energy



Glycolysis: Step 10

- 10) More ATP is produced by the transfer of a phosphate group from PEP to ADP (2nd instance of substrate-level phosphorylation)
  - Since this step occurs twice for each glucose, 2 ATP are formed
    - This brings the total ATP formed to 4
    - However, 2 *NET* ATP are formed since 2 have been used
  - PEP is thus converted to a molecule called ***pyruvate***, the end product of glycolysis



Concept Check 9.2

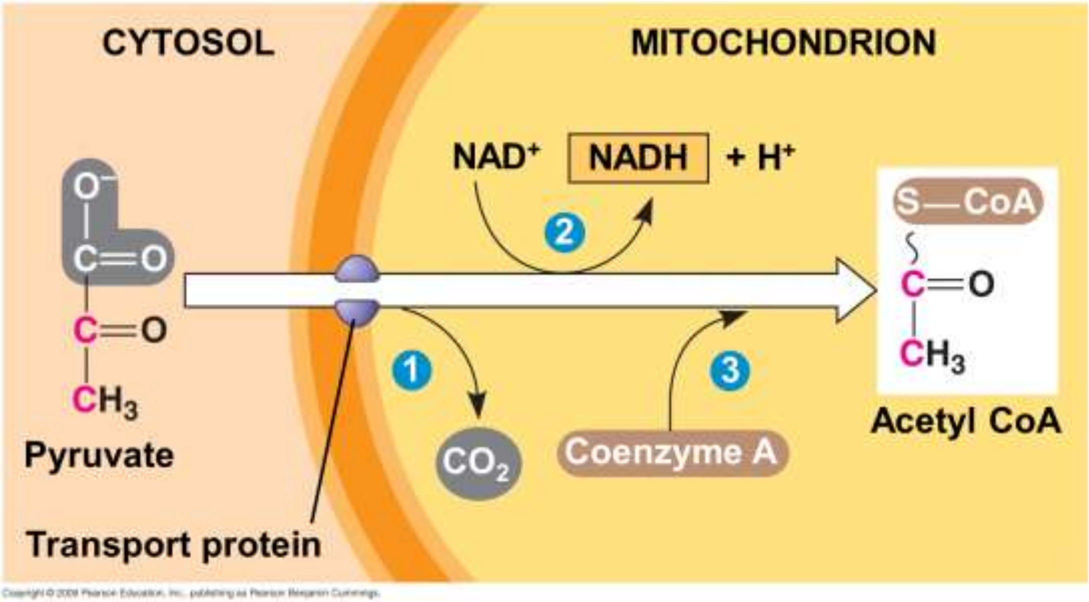
- 1) During the redox reaction in glycolysis (step 6 in Figure 9.9, pp. 169), which molecule acts as the oxidizing agent? The reducing agent?

- 2) Step 3 in Figure 9.9 (pp. 168) is a major point of regulation of glycolysis. The enzyme phosphofructokinase is allosterically regulated by ATP and related molecules. Considering the overall result of glycolysis, would you expect ATP to inhibit or stimulate activity of this enzyme? (Hint: make sure you consider the role of ATP as an allosteric regulator, not as a substrate of the enzyme.)

Concept 9.3:
The citric acid cycle completes the energy-yielding oxidation of organic molecules

Formation of Acetyl CoA

- If oxygen is present, pyruvate enters the mitochondrion (or cytosol in prokaryotes)
  - Here, enzymes of the citric acid cycle complete the oxidation of glucose
- Upon entering mitochondrion (via active transport), pyruvate must first be converted to ***acetyl coenzyme A (acetyl CoA)***, which occurs in 3 steps:
  - 1) A carboxyl group is removed from pyruvate and given off as a molecule of CO_2
  - 2) The remaining 2-carbon fragment is oxidized (electrons removed), forming acetate
    - The electrons are transferred to NAD+, forming NADH
  - 3) ***Coenzyme A (CoA)***, a sulfur-containing compound derived from vitamin B, is attached to acetate with an unstable bond
    - Instability of this bond makes the product, acteyl CoA ,very reactive and high in potential energy



Overview of the Citric Acid Cycle

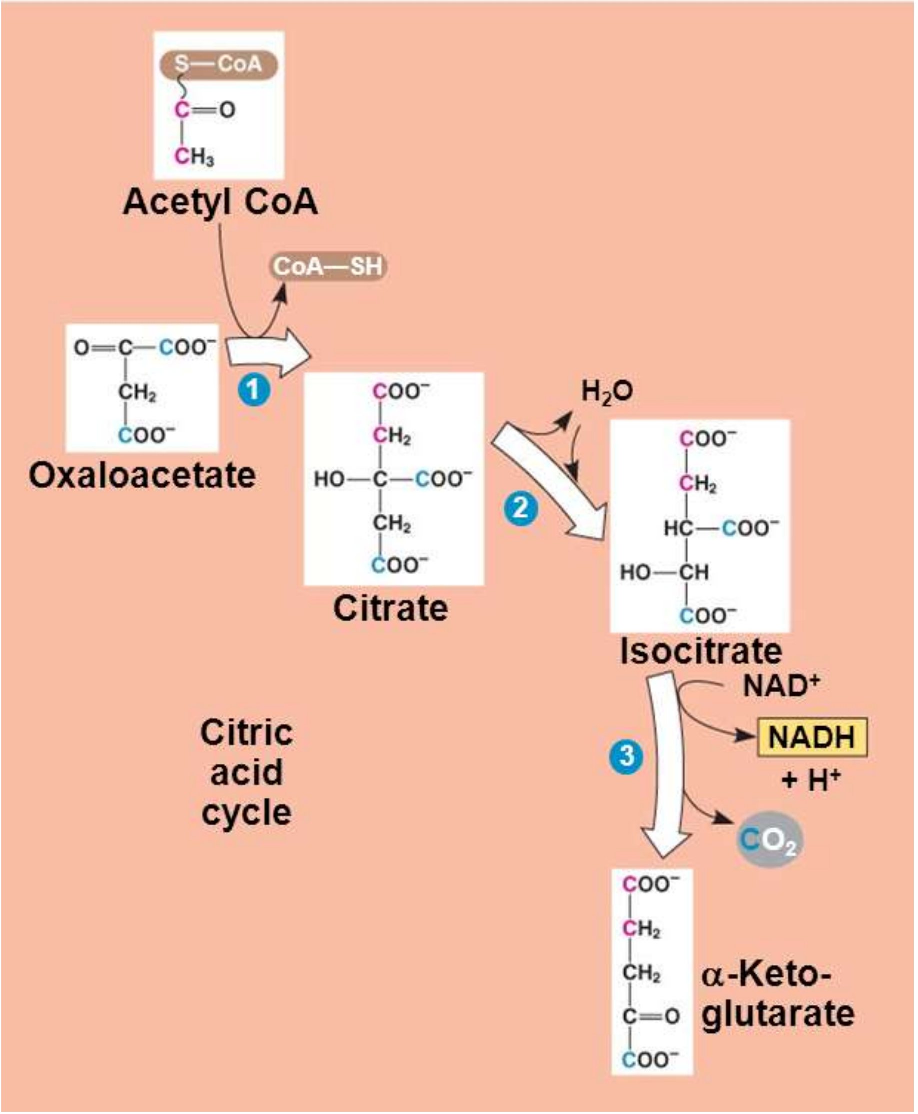
- The citric acid (Krebs) cycle takes place in the mitochondrial matrix
  - Organic fuel derived from pyruvate is oxidized, forming (per turn):
    - 1 ATP
    - 3 NADH
    - 1 $FADH_2$
  - Most of the chemical energy is still transferred to the electron carriers NADH and $FADH_2$
    - NADH and $FADH_2$ then shuttle these high-energy electrons to the ETC

Overview of the Citric Acid Cycle

- The citric acid cycle has 8 steps, each catalyzed by a specific enzyme
    - The cycle begins when acetyl CoA combines with oxaloacetate, forming citrate
  - The next 7 steps decompose citrate back to oxaloacetate
    - This regeneration of oxaloacetate makes the process a CYCLE
  - For each acetyl group entering cycle, 3 NAD+ are reduced to NADH
    - Electrons are also transferred to FAD in step 6 forming $FADH_2$
  - Most of the ATP produced by respiration results from oxidative phosphorylation
    - Here NADH and $FADH_2$ produced by TCA cycle relay their high-energy electrons extracted from food to the ETC

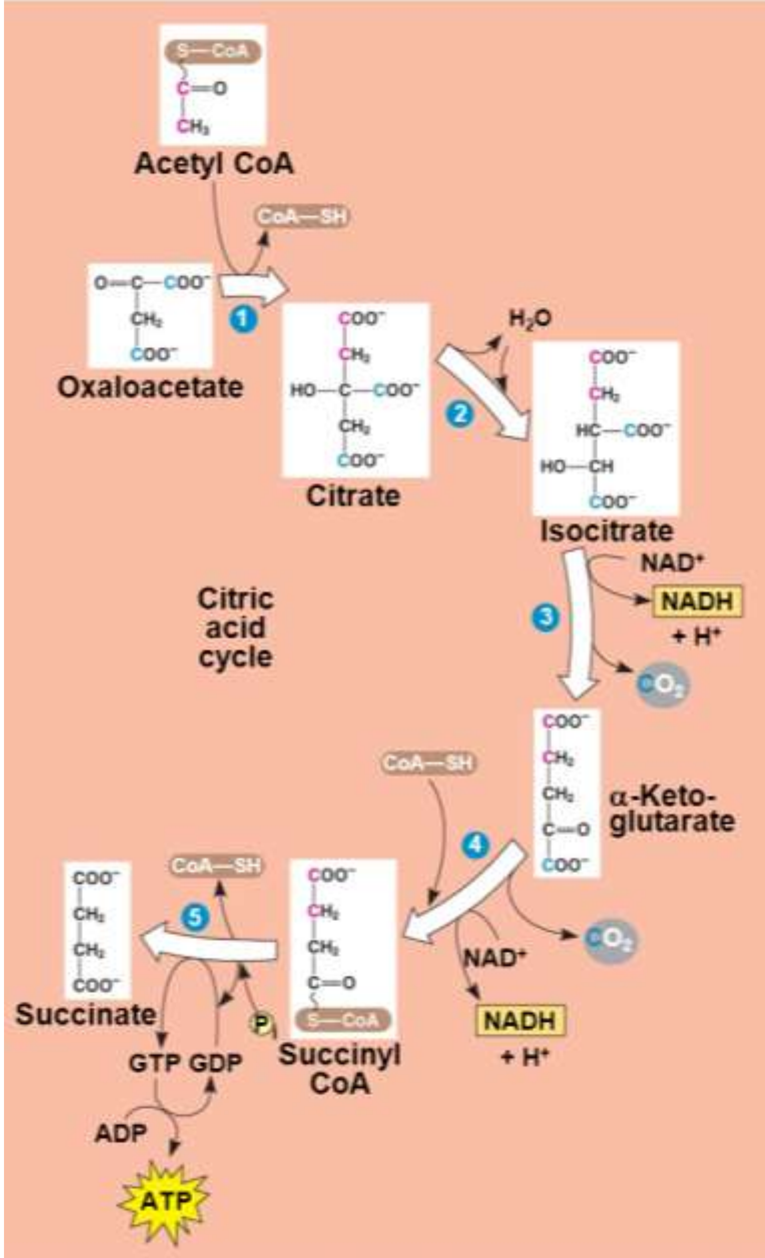
The Citric Acid Cycle: Steps 1-3

- 1) Acetyl CoA adds its 2-carbon acetyl group to oxaloacetate, forming ***citrate***
- 2) Citrate is converted to its isomer, ***isocitrate***, by removal of one water molecule and addition of another
- 3) Isocitrate is oxidized as electrons are transferred to NAD+ , forming NADH
  - Then, the resulting compound loses a CO_2 molecule, forming ***alpha-ketoglutarate***



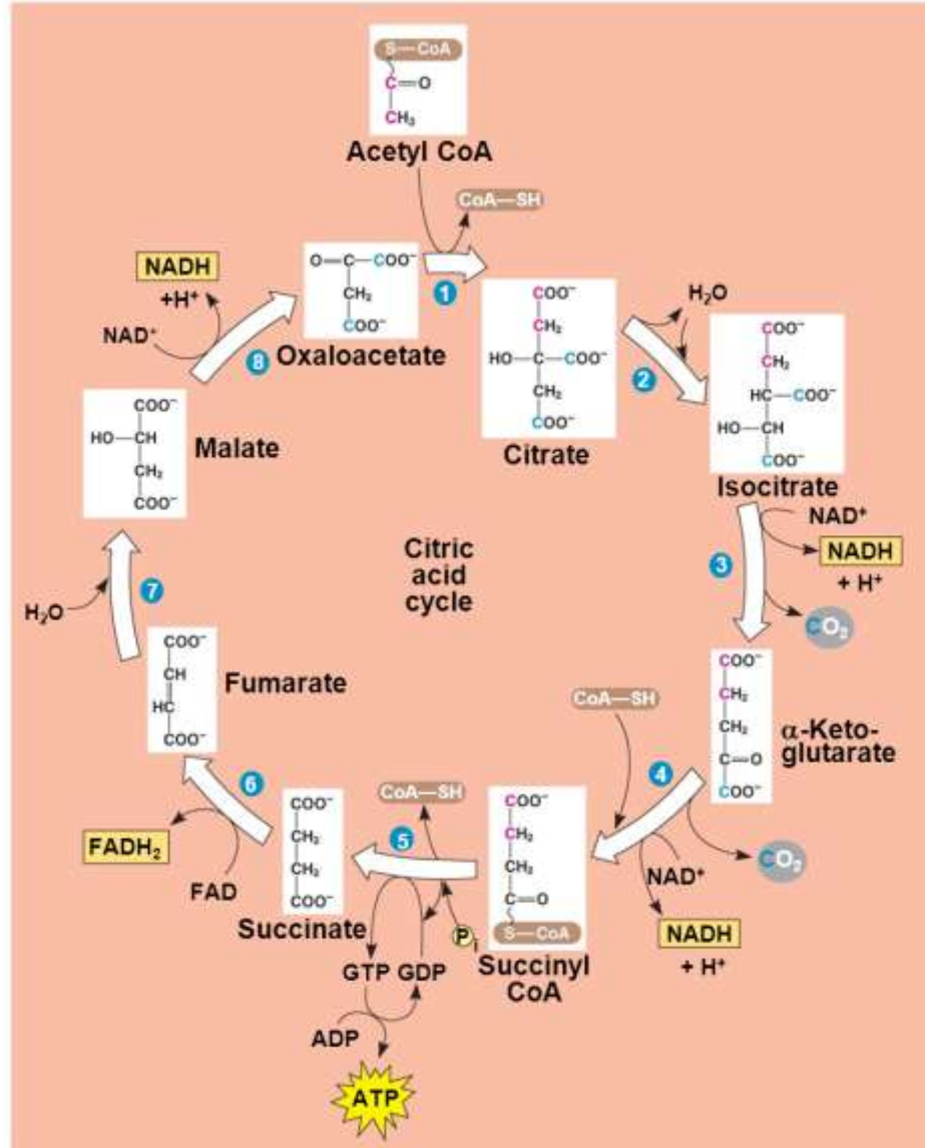
The Citric Acid Cycle: Steps 4-5

- 4) Another CO_2 is now lost from α-keto-glutarate, and the resulting compound is oxidized
    - Electrons are again added to NAD+, forming NADH
  - – The remaining molecule is attached to coenzyme A by an unstable bond, forming ***succinyl CoA***
- 5) CoA is displaced by a phosphate group, forming ***succinate***
  - – This phosphate group is then transferred to GDP, forming GTP
    - GTP has functions similar to ATP; can be used in some cases to make ATP



The Citric Acid Cycle: Steps 6-8

- 6) Two hydrogens are transferred to FAD, forming $FADH_2$
  - As a result, succinate is oxidized to ***fumarate***
- 7) A water molecule is added to fumarate, forming ***malate***
- 8) Malate is oxidized, reforming ***oxaloacetate***
  - The electrons are added to NAD+, forming a 3rd molecule of NADH



Concept Check 9.3

- 1) Name the molecules that conserve most of the energy from the citric acid cycle's redox reactions. How is this energy converted to a form that can be used to make ATP?
- 2) What cellular processes produce the carbon dioxide that you exhale?
- 3) The conversions shown in Figure 9.10 (pp.170) and step 4 of Figure 9.12 (pp. 171) are each catalyzed by a large multienzyme complex. What similarities are there in the reactions that occur in these two cases?

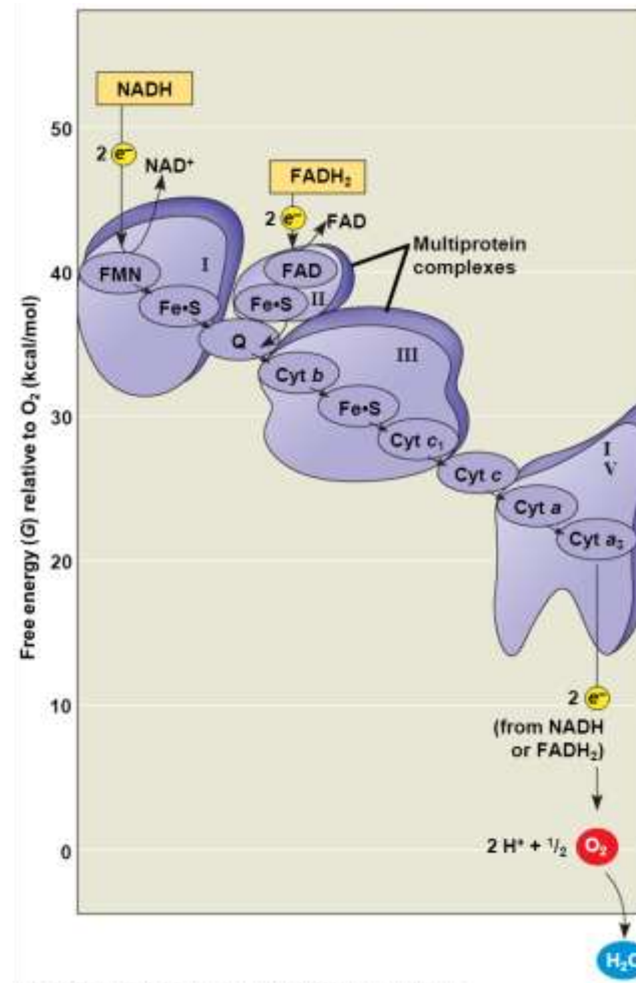
Concept 9.4:
During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

A Preview: Oxidative Phosphorylation

- So far, glycolysis and TCA cycle have produced only 4 ATP molecules per glucose, all via substrate-level phosphorylation
  - 2ATP from glycolysis
  - 2 ATP from TCA cycle
- At this point, molecules of NADH and $FADH_2$ account for most of the energy extracted from glucose
  - These molecules donate these high-energy electrons to the ETC
    - Here, energy released by the ETC will be used to power ATP synthesis via oxidative phosphorylation

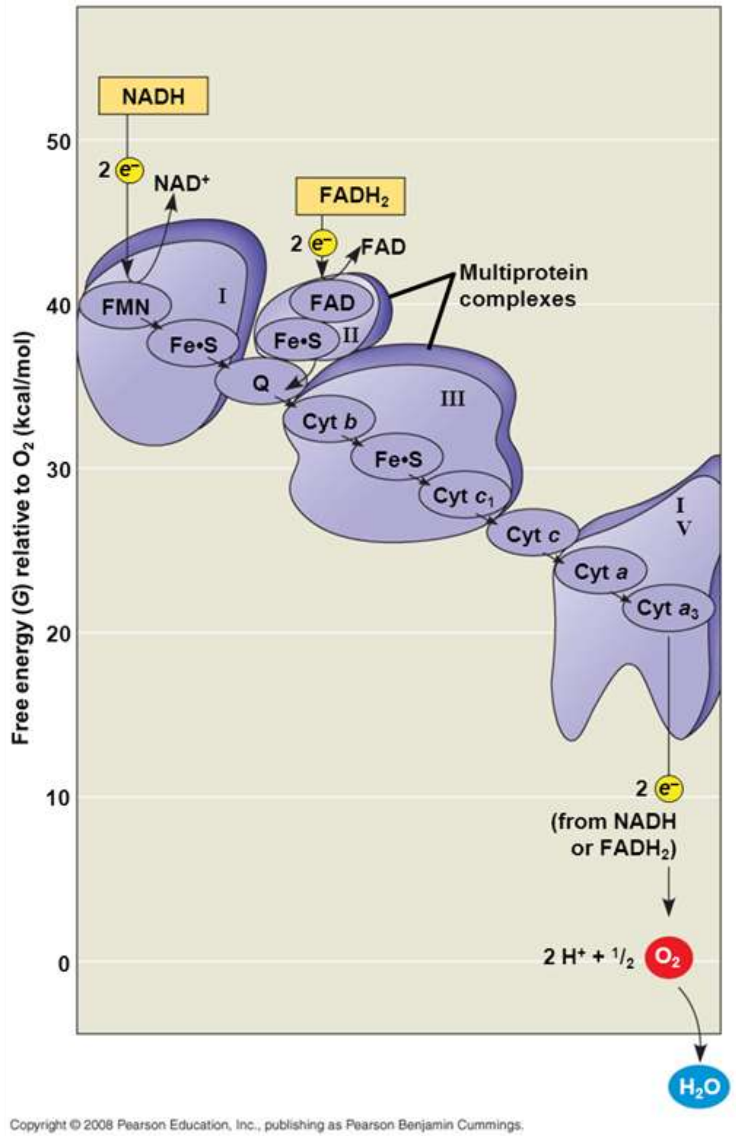
Structure of the ETC

- The ETC is a collection of molecules embedded in the inner membrane of the mitochondria
    - In prokaryotes, ETC is located in the plasma membrane
- The inner membrane of mitochondria has many infoldings, which increases its surface area
    - As a result, 1000s of copies of the ETC exist in each mitochondrion
- Most of the components of the ETC are proteins that exist in multiprotein complexes (numbered I-IV)
    - Prosthetic groups are tightly attached to these proteins
        - These prosthetic groups are nonprotein components that are essential for the catalytic function of certain enzymes



The Pathway of Electron Transport

- During electron transport down the chain, electron carriers alternate between reduced and oxidized states
  - An electron carrier becomes reduced as it accepts electrons from its "uphill" neighbor
    - This uphill neighbor has a lower affinity for electrons because it is less electronegative
    - This same electron carrier then returns to its oxidized form as it passes its electrons to its "downhill" more electronegative neighbor
  - As electrons move along the ETC, they drop in free-energy until they are finally passed to O_2, forming H_2O
    - The overall energy drop for electrons traveling from NADH to O_2 is 53 kcal/mol



Cytochromes

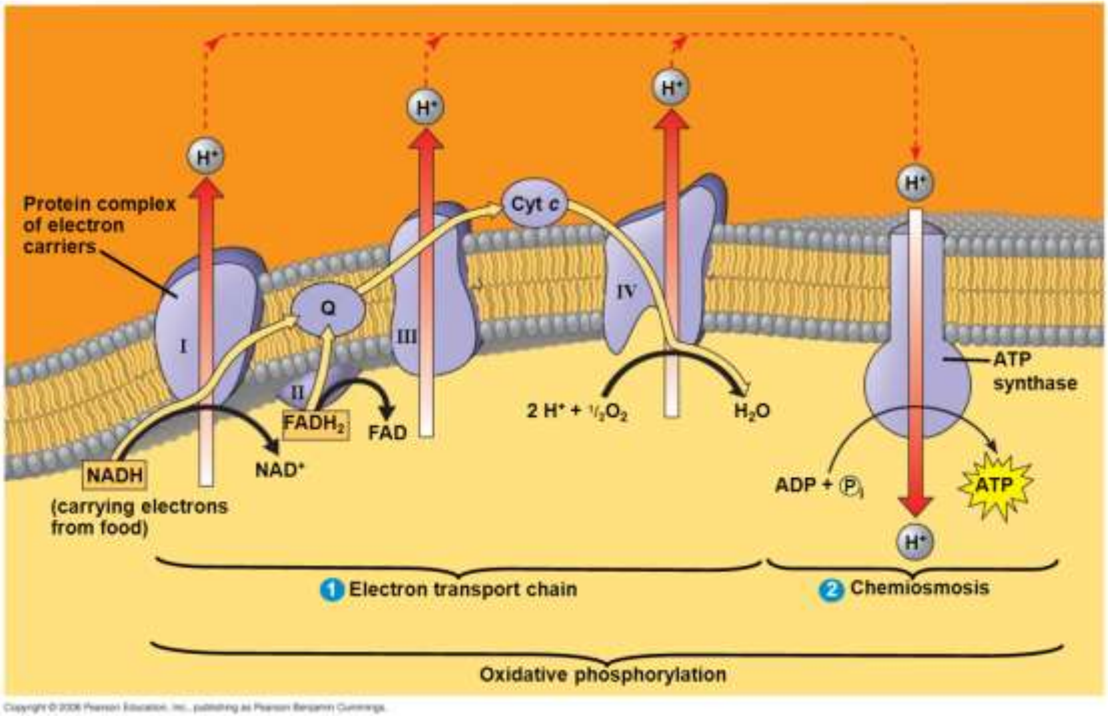
- Electrons from NADH and $FADH_2$ are transferred to the ETC
    - Once in the ETC, they are passed through a series of proteins, including ***cytochromes***, before reaching O_2
  - Cytochromes have a prosthetic group called a heme group
    - This heme group has an iron atom that accepts and donates electrons
  - The ETC has several types of cytochromes, each with a slightly different heme group
- The ETC makes no ATP directly
  - Instead, its function is simply to ease the fall of electrons from food to oxygen, which releases energy in manageable amounts

Chemiosmosis: The Energy-Coupling Mechanism

- There are many copies of another protein complex called ***ATP synthase*** in the inner mitochondrial membrane
    - This enzyme makes ATP from ADP and inorganic phosphate
- – ATP synthase uses the energy of an existing ion gradient to power ATP synthesis
    - The power source for ATP synthase is a difference in concentration of H+ ions on opposite sides of the inner mitochondrial membrane
        - – This concentration gradient is created as electrons are transferred down the ETC, which causes proteins to pump H+ from the mitochondrial matrix to the intermembrane space
    - The exergonic flow of these H+ ions back down their concentration gradient is used to drive the phosphorylation of ATP
        - – This is an example of ***chemiosis*** – the use of energy in H+ ion gradients to drive cellular work

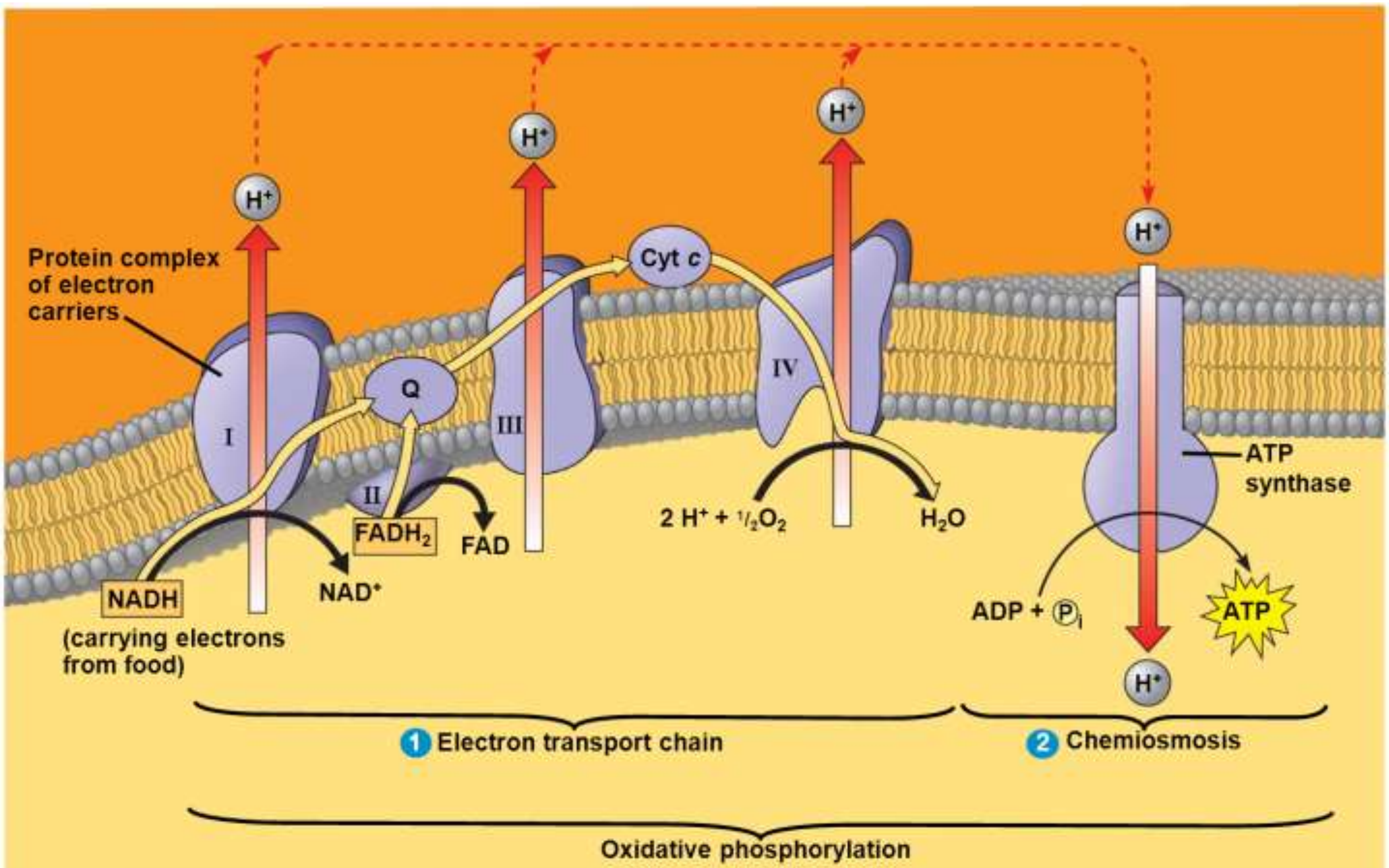
Steps of Oxidative Phosphorylation

- 1) NADH and $FADH_2$ shuttle high-energy electrons extracted from food to the ETC
    - Yellow arrows trace transport of electrons
  - Electrons finally pass to oxygen at the end of the ETC, forming water
- Most of the electron carriers are grouped into 4 complexes
  - There are 2 mobile carriers, ubiquinone (Q) and cytochrome c (Cyt C)
    - These carriers move rapidly, passing electrons between the large complexes
  - As protein complexes accept and then donate electrons, they pump protons from the mitochondrial matrix into the intermembrane space



Steps of Oxidative Phosphorylation

- 2)During chemiosis, protons flow back down their gradient via ATP synthase
  - ATP synthase harnesses this proton-motive force and phosphorylates ADP, forming ATP



An Accounting of ATP Production by Cellular Respiration

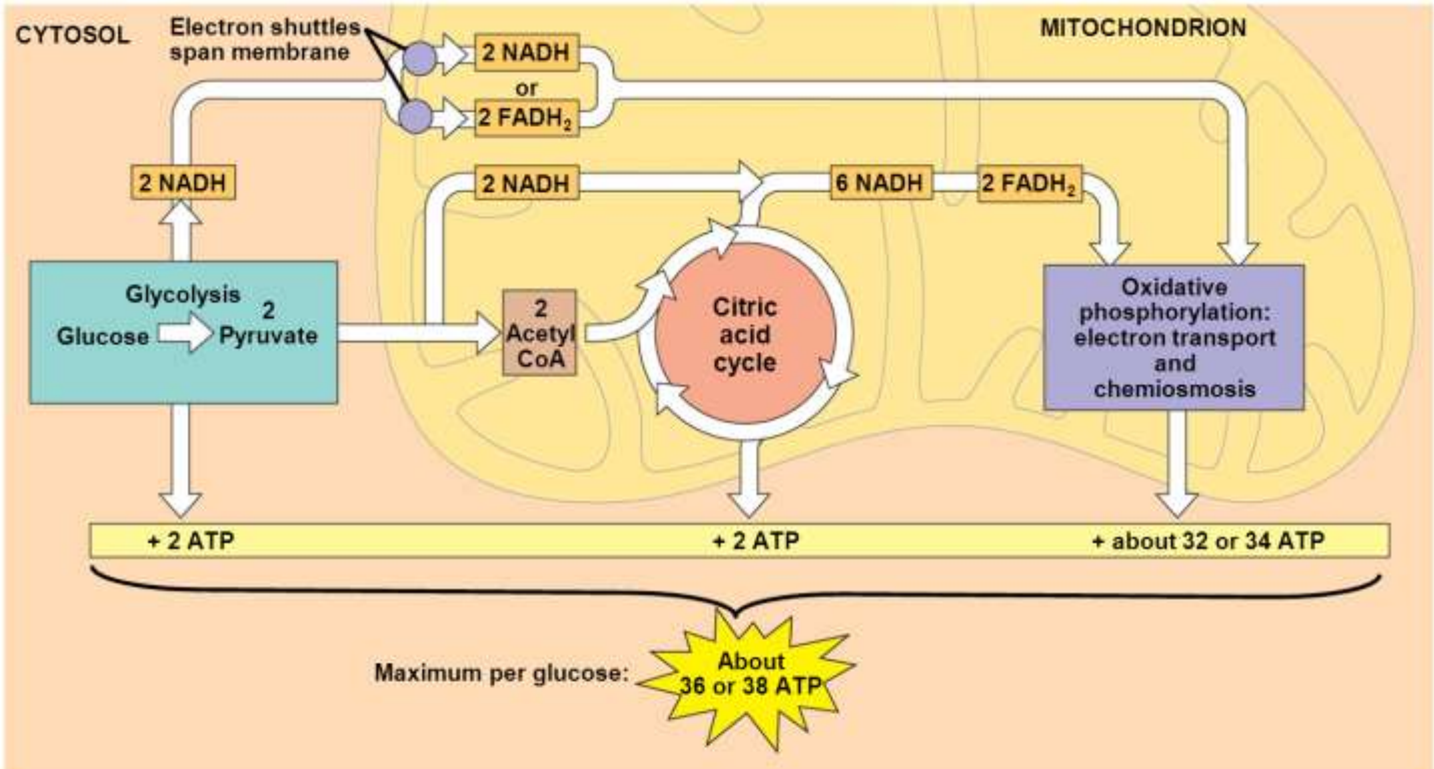
- During cell respiration, most energy flows in this sequence:

  glucose → NADH → electron transport chain → proton-motive force → ATP

- About 40% of the potential chemical energy in glucose is transferred to ATP during cellular respiration
  - This produces about 38 ATP per glucose molecule
    - The rest of the stored energy in glucose is lost as heat
      - Humans use some of this heat to maintain their relatively high body temperature
      - We dissipate the rest through sweating and other cooling mechanisms
  - Cellular respiration is very efficient overall
    - By comparison, the most efficient automobile converts only about 25% of the energy stored in gas to energy that moves the car

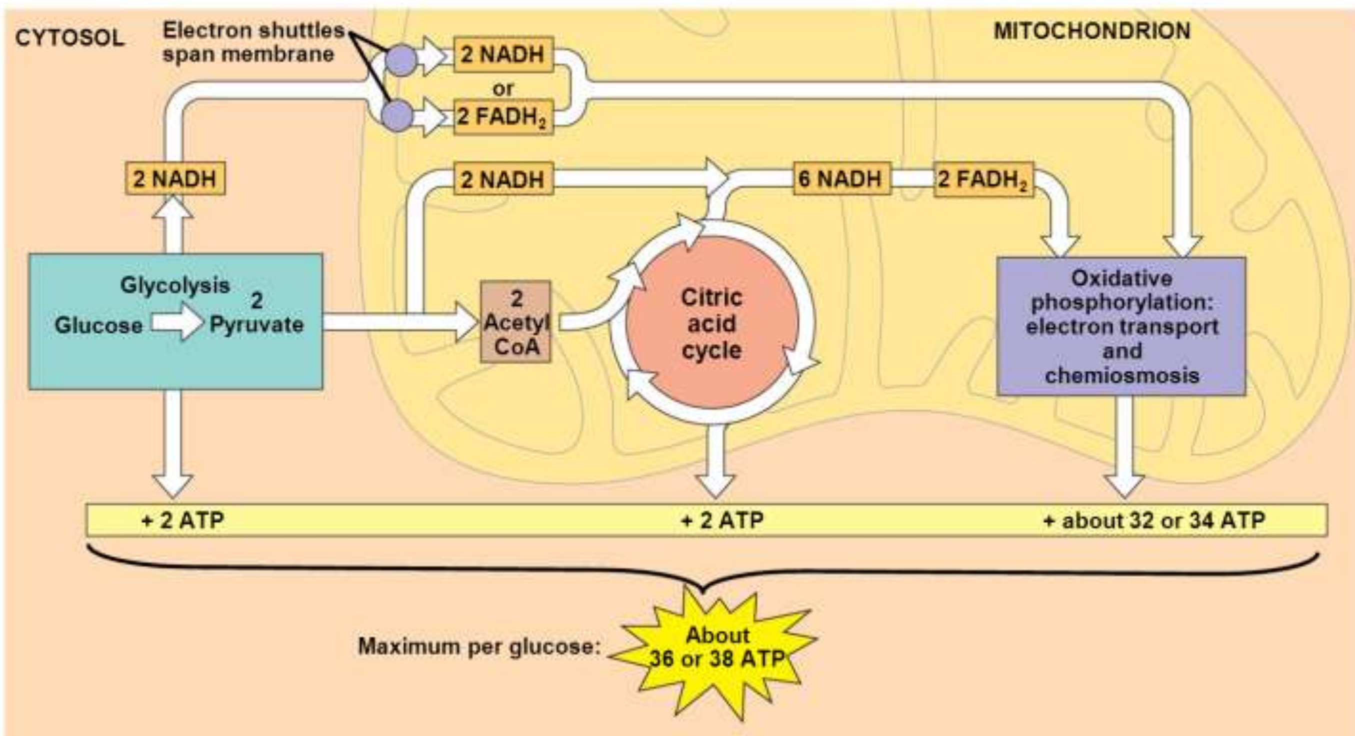
Cellular Respiration: A Review

- ATP yield per molecule of glucose at each stage of cellular respiration:
  - 2 ATP produced during glycolysis by substrate level phosphorylation
  - 2 ATP produced during TCA cycle by substrate level phosphorylation
  - 32-34 ATP produced during oxidative phosphorylation



Cellular Respiration: A Review

- ATP production depends on the type of shuttle used to transport electrons from cytosol into mitochondrion
  - The mitochondrial membrane is impermeable to NADH
    - ATP yield varies depending on if the electrons from NADH in cytosol are passed to NAD+ or FAD in the mitochondria
  - The maximum ATP yield per glucose molecule is 36 or 38 ATP



Concept Check 9.4

- 1) What effect would an absence of oxygen have on the process of oxidative phosphorylation (Figure 9.16, pp. 175)?

- 2) In the absence of oxygen, as in question 1, what do you think would happen if you decreased the pH of the intermembrane space of the mitochondrion? Explain your answer.

Concept 9.5: Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

Production of ATP Under Anaerobic Conditions

- If no oxygen is present, there is no electronegative force present to pull electrons down the ETC
    - Thus, oxidative phosphorylation ceases
  - There are 2 general mechanisms by which cells can oxidize organic fuel and generate ATP without the use of oxygen
    - Anaerobic respiration
    - Fermentation

Anaerobic Respiration and Fermentation

- Anaerobic respiration uses an ETC like aerobic respiration
  - The difference is that. in anaerobic respiration, oxygen is NOT the final electron acceptor
    - A commonly used substance is instead the sulfate ion
- Fermentation does not use oxygen or an ETC
  - Fermentation is an expansion of glycolysis
    - ATP is continually generated by substrate level phosphorylation of glycolysis

Types of Fermentation

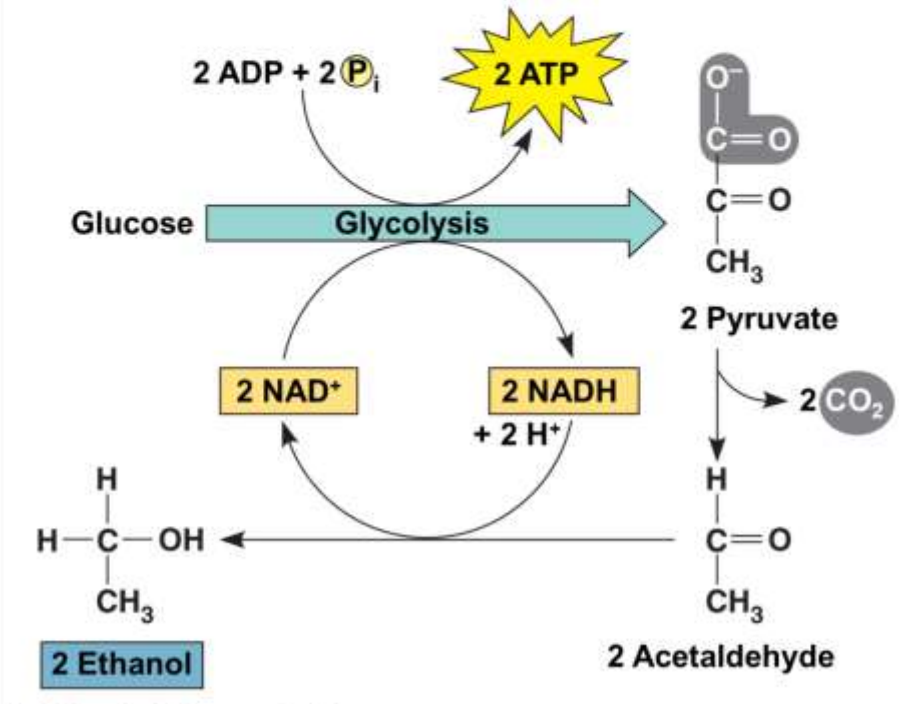
- Fermentation consists of glycolysis, plus reactions that generate NAD+ by transferring electrons from NADH to pyruvate or derivatives of pyruvate
    - NAD+ can then be reused in glycolysis
  - Otherwise, glycolysis would deplete the cell's pool of NAD+ by reducing it all to NADH
- There are many types of fermentation that differ in the end products formed from pyruvate
  - 2 common types are :
    - Alcohol fermentation
    - Lactic acid fermentation

Alcohol Fermentation

- In ***alcohol fermentation***, pyruvate is converted to ethanol in 2 steps
  - 1) Carbon dioxide is released from pyruvate
    - Pyruvate is thereby converted to a 2-carbon compound called ***acetaldehyde***
  - 2) Acetaldehyde is reduced by NADH to ***ethanol***
    - This regenerates the supply of NAD+ needed for continuation of glycolysis
- Many bacteria and yeast carry out alcohol fermentation
  - For 1000s of years, humans have used yeast in brewing, winemaking, and baking
    - CO_2 bubbles generated by baker's yeast during alcohol fermentation allows bread to rise

PLAY

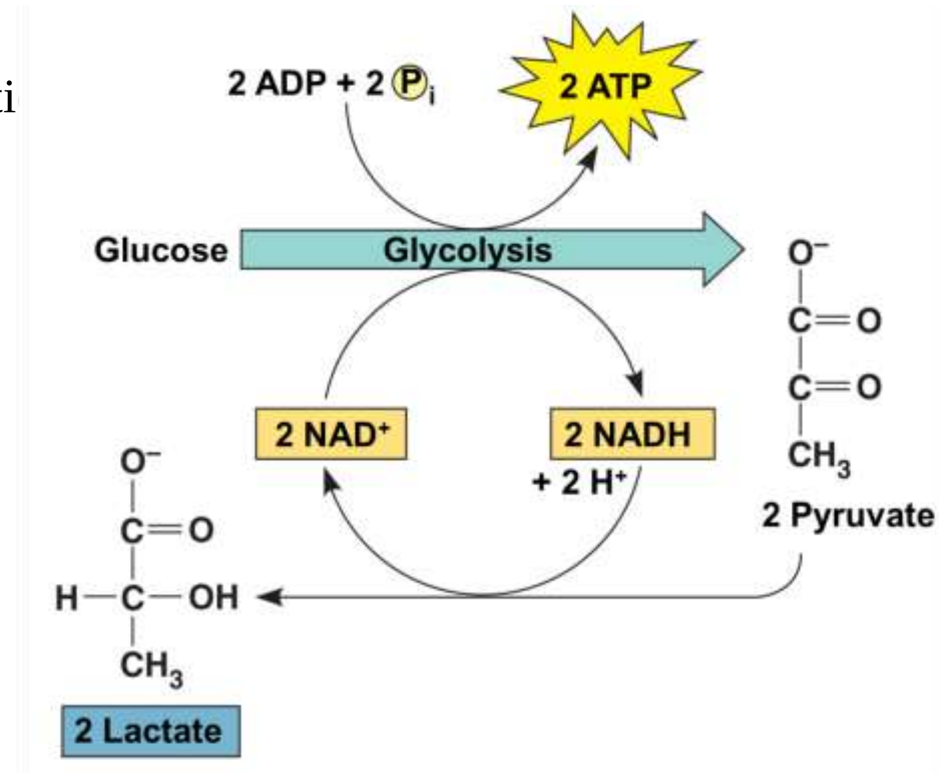
Animation: Fermentation Overview



(a) Alcohol fermentation

Lactic Acid Fermentation

- During ***lactic acid fermentation***, pyruvate is reduced directly by NADH, form ***lactate*** as an end product, with no release of CO_2
  - Lactic acid fermentation by certain fungi and bacteria is used in the dairy industry to make cheese and yogurt
  - Human muscle cells make ATP by lacti
    - This occurs during the early stages of strenuous exercise when breakdown of glucose outpaces the muscle's supply of oxygen from the blood



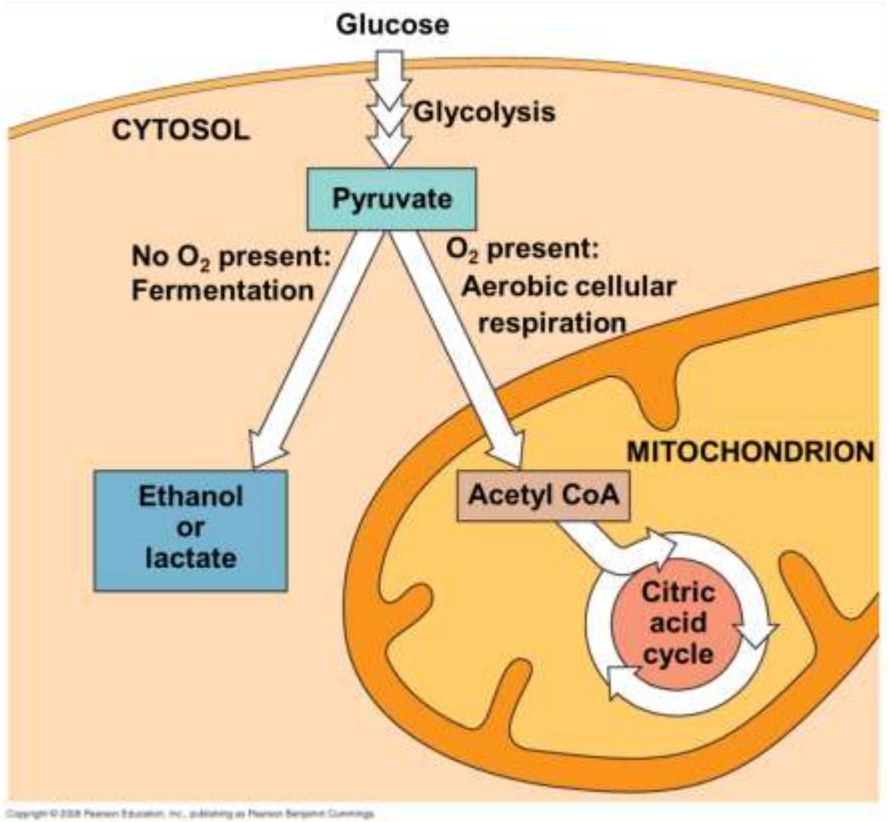
(b) Lactic acid fermentation

Fermentation and Aerobic Respiration Compared

- Both fermentation and aerobic respiration use glycolysis to oxidize glucose and other organic fuels to pyruvate, with a net production of 2 ATP by substrate level phosphorylation
  - In both processes, NAD+ is the oxidizing agent that accepts electrons from food during glycolysis
- A key difference, however, is the mechanism for oxidizing NADH back to NAD+
  - In fermentation, the final electron acceptor is an organic molecule like pyruvate or acetaldehyde
  - In aerobic respiration, the final acceptor for electrons from NADH is oxygen
- Another difference between fermentation and aerobic respiration is overall ATP production
  - Cellular respiration can produce up to 38 ATP per glucose molecule
  - Fermentation can only produce 2 ATP per glucose molecule

Obligate and Facultative Anaerobes

- Some organisms called ***OBLIGATE ANAEROBES*** carry out only fermentation or anaerobic respiration
  - These organisms cannot survive in presence of oxygen
- Other organisms (ex: yeast, many bacteria) can make enough ATP to survive using either fermentation or respiration
    - These species are called ***FACULTATIVE ANAEROBES***
  - In these organisms, pyruvate is a fork in the road and can either continue on in aerobic respiration or undergo fermentation



The Evolutionary Significance of Glycolysis

- The fact that glycolysis occurs in nearly all organisms suggests it evolved very early in the history of life
  - Ancient prokaryotes probably used glycolysis to make ATP long before oxygen was present in Earth's atmosphere
    - This suggests that glycolysis evolved more than 2.7 bya
  - In addition, the fact that glycolysis occurs in the cytosol also implies that glycolysis is very old
    - This process does not require the membrane-bound organelles of the eukaryotic cell, which evolved about 1 billion years after the evolution of the prokaryotic cell

Concept Check 9.5

- 1) Consider the NADH formed during glycolysis. What is the final acceptor for its electrons during aerobic respiration?

- 2) A glucose-fed yeast cell is moved from an aerobic environment to an anaerobic one. For the cell to continue generating ATP at the same rate, how would its rate of glucose consumption need to change?

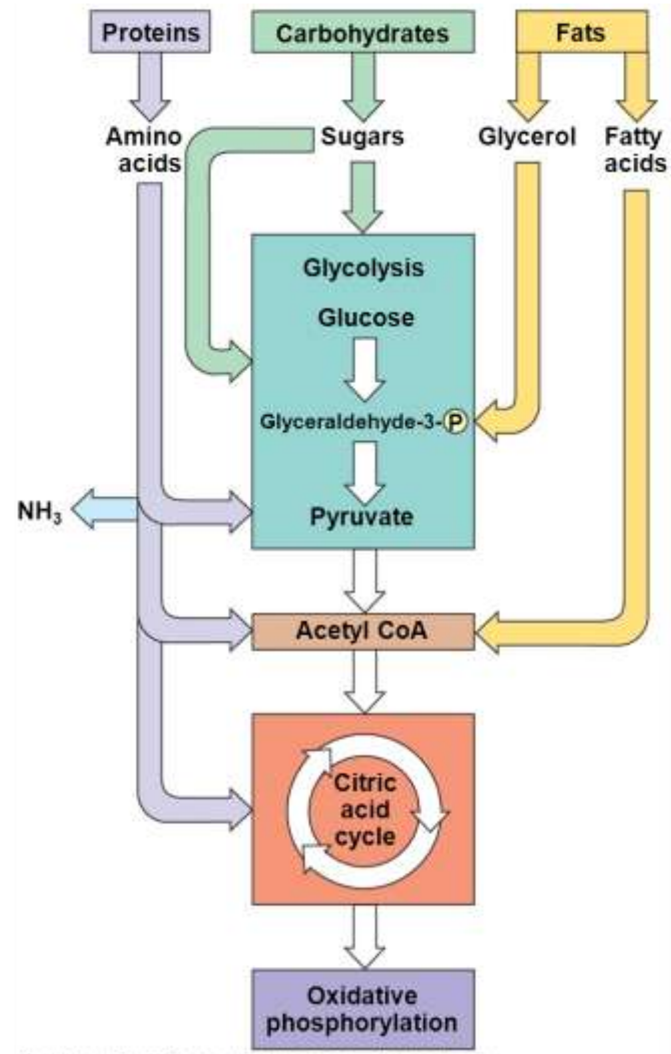
Concept 9.6:
Glycolysis and the citric acid cycle connect to many other metabolic pathways

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

- So far ,we have looked at the oxidation of glucose in isolation from the overall metabolism of the cell
  - In reality, glycolysis and the TCA cycle are major intersections to various catabolic and anabolic pathways in the cell

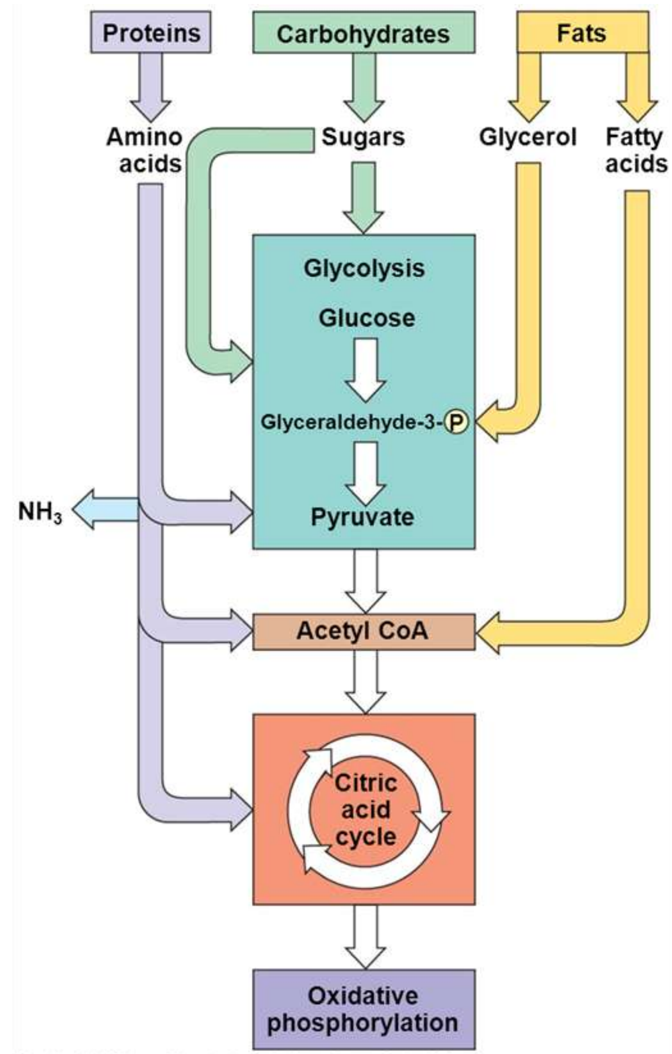
The Versatility of Catabolism

- So far, we have only looked at glucose as the fuel for cell respiration
  - Free glucose molecules, however, are not common in the diets of humans and other animals
    - We get most of our calories from fats, protein, sucrose, and starch
  - All of these organic molecules can be used by cell respiration to make ATP
    - Carbohydrates and starches like glycogen can be broken down into their glucose monomers
      - These glucose molecules are then made available to enter glycolysis and the citric acid cycle
    - Proteins can also be used for fuel, but they must first be broken down into their amino acids
      - Amino acids can then be converted by enzymes into intermediates of glycolysis and the citric acid cycle



Fats and Cellular Respiration

- Fats can also used in cellular respiration
  - They can first be broken down to glycerol and fatty acids
    - Glycerol can then be converted to glyceraldehyde-3-phosphate (G3P), an intermediate of glycolysis
    - Fatty acids are broken down during a process called BETA OXIDATION into 2-carbon fragments that enter TCA cycle as acetyl CoA
  - Fats are an excellent fuel source
    - A gram of fat oxidized by respiration produces more than twice as much ATP as a gram of carbohydrate

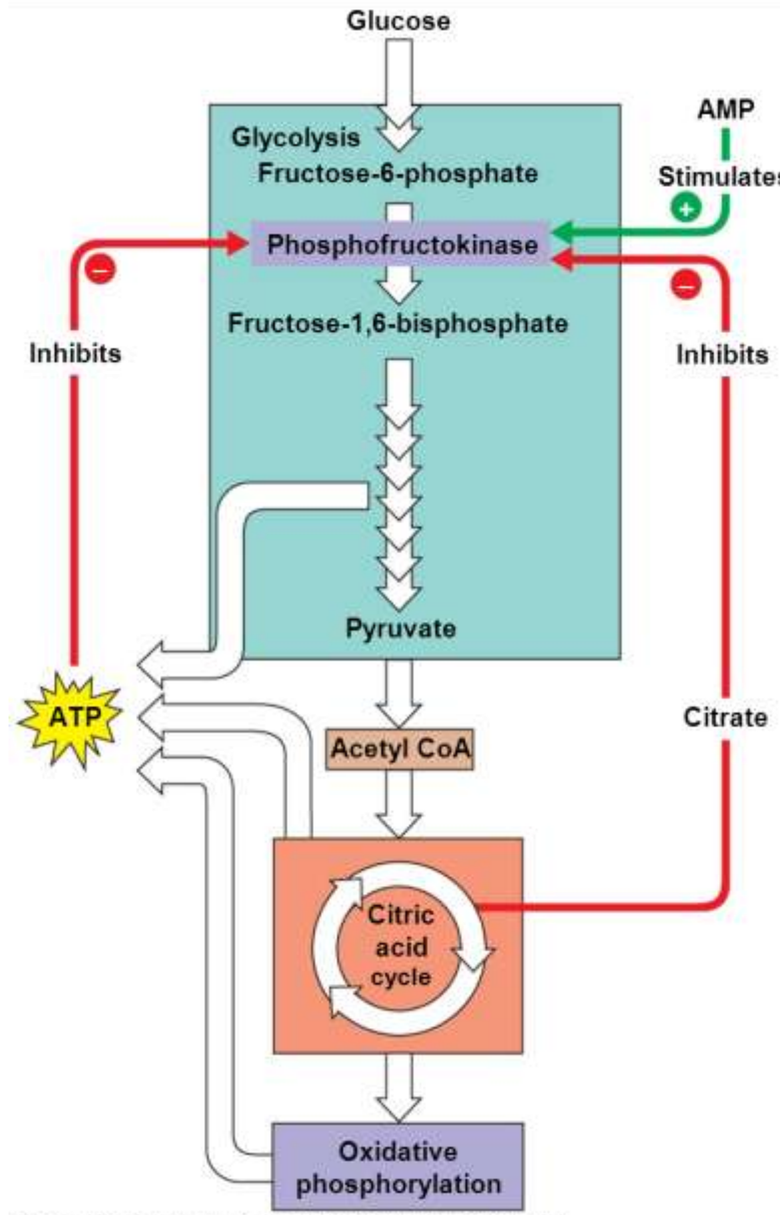


Biosynthesis (Anabolic Pathways)

- Not all organic molecules of food are oxidized as fuel to make ATP
    - In addition to calories, food must also provide the carbon skeletons that cells need to make their own molecules
  - Compounds formed as intermediates of glycolysis and the TCA cycle can be diverted into anabolic pathways as precursors from which the cell can make the molecules it requires
    - Ex) Cells can make about ½ of the 20 amino acids by modifying compounds that are siphoned away from the TCA cycle (the rest need to be consumed in the diet)

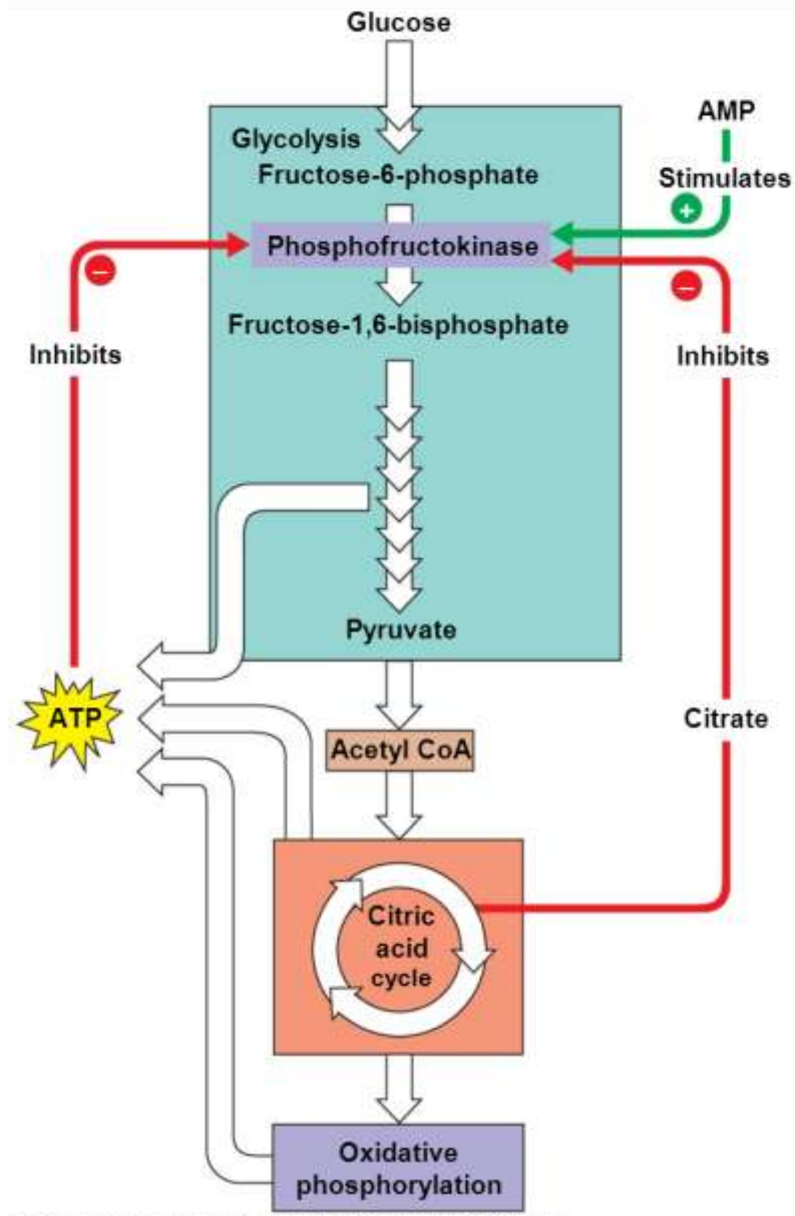
Regulation of Cellular Respiration via Feedback Mechanisms

- Basic principles of supply and demand regulate the metabolism so that the cells don't waste energy making more of something than it needs
  - The most common method of control of metabolism is ***FEEDBACK INHIBITION***
    - Here, the end product of an anabolic pathway inhibits the enzyme that catalyzes an early step of the pathway
      - This stops production of the end product



Regulation of Cellular Respiration via Feedback Mechanisms

- Cells also control their catabolism
    - When there is plenty of ATP to meet demand, respiration slows down
  - Control is again mainly based on regulating the activity of enzymes in the catabolic pathway
    - Ex) One important switch is phosphofructokinase, the enzyme that catalyzes step 3 of glycolysis
      - Phosphofructokinase is stimulated by AMP but inhibited by ATP and citrate
      - By controlling the rate of this step, the cell can speed up or slow down the entire process of glycolysis



Concept Check 9.6

- 1) Compare the structure of a fat (Figure 5.11, pp. 75) with that of a carbohydrate (see Figure 5.3, pp. 70). What features of their structures make a fat a much better fuel?
- 2) Under which circumstances might your body synthesize fat molecules?
- 3) What will happen in a muscle cell that has used up its supply of oxygen and ATP (See Figures 9.19, pp.179, and 9.21, pp. 181).

You should now be able to:

1. Explain in general terms how redox reactions are involved in energy exchanges
2. Name the three stages of cellular respiration; for each, state the region of the eukaryotic cell where it occurs and the products that result
3. In general terms, explain the role of the electron transport chain in cellular respiration

4. Explain where and how the respiratory electron transport chain creates a proton gradient
5. Distinguish between fermentation and anaerobic respiration
6. Distinguish between obligate and facultative anaerobes