

Metabolism Notes

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1 Definitions

1.1 Energy

Energy is the ability to do work.

1.2 Kinetic energy

Kinetic energy is a form of energy associated with the motion of objects. Examples of kinetic energy include:

- A cheetah running
- A hummingbird vibrating its wings
- A bacterium swimming
- Blood flowing inside the veins

1.3 Heat energy

Heat or thermal energy is generated by the random movement of atoms or molecules. In living systems, metabolic activities generate heat. Accumulation of this heat may often require mechanisms to dissipate (through homeostasis), like by sweating or panting in order to maintain the normal body temperature.

1.4 Electrical energy

Electrical energy is manifested in different ways in biological systems. Some examples include electrical impulses in neurons and electrical currents on the surface of electric eels.

1.5 Light energy

Light energy can be captured by living systems such as during photosynthesis and transformed to other forms such as chemical energy stored in ATP and glucose. Some organisms are able to produce light from chemical energy, such as fireflies and some marine animals.

1.6 Potential energy

Potential energy is the energy that matter carries because of its location or structure.

1.7 Chemical energy

Chemical energy is a form of potential energy stored in molecules because of the arrangement of their atoms.

1.8 System

A system is defined as a part of the universe which we choose to study.

1.8.1 Isolated system

An isolated system is a system that **does not have any exchange** of matter or energy with its surroundings. A thermos bottle containing hot water is one example, as the hot water does not spill out and the water stays hot.

1.8.2 Closed system

A closed system is a system that **only exchanges energy** with its surroundings. A closed system does not exchange matter with its surroundings. A mercury thermometer is one example.

1.8.3 Open system

An open system is a system where **both matter and energy** is exchanged with its surroundings. A bacterial cell is an open system, as it takes in organic matter from its surroundings, and releases heat and waste compounds to its surroundings.

1.9 First law of thermodynamics

The first law of thermodynamics states that energy can be transformed or transferred, but it cannot be created or destroyed.

$$\Delta E = W + q$$

1.9.1 ΔE

ΔE refers to the **total energy change** in a system, meaning the difference between the initial energy and the final energy of the system. It is generally difficult to measure initial energy or final energy directly, but ΔE can be calculated if the work energy and the heat energy transferred are known.

1.9.2 W

The work energy is conventionally denoted by W . Work can be manifested in various forms, as mechanical energy in muscle contraction, as electrical energy in nerve impulse transmission, and as light energy in firefly illumination.

When the **system does work on the surroundings**, W is **negative**, because the system **loses energy** in the form of work. When the **surroundings do work on the system**, W is **positive**, because the system **gains energy** in the form of work.

1.9.3 q

The heat energy is conventionally denoted by the symbol q . When heat is exchanged between the system and the surroundings, this exchange or transfer of heat can be classified into **exothermic** and **endothermic**.

In an exothermic reaction, the system **generates and releases** heat which flows out of the system. Thus, the system **loses energy** in the form of heat, and q is **negative**.

In an endothermic reaction, heat from the surroundings is **absorbed** by the system. Thus, the system **gains energy** in the form of heat, and q is **positive**.

1.10 Exothermic reactions

In an exothermic reaction, the system **generates and releases** heat which flows out of the system. Thus, the system **loses energy** in the form of heat, and q is **negative**.

1.11 Endothermic reactions

In an endothermic reaction, heat from the surroundings is **absorbed** by the system. Thus, the system **gains energy** in the form of heat, and q is **positive**.

1.12 Enthalpy (ΔE)

Enthalpy is the energy change in the system due to heat.

1.13 Enthalpy of reaction (ΔH_r)

The enthalpy of reaction is the heat absorbed in a reaction at **1 atmospheric pressure**, with the **number of moles of reactants shown in any chemical equation**.

1.14 Enthalpy of formation (ΔH_f)

The enthalpy of formation is the heat absorbed **per mole of a compound** when it is formed from its elements.

1.15 Enthalpy of combustion (ΔH_c)

The enthalpy of combustion is the heat absorbed **per mole of substance burnt** (oxidised) in oxygen. It is always negative since heat is always generated and released during combustion.

1.16 Enthalpy of neutralisation (ΔH_n)

The enthalpy of neutralisation is the amount of heat absorbed **per mole of water produced** when an acid and a base react.

1.17 Calorie value of food

The calorie value of food is derived from the enthalpy of combustion of that food item $1 \text{ kcal} = 4.18 \text{ kJ}$. It is usually expressed as Calorie (with a capital C), which is actually a kilocalorie or kcal. The average human requires about 6000 kJ of energy to sustain body functions, which means that the total ΔH from all daily biological reactions is about 6000 kJ .

1.18 Entropy (S)

Entropy is a quantity used as a **measure of disorder or randomness**. The more random a process is, the greater is its entropy. A **highly ordered** state is said to have **low entropy** and a **less ordered state** is said to have **higher entropy**. A process in an isolated system tends to proceed when the entropy of the system increases, that is, when ΔS is **positive**.

1.19 The second law of thermodynamics

The second law of thermodynamics states that every energy transfer or transformation tends to move in a direction so that the **entropy of the universe or an isolated system increases**.

In spite of the unstoppable trend of the universe towards increasing the disorder, it is possible for order to **increase locally** within an organism. The entropy of a system, such as an organism, may decrease as long as the total entropy of the universe, which is the system plus its surroundings, increases.

Since an organism is **not isolated from the universe**, we cannot predict whether any biological reaction will happen spontaneously just based on **entropy inside a cell**, as spontaneity is driven by the **resultant entropy of the universe**.

1.20 Free energy (G)

- If the free energy change ΔG is **negative** for a reversible chemical reaction, the reaction **will tend to occur spontaneously**, in the **forward** direction.
- Conversely, if ΔG is **positive**, the reaction is **non-spontaneous**, in the **forward** direction. Hence, it will tend to occur in the reverse direction.
- If ΔG is **zero**, **no net reaction** occurs in either direction and the reaction is said to be **at equilibrium**.

$$\Delta G = \Delta H - T\Delta S$$

1.20.1 $\Delta H = T\Delta S$

$$\Delta G = 0$$

The reaction is not favoured to go in either forward or reverse direction, and the system is in **equilibrium**.

1.20.2 $\Delta H > T\Delta S$

$$\Delta G > 0 \text{ or } \Delta G \text{ is positive}$$

The reaction is not favoured in the forward direction, but favoured in the **reverse direction**. The reaction is **not spontaneous**.

1.20.3 $\Delta H < T\Delta S$

$$\Delta G < 0 \text{ or } \Delta G \text{ is negative}$$

The reaction is favoured in the forward direction and hence the reaction is **spontaneous**.

1.21 Standard free energy change (ΔG°)

The standard free energy change is the free energy change (ΔG) under standard conditions.

1.22 Exergonic reactions

Exergonic reactions are reactions that can occur without the addition of energy. Basically, it's another way to say a reaction is **spontaneous**.

1.23 Endergonic reaction

Endergonic reactions are reactions that require additional energy to occur. Basically, it's another way to say a reaction is **non-spontaneous**.

1.24 Extracellular metabolism

In extracellular metabolism, ingested foodstuff such as lipids, carbohydrates and proteins are digested (broken down) into smaller molecules through a set of reactions that occur in the digestive system.

1.25 Intracellular metabolism

Intracellular metabolism comprises chemical reactions that occur in living cells. This phase happens after extracellular metabolism has broken down the foodstuff into smaller molecules, which can then enter the cell.

1.26 Gastrointestinal (GI) system

The gastrointestinal system consists of two parts, the gastrointestinal tract and the accessory organs.

1.27 Gastrointestinal (GI) tract

The gastrointestinal tract includes the mouth, esophagus, stomach, small intestine and the large intestine.

1.28 Lumen of the gastrointestinal (GI) tract

The lumen of the refers to the **central hollow portion** of the gastrointestinal tract, where food substances pass through.

1.29 Accessory organs

Accessory organs include the salivary glands, the liver, the pancreas, and the gallbladder. These have portals that attach to some parts of the gastrointestinal tract, allowing secretion to be introduced into the lumen.

It is important to note that the lumen of the GI tract is continuous with the outside environment, and is "separated" from the "inside" of the body which forms the walls of the GI tract.

This is why digestive activities in the lumen are referred to as "extracellular" metabolism.

1.30 Villus (plural: villi)

Villus refers to any of the small, slender, vascular projections that increase the surface area of a membrane.

1.31 Epithelium

The epithelium is the thin, continuous, protective layer of compactly packed cells with a little intercellular matrix.

1.32 Epithelial cells

Epithelial cells are the compactly packed cells in the epithelium.

1.33 Catabolism

Catabolism means "breaking down", which means that larger molecules are being broken down into smaller molecules.

1.34 Anabolism

Anabolism means "building up", which means that smaller molecules are being combined to form larger molecules.

1.35 Metabolic pathway

Metabolic pathways are a sequence of reactions that produces a specific product from a given substrate. Most of the reactions in a metabolic pathway require enzymes for catalysis.

1.35.1 Example

Glycolysis is a metabolic pathway where glucose is the substrate from which the product pyruvate is produced through a sequence of 10 reactions.

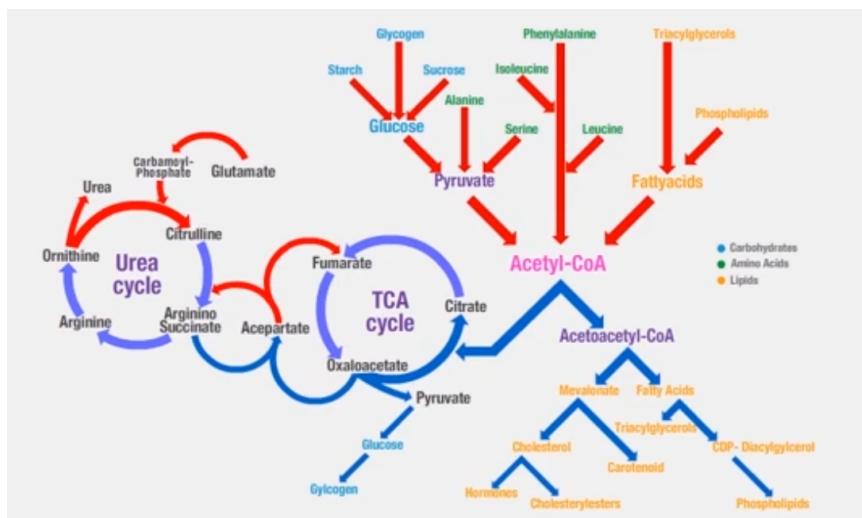
1.35.2 Types

1. **Linear** metabolic pathways, which are pathways in a single straight line.
2. **Branched** metabolic pathways, which have branches that either become one path (convergent), or are split from a single pathway (divergent).
3. **Cyclic** metabolic pathways, which generate a product that can be fed back into the pathway as a substrate to start the next cycle of reactions.
4. **Spiral** metabolic pathways, which are better understood as looped pathways. It is similar to a cyclic pathway, but the products of each cycle progressively change instead of remaining as the same product.
5. **Catabolic** pathways, which are pathways where large molecules are broken down into smaller molecules, accompanied by a release of energy. Energy is generally stored in the form of ATP, NADH, NADPH, or $FADH_2$. Catabolic pathways are generally oxidative pathways. An example is glycolysis, where glucose (6 carbon atoms) is oxidised to form two smaller molecules of pyruvate (3 carbon atoms) along with the production of ATP and NADH.
6. **Anabolic** pathways, which are biosynthetic pathways, which means that small molecules are used to produce larger molecules by spending energy which is available from molecules like ATP and NADH. Anabolic pathways are generally reductive pathways. An example is gluconeogenesis, where pyruvate (3 carbon atoms) is used to form glucose (6 carbon atoms).

1.35.3 Common metabolic pathways

Metabolic Pathway	Purpose
Glycolysis	Glucose is broken down to pyruvate
TCA Cycle or Kreb Cycle	Acetyl CoA is oxidized to CO ₂
Glycogenolysis	Glycogen is broken down to glucose
Glycogenesis	Glycogen is synthesized from glucose
Fatty Acid Oxidation	Fatty acids are oxidized sequentially to form acetyl CoA
Fatty Acid Synthesis	Fatty acids are synthesized sequentially from acetyl CoA
Amino Acid Oxidation	Surplus amino acids (beyond the needs of protein synthesis) are degraded to ammonia and α-keto acid
Urea Cycle	Toxic ammonium ion (formed during amino acid oxidation) is removed

1.35.4 Overall cellular metabolism



1.35.5 Compartmentalisation of metabolic pathways

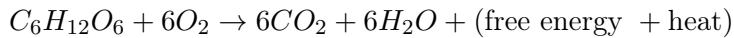
In prokaryotes, almost all metabolic pathways occur in the cytoplasm, with some occurring across the cell membrane.

In eukaryotes however, more sophisticated organisation for metabolism can be achieved using organelles such as mitochondrion, chloroplast, endoplasmic reticulum, and nucleus as compartments. This feature of cellular compartmentalisation allows cells to develop strategies of metabolic regulation through physical separation accorded by the organelle structures.

1.36 Cellular respiration

Cellular respiration is a metabolic process by which the chemical energy of organic substrates such as glucose is converted into the energy currency of ATP and reducing powers such as NADH, NADPH and $FADH_2$. It is a universal process occurring both in eukaryotes and in prokaryotes.

Using glucose as the carbohydrate, the process can be summarised as:



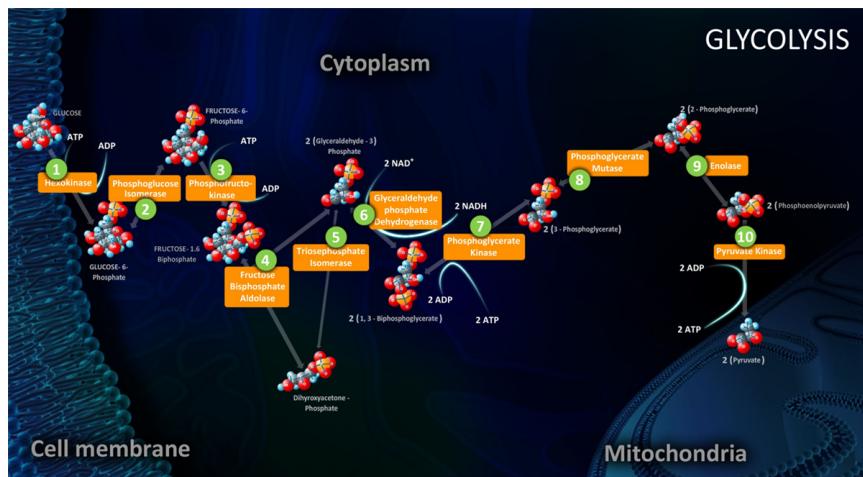
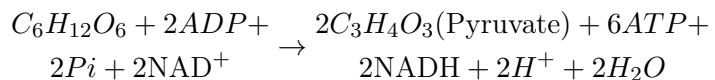
Part of the free energy is coupled to the formation of ATP molecules. Hence, respiration is a catabolic process where glucose is fully oxidised to CO_2 with the liberation and storage of free energy.

Cellular respiration does not occur in one step. It consists of 3 metabolic pathways occurring in **4 phases, glycolysis, pyruvate oxidation, tricarboxylic acid (TCA) cycle and electron transfer (transport) chain (ETC) coupled to ATP synthesis**.

In eukaryotic cells, these phases do not occur in one compartment (as they do in prokaryotic cells' cytoplasm) but at three cellular locations, the cytoplasm, the mitochondrial matrix and the inner mitochondrial membrane.

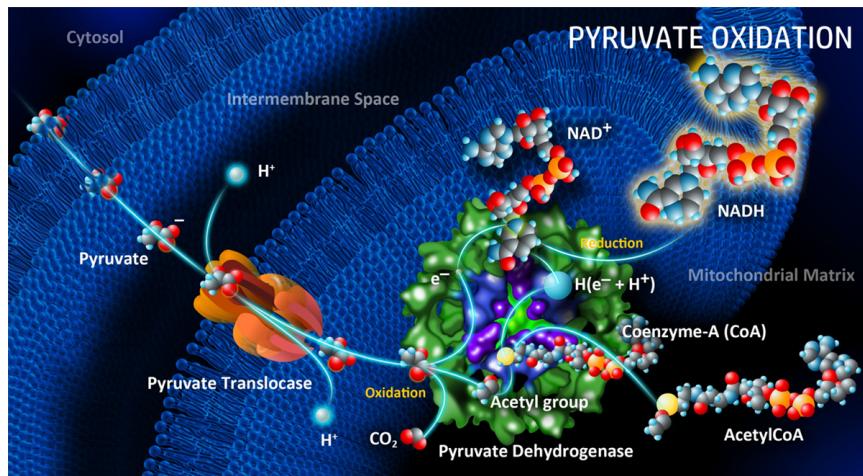
1.37 Glycolysis

Glycolysis is the metabolic pathway which converts a glucose molecule to 2 pyruvate molecules in the cytoplasm through a series of 10 reactions catalysed by 10 enzymes. Along the way, the two molecules of NAD^+ are reduced to NADH. In addition, two molecules of ADP are phosphorylated to two molecules of ATP. Thus, the net reaction of glycolysis for glucose is:



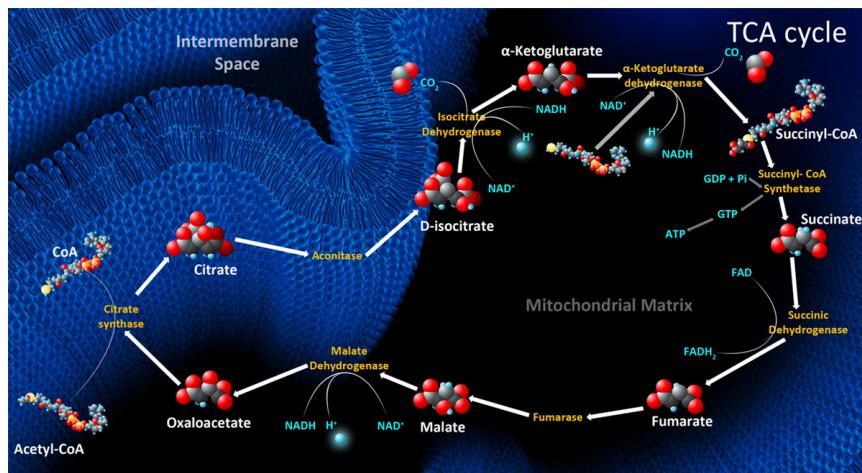
1.38 Pyruvate oxidation

A pyruvate molecule is transported from the cytoplasm to the mitochondrial matrix. There, one of the 3 carbon atoms of pyruvate is cleaved and released as CO_2 . The outcome of this reaction is that pyruvate is oxidised by losing two electrons and two protons. NAD^+ is reduced, and the remaining acetyl group is attached to CoA, forming acetyl-CoA.



1.39 TCA cycle

The TCA cycle, also called the citric acid cycle or the Kreb's cycle, is a cyclic pathway that consists of several reaction steps which are mostly oxidative in nature. The cycle occurs in the mitochondrial matrix. The cycle "starts" with the 2-carbon acetyl group of acetyl-CoA combining with a 4 - carbon molecule (oxaloacetic acid, OAA) resulting in a 6 - carbon molecule, citric acid (TCA). The resulting citrate in the first reaction of the cycle undergoes a sequence of oxidative reactions whereby two carbon molecules are oxidised to CO_2 and the OAA molecule is regenerated. This completes one turn of the cycle and allows another turn to start.



1.39.1 Energetics of the TCA cycle

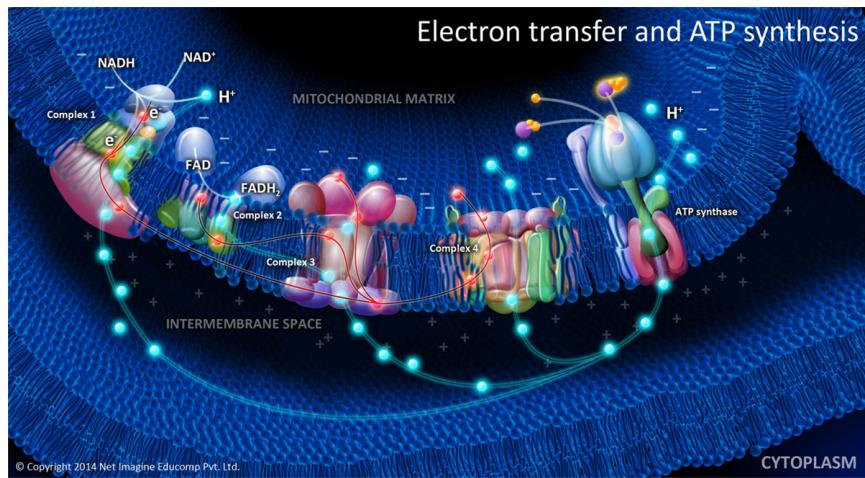
Note that both ATP and reducing molecules like NADH and $FADH_2$ are generated as a result of these 2 turns of TCA.

The inputs and outputs for two turns of the TCA cycle are shown below:

INPUT	OUTPUT
2 Acetyl groups	4 CO_2
6 NAD ⁺	6 NADH + H ⁺
2 FAD	2 $FADH_2$
2 GDP + 2Pi	2 ATP

1.40 Electron transfer chain (ETC) driven ATP synthesis

This is the final phase of cellular respiration, NADH and $FADH_2$ molecules are oxidised, releasing electrons. The free energy generated from the oxidation of NADH and $FADH_2$ is used to make more ATP. This phase is divided into three parts: electron transfer chain, formation of proton gradient, and ATP synthesis.



1.40.1 Electron transfer chain (ETC)

The electron transfer chain consists of several electron carriers over which the electrons "hop" through. It starts from NADH and $FADH_2$ and ends at O_2 . In some bacteria and archaea, in the absence of molecular oxygen, different electron acceptors may be used.

1.40.2 Formation of the proton gradient

The electron carriers are localised and embedded in the inner mitochondrial membrane with specific orientations to facilitate electron transfer as well as the formation of the proton gradient. As the electrons pass through the chain, the free energy liberated is used to form a proton gradient across the inner mitochondrial membrane.

1.40.3 ATP synthesis

Any concentration gradient is a potential source of free energy which can be coupled with endergonic processes. In mitochondria, the proton gradient created by the electron transfer chain across its inner membrane is dissipated through a protein complex and the released free energy is captured to synthesise ATP from ADP and Pi. This protein complex is called the ATP synthetase.

1.41 Autotrophs

Autotrophs just mean that an organism can produce its own food. Autotrophs are able to make use of simple molecules like CO_2 as a carbon source to build complex organic molecules such as polysaccharides and proteins that form the bulk of their body.

Because of this, an autotroph is called a "producer" in the food chain, because this organism "produces" complex organic biomolecules from simple substances present in its surroundings. There are 2 types of autotrophs, photoautotrophs and chemoautotrophs.

1.42 Photoautotrophs

Photoautotrophs use energy from sunlight to produce the energy currency ATP and to convert water (electron source) and carbon dioxide (carbon source) from the air into glucose via a process called photosynthesis. From glucose, other intermediates are further generated for biosynthesis. Examples of photoautotrophs include plants, algae, photosynthetic protists, and cyanobacteria.

1.43 Chemoautotrophs

Chemoautotrophs use energy from chemical compounds to produce ATP and reducing powers, through a process called chemosynthesis. The chemical reactions involve making use of simple inorganic compounds such as H_2 , H_2S , NH_3 and Fe^{2+} as electron sources, leading to their oxidation. Examples of chemoautotrophs include certain extremophiles such as bacteria and archaea found inside or near active volcanoes, hydrothermal vents in the sea floor and hot water springs.

1.44 Heterotrophs

Heterotrophs are basically organisms that eat plants or animals for energy. Heterotrophs require more complex organic compounds as the source of carbon. Hence, the lives of heterotrophs are dependent on autotrophs, because these complex substances are made available only through the metabolism of autotrophs.

Therefore, heterotrophs are called "consumers" in the food chain because they live on "producers", which are the autotrophs. There are 2 types of heterotrophs, photoheterotrophs and chemoheterotrophs.

1.45 Photoheterotrophs

Some heterotrophs are versatile enough to use light together with chemical compounds. These heterotrophs use light as an energy source and rely on chemical compounds as electron and carbon sources. Examples of photoheterotrophs are:

- Purple photosynthetic bacteria. They use light as a source of energy, while using inorganic hydrogen, sulfide or sulfur as electron sources.
- Pitcher plant. These plants are capable of normal photosynthesis using light, CO_2 and water, and hence are partially photoautotrophs. However, they are also carnivorous, feeding on small insects, hence taking on photoheterotrophic metabolism.

1.46 Chemoheterotrophs

Chemoheterotrophs make use of chemical compounds for all 3 requirements, which are energy, electrons, and carbon. Examples of chemoheterotrophs are parasites, most bacteria, all fungi, most protozoa, and all animals, which also include humans.

1.47 Metabolic network

A metabolic network is the interconnected pathways of biochemical reactions within living cells.

1.48 Metabolic integration (metabolic homeostasis)

Metabolic integration is the coordination between different metabolic pathways inside the body and hence metabolic integration is multistep.

1.48.1 Advantages of metabolic integration

1. Being more energetically efficient. More energy is wasted as heat when a large amount of free energy is released in one single step, compared to when smaller amounts of free energy is being released in a step-wise fashion.
2. Ease of coupling between exergonic and endergonic reactions. With simpler reaction steps, it is more feasible to couple an endergonic reaction to exergonic reactions such as hydrolysis of ATP molecules.
3. Introduction of regulatory mechanisms. Fine-tuning, back-up provision, and coordination with other pathways will be possible with multiple steps of simple reactions, but not if the whole process occurs in one single complex step.
4. Common intermediates allow for metabolic integration. If an intermediate in a particular pathway is also found in other pathways, this intermediate can potentially be made to "multitask" to achieve metabolic integration.

1.48.2 Reduce-reuse-recycle approach

Take the example of the cycling of NADH and NAD⁺ in carbohydrate metabolism.

In glycolysis, an NAD⁺ molecule is reduced to NADH in one of the reactions. For continuous glycolysis, there must be a continuous supply of NAD⁺. However, the NAD⁺ pool in the cytoplasm is limited. Hence, NADH is re-oxidised via another reaction in the cytoplasm to produce NAD⁺ again, essentially "recycling" the NADH.

There are two ways to re-oxidise NADH in the glucose metabolism:

1. Lactate fermentation

In skeletal muscle cells, NADH is recycled to regenerate NAD⁺ through lactate fermentation. Pyruvate (generated during glycolysis) is reduced to lactate in one reaction which oxidises NADH to NAD⁺.

2. Alcoholic fermentation

In yeast and some other bacteria, NADH is recycled to regenerate NAD⁺ through alcoholic fermentation. Under anaerobic conditions, they reduce pyruvate (generated during glycolysis) to ethanol by oxidising NADH to NAD⁺.

1.48.3 Common intermediates in the reduce-reuse-recycle approach

Pyruvate can be used to generate either lactate or ethanol while recycling NAD⁺. It can also be used to synthesise glucose by following a metabolic pathway known as gluconeogenesis. Pyruvate is the common intermediate in the two tracks of metabolic pathways aforementioned. However, the starting molecule for gluconeogenesis need not always be pyruvate. Lactate or amino acids such as alanine can serve as the substrate too. This means that glucose production by gluconeogenesis can be orchestrated by pathways that influence the cellular levels of pyruvate, lactate and amino acids.

1.49 Insulin

Insulin is a soluble protein that binds to its cell membrane receptor to induce a signal.

1.50 Homeostasis

Homeostasis refers to the ability or tendency of an organism to maintain its internal condition fairly stable, i.e., within a range of physiological parameters, such as temperature, blood pressure, pH, as well as the concentrations of blood glucose, other metabolites and ions. When an external event disturbs the balanced state, the organism counteracts the disturbance by coordinating the functions of all organs and tissues via their metabolic pathways. When the homeostatic mechanism fails due to defective enzymes or extreme environmental fluctuations, disease or disorder sets in.

1.51 Glucose homeostasis

The maintenance of normal glucose level in blood is called glucose homeostasis. Glucose homeostasis strives to maintain the blood glucose concentration at about 5 mM (90 mg/100 ml) under all conditions. This is especially crucial for our brain, as it uses glucose exclusively as the metabolic fuel, has no fuel storage system, and yet consumes a large amount of energy accounting for at least 20% of the total energy demand of the body.

If blood glucose falls below a critical level of about 2.2 mM (40 mg/100 ml), severe and sometimes irreversible damage to brain function may occur. Thus, the first priority of metabolic integration is to maintain glucose homeostasis at any cost with a view to save the brain. Diabetes mellitus is a condition whereby glucose homeostasis is defective.

Glucose metabolism needs to be considered in the context of a fed-starved cycle. The cycle has two stages, the post-absorptive state after a meal of about 2 - 3 hours, and a fasting or starved state after that, before the next meal. The homeostatic responses in each state, involving the hormones insulin and glucagon, lead to the activation and inhibition of the appropriate sets of metabolic pathways that can alter the balance of glucose (the usable form) versus glycogen (the storage form).

1.51.1 Post-absorptive state

1. Soon after a meal that contains carbohydrates as a component, extracellular metabolism works to ensure that glucose from the intestine enters the bloodstream.
2. This results in an increase in the blood glucose level, which is sensed by the pancreas, stimulating it to produce the hormone insulin.
3. Insulin is released into the blood and carried to other organs including its targets: liver, muscle and adipose tissue, where it works to stimulate glucose uptake by the cells, bringing blood glucose concentration down to a normal level.
4. Inside the target cells, metabolic pathways that can decrease cellular glucose concentration by converting glucose to the storage form (glycogen) for future use, are activated.

1.51.2 Starved or fasting state

1. In this state, even in the absence of visible physical activity, like during sleep, blood glucose is consumed (mainly by the brain) and the level falls below normal.
2. Lowered blood glucose triggers the secretion of glucagon and inhibits insulin release from the pancreas.
3. The main target organ of glucagon is the liver, where glucose production is stimulated. This increases cellular glucose concentration, allowing the liver to export glucose to the blood, restoring glucose level to normal.

1.52 Signal transduction

Signal transduction is a mechanism that transmits the effects of hormones, such as insulin, to target cells. Signal transduction involves a "message" being transmitted from one site (usually remote) to another, most often from the outside to the inside of a cell. It occurs in three steps.

1.52.1 Reception

During the reception step, a signal molecule (a messenger) binds to a receptor protein on the target cell's membrane. A part of the receptor molecule protrudes is on the outside of the cell and a part of it is inside the cell.

For example, the hormone insulin is a messenger sent by the pancreas in response to high glucose concentration in blood. Insulin binds to its specific receptor protein embedded in the plasma membrane of cells of the liver, the muscles and the adipocytes.

1.52.2 Transduction

During the transduction steps, the part of the receptor molecule inside the cell relays the message to activate the appropriate cellular response.

In the example of insulin, as it binds to the receptor and activates it, certain reactions that produce the second (secondary) messenger molecules are initiated. The second messengers then transmit the signal to the target site by activating a series of reactions sequentially. Cyclic AMP (cAMP) is a common secondary messenger in many signal transduction processes.

1.52.3 Response

The sequence of reactions initiated through the second messenger eventually reach the end enzyme in this series, which when activated, stimulates or inhibits the target metabolic pathway, which is the intended response. For instance, the transduction process initiated by insulin will eventually reach the regulator that will stimulate consumption of glucose to decrease glucose concentration.

1.52.4 Versatility of the signal transduction system

Signal transduction is versatile because of the many ways signal transduction can be configured. The second messengers can be designed to activate not just one series of reactions for targeting one metabolic pathway, but several series of reactions.

For instance, when one insulin binds to its receptor in a liver cell, several metabolic pathways related to the desired response are regulated, like the stimulation of glucose uptake, glycogen synthesis, glycolysis, and fatty acid synthesis.

1.52.5 Cascade effect

Consider one insulin molecule binding to a receptor and activated 10 second messenger molecules per second. If each second messenger molecule activates 10 enzymes in the cascade per second, 10 messengers will activate 100 enzyme molecules per second.

2 Energy scheme

Energy → work → system. Whenever some work is done, energy is needed. For example, our body needs energy to do work, and our body gets energy from the food we eat. Another example is that a seed needs energy to sprout, and so the seed gets energy from the chemicals stored inside.

3 Energy change in living systems

1. Most reactions in living things work **under constant pressure**.
2. Most processes occur in solid and liquid phases, which are mostly **constant in volume**. Even the occasional by-products of gases end up being dissolved in liquids.

Since W is affected by changes in pressure and volume and those are constant in living systems:

$$\Delta E = q$$

Under such conditions:

- ΔE is referred to as the enthalpy of a system, or $\Delta E = \Delta H$
- Due to this relationship, the term enthalpy often appears when heat exchange is described in biological reactions.

4 Adenosine triphosphate (ATP) as energy

- ATP hydrolysis is a common exergonic reaction which is coupled to many endergonic reactions of metabolic pathways.
- Various activities in a cell are nearly always powered by the hydrolysis of ATP.
- ATP is a renewable resource that can be regenerated by the addition of a phosphate group to ADP (which is powered by exergonic reactions during cellular respiration).
- The turnover of ATP is very high in living organisms. A resting human adult consumes roughly 40 kg of ATP per day and a working muscle cell recycles its entire pool of ATP once each minute. More than 10 million ATP molecules are consumed and regenerated per second per cell.

5 Extracellular metabolism

5.1 Carbohydrates

- Starch is the major carbohydrate in our food. Other carbohydrates that can be found in foodstuff are sucrose, lactose and sometimes maltose.
- Starch digestion is started in the mouth by the enzyme amylase, which is secreted by the salivary glands and continues in the upper part of the stomach.
- Starch, sucrose, lactose, and maltose are then fully digested to monosaccharides (glucose, galactose and fructose) in the small intestine by pancreatic amylase.
- The monosaccharides need to be absorbed "into the body" across the epithelial cells lining the villus.
- Fructose enters the epithelial cells by facilitated diffusion, while glucose and galactose enter by active transport.
- They then move through the epithelial cells and cross the membrane by facilitated diffusion in order to enter the blood.
- They are then distributed to and taken up by cells, within which cellular metabolism occurs.

5.2 Proteins

- The extracellular metabolism of proteins begins in the stomach.
- In the acidic pH of the stomach, the dietary proteins are first unfolded (denatured).
- The enzyme pepsin then cleaves some peptide bonds in these unfolded proteins, thereby making small peptides.
- These small peptides are then carried to the small intestine where the pH is near neutral. The peptides cannot refold since they are only fragments of the original proteins.
- In the small intestine, the peptides are further cut by other enzymes, such as trypsin, into amino acids and smaller peptides.
- They are now ready to be transported across the epithelial cells of the intestine to the inside of the body. Similar to the monosaccharides, amino acids cross the epithelial cell membranes into the capillaries to enter the blood, and get circulated to be taken up by cells to enter the cellular metabolism phase.

5.3 Fats (triglycerides)

- Fats are insoluble in the aqueous medium such as the cytosol or blood.
- Thus, fats in our food first aggregate into large droplets through hydrophobic interaction in the upper part of the stomach and move to the intestine.
- Here, these large lipid droplets are emulsified into smaller droplets by bile salt and phospholipids which have been secreted into the small intestine by the liver (stored in the gall bladder).
- Emulsified droplets of fat are then digested by the enzyme lipase, secreted by the pancreas, into fatty acids and monoglycerides.
- The fatty acids and monoglycerides then diffuse into the intestinal epithelial cells, where they are recombined by enzymes into triglycerides again.
- These triglycerides aggregate and are released as chylomicrons through the other side of the epithelial cells via exocytosis.
- Chylomicrons find their way into the lymphatic system and are then delivered to the systemic veins to enter the circulation for eventual uptake by the liver, to be broken down into fatty acids again.

6 Large amount of water is needed to digest food

- For an average adult, over 8 litres of water enters the GI tract to digest less than 1 kg for foodstuff.
- Of this 8 litres of water, 99% is absorbed back into the blood at the end of the process.

The reason for requiring is due to water being needed to hydrolyse the macromolecules into their monomeric units (monosaccharides, amino acids, nucleotides and fatty acids).

Enzyme	Digestion
Salivary amylase	$\text{Starch} + \text{H}_2\text{O} \rightarrow \text{maltose}$
Pancreatic amylase	$\text{Starch} + \text{H}_2\text{O} \rightarrow \text{maltose}$
Maltase	$\text{Maltose} + \text{H}_2\text{O} \rightarrow \text{glucose} + \text{glucose}$
Pepsin	$\text{Protein} + \text{H}_2\text{O} \rightarrow \text{pepti}$
Trypsin	$\text{Protein} + \text{H}_2\text{O} \rightarrow \text{peptides}$
Peptidases	$\text{Peptide} + \text{H}_2\text{O} \rightarrow \text{amino acids}$
Nuclease	$\text{RNA and DNA} + \text{H}_2\text{O} \rightarrow \text{nucleotides}$
Nucleosidases	$\text{Nucleotide} + \text{H}_2\text{O} \rightarrow \text{base} + \text{sugar} + \text{phosphate}$
Lipase	$\text{Fat droplet} + \text{H}_2\text{O} \rightarrow \text{glycerol} + \text{fatty acids}$

Figure 1: Water is used for the hydrolysis of most macromolecules.

6.1 Water in digestion

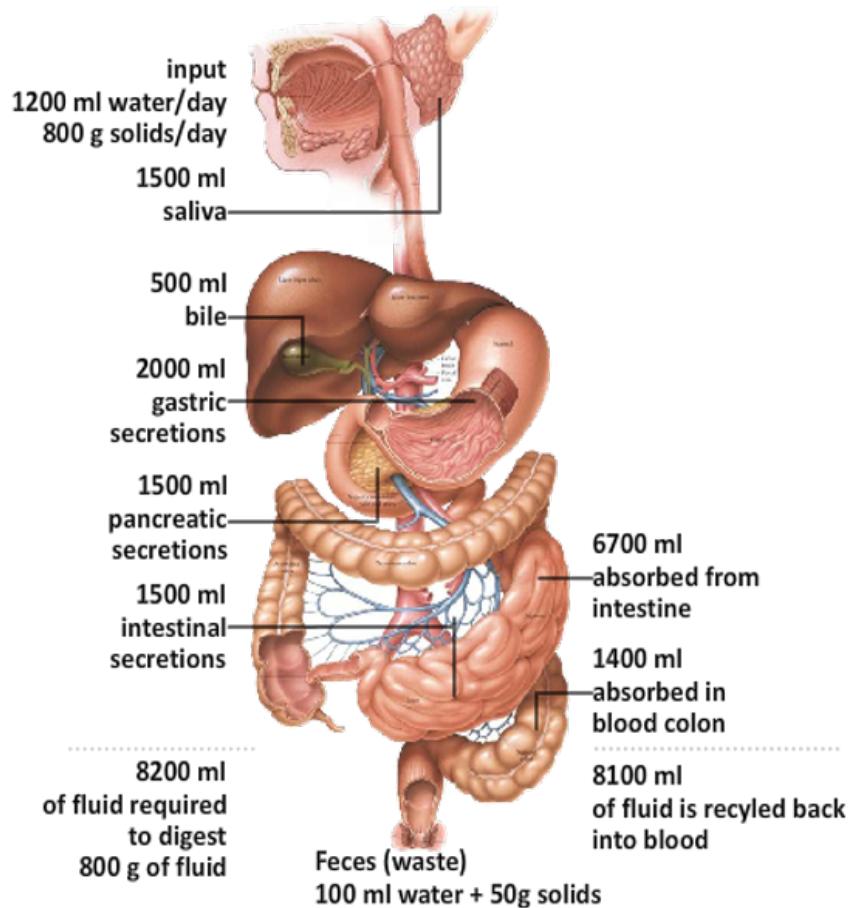


Figure 2: The amount of water used or absorbed in the body during digestion.

7 Metabolic fates of pyruvate

Pyruvate can be channelled to one of the 4 options of metabolism below:

7.1 Pyruvate oxidation

Pyruvate forms acetyl CoA. This happens in plants, animals, and bacteria, under aerobic conditions.

7.2 Lactate fermentation

Pyruvate forms lactate. This happens in red blood cells, highly active muscles, and bacteria under oxygen limiting (anaerobic) conditions.

7.3 Ethanol fermentation

Pyruvate forms ethanol. This happens in yeast and some bacteria under anaerobic conditions.

7.4 Gluconeogenesis

Pyruvate goes into an anabolic pathway to form back glucose.

8 Specifying a metabolic type

There are 3 primary requirements that need to be examined when considering the metabolic type of an organism.

1. Energy source

The energy source is form of energy that gets transferred from the environment into the organism.

2. Electron source

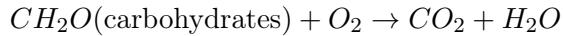
Electron source is compound used by the organism to ultimately generate its reducing powers (reductants), such as NADH and $FADH_2$.

3. Carbon source

The carbon source is used to build up the physical body.

8.1 Animal example

In animals, organic material such as carbohydrates can be the source of all 3 requirements, achieved through the overall reaction shown below:



As seen in the process of cellular respiration, the organic material carbohydrates satisfy all three requirements in the following ways:

8.1.1 Energy source

The energy source is chemical potential energy. The oxidation of carbohydrates generates energy as ATP.

8.1.2 Electron source

The oxidation of carbohydrates produce reducing powers in the form of NADH and $FADH_2$.

8.1.3 Carbon source

The breakdown of carbohydrates to smaller units generates a pool of carbon sources that can be drawn upon to make metabolic intermediates and various biomolecules.

8.2 Plant example

In photosynthetic organisms, the three requirements are coming from different sources. In green plants, for example, the requirements are satisfied by having light, water and carbon dioxide, achieved through the overall reaction shown below:



8.2.1 Energy source

The energy source is light. The source of energy that oxidises water to generate energy as ATP and also fix CO_2 is light.

8.2.2 Electron source

H_2O is the source of electrons needed to produce NADPH, which is the reducing power found primarily in plants.

8.2.3 Carbon source

CO_2 is fixed into organic compounds to become metabolic intermediates for making various biomolecules of the plant body.

9 Metabolic division of labour among organs

Each organ has its own metabolic profile specified by its function:

- Skeletal muscle performs motion
- Adipose tissue stores and releases fats
- The brain pumps ions to produce electrical signals and synthesise neurotransmitters
- The liver plays a central role by performing functions as the "watch dog" of all the other organs.

Each organ is specialised in terms of the metabolic fuel used, the type of fuel stored, and the metabolic fuel available to transport to other organs. Let's take the example of glucose metabolism.

1. During prolonged movement, skeletal muscle cells utilise glucose (by initiating glycolysis) to produce energy for muscular action, and produce excess lactate (from pyruvate, generated during glycolysis) as a result.
2. The lactate from muscles is then transported via blood circulation to the liver. Here, lactate is converted to glucose by gluconeogenesis, a metabolic pathway not present in muscle cells.
3. This pool of "new" glucose produced by the liver is then transported to muscles here it can be used to further generate energy to sustain more muscular activities.

The above is a metabolic division of labour between skeletal muscles and the liver. The skeletal muscles specialise in using glucose, whereas the liver takes care of the recycling of glucose from lactate produced by the muscles.