General Biology
Unit 4
Cellular Metabolism and Metabolic Disorders

Contents

4.1. Cellular metabolism

4.2. Enzymes and their role in metabolism

- **Chemical nature and classification of enzymes**
- **Mechanisms of enzyme action**
- **Factors affecting enzyme activities**

4.3. Bioenergetics and biosynthesis

- **Cellular respiration**
- **Biosynthesis**

4.4. Metabolic disorders, diagnosis and treatments

Objectives of the unit

At the end of this unit you will be expected to:

- ***define*** metabolism, enzymes, bioenergetics and biosynthesis
- ***Classify*** enzymes
- ***describe*** the nature, mechanisms of action and factors affecting activities of enzymes
- ***explain*** the processes of cellular respiration and biosynthesis (photosynthesis)
- ***list and describe*** metabolic disorders
- ***describe*** diagnosis and treatments of metabolic disorders

4.1. Cellular Metabolism

☑ Living cells are in a **constant activity**
☑ Macromolecules are **assembled** and **broken down**,
☑ substances are transported across **cell membranes**, and
☑ genetic instructions are transmitted
☑ All of these cellular activities **require energy**
☑ Living organisms are unique in that they can extract energy to carry out activities such as
  – movement,
  – growth and development,
  – reproduction

❑ **How living organisms or, their cells extract energy?**

Metabolism is thus the sum of all chemical reactions that takes place within each cell of a living organism
  – provides **energy** and **synthesizing** of new organic materials
- Broadly, these reactions can be divided into
  – **catabolic reactions** that convert nutrients to energy and
  – **anabolic reactions** that lead to the synthesis of larger biomolecules

Metabolic pathway:
✓ **Catabolic pathways** release energy by breaking down larger molecules into smaller molecules
✓ **Anabolic pathways** use the energy released to build larger molecules from smaller molecules

✓ **Question**: ***Give examples of catabolic and anabolic pathways***

❖ The reactants and products of these chemical reactions are **metabolites**
  ◎ include proteins, carbohydrates, nucleotides, lipids, coenzymes, and cofactors
  ◎ these metabolites involved in cellular respiration (e.g., glycolysis, Krebs cycle, other pathways) and
  ◎ in the production of building blocks for synthesis of large biopolymers DNA, RNA, proteins, and oligosaccharides

❖ At the cellular level the main chemical processes of all living matter are **similar**, if **not identical**
❖ This is true for animals, plants, fungi, or bacteria

4.2. Enzymes and their role in metabolism

- most chemical reactions require biological catalyst called **enzymes**
- Enzymes are **protein** catalysts that **speed up** chemical reactions;
- They make a chemical reaction **millions** times **faster** than without their involvement
- almost **all** metabolic processes in cell need enzyme catalysis
- Enzymes **bind** with particular reactants until the chemical reaction occurs, then **free themselves**

❑ How do enzymes speed up chemical reactions?

- Enzymes speed up reactions by **lowering activation energy**
- Many enzymes change **shape** when substrates bind
- This is termed "**induced fit**",
  - Meaning the precise **orientation** of the enzyme required for catalytic activity can be induced by the binding of the substrate

❑ What is activation energy?

4.2.1. Chemical nature and classification of enzymes

- All known enzymes are **proteins** except recently discovered **RNA enzymes**
- Some enzymes contain additional **non-protein group**
- Enzymes are **high molecular weight** compounds made up of chains of **amino acids** linked together by peptide bonds
- Many enzymes require other compounds (**cofactors**) before their catalytic activity can be exerted
- This **entire** active complex is referred to as the **holoenzyme**;
  - ☑ i.e., **apoenzyme** (protein portion) + **cofactor** (coenzyme, prosthetic group or metal-ion-activator)

❑ Thus, based on chemical nature, enzymes may be described as follows:

❖ **Simple enzymes:** are made up of **only protein** (polypeptide)
- contain **no chemical groups**
- E.g: digestive enzymes (**pepsin** and **trypsin)**

❖ **Conjugate enzymes**: is formed of two parts;
- a protein part called **apoenzyme** (e.g., flavoprotein) and a non-protein part **cofactor**

- **apoenzyme** + **cofactor** ➔ **holoenzyme**
- only enzymatic activity present when **both** components (apoenzyme and cofactor) are present together

- The cofactor is sometimes a
  - simple divalent metallic ion (e.g. Ca, Mg, Zn, Co, etc), and
  - sometimes a nonprotein organic compound
- If the cofactor is **firmly bound** to the apoenzyme, it is called **prosthetic group**
  - e.g. **cytochromes** are the enzymes that possess **porphyrins** as their prosthetic groups
- If, instead of being **more or less permanently** bound to the apoenzyme,
  - the cofactor attaches itself to the apoenzyme **only** at the **time of reaction**, it is called a **coenzyme**

❖ **Metallo-enzymes:**
- metal cofactors involved in enzymic reactions are
  - monovalent (K_+) and divalent cations (Mg_{++}, Mn_{++} and Cu_{++}).
- These may be **loosely held** by the enzyme, or as in some cases, go into the **composition** of the molecule itself
- If the metal forms part of the molecule, as iron of haemoglobin or cytochrome is, the enzymes are called **metallo-enzymes**

❖ **Isoenzymes (Isozymes):**
- are **enzymes** that differ in amino acid sequence but catalyze the same chemical reaction

  e.g. lactate dehydrogenase

- **Classes of enzymes based on the substrate they act up on**

Table 4.1. Major classes of Enzymes

S.No.	Type of reaction	Description of reaction	Enzyme class
1.	Oxidation – reduction	Transfer of electrons.	Oxidoreductases
2.	Group transfer	Transfer of a functional group from one molecule to another.	Transferases
3.	Hydrolysis	Cleavage of bonds by the addition of water.	Hydrolases
4.	Nonhydrolytic cleavage	Cleaving/splitting a molecule by nonhydrolytic processes.	Lyases
5.	Isomerization & rearrangements	Rearrangement of atoms to form isomers.	Isomerases
6.	Ligation using energy from ATP	Formation of Carbon and other bonds with energy from ATP.	Ligases

(Source: Concepts in Biochemistry; Rodney Boyer)

4.2.2. Mechanisms of enzyme action

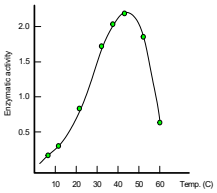
- Mechanisms of enzyme catalysis **vary**, but are all **similar in principle** to other types of chemical catalysis
- The reduction of activation energy **increases** the fraction of reactant molecules that can overcome this barrier and form the **P**
- An **E** attracts **S** to its **active site**, catalyzes the chemical reaction by which **P** are formed, and then allows the **P** to separate
- The combination formed by an **E** and its **S** is called the **E-S complex**
- The **S** are attracted to the active site by **electrostatic and hydrophobic forces**, which are called **noncovalent bonds**
  - because they are physical attractions and not chemical bonds

4.2.3 Factors affecting enzymatic activities

- The activity of an enzyme is affected by its environmental conditions such as **T** and **pH**

❖ **Temperature (T):**

- Increasing **T** increases the **kinetic energy** of molecules
- Since **E** catalyze reactions by randomly colliding with **S**, increasing **T** increases the **rate of reaction**, forming more **P**



- However, increasing **T** also increases the **vibrational energy** that **E** have, which damage the bonds that hold them together
- As **T** increases, weaker hydrogen and ionic bonds, will break
- Breaking bonds within the **E** will cause the **active site to change shape**
- change in shape of **active site,** is **less** complementary to the shape of the **S**, so that it is less likely to catalyze the reaction
- Higher **T** will **denature** the **E** and will no longer function
- **Optimal temperature** (T_o) is the **T** at which an **E** has the maximal catalytic power
- This varies with the type of **E**
- Reaction rates increase by **2 folds** for every **10°C rise**

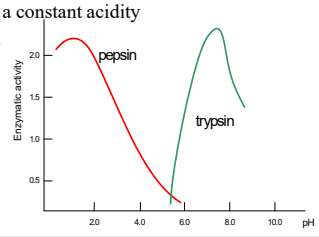
❖ **pH - Acidity and Basicity:**

- Lower pH values mean higher [H+] and lower [OH-]
- H+ and OH- ions are charged and so, interfere with H and ionic bonds that hold together an **E**, since they will be **attracted** or **repelled** by the charges created by the bonds
- This interference causes a change in shape of **E** and its **active site**
- Different **E** have different optimum pH values
- At the optimum pH, the rate of reaction is at an optimum
- Any change in pH above or below the optimum will quickly cause a decrease in the rate of reaction
- Small changes in pH above or below the optimum **do not** cause a permanent change to the enzyme

- However, extreme changes in pH can cause enzymes to denature and permanently lose their function
- E in different locations of our body have different optimum pH values since their environmental conditions may be different
- For example, the enzyme **pepsin** functions best at around pH-2 and is found in the stomach, which contains HCl
- most living systems are highly buffered; i.e., they have mechanisms that enable them to maintain a constant acidity
- Optimal pH is the pH at which the enzyme has the maximal catalytic power.
- pH 7.0 is suitable for most enzymes.

  pH (pepsin) = 1.8

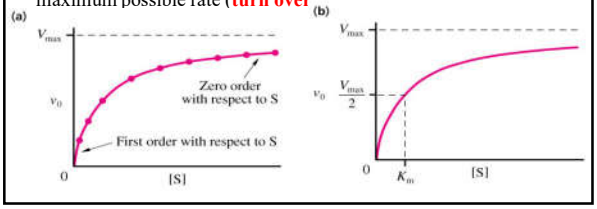
  pH (trypsin) = 7.8



Substrate and enzyme concentration

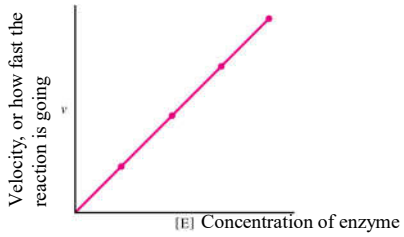
Substrate concentration

- Increasing **[S]** increases the rate of reaction
- This is because more S molecules will be colliding with **E** molecules, so more **P** will be formed
- But, after a certain **[S]**, any increase will have **no effect** on the rate of reaction, since **[S]** will no longer be the limiting factor
- The **E** will effectively become **saturated**, and will be working at their maximum possible rate (**turn over rate**)



Enzyme concentration

- Increasing **[E]** will increase the rate of reaction, as more **E** will be colliding with **S** molecules
- However, this too will only have an effect up to a certain concentration, where the **[E]** is no longer the limiting factor



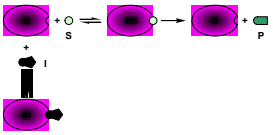
4.2.4. Enzyme inhibitors

- **E** activity can be inhibited in various ways
- Inhibition could be **reversible** or **irreversible**

Reversible inhibition

❖ **Competitive inhibition:**

- occurs when molecules very similar to the **S** molecules bind to the **active site** and **prevent binding** of the **actual S**
- **Penicillin**, is a competitive inhibitor that **blocks** the active site of an **E** that many bacteria use to construct their **cell walls**
- Inhibitors can be **normal** body metabolites and **foreign** substances (**drugs and toxins**)



❖ **Noncompetitive inhibition**:

- occurs when an inhibitor binds to the **E** at a location **other than the active site**
- In this case, the binding of the inhibitor is believed to **change the shape** of the **E** molecule, thereby **deforming** its active site and preventing it from reacting with its **S**
  - Noncompetitive inhibition is called **allosteric inhibition**; the place where the inhibitor binds to the **E** is called the *allosteric site*

Frequently, an end-product of a metabolic pathway serves as an **allosteric inhibitor** on an earlier enzyme of the pathway

- This inhibition of an enzyme by a product of its pathway is a form of **negative feedback**
- **Activators:** allosteric control can involve **stimulation** of **E** action as well as **inhibition**
- An activator molecule can be bound to an allosteric site and induce a reaction at the active site by changing its shape to fit a **S**
- Common activators include **hormones** and the products of earlier enzymatic reactions
- Allosteric **stimulation** and **inhibition** allow production of energy and materials by the cell when they are needed and inhibit production when the supply is adequate

❖ **Irreversible inhibition**

- covalently modify an **E**, and inhibition can not be reversed
- often contain reactive functional groups
- Is different from reversible **E** inactivation
- are generally **specific** for one class of **E** and
- **do not** inactivate all proteins;
- they ***do not*** function by destroying protein structure but by specifically **altering** the active site of their target

Review questions

1. Give examples of enzymes by types of substrates on which they act
2. Describe the two common models for mechanisms of actions of enzymatic catalysis
3. Give examples of enzyme inhibitions
4. Why are several enzymes needed in a particular metabolic pathway?
5. Discuss negative feedback inhibition and its importance

4.3. Bioenergetics and biosynthesis

4.3.1. Cellular respiration

- Most living organisms obtain energy by **breaking** down organic molecules during cellular respiration
- cellular respiration is to harvest electrons from C compounds (glucose) and use that energy to make ATP
- ATP is used to provide **immediate energy** for cells to do work
- This catabolic process can be divided into 3 phases

- **Phase I** - breakdown polysaccharides, proteins and lipids into their respective building blocks (**hydrolysis**)
  -this stage does **not** release much energy ➔Glycolysis
- **Phase II** - these building blocks are oxidized to **acetyl-CoA**
- Also, **pyruvate** or other TCA intermediates may be formed
- **Phase III** - consists of **TCA** followed by **ETC** and **oxidative phosphorylation**
- Energy released by ETC to O2 is coupled to **ATP synthesis**
- TCA cycle and ETC release much energy

- Cellular respiration occurs in **two** main parts:
  - glycolysis and
  - aerobic respiration
- glycolysis is an **anaerobic** process
  - **does not require O2**
- Aerobic respiration occurs at **Krebs cycle** and **ETC**
  - processes **require O2**

A. Glycolysis: anaerobic respiration

- **Glucose** is a key metabolite in metabolism
- Various pathways that are concerned with the **utilization**, **storage**, and **regeneration** of glucose exist
- **Glycogen** is a polymeric storage form of glucose in human and in the liver and in striated muscle, some amount is found in other tissues
- Glycogen is synthesized when glucose supply is **high**, and
  - its degradation helps to **maintain the blood glucose level** when during fasting
- When glycogen is **depleted**, more glucose is synthesized from scratch in **gluconeogenesis**
- Gluconeogenesis occurs in the **liver** and in the **kidneys**

- The first step in the degradation of glucose is **glycolysis**
- breaks down glucose (6C) to **pyruvate (two 3C)**
- glycolysis generates **ATP**
- A modest amount of ATP is produced in glycolysis **directly**
- much more ATP is formed downstream of glycolysis through complete oxidation of pyruvate
- Glycolysis is found in **animals**, **plants** and **microorganism**
- This pathway is used by anaerobic as well as aerobic organisms
- The process takes place in the **cytoplasm** of prokaryotes and eukaryotes and **does not require O2**
- Under aerobic conditions, pyruvate undergoes complete oxidative to CO2 and H2O

- Pyruvate intended for complete degradation is transported to the **mitochondria**,
  - where it is **decarboxylated** to acetyl-CoA by **pyruvate dehydrogenase**
- Acetyl-CoA is completely degraded in the **TCA** cycle
- The H2 that is produced here is **not gaseous** but bound to co-substrates as,
  - **NADH** and **FADH2**, which is subsequently oxidized in the respiratory chain

❖ Glycolysis involves **ten** enzymatic reactions;

❖ The first five are **preparatory phases or investment phase**.

1. The phosphorylation of glucose at C-6 by **hexokinase** forming glucose 6-phosphate (**G6P**)
2. The conversion of G6P to fructose-6-phosphate (**F6P**) by **phosphohexose isomerase**
3. The phosphorylation of F6P to the 1,6-bisphosphate (**F1,6-BP**) by **phosphofructokinase**,
4. The cleavage of F1,6-BP by **aldolase**. This yields two different products, dihydroxyacetone phosphate (**DHAP**) and glyceraldehyde-3-phosphate (**GADP**),
5. The isomerization of **DHAP** to a second molecule of **GADP** by **triose phosphate isomerase**,

6. The dehydrogenation and concomitant phosphorylation of **GADP** to 1,3-bis-phosphoglycerate by **glyceraldehyde-3-phosphate dehydrogenase**,
7. The transfer of the 1-phosphate group from 1,3-PG to ADP by **phosphoglycerate kinase**, which yields ATP and 3-PG
8. The isomerization of 3PG to 2PG by **phosphoglycerate mutase**,
9. The dehydration of 2PG to phosphoenolpyruvate by **enolase**
10. The transfer of the phosphate group from phosphoenolpyruvate to ADP by **pyruvate kinase**, to yield a second molecule of **ATP**

❖ Step 6 to10 are called **energy conserving stages**

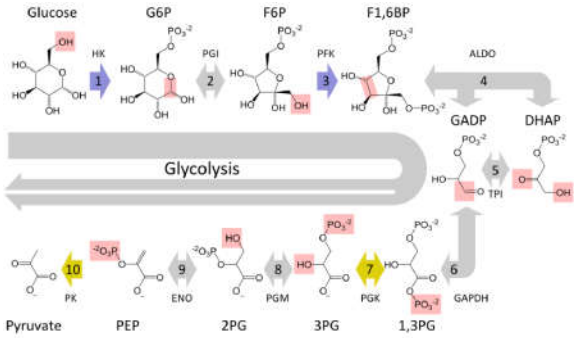


Fig: 4.1a. Glycolysis steps

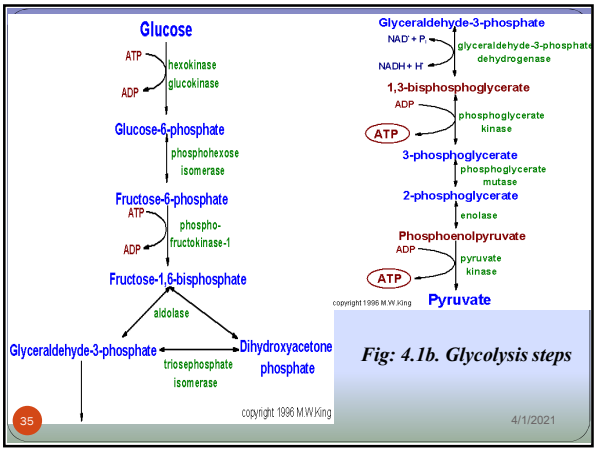


Fig: 4.1b. Glycolysis steps

B. Formation of Acetyl CoA

- One fate of pyruvate is that it enters to TCA for complete oxidation
- But there are **intermediate** processes that convert pyruvate to a acetyl-CoA
- The **enzyme complex** converts pyruvate into Acetyl-CoA by the following chemical changes:
  - Decarboxylation of pyruvate (loss of CO2)
  - Formation of acetyl group
  - Linkage of acetyl group to coenzyme A forming acetyl-CoA

C. TCA cycle and ETC: Aerobic respiration

i. The Tricarboxylic Acid (TCA) Cycle (Phase III)

- The TCA cycle is considered as **central** pathway of **aerobic** metabolism, as it serves two purposes-
  - **bioenergetics** and **biosynthesis**:

❖ **Bioenergetic** - the cycle carries out complex degradation of acetyl group in acetyl-CoA to CO2,

- resulting in release of energy (**ATP or GTP**) and reducing power (**NADH** and **FADH2**)

❖ **Steps of the Krebs cycle (After Hans Adolf Krebs)**

- Prior to the Krebs cycle, pyruvate first reacts with coenzyme A (CoA) to form **acetyl-CoA**
- At the same time, **CO2** is released and NAD is converted to **NADH**
- Then acetyl-CoA moves to the **mitochondrial matrix** resulting **2CO2** and **2NADH**
- The Krebs cycle **begins** with acetyl-CoA combining with a 4-C compound to form a 6-C compound known as **citric acid**
- Citric acid is then broken down in the next series of steps, releasing **2CO2** and**1GTP**, **3NADH**, and **1FADH2**
- FAD is another electron carrier similar to NADH and NADPH
- Finally, acetyl-CoA and citric acid are generated and the cycle continues

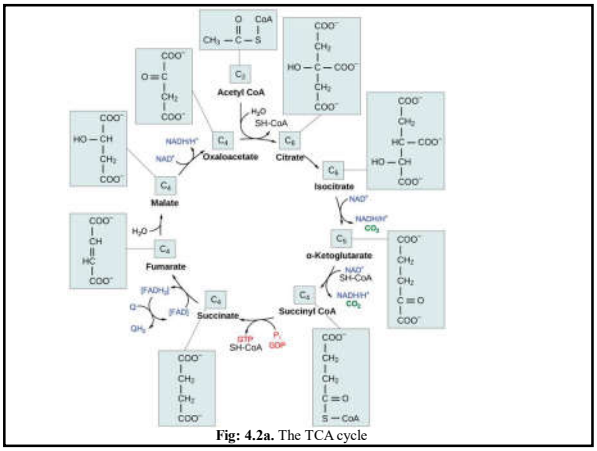


Fig: 4.2a. The TCA cycle

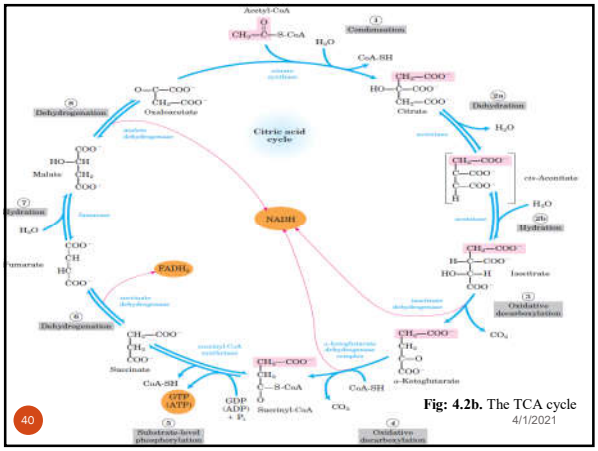


Fig: 4.2b. The TCA cycle

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❖ Recall that **two pyruvate** molecules are formed during glycolysis, resulting in **two turns** of the Krebs cycle for each glucose molecule

❖ The net yield from the Krebs cycle is

- **6CO2** molecules (2 during Acetyl-CoA formation and 4 within the cycle),
- **2GTP** (ATP),
- **8NADH** (2 during Acetyl-CoA formation and 6 within the cycle), and
- **2FADH2**

❖ NADH and FADH2 move on to play a significant role in the next stage of aerobic respiration

❖ **Biosynthesis** - supplies precursors for several biosynthetic pathways of amino acids, pyrimidines, purines etc.

- the TCA cycle is also an important source of biosynthetic precursors
  - **e.g.** α-ketoglutarate and oxaloacetate are used for synthesis of a number of amino acids like **glutamic acid**, **asparatic acid** etc.
  - Succinyl-CoA is used to form **porphyrin** ring of cytochromes, chlorophyll etc.
  - Oxaloacetate can also be converted to **phosphoenolpyruvate**, which is a precursor of glucose
  - Acetyl-CoA is the starting material for **fatty acid** biosynthesis

ii. Electron Transport Chain

- In aerobic respiration, **electron transport** is the final step in the break-down of glucose
- It is the point at which **most of the ATP** is produced
- High-energy electrons and H+ from NADH and FADH2 produced in the TCA are used to convert ADP to ATP

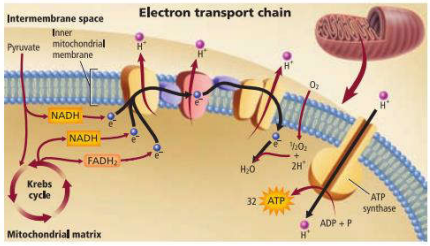


Fig: 4.3. Electron Transport Chain

- Electrons move along the **mitochondrial membrane** from one protein to another
- As NADH and FADH2 electrons, the energy carriers are converted to NAD+ and FAD2+, and H ions are released into the **mitochondrial matrix**
- The H+ are pumped into the mitochondrial matrix across the **inner mitochondrial membrane**
- H+ then diffuse down their concentration gradient back across the membrane and into the matrix through **ATP synthase** molecules in **chemiosmosis**
- Electron transport and chemiosmosis in cellular respiration are similar to these processes in photosynthesis
- O2 is the final electron acceptor in ETC in cellular respiration
- Protons and electrons are transferred to O2 to form H2O

Summary of cellular respiration

Process	Inputs	Outputs
Glycolysis	1 Glucose 2ATP	2 Pyruvate 2 NADH 4 ATP
Link reaction	2 Pyruvate	2 CO2 2 Acetyl CoA 2 NADH
Krebs cycle	2 Acetyl CoA	4 CO2 2 ATP 6 NADH 2NADH2
Electron transport chain	10 NADH*3ATP 2 FADH2*2ATP O2	34 ATPs H2O

Review questions

1. What is the importance of converting glucose into G6P during the first step of glycolysis
2. Describe gluconeogenesis
3. Indicate places where glycolysis, link reaction, TCA cycle and ETC occur in cellular respiration
4. Calculate the total number of ATP obtained from a molecule of glucose
   - From substrate-level phosphorylation
   - From oxidative phosphorylation
   - Total number of ATP from cellular respiration

4.3.2 Biosynthesis

- is a multi-step enzyme-catalyzed process in living organisms
- In biosynthesis,
  - simple compounds are modified,
  - converted into other compounds, or
  - joined together to form macromolecules
- This process often consists of metabolic pathways located within
  - a single cellular organelle,
  - others involve enzymes located within multiple cellular organelles

  e.g, production of lipid membrane components and nucleotides
- Biosynthesis is usually synonymous with anabolism

- The prerequisite elements for biosynthesis include:
  - precursor compounds,
  - chemical energy (e.g. ATP), and
  - catalytic enzymes which require coenzymes (e.g.NADH, NADPH).
- These elements create **monomers**, the building blocks for **macromolecules**
- Some important biological macromolecules include:
  - **proteins**, which are composed of **amino acid monomers** joined via peptide bonds, and
  - **DNA** molecules, composed of **nucleotides** joined via phosphodiester bonds

- The focus of the biosynthesis will be related to photosynthesis:

1. **Photosynthesis**
   a) **The importance of photosynthesis**
   b) **Variants of photosynthesis** (oxygenic vs anoxygenic)
2. **The photosynthetic apparatus**
   a) **Plastids** (chloroplasts, chromopalsts, proteinoplasts, leucoplasts)
   b) **Pigments** (chlorophylls, carotenoids, phycobilins)
   c) **Antenna**
   d) **Reaction centers**
3. **The photosynthetic process**
   a) **Light dependent reactions**
   b) **Light independent reactions** (carbon fixation, reduction and regeneration)
   c) **Alternative pathways** (C4 pathway, CAM)

A. Photosynthesis

- Is the process by which **autotrophs** convert light energy into chemical energy

The importance of photosynthesis

- Directly or indirectly, photosynthesis nourishes **almost the entire living world**
- **all organisms**, from bacteria to humans require **energy**
- To get this, many organisms access stored energy by **eating food**
- **Carnivores** eat other **animals** and **herbivores** eat **plants**

❖ But where does the stored energy in food originate?

- All of this energy can be traced back to the process of **photosynthesis** and light energy from the **sun**

- Photosynthesis is essential to **all life** on earth
- It is the only biological process that captures energy from **sunlight**
- converts it into chemical energy in the form of **G3P**
- which in turn made into sugars, proteins, lipids, and nucleic acids
- Plants use these compounds in all of their metabolic processes;
- plants do not need to consume other organisms for food
- Unlike plants, animals need to consume other organisms

- During photosynthesis,
  - molecules in leaves capture sunlight and energize electrons,
  - then stored in the covalent bonds of carbohydrate molecules
  - those covalent bonds are broken to release energy by cell respiration
- **Photoautotrophs** (self-feeders using light)
  - Plants, algae, and cyanobacteria
- **Heterotrophs** (other feeders): animals, fungi, and most other bacteria,
  - rely on photosynthetic organisms for their energy needs
- **Chemoautotrophs**:
  - synthesize sugars by extracting energy from inorganic chemical,
  - Do not use sunlight e,g, other bacteria

- Those **carbohydrates** are the energy source that heterotrophs use to power the synthesis of ATP via respiration
- Therefore, photosynthesis powers **99%** of Earth's ecosystems
- Energy path: sun light ➔ vegetation ➔to deer ➔finally to wolf

E.g,



Variants of photosynthesis

- Common photosynthetic known as **oxygenic photosynthesis**
- The other type is termed as **anoxygenic photosynthesis**
- Their general principles are very similar

❖ **Oxygenic photosynthesis**,
- ✓ Commonly seen in plants, algae and cyanobacteria
- ✓ light energy transfers e- from H2O to CO2, to produce carbohydrates
- ✓ the CO2 is "**reduced**," or receives electrons, and
- ✓ the water becomes "**oxidized**," or loses electrons
- ✓ Ultimately, **oxygen** is produced along with carbohydrates

❖ **Anoxygenic photosynthesis**,
- uses electron donors other than water
- occurs in **purple bacteria** and **green sulfur bacteria**
- **does not** produce **oxygen**
- What is produced depends on the electron donor

E.g, many bacteria use H2S, producing solid S as a byproduct

- The overall process of both types of photosynthesis can be neatly summarized as a chemical equation

❖ Oxygenic photosynthesis is written as follows:

$6CO_2 + 12H_2O + \text{Light Energy} \rightarrow C_2H_{12}O_6 + 6O_2 + 6H_2O$

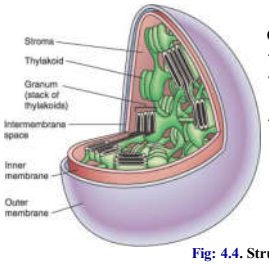
❖ Anoxygenic photosynthesis reactions can be represented as a single generalized formula:

$CO_2 + 2H_2A + \text{Light Energy} \rightarrow [CH_2O] + 2A + H_2O$

B. The photosynthetic apparatus

- **Plastids**
- Photosynthetic eukaryotic organisms contain organelles called plastids in their cytoplasm
- Plastids generally contain **pigments** or can **store nutrients**
- The undifferentiated **protoplastids** in plants can differentiate into several types, each with a distinct function
  - **Chloroplasts** contains **chlorophyll** for photosynthesis
  - **Chromoplasts** for pigment **storage** (contain **carotenoids**)
  - **Proteinoplasts** for **protein** storage
  - **Leucoplasts** for storage of **fats** and **starch**; colorless and nonpigmented
- Photosynthesis occurs in the chloroplasts; specifically, in **grana** and **stroma** regions

- The grana is the **innermost** portion of the organelle; a collection of **disc-shaped membranes**, stacked into **columns** like plates
- The individual discs are called **thylakoids**
- It is here that the transfer of electrons takes place
- The **empty spaces** between columns of grana constitute the **stroma**



Chloroplasts are similar to mitochondria,
- ✓ the **energy centers** of cells,
- ✓ have their own **genome**, or collection of genes,
- ✓ contained within **circular DNA**

Fig: 4.4. Structure of chloroplast

Pigments

- are molecules that **bestow color** on plants, algae and bacteria,
- responsible for effectively **trapping sunlight**
- Pigments of different colors absorb different wavelengths of light
- Below are the three main groups.

❖ **Chlorophylls**:

- are green-colored pigments
- are capable of trapping **blue** and **red** light
- have 3 subtypes, chlorophyll **a, b** and **c**
- also a bacterial variant named bacteriochlorophyll,
  - which absorbs **infrared** light
  - mainly seen in **purple and green bacteria**, which perform anoxygenic photosynthesis

❖ **Carotenoids:**

- ☑ **red**, **orange** or **yellow**-colored pigments
- ☑ absorb **bluish-green light**
- ☑ e.g, **xanthophyll** (yellow) and **carotene** (orange) from which carrots get their color
- ☑ Carotenoids **cannot** transfer sunlight energy directly to the photosynthetic pathway,
  - For this reason, they are called **accessory** pigments. e,g **fucoxanthin**

❖ **Phycobilins**:

- these **red** or **blue** pigments
- absorb wavelengths of light that are **not well** absorbed by chlorophylls and carotenoids
- They are seen in **cyanobacteria** and **red algae**

Antennae

- A large collection of **100-5,000** pigment molecules constitutes antennae
- capture light energy from the sun, in the form of **photons**
- Ultimately, light energy transferred to a **pigment-protein** complex that can convert it to chemical energy, in the form of electrons
- In plants, light energy is transferred to chlorophyll pigments
- The conversion to chemical energy is accomplished when a chlorophyll pigment expels an electron, which can then move on to an appropriate recipient
- The **pigments** and **proteins**, which convert light energy to chemical energy and begin the process of electron transfer, are known as **reaction centers**

C. The photosynthetic process

- The reactions of plant photosynthesis are divided those that;
  - require the presence of sunlight and those that do not
- Both types of reactions take place in chloroplasts:
  - light-dependent reactions in the **thylakoid** and
  - light-independent reactions in the **stroma**

❑ **Light-dependent reactions** (also called light reactions):

- When a photon of light **hits** the reaction center, a pigment chlorophyll **releases an electron**
- The released electron escape by traveling through an **ETC**, which generates the energy needed to produce **ATP** and **NADPH**
- The "**electron hole**" in the original chlorophyll pigment is filled by taking an electron from **water**
- As a result, **oxygen** is released into the atmosphere

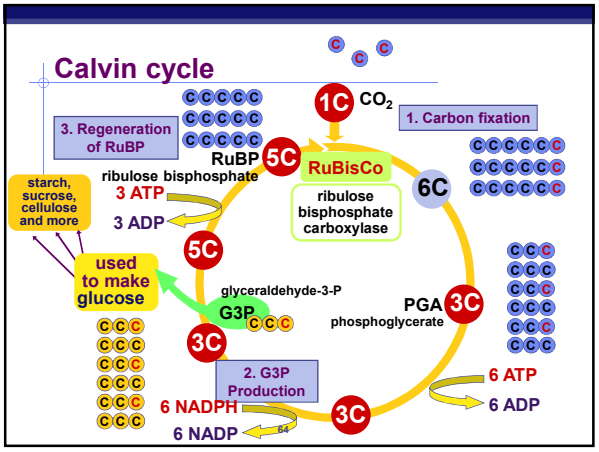
❑ **Light-independent reactions:**

- called **dark reactions** and known as the **Calvin cycle (after Melvin Calvin)**
- Light reactions produce **ATP** and **NADPH**, which are the rich energy sources that drive dark reactions
- NADPH and ATP provide cells with large amounts of energy
  - But these molecules are **not stable** enough to store chemical energy for long periods of time

❖ Thus, there is a second phase of photosynthesis called the **Calvin cycle** in which **energy is stored in organic** molecules such as glucose

- Three chemical reaction steps make up the Calvin cycle:
  - ☑ **carbon fixation,**
  - ☑ **reduction and**
  - ☑ **regeneration**.
- These reactions use **water** and **catalysts**
- The carbon atoms from CO2 are "**fixed**," when they are built into organic molecules that ultimately form **3C sugars** (**six** CO2 and **six** 5-C compounds form **twelve 3-C** compound – 3PGA = 3 Phosphoglycerate)
- These sugars are then used to make **glucose** or are recycled to initiate the Calvin cycle again
- **RuBisCo** converts inorganic CO2 into organic molecules that can be used by the cell
  - it is considered one of the most important biological enzymes
- The Calvin Cycle just described is known as the **C3 pathway** because the first stable organic molecule formed is a three carbon sugar!

  e.g, **C3 plants** are: grass, oak trees, maple trees, rose bushes, etc.



Summary of light dependent and independent reactions

Reaction	Input	Output
Light dependent reaction	H20, Light energy	O2, ATP, NADPH
Light independent reaction	CO2, ATP, NADPH	Glucose, NADP, ADP, Pi

The rate of photosynthesis can be limited by:
light intensity, CO2 concentration, water and temperature.
How???

Alternative Pathways

- The **environment** in which an organism lives can impact the organism's ability to carry out photosynthesis
- Environments in which the amount of **water** or **CO2** is insufficient can **decrease** the ability of a photosynthetic organism to convert light energy into chemical energy
- e.g, plants in hot, dry environments are subject to **excessive water loss** that can lead to decreased photosynthesis
- Many plants in extreme climates have altered native photosynthesis pathways to maximize energy conversion

❖ **C4 plants** one adaptive pathway that helps to maintain photosynthesis while **minimizing water** loss is called the **C4 pathway**

- Occurs in plants such as **sugar cane** and **corn**
- Are called C4 plants because they fix CO2 into **4C cpds** instead of 3C during the Calvin cycle
- C4 plants have significant **structural modifications** in the arrangement of cells in the leaves
- C4 plants keep their **stomata** (pores) **closed** during hot days, while the 4C cpds are transferred to special cells where CO2 enters the Calvin cycle.
  - This allows for **sufficient CO2 uptake**, while simultaneously **minimizing water loss**

❖ **CAM plants** another adaptive pathway used by some plants to maximize photosynthetic activity is called **crassulacean acid metabolism** (CAM photosynthesis)

- The CAM pathway occurs in water conserving plants that live in **deserts**, **salt marshes**, and others where access to water is limited
- CAM plants, such as **cacti**, **orchids**, and **pineapple** allow CO2 to enter the leaves only at **night**, when the atmosphere is cooler and more humid
- At night, these plants fix CO2 into **organic compounds**
- During the **day**, CO2 is released from these compounds and enters the **Calvin cycle**
- This pathway also allows for sufficient CO2 uptake, while minimizing water loss

Review Questions

1. Discuss variants in photosynthesis
2. List and describe functions of different types of plastids and pigments
3. What are **photosystems**? And where are they located?
4. What are **antenna** and **reaction centers**?
5. How are photosystems related to **antenna** and **reaction centers**?
6. Discuss light dependent and light independent reactions
7. Discuss the alternative pathways of photosynthesis

4.4. Metabolic disorders, diagnosis and treatments

- Metabolism is the breaking down of food to its simpler components
- Metabolic disorders occur when these normal processes become **disrupted**

A. Types of metabolic disorders

- They can be **inherited**, in case known as **inborn errors of metabolism**, or they may be **acquired** during ones lifetime

Inherited metabolic disorders

- occur when a **defective gene** causes an enzyme deficiency
- These diseases are known as **inborn errors of metabolism**
- Also occur when the **liver** or **pancreas** do not function properly

❑ Inherited causes of metabolic disorders include:

➢ **Carbohydrate disorders**; examples include
- ***Diabetes insipidus*** *(excessive dilute urine up to 20l/day)*,
- hereditary **fructose intolerance** (malabsorption from the intestine),
- **Galactosemia** (accumulation in the blood),
- pyruvate metabolism disorders,
- **von Gierke's disease** (failure of liver to break down glycogen),
- **McArdle disease** (muscle glycogen storage disease – myophosphorylase defi),
- **Pompe's disease** (glycogen accumulation inside lysosome), and
- **Forbes' disease** (deficiency of glycogen debranching enzymes)

➢ **Fatty acid oxidation defects**; examples include
- **Gaucher's disease** (accumulation of glucosyleceramide in cells),
- **Niemann-Pick disease** (sphingomyelin accumulation in lysosome),
- **Fabry's disease** (sphingolipids accumulation in blood vessels), and
- medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency

➢ **Amino acid disorders**; examples include
- Tay-Sachs disease,
- phenylketonuria,
- tyrosinemia,
- maple syrup urine disease, and
- homocystinuria

❑ Some of the disorders **associated** with metabolism

- ✓Acid-base imbalance,
- ✓Disorders of calcium metabolism,
- ✓DNA repair-deficiency disorders,
- ✓Iron metabolism disorders,
- ✓Mitochondrial diseases,
- ✓Phosphorus metabolism disorders,
- ✓Malabsorption syndromes,
- ✓Water-electrolyte imbalance

Other causes of metabolic disorders

- Metabolic disorders can be due to other factors, such as a **combination of inherited** and **environmental factors**
- Some of the conditions that can cause metabolic disorders include:
  - Alcohol abuse, Diabetes (chronic, affects body's ability to use sugar)
  - Diuretic abuse, Gout (type of arthritis caused by a buildup of uric acid in the joints)
  - Ingestion of poison or toxins, including excessive aspirin, bicarbonate, alkali, ethylene glycol, or methanol
  - Kidney failure, Pneumonia, respiratory failure, or collapsed lung
  - Sepsis (life-threatening bacterial blood infection)

B. Risk factors of metabolic disorders

- A number of factors increase the risk of developing metabolic disorders
- Not all people with risk factors will get metabolic disorders
- Risk factors for metabolic disorders include:
  - chronic medical conditions, such as lung or kidney disease and Diabetes
  - Family history of genetic metabolic disorder.
  - Race and ethnicity: people with African, Hispanic, First Nations, Asian, and Pacific Islander backgrounds are at higher risk than whites for type 2 diabetes
  - HIV/AIDS and other diseases; the risk of metabolic syndrome is higher if a person ever had nonalcoholic fatty liver disease, polycystic ovary syndrome or sleep apnea
  - Age- the risk of metabolic syndrome increases with age
  - Obesity and lack of exercise: carrying too much weight, especially in abdomen area, increases risk of metabolic syndrome
  - Hormone imbalance: a hormone disorder such as polycystic ovary syndrome (PCOS), a condition in which the female body produces too much of certain hormones, is linked with metabolic syndrome
  - Insulin resistance: a situation in which a body cannot use insulin properly

C. Diagnosis of metabolic disorders

❖ Metabolic syndrome is more effectively diagnosed by testing different;
  - blood markers (specific markers of insulin resistance),
  - obesity (especially abdominal obesity),
  - high blood pressure, and
  - lipid abnormalities

❖ Specifically, metabolic syndrome is diagnosed if **any three of the following five markers** are present:
  - Elevated **waist circumference**: 40 inches or more for men; 35 inches or more for women
  - Elevated **triglycerides**: 150 mg/dL or higher
  - Reduced **high-density lipoprotein** (HDL) levels (AKA "good" cholesterol): less than 40 mg/dL in men; less than 50 mg/dL in women
  - Elevated **blood pressure**: 130/85 mm Hg or higher or are already taking blood pressure medications
  - Elevated **fasting glucose**: 100 mg/dL or higher or are already taking glucose-lowering medications

D. Treatments of metabolic disorders

- The treatment approach for metabolic disorders depends on the specific disorder
- Multiple treatment options are available for inborn (inherited) errors of metabolism and examples include:
  - bone marrow transplantation,
  - enzyme replacement therapy in selected patients,
  - gene therapy in selected patients,
  - medications to reduce symptoms, such as pain or low blood sugar,
  - mineral supplementation,
  - periodic assessment,
  - physical therapy
  - nutritional counseling and support,
  - surgery to relieve pain or symptoms, vitamin supplementation and etc.

- Acquired metabolic disorder treatment will include
  - normalizing the metabolic balance by both reversing the cause and administering medications.

❑ **Potential complications of metabolic disorders**

- Complications of untreated metabolic disorders can be serious, even life threatening in some cases
- The risk of serious complications can be minimized following the treatment plan designed by health care professional
- Complications of metabolic disorders include:
  - organ failure/dysfunction,
  - seizures and tremors, and
  - unconsciousness and coma