College of Health and Medical Technologies - Al-Dour
Department of Physical Therapy
The second stage

Metabolism

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METABOLISM

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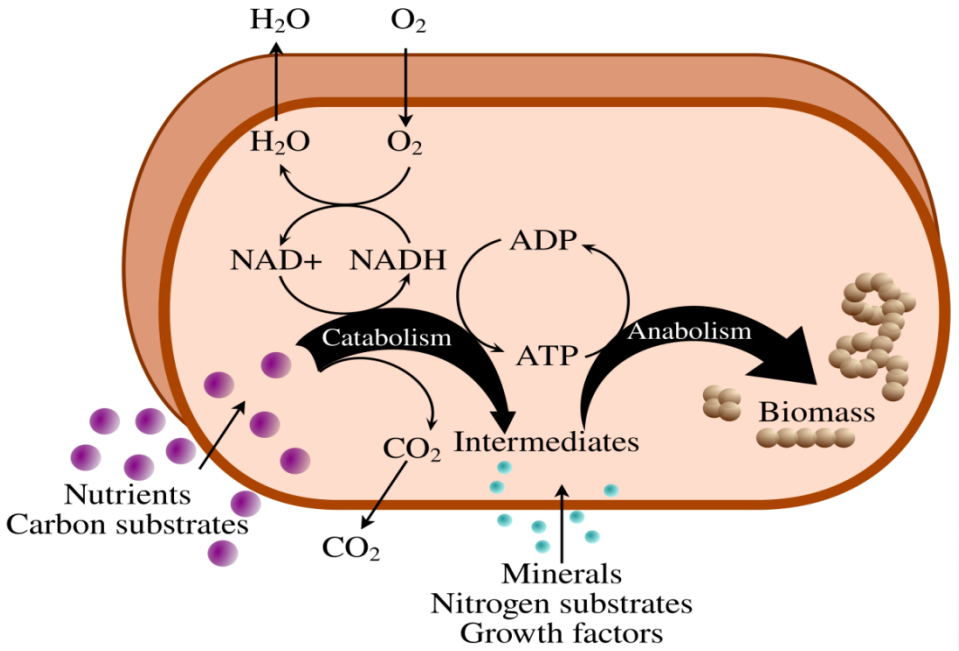
Metabolism

refers to all the chemical processes going on continuously inside your body that allow life and normal functioning (maintaining normal functioning in the body is called homeostasis). These processes include those that break down nutrients from our food, and those that build and repair our body



metabolism

from Greek: metabolē, "change") is the set of life-sustaining chemical reactions in organisms.

The three main functions of metabolism are:

1. the conversion of the energy in food to energy available to run cellular processes;
2. the conversion of food to building blocks of proteins, lipids, nucleic acids, and some carbohydrates
3. the elimination of metabolic wastes

What are the stages of metabolism

- **Stage 1**: Glycolysis for glucose, β-oxidation for fatty acids, or amino acid catabolism.
- **Stage 2**: Citric Acid Cycle (or Krebs cycle)
- **Stage 3:** Electron Transport Chain and ATP synthesis

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Metabolic reactions

may be categorized as

1. catabolic—the breaking down of compounds (for example, of glucose to pyruvate by cellular respiration); or
2. anabolic—the building up (synthesis) of compounds (such as proteins, carbohydrates, lipids, and nucleic acids).

Usually, catabolism releases energy, and anabolism consumes energy.

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Metabolic rate

Your body's metabolic rate (or total energy expenditure) can be divided into 3 components, which are:

- **Basal metabolic rate (BMR)** – even at rest, the body needs energy (kilojoules) to keep all its systems functioning correctly (such as breathing, keeping the heart beating to circulate blood, growing and repairing cells and adjusting hormone levels). The body's BMR accounts for the largest amount of energy expended daily (50 to 80% of your daily energy use).
- **Thermic effect of food (also known as thermogenesis)** – your body uses energy to digest the foods and drinks you consume and also absorbs, transports and stores their nutrients. Thermogenesis accounts for about 5 to 10% of your energy use.

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- **Energy used during physical activity** – this is the energy used by physical movement and it varies the most depending on how much energy you use each day. (Based on a moderately active person (30 to 45 minutes of moderate-intensity physical activity per day), this component contributes 20% of our daily energy use).

Physical activity includes planned exercise (like going for a run or playing sport) but also includes all incidental activity (such as hanging out the washing, playing with the dog or even fidgeting!).

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Basal metabolic rate (BMR)

The BMR refers to the amount of energy your body needs to maintain homeostasis.

Factors that affect our BMR:

1. Body size – larger adult bodies have more metabolising tissue and a larger BMR.

2. Amount of lean muscle tissue – muscle burns kilojoules rapidly.

3. Amount of body fat – fat cells are 'sluggish' and burn far fewer kilojoules than most other tissues and organs of the body.

4. Crash dieting, starving or fasting – eating too few kilojoules encourages the body to slow the metabolism to conserve energy. BMR can drop by up to 15% and if lean muscle tissue is also lost, this further reduces BMR.

5. Age – metabolism slows with age due to loss of muscle tissue, but also due to hormonal and neurological changes.

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4. Growth – infants and children have higher energy demands per unit of body weight due to the energy demands of growth and the extra energy needed to maintain their body temperature.

5. Gender – generally, men have faster metabolisms because they tend to be larger.

Genetic predisposition – your metabolic rate may be partly decided by your genes.

6. Hormonal and nervous controls – BMR is controlled by the nervous and hormonal systems. Hormonal imbalances can influence how quickly or slowly the body burns kilojoules.

7. Environmental temperature – if temperature is very low or very high, the body has to work harder to maintain its normal body temperature, which increases the BMR.

8. Infection or illness – BMR increases because the body has to work harder to build new tissues and to create an immune response.

9. Amount of physical activity – hard-working muscles need plenty of energy to burn. Regular exercise increases muscle mass and teaches the body to burn kilojoules at a faster rate, even when at rest.

10. Drugs – like caffeine or nicotine, can increase the BMR.

11. Dietary deficiencies – for example, a diet low in iodine reduces thyroid function and slows the metabolism.

Energy used during physical activity

During strenuous or vigorous physical activity, our muscles may burn through as much as 3,000 kJ per hour. The energy expenditure of the muscles makes up only 20% or so of total energy expenditure at rest, but during strenuous exercise, it may increase 50-fold or more.

Energy used during exercise is the only form of energy expenditure that we have any control over.

Moderate exercise means you can talk while you're exercising, but you can't sing.

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Metabolism and age-related weight gain

Muscle tissue has a large appetite for kilojoules. The more muscle mass you have, the more kilojoules you will burn.

People tend to put on fat as they age, partly because the body slowly loses muscle. It is not clear whether muscle loss is a result of the ageing process or because many people are less active as they age. However, it probably has more to do with becoming less active. Research has shown that strength and resistance training can reduce or prevent this muscle loss.

Hormonal disorders of metabolism

Hormones help regulate our metabolism. Some of the more common hormonal disorders affect the thyroid. This gland secretes hormones to regulate many metabolic processes, including energy expenditure (the rate at which kilojoules are burned).

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Thyroid disorders include:

- **Hypothyroidism (underactive thyroid)** – the metabolism slows because the thyroid gland does not release enough hormones. A common cause is the autoimmune condition Hashimoto's disease. Some of the symptoms of hypothyroidism include unusual weight gain, lethargy, depression and constipation.
- **Hyperthyroidism (overactive thyroid**) – the gland releases larger quantities of hormones than necessary and speeds the metabolism. The most common cause of this condition is Graves' disease. Some of the symptoms of hyperthyroidism include increased appetite, weight loss, nervousness and diarrhoea.

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Genetic disorders of metabolism

Our genes are the blueprints for the proteins in our body, and our proteins are responsible for the digestion and metabolism of our food.

Sometimes, a faulty gene means we produce a protein that is ineffective in dealing with our food, resulting in a metabolic disorder. In most cases, genetic metabolic disorders can be managed under medical supervision, with close attention to diet.

The symptoms of genetic metabolic disorders can be very similar to those of other disorders and diseases, making it difficult to pinpoint the exact cause.

- **Fructose intolerance (**the inability to break down fructose, which is a type of sugar found in fruit, fruit juices, sugar).
- **Galactosaemia (**the inability to convert the carbohydrate galactose into glucose. Galactose is not found by itself in nature. It is produced when lactose is broken down by the digestive system into glucose and galactose.).
- **Phenylketonuria (PKU) (**the inability to convert the amino acid phenylalanine into tyrosine. High levels of phenylalanine in the blood can cause brain damage .

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METABOLISM

ENZYMES

Enzymes

enzymes are biological catalysts which bring about chemical reaction in the living cell.

- produced by the living organism in small amounts.
- Functions: digestion, breathing, synthesis and break down of CHOS, proteins, fats
- enzymes acts upon substance called substrate.
- enzymes convert substrate into product.

Ex: lactose $\xrightarrow{\text{lactase}}$ galactose + glucose

- 16% of weight is nitrogen.

physical properties: 1. Heat labile 2. Soluble in water

3. Precipitate by precipitating agent (ammonium sulphate or trichloroacetic acid)

General properties of enzymes:

1. 1. all enzymes are proteins.
2. 2. enzymes accelerate the reaction but: a. do not alter the reaction equilibrium b. not consumed in overall reaction c. required in very small quantities.
3. 3. enzymes are highly specific for their substrate.
4. 4. enzymes possess active site, at which interaction with substrate take place.

Sources of enzymes:

- Endoenzymes: enzymes that function within the cells, most of enzymes are these types. Ex: metabolic oxidase.
- Exoenzymes: enzymes that are liberated by cells and catalyze reactions outside the cell. Ex: digestive enzymes (amylase, lipase, protease).

Chemical composition of enzymes:

Enzymes classified according to their chemical composition into.

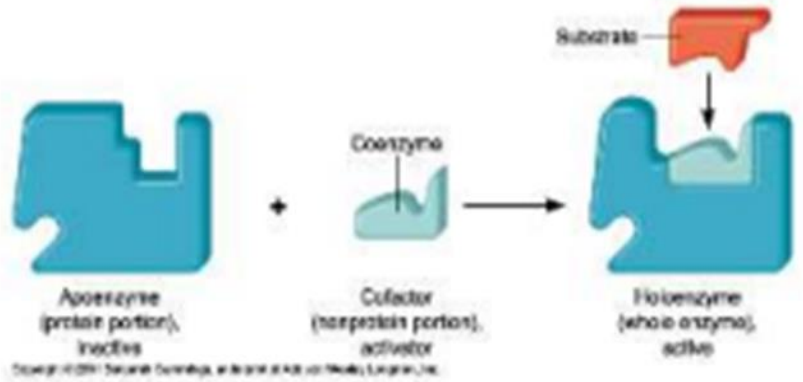
1. Enzyme consist of only protein. Ex: pepsin, trypsin (amino acids binding peptide bonds).
2. Enzyme consist of : protein (enzyme) + Co - Enzyme = Holoenzyme (apoenzyme)
3. Enzyme consist of:

Protein (enzyme) + prosthetic group (Co – factor) = Holoenzyme

Chemical composition of enzymes

(1) Simple protein

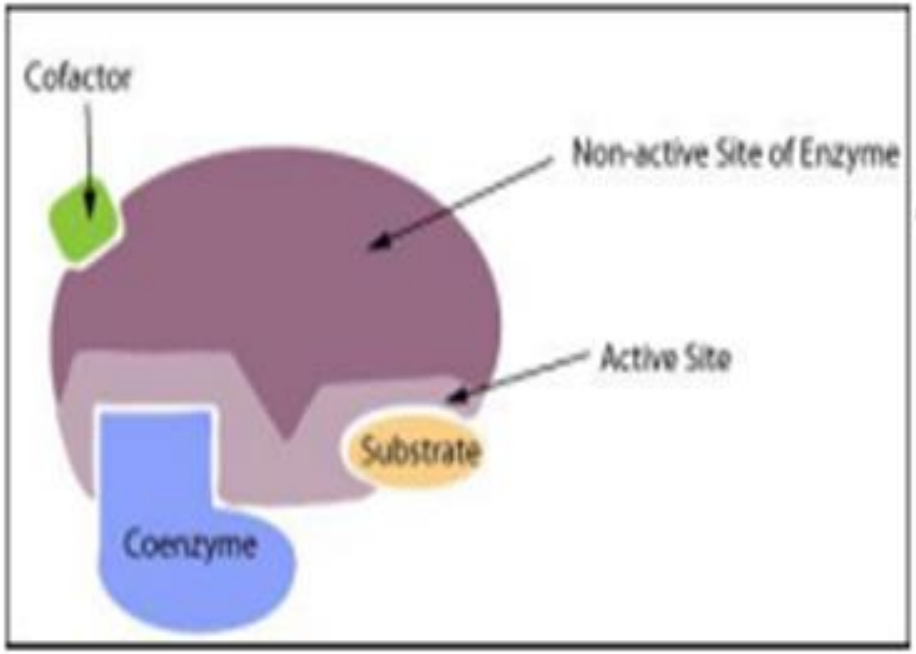
(2) Conjugated protein

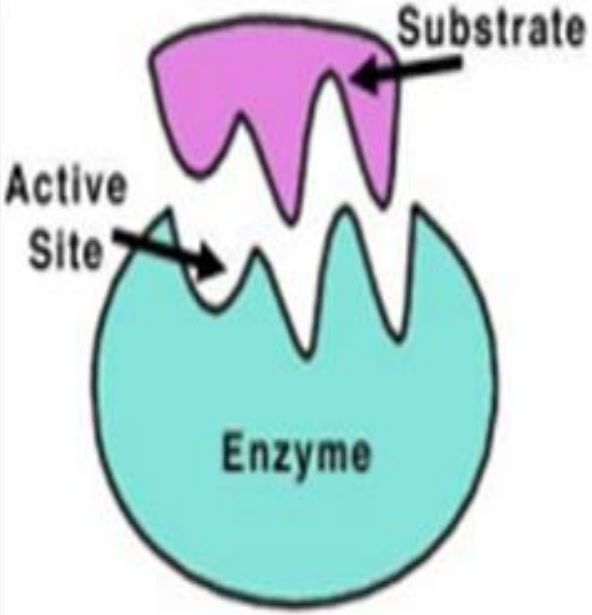


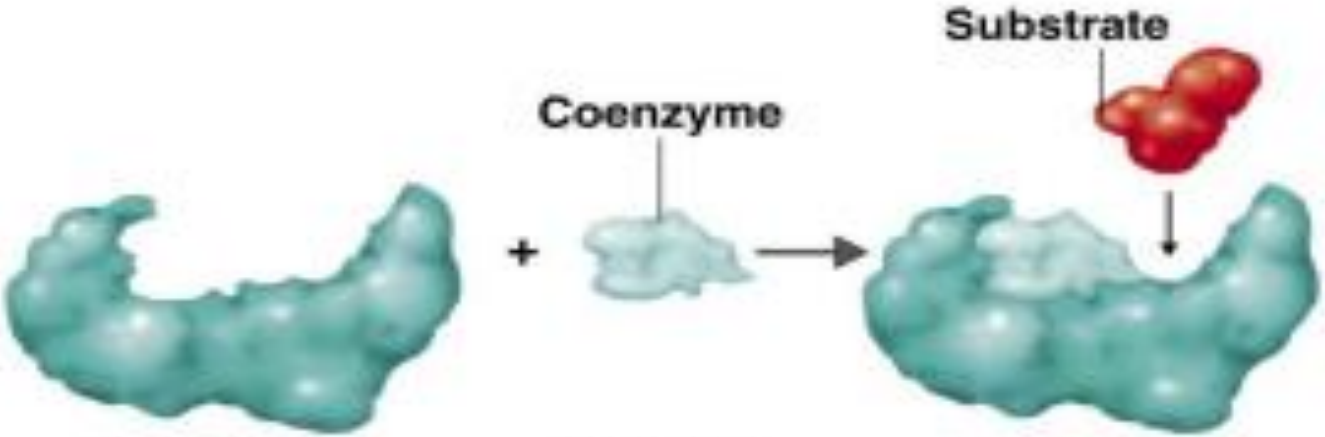
Holoenzyme= Apoenzyme+ Cofactor

Cofactor

- Coenzyme : loosely bound to enzyme (non-covalently bound).
- Prosthetic group : very tightly or even covalently bound to enzyme (covalently bound)







Apoenzyme (protein portion), inactive

Cofactor (nonprotein portion), activator

Holoenzyme (whole enzyme), active

- Co enzymes : are typically organic molecules, used by enzymes to help catalyse reactions, contain functionalities not found in proteins.
- Co factors : are catalytically essential molecules or ions that are covalently(تساهميا) bound to the enzyme.
- Holoenzyme : enzyme consist of Apoenzyme + prosthetic group
- Apoenzyme : term refers to the protein part of enzyme.
- Active site of enzyme: the point in the enzyme which interaction with substrate, co-enzyme, inhibitor take place.
- Zymogen: the active form of enzyme.

Ex: pepsinogen Hcl pepsin (active)

Ex: trypsinogen enterokinase trypsin (active)

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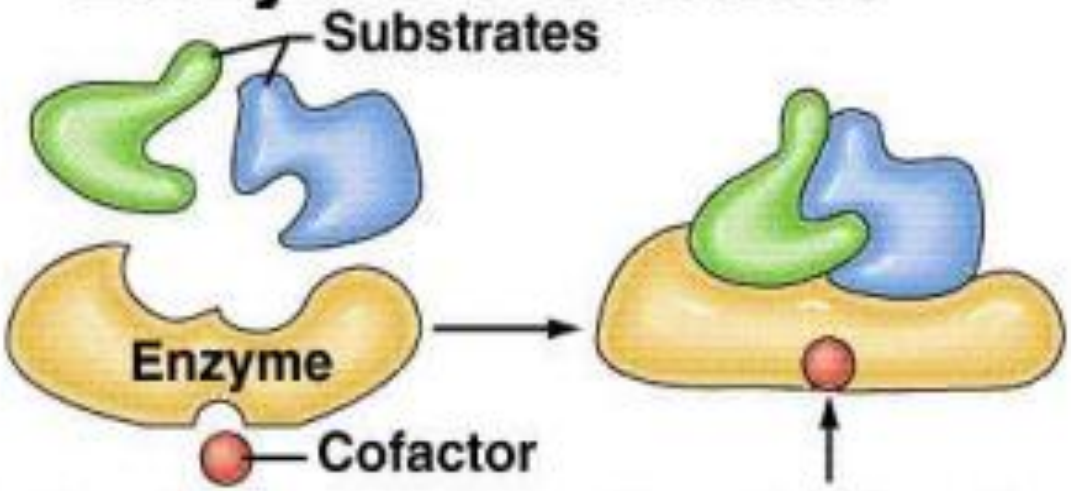
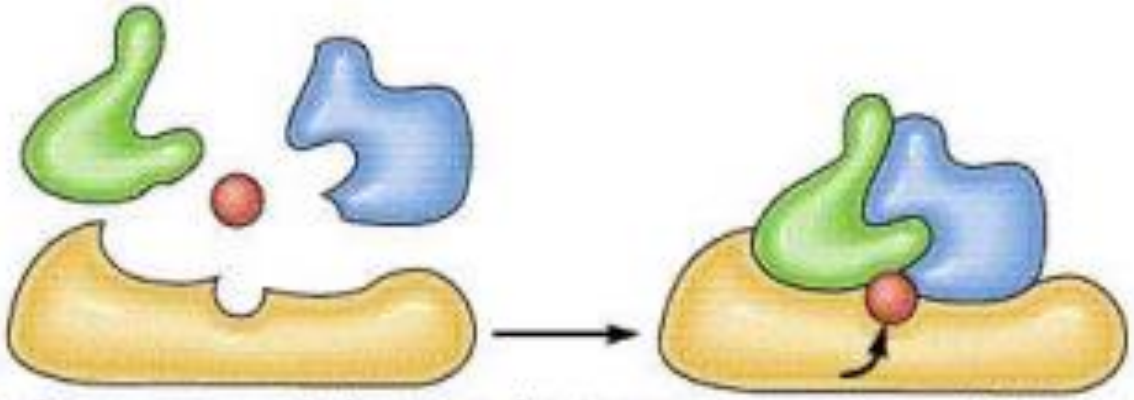
Roles of Cofactors in Enzyme Function



Cofactor changes conformation of active site.



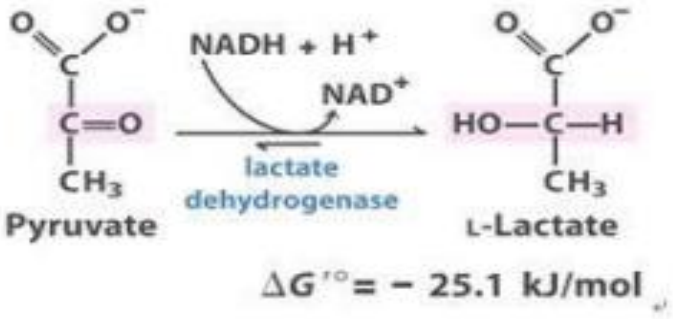
Cofactor participates in temporary bonding between active site and substrates.

The difference between Co-enzymes and Co- factors

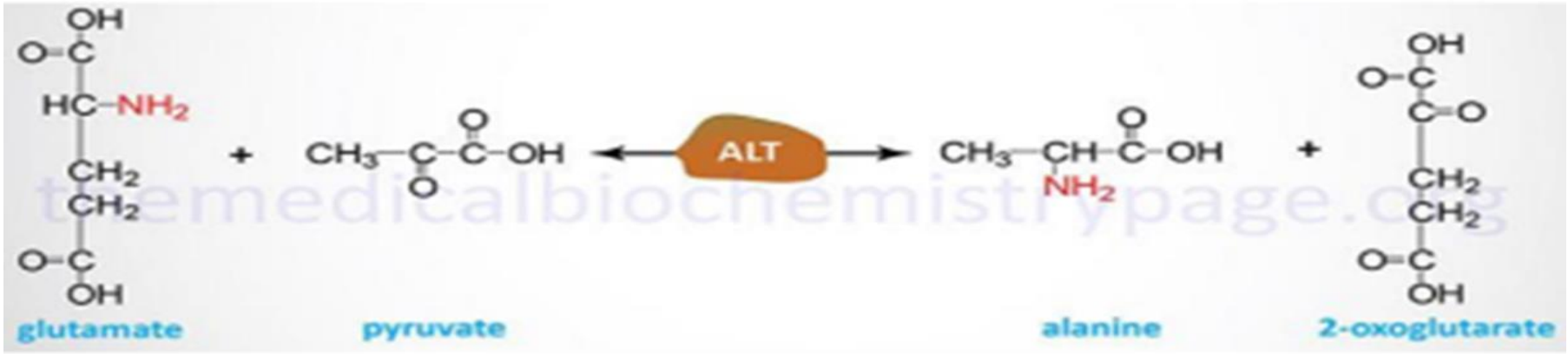
Co-enzymes	Co - factors
binds loosely and can easily separated from enzyme by dialysis	conjugated with protein(enzyme)
organic compounds (ex: water soluble vitamins such as Vit C and B	metallic ions (Fe, Mn, Cu,Mg)
non protein	has low molecular weight
heat resistance	
their function as co-substrate.	

Classification of enzymes

1. Oxide reductases: one compound oxidized, another reduced. Ex: lactate dehydrogenase, tyrosinase



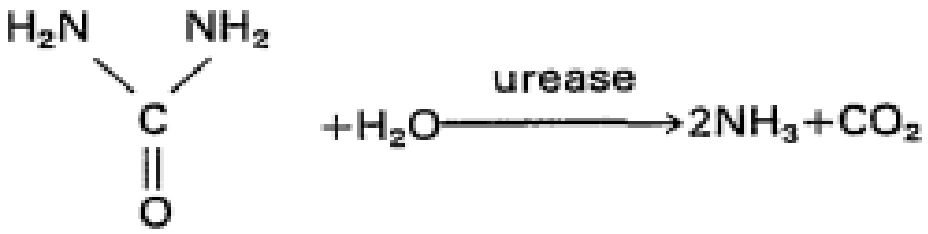
2. Transferees: Enzyme transfer group containing C, N or S, from one substrate to another substrate Transaminase (glutamate oxaloacetate transaminase(GOT) or Aspartate transaminase (AST). and glutamate pyruvate transaminase(GPT), alanine transaminase(ALT) (transfer of amine group).



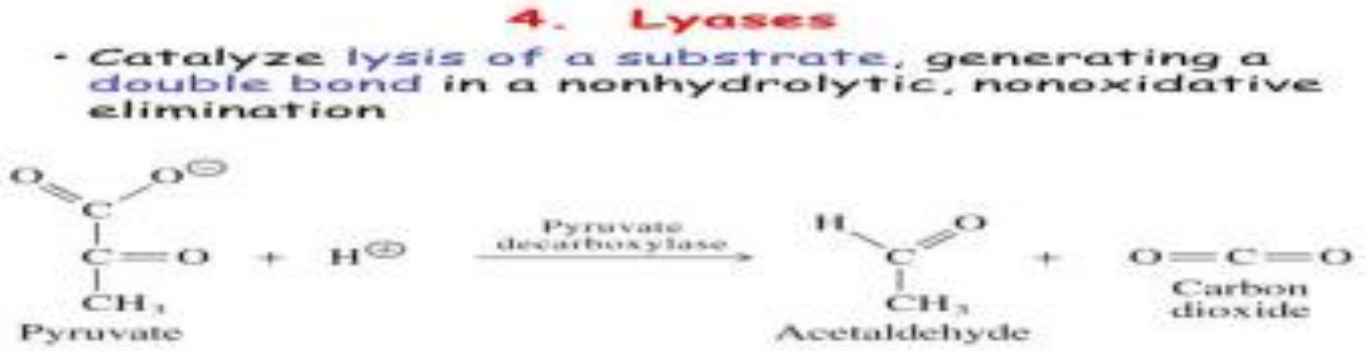
3. Hydrolase: Catalyse hydrolysis of ester, peptide or glycoside bound by addition of H2O across the bond.

Urea + H2O urease 2NH3 + CO2

Maltose + H2O maltase glucose + glucose

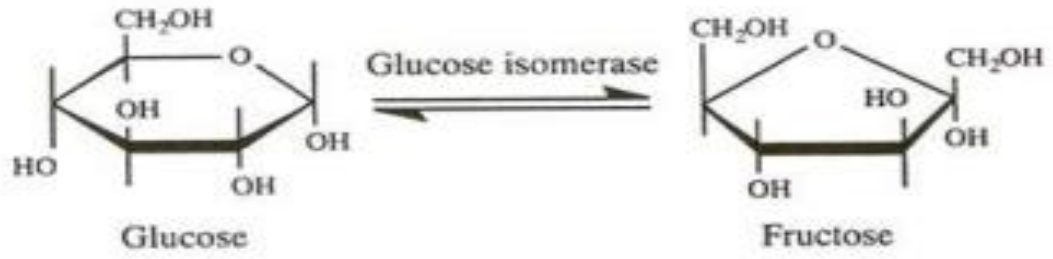


4. Lyasis: Additional or removal of group without hydrolysis, oxidation, reduction producing double Bond.

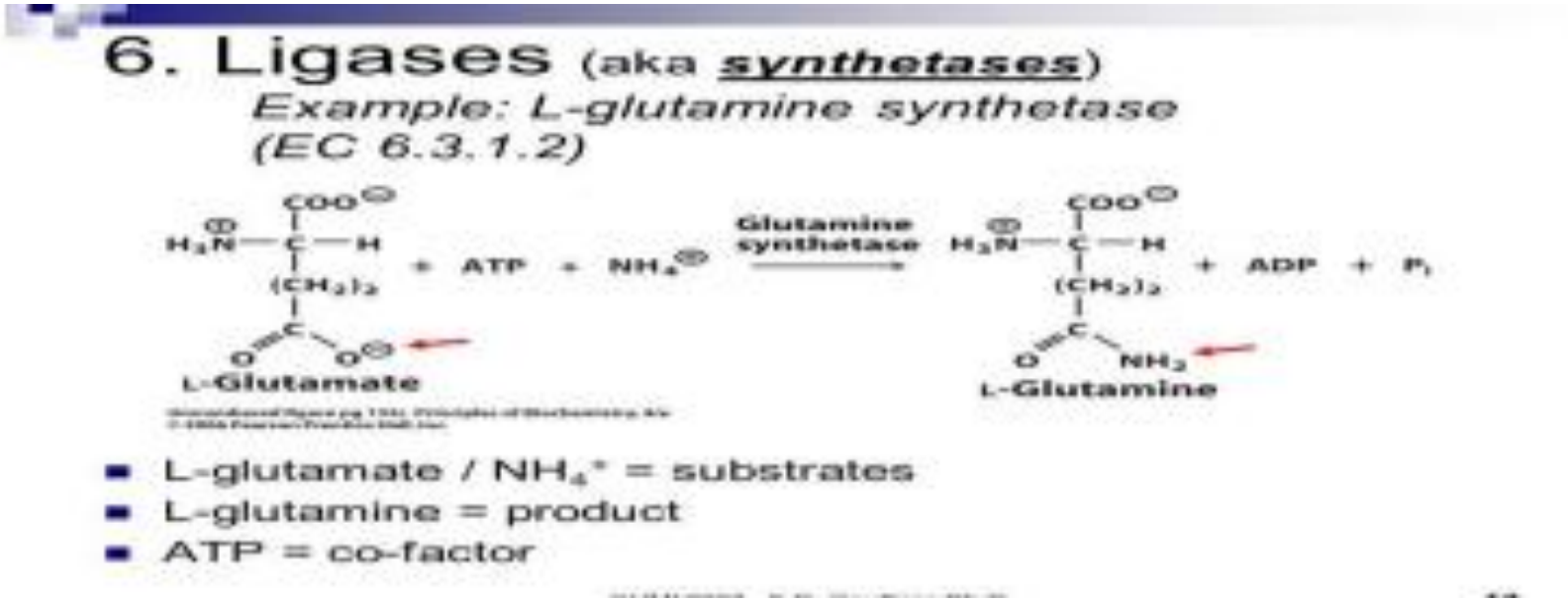


5. Isomerize : Produce optical, geometric or position isomer of substrates by intermolecular rearrangement.

Ex: D- alanine racemase L – alanine



6. Ligases or synthetase: link two substrate together usually by pyrophosphate bound.



Classification of enzymes

1) By their composition

I. Monomeric enzyme

II. Oligomeric enzyme

III. Multienzyme complex: such as

Fatty acid synthase

2) Nomenclature

- **Recommended name**

Enzymes are usually named according to the reaction they carry out. To generate the name of an enzyme, the Suffix -ase is added to the name of its substrate (actase is the enzyme suffix -ase is added to the name of its substrate (e. g. , lactase is the enzyme that cleaves lactose) or the type of reaction (DNA polymerase forms DNA polymers).

- Systematic name (International classification)

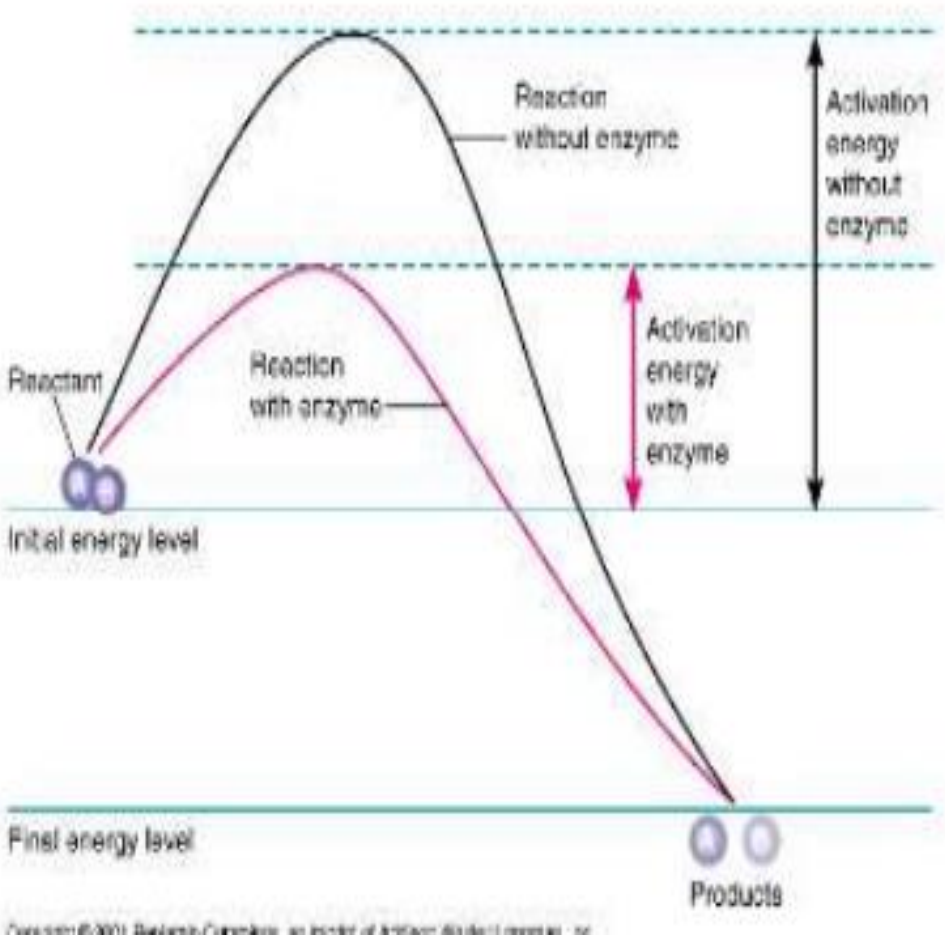
By the reactions they catalyze (Six Classes)

How enzymes work (important!)

Enzymes lower a reaction's activation energy

– All chemical reactions have an energy barrier, called the activation energy, separating the reactants and the products.

– activation energy: amount of energy needed to disrupt stable molecule so that reaction can take place



HOME WORK

What is the difference between an enzyme and a protein?

&

THANK YOU

Michaelis-Menten kinetics

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Michaelis-Menten kinetics

Also known as: Michaelis-Menten hypothesis

Michaelis-Menten kinetics, a general explanation of the velocity and gross mechanism of enzyme-catalyzed reactions.

it assumes the rapid reversible formation of a complex between an enzyme and its substrate (the substance upon which it acts to form a product)

It also assumes that the rate of formation of the product, P, is proportional to the concentration of the complex.

The velocity of such a reaction is greatest when all the sites at which catalytic activity can take place on the enzyme molecules (active sites) are filled with substrate i.e., when the substrate concentration is very high.

These relationships provide the basis for all kinetic studies of enzymes and also have been applied to investigations of the effects of carriers upon the transport of substances through cell membranes.

Key Components:

1. Enzyme (E) and Substrate (S): The enzyme catalyzes the conversion of substrate into product (P).

2. Michaelis Constant (Km): This is the substrate concentration at which the reaction rate is half of its maximum (Vmax). It reflects the affinity of the enzyme for the substrate—lower Km means higher affinity.

3. Maximum Velocity (Vmax): The maximum rate of the reaction when the enzyme is saturated with substrate.

Introduction

The general reaction scheme of an enzyme-catalyzed reaction is as follows:

$$E+S \underset{}{\overset{k1}{\rightarrow}} [ES] \overset{k2}{\rightarrow} E+P \quad (1)$$

The enzyme interacts with the substrate by binding to its active site to form the enzyme-substrate complex, ES. That reaction is followed by the decomposition of ES to regenerate the free enzyme, E, and the new product, P.

To begin our discussion of enzyme kinetics, let's define the number of moles of product (P) formed per time as *V*. The variable, *V,* is also referred to as the rate of catalysis of an enzyme. For different enzymes, *V* varies with the concentration of the substrate, S. At low S, *V* is linearly proportional to S, but when S is high relative to the amount of total enzyme, *V* is independent of S. The concentration of S is important in determining the initial rate of an enzyme-catalyzed reaction. A more thorough explanation of enzyme rates can be found here: Definition of Reaction Rate.

To understand Michaelis-Menten Kinetics, we will use the general enzyme reaction scheme shown below, which includes the back reactions in addition the the forward reactions:

$$E+S \underset{}{\overset{k1}{\rightarrow}} [ES] \overset{k2}{\rightarrow} E+P \quad (2)$$

$$E+S \underset{k3}{\overset{}{\leftarrow}} [ES] \overset{k4}{\leftarrow} E+P. \quad (3)$$

The table below defines each of the rate constants in the above scheme :

Rate Constant	Reaction
k1	The binding of the enzyme to the substrate forming the enzyme substrate complex.
k2	Catalytic rate; the catalysis reaction producing the final reaction product and regenerating the free enzyme. This is the rate limiting step.
k3	The dissociation of the enzyme-substrate complex to free enzyme and substrate .
k4	The reverse reaction of catalysis.

Substrate Complex

E+S−→k1ESE+S→k1ES v_o=k1[E][S]vo=k1[E][S]

ES−→k2E+SES→k2E+S v_o=k2[ES]vo=k2[ES]

ES−→k3E+PES→k3E+P v_o=k3[ES]vo=k3[ES]

E+P−→k4ESE+P→k4ES v_o=k4[E][P]=0vo=k4[E][P]=0

The ES complex is formed by combining enzyme E with substrate S at rate constant k_1. The ES complex can either dissociate to form E_F (free enzyme) and S, or form product P at rate constant k_2 and k_3, respectively. The velocity equation can be derived in either of the 2 methods that follow.

Method 1: The Rapid Equilibrium Approximation

E, S, and the ES complex can equilibrate very rapidly. The instantaneous velocity is the catalytic rate that is equal to the product of ES concentration and k2 the catalytic rate constant.

$$V_o = k_2[E-S] \quad (4)$$

The total enzyme concentration (ET) is equal to the concentration of free enzyme E (EF) plus the concentration of the bound enzyme in ES complex:

$$[E]_T = [E_F] + [ES] \quad (5)$$

$$K_s = k_2/k_1 = [E][S]/[ES] \quad (6)$$

$$K_s([E_o] - [ES])[S]/[ES] \quad (7)$$

Method 1: The Rapid Equilibrium Approximation

$$[ES]=[E_o][S]/K_s+[S] \qquad (8)$$

$$v_o=(Dp/dt)_o=k_3[ES] \qquad (9)$$

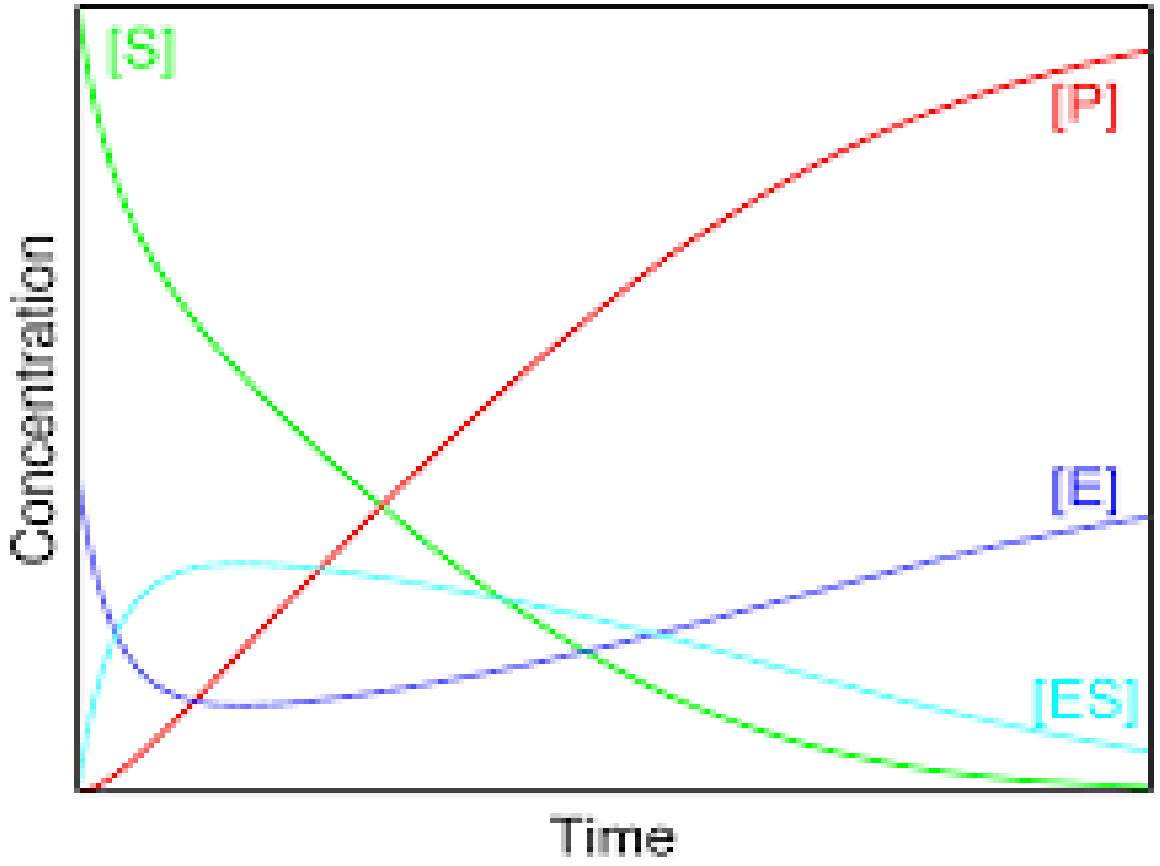
$$v_o=(dP/dt)_o=k_3[E_o][S]/K_s+[S] \qquad (10)$$

At high substrate concentrations, $[S] >> K_s$ we get:

$$\mathbf{V_o=(dP/dt)_o=k_3[E_o]=Vmax} \qquad (1)$$

Method 2: The Steady-State Approximation

Figure 1 below shows the relatively low and constant concentration of the enzyme-substrate complex due to the complex's slow formation and rapid consumption. Note the falling substrate concentration and the rising product concentration.



The rates of formation and breakdown of the E - S complex are given in terms of known quantities:

- The rate of formation of E-S = $k_1[E][S]$
  (with the assumption that [P] =0)

The rate of breakdown of E-S = $k2[ES]+k3[ES]=(K2+K3)[ES]$

At steady state,

$$\mathbf{d[ES]dt = k_1[E][S]+k_2[ES]+ k_3[ES]= 0} \quad \mathbf{(11)}$$

Therefore, rate of formation of E-S is equal to the rate of breakdown of E-S

So,

$$\mathbf{k1[E][S]=(k_2+k_3)[ES]} \quad \mathbf{(12)}$$

Dividing through by k1:

$$\mathbf{[E][S]=(k_2+k_3)/k1\ *[E-S]} \quad \mathbf{(13)}$$

Substituting (k2+k3)/k1 with kM:

[E][S]=KM[ES]

$$\mathbf{KM=breakdown[ES]/formation[ES]} \quad \mathbf{(14)}$$

The factors that affect Km are:

- pH
- temperature
- ionic strengths
- the nature of the substrate

Substituting EF] with [ET]-[ES]: ET = [ES] + [EF]

([ET] - [ES]) [S] = k_M [ES]

[ET] [S] -[ES][S] = k_M [ES]

[ET] [S] = [ES] [S] + k_M [ES]

[ET] [S] = [ES] ([S] + KM)

Solving for [ES]:

[ES] = ([ET][S]) / ([S]+K_M)

The rate equation from the rate limiting step is:

$$\mathbf{V_o = dp/dt = k2[ES]}$$

Multiplying both sides of the equation by k2:

$$k_2[ES]=k2(([ET][S])/(KM+[S]) \qquad (15)$$

$$V_o=k2(([ET][S])/(KM+[S]) \qquad (16)$$

When S>>KM, Vo is approximately equal to k2[ET]. When the [S] great, most of the enzyme is found in the bound state ([ES]) and Vo = Vmax

We can then substitue k2[ET] with Vmaxto get the Michaelis Menten Kinetic Equation:

$$\textit{vo = (vmax[S])/(KM+[S])}$$

THANK YOU

METABPLISM

Carbohydrates Metabolism

LEC.4

Carbohydrates Metabolism

Definition of Metabolism: The chemical processes occurring within a living cell or organism that are necessary for the maintenance of life. All these are called **anabolism and catabolism**.

- Anabolic reaction :

1. synthesis of complex molecules from simple compound.
2. energy is needed for synthesis (endergonic reaction)

- catabolic reaction :

1. 1.break down of large molecules Such as polysaccharides, proteins Into small molecules like, CO_2, NH_3, H_2O.
2. liberated energy. (exergonic reaction)

Digestion and absorption:

Digestion of CHO is accomplished by the enzymes of digestive fluids, saliva, pancreatic juice and

intestinal juice.

1. **mouth**: salivary glands secrete saliva Saliva contains: α- amylase (ptyalin), water 99.5% and glycoprotein as food lubricant. α- amylase, hydrolysis starch to dextrin and maltose. PH of α- amylase = 5.8 – 7.1 less than 4.0 is in active
2. **stomach** ---------- no digestion is seen in stomach , amylase is in active Because the PH of stomach (1 - 2) very acidic.
3. **small intestine**: it is the major site of digestion of CHO, pancreatic amylase hydrolyze dextrin into maltose. The optimum PH of amylase = 7.1

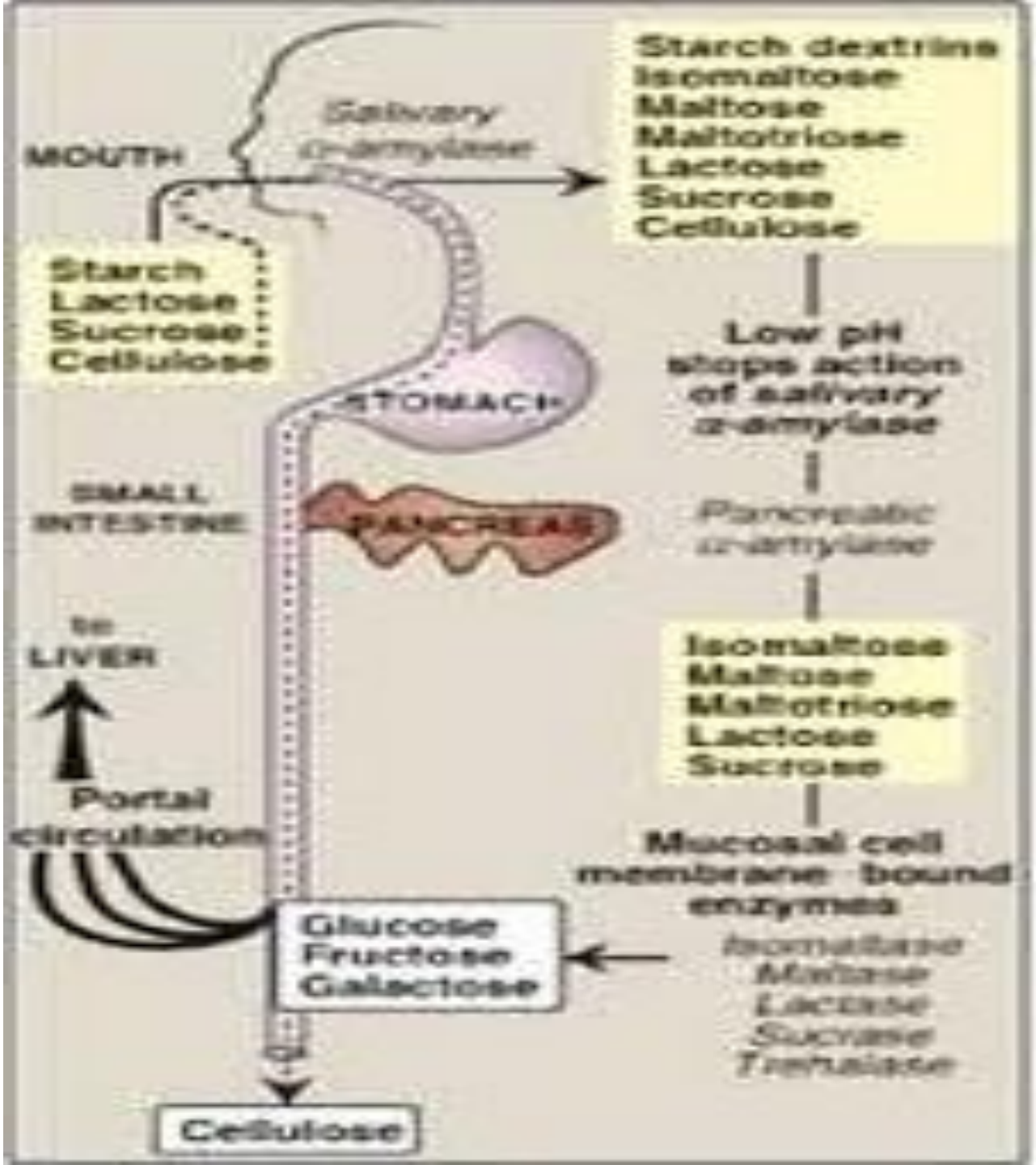
4. **intestinal mucosal** : mucosal cell membrane – bound enzymes , the site where disaccharides hydrolyze.

Maltose $\xrightarrow{\text{maltase}}$ glucose + glucose

Sucrose $\xrightarrow{\text{sucrase}}$ glucose + fructose

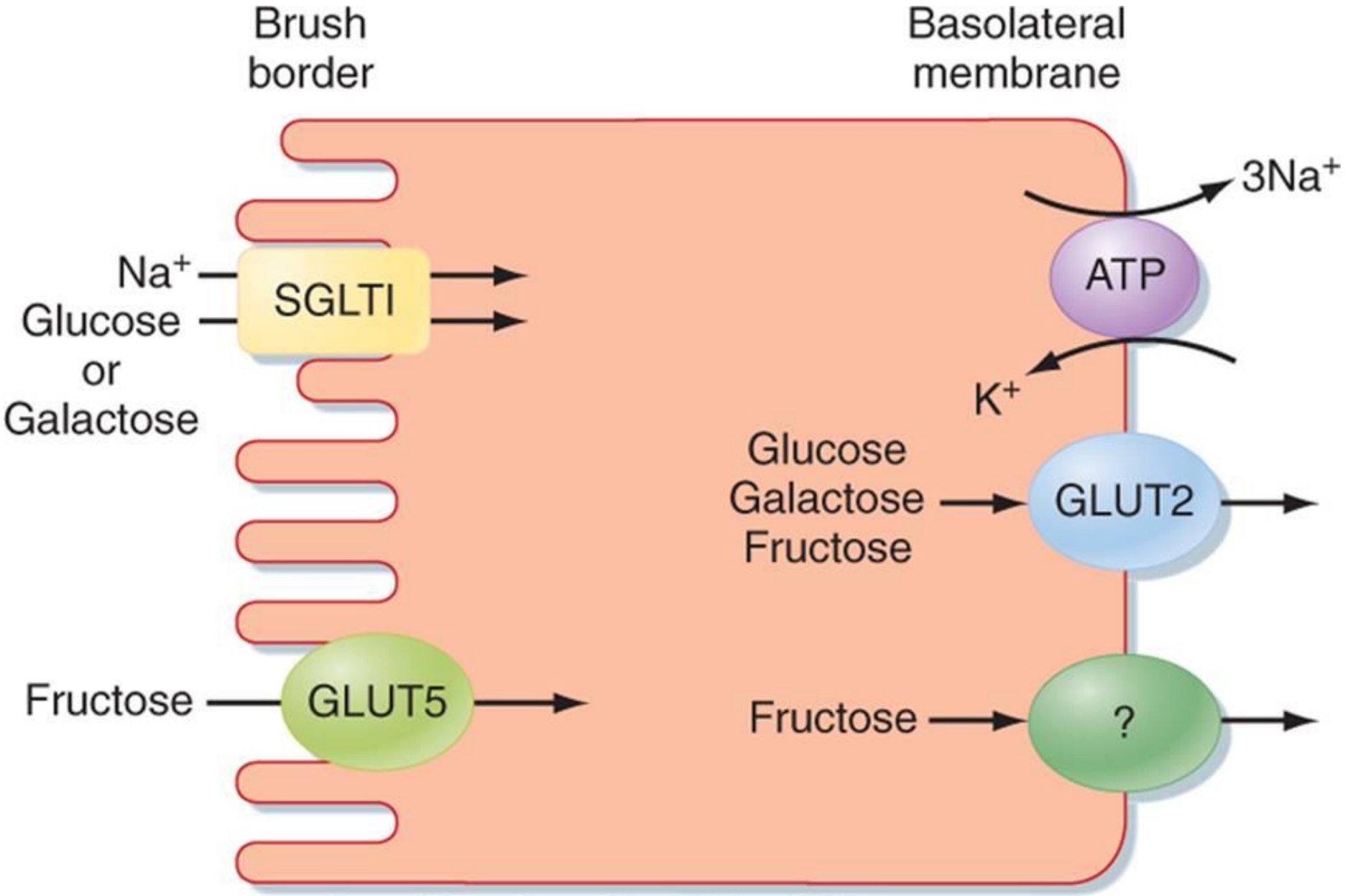
Lactose $\xrightarrow{\text{lactase}}$ glucose + galactose

Digestion of carbohydrate



Absorption of Carbohydrates

intestine



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.
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Absorption of Carbohydrates:

1. transport into epithelial cells (of the villi) glucose and galactose are transported by active transport, while fructose is transported by facilitated diffusion.
2. transport from epithelial cells into the blood stream is by facilitated diffusion.

Fate of glucose after absorption

In the liver, glucose undergoes variety of chemical changes depending upon the physiological need of the body.

1. Body need for energy: glucose oxidized completely to CO2, H2O and energy by (glycolysis and citric acid cycle).
2. Excess glucose may be converted to glycogen, deposit in liver, muscle tissues By (glycogenesis).
3. To maintain glucose blood level, liver glycogen reconverted to glucose enters blood By (glycogenolysis).
4. excess glucose after conversion to glycogen , convert to fatty acids stored in adipose tissue as triglycerides (lipogenesis).
5. small amounts of glucose may be utilized for the synthesis of ribose and deoxyribosee for synthesis of nucleic acids.
6. in muscle contraction, only partial degradation of glucose may take place, resulting in formation of lactic acid disposed off by the liver.

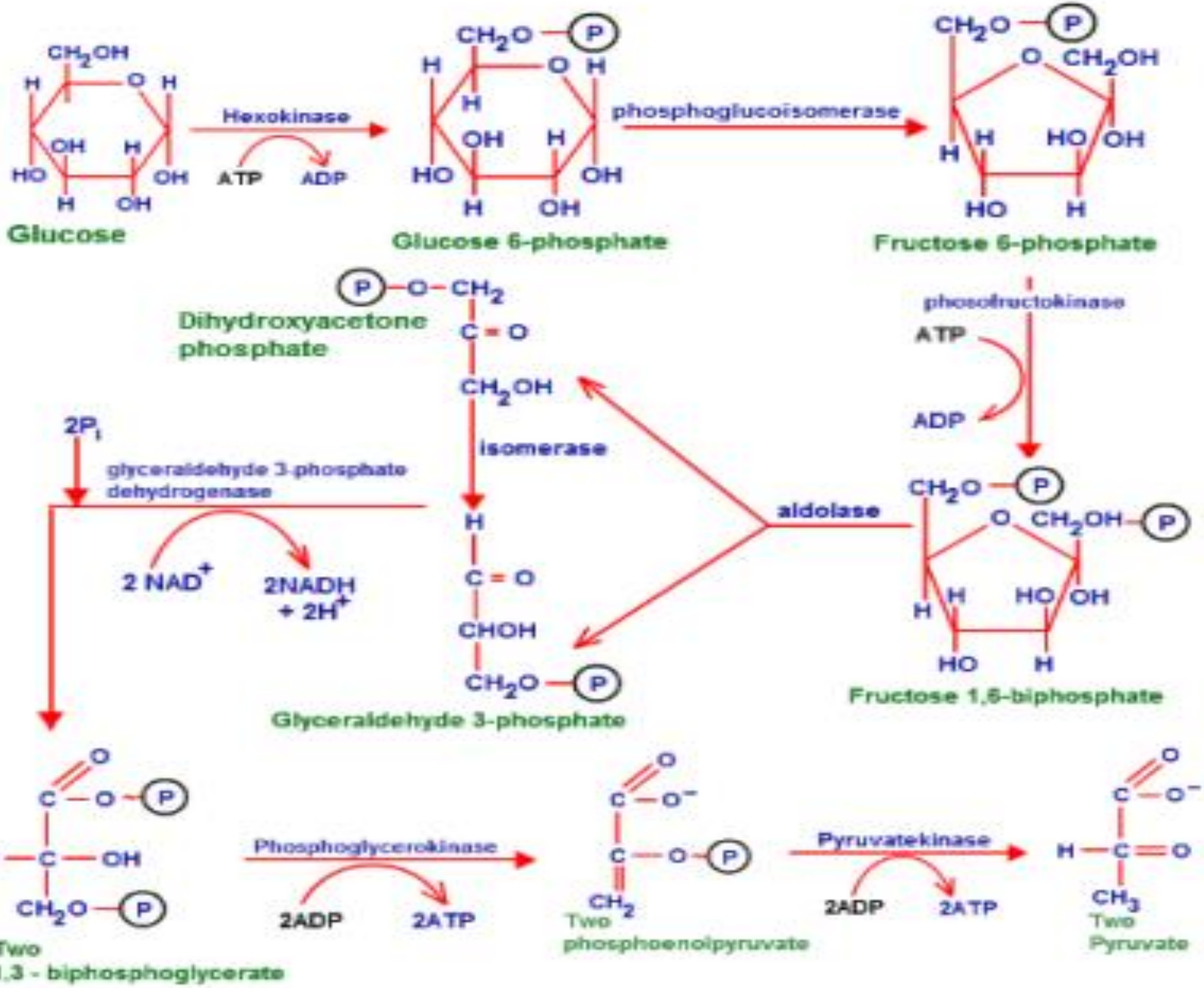
The metabolism of CHO may be subdivided in the following categories.

Glycolysis: (from glycose, an term for glucose + -lysis degradation)

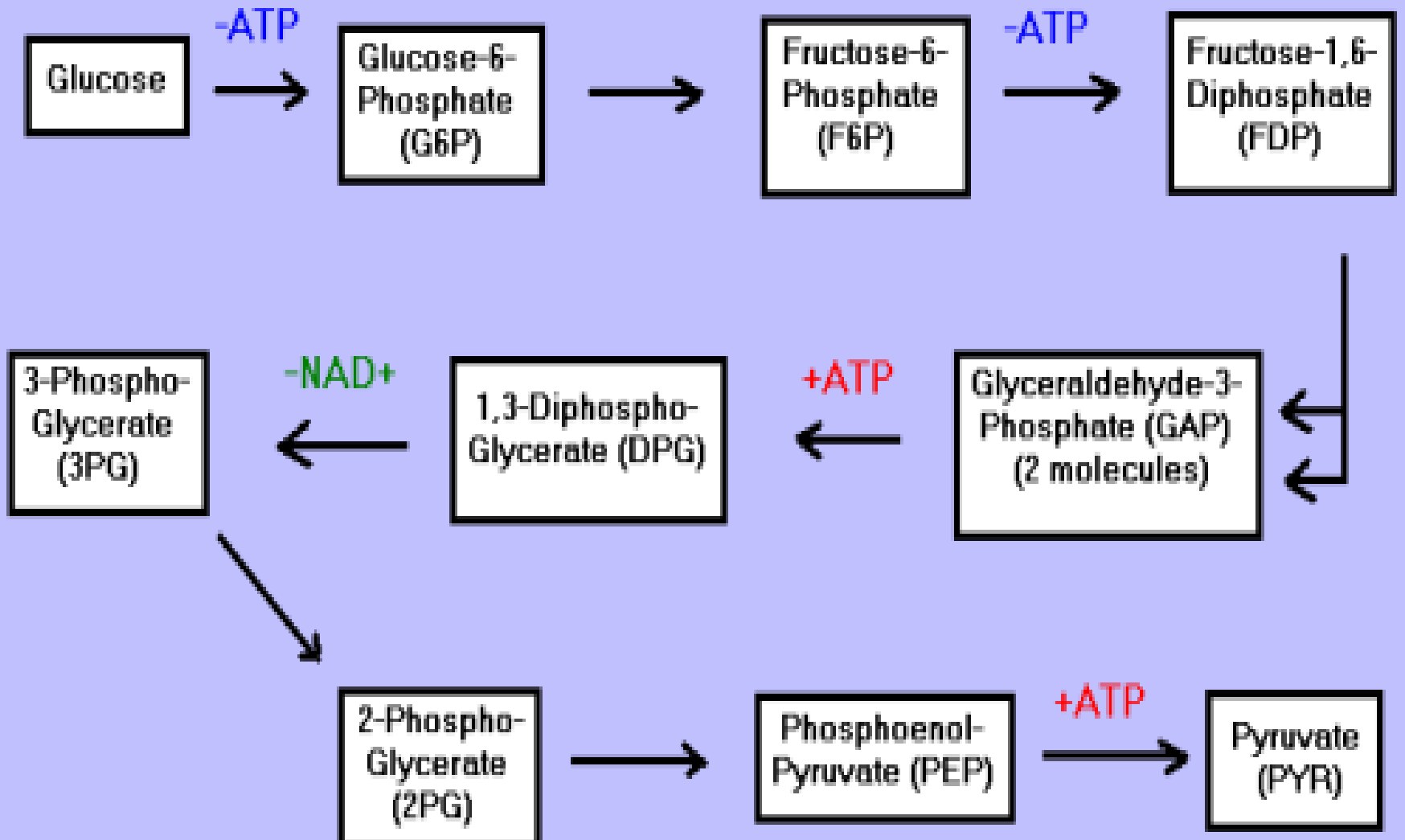
1. It is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate.
2. The free energy released in this process is used to form the high-energy molecules ATP and NADH.
3. Glycolysis is an oxygen independent metabolic pathway, said to be anaerobic.
4. Glycolysis occurs in the cytosol (cytoplasm) of the cell.
5. The most common type of glycolysis is the Embden–Meyerhof–Parnas (EMP), which was discovered by Gustav Embden, Otto Meyerhof, and Jakub Karol Parnas.
6. The glucose in the blood circulation, when enter the cell become phosphorylated given by ATP (Activation by phosphate group).
7. This phosphorylation occurs on the cell membrane by the action of two enzymes.

- 1. specific enzyme (glucokinase) in the liver.
- 2. nonspecific enzyme (hexokinase), Present in liver and other extra hepatic cell

8. Glu-6- p is an important compound for several metabolic pathways. The reaction is irreversible.


Glucose
Hexokinase
ATP
ADP
Glucose 6-phosphate
phosphoglucoisomerase
Fructose 6-phosphate
phosofructokinase
ATP
ADP
Dihydroxyacetone phosphate
isomerase
aldolase
Fructose 1,6-biphosphate
Glyceraldehyde 3-phosphate
2Pi
glyceraldehyde 3-phosphate dehydrogenase
2 NAD+
2NADH + 2H+
Phosphoglycerokinase
2ADP
2ATP
Two 1,3 - biphosphoglycerate
Two phosphoenolpyruvate
Pyruvatekinase
2ADP
2ATP
Two Pyruvate

GLYCOLYSIS


Glucose
-ATP
Glucose-6-Phosphate (G6P)
Fructose-6-Phosphate (F6P)
-ATP
Fructose-1,6-Diphosphate (FDP)
Glyceraldehyde-3-Phosphate (GAP) (2 molecules)
+ATP
1,3-Diphospho-Glycerate (DPG)
-NAD+
3-Phospho-Glycerate (3PG)
2-Phospho-Glycerate (2PG)
Phosphoenol-Pyruvate (PEP)
+ATP
Pyruvate (PYR)

Energy production: The net of ATP molecules during glycolysis is equal to (8).

ATP used 1. (glu glu-6-pho) 1 ATP

2. (F-6-pho F-1,6 - di pho) 1 ATP

ATP gain Gly-3- pho → 1,3-diphoGly NADH × 2

1,3 –diphoGlyc → 3phoGly 1 ATP × 2

PEP → pyruvate 1 ATP × 2

Net of ATP from anaerobic glycolysis 10 – 2 = 8 ATP

Formation of lactate from pyruvate is the major steps in RBCs, lens and cornea, kidney, medulla, and leukocytes.

THANK YOU

Lactic Acid Fermentation

LAB.5

Lactic Acid Fermentation

Lactic acid fermentation (e.g., fermented milks and cereals) is mainly of anaerobic respiration carried out by bacteria (Lactobacillus and others) to convert the 3-carbon pyruvate to the 3-carbon lactic acid ($C_3H_6O_3$) and regenerate NAD+ in the process, allowing glycolysis to continue to make ATP in low-oxygen conditions

$C_3H_3O_3$pyruvate+NADH→$C_3H_6O_3$lacticacid+NAD+

Biotechnological processes for the production of lactic acid usually include lactic acid fermentation and biochemical changes

In the lactic acid fermentation process, sugar molecules are converted into lactic acid with the help of organisms such as Leuconostoc, Streptococcus, and Lactobacillus bacteria

Lactic acid fermentation is a process by which sugars such as glucose, fructose, and sucrose are converted into cellular energy and the metabolic byproduct lactate.

Enzymatic conversions of starch

Lactic Acid Fermentation

The pyruvate resulting from glycolysis is further oxidized completely, generating additional ATP and NADH in the citric acid cycle and by oxidative phosphorylation. this process can occur only in the presence of oxygen. Oxygen is toxic to organisms that are obligate anaerobes and is not required by facultative anaerobic organisms

Lactic acid fermentation is one of the processes for regenerating NAD+ in the anaerobic processes, that is, in the absence of oxygen.

Once glucose is generated from starch, it is split through glycolysis into pyruvic acid, and lactic acid fermentation may start.

<u>The LAB were divided early on into two main groups, depending on their fermentation products</u>

- One group included those bacteria that convert carbohydrates essentially into lactate.
- while the other group included those producing, in addition, substantial quantities of volatile acids and carbon dioxide.

There are two pathways Lactic Acid Fermentation

- homoplastic (only product is L-LACTATE)
- heterolactic (phosphoketolase)

first of them, one glucose molecule produces two molecules of lactic acid:

$C_6H_{12}O_6 \rightarrow 2CH_3COCO_2 \rightarrow 2CH_3CHOHCO_2H$

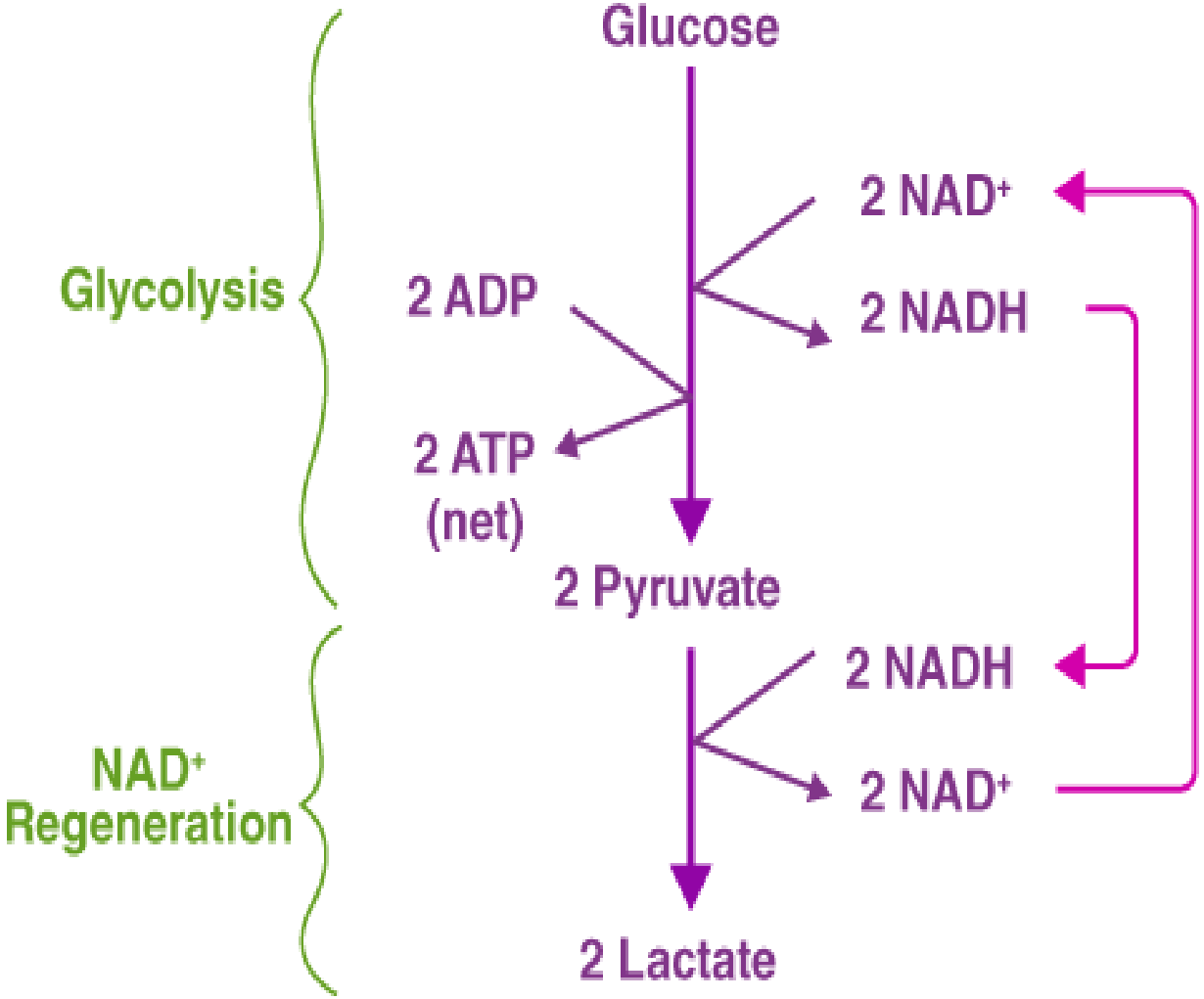
whereas in the second process, from one glucose one molecule of lactic acid is produced, together with one molecule of ethanol and one molecule of CO_2:

$C_6H_{12}O_6 \rightarrow 2CH_3COCO_2H \rightarrow CH_3CHOHCO_2H + C_2H_5OH + CO_2$

- ❑ Several fungi and bacteria cause lactic acid fermentation. Lactobacillus is the most common among them. Leuconostoc mesenteroides, Pediococcus cerevisiae, Streptococcus lactis, and Bifidobacterium bifidus are also quite common

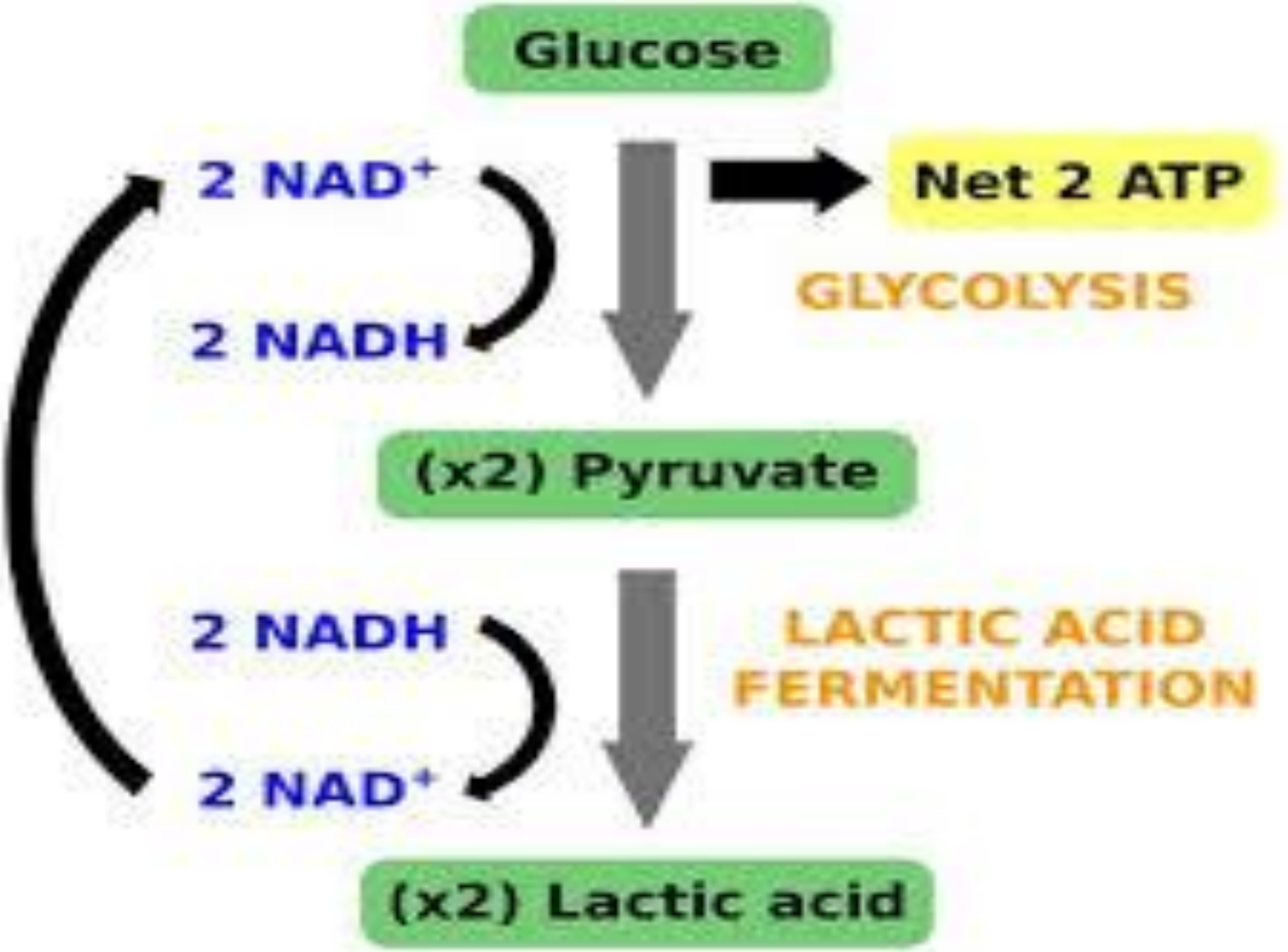
The lactic acid bacteria (LAB) are a group of Gram positive bacteria that produce lactate as the major end product of the fermentation of carbohydrates.

Steps Involved in Lactic Acid Fermentation



Steps Involved in Lactic Acid Fermentation

- The glucose or 6-carbon molecule is broken down into Glyceraldehyde 3-phosphate, and then to 3-Phosphoglyceric acid.
- During this, NAD+ is converted into NADH+H+.
- The 3-Phosphoglyceric acid forms Phosphoenol pyruvic acid, which later forms the Pyruvic acid.
- Net 2 ATP molecules are formed in this process (glycolysis).
- This Pyruvic acid is reduced to Lactic acid with the help of reducing agent NADH+H+, which reoxidises to NAD+.
- This process produces two lactate/lactic acid molecules from two pyruvate/pyruvic acid molecules. This reaction happens in the presence of the enzyme lactate dehydrogenase.


Glucose
2 NAD+
2 NADH
Net 2 ATP
GLYCOLYSIS
(x2) Pyruvate
2 NADH
2 NAD+
LACTIC ACID FERMENTATION
(x2) Lactic acid

Thank U

Citric and cycle /TCA cycle / Krebs cycle

LEC.6

Krebs cycle

It is a series of eight-step processes, where the acetyl group of acetyl-CoA is oxidised to form two molecules of CO_2 and in the process, one ATP is produced. Reduced high energy compounds, NADH and $FADH_2$ are also produced. Two molecules of acetyl-CoA are produced from each glucose molecule so two turns of the Krebs cycle are required which yields four CO_2, six NADH, two $FADH_2$ and two ATPs.

Krebs Cycle is a part of Cellular Respiration

Cellular respiration is a four-stage process. In the process, glucose is oxidised to carbon dioxide and oxygen is reduced to water. The energy released in the process is stored in the form of ATPs. 36 to 38 ATPs are formed from each glucose molecule.

The four stages of Cellular respiration

1. **Glycolysis:** Partial oxidation of a glucose molecule to form 2 molecules of pyruvate. This process takes place in the cytosol.
2. **Formation of Acetyl CoA:** Pyruvate formed in glycolysis enters the mitochondrial matrix. It undergoes oxidative decarboxylation to form two molecules of Acetyl CoA. The reaction is catalysed by the pyruvate dehydrogenase enzyme.

$$2Pyruvate + 2NAD^{+} + 2CoA \xrightarrow{Pyruvate\ dehydrogenase} 2AcetylCoA + 2NADH + CO_2$$

3. **Krebs cycle (TCA cycle or Citric Acid Cycle):** It is the common pathway for complete oxidation of carbohydrates, proteins and lipids as they are metabolised to acetyl coenzyme A or other intermediates of the cycle. The Acetyl CoA produced enters the Tricarboxylic acid cycle or Citric acid cycle. Glucose is fully oxidized in this process. The acetyl CoA combines with 4-carbon compound oxaloacetate to form 6C citrate. In this process, 2 molecules of CO_2 are released and oxaloacetate is recycled. Energy is stored in ATP and other high energy compounds like NADH and $FADH_2$.
4. **Electron Transport System and Oxidative Phosphorylation:** ATP is generated when electrons are transferred from the energy-rich molecules like NADH and $FADH_2$, produced in glycolysis, citric acid cycle and fatty acid oxidation to molecular O_2 by a series of electron carriers. O_2 is reduced to H_2O. It takes place in the inner membrane of mitochondria.

Krebs Cycle Steps

Step 1: The first step is the condensation of acetyl CoA with 4-carbon compound oxaloacetate to form 6C citrate, coenzyme A is released. The reaction is catalysed by citrate synthase.

Step 2: Citrate is converted to its isomer, isocitrate. The enzyme aconitase catalyses this reaction.

Step 3: Isocitrate undergoes dehydrogenation and decarboxylation to form 5C **α**-ketoglutarate. A molecular form of CO2 is released. Isocitrate dehydrogenase catalyses the reaction. It is an NAD+ dependent enzyme. NAD+ is converted to NADH.

Step 4: **α**-ketoglutarate undergoes oxidative decarboxylation to form succinyl CoA, a 4C compound. The reaction is catalyzed by the **α**-ketoglutarate dehydrogenase enzyme complex. One molecule of CO2 is released and NAD+ is converted to NADH.

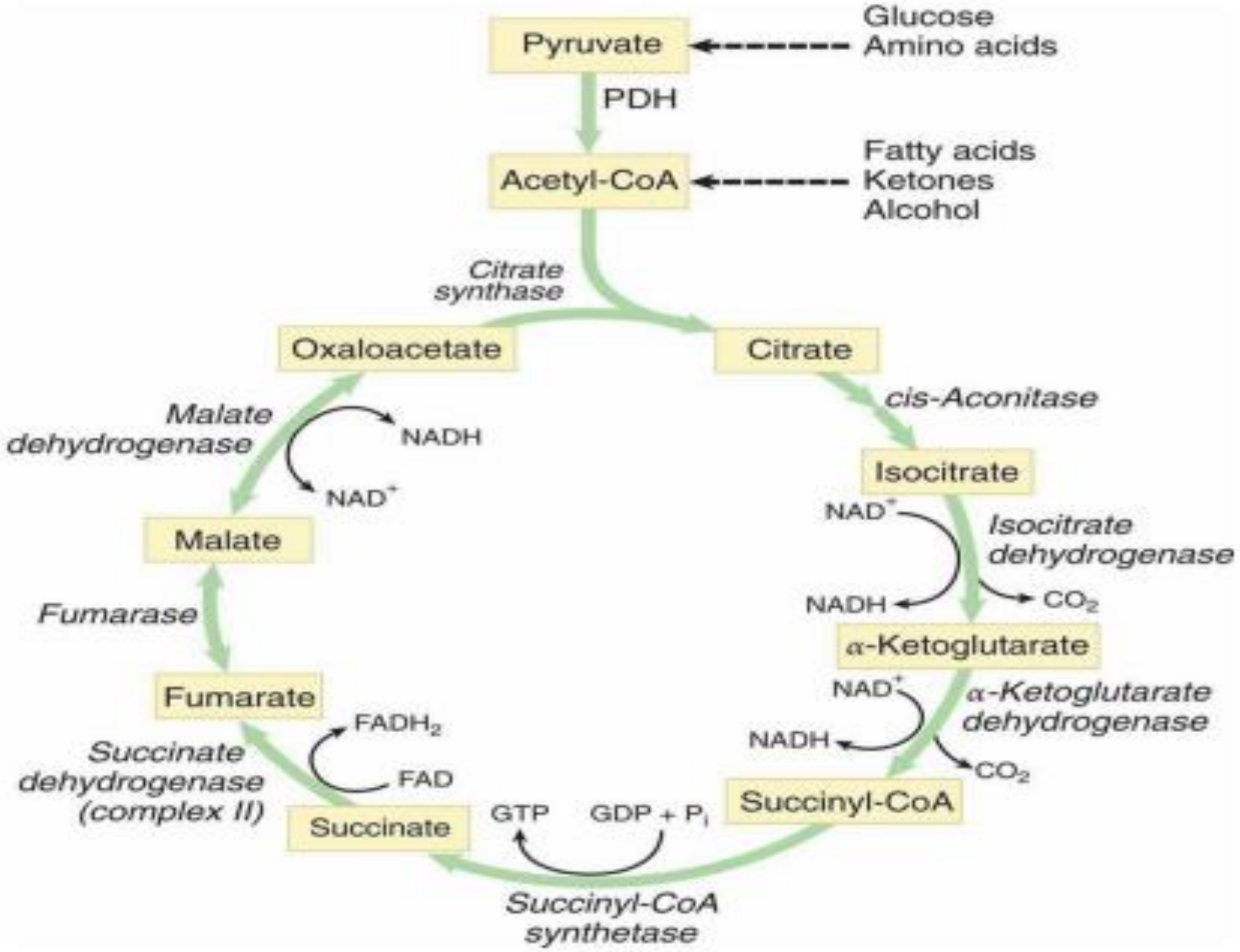
Krebs Cycle Steps

Step 5: Succinyl CoA forms succinate. The enzyme succinyl CoA synthetase catalyses the reaction. This is coupled with substrate-level phosphorylation of GDP to get GTP. GTP transfers its phosphate to ADP forming ATP.

Step 6: Succinate is oxidised by the enzyme succinate dehydrogenase to fumarate. In the process, FAD is converted to FADH2.

Step 7: Fumarate gets converted to malate by the addition of one H2O. The enzyme catalysing this reaction is fumarase.

Step 8: Malate is dehydrogenated to form oxaloacetate, which combines with another molecule of acetyl CoA and starts the new cycle. Hydrogens removed, get transferred to NAD+ forming NADH. Malate dehydrogenase catalyses the reaction.


Pyruvate
Glucose
Amino acids
PDH
Acetyl-CoA
Fatty acids
Ketones
Alcohol
Citrate synthase
Oxaloacetate
Citrate
cis-Aconitase
Malate dehydrogenase
NADH
NAD+
Isocitrate
Malate
NAD+
Isocitrate dehydrogenase
NADH
CO2
Fumarase
α-Ketoglutarate
Fumarate
NAD+
α-Ketoglutarate dehydrogenase
FADH2
NADH
CO2
Succinate dehydrogenase (complex II)
FAD
Succinyl-CoA
Succinate
GTP
GDP + Pi
Succinyl-CoA synthetase

ATP generated in TCA cycle Convertion of :

pyruvic acid to acetyl COA	1 NADH	= 3ATP
Isocitric acid to α-ketoglutarate	1NADH	= 3ATP
α –ketoglutarare to succinyl COA	1NADH	= 3ATP
Succinyl COA to succinic acid	1GTP	= 1ATP
Succinic acid to fumeric acid	1FAD	= 2 ATP
Malic acid to oxaloacitic acid	1NADH	= 3ATP

total 15 ATP

Net ATP produced per glucose molecule = 15 × 2= 30 ATP

Total ATP per glucose (aerobic oxidation + anaerobic) 30 + 8= 38 ATP

Glycolysis		**Citric acid cycle (Krebs cycle)**	
1.	It is a linear pathway.	1.	It is a cyclic pathway.
2.	It occurs in the cell cytoplasm.	2.	It occurs in the mitochondrial matrix.
3.	It occurs in both aerobic and anaerobic respiration.	3.	It occurs in aerobic respiration.
4.	One glucose molecule breaks down to generate 2 $NADH_2$ and 2 ATP molecules.	4.	It produces 6 $NADH_2$, 2 $FADH_2$, and 2 ATP molecules on breakdown of two acetyl-coA molecules.

Citric acid cycle

Krebs cycle, tricarboxylic acid cycle TCA

The central function is the oxidation of acetyl CoA to CO2

- It is the final common pathway for oxidation of fuel molecules
- Acetyl Co is derived from the metabolism of fuel molecules as amino acids, fatty acids, and carbohydrates.
- Citric acid cycle is also an important source of precursors
    - Some intermediates are precursors of amino acid
    - One of the intermediates is used in the synthesis of porphorins
    - Another is used in the synthesis of fatty acids and sterols.
- Citric Acid Cycle located in the mitochondrial matrix

Glycogenesis (glycogen synthesis): formation of glycogen from glucose.

1. **Glycogen** is serves as an energy store primarily in muscle and liver, when glucose and ATP are present in relatively high amounts.
2. **the excess of insulin** promotes the glucose conversion into glycogen for storage in liver and muscle cells.
3. It is stored in the form of granules **cytoplasm** in the cell.
4. The concentration of glycogen in **muscle is low (**1-2 % fresh weight) compared to the levels **stored in the liver** (up to 8% fresh weight).
5. Glycogen is an **energy reserve** that can be quickly mobilized to meet a sudden need for glucose.

Glycogenolysis

biochemical breakdown of glycogen to glucose.

1. take place in the cells of muscle and liver tissues in response to hormonal and neural signals.
2. Glycogenolysis occurs in the cytoplasm and is stimulated by glucagon and adrenaline hormones.
3. glycogenolysis plays an important role in the adrenaline-induced fight-or-flight response and the regulation of glucose levels in the blood.
4. The enzymes required for this process are glycogen phosphorylase, debranching enzyme, and amylo-α-1, 6-glucosidase

DIFFERENCE BETWEEN MUSCLE &LIVER GLYCOGEN

	Liver glycogen	Muscle glycogen
Amount	-	More
Source	Glucose and other precursors	Glucose only
Hydrolysis	Give blood glucose	Give lactic acid
Starvation	Converted into blood glucose	Not affected
Muscular exercise	Depleted later on	Depleted first

BLOOD SUGAR LEVEL CHART

	FASTING	JUST ATE	3 HOURS AFTER EATING
NORMAL	80-100	170-200	120-140
PRE-DIABETIC	101-125	190-230	140-160
DIABETIC	126+	220-300	200+

THANK YOU

The electron transport chain

Lec.7

The electron transport chain

The electron transport chain is a series of four protein complexes that couple redox reactions, creating an electrochemical gradient that leads to the creation of ATP in a complete system named oxidative phosphorylation. It occurs in mitochondria in both cellular respiration and photosynthesis. In the former, the electrons come from breaking down organic molecules, and energy is released. In the latter, the electrons enter the chain after being excited by light, and the energy released is used to build carbohydrates

The electron transport chain is a cluster of proteins that transfer electrons through a membrane within mitochondria to form a gradient of protons that drives the creation of adenosine triphosphate (ATP). ATP is used by the cell as the energy for metabolic processes for cellular functions.

summary

Aerobic cellular respiration is made up of three parts:

1. **glycolysis,**
2. **the citric acid (Krebs) cycle, and**
3. **oxidative phosphorylation**

In glycolysis, glucose metabolizes into two molecules of pyruvate, with an output of ATP and nicotinamide adenine dinucleotide (NADH). Each pyruvate oxidizes into acetyl CoA and an additional molecule of NADH and carbon dioxide (CO_2).

The acetyl CoA is then used in the citric acid cycle, which is a chain of chemical reactions that produce CO_2, NADH, flavin adenine dinucleotide ($FADH_2$), and ATP.

In the final step, the three NADH and one $FADH_2$ amassed from the previous steps are used in oxidative phosphorylation, to make water and ATP.

Oxidative phosphorylation

has two parts

1. **the electron transport chain (ETC)**
2. **chemiosmosis.**

The ETC is a collection of proteins bound to the inner mitochondrial membrane and organic molecules, which electrons pass through in a series of redox reactions, and release energy. The energy released forms a proton gradient, which is used in chemiosmosis to make a large amount of ATP by the protein ATP-synthase.

Photosynthesis is a metabolic process that converts light energy into chemical energy to build sugars. In the light-dependent reactions, light energy and water are used to make ATP, NADPH, and oxygen (O2). The proton gradient used to make the ATP forms via an electron transport chain. In the light-independent reactions, sugar is made from the ATP and NADPH from the previous reactions.

Steps of the Electron Transport Chain

In the electron transfer chain, electrons move along a series of proteins to generate an expulsion type force to move hydrogen ions, or protons, across the mitochondrial membrane.

The electrons begin their reactions in Complex I, continuing onto Complex II, traversed to Complex III and cytochrome c via coenzyme Q, and then finally to Complex IV. The complexes themselves are complex-structured proteins embedded in the phospholipid membrane. They are combined with a metal ion, such as iron, to help with proton expulsion into the intermembrane space as well as other functions. The complexes also undergo conformational changes to allow openings for the transmembrane movement of protons.

These four complexes actively transfer electrons from an organic metabolite, such as glucose. When the metabolite breaks down, two electrons and a hydrogen ion are released and then picked up by the coenzyme NAD+ to become NADH, releasing a hydrogen ion into the cytosol.

These four complexes actively transfer electrons

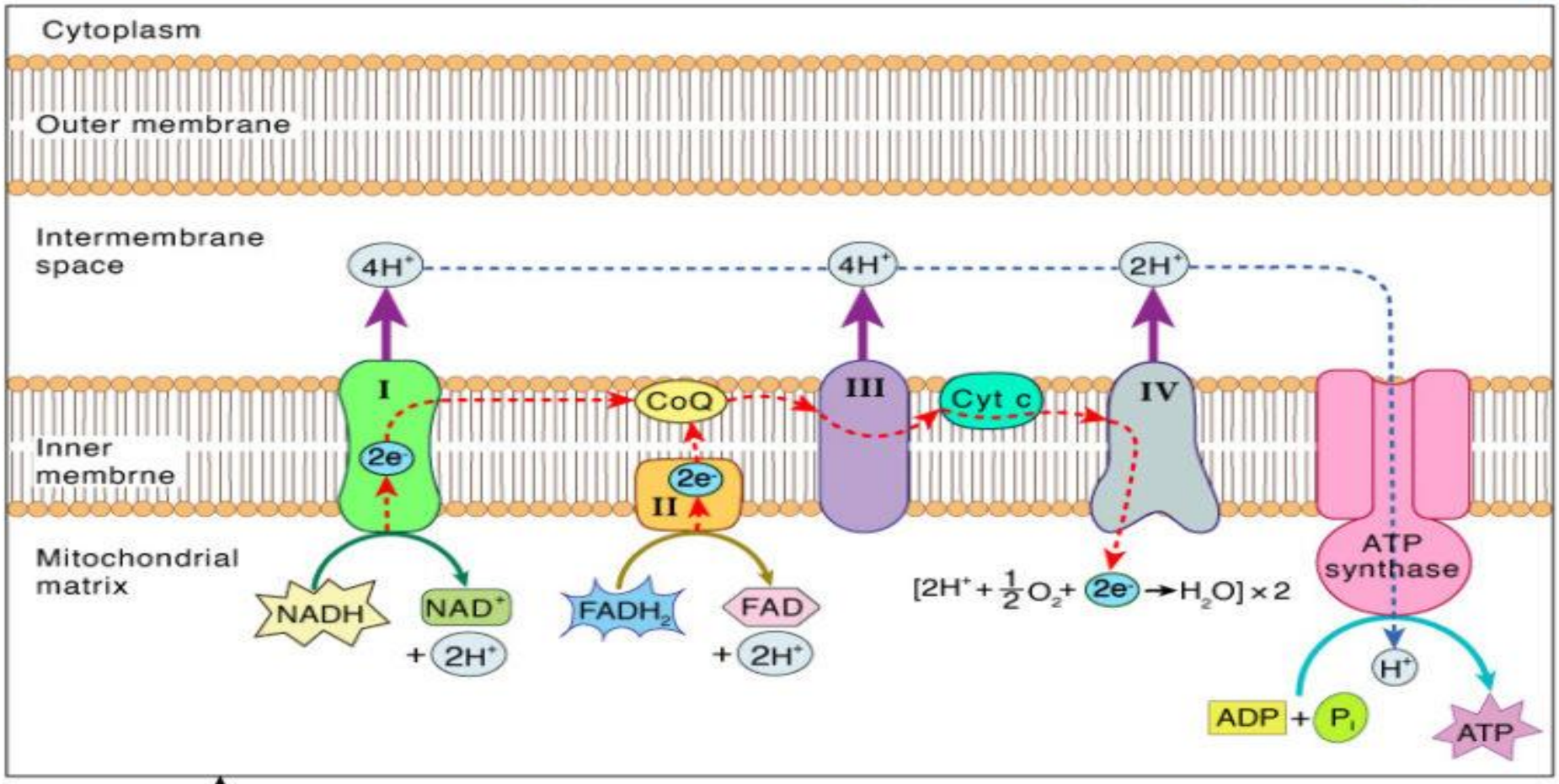
The NADH now has two electrons passing them onto a more mobile molecule, ubiquinone (Q), in the first protein complex (Complex I). Complex I, also known as NADH dehydrogenase, pumps four hydrogen ions from the matrix into the intermembrane space, establishing the proton gradient. In the next protein, Complex II or succinate dehydrogenase, another electron carrier and coenzyme, succinate is oxidized into fumarate, causing FAD (flavin-adenine dinucleotide) to be reduced to FADH2. The transport molecule, FADH2 is then reoxidized, donating electrons to Q (becoming QH2), while releasing another hydrogen ion into the cytosol. While Complex II does not directly contribute to the proton gradient, it serves as another source for electrons.

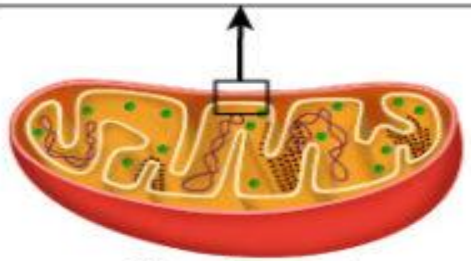
These four complexes actively transfer electrons

Complex III, or cytochrome c reductase, is where the Q cycle takes place. There is an interaction between Q and cytochromes, which are molecules composed of iron, to continue the transfer of electrons. During the Q cycle, the ubiquinol (QH2) previously produced donates electrons to ISP and cytochrome b becoming ubiquinone

ISP and cytochrome b are proteins that are located in the matrix that then transfers the electron it received from ubiquinol to cytochrome c1. Cytochrome c1 then transfers it to cytochrome c, which moves the electrons to the last complex.

Electron Transport Chain





Mitochondrion

I - Complex I: (NADH-CoQ oxidoreductase)

II - Complex II: (Succinate dehydrogenase)

CoQ - Coenzyme Q (Ubiquinone)

III - Complex III: (Cytochrome bc1 complex)

IV - Complex IV: (Cytochrome c oxidase)

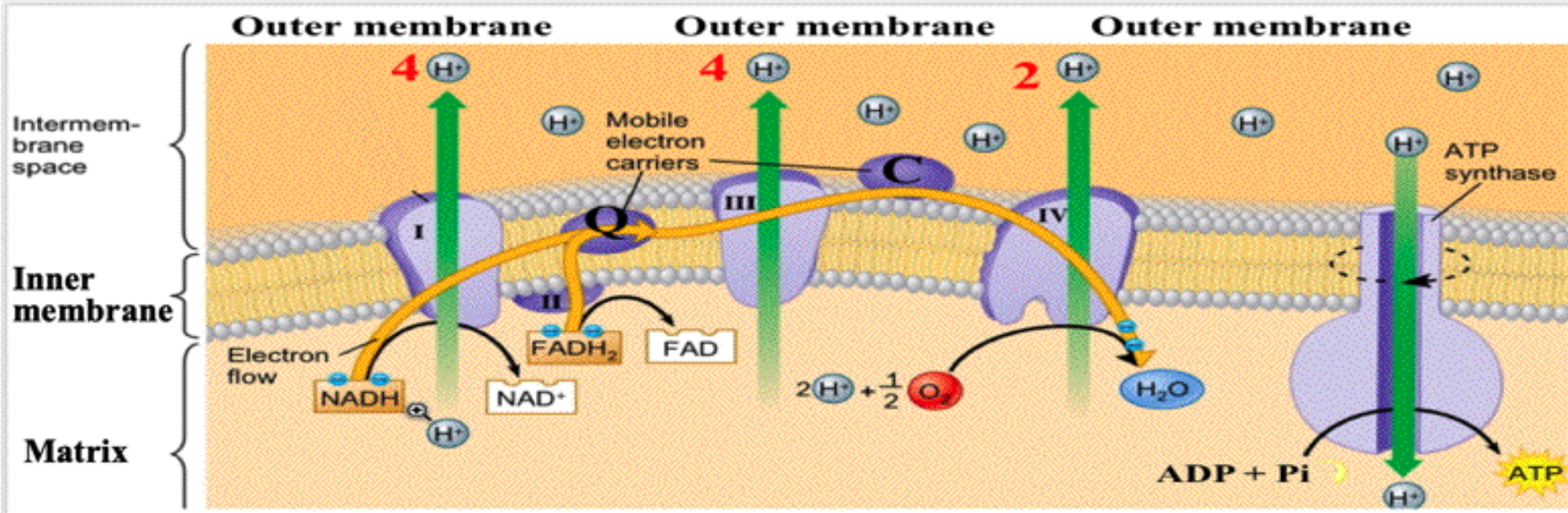
Cyt c - Cytochrome c

The electron transport chain has two essential functions in the cell:

1. Regeneration of electron carriers: Reduced electron carriers NADH and $FADH_2$ pass their electrons to the chain, turning them back into NAD^+ and FAD. This function is vital because the oxidized forms are reused in glycolysis and the citric acid cycle (Krebs cycle) during cellular respiration.
2. Generating proton gradient: The transport of electron through the chain results in a gradient of a proton across the inner membrane of mitochondria, later used in ATP synthesis

The critical steps of the electron transport chain and chemiosmosis are:

1. **Donation of electrons by electron carriers NADH and FADH2**: Two reduced electron carriers NADH and FADH2 produced during earlier stages of cellular respiration transfer their electrons to the specific complex at the start of ETC.
2. **Transfer of electrons by mobile electron carriers and proton pumping**: As electrons flow through the chain, they lose energy, which helps to pump protons (H+ ions) out of the mitochondrial matrix to the intermembrane space. This process creates a proton gradient, also known as the electrochemical gradient.
3. **Splitting of oxygen to form water**: This happens at the end of ETC, where electrons are finally transferred to molecular oxygen, forming a water molecule by accepting H+ ions.
4. **Synthesis of ATP**: As H+ returns to the matrix through the concentration gradient, they pass through a multi-subunit enzyme complex called ATP synthase and result in ATP synthesis



1. Redox of NADH+H+ at Complex I, electrons go to Complex I, four protons pumped from matrix to intermembrane space

2. Redox of $FADH_2$ at Complex II, Coenzyme Q picks up electrons (from Complex I and II) and transports to Complex III

3. Redox of Complex III, four protons pumped from matrix to intermembrane space, carrier C transports electrons to Complex IV

4. Redox of Complex IV, two protons pumped from matrix to intermembrane space, formation of H_20 (20% of water in body)

5. ATP Synthase action, pumps protons from intermembrane space to matrix, produces ATP from ADP + Pi + energy

Quiz

Where is the higher concentration of protons while the electron transport chain is activated?

A. Phospholipid layer

B. Mitochondrial matrix

C. Intermembrane space

D. Cell membrane

THANK YOU

Fructose Metabolism

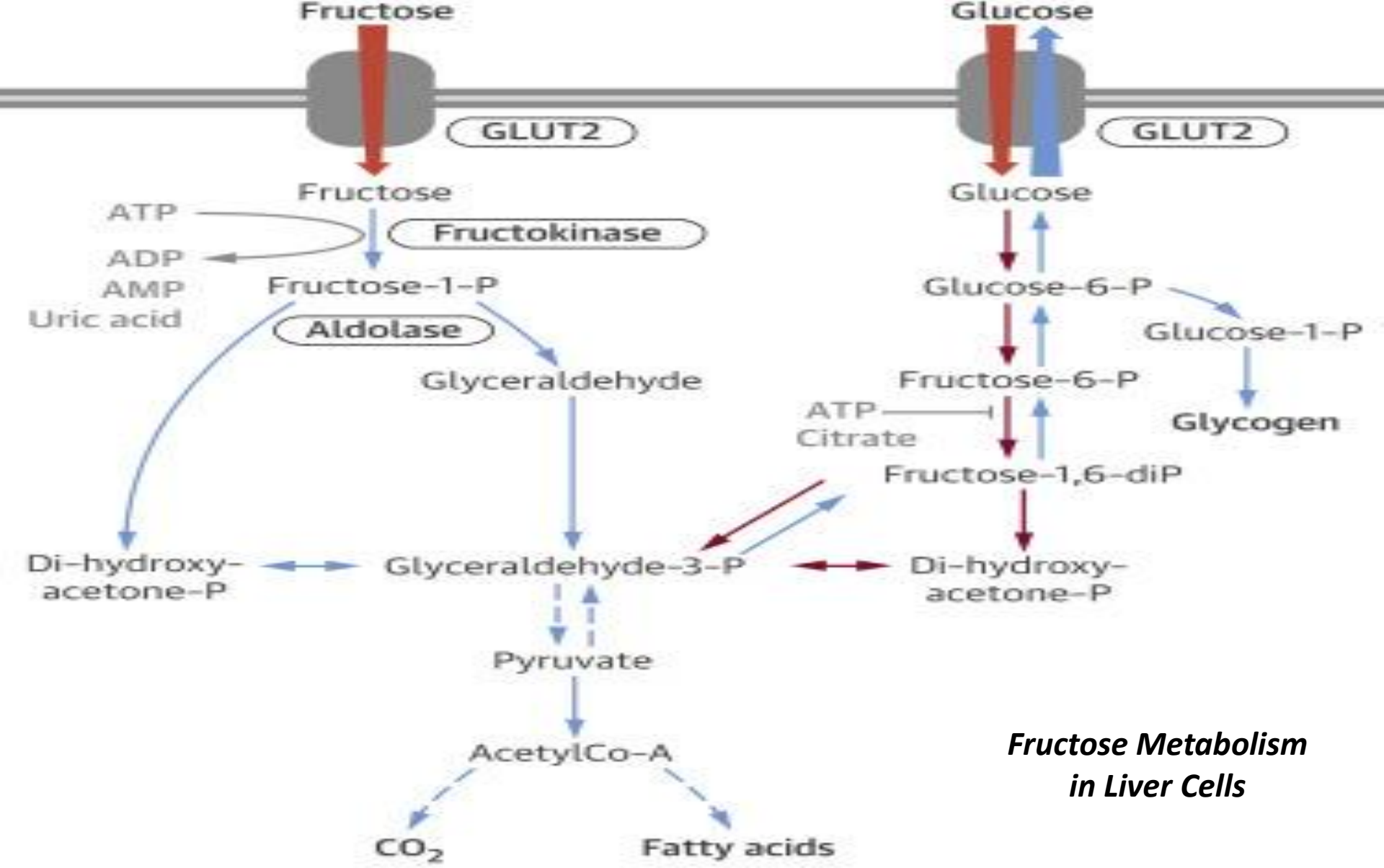
Lec8

Fructose Metabolism

Fructose is absorbed from the gut into the portal vein and is metabolized in the liver, where it is converted into fructose-1-phosphate by the enzyme fructokinase. Fructose-1-phosphate is then split into 2 3-carbon molecules, namely **glyceraldehyde** and **dihydroxyacetone phosphate**, by **aldolase**.

Aldolase is a glycolytic enzyme that catalyzes the conversion of fructose 1-6-diphosphate to glyceraldehyde 3-phosphate and dihydroxy-acetone phosphate via the glycolysis metabolic pathway.

Fructose metabolism differs from that of glucose in 2 major ways



Fructose Metabolism in Liver Cells

Fructose metabolism (red arrows) differs from glucose (blue arrows) due to: 1) a nearly complete hepatic extraction; and 2) different enzyme and reactions for its initial metabolic steps.

Fructose Metabolism

unlike glucose, fructose can bypass the main rate limiting step of glycolysis at the level of phosphofructokinase, allowing it to act as a substrate for hepatic de novo lipogenesis and production of lipids. Thus, intake of fructose in high amounts can promote triglyceride synthesis from unchecked pathways.

The actual amount of fructose needed to increase blood triglyceride levels is debated

Fructose Metabolism

Fructose is a

- Hexose carbohydrate / suger
- monosaccharide found in sucrose or table sugar, honey, fruits, vegetables, and plants. It also exists in a number of oligosaccharides, such as raffinose (a trisaccharide) and stachyose (a tetrasaccharide). Stachyose is found abundantly in legumes. Ingested sucrose is hydrolyzed by intestinal sucrase to glucose and fructose.

The oligosaccharides raffinose and stachyose, which also contain galactose and glucose, are not digested in humans.

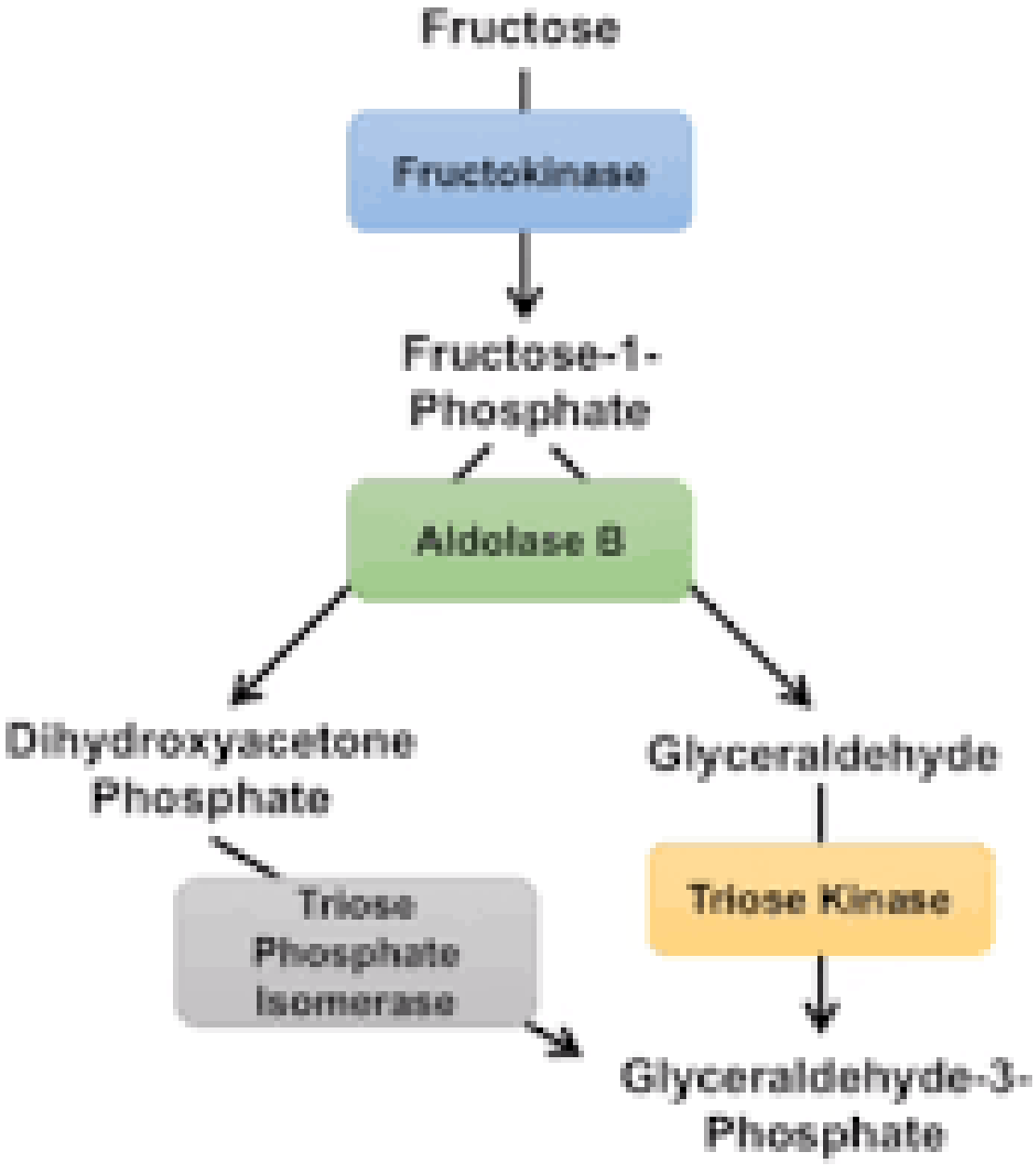
The liver plays a dominant role in the metabolism of fructose; other organs metabolize fructose but to a lesser extent .

The overall process results in conversion of the sugar to glycolytic intermediates, leading to the formation of either glucose or lactic acid

Fructose Metabolism

In the liver, fructose is phosphorylated to fructose-1-phosphate (F-1-P) in the presence of **fructokinase**. The enzyme is also present in kidney and intestinal mucosa. **Fructokinase** is not present in muscle, adipose tissue, and blood cells, and in these tissues, fructose is phosphorylated to fructose-6-phosphate by hexokinase.

In the liver, F-1-P is further metabolized to d-glyceraldehyde and dihydroxyacetone phosphate by F-1-P aldolase (aldolase B/fructose-1,6-bisphosphonate aldolase)


Fructose
Fructokinase
Fructose-1-Phosphate
Aldolase B
Dihydroxyacetone Phosphate
Glyceraldehyde
Triose Phosphate Isomerase
Triose Kinase
Glyceraldehyde-3-Phosphate

Disorders of Fructose Metabolism

There are three disorders of fructose metabolism, all inherited in an autosomal recessive fashion.

Fructose is widely distributed in the diet as the primary sugar in fruits, vegetables, and honey. It is also derived from sucrose and sorbitol, which are found in large variety of products, including infant formulas and intravenous fluids.

The toxic effect of fructose is due to inhibition of gluconeogenesis by high levels of fructose-1-phosphate and subsequent depletion of inorganic phosphate and, thus, adenosine triphosphate.

Fructose and Sorbitol Metabolism

Fructose is a ketohexose found in honey and a wide variety of fruits and vegetables. Combined with glucose in an α(1→2)β linkage, it forms sucrose

Fructose absorption

The absorption rate of fructose alone from the small intestine is slower than that of glucose. This is partly due to the differences in the absorption process between the two monosaccharides. Glucose is absorbed from the intestine into the plasma via more than one active glucose co-transporter protein.

Compared with glucose, fructose absorption appears to be quantitatively limited. Some individuals may have a low capacity to absorb fructose and develop symptoms of diarrhea and flatulence after fructose loading , more particularly when fructose is ingested without glucose.

Once inside the enterocyte, part of the fructose appears to be converted into lactate and released into the portal circulation.

THANK YOU