AEROBIC RESPIRATION

Aerobic respiration needs free O_2. In aerobic respiration organic food is completely broken down into CO_2 and H_2O and the stored energy is released.

OVERALL EQUATION

The overall equation of aerob respiration for glucose breakdown can be written as follows:

$$C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O + 36ATP$$

Glucose and oxygen are used and carbondioxide and water are produced. Energy is released which is used in the synthesis of ATP molecules. This is just the opposite of photosynthesis where glucose and oxygen are produced and CO_2 and water are used as raw materials.

The overall equation of aerobic respiration gives a perception that oxygen combines with glucose molecule which is broken down into water and carbondioxide and stored energy is released. But infact this doesnot happen. Complete breakdown of glucose molecule in aerobic respiration, occ in different steps

STEPS OF AEROBIC RESPIRATION

Aerobic respiration occurs in three different steps:

1. Glycolysis
2. Kreb's cycle
3. Electron Transport Chain

SITES OF DIFFERENT STEPS

Glycolysis occurs in cytosol (cytoplasm) while the latter two stages i-e Kreb's cycle and Electron Transport Chain occur in mitochondria.

SYNTHESIS OF ATP MOLECULES

Organic food molecules are used by the living organisms as building materials and source of energy. Among the food molecules carbohydrates are the primary source of energy broken down by the living cells for the synthesis of ATP molecules. ATP are energy rich molecules also called the energy currency of the cells.

PURPOSE OF RESPIRATION

The purpose of respiration is to release energy stored in organic food molecules and ATP are produced. Why living cells don't acquire direct energy from the breakdown of [illegible]

Why do they synthesize ATP? This is bcz if whole amount of energy of glucose is released it will be too great for individual reactions. This will result in heating up of the cells and also a large amount of energy will be wasted. ATP contains the right amount of energy available to the cells for its functions when it is broken down into ADP and inorganic phosphate. All living cells therefore use ATP molecules for energy requirement.

1. GLYCOLYSIS

Glyco → glucose
lysis → splitting

Glycolysis is the breake down of glucose, a 6-C molecule, in two molecules of pyruvate (3-C molecule) and a net gain of two ATP molecules. It takes place in cytosol (cytoplasm) and is common in both aerobic and anaerobic respiration. Glycolysis doesnot need free oxygen.

Glycolysis completes in two phases i-e preparatory phase and oxidative phase.

1) PREPARATORY PHASE

Preparatory phase is phospho-rylation of glucose by two ATP molecules. It is energy consumption phase. It occurs in the following steps:

1. PHOSPHORYLATION OF GLUCOSE

Glycolysis starts when glucose reacts with ATP molecule. ATP transfers energy and phosphate to glucose forming glucose-6 Phosphate and itself converts to ADP

Glucose + ATP → Glucose-6 Phosphate + ADP

2. ISOMERIZATION

Glucose-6 Phosphate is isomerised into Fructose-6 Phosphate in the presence of enzyme isomerase.

Glucose-6 Phosphate $\xrightarrow{\text{isomerase}}$ Fructose-6 Phosph

3. FORMATION OF FRUCTOSE-1-6 BIPHOSPHATE

Fructose-6 phosphate reacts with another ATP molecule. The phosphate from ATP molecule attaches to carbon 1 of Fructose-6 Phosphate forming Fructose-1-6 Biphosphate.

Fructose-6 Phosphate + ATP → Fructose-1-6-Biph... + ADP

4. SPLITTING OF FRUCTOSE-1-6 BISPHOSPHATE

Fructose-1-6 Biphosphate splits into 3-carbon Phosphosglyceraldehyde (PGAL) and dihydroxy acetone phosphate (DAP). Both PGAL and DAP are isomers of eachother and both are 3-C compounds. PGAL and DAP are interconvertable as they are isomers of each other.

Fructose-1-6 Biphosphate → PGAL + DAP

5. CONVERSION OF DAP

Dihydroxy Acetone Phosphate (DAP) changes to phosphoglyceraldehyde (PGAL).

DAP → PGAL

Preparatory phase completes with the splitting of fructose biphosphate into PGAL and DAP.

ii) Oxidative Phase

In oxidative phase PGAL is oxidized to PGA (phosphoglycerate). Hydrogen is removed from PGAL and the energy of oxidation results in the formation of high energy phosphate bonds and the generation of ATP molecules.

This is an energy production phase. It involves the following steps:

1. OXIDATION OF PGALs

1. PRODUCTION OF 1-3-BIPHOSPHOGLYCERATE

The process begins when two hydrogen atoms are removed from 3-Phosphoglyceraldehyde (PGAL) and transferred to a molecule of NAD, a coenzyme. Thus PGAL is oxidized to PGA and NAD is reduced to $NADH_2$. This step and the subsequent step occurs twice because two PGAL are produced at the end of preparatory phase. Although two NADH are produced in the process. This reaction is accompanied by the addition of phosphate groups. The resultant molecules are 1-3 biphospho--glycerate.

ADDITION OF PHOSPHATE

$$2PGAL + 2Pi \longrightarrow 2BPGA + 2H_2$$

$$2NAD + 2H_2 \longrightarrow 2NADH_2$$

2. SYNTHESIS OF ATP

Each molecule of 1-3 biphosphoglycerate converts into 2-Phosphoenol pyruvate transfers high energy phosphate to ADP forming ATP molecule and itself changes to 3-Phosphoglycerate.

1-3 biphosphoglycerate + ADP ⟶ 3-Phosphoglycerate + ATP

3) 2-PHOSPHOENOL PURUVATE

In next step 3-Phosphoglycerate converts into 2-Phosphoenol pyruvate (PEP) with the elimination of one water molecule

$$2\,PGA \longrightarrow PEP + H_2O$$

4) FORMATION OF PYRUVIC ACID

In last step phosphoenol pyruvate reacts with ADP forming an ATP and Pyruvic acid. In this step phosphoenol pyruvate gives up a phosphate group to ADP generating ATP and itself oxidizing to pyruvic acid.

PEP + ADP ⟶ Pyruvic acid + ATP

END PRODUCT

Two molecules of pyruvate are the end product of glycolysis.

NET GAIN OF ATP MOLECULES

Since two molecules of ATP are utilized to start the process of glycolysis and four molecules of ATP are produced in the metabolic pathway, therefore there is a net gain of two molecules of ATP.

SUBSTRATE LEVEL PHOSPHORYLATION

The generation of ATP in the process of glycolysis is called substrate level phosphorylation bcz high energy phosphate bonds are transferred from substrate to ADP.

NOTE

In aerobic respiration also called cellular respiration further steps occur in mitochondria. Pyruvate from glycolysis is completely oxidized through linked reactions, Krebs cycle, and electron transport chain to carbondioxide and water. During the pathways mostly hydrogen atoms are removed from organic compounds. These hydrogen atoms are picked up by oxidized NAD and FAD and are reduced to $NADH_2$ and $FADH_2$. These reduced coenzymes transfer electrons to oxygen through an electron transport system with generation of ATP. Oxygen is the final electron acceptor and water is formed

LINKED REACTION

(CONVERSION OF PYRUVATE TO ACETYL-COA)

SITE OF LINKED REACTION

Linked Reaction takes place in mitochondria. "Pyruvate carrier" carry pyruvate from cytosol to mitochondria.

PROCESS

* **OXIDATION OF PYRUVATE**

Pyruvate doesnot enter the Krebs cycle directly. Before entering the Krebs cycle pyruvate is oxidized to a carbondioxide and a two carbon molecule called acetyl group.

$$\text{Pyruvic Acid} \longrightarrow \text{Acetyl Group} + CO_2 + 2H$$

* **ATTACHMENT TO COENZYME A**

The acetyl group attaches to coenzyme A (CoA) forming a group called acetyl CoA. Coenzyme A consists of a nucleotide and a portion of one of the B vitamins.

$$\text{Acetyl Group} + CoA \longrightarrow \text{Acetyl CoA}$$

REDUCTION OF NAD

During the process hydrogen is removed from the pyruvate which is taken by NAD. By getting hydrogen NAD is reduced to $NADH_2$.

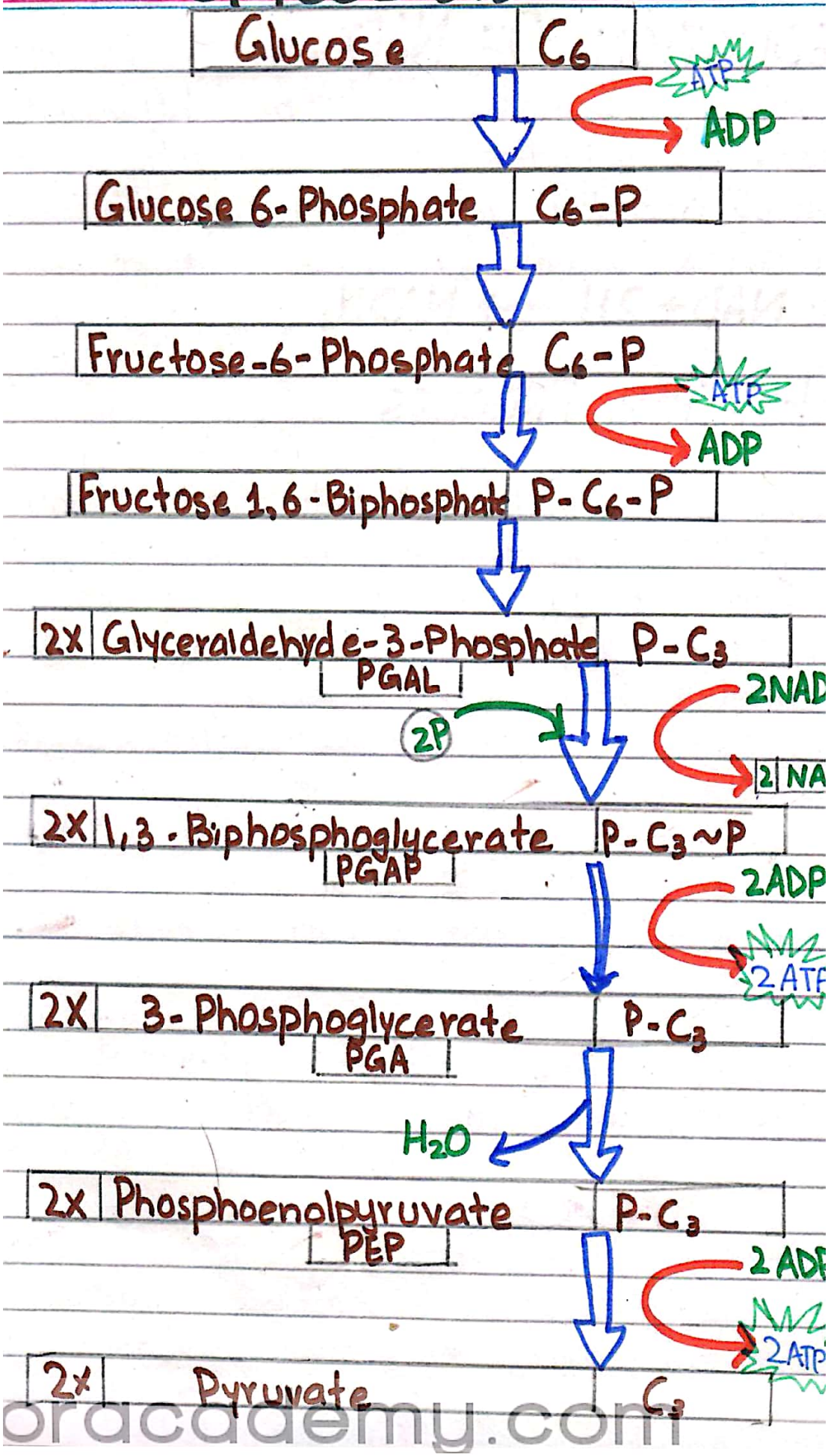
$$NAD + 2H \longrightarrow NADH_2$$

FURTHER PROCESS

Acetyl-Co A enters the Krebs cycle. This process is called linked reaction bcz it links Glycolysis to the Krebs cycle.

Further oxidation of acetyl-CoA takes place in a cyclic manner. This manner is called Krebs cycle.

GLYCOLYSIS



2. KREBS CYCLE OR TRICARBOXYLIC ACID CYCE (TCA)

Krebs cycle is also known as Citric Acid Cycle. The Krebs cycle is named after the British biochemist Hans Krebs.

The Krebs cycle takes place in the mitochondrial matrix.

The acetyl-CoA produced in the linked reaction enters into a cycle called Krebs cycle. In Krebs cycle the metabolic pathway takes the course of cycle where Acetyl CoA (2-C compound) is completely oxidized into two molecules of CO_2 and hydrogen atoms are removed which reduces NAD and FAD to $NADH_2$ and $FADH_2$ respectively.

STEPS

1. FORMATION OF CITRIC ACID

The first reaction of the citric acid cycle is catalyzed by the enzyme citrate synthase. In this step, Acetyl CoA combines with preexisting oxaloacetate (4-C) (present in the mitochondrial matrix) to form citric

acid (6-C). Once the two molecules are joined, a water molecule attacks the acetyl leading to the release of coenzyme A from the complex. Co-A becomes free and is ready to react with another acetyl group.

(2-C) (4-C) (6-C)

Acetyl Co.A + Oxaloacetate → Citrate + Co.A

* ISOCITRATE

[Citrate is converted into isocitrate.]

The next reaction of the krebs cycle is catalyzed by the enzyme ~~acontinase~~ aconitase. In this reaction, a water molecule is removed from the citric acid and then put back on in another location. The overall effect of this conversion is that the -OH group is moved from the 3' to the 4' position on the molecule. This transformation yields the molecule isocitrate.

(6-C) (6-C)

Citrate → Isocitrate

* KETOGLUTARATE

Iso-citrate is oxidized to alpha ketoglutarate (5-C)

In this step one carbon of isocitrate is oxidized to CO_2 and hydrogen is removed which is picked up by NAD reducing into $NADH_2$.

* FORMATION OF SUCCINYL CO-A

One carbon of -Ketoglutarate is oxidized into carbondioxide. The CO_2 is released from the cycle. This is second CO_2 molecule produced in the Krebs cycle. The two carbons of the acetyl group which has entered into the Krebs cycle are oxidized into two molecules of CO_2. Hydrogen atoms are released which are accepted by oxidized NAD. By accepting hydrogen atoms NAD is reduced to $NADH_2$. The -Ketoglutarate is converted into succinyl group (4-C). Co-A (This CoA comes from Acetyl CoA) reacts with succinyl group forming succinyl Co-A.

* SUCCINATE ACID (4-C)

In the next step succinyl Co-A is converted to succinate Acid (4-C) and Co-A is released.

* SUBSTRATE LEVEL PHOSPHORYLATION

Some of the energy produced in the oxidation is used in the synthesis of ATP. The energy of the substrate used in the generation of ATP is called substrate-level phosphorylation.

FUMARATE (4-C)

The enzyme succinate dehydrogen catalyzes the removal of two hydrogens from succinate. In the reaction, a molecule of FAD (Flavin Adenine Di-nucleotide) a coenzyme similar to NAD, is reduced to $FADH_2$ as it takes the hydrogens from succinate. The product of this reaction is fumarate.

Although FAD and NAD perform the same oxidative and reductive roles in reactions, FAD and NAD work on different classes of molecules. FAD oxidizes carbon-carbon double and triple bonds while NAD oxidizes mostly carbon-oxygen bonds.

MALATE

Fumarate is converted to malate (4-C) in the presence of enzyme fumarase.

OXALOACETATE

In last step malate oxidizes to oxaloacetate. A molecule of NADH is produced during this step. The oxaloacetate is now able to react with another acetyl Co-A and continue the cycle.

ELECTRON TRANSPORT CHAIN

INTRODUCTION

The last step in aerobic respiration is the oxidation of reduced coenzymes $NADH_2$ and $FADH_2$ produced in glycolysis and Krebs cycle by molecular oxygen.

The pairs of hydrogen atoms released from glucose during glycolysis and Krebs cycle of aerobic respiration are not received directly by oxygen but pass along a series of electron carriers called coenzymes and cytochromes. This series of electron carriers constitute respiratory electron transport chain. The final electron acceptor at the end of the electron transport chain is oxygen forming water.

Various molecules involved in the electron transport are $NADH_2$, $FADH_2$, coenzyme Q, cytochrome b (Cyt. b), cytochrome c (Cyt. c), cytochrome a (Cyt. a), and Cytochrome a_3 (Cyt a_3). The coenzyme Q and cytochromes are alternately reduced and oxidized.

Electrons are passed along a

series of carriers as they lose energy at each transfer. Some of this energy is used in the formation of ATP from ADP and inorganic phosphate. In the electron transport chain each next molecule is at lower energy level than the previous one. At the end oxygen accepts electrons and hydrogen to form water.

DETAILED PROCESS

The electron transport chain is the final and most important step of cellular respiration. While Glycolysis and the Krebs cycle make the necessary precursors, the electron transport chain is where a majority of the ATP is created.

CHEMIOSMOTIC ATP SYNTHESIS

The synthesis of ATP from ADP and inorganic phosphate in the electron transport system through the joint event of chemical and osmotic processes is called chemiosmotic ATP synthesis.

Chemiosmotic theory of ATP synthesis suggests how ATP formation is coupled with the the energy release in the electron transport chain.

SITE OF ELECTRON TRANSPORT CHAIN (ETC)

The electron transport chain takes place in mitochondria. Mitochondria are surrounded by double membrane. The outer membrane is smooth while the inner membrane forms enfolding which are shelf-like projections or protuberances called cristae. The cristae are present in the inner chamber or mitochondrial matrix that is filled with a gel-like substance. The carriers of ETC are present on the cristae. A space is present between the outer and inner membrane called intermembrane space.

PROTEIN COMPLEXES

There are four protein complexes (labeled complex I-IV) in the electron transport chain, which are involved in moving electrons from $NADH_2$ and $FADH_2$ to molecular oxygen.

A complex is a structure consisting of a central atom, molecule, or protein weakly connected to surrounding atoms, molecules, or proteins.

OXIDATIVE PHOSPHORYLATION

Oxidative Phosphorylation is the metabolic pathway in which electrons are transferred from electron donors to electron acceptors in redox reactions; this series of reactions releases energy which is used to form ATP.

As electrons pass from complex to complex, they power the movement of hydrogen ions/atoms from the mitochondrial matrix into the intermembrane space. As a result hydrogen ions accumulate on the outside of the inner membrane in the intermembrane space. Difference of hydrogen ion concentration increases across the membrane which develops a gradient of hydrogen ions between the matrix and the intermembrane space i-e across the inner membrane. Hydrogen ions diffuse down (flows back) the inner membrane through electrochemical gradient from the Intermembrane space into the matrix. The passage of hydrogen ions through the membrane is coupled to ATP synthesis from ADP and inorganic phosphate through ATP synthase complex. This process of ATP synthesis is called chemiosmosmis bcz electrochemical and osmotic events are involved.

COMPLEX I

NADH just floats over to the inner-member and can enter the ETC at complex I.

Complex I establishes the hydrogen ion gradient by pumping four hydrogen ions across the membrane from the matrix into the intermediate space.

COMPLEX II

$FADH_2$ enters the transport chain at complex II. NADH and $FADH_2$ are known as electron carriers. This means they are capable of donating electrons to the transport chain.

COMPLEX III

Ubiquinone (Q) accepts the electrons from both complex I and II and delivers them to complex III.

Complex III pumps protons through the membrane and passes its electrons to cytochrome c for transport to fourth complex of protein and enzymes.

COMPLEX IV

Complex The Fourth Complex is composed of cytochrome proteins c, a and a_3. The cytochromes hold an oxygen molecule very tightly until the oxygen

is completely reduced. The reduced oxygen then picks up two hydrogen ions from the surrounding medium to produce water (H_2O)

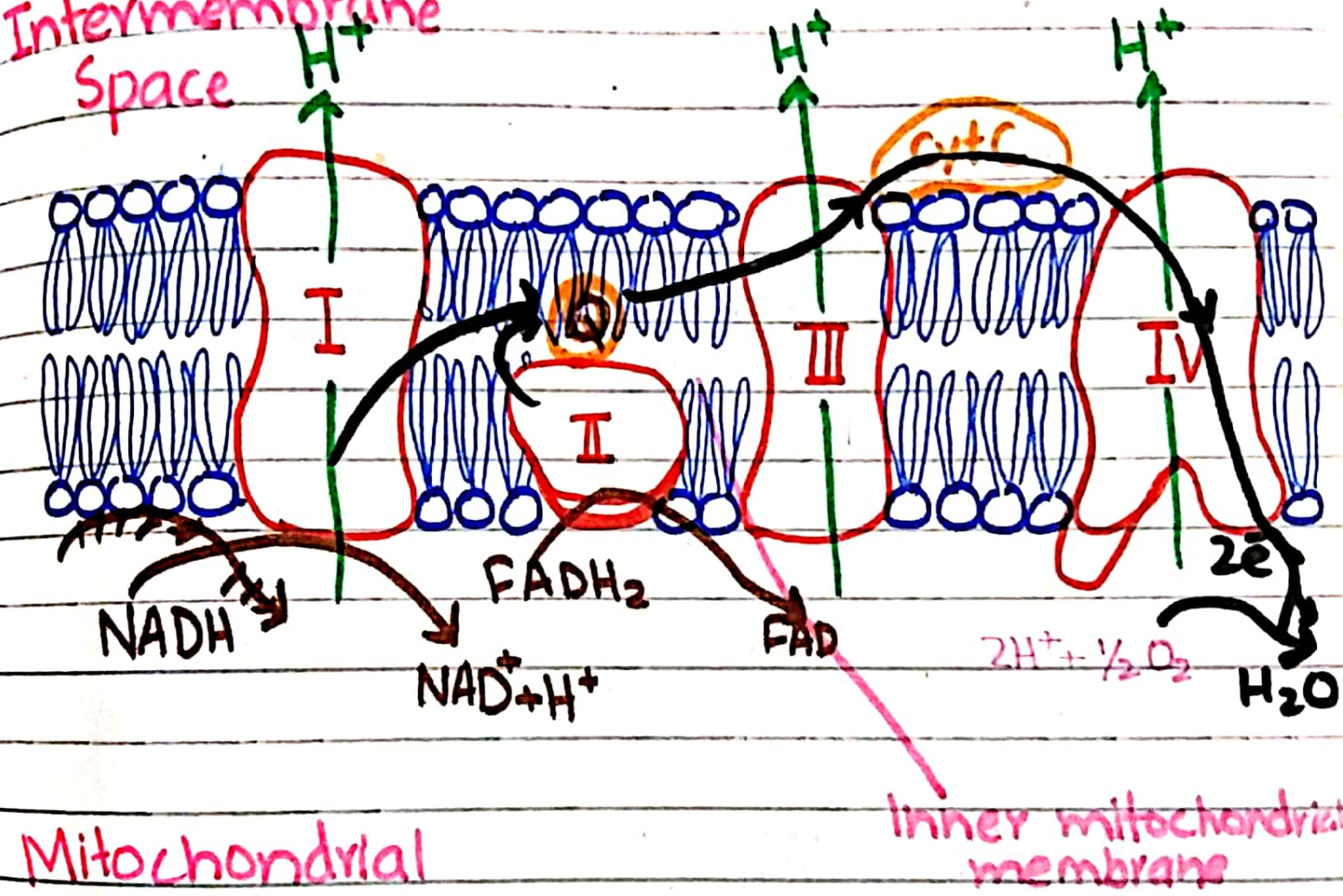


Fig: Electron Transport Chain