Module - 2

Bioenergetics

It is the quantitative study of the energy transductions that occur in living cells of the nature & function of the chemical process underlying these transductions.

Biological energy transductions obey laws of thermodynamic

Living organisms preserve their internal order by taking free energy from their surrounding in the form of nutrients or sunlight & returning to their surroundings an equal amount of energy as heat and entropy.

First Law of Thermodynamics :-

(It is also known as law of conservation of Energy)

It states that for any physical or chemical change, the total amount of energy in the universe remains constant ; energy may be changed from it or it may be transported or transferred from one region to other, but it cannot be created or destroyed.

$$\Delta U = q + w$$

ΔU : change in Internal energy

q : sum of heat that flows across its boundries

w : work done on the system by surroundings.

The second law of Thermodynamics

The universe always tends toward increasing disorder i.e. in all natural processes the entropy of the universe increases.

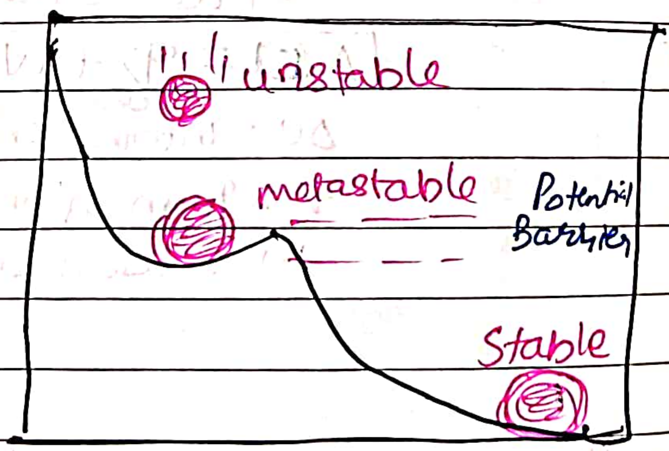
Isolated systems spontaneously evolve towards thermal equilibrium. (The state of maximum entropy of the system).

The Third law of thermodynamics

It states that entropy of a system approaches a constant value as the temp. approaches the absolute zero. The entropy of a system at absolute zero is typically zero & in all cases is determined only by the number of diff. ground states it has.

Entropy of a pure crystalline substance (perfect order) at absolute zero temp is zero.

Energy States



- Unstable: falling or rolling
- Stable: at rest in lowest energy state
- metastable: in low-energy perch.

Gibbs free Energy

Gibbs free Energy (G): G expresses the amount of energy capable of doing work during a reaction at constant temperature & pressure.

All chemical systems tend naturally towards states of minimum Gibbs free Energy.

- under the constant temperature & pressure changes in free energy, enthalpy & entropy in biological systems are related to each other by the equation.

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

ΔG = Change in Gibbs free energy of the reacting system ($G_{products} - G_{reactives}$)

ΔH = change in enthalpy of the reacting system. ($H_{products} - H_{reactives}$)

ΔS = Change in entropy of the reacting system ($S_{products} - S_{reactives}$)

- when a reaction proceeds with the release of free energy (that is, when the system changes so as to possess less free energy) ΔG has a negative value & the reaction is said to be exergonic reaction.

- in endergonic reactions, the system gains free energy & ΔG is positive.

  - Favourable or spontaneous rxn, $\Delta G^{\circ} < 0$

Aerobic Respiration & Anaerobic Respiration :-

Living organisms use energy released by respiration for their life processes. There are two types of respiration - aerobic (which needs oxygen) & anaerobic (which doesn't need oxygen).

Aerobic Respiration	Anaerobic Respiration
A chemical process in which oxygen is used to make energy from carbohydrates (sugars). Also called aerobic metabolism, cell respiration & oxidative metabolism	Anaerobic respiration is the type of respiration through which cells can break down sugars to generate energy in the absence of oxygen.

Aerobic Respiration :-

Mammals & birds need energy to maintain a constant body temperature.

Energy is also needed for the following life processes.

- growth
- cell division
- Muscle contraction
- Protein syntheses
- active transport
- nerve Impulses

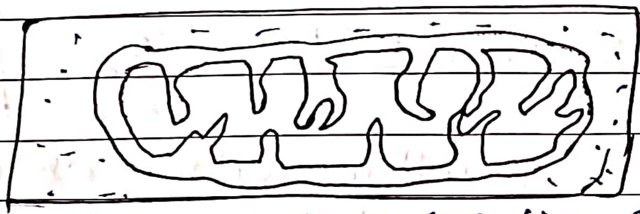
Respiration involves chemical reactions that break down nutrient molecules in living cells to release energy

Aerobic respiration needs oxygen. It is the release of a relatively large amount of energy in cells by the breakdown of food substances in the presence of oxygen.

Glucose + oxygen ⟶ Carbon Dioxide + Water.

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

Aerobic respiration happens all the time in animals & plants. Note that respiration is different to breathing (ventilation). Most of the reactions in aerobic respiration happen inside the mitochondria in cells.



Mitochondria are tiny organelles found in the cell cytoplasm

Anaerobic Respiration :

Unlike aerobic respiration, anaerobic respiration does not need oxygen. It is the release of a relatively small amount of energy in cells by the breakdown of food substances in the absence of oxygen.

Anaerobic respiration in muscles

Anaerobic respiration happens in muscles during hard exercise.

glucose ⟶ lactic acid

$$C_6H_{12}O_6 \longrightarrow 2C_3H_6O_3$$

Glucose is not completely broken down, so much less energy is released than during the aerobic respiration.

There is a build-up of lactic acid in the muscles during vigorous exercise. The lactic acid needs to be oxidised to carbon dioxide & water later.

This causes an oxygen debt : known as Excess post-exercise oxygen consumption (EPOC) that needs to be repaid after the exercise stop. This is why we keep on breathing deeply for a few minutes after we have finished exercising.

Anaerobic respiration in plants & yeast.

Anaerobic respiration also happens in plant cells & some other microorganisms.
Anaerobic respiration in yeast is used during brewing & bread-making :-

glucose → ethanol + Carbondioxide

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

Ethanol is the alcohol found in alcoholic drinks like beer & wine. In bread-making bubbles of CO_2 gas expands the dough & help bread rise.

Anaerobic Respiration.
(no oxygen)
↓
Glycolysis
(Cytoplasm)
↓
Fermentation
I) alcoholic Fermentation
II) lactic acid fermentation
(cytoplasm)
↓
2ATP/Glucose

Aerobic Respiration
(requires oxygen)
↓
Glycolysis
(Cytoplasm)
↓
Kreb's Cycle
(Mitochondria)
↓
Electron Transport
(Mitochondria)
↓
36 ATP/Glucose

↓

Glycolysis
(in Cytoplasm)

↓

Pyruvate
(2 ATP)

← Anaerobic Respiration (in Cytoplasm)

→ Aerobic Respiration (in mitochondria)

Anaerobic Respiration:

- Animal: Lactic Acid ($C_3H_6O_3$)
- Plant: Ethanol + CO_2 (C_2H_5OH)

Aerobic Respiration:

- $CO_2 + H_2O$ [36-38 ATP]

Glucose → Glycolysis → Pyruvate

Cytoplasm: Anaerobic (without oxygen)

Mitochondria: Aerobic (oxygen Present)

Pyruvate → Fermentation → Lactic Acid / Alcohol & CO_2

Pyruvate → Aerobic Respiration → Krebs Cycle → Electron Transport chain

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Glucose → Pyruvate

- Aspergillus → Lactic Acid, eg- Soya sauce
- Lactobacillus → Lactic acid, eg. cheese, yogurt
- Saccharomyces → Ethanol + CO_2, eg. Beer; Ethanol, wine; CO_2, Bread.

Metabolism

Catabolic Reactions: [Mitochondria]

complex molecules → simple molecules + Energy.

Anabolic Reactions: (cytoplasm) (Biosynthetic Reactions)

simple molecules + Energy (in cell) → complex molecules

Glycolysis :-

- ✓ Glycolysis occurs in almost every living cell.
- ✓ It was the First metabolic sequence to be studied.
- ✓ This pathway is also called Embden Meyerhof pathway (EM-Pathway).
- ✓ It occurs in cytosol.
- ✓ Glycolysis is defined as the sequence of reactions converting glucose to pyruvate or lactate with the production of ATP.

- ✓ Glycolysis occurs in the absence of Oxygen (O_2) (anaerobic) or in presence of oxygen (O_2) (aerobic)

Overall of glycolysis

$$C_6H_{12}O_6 + 2NAD^+ \xrightarrow{2ADP \rightarrow 2ATP} 2\,CH_3-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-O^- + 2NADH + 2H^+$$

Pyruvate

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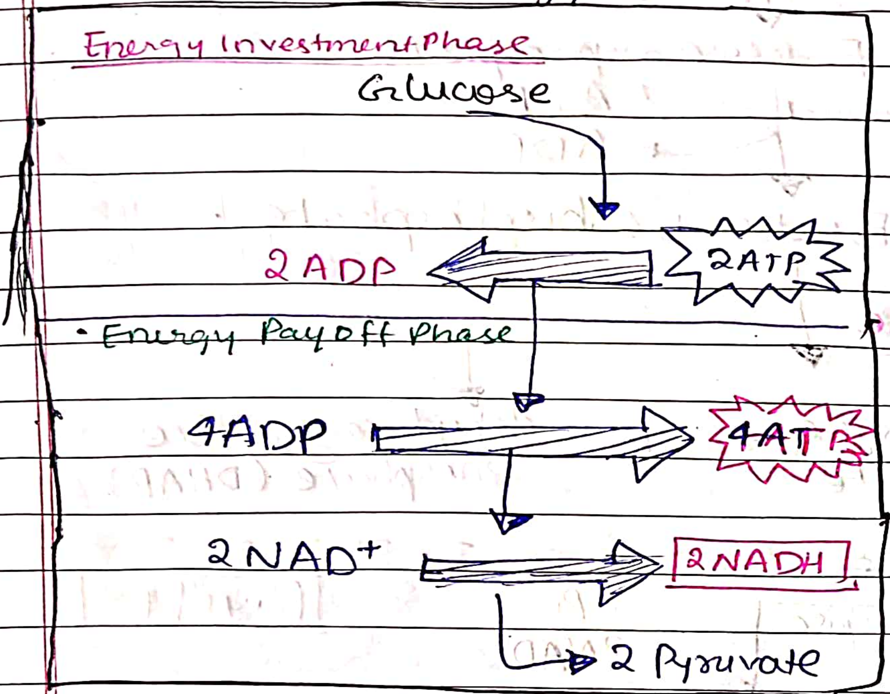
Reactions of Glycolysis

- Divided into three distinct phases.
  - i) Energy Investment Phase (Priming Phase)
  - ii) Splitting Phase.
  - iii) Energy generation Phase.



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Glycolysis

Glucose

1. Hexokinase — ATP → ADP

glucose 6-phosphate

2. Phosphohexose-isomerase (Phosphoglucoisomerase)

Fructose 6-phosphate

3. Phosphofructokinase-1 — ATP → ADP

Fructose 1,6 bisphosphate.

4. Aldolase

glyceraldehyde 3-Phosphate (G3P) ↔ **dehydroxyacetone Phosphate (DHAP)**

Payoff

5. Isomerase

6. Triose Phosphate Dehydrogenase — 2Pi, $2NAD^+$ → $2NADH + H^+$

1,3-bisphosphoglycerate(2)

7. Phosphoglycerate-kinase — 2ADP → 2ATP

3-phosphoglycerate(2)

8. Phosphoglycerate-mutase

2-Phosphoglycerate(2)

9. Enolase — → $2H_2O$

Phosphoenolpyruvate (PEP)

10. Pyruvate kinase — 2ADP → 2ATP

Pyruvate

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Energy-requiring Phase :-

In this phase, the starting molecule of glucose gets rearranged & two phosphate groups are attached to it. The phosphate groups make the modified sugar - now called fructose-1,6 biphosphate unstable allowing it to split in half & form two phosphate-bearing 3-carbon sugars. Because the phosphates used in these steps come from ATP, 2 ATP molecules gets used up.

Splitting Phase :-

In this step, fructose 1,6 diphosphate get dissociated to get glyceraldehyde-3-phosphate (G3P) & dihydroxyacetone phosphate (DHAP).

Energy releasing Phase :-

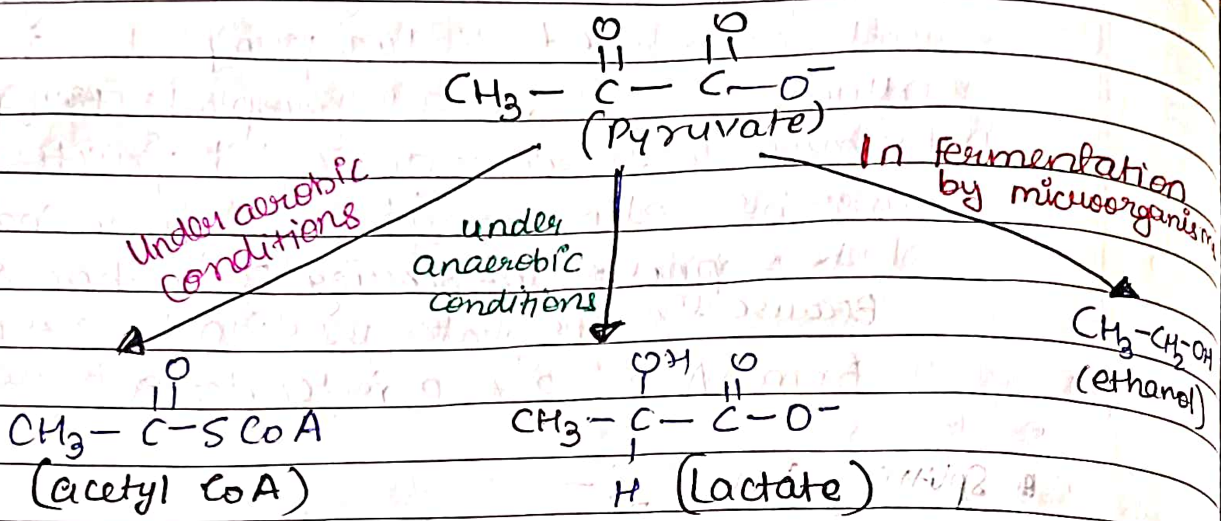
In this phase, each 3-C sugar is converted into another 3-carbon molecule, pyruvate, through a series of rxn. In these rxns 2 ATP molecules and one NADH molecule are made. B'coz this phase takes place twice, once for each of the two 3C-sugars it makes 4 ATP & 2 NADH overall.

→ overall, glycolysis converts one 6-C molecule of glucose into two 3-C molecules of pyruvate.

→ The net production of this process are 2 molecules of ATP & 2 molecules of NADH.

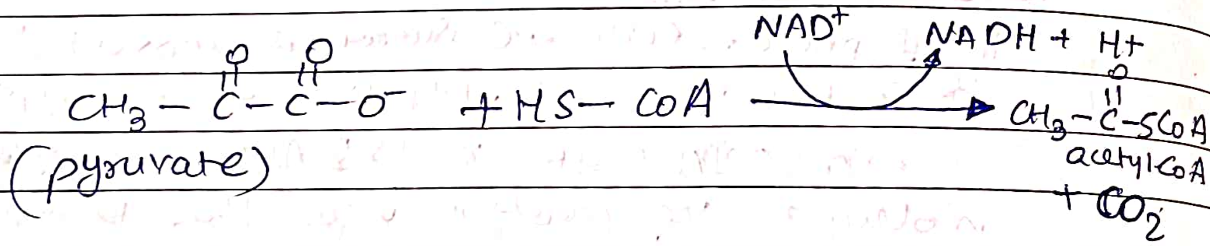
Glucose + 2ATP + 2NAD + 4ADP + 2P → Pyruvate + 4ATP + 2N

The fate of Pyruvate



Aerobic conditions

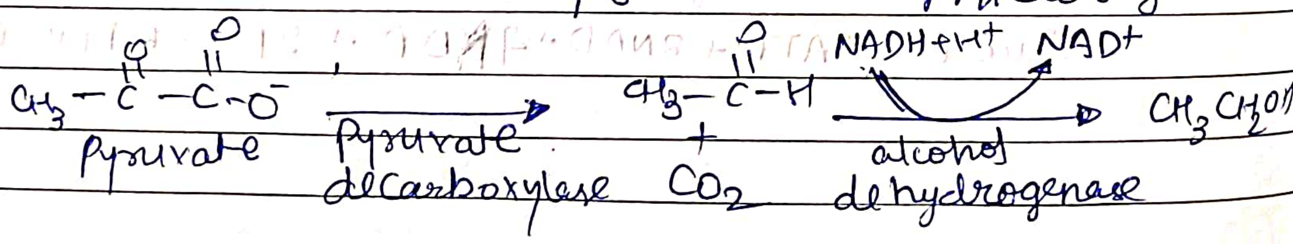
Pyruvate must diffuse across the outer & inner membrane of the mitochondria into the matrix.



The NADH formed needs O_2 to return to NAD^+, so without O_2 no additional pyruvate can be oxidized.

Fermentation

Fermentation is the anaerobic conversion of glucose to ethanol & CO_2 by yeast & other microorganisms.



Gluconeogenesis :-

- Gluconeogenesis is the synthesis of new glucose molecules from pyruvate, lactate, glycerol, or other amino acids alanine or glutamine.
- The process takes place primarily in the liver during periods of low glucose, that is under conditions of fasting, starvation & low carbohydrate diets
- So, the question can be raised as to why the body would create something it has just spent a fair amount of effort to break down? Certain key organs, including the brain can use only glucose as an energy source. therefore, it is essential that body maintain a minimum blood glucose concentration.
- when the blood glucose concentration falls below that certain point, new glucose is synthesized by the liver to raise the blood concentration to normal.

Energetics of Glycolysis Pathway

ATP formed:

1. Gly-3-PO_4 → 1,3-Bisphosphoglycerate = 6 ATP
2. 1,3 Bisphoglycerate → 3-Phosphoglycerate = 2 ATP
3. Phosphoenolpyruvate → Enol Pyruvate = 2 ATP

ATP consumed

4. Glucose → Glucose-6-PO_4 = 1 ATP
5. Fru-6-PO_4 → Fru-1,6-bisphosphate = 1 ATP

Net ATP Produced = 8 ATP.

Regulation of Glycolysis :-

Two types controls for metabolic reactions :-

a) **Substrate limited** : when concentrations of reactant & products in the cell are near equilibrium, then it is the availability of substrate which decides the rate of reac.

b) **Enzyme limited** : when concentrations of substrate & products are far-away from the equilibrium, then it is activity of enzyme that decides the rate of reaction. These reactions are the one which control the flux of the overall pathway.

There are 3 steps in glycolysis that have enzymes which regulate the flux of glycolysis.

I. The Hexokinase (HK)

II. The phosphofructokinase (PFK)

III. The pyruvate kinase.

Hans Krebs (1937)
Discovered
Nobel Prize : 1953 (Physiology or medicine)

Krebs Cycle [Citric Acid cycle] [TCA cycle]

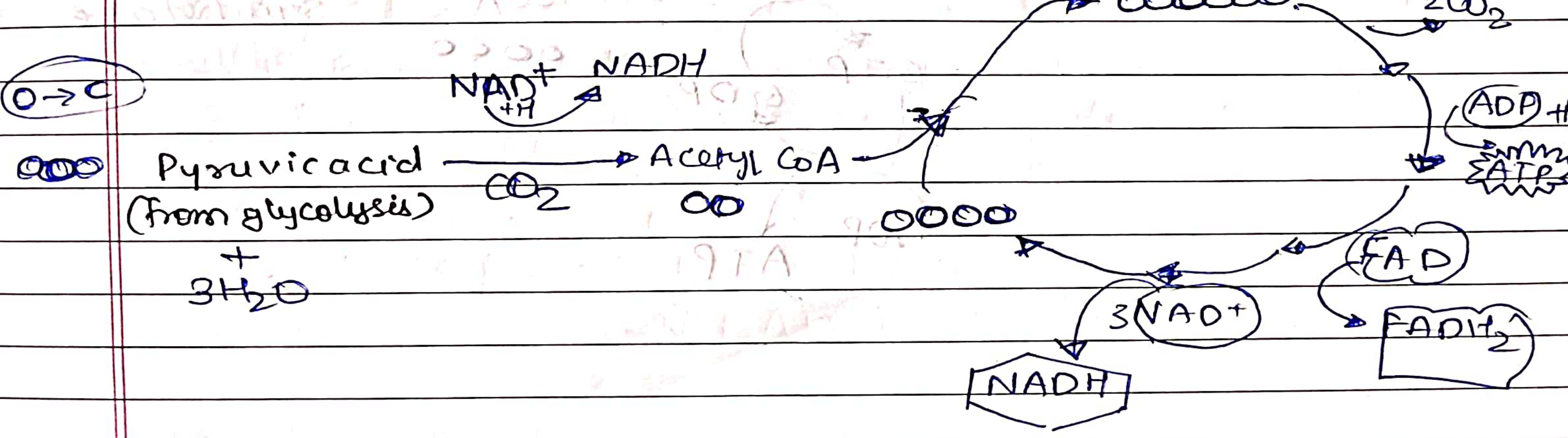
Location : in the Mitochondrial Matrix

Main Goal : To break down pyruvate (pyruvic acid) into carbon dioxide and acetyl Co-A and release more energy.

Process :

↳ Each pyruvate loses one C and makes a 2-C molecule called Acetyl Co A.
↳ The carbon joins with Oxygen (aerobic) that breathe in to create CO_2 we Exhale.
↳ The Acetyl Co-A can then diffuse into the matrix of Mitochondria

There is a preparation step that must take place b/w glycolysis & Kreb's cycle.
↳ This Preparation step changes pyruvates into Acetyl Co A.
↳ This step moves us from the first stage of cellular respiration to the second stage.



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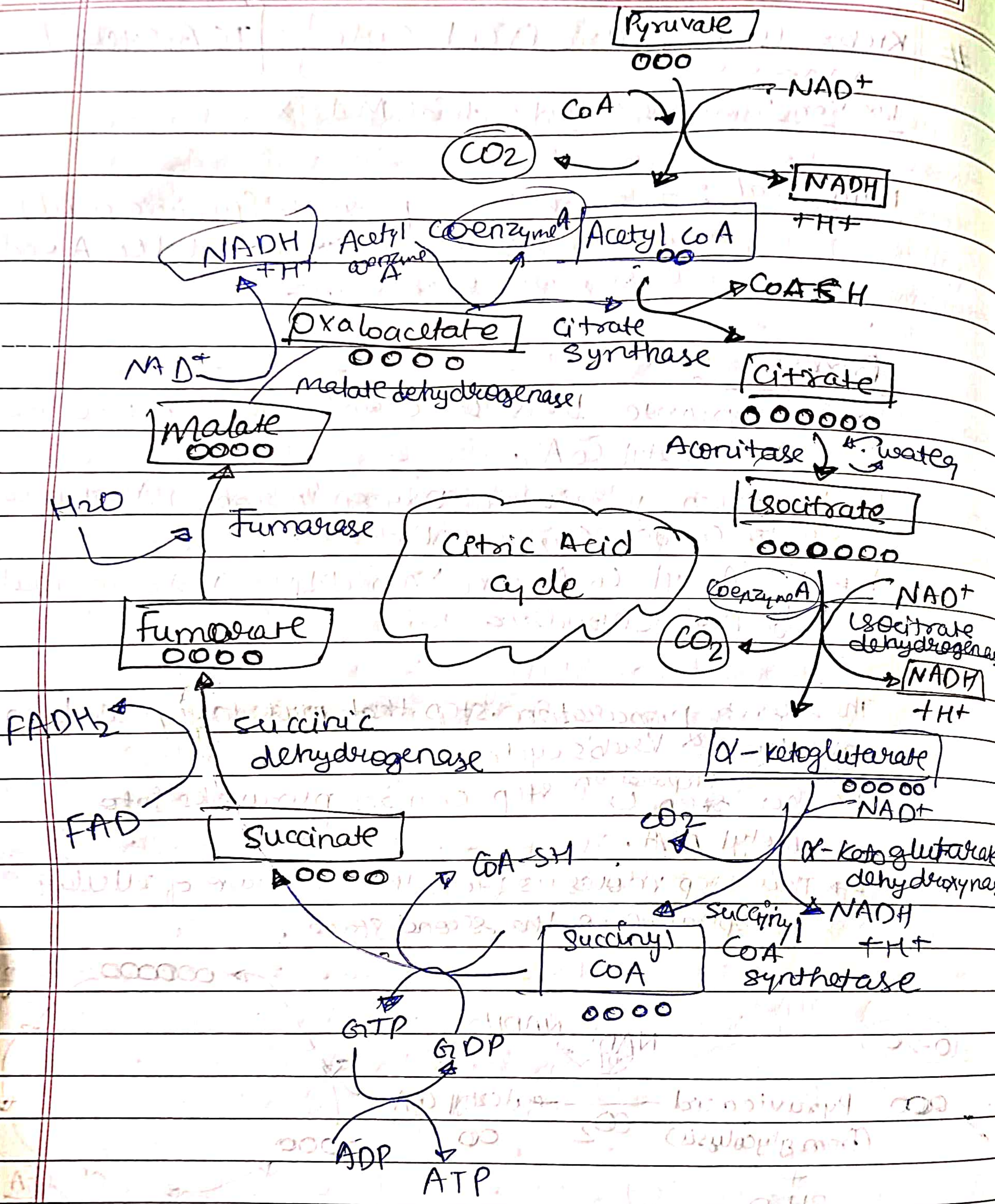
Pyruvate
000
CoA
NAD+
CO2
NADH
+H+
NADH
+H+
Acetyl coenzyme A
Coenzyme A
Acetyl CoA
00
CoASH
Oxaloacetate
0000
Citrate synthase
NAD+
Malate dehydrogenase
Citrate
000000
Malate
0000
Aconitase
water
H2O
Fumarase
Isocitrate
000000
Citric Acid cycle
Coenzyme A
NAD+
Isocitrate dehydrogenase
CO2
NADH
+H+
Fumarate
0000
FADH2
succinic dehydrogenase
α-ketoglutarate
00000
NAD+
CO2
FAD
Succinate
0000
CoA-SH
α-Ketoglutarate dehydroxynase
Succinyl CoA synthetase
NADH
+H+
Succinyl CoA
0000
GTP
GDP
ADP
ATP

$2\ Acetyl\ CoA + 6NAD^+ + 2FAD + 2ADP + 2Pi + 2H_2O$

$\downarrow$

$4CO_2 + 6NADH + 2FADH_2 + 2ATP + 2CoA$.

Reactants — Products

Products From Glycolysis

Pyruvate to Acetyl CoA	→ 4 carbon Molecule to be recycle
ADP	→ ATP
Oxygen	→ CO_2
FAD	→ $FADH_2$
NAD+	→ NADH

Significance of Kreb's cycle

- Krebs cycle or citric acid cycle is the final pathway of oxidation of glucose, fats & amino acids
- It is the major source of ATP production in the cells A large amount of energy is produced after complete oxidation of nutrients
- It plays an important role in gluconeogenesis & lipogenesis & interconversion of amino acids.
- Many intermediate compounds are used in the synthesis of amino acids; nucleotides, cytochromes & chlorophylls etc.
- Regulation of Kreb's cycle depends on the supply of NAD^+ & utilization of ATP in physical & chemical work.

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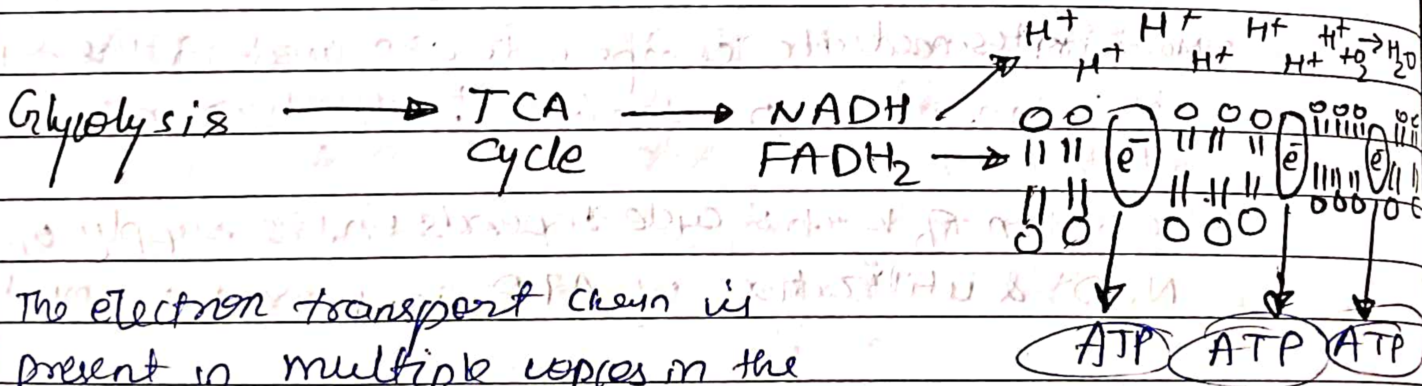
Electron Transport chain

An electron transport chain is a series of protein complexes & other molecules that transfer electrons from electron donors to electron acceptors via redox rxn & couples this electron transfer with transfer of protons across a membrane.

This causes Hydrogen ions to accumulate within the matrix space. Therefore a concentration gradient forms in which hydrogen ions diffuse out of the matrix space by passing through ATP synthase.

The current of hydrogen ions powers the catalytic action of ATP synthase, which phosphorylates ADP, producing ATP.



- The electron transport chain is present in multiple copies in the inner mitochondrial membrane of eukaryotes & the plasma membrane of prokaryotes

- The electron transport chain is the last component of aerobic respiration & is the only part of glucose metabolism that uses atmospheric oxygen

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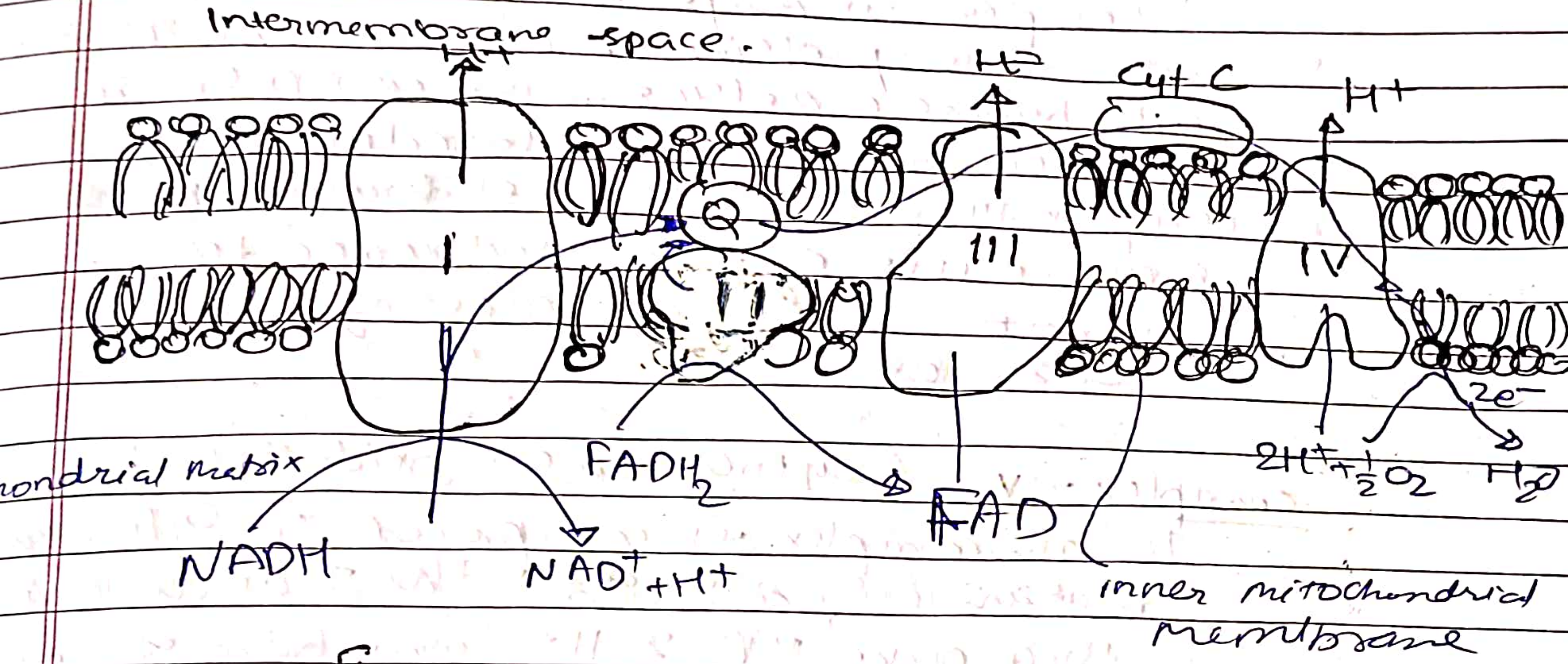
there are 4 complexes composed of proteins



Complex-1 [NADH dehydrogenase]

To start, 2 ē are carried to 1st complex aboard NADH. This complex (NADH dehydrogenase), labelled I is composed of flavin mononucleotide (FMN) & iron sulfur (Fe-S) containing protein. Complex-1 can pup 4 H^+ ions across membrane from matrix into intermembrane space

Q & complex-II [succinate dehydrogenase

complex-II directly receives $FADH_2$, which does not pass through complex-1. The compd connecting Ist & IInd complexes to 3rd is ubiquinone (Q). It delivers its electrons to the next complex in the electron transport chain. Q receives the electrons derived from NADH from complex 1 & ē from derived $FADH_2$ from complex-II

Complex – III (Cytochrome bc_1)

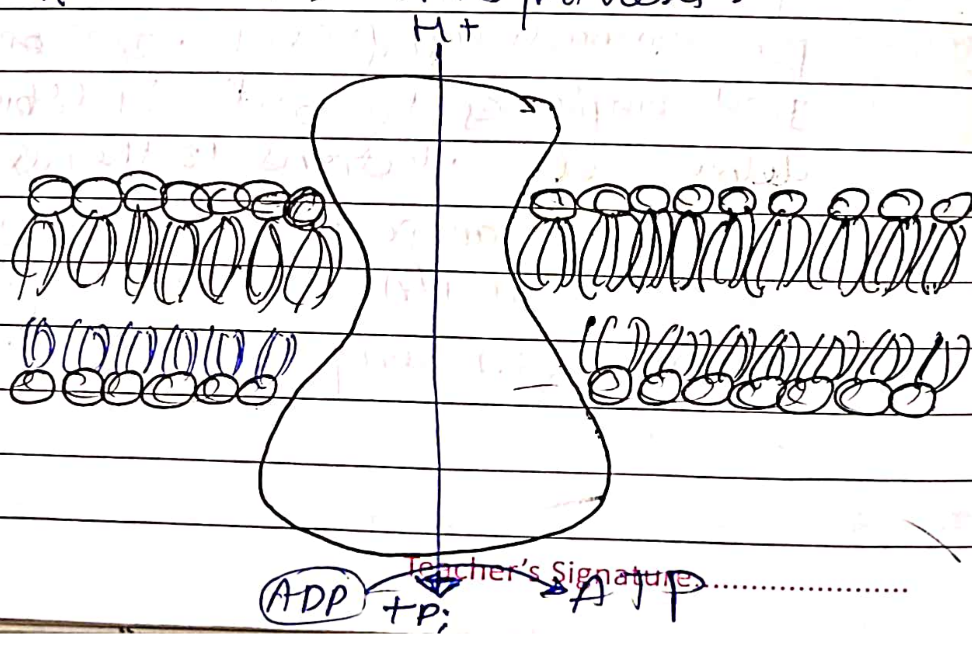
3rd complex is composed of cytochrome B, another Fe-S protein, Rieske center (2Fe-2S center) & cytochrome C proteins ; this complex is also called cytochrome oxidoreductase, Complex III pumps protons through membrane & passes its e⁻ to cytochrome C for transport to 4th complex of proteins & enzymes

Complex – IV (Cytochrome C oxidase)

The 4th complex is composed of cytochrome proteins C, a & a_3. The reduced oxygen then picks up 2 H+ ions from surrounding medium to make water (H_2O)

7) ATP synthase : Machinery to synthesize ATP :–

ATP synthase uses the proton gradient energy to produce ATP. It is the release of the energy in the gradient back through the membrane through the protein ATP synthase that drives ATP synthesis.



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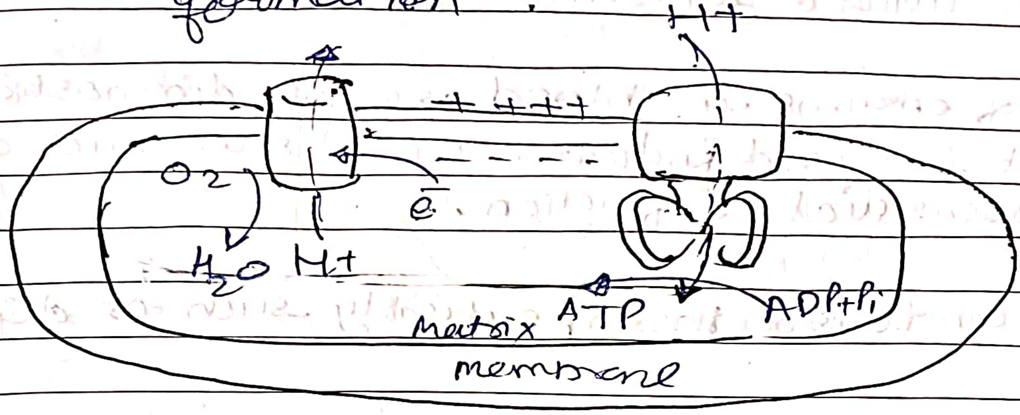
The chemiosmotic Hypothesis

↳ Proposed by Peter Mitchell in 1960's (Nobel Prize in 1978)

↳ A proton concentration gradient serves as the energy reservoir for driving ATP formation.



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Beta oxidation

Lipid metabolism

Fatty acids have 4 major physiologic roles in cell :
→ 1) Building blocks of phospholipids and glycolipids
2) Added onto proteins to create lipoproteins which targets them to membrane locations
3) fuel molecules - source of ATP.
4) Fatty acid derivatives serves as hormones & intracellular messengers

Absorption & Mobilisation of fatty acids

- Most lipids are triacylglycerols some are phospholipids & cholesterol.
- Digestion occurs primarily in the small intestine.
- Fat particles are coated with bile salts (amphipathic) from gall bladder.
- Degraded by pancreatic lipase (hydrolyzes C-1 & C-3 → 2 fatty acid & 2 mono acyl glycerol)
- can then be absorbed by intestinal epithelial cells bile salts are recirculated after being absorbed by the intestinal epithelial cells.
- in the cells fatty acids are converted by fatty acyl CoA molecules

- Phospholipids are hydrolyzed by pancreatic phospholipases primarily phospholipase A2
- cholesterol esters are hydrolyzed by esterases to form free cholesterol which is solubilized by bile salts and absorbed by the cells.
- lipids are transported throughout the body as lipoproteins.
- Lipoproteins consists of a lipid (triacylglycerol, cholesterol, cholesterol ester) core with amphipathic molecules forming layer on outside

Lipoproteins

- Both transported in form of lipoprotein particles which solubilize hydrophobic lipids and contain cell-targeting signals.
- Lipoproteins classified according to their density
  1) Chylomicrons - contain dietary triacylglycerols
  ii) Chylomicron remnants - contain dietary cholesterol ester.

  iii) very low density lipoproteins (VLDLs)
  Transport endogenous triacylglycerols which are hydrolyzed by lipoproteins lipase at capillary surface.

IV) Intermediate-density Lipoproteins (IDL)

Contain endogeneous cholestrol esters, which are taken up by liver cells via receptor-mediated endocytosis & converted to LDLs.

V) Low Density Lipoproteins

Contains endogeneous cholestrol esters, which are taken up by liver cells via receptor mediated endocytosis major carrier of cholestrol in blood, regulates de novo cholestrol synthesis at level of target cell.

VI) High density Lipoproteins

contain endogeneous cholestrol esters released from dying cells and membranes undergoing turnover.

Storage of fatty acids

- Triacyl glycerols are transported as chylomicrons & VLDLs to adipose tissue; there, they are hydrolysed to fatty acids, which enter adipocytes & are esterified for storage.

- Mobalization is controlled by hormones particularly epinephrine, which binds to adrenergic receptors on adipocyte membrane

→ protein kinase A activated → phosphorylates hormone sensitive lipase ← converts triacyl glycerols to free fatty acids & monoacyl-glycerol

- Insulin inhibits lipid mobilization (eg. reciprocal regulation)
- Monoacylglycerols formed are phosphorylated & oxidised to DHAP (intermediate of glycolysis & gluconeogenesis.

glycerol —(ATP → ADP; glycerol kinase)→ glycerol 3-phosphate —(NAD → NADH + H^+; glycerol phosphate dehydrogenase)→ dihydroxy acetone phosphate

Can be converted to glucose (gluconeogenesis) or pyruvate (glycolysis) in the liver.

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Fatty acid Oxidation (Beta oxidation) (β-oxid^n)

→ Fatty acids are degraded by oxidation of β-carbon by β-oxid^n.

→ Pathway that removes 2-C units at a time
→ acetyl CoA → citric acid cycle → ATP.

→ 3 stages of β-oxid^n

1) Activation of fatty acids in cytosol catalyzed by acyl CoA synthetase; two high energy bonds are broken to produce AMP.

2) Transport of fatty acyl CoA into mitochondria via carnitine shuttle

3) β-oxid^n → cyclic pathway in which many of same enzymes are used repeatedly.

Fatty acid Metabolism

- lipolysis is carried out by lipases
- once freed from glucose, free fatty acids can enter blood and muscle fiber by diffusion.
- β-oxid^n splits long carbon chains of fatty acids into acetyl CoA. which can eventually enter TCA cycle.

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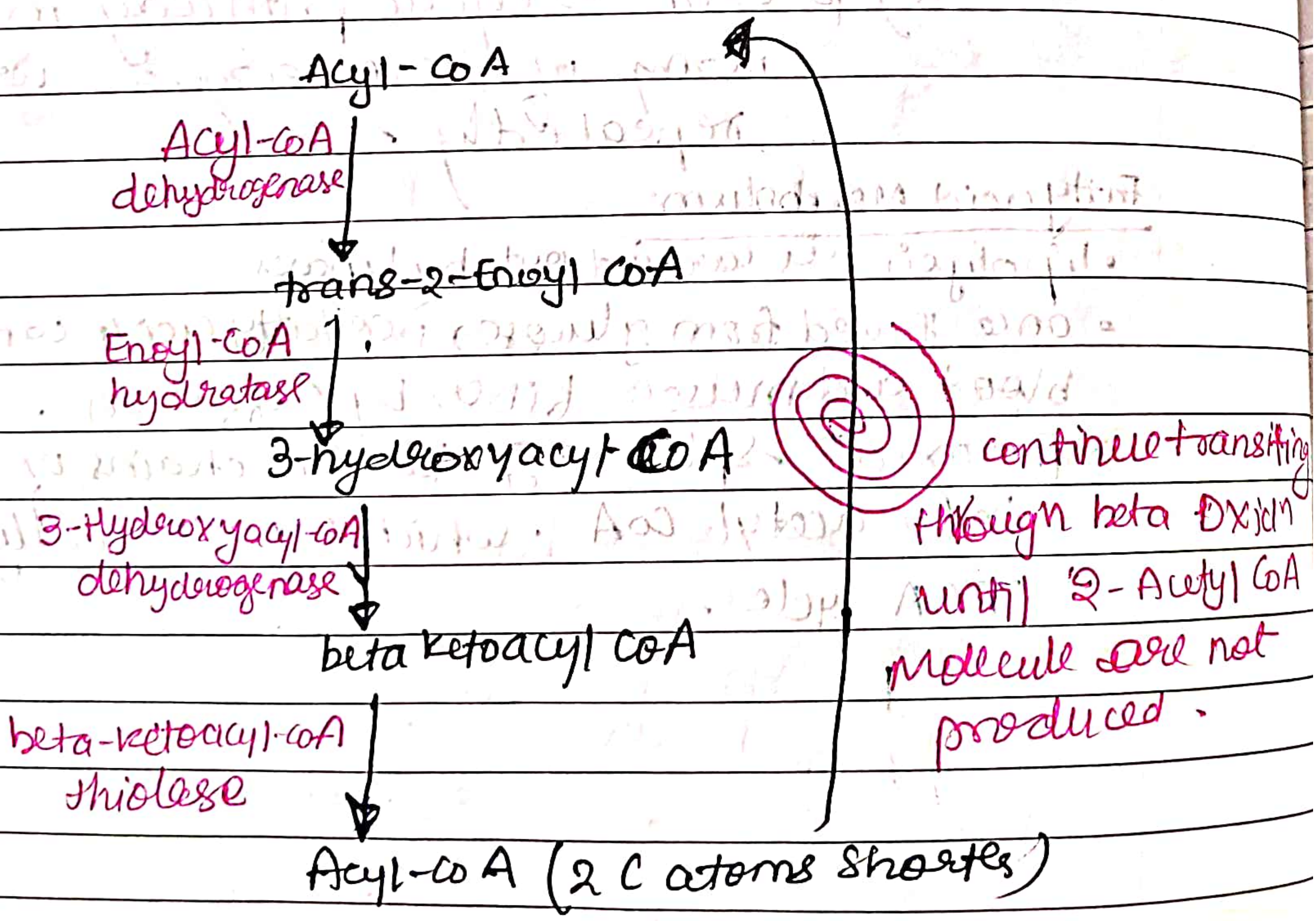
Briefly β-oxidⁿ or lipolysis of free fatty acids is as follows:

1. Dehydrogenation by acyl-CoA dehydrogenase, yielding 1 $FADH_2$.
2. Hydration by enoyl-CoA hydratase
3. Dehydrogenation by 3-hydroxyl-CoA dehydrogenase yielding 1 NADH
4. Cleavage by thiolase, yielding 1 acetyl CoA and a fatty acid that has now been shortened by 2 carbons (acyl-CoA)



Fatty acid degradation includes :

- → Activation & transport into Mitochondria (by Carnitine-palmitoyl transferase-I) (CPT-I)
- → β oxidn
- → ATP generation
- → Regulation of fatty acid oxidn

Photosynthesis

Photosynthesis is the process in which phototrophs convert light energy into chemical energy, which is later used to fuel cellular activities. The chemical energy is stored in the form of sugars which are created from water & CO_2.

$$CO_2 + H_2O \xrightarrow{light} [CH_2O] + O_2$$

$$2H_2A + CO_2 \xrightarrow{light} 2A + CH_2O + H_2O$$

$$6CO_2 + 12H_2O \xrightarrow{light} C_6H_{12}O_6 + 6H_2O + 6O_2$$

($C_6H_{12}O_6$ → glucose)

→ within chloroplast there is membranous system consisting of grana, the stroma lamellae, & matrix stroma. There is a clear division of labour within the chloroplast.
The membrane system is responsible for trapping light energy and also for synthesis of ATP & NADPH.

→ In stroma, enzymatic reactions synthesise sugar, which in turns forms starch.

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Light Reaction (Photochemical phase)

- Light absorption
- water splitting
- oxygen release
- formation of high energy chemical intermediates (ATP & NADPH

Pigments → Two descrete photochemical light harvesting complexes (LHC) within Photosystem I (PS I) & Photosystem II (PS II)

Each photosystem has all the pigments except one molecule of Chlorophyll α) forming a Light harvesting system called antennae.

PS I → P700

PS II → P680

→ Carbon fixing rxn

dark reaction : It is light independent process in which sugar molecules are formed from CO_2 & water molecules It occurs in stroma of . of chloroplast where they utilize products of light reaction

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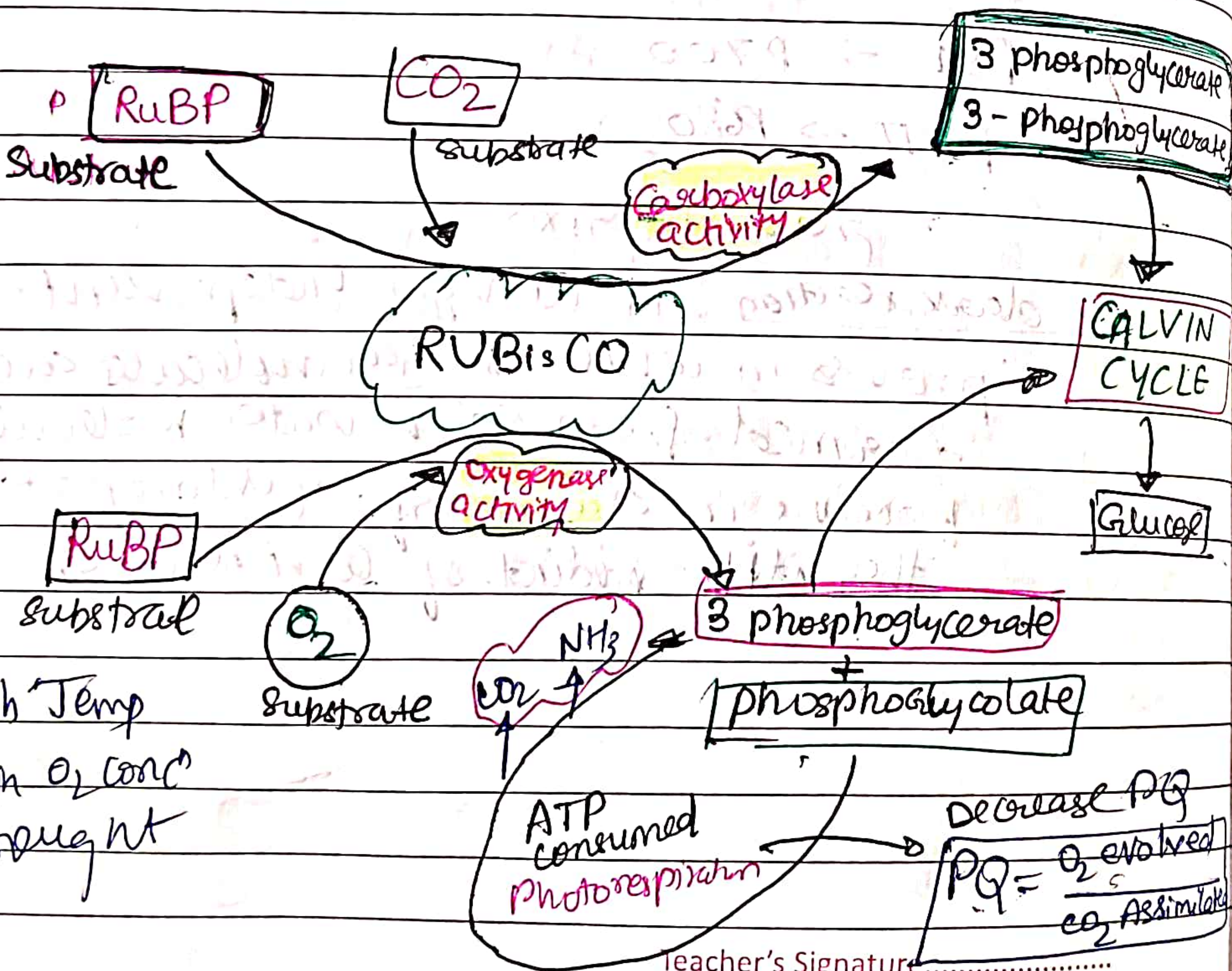
Photorespiration :-

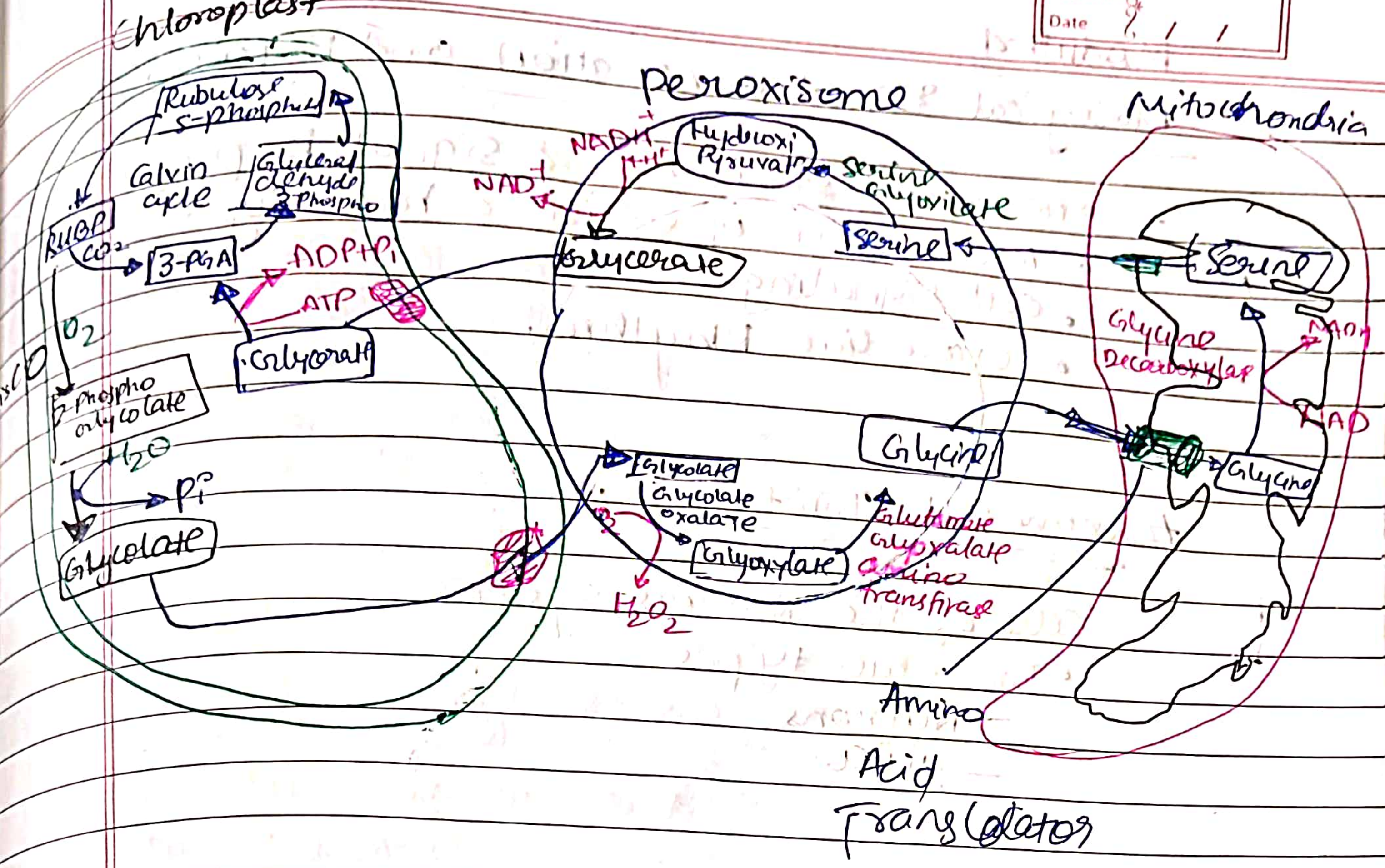
- Plant Metabolism
  - Oxygenation of RuBP by RUBISCO enzyme
  - RUBISCO Enzyme fixes O_2 instead of CO_2
  - Light dependent evolution of CO_2

RUBISCO

RuBisCO : Ribulose, 1,5-bisphosphate carboxylase / oxygenase.



- High Temp
- High O_2 conc
- Drought


Chloroplast
Peroxisome
Mitochondria
Rubulose 5-phosphate
Calvin cycle
Glyceraldehyde 3 Phospho
RUBP
CO2
3-PGA
ADP+Pi
ATP
Glycerate
O2
2-Phospho glycolate
H2O
Pi
Glycolate
NADH
NAD+
Hydroxi Pyruvate
Serine Glyoxilate
Serine
Glycerate
Glycolate
Glycolate oxalate
O2
H2O2
Glyoxylate
Glycine
Glutamate glyoxalate Amino transferase
Serine
Glycine Decarboxylase
NADH
NAD
Glycine
Amino Acid Translator