

Theory of Evolution (M.A.)



- Overproduction :- Most species produce far more offspring than are needed. (while only a small fraction make it).
- Competition :- Living space & food are limited so offspring of each generation should compete (according to the small fraction).
- Variation (Genetic) : Characteristics in individuals in any species are not exactly alike. (Darwin studied finch - a bird in different islands). They have different beaks due to different eating habits.
But how is it happening? Think!

T G A G C T A .

Hint : Mutation (change in the DNA sequence).

- Adaptation : An 'inherited trait' that increases an organism's chance of survival & reproduction in a given environment.
- Natural selection :- Nature / environment selects for. During organisms with better suited traits to survive & reproduce..
- speciation :- Over many generations, favorable adaptation (in a particular environment) gradually accumulates in a species & bad ones disappear. This takes many many generations to do so. (?) (not explained)

Obs 1 :- Individuals have potential for rapid reproduction
Obs 2 :- Limited resources
Conclusion 1 :- Survival of the fittest.

Obs 3 :- Genetic variation
Conc 2 :- Evolves to adaptation.

Obs 4 :- Variations continuously occur
Conc 3 :- After so many generations all these variations accumulate & we get a new species.

The theory states :-

- 1) Evolution
- 2) Natural Selection
- 3) Survival of the fittest.

Ex :- Usually 'natural selection' takes hundreds or thousands of years to produce a noticeable change in phenotype.

(a) Industrial melanism :- Before & after industrial revolution. (Trunks of trees became black. So, moths became black from white to evolve to camouflage).

(b) Bacteria :- Bacteria ~~replicate~~ at a very fast rate. a new generation every 20 minutes. Antibiotics easily wipe out most bacteria.

Scientific Evidence of Evolution :-

1) Fossil Record :-

Chronological Appearance of organisms -
Example : bacteria - invertebrates - fish - amphibians - reptiles - birds - mammals.

2) Comparative Anatomy :- Homologous structures - structures that are similar in function & similar in anatomy. (This suggests similar anatomy = common ancestor).

Morphological diversity - Forelimbs of mammals are constructed from the same skeletal elements.

c) Comparative embryology - Closely related organisms go through a shared program of embryonic development. For eg:- Human embryos till date have gill pouches & tail!

Q1 Comparative Biochemistry / Molecular Biology

QUESTION Does environment create genetic variation between individuals?

Ans. Environment does not create it, they only choose it.

> Does survival of the fittest mean that only the fastest, smartest & strongest survive?

Ans. No, only the environment decide if they have an edge over the rest.

> Do individuals evolve?

Ans. No, its population that evolves

Q2 Does natural selection breed perfection?

Ans. No, it only gives you that is suitable for this environment.
(HW - find examples).

> Did humans evolve from monkeys?

Ans.) No, we have co-evolved from monkeys.
We must have that a common ancestor.

- Competition . → Adaptation
- Genetic variation .
- speciation

Task of digestive system + convert raw materials of food into nutrients & energy.

Lat \rightarrow Mouth, Mouth \rightarrow Oesophagus \rightarrow Stomach

Pancreas \leftarrow Gall bladder \leftarrow Liver
 ↓
 (stores bile), (makes bil).

Small intestine \rightarrow Large intestine \rightarrow Rectum - anus
 (alias colon).

DIVISION

- > Gastro-intestinal track. (30-40 m).
- > Liver, Gallbladder, Pancreas
- > Enzyme, Hormones, Nerves & Blood
- > Mesentery: — Large stretch of tissue that support & positions all the digestive organs in abdomen.
- > Glands of our mouth secrete saliva just by anticipation - even before food entry!
- > Saliva mixed ~~to~~ helps in mechanical breakdown of food (bolus (moist food)).
- > Trigger peristalsis. (in oesophagus).
We can even eat against gravity due to this!
- > Mixing with gastric juice, bolus is broken down in the contractions of the stomach thus forming a liquid called chyme.
- > Bile produced by liver is added to chyme in small intestine where it absorbs all the nutrients & put in blood stream.
Villi & microvilli contributes to the large surface area of small intestine

Left over food enter large intestine where they suck off the remaining nutrients producing solid stool.

* Homeostasis - A state of balance in the body.

Body temp. = 37°C .

Blood glucose \rightarrow 80-100 mg/dL.

Imbalance \Rightarrow disease.

Less blood sugar \rightarrow hypoglycemia.

normal,

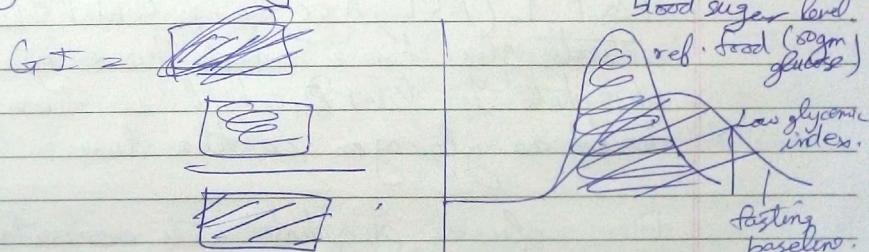
more blood sugar \rightarrow hyperglycemia (diabetes).

NORMAL

FASTING < JUST ATE >

Ranking carbohydrates by different blood glucose level \rightarrow glycemic index (GI).

High GI \rightarrow rapidly digested & absorbed \rightarrow rapid rise in blood sugar level



high GI : ≥ 70
medium GI : $56-69$
low : ≤ 55

Blood sugar in the body is regulated by liver & pancreas.

- > Liver stores glucose in form of glycogen.
- > When we are fasting, pancreas releases glucagon which breaks down glycogen in liver to glucose.
- > insulin-action on glucose transport is thought to be by endocytosis mechanism.
- > Diabetes occur because pancreas does not produce pancreas. (Type 1).
- > (Type-2) — If the interaction between insulin & receptors is inhibited due to some reason then type-2 diabetes occurs.

→ Liver detoxify substance that are harmful to our body.

- > When insulin binds with receptor, it releases IRS-1, which creates the enzymes, SREB-1 (ACL, ACC, PAs) which also activates glycokinase which have glucose phosphate in liver which is then stored as glycogen in the liver.

Else glucose phosphate gets converted to pyruvate which can go to mitochondria to produce ATP.

In mitochondria TCA cycle performs which generates ATP & forms citrate.

This citrate is acted upon by ACL, ACC & PAs which converts it into VLDL (Very Low Density Lipoprotein).

This formation is not a good thing but it is + dangerous because most of the carbohydrate goes to other parts of the body.

- * When someone consumes alcohol, liver should work ~~more~~ 4 times more than normal
- * ethanol does not need insulin to enter into the cell.
- When alcohol enters the body it gets converted to acetaldehyde & then ~~is~~ into Reactive oxygen species (ROS) ($\text{O}_2^{-\cdot}$), protein damage, aging, (radical is too reactive!). cancer

Else acetaldehyde \rightarrow acetate \rightarrow mitochondria.
Here TCA cycle happens, ester is formed & VLDL fat is formed by ACe, ACh & PAs but in large amount! So people get beer belly.

If there are even few citrate, then got converted lipid droplets \rightarrow alcoholic fatty liver disorder.

Also, ROS & ethanol can activate JNK-
This inactivates IRS-1! (which is needed for glucose metabolism). Also causes inflammation.

- ~~Sugars~~ ^{toxic}
- > Sugar = glucose + fructose
Fructose 100% goes to liver.
 - * Liver should work 5 times more than normal.
& sugar can enter without permission into liver.

> Fructose after entering body is acted upon by enzyme fructokinase → pyruvate
sugar belly. ← extreme miochondria overacid formation

* Our body never wants to burn fat. It only wants to burn glycogen.

> Green vegetables like broccoli, grapefruit, walnuts, lemons, sprouts, avocados, carrots, beets, leafy greens, green tea can clean up the liver.

This because it contain lots of potassium.

- IRS - 1 (Insulin receptor substrate).
- ATP citrate lyase (ACL)
- acetyl-CoA-carboxylase (ACe)
- fatty-acid synthase (FAS).
- C-Pun-N-Terminal kinase (CINK)
- sterol regulatory element

Evolution:

Tamark proposed 'adaptive' evolution.
Darwin proposed 'random' evolution.

3 domains of life:

Bacteria, Archaea, Eukarya.

Common Ancestor.

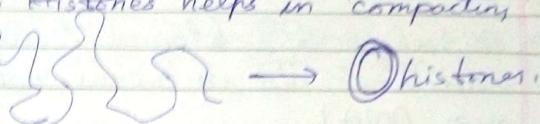
Eukaryotic cells evolved from prokaryotes.
Bacteria & Archaea are prokaryotes.

Earliest eukaryote → 1.5 billion years ago.

Three major changes for evolution of eukaryotes:

i) DNA protein complexes (chromosomes) developed

At DNA has no boundary in prokaryotes while that of eukaryotes have histones (protein molecules). Histones helps in compacting the DNA.



ii) Intracellular membrane: Prokaryotes have no membrane inside the cell. While in eukaryotes, there is a membrane even within the DNA. So, it is completely separated from the surroundings.

iii) Endosymbiosis: How the specialised organelles came into existence is called endosymbiosis.

ENDOSYMBIOSIS

Eukaryotes need more energy to work. The ancestral eukaryote was anaerobic (\because there was no oxygen). It developed a membrane around the DNA. Over this is the nuclear wall outside the nucleus is called cytoplasm.

This eukaryote engulfed an ~~anaerobic~~ bacteria. So ~~the~~ bacteria started using oxygen & cell ~~that~~ too was in advantage since it was anaerobic. This bacteria evolved to today's 'mitochondria'.

So, now this eukaryote can use oxygen which is more energy-efficient.

Now, this cell engulfed a cyanobacterium which has chlorophyll! It does photosynthesis & so now this cell can produce its own food! This cyanobacterium evolved to today's chloroplast.

- * Endosymbiosis theory is supported by the following evidences :-
- > Mitochondria & chloroplast are two additional sites in a cell who have their own DNA!
- > ~~And~~ This DNA is not like the DNA of the nucleus! But this is very similar to bacterial DNA.
- > ~~Mitochondria~~ They also have their own ribosomes (which are needed to make proteins). ~~and~~ (similar to bacterial ribosomes).
- > They replicate by binary fission - not mitosis (like a bacteria!).

~~There is so much diversity in eukaryotes. Why is this?~~

Explanation: Two words: Mutation & gene duplication.

copy = alleles. (Bacteria divide once
Page in 20 minutes)

Species A

Gene 1

Function 1

Mutation

Species B

Gene 1*

Function 1

Same DNA sequence in different organisms
→ homologues.

But if they are in same organism as
two copies → gene duplication

↓
duplic.

Gene 1

Gene 1 copy

Function 1

Function 1

Mutation

] Mutation of the copy

Gene 1

Function 1

Gene 2

Function 2

> ~~Ques~~ How does a cell know its size? Why does the size remain the same? [The cells are of the same size for a rat & a elephant, why?].

~~A~~ Surface area to volume ratio is an important factor that governs this size. It needs to maintain this ratio to ~~expel~~ expel an equal proportion of cells' waste.

Most large-bacteria either maintain a high surface-to-volume ratio by being long & thin.

After reaching this ideal ratio, they either divide or stop metabolism.

~~→ Fts 2~~ is an important DNA content. If we remove this protein from the cell, the bacteria become bigger & bigger. So the cell does not know how big to become.

→ Diffusion ~~also~~ regulate the size.

→ ~~Bacteria~~ If one-cell (eukaryote) is able to do everything why did multi-cellular eukaryotes evolve (like us)?

The early steps of evolution was the association of unicellular organism to form colonies. They divide but not separate.

Benefits :-

1) Increased size - It is easier to get nutrients into & waste products out of, a large body.

2) Division of labour - Specialization.

3) Longer lives - The life span of a multicellular individual is not limited to the life span of a particular cell. They can live & produce offspring, for a longer period of time.

4) Escape predators by locomotion.

→ One ~~bacterium~~ found recently & interestingly makes the surface area to volume ratio by reducing the volume. (1) It is an example of the largest bacteria because there is nothing inside the cell membrane.

Binary fission - prokaryote

Mitosis or meiosis - eukaryote

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Cell theory :-

- > Cells are fundamental unit of life.
- > All organisms are unicellular / multicellular.
- > Cells arise from pre-existing cells.
- 'Cell' → coined by Robert Hooke. (Looked dead cell)
- Anton van Leeuwenhoek → first to view living cells.
Also credited for first simple microscope.

Matthias Schleiden, Theod'

Cell of prokaryote :-

- 1) Cytoplasm : Most enzymes are harboured. Most reactions in for energy.
- 2) Ribosomes : Smaller than eukaryotic ribosomes. Scattered in cytoplasm. DATA.
- 3) Cell envelope : Three layers :-
 - (a) Cell membrane → covering cell membrane.
 - (b) Cell wall : covers ~~before~~ cell membrane
 - (c) Capsule : covers cell wall.
- 4) Flagella → locomotory structure. (Generates movement. Generate Energy!).
- 5) pili → Required to attach to a surface. (Hair-like structures).
- In binary fission, first the genetic material is divided into two, then the septum is formed & the two diff. cells arise.
- Q) Then what happens to mitochondria & chloroplast during binary fission?

A) They replicate independently. It happens before septum formation.

In laboratories generation time (G) of an organism is given by $\frac{t}{n}$ where $n = \text{no. of times the division happen in time } t$.

For $E. coli$, $G = 20 \text{ min}$.

Eukaryotic Cell :-

One similarity of prokaryotic & eukaryotic cell is that both have a cell membrane.

1) Cell membrane

Why is it needed? → To define boundary
To maintain diff. between cytoplasm & extracellular environment.

Plant Cell

- > Cell wall ✓
- > Large vacuole
- > Chloroplast ✓

Animal Cell

- No cell wall.
- Small vacuole
- No chloroplast.

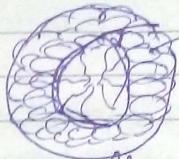
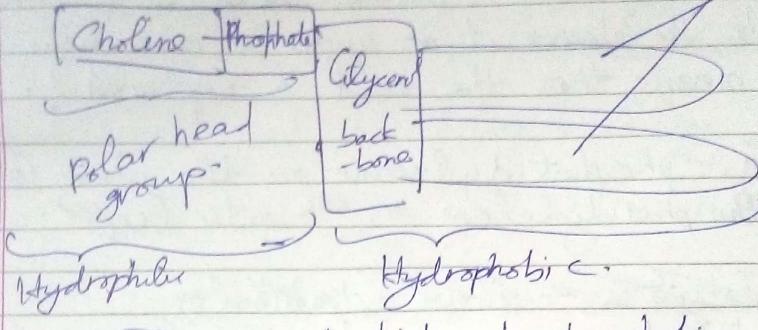
Membrane is composed of ~~phos~~ phospholipids & sterols. There are integral & peripheral proteins. There are glycolipids & glycoproteins ~~with~~ carbohydrates. Thickness - 8 nm.

Electro-microscopy ~~lets us~~ used to visualize ~~more~~ cell membrane.

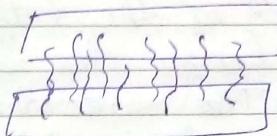
This membrane is flexible. ~~There should not~~
It should be self-sealing (in case of a rupture). ~~It needs to be~~ permeable to solutes.
It should be of fluid-mosaic model

These membranes are not merely passive barriers.

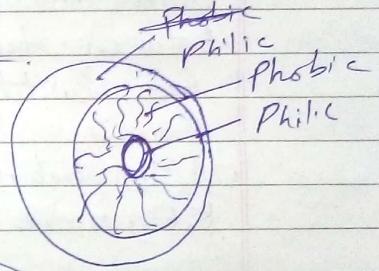
Lipid molecule :



Micelle



Bi layer sheet



Liposome

Self-assembly
of molecules to hide
hydrophobic part from water
(from extracellular & water from cytoplasm),

Liposome

Membrane lipids are amphipatic (both polar & non-polar at the same time).

> All cell organelles are bounded by membranes in eukaryotes. All these membranes are composed of phospholipids. The levels of ~~cholesterol~~ cholesterol, sphingolipids, cardiolipin, ~~proteins~~ etc. are different for every one. (Type)

~~Phagocytosis - mechanism by which extracellular substances can enter the cell.~~

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Membranes are asymmetric.

- If we stain a particular ~~content~~ content of the membrane which is inside the cell & we are able to observe it ~~in~~ under a microscope, it means that the cell is ruptured!

Eg:- phosphatidylserine on the inner leaflet.
Phosphatidylcholine on the outer leaflet.

~~Phagocytosis allows extracellular~~
Fluid-mosaic model - ~~the~~ Cell organelles are more mobile inside.

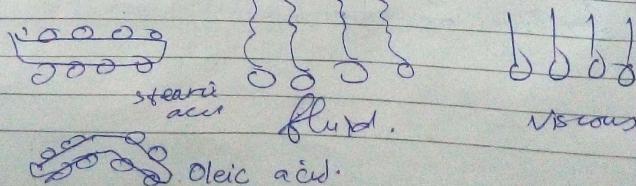
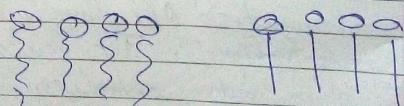
1) The length of the fatty acid tail can vary. The longer the length the more the interaction. The more strongly bonding between two ~~tail~~ acid molecules. So less fluidity.

2) Temperature: Higher the temp, higher the KE, more fluid.

3) Cholesterol content of b layers. It has a rigid structure. It comes in between two lipid molecules. More static.

4) The degree of saturation of fatty acid tails → less fluidity. Then, the tail becomes a linear saturated.

Double bond causes bending.

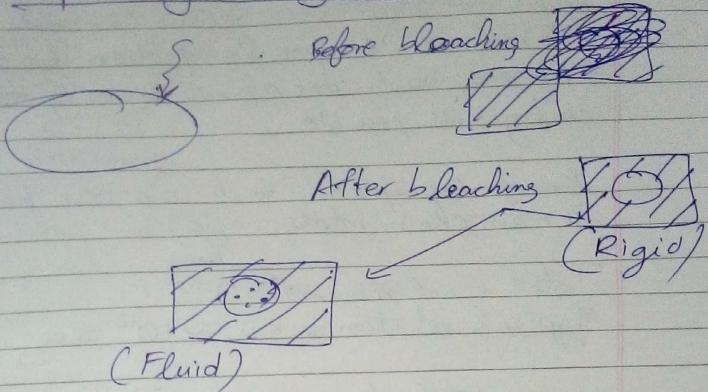


Laser beam (high intense) can bleach the cell membrane.

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FRAP (Fluorescence Recovery after photo bleaching)

Lipid Bilayer is dynamic.

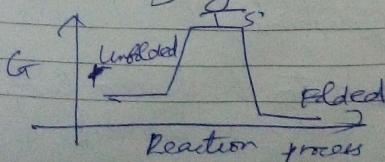


SATPATTI

- > Protein is inactive in denatured (unfolded) state.
- > It is the folding of proteins that gives protein their characteristic function.
- > Protein can be unfolded by urea, guanidine hydrochloride & heat → These are called denaturing agents.
- > Extent of protein can be measured by determining residual function of protein.
- > At MP, denaturation = 50%.
- > The sequence of arrangement of amino-acid hydrophilic - hydrophobic factors determine the folding of protein.

Anfinsen's Exp.

- > Proof: Renatured ribonuclease after denaturation by connecting sulfide bridge. (By removing the denaturing agent - circa 2 mercapto ethanol)



> Cys residues can form disulfide bonds.

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How proteins fold?

Protein :- There are 101 amino-acids.

∴ There are 100 possible peptide bonds.

> Peptides bonds are planar & only trans config. is possible.

amino acid

At ~~each~~ Assumption: Each aa can have
3 main chair rotation angle.

Total no. of minimum ^{rotations} = 3^{100}

Typical rotation takes $\sim 10^{-12}$ sec.

∴ So total time = 1.6×10^{27} (!).

But it is found that small proteins fold spontaneously on a millisecond or even microseconds time scale!

Levinthal's paradox !!



Reptation ~~problem~~

Solution :- Folding isn't random.

> ϕ, ψ not all are stable.

Sickle-cell disease :-

So, it cannot carry oxygen this clogglots RBC for the disease - in the blood vessel.



Linus Pauling found that the problem lies in the fact that one amino-acid is different. One glutamate (^{hydrophilic}) is converted into valine (^{hydrophobic}).

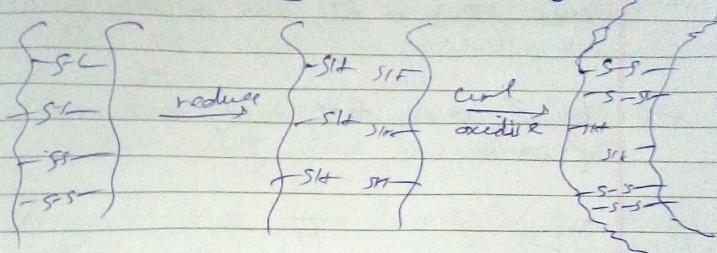
So, they stick together & form lumps to escape water in blood!

> Ribbon diagram → best way to represent protein.

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Hair Chemistry :-

Hair is made of keratin.
They are ~~one~~ α -helix. When two of them come together, they form a tertiary structure.



Human Haemoglobin
Made up of α & β units.

Sources of Requirement of protein

Male \rightarrow 56 g/day

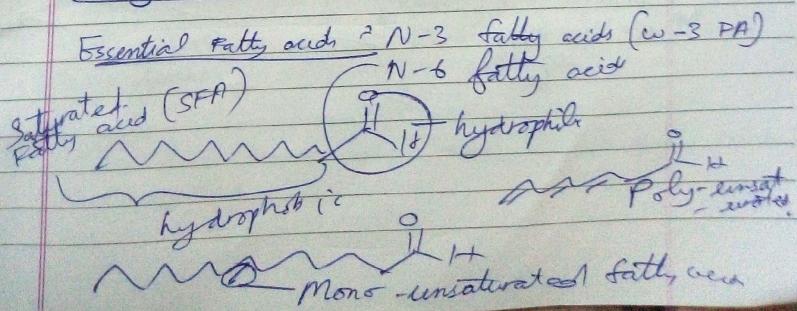
Female \rightarrow 46 g/day

Essential amino acids (9) \rightarrow Histidine, isoleucine, leucine, tyrosine, methionine, phenylalanine, threonine, tryptophan, valine.

Complete protein : - Supply all essential a-a.
Incomplete " : - Do not " " " "

Fats with structural & Biological Imp.

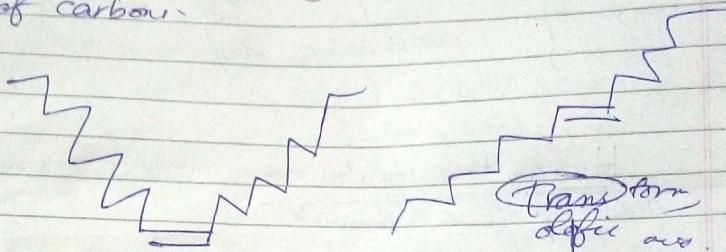
Fatty Acids \leftarrow SFA \rightarrow MUFA \rightarrow PUFA.



* Lipids are non-polar (hydrophobic) compounds soluble in organic solvents

Membrane

- Double bonds in fatty acids usually have cis nature.
- Naturally occurring fatty acids, ^{usually} have even no. of carbons.

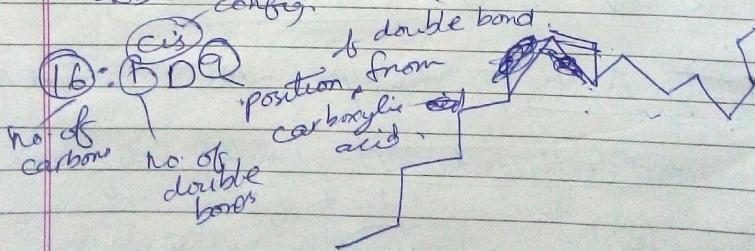


* Body needs cis protein

Behave like saturated fat

→ So, if heat enters then in the body, cis double bond gets hydrogenated then the protein becomes trans (more stable) immediately.

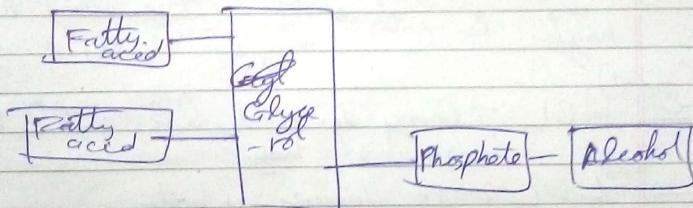
∴ Hence, we get trans fat. This is ~~BAD~~.



omega 3 (alpha-linolenic acid) & omega 6
are two essential fatty acids.

- SFA are solid at room temp.
- Melting point depends on chain length & degree of saturation.
 - 1) Unsaturated fatty acids have lower MP.
 - 2) Shorter fatty acids have lower MP
- Cis double bonds → low MP. (due to less intermolecular packing).
- Lipids →
 - Phospholipid → glycerophospholipid
 - glycerol → sphingophospholipid
 - glycerol → glycolipid
 - cholesterol → sphingolipid

Phospholipid



Glycolipid ← Sphingosine + sugar.

glycerol + 3 fatty acids → triglyceride.

CITOLSTEROL → Lipid based on steroid nucleus.
(hydrophobic)

> Cholesterol has one polar group, a hydroxyl makes it amphiphatic.

> Almost all cholesterol in our body is made by our body.

→ Body makes 3g / day.

Why is this needed?

- 1) Cell membranes (Brain: lots & lots of cholesterol)
 - 2) Bile production.
 - 3) Vitamin D, A, K₂, E.
 - 4) Adrenal hormone (stress).
 - 5) Sex hormone
 - 6) Myelin synthesis (lipid layer around nervous system).
 - 7) Helps immune system (control w/o). system.
 - 8) Bind & neutral toxin from bacteria.
Lipoprotein binds with cholesterol to avoid clumping.

> Based on the density, there are five classes. due to

118. $\text{P}_2\text{O}_5 + 3\text{H}_2\text{O} \rightarrow 2\text{H}_3\text{PO}_4$ (acid)

High, low intermediate (Chylomicron) water.
Very low density lipoprotein

(good) HDL :- Carry unused cholesterol & bring back to body

(back) backs to body.

\downarrow LDL - it deposits in body

SHRI SIDDH
MEAN

Transverse diffusion

- > Flip Flop (movement of lipid layer).
- > From one bilayer lipid to another.
- > Very slow without catalyst.
- > Catalyst required → flippase

Membrane proteins: Membrane functions mainly dependent on membrane protein

• Myelin sheet → insulates neurons
+ only 25% protein → ~~does not do~~ not much work.

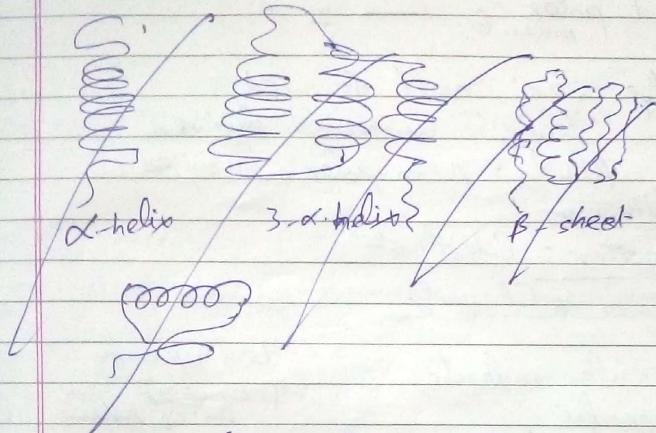
Chloroplast
Mitochondria membrane → 25% protein because it needs more protein for energy

3-classes of membrane protein

> Integral/intrinsic

> Peripheral/extrinsic

> Lipid-linked



Integral membrane proteins

> strongly associated with membrane
- hydrophobic interaction

> Amphiphilic.

Function of membrane proteins: Depends on which membrane they are present

> Transport of solute

> Enzymatic activity

> Signal transduction

> Intercellular joining (During cell division)

> Cell-cell recognition

> Attached to the cytoskeleton & extracellular matrix (etc)

(Vesicles' transport)

~~Permeability~~ Permeability of plasma membranes

Gaseous molecule → Permeable (P)

Small uncharged polar molecules (ethanol) → P.

H₂O, urea → slightly P.

uncharged large polar molecule → I P.

Ions → IP
charged polar molecule → I P.

★ Size: Small favoured

Charge: uncharged favoured

Polarity: Non-polar favoured.

It needs to interact with destination

Transporter: Classification

b) Carriers & Channels

- > carry a particular molecule
- > It is very specific
- > Bind their substrates with high specificity & catalyse transport
- > are saturable (only a given no. of carriers can transport a given no. of solutes)
- > Less specific
- > Transport large no. of molecules
- > Faster transport
- > Non-saturable.

2) Based on solute -

(a) Uniporter : Transport only one type of molecule

(b) Symporter : 2 different molecules in same direction

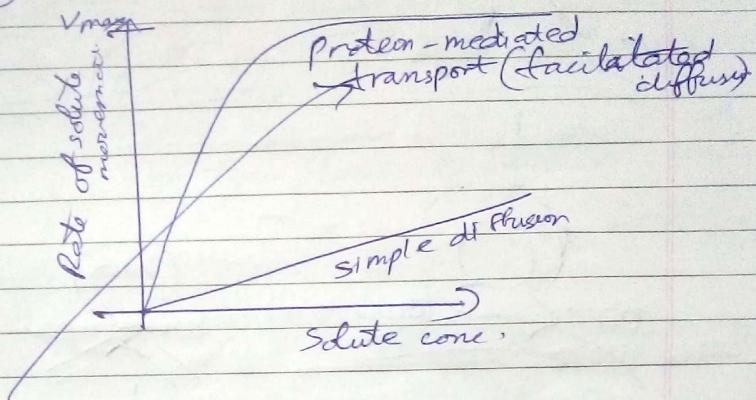
(c) Antiporter : 2 diff. in " opp. direction

Dif modes of transport

→ Passive diff. & Active transport

↓
Does not require
consumption of
energy. Follows
conc. gradient.

↓
Consumes energy - Against
conc. gradient.
Eg. $\text{Na}^+ - \text{K}^+$ pump.



Not exactly linear because there is a limit to the no. of membrane proteins that can be used for transport (by carriers).

→ GLUT 1 mediated glucose transport.

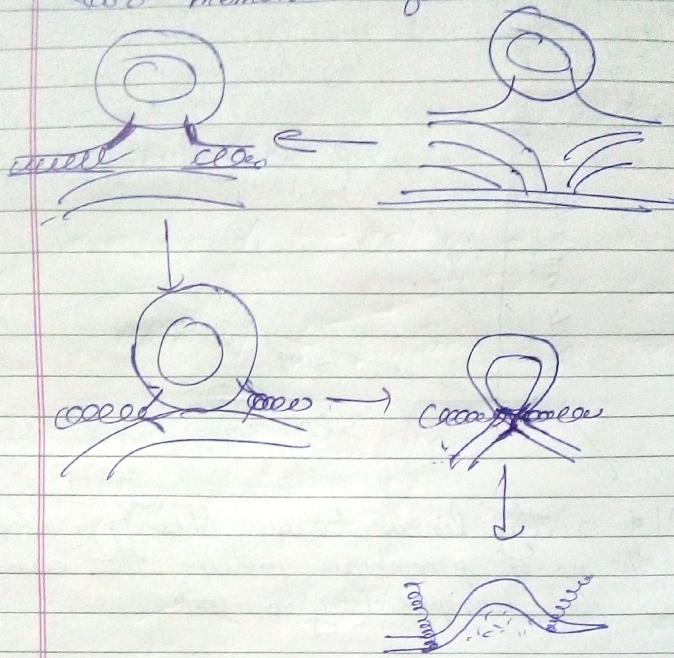
If GLUT 1 does not perform well, then glucose transport inhibits loading to diabetes.

→ Transport of water

Can happen to a certain extent through diffusion through lipid membranes. But, this is not enough for some organelles. So, there is a specialized channel made up of proteins called Aquaporins (transmembrane proteins). Eg:- During production of urine. There is a process called reabsorption of water in the duct of kidneys to avoid huge volume-water loss.

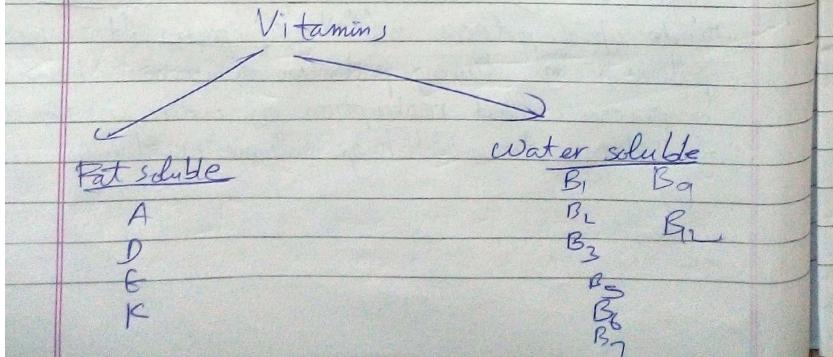
Fusion of two membranes via proteins

Eg - In brain cell, ^{neuro-transmitter} signal has to go from one neuron to another ~~across~~ neurons. So two membranes to fuse.



SATPARI SIX

- > Vitamins are essential organic nutrients, required in small amounts
- > Mostly obtained from our diet, ~~but also from~~
- > Required for growth, maintenance, reproduction & lactation



Enzymes - Biological catalysts (reduce activation energy.)
They are faster than chemical catalyst.

Not all enzymes are made of proteins.

Eg :- RNA is also a catalyst (without protein)

If
> Ribosome joins two amino acids together & keeps on going forming peptide bond formation - The RNA part of ribosome does this.

Simple Enzymes (That consists of protein)
Eg :- Pepsin, breaks food molecules

Enzymes

Apoenzymes (protein)

Holoenzymes

co-factor (non-protein)

metal ions
(inorganic)

Eg :- Alcohol dehydrogenase
(Zn²⁺)

converts alcohol
into aldehyde

Prosthetic

Eg :- Heme
(Tightly bound,
remain unchanged)

Coenzyme (organic)

Co-substrate.

Eg :- Coenzyme A.

(Loosely bound during
reaction)
Eg :- NAD⁺, FAD

Holoenzymes do not work on their own.
Simple enzymes work on their own.

Heme groups Co-substrates usually deliver a substance.

VITAMIN

Eg. of co-substrate :-

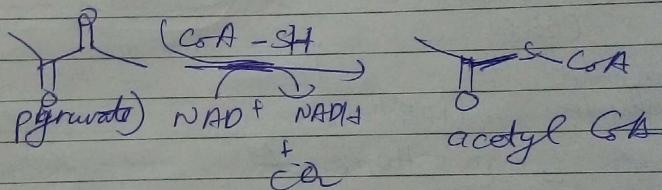
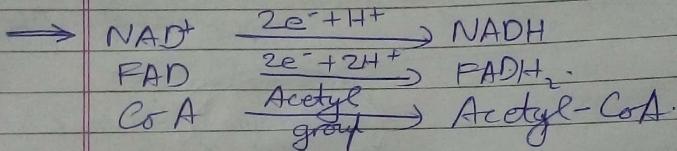
NAD⁺, FAD, coenzyme A

- NAD⁺ is made up of vitamin B_3 .
- FAD is made up of vitamin B_2 .

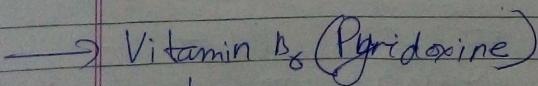
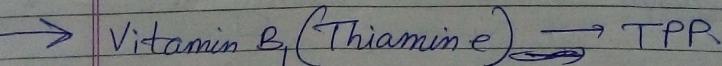
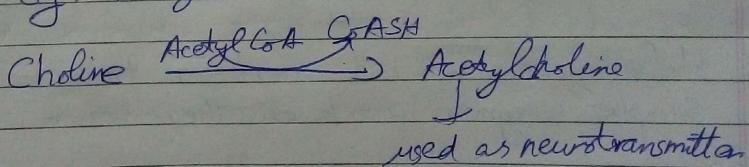
$\text{FMN} \rightarrow \text{ATP}$ - dependent phosphorylation
of riboflavin

FAD (Flavin adenine dinucleotide) \rightarrow
further reaction with ATP

- Co-enzyme A \rightarrow made up of vitamin B_5
(CoA) (panthothenic acid)
- made up of β -alanine & pantoic acid



Eg: Acetylation reaction.

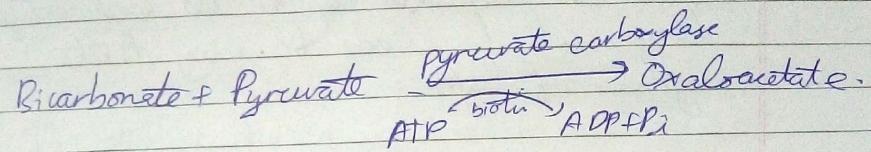


(Pyridoxal phosphate PLP is prosthetic group for enzymes involved in amino acid metabolism)

→ Vitamin B_7 → ~~Biotin~~

Avidin is a molecule which binds to Biotin very tightly & may cause deficiency.

→ Pyruvate carboxylase → uses Biotin as a prosthetic group. Biotin has a side chain forms a long swinging arm.



→ Vitamin B_9 (Folic Acid):- This is used to make

DNA. During pregnancy, this is a very important constituent needed. This is a very important DNA.

→ Vitamin C (Ascorbic Acid) → It comes as L-ascorbic acid & L-dehydroascorbic acid.

(1) Production & maintenance of collagen (muscle)

> Proline → hydroxyproline

> Lysine → hydroxyllysine.

→ ~~Vitamin A~~ → ~~not~~ produced from β -carotene.

comes in 3 forms → retinol, retinal & retinoic acid collectively known as retinoids.

> stored in liver. Used for gene expression/differentiation (used to)

> Retinol is ~~used to~~ stored in the body (liver) as retinyl ester

> Retinal isomerization gives rise to vision.

> Retinoic acid → gene regulation (cell differentiation)

Vision

- > 11-Cis-Retinal isomerisation gives rise to vision.
— Very first signal for vision

Alone this protein is useless. This is bound to 'opsin'. When light ~~enters~~ interactions with opsin, its conformation changes which leads to very first signal of light.

Vitamin D -

Fat soluble.

Stored in liver

Synthesized from cholesterol

Gene expression and immune system

imp. for
calcium
metabolism.

Vitamin E → comes in 8 types

acts as anti-oxidant, helping to protect cells from damage & caused by free radicals (ROS).

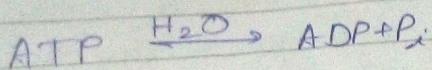
Vitamin K → amino acid metabolism
blood clotting
napthoquinone derivative

MINERALS

Macro

Micro

Water
Water is used to hydrolyse ATP! (Very Imp)



by increasing +ve charge on a phosphorous atom

Shri Shriram Ma'am :

> Cystic fibrosis transmembrane receptor (CFTR).

This is the disease that is caused by.
The disease caused by problem in this protein is called cystic fibrosis.

→ This protein is used to transport ions. It is used to transport chloride ions from inside the epithelial cells (in the lungs) to outside it (mucus).

Positively charged sodium ion follow passively, increasing the total electrolyte concentration in the mucus, resulting in movement of the cell via osmosis.

More mucus → more bacteria decomposition.

CARBOHYDRATES

Two types are present on the membrane:
Glycoproteins & glycolipids.

Most of them are present in the outer monolayer of the plasma membrane, facing the extracellular space.

Carbohydrates of the plasma membrane ^{no} → glycocalyx.

every step for erythrocytes

Two main functions are cell recognition & adhesion.

The entry of any pathogen is due to interaction with glycoprotein. ~~so it~~
It all works in cell-cell signaling & as a physical barrier to pathogens.

→ The body does not make antibodies to its own antigen.

Diff. between plasma membrane of prokaryotes & eukaryotes

→ Bacteria (prokaryotes) do not have sterols.
But, they have some similar to it.

Archaeal plasma membrane are very diff. from ~~bacteria~~ pro & eu - eukaryotes

They are extremophiles because they survive in extreme saline, acidic etc. condition.

Plasma membrane of archaea.

1) chirality of glycerol. (It has L-glycerol while eukaryotes have D-glycerol)

2) ether linkage

eukaryotes 3) isopropenoid chains. (branched) have

ester ester linkage.

4) branching of side chains.

so different bonds with fatty acids

In chemistry ether bonds are stronger than ester bonds.

eukaryotes have linear fatty acid chains.

So, archaeal membrane is more rigid because it has to survive in very extreme conditions.

Page :
Date :

> In some archae, the bilayer of the plasma membrane becomes a pseudo monolayer (while in eukaryotes, the plasma membrane is always bilayer).

Q) Membrane proteins are present on the membrane. From where do they come?

Two imp. organelles which makes the protein compartmentalized are -

> Endoplasmic reticulum & Golgi Apparatus.

(ER)

It has ribosomes attached to it.

Two types based on the function :

Protein synthesis & Lipid synthesis

has ribosomes

→ Rough Endoplasmic reticulum

→ Smooth Endoplasmic reticulum

)

does not have ribosome

> Proteins are formed in the cytosol by RNA.

→ After protein is made modifications are made by the golgi complex & then segregation of proteins happen. Those proteins which need to traffic to the plasma membrane are sent to ER.

Those proteins which need to go to nuclear membrane are sent to cytosol & from there they go to their destination by various other signals.

Glycosylation (Formation of glycoproteins)
also form in ER.

Glycosylated protein on ER (protein capriged
~~detaches~~ detaches from ER & goes to Golgi
complex where further modification happens
& then it is directed to plasma membrane.

GOLGI APPARATUS, Made up of flattened
cisternae.

There are two types of Golgi

Cis :- Facing towards ER

Trans :- Facing away from ER.

Proteins coming from ER enters cis Golgi.
Then they move through Golgi cisternae
& finally reach the Trans Golgi.

From there they are segregated to
lysosome, cytosol, nuclear membrane, etc.
(destination) by the help of its receptors.

Lysosome → Compartment to degrade
waste

[Mannose \rightarrow Carbohydrate]

The receptor & protein are pinched off
from the Golgi as a vesicle. Then they
reach the ~~recept~~ destination. Protein is
delivered & then the receptor is recycled.

Vesicles $\xrightarrow{\text{made up of}}$ actin & myosin.

A point we missed: DNA Nucleus contains
DNA. This DNA is transcribed to RNA.

RNA comes out of this nucleus. Now
this RNA has to make proteins by the
cycle described above.

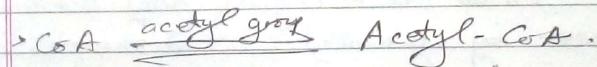
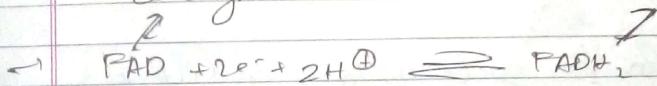
~~fact~~,
There is a retrograde mechanism at the Golgi which brings back the proteins which need not be present at the Golgi to the endoplasmic reticulum.

- * Now these proteins also have a targeting signals which takes them to different cell organelles.

SAPATI SIR

Bioenergetics (Metabolism)

→ Cellular respiration involves break down of glucose into ATP.

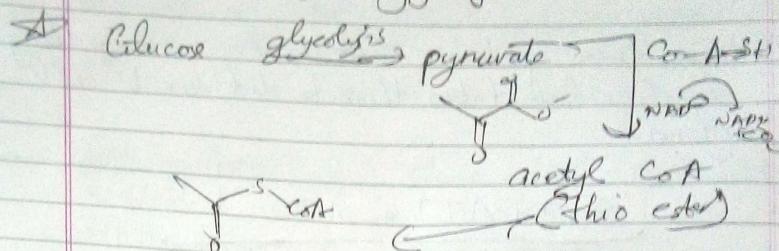


→ First glucose enters the body. Then it undergoes 'glycolysis' (from which ATP is generated) & is converted to 2-pyruvate molecule (from one glucose molecule). This pyruvate enters mitochondria & thereafter is converted to acetyl CoA. Once this is formed, it undergoes TCA (citric acid cycle) due to which 2 CO₂ molecules is released. This cycle also produces reduced coenzyme. They contain one electron. They deliver this to protein on mitochondrial membrane from which ATP is generated. This electron transport chain involves oxygen. The mechanism is called oxidative phosphorylation.

ATP
NADH
FADH₂

If this oxygen is absent, then the pyruvate is converted into lactate by fermentation.

Even outside the mitochondria, body can make ATP (from glycolysis).



CAC (Citric acid cycle / Kreb's cycle)

- > 2 C in & 2 C out.
- > Reduced co-enzyme formation
- > ΔATP ΔNADH ΔFADH_2

In this cycle itself, a GTP is produced (similar to ATP just that adenine is replaced by guanine). \rightarrow Energy currency.

One imp reaction of this cycle is
Oxaloacetate + Acetyl CoA \rightarrow citrate
 \downarrow dehydration

Iso-citrate $\xrightarrow{\text{Hydration}}$ chiral product
 \downarrow release CO_2

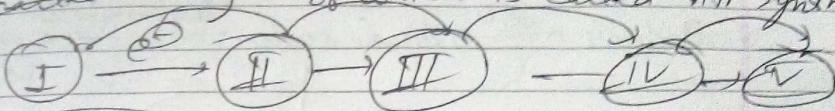
Product 1 $\xrightarrow{\text{CO}_2}$ Product 2 $\xrightarrow{\text{oxidation}}$

Here GTP is

Δ^2 alcohol is easily oxidized product

ETC (electron transport chain) →

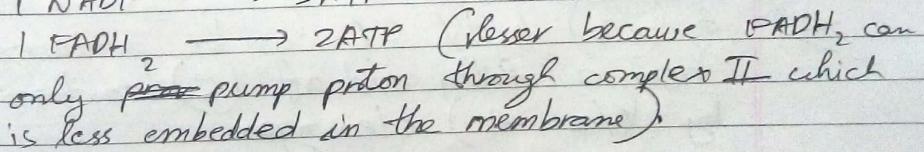
The electron released by reduced coenzymes + oxidation of goes to proteins on inner membrane of mitochondria. These proteins are a group of 3 complexes collectively called ATP, 5 of which is called ATP synthase.



They pump the protons in this process. So, these protons are higher inside the mitochondria than the cytoplasm - so they go to cytoplasm (↓ con. gradient) through ATP synthase.

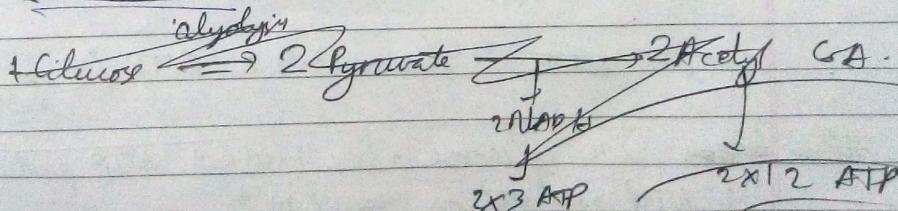
(I) (II) & (IV) are almost fully in the mitochondrial membrane while (III) is just in almost outside (except for the tip).

This protons are pumped by NADH and FADH_2 from matrix to intermembrane space.



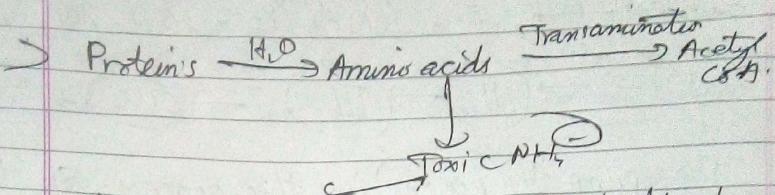
Q) How many ATP per glucose molecule. (in presence of oxygen)

A) 38 ATP

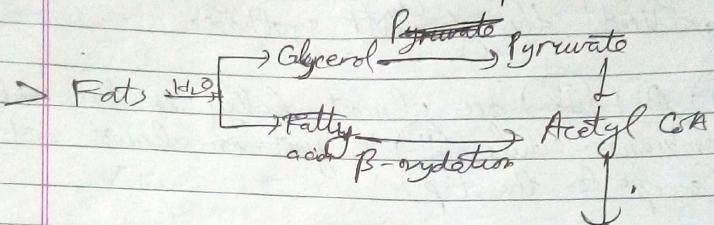


Q) How ATP is produced in absence of oxygen (per glucose molecule).

A) 2 ATP.



It undergoes urea cycle to convert this toxic ammonium ion to urea & proceed to excretion.



Q) How many ATP is produced from FAT?

A) Each time we cleave a fatty acid chain (in chair) we get 1 FADH₂, 1 NADH & 1 acetyl CoA.

★ (C/2) Acetyl CoA can be produced from a fatty acid of (C) carbons by (C/2 - 1) cleavages.

Q) Let's consider a fatty acid (Lauric Acid). It can produce 9.5 ATP molecules. (n).

$$\cancel{9/12} = 7.92 \text{ ATP/C in fat.}$$

~~Q)~~ In glucose-facilitated ATP production,

1 ATP production = 4 H⁺

1 NADH = 10 H⁺ = 2.5 ATP

1 FADH₂ = 6 H⁺ = 1.5 ATP

→ There is a shuttle system to reuse the NADH after producing ATP via fermentation.

Ma'am :

Next trafficking root in the cell is cytosol.
Some proteins ~~which remain in~~ ^{which remain in} cytosol does not have any targeting signals or sequences.
~~(These)~~

There is a signal sequence which directs a protein which is removed after it reaches its target destination. This is also there in bacteria. The targeting of proteins via signals happens in it too.

Bacteria can target protein to the inner or outer membranes, the periplasmic space between this membrane, or to the extracellular medium.

For blood groups

$$\text{dominant } (+) + (+) = (+)$$

, dominant

$$+ + - = -$$

$$\text{dominant } (+) + (-) = (+)$$

$$- + - = -$$

MITOCHONDRIA :

Seen by electron-micrograph.

Mitochondria is a double membraned organelle

There is DNA, ribosomes, granules, cristae ^(site of ATP synthesis), intermembrane space, matrix in the mitochondria.

inner cristae are the ~~in~~ invagination of the membranes of mitochondria. This gives more surface area for ATP synthesis.

One imp. feature of mitochondria ~~is~~ ~~apoptotic signalling~~ → during cell death. This is why fusion of inner & outer membranes are needed.

* Mitochondria produces only 13 proteins from its own DNA. It has 1000s of others. These are made from nuclear DNA.

→ Most mitochondrial proteins are synthesized by cytosolic ribosomes.

* Cytoskeleton.

> Scaffold on which the membrane rests

Actin (microfilaments) Tubulin (microtubules) intermediate filament

* Cytoskeleton need to be in place to help in protein transport.

Cytoskeleton is a polymer of a distinct type of protein.

* Microfilaments are polymers of the protein actin & are 7nm in diameter.

* Microtubules are composed of tubulin & are 25nm in diameter.

* Intermediate filaments are composed of 8-12nm diameter proteins.

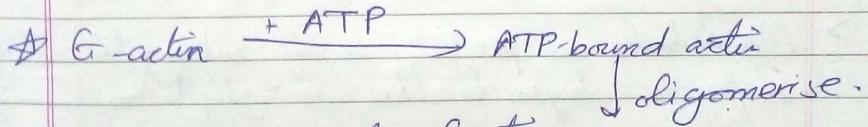
→ All filaments interact with each other & accessory proteins to help the vesicles move.

Functions of cytoskeleton:

- 1) Cell movement → Actin & Tubulin rearrange for cell movement.
- 2) Cell shape support → Meshwork.
- 3) Tracks for motor supports → for vesicle (protein) transport.
- 4) Cell adhesion → cell-to-cell attachment especially in tissues favoured by actin.
- 5) Maintains organelle ~~structure~~ structure (nucleus - lamins)

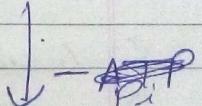
Actin :- present are two forms G-actin (globular monomeric) & F-actin (filamentous actin).

G-actin combines to form a polymer which forms microfilament.



aggregator $\xrightarrow{\text{nucleus formation}}$ stable actin oligomer

assembly $\xrightarrow{\text{extended to a long helical structure}}$

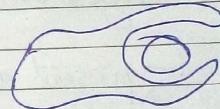
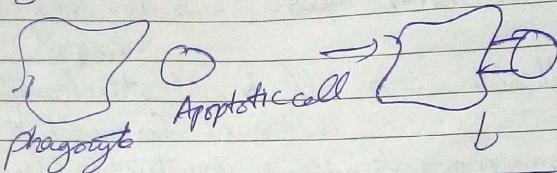


F-actin.
(ATP bound)

- Only ~~F-actin~~ can transport the vesicles.
- > F-actin can transport the vesicles.
- > When no transport is needed then it goes back to G-actin form.

→ Actin is a house-keeping gene (dead ones).

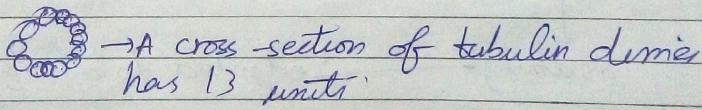
★ Apoptotic cell is ~~released from the~~ engulfed by phagocyte to degrade them.



The above mechanism happens only because of polymerisation of G-actin to F-actin.

> Microtubules are present in all eukaryotic cells & provide shape to the cell cytoplasm.

Tubulin dimer \rightarrow α -tubulin + β -tubulin.



↳ Microtubulin splits chromosomes into 2 parts.

> ~~microtubules bound with Kinesin motor protein helps in vesicle~~ ~~cargo~~ transport.
 actin as accessory protein.

because their diameter is midway between the ~~the other~~ two.

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(Intermediate) filaments

Intermediate filaments that holds the nuclear structure are made of laminins.

- ★ Intermediate filaments do not bind for a nucleoside triphosphate. So, they do not depend on energy formation. They exist in monomer, dimer & tetramer.

~~spindle~~ [Actin also helps in extracellular movement].

It is the structure of proteins that give similarity in cytoskeleton functions of prokaryotes & eukaryotes.

- Q) Do all cells divide similarly?

A) The mechanism is similarly, but frequency of division varies as cell type.

★ Nerve cells do not divide once they get their function. They do not divide.

So are ~~highly~~ similarly, highly differentiated cells like nerve cells, heart cells, RBCs.

★ RBCs are formed from bone marrow. When it is formed, it is like a typical eukaryotic cell. But as soon as it gets its function, it loses its nucleus (it gets de-nucleated) because the most imp. comp. of RBC is haemoglobin which needs to bind with O₂. So, it kicks off unnecessary stuff like nucleus from it.

→ If nerve cells die, you get neuro-degenerative disease like ~~Alzheimer~~ & Parkinson's disease.

> Some cells like liver cells & WBCs divide only on demand. These

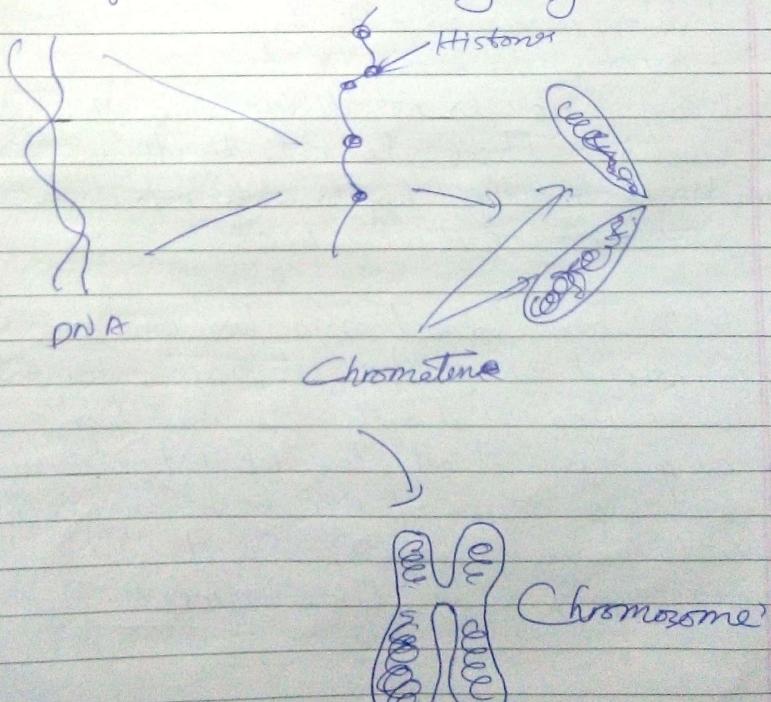
WBCs are needed only to get rid of infection or virus.

→ Some cells like skin cells & gut cells are continuously replenished.

> Avg. cell division time for human cells → 24 hours.

→ A condensed form of DNA (due to presence of proteins called histones) is called chromosome.

> When cell division needs to happen, the extent of chromosome is very high.



Cell cycle -

Every cell organelle has to be duplicate before cell division. So do the DNA content.

STEPS →

- 1) Interphase → First phase of cell division.
This has further sub-phases → G₁, S, G₂.

First task is to duplicate the DNA.

& then

- 2) M-phase → Now a nucleus has to divide ~~cell membrane has to~~ division has to take place. (nuclear division)

It has two processes → Karyokinesis &

Cytokinesis

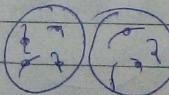
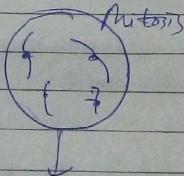
(Cell division)

It has several sub-phases Prophase, Metaphase, Anaphase & Telophase.

- 3) G₀ phase → This is ~~cell~~ when cell exits cell division. & does not enter G₁ cells.

Two types of cell division →

- Mitosis → all cells except gamete (sex cells)
- Meiosis → Only in sex cells.

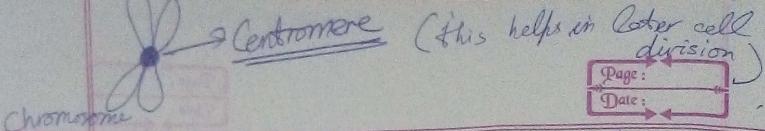


Same no. of chromosomes

Meiosis

Only half no. of chromosome in daughter cell because in zygote formation one father cell & one mother cell combine to form zygote gamete.

Here there is a crossing over of genes too! This is why we are different from our parents.



Chromosome

Mitosis → results in production of only two daughter cells.

Mitosis stages:

- > Interphase → Takes the longest time in cell division. (~~G1 cycle~~ (95% of time))

in G1 phase → DNA condensation ATP production

in S phase → Copying of DNA takes place.

in G2 phase → Actin polymerisation microtubule formation All machinery needed produced.

- > M phase → Karyokinesis & Cytokinesis both happen in this phase

CDK & cyclin are two imp. protein (cyclin dependent kinase) needed in this phase

in prophase → DNA is distributed inside

The nuclear membrane is disintegrated

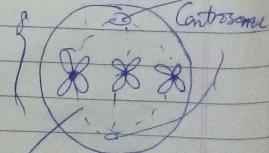
(vanishes) So the two copies of chromosomes are present in the cytosol.

Now these chromosomes attach to centrosome (protein)

in metaphase → all these chromosomes line up in the center of the cell.

Microtubules enter from the centrosome & attach to the chromosomes

equatorial plane. Microtubules Metaphase



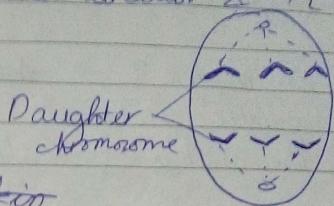
Spindle fibres arise from centrosomes & bind with the kinetochore (protein complex around the centromere).

centromere alias centriole

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in anaphase → the centromeres divide.

The spindle fibres pull against the chromosomes.
 $\frac{1}{2}$ are pulled in one direction & $\frac{1}{2}$ in other direction



in telophase & cytokinesis

DNA spreads out, spindle fibre disintegrate,
2 nuclei are formed.
(nuclear membrane)

After telophase, cytokinesis occurs.

[In plant cell, ~~so~~ first cell plate formation occurs at the center. This is because the rigidity of cell ~~flat~~ wall makes it difficult to cleave it unlike cells of animals which are easily cleaved by actin].

Centrosomes are absent in plant cells.

M EIOSIS

Four daughter cells are formed.

Eggs & sperm are produced.

Daughter cell have half the no. of chromosomes.

→ During meiosis, DNA replicates once, but nucleus divides twice

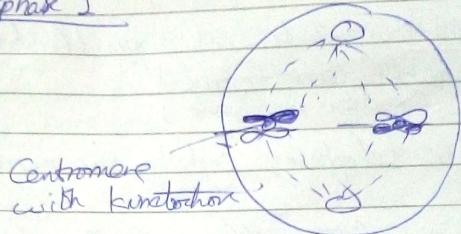
There are 23 chromosomes in each mother & father cells.

Miosis I & Miosis II

in interphase \rightarrow 46 chromosomes are formed.
(replicated) (23 from mother & 23 from father)

in prophase I \rightarrow ~~over~~ chiasmata, genetic material is exchanged between the mother & father chromosome.

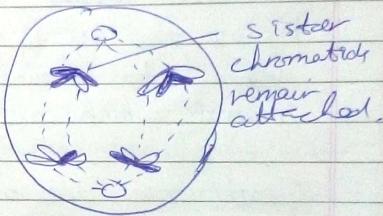
metaphase I



Anaphase I



Homologous chromosomes separate.



SATPATI SIR
G O O D Q

ATP synthase & laws of thermodynamics.

It can be divided into 2 regions \rightarrow P₁, R₁.

P₁ region lies in mitochondrial matrix.

P₁ consists of 5 types of protein +

$\alpha, \beta, \gamma, \delta, \epsilon$.

$\Rightarrow \alpha, \beta$ ring (hexameric) form a ~~hexamer~~ structure type

$\gamma\&\delta$ acts as the rotor stalk.

FO region (mostly hydrophobic & is embedded in the membrane).

H^+ transfer occurs in the FO region ('a' region)

$ADP + P_i \rightarrow ATP$. This region occurs in F1 region, specifically in the $\alpha_3\beta_3$ ^{hexameric} region.

* On top of $\alpha_3\beta_3$ region is δ . (acting as the cherry of the cake).

* When H^+ moves through 'a' region of FO, it induces a rotation in the rotor stalk which thereby stimulates ATP formation.

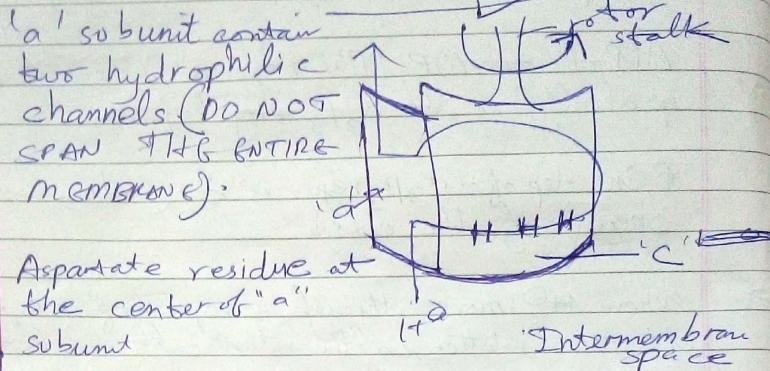
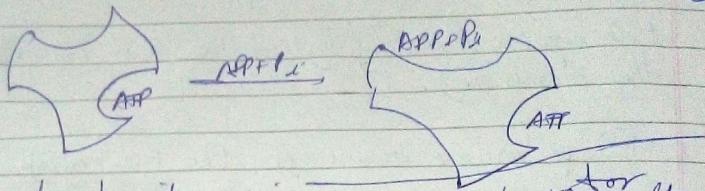
ATP synthase can be divided into two parts.
Rotatory region : C101 + $\gamma\&\delta$.
Stationary region Everything else.

> Rotation of γ stalk can induce conformational change in α/β unit.

Reason:- α/β unit (cross-section) is as shown →

There is one site to which ADP binds - one site to which ATP binds. Then γ rotates bring them in vicinity & then ATP is formed. There is one more site which binds with amino acid - to catalyse the reaction.

360° rotation of $\gamma \Rightarrow 3$ ATP molecules formed.



Mechanism: High H^+ \rightarrow Low H^+ through Asp protonation, Brownian motor.

→ How many H^+ diffusion is required for 1 ATP?

$$\# 360^\circ \text{ rotation} = 3 \text{ ATP}$$

$$\# 360^\circ \text{ rotation} = 10 - 14 H^+$$

$$\Rightarrow 1 \text{ ATP} = 3.33 - 4 \cdot 6.7 = [4 H^+]$$

(Q) What if we burns ATP to $ADP + P_i$? would the movement of rotor reverse?

A) Yes! (Experiments have proved).

a) How did they prove?

A There is an actin filament connected to protein. Using some 'special' light, it can be seen. By inducing $ATP \rightarrow ADP + P_i$, indeed the \rightarrow rotation of the actin filament was reversed.

$\Delta G > 0 \rightarrow$ Endergonic, $\Delta G < 0 \rightarrow$ Endergonic.

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Bioenergetics (Study of energy transduction)

Biological energy transduction → obey laws of Thermodynamics.

* Thermodynamics & Biology

In non-living things, flow of heat → work.
Ex: Carnot engine.

In living things, work is done by various factors like electric gradient, etc.

Chemical reaction in lab: closed system
Living cell: open system (exchange of mass & energy possible)

(exchanges heat)

Laws of thermodynamics:

0) Zeroeth law: Heat Energy conservation
path function.

1) $\Delta U = Q + W$
 U = state function

$$\Delta H = \Delta U + P\Delta V + V\Delta P$$

$$(\text{At constant press., } \Delta H = \nabla(U + PV))$$

At constant press.,

$$\Delta U = -P\Delta V$$

Heat added to system
 $Q = +$

Heat released by system
 $Q = -$

Work done on the system
 $W = +$

Work done by the system
 $W = -$

At constant pressure,

$$\Delta H = \Delta U + P\Delta V$$

$$= Q + W - W$$

$$\Delta H = Q$$

ΔH (enthalpy) \rightarrow state function

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At constant volume, $\Delta U = \Delta Q$

For reactions involving liquid/solid, $\Delta Q \approx \Delta H$.

$\Delta H +ve \rightarrow$ endothermic
 $-ve \rightarrow$ exothermic.

\rightarrow Hess' Law

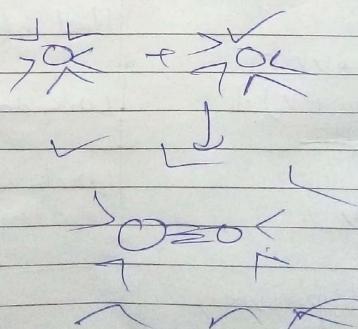
2) ΔS_{univ}) For spontaneous process, entropy S of the universe increases.

$$\Delta S_{\text{univ}} > 0 \quad \Delta S_{\text{univ}} \neq 0$$

Temperature is the average K_F of the system.

(Randomness)/(Temp) \rightarrow state function giving directionality of time.

Apparent Contradiction to 2nd law of thermodynamics?
— crystallisation : or not
— life on earth.



$$\Delta S_{\text{system}} < 0$$
$$\Delta S_{\text{surroundings}} > 0$$

$$\Delta S_{\text{universe}} > 0$$

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Conditions in cell are at constant pressure.

$$\Delta S_{\text{surrounding}} = \frac{\Delta Q_{\text{surrounding}}}{T} = -\frac{\Delta Q_{\text{system}}}{T}$$

$$\Rightarrow (\Delta H - T\Delta S)_{\text{state function}} \leq 0 \quad (\text{const. } T) \quad (G = H - TS)$$

At constant volume,

$$\Delta (U - TS) \leq 0$$

$$\Delta A \leq 0$$

ΔF (Helmholtz Free Energy)
state function

★ $\Delta G = -\omega_{\text{non-mech}} + V\Delta P - S\Delta T$

$$\Delta G_{\text{PST}} = -\omega_{\text{non-mech}}$$