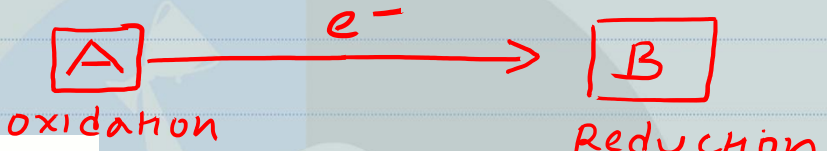
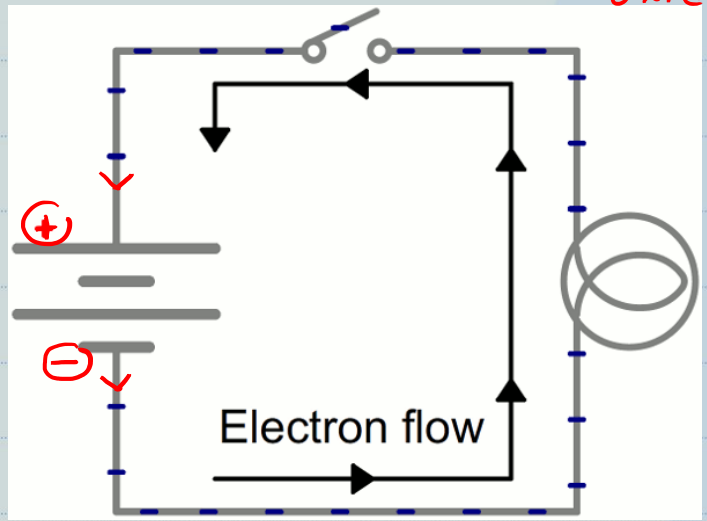
LECTURE 20

Biological Oxidation

Oxidative Phosphorylation

BIOLOGICAL OXIDATION : Loss of electron





Electron flow
↓
Energy
↓
use for work

The Flow of Electrons (emf) Can Do Biological Work

Four types of electron transfer occur in cells

1. Directly as electrons:

$$Fe^{2+} \longrightarrow Fe^{3+} + e^-$$

$$Cu^{+} \longrightarrow Cu^{2+} + e^-$$

2. As hydrogen atoms:

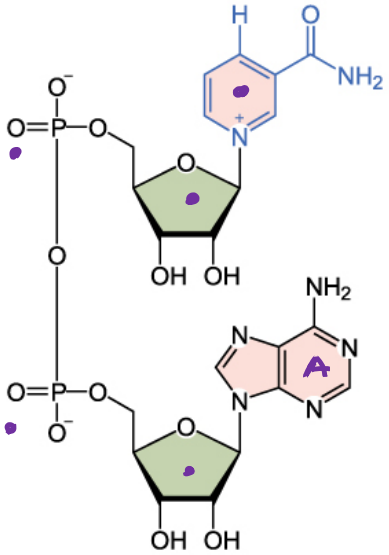
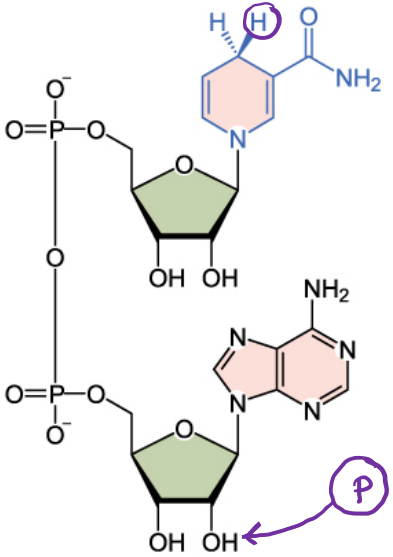
$$H \longrightarrow H^+ + e^-$$

Succinate $\rightleftharpoons$ fumarate (FAD / $FADH_2$)

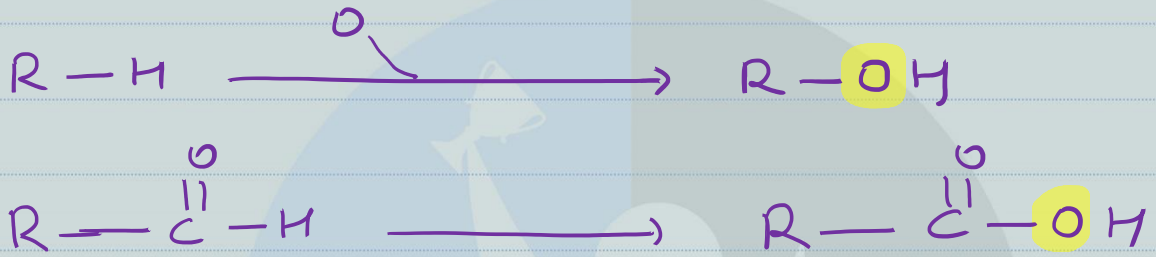
3. As a hydride ion ($:H^+$) which has two electrons:

$$NADH \longrightarrow NAD^+ + [2e^- + H^+]$$

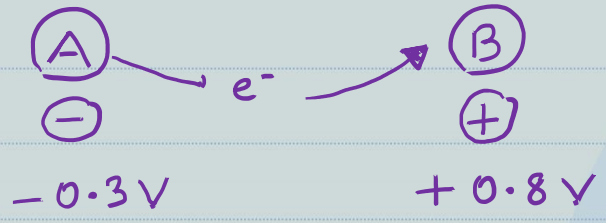
$$NADPH \longrightarrow NADP^+ + [2e^- + H^+]$$

NAD^+	NADH
	

4. Through direct combination with oxygen:



Reduction potentials measure affinity for electrons (measure in volts)



⊕ High tendency to accept electron

⊖ High tendency to loose electron

0 V ← Ability of H^+ to accept electron & convert into hydrogen gas

The **standard reduction potential, E^0** Standard condition

Electron donor 1M

E^0 Electron Acceptor 1M

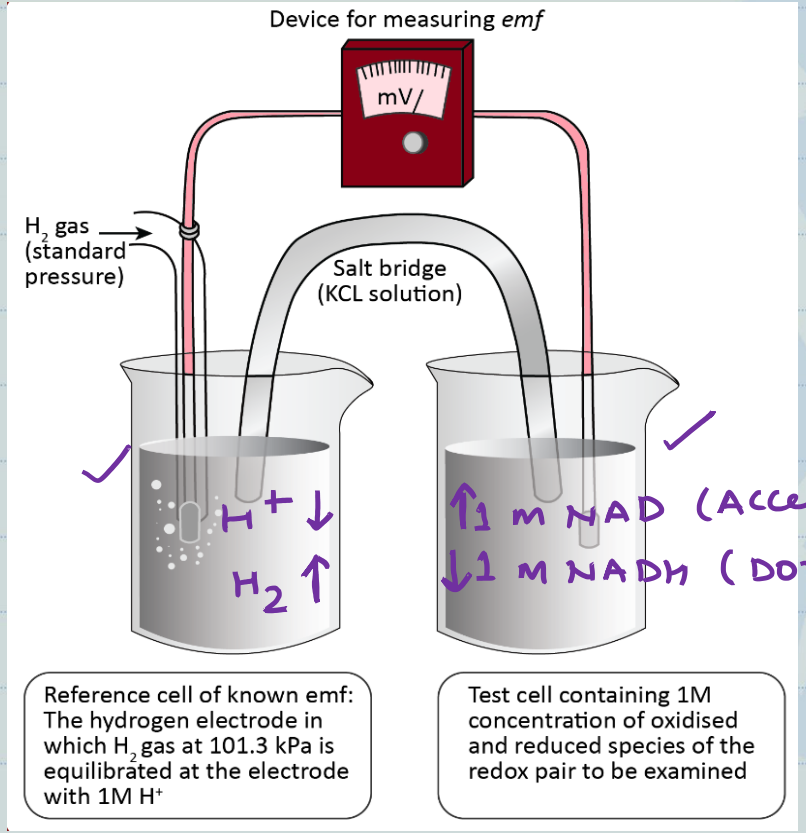
$E^{0\prime}$ Temperature 25°C

Pressure 1 atm

pH = 0 (Biological system = pH=7)

Standard reference

− 0.32 V



$H^+ + e^- \rightarrow \frac{1}{2} H_2$ '0 Volt'

Test cell containing 1M (Oxidised/Reduced species)

$\downarrow H^+ + e^- \longrightarrow H_2 \uparrow$

$\downarrow NADH \longrightarrow NAD \uparrow$

Half-reaction	E'° (V)
$\frac{1}{2}O_2 + 2H^+ + 2e^- \longrightarrow H_2O$	0.816
$Fe^{3+} + e^- \longrightarrow Fe^{2+}$	0.771
$NO_3^- + 2H^+ + 2e^- \longrightarrow NO_2^- + H_2O$	0.421
Cytochrome f (Fe^{3+}) + e^- $\longrightarrow$ cytochrome f (Fe^{2+})	0.365
$Fe(CN)_6^{3-}$ (ferricyanide) + $e^- \longrightarrow Fe(CN)_6^{4-}$	0.36
Cytochrome a_3 (Fe^{3+}) + e^- $\longrightarrow$ cytochrome a_3 (Fe^{2+})	0.35
$O_2 + 2H^+ + 2e^- \longrightarrow H_2O_2$	0.295
Cytochrome a (Fe^{3+}) + e^- $\longrightarrow$ cytochrome a (Fe^{2+})	0.29
Cytochrome c (Fe^{3+}) + e^- $\longrightarrow$ cytochrome c (Fe^{2+})	0.254
Cytochrome c_1 (Fe^{3+}) + e^- $\longrightarrow$ cytochrome c_1 (Fe^{2+})	0.22
Cytochrome b (Fe^{3+}) + e^- $\longrightarrow$ cytochrome b (Fe^{2+})	0.077
Ubiquinone + $2H^+ + 2e^- \longrightarrow$ ubiquinol + H_2	0.045
$Fumarate^{2-} + 2H^+ + 2e^- \longrightarrow succinate^{2-}$	0.031
$2H^+ + 2e^- \longrightarrow H_2$ (at standard conditions, pH 0)	0.000
Crotonyl-CoA + $2H^+ + 2e^-$ $\longrightarrow$ butyryl-CoA	−0.015
$Oxaloacetate^{2-} + 2H^+ + 2e^- \longrightarrow malate^{2-}$	−0.166
$Pyruvate^- + 2H^+ + 2e^- \longrightarrow lactate^-$	−0.185
Acetaldehyde + $2H^+ + 2e^-$ $\longrightarrow$ ethanol	−0.197
FAD + $2H^+ + 2e^- \longrightarrow FADH_2$	−0.219*
Glutathione + $2H^+ + 2e^-$ $\longrightarrow$ 2 reduced glutathione	−0.23
$S + 2H^+ + 2e^- \longrightarrow H_2S$	−0.243
Lipoic acid + $2H^+ + 2e^-$ $\longrightarrow$ dihydrolipoic acid	−0.29
$NAD^+ + H^+ + 2e^- \longrightarrow NADH$	−0.320
$NADP^+ + H^+ + 2e^- \longrightarrow NADPH$	−0.324
Acetoacetate + $2H^+ + 2e^-$ $\longrightarrow$ β-hydroxybutyrate	−0.346
α-Ketoglutarate + $CO_2 + 2H^+ + 2e^-$ $\longrightarrow$ isocitrate	−0.38
$2H^+ + 2e^- \longrightarrow H_2$ (at pH 7)	−0.414
Ferredoxin (Fe^{3+}) + e^- $\longrightarrow$ ferredoxin (Fe^{2+})	−0.432

Change in

Standard reduction potentials can be used to calculate the free-energy change

$$\Delta G^{\circ} = -n F \Delta E^{\circ}$$

n = number of electron

F = Faraday constant

(KJ = 96.5 , K.cal = 23)

ΔE° = Change in Reduction potential

$$\Delta E^{\circ} = E^{\circ}_{Acceptor} - E^{\circ}_{Donor}$$

ΔE° = +ve $\quad \Delta G^{\circ}$ = −ve Spontaneous

ΔE° = −ve $\quad \Delta G^{\circ}$ = +ve Non-spontaneous

F= Faraday constant (96.5 kJ/V. mol or ~~23 kJ/V. mol~~)

Consider the reaction in which acetaldehyde is reduced by the biological electron carrier NADH:

Acceptor Donor

Acetaldehyde + NADH + H^+ → ethanol + NAD^+

The relevant half-reactions and their $E^{0'}$ values are:

(1) Acetaldehyde + $2H^+$ + $2e^-$ → ethanol $E^{0'}$ = - 0.2 V Acceptor

(2) NAD + $2H^+$ + $2e^-$ → NADH + H^+ $E^{0'}$ = - 0.3 V Donor

Calculate $\Delta G^{o'}$ *(Given F = 96.5 kJ/V.mol)?*

$$\Delta G^\circ = -nF\Delta E^\circ$$
$$= -2 \times 96.5 \times 0.1$$
$$= -2 \times 9.65$$
$$\Delta G^\circ = -19.30 \text{ KJ/mole}$$

$$\Delta E^\circ = (E^\circ_A) - (E^\circ_D)$$
$$= (-0.2) - (-0.3)$$
$$= -0.2 + 0.3$$
$$= +0.1$$

Nerst Equation:

cellular conc^{n}

$$E_A = E^0 + \frac{0.26}{n} ln \frac{(Electron\ Acceptor)}{(Electron\ Donor)}$$

Standard Reduction potential

Physiological Reduction potential

Biological system

ΔG

$\Delta G = -n F (\Delta E)$

$\Delta E = (E_A) - (E_D)$

Electron Transport Chain

Location: Inner mitochondrial membrane
Bacterial Plasma membrane.

ELECTRON TRANSPORT CHAIN COMPONENTS

* 4 Immobile complex — I, II, III, IV

* 2 mobile carrier

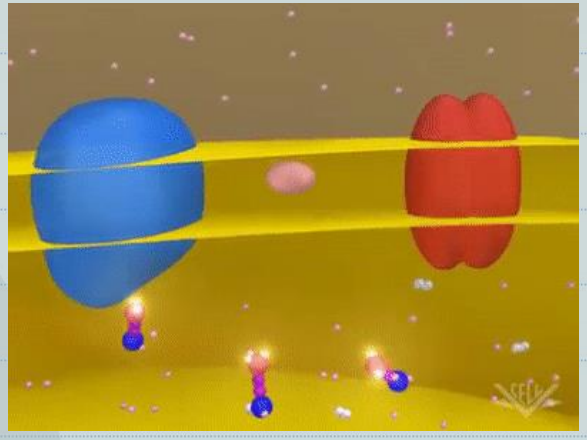
I → III
II ↗ → Ubiquinone (lipid soluble)

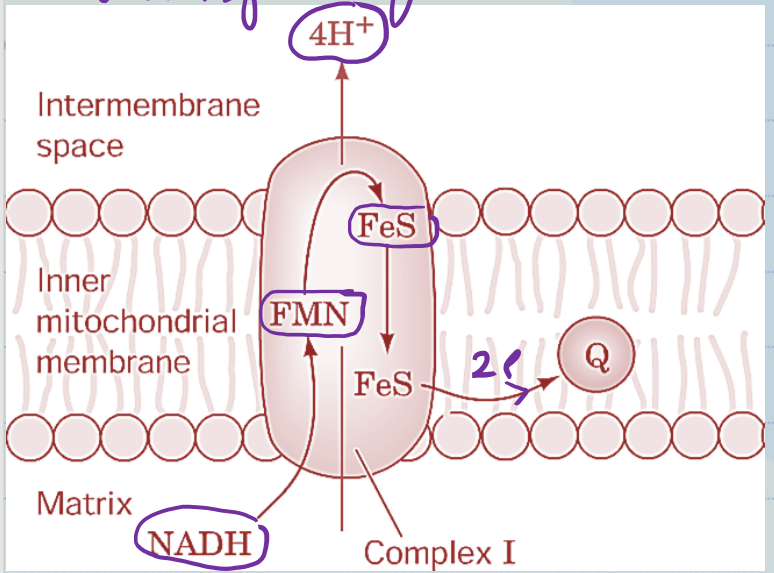
cytochrome C (protein)

III → IV

NADH Dehydrogenase complex

- **NADH-Q reductase (Complex I):**
- Transfer 2 e^- from NADH to ubiquinone
- Flavoprotein (FMN) & Fe-S protein
- Pump 4 H^+ outside matrix during transfer of two electrons to UQ.



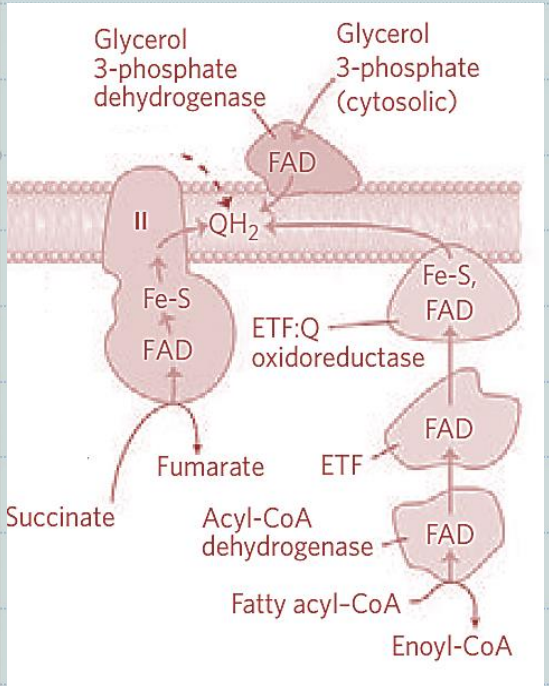


NADH $\xrightarrow{2e^-}$ FMN $\xrightarrow{2e^-}$ FeS $\xrightarrow{2e^-}$ UQ $\rightarrow$ III

Complex II: Succinate dehydrogenase complex

- TCA cycle enzyme
- Oxidize succinate & transfer 2 electron to UQ

Succinate $\xrightarrow{2e^-}$ FAD $\xrightarrow{2e^-}$ Fes $\xrightarrow{2e^-}$ UQ



- Flavoprotein (FAD)
- Fe-S protein (Fe-S)
- donot pump H^+.

I → UQ → III

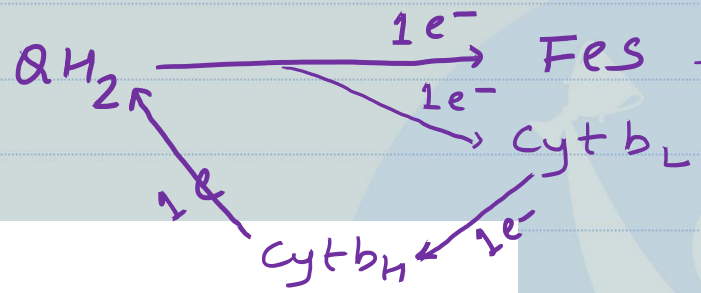
II → UQ

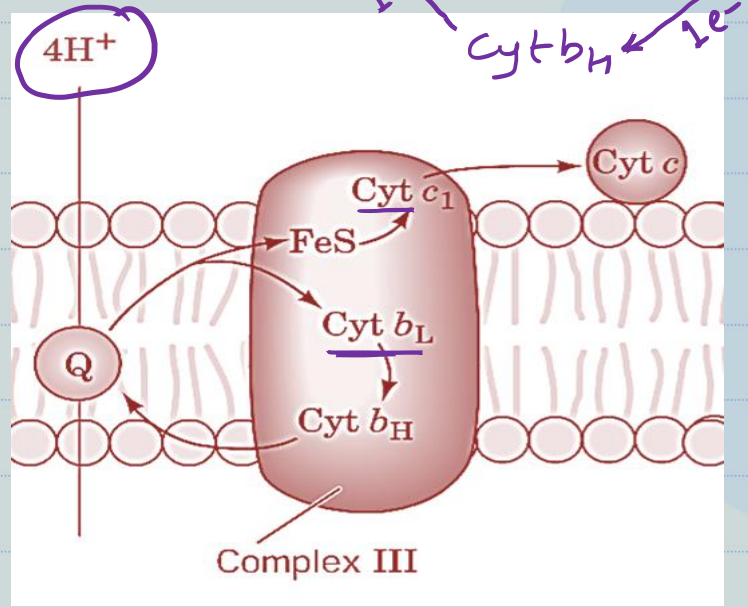
- Polyterpene
- lipid soluble
- Accept 1 or 2 electron.

- Cyt b – c_1 complex

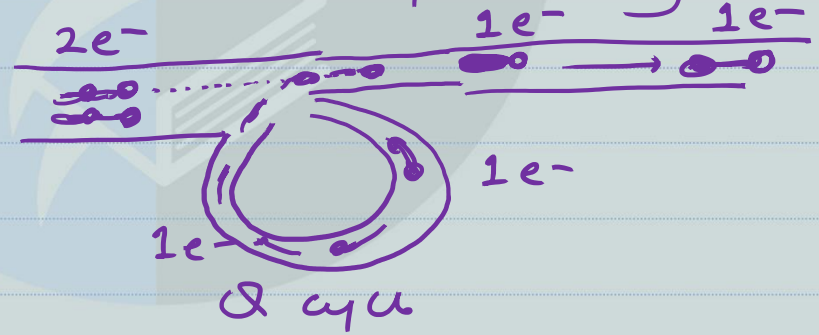
Q-cytochrome c reductase (Complex III):

- Fe-S protein
- Haeme protein





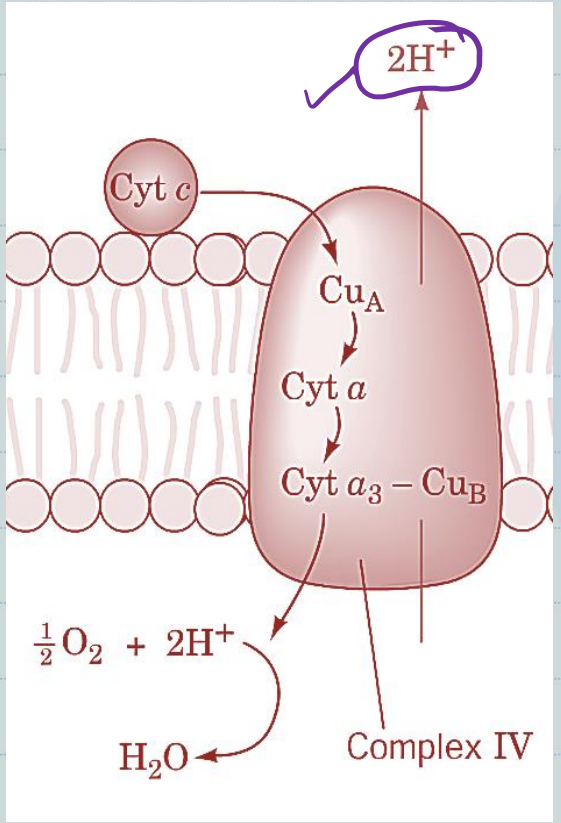
- Two electrons are transferred from ubiquinone to cyt C
- 4 protons are also transported against gradient



Cytochrome c oxidase (Complex IV):

cyt c : Peripheral Protein (heme)

III — IV



cyt c $\xrightarrow{2e^-}$ cyt a – Cu_A

↓

cyt a_3 — Cu_B

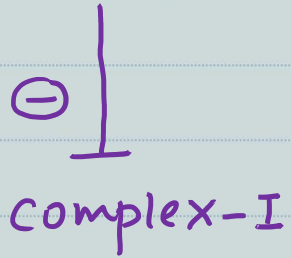
↓ $2e^-$

O_2

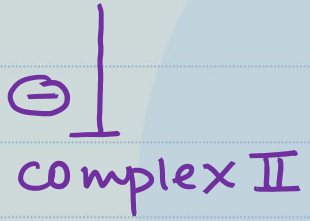
- Haeme-cyano protein
- 2 proton are transported outside matrix

Electron transport chain inhibitors:

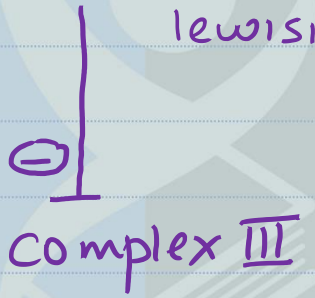
Rotenone
Amytal
Barbiturates
Piercidin



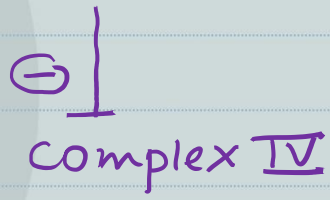
Malonate
Carboxin



Phenformin
Dimercaprol
Antimycin A
BAL (British Anti lewisite)



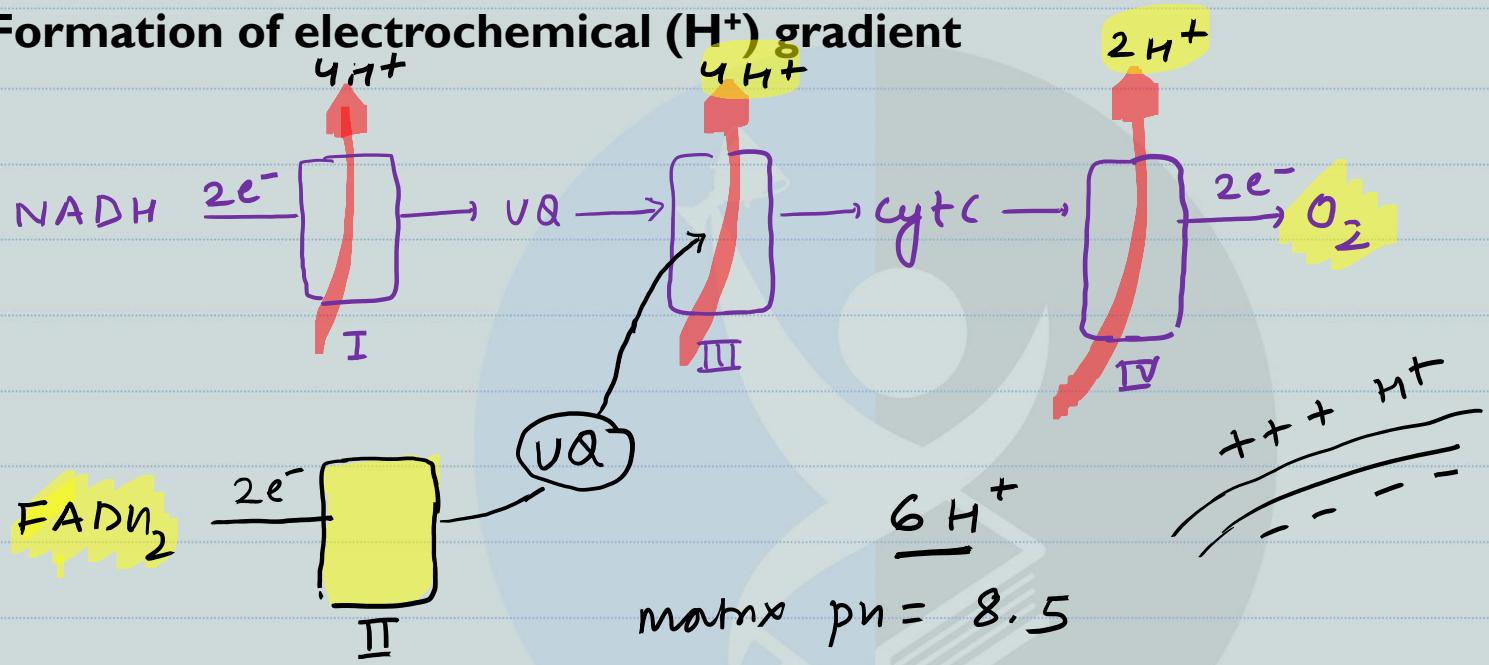
Cyanide
Azide
CO
H_2S



Electron flow

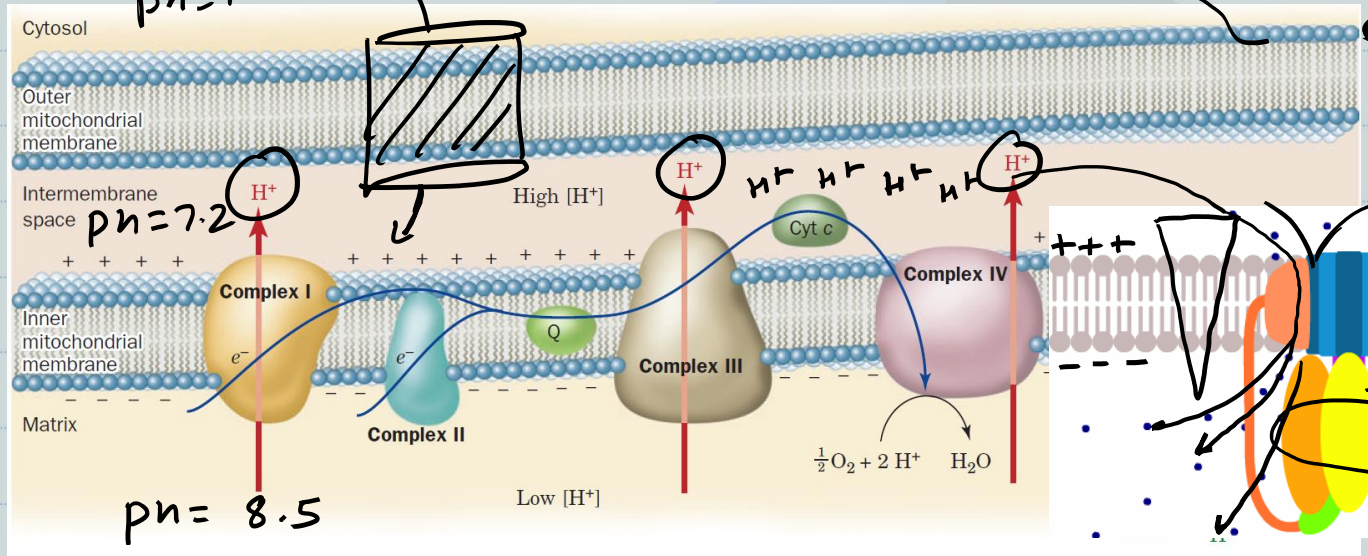
Intermembrane space = 7.2 ph

Formation of electrochemical (H^+) gradient



coupled with ETC
- ATP Synthase
- F_0-F_1 Particle
- oxysome

Oxidative phosphorylation:



ADD

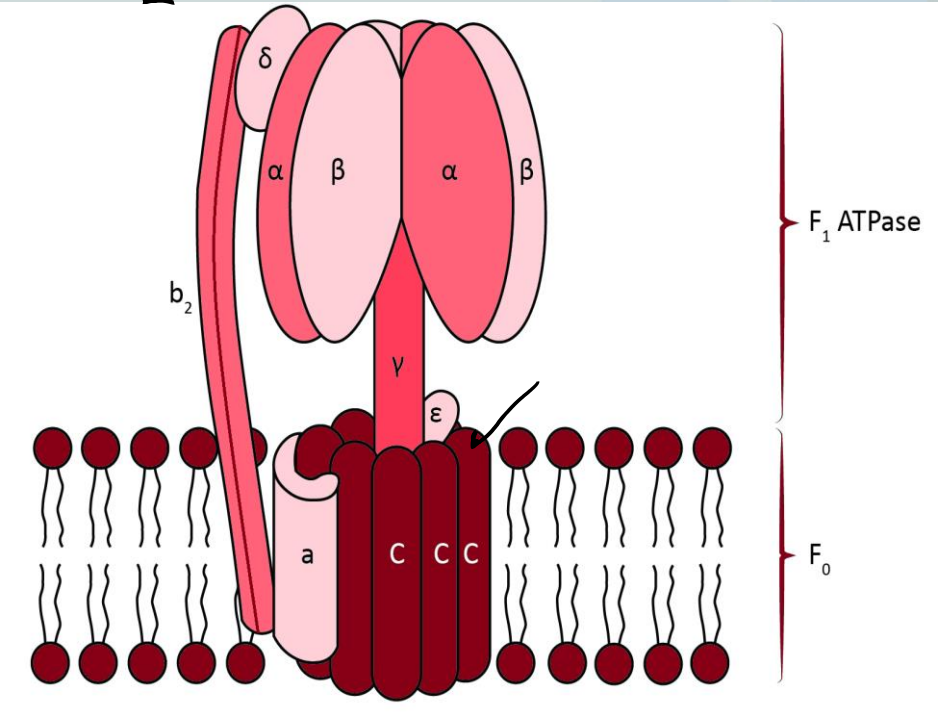
IP

Rotational catalysis

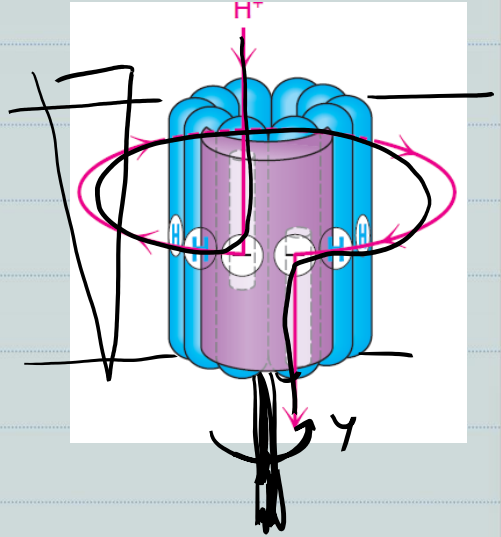
ATP

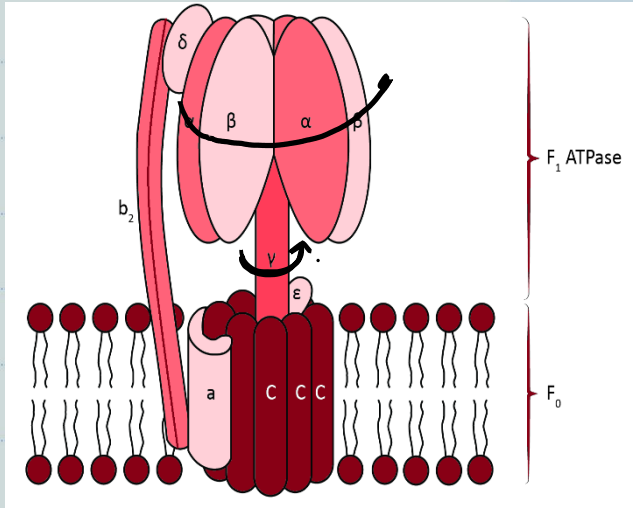
ATP Synthase Is Driven by the Flow of Protons

- The F1 Component Has Pseudo-Threefold Symmetry — 3α, 3β, 1γ, 1δ, 1ε
- The Fo Component Includes a Transmembrane Ring — 1a, 2b, 10c



- **ATP Is Synthesized by the Binding Change Mechanism.**
  - Catalytic role = β-Subunit of F_1
  - Rotational Catalysis
  - Chemi-Osmotic hypothesis = Mitschell



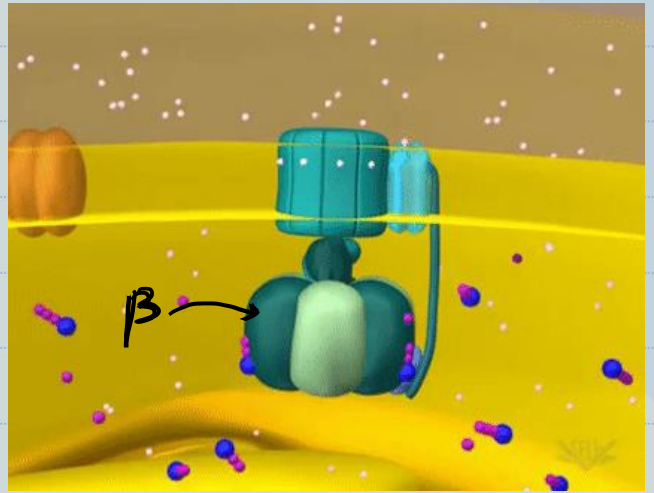


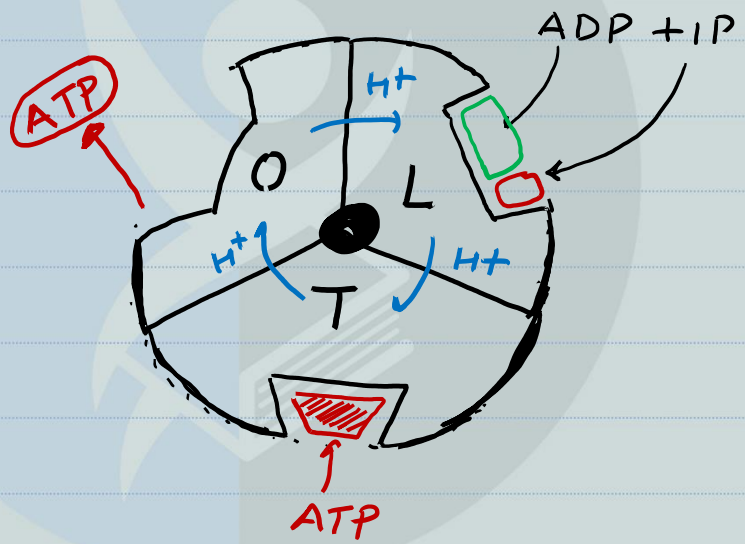
Each of the β (nucleotide binding sites) three subunits cycle through 3 different conformations due to rotation of Ɣ subunit:

(O)pen: little affinity; ADP and Pi are free to enter (ATP is free to leave) the catalytic site

(L)oose: higher affinity; lose binding of ADP and Pi

(T)ight: Packing the ADP and Pi together tightly; facilitating the condensation





$3H^+$

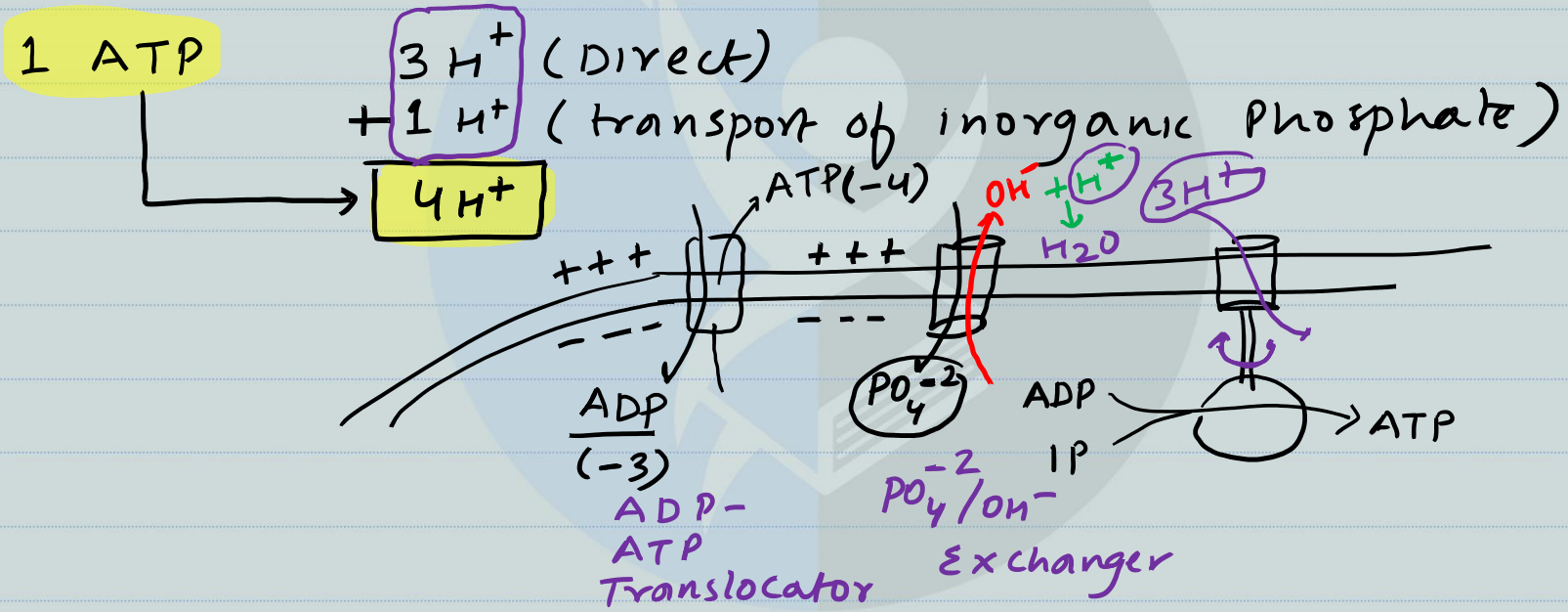
360° rotation

$10\ H^+$ $\quad 10\ H^+/4\ H^+ = 2.5\ ATP$

The free energy from NADH to O_2 can drive the synthesis of approximately 2.5 ATP

The free energy from FADH2 to O_2 can drive the synthesis of approximately 1.5 ATP

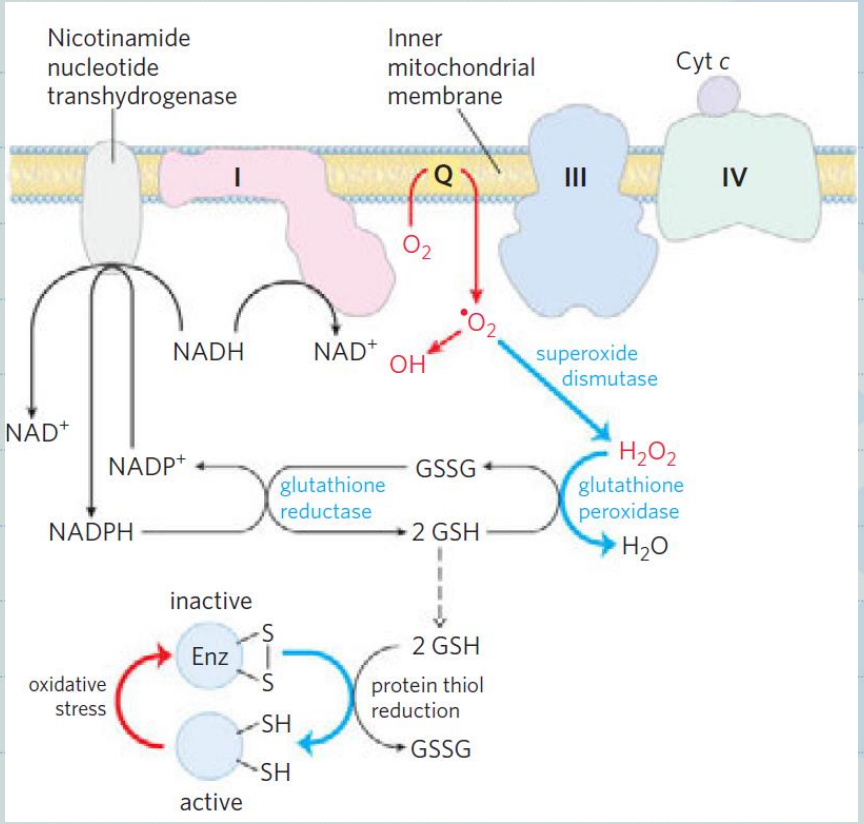
$6\ H^+$ $\quad 6\ H^+/4\ H^+$



ATP synthase Inhibitors

- Oligomycin
- Dicyclohexylcarbodiimide (DCCD)

Reactive Oxygen Species Are Generated during Oxidative Phosphorylation

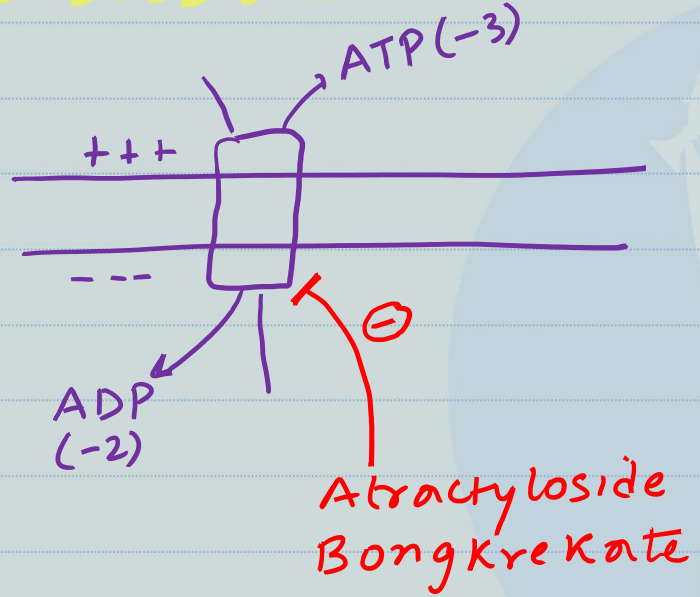


✓ O_2^- & ✓ H_2O_2

Anti-oxidant Enzyme

- Super oxide dismutase
- Glutathione peroxidase

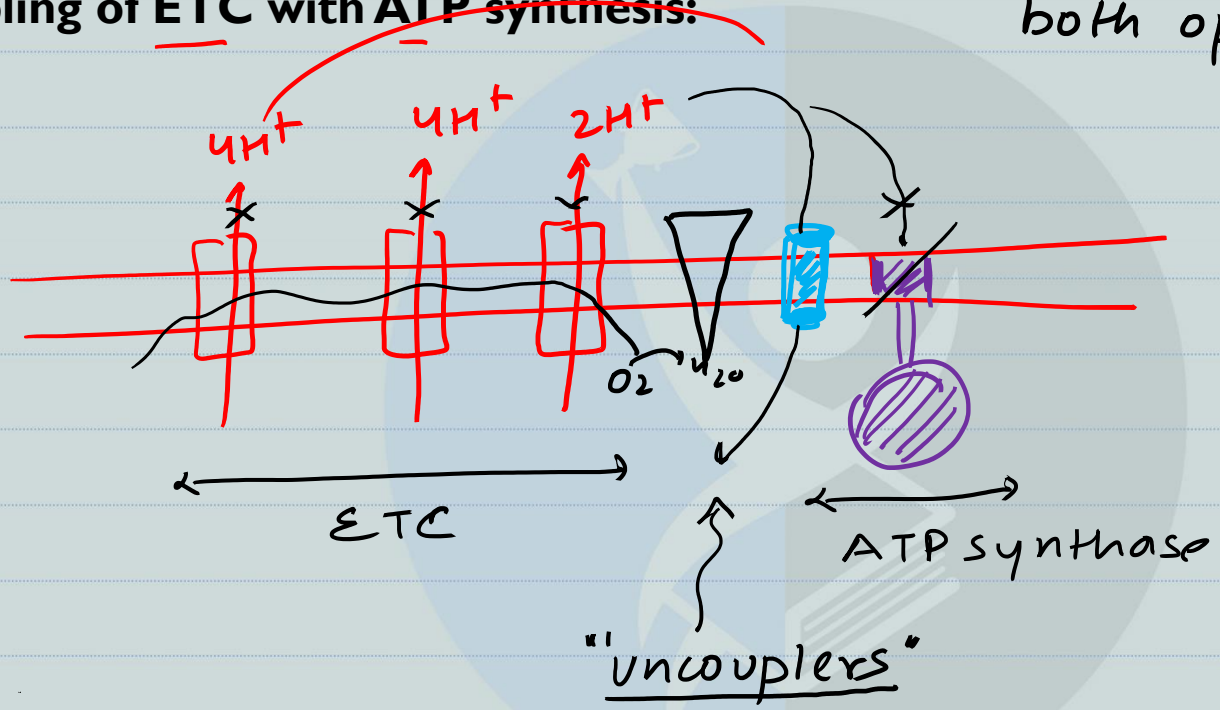
ADP/ATP transport systems



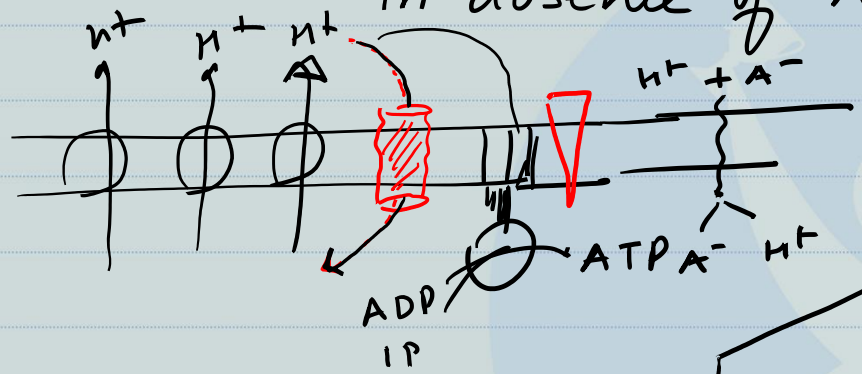
Atractyloside and bongkrekic acid/ bongkrekate

ETC & ATP synthase both operate together

Coupling of ETC with ATP synthesis:



Uncouplers : Allow electron transport chain to operate in absence of ATP synthesis.



- Energy will be released in form heat.

Ionophore

Ion-carrier

- Brown fat
- **Brown adipose tissue**

eg.

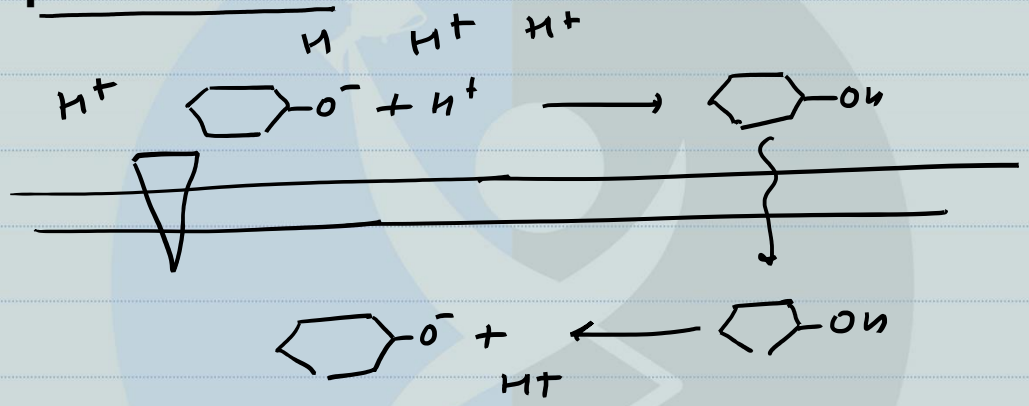
- **Thermogenin** (or uncoupling protein).

Physiological uncouplers (ion carriers)

- Thyroxine
- Bilirubin

Synthetic uncouplers (Ion carriers):

- **2,4-dinitrophenol**: **proton carrier**



- **Dinitro cresol,**
- **Penta chlorophenol,**
- **Trifluoro carbonylcyanide phenyl hydrazone** (FCCP).
- **Aspirin** (methyl salisylate)

Ionophores : Pore on inner membrane

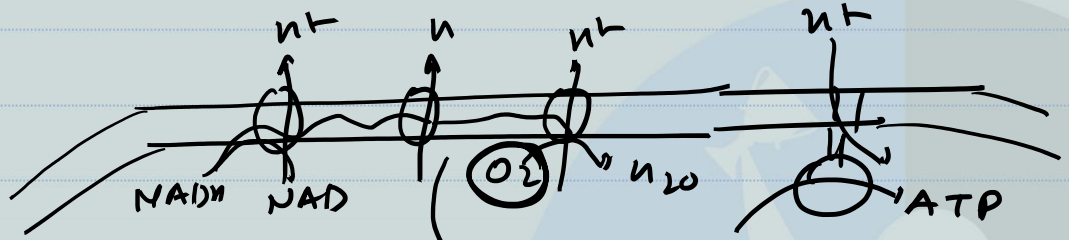
- Valinomycin
- Nigrerein

→ amphipathic helix
→ L-aa -D-aa -L-aa -D-aa ----

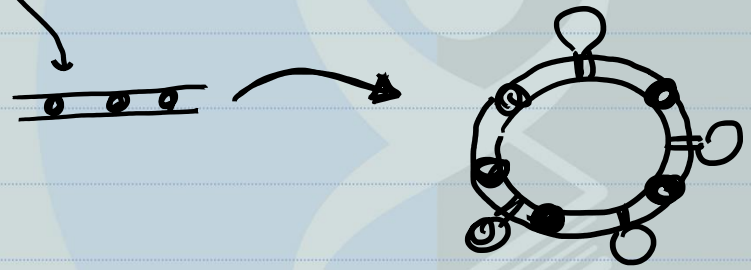
K^+ → Ionophore

Antibiotics **valinomycin** and **nigercin** act as **ionophores for K^+** ion

- **Study of effect of various molecules on electron transport chain**

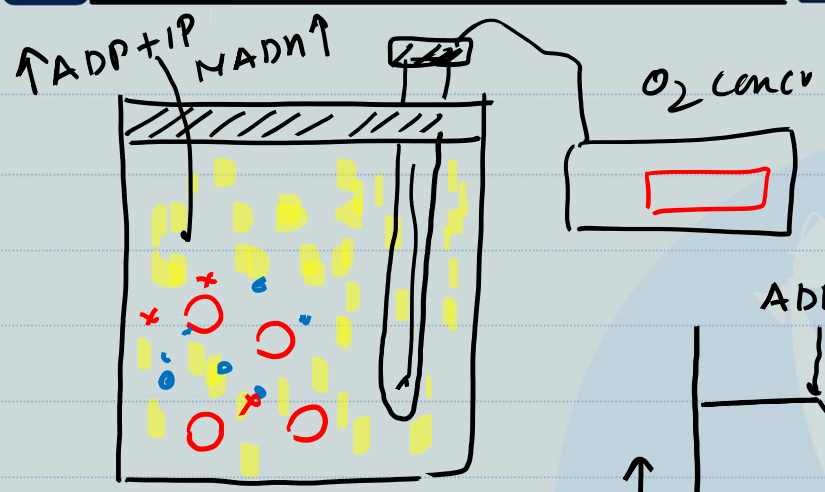


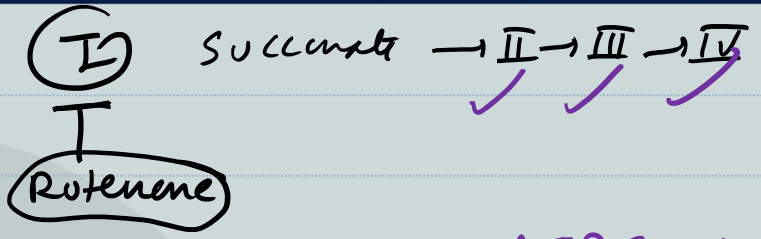
If ETC operates then O_2 will be consumed



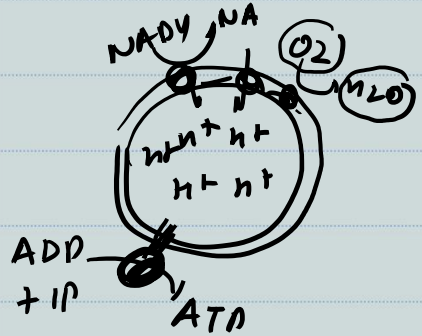
ADP
iP
NADH

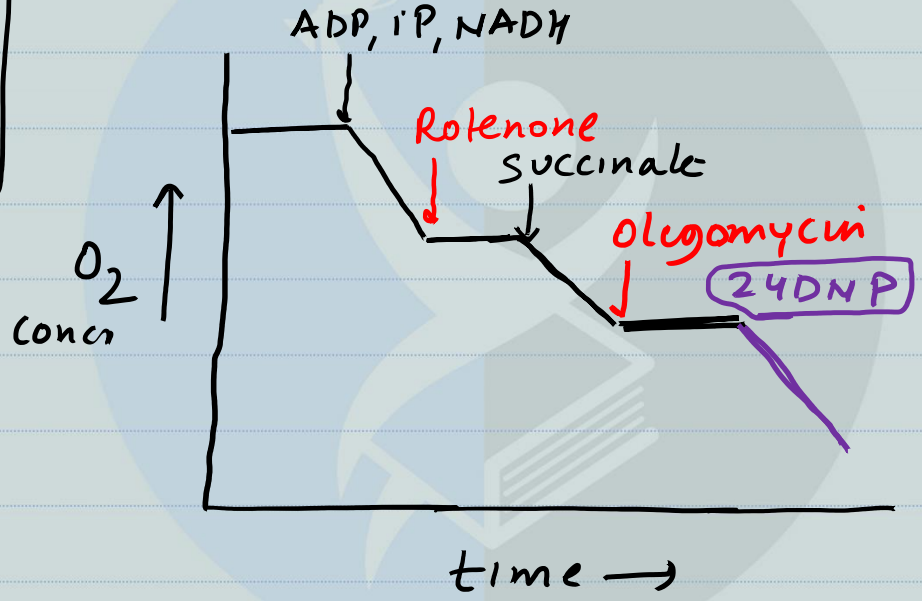
Microsome



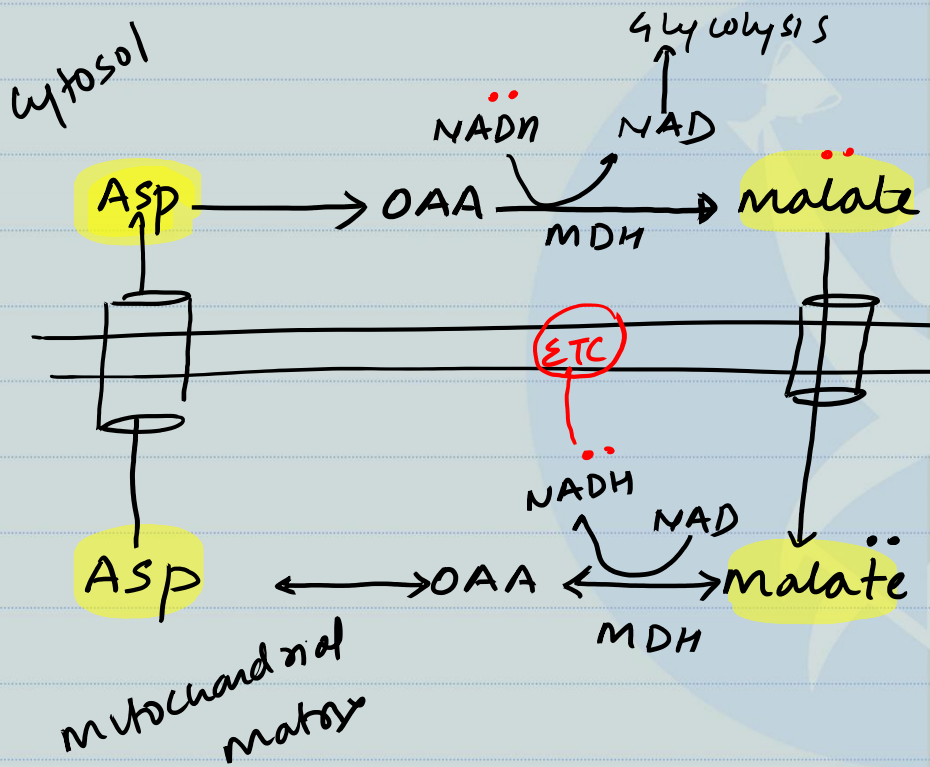


ATP Synthase





- **Malate-Aspartate Shuttle (Heart, liver and kidney):**



Glycolysis
- 2 ATP
- 2 NADH → ? → ETC

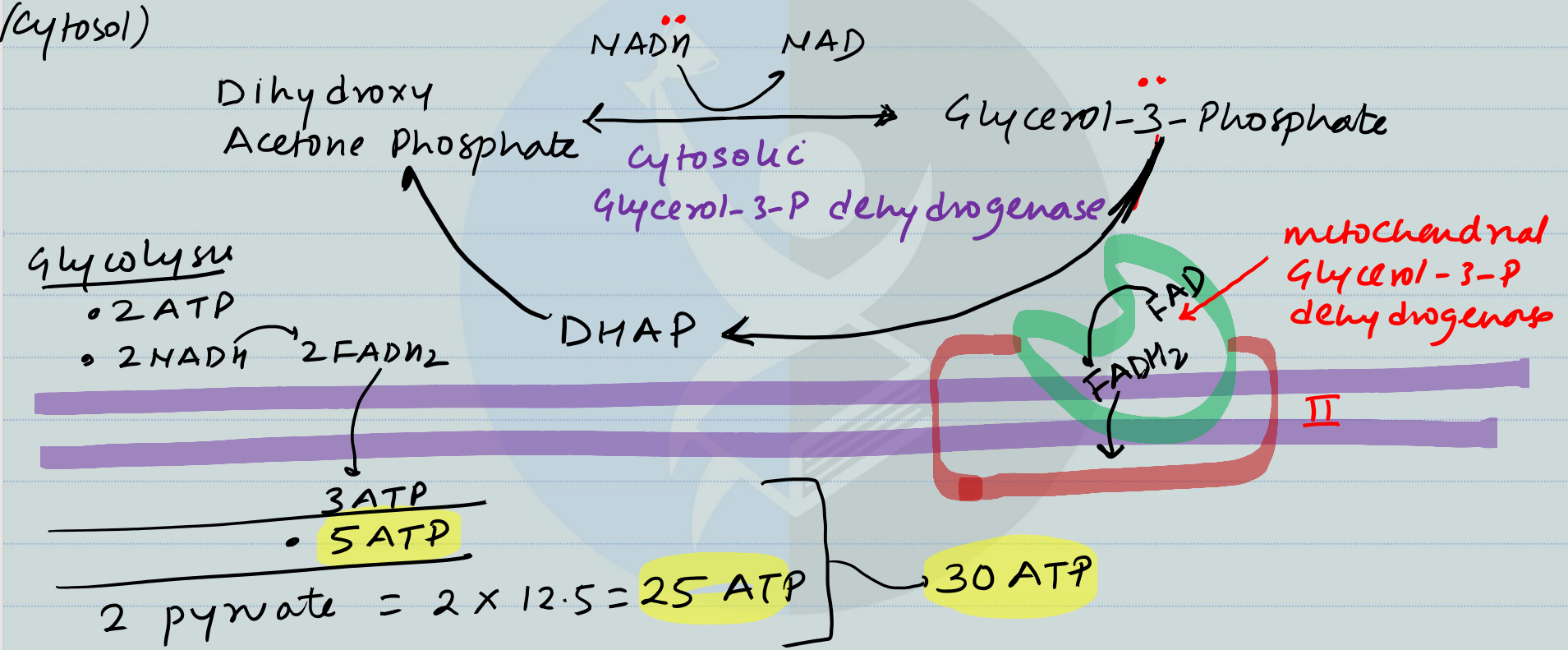
(cytosol)

Glycolysis
- 2 + 5 ATP = 7 ATP
- 2 Pyruvate = 2 × 12.5 ATP
  = 25 ATP

1 glucose ⇝ 32 ATP

2 NADH → 2 $FADH_2$

The glycerophosphate shuttle (brain and muscles): , Plants



HAPPY LEARNING

THANKS

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