Bioinorganic Chemistry

M.Sc. III SEM
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Introduction

- Bioinorganic chemistry is the branch of inorganic chemistry which identify the role of inorganic compounds in biological processes and to study the structure and functioning of these compounds.
- Analysis of ash of animal tissue exposed that it is having at least 30 elements. These elements can be classified in two types of constituents,

(A) Organic constituents:

comprises of about 90% of solid matter. Main elements are C, N, H, O. Examples of organic constituents are carbohydrates, proteins and lipids.

(B**) Inorganic Constituents**:

comprises of about 10% of solid matter. Main elements are Na, K, Cl, Mg, Fe, Ca etc.

Normally essential elements are present at lower concentrations and if are present at higher concentrations they become toxic. For example NaCl is toxic at higher concentrations because it upsets the essential electrolyte balance.

Essential and non-essential elements

The 30 elements can be divided into two groups essential and non-essential elements:

(A) Essential elements:

The elements which are necessary for the normal functioning of a tissue or living being. On the Basis of their amounts in tissue they can be further classified in two categories,

(i) Macro elements: Required in diet more than >1 mg. form 60-80% of all inorganic material present in body.

12 macro elements: C, H, O, N, P, Na, K, Ca, Fe, Mg, Cl, S.

(ii) Micro elements: Required in micrograms or in miligrams.

8 micro elements: Cu, Zn, Co, Mn, Mo, I, F etc.

(B) Non-essential elements: Their function in the body is not known yet.

10 elements: Br, B, Si, As, Ni, Al, Pb, Sn, V, Ti.

Metallobiomolecules

Natural products which contains one more metallic elements.

Metallobiomolecules

- **Transport & storage proteins**
  - Electrons carriers
    - Cytochromes (Fe)
    - Iron-sulfur (Fe)
    - Blue copper (Cu)
  - Metal storage, carrier & structural
    - Ferritin (Fe)
    - Transferritin (Fe)
    - Ceruloplasmin (Cu)
  - O_2 binding
    - Myoglobin (Fe)
    - Hemoglobin (Fe)
    - Hemerythrin (Fe)
    - Hemocyanin (Cu)
- **Enzymes**
  - Hydrolases
    - Carboxypeptidases (Zn)
    - Aminopeptidases (Mg, Mn)
    - Phosphatases (Mg, Zn, Cu)
  - Oxido-reductases
    - Oxidases (Fe, Cu, Mo)
    - Dehydrogenases (Fe, Cu, Mo) (reductases)
    - Hydroxylases (Fe, Cu, Mo)
    - Oxygenases (Fe)
    - Superoxide dismutase (Cu, Zn, Mn)
    - Nitrogenases (Fe, Mo)
    - Hydrogenases (Fe)
  - Isomerases & synthetases
    - Vitamin B-12 coenzyme (Co)
- **Nonproteins**
  - Metal transport & structural
    - Siderophores (Fe)
    - Skeletal (Ca, Si)
  - Photoredox
    - Chlorophyll (Mg)
    - PS II (Mn, Mg)

Biochemistry of Na, K and Cl

- **Source**
- **Absorption**
- **Distribution**
- **Fuctions**

✓Maintainance of normal hydration and osmotic pressure
✓Maintainance of normal acid-base equilibrium
✓Transport of CO2
✓Neuromuscular irritability
✓Maintainance of proper viscosity of blood
✓In secretion of digestive fluids
✓In the storage of protein and glycogen
✓In antibiotics
✓Excretion

The sodium potassium pump

Also known as Na^+-K^+ ATPase

Active transport

Required energy (in form of ATP)

Examples: Na^+-K^+ transport

H^+-K^+ transport

Ca^{2+} transport

Passive transport

Does not required energy

Transport is along the concentration gradient

The sodium potassium pump

- In order to maintain the cell potential, cells must keep a low concentration of Na^+ ions and high levels of K^+ ions within the cell. The Na^+-K^+ ATPase helps to keep lower concentration of Na^+ ions within the cell.

- In neural tissue 70% of total metabolic energy is consumed in maintaining these ion gradients.

- This is an energy dependent ion pump, which transport three Na^+ ions outside the cell and imports two K^+ ions inside the cell at hydrolysis of one ATP molecule.

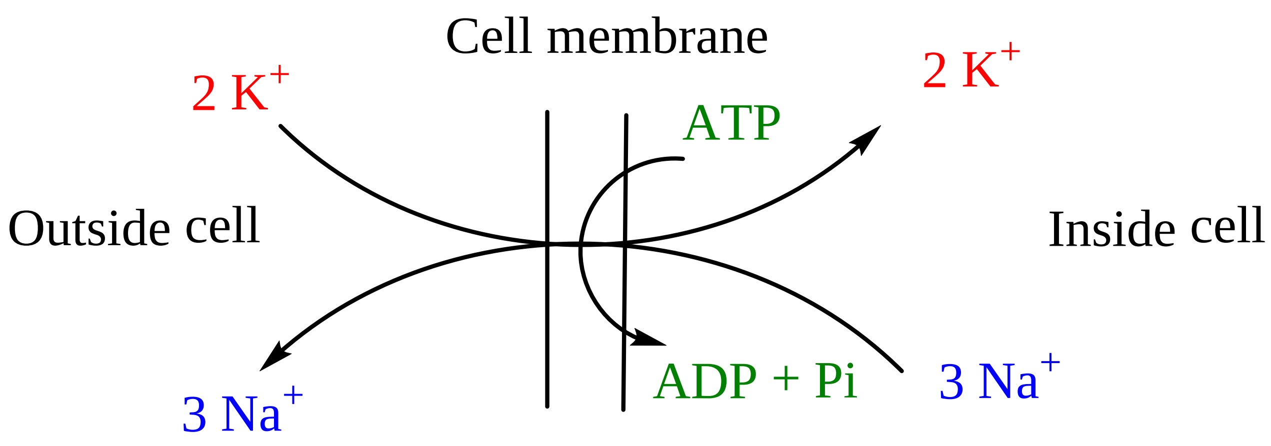
- This pump is electrogenic in nature as there is net movement of one positive charge outward percycle.

- The net process is ,

$$3\,Na^+{}^{(in)} + 2\,K^+{}^{(out)} + ATP + H_2O \rightleftharpoons 3\,Na^+{}^{(out)} + 2\,K^+{}^{(in)} + ADP + Pi$$

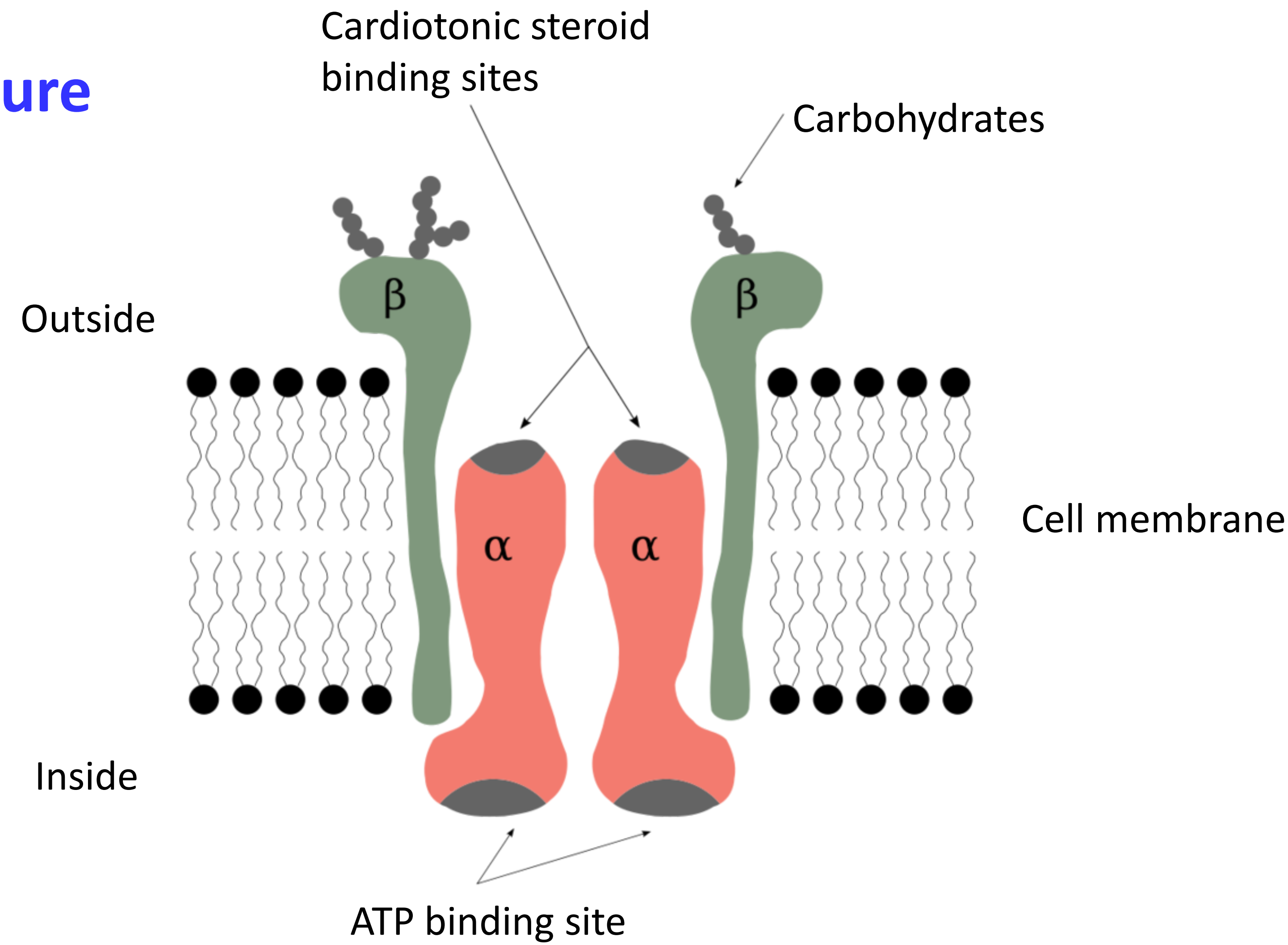
The sodium potassium pump

In most animal cells concentration gradient is,
Inside the cell
K+ = 0.15 M, Na+ = 0.01 M
Outside the cell
K+ = 0.004 M, Na+ = 0.15M



The sodium potassium pump

Structure

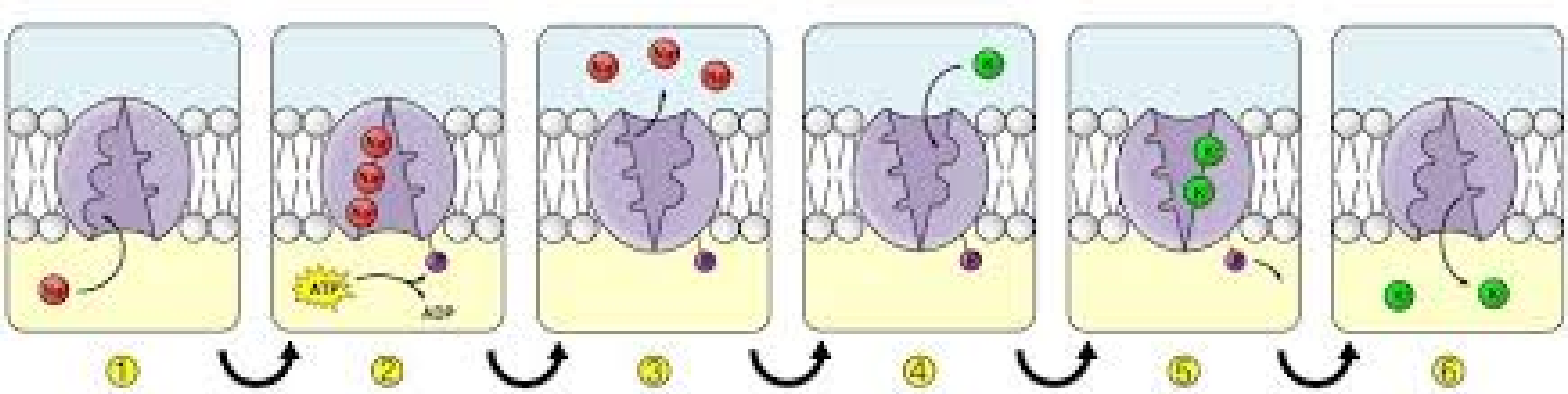


Source: image Wikipedia

The sodium potassium pump

Operation of pump

Outside cell



Inside cell

Na^+ ion

K^+ ion

✓ **Importance Na^+-K^+ pump**

Source image: internet (BioNinja)

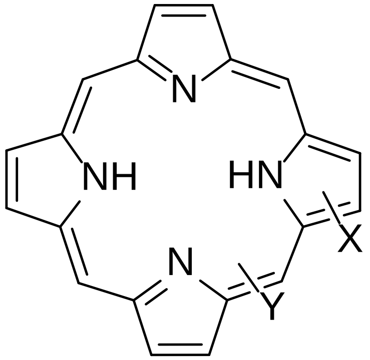
Cytochromes

- Electron transfer proteins in biological systems
- Found in all aerobic forms of life
- Heme proteins with Fe containing prosthetic group.
- Operated by shuttling of the iron atom between Fe(II) and Fe(III).

$$\mathrm{Fe(II)} \underset{+e}{\overset{-e^-}{\rightleftharpoons}} \mathrm{Fe(III)}$$ Redox intermediate

- Cytochromes are classified according to the type of porphyrin they contain.

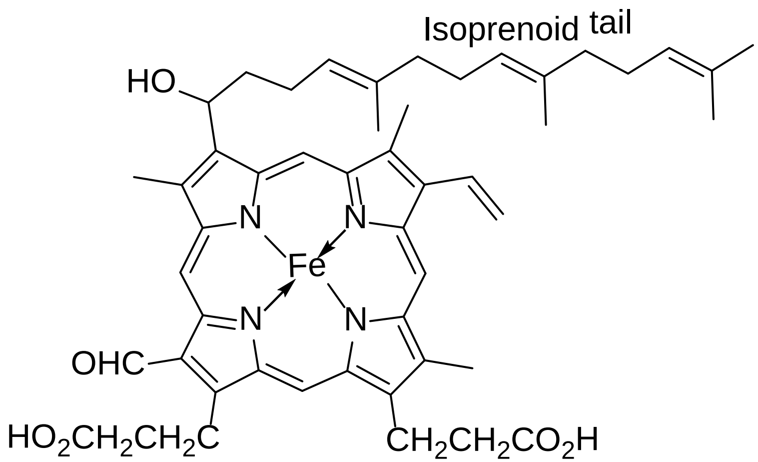
Broadly devided into cyt. a, b and c.



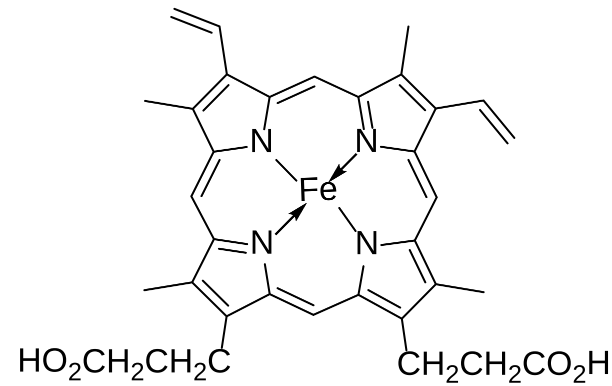
Porphyrin

Nature of substituents on porphyrin (EWG/ERG) helps to vary redox properties and interaction with protein chain.

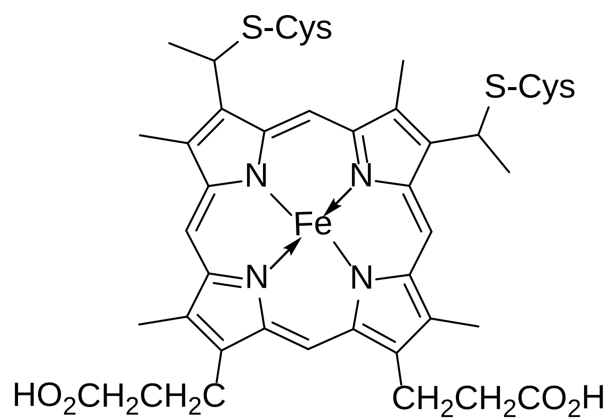
Cytochromes



Heme a
600 nm



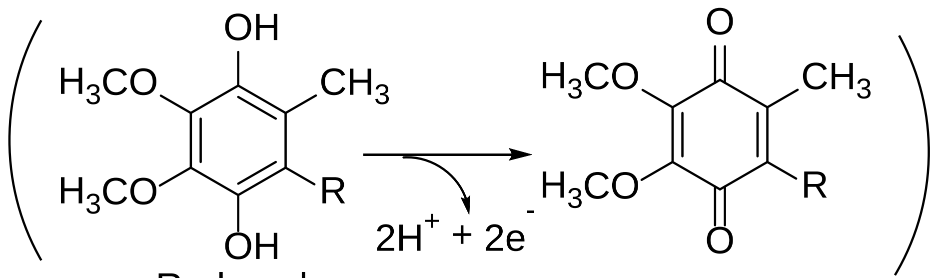
Heme b
560 nm



Heme c
550 nm

✓ In cyt. A and cyt. B, there is no covalant bond between heme and protein chain whereas in cyt. c heme and protein chain are connected with covalent thioether bond.

Cytochromes



Reduced — Oxidised

Reduced CoQ

↓

Cytochrome b (Cyt. b)

↓

Cytochrome c_1 (Cyt. c_1)

↓

Cyt. c

↓

Cyt a + Cyt. a_3

(Cytochrome c oxidase)

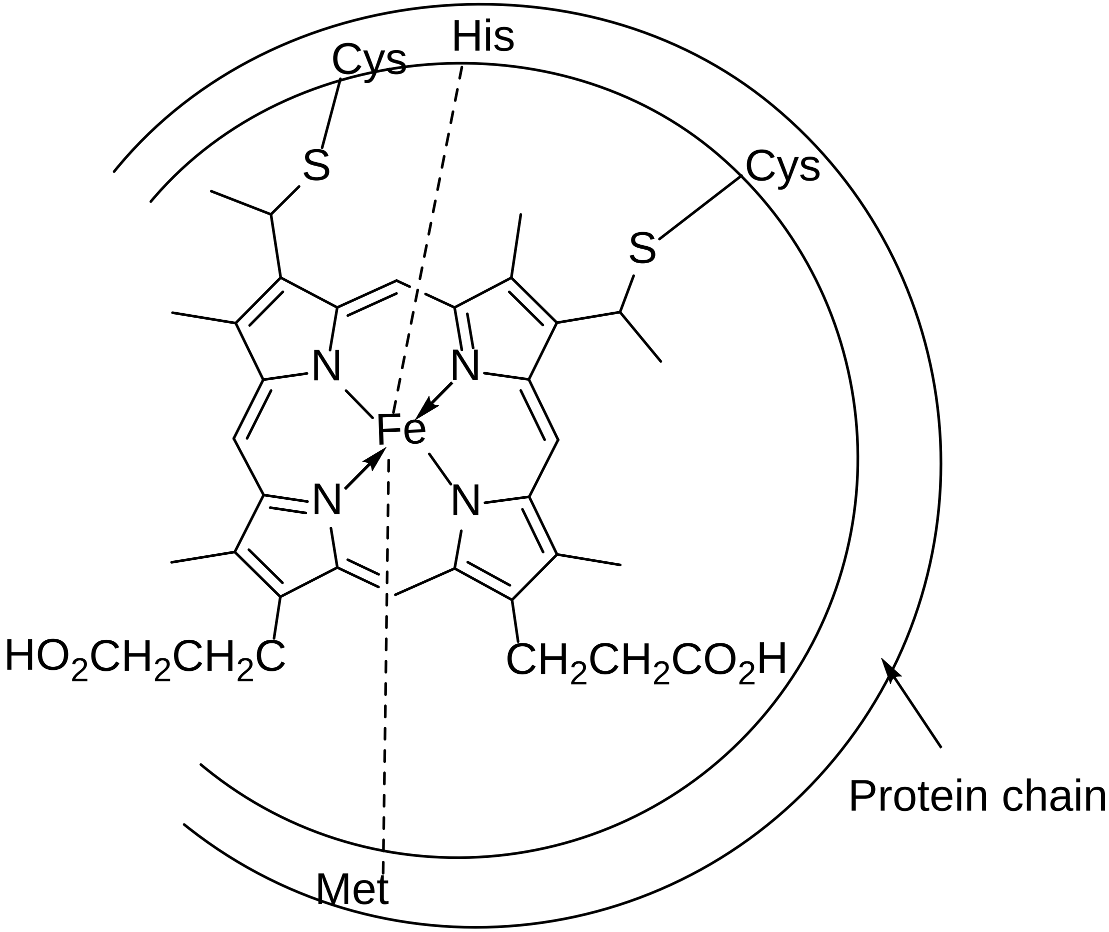
O_2 + $4H^+ + 4e^-$ → $2H_2O$

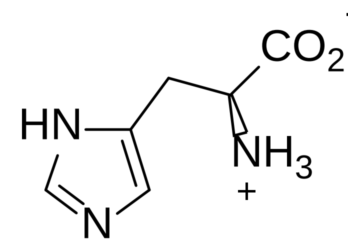
Standerd reduction potential (E_0) of Cyt.

Cyt. b (Fe^{2+}/Fe^{3+})	= +0.07
Cyt. c_1 (Fe^{2+}/Fe^{3+})	= +0.23
Cyt. c (Fe^{2+}/Fe^{3+})	= +0.25
Cyt. c oxidase (Fe^{2+}/Fe^{3+})	= +0.29
$1/2O_2/H_2O$	= +0.82

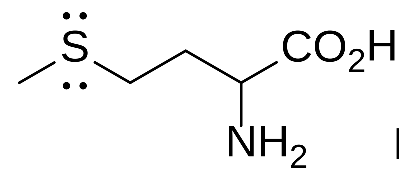
Sequence of cytochromes that intervene between coenzyme Q and the reduction of dioxygen

Cytochrome c





Histidine



Methionine

- Heme type c
- Covalently bound with protein chain
- Coordination number of iron is 6, so can’t bind with oxygen
- Can react only via elecron transfer mechanism not by simple coordination

Cytochrome c oxidase

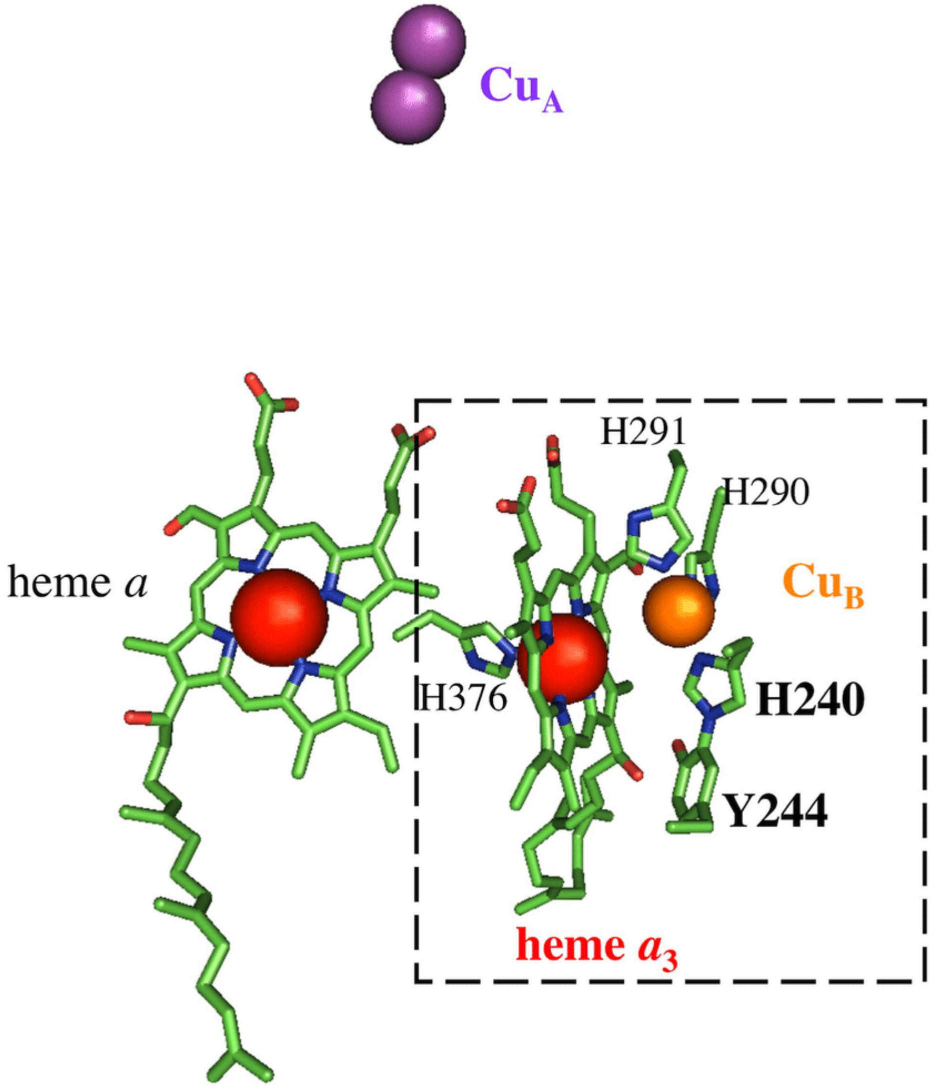
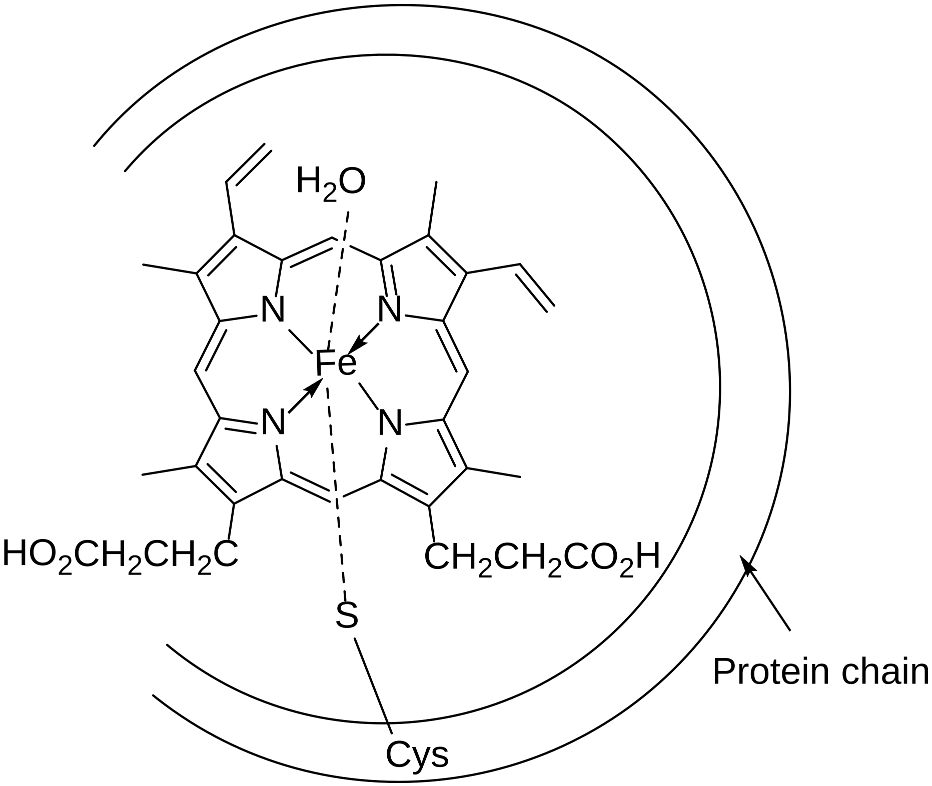


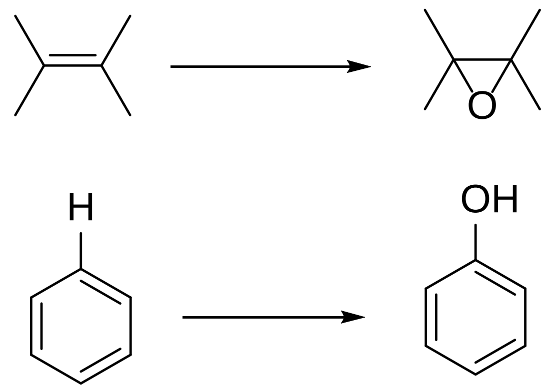
Image source: William James McDonald, Univ. of California

Cytochrome P-450



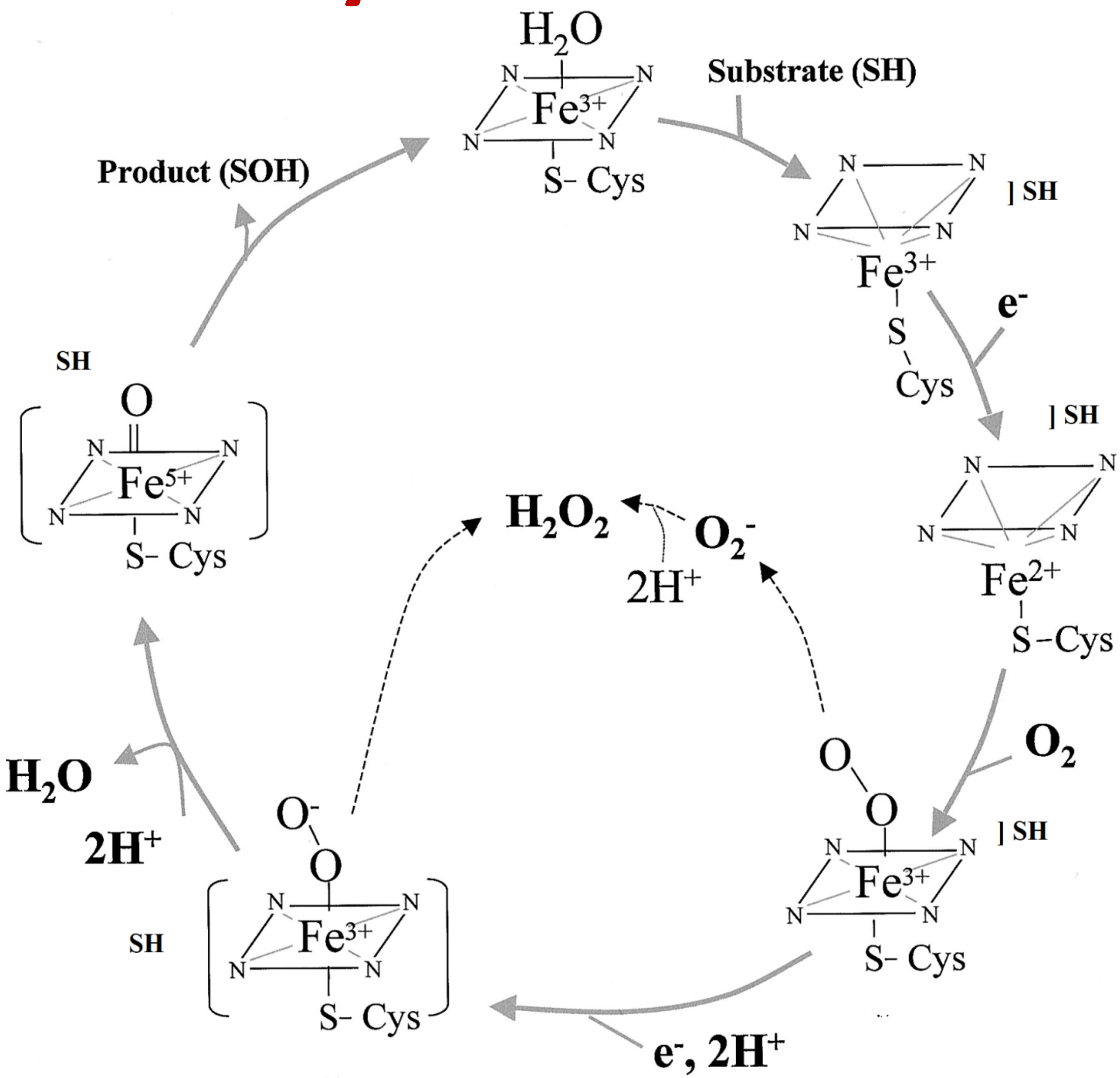
- Heme type b
- Name Cyt. P-450: Its complex with CO absorbs at λmax = 450 nm
- Detoxification
- Oxigenate the substrates

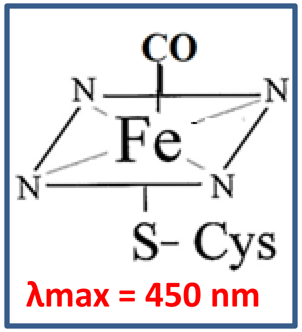
$$\text{R-H} + {}^{1}/_{2}\,O_2 \longrightarrow \text{R-OH}$$



$$\text{Ph–O–CH}_3 \longrightarrow \text{Ph–O–H} + \text{HCHO}$$

Cytochrome P-450





The cycle of reactions of P-450

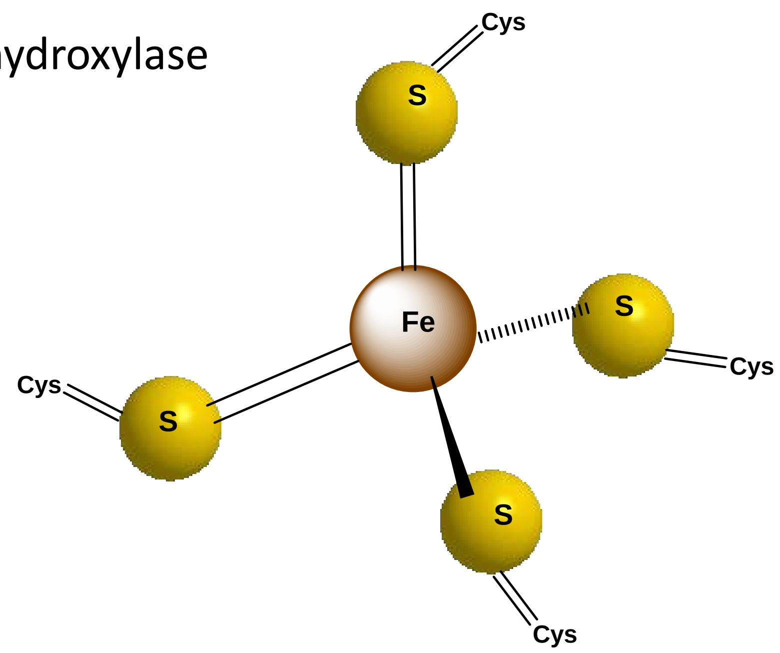
Source image: I. Fleming, Circulation res. 2001, 89, 753.

Iron-Sulfur Proteins

- Nonheme proteins containing Fe-S clusters
- Involved in electron transfer reactions (redox reaction)
- All types of Fe-S proteins participate in one electron transfers irrespective to the number of iron atoms
- almost all Fe centres are tetrahedrally coordinated to sulfur atoms
- Present in anaerobic and aerobic bacteria, algae, fungi, higher plants and animals
- Classified into two types (1) Rubredoxin (Rd) and (2) Ferredoxin (Fd)

Rubredoxin

- Singel iron atoms tetrahydrally coordinated by four sulfur atoms $(Cys\text{-}S)_4Fe$
- Do not have acid labile sulfide
- Ligands are cysteines which provide four thiolate donors
- Iron atom in rubredoxin exhibits +2 and +3 oxidation states
- Molecular weight around 6000 with 54 amino acid residues
- Oxidized form is red and reduced form is colorless
- It receives electron from NADH and turns to Fe(II) and rexoidized to Fe(III) after releasing electron to hydroxylase

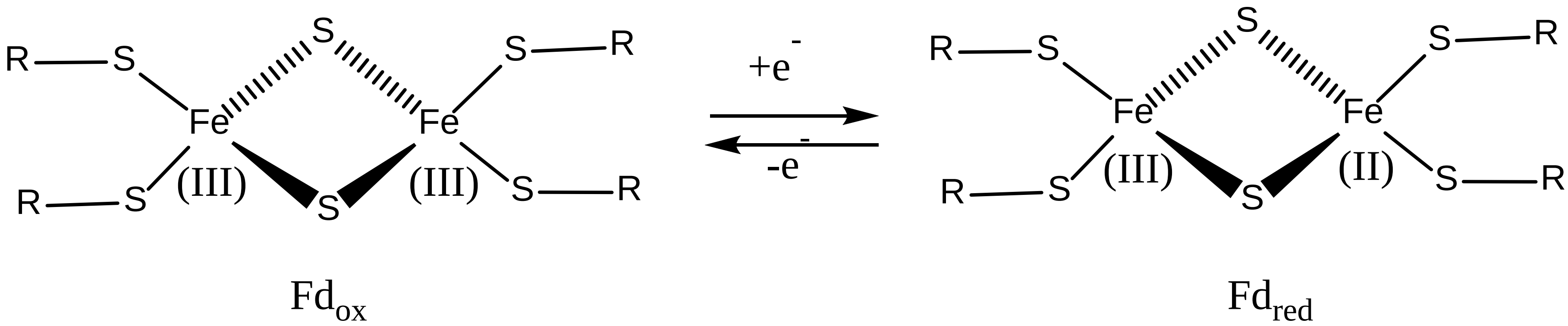


Ferredoxins

2Fe-2S and 4Fe-4S are most common ferredoxins

2Fe-2S

- $[Fe_2S_2(S\text{-}Cys)_4]^{2-}$ cluster
- The two Fe(III) sites are antiferromagnetically coupled and resulting in diamagnetic cluster
- Donate electrons to Cyt P-450 monooygenase and Cyt P-450 camphormonooxygenase



Ferredoxins

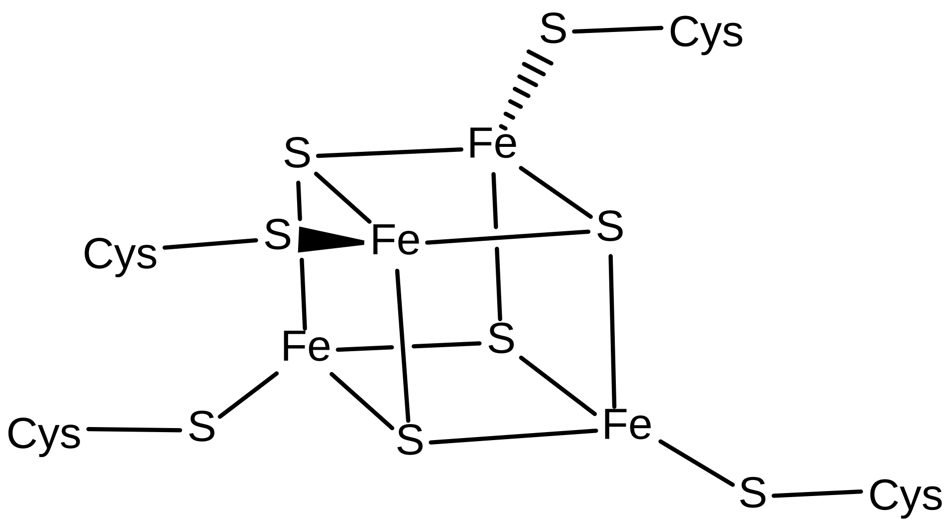
4Fe-4S

Subdevided into Low potential and High potential (HiPIP) ferredoxins

In Low potential ferredoxin [$2Fe^{3+}$, $2Fe^{2+}$] or [$1Fe^{3+}$, $3Fe^{2+}$]

In High potential ferredoxin [$3Fe^{3+}$, $1Fe^{2+}$] or [$2Fe^{3+}$, $2Fe^{2+}$]

- **Play an important role in biological nitrogen fixation.**

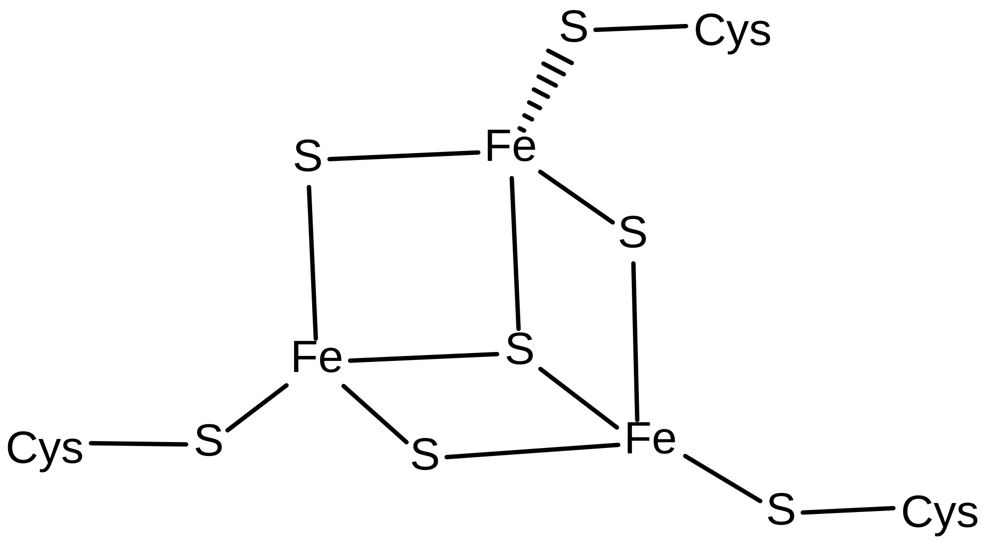


$$Fe_4S_4^{3+} \underset{}{\overset{+e^-}{\rightleftharpoons}} Fe_4S_4^{2+} \underset{}{\overset{+e^-}{\rightleftharpoons}} Fe_4S_4^{+}$$

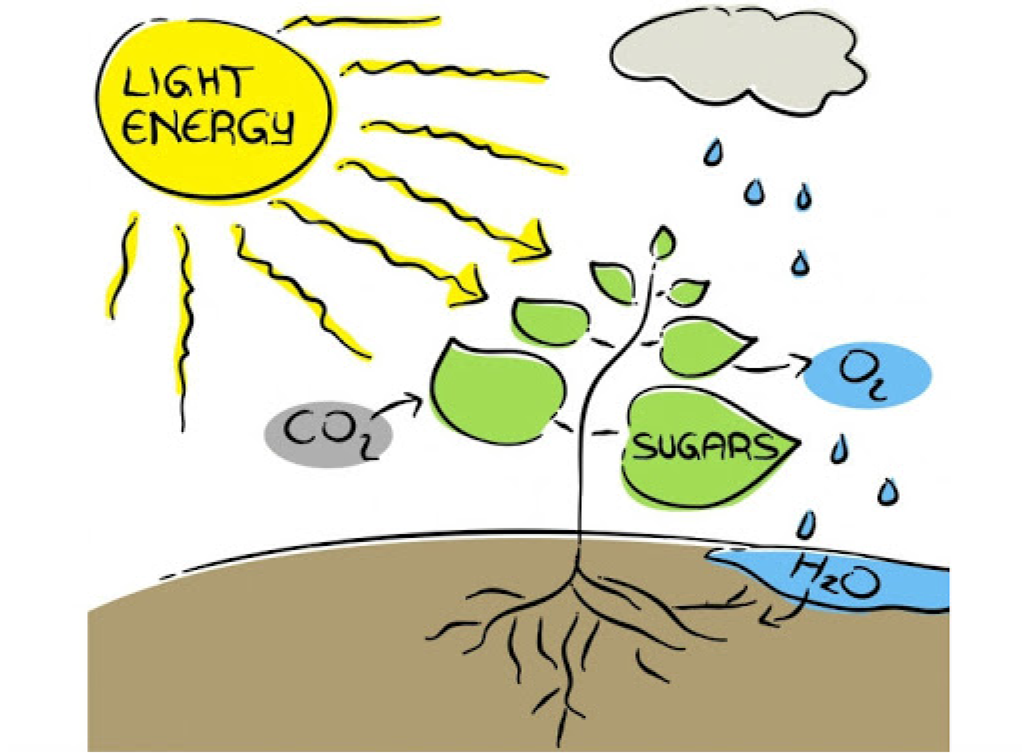
[Fe(III)$_3$Fe(II)]	[Fe(III)$_2$Fe(II)$_2$]	[Fe(III)Fe(II)$_3$]
oxidized HiPIP	reduced HiPIP	

Ferredoxins

3Fe-4S



Photosynthesis



$$nCO_2 + nH_2O \xrightarrow[\text{Chlorophyll}]{\text{Light}} (CH_2O)_n + nO_2$$

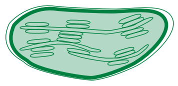
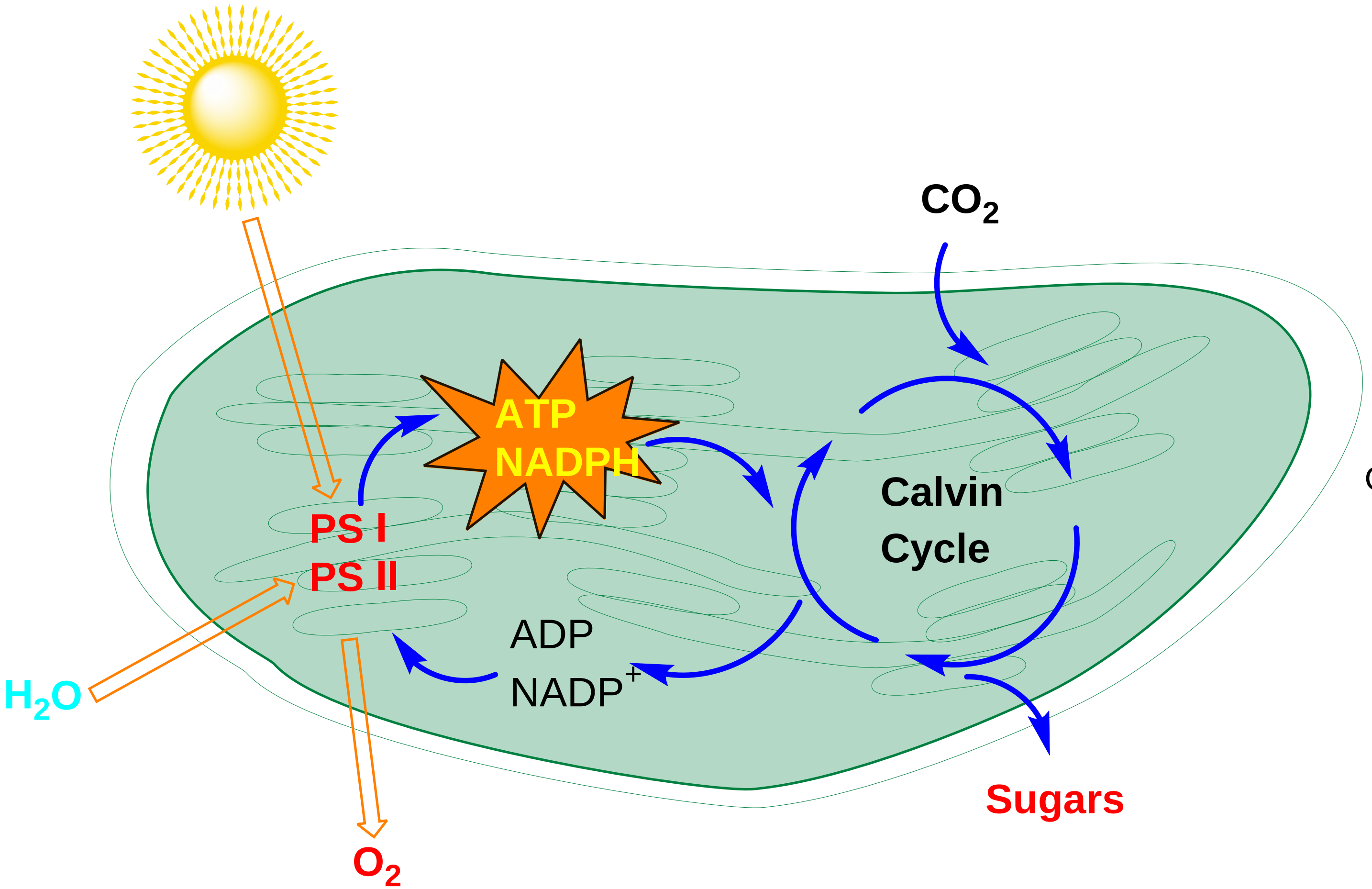
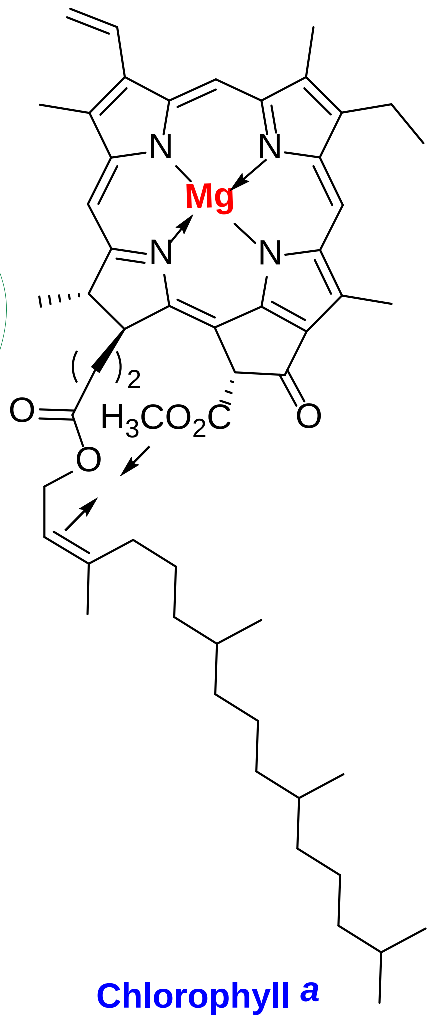


Image source: *Credit Shutterstock, Earth Times*

Photosynthesis: Chlorophyll



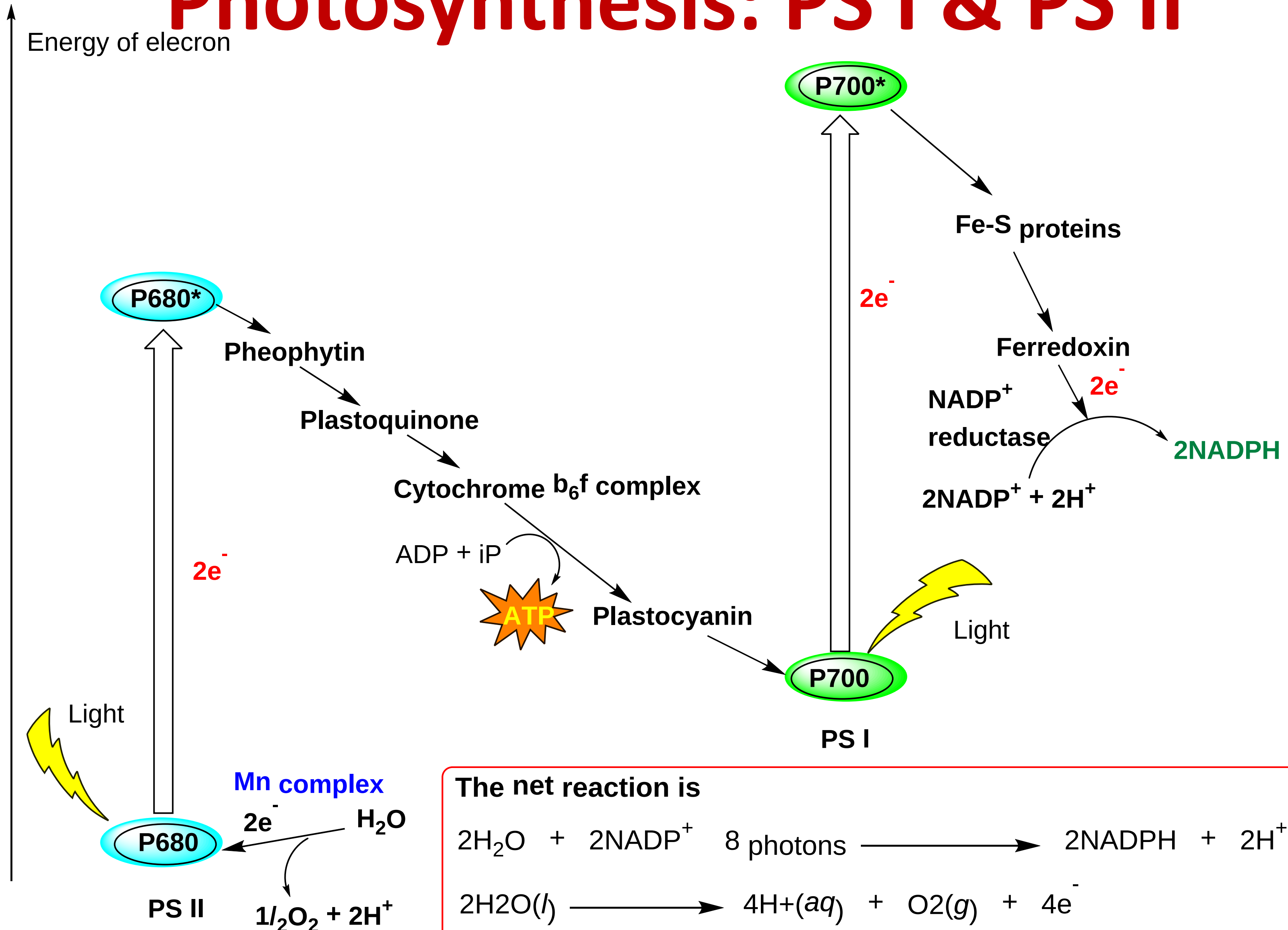


Chlorophyll *a*

PS I : contains about 200 molecules of Chl. A and 50 carotenoid pigments, absorption at 700 nm

PS II : contains Chl. a, Chl. B and othe rassociated pigments, absorption at 680 nm

Photosynthesis: PS I & PS II



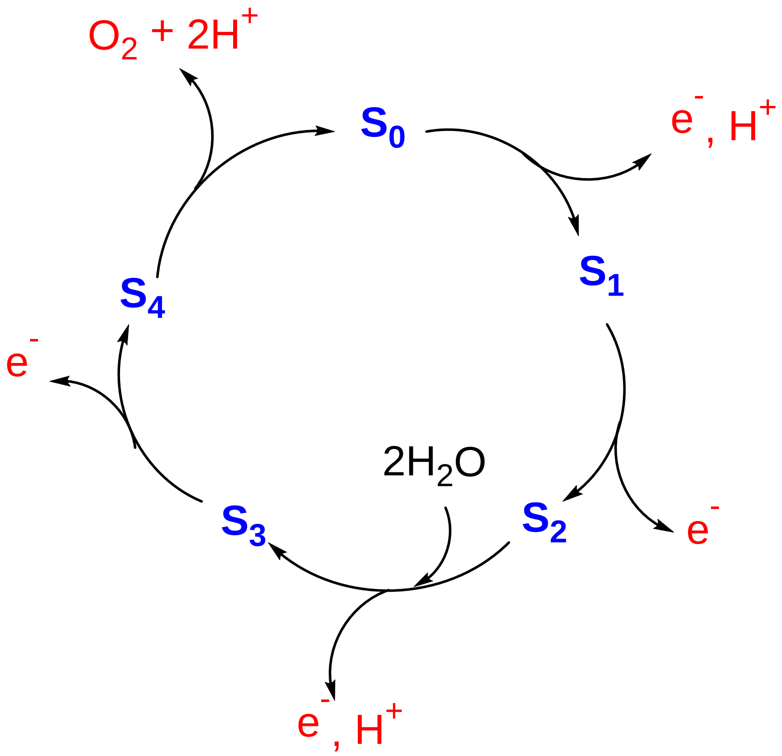
The net reaction is

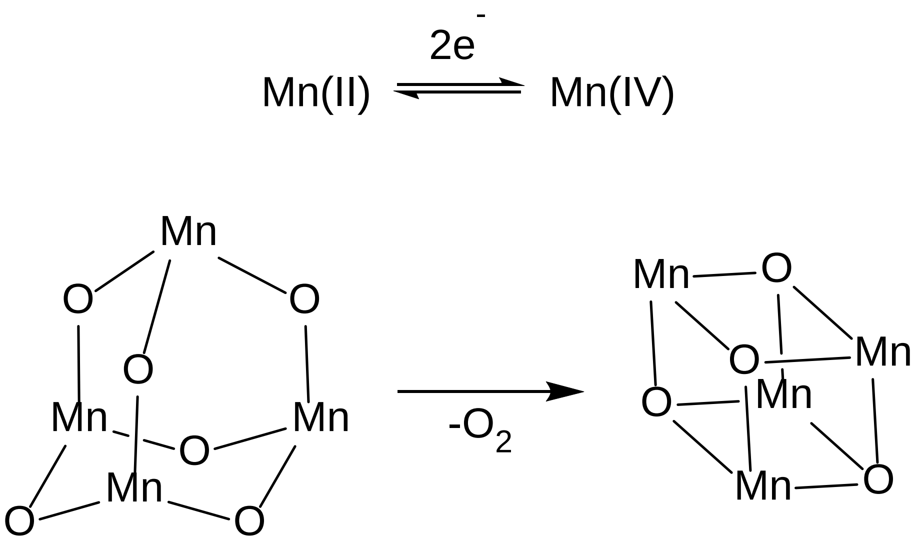
$2H_2O$ + $2NADP^+$ 8 photons $\longrightarrow$ 2NADPH + $2H^+$ + O_2

2H2O(*l*) $\longrightarrow$ 4H+(*aq*) + O2(*g*) + $4e^-$

The Pathway of electron transfer from H_2O to NADP+ in two Photosystems for green plants

Photosynthesis





S_4 Adamantane form *S_0* Cubane form

Proposal for the cyclic four steps of oxidation that release O_2 in PS II