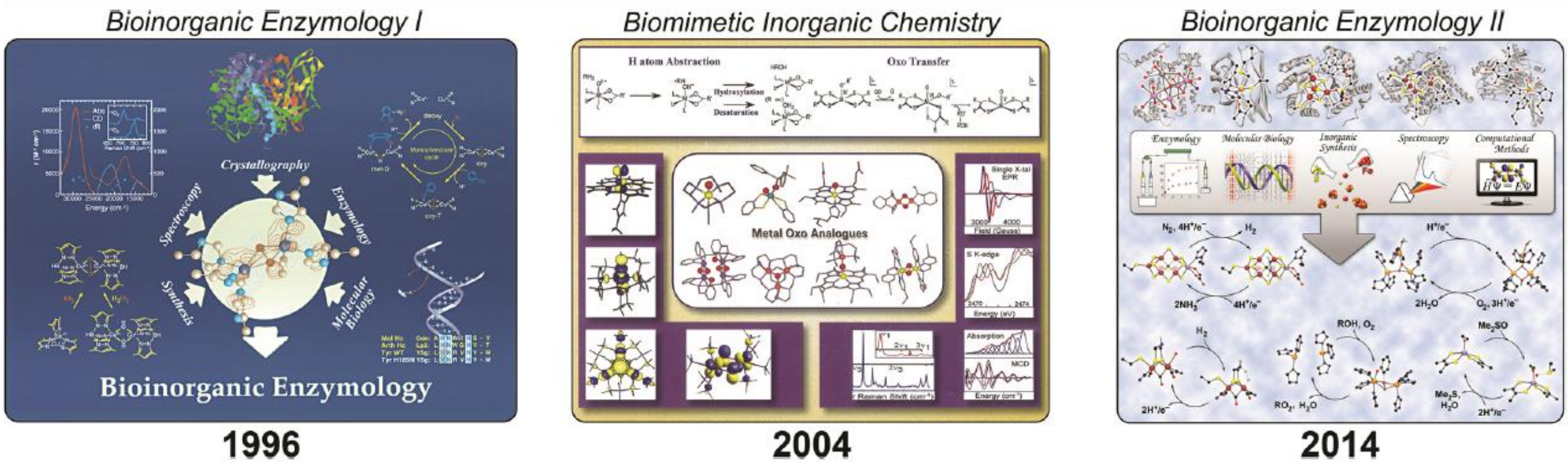
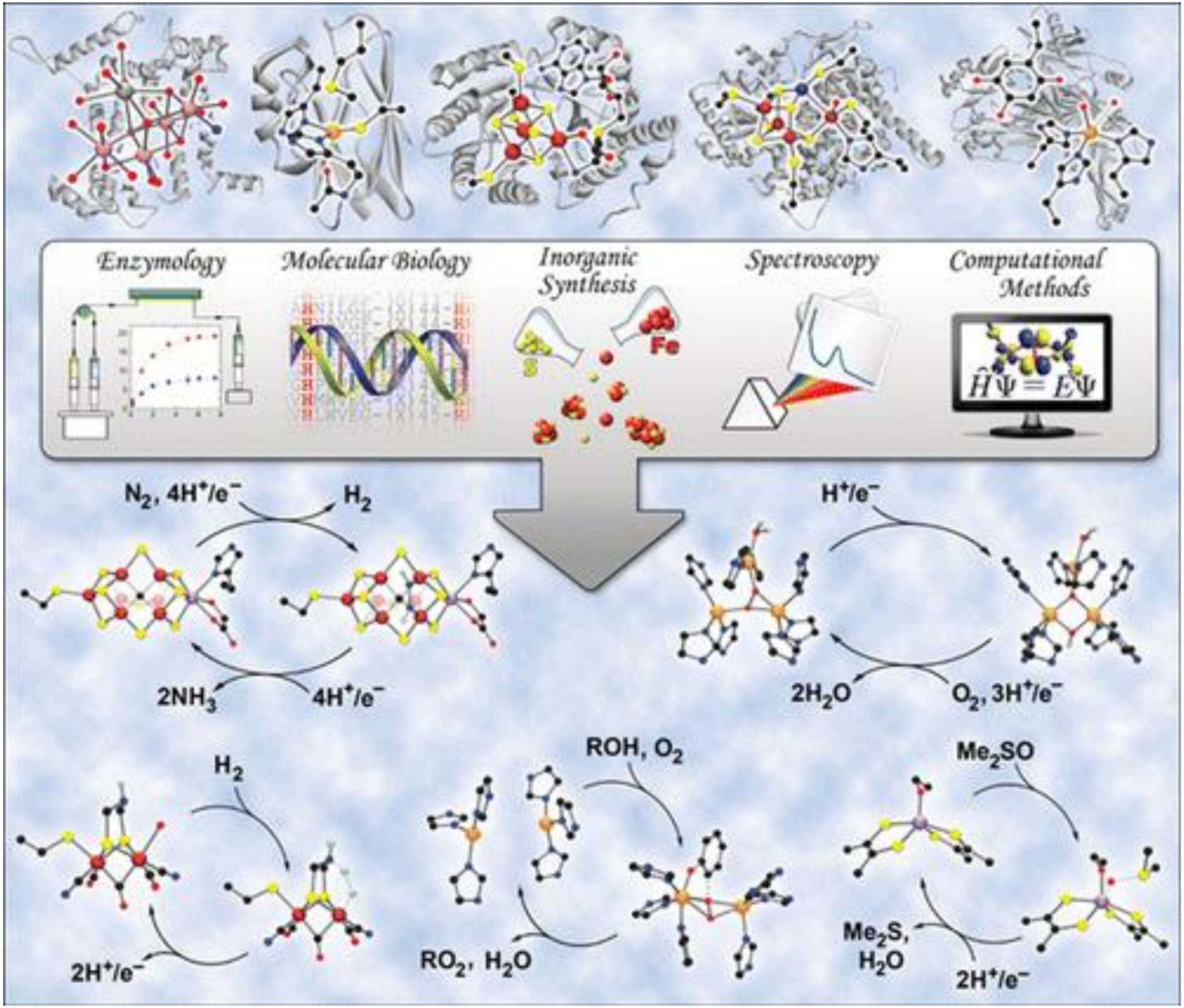
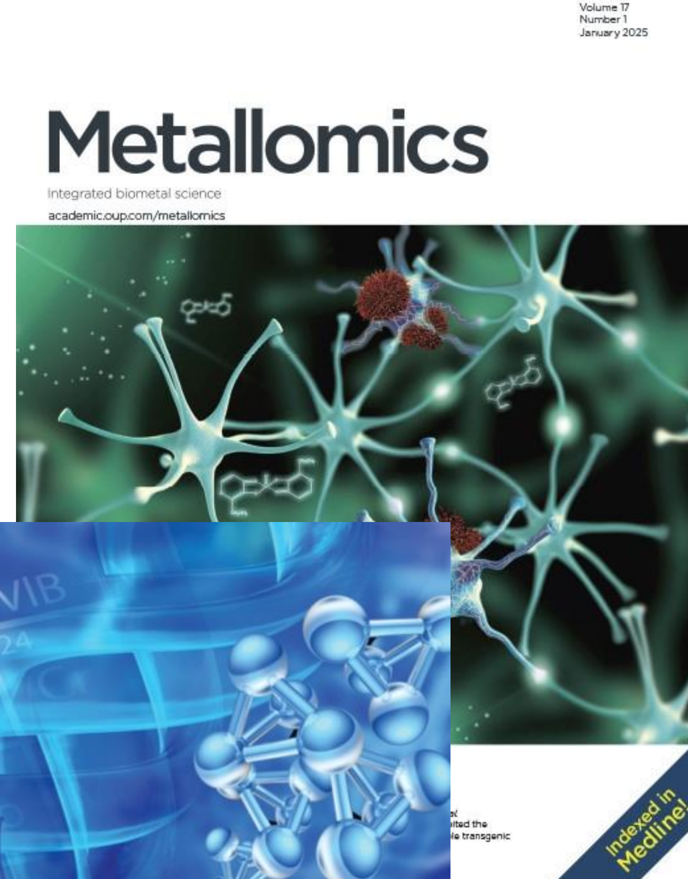
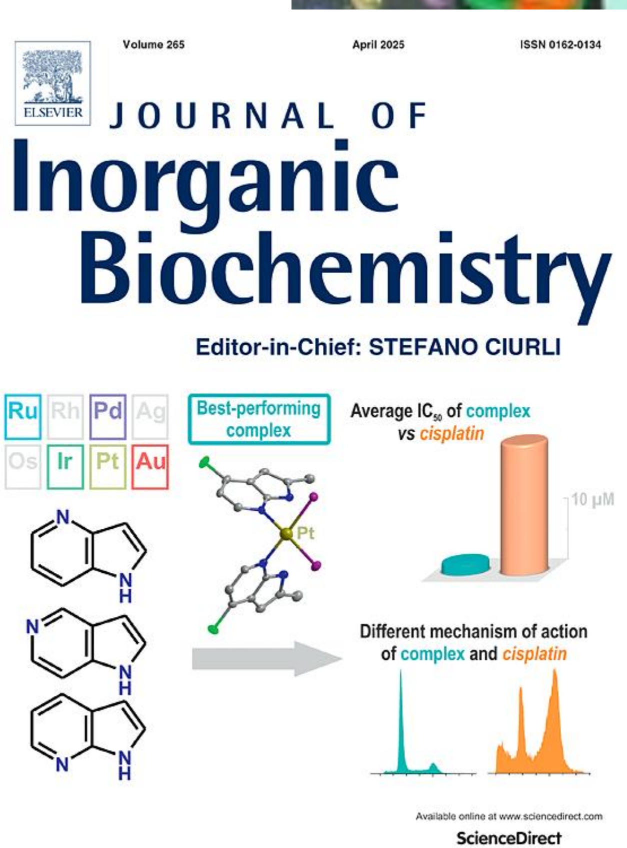
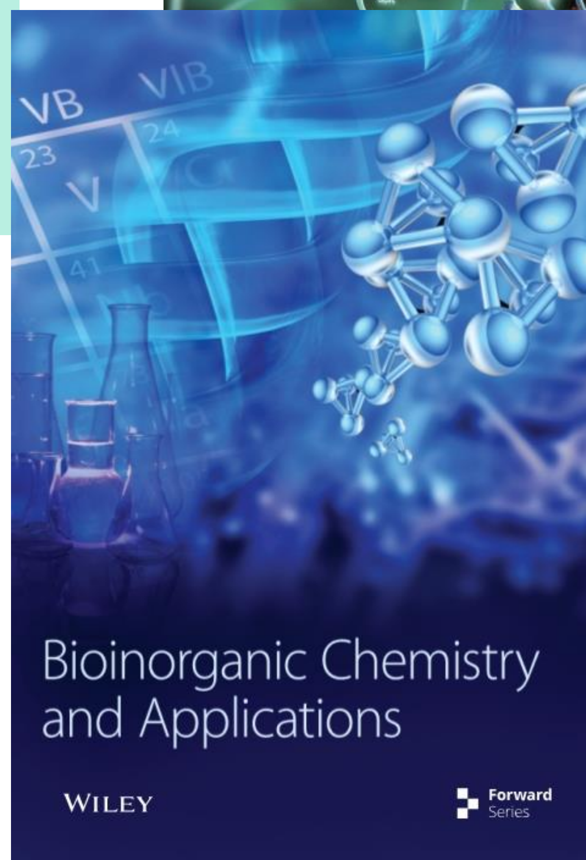


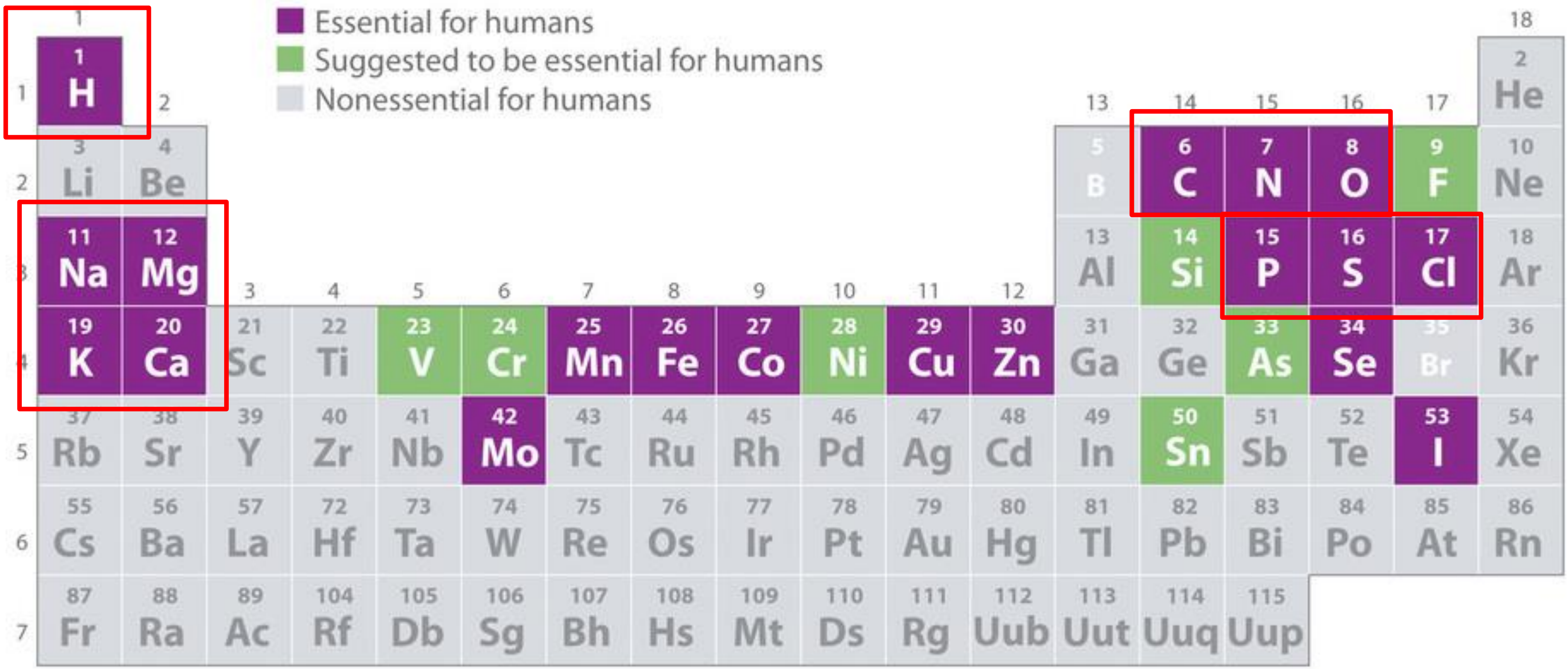
Figure 1. Covers of the triad of *Chemical Reviews* thematic issues on Bioinorganic Chemistry (1996, 2004, 2014).



Enzymology
Molecular Biology
Inorganic Synthesis
S
Fe
Spectroscopy
Computational Methods
$\hat{H}\Psi = E\Psi$
N_2, $4H^+/e^-$
H_2
$2NH_3$
$4H^+/e^-$
H^+/e^-
$2H_2O$
O_2, $3H^+/e^-$
H_2
$2H^+/e^-$
ROH, O_2
RO_2, H_2O
Me_2SO
Me_2S, H_2O
$2H^+/e^-$


JBIC
2021
Journal of
Biological
Inorganic
Chemistry

Volume 17
Number 1
January 2025
Metallomics
Integrated biometal science
academic.oup.com/metallomics
Indexed in Medline!

Volume 265
April 2025
ISSN 0162-0134
ELSEVIER
JOURNAL OF
Inorganic
Biochemistry
Editor-in-Chief: STEFANO CIURLI
Ru Rh Pd Ag
Os Ir Pt Au
Best-performing complex
Average IC50 of complex vs cisplatin
10 μM
Different mechanism of action of complex and cisplatin
Available online at www.sciencedirect.com
ScienceDirect

Bioinorganic Chemistry
and Applications
WILEY
Forward
Series

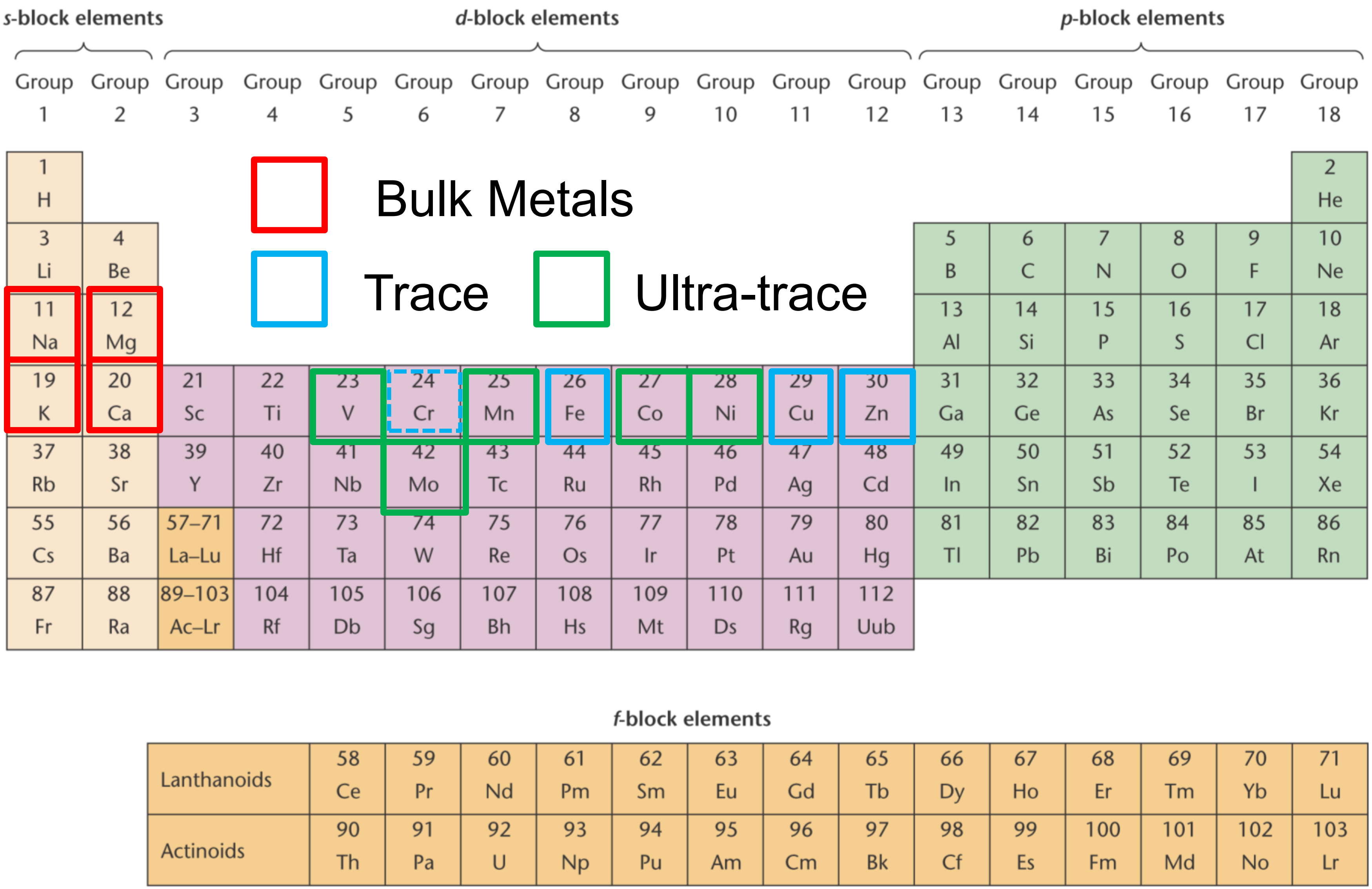
Essential elements in living organisms



11 elements (red frame) are predominant and ca. constant in terms of atoms % in all living organisms (99.9% of total atoms)

C + H + O + N = 99% of total atoms

12/13 metallic elements are essential for living organisms



Abundance of essential metallic elements in living organisms

Metal	g/75 kg
Na	70 – 120
K	160 – 200
Ca	1100
Mg	25
Fe	4 – 5
Zn	2 – 3
Cu	$80 – 120 \times 10^{-3}$
V	15×10^{-3}
Mn	1×10^{-2}
Co	1.2×10^{-3}
Mo	10×10^{-3}
Ni	?

Average intracellular concentration in eucariotic cells:

$[Fe]_{total}$ = 0.5 mM
$[Zn]_{total}$ = 0.5 mM
$[Cu]_{total}$ = 50 μM

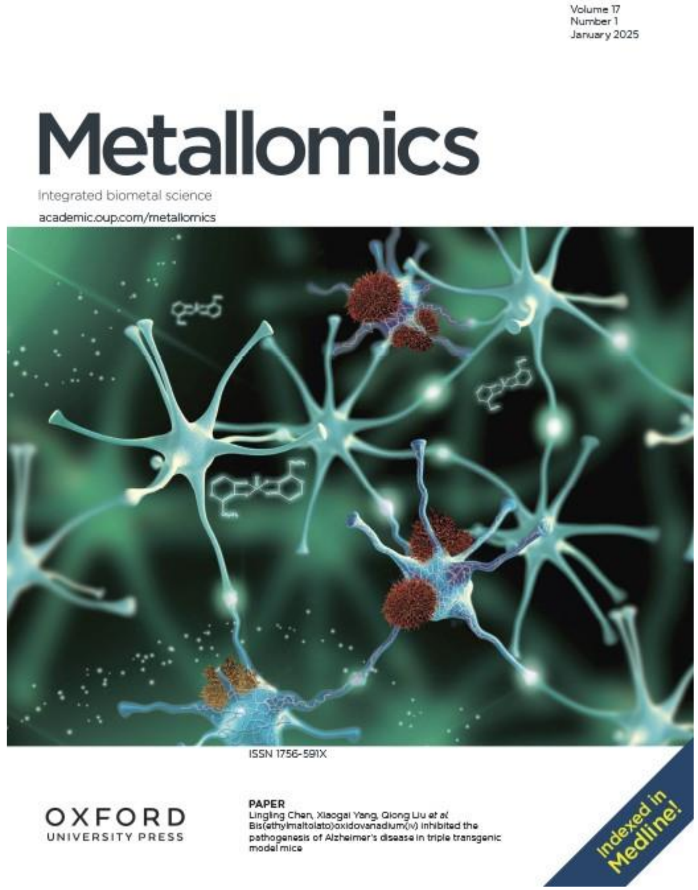
[Fe] corresponds to ca. 10^6 Fe atoms per cell

Cells are capable of accumulating essential metal ions

Metallome

Each species is characterized by a specific **metallome**

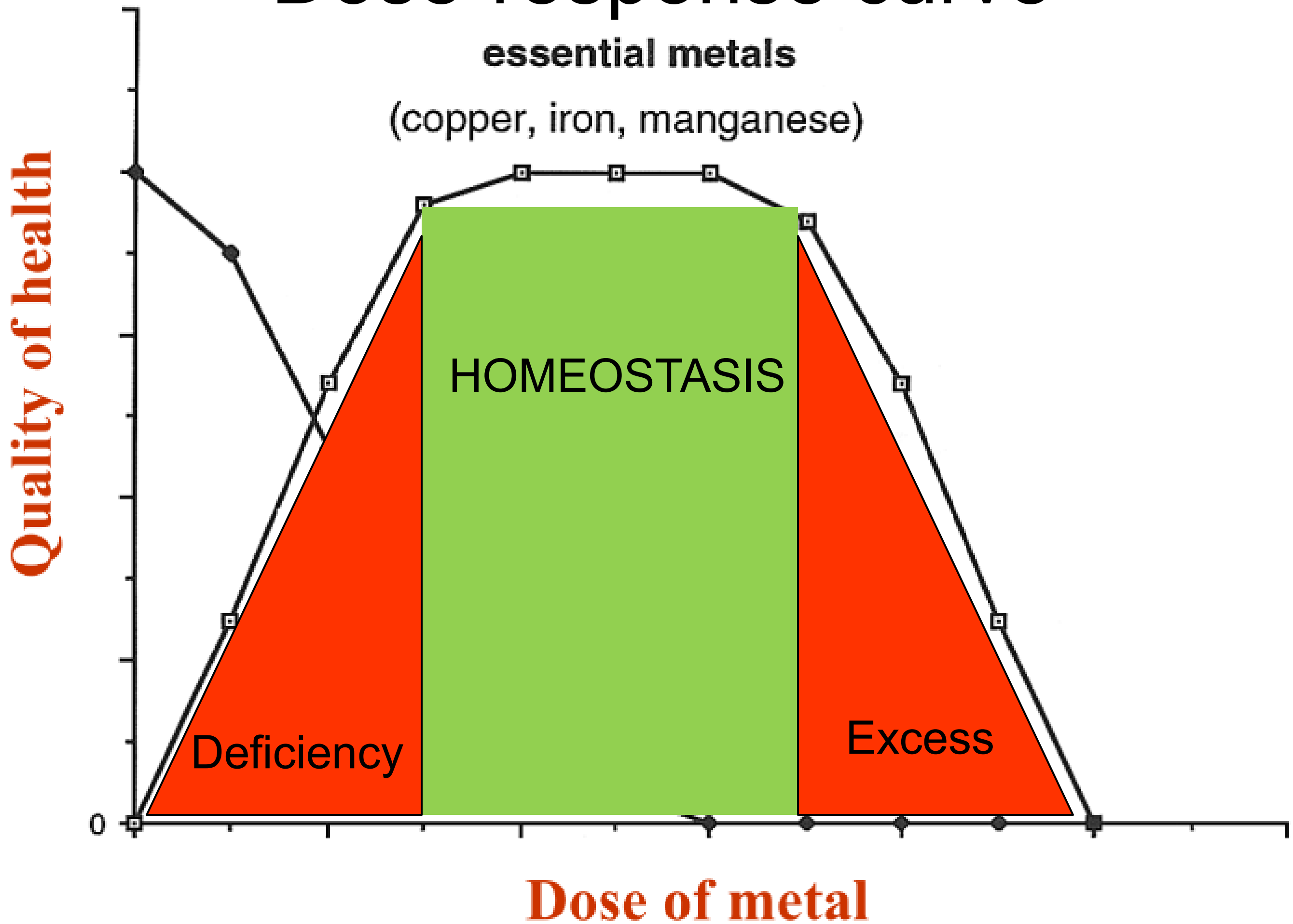
Defined as the pool of metals that are present in each type of cell of that species, each one with its specific **amount**, **speciation**, and **localization** inside each cell

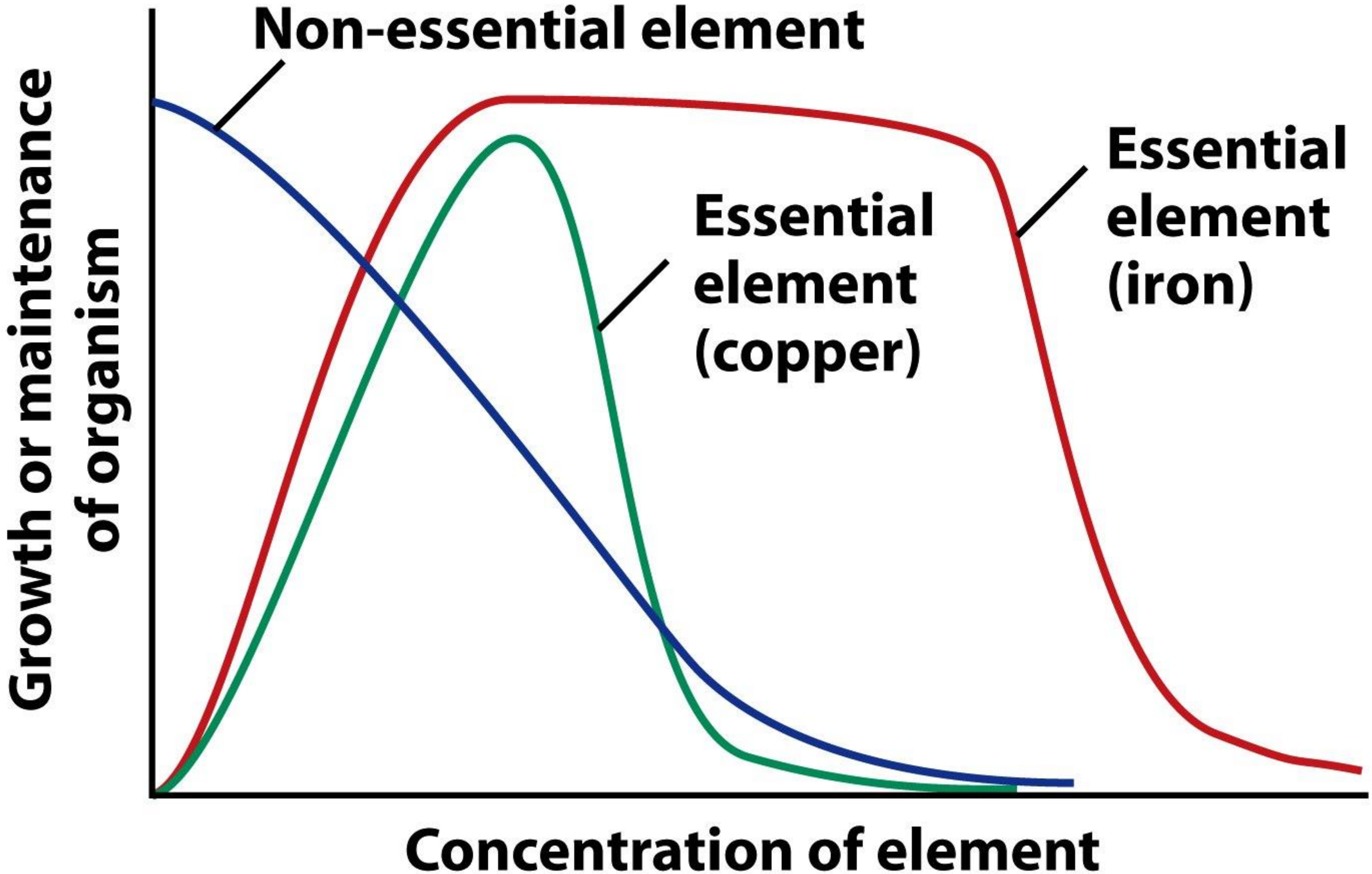


How an element can be established as being essential for a particular species?

An ***essential*** *element is defined as one that is* *<u>systematically</u>* *present in a certain biological species and such that its absence (or deficiency) in the nutrient sources of that species causes disease, metabolic or developmental disorders. Negative effects are also caused by its excess.*

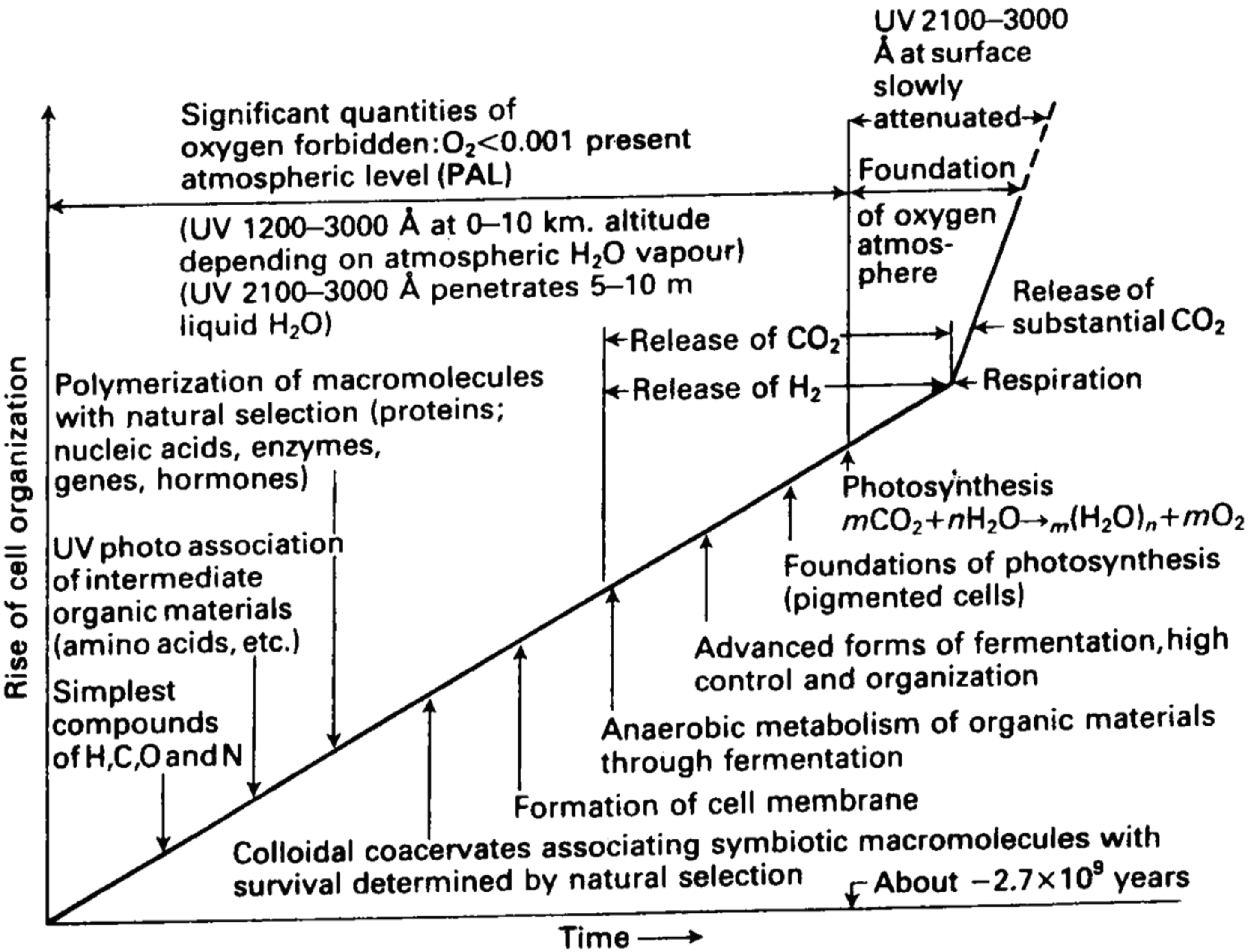
Dose-response curve




Non-essential element
Essential element (iron)
Essential element (copper)
Growth or maintenance of organism
Concentration of element

Element	Deficiency symptoms	Excess symptoms
Ca	Delay in skeletal growth	
Mg	Muscle cramps, convulsions	
Fe	Anemia, disorders in the immune system	Oxidative stress
Zn	Damage to the skin, delayed sexual maturation	
Cu	Weakness of the arteries, liver disorders, secondary anemia, Menkes Syndrome	Wilson Syndrome
Mn	Infertility, reduced skeletal growth	Psychiatric disorders
Mo	Delay in cell growth, propensity to caries	Anemia
Co	Pernicious anemia	Cardiac disorders
Si	Disorders in skeletal growth	
F	Caries	
I	Gout, Thyroid disorders, delayed metabolism	Gout
Se	Muscle weakness, cardiomyopathy	
As	Delayed growth	

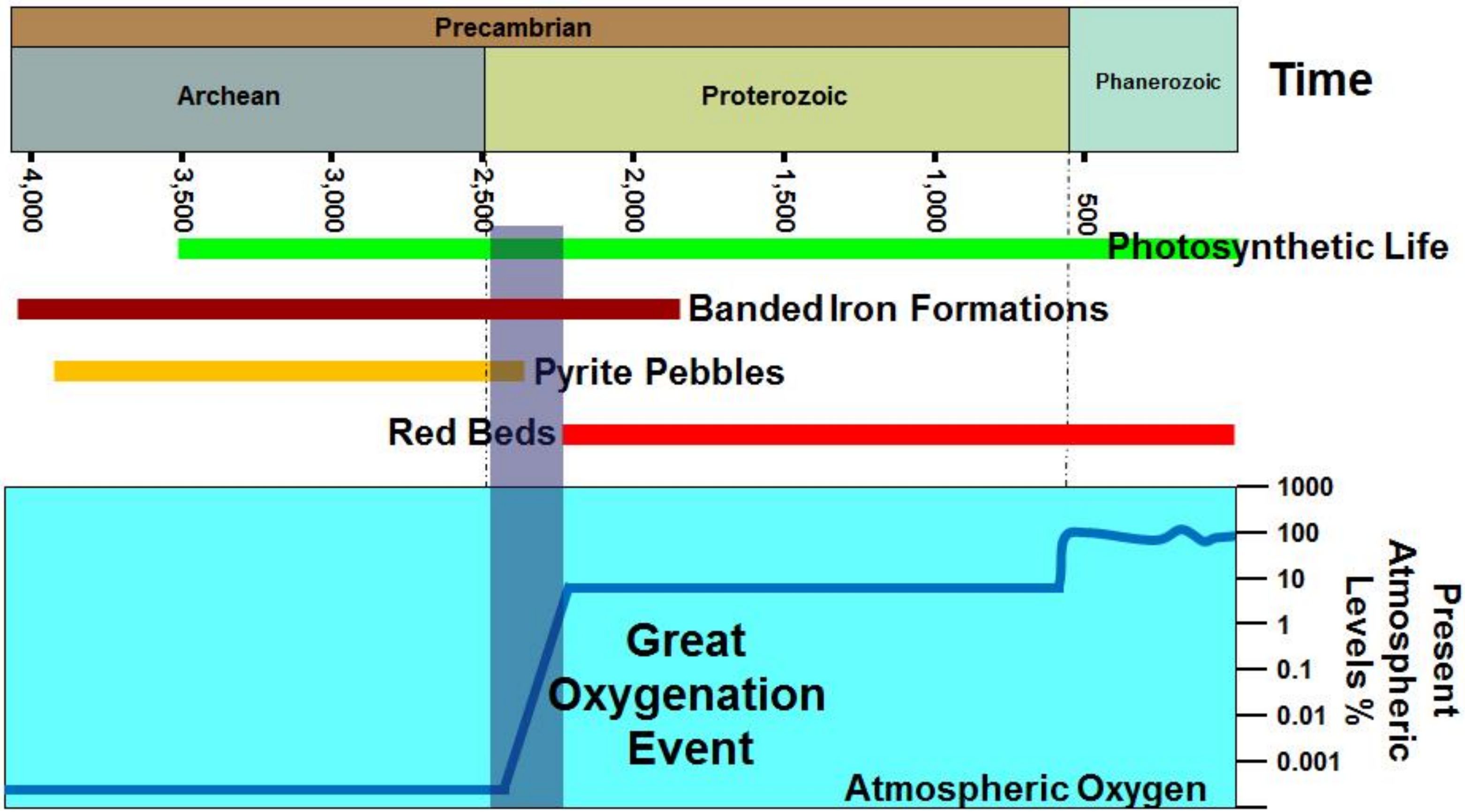
Bioavailability of the elements



Great Oxygenation Event

In 200 milion years the atmospheric concentration of O_2 increased 10^4 times

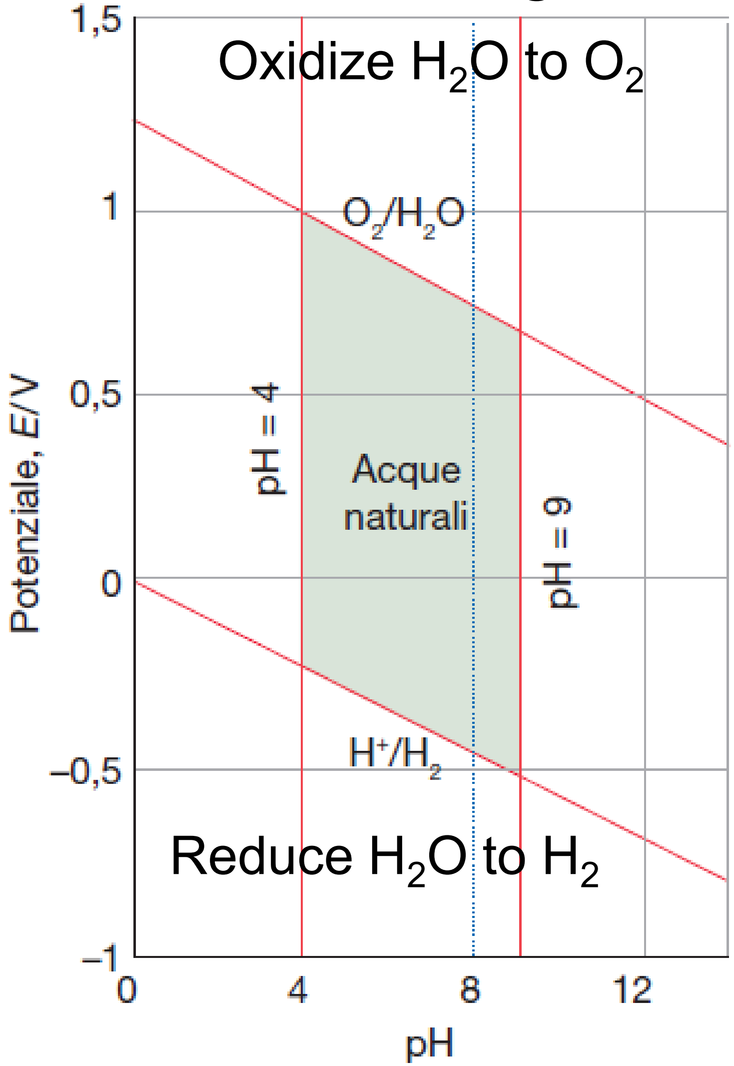
The Great Oxygenation Event



Redox potentials accessible in water at pH 7: between –0.4 V (H^+/H_2) and +0.8 V (O_2/OH^-)

Primeval redox potentials accessible in water at pH 7: between –0.4 V (H^+/H_2) and ca.0.0 V (S_n/H_2S)

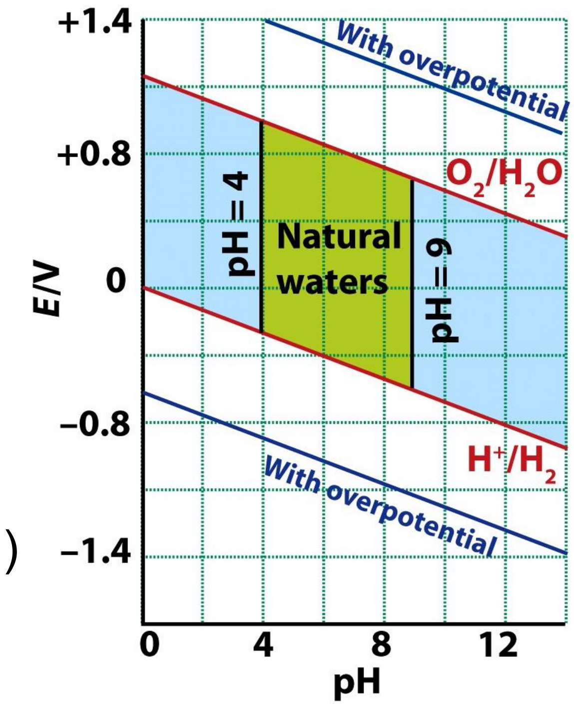
Pourbaix diagram



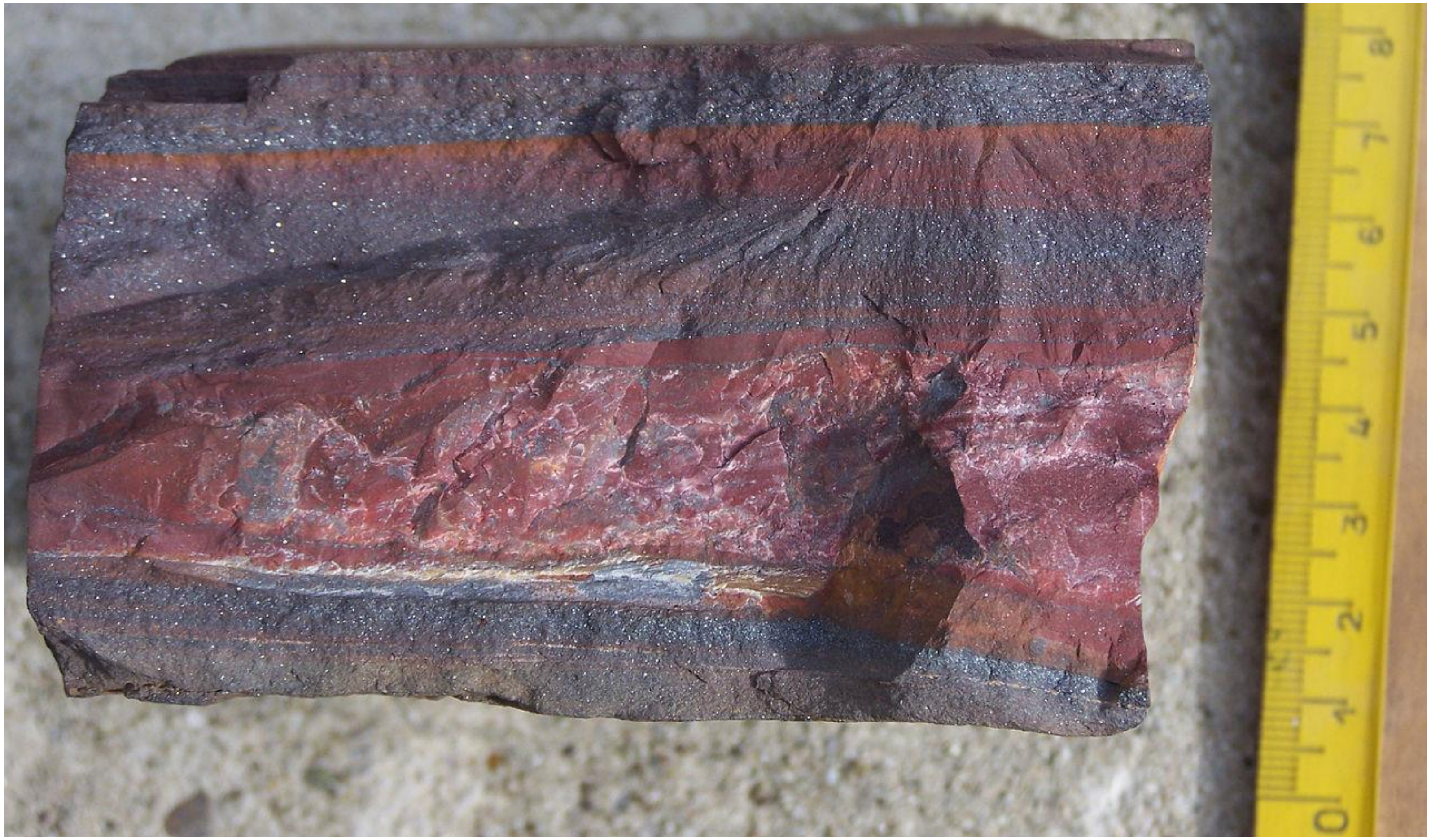
E = 1.23 V – (0.059 V × pH)

$E°(Fe^{3+}/Fe^{2+})$ = + 0.77 V

E = –0.059 V × pH



Banded iron bed



	Bio-availability	
Element	**Reducing environment (anaerobic)**	**Oxidizing environment (aerobic)**
Fe	Fe(II), (high)	Fe(III), (low)
Cu	as sulfide CuS (low)	Cu(II), (moderate)
S	HS^- (high)	SO_4^{2-} (high)
Mo	MoS_2, $(MoO_nS_{4-n})^{2-}$ (low)	MoO_4^{2-} (moderate)
V	V^{3+}, sulfides of V(IV) (moderate)	VO_4^{3-} (moderate)

*The **bio-availability** of an element in aqueous solution depends not only on its **abundance** but also on its **speciation** (i.e., in what form it is found) and the **solubility** of its compounds*

Roles of metals in biological systems

Structural role

Endo- and exoskeletons, stabilization of DNA, RNA and proteins

Functional role

- Charge transport (Na^+, K^+, Ca^{2+})
- Synthesis and metabolism of organic molecules (Lewis acids: Zn^{2+}, Mg^{2+}…..)
- Electron transfer ($Fe^{2+/3+}$, $Cu^{+/2+}$)
- Activation of small molecules, O_2, N_2, CO_2 (Fe, Cu, Mn, Mo…). Assets: capacity of providing unpaired electrons, σ-donation + π-acception
- Organometallic reactivity (Co): radical production, reductive alkylation

Biological ligands

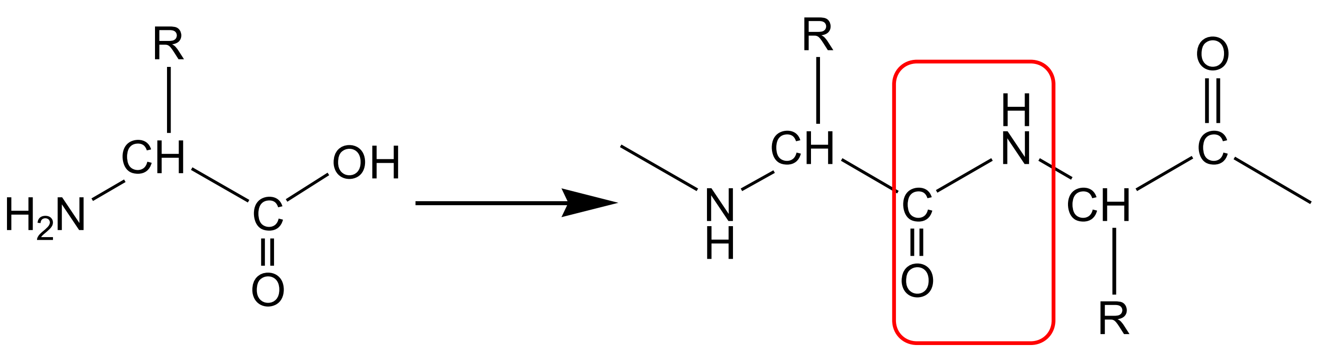
Anions

OH^-, O^{2-}, HPO_4^{2-}, CO_3^{2-}, Cl^-, S^{2-}

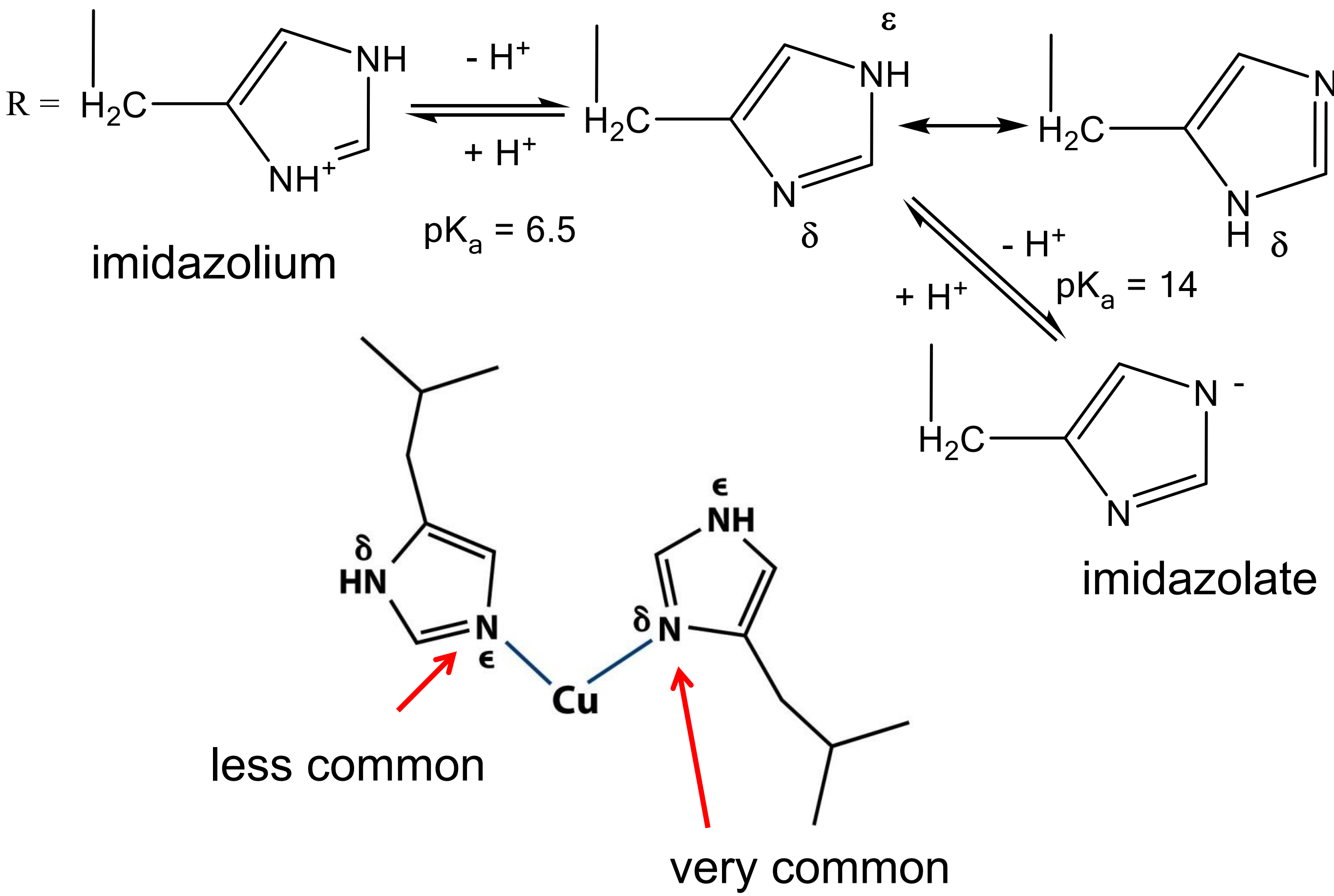
Water

H_2O

Aminoacid side-chains

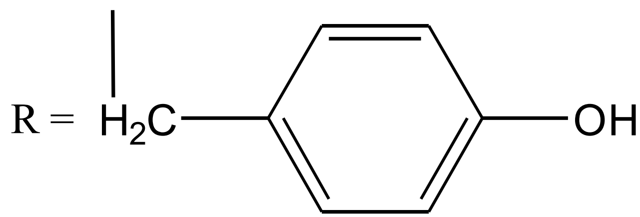


Histidine (His)

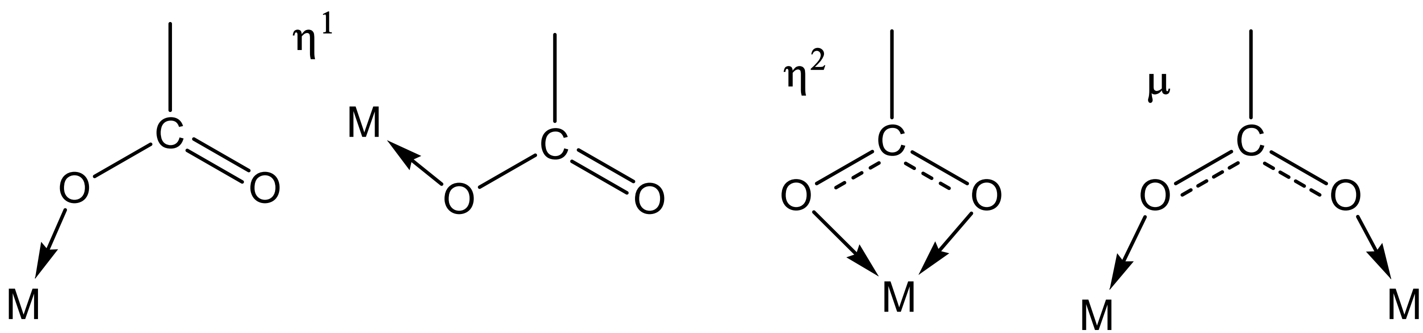


$R = CH_2SH$
Cysteine (Cys), $pK_a = 8.5$

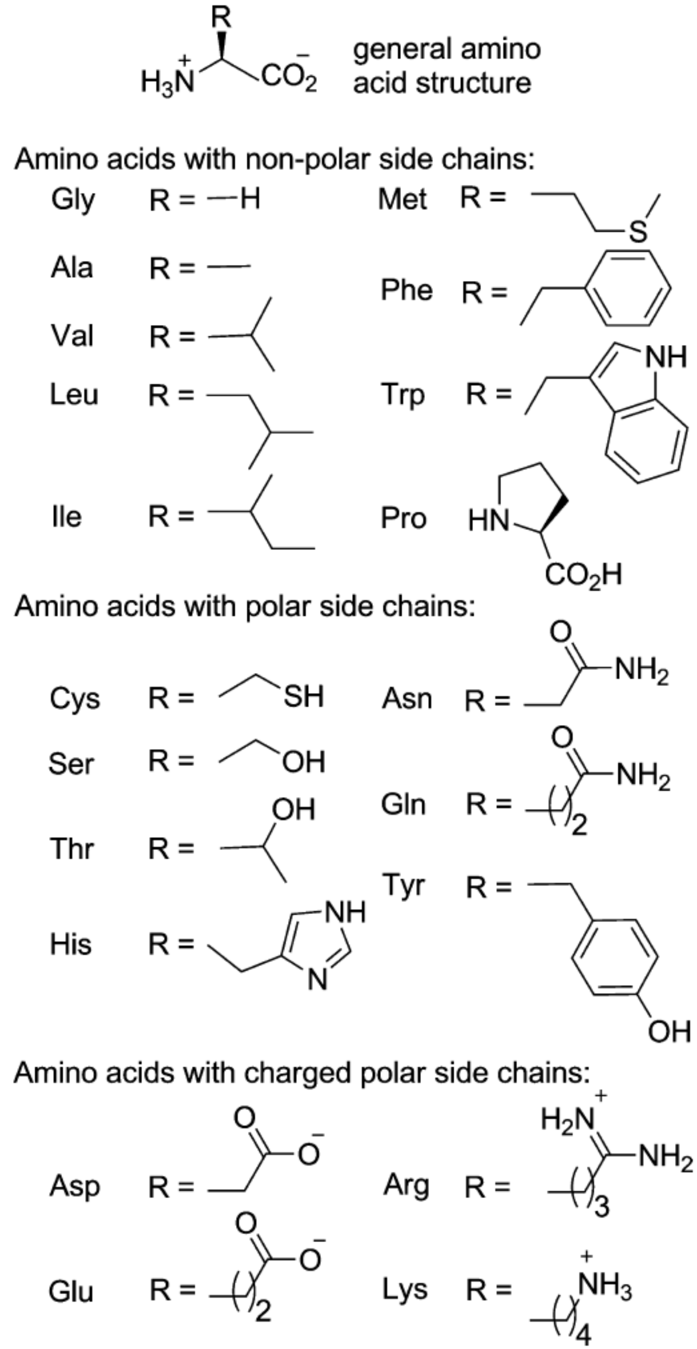
$R = -CH_2CH_2SCH_3$
Methionine (Met)



Tyrosine, $pK_a = 10$

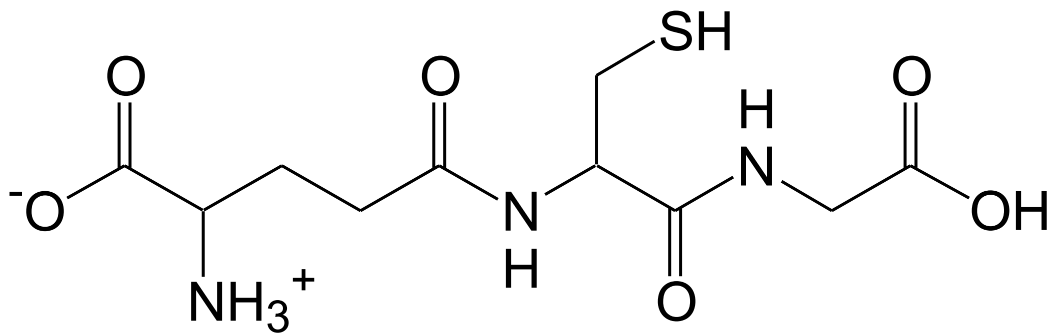


Glutamate (Glu): $R = -CH_2CH_2COO^-$ Aspartate (Asp): $R = -CH_2COO^-$
$pK_a = 4.5$



R
H3N+ CO2−
general amino acid structure
Amino acids with non-polar side chains:
Gly R = —H
Ala R =
Val R =
Leu R =
Ile R =
Met R =
S
Phe R =
Trp R =
NH
Pro
HN
CO2H
Amino acids with polar side chains:
Cys R =
SH
Ser R =
OH
Thr R =
OH
His R =
NH
N
Asn R =
O
NH2
Gln R =
O
NH2
2
Tyr R =
OH
Amino acids with charged polar side chains:
Asp R =
O
O−
Glu R =
O
O−
2
Arg R =
H2N+
NH2
3
Lys R =
NH3+
4

Glutathione: the most important intracellular thiol



GSH

Glu-Cys-Gly

0.5 – 10 mM intracellular

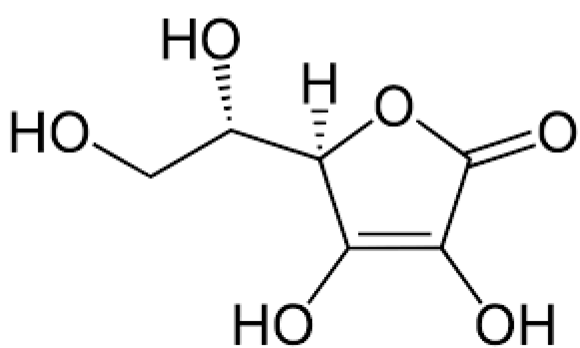
(also a monoelectronic reductant)

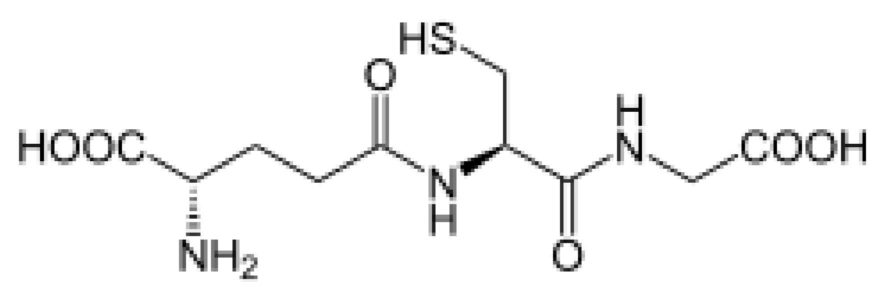
Endogenous reducing agents

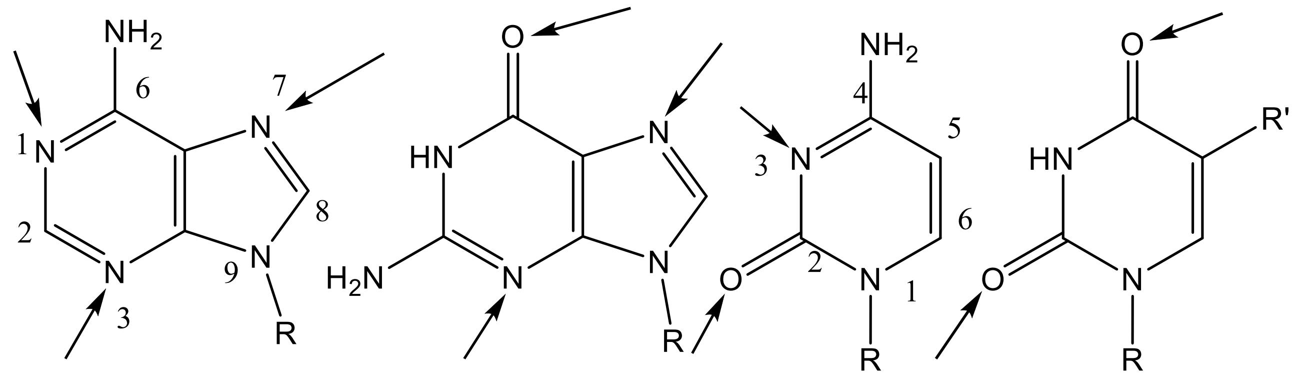
Electron transfer enzymes

Ascorbic acid: 11–79 μM in the blood

Glutathione: 0.5 – 10 mM intracellular







Adenina Guanina Citosina

Basi puriniche

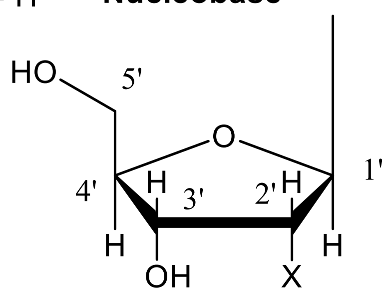
R' = H = Uracile

R' = CH_3 = Timina

Basi pirimidiniche

R = H **Nucleobase**

R =

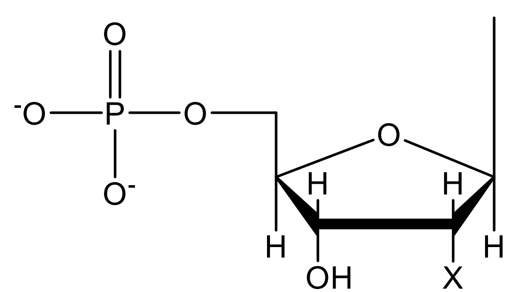


Nucleoside

X = OH ribosio

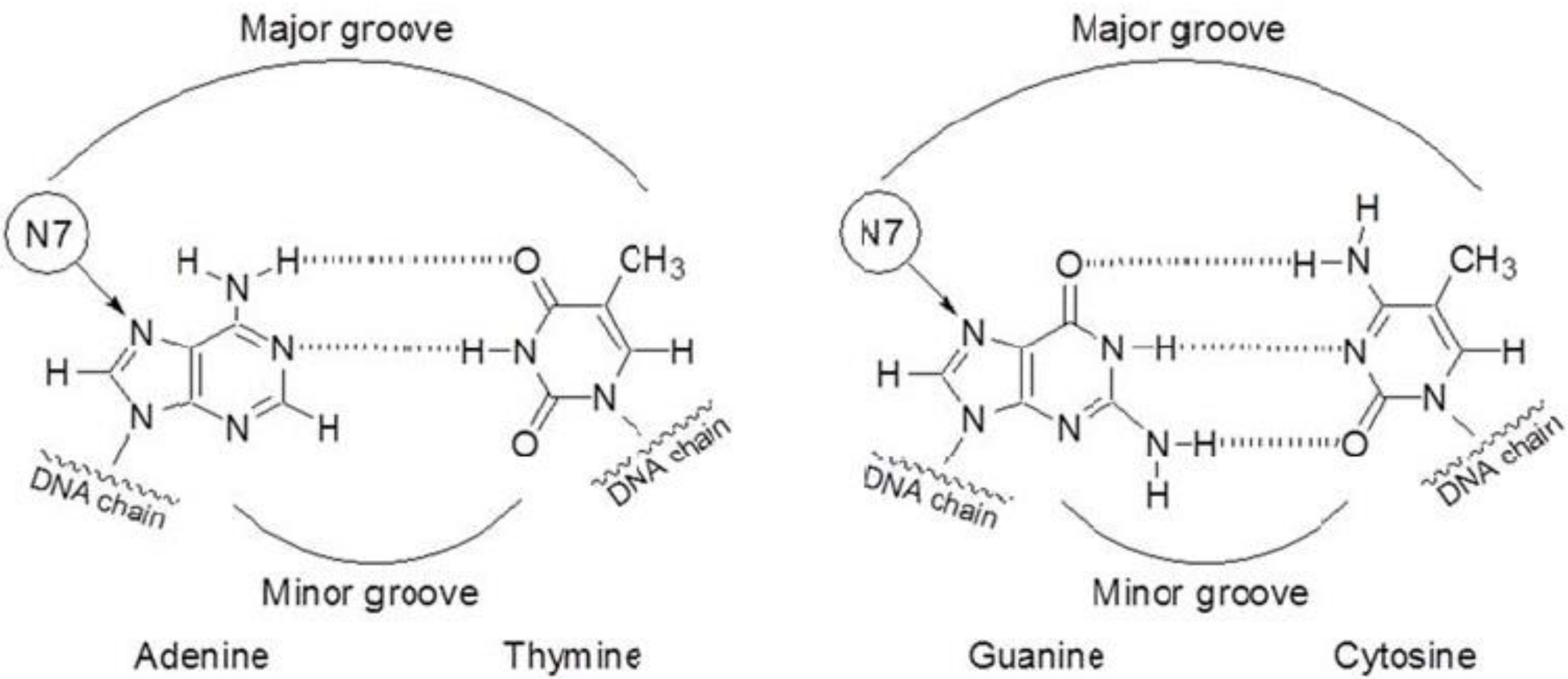
X = H desossi-ribosio

R =



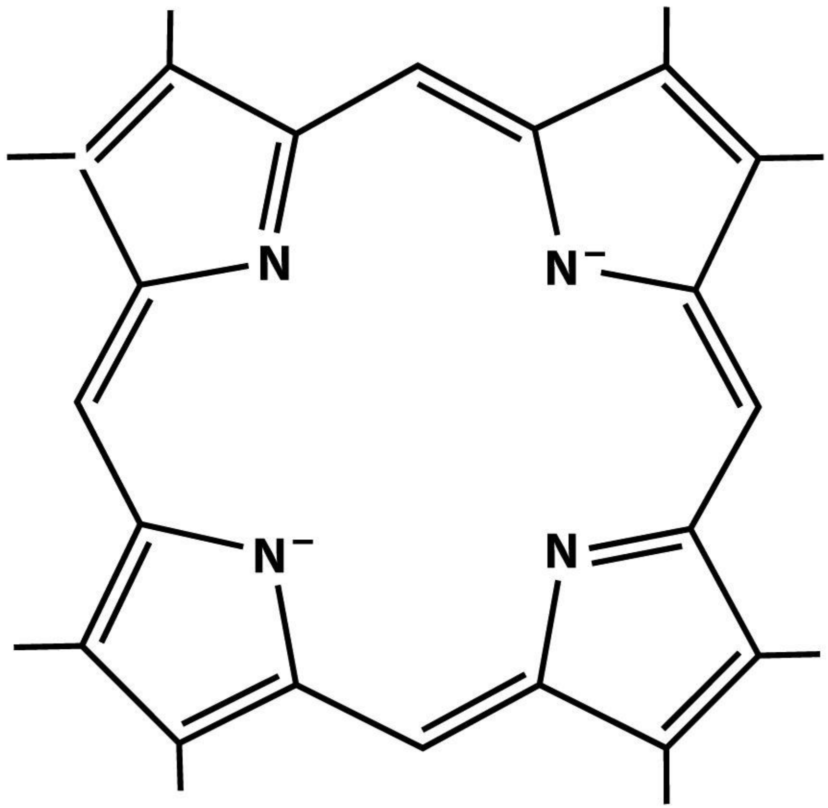
Nucleotide

Watson-Crick type hydrogen bonds

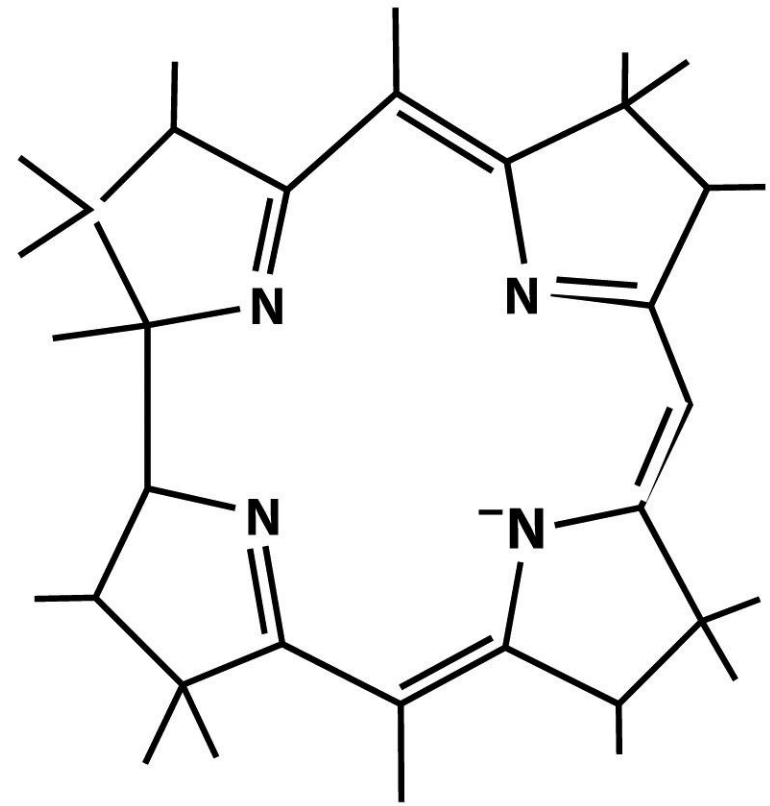


The N7 atoms of adenine and guanine are the main binding sites of nucleobases

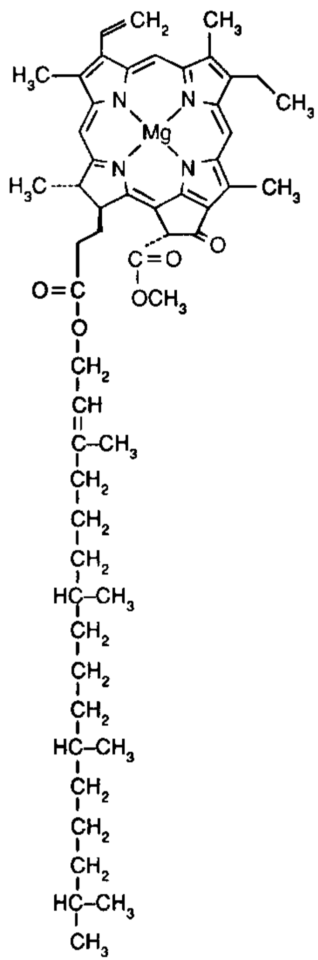
Tetrapyrrole ligands



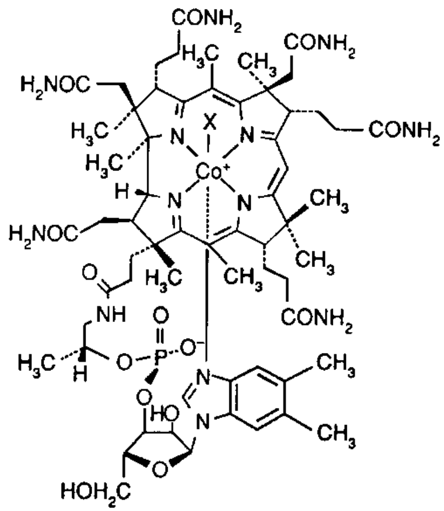
Porphyrin^{2-}



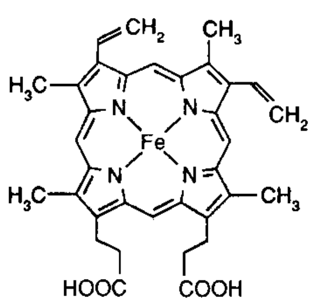
Corrin^{-}



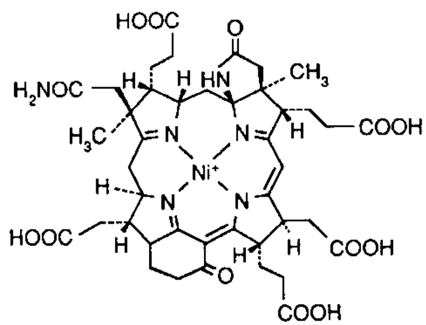
chlorophyll *a*



vitamin B_{12} (X = CN)



heme
(Fe-protoporphyrin IX)



coenzyme F430

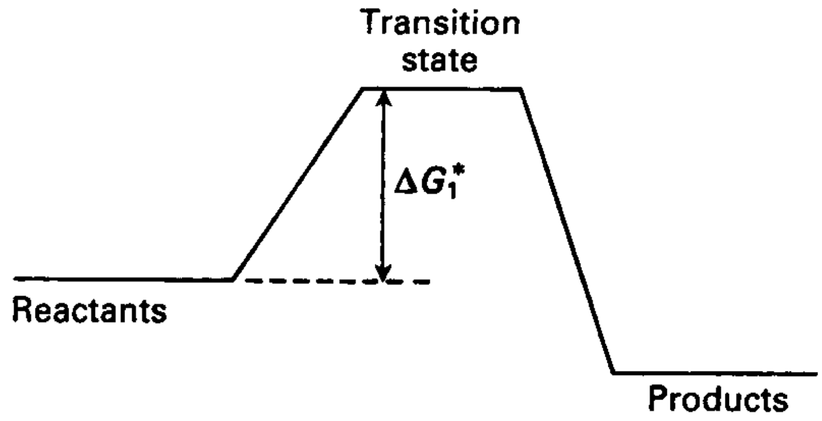
- Planar macrocycles
- Very stable
- After deprotonation inner charge 2- (1- for corrin ring)
- Rather rigid, best fit for cations with ionic radius of 0.6 – 0.7 Å
- Two available axial coordination positions
- Extended π-conjugation leads to a small energy gap between HOMO and LUMO → favorable redox and photophysical properties

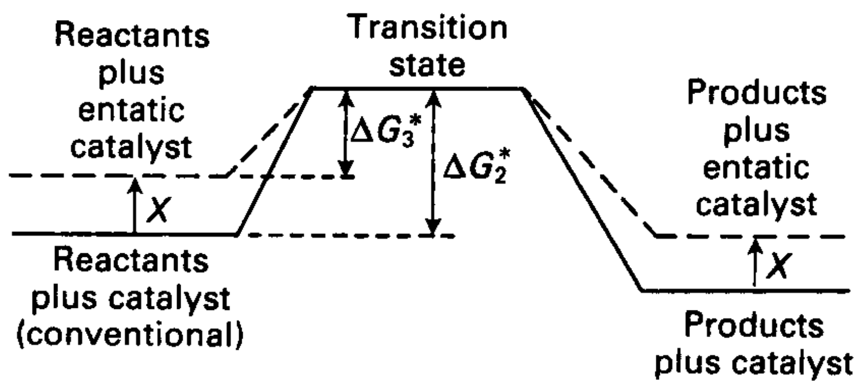
Type	Cations	Donor atoms
Hard	H^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Mn^{2+}, Mn^{3+}, Fe^{3+}	Oxygen in H_2O, $OH^–$, $OR^–$, $O^{2–}$, $PO_4^{3–}$, $NO_3^–$, $CO_3^{2–}$, $RCOO^–$ (including glu, asp, tyr, ser, thr), -C=O (peptide), $F^–$, $Cl^–$, NH_3
Soft	Cu^+, Ag^+, Pt^{2+}, Cd^{2+}, Hg^+, Hg^{2+}	$CN^–$, CO, $S^{2–}$, RSH e R_2S (including cys and met), $I^–$
Borderline	Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}	Any N, O and S donor

Table 2.6 Typical coordination environments of metal centers in proteins

metal oxidation state	bond stability	typical number and type of side chain ligands	typical coordination geometry
Zn(II)	high	3: His, Cys^-, (Glu^-)	severely distorted tetrahedron
Cu(I)	high	3,4: His, Cys^-, Met	severely distorted tetrahedron
Cu(II)	high	3,4: His, (Cys^-)	distorted square planar arrangemer
Fe(II), Ni(II) Co(II), Mg(II)	low	4-6: His, Glu^-, Asp^-	distorted octahedron
Fe(III)	high	4-6: Glu^-, Asp^-, Tyr^-, Cys^-	distorted octahedron

Entatic state theory for metal enzymes





Entatic state theory for metal enzymes