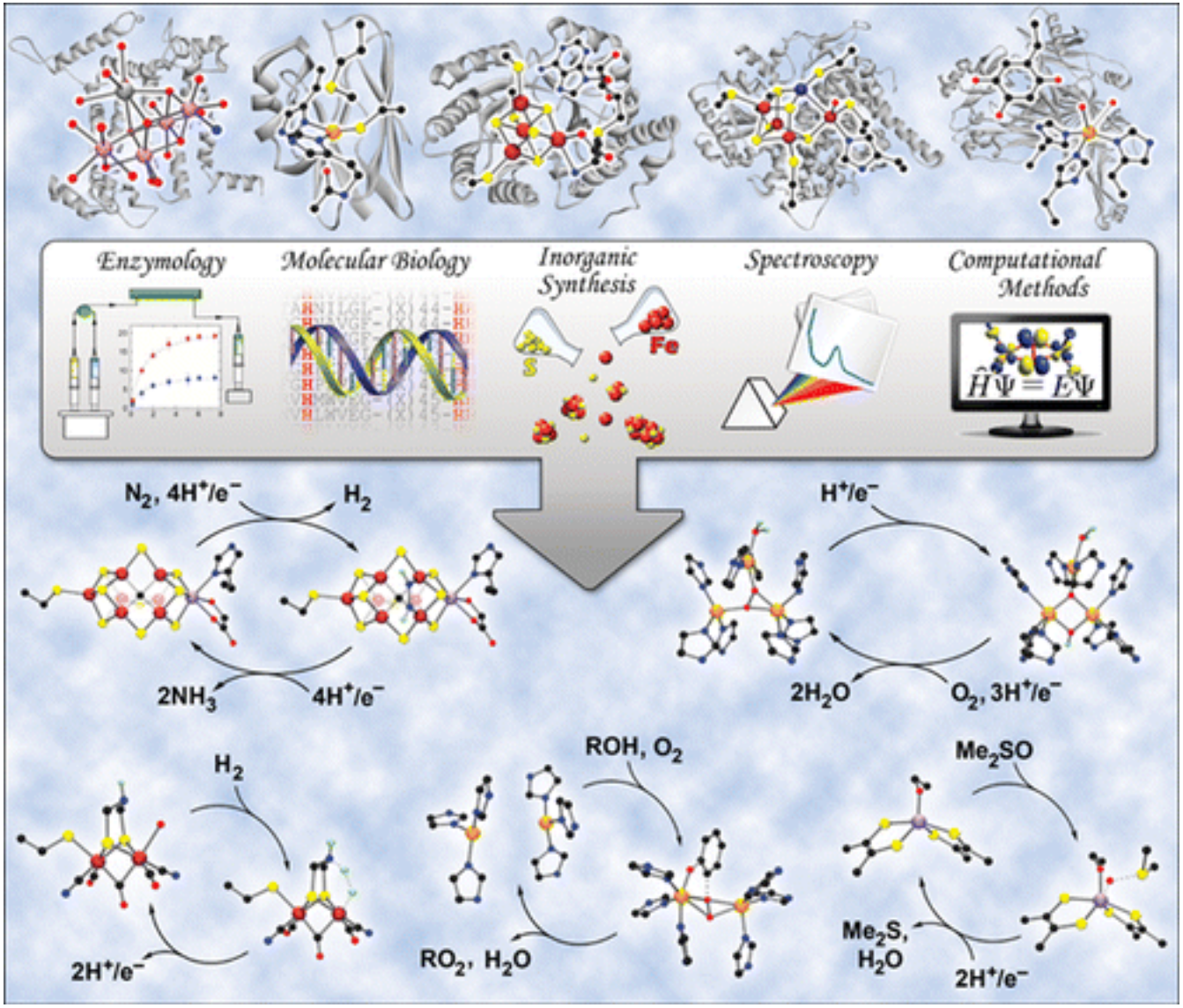
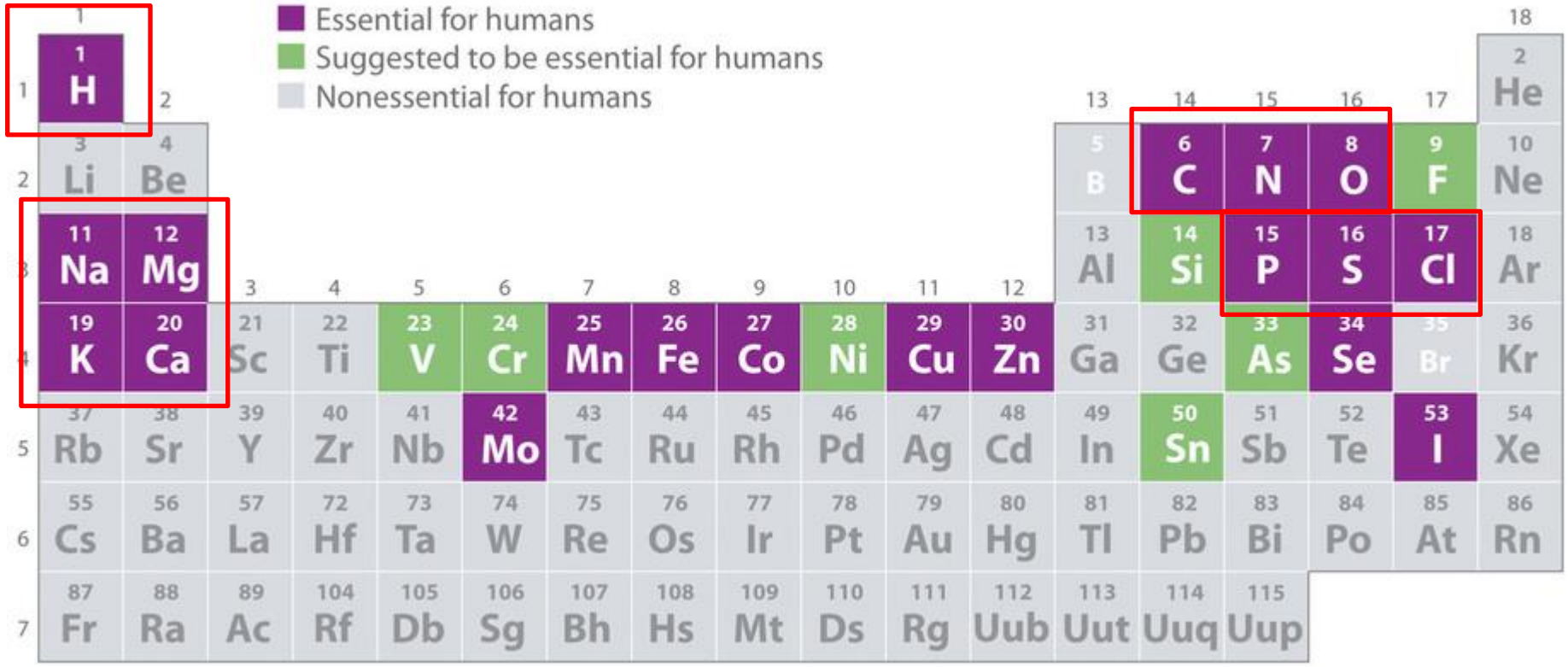

Enzymology
Molecular Biology
Inorganic Synthesis
Spectroscopy
Computational Methods
Fe
S
$\hat{H}\Psi = E\Psi$
N_2, $4H^+/e^-$
H_2
$2NH_3$
$4H^+/e^-$
H^+/e^-
$2H_2O$
O_2, $3H^+/e^-$
H_2
$2H^+/e^-$
ROH, O_2
RO_2, H_2O
Me_2SO
Me_2S, H_2O
$2H^+/e^-$

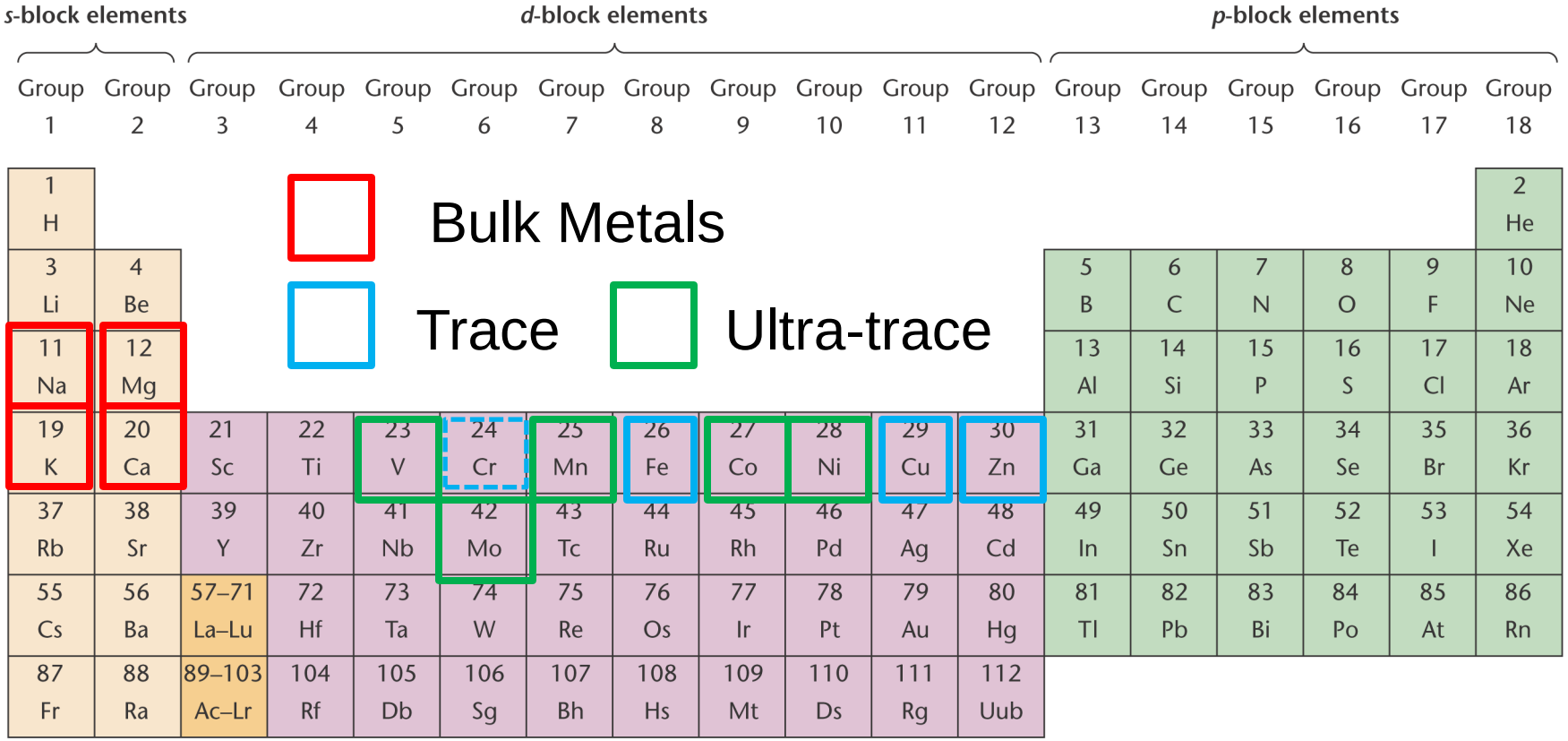
Elementi essenziali nelle specie viventi



11 elementi predominanti e ca. costanti in tutte le specie viventi
(99.9% del totale degli atomi)

C + H + O + N = 99% del totale degli atomi

12 elementi metallici essenziali per le specie viventi



f-block elements

Lanthanoids	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb	71 Lu
Actinoids	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No	103 Lr

Abbondanza degli elementi metallici essenziali nelle specie viventi

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:

$[Fe]_{total}$ = 0.5 mM

$[Zn]_{total}$= 0.5 mM

$[Cu]_{total}$= 50 μM

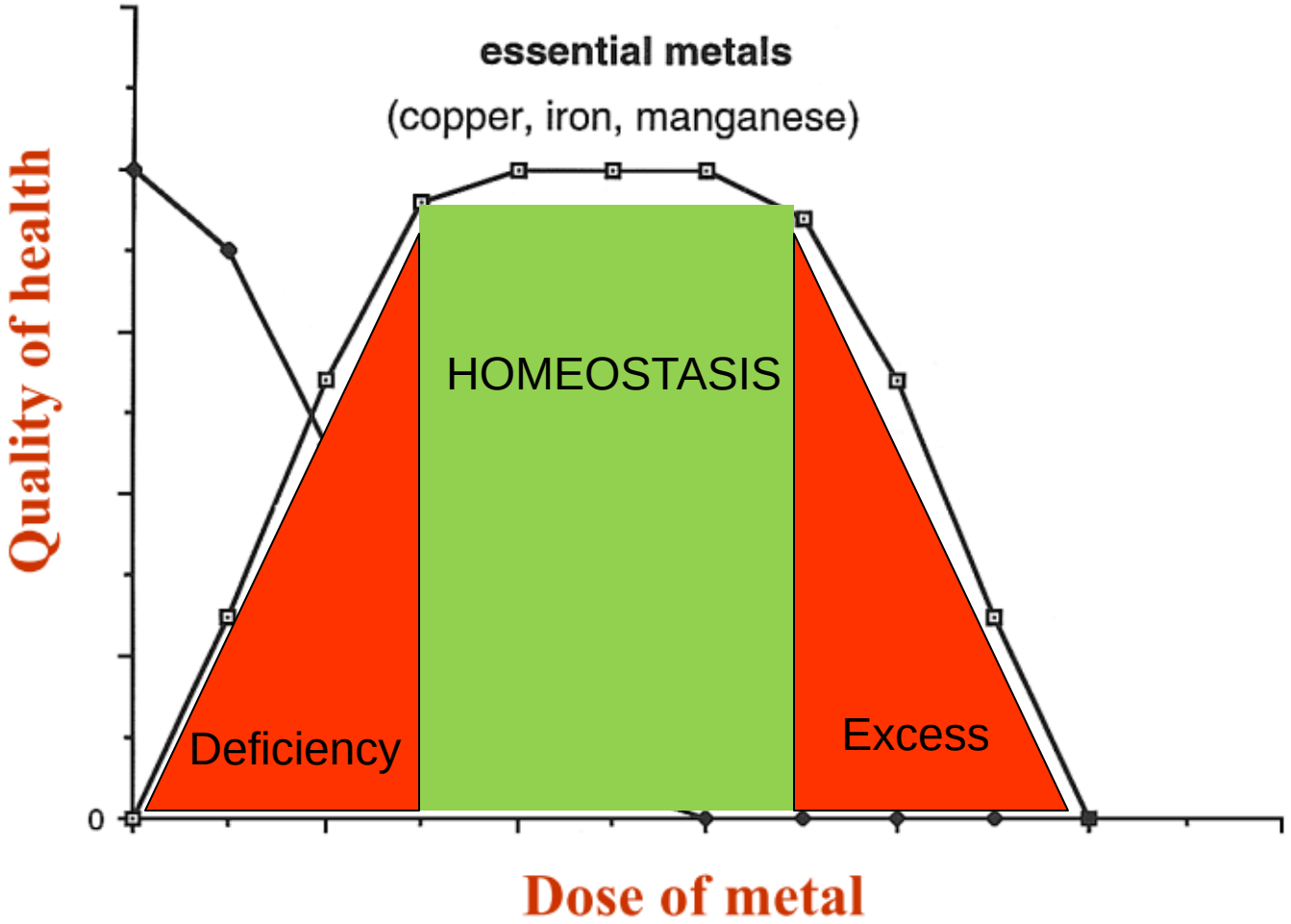
Metalloma

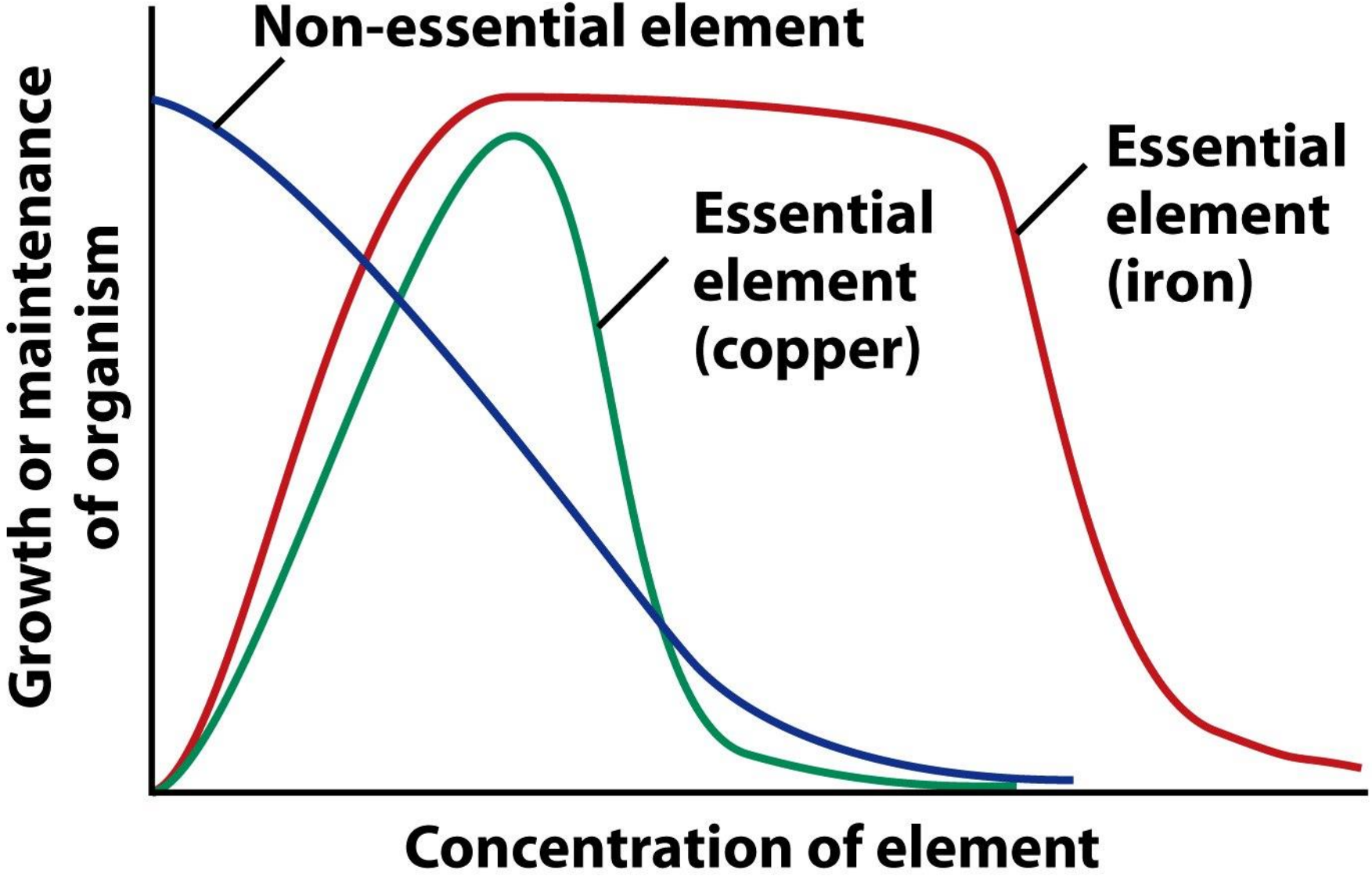
Ogni specie è caratterizzata da uno specifico
metalloma
definito come l'insieme dei metalli contenuti in ogni tipo di cellula di quella specie, ognuno con la sua specifica **quantità**, **speciazione** e **localizzazione** all'interno di ogni cellula

Come si stabilisce se un elemento è essenziale per una specie?

*Si definisce **essenziale** un elemento sistematicamente presente in una certa specie biologica e tale che la sua assenza (o carenza) nelle fonti nutritive di quella specie sia causa di malattie, disturbi metabolici o dello sviluppo*

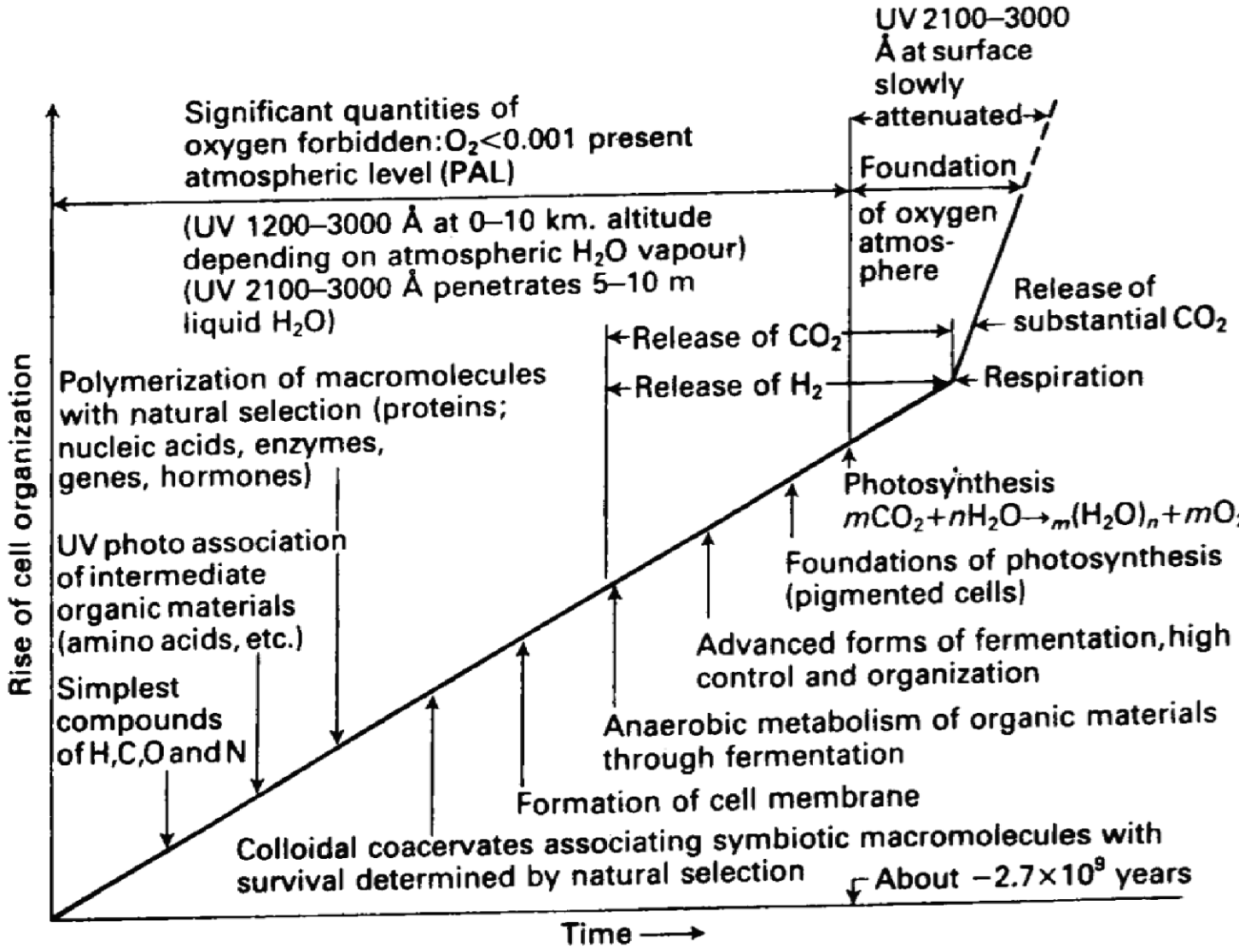
Dose-response curve




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

Elemento	Sintomi da deficienza	Sintomi da eccesso
Ca	Ritardo nella crescita dello scheletro	
Mg	Crampi muscolari, convulsioni	
Fe	Anemia, disordini nel sistema immunitario	Stress ossidativo
Zn	Danni alla pelle, ritardata maturazione sessuale	
Cu	Debolezza delle arterie, disordini del fegato, anemia secondaria, Sindrome di Menkes	Sindrome di Wilson
Mn	Infertilità, ridotta crescita dello scheletro	Disturbi psichiatrici
Mo	Ritardo nella crescita delle cellule, propensione alla carie	Anemia
Co	Anemia perniciosa	Disturbi cardiaci
Si	Disordini nella crescita dello scheletro	
F	Carie	
I	Gotta, disordini tiroidei, metabolismo ritardato	Gotta
Se	Debolezza muscolare, cardiomiopatia	
As	Crescita ritardata	

Biodisponibilità degli elementi



Great Oxidation Event

In 200 milioni di anni la concentrazione atmosferica di O_2 aumentò di 10mila volte

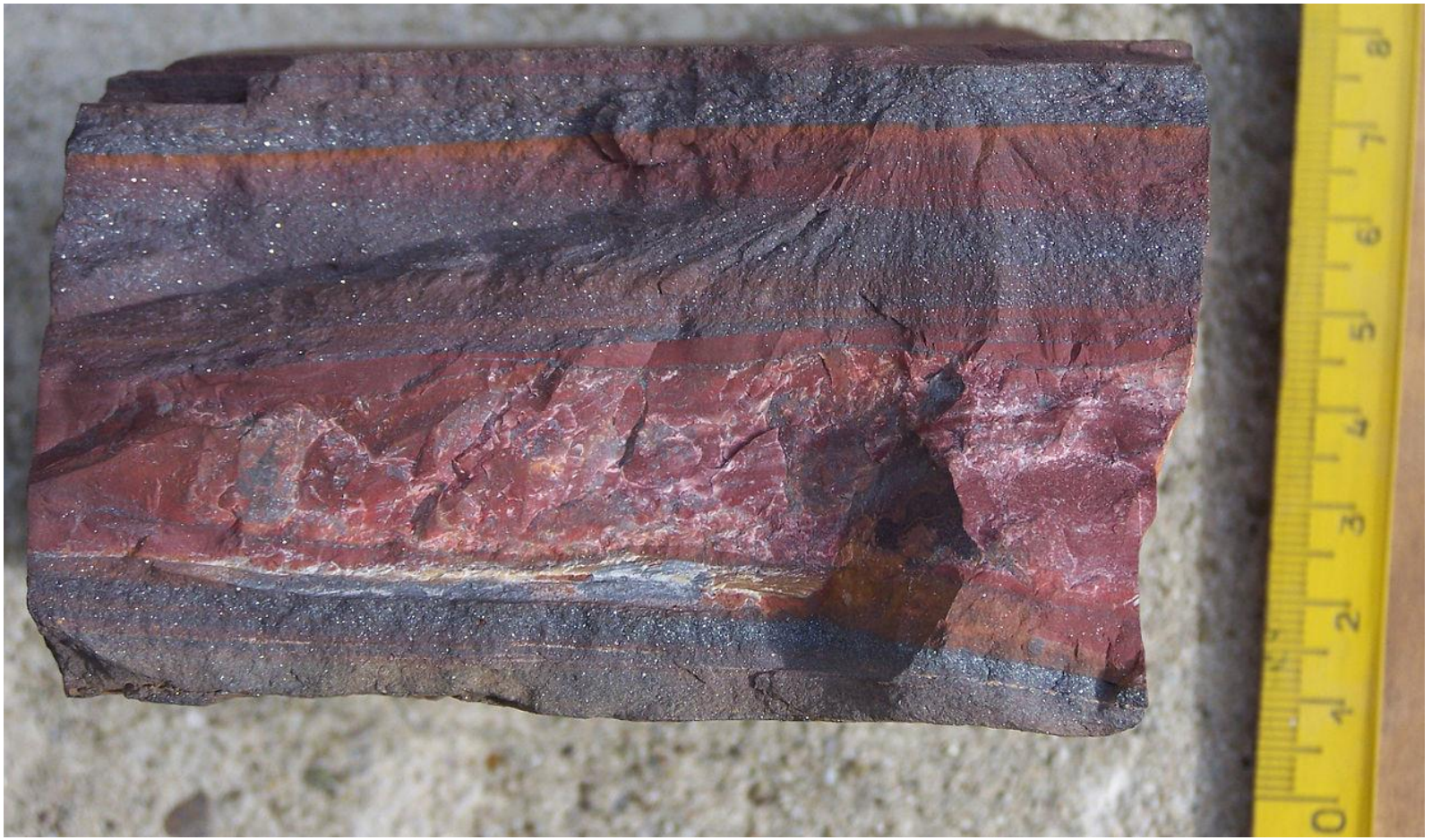
Potenziali redox accessibili in acqua a pH 7: fra –0.4 V (H^+/H_2) e +0.8 V (O_2/OH^-)

Potenziali redox primordiali in acqua a pH 7: fra –0.4 V (H^+/H_2) e ca.0.0 V (S_n/H_2S)

	Biodisponibilità	
Elemento	**Ambiente riducente (anaerobico)**	**Ambiente ossidante (aerobico)**
Fe	Fe(II), (alta)	Fe(III), (bassa)
Cu	Come solfuro (bassa)	Cu(II), (moderata)
S	HS^- (alta)	SO_4^{2-} (alta)
Mo	MoS_2, $(MoO_nS_{4-n})^{2-}$ (bassa)	MoO_4^{2-} (moderata)
V	V^{3+}, solfuri di V(IV) (moderata)	VO_4^{3-} (moderata)

*La bio-disponibilità di un elemento in soluzione acquosa dipende, oltre che dall'**abbondanza**, anche dalla **speciazione** (cioè sotto che forma si trova) e dalla **solubilità** dei suoi composti.*

Orizzonti ferriferi a bande



Ruoli dei metalli nei sistemi biologici

Ruolo strutturale

Endo- ed esoscheletri, stabilizzazione di DNA, RNA e proteine

Ruolo funzionale

- Trasporto di carica
- Sintesi e metabolismo di molecole organiche
- Trasferimento di elettroni
- Attivazione di piccole molecole
- Reattività organometallica

Biological ligands

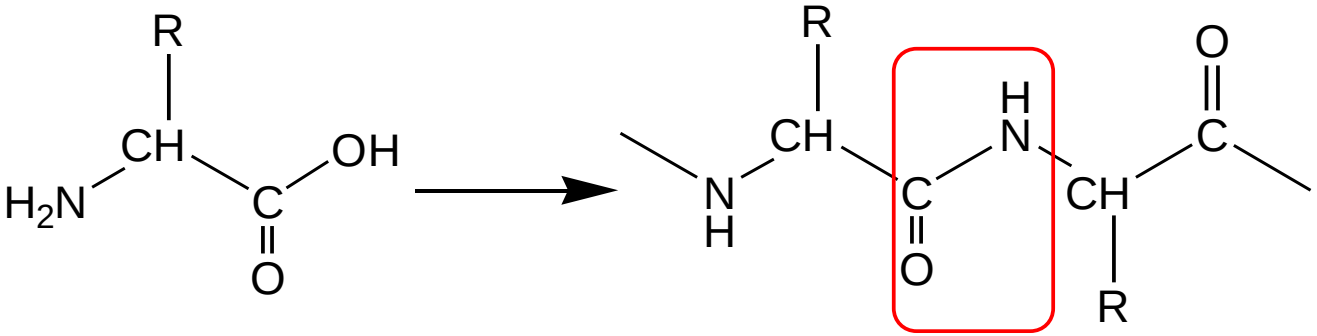
Anions

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

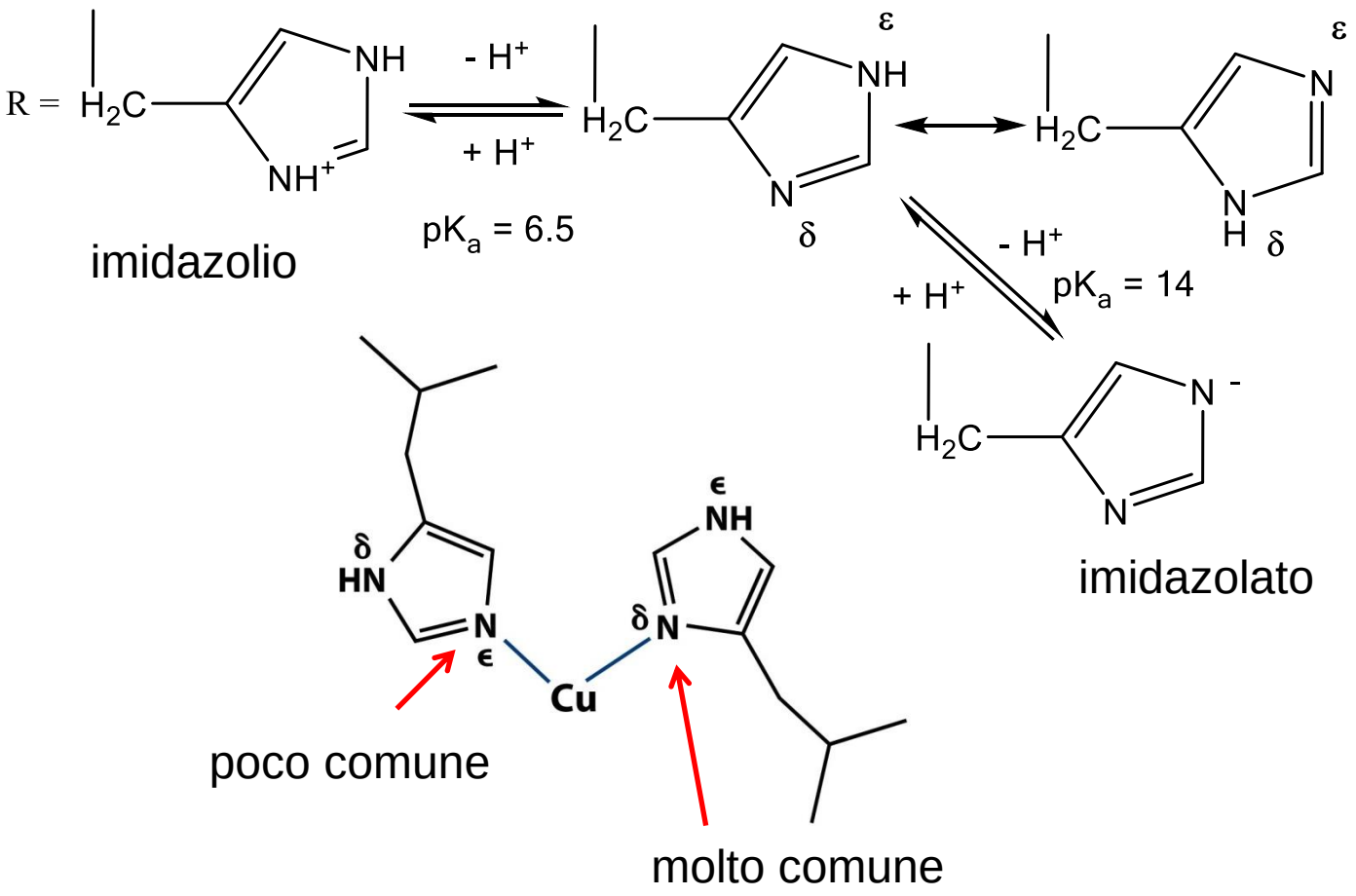
Water

H_2O

Aminoacid side-chains



Istidina (His)

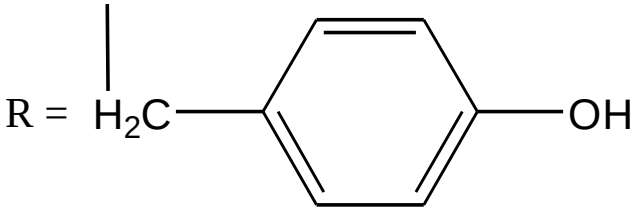


R = CH_2SH

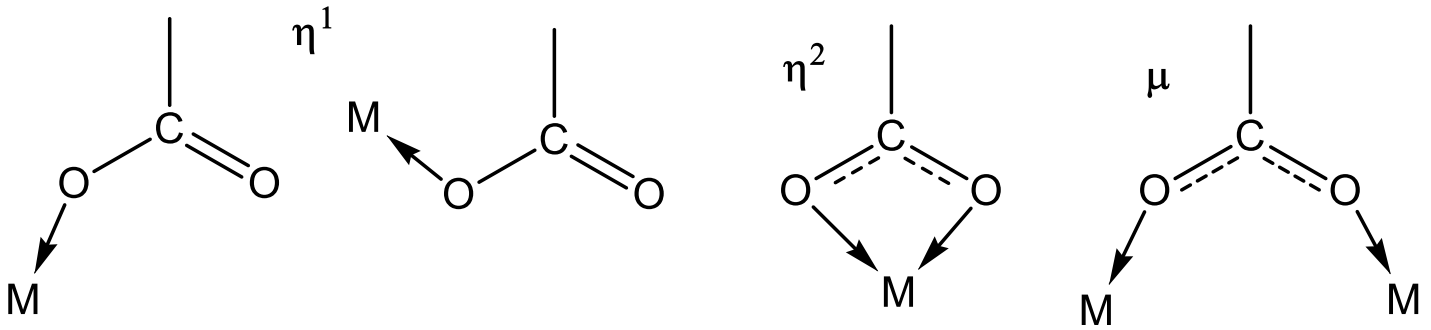
Cisteina (Cys), $pK_a = 8.5$

R = $–CH_2CH_2SCH_3$

Metionina (Met)

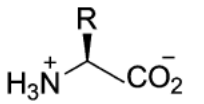


Tirosina, $pK_a = 10$



Glutammato (Glu): R = $–CH_2CH_2COO^–$ Aspartato (Asp): R = $–CH_2COO^–$

$pK_a = 4.5$



general amino acid structure

Amino acids with non-polar side chains:

Gly R = —H

Ala R = —

Val R =

Leu R =

Ile R =

Met R =

Phe R =

Trp R =

Pro

Amino acids with polar side chains:

Cys R =

Ser R =

Thr R =

His R =

Asn R =

Gln R =

Tyr R =

Amino acids with charged polar side chains:

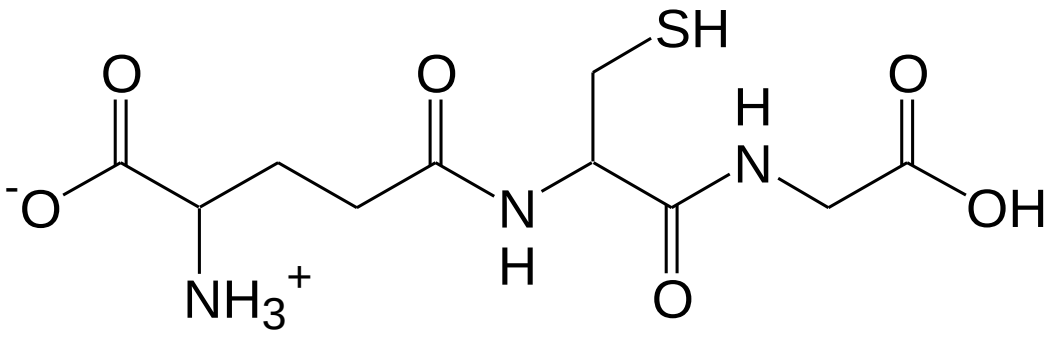
Asp R =

Glu R =

Arg R =

Lys R =

Glutatione: il più importante tiolo intracellulare

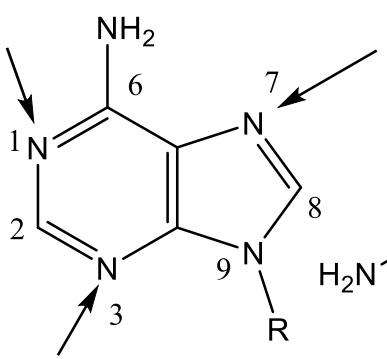


GSH

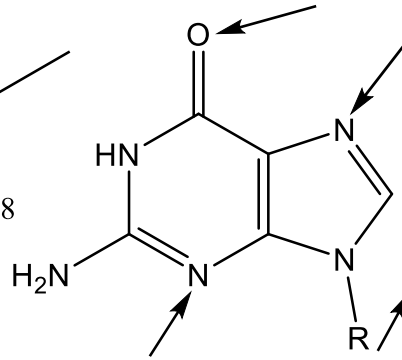
Glu-Cys-Gly

0.5 – 10 mM intracellulare

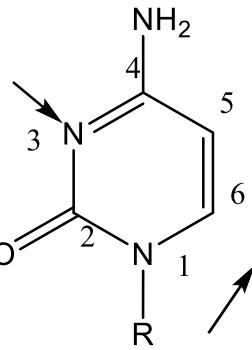
(anche riducente monoelettronico)



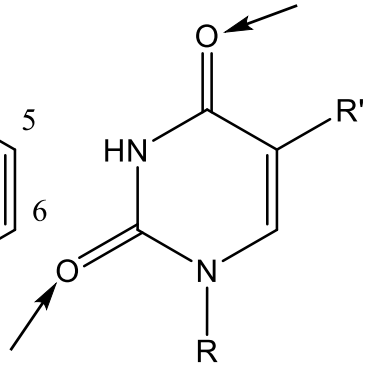
Adenina



Guanina



Citosina



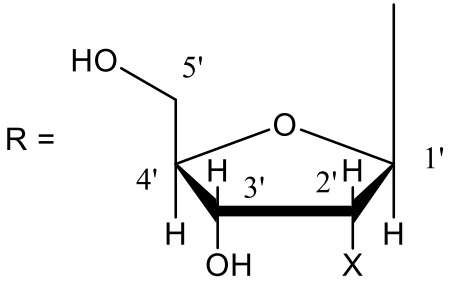
R' = H = Uracile

R' = CH_3 = Timina

Basi puriniche

Basi pirimidiniche

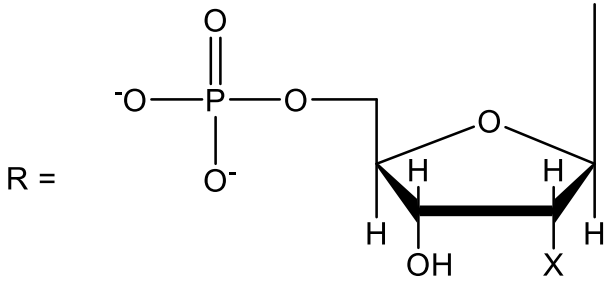
R = H **Nucleobase**



Nucleoside

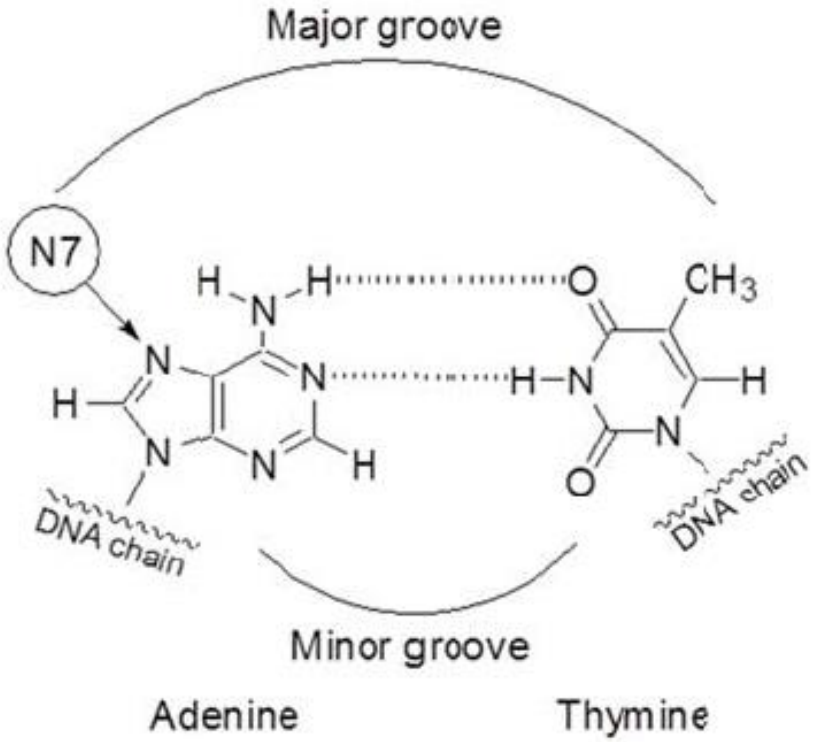
X = OH ribosio

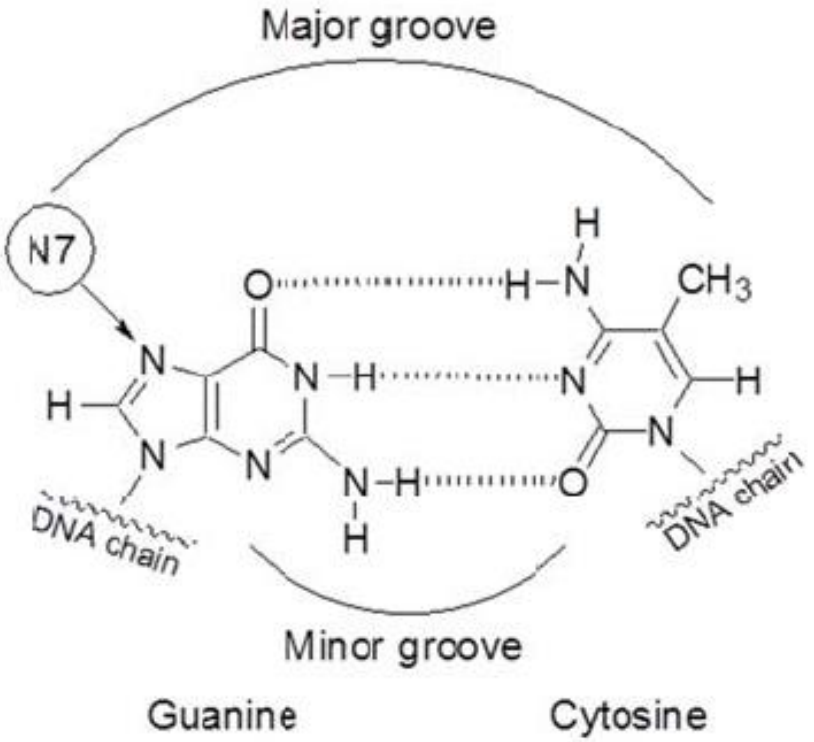
X = H desossi-ribosio



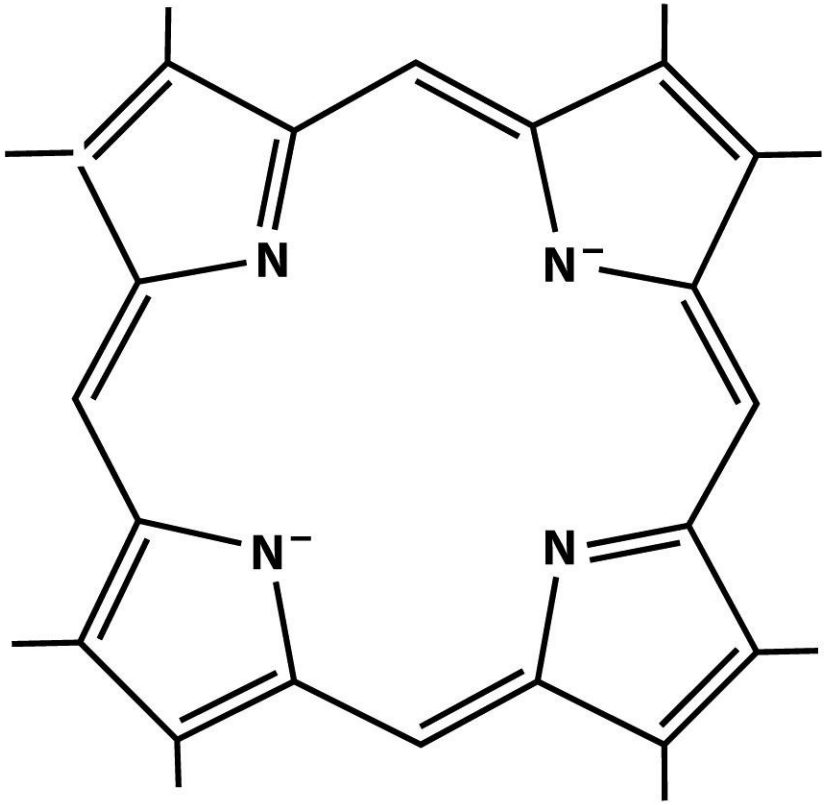
Nucleotide

Legami a idrogeno di tipo Watson-Crick

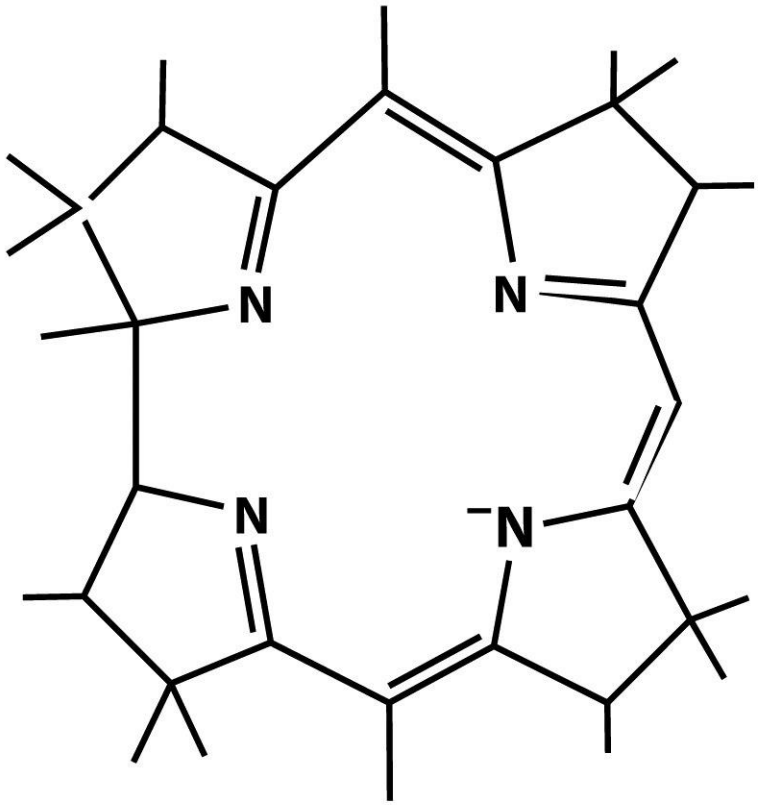




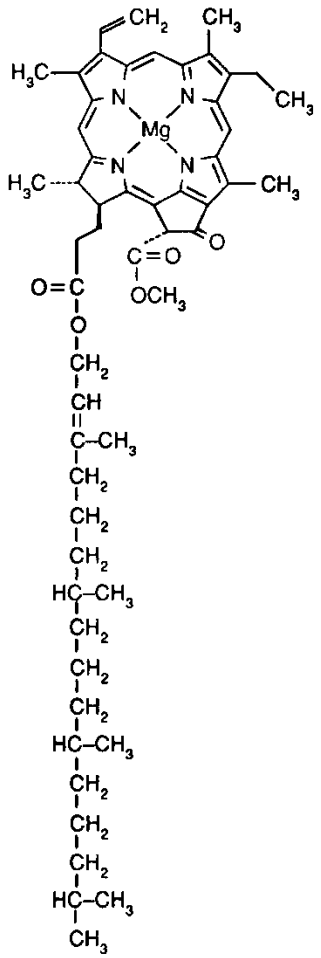
Leganti tetrapirrolici



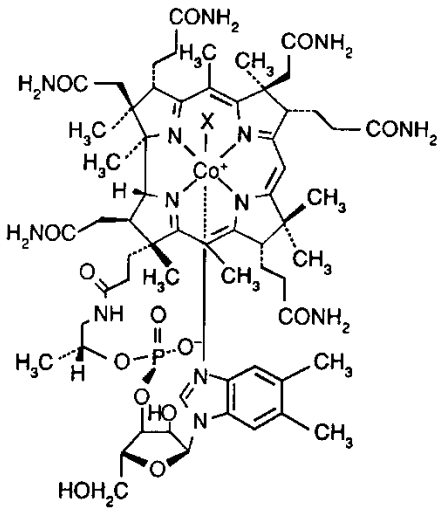
Porphyrin^{2-}



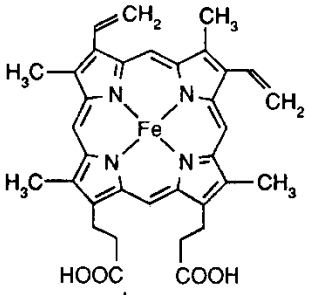
Corrin^{-}



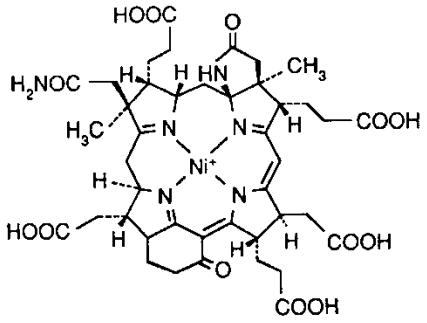
chlorophyll *a*



vitamin B_{12} (X = CN)



heme
(Fe-protoporphyrin IX)



coenzyme F430

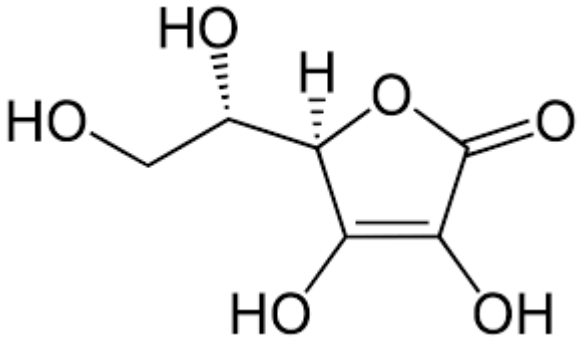
Tipo	Cationi	Atomi donatori
Hard	H^+, Na^+, K^+, Mg^{2+}, Ca^{2+}, Mn^{2+}, Mn^{3+}, Fe^{3+}	Ossigeno in H_2O, OH^-, OR^-, O^{2-}, PO_4^{3-}, NO_3^-, CO_3^{2-}, $RCOO^-$ (inclusi glu, asp, tyr, ser, thr), -C=O (peptide), F^-, Cl^-, NH_3
Soft	Cu^+, Ag^+, Pt^{2+}, Cd^{2+}, Hg^+, Hg^{2+}	CN^-, CO, S^{2-}, RSH e R_2S (inclusi cys e met), I^-
Borderline	Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}	Qualsiasi donatore N, O ed S

Endogenous reducing agents

Electron transfer enzymes

Ascorbic acid: 11–79 μM in the blood

Glutathione: 0.5 – 10 mM intracellular



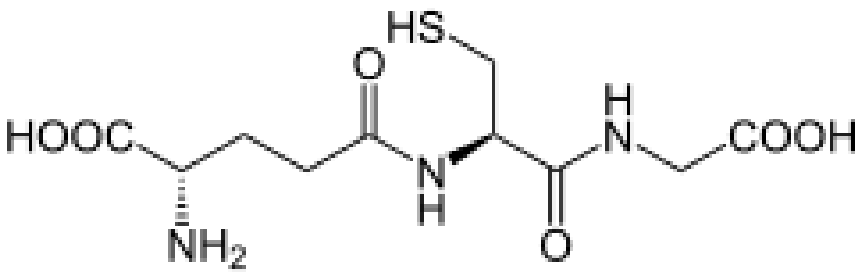
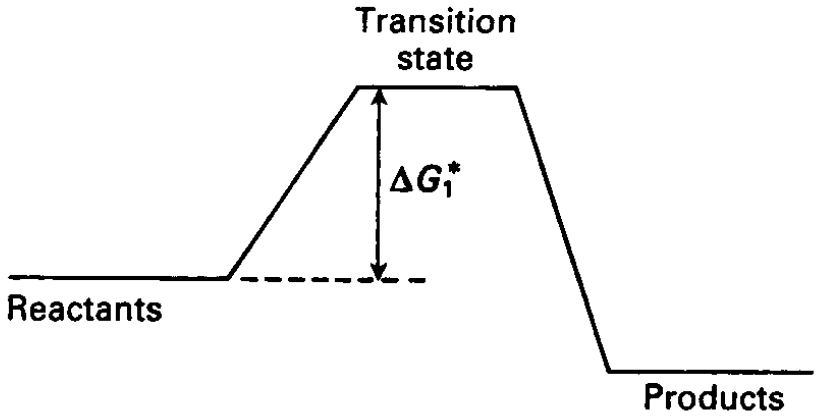
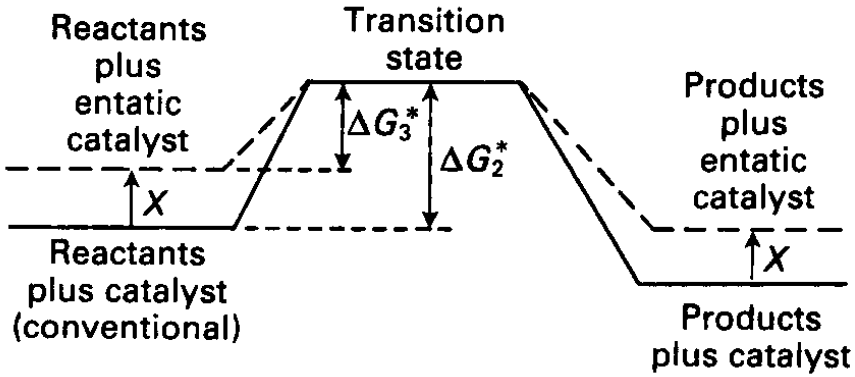


Table 2.6 Typical coordination environments of metal centers in proteins

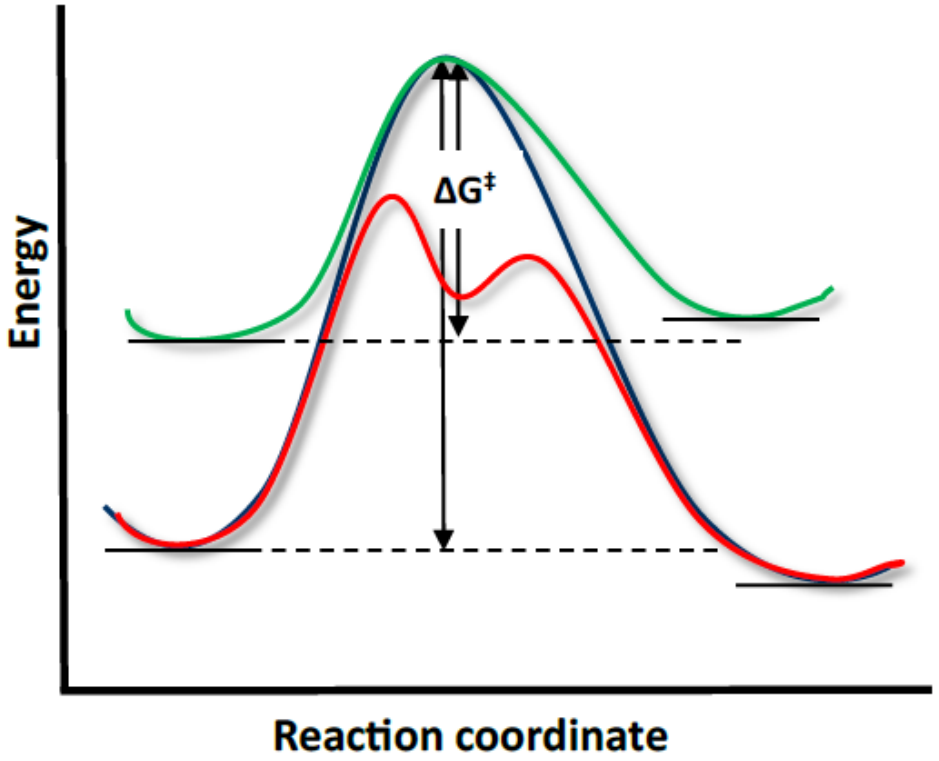
metal oxidation state	bond stability	typical number and type of side chain ligands	typical coordination geometry
Zn(II)	high	3: His, Cys^-, (Glu^-)	severely distorted tetrahedron
Cu(I)	high	3,4: His, Cys^-, Met	severely distorted tetrahedron
Cu(II)	high	3,4: His, (Cys^-)	distorted square planar arrangemer
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

Stato entatico





Stato entatico



Stato entatico