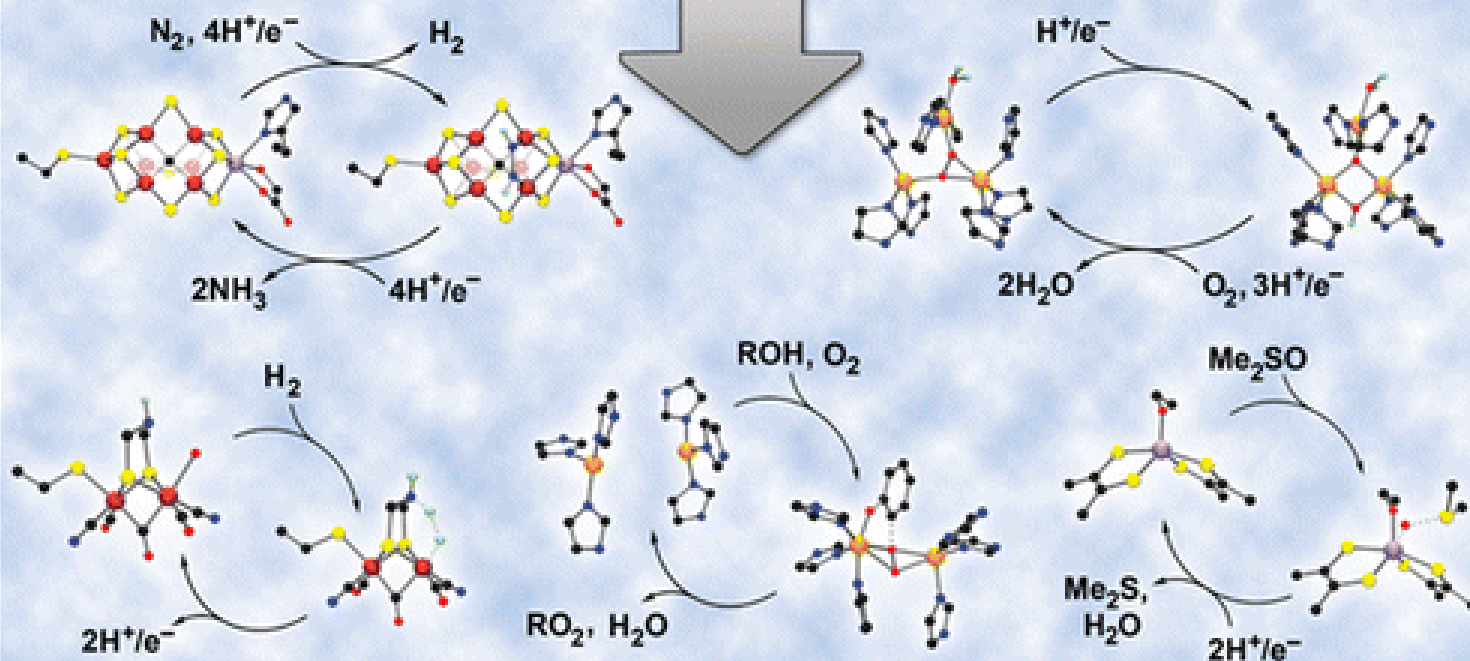
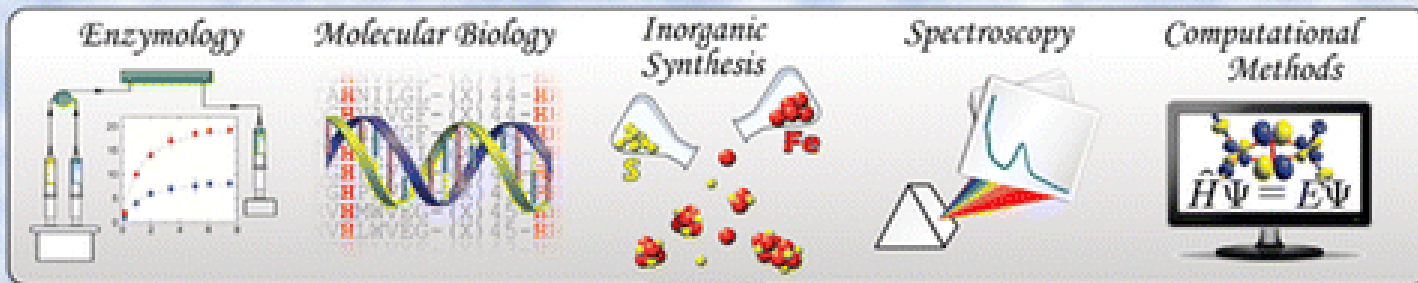
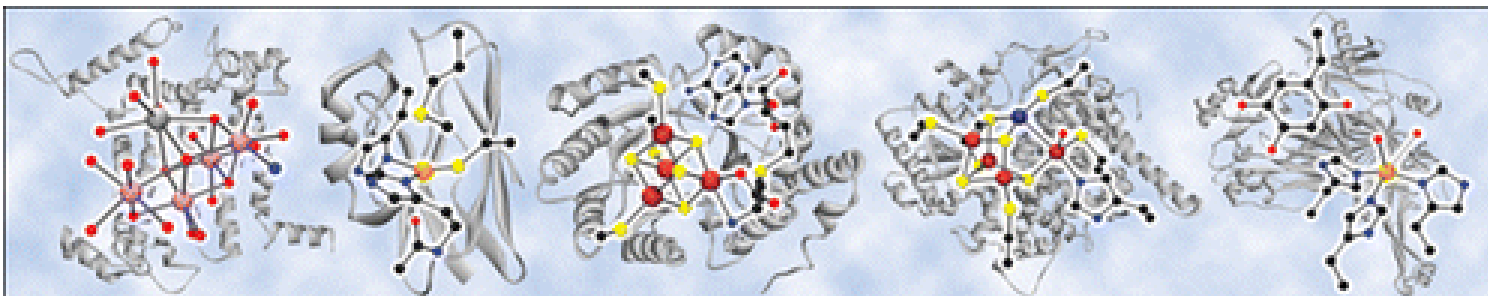


Figure 1. Covers of the triad of *Chemical Reviews* thematic issues on Bioinorganic Chemistry (1996, 2004, 2014).



# Elementi essenziali nelle specie viventi

Legend:

- Essential for humans (Purple)
- Suggested to be essential for humans (Green)
- Nonessential for humans (Grey)

1	2											13	14	15	16	17	18	
1												5	6	7	8	9	10	
2	Li	Be											B	C	N	O	F	Ne
3												13	14	15	16	17	18	
4	Na	Mg										Al	Si	P	S	Cl	Ar	
5																		
6	K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
7																		
8	Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
9																		
10	Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
11																		
12	Fr	Ra	Ac	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Uub	Uut	Uuq	Uup			

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

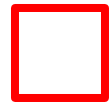
s-block elements

d-block elements

p-block elements

Group 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

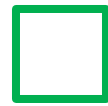
1 H																	2 He	
3 Li	4 Be												5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg												13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr	
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe	
55 Cs	56 Ba	57-71 La-Lu	72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn	
87 Fr	88 Ra	89-103 Ac-Lr	104 Rf	105 Db	106 Sg	107 Bh	108 Hs	109 Mt	110 Ds	111 Rg	112 Uub							



Bulk Metals



Trace



Ultra-trace

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	$15 \times 10^{-3}$
Mn	$1 \times 10^{-2}$
Co	$1.2 \times 10^{-3}$
Mo	$10 \times 10^{-3}$
Ni	?

Average intracellular concentration:

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

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

$$[\text{Cu}]_{\text{total}} = 50 \text{ } \mu\text{M}$$

# Metalloma

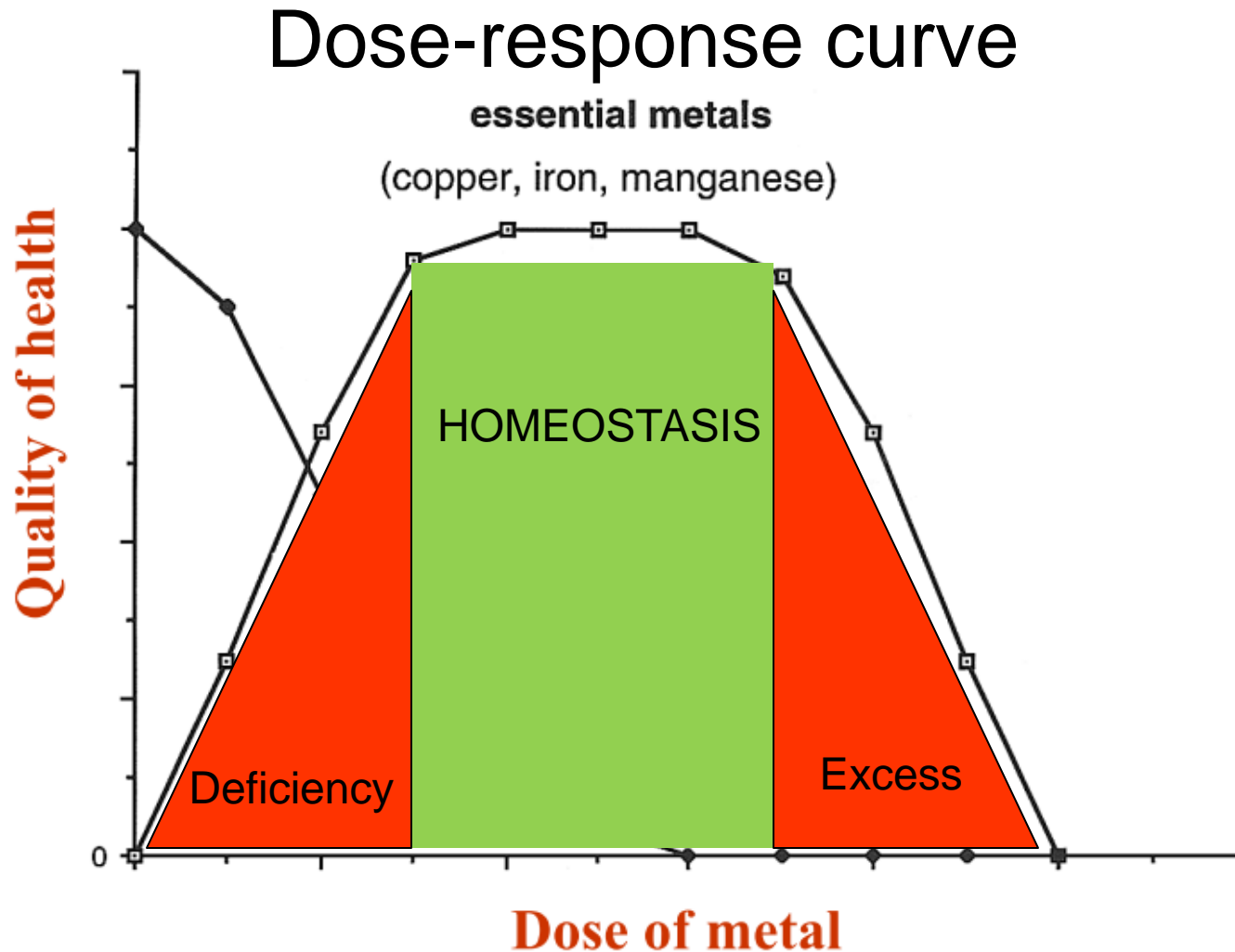
Ogni specie è caratterizzata da uno specifico

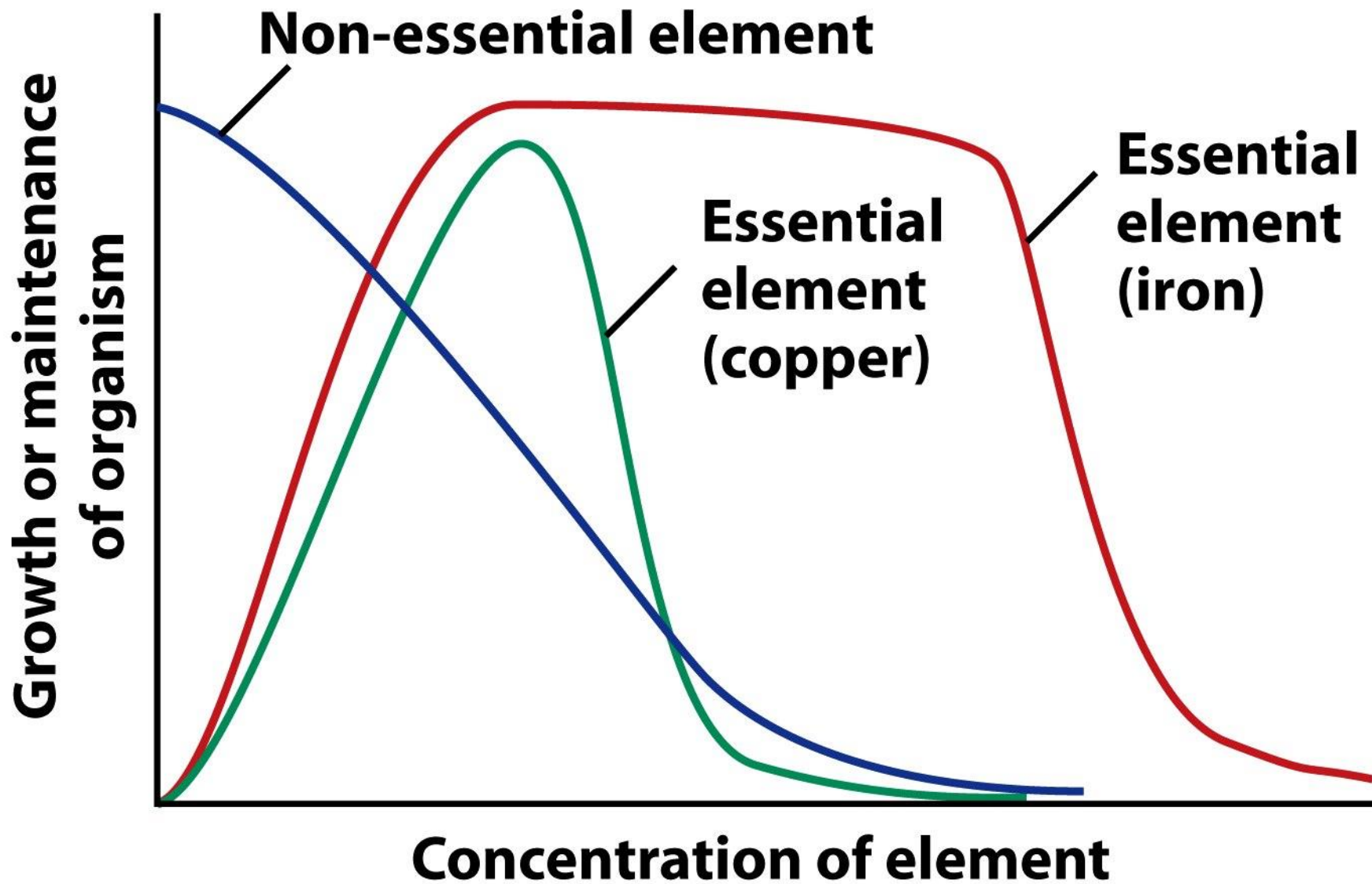
**metalloma**

definito come l'insieme dei metalli contenuti in ciascun tipo di cellula di quella specie, ognuno con la sua specifica **quantità, speciazione e localizzazione** all'interno di ciascuna 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

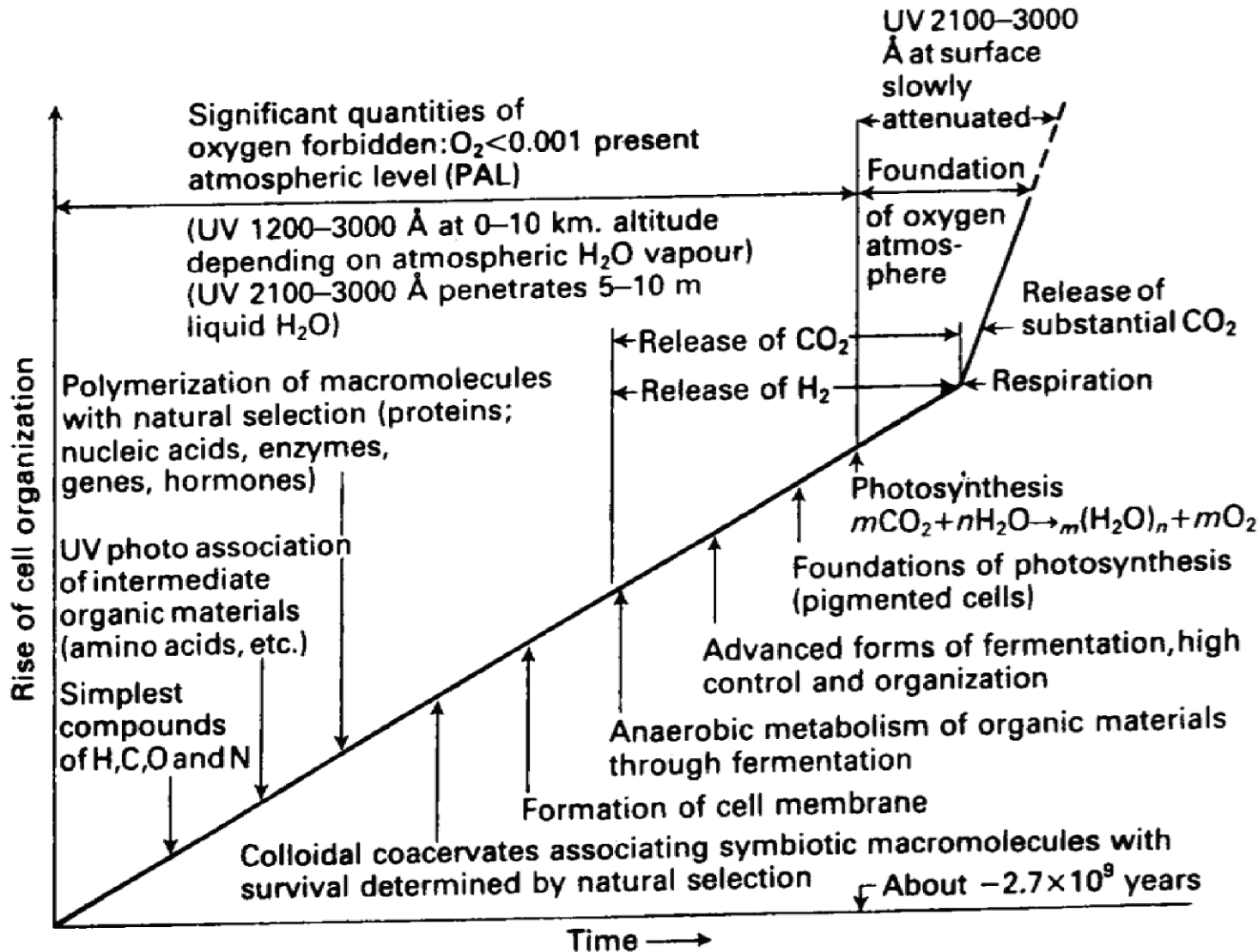






<b>Elemento</b>	<b>Sintomi da deficienza</b>	<b>Sintomi da eccesso</b>
Ca	Ritardo nella crescita dello scheletro	
Mg	Crampi muscolari, convulsioni	
Fe	<b>Anemia</b> , disordini nel sistema immunitario	Stress ossidativo
Zn	Danni alla pelle, ritardata maturazione sessuale	
Cu	Debolezza delle arterie, disordini del fegato, anemia secondaria, <b>Sindrome di Menkes</b>	<b>Sindrome di Wilson</b>
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

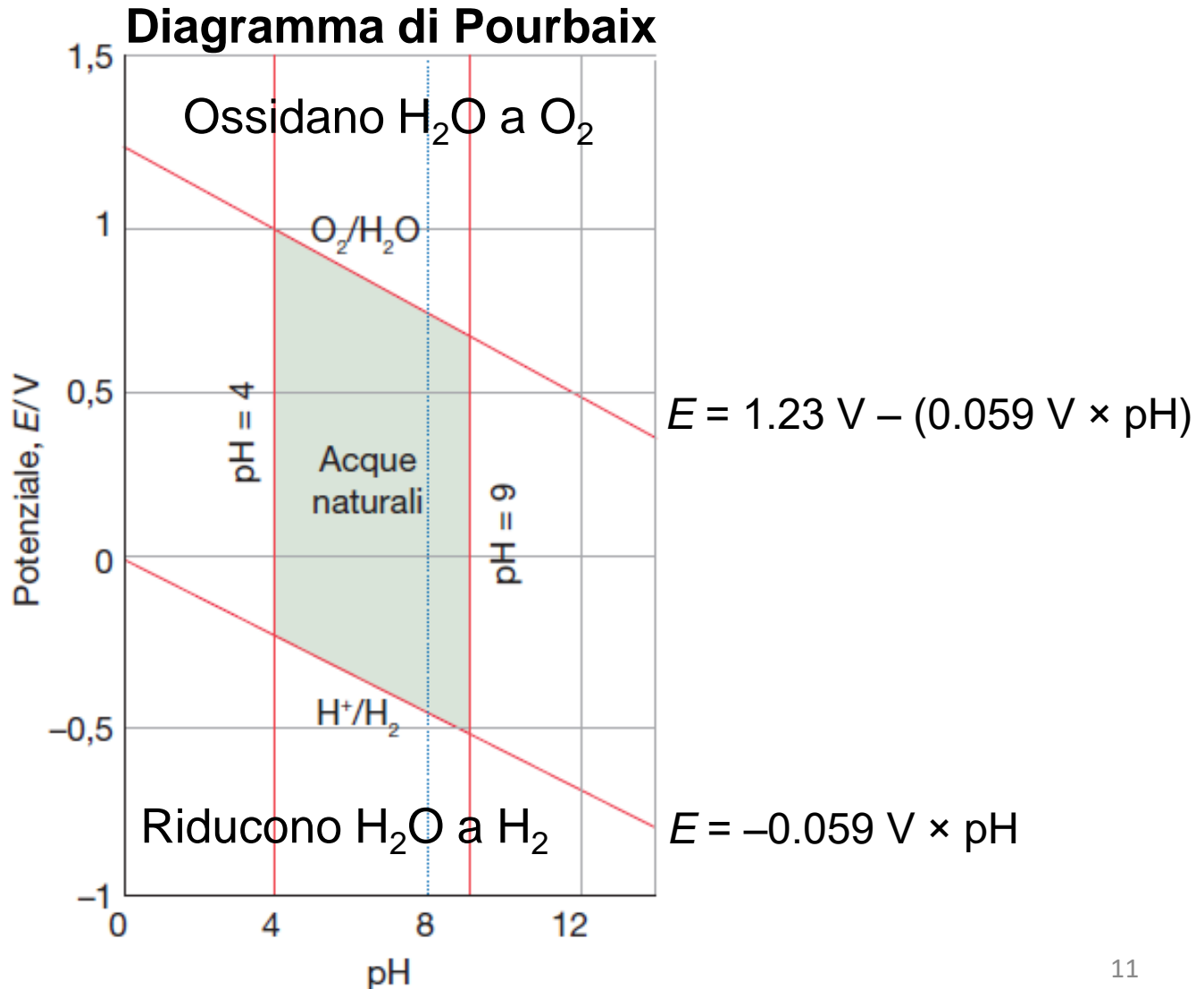


## Great Oxidation Event

In 200 milioni di anni la concentrazione atmosferica di  $\text{O}_2$  aumentò di 10 mila volte

Potenziali redox accessibili in acqua a pH 7: fra  $-0.4 \text{ V}$  ( $\text{H}^+/\text{H}_2$ ) e  $+0.8 \text{ V}$  ( $\text{O}_2/\text{OH}^-$ )

Potenziali redox primordiali in acqua a pH 7: fra  $-0.4 \text{ V}$  ( $\text{H}^+/\text{H}_2$ ) e ca.  $0.0 \text{ V}$  ( $\text{S}_n/\text{H}_2\text{S}$ )



Elemento	Biodisponibilità	
	Ambiente riducente (anaerobico)	Ambiente ossidante (aerobico)
Fe	Fe(II), (alta)	Fe(III), (bassa)
Cu	Come solfuro (bassa)	Cu(II), (moderata)
S	HS <sup>-</sup> (alta)	SO <sub>4</sub> <sup>2-</sup> (alta)
Mo	MoS <sub>2</sub> , (MoO <sub>n</sub> S <sub>4-n</sub> ) <sup>2-</sup> (bassa)	MoO <sub>4</sub> <sup>2-</sup> (moderata)
V	V <sup>3+</sup> , solfuri di V(IV) (moderata)	VO <sub>4</sub> <sup>3-</sup> (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

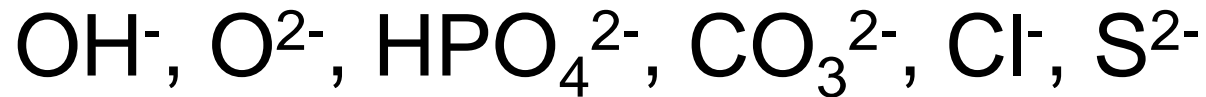
Endo- ed esoscheletri, stabilizzazione di DNA, RNA e proteine

## Ruolo funzionale

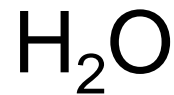
- Trasporto di carica ( $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ )
- Sintesi e metabolismo di molecole organiche ( $\text{Zn}^{2+}$ ,  $\text{Mg}^{2+}$ )
- Trasferimento di elettroni ( $\text{Fe}^{2+/3+}$ ,  $\text{Cu}^{+/2+}$ )
- Attivazione di piccole molecole (Fe, Cu, Mn, Mo...)
- Reattività organometallica (Co)

# Biological ligands

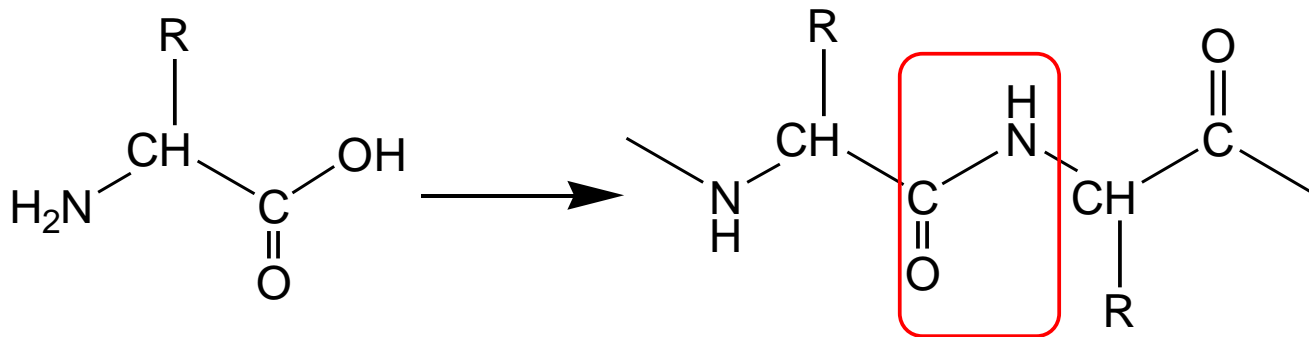
## Anions



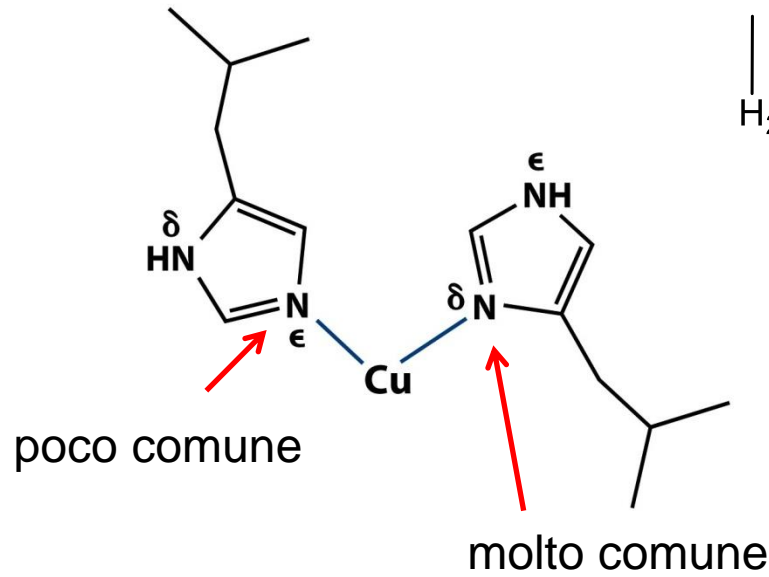
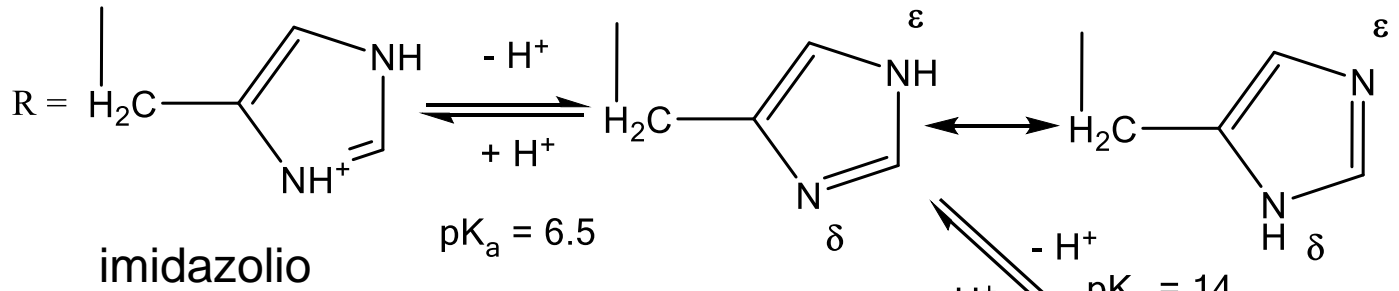
## Water



## Aminoacid side-chains



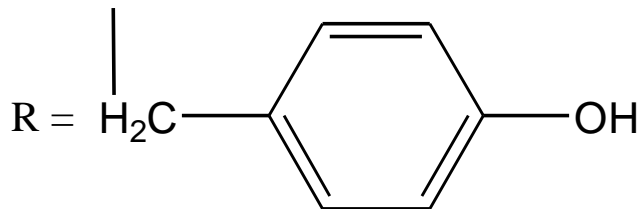
# Istidina (His)



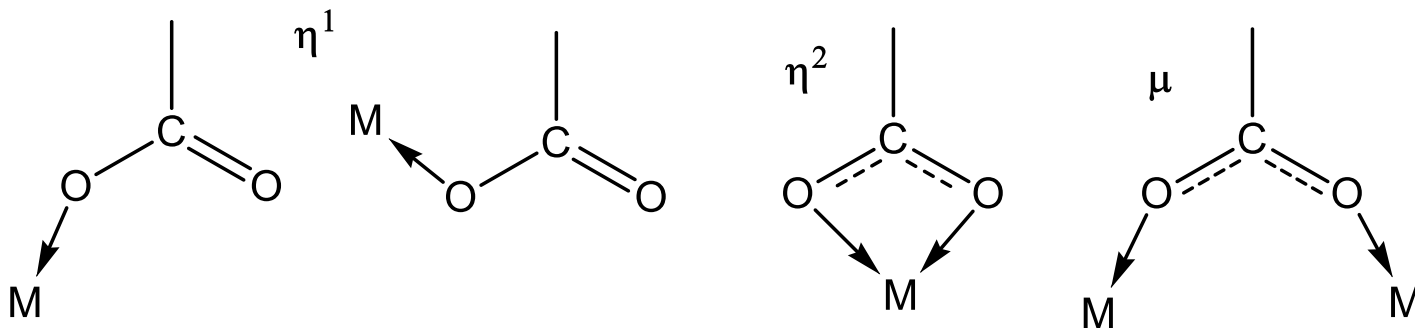


R = CH<sub>2</sub>SH  
Cisteina (Cys), pK<sub>a</sub> = 8.5

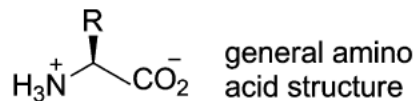
R = -CH<sub>2</sub>CH<sub>2</sub>SCH<sub>3</sub>  
**Metionina (Met)**



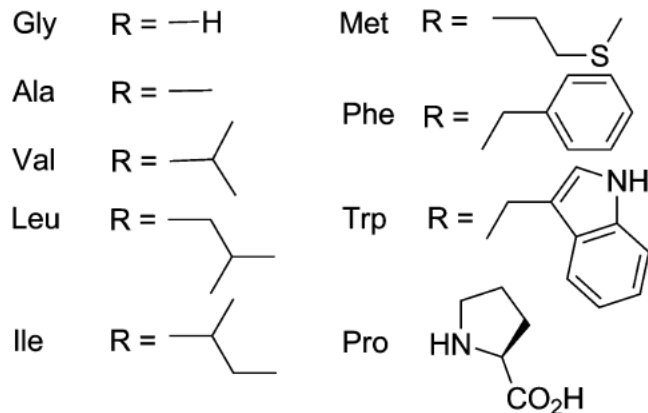
Tirosina, pK<sub>a</sub> = 10



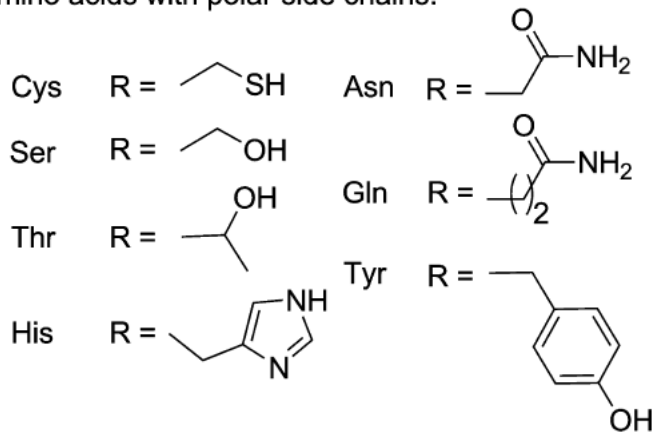
Glutammato (Glu): R = -CH<sub>2</sub>CH<sub>2</sub>COO<sup>-</sup> Aspartato (Asp): R = -CH<sub>2</sub>COO<sup>-</sup>  
pK<sub>a</sub> = 4.5



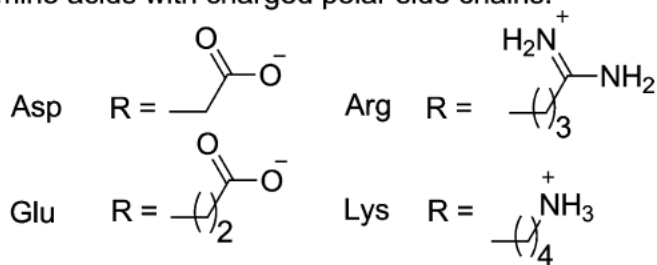
Amino acids with non-polar side chains:



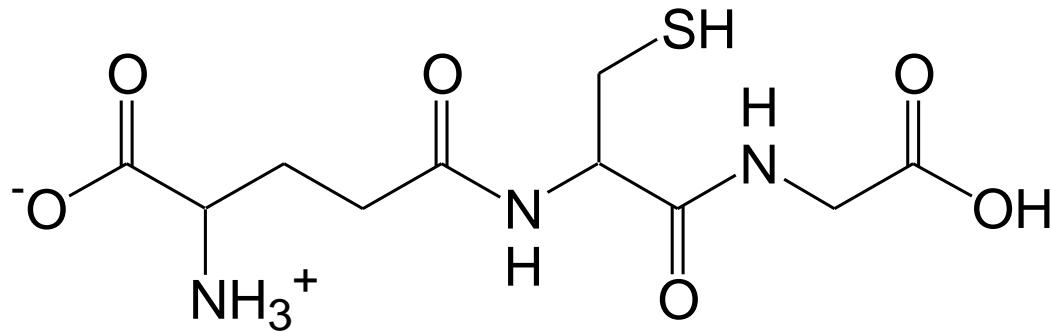
Amino acids with polar side chains:



Amino acids with charged polar side chains:



# Glutatione: il più importante tiolo intracellulare

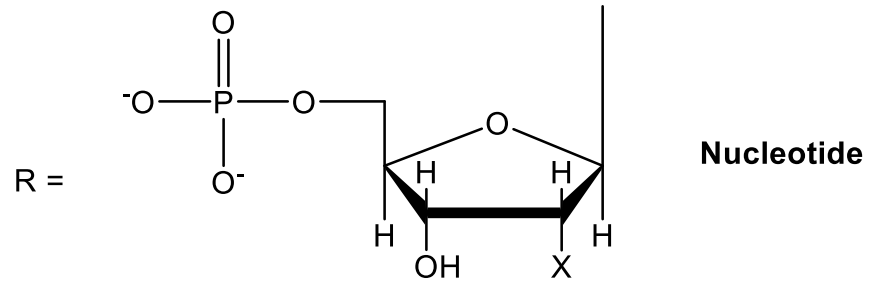
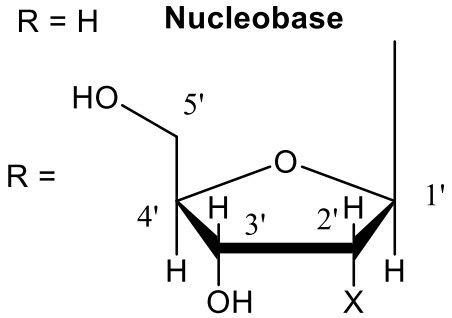
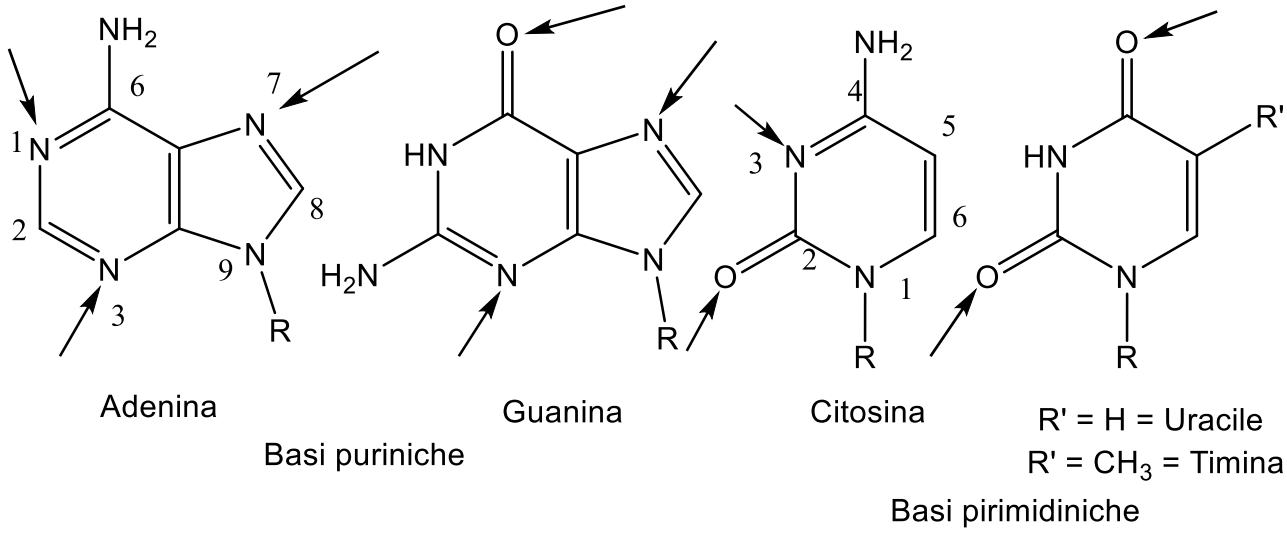


GSH

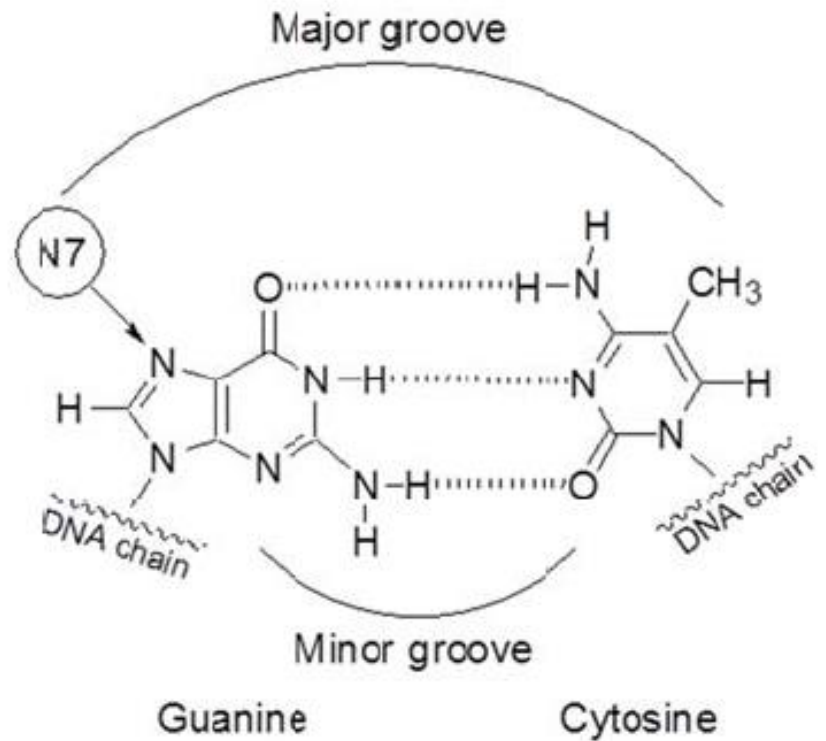
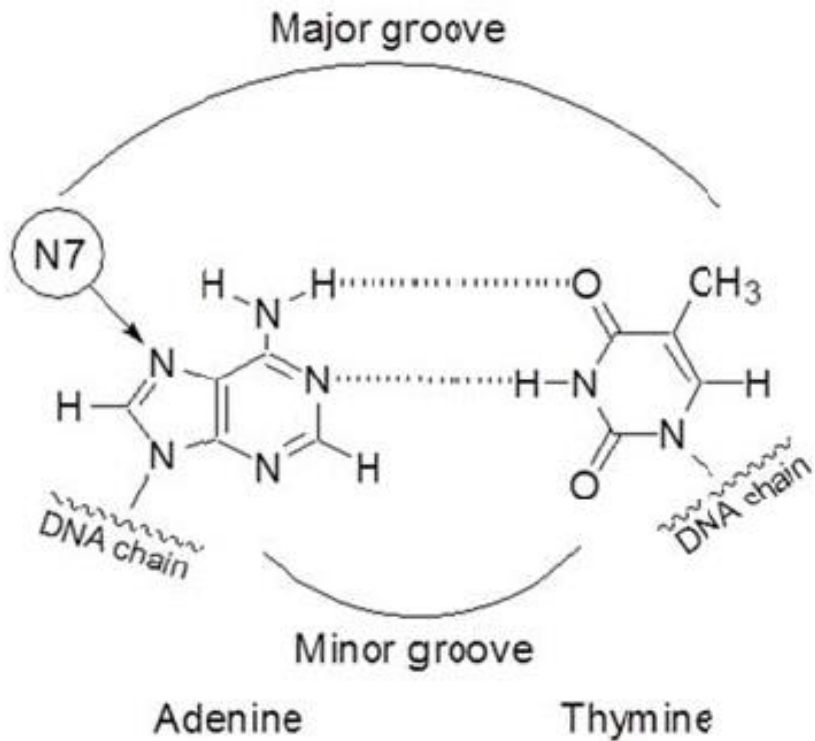
Glu-Cys-Gly

0.5 – 10 mM intracellulare

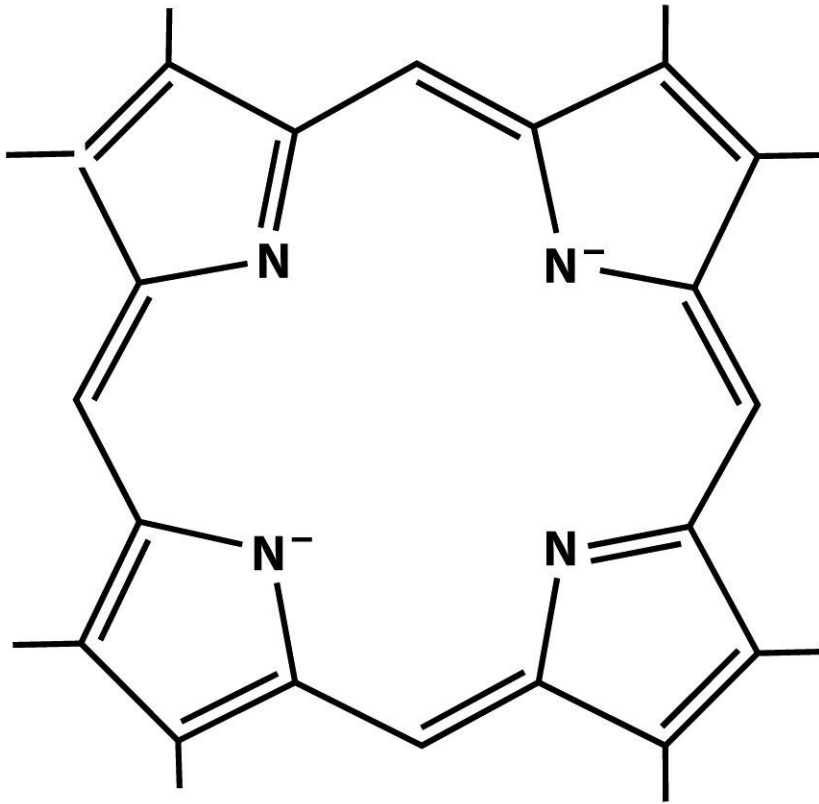
(anche riducente monoeletttronico)



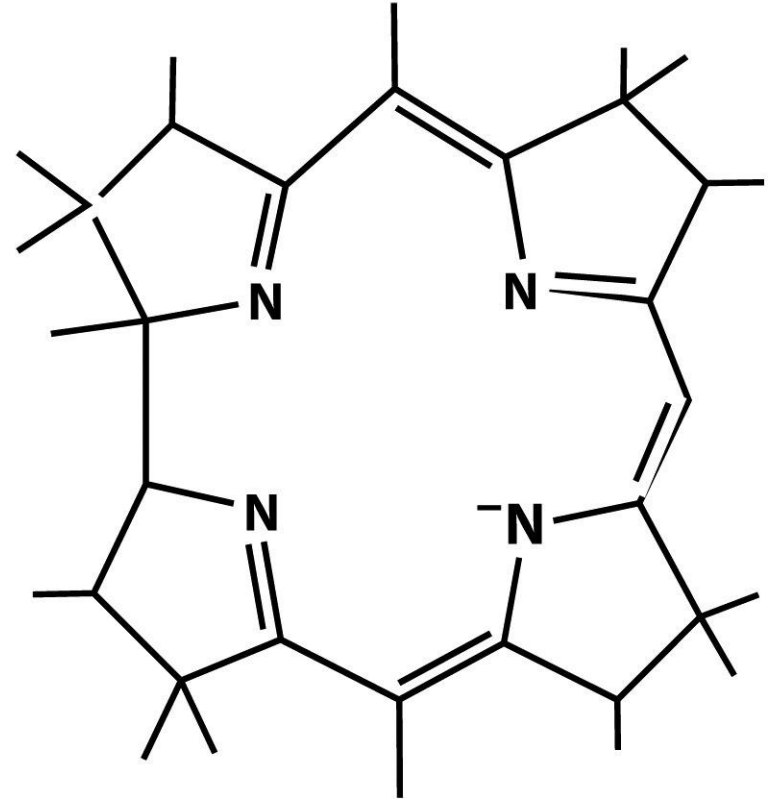
# Legami a idrogeno di tipo Watson-Crick



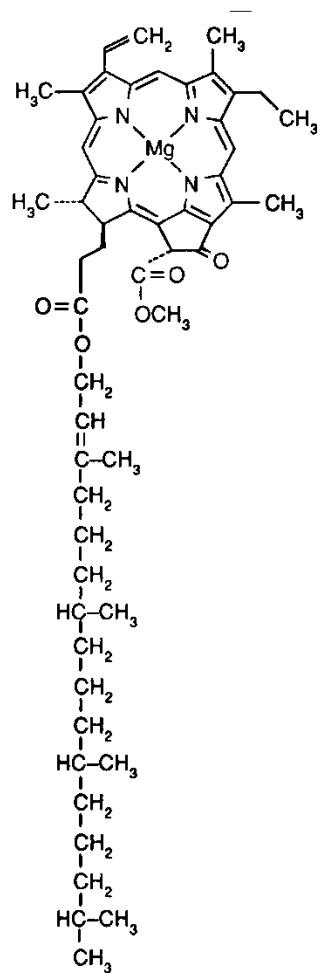
# Leganti tetrapirrolici



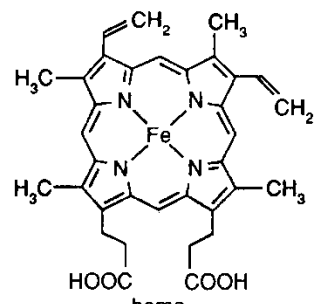
**Porphyrin<sup>2-</sup>**



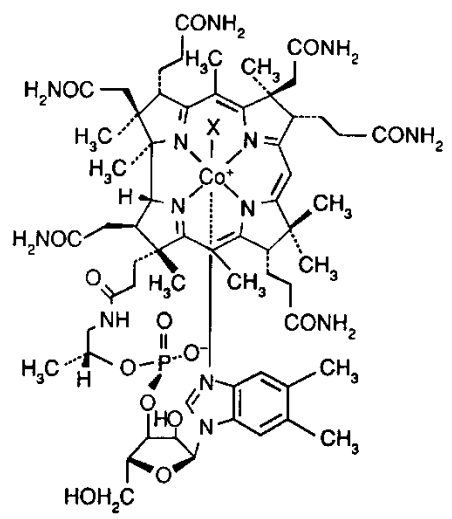
**Corrin<sup>1-</sup>**



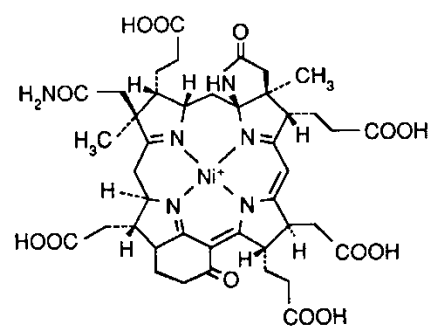
chlorophyll a



heme  
(Fe-protoporphyrin IX)



vitamin B<sub>12</sub> (X = CN)



coenzyme F430

Tipo	Cationi	Atomi donatori
<i>Hard</i>	$H^+$ , $Na^+$ , $K^+$ , $Mg^{2+}$ , $Ca^{2+}$ , $Mn^{2+}$ , $Mn^{3+}$ , $Fe^{3+}$	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), $F^-$ , $Cl^-$ , $NH_3$
<i>Soft</i>	$Cu^+$ , $Ag^+$ , $Pt^{2+}$ , $Cd^{2+}$ , $Hg^+$ , $Hg^{2+}$	$CN^-$ , $CO$ , $S^{2-}$ , $RSH$ 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

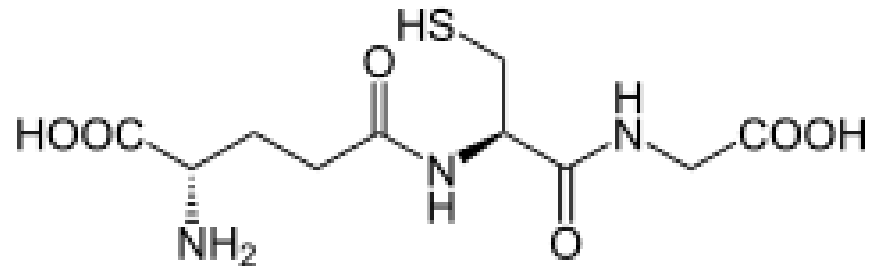
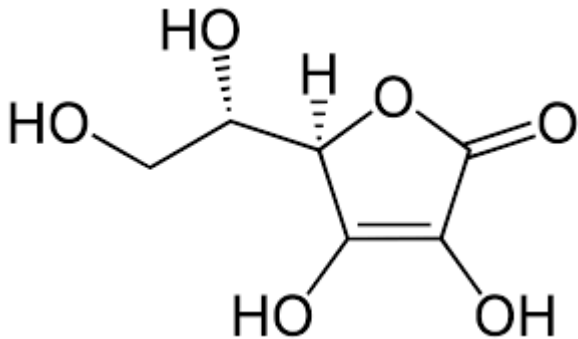


# Endogenous reducing agents

Electron transfer enzymes

**Ascorbic acid:** 11–79  $\mu\text{M}$  in the blood

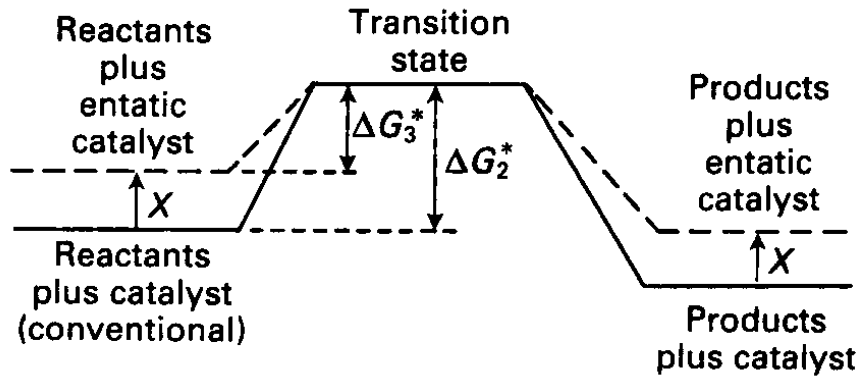
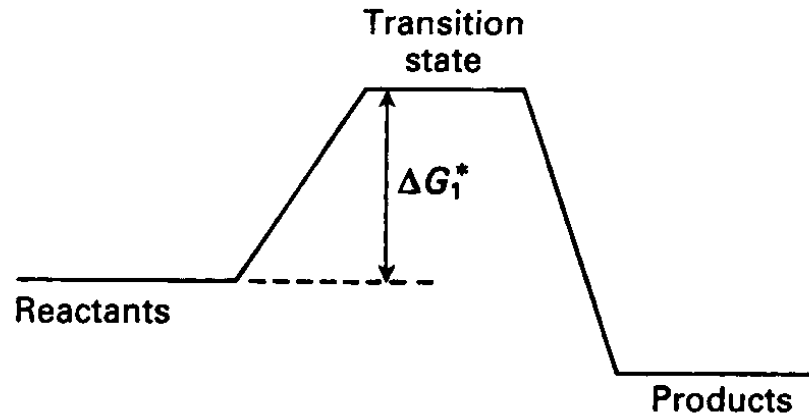
**Glutathione:** 0.5 – 10 mM intracellular



**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 <sup>-</sup> , (Glu <sup>-</sup> )	severely distorted tetrahedron
Cu(I)	high	3,4: His, Cys <sup>-</sup> , Met	severely distorted tetrahedron
Cu(II)	high	3,4: His, (Cys <sup>-</sup> )	distorted square planar arrangement
Fe(II), Ni(II) Co(II), Mg(II)	low	4-6: His, Glu <sup>-</sup> , Asp <sup>-</sup>	distorted octahedron
Fe(III)	high	4-6: Glu <sup>-</sup> , Asp <sup>-</sup> , Tyr <sup>-</sup> , Cys <sup>-</sup>	distorted octahedron

# Stato entatico



# Stato entatico

