

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

○ Bulk biological elements

□ Trace elements believed to be essential for bacteria, plants or animals

⋯ Possibly essential trace elements for some species

11

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

Na (100g), K (170g), Mg (25g), Ca (1100g) = *bulk metals*

Fe, Cu, Zn, V, Cr, Mo, Mn, Co, Ni = *trace* e *ultra-trace metals*

13 metalli essenziali

Metal	Mass / mg	Biological roles
V	0.11	Enzymes (nitrogenases, haloperoxidases)
Cr	14	Claimed (not yet proven) to be essential in glucose metabolism in higher mammals
Mn	12	Enzymes (phosphatase, mitochondrial superoxide dismutase, glycosyl transferase); photoredox activity in Photosystem II (see equation 22.54 and discussion)
Fe	4200	Electron-transfer systems (Fe-S proteins, cytochromes); O ₂ storage and transport (haemoglobin, myoglobin, haemerythrin); Fe storage (ferritin, transferritin); Fe transport proteins (siderophores); in enzymes (e.g. nitrogenases, hydrogenases, oxidases, reductases)
Co	3	Vitamin B ₁₂ coenzyme
Ni	15	Enzymes (urease, some hydrogenases)
Cu	72	Electron transfer systems (blue copper proteins); O ₂ storage and transport (haemocyanin); Cu transport proteins (ceruloplasmin)
Zn	2300	Acts as a Lewis acid (e.g. in hydrolysis processes involving carboxypeptidase, carbonic anhydrase, alcohol dehydrogenase); structural roles
Mo	5	Enzymes (nitrogenases, reductases, hydroxylases)

Concentrazione intracellulare media dei *trace elements* nelle cellule di eucarioti:

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

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

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

Metalloma

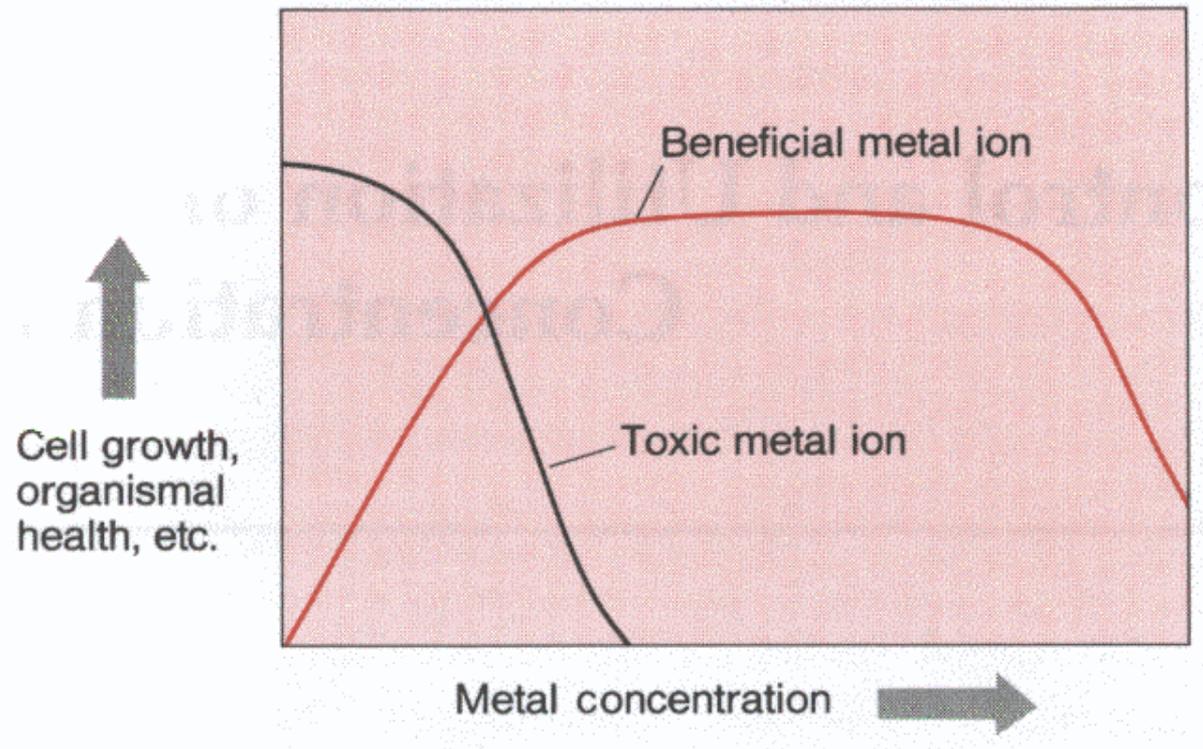
Ogni specie è caratterizzata da uno specifico

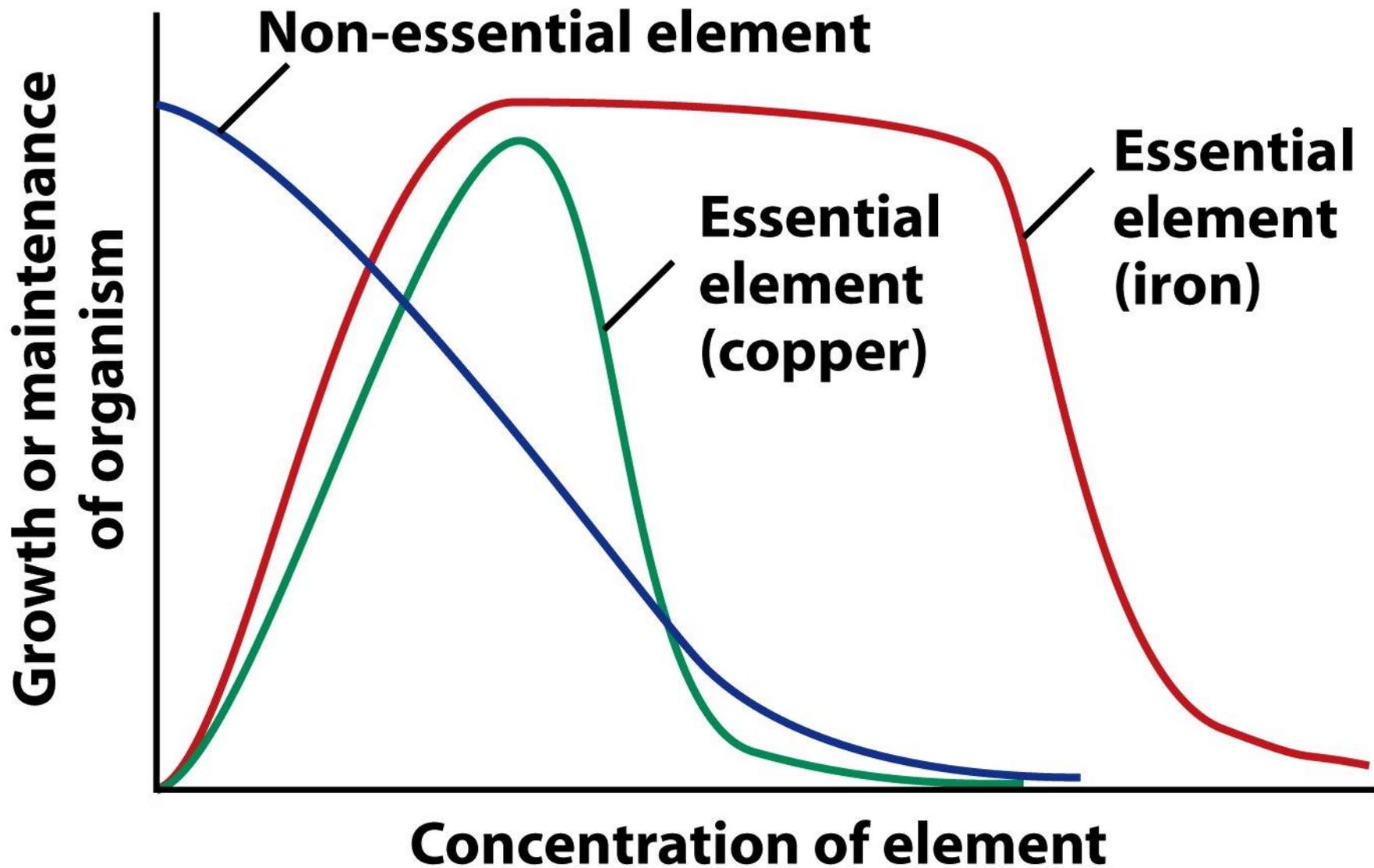
metalloma

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

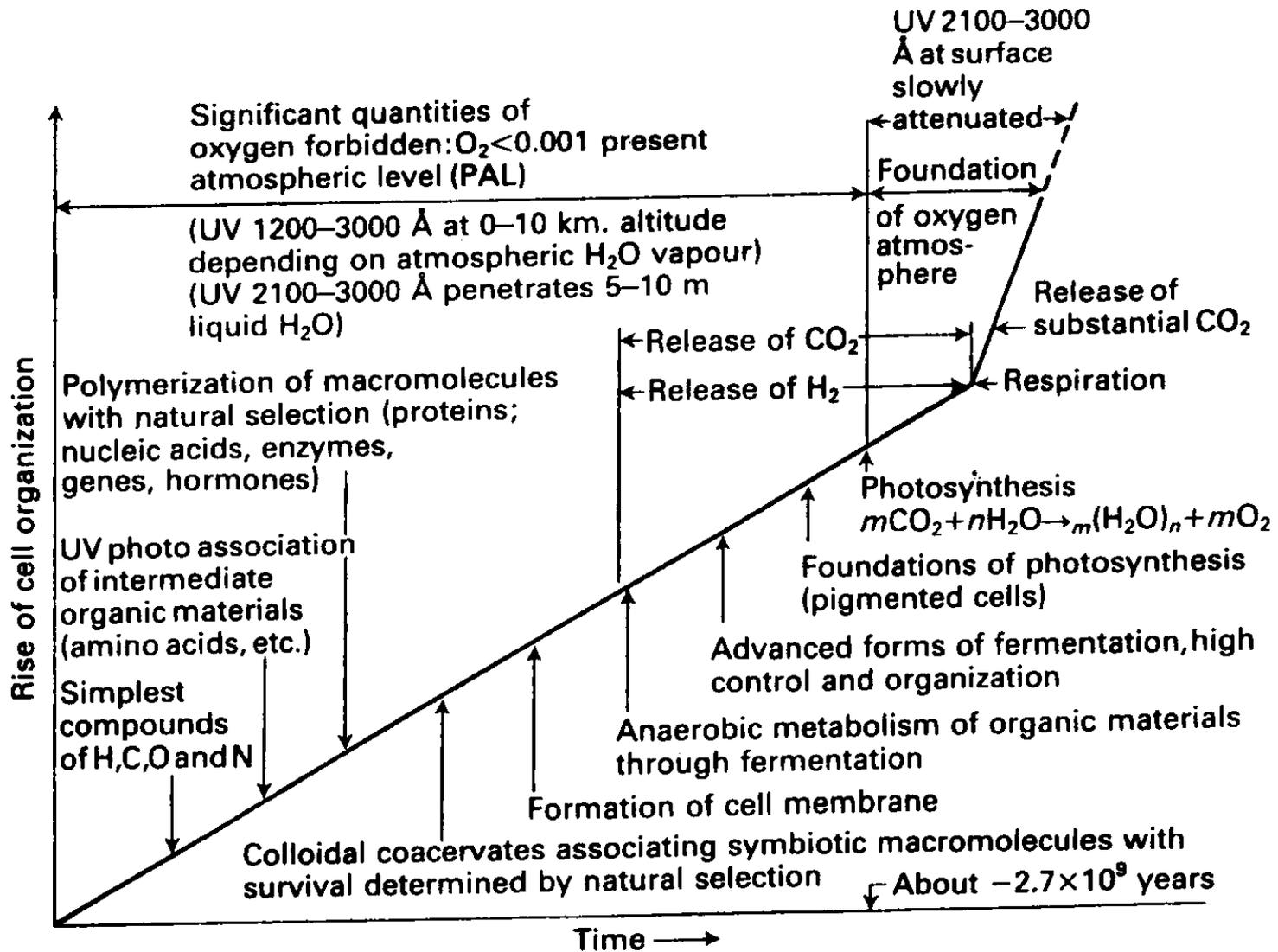
Come si stabilisce se un elemento è essenziale per una specie?

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





Biodisponibilità degli elementi



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

Elemento	Ambiente riducente	Ambiente ossidante
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 _n S _{4-n}) ²⁻ (bassa)	MoO ₄ ²⁻ (moderata)
V	V ³⁺ , solfuri di V(IV) (moderata)	VO ₄ ³⁻ (moderata)

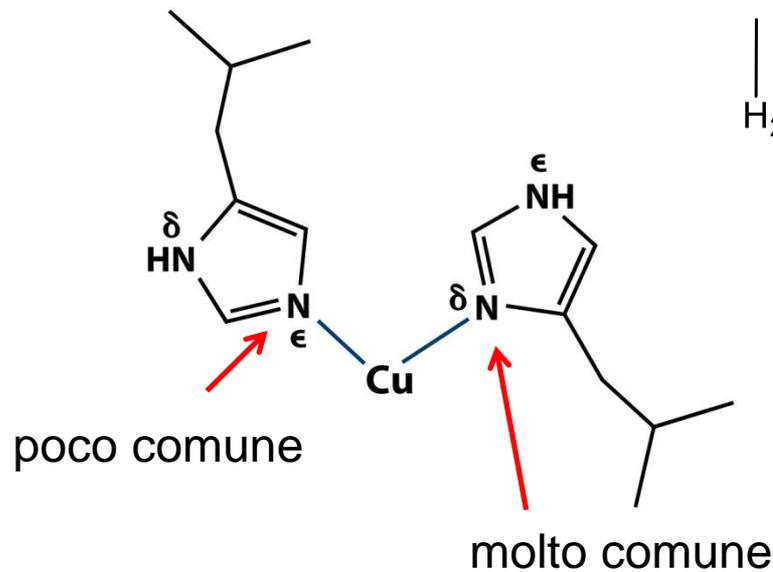
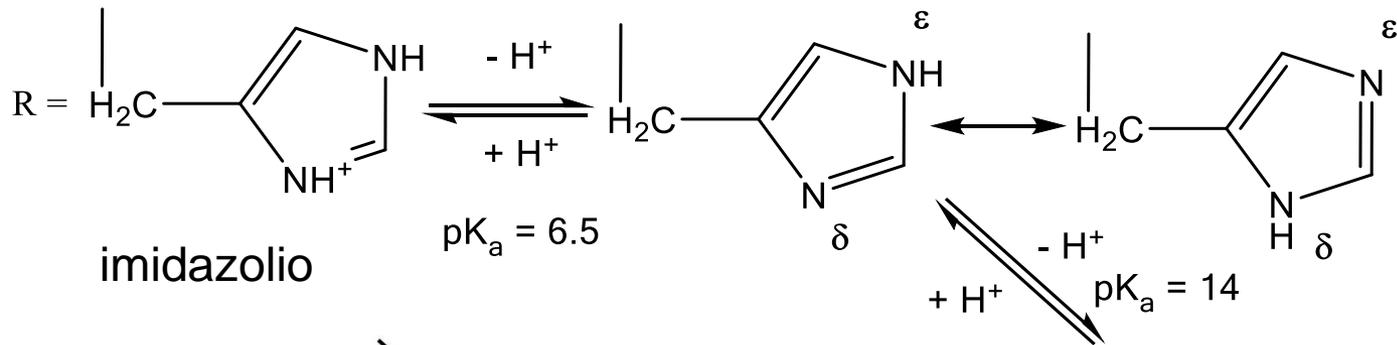
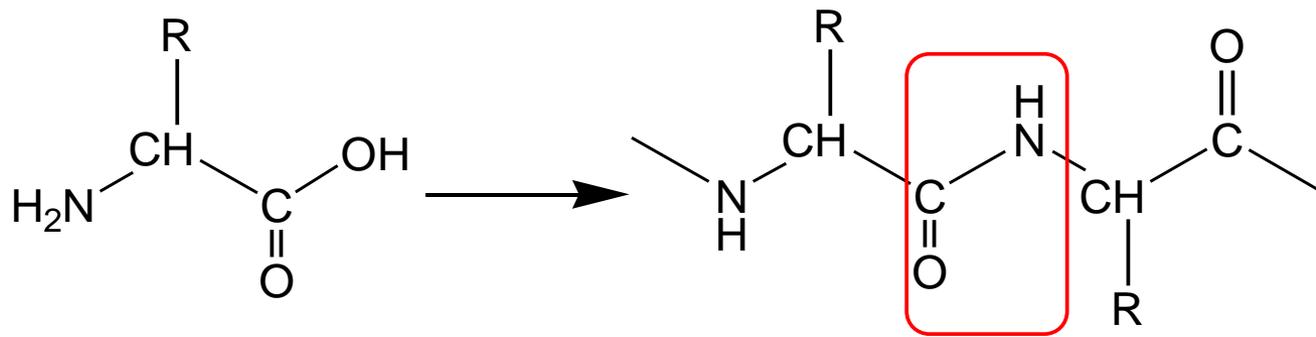
Ruoli dei metalli nei sistemi biologici

Ruolo strutturale

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

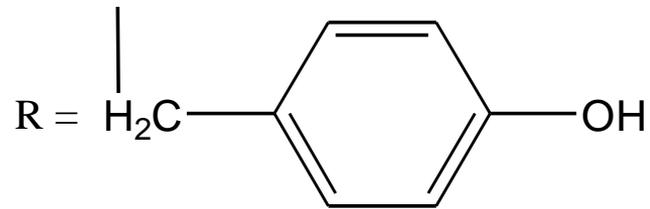
Ruolo funzionale

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

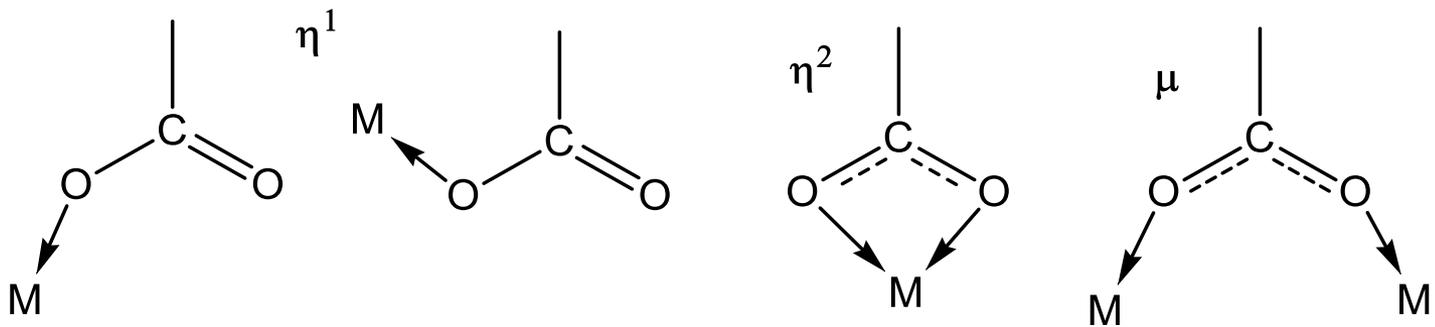


R = CH₂SH
Cisteina (Cys), pK_a = 8.5

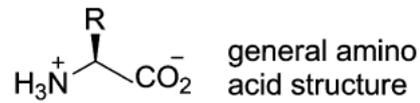
R = -CH₂CH₂SCH₃
Metionina (Met)



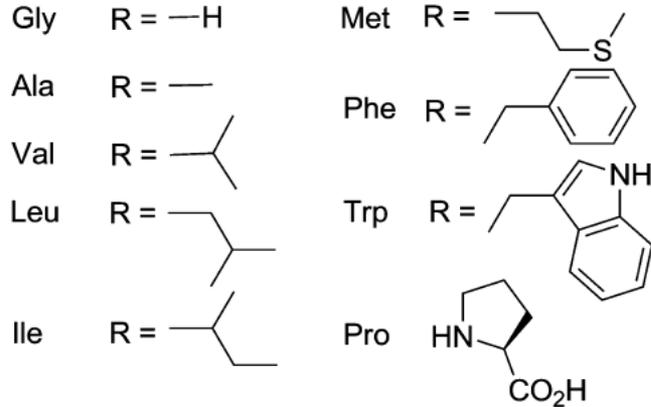
Tirosina, pK_a = 10



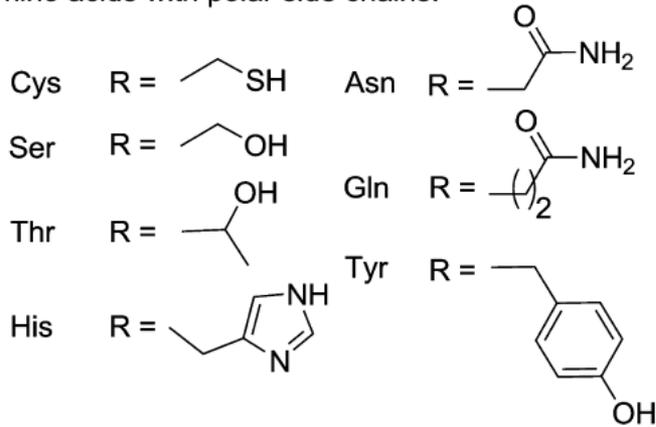
Glutammato (Glu): R = -CH₂CH₂COO⁻ Aspartato (Asp): R = -CH₂COO⁻
pK_a = 4.5



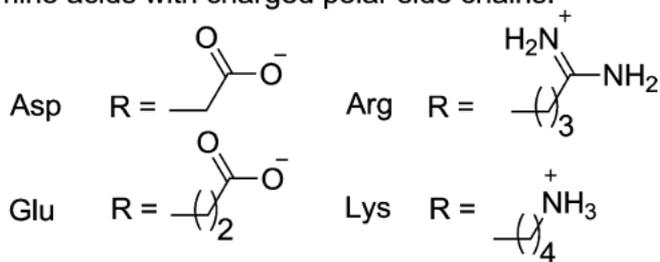
Amino acids with non-polar side chains:



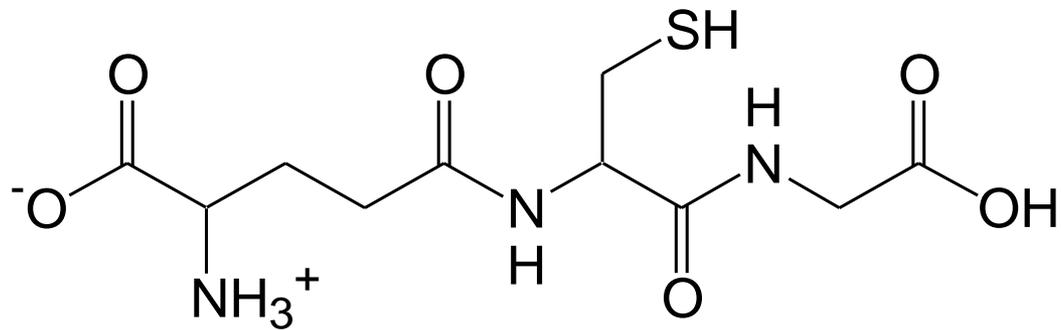
Amino acids with polar side chains:



Amino acids with charged polar side chains:



GLUTATIONE

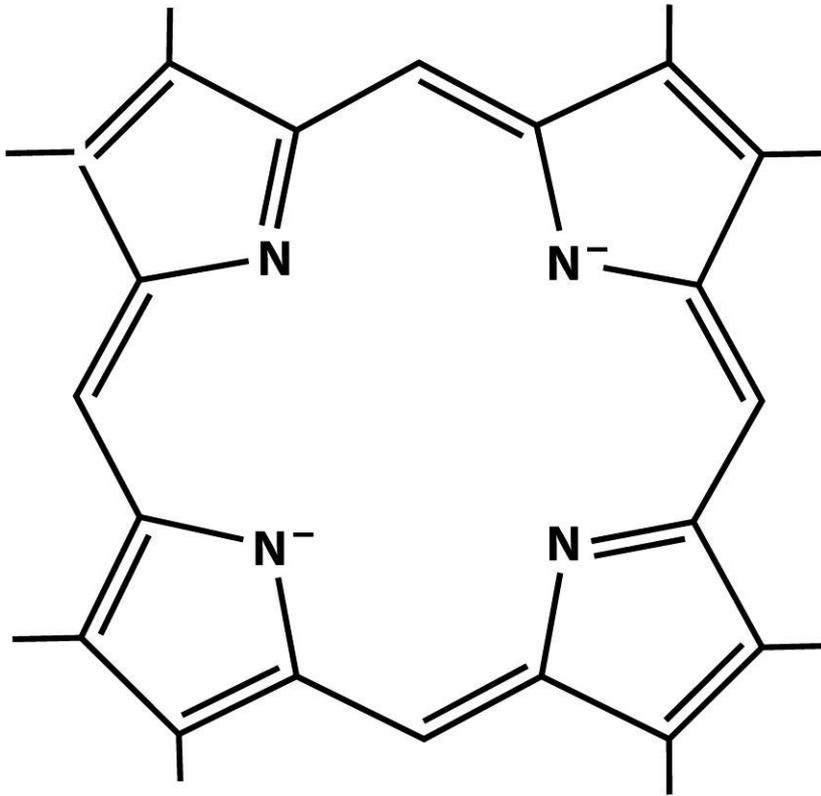


GSH

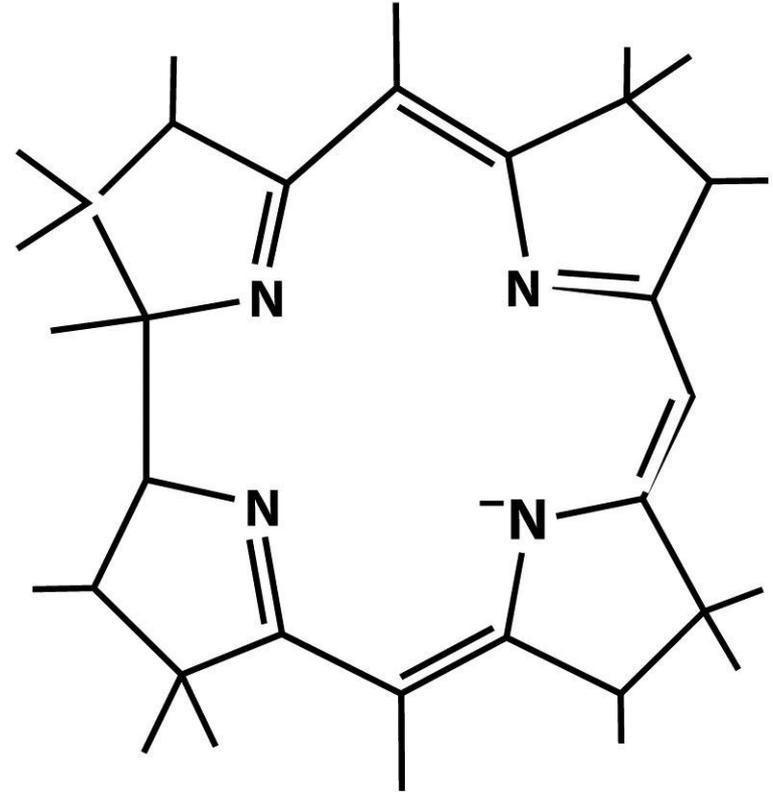
Glu-Cys-Gly

0.5 – 10 mM intracellulare
(riducente monoelettronico)

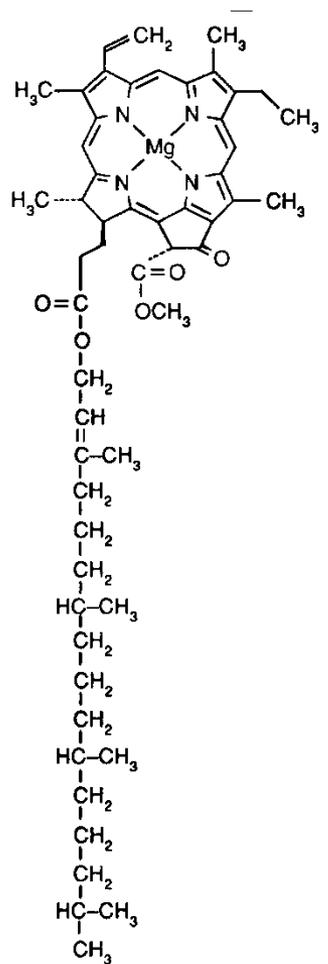
Leganti tetrapirrolici



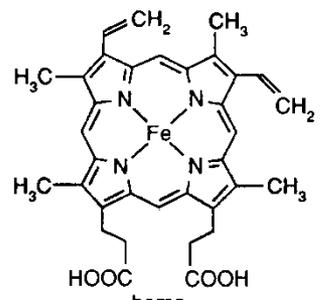
Porphyrin²⁻



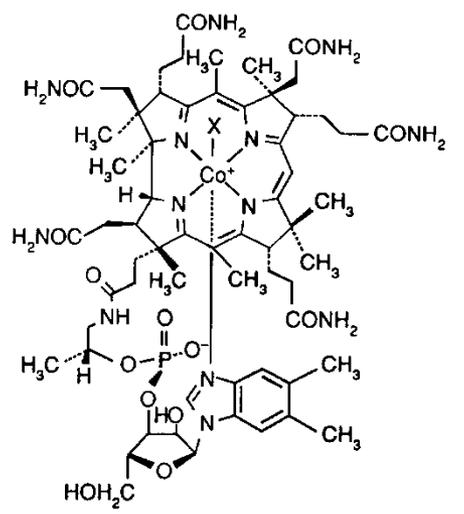
Corrin¹⁻



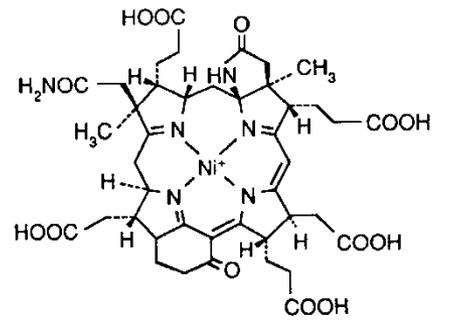
chlorophyll a



heme
(Fe-protoporphyrin IX)



vitamin B₁₂ (X = CN)

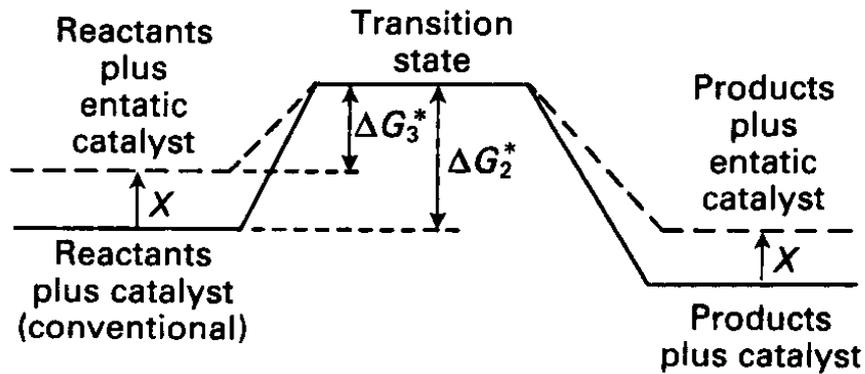
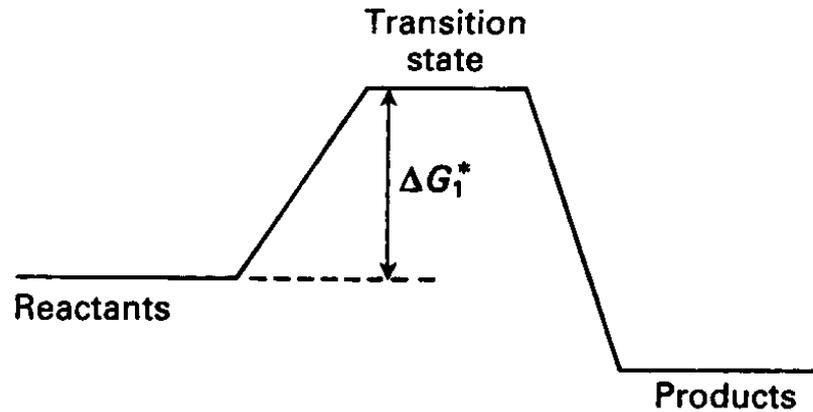


coenzyme F430

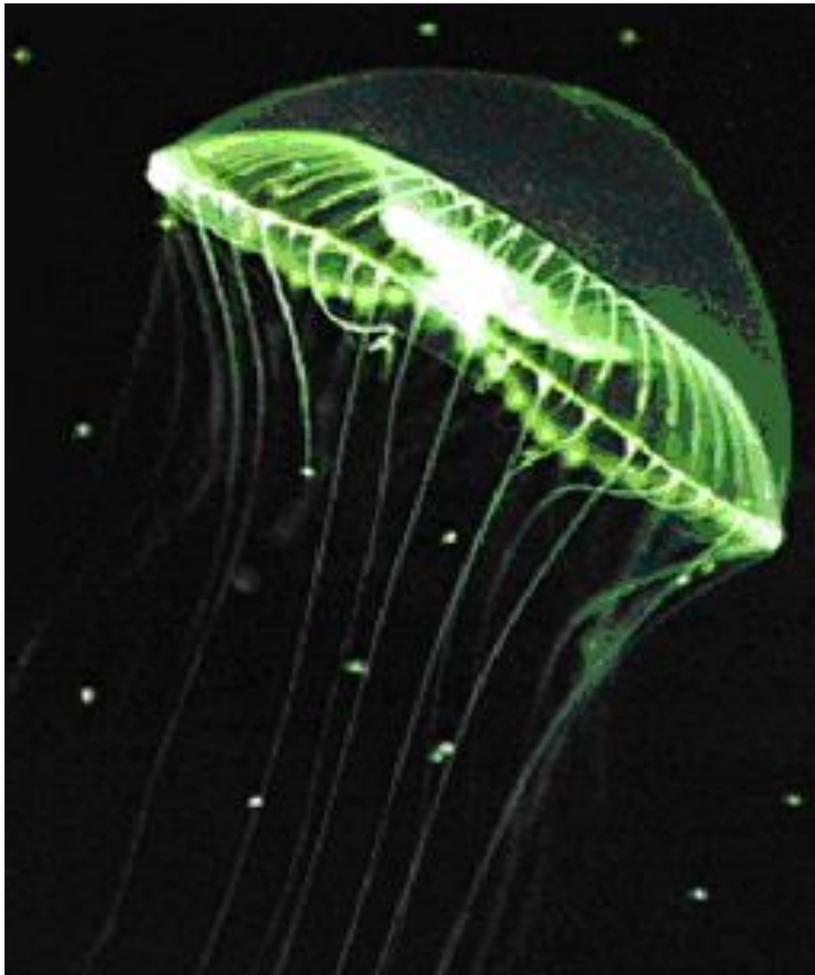
Table 2.6 Typical coordination environments of metal centers in proteins

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 arrangement
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

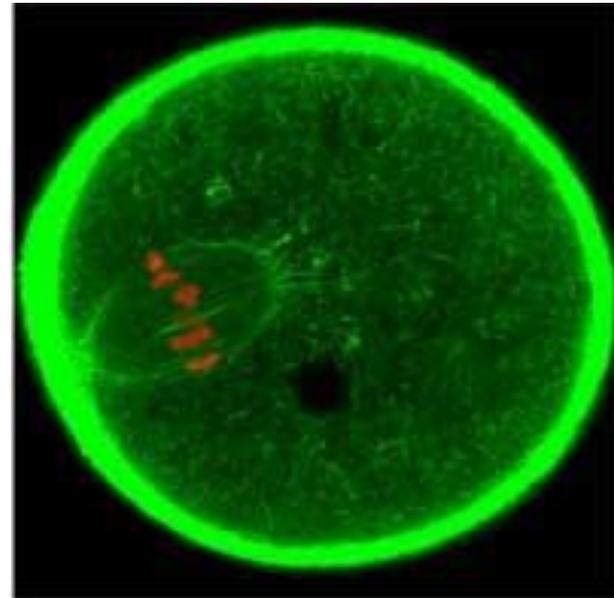
Stato entatico



Ione	Raggio (Å)	Ione	Raggio (Å)
Na ⁺	1.02	Mg ²⁺	0.72
K ⁺	1.38	Ca ²⁺	1.00

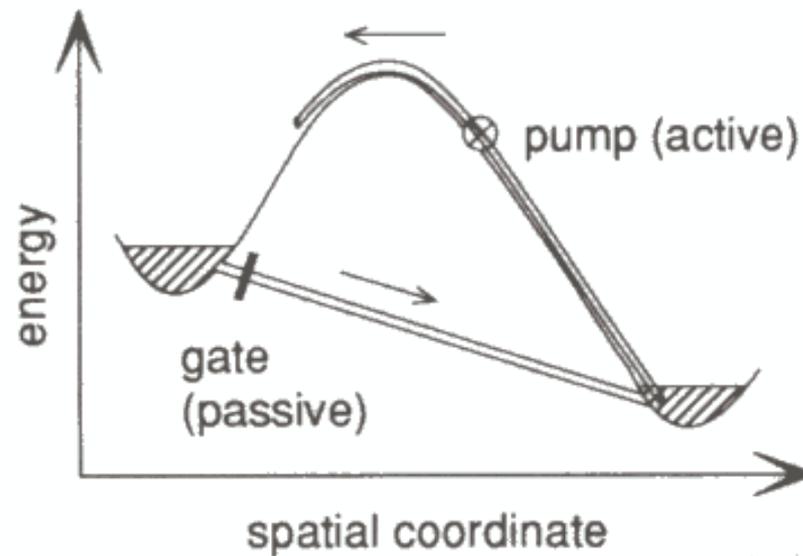


Green Fluorescent Protein (GFP) =
sensore fluorescente per Ca²⁺

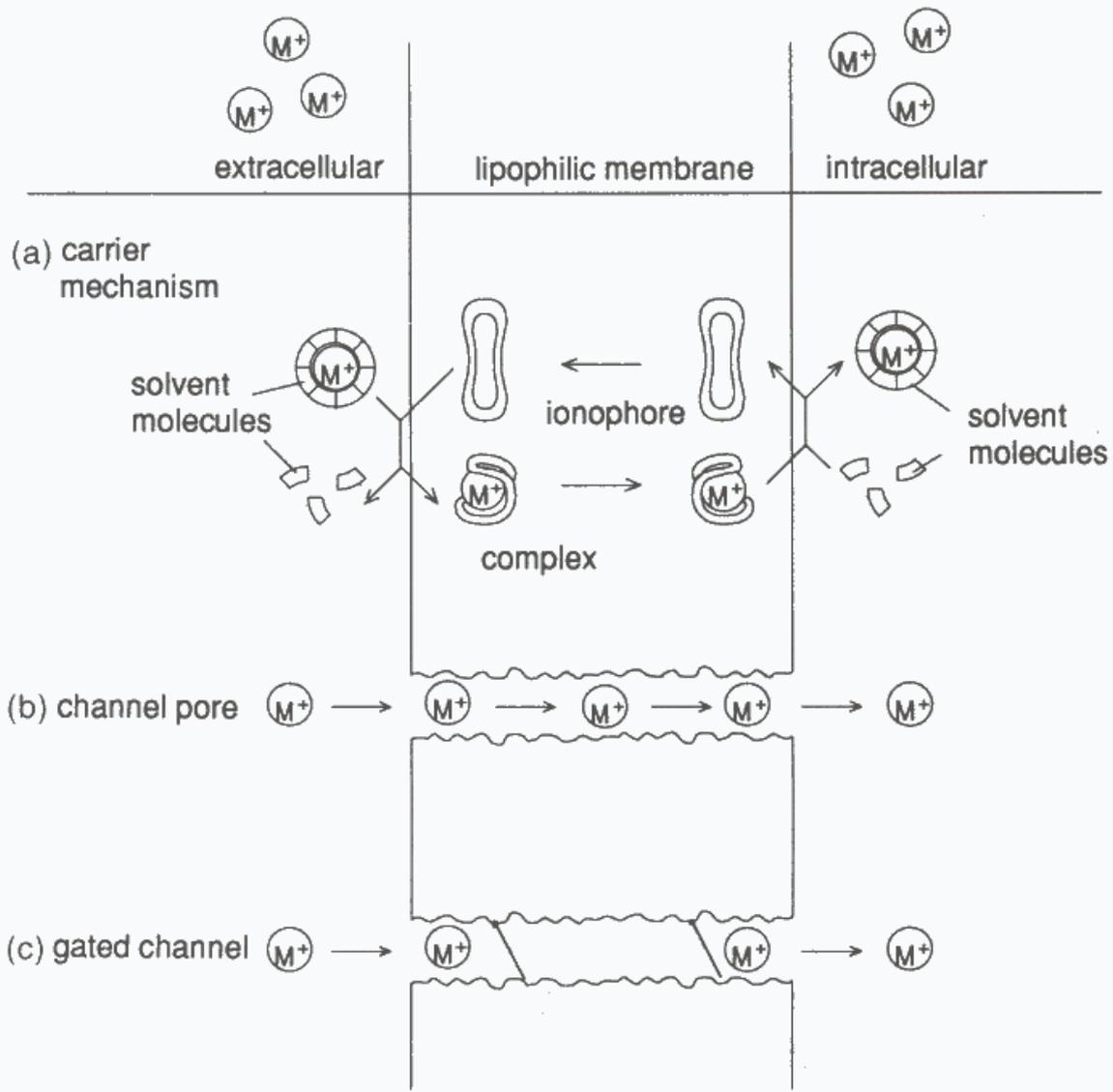


Ione	Intracellulare (mM)	Extracellulare (mM)
Na ⁺	10	150
K ⁺	100	5
Mg ²⁺	2.5	1.5
Ca ²⁺	0.1 ^a	2.5
Cl ⁻	4	100

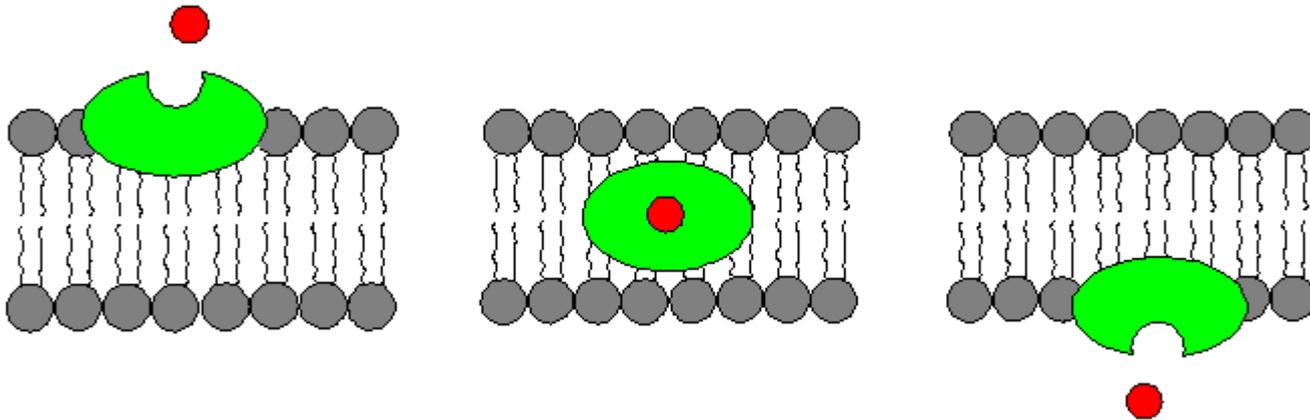
^a0.1 μM nel citoplasma della cellula a riposo



ion-transport mechanisms

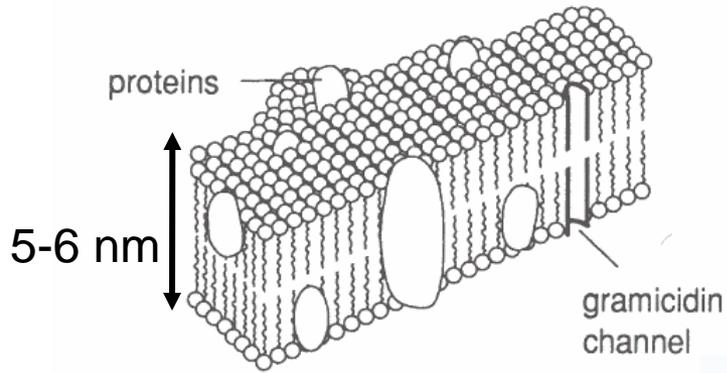


Ionofori



La valinomicina trasporta $10^3 - 10^4$ ioni K^+ al secondo attraverso la membrana dei mitocondri.
La selettività K^+/Na^+ è dell'ordine di 10^4

Ion channels



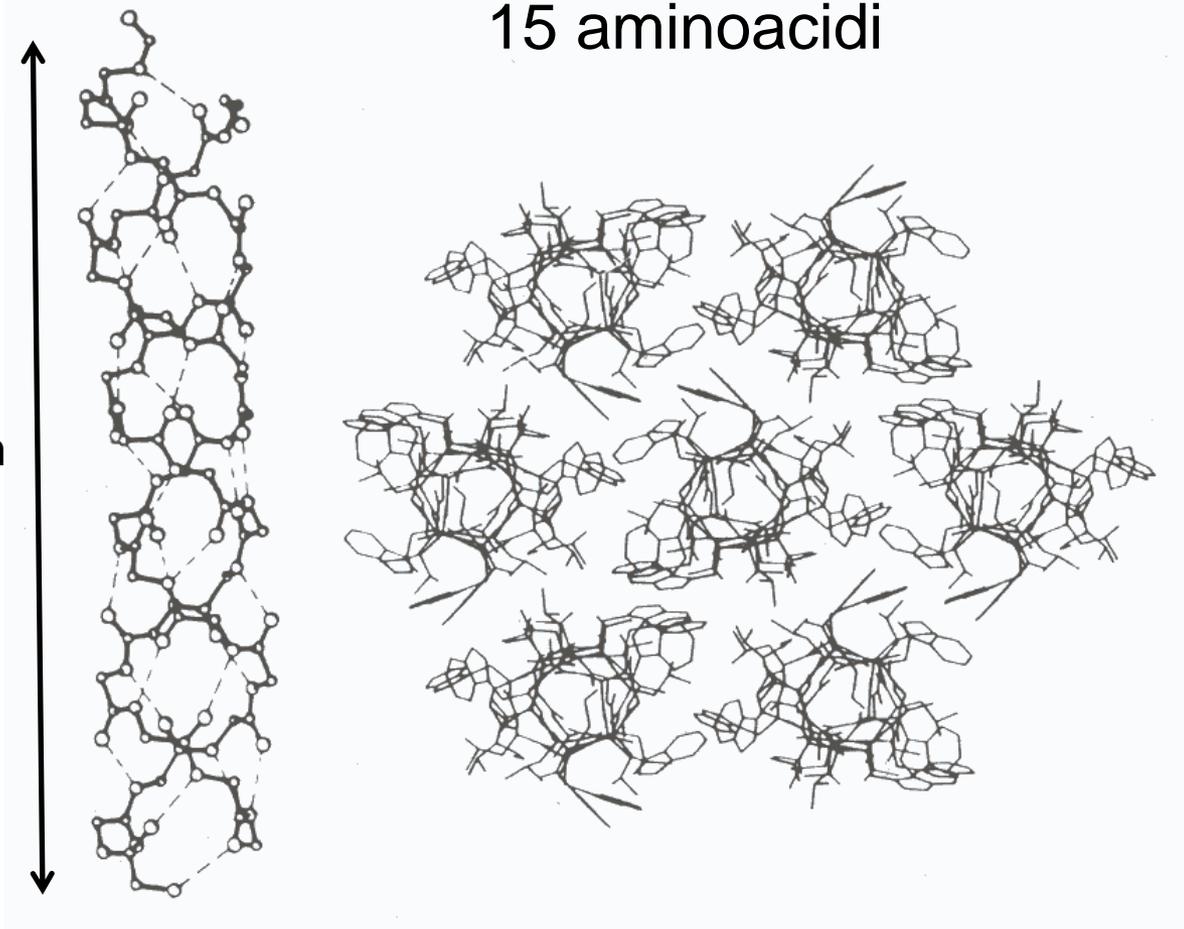
fluid double layer

gramicidin channel

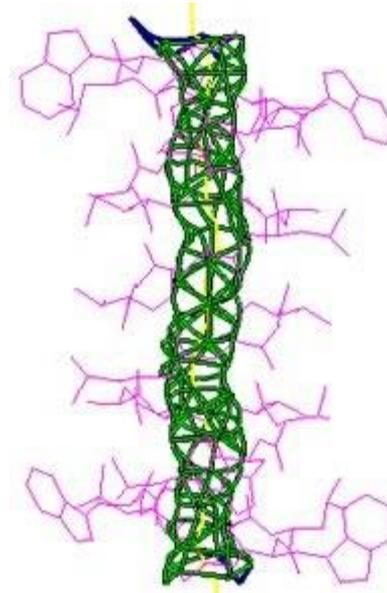
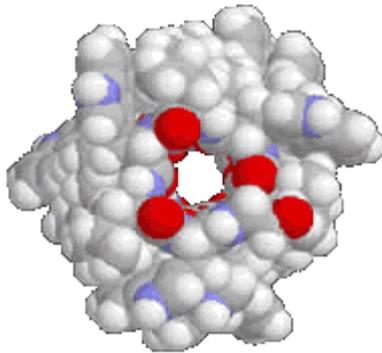
0.4 nm

3 nm

Gramicidina A
15 aminoacidi

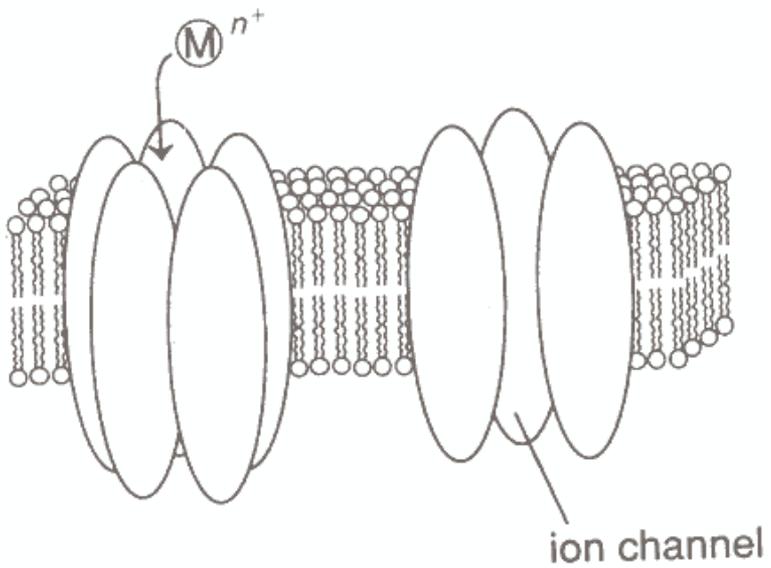


Gramicidina A

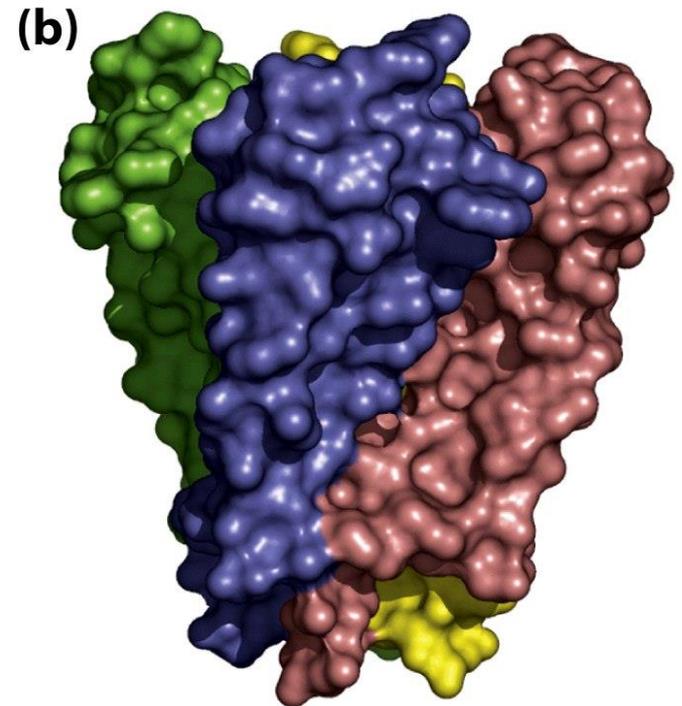
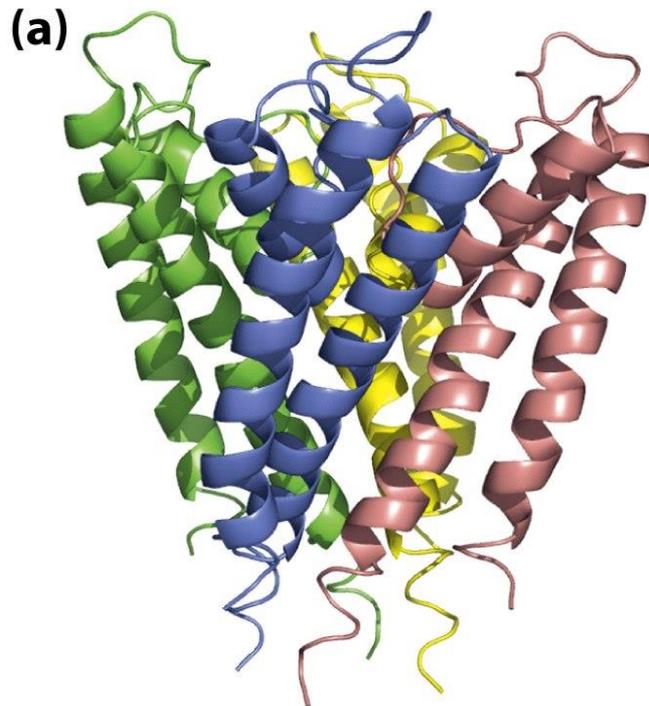


La gramicidina A trasporta 10^7 ioni K^+ o Na^+ al secondo attraverso la membrana. I cationi divalenti bloccano il poro.

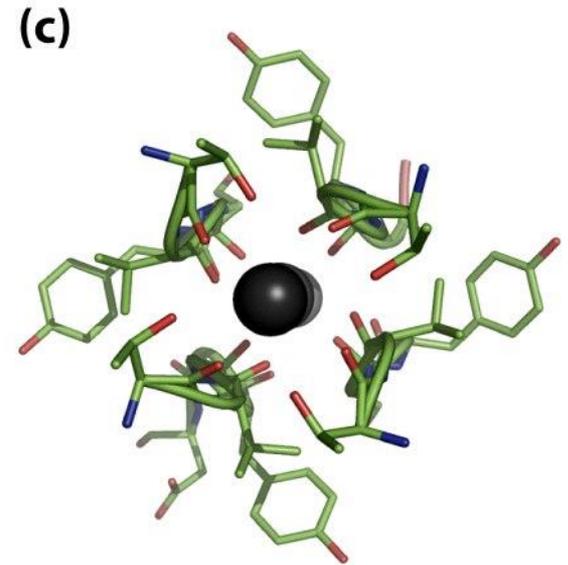
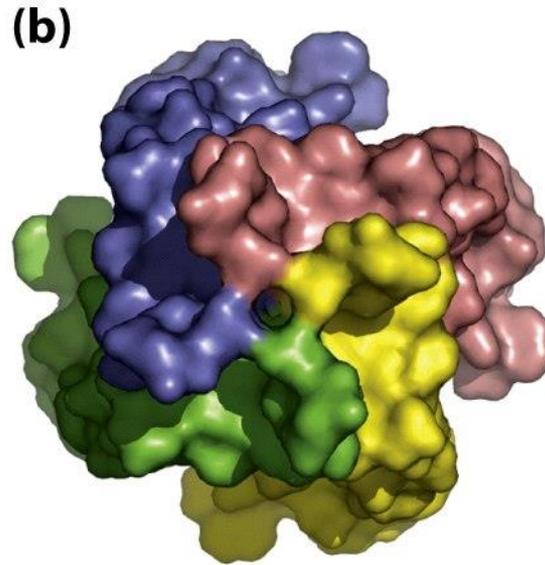
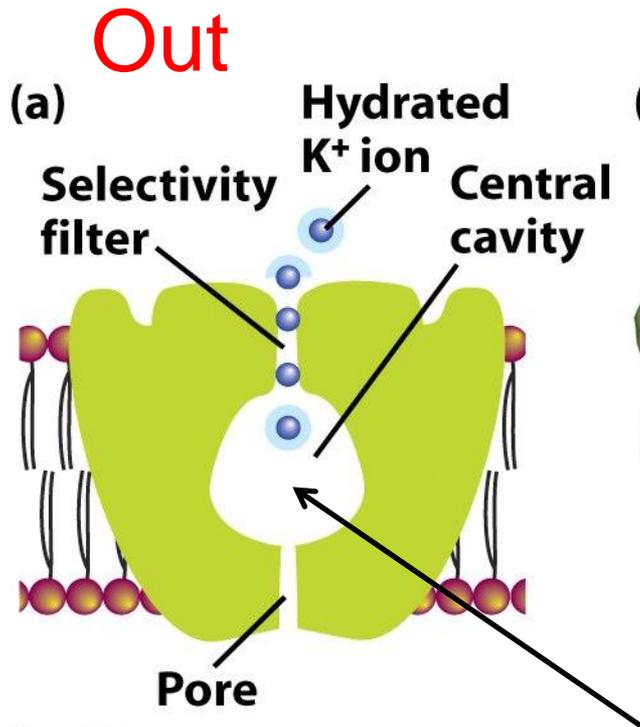
Proteine trans-membrana



Canale del K^+

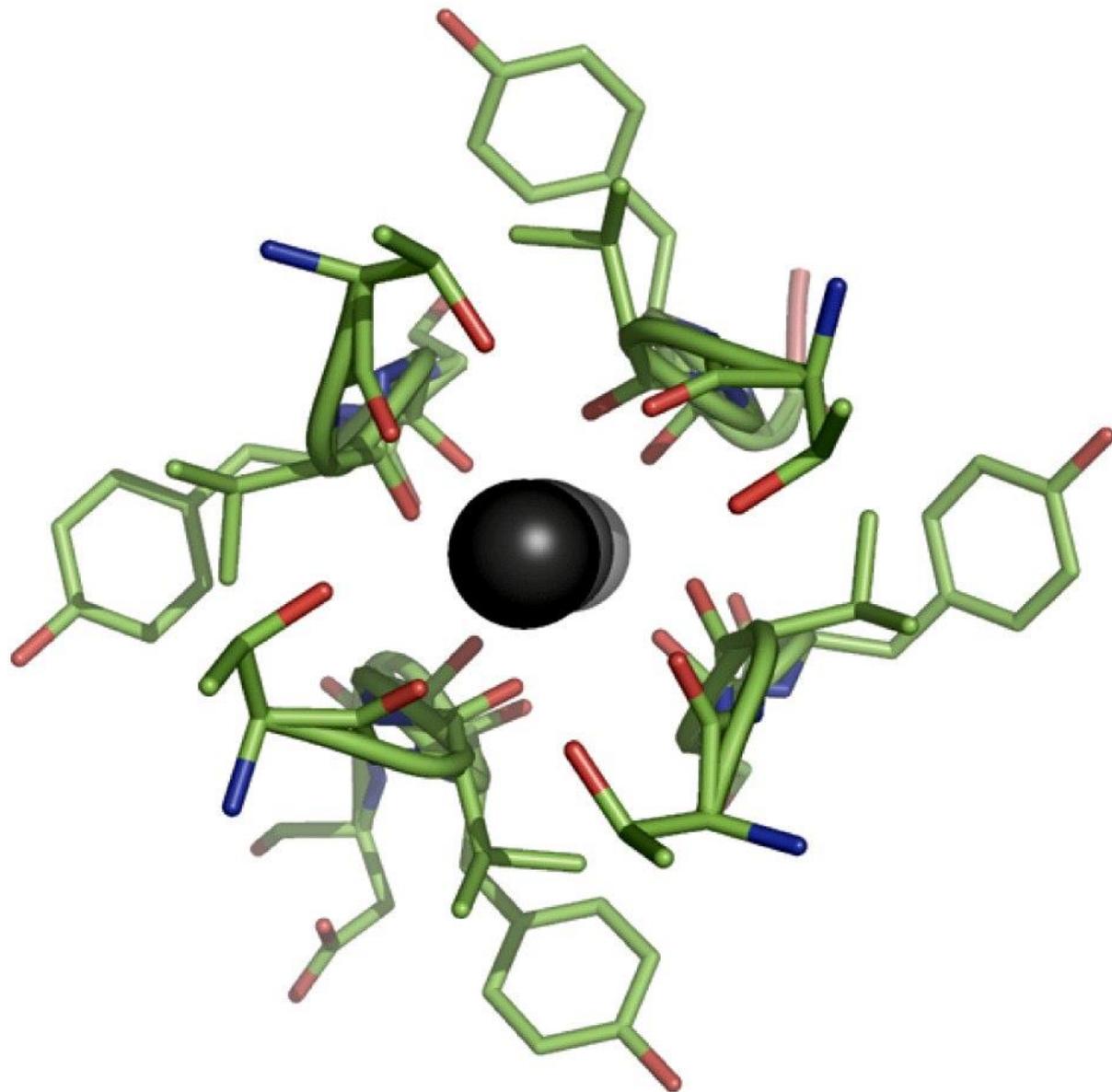


Canale del K⁺ *potential gated*

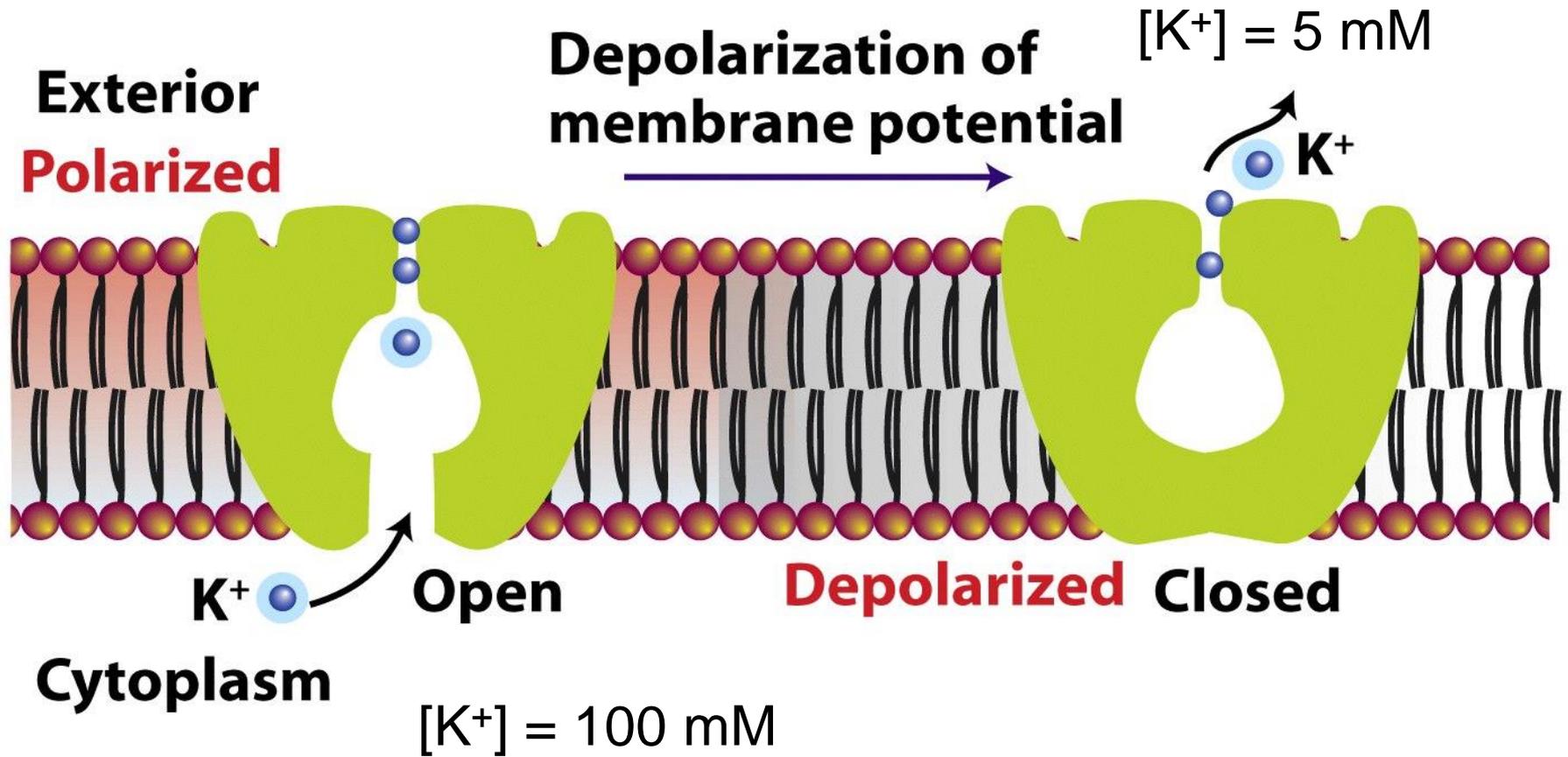


In

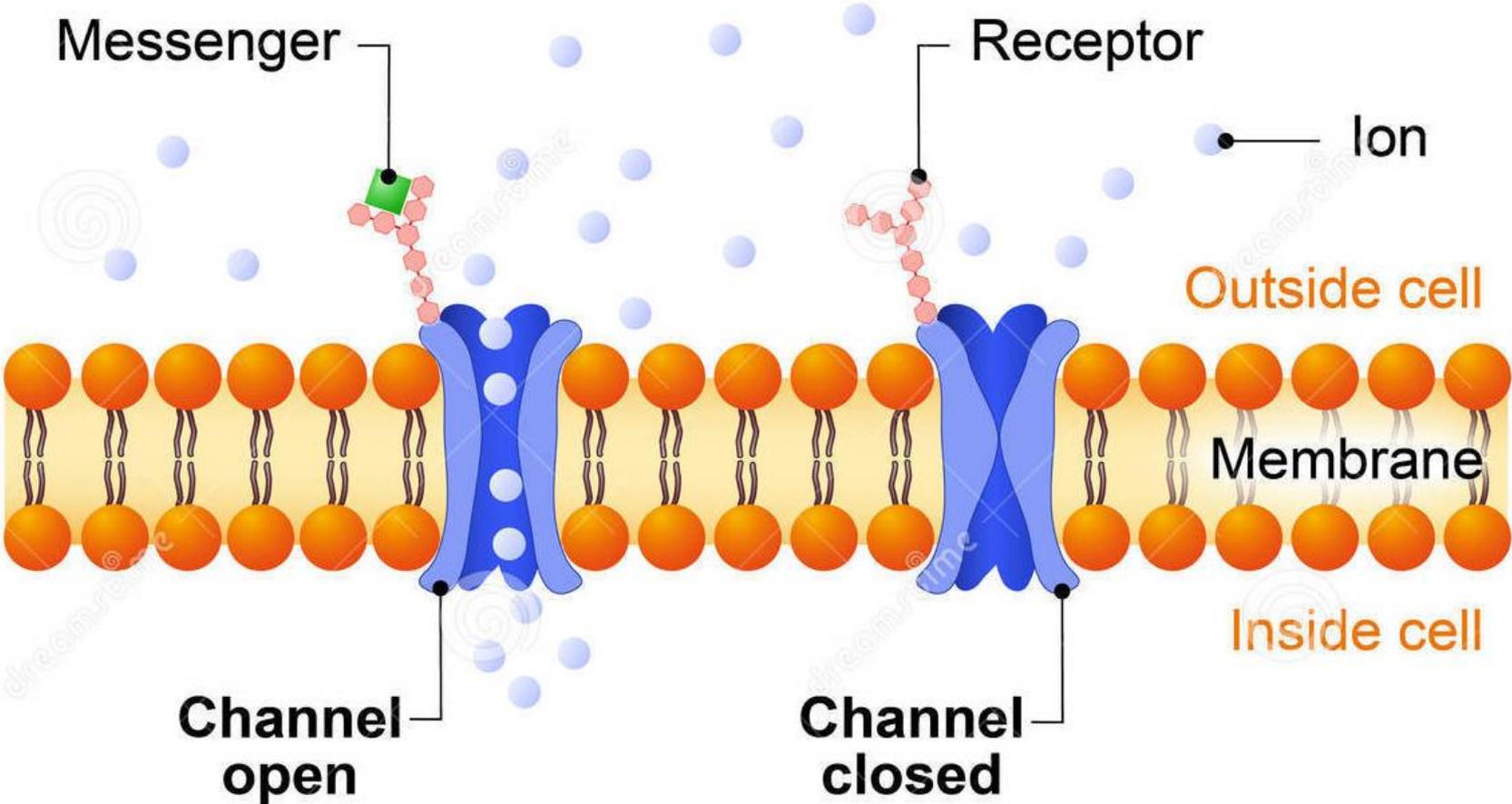
$\varnothing = 1 \text{ nm}$
 $[\text{K}^+] = 2 \text{ M}$



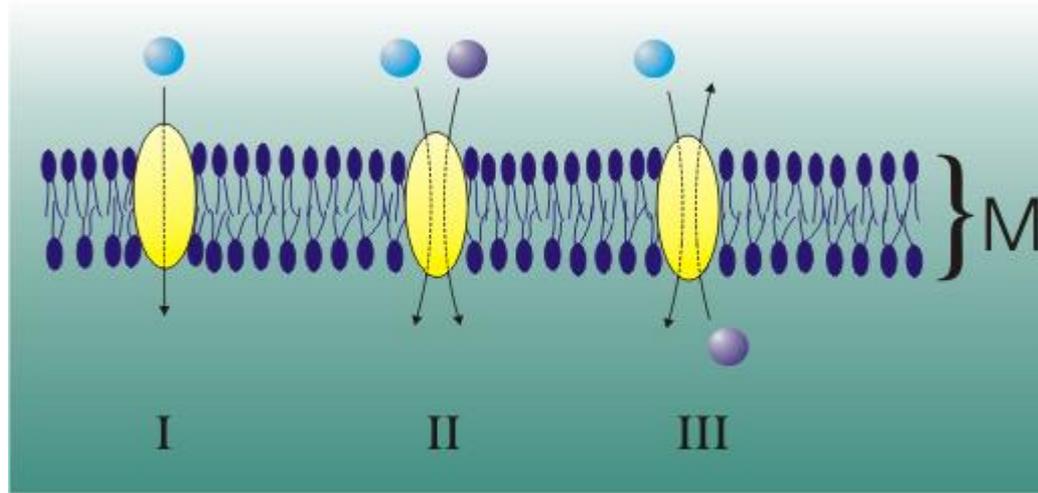
Canale del K^+ *potential gated*



Ligand-gated ion channel



Pompe ioniche (ATPasi)

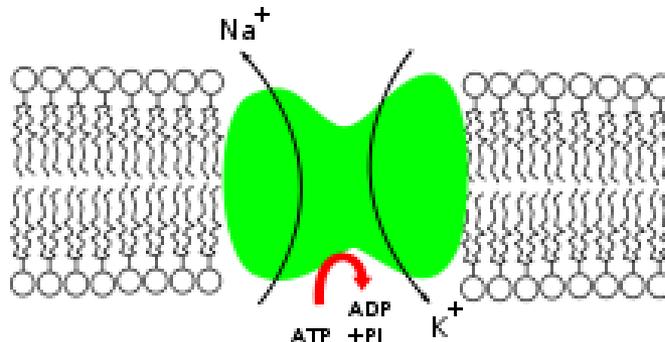


Uniporto

Simporto

Antiporto

Pompa ionica *antiporto* Na^+/K^+ -ATPasi

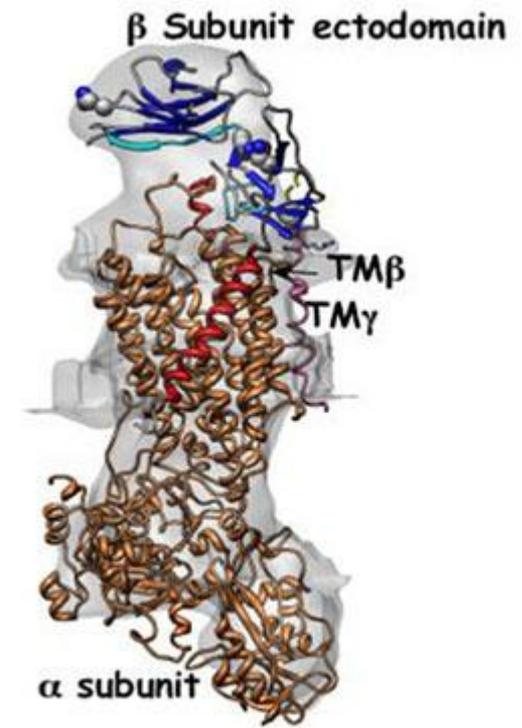
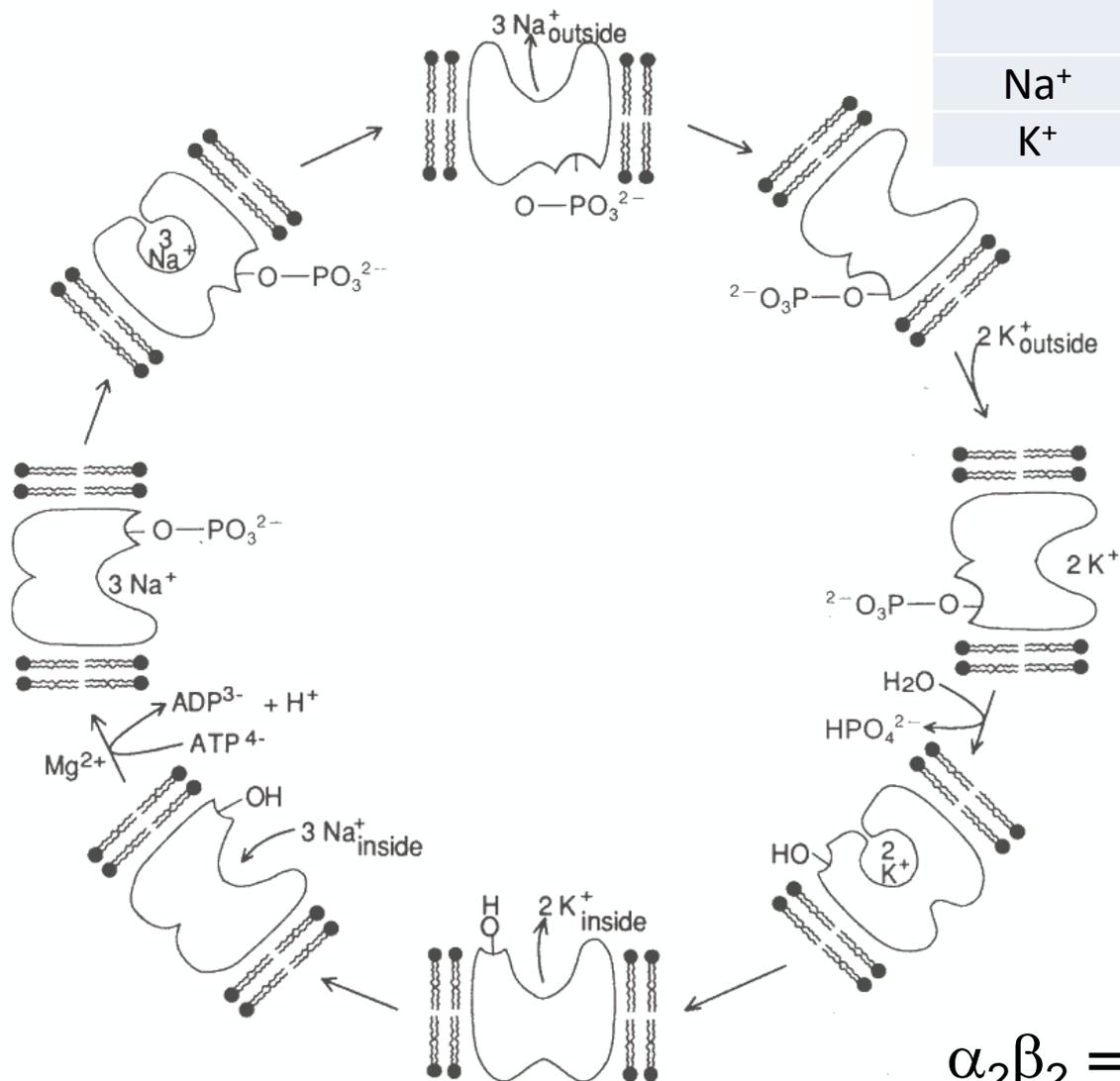


Ione	Intracellulare (mM)	Extracellulare (mM)
Na^+	10	150
K^+	100	5

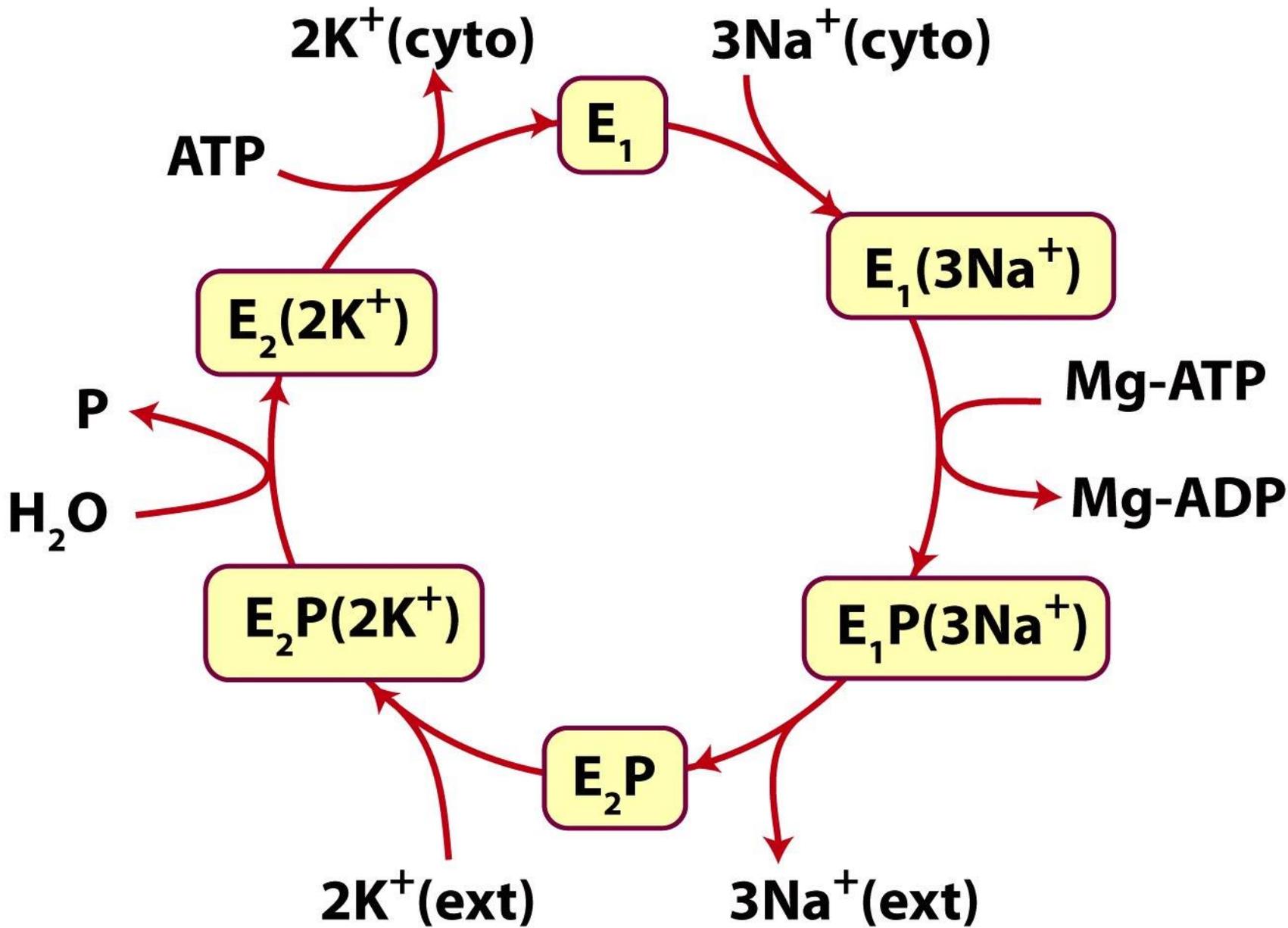
Pompa ionica *antiporto* Na⁺/K⁺-ATPasi



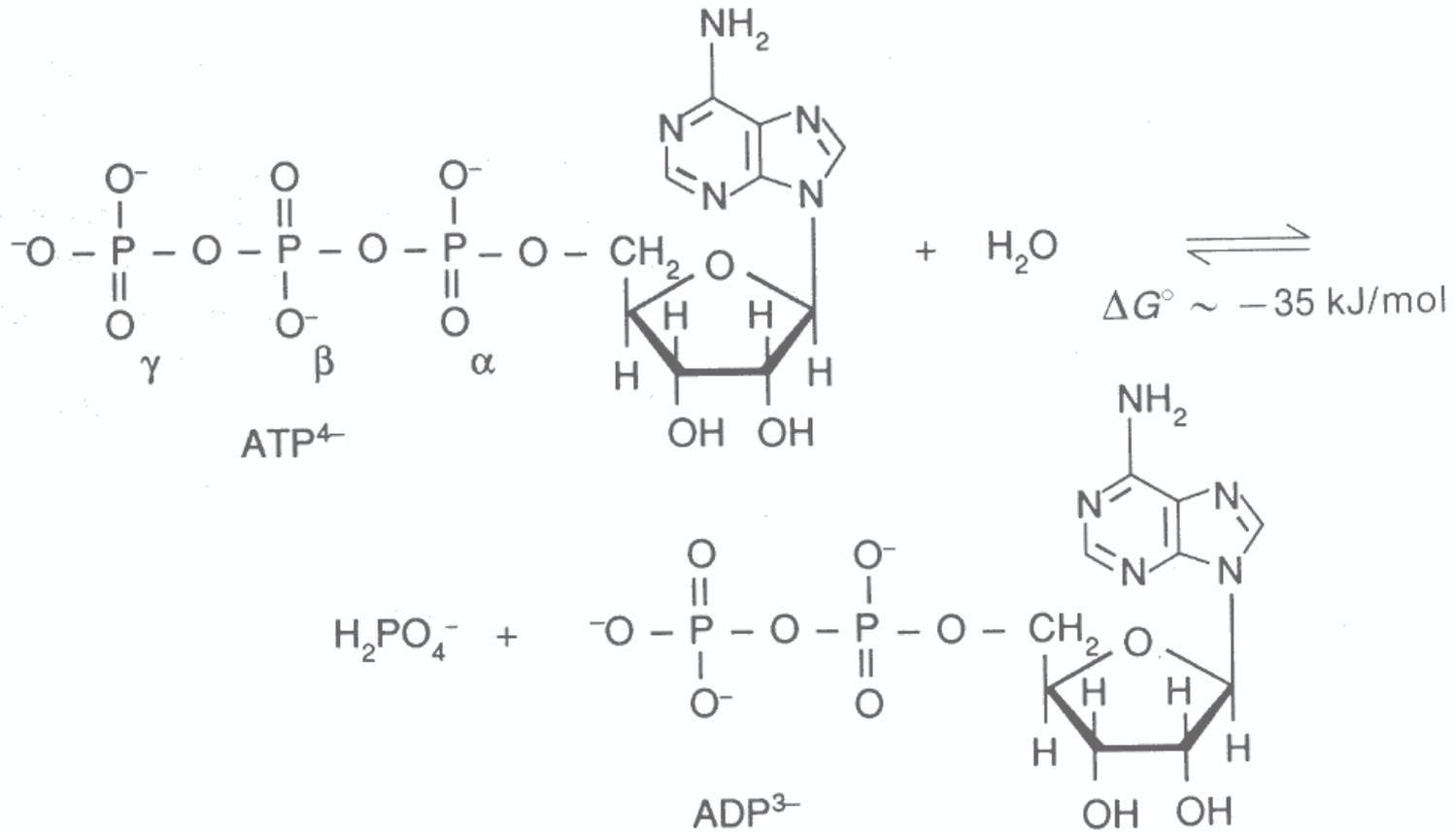
Ione	Intracellulare (mM)	Extracellulare (mM)
Na ⁺	10	150
K ⁺	100	5



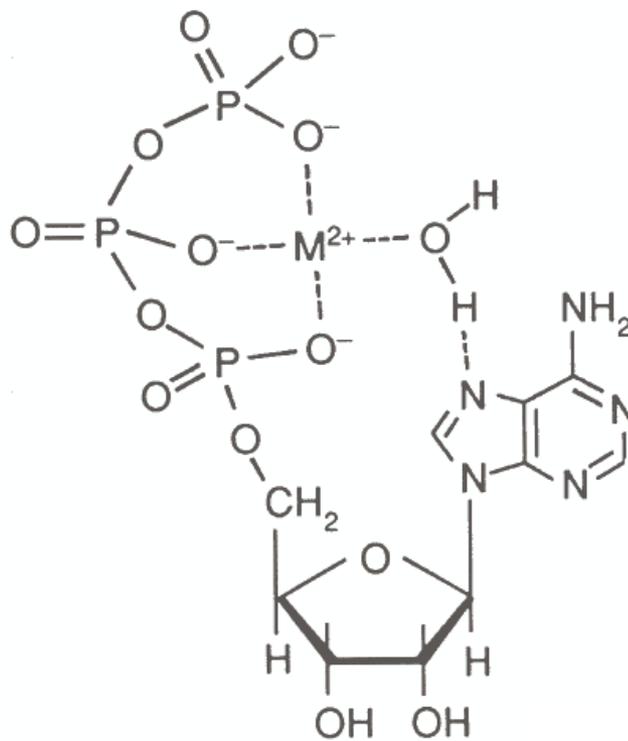
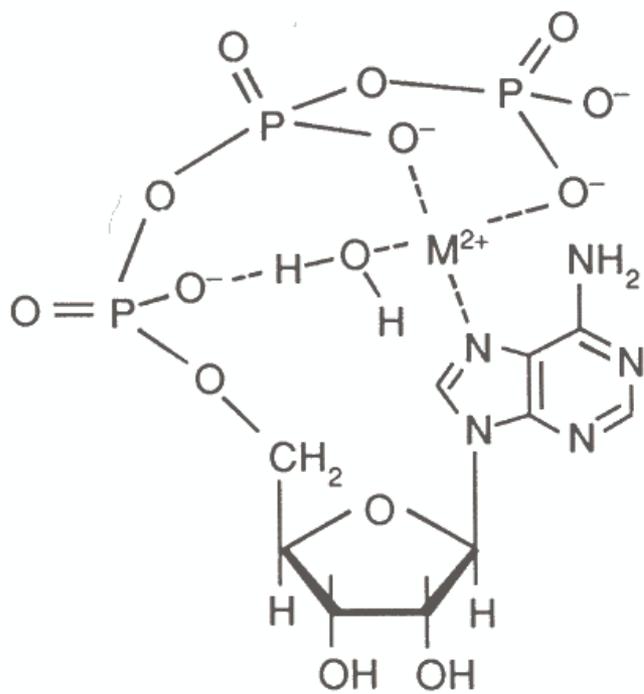
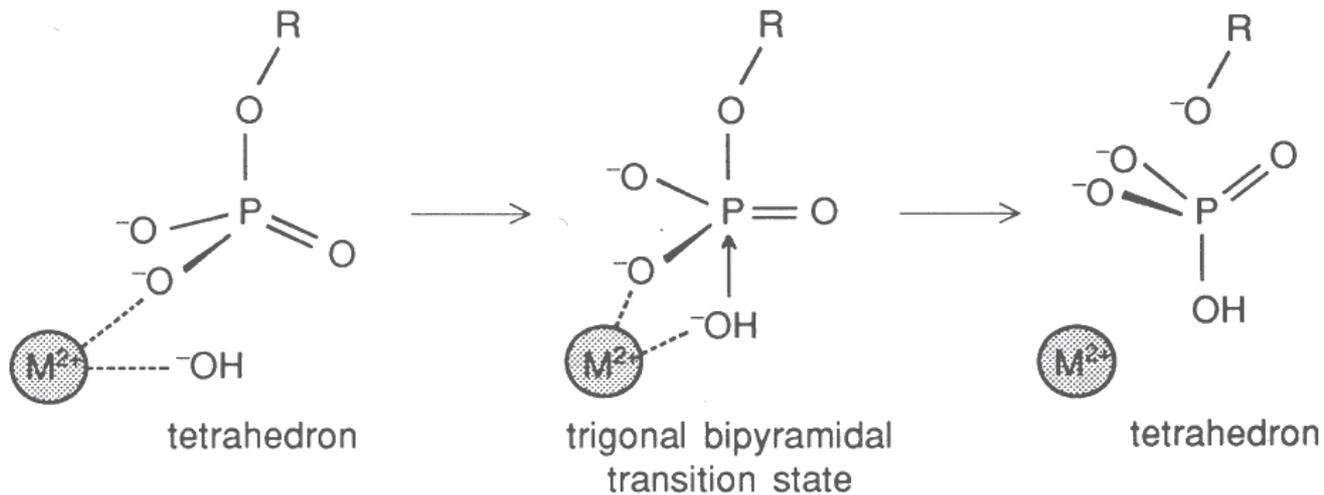
$$\alpha_2\beta_2 = 2 \times 112(\alpha) + 2 \times 35(\beta)$$

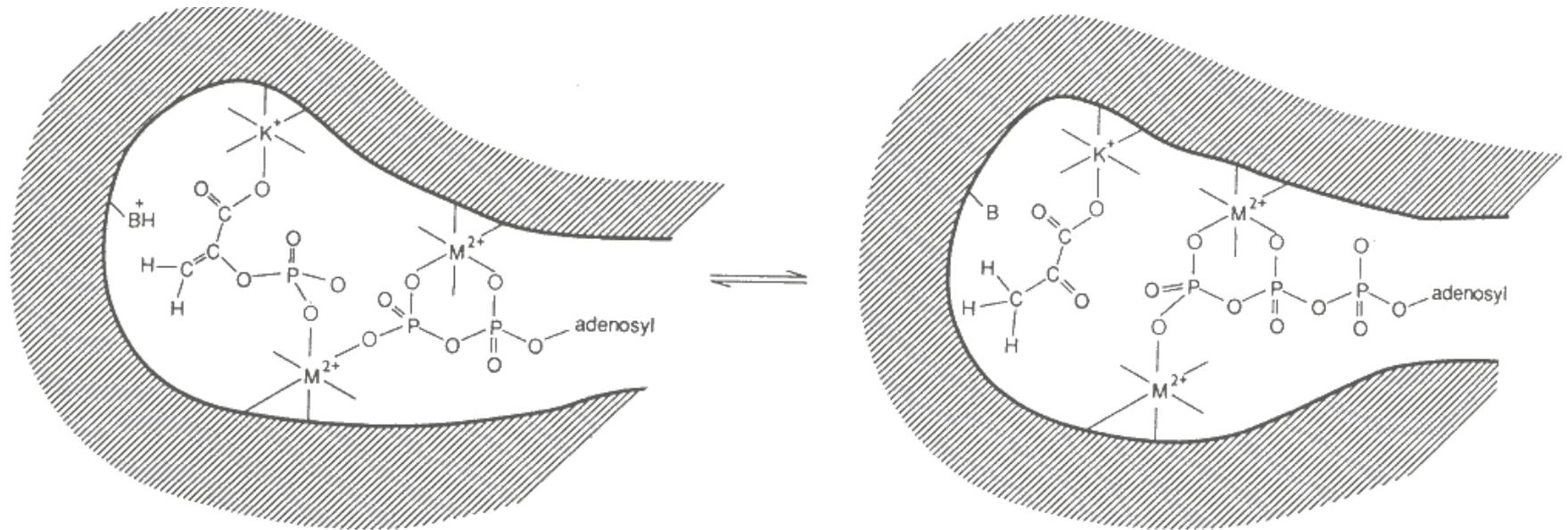
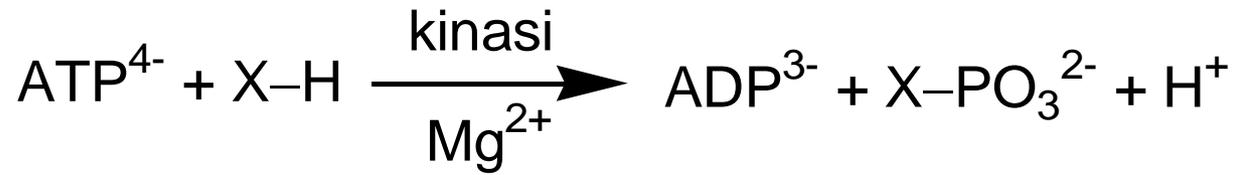


Magnesio



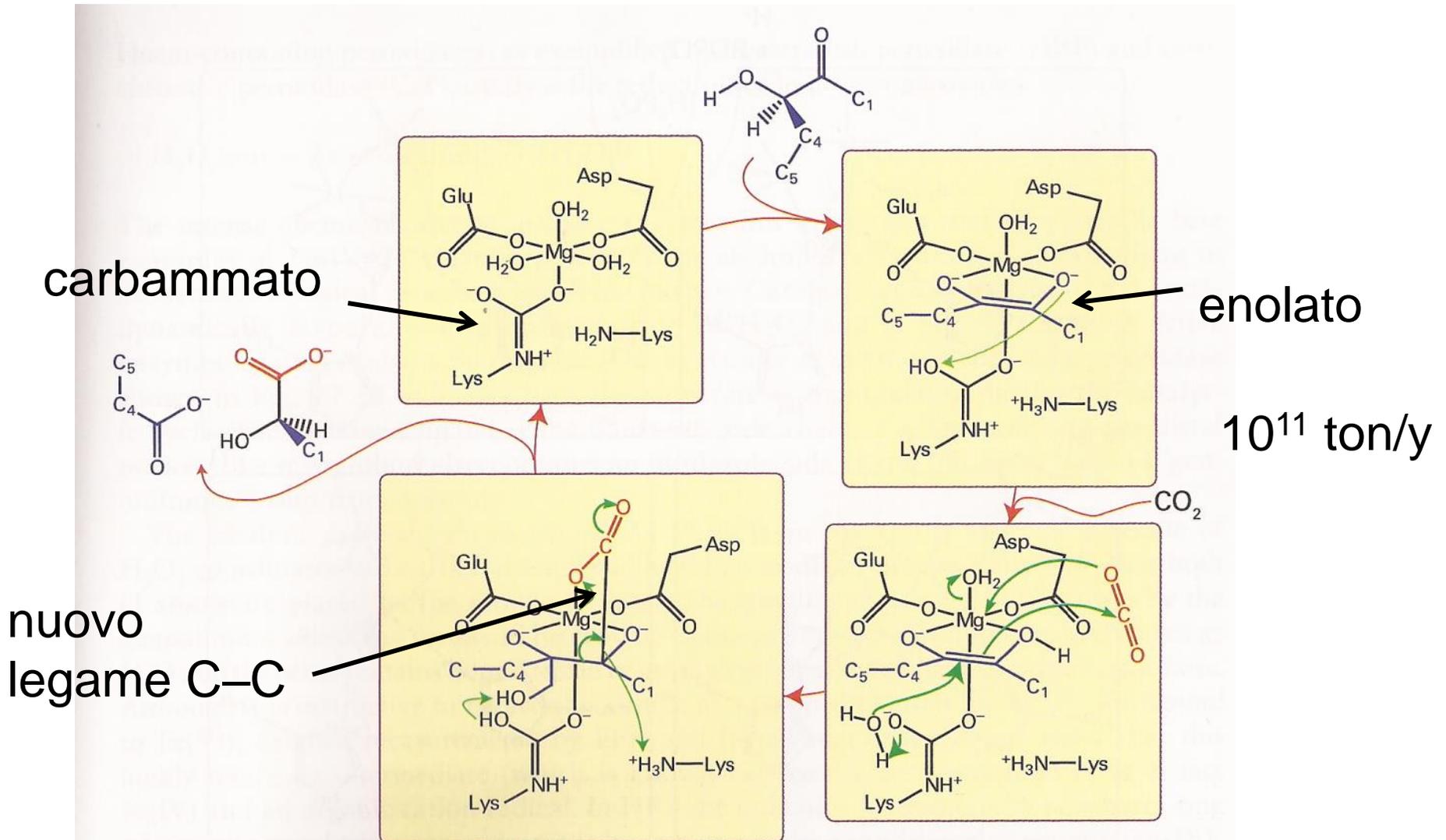
S_N2



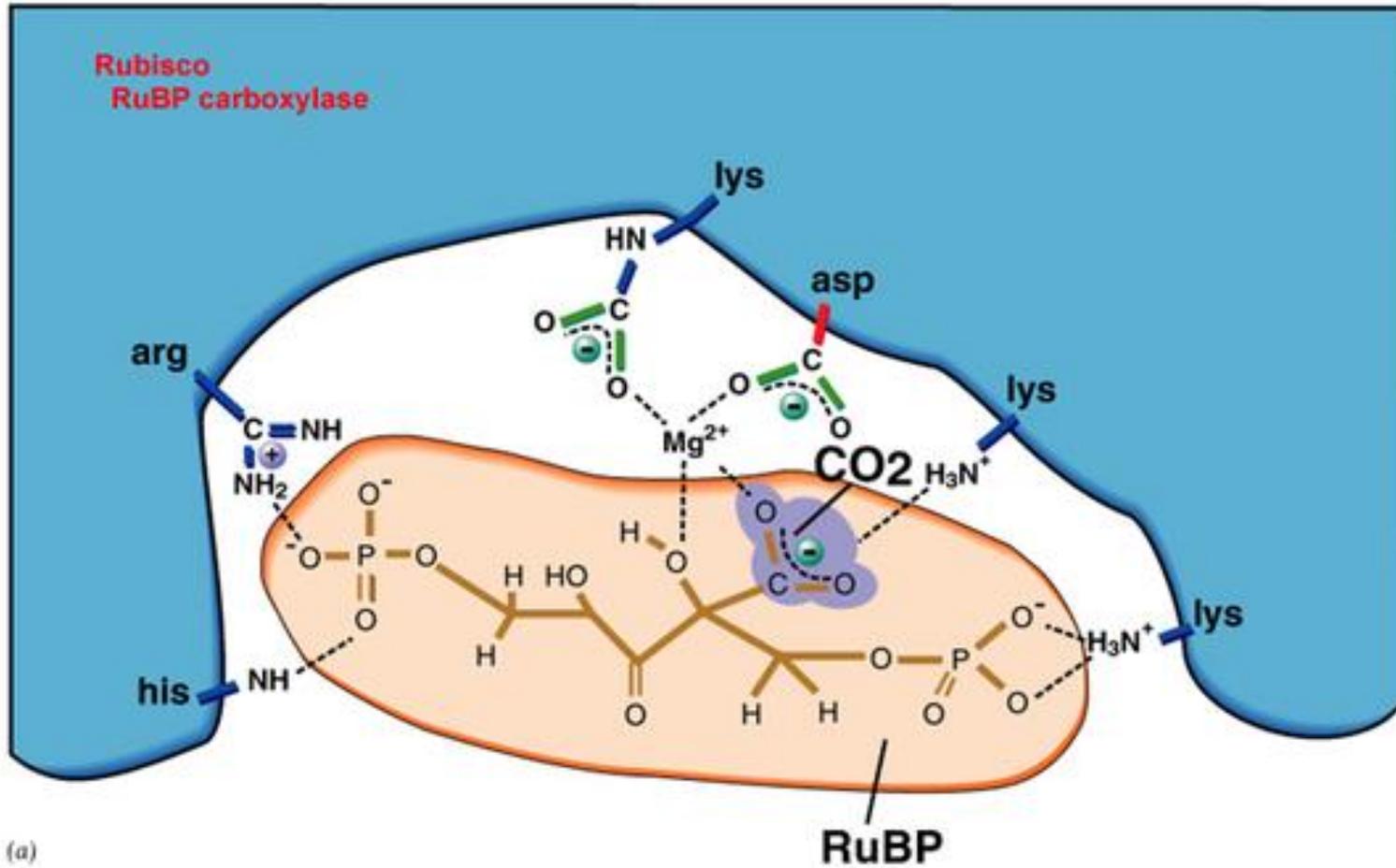


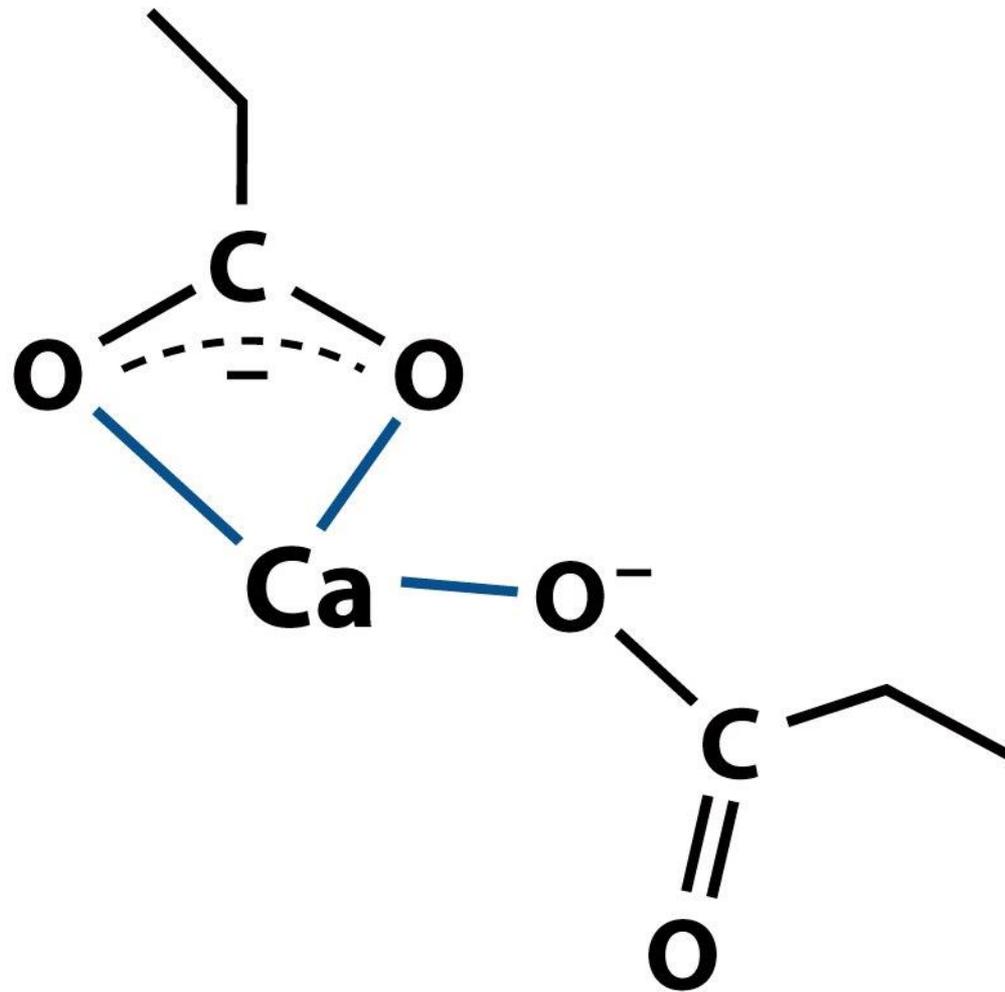
Piruvato-kinasi

Ribulosio bisfosfato carbossilasi '*rubisco*'



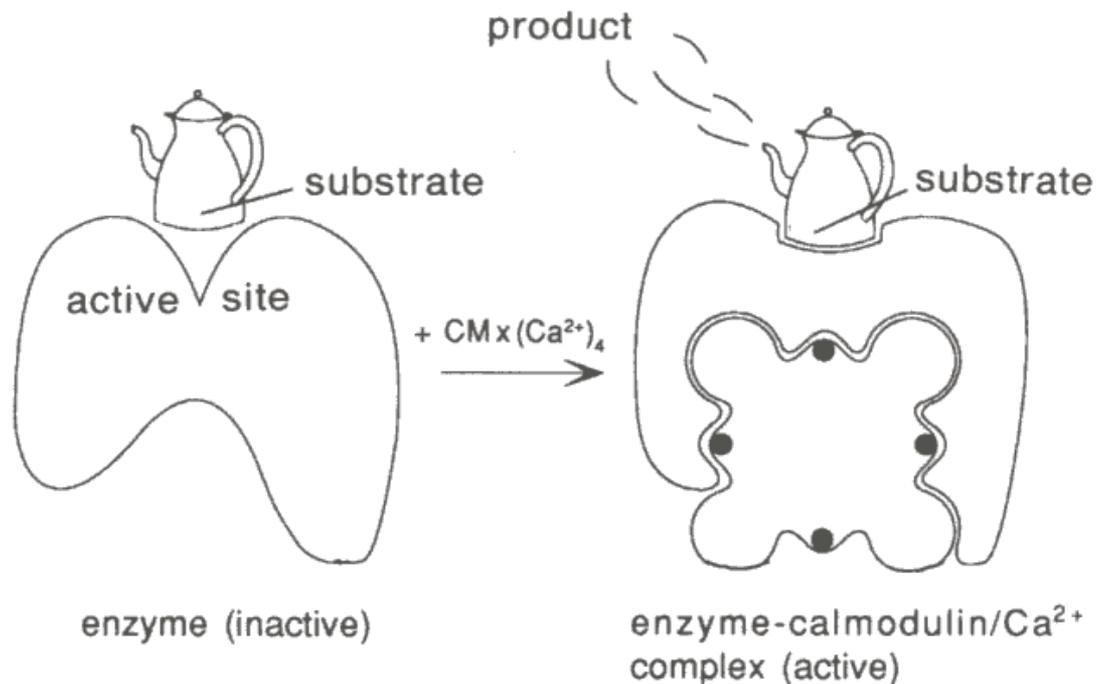
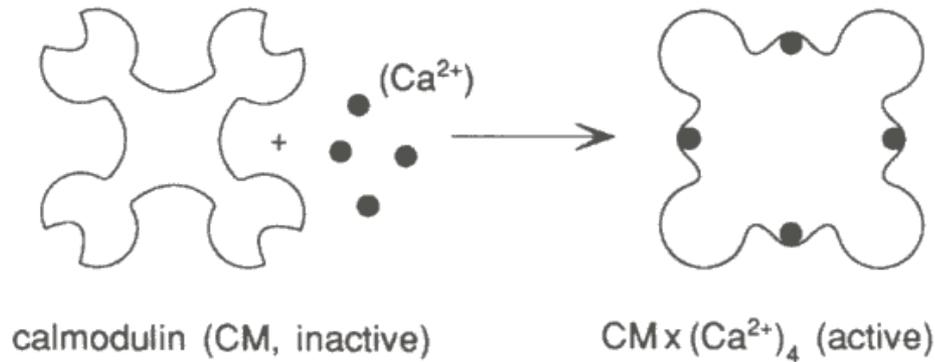
Rubisco





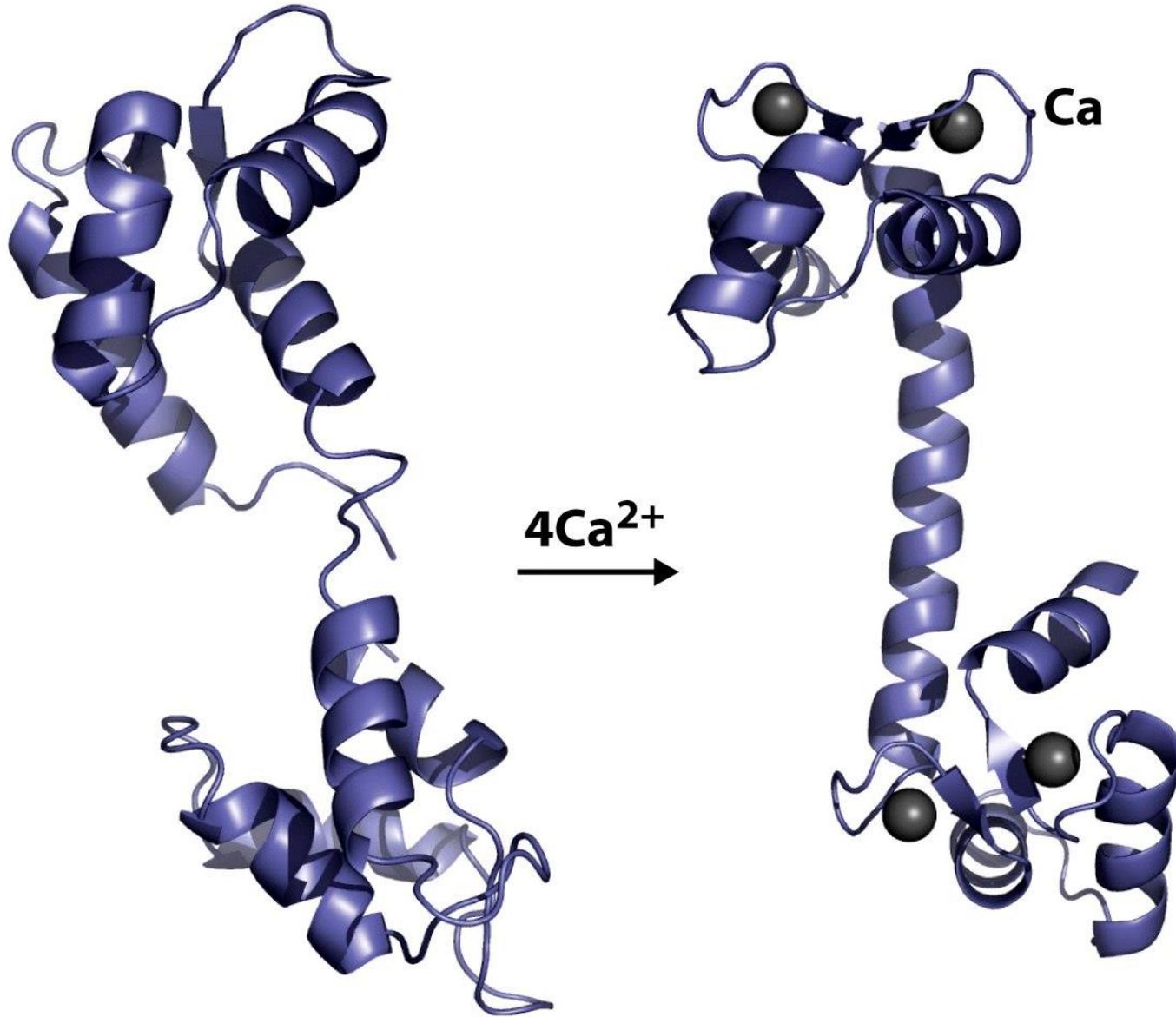
Ca^{2+} coordination

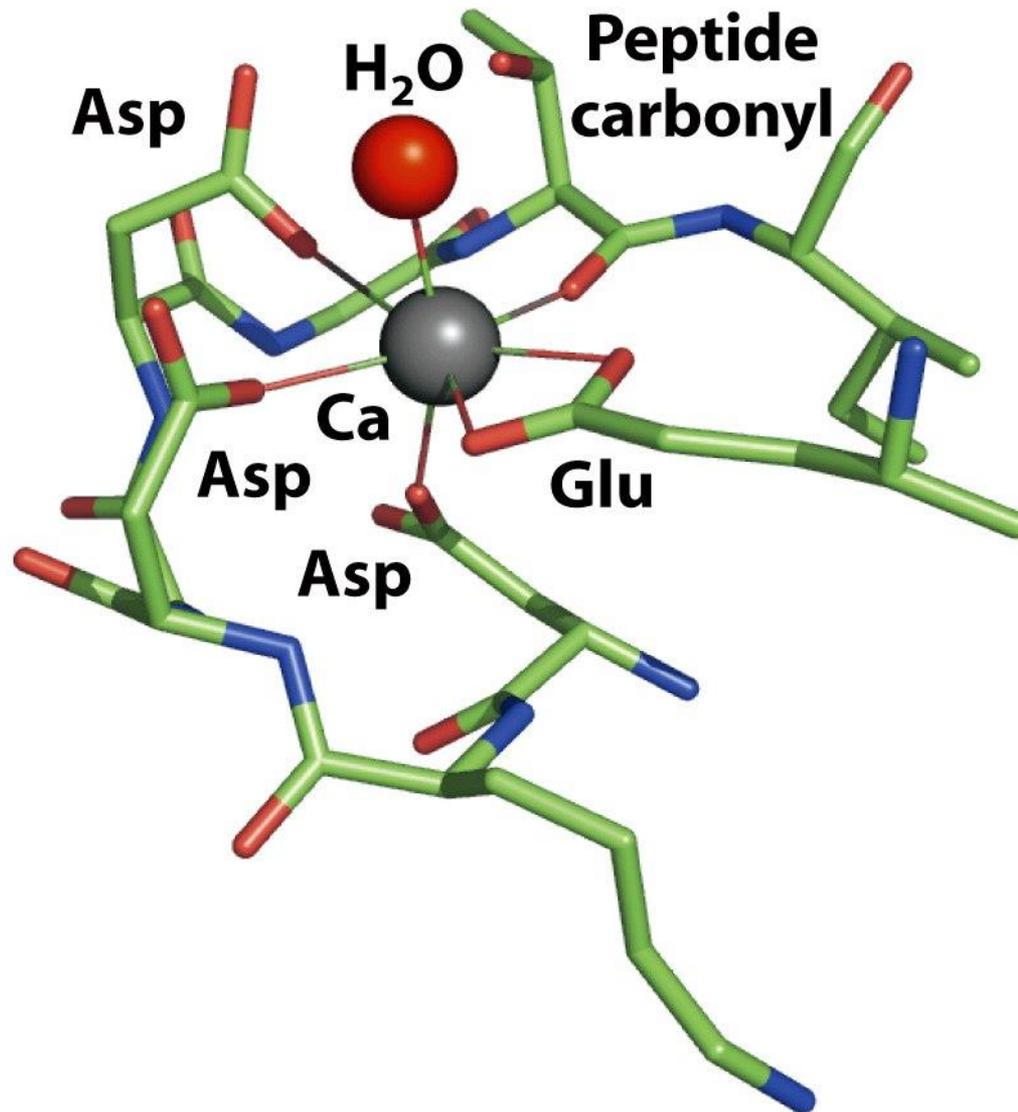
Ca²⁺: messaggero secondario



e.g.: NO sintasi (NO), adenilato e guanilato ciclasti (cAMP, cGMP), NAD kinasi (NADP)

CALMODULINA





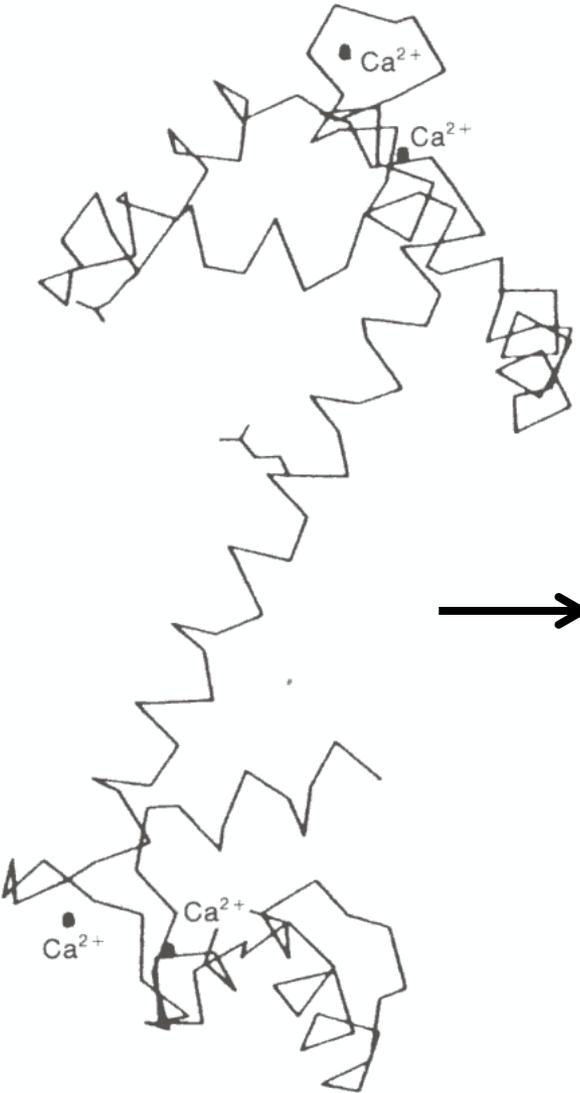
Uno dei siti di coordinazione del Ca^{2+} della apo-calmodulina

TROPONINA-C

Siti di binding ad affinità minore



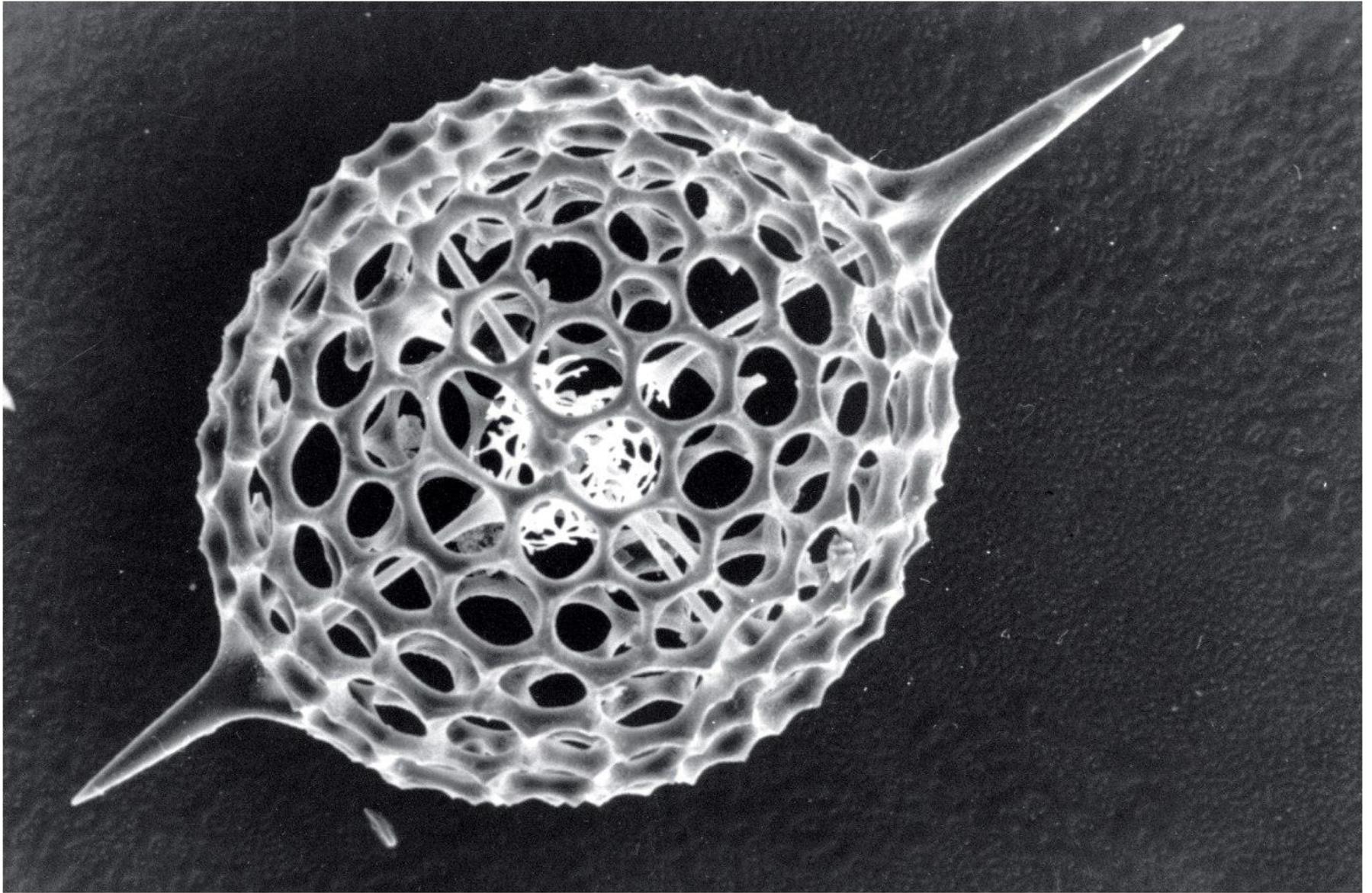
Siti di binding ad elevata affinità ($K > 10^6$)



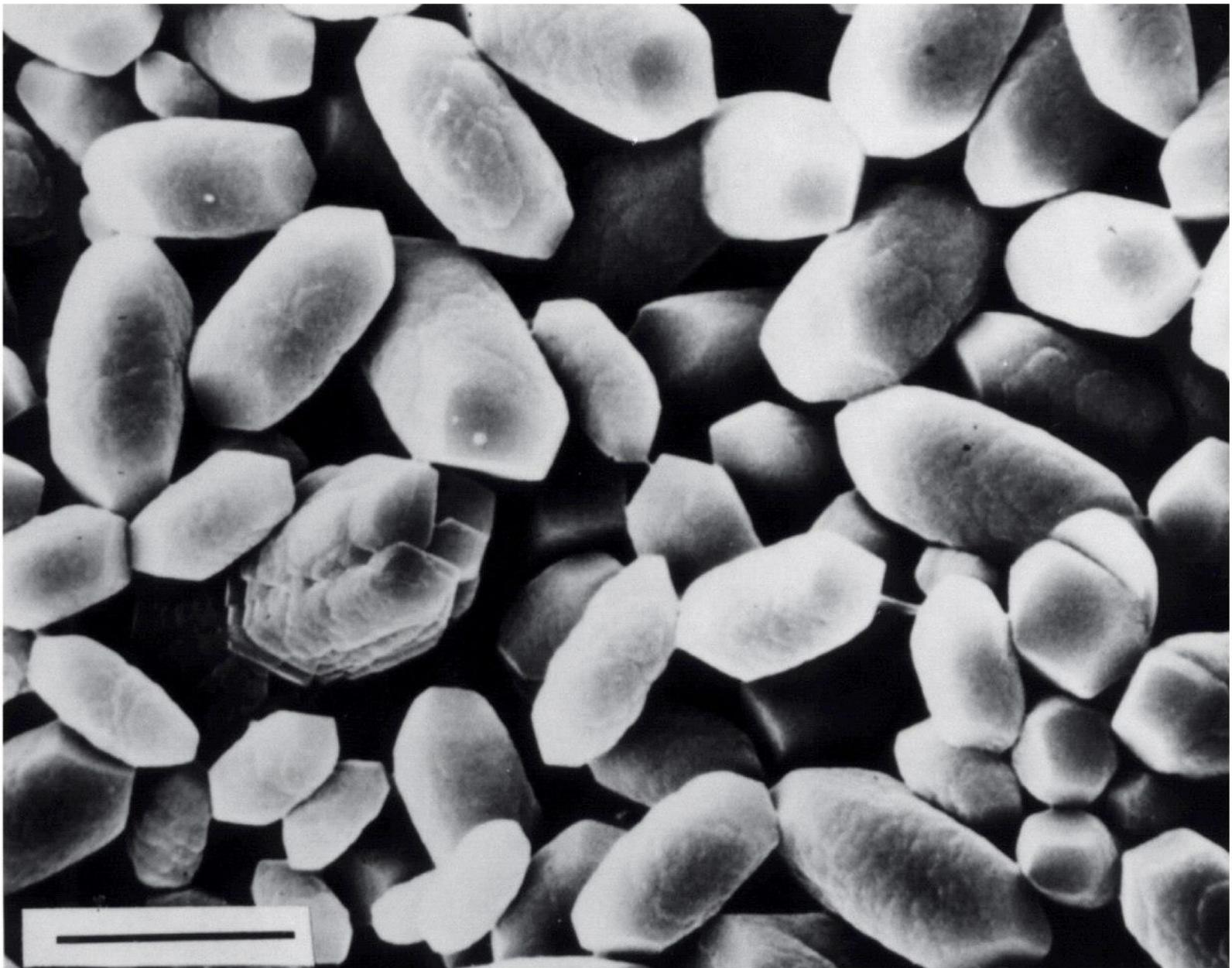
actina
miosina

I principali biominerali di elementi alcalino-terrosi

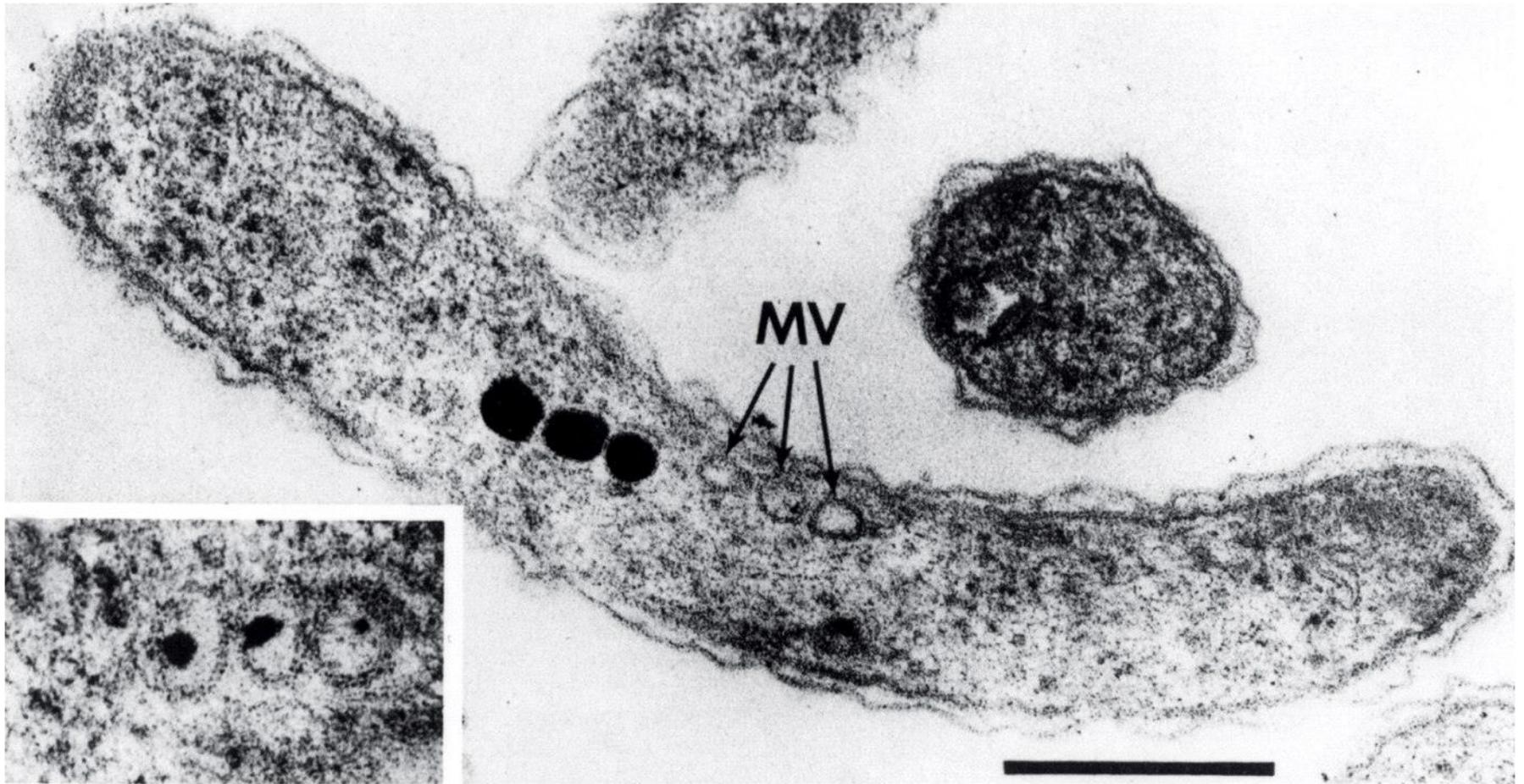
Composto	Minerale	Presenza negli organismi viventi
MgCO_3	Magnesite	Scheletro del corallo
CaCO_3	Aragonite	Conchiglie e perle
CaCO_3	Calcite	Uova di uccello, sistemi gravitazionali nell'orecchio interno
$\text{CaCO}_3 \cdot n\text{H}_2\text{O}$	Amorfo	Immagazzinamento di calcio nelle piante
$\text{Ca}(\text{C}_2\text{O}_4) \cdot n\text{H}_2\text{O}$	Whewellite (n = 1) Weddellite (n = 2)	Immagazzinamento di calcio nelle piante, calcoli renali
$3\text{Ca}_3(\text{PO}_4)_2 \cdot \text{Ca}(\text{OH})_2$	Idrossiapatite	Ossa e denti nei vertebrati
$\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$	Gesso	Sistema gravitazionale nelle meduse
SrSO_4	Celestite	Esoscheletro di certo plankton
BaSO_4	Barite	Sistema gravitazionale nelle alghe



Microscheletro siliceo di una radiolaria



Cristalli di calcite nell'orecchio interno: sensori gravitazionali



Cristalli di magnetite in archeobatteri magnetotattici

Table 26.1 The approximate concentrations (mol dm⁻³), where known, of elements (apart from C, H, O, N, P, S, Se, Br, I, B, Si and W) in different biological zones

Element	External fluids (sea water)	Free ions in external fluids (blood plasma)	Cytoplasm (free ions)	Comments on status in cell
Na	$> 10^{-1}$	10^{-1}	$< 10^{-2}$	Not bound
K	10^{-2}	4×10^{-3}	$\leq 3 \times 10^{-1}$	Not bound
Mg	$> 10^{-2}$	10^{-3}	$\approx 10^{-3}$	Weakly bound as ATP complex
Ca	$> 10^{-3}$	10^{-3}	$\approx 10^{-7}$	Concentrated in some vesicles
Cl	10^{-1}	10^{-1}	10^{-2}	Not bound
Fe	10^{-17} (Fe(III))	10^{-16} (Fe(III))	$< 10^{-7}$ (Fe(II))	Too much unbound Fe is toxic (Fenton chemistry) in and out of cells
Zn	$< 10^{-8}$	10^{-9}	$< 10^{-11}$	Totally bound, but may be exchangeable
Cu	$< 10^{-10}$ (Cu(II))	10^{-12}	$< 10^{-15}$ (Cu(I))	Totally bound, not mobile. Mostly outside cytoplasm
Mn	10^{-9}		$\approx 10^{-6}$	Higher in chloroplasts and vesicles
Co	10^{-11}		$< 10^{-9}$	Totally bound (cobalamin)
Ni	10^{-9}		$< 10^{-10}$	Totally bound
Mo	10^{-7}		$< 10^{-7}$	Mostly bound