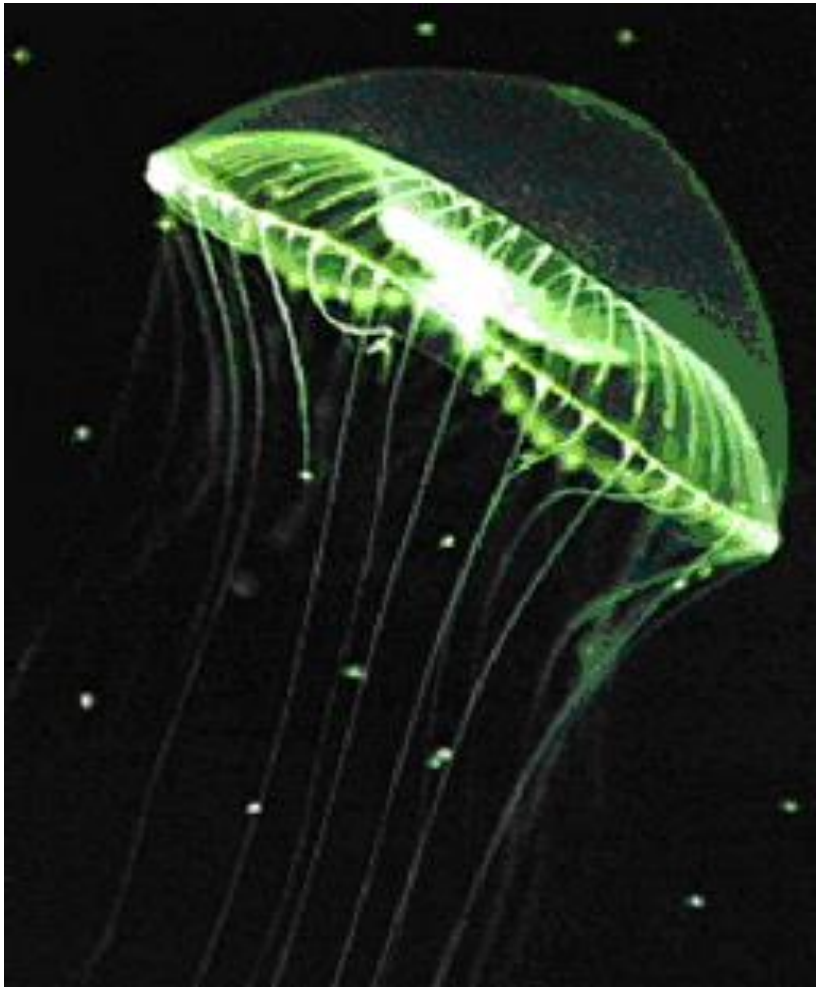
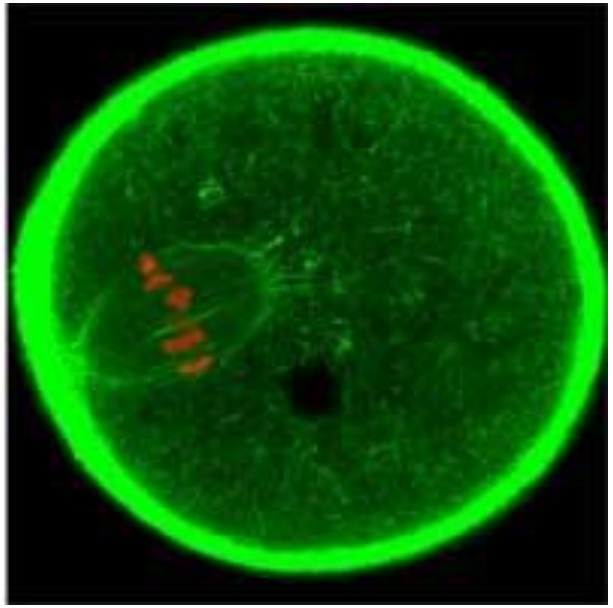
Ion	Radius (Å)	Ion	Radius (Å)
Na^+	1.02	Mg^{2+}	0.72
K^+	1.38	Ca^{2+}	1.00

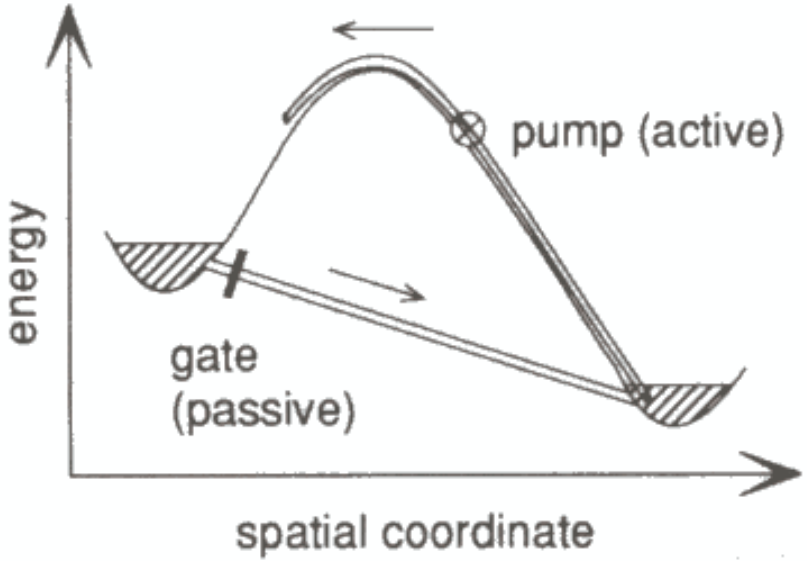


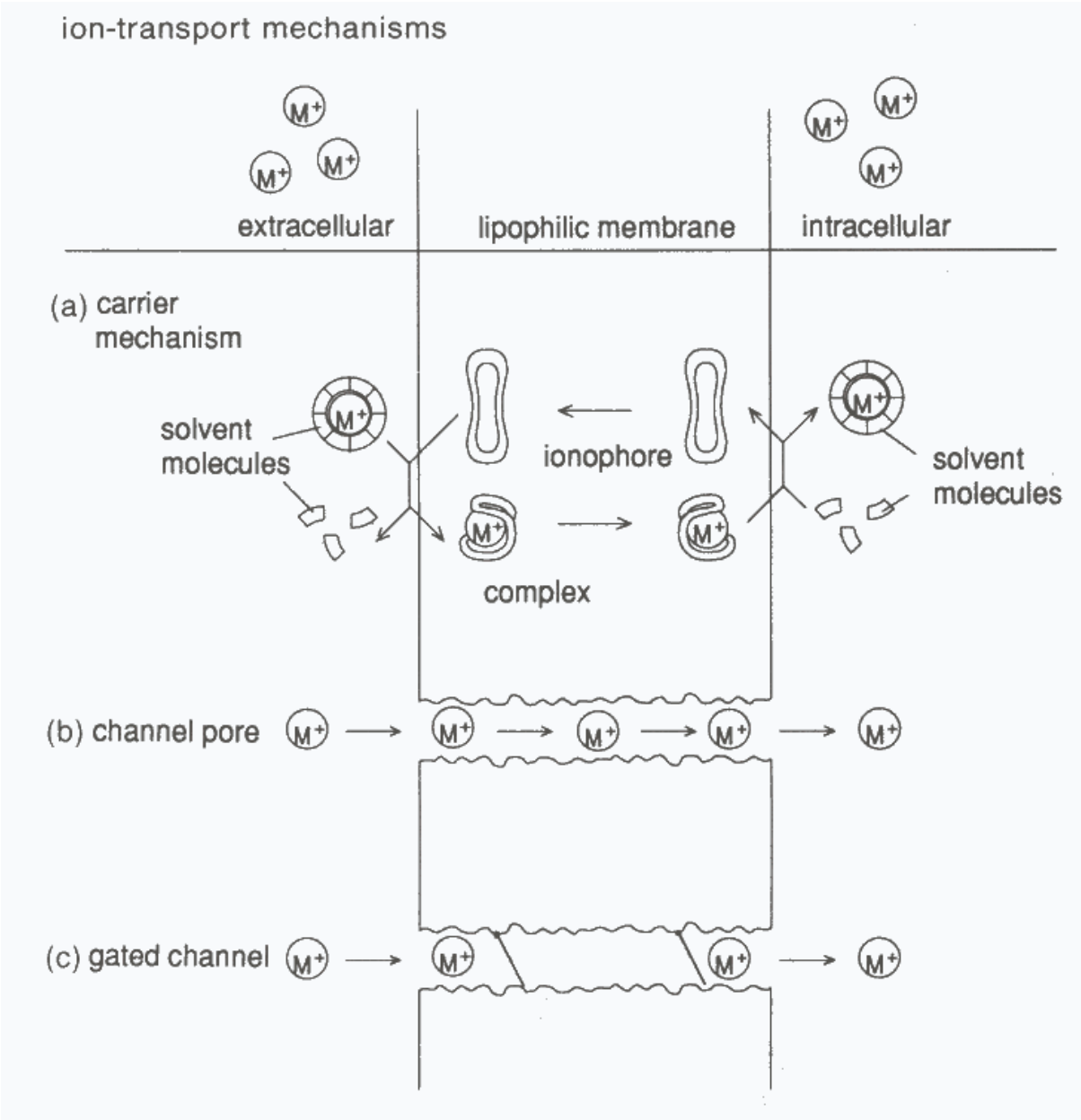
Green Fluoerescent Protein (GFP) = fluorescent sensor for Ca^{2+}



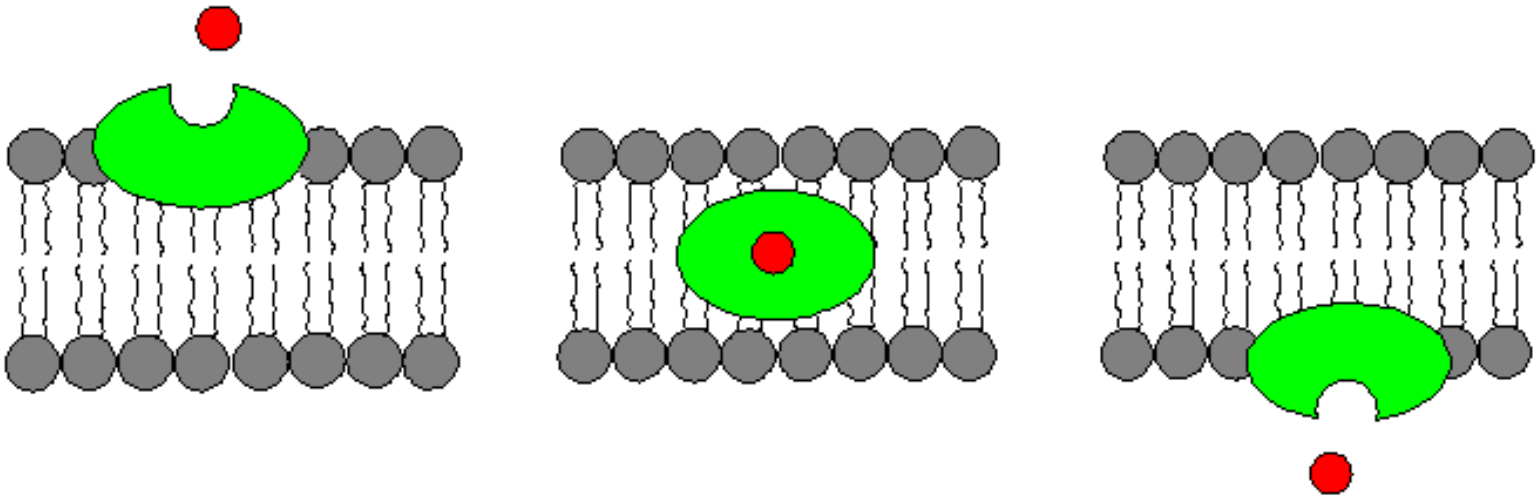
Ion	Intracellular (mM)	Extracellular (mM)
Na^+	10	150
K^+	100	5
Mg^{2+}	2.5	1.5
Ca^{2+}	0.1[a]	2.5
Cl^-	4	100

[a]0.1 μM inside the cytoplasm of resting cell, i.e. 10^4 times less than outside

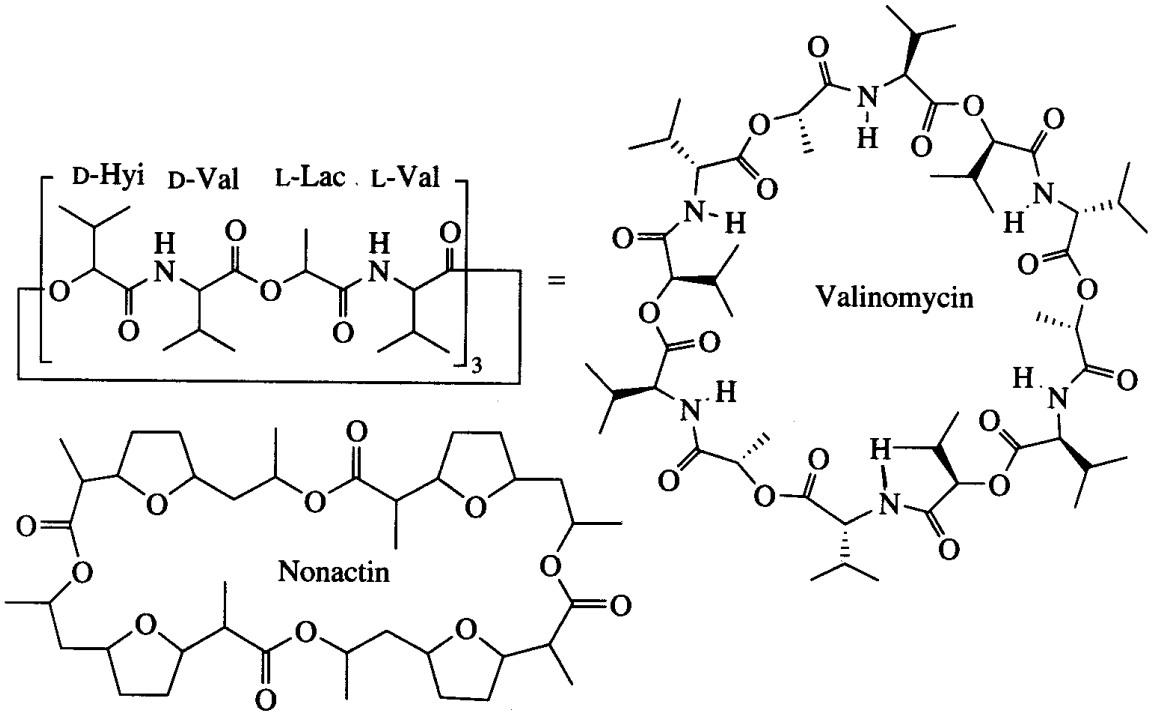


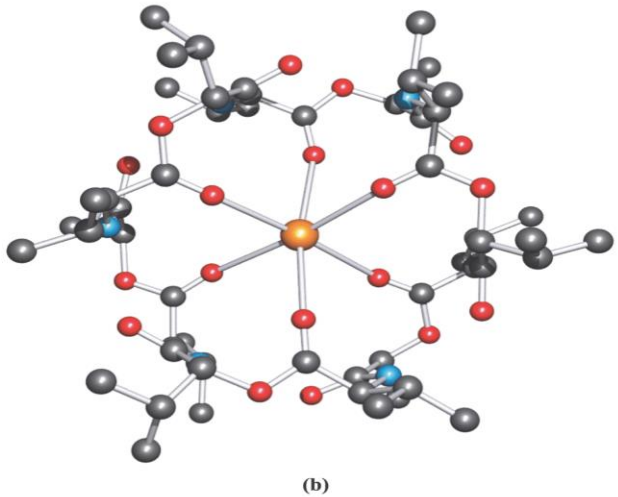

ion-transport mechanisms
M+
extracellular
lipophilic membrane
intracellular
(a) carrier mechanism
solvent molecules
ionophore
solvent molecules
complex
(b) channel pore
(c) gated channel

Ionophores

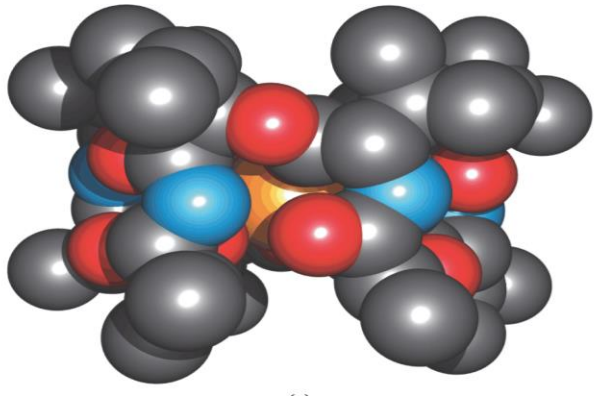


Ionophores



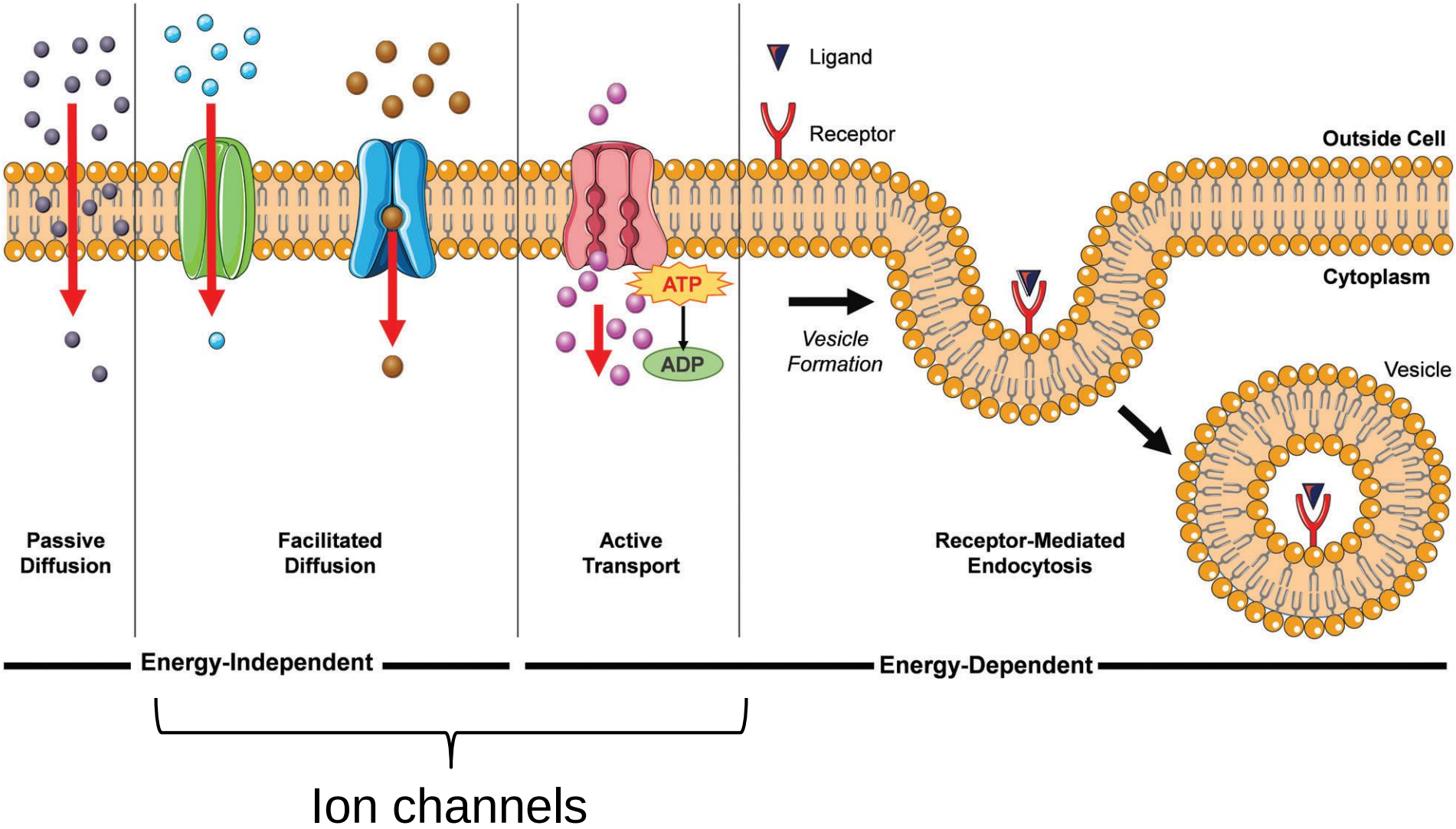


Valinomycin adduct with K^+



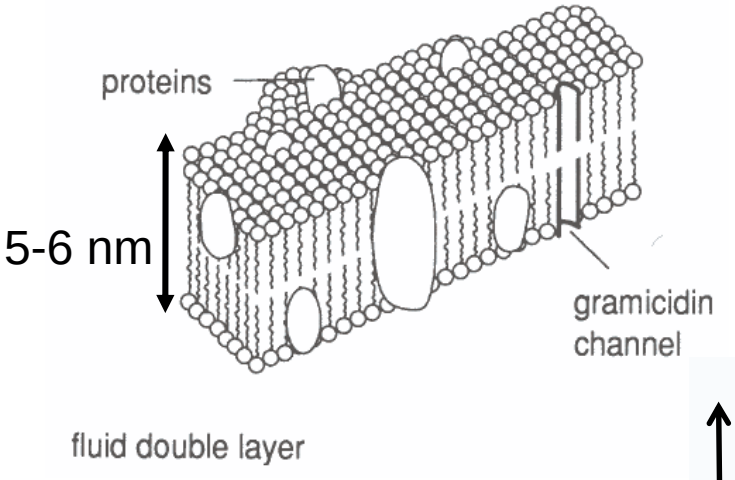
Valinomycin transports through the mitochondrial membrane 10^3 – 10^4 K^+ ions per second without affecting the concentration of Na^+ ions.
The K^+/Na^+ selectivity is ca. 10^4.

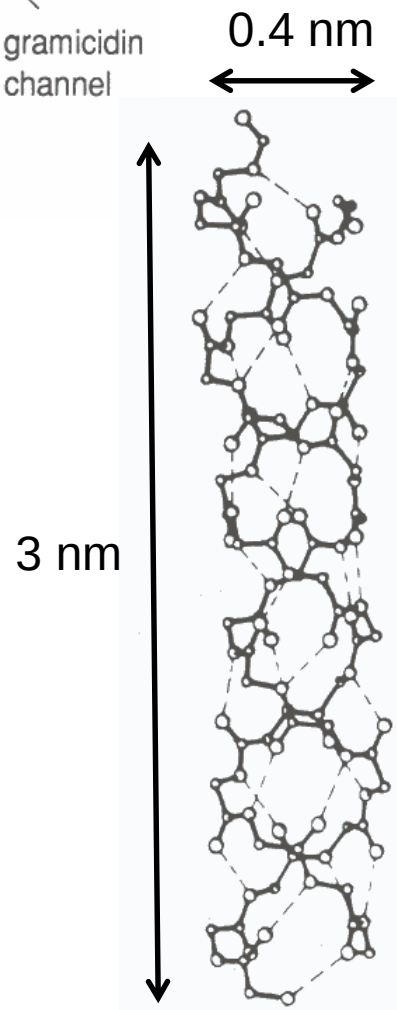
trans-membrane transport mechanisms



Ion channels

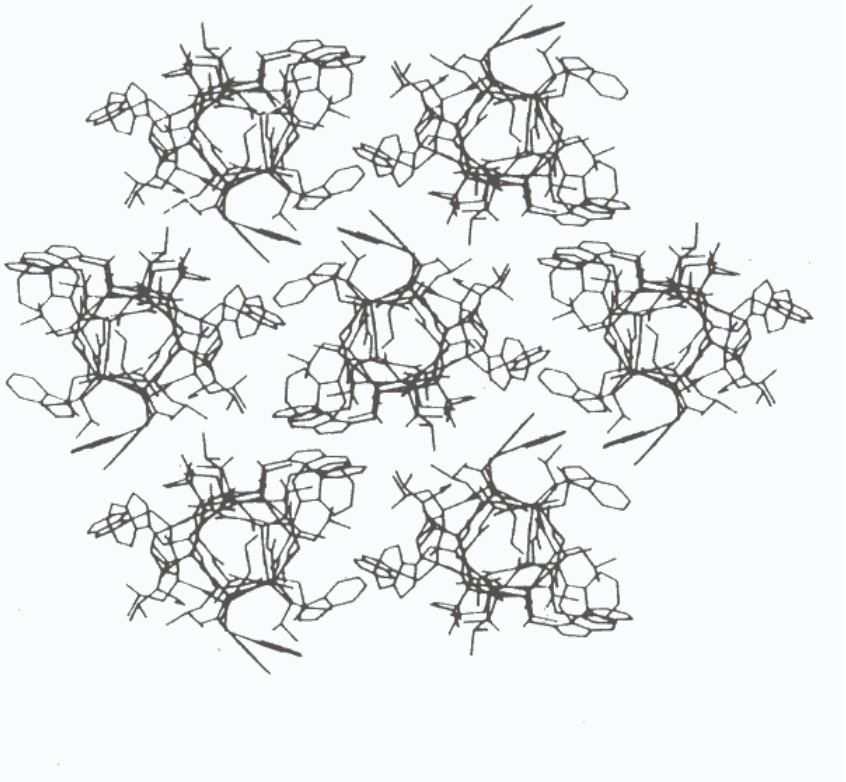
Ion channels



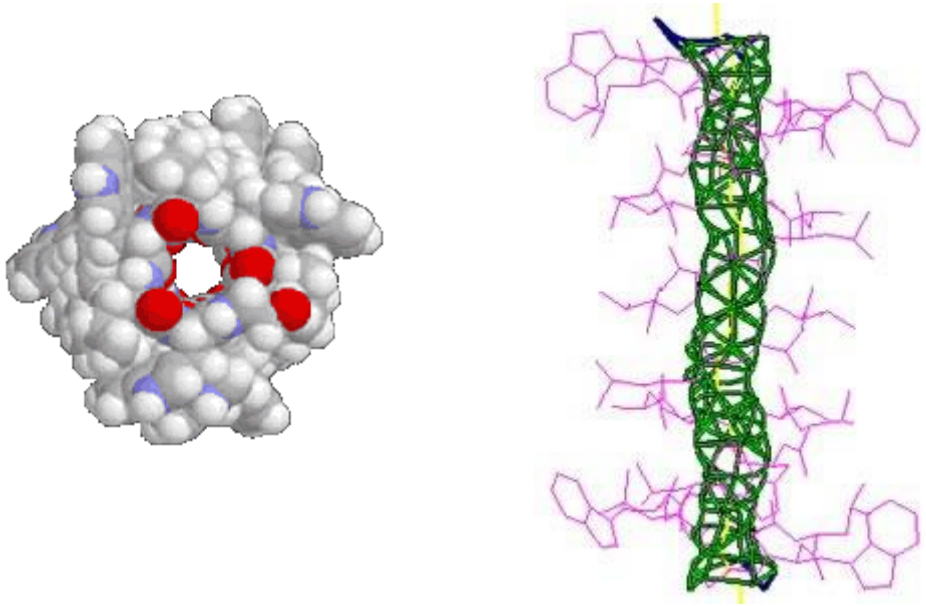


Gramicidin A

15 aminoacids

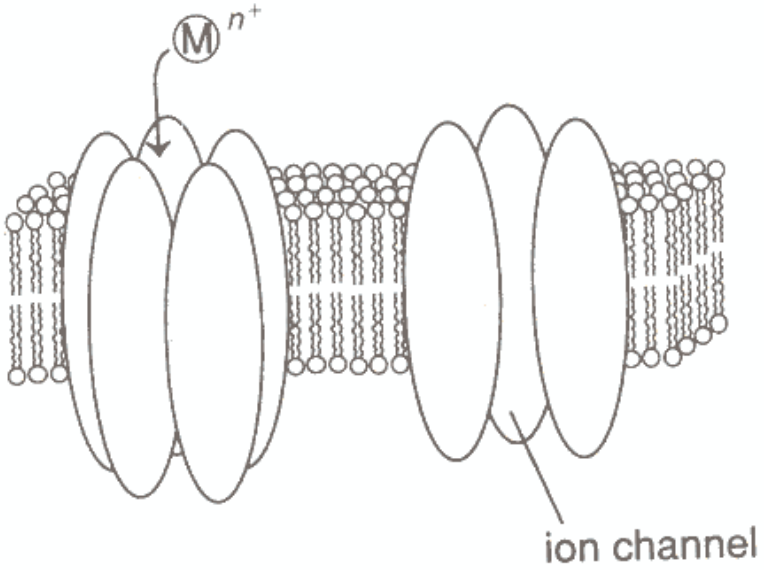


Gramicidin A

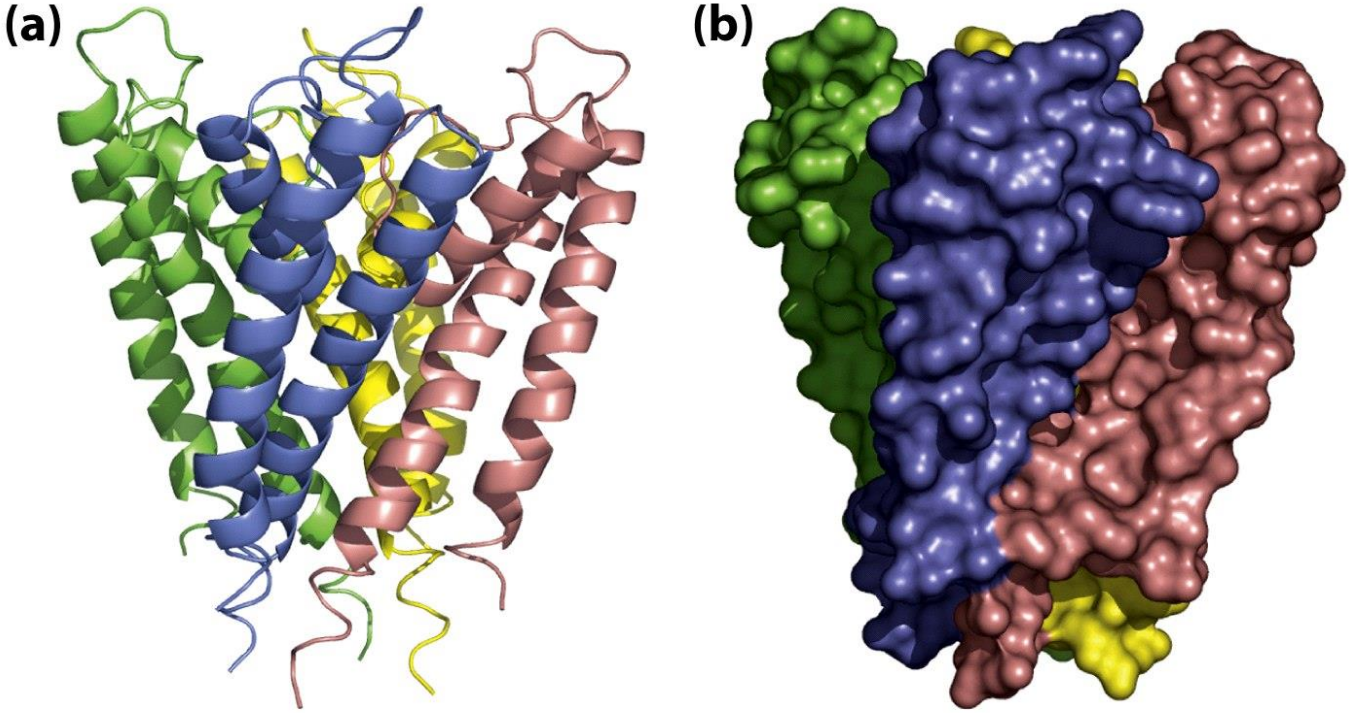


Gramicidin A transports through the cell membrane 10^7 K^+ or Na^+ ions per second. The divalent cations block the pore.

trans-membrane proteins

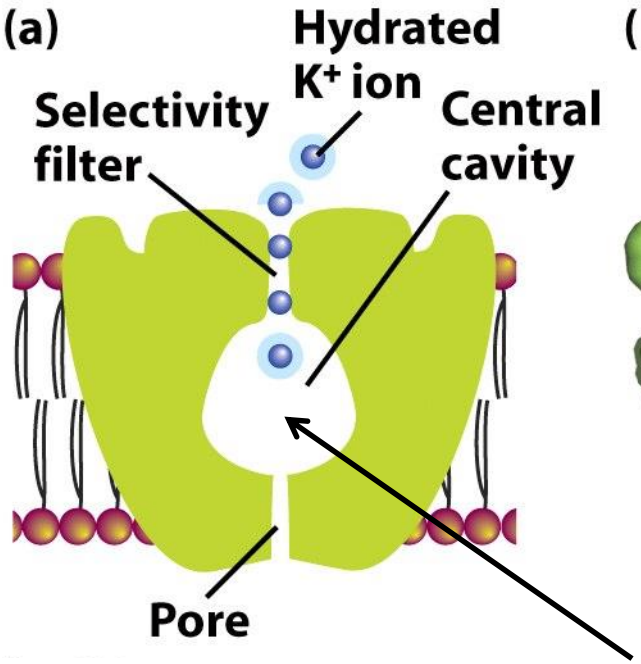


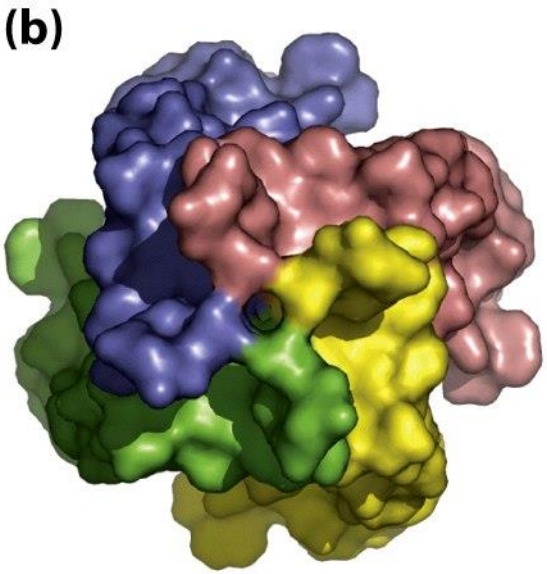
K^+ Channel

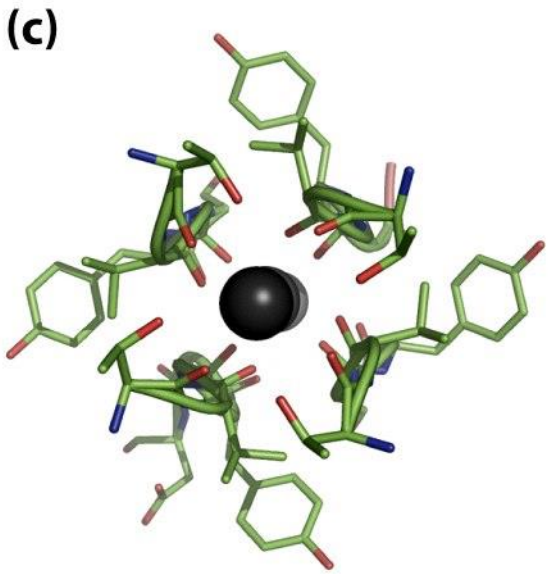


potential gated K^+ channel

Out $[K^+] = 5$ mM



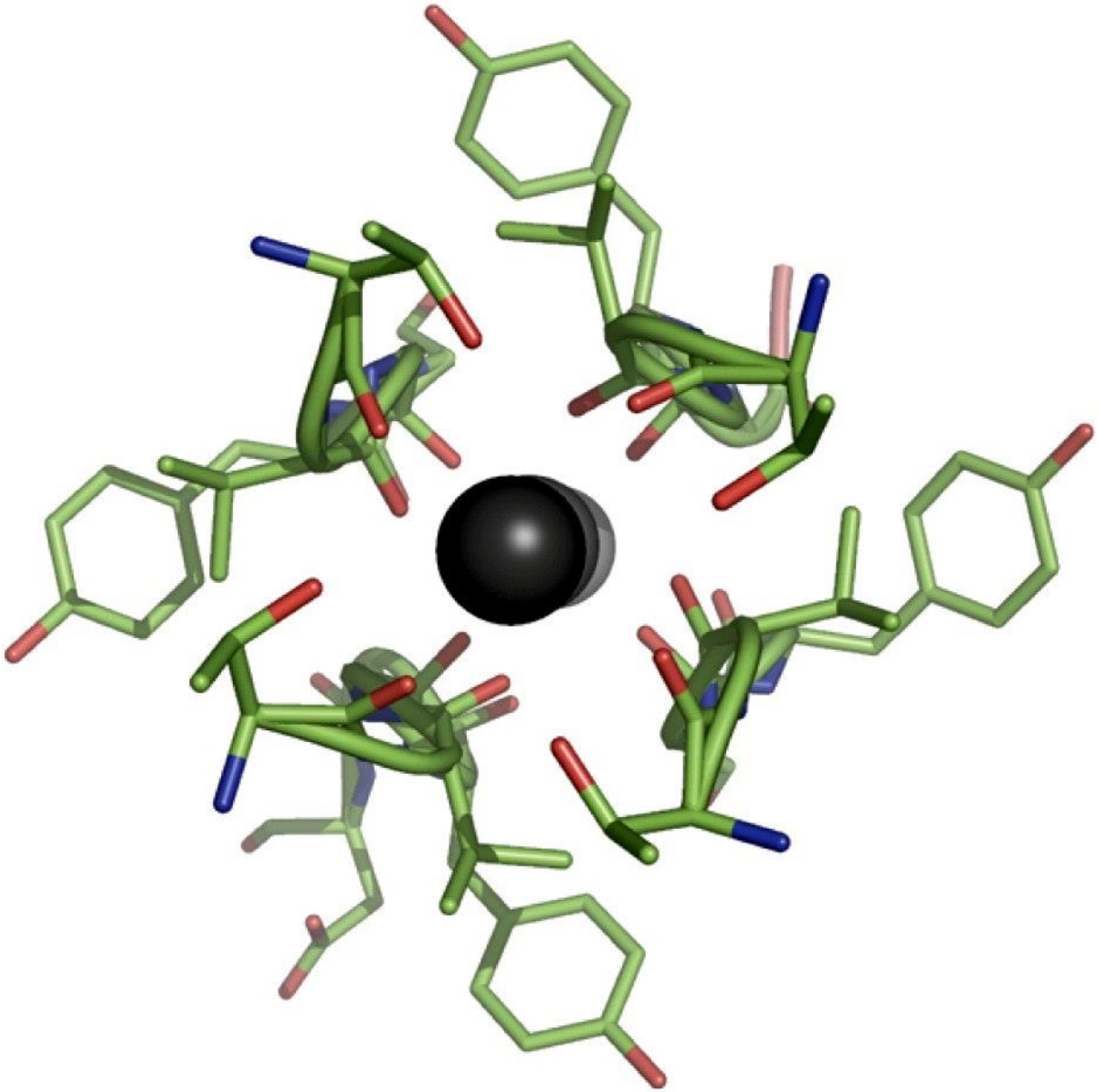




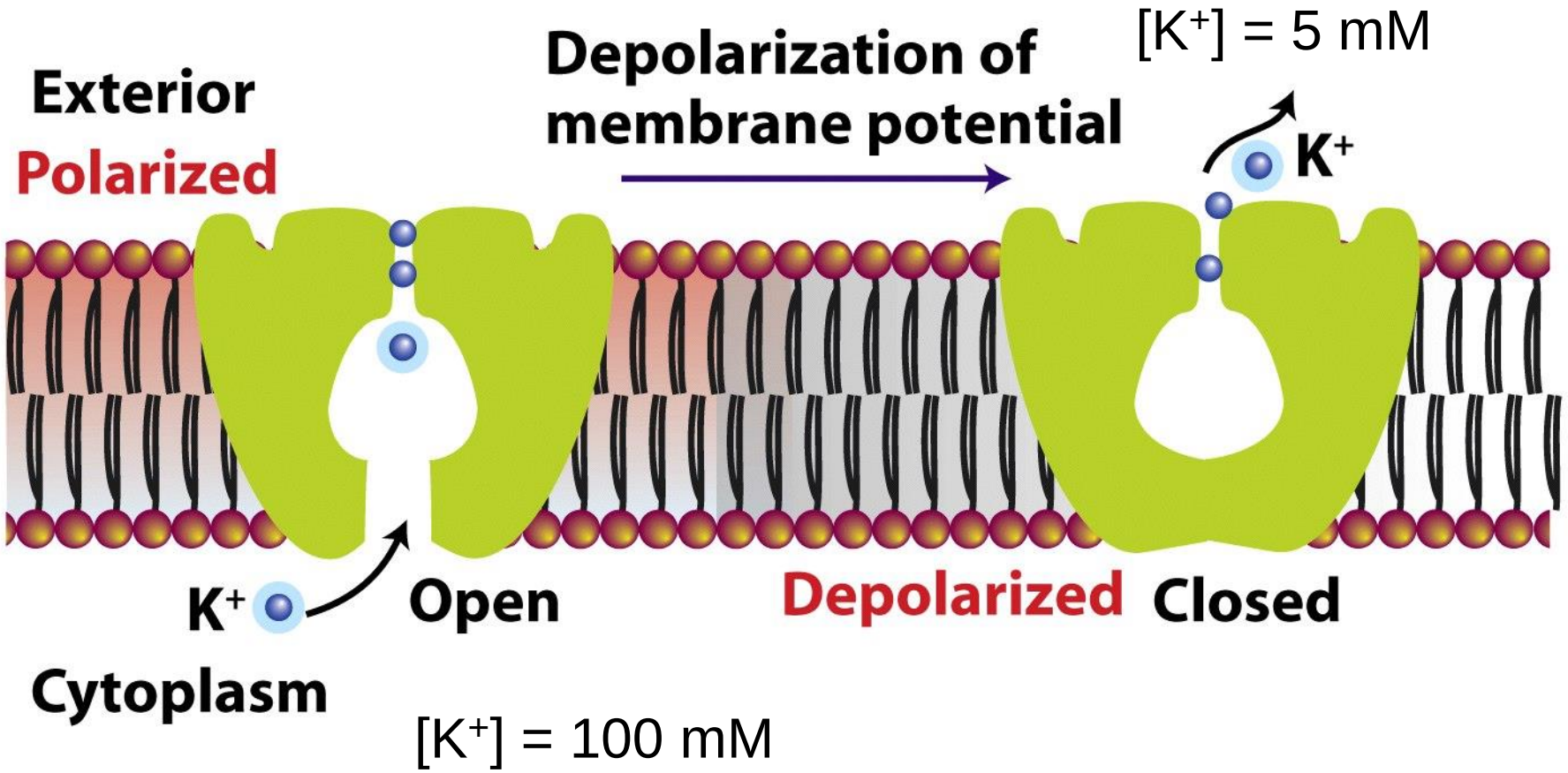
Ø = 1 nm
$[K^+] = 2$ M

In

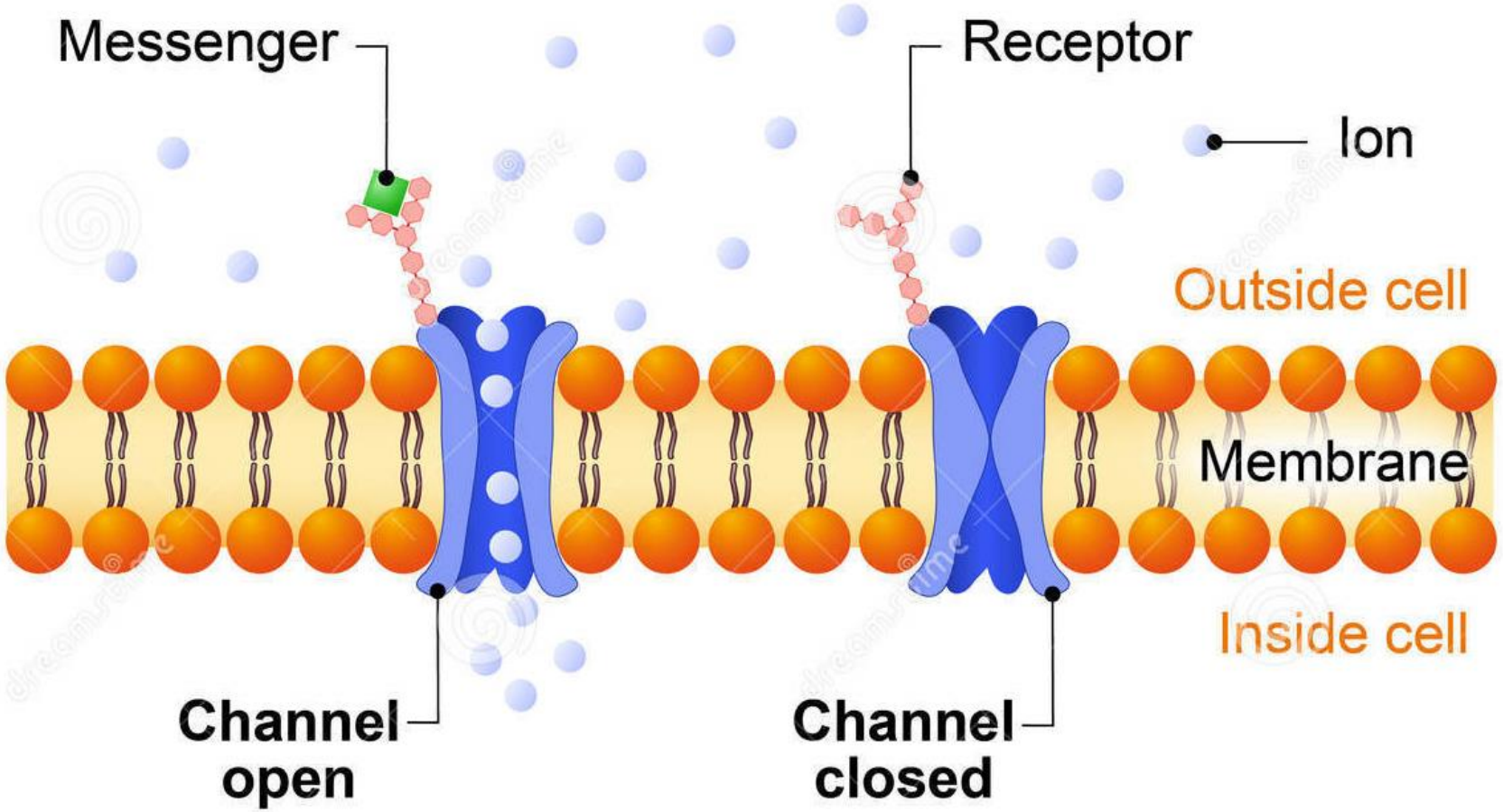
$[K^+] = 100$ mM



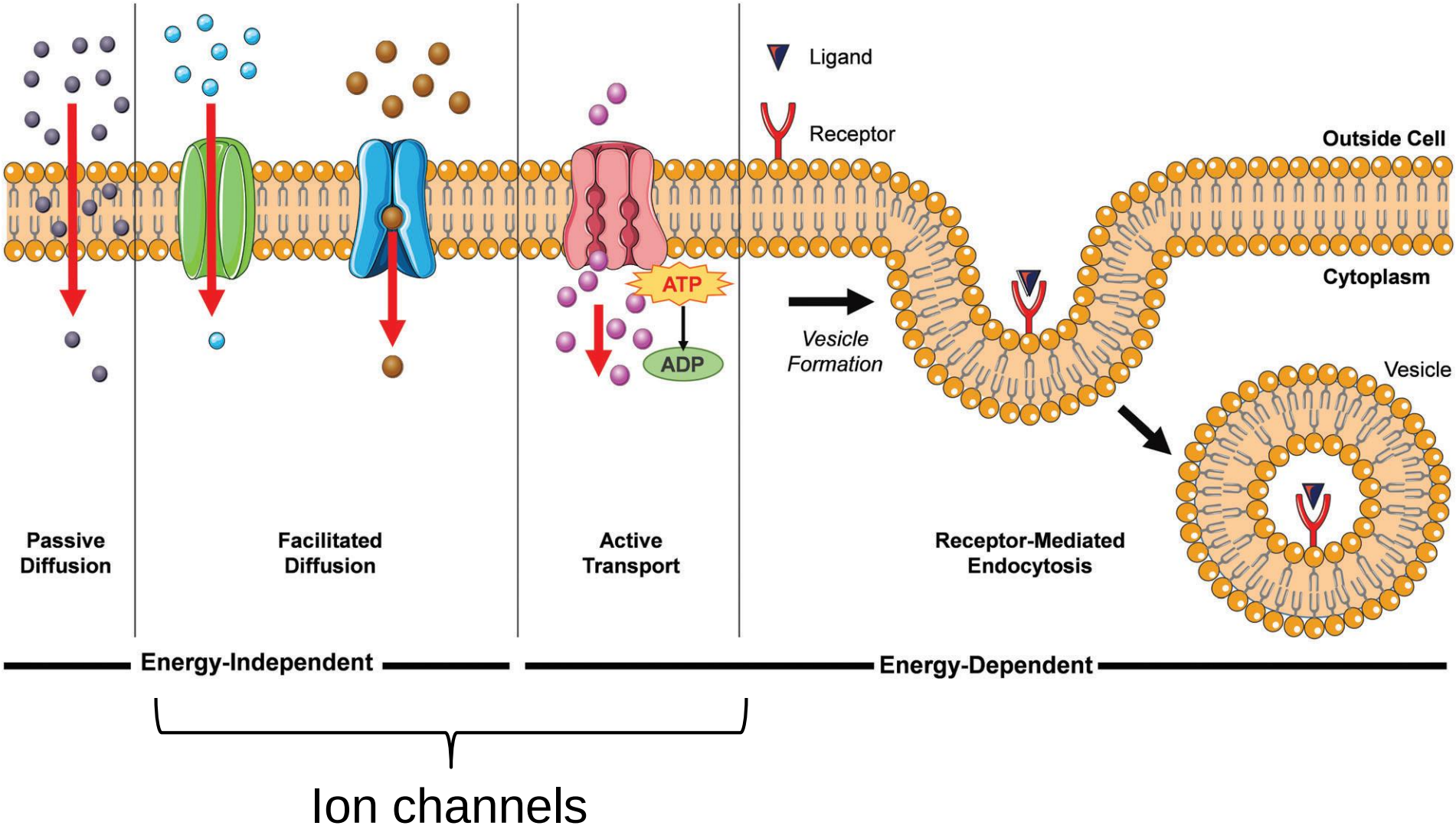
potential gated K^+ channel



Ligand-gated ion channel

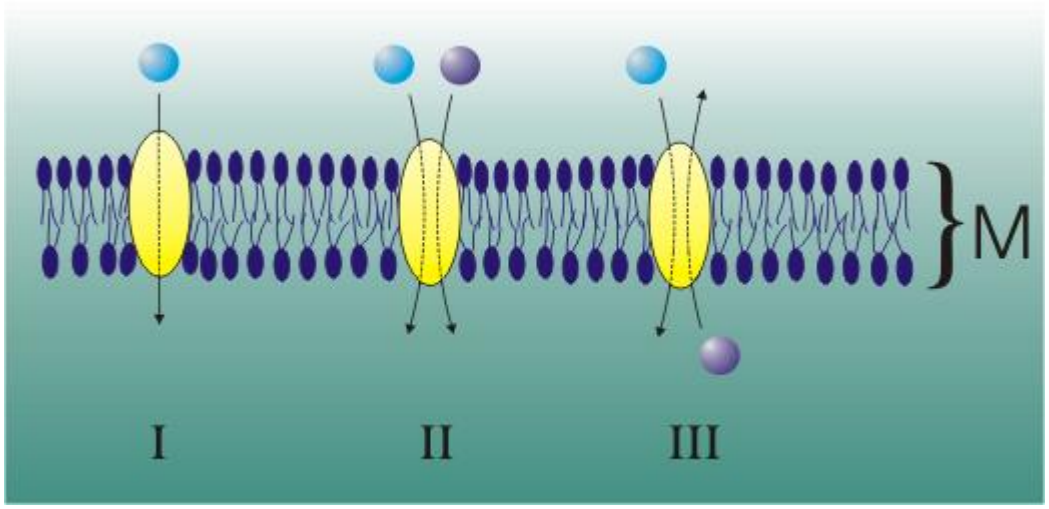


trans-membrane transport mechanisms



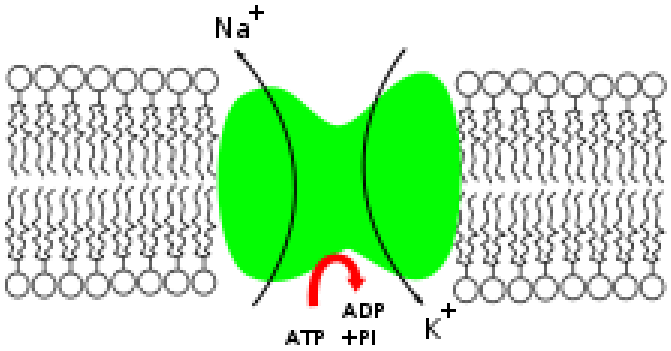
Ion channels

Ionic pumps (ATPases)



Uniporter *Symporter* *Antiporter*

Na^+/K^+-ATPase *antiporter* ionic pump

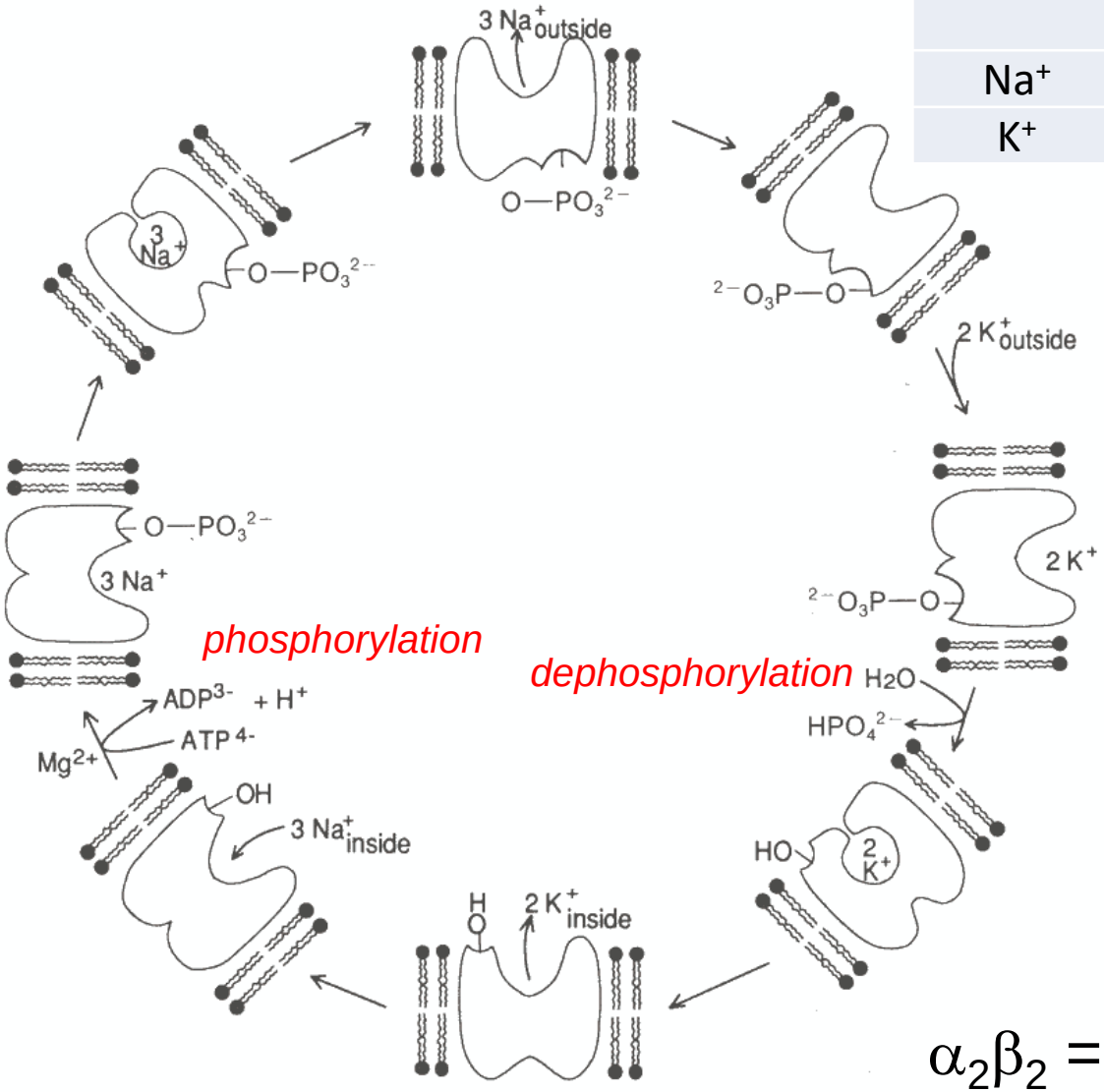


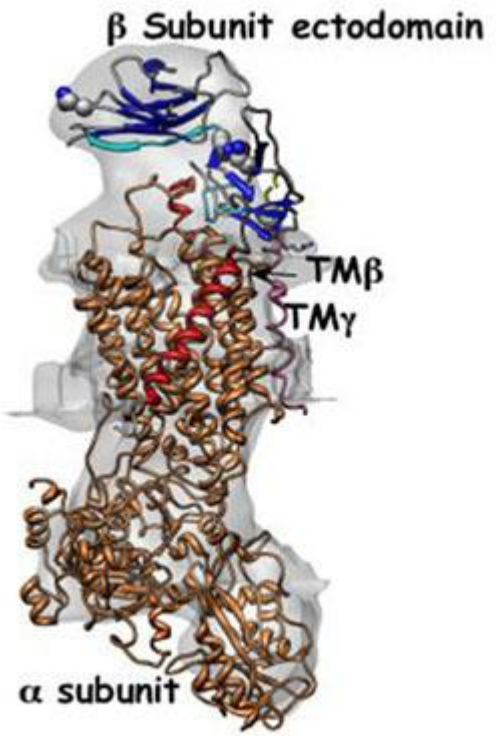
Ion	Intracellular (mM)	Extracellular (mM)
Na^+	10	150
K^+	100	5

antiporter Na^+/K^+-ATPase ionic pump

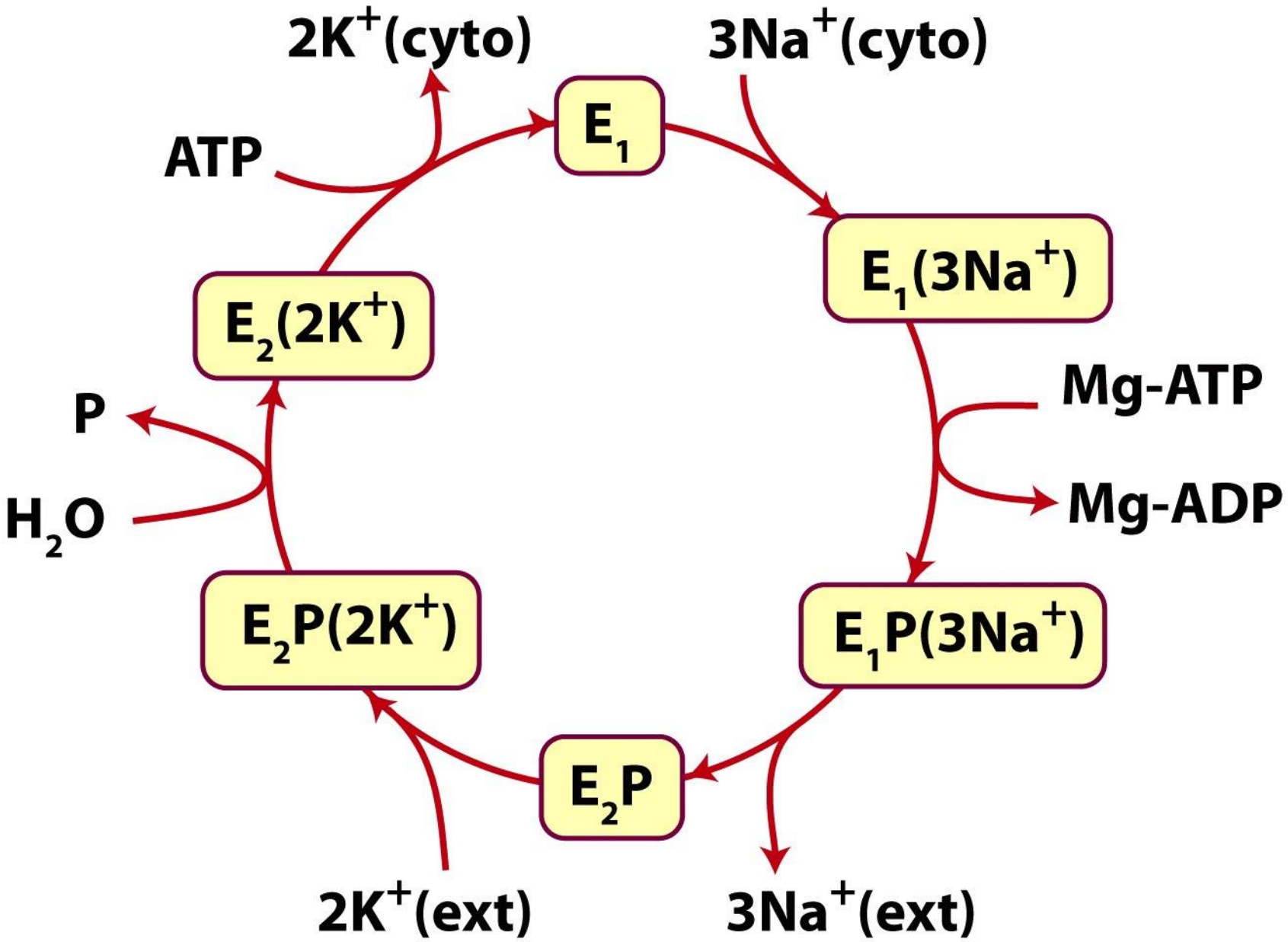
$3Na^+(in) + 2K^+(out) + Mg^{2+}ATP^{4-} + H_2O \rightarrow 3Na^+(out) + 2K^+(in) + Mg^{2+}ADP^{3-} + HPO_4^{2-} + H^+$

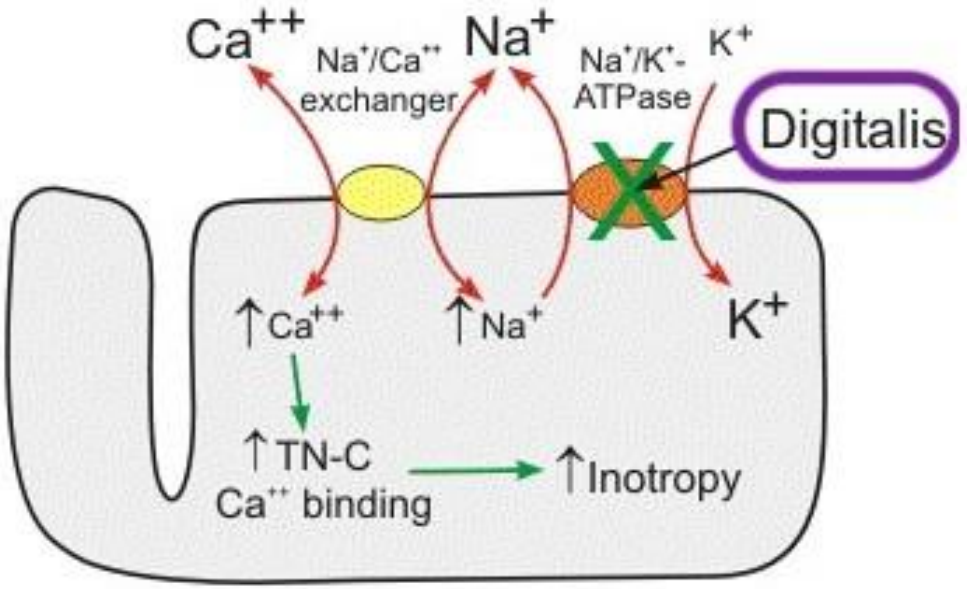
Ion	Intracellular (mM)	Extracellular (mM)
Na^+	10	150
K^+	100	5





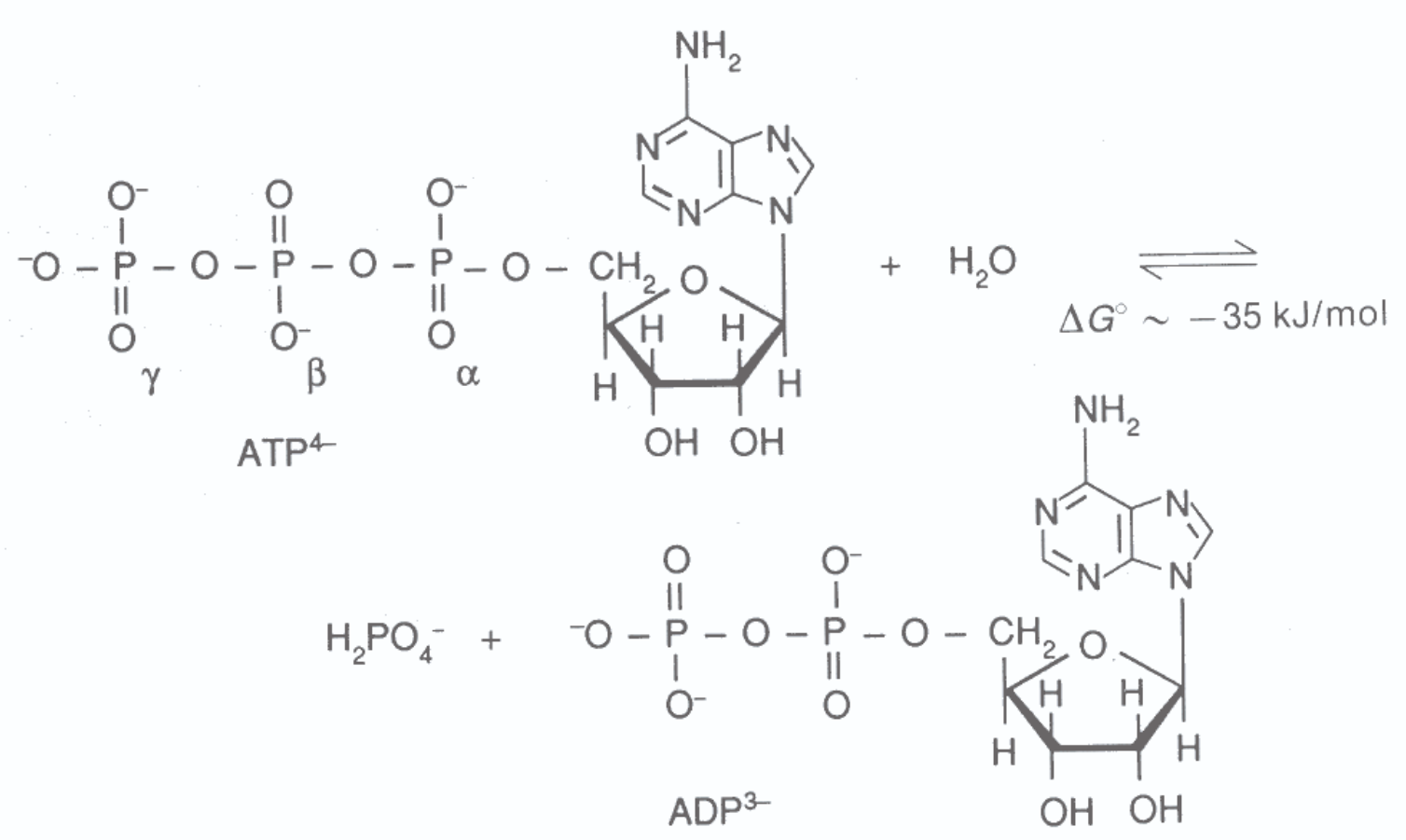
$\alpha_2\beta_2 = 2 \times 112(\alpha) + 2 \times 35(\beta)$


2K+(cyto)
3Na+(cyto)
ATP
E1
E1(3Na+)
E2(2K+)
Mg-ATP
P
H2O
Mg-ADP
E2P(2K+)
E1P(3Na+)
E2P
2K+(ext)
3Na+(ext)



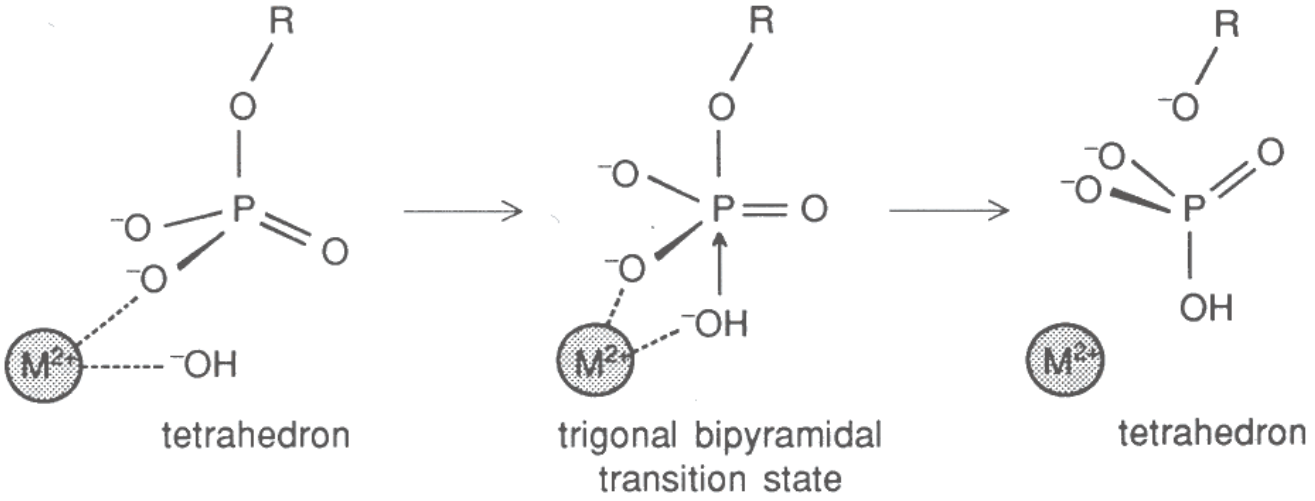
At the level of cardiac muscle, inhibition of the Na^+/K^+ pump by **digitalis** increases $[Na^+]$ within the cell, leading to activation of the **Na^+/Ca^{2+} antiport pump**, and thus to an increase in intracellular $[Ca^{2+}]$ that – by binding to troponin-C – results in intensification of muscle contraction (cardiotonic effect).

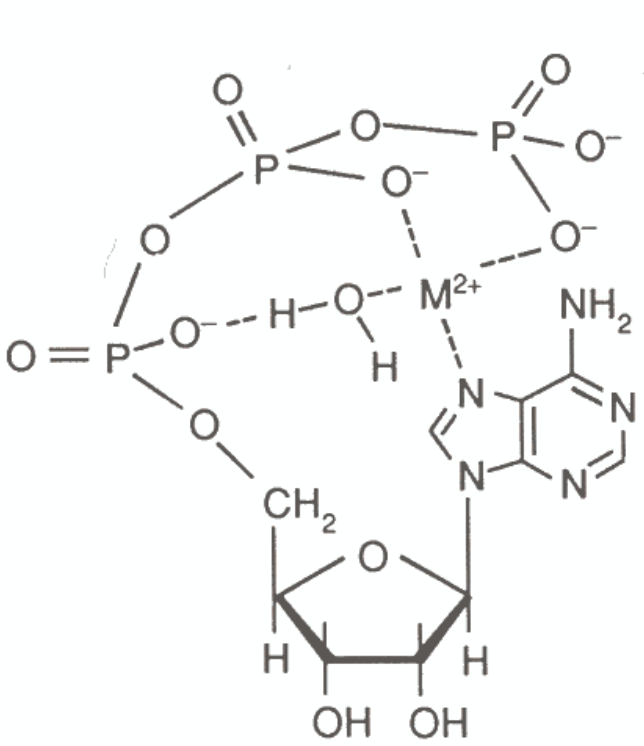
Magnesium

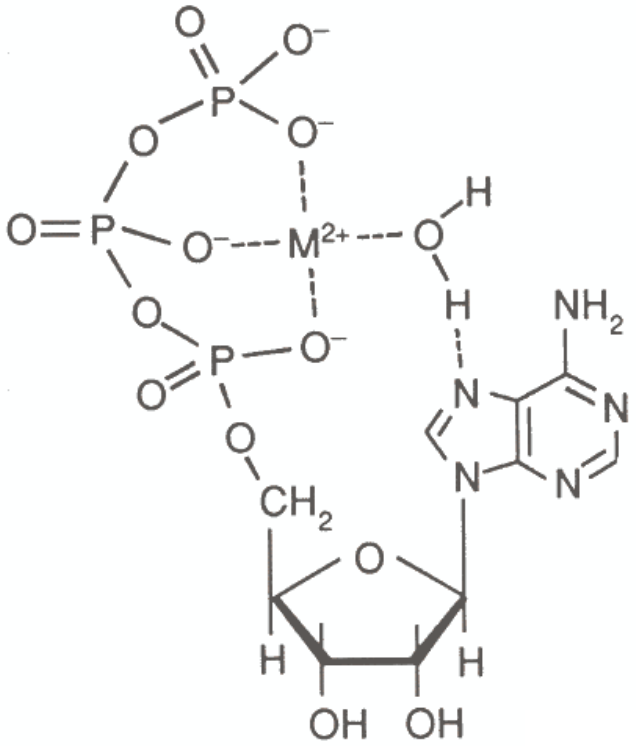


On average, every single day an adult synthesizes and uses an amount of ATP corresponding to its own body weight

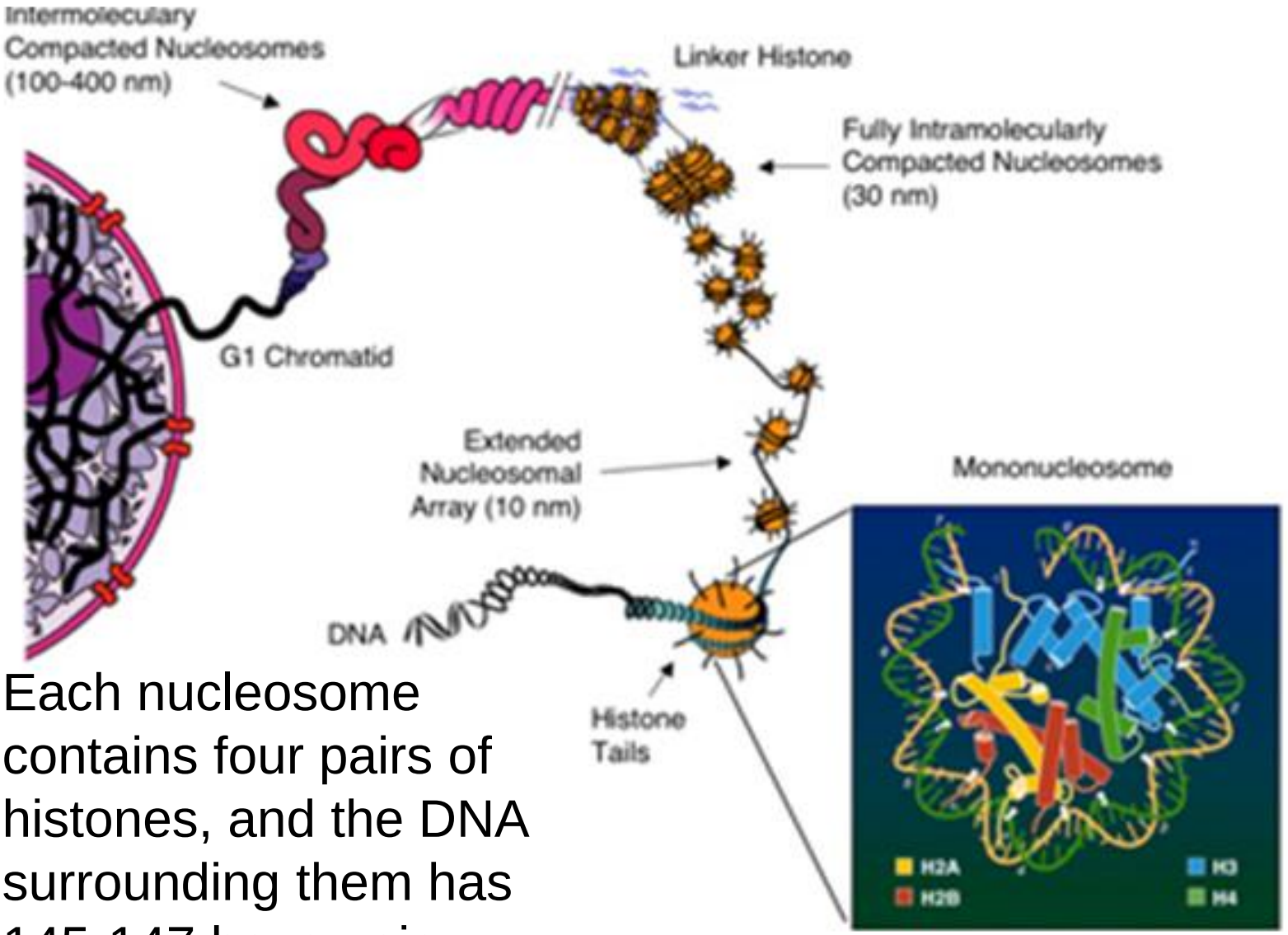
S_N2


R
O
P
O
$^{-}$O
$^{-}$O
M^{2+}
$^{-}$OH
tetrahedron
trigonal bipyramidal
transition state
tetrahedron


O
P
O^{-}
M^{2+}
H
NH$_2$
N
CH$_2$
OH

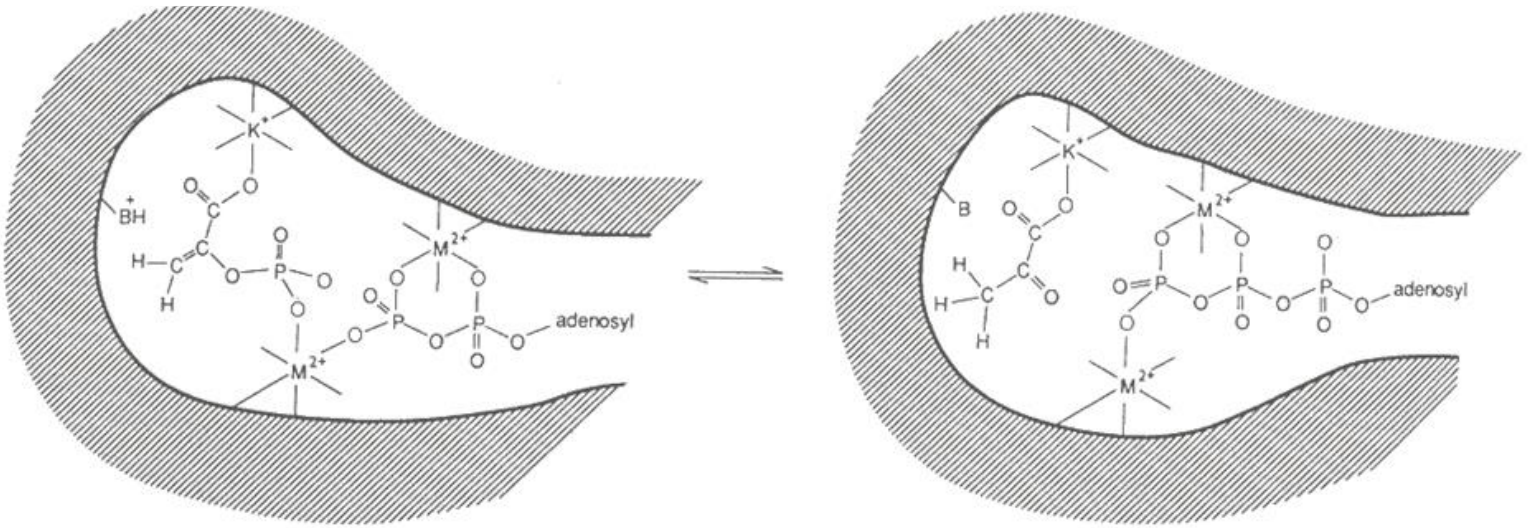

O
P
O^{-}
M^{2+}
H
NH$_2$
N
CH$_2$
OH

Structural role of Mg^{2+}: the folding of DNA in the nucleus (Chromatine, Nucleosomes and Histones)



Each nucleosome contains four pairs of histones, and the DNA surrounding them has 145-147 base pairs

$$ATP^{4-} + X\text{–}H \xrightarrow[Mg^{2+}]{\text{kinasi}} ADP^{3-} + X\text{–}PO_3^{2-} + H^{+}$$

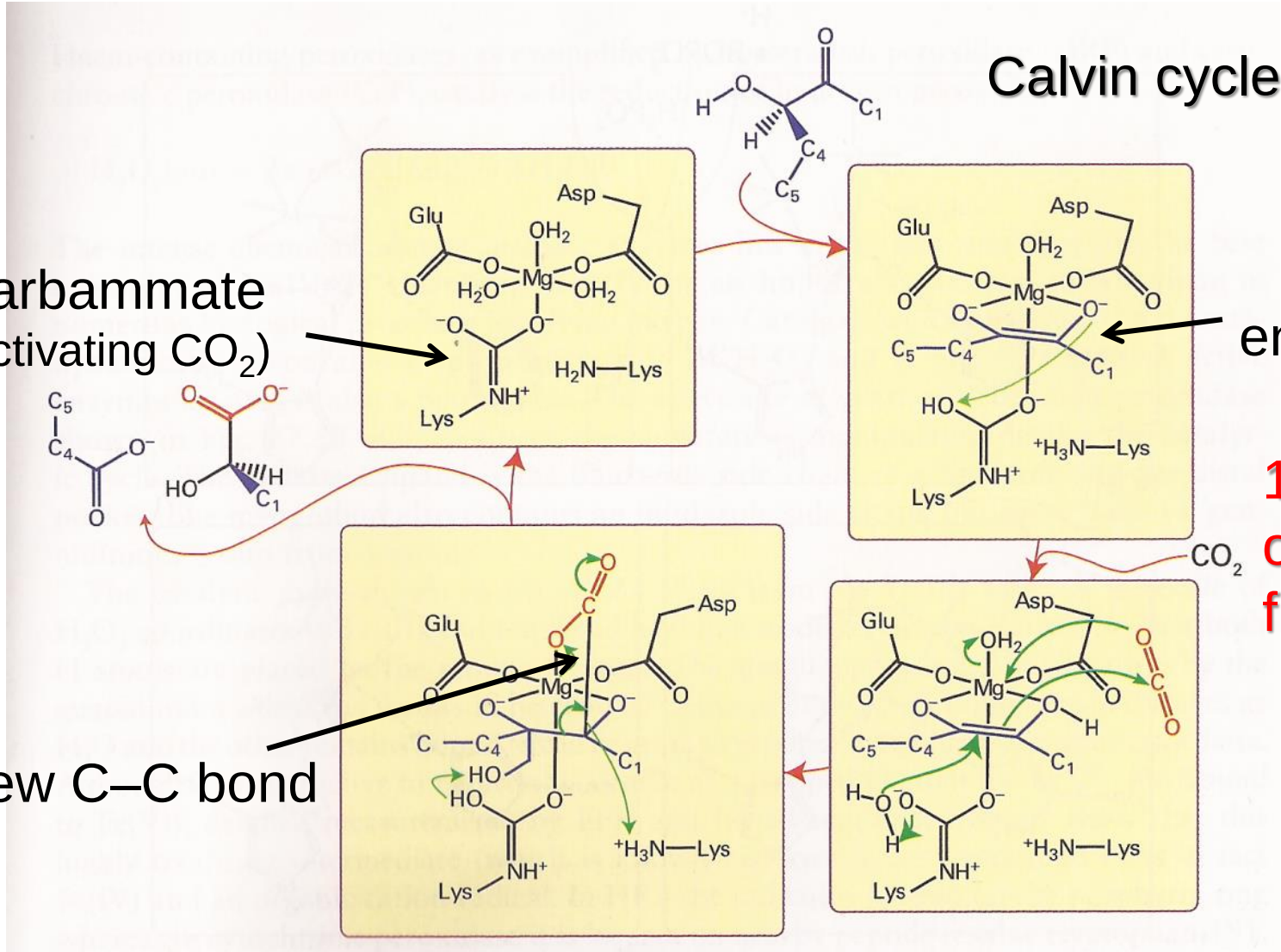


Pyruvate-kinase

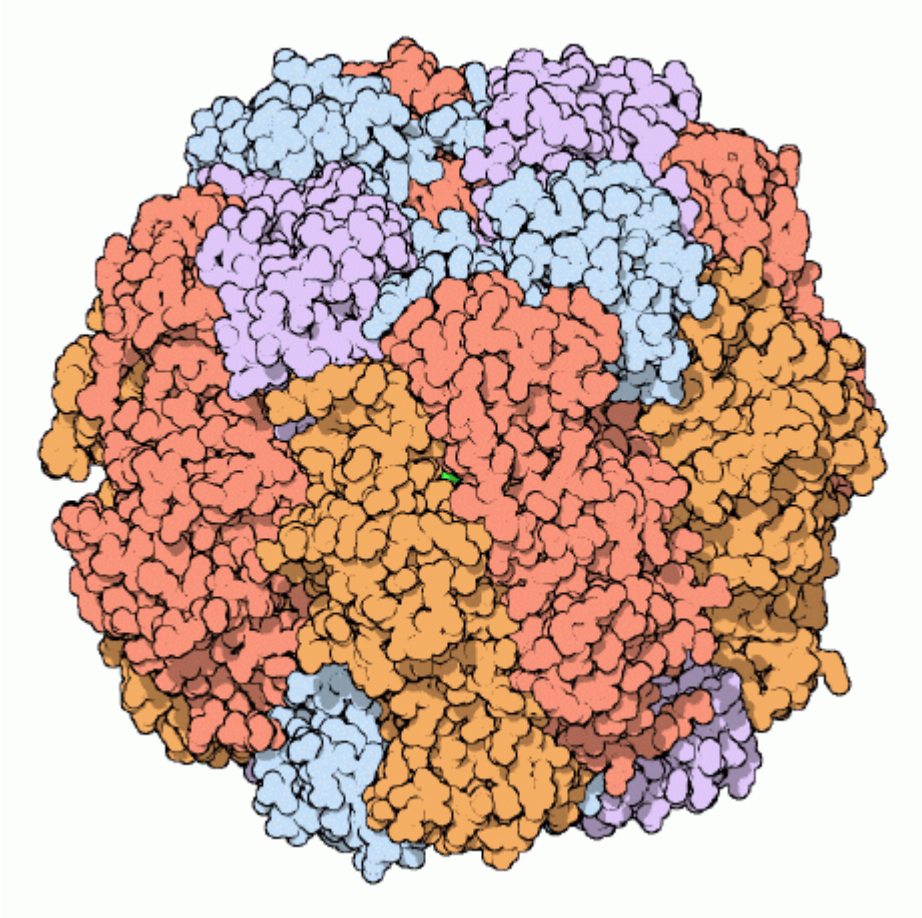
Ribulose 5-bisphosphate carboxylase (*RuBisCo*)

The most abundant protein (enzyme) on Earth

It catalyzes the carbonylation of ribulose 1,5-disphosphate



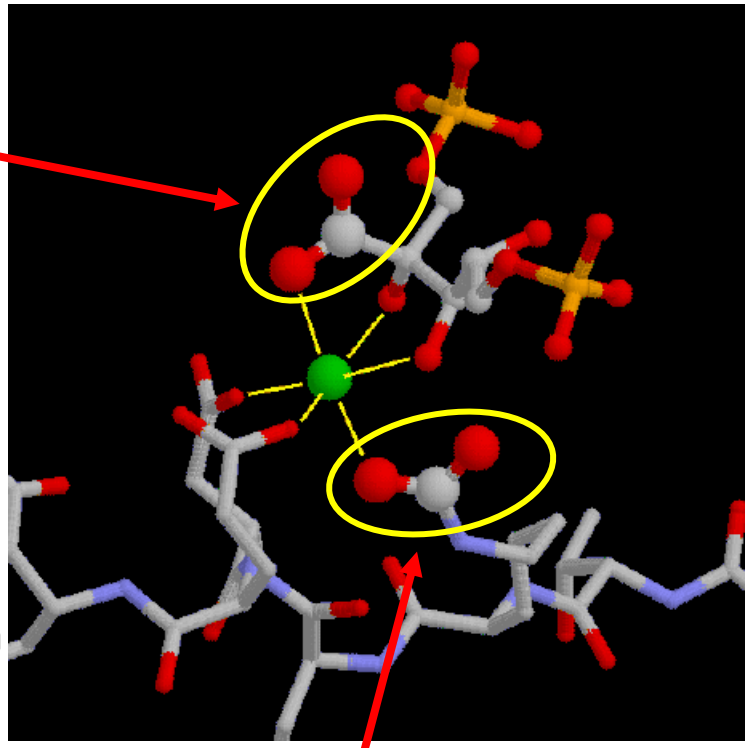
Rubisco



16 subunits L_8S_8

Two Mg active sites at the interface of each L_2 pair

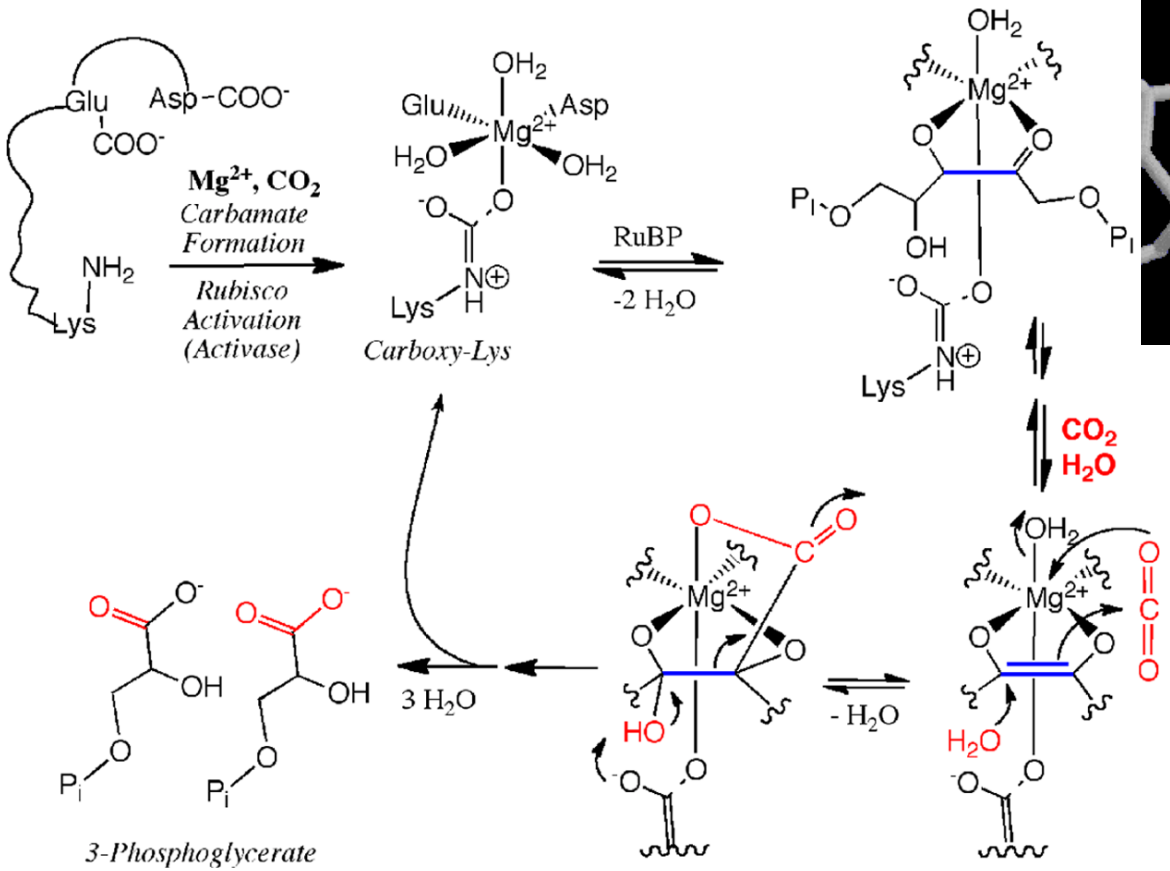
Rubisco



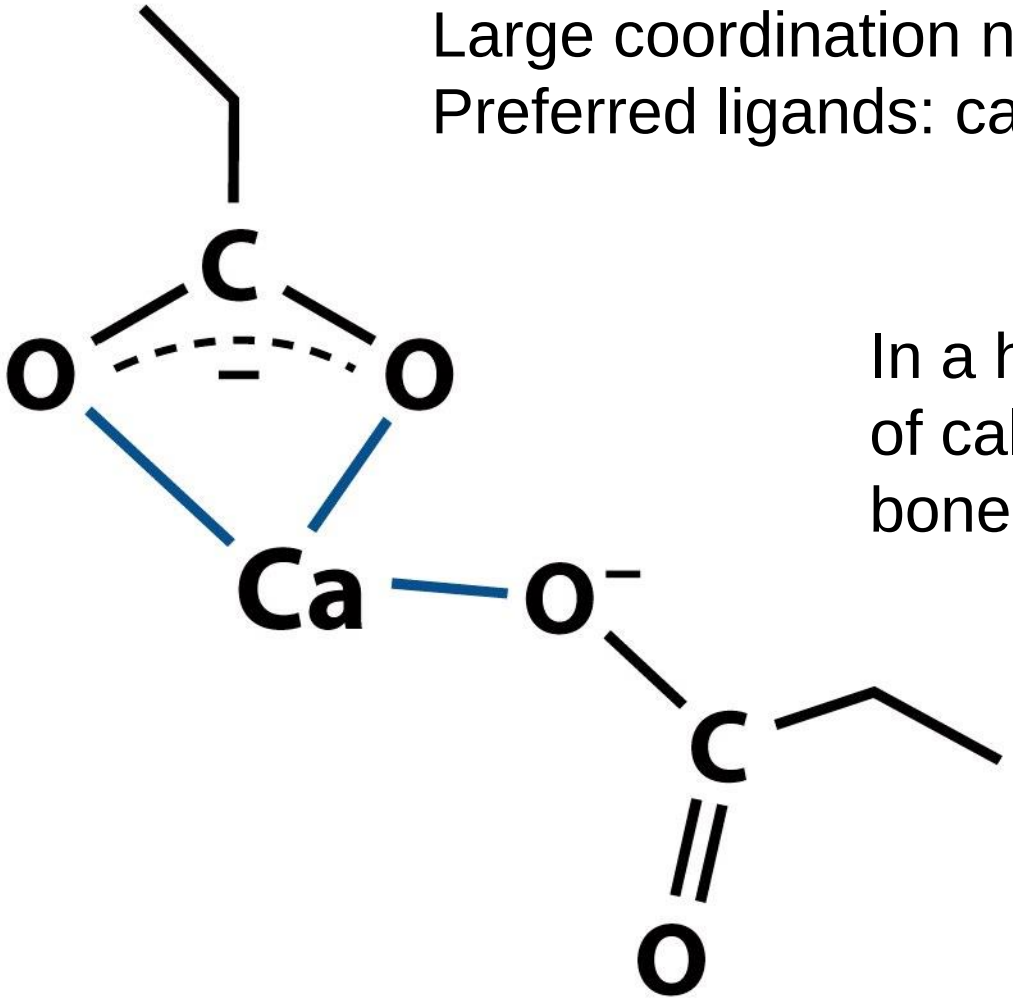
Substrate CO_2

only 3 cycles/second

Activating CO_2



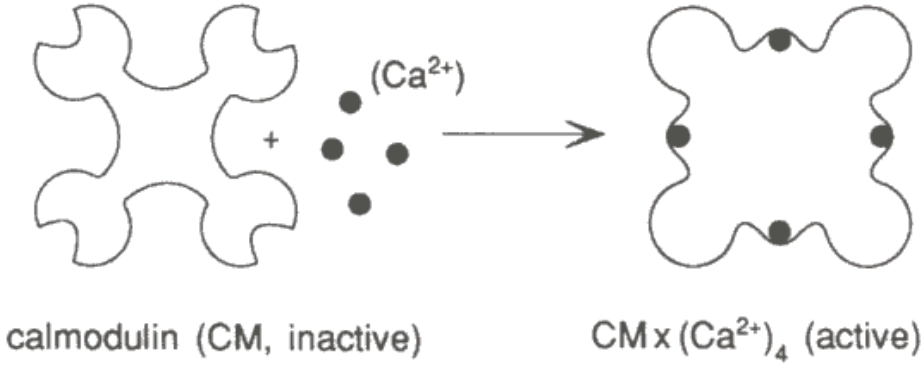
Calcium

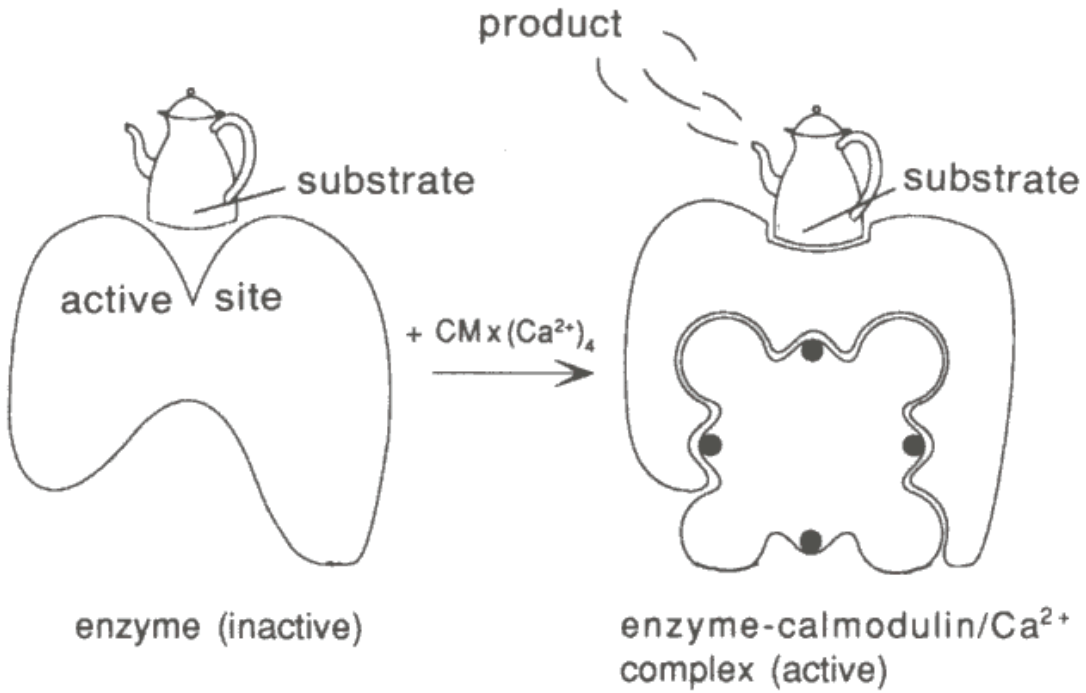


Large coordination numbers: 7 – 8
Preferred ligands: carboxylates

In a human being, ca. 10g of calcium do not belong to bones and teeth

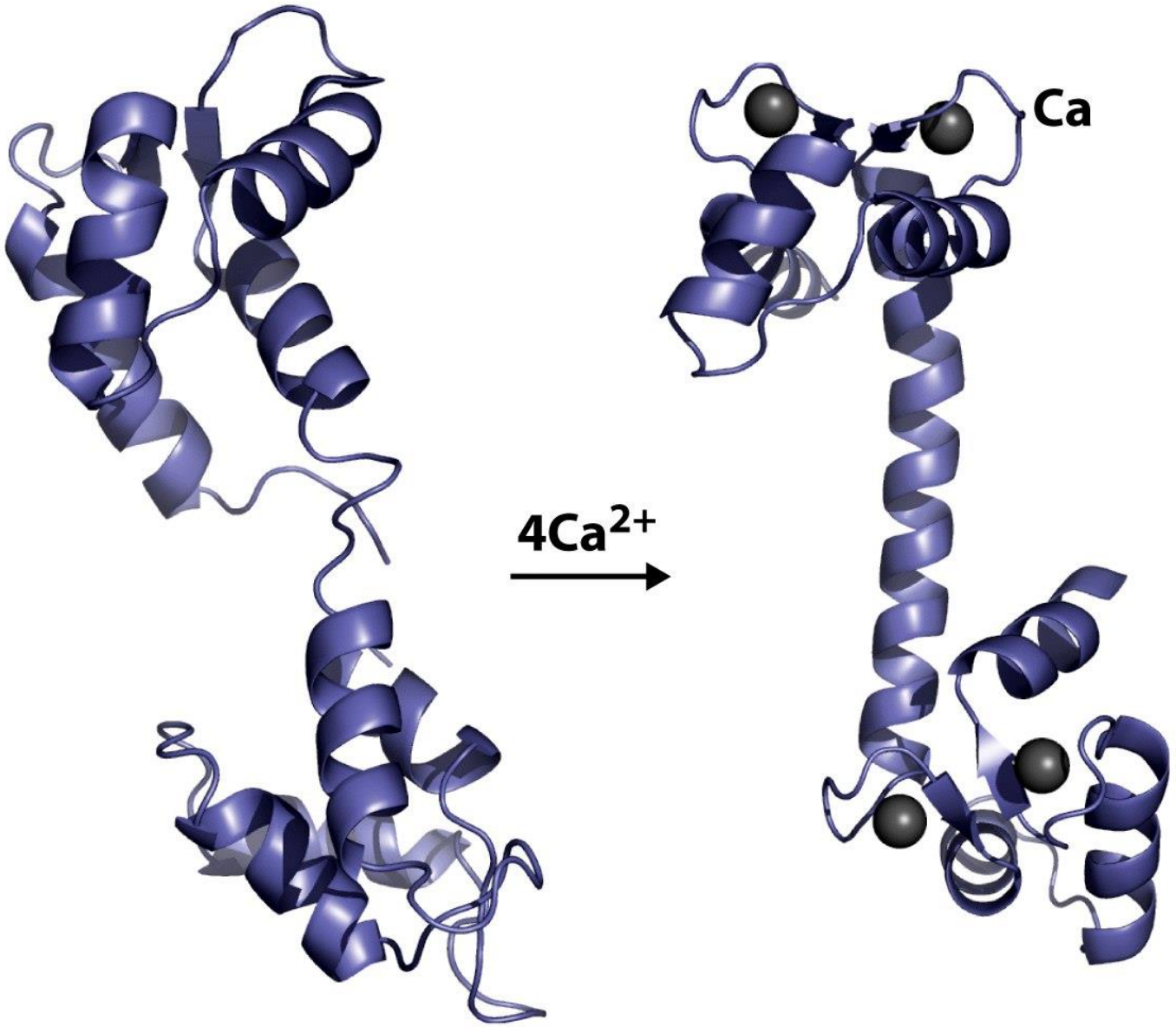
Ca^{2+}: a secondary messenger inside cells



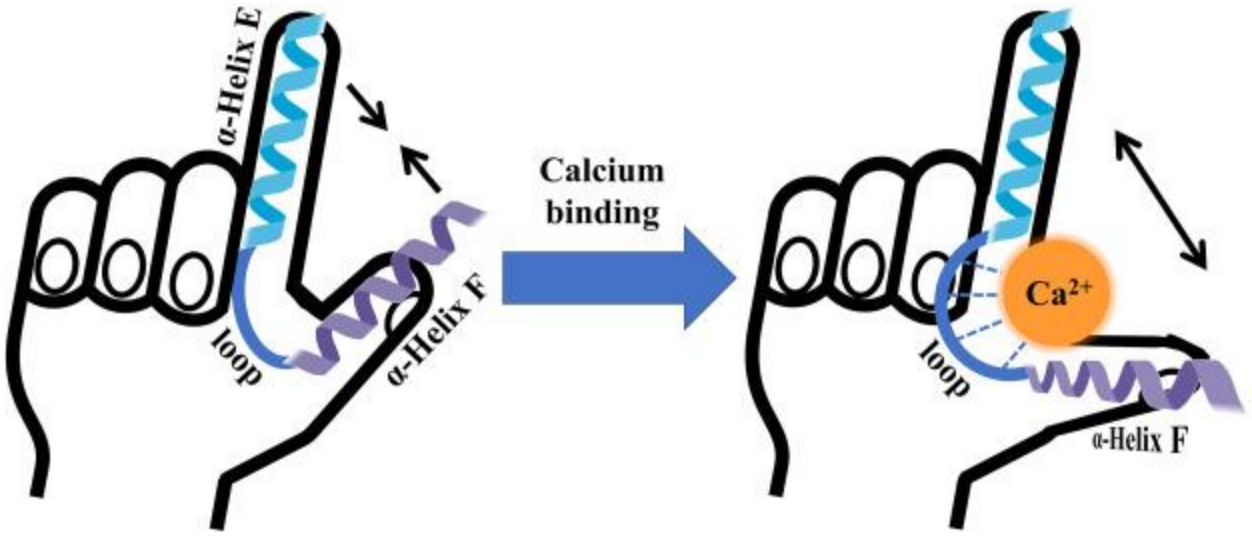


e.g.: NO synthase (NO), adenylate and guanylate cyclase (cAMP, cGMP), NAD kinase (NADP)

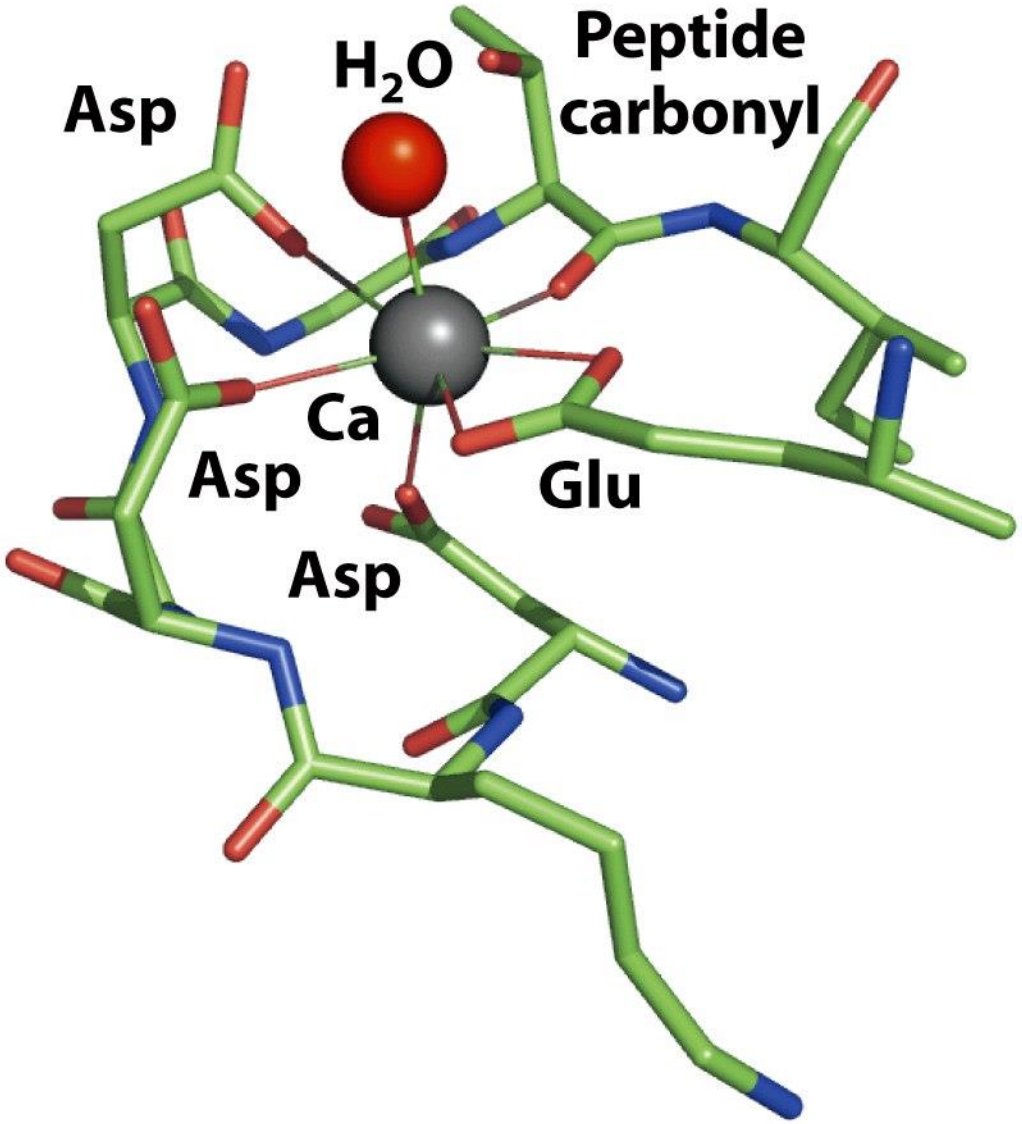
Conformational variation in a calmodulin



The EF hand calcium binding motif



Ca^{2+} ions are coordinated by ligands within the loop

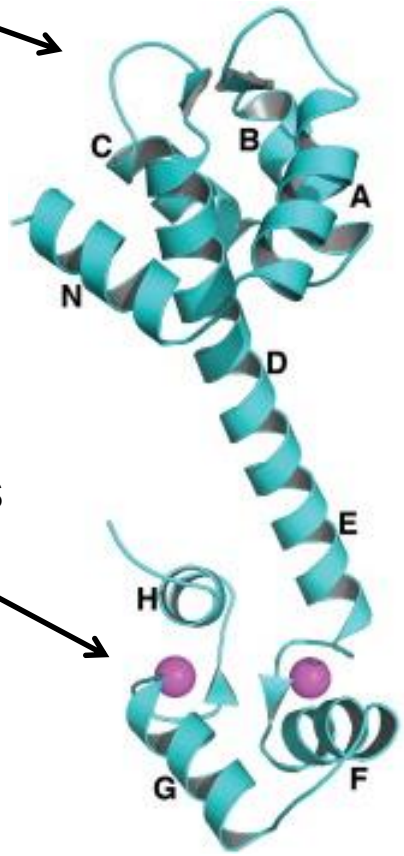


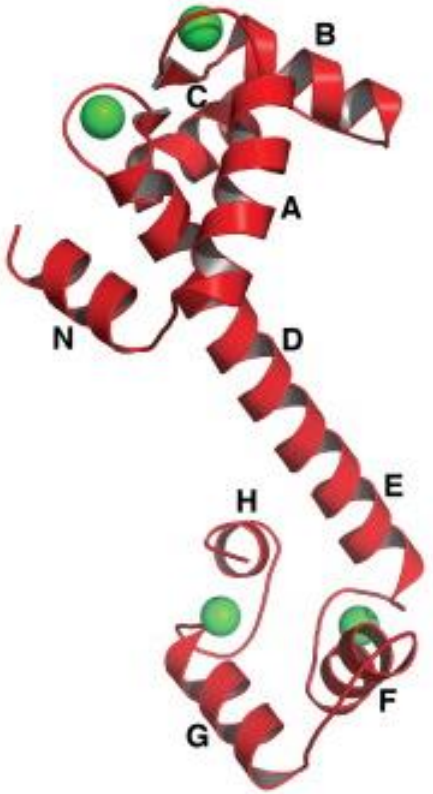
One of the Ca^{2+} coordination sites of a calmodulin

Troponin-C

Lower affinity binding sites

High affinity binding sites
($K > 10^6$)



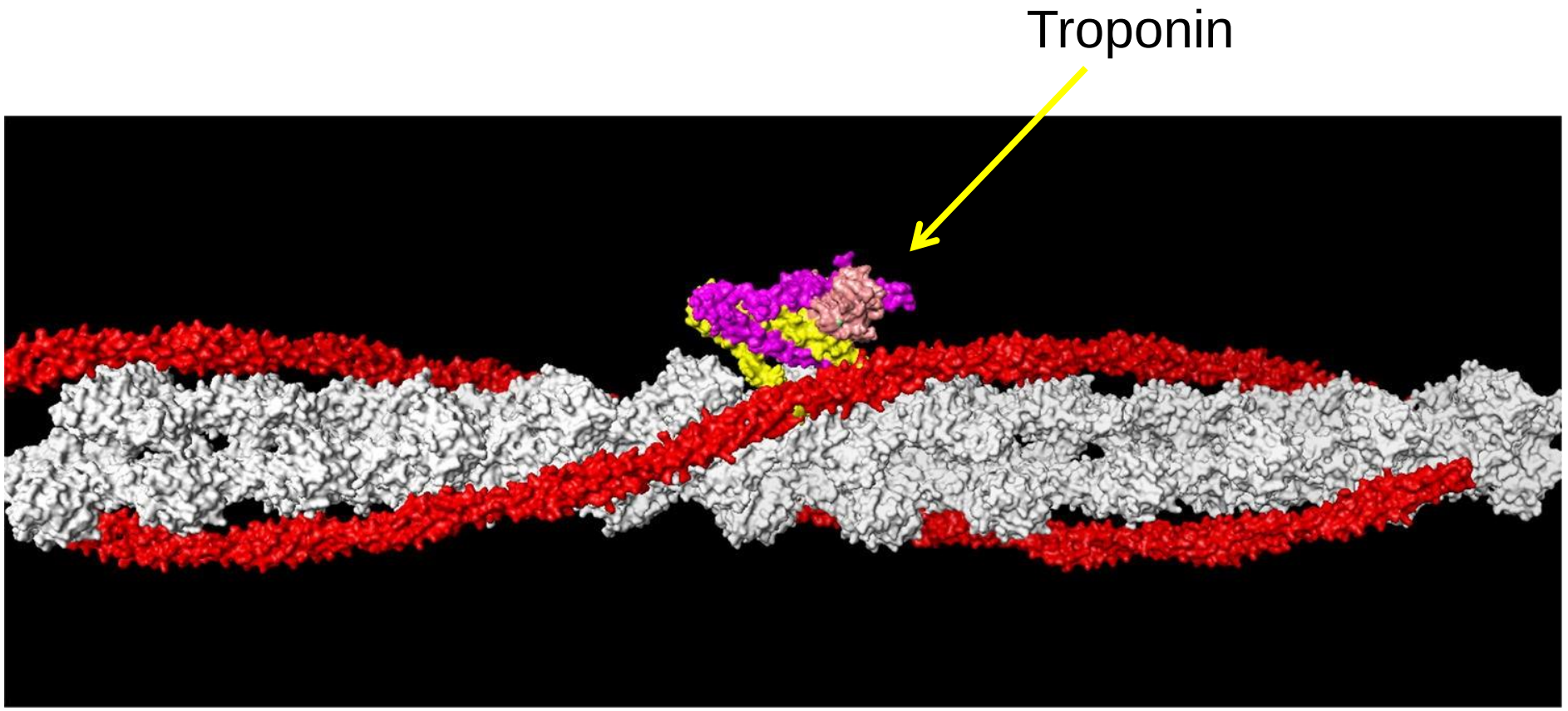


actin
myosin

(protein components of muscular filaments)

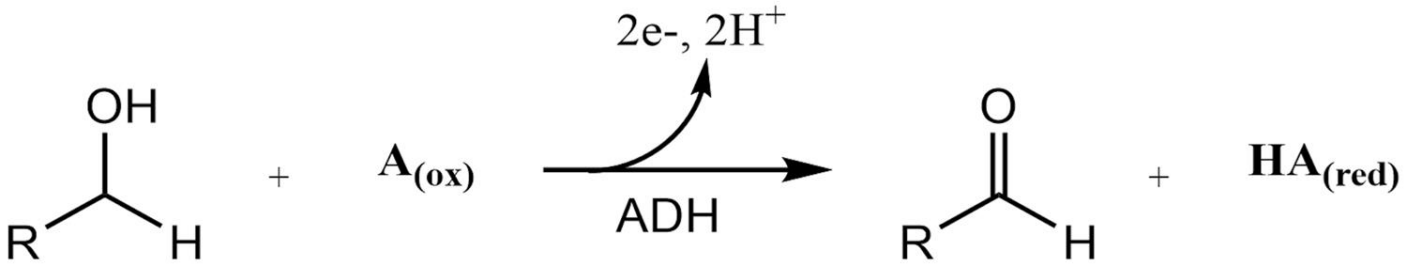
https://www.youtube.com/watch?v=nTZnBdeIb5c

Model of a muscular filament

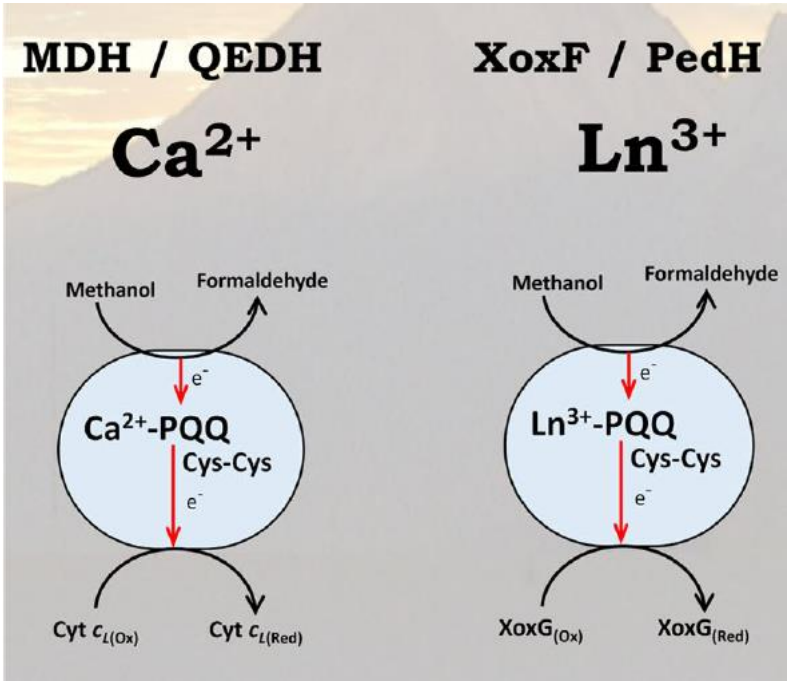


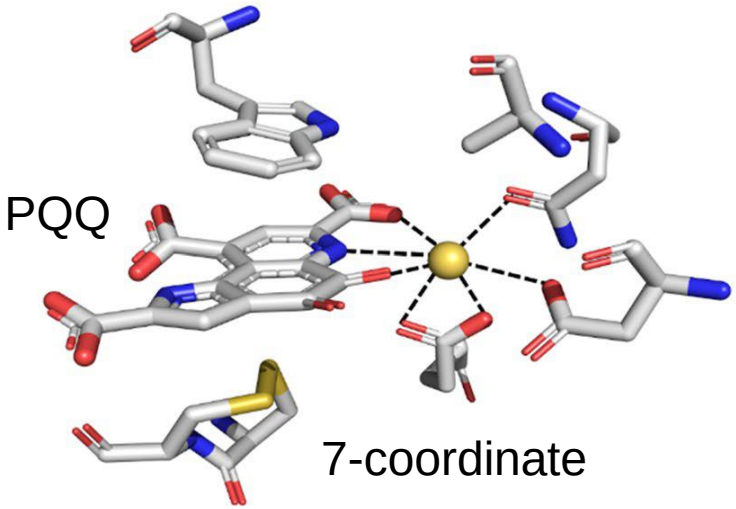
Actin = white
Tropomyosin = red

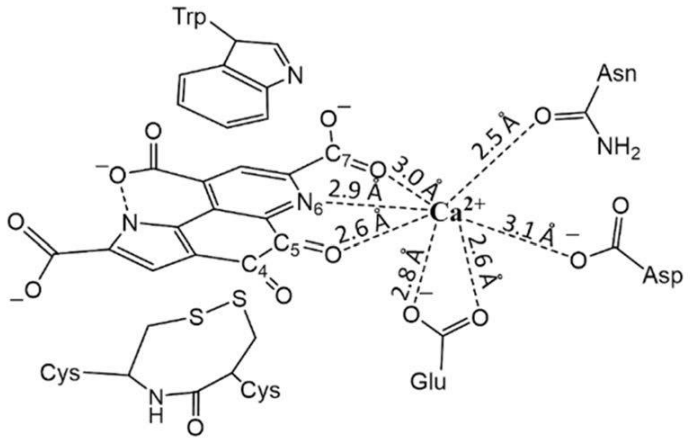
PQQ-dependant alcohol dehydrogenases (ADHs) (PQQ = Pyrroloquinoline quinone)



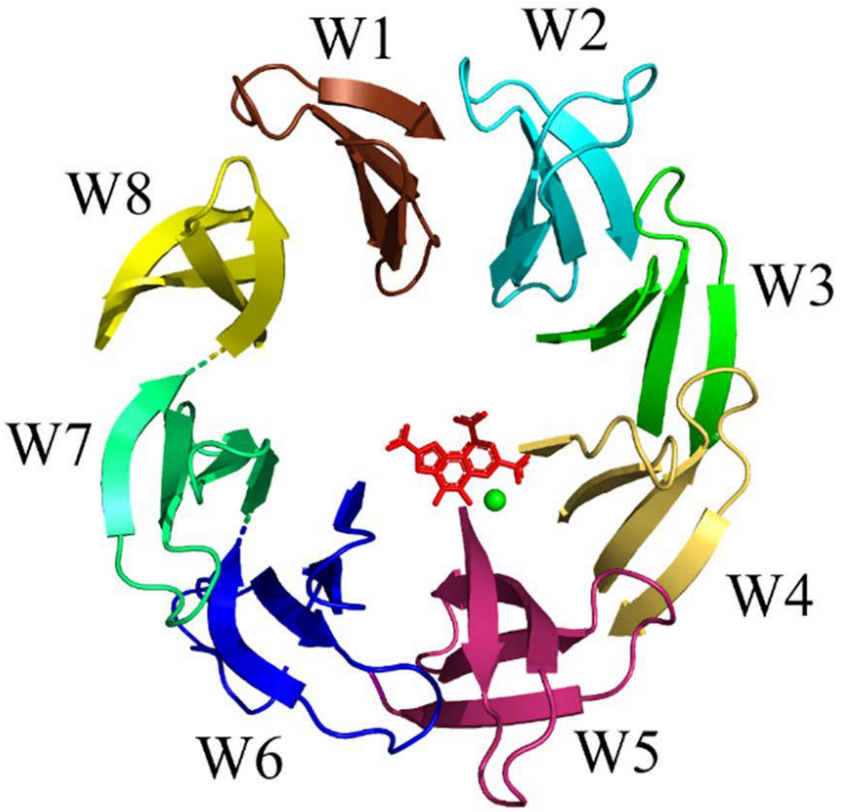
R, usually: CH_3, CH_2CH_3, $CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$



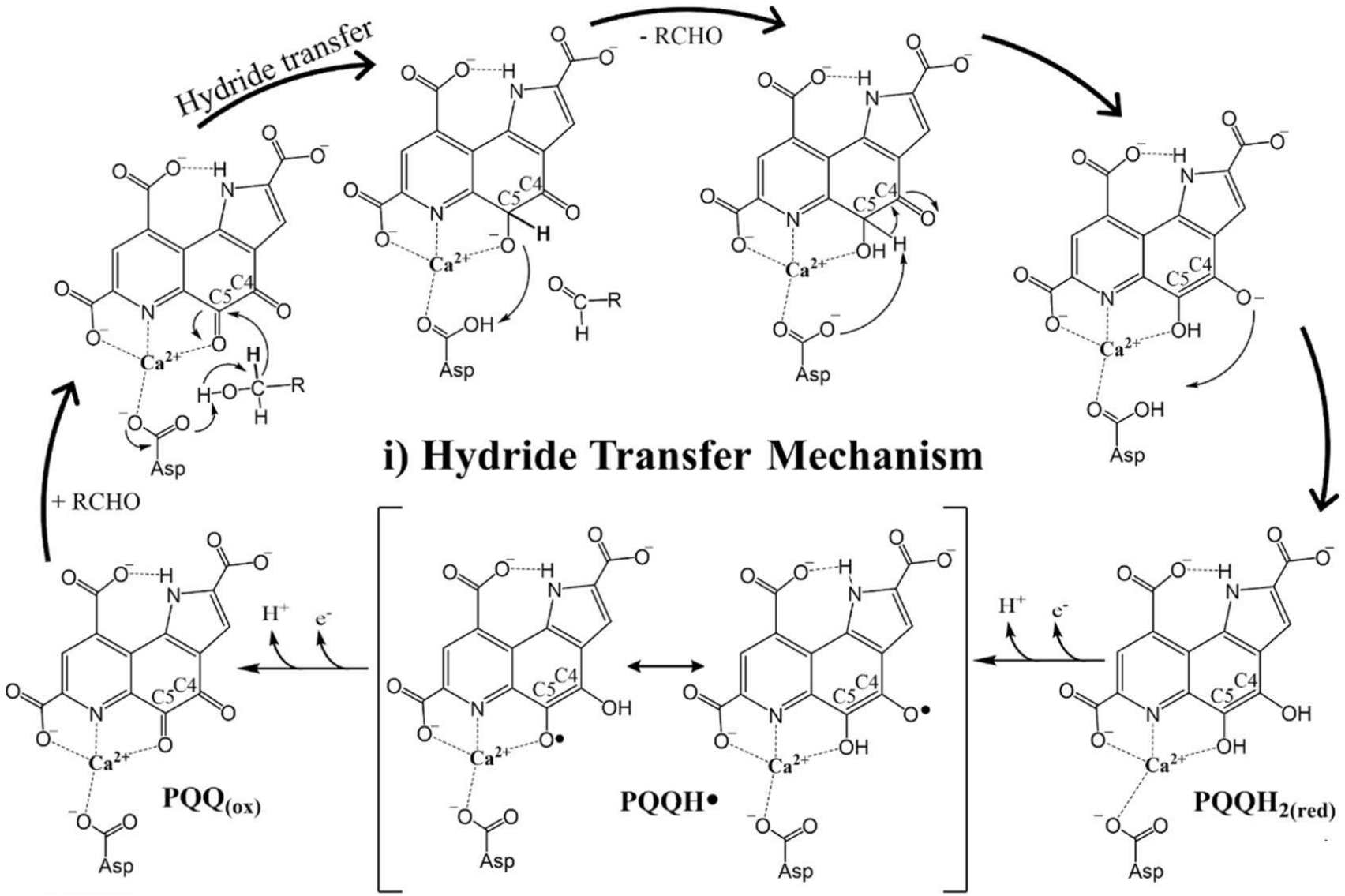


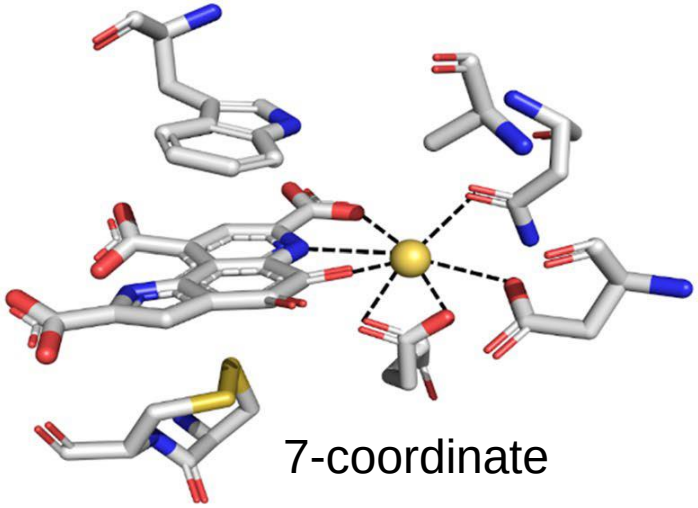


Ca^{2+}-PQQ active site of *methanol dehydrogenase*, MDH

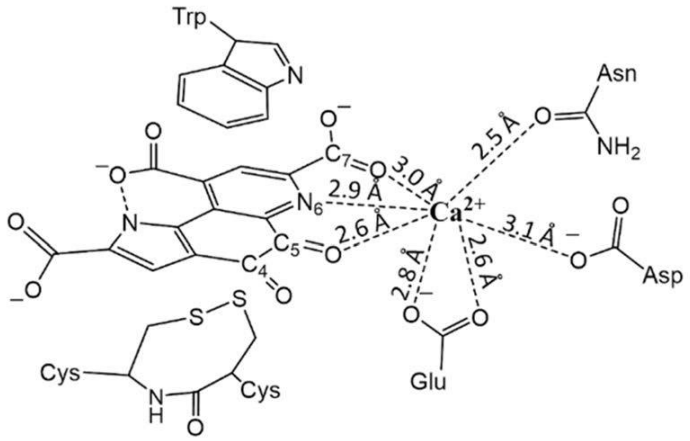


Hypothetical mechanism

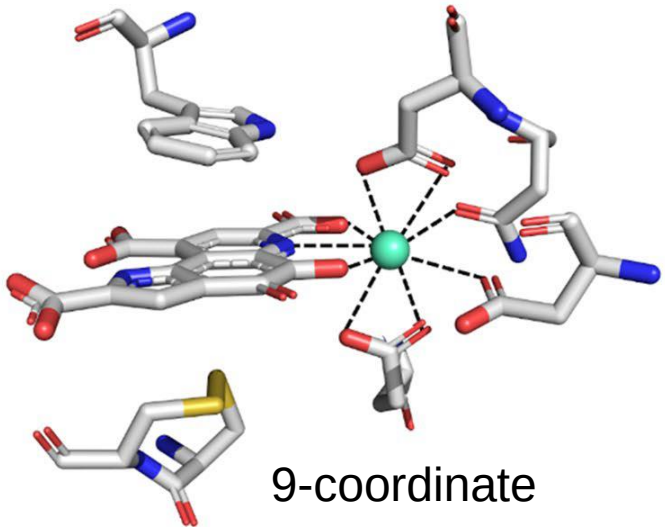




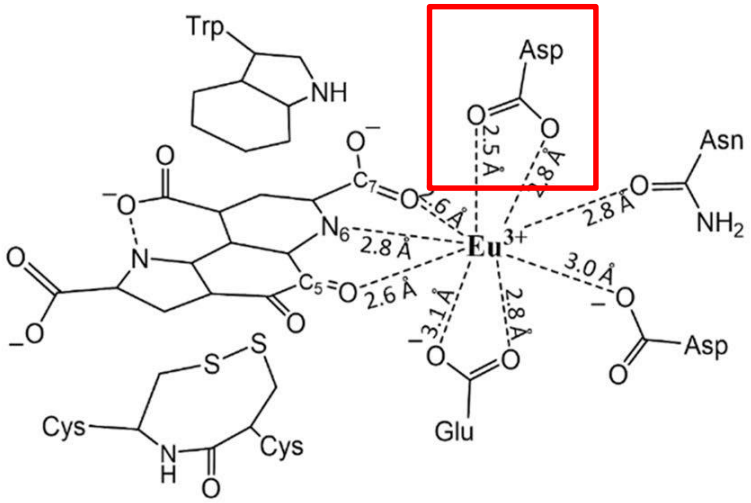
7-coordinate



Ca^{2+}-PQQ active site of *methanol dehydrogenase*, MDH

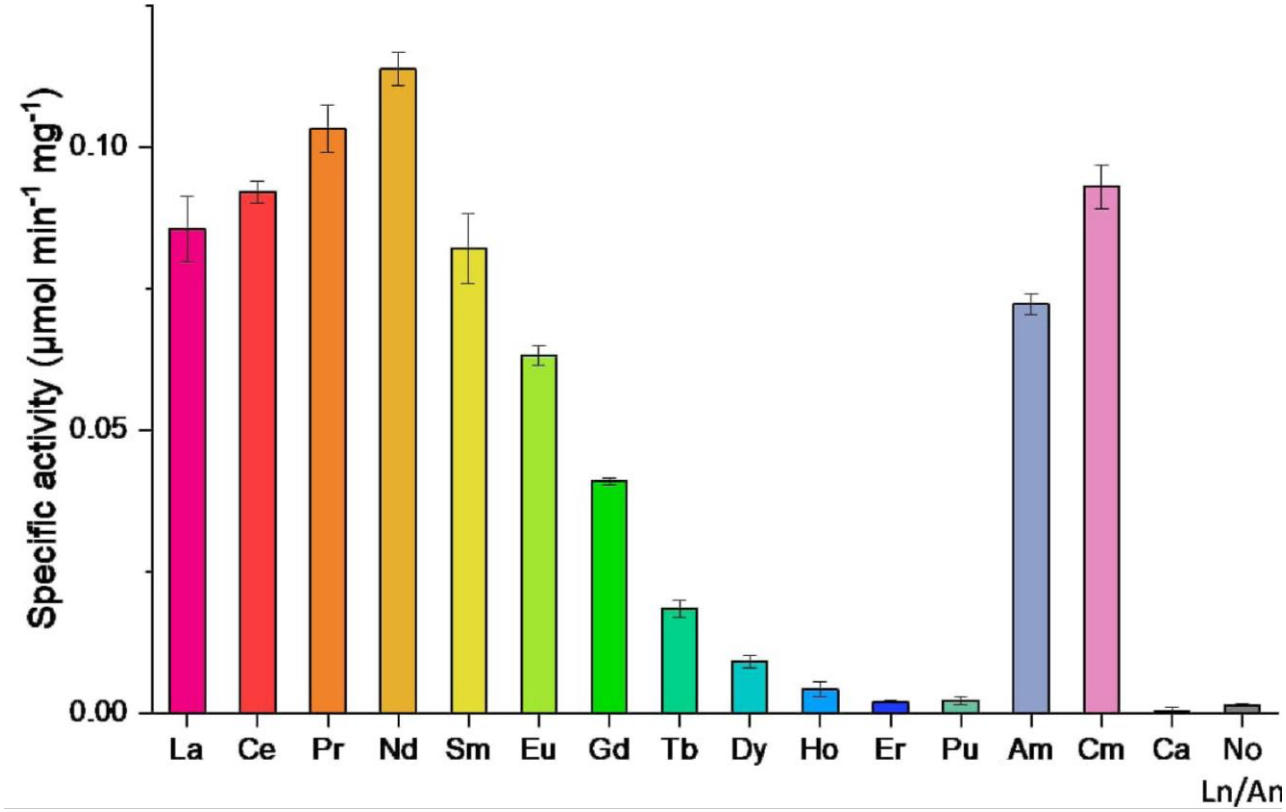


9-coordinate

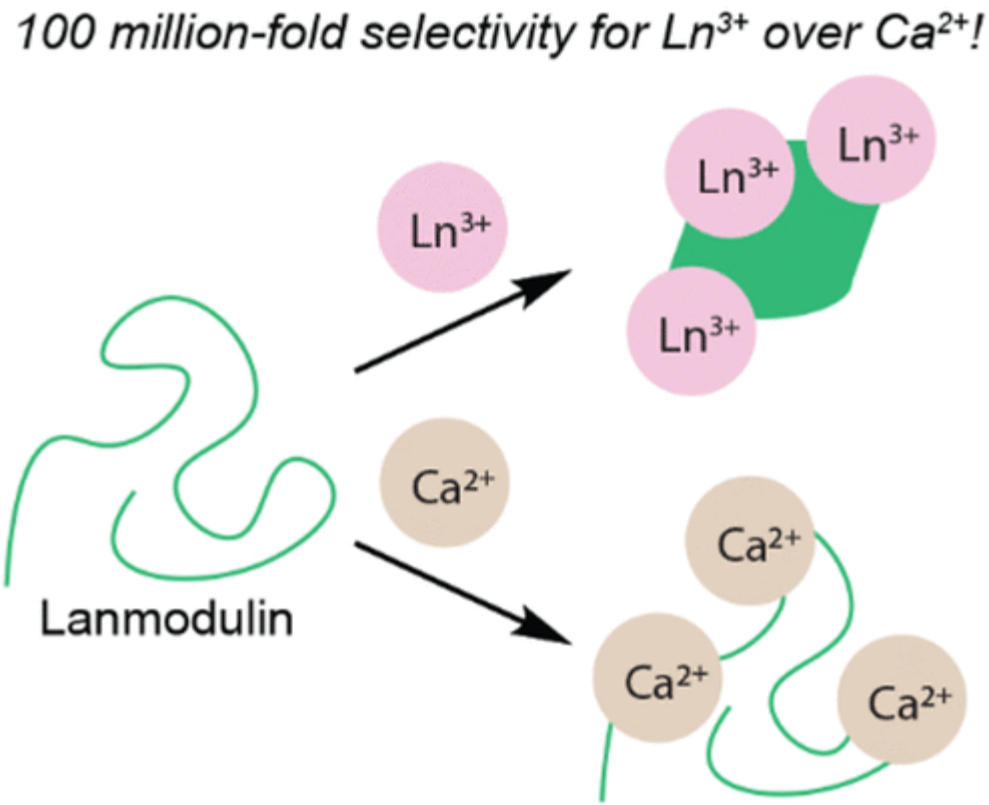


Ln^{3+}-PQQ active site of *methanol dehydrogenase*, MDH

enzimatic activity depends on the nature of Ln^{3+}



Lanmodulin


100 million-fold selectivity for Ln^{3+} over Ca^{2+}!
Ln^{3+}
Ln^{3+}
Ln^{3+}
Ln^{3+}
Ca^{2+}
Ca^{2+}
Ca^{2+}
Ca^{2+}
Lanmodulin