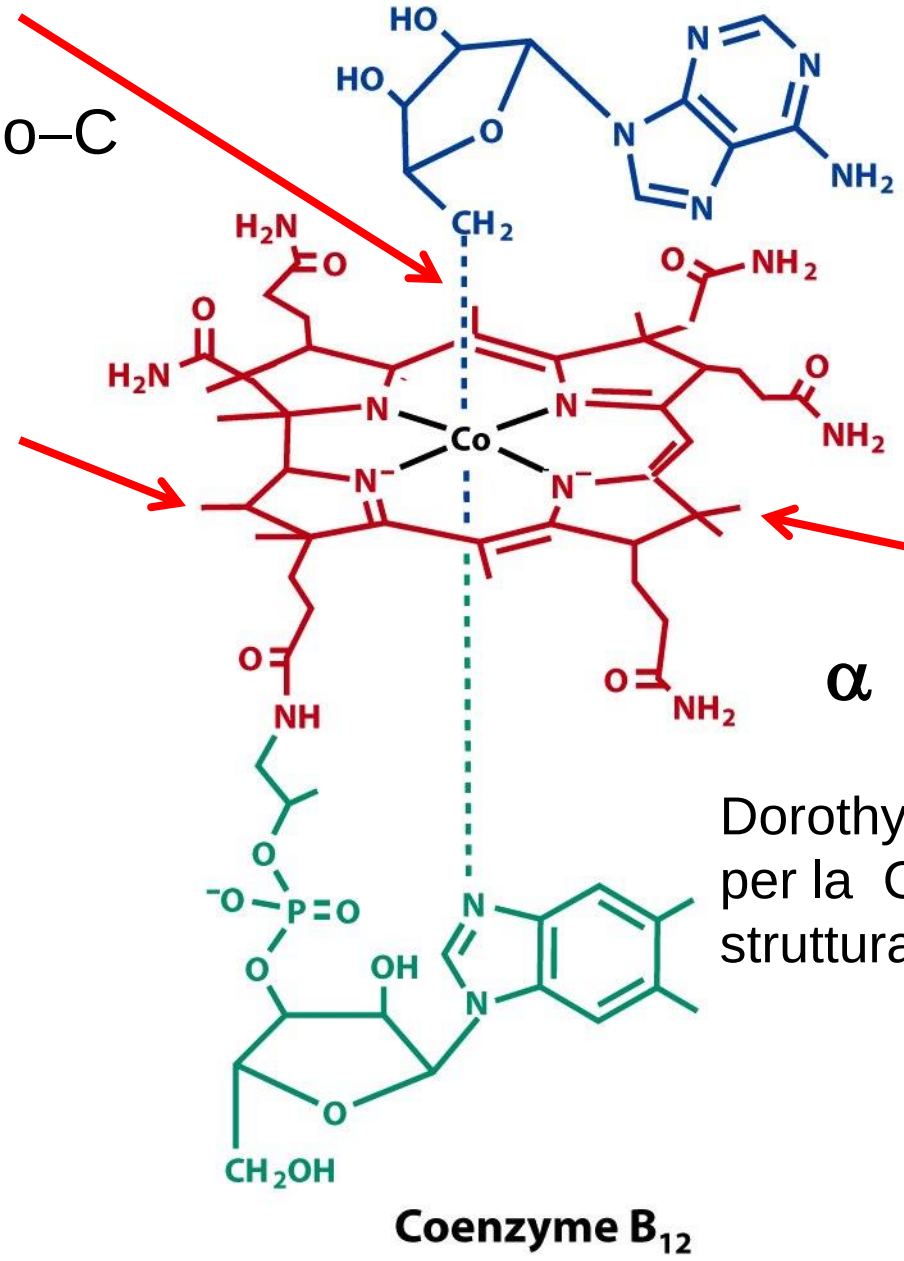
Legame Co–C

1958

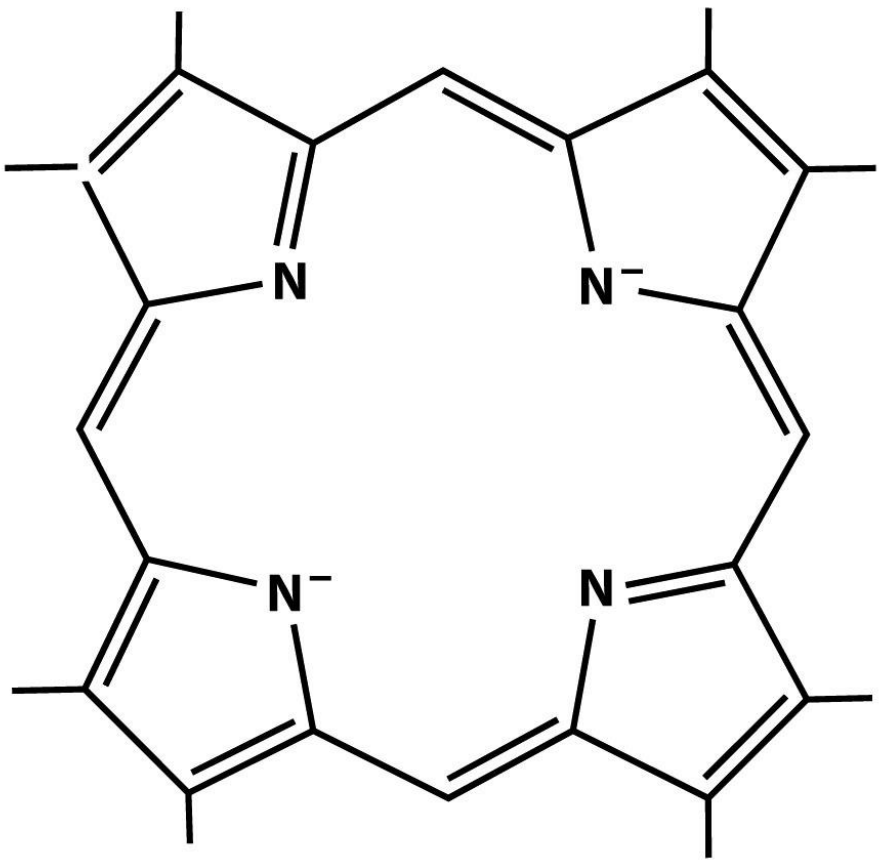


catena amidica

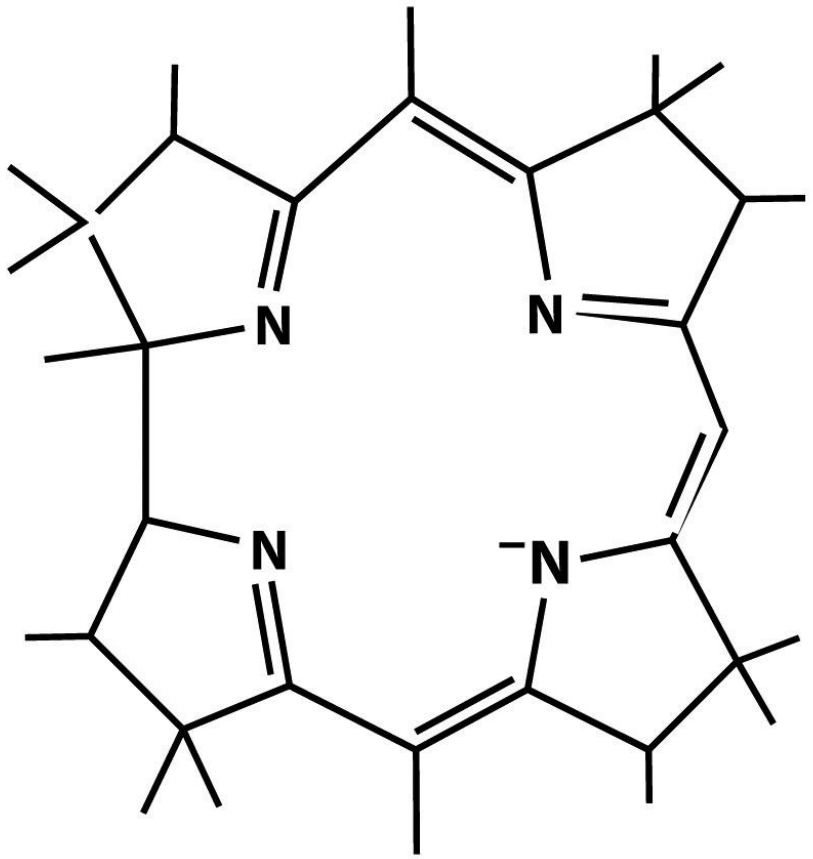
Anello corrinico

Dorothy Hodgkin, premio Nobel per la Chimica nel 1964 per la struttura ai raggi X

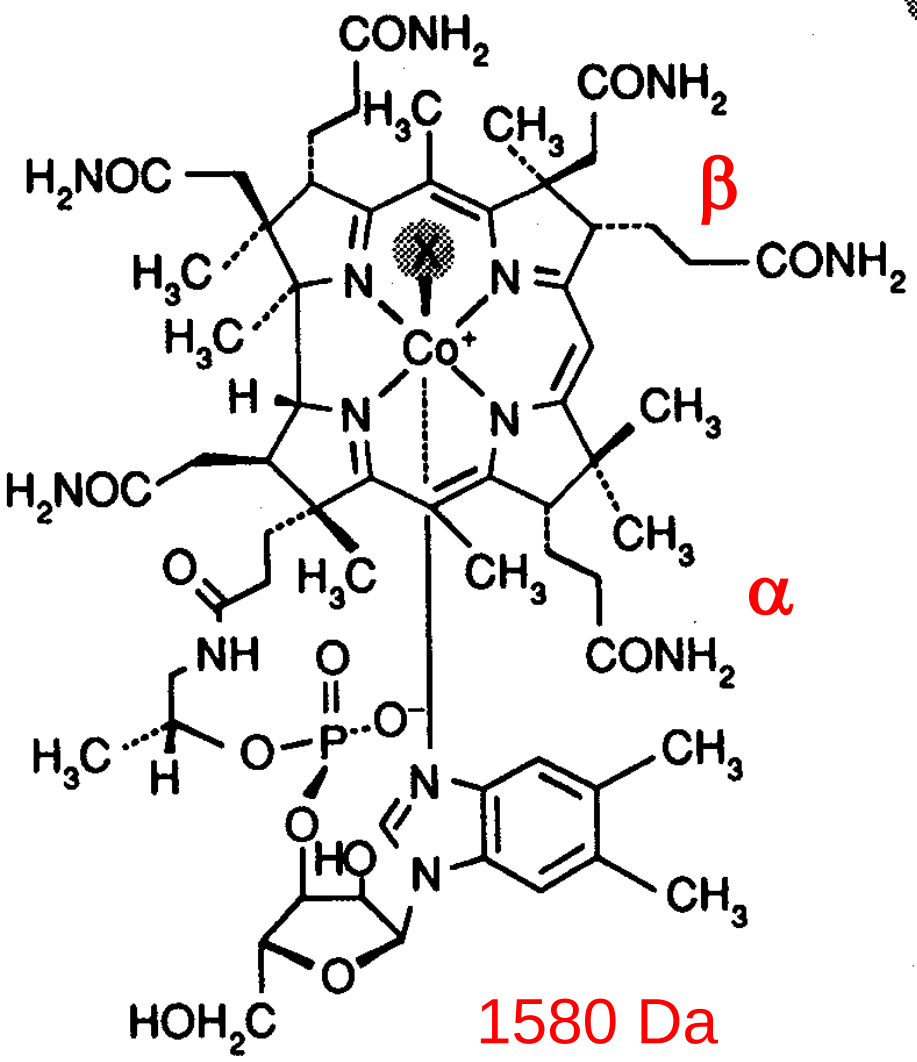
5′-desossiadenosilcobalamina



Porphyrin^{2-}



Corrin^{-}



1580 Da

= CH_3 : methylcobalamin (MeCbl or MeB_{12})

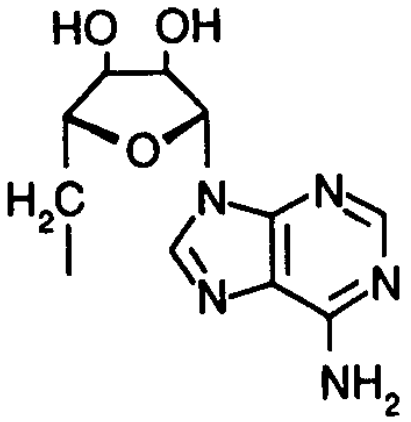
CN : cyanocobalamin (vitamin B_{12})

OH : hydroxycobalamin

H_2O : aquacobalamin

R : 5'-deoxyadenosyl-cobalamin (coenzyme B_{12}, AdoCbl or $AdoB_{12}$)

R = 5'-deoxyadenosyl



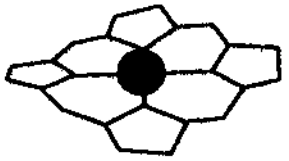
7 catene amidiche laterali,
9 centri chirali

in-plane coordination
(side view)

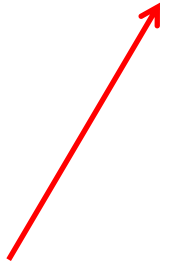
out-of-plane coordination
(side view)

'doming' of the
macrocycle

saddle-shaped
macrocycle



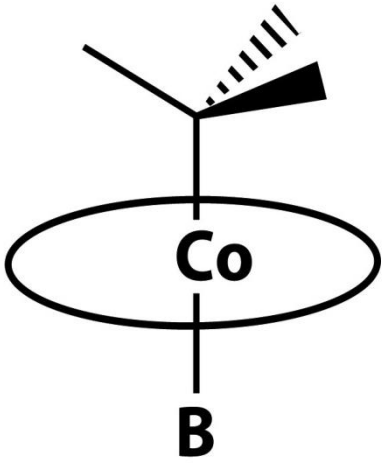
'ruffling' of the
macrocycle



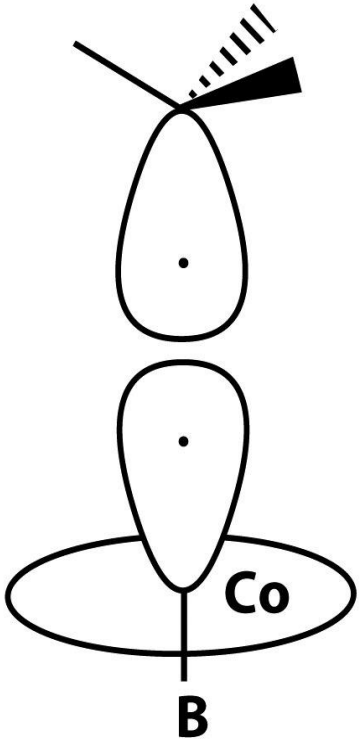
Distorsione nelle cobalamine

Co sempre basso spin

Co(III) d^6



C. N. = 6

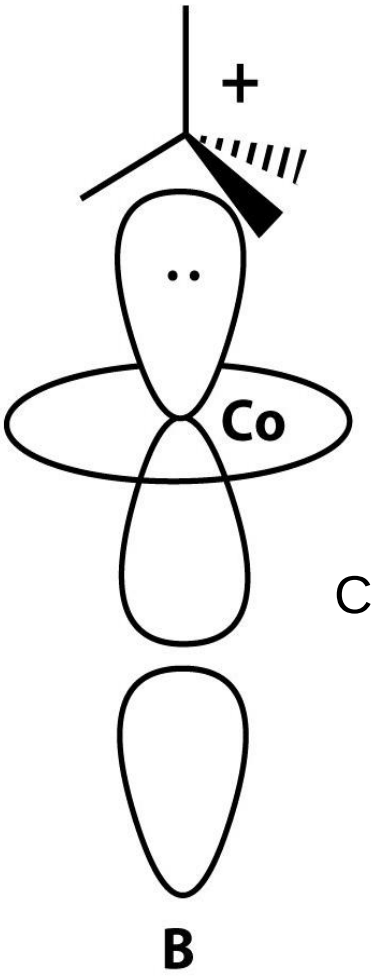


Co(II) d^7

C. N. = 5

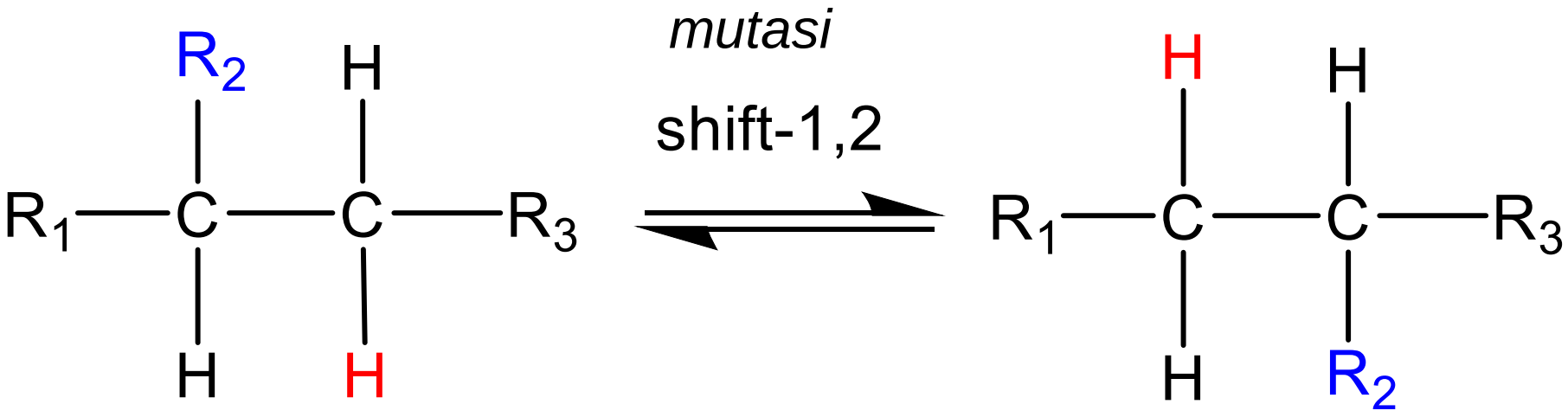
supernucleofilo

Co(I) d^8



C. N. = 4

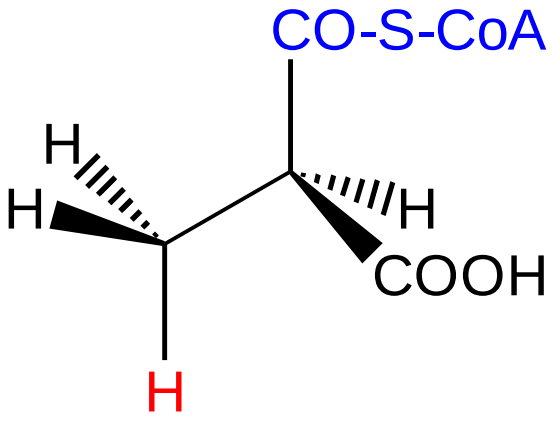
Reazioni catalizzate dal coenzima B_{12}



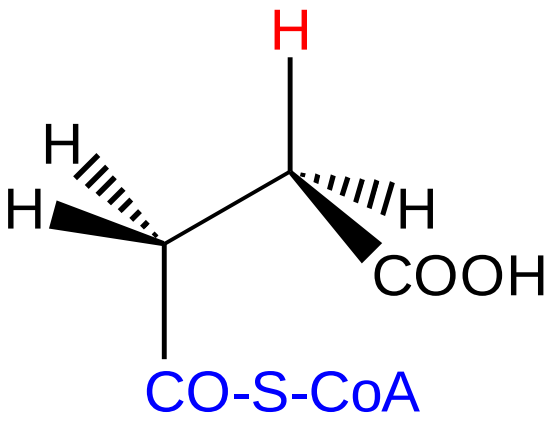
Enzima	**R_1**	**R_2**	**R_3**
Diolo deidratasi	CH_3	OH	OH
Etanolamina deaminasi	H	NH_2	OH
Glutammato mutasi	H	$CH(NH_2)COOH$	COOH
Glicerolo deidratasi	CH_2OH	OH	OH

MetilMalonil-Coenzima A-Mutasi

(*succinil-CoA necessario nel ciclo di Krebs*)

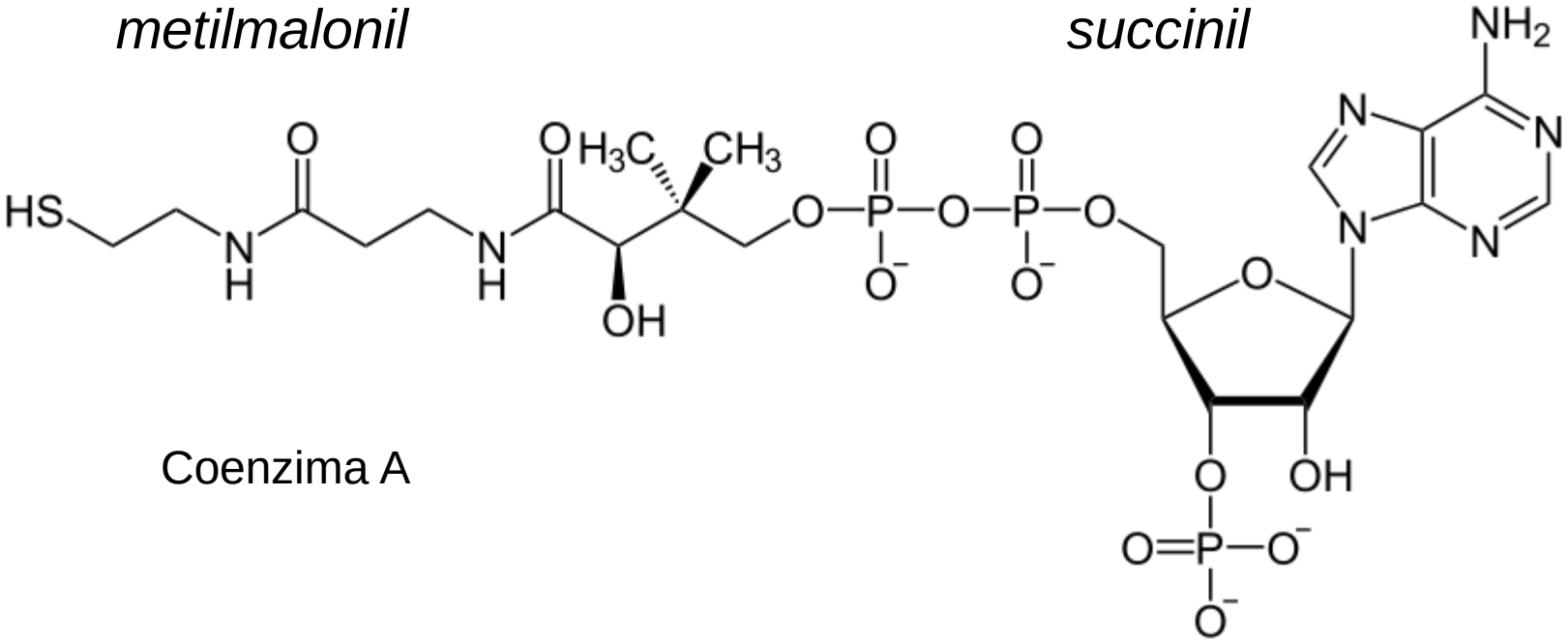


MMCM

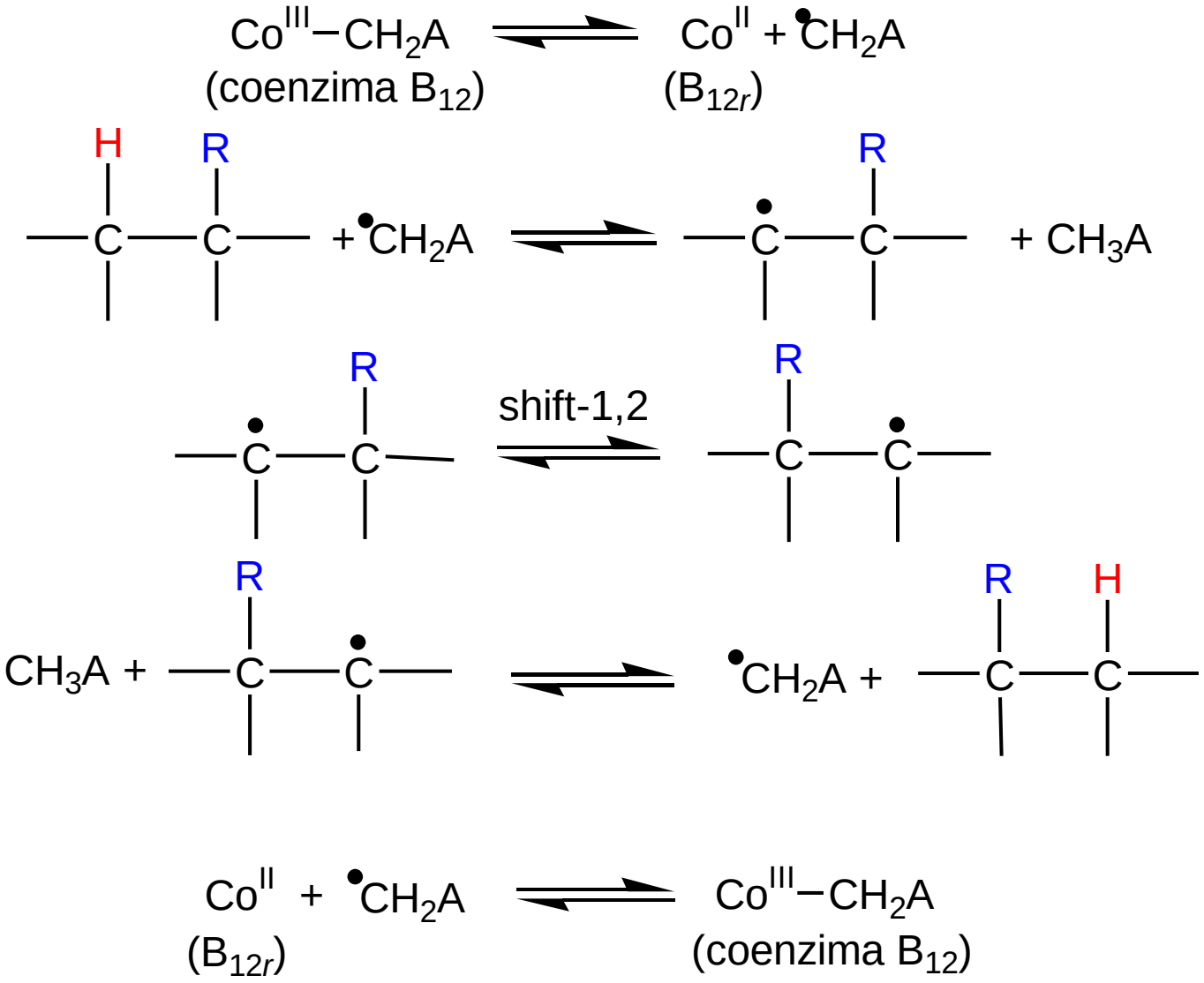


metilmalonil

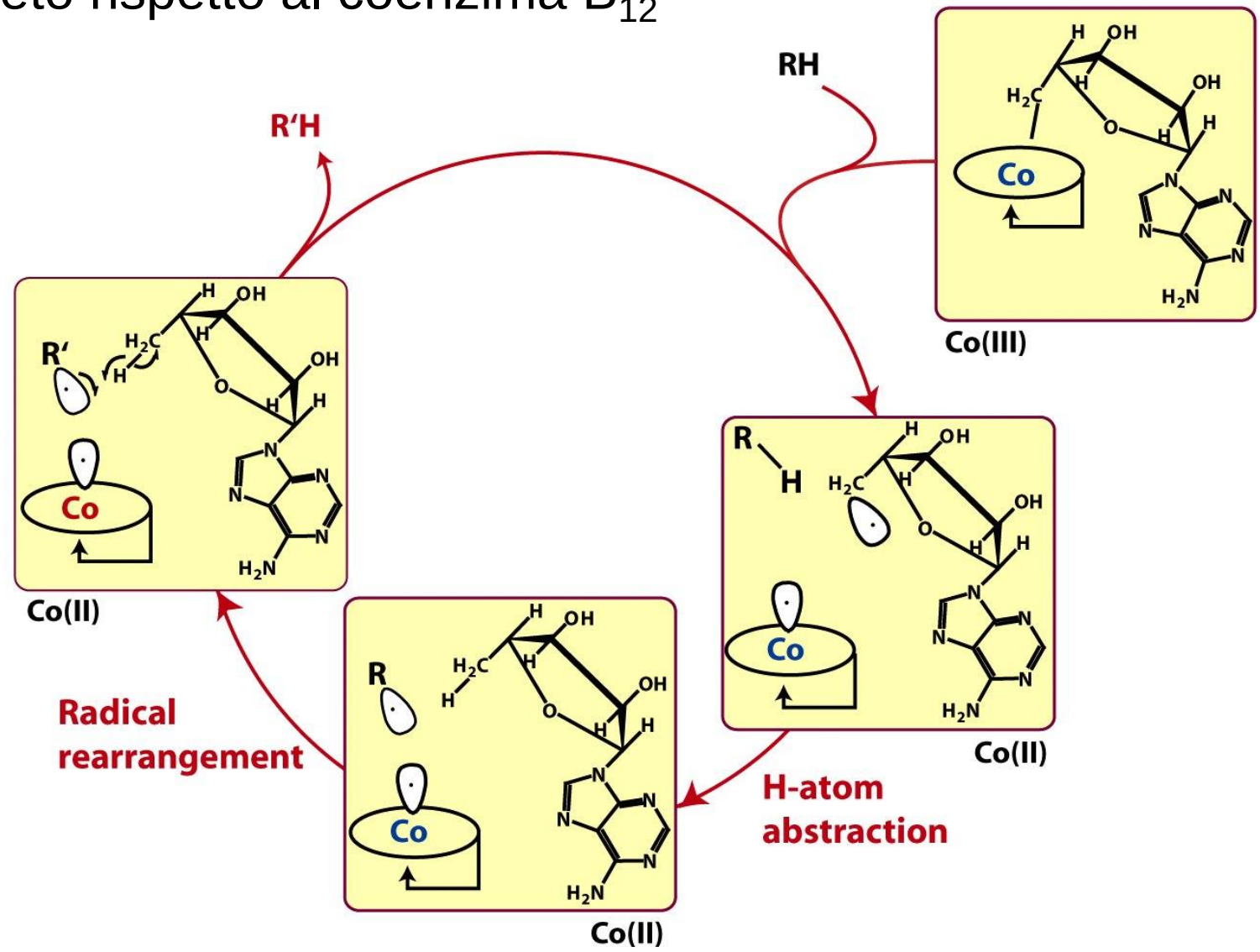
succinil



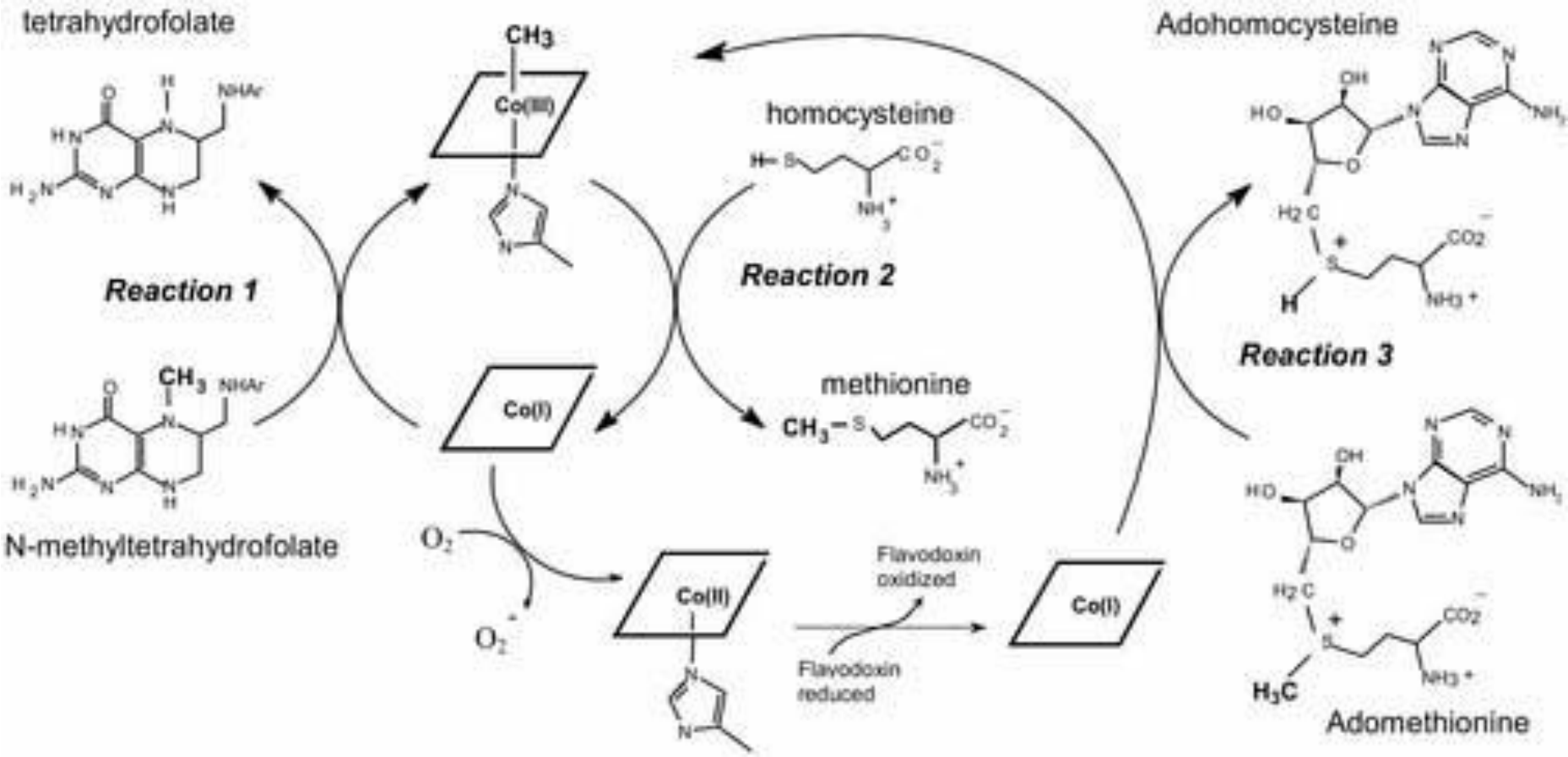
Coenzima A


Co^III–CH2A
(coenzima B12)
Co^II + •CH2A
(B12r)
H
R
•CH2A
+ CH3A
shift-1,2
CH3A +
•CH2A +
Co^II + •CH2A
(B12r)
Co^III–CH2A
(coenzima B12)

La rottura del legame Co–C è 10^{12} volte più veloce nell'enzima completo rispetto al coenzima B_{12}



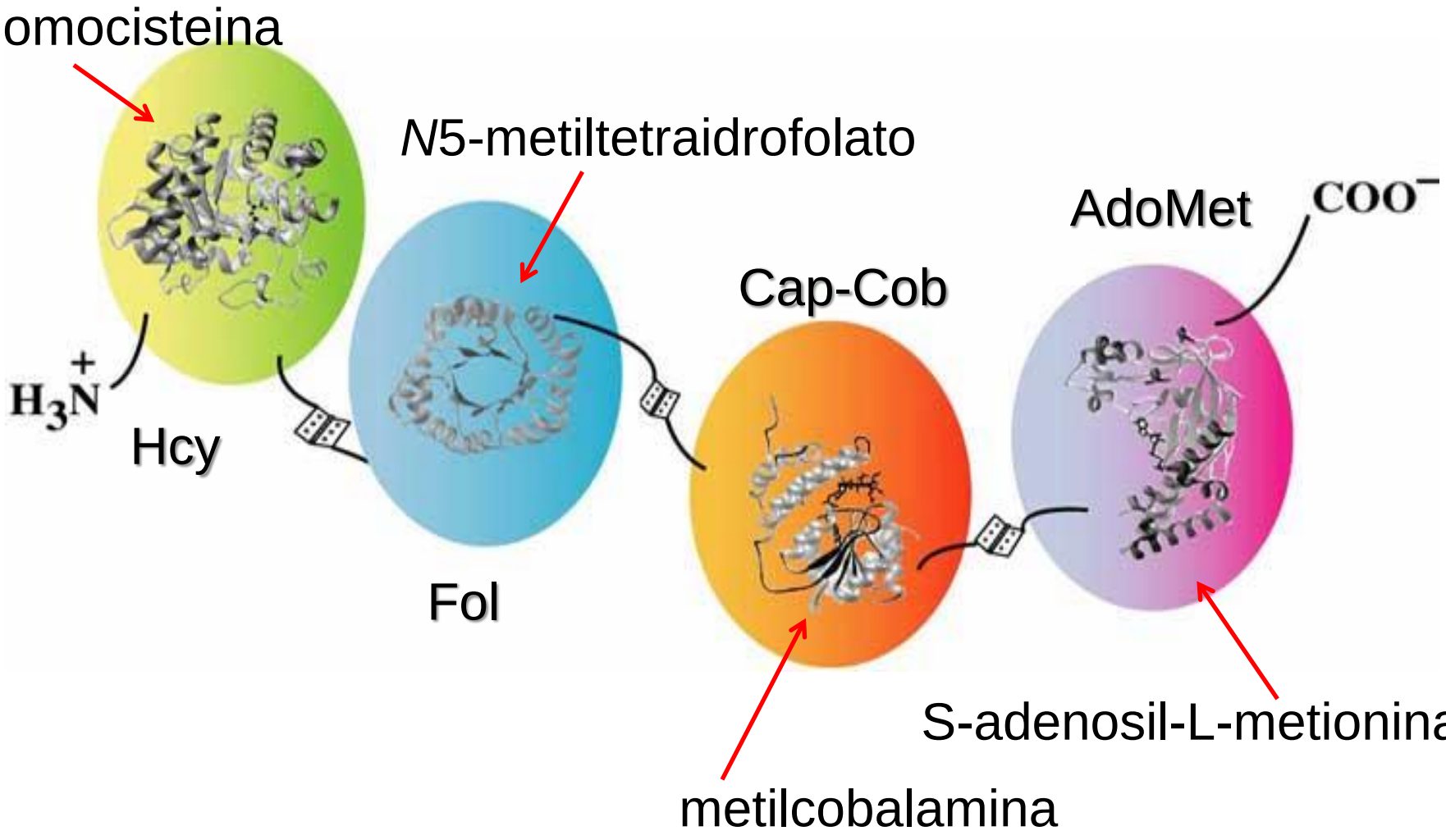
Metilcobalamina: cofattore della Metionina Sintasi



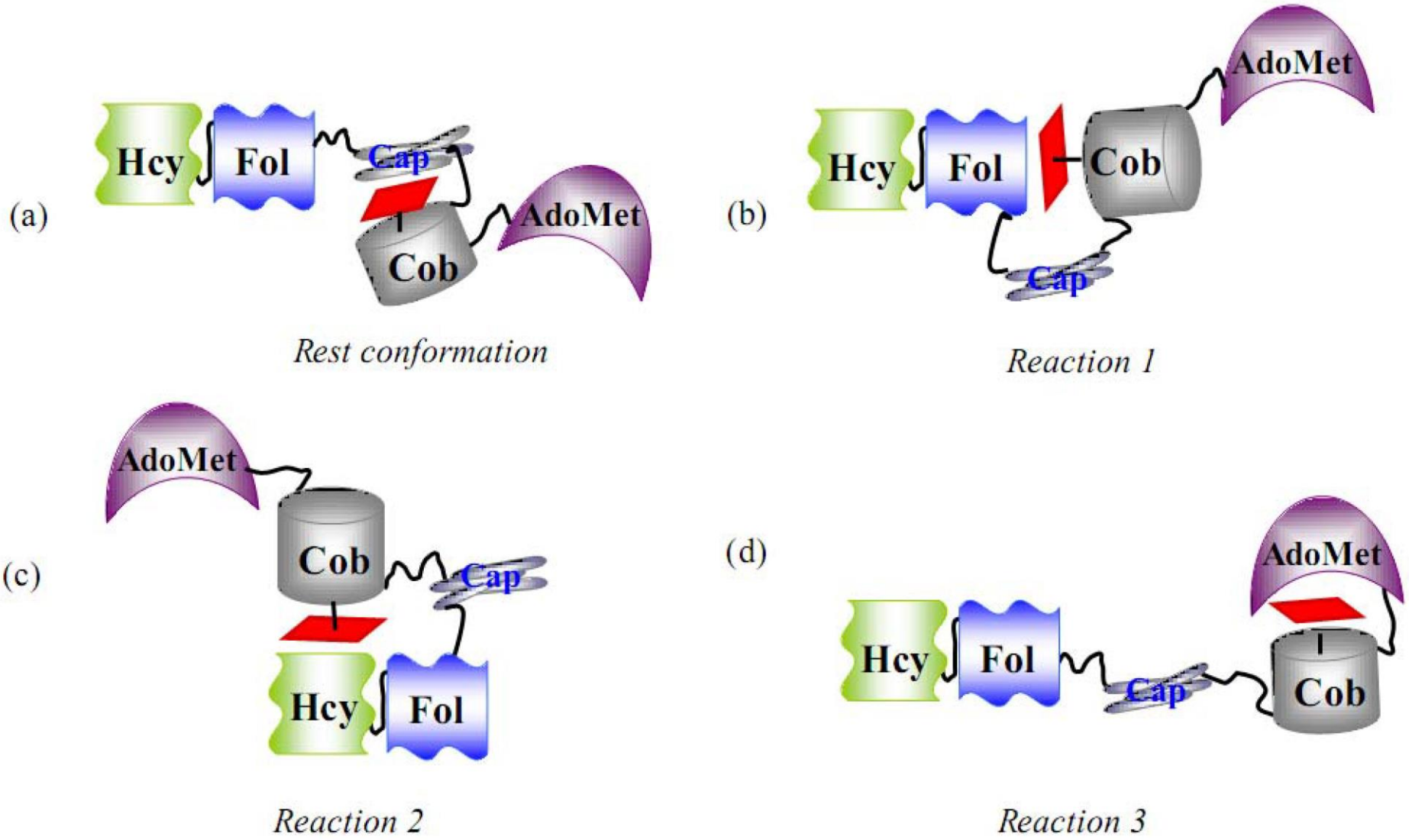
S-adenosil-L-metionina

Metile traferito come CH_3^+

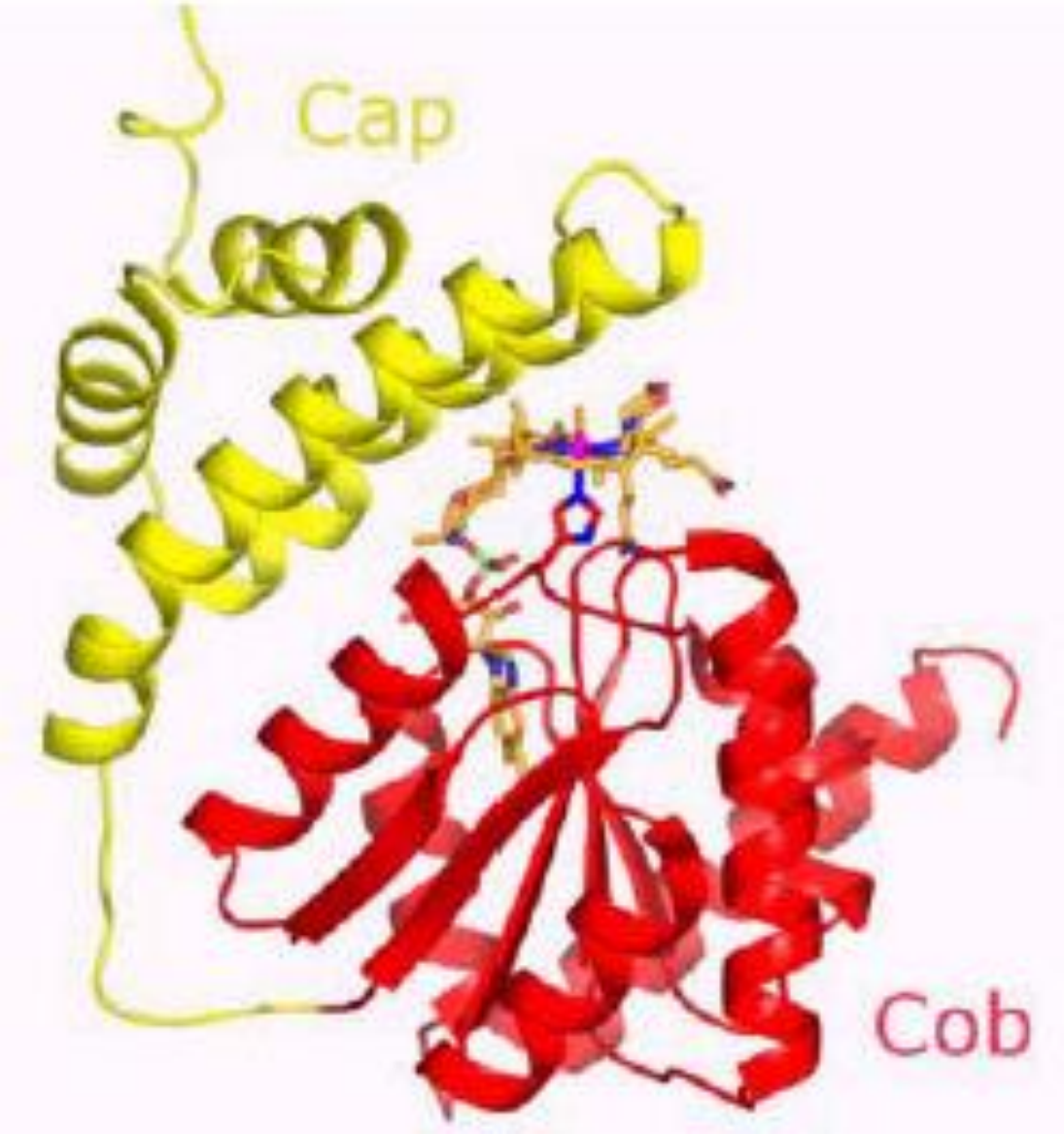
Metionina Sintasi



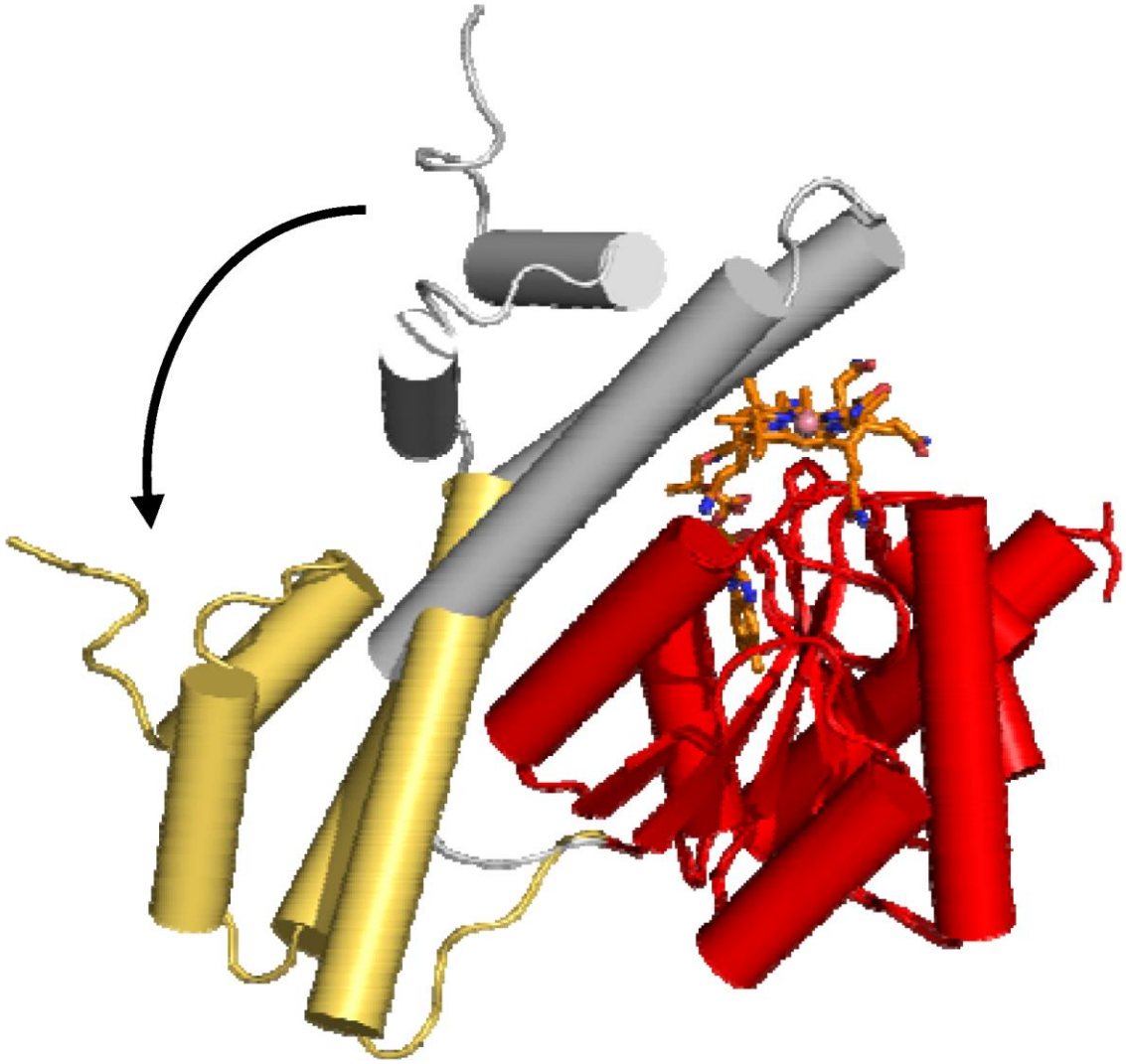
Variazioni conformazionali della metionina sintasi



Metilcobalamina in Cap-Cob: *base-off/His-on*



Variazioni conformazionali in Cap-Cob

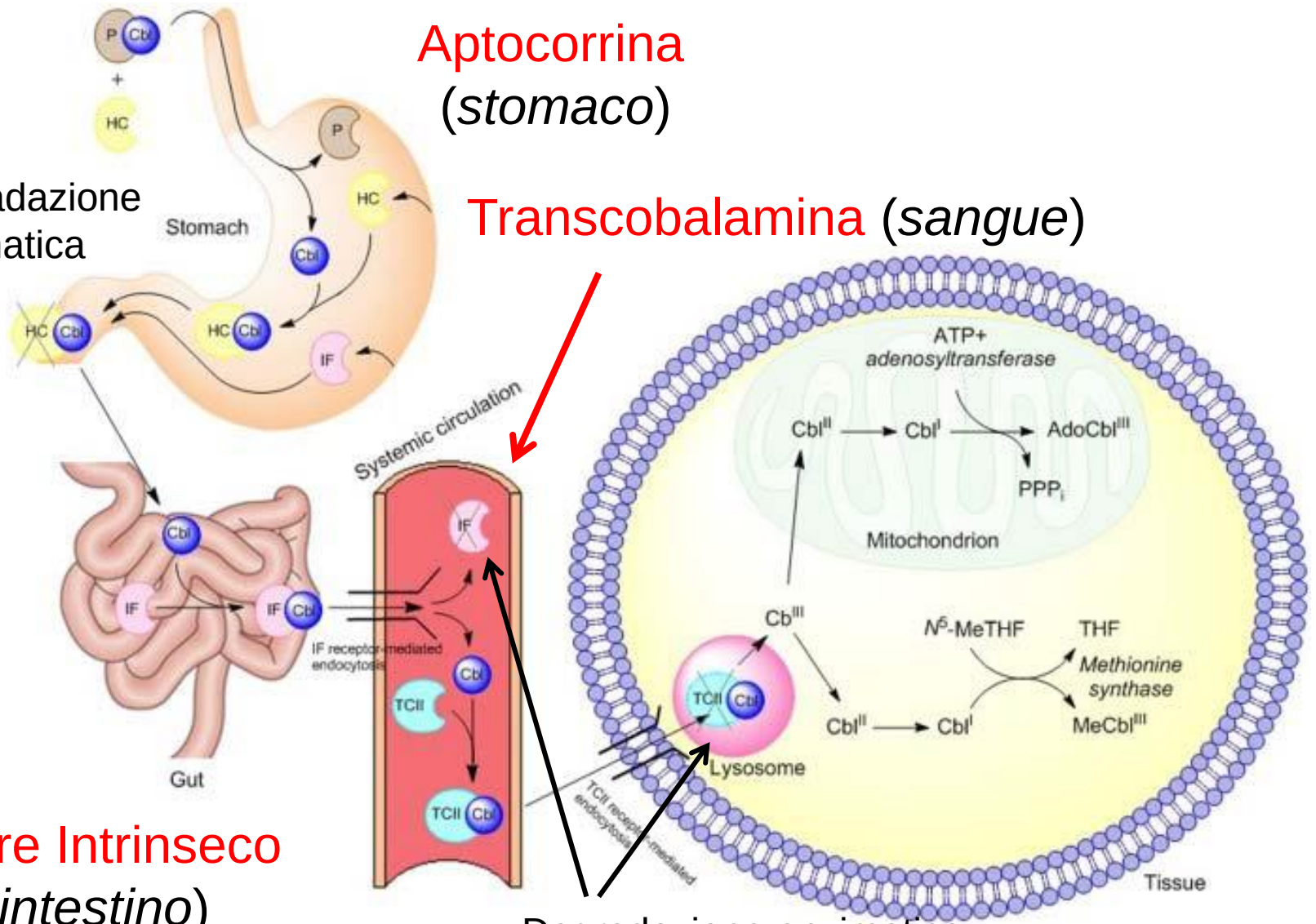


Uptake e Trasporto della Cobalamina

Aptocorrina
(*stomaco*)

Degradazione
enzimatica

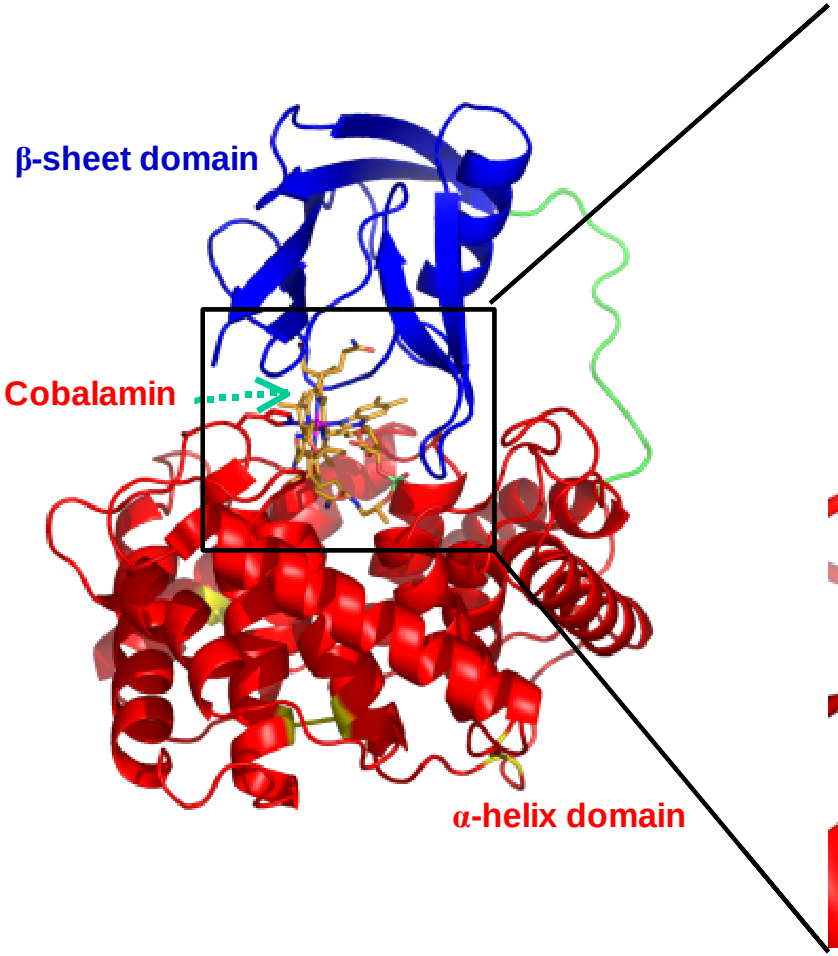
Transcobalamina (*sangue*)

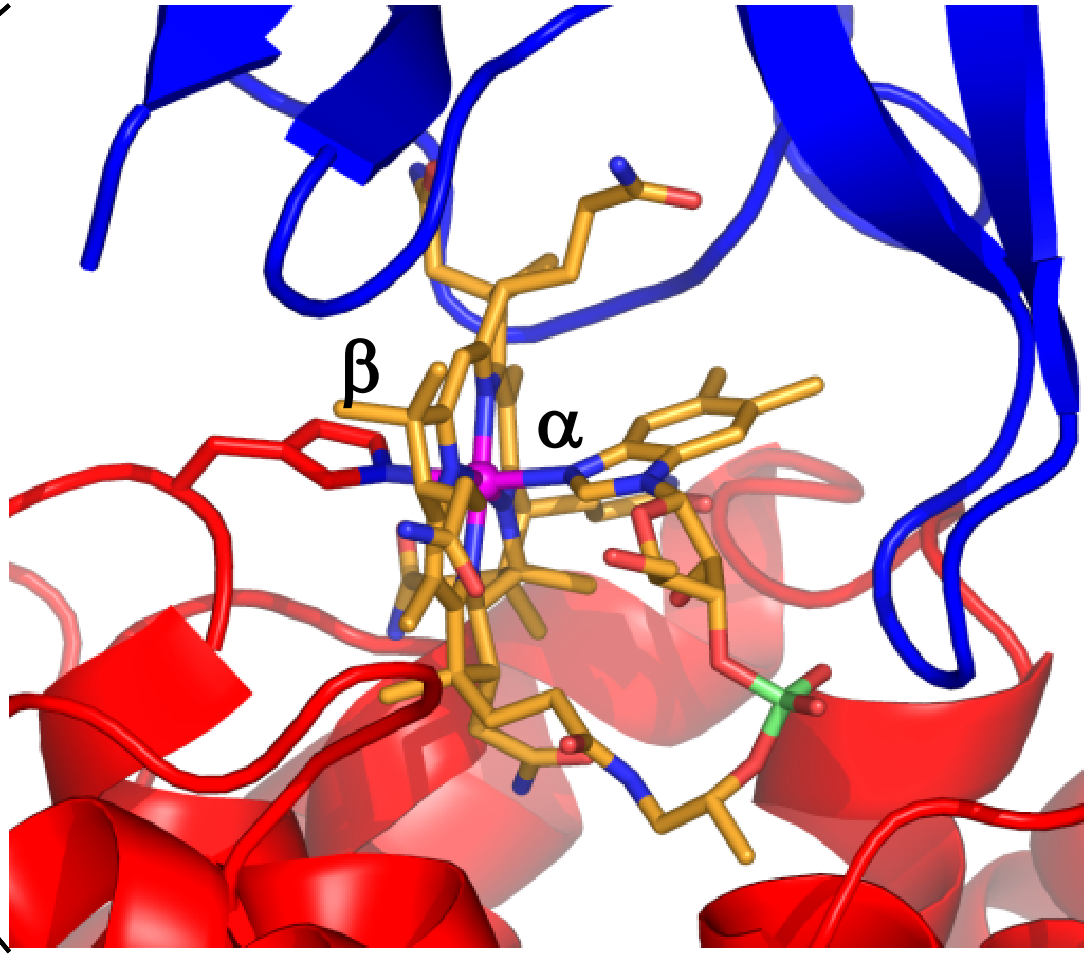


Fattore Intrinseco
(*intestino*)

Degradazione enzimatica
lisosomiale

Struttura TC+Cobalamina (2006)

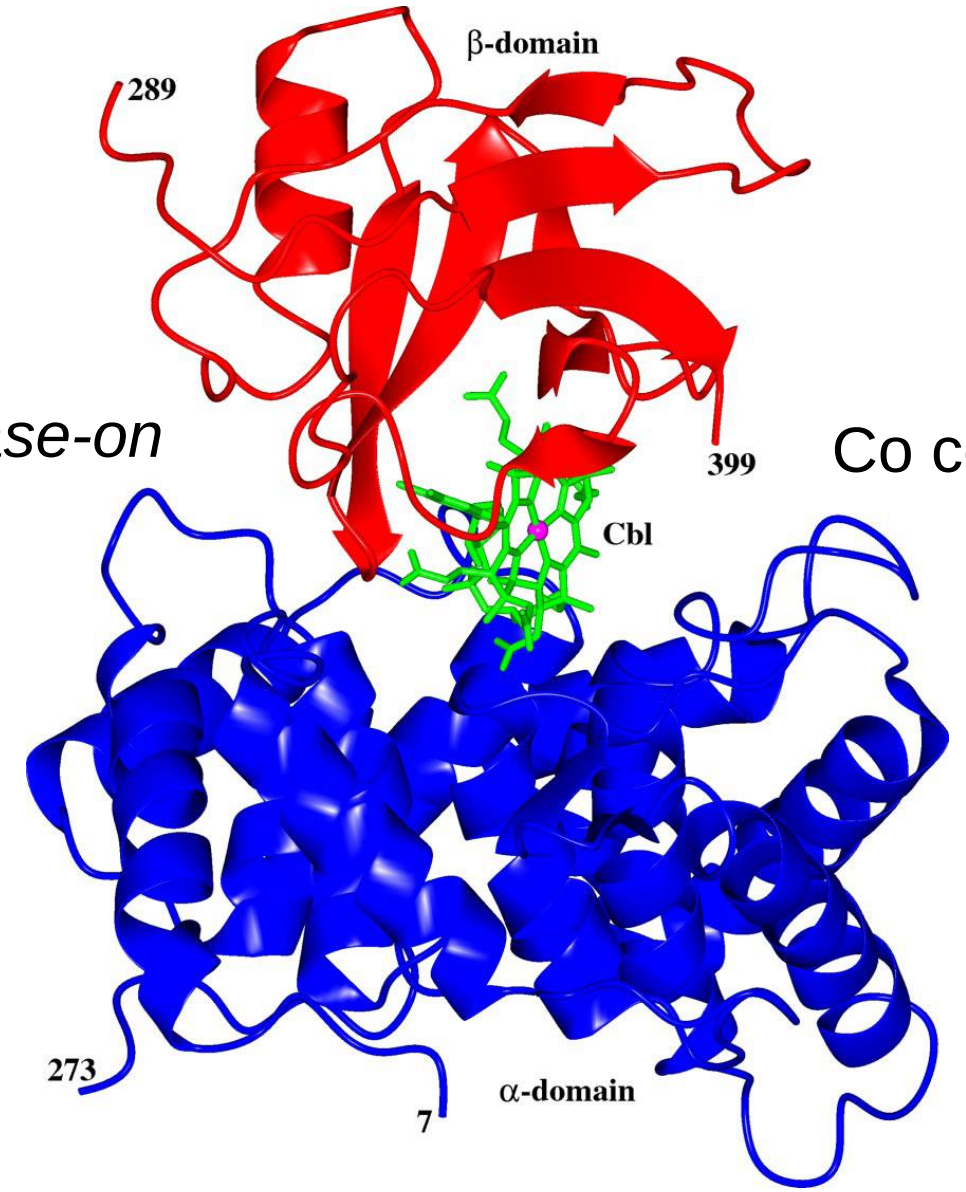




Coordinazione *base-on/His-on* (su β)

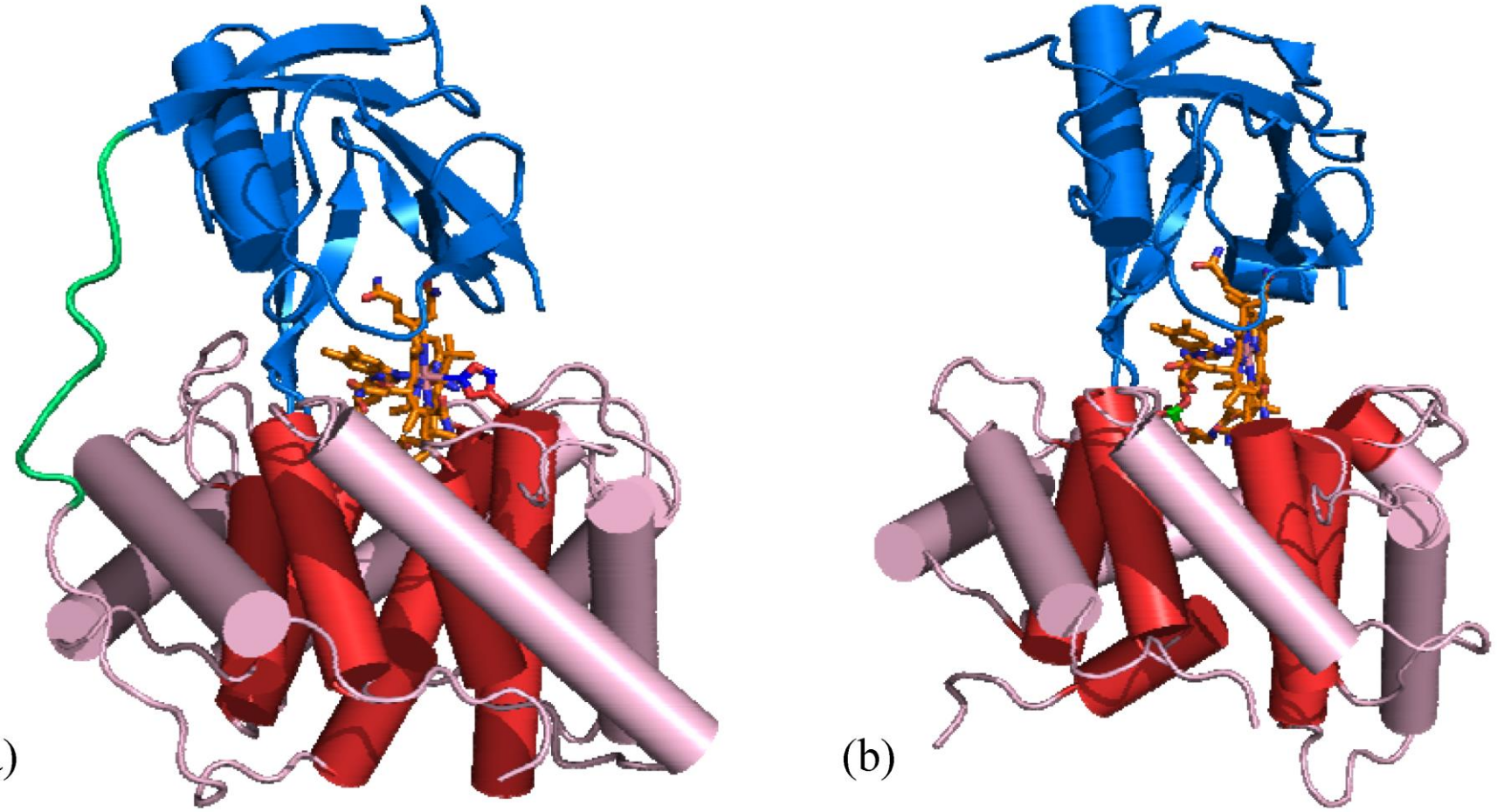
Complesso IF-Cbl (2007)

Coordinazione *base-on*



Co come Co(II)

Confronto fra le strutture di TC-Cbl (a) e IF-Cbl (b)



Addotto IF-Cbl con CUB_{5-8} recettori della cubilina