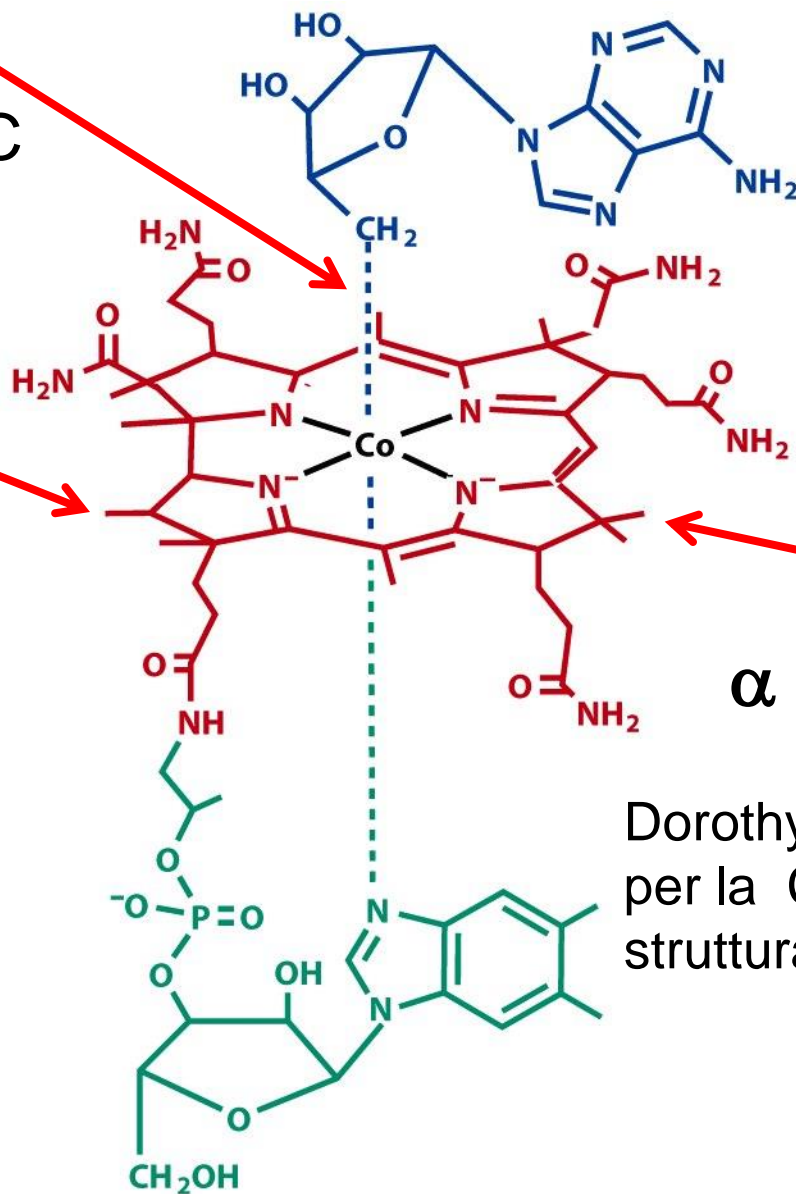


Legame Co-C

1958

catena amidica
(errore nel
disegno)



β

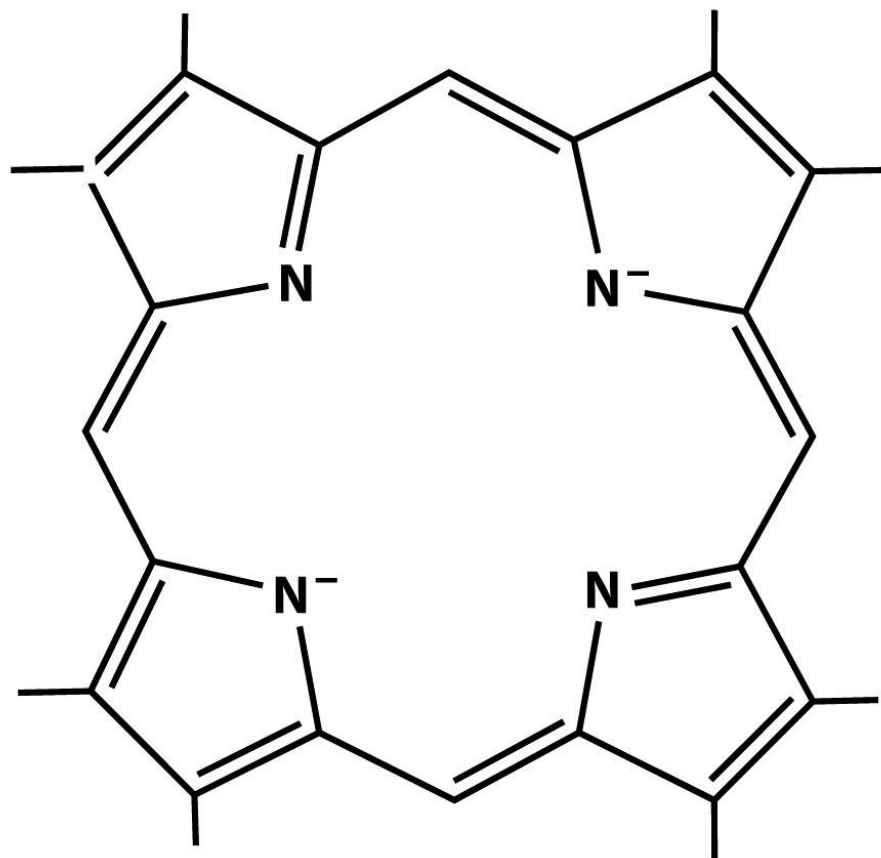
Anello corrinico

α

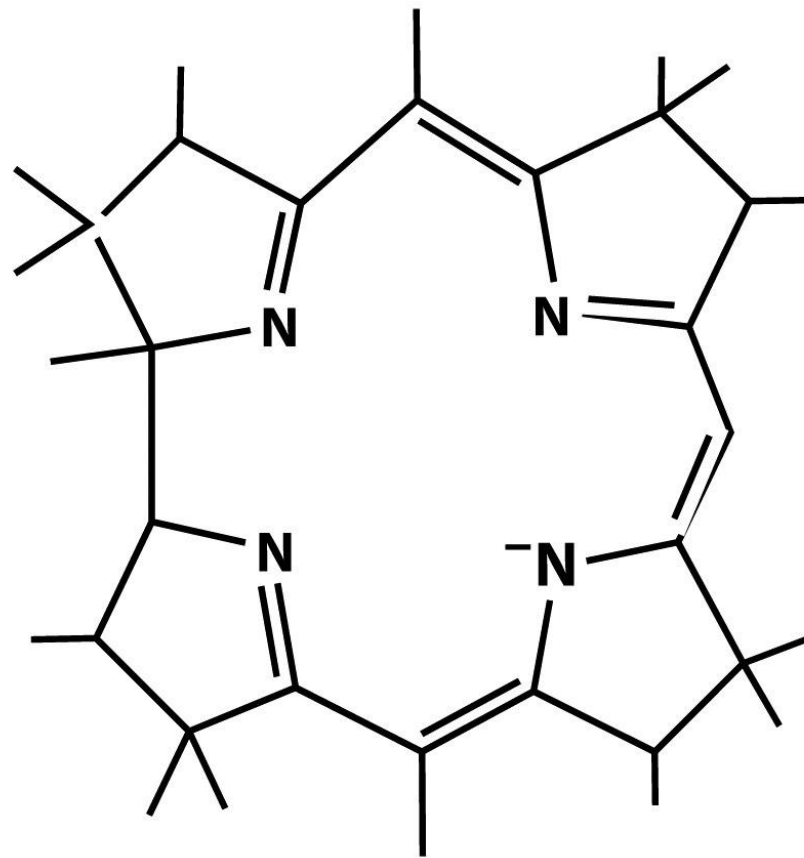
Dorothy Hodgkin, premio Nobel
per la Chimica nel 1964 per la
struttura ai raggi X

Coenzyme B₁₂

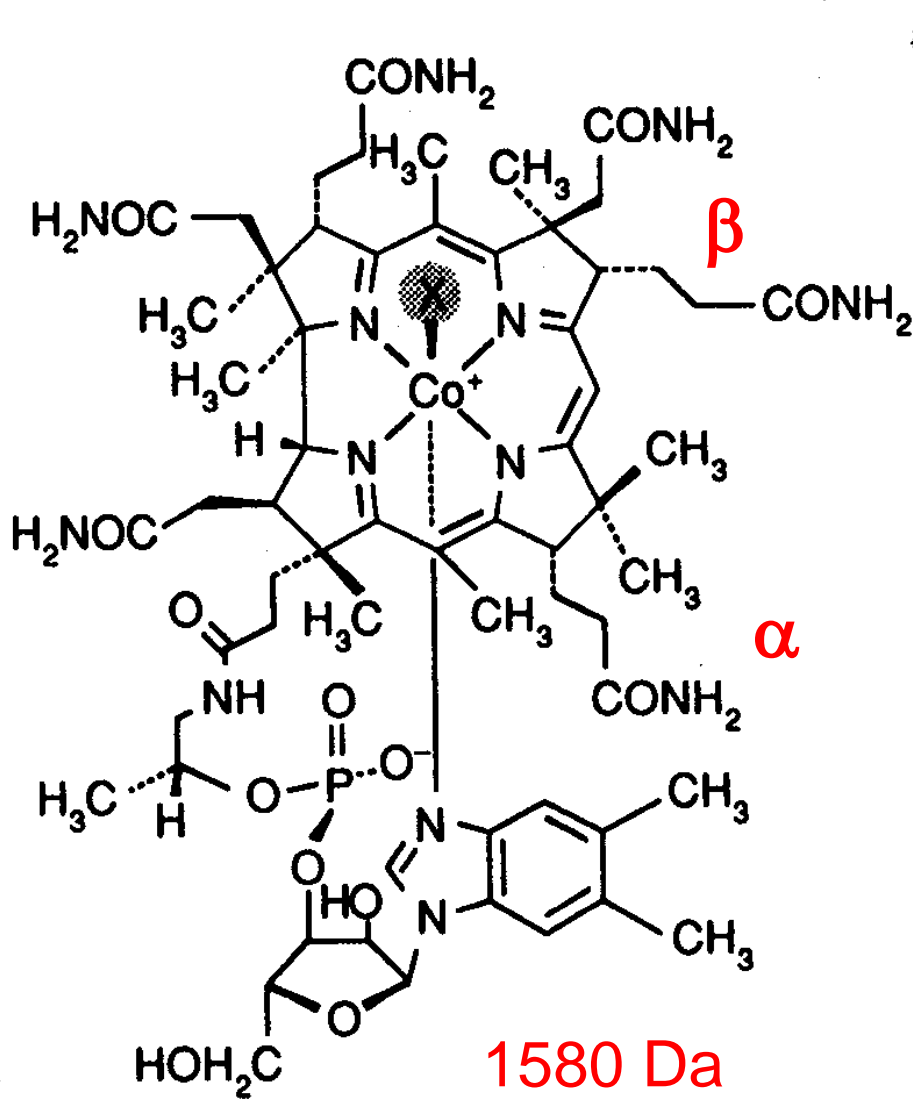
5'-desossiadenosilcobalamina




Porphyrin²⁻

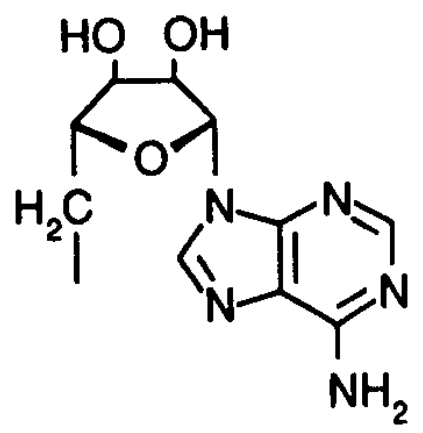


Corrin¹⁻



-  = CH₃ : methylcobalamin (MeCbl or MeB₁₂)
- CN : cyanocobalamin (vitamin B₁₂)
- OH : hydroxycobalamin
- H₂O : aquacobalamin
- R : 5'-deoxyadenosylcobalamin (coenzyme B₁₂, AdoCbl or AdoB₁₂)

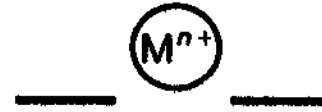
R = 5'-deoxyadenosyl



7 catene amidiche laterali,
9 centri chirali



in-plane coordination
(side view)



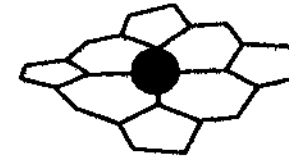
out-of-plane coordination
(side view)



'doming' of the
macrocycle



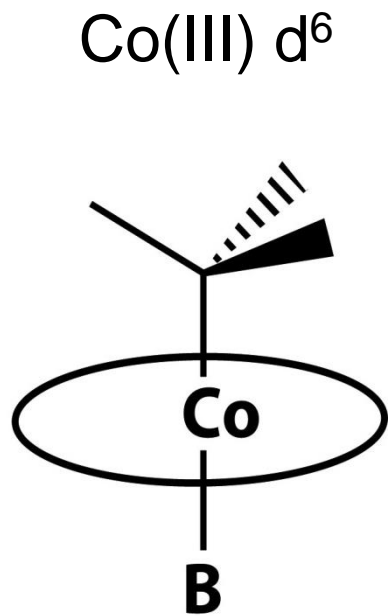
saddle-shaped
macrocycle



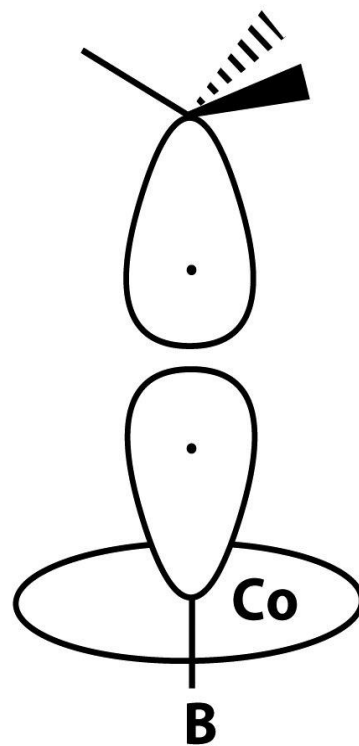
'ruffling' of the
macrocycle

Distorsione nelle cobalamine

Co sempre basso spin



C. N. = 6

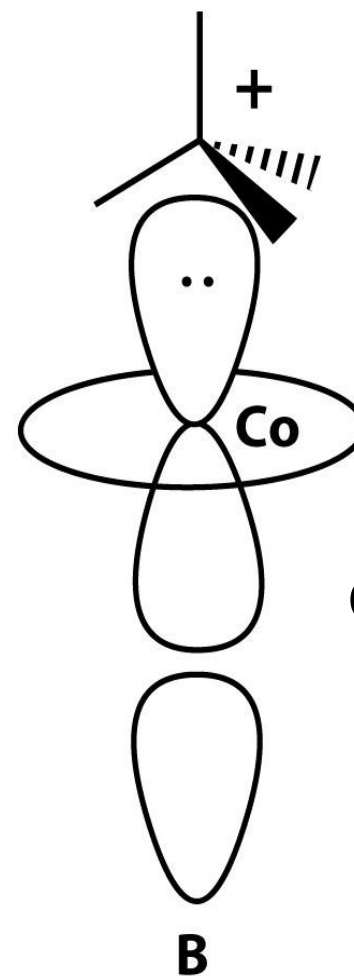


Co(II) d^7

C. N. = 5

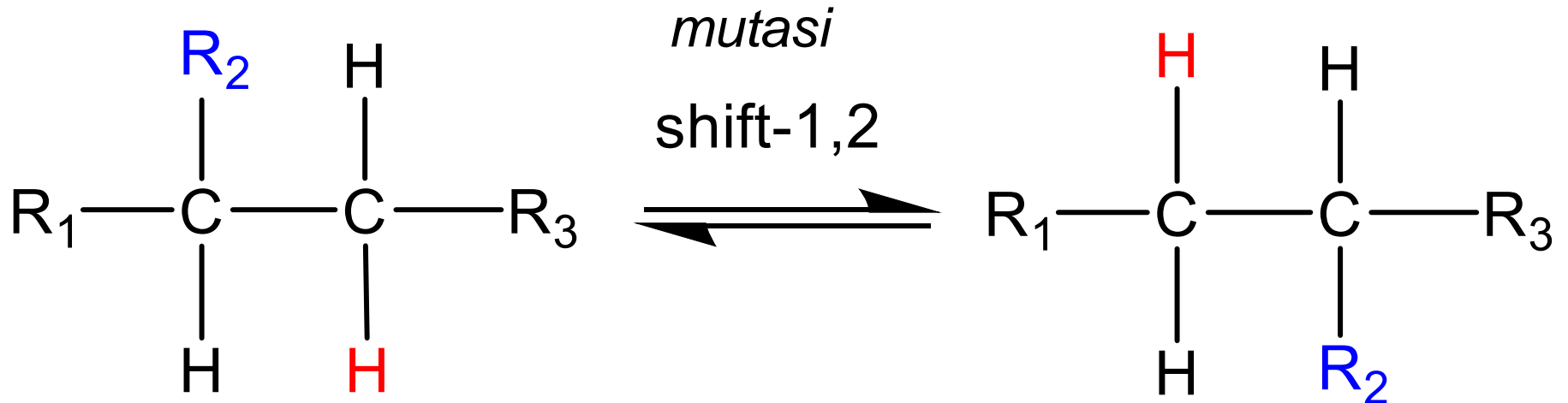
supernucleofilo

Co(I) d^8



C. N. = 4

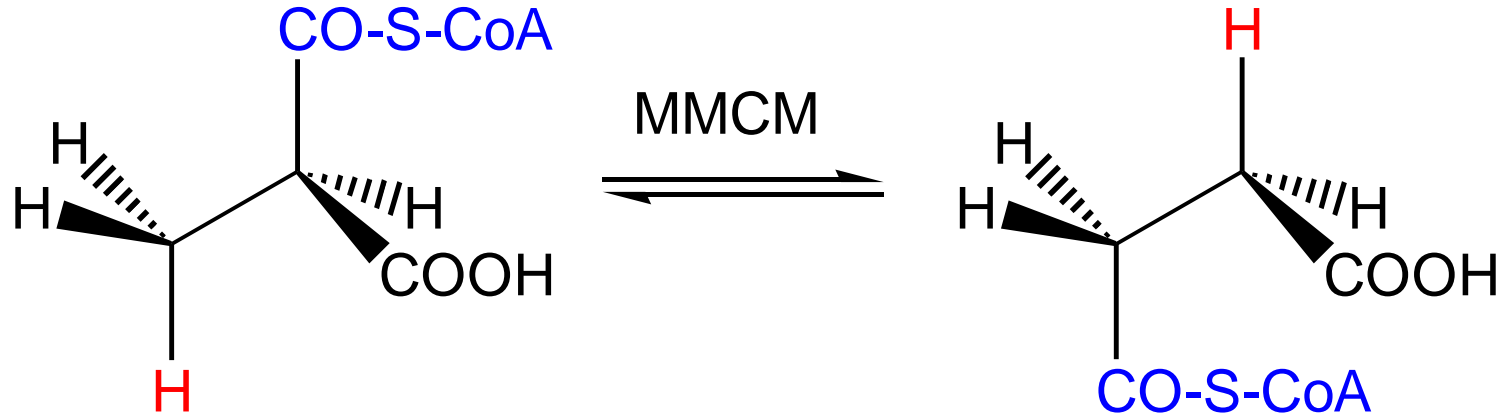
Reazioni catalizzate dal coenzima B₁₂



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)COO H	COOH
Glicerolo deidratasi	CH ₂ OH	OH	OH

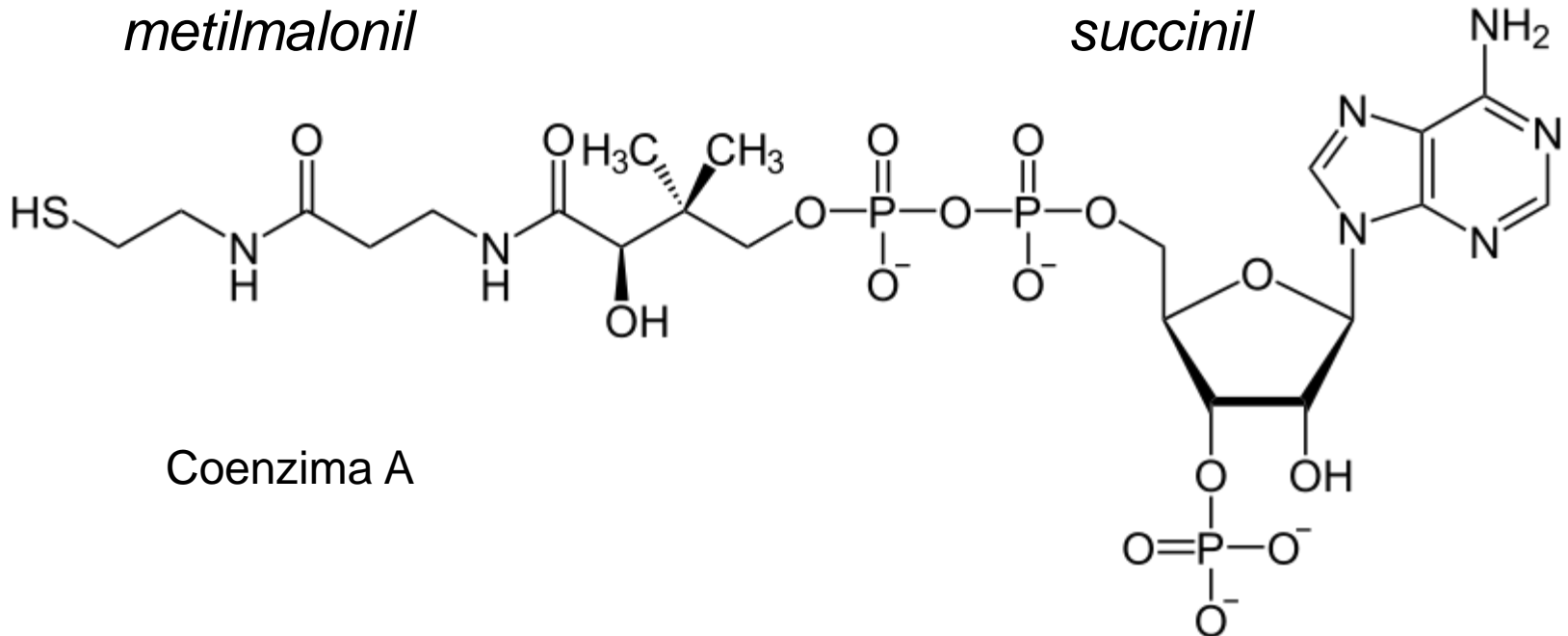
MetilMalonil-Coenzima A-Mutasi

(succinil-CoA necessario nel ciclo di Krebs)

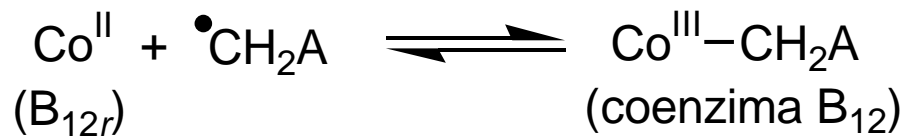
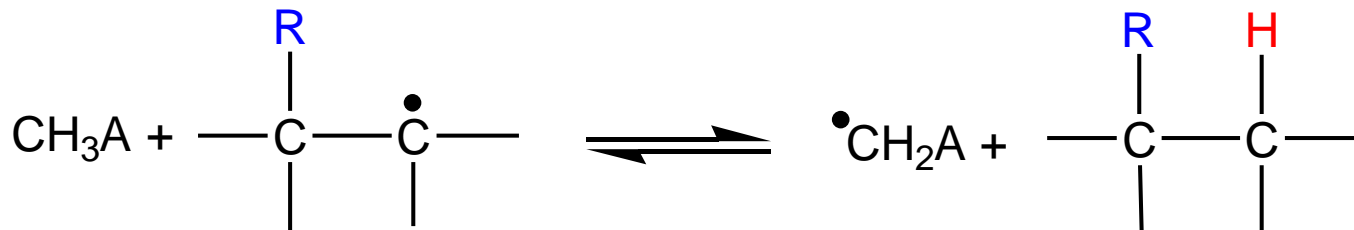
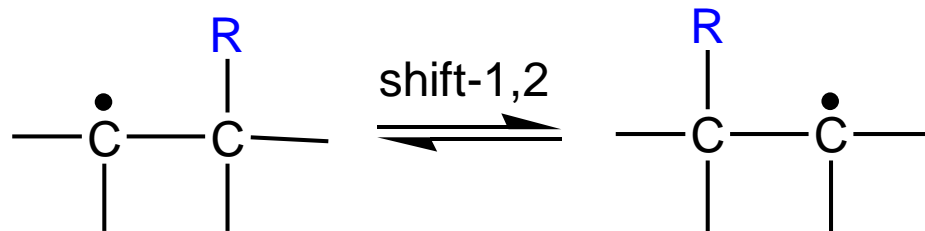
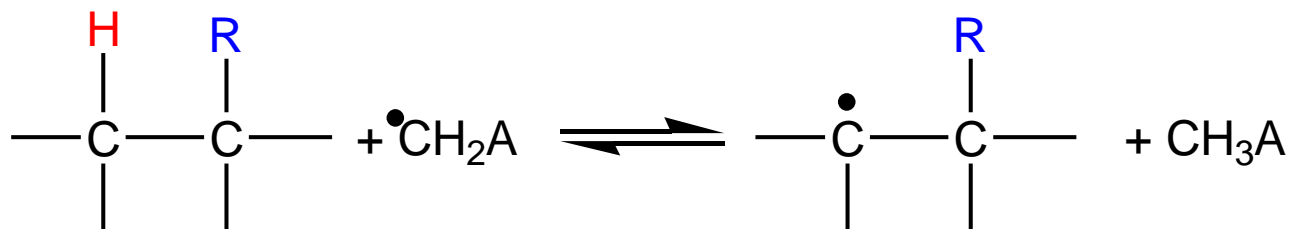
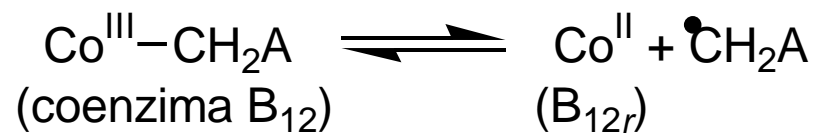


metilmalonil

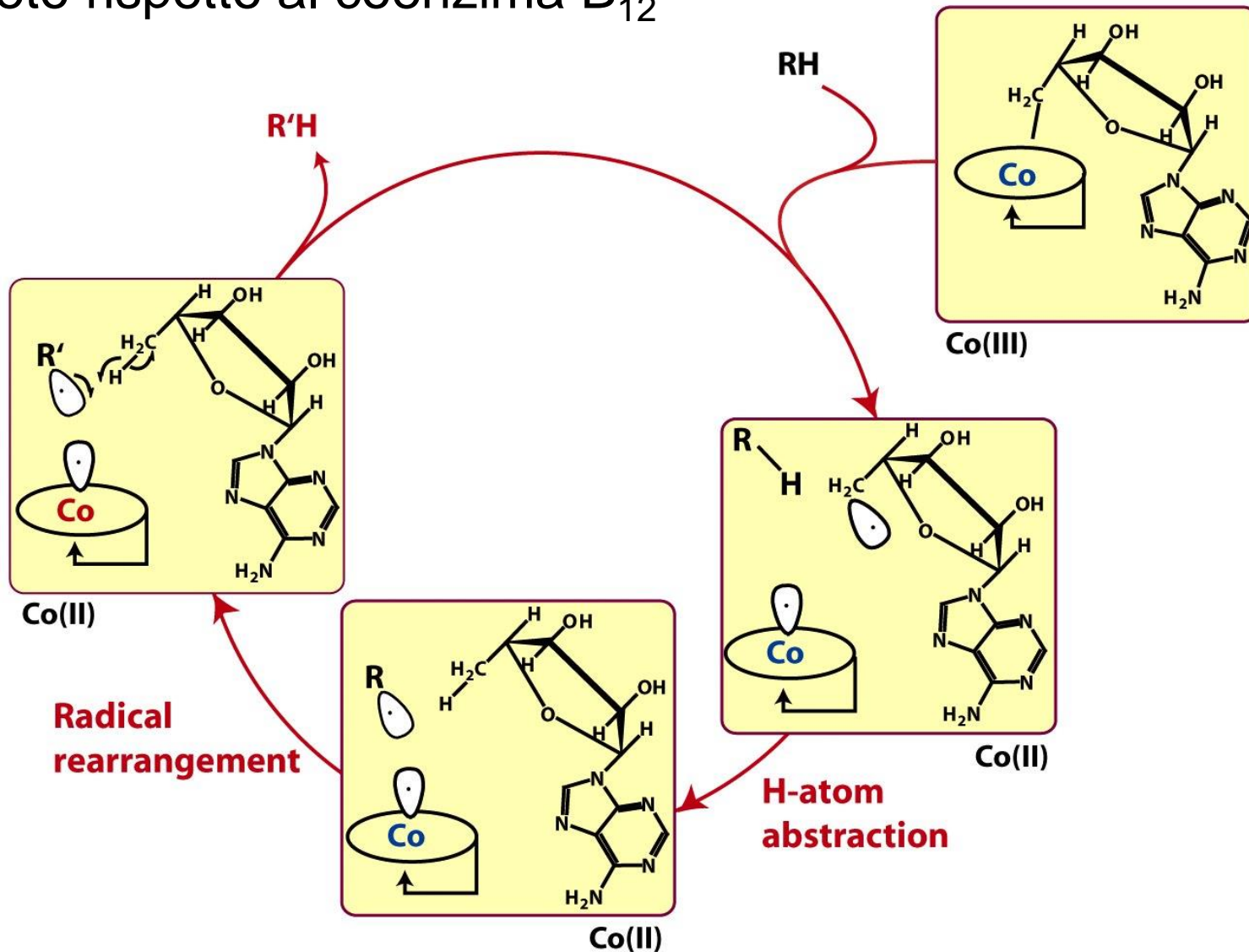
succinil



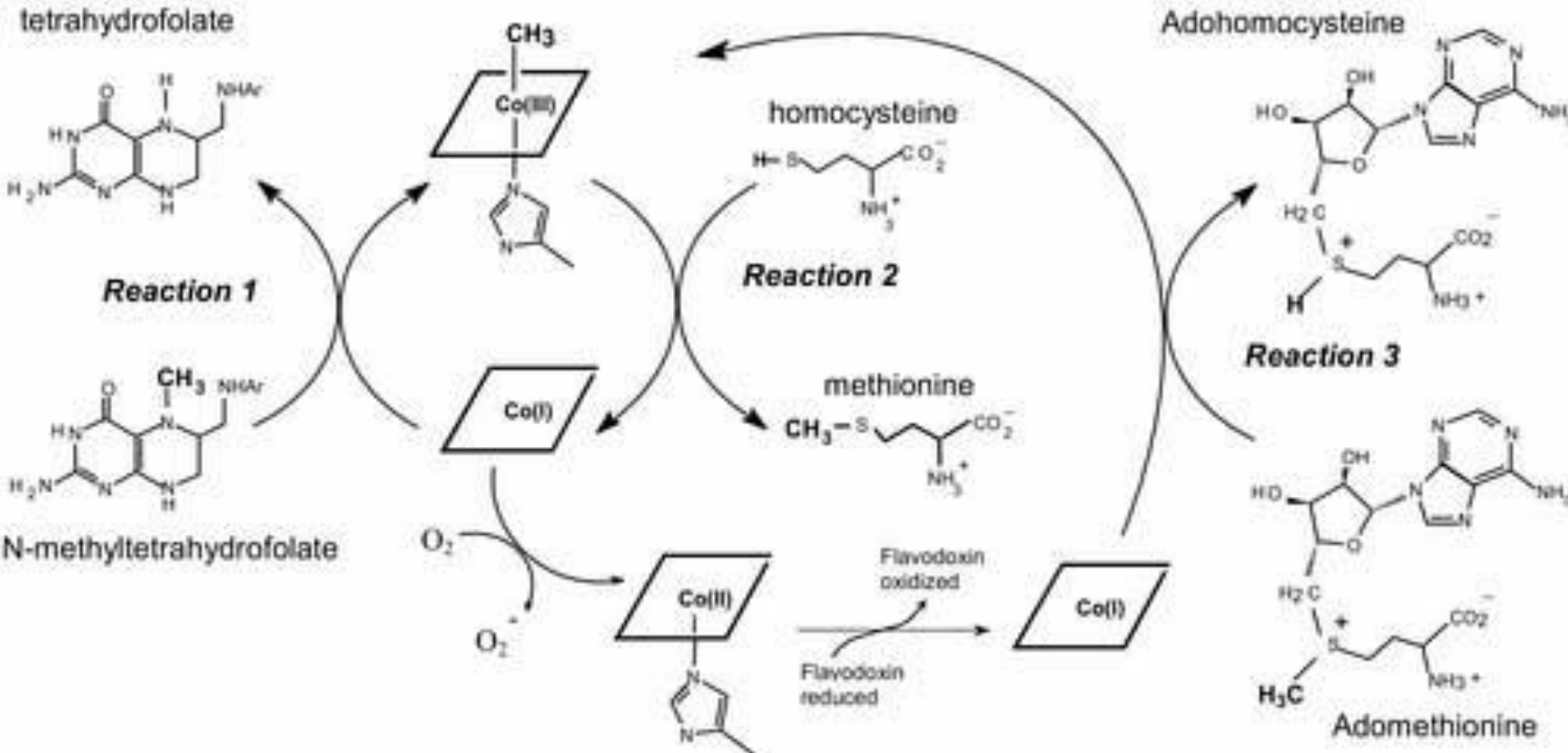
Coenzima A



La rottura del legame Co–C è 10^{12} volte più veloce nell'enzima completo rispetto al coenzima B₁₂



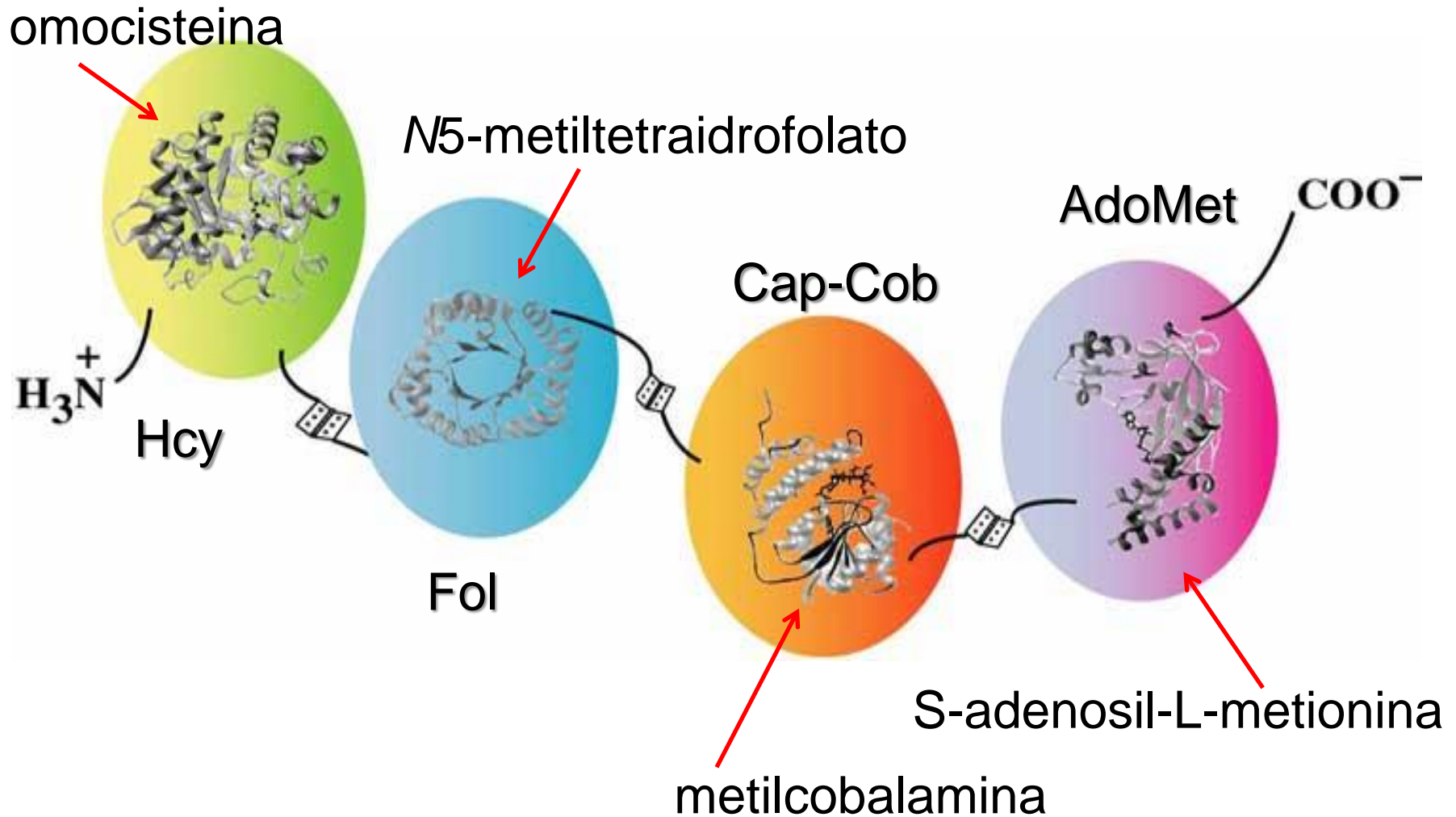
Metilcobalamina: cofattore della Metionina Sintasi



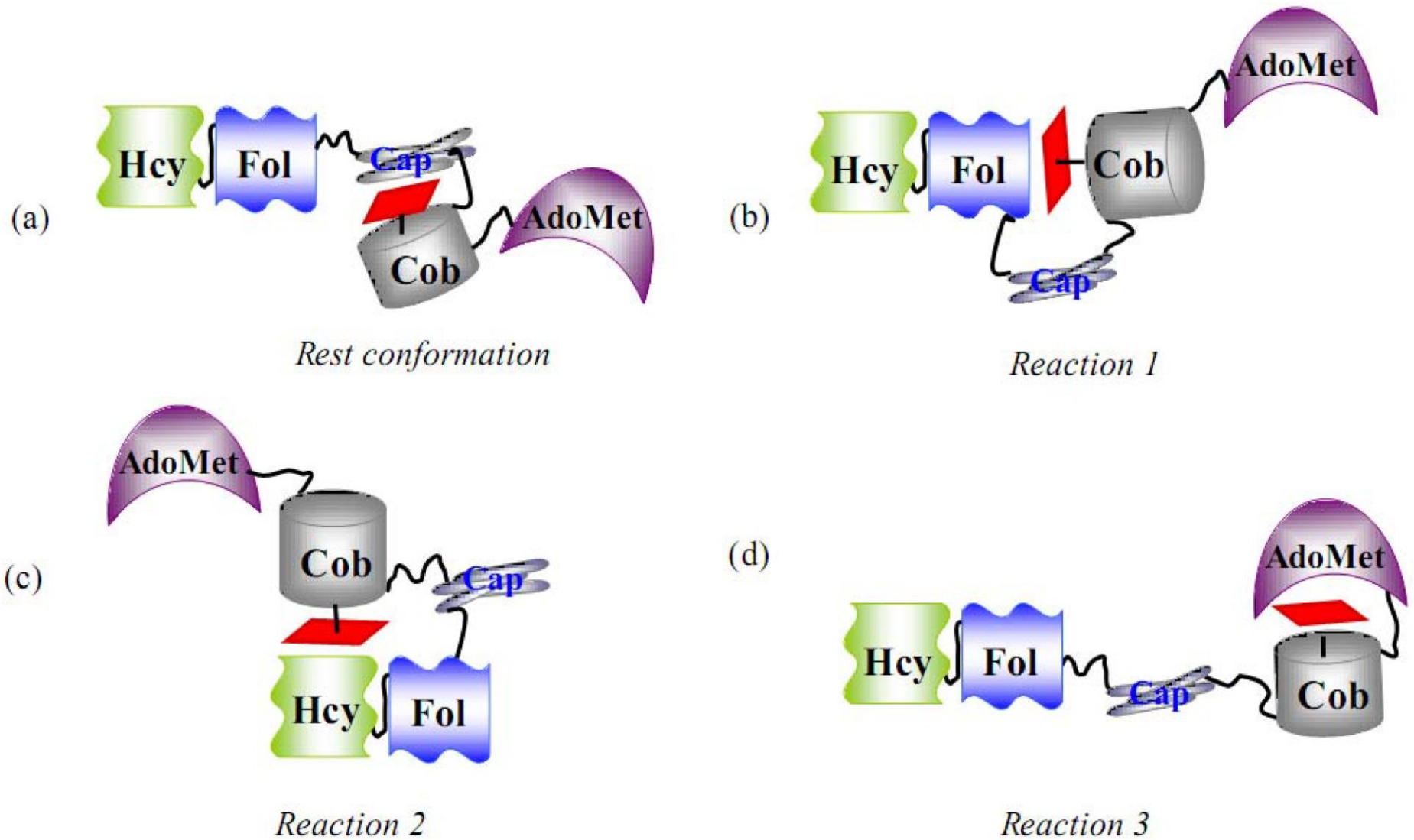
S-adenosil-L-metionina

Metile trasferito come CH₃⁺

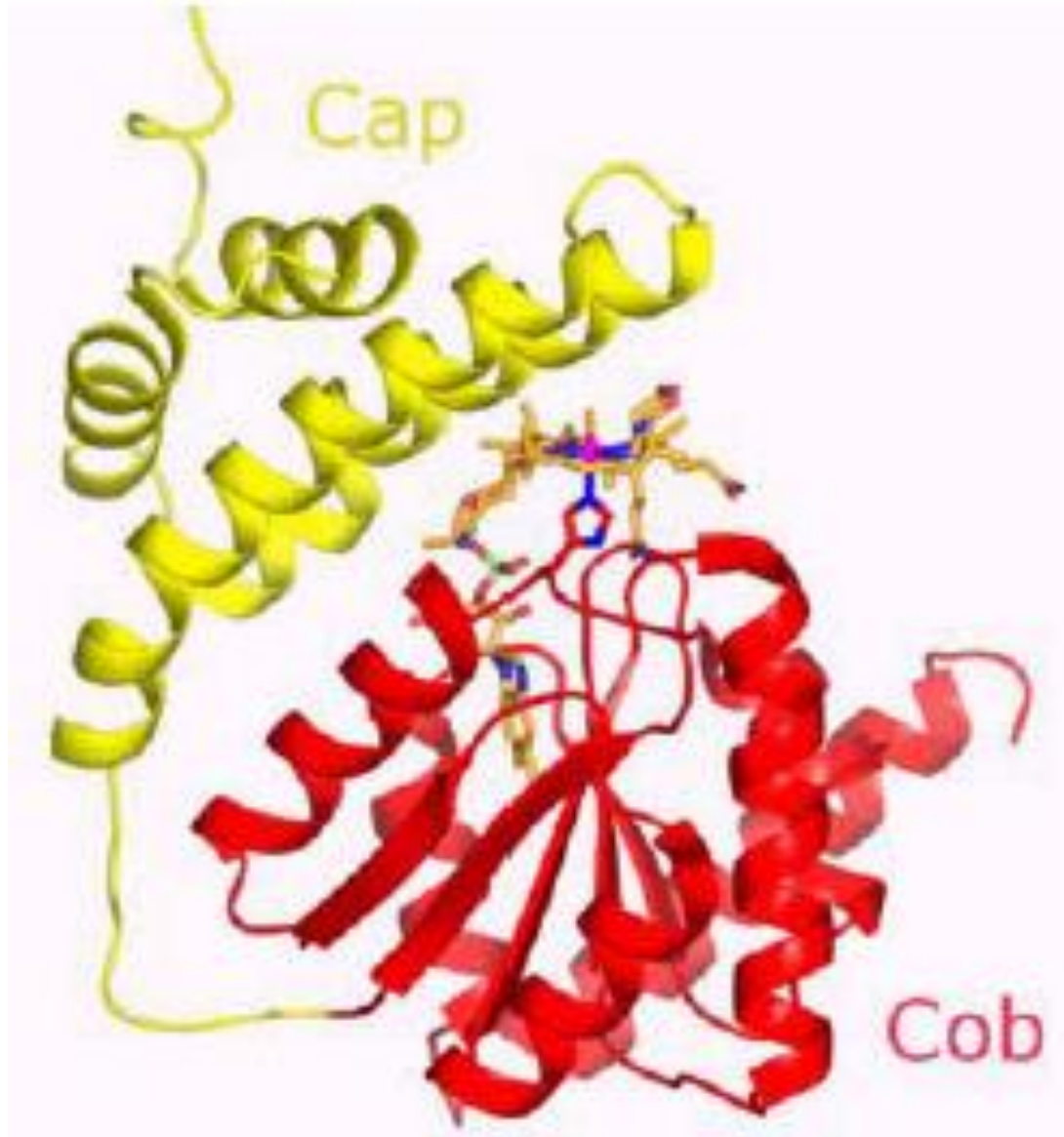
Metionina Sintasi



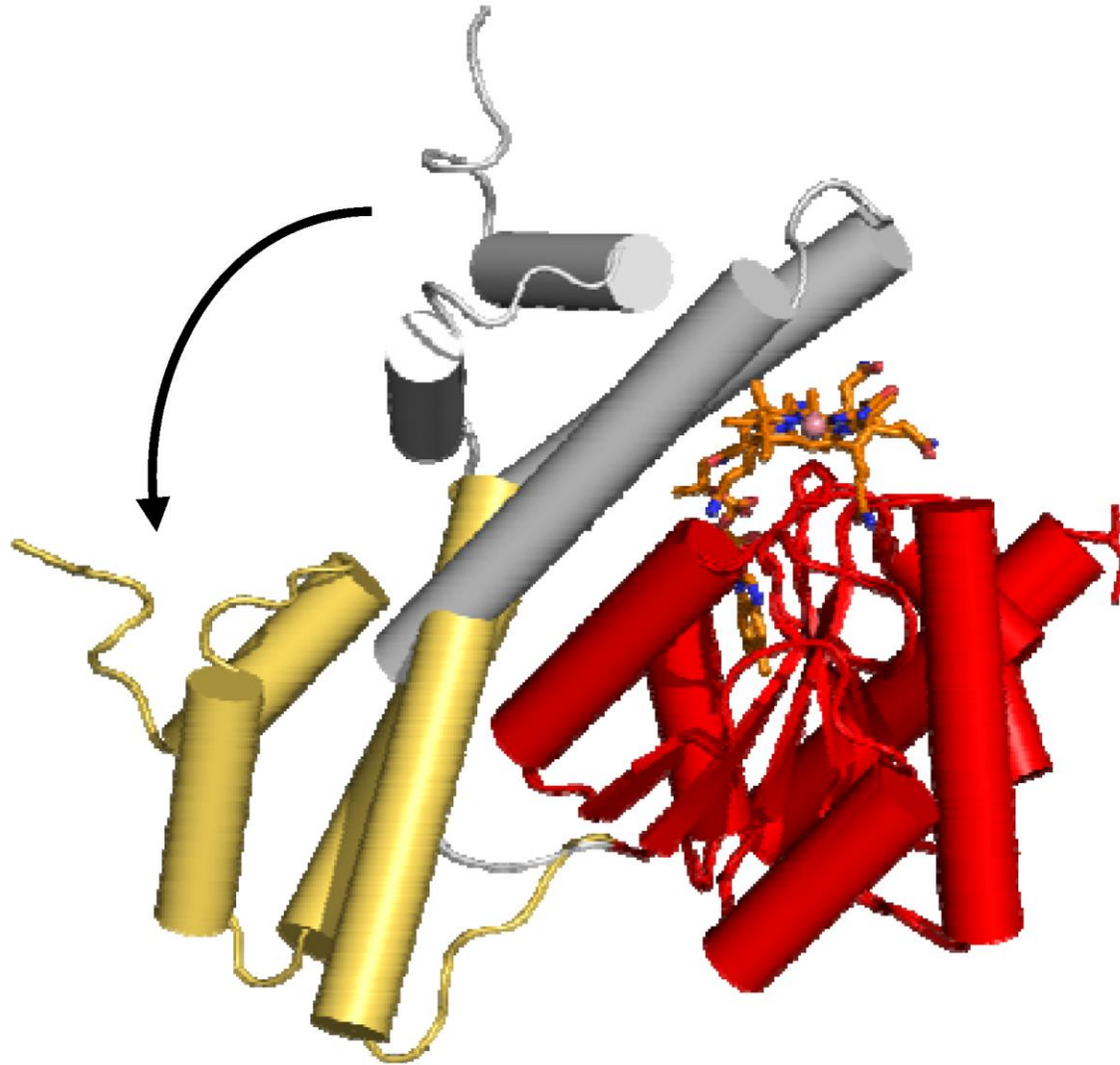
Variazioni conformazionali della metionina sintasi



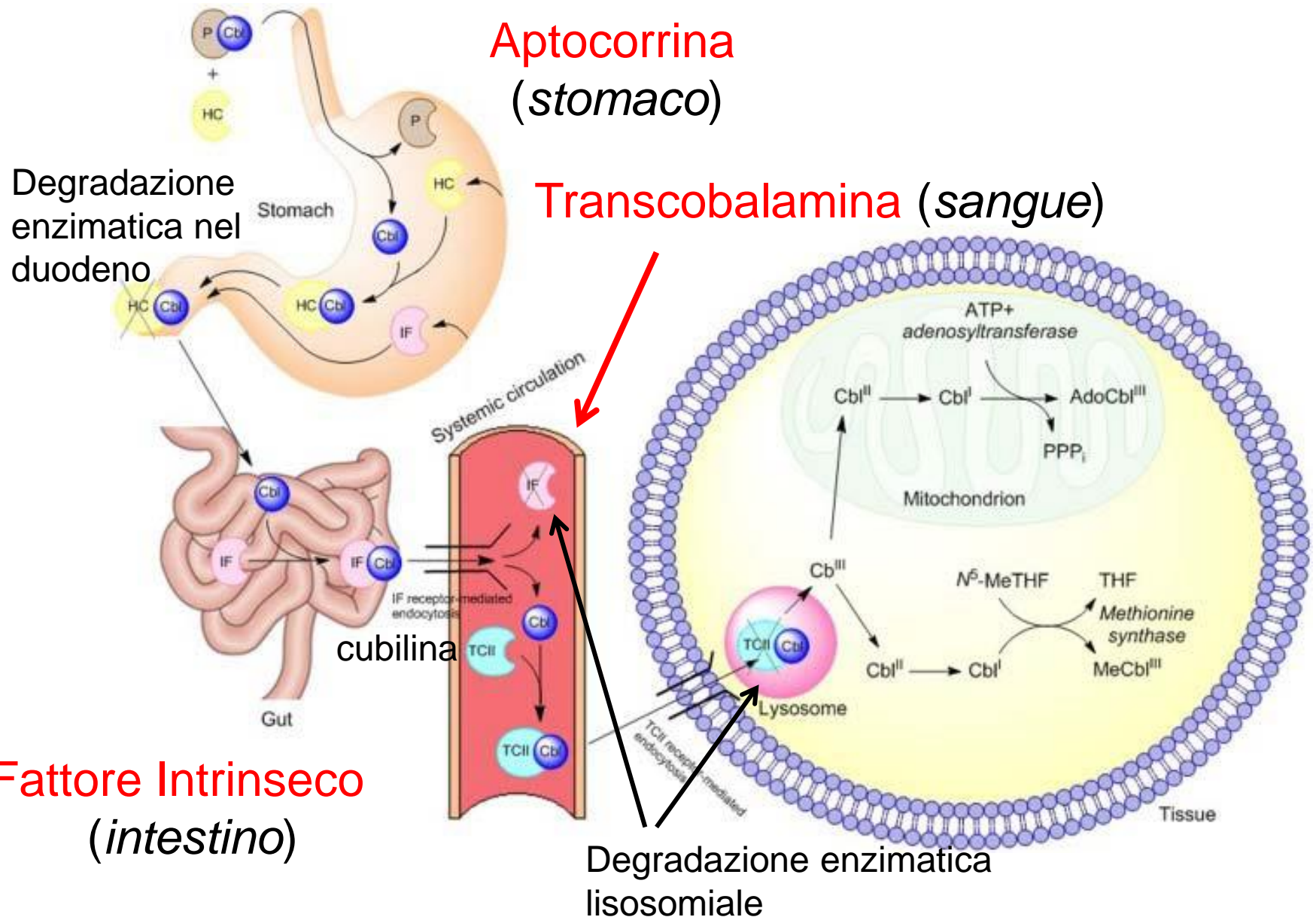
Metilcobalamina in Cap-Cob: *base-off/His-on*



Variazioni conformazionali in Cap-Cob



Uptake e Trasporto della Cobalamina



Aptocorrina
(*stomaco*)

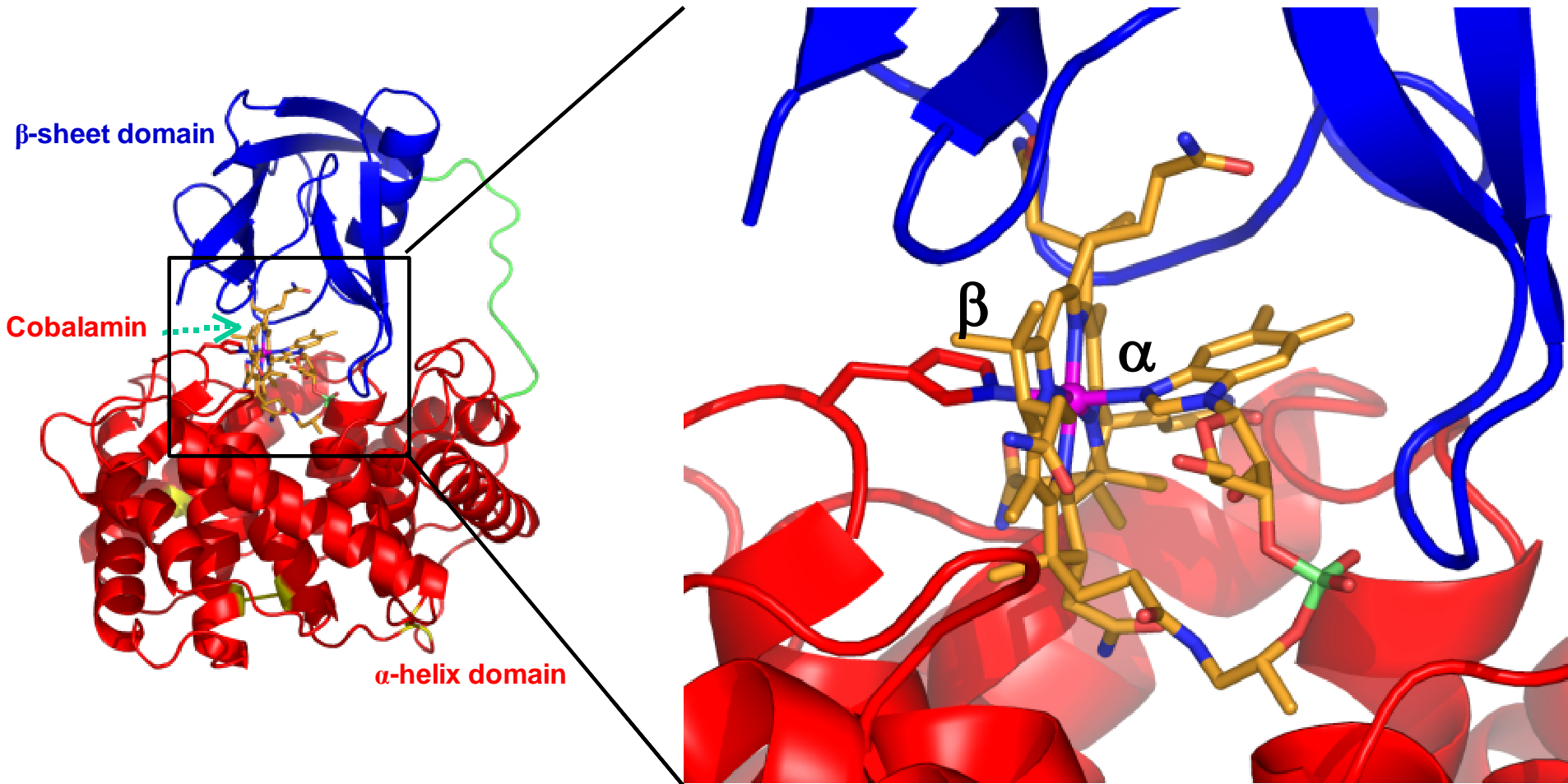
Transcobalamina (*sangue*)

Degradazione enzimatica nel duodeno

Fattore Intrinseco
(*intestino*)

Degradazione enzimatica lisosomiale

Struttura TC+Cobalamina (2006)

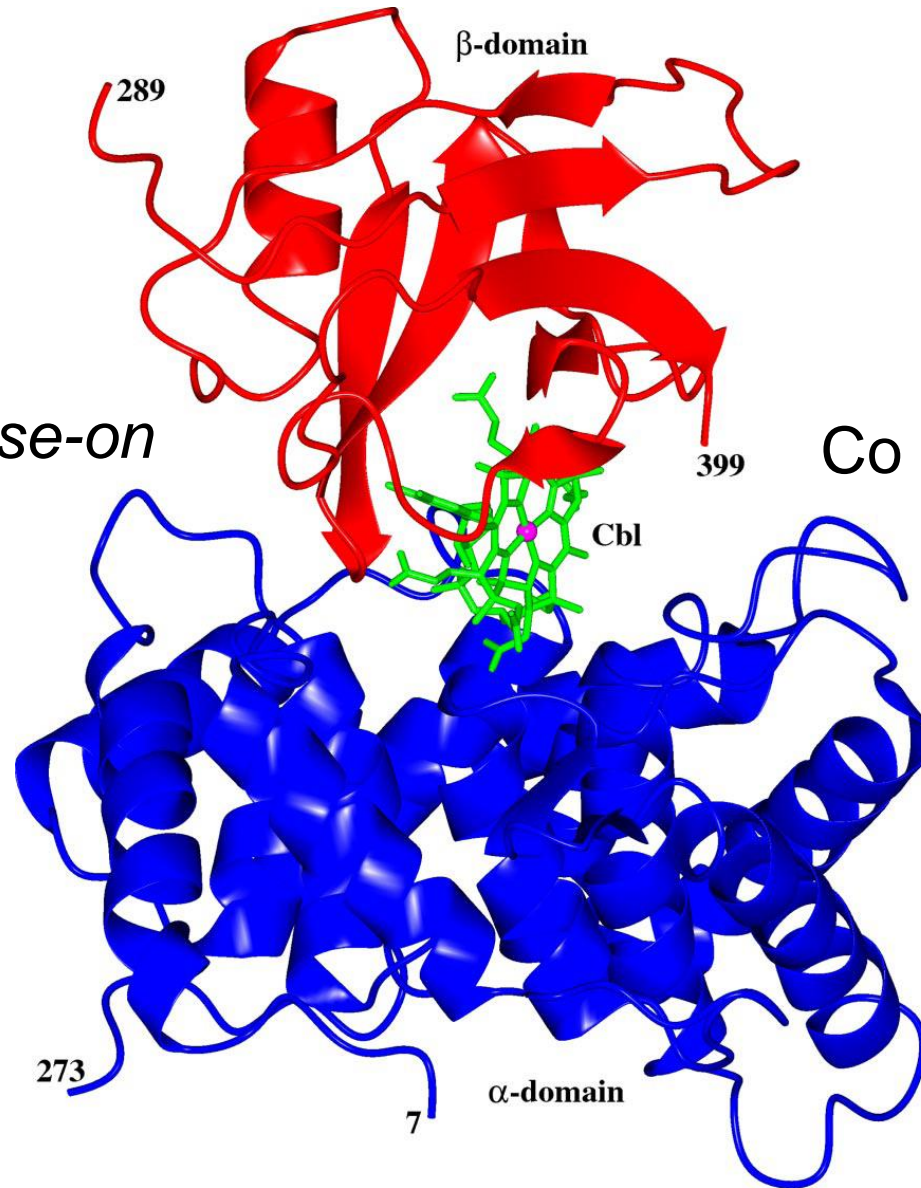


Coordinazione *base-on/His-on* (su β)

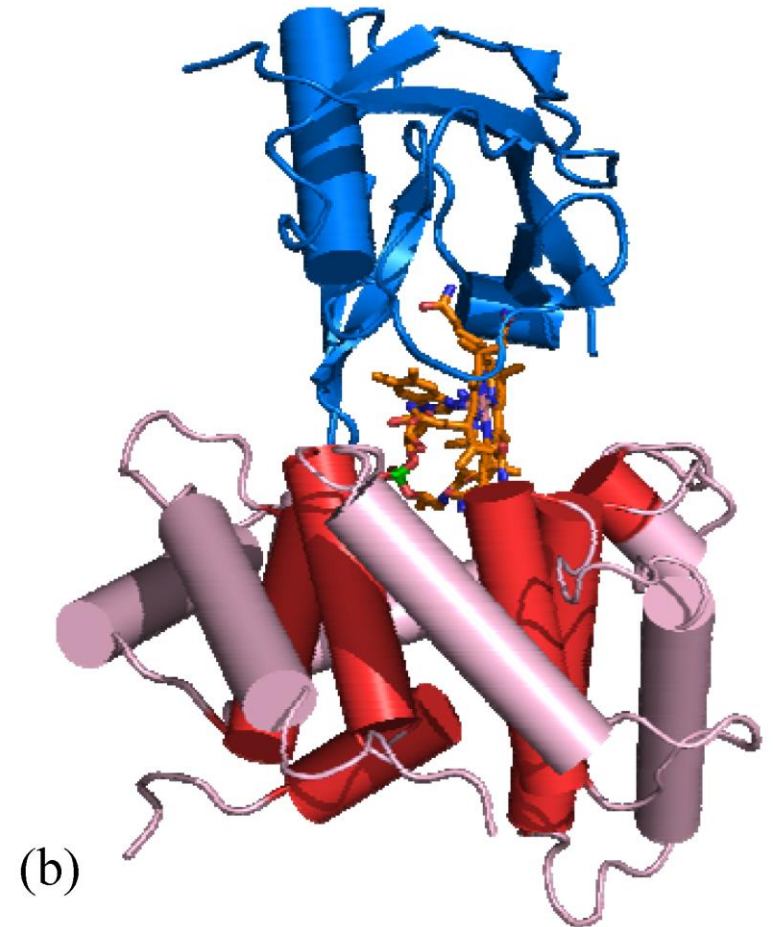
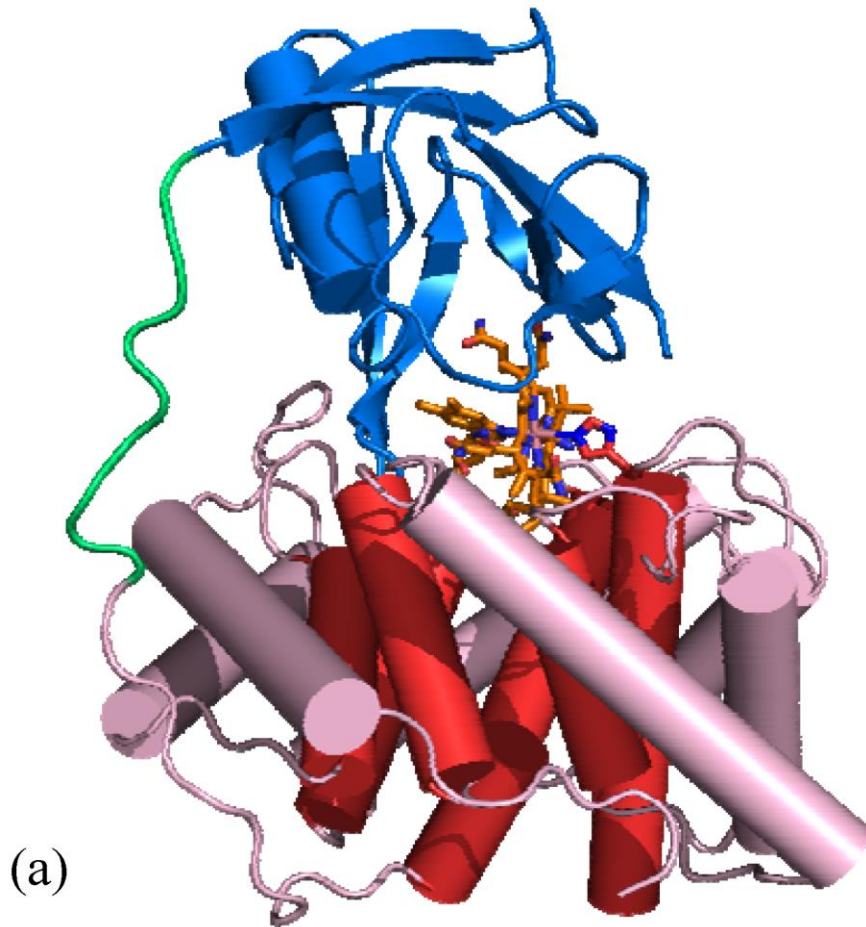
Complesso IF-Cbl (2007)

Coordinazione *base-on*

Co come Co(II)



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



Addotto IF-Cbl con CUB₅₋₈ recettori della cubilina

