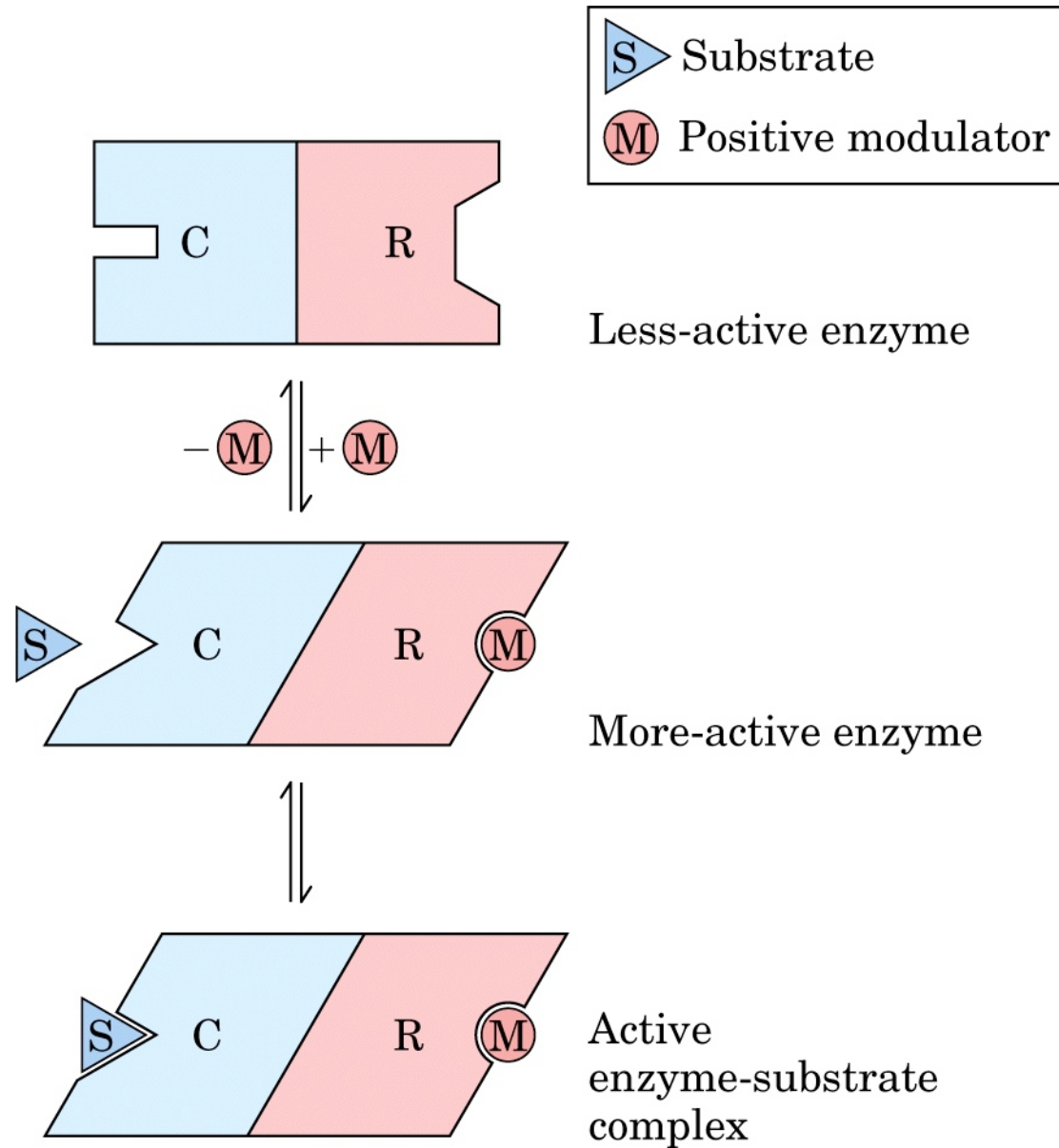
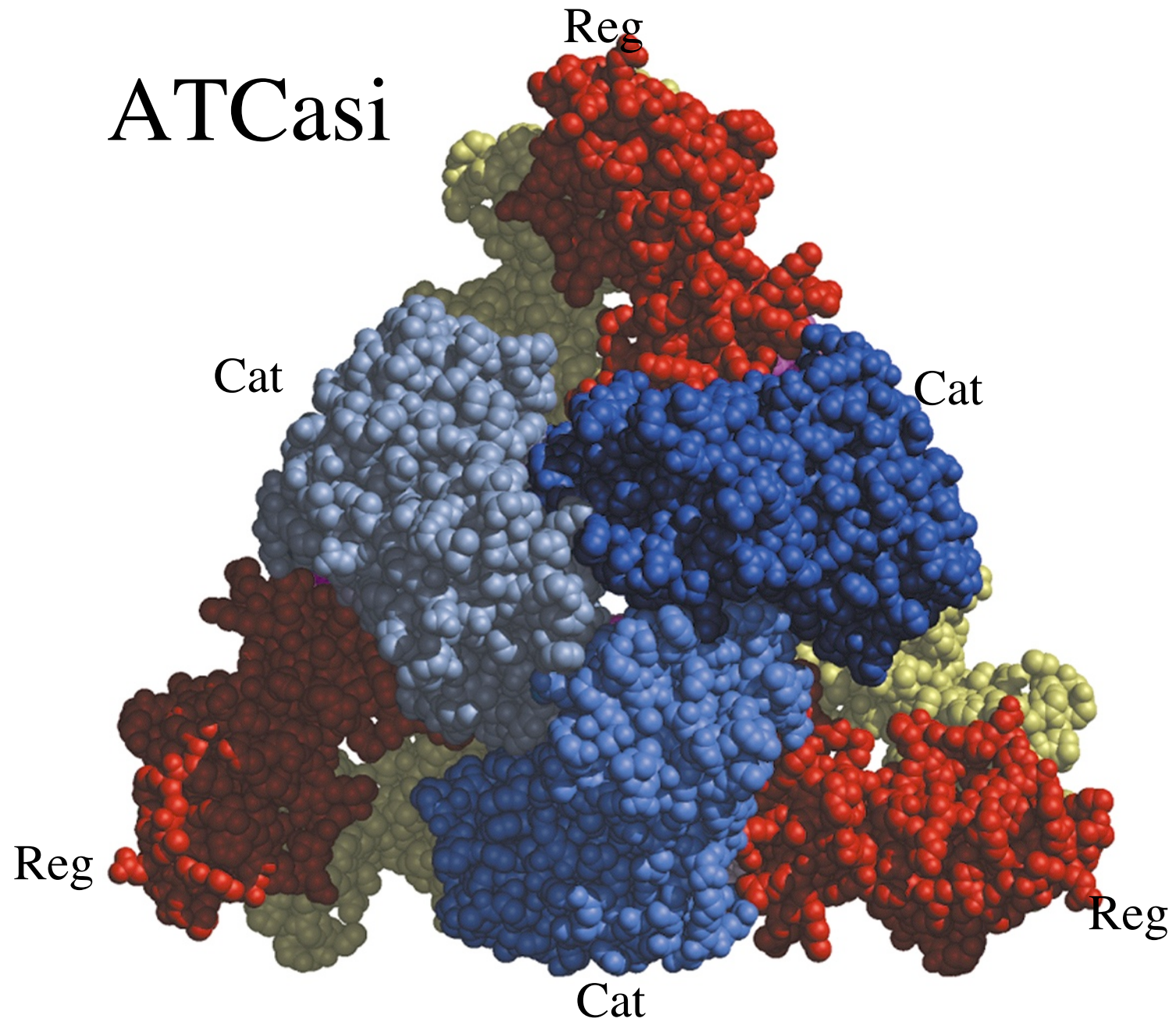


ENZIMI REGOLATORI

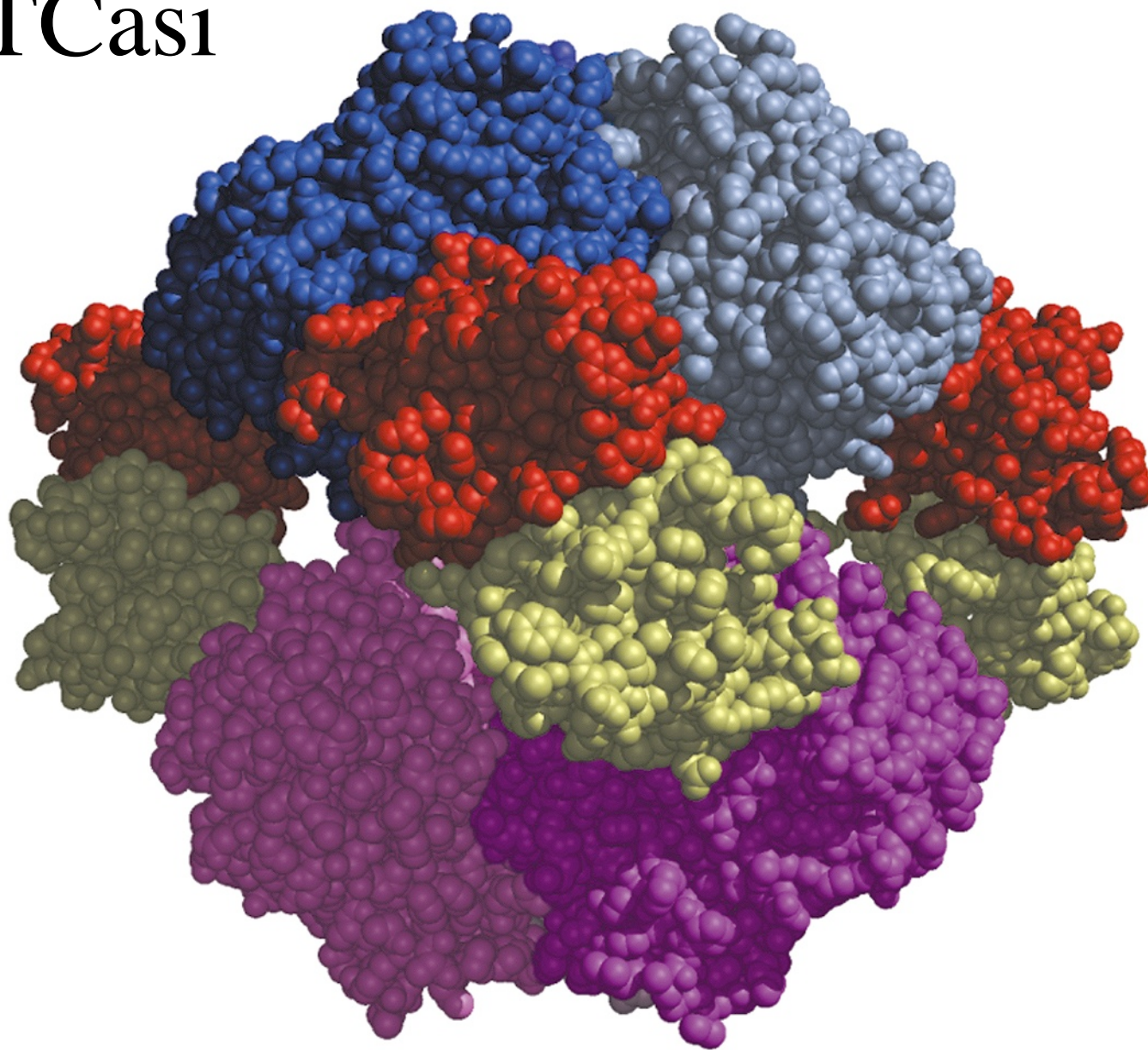
REGOLAZIONE ALLOSTERICA



ATCasi

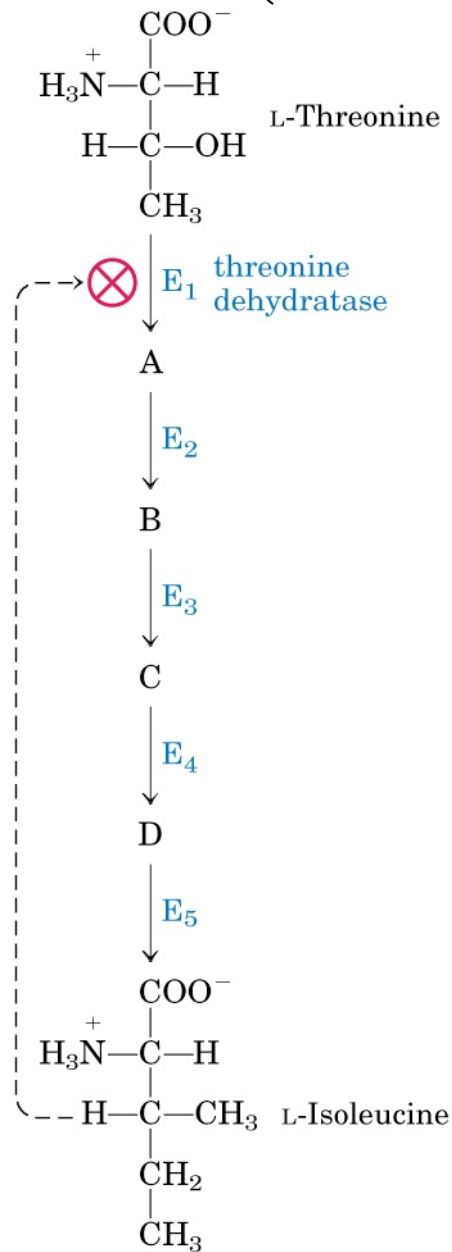


ATCasi

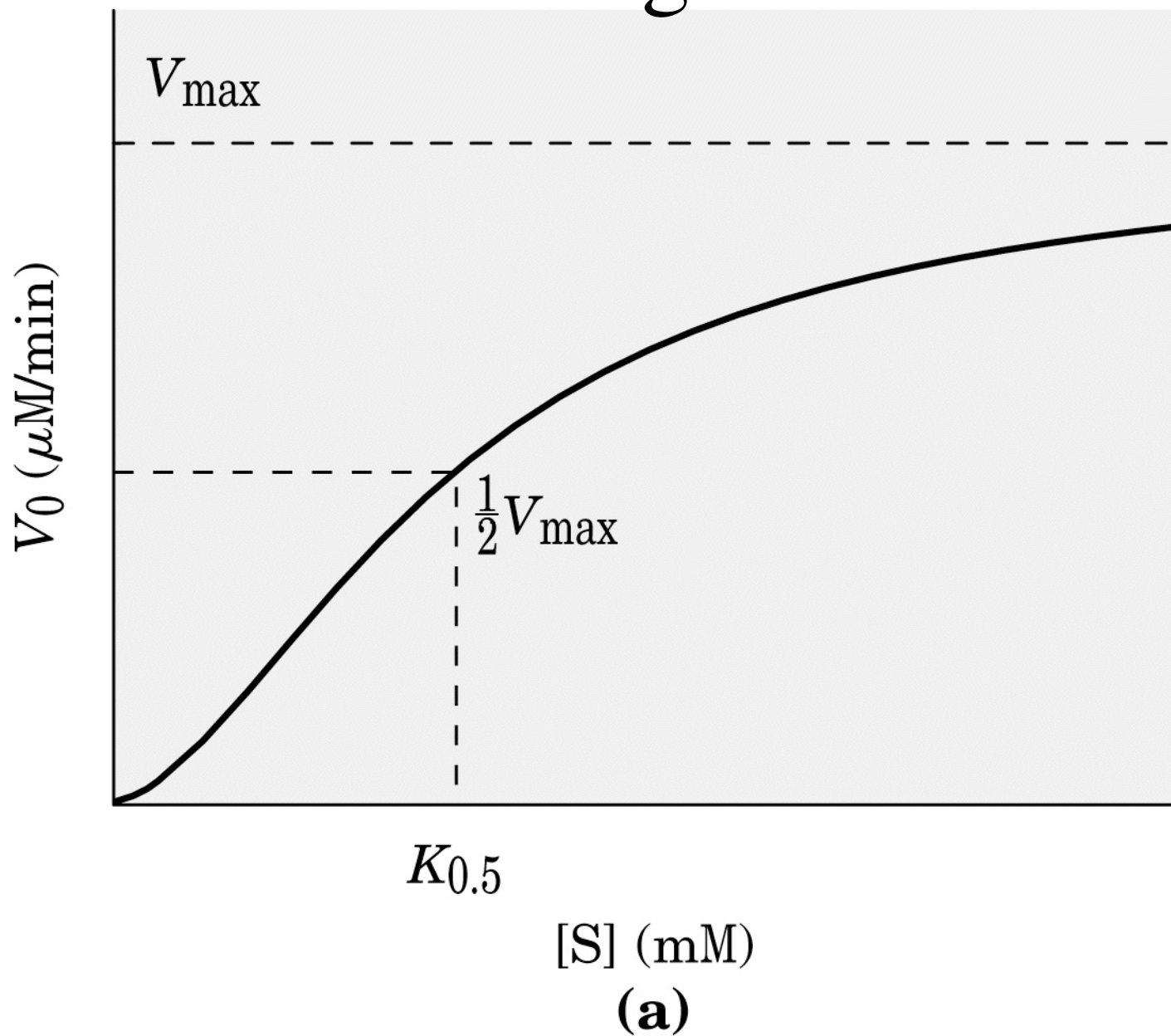


Regolazione delle vie metaboliche

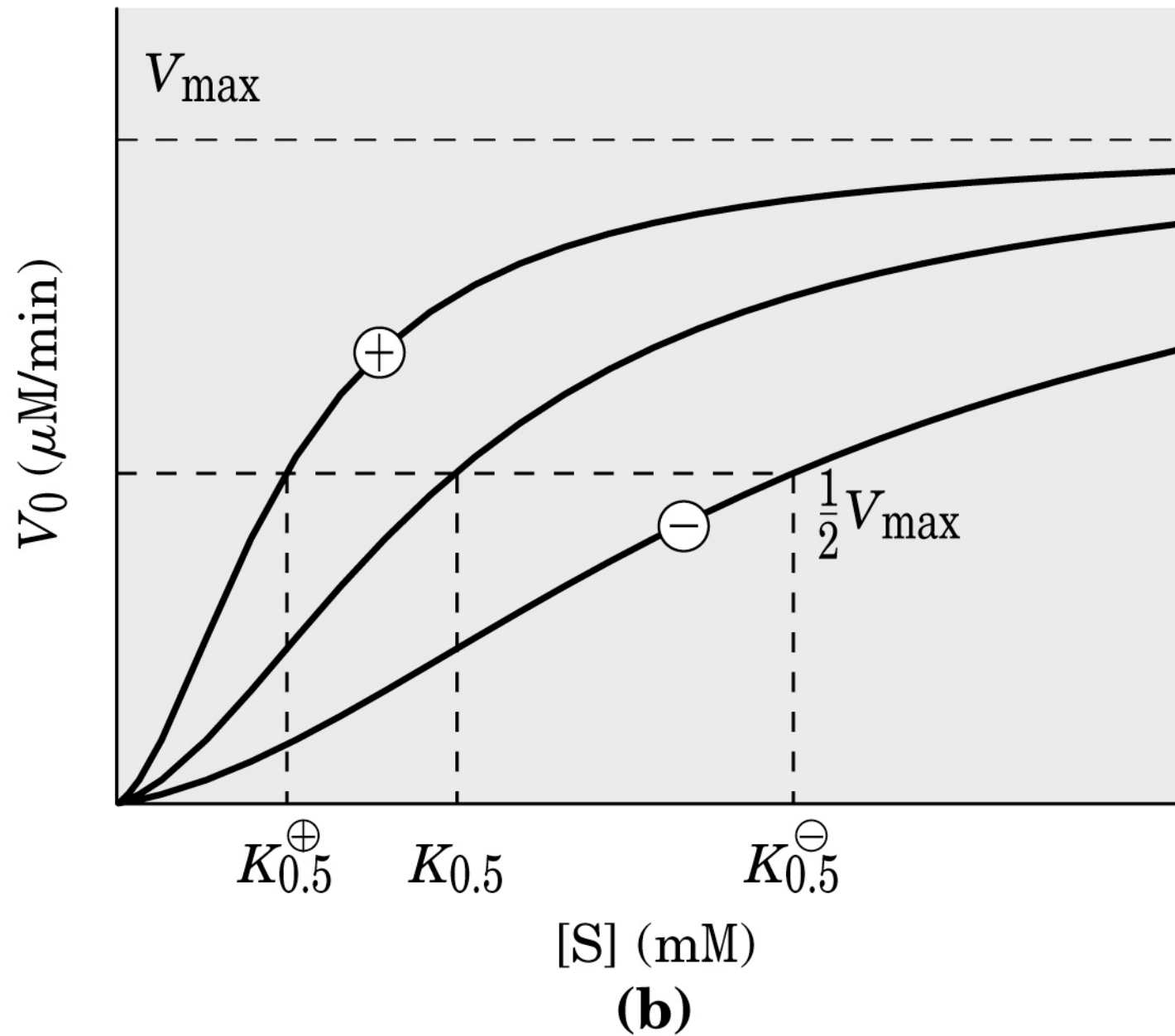
Inibizione retroattiva (feed-back negativo)



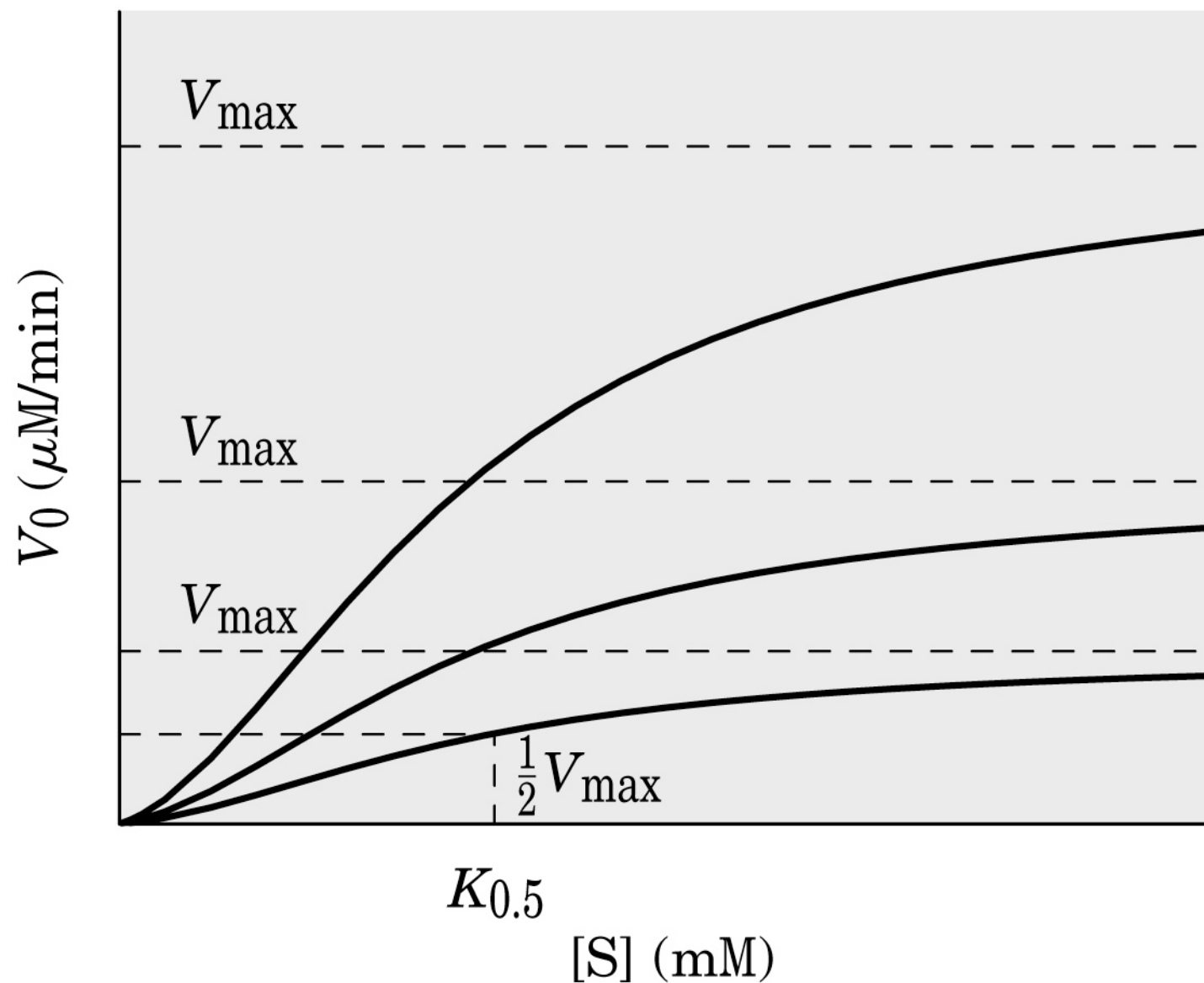
Cinetica sigmoidea



Modulazione di K_m



Modulazione di $V_{\max}$

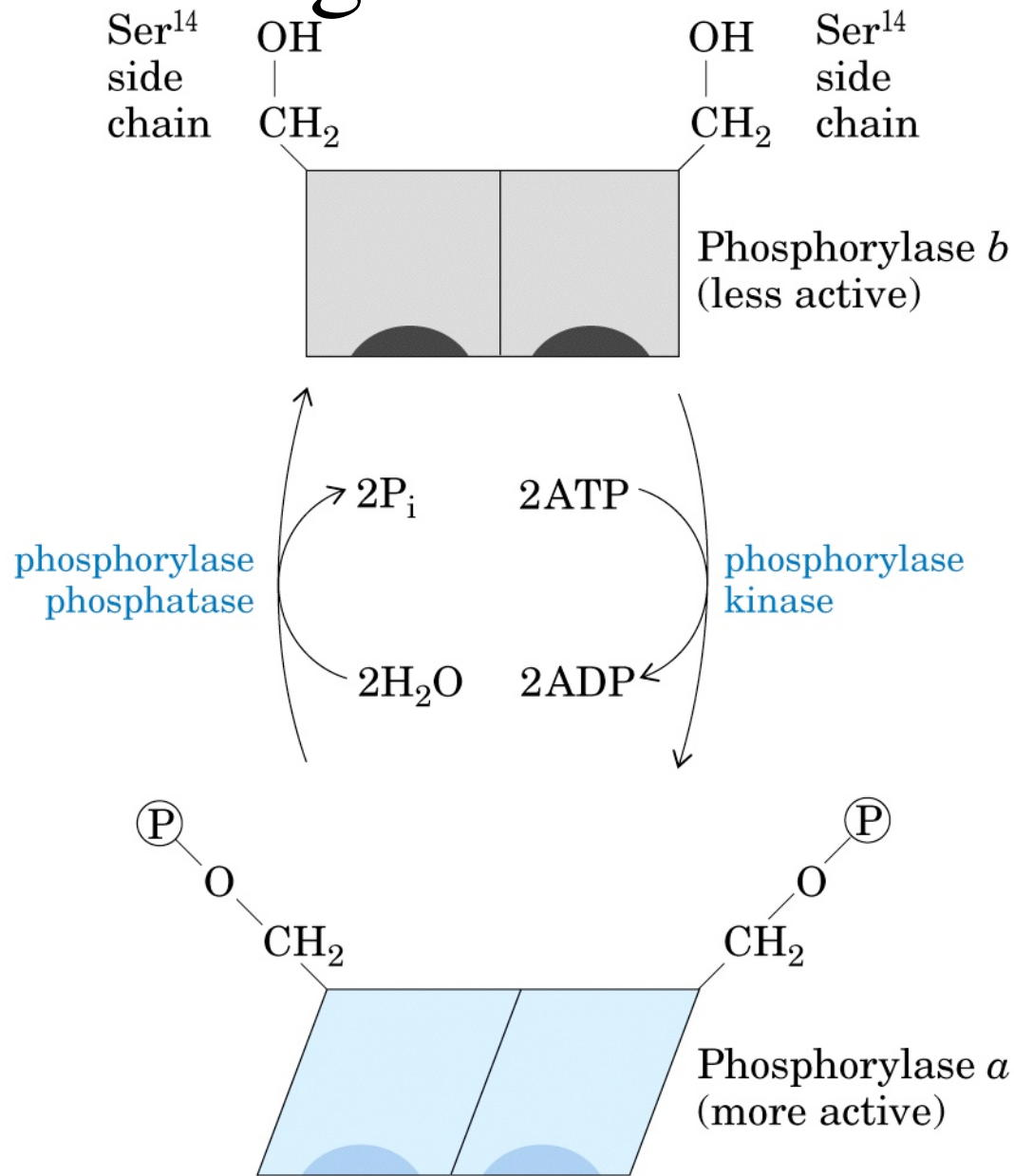


(c)

Regolazione per modificazione covalente

Covalent modification	Amino acid residues known to accept covalent modification
Phosphorylation $\text{Enz} \xrightarrow{\text{ATP} \rightarrow \text{ADP}} \text{Enz}-\text{P}(=\text{O})(\text{O}^-)_2$	Tyr, Ser, Thr, His
Adenylylation $\text{Enz} \xrightarrow{\text{ATP} \rightarrow \text{PP}_i} \text{Enz}-\text{P}(=\text{O})(\text{O}^-)-\text{O}-\text{CH}_2-\text{ribose}-\text{Adenine}$	Tyr
Uridylylation $\text{Enz} \xrightarrow{\text{UTP} \rightarrow \text{PP}_i} \text{Enz}-\text{P}(=\text{O})(\text{O}^-)-\text{O}-\text{CH}_2-\text{ribose}-\text{Uridine}$	Tyr
ADP-ribosylation $\text{Enz} \xrightarrow{\text{NAD} \rightarrow \text{nicotinamide}} \text{Enz}-\text{ribose}-\text{CH}_2-\text{O}-\text{P}(=\text{O})(\text{O}^-)-\text{O}-\text{P}(=\text{O})(\text{O}^-)-\text{O}-\text{CH}_2-\text{ribose}-\text{Adenine}$	Arg, Gln, Cys, diphthamide (a modified His)
Methylation $\text{Enz} \xrightarrow{\text{S-adenosyl-methionine} \rightarrow \text{S-adenosyl-homocysteine}} \text{Enz}-\text{CH}_3$	Glu

Glicogeno fosforilasi



SITI DI FOSFORILAZIONE PROTEICA

SERINA
TREONINA



Ser/thr -chinasi

TIROSINA Tyr-chinasi

SEQUENZE CONSENSO PER LE PROTEINE CHINASI

table 8-9

Consensus Sequences for Protein Kinases	
Protein kinase	Consensus sequence and phosphorylated residue*
Protein kinase A	-X-R-(R/K)-X-(S/T)-B-
Protein kinase G	-X-R-(R/K)-X-(S/T)-X-
Protein kinase C	-(R/K)-(R/K)-X-(S/T)-B-(R/K)-(R/K)-
Protein kinase B	-X-R-X-(S/T)-X-K-
Ca ²⁺ /calmodulin kinase I	-B-X-R-X-X-(S/T)-X-X-X-B-
Ca ²⁺ /calmodulin kinase II	-B-X-(R/K)-X-X-(S/T)-X-X-
Myosin light chain kinase (smooth muscle)	-K-K-R-X-X-S-X-B-B-
Phosphorylase b kinase	-K-R-K-Q-I-S-V-R-
Extracellular signal-regulated kinase (ERK)	-P-X-(S/T)-P-P-
Cyclin-dependent protein kinase (cdc2)	-X-(S/T)-P-X-(K/R)-
Casein kinase I	-(Sp/Tp)-X-X-(X)-(S/T)-B
Casein kinase II	-X-(S/T)-X-X-(E/D/Sp/Yp)-X-
β -Adrenergic receptor kinase	-(D/E) _n -(S/T)-X-X-X-
Rhodopsin kinase	-X-X-(S/T)-(E) _n -
Insulin receptor kinase	-X-E-E-E-Y-M-M-M-M-K-K-S-R-G- D-Y-M-T-M-Q-I-G-K-K-L-P-A- T-G-D-Y-M-N-M-S-P-V-G-D-
Epidermal growth factor (EGF) receptor kinase	-E-E-E-E-Y-F-E-L-V-

Sources: Pinna, L.A. & Ruzzene, M.H. (1996) How do protein kinases recognize their substrates? *Biochim. Biophys. Acta* **1314**, 191-225. Kemp, B.E. & Pearson, R.B. (1990) Protein kinase recognition sequence motifs. *Trends Biochem. Sci.* **15**, 342-346. Kennelly, P.J. & Krebs, E.G. (1991) Consensus sequences as substrate specificity determinants for protein kinases and protein phosphatases. *J. Biol. Chem.* **266**, 15,555-15,558.

*Shown here are deduced consensus sequences (in roman type) and actual sequences from known substrates (italic). The Ser (S), Thr (T), or Tyr (Y) residue to undergo phosphorylation is in red; all amino acid residues are shown as their one-letter abbreviations (see Table 5-1). X represents any amino acid; B, any hydrophobic amino acid; Sp, Tp, and Yp, already phosphorylated Ser, Thr, and Tyr residues.

REGOLAZIONE DA FOSFORILAZIONI MULTIPLE



Kinase	Glycogen synthase sites phosphorylated	Degree of synthase inactivation
Protein kinase A	1A, 1B, 2, 4	+
Protein kinase G	1A, 1B, 2	+
Protein kinase C	1A	+
Ca ²⁺ /calmodulin kinase	1B, 2	+
Phosphorylase <i>b</i> kinase	2	+
Casein kinase I	At least 9 sites	+ + + +
Casein kinase II	5	0
Glycogen synthase kinase 3	3A, 3B, 3C	+ + +
Glycogen synthase kinase 4	2	+

ATTIVAZIONE MEDIANTE PROTEOLISI

