Interações de van der Waals

$U_{london}(r)$ = -14.54x10^{-21} J para duas moléculas de HCl (r=3 Å) a 300K

$U_{dipolo\text{-}dipolo}(r)$ = -2.5x10^{-21} J

$U_{dipolo\text{-}dipoloinduzido}(r)$ = -0.77x10^{-21} J

k_BT = 4.1x10^{-21} J a 300K

$C_6 = U_{london} + U_{dipolo\text{-}dipolo} + U_{dipolo\text{-}dipolo\ induzido}$ **(moléculas polares)**

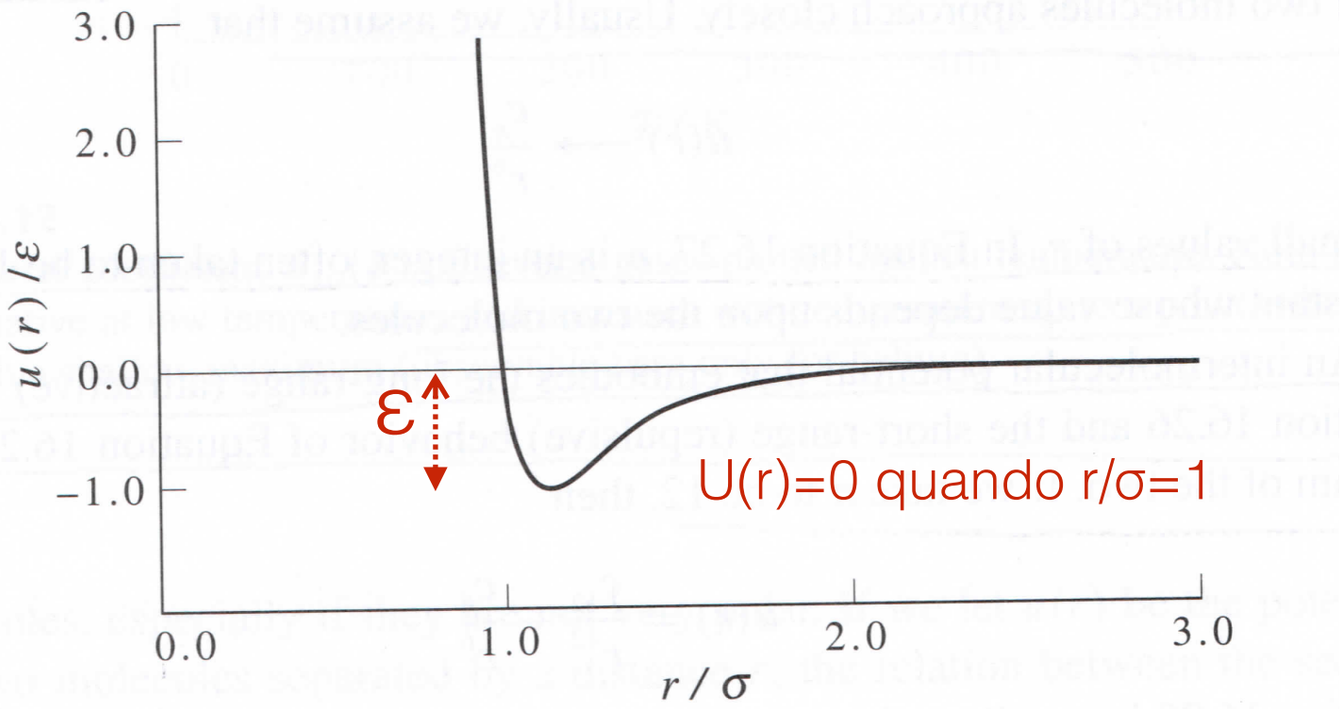
$C_6 = U_{london}$ **(moléculas apolares)**

$$U(r) = \frac{C_{12}}{r^{12}} - \frac{C_6}{r^6}$$

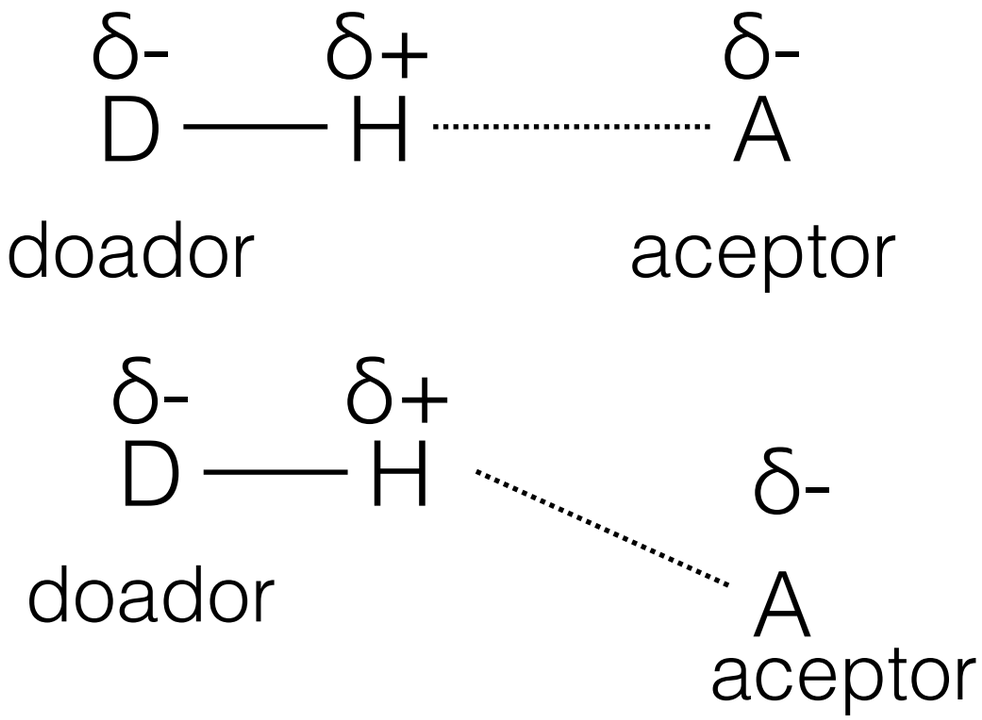
$$U(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

repulsão

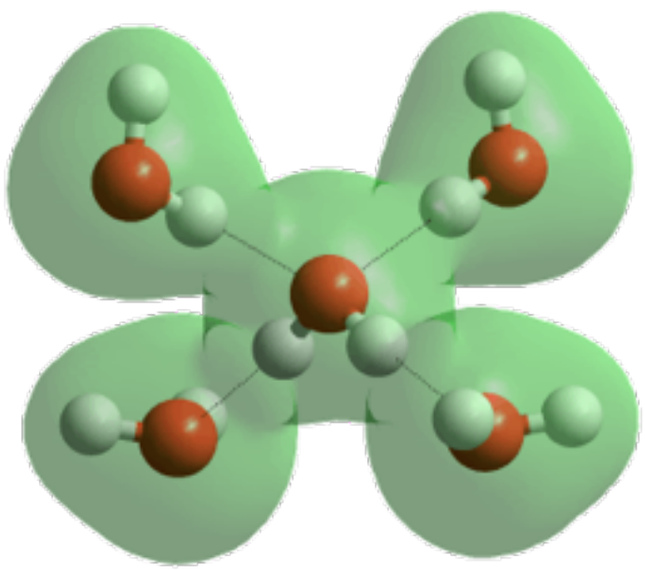
atração



Ligações de hidrogênio



Caráter de ligação é 90% eletrostático e 10% covalente



Energia de ligações covalentes

Ligação	u (kcal/mol)
H—C	80.6
C—C	98.3

Ligação de hidrogênio:

Interação	Energia (kcal/mol)
Água/Água	5.5
Dipolo-dipolo	0.5
dipolo-dipolo induzido	0.012

Dill, K. et al. Molecular Driving Forces, Garland Science, 1ª. ed., 2003, Madison

Como as ligações de hidrogênio são muito mais fracas do que ligações covalentes o tempo de vida das ligações de hidrogênio é muito curto

Energias envolvidas na formação de interações não covalentes vs. covalentes

$$u(r) = (constant)r^{-p}$$

Diferentes tipos de energia u(r)

Tipo	u (kcal/mol)	Dependência em r
iônica	66	1/r
íon/dipolo	4	$1/r^2$
dipolo/dipolo	0.5	$1/r^3$
dipolo/dipolo induzido	0.012	$1/r^6$

Energia de ligações covalentes

Ligação	u (kcal/mol)
H—C	80.6
C—C	98.3

Ponte de hidrogênio:

Água/Água	5.5 kcal/mol

Dill, K. et al. Molecular Driving Forces, Garland Science, 1ª. ed., 2003, Madison

A estabilidade da proteína é da mesma ordem de grandeza que 4-5 ligações de hidrogênio

Termodinâmica de enovelamento de proteínas

Proteína	ΔG^0 (kcal/mol)	ΔH^0 (kcal/mol)	$T\Delta S^0$ (kcal/mol)
CI2	-6.62	-32.26	-25.64
EglinC	-8.82	-27.48	-18.66
RNAse T1	-8.96	-67.16	-58.22
Citocromo c	-8.87	-21.27	-12.40
Barnase	-11.69	-73.37	-61.71

Fonte: Lesk, A. *Introduction to protein science*. Oxford University Press, 2ª edição, p. 352 (2010)

TABLE 8.5 Turnover numbers of some enzymes

Enzyme	Turnover number (per second)
Carbonic anhydrase	600,000
3-Ketosteroid isomerase	280,000
Acetylcholinesterase	25,000
Penicillinase	2,000
Lactate dehydrogenase	1,000
Chymotrypsin	100
DNA polymerase I	15
Tryptophan synthetase	2
Lysozyme	0.5

TABLE 8.7 Enzymes for which k_{cat}/K_M is close to the diffusion-controlled rate of encounter

Enzyme	k_{cat}/K_M (s^{-1} M^{-1})
Acetylcholinesterase	1.6×10^8
Carbonic anhydrase	8.3×10^7
Catalase	4×10^7
Crotonase	2.8×10^8
Fumarase	1.6×10^8
Triose phosphate isomerase	2.4×10^8
β-Lactamase	1×10^8
Superoxide dismutase	7×10^9

Source: After A. Fersht, *Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding* (W. H. Freeman and Company, 1999), Table 4.5.

Chymotrypsinogen

1 15 245

Trypsin

Π-Chymotrypsin

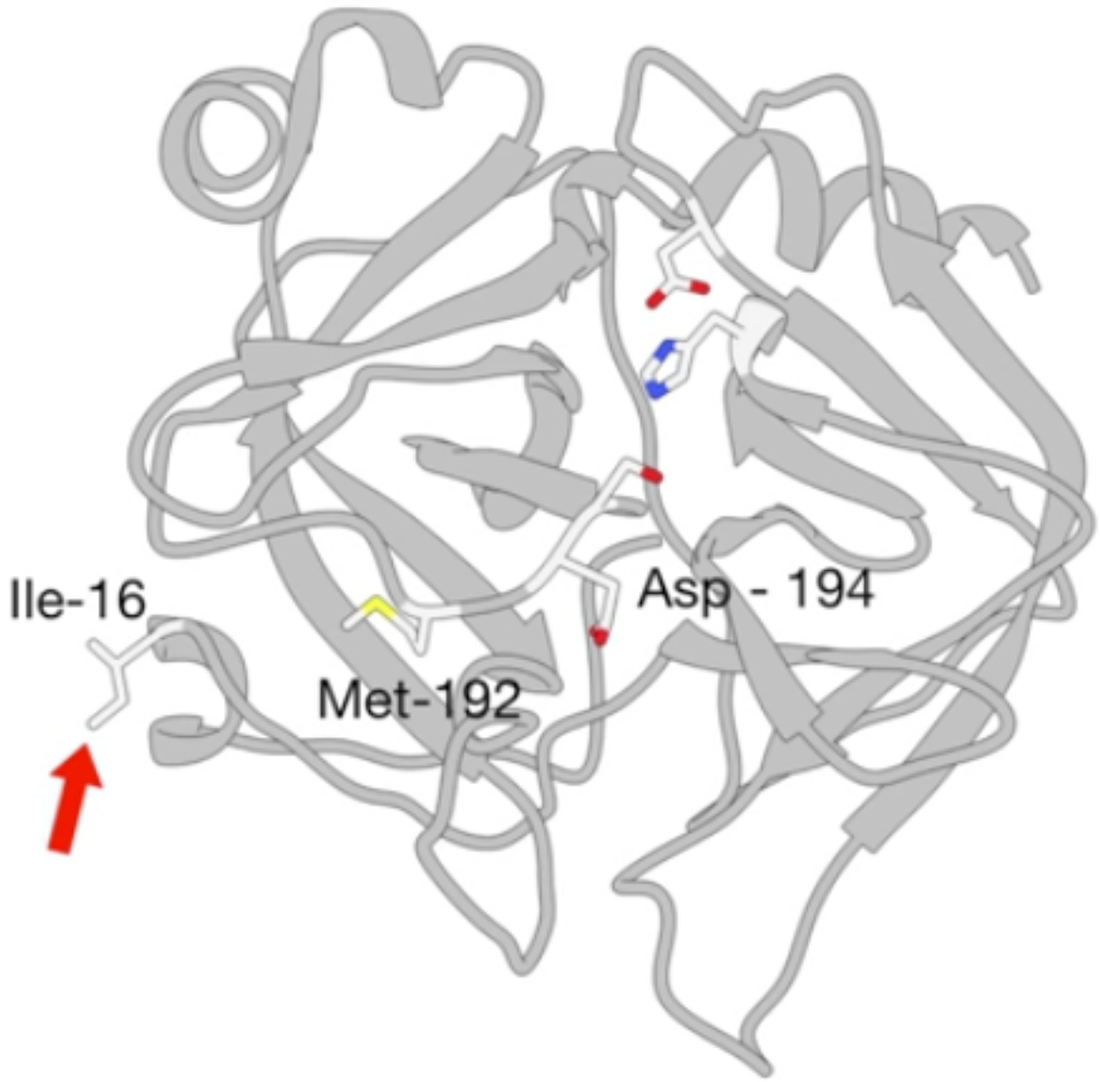
1 15 16 245

Autolysis

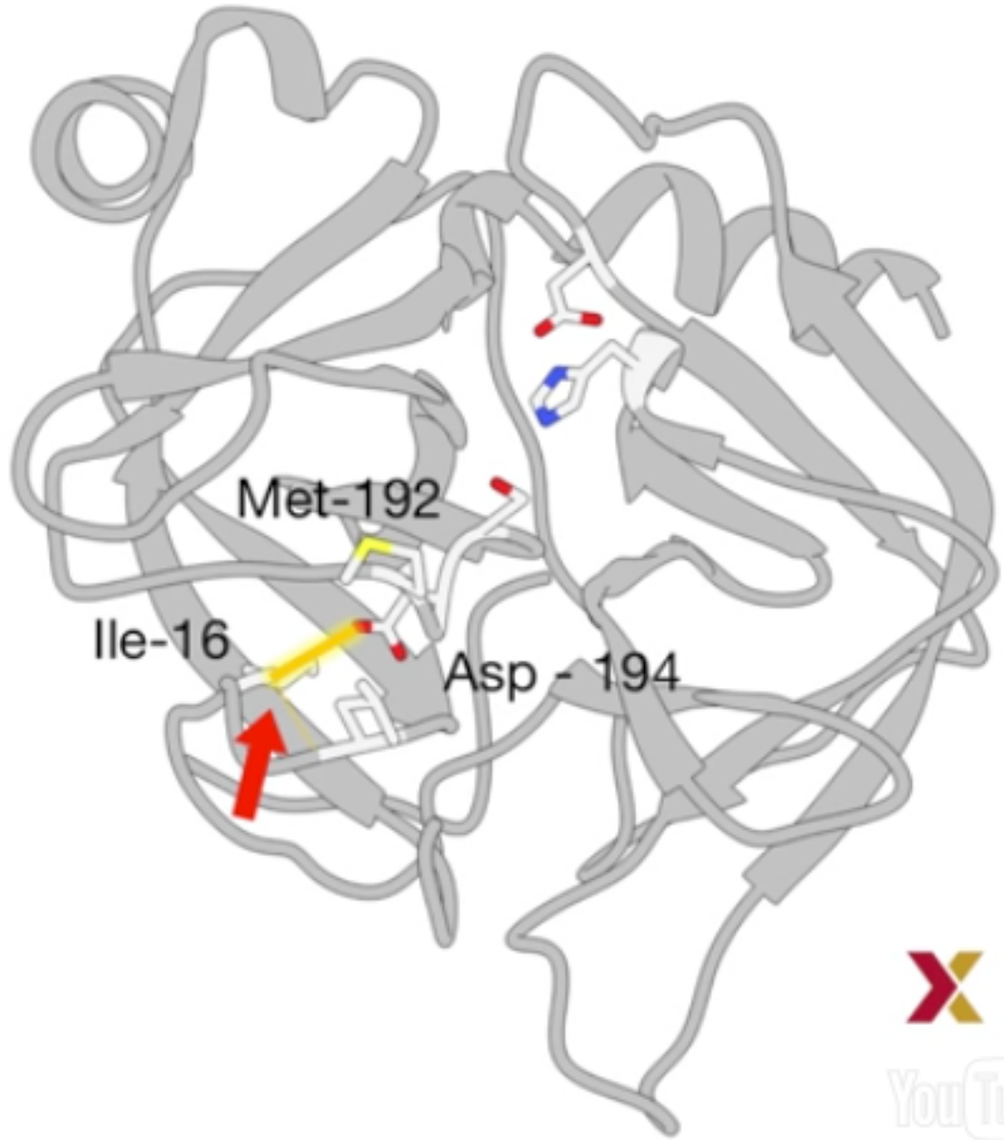
α-Chymotrypsin

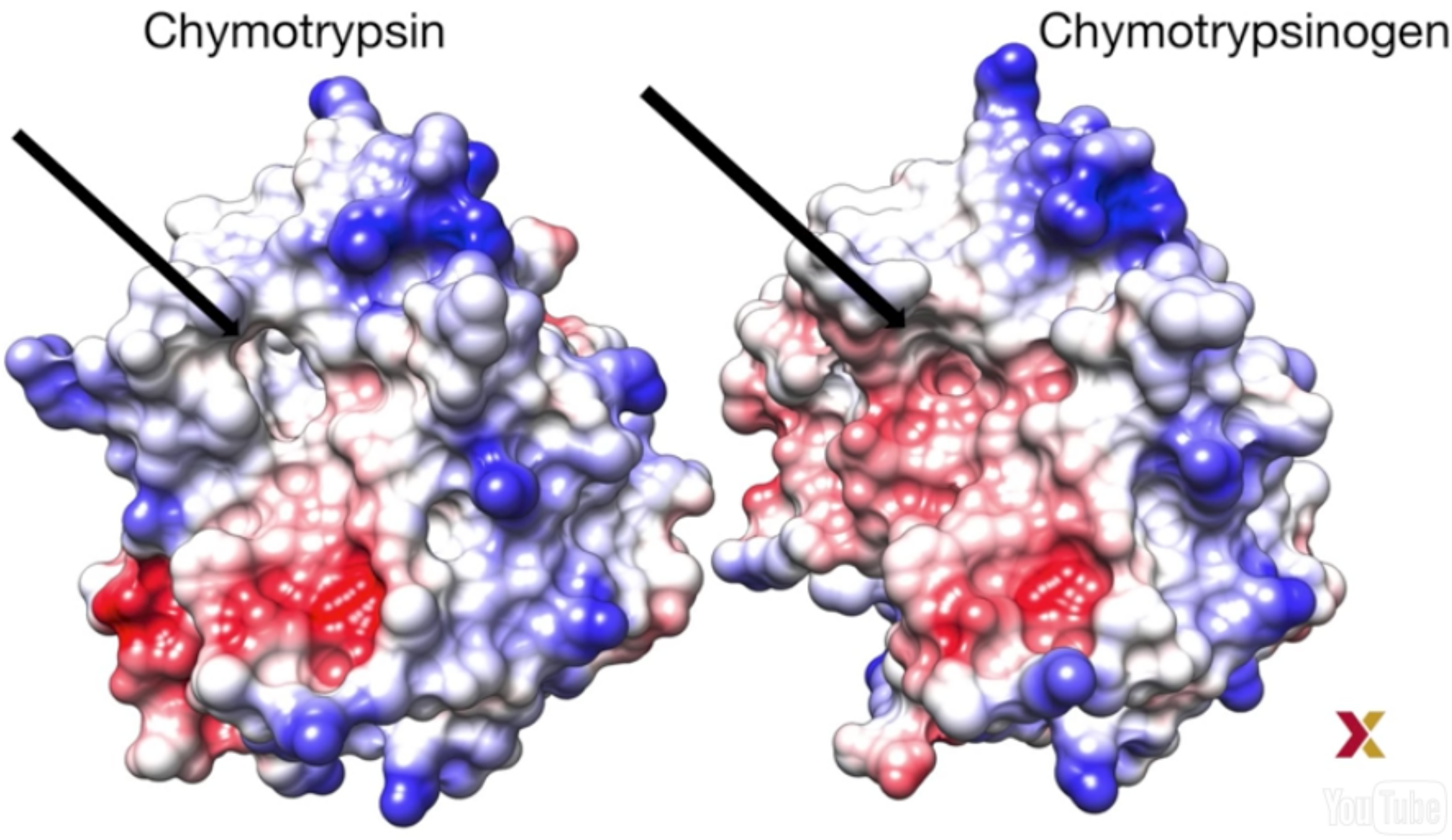
1 13 16 146 149 245

Chymotrypsinogen

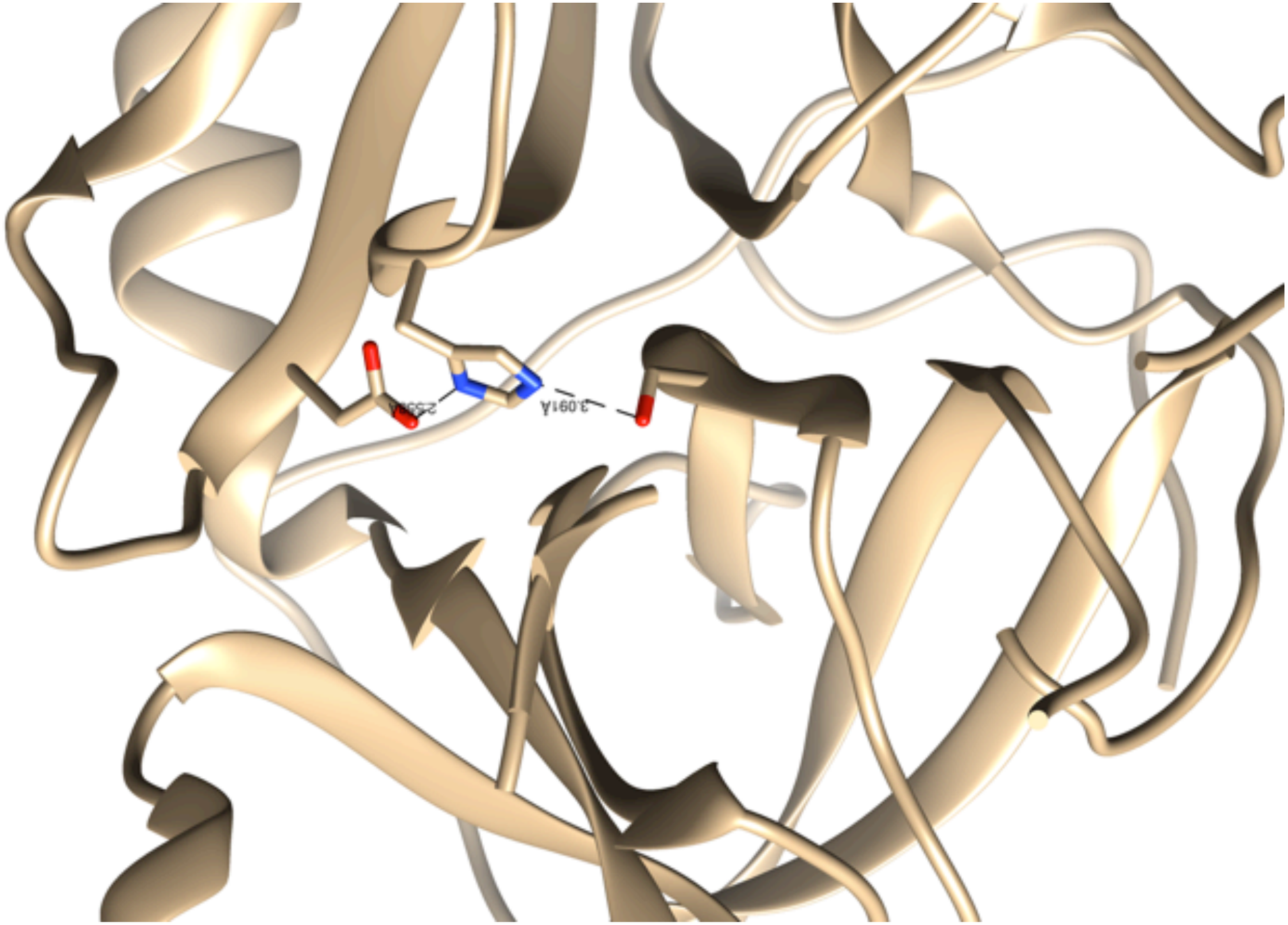


Chymotrypsin

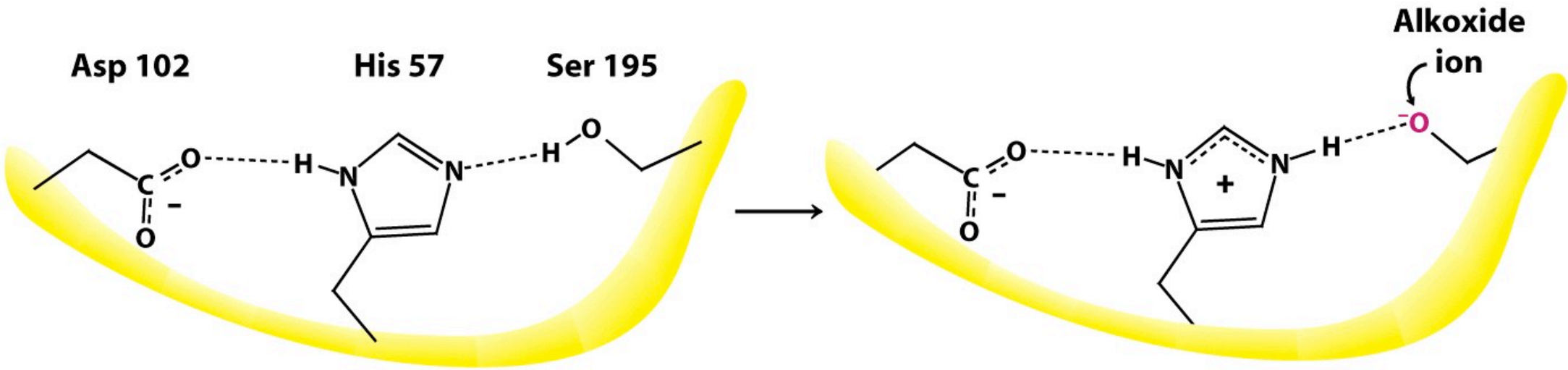




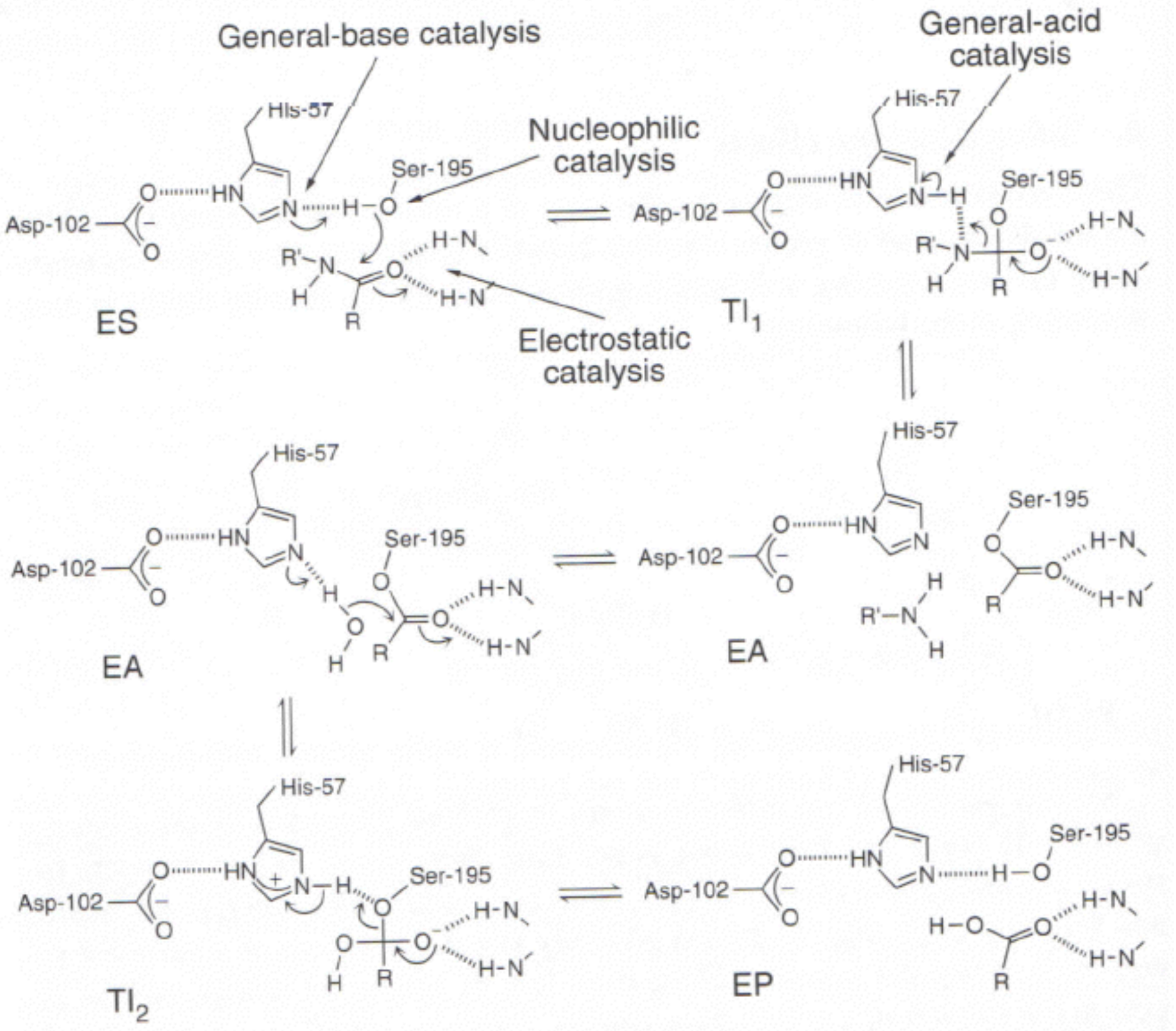
Active enzyme ***Inactive enzyme***


3.091Å

A tríade catalítica converte a Ser^{195} em um potente nucleófilo



Mecanismo de hidrólise da ligação peptídica pela chymotrypsin



Mutação sítio-dirigida de resíduos da tríade catalítica da subtilisina

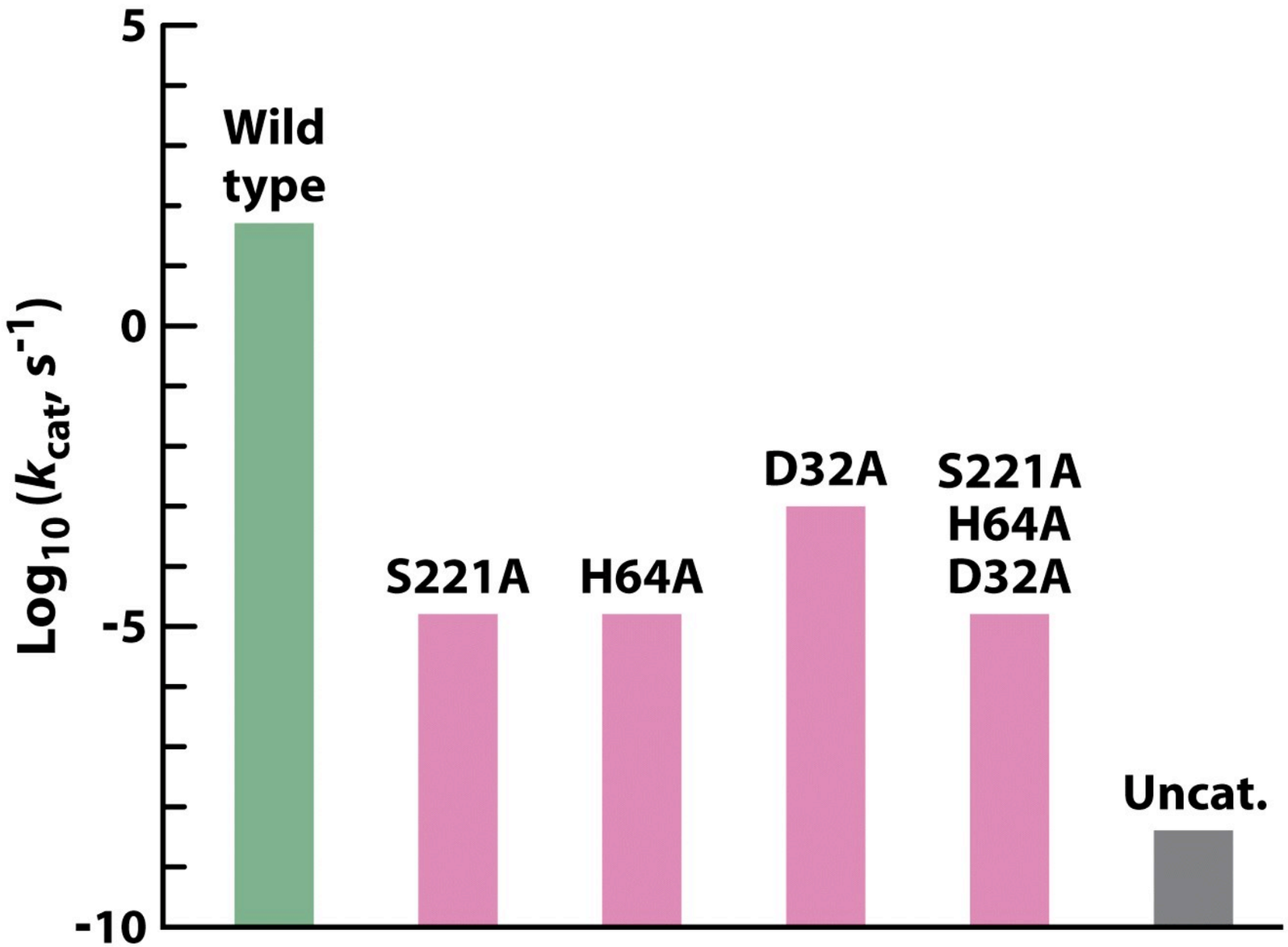
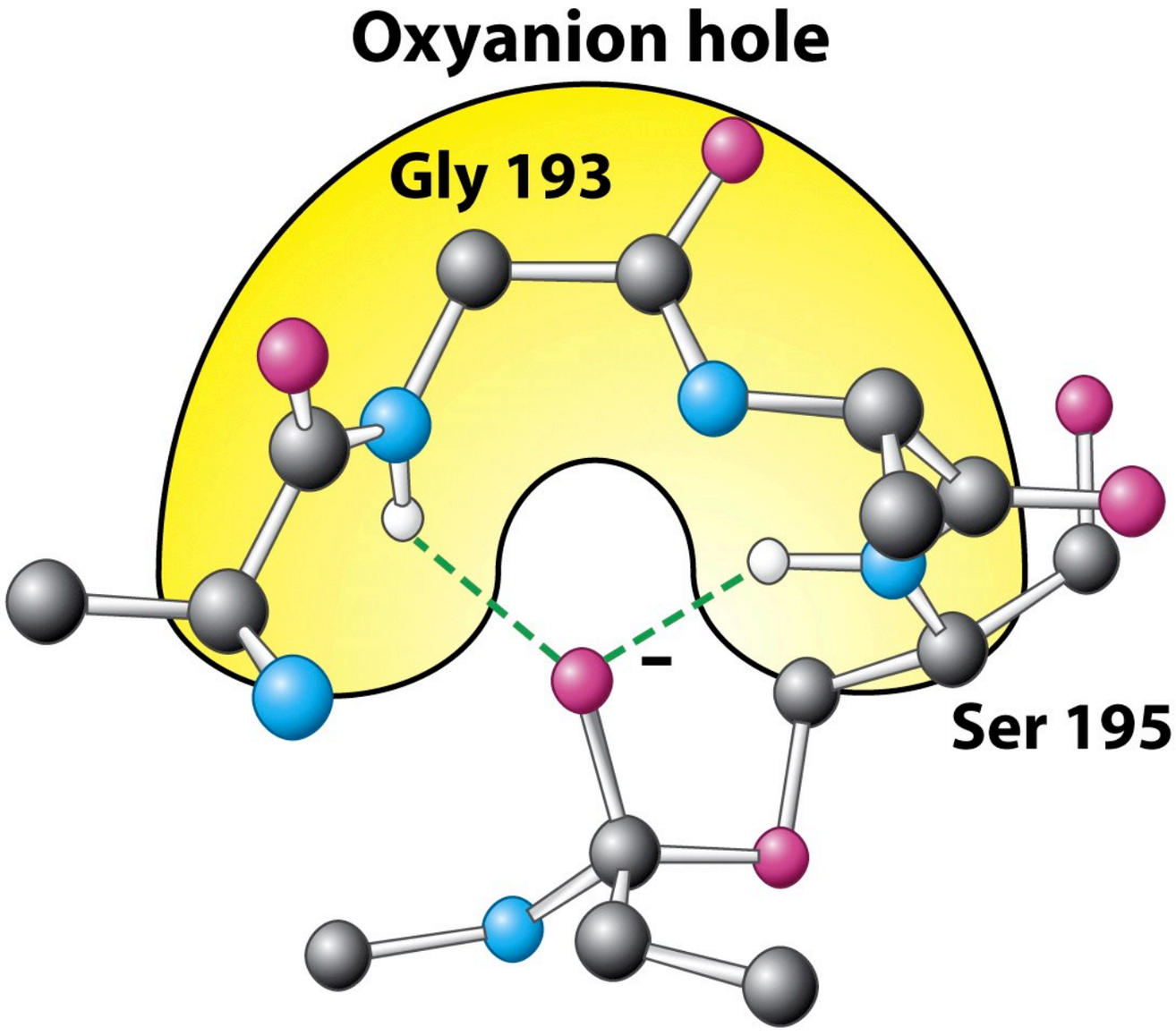
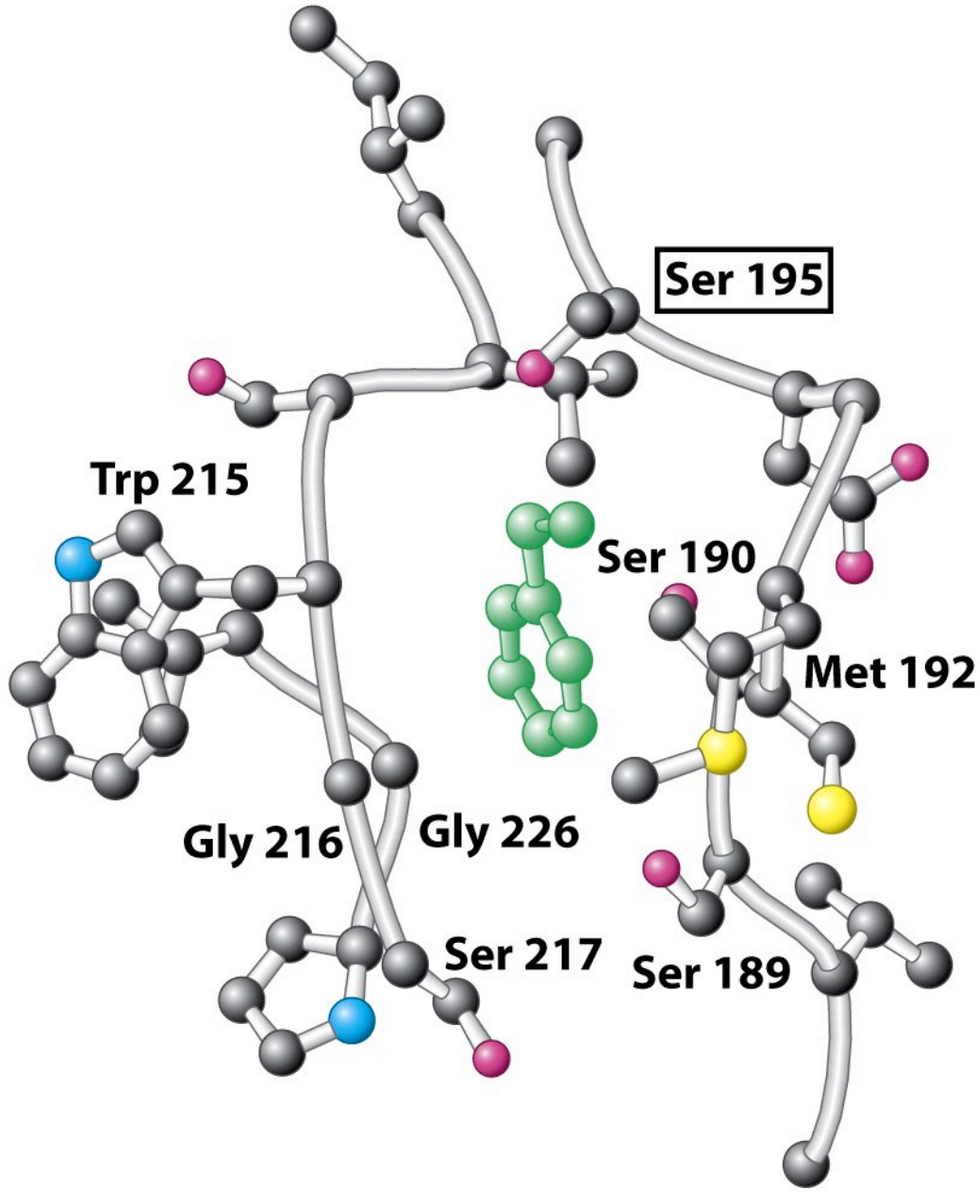


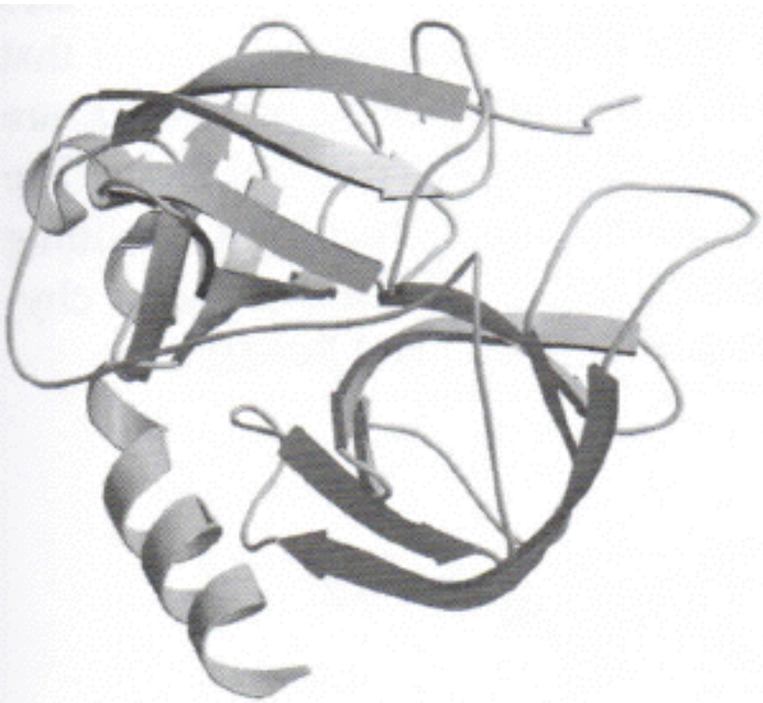
Figure 9-16
Biochemistry, Sixth Edition

Estabilização do intermediário tetraédrico



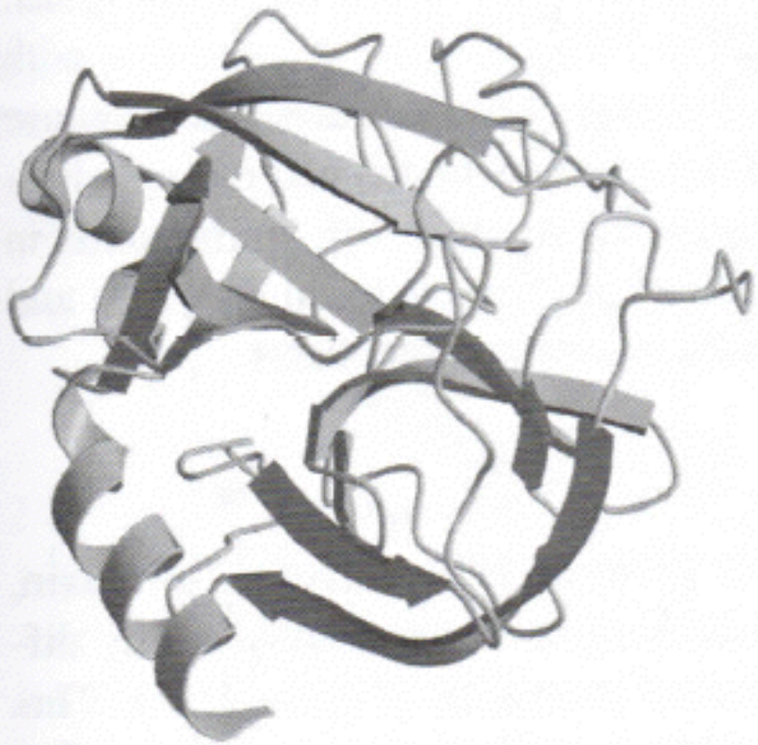
Explicação para a especificidade da enzima



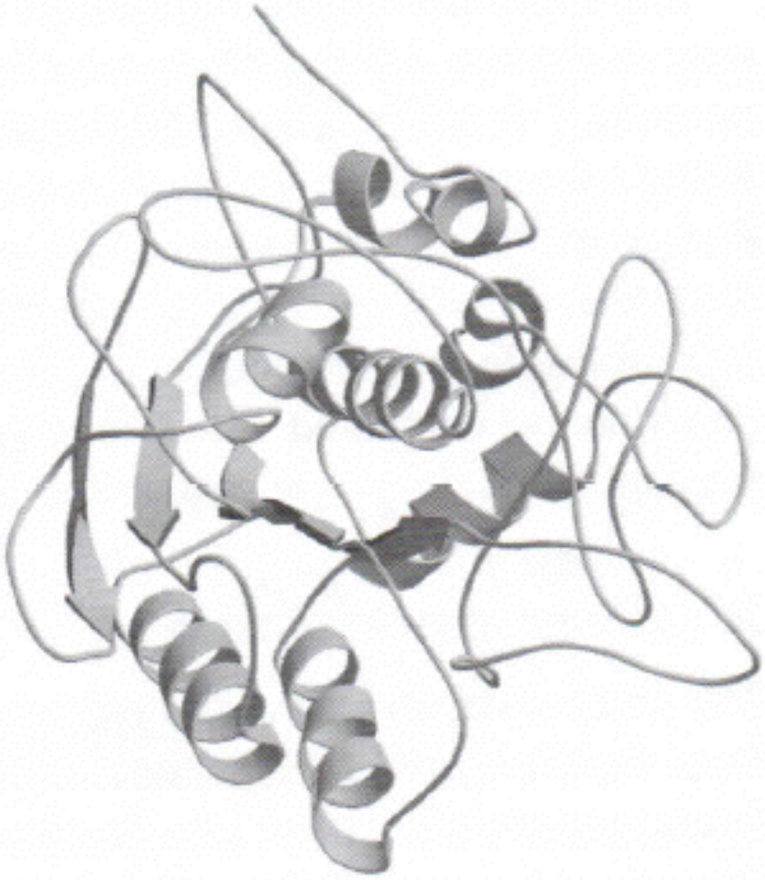


(a) Chymotrypsin

(b) Elastase

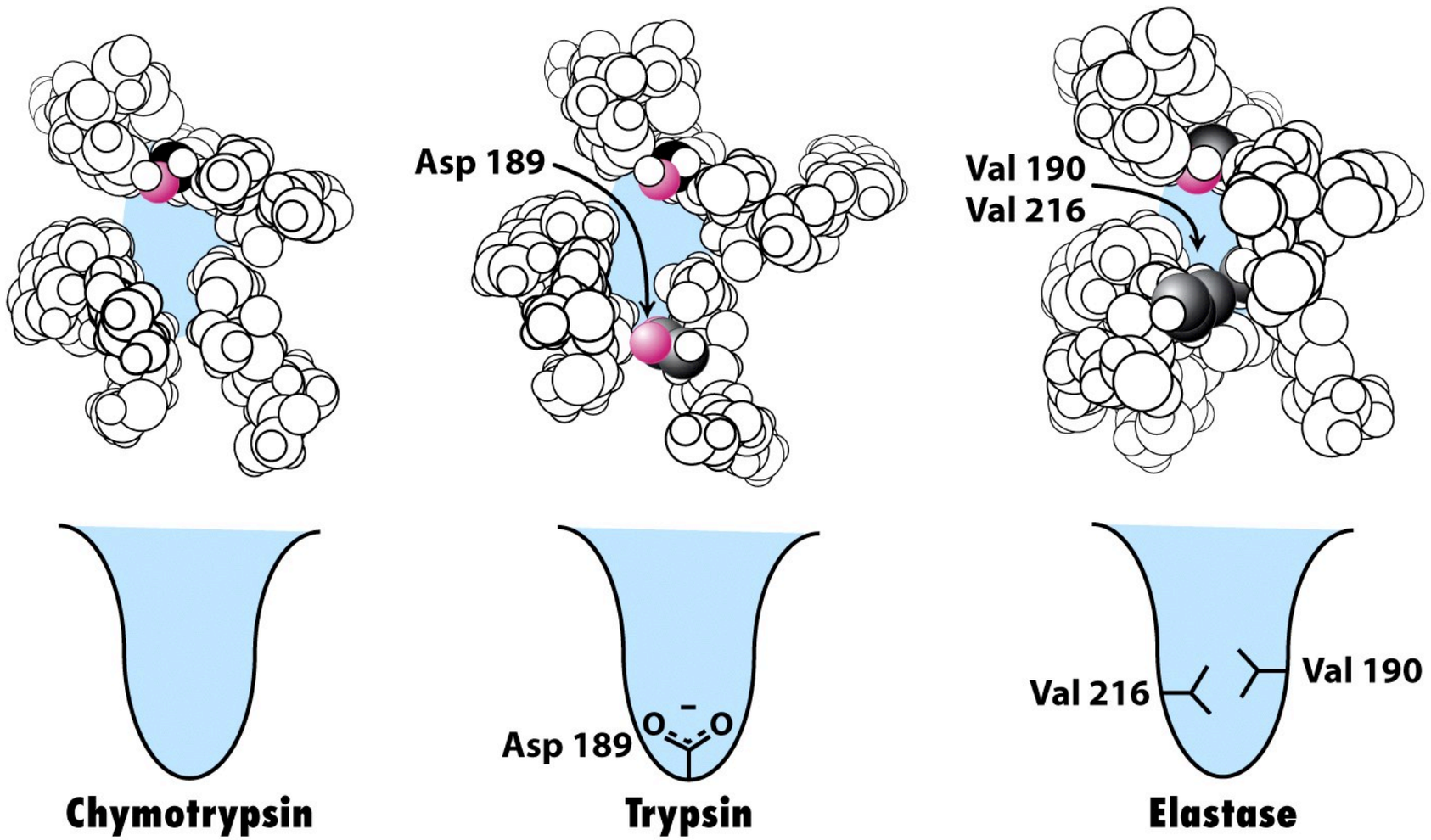


(c) Trypsin

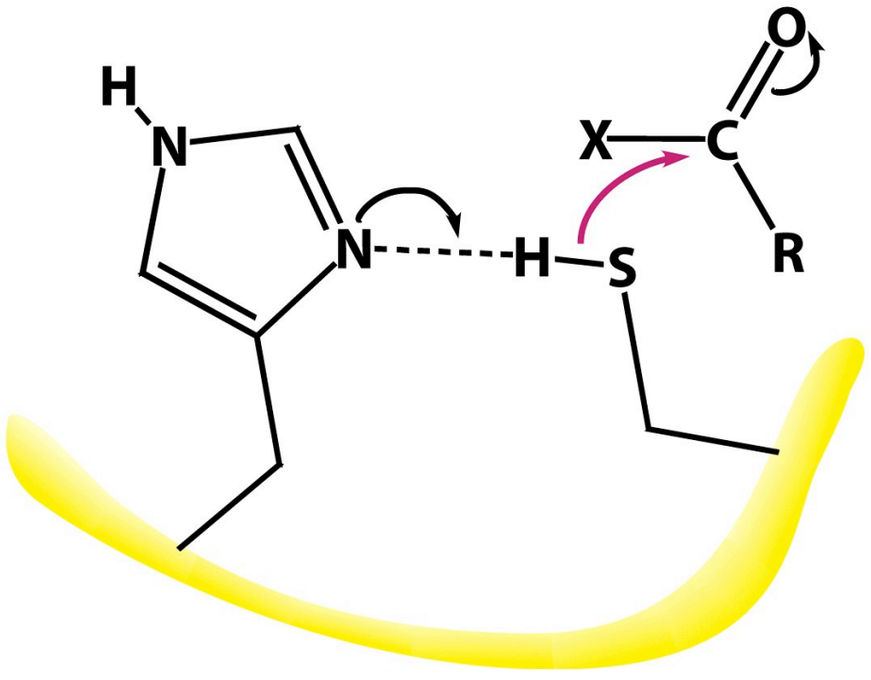


(d) Subtilisin

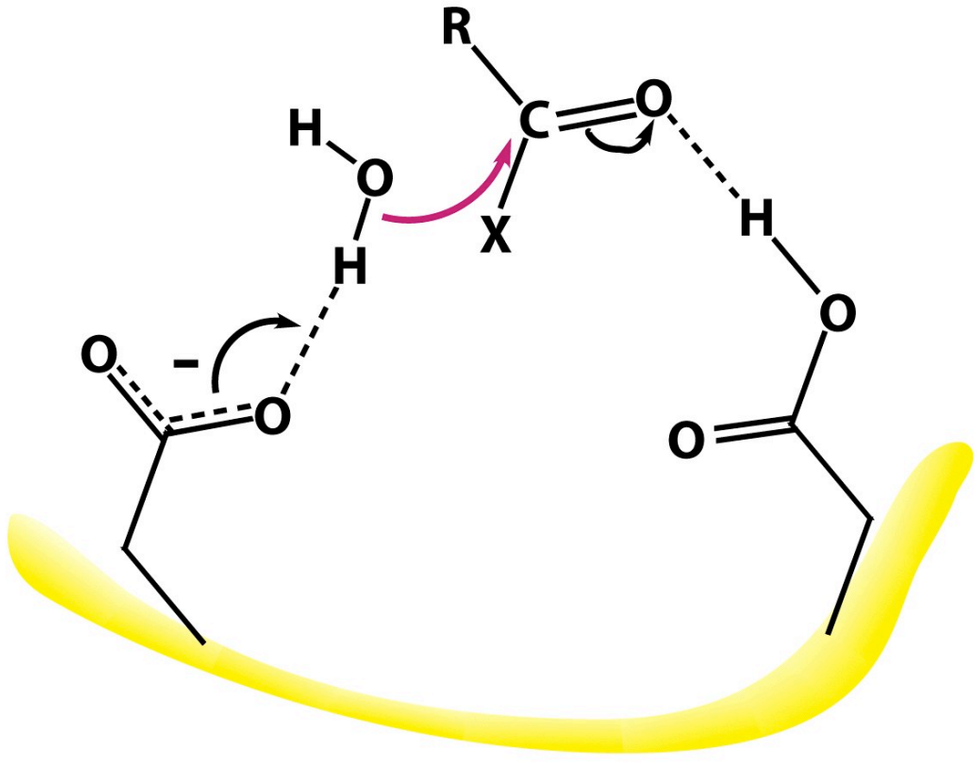
Explicação para as diferentes especificidades demonstradas por chymotrypsin, trypsin, elastase



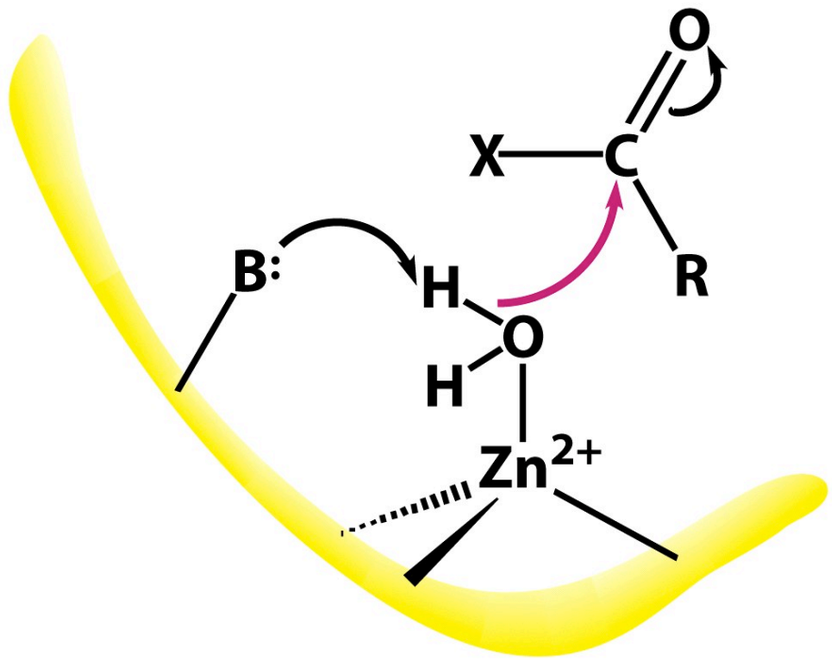
CYSTEINE PROTEASES

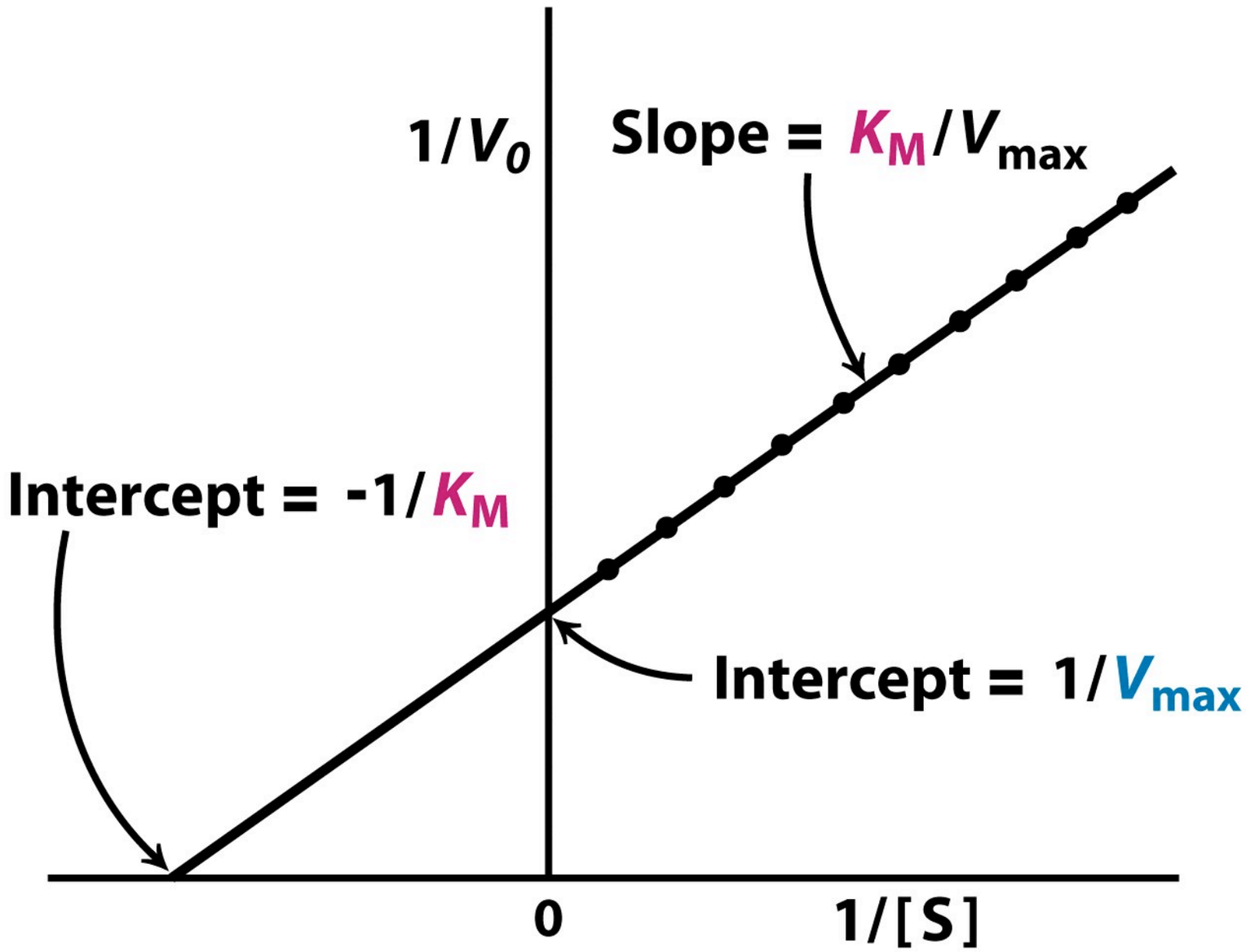


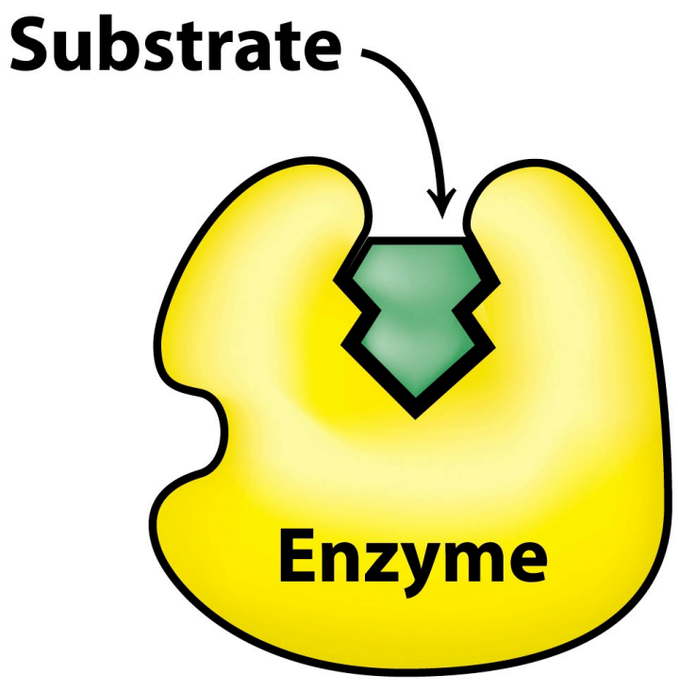
ASPARTYL PROTEASES

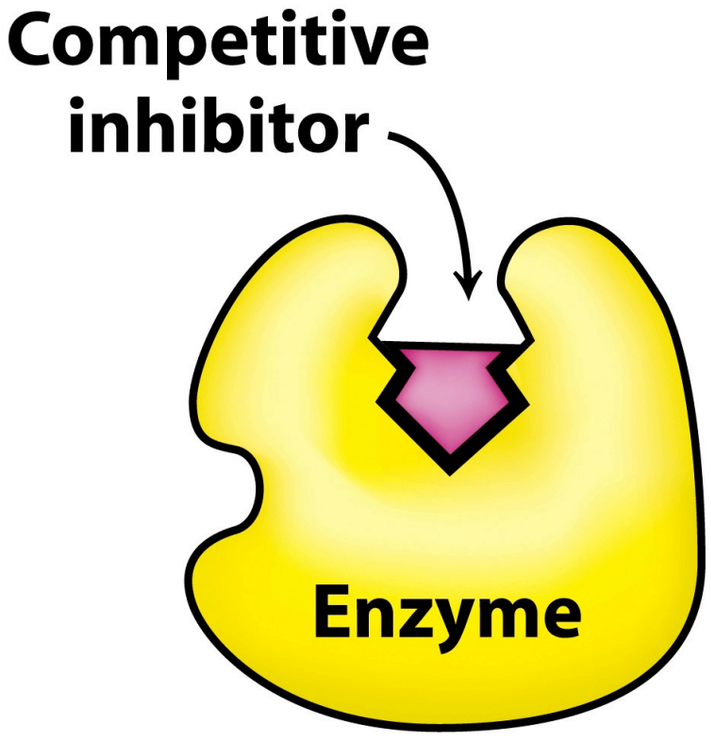


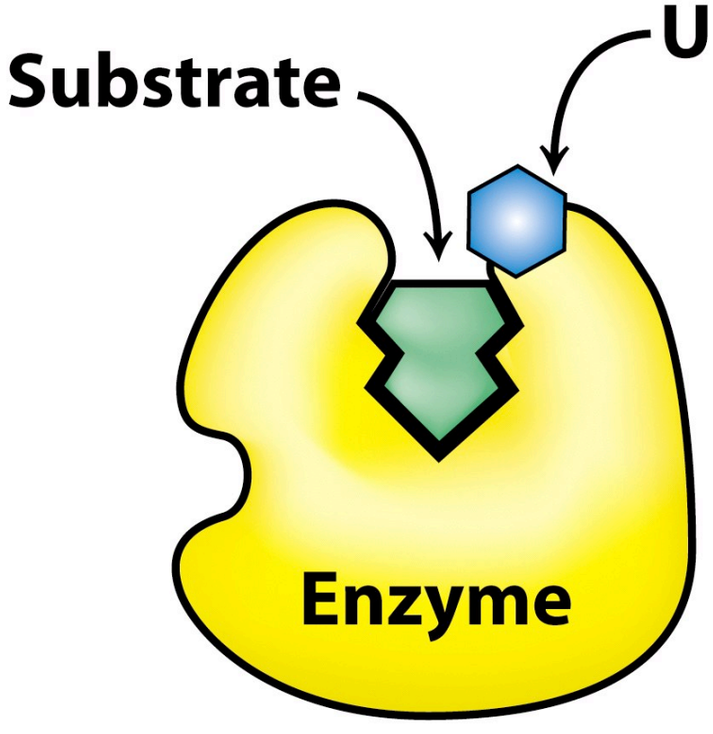
METALLOPROTEASES

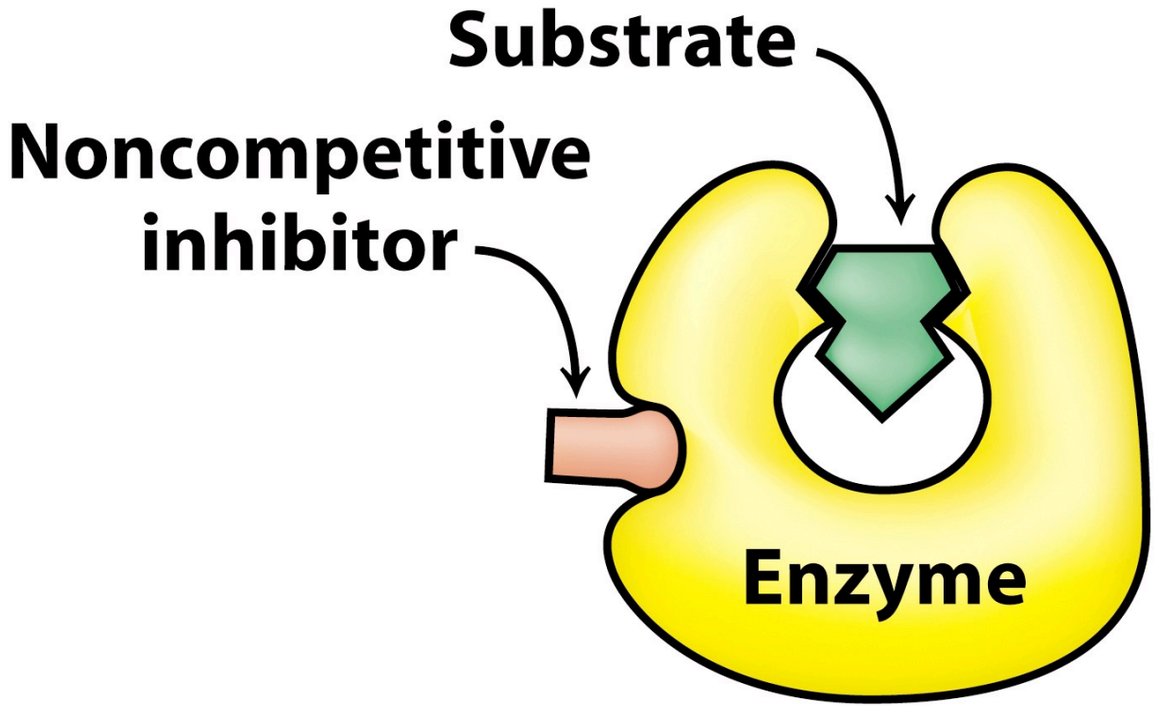


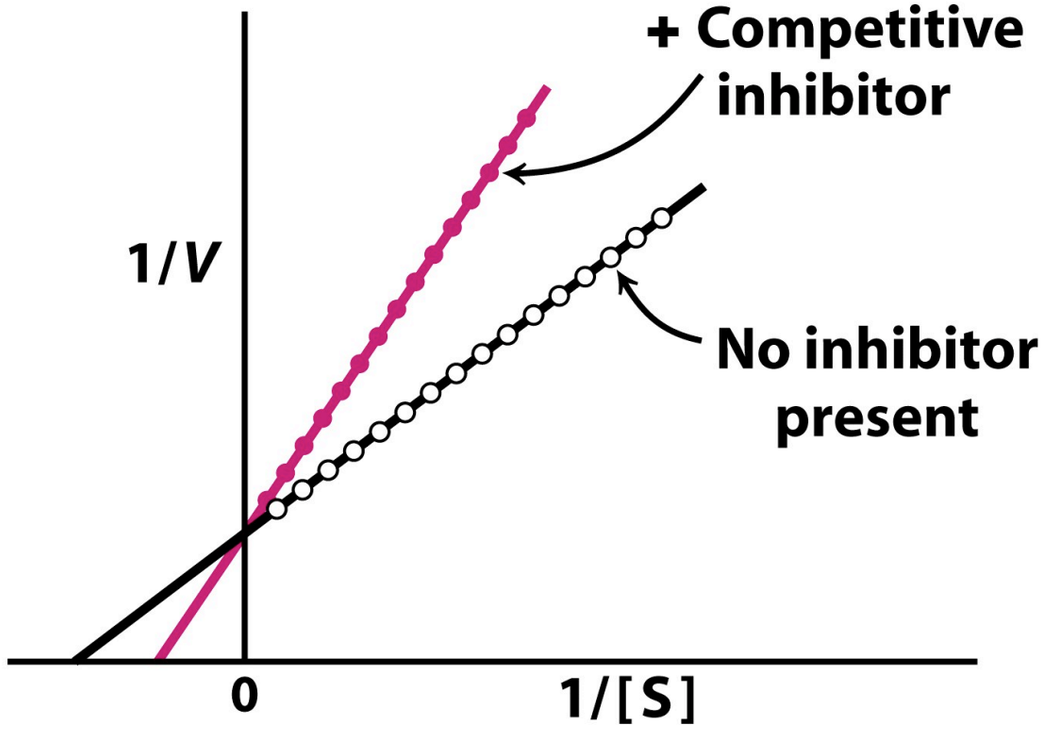

1/V_0
Slope = K_M/V_{max}
Intercept = -1/K_M
Intercept = 1/V_{max}
0
1/[S]

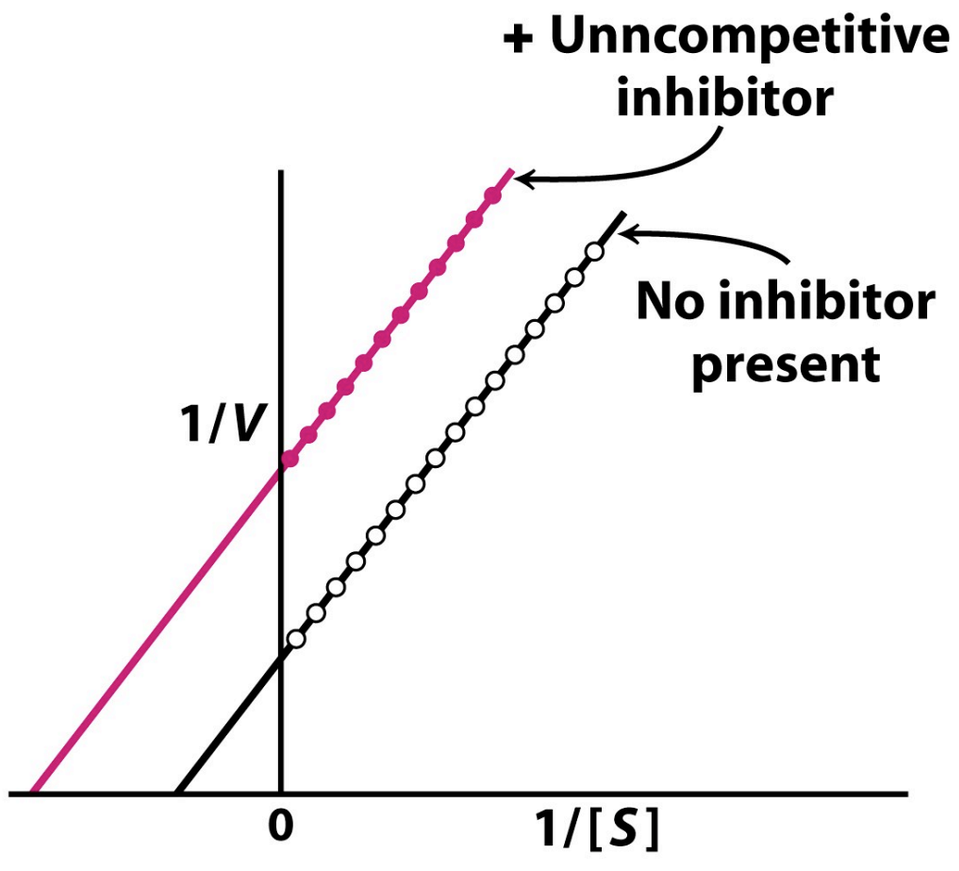

Substrate
Enzyme

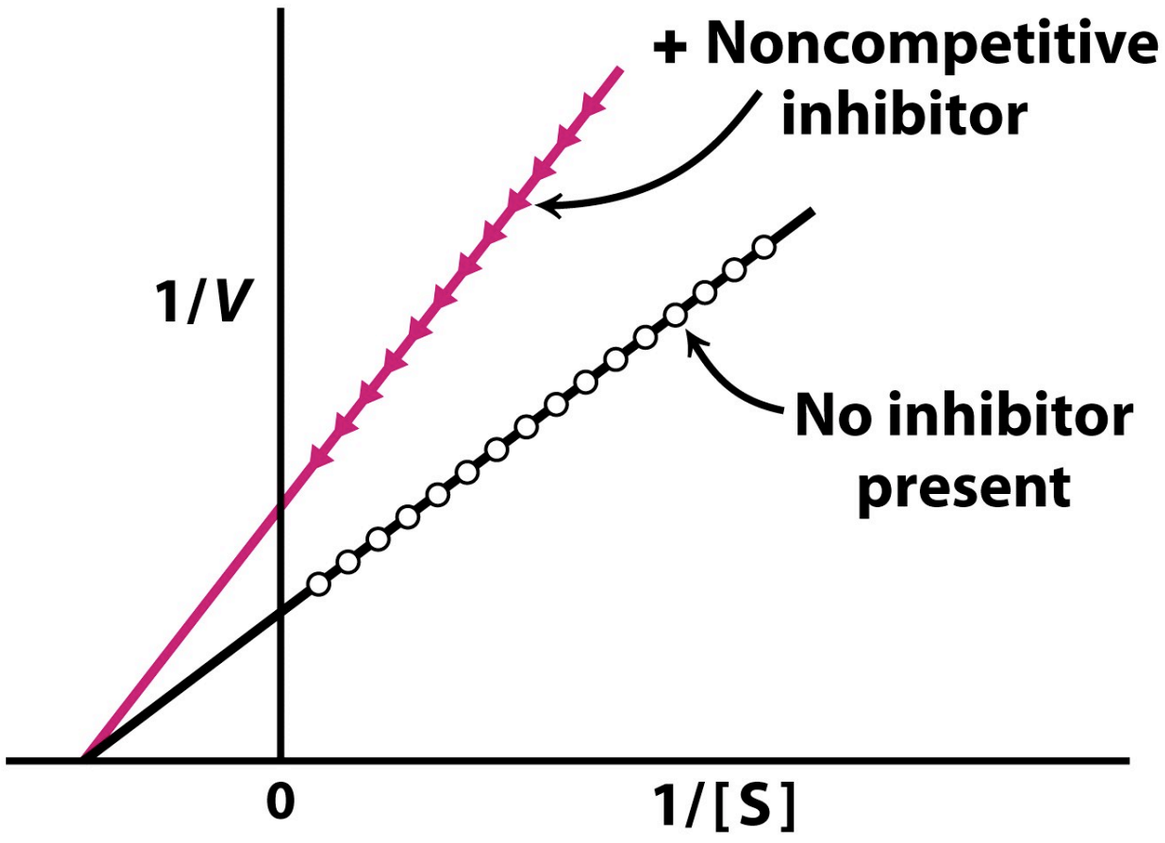

Competitive
inhibitor
Enzyme


Substrate
Uncompetitive
inhibitor
Enzyme


Substrate
Noncompetitive
inhibitor
Enzyme


+ Competitive inhibitor
No inhibitor present
1/V
0
1/[S]


+ Unncompetitive inhibitor
No inhibitor present
1/V
0
1/[S]


+ Noncompetitive inhibitor
No inhibitor present
1/V
0
1/[S]