Enzymes

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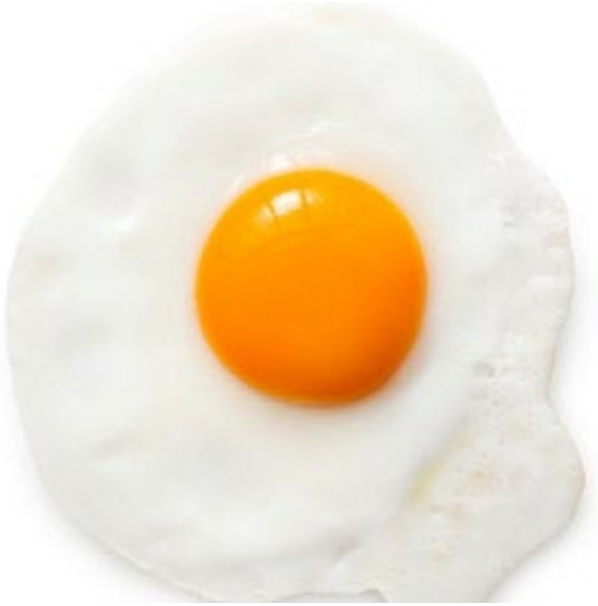
Think about your food

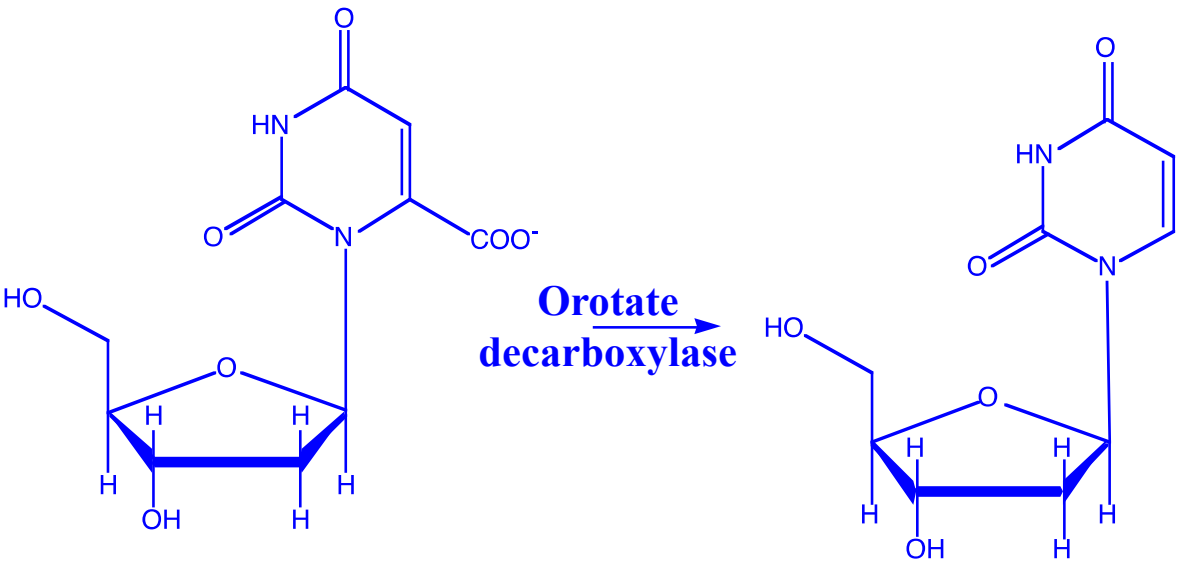


If eaten, digested in hours;

If not eaten, stay for years…..

Enzymes are biological catalysts.
酶是生物催化剂。

Enzymes affect reaction rates, not equilibria.
酶只影响反应速度，而不影响反应平衡。



k_{cat}= 39 s^{-1} ➔ 25 × 10^{-3} second

k_{non} = 2.8 ×10^{-16} s^{-1} ➔ 78 × 10^{6} year

k_{cat} / k_{non} = 1.4 × 10^{17}

Why do people study enzymes?

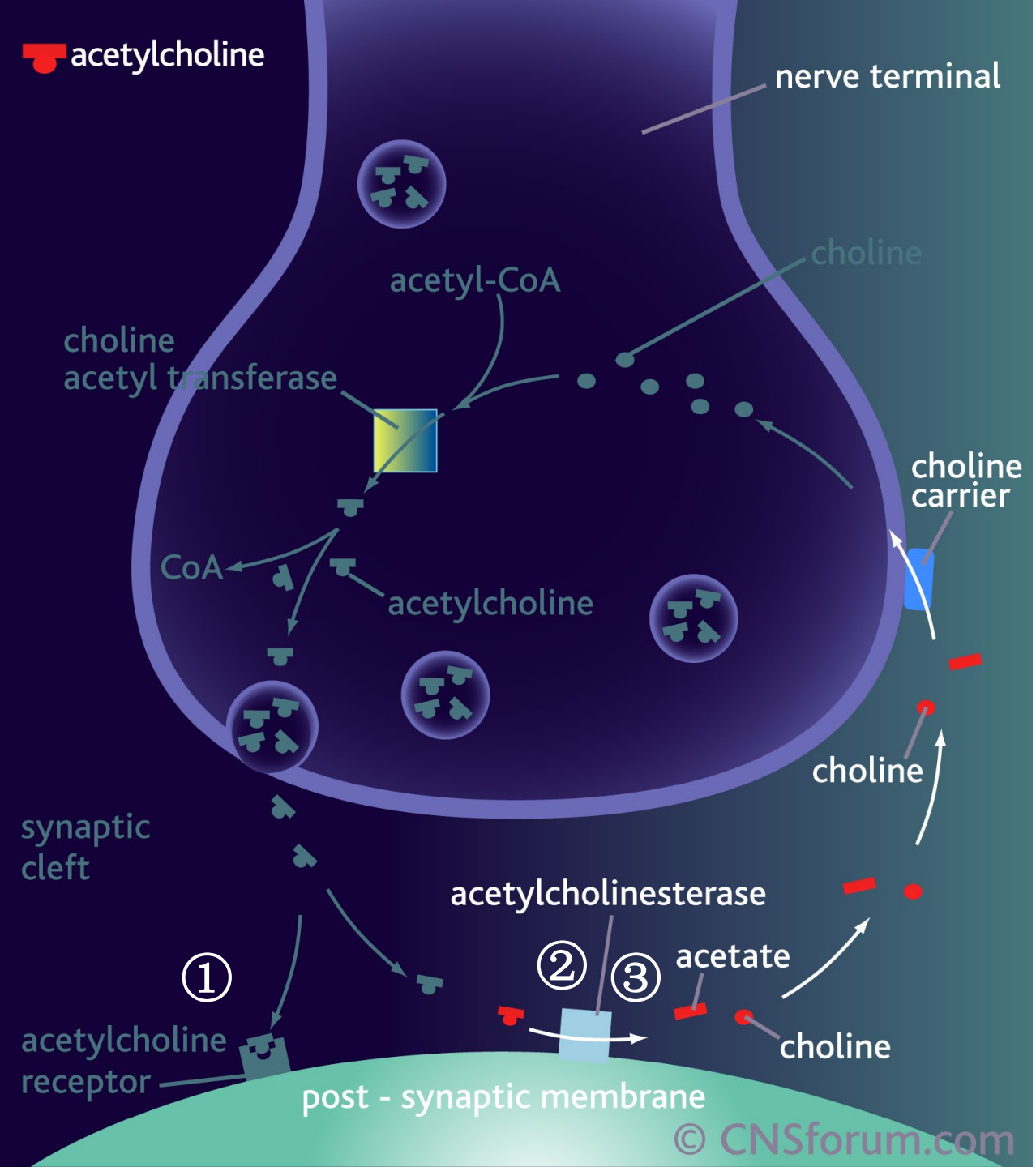
Science & Technology

Enzyme-inhibitor examples

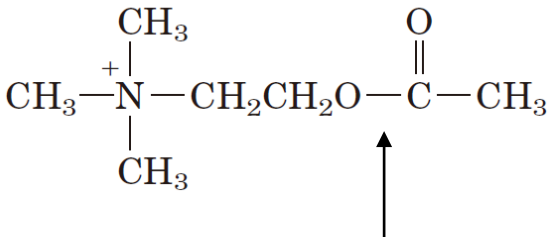
Lipase inhibitor;

Anti-AIDS cock-tail therapy;

Acetylcholinesterase inhibitor.乙酰胆碱酯酶抑制剂



acetylcholine



acetylcholinesterase

① Indian curare

② Organophosphorus

③ AD-treating medicine

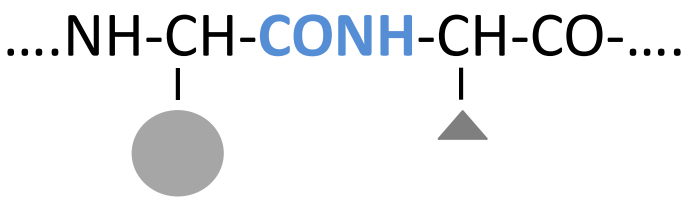
How do enzymes work?

Chymotrypsin 胰凝乳蛋白酶

VNQHLCGSHLVEALYLVCGERG **Substrate 底物**

chymotrypsin

VNQHLCGSHLVEALY LVCGERG **Product 产物**

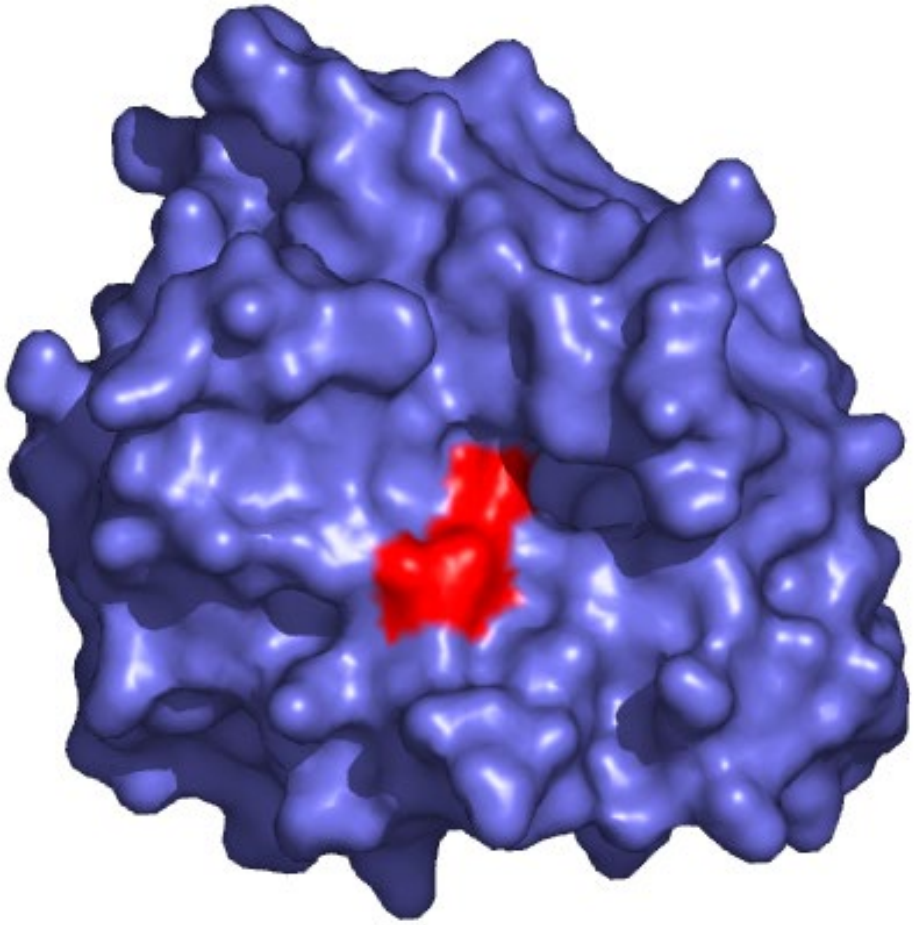


chymotrypsin

Chymotrypsin 胰凝乳蛋白酶

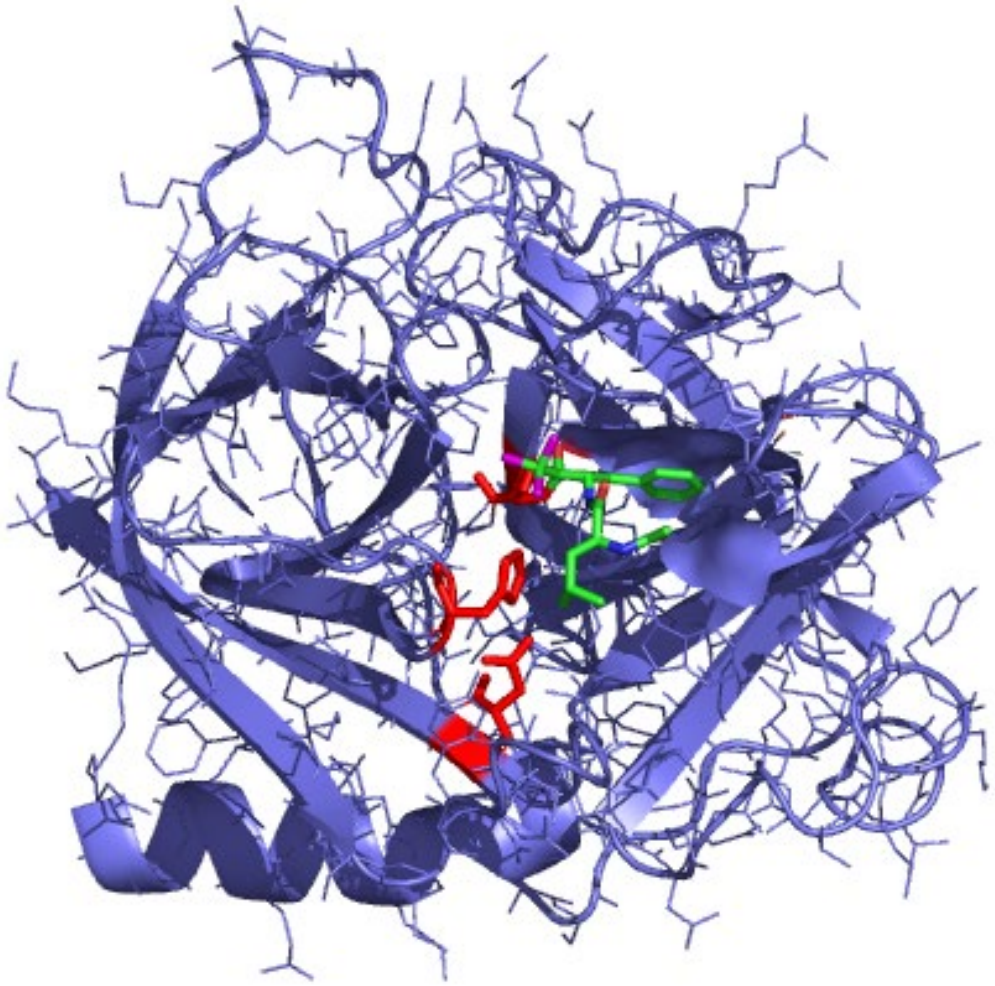
(PDB 7GCH)

Chymotrypsin 胰凝乳蛋白酶



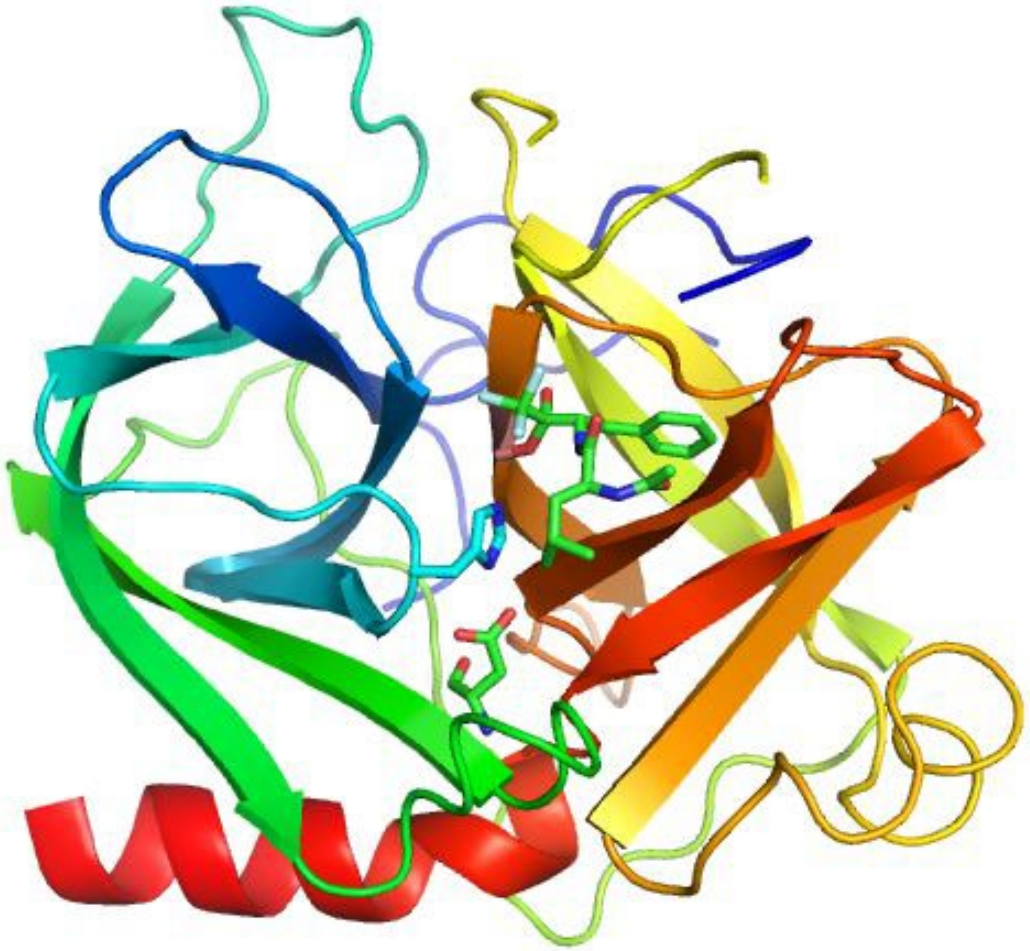
Active site 活性位点

Chymotrypsin 胰凝乳蛋白酶

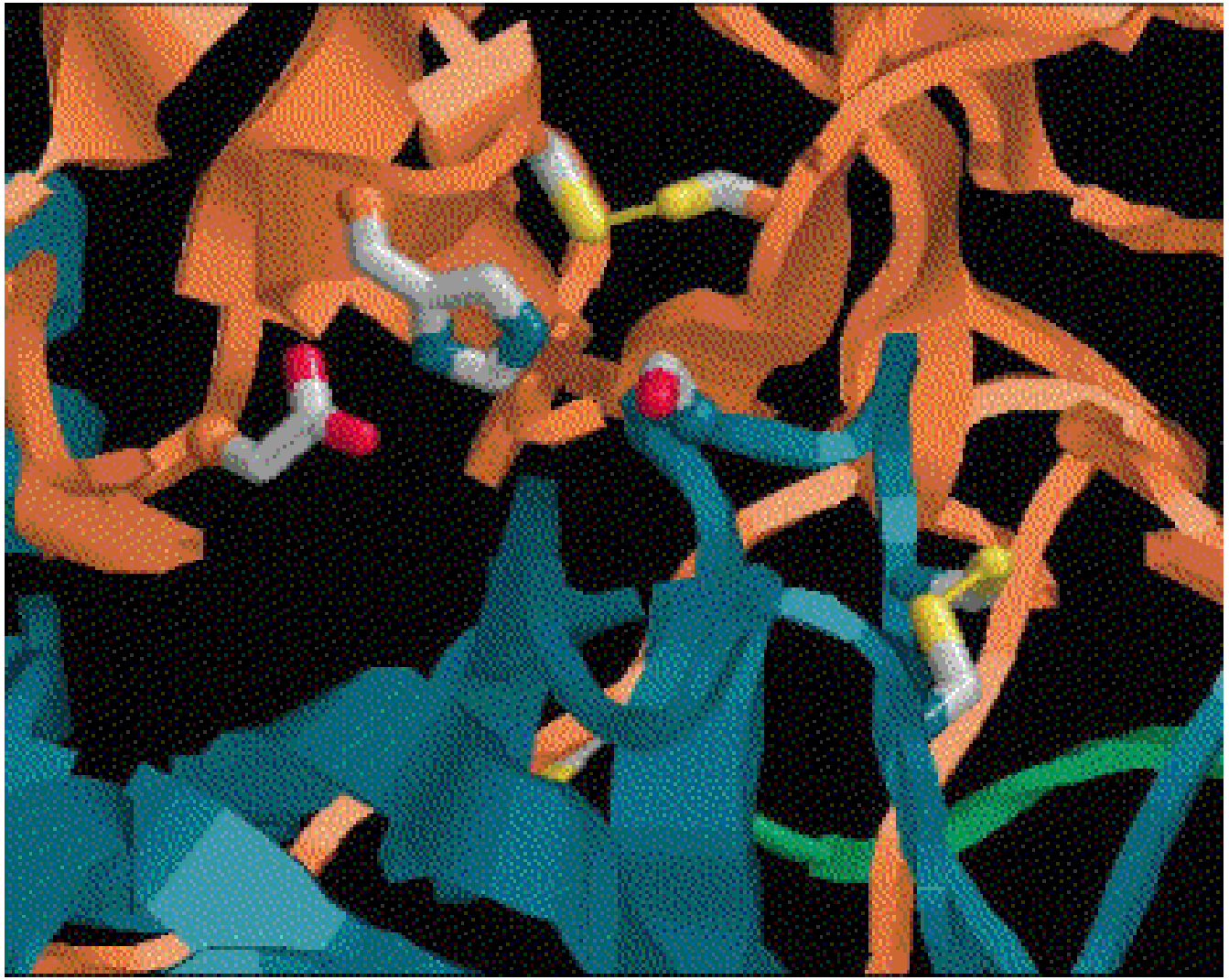


Catalytic triad: Ser195, His57, Asp102. **Inhibitor 抑制剂**

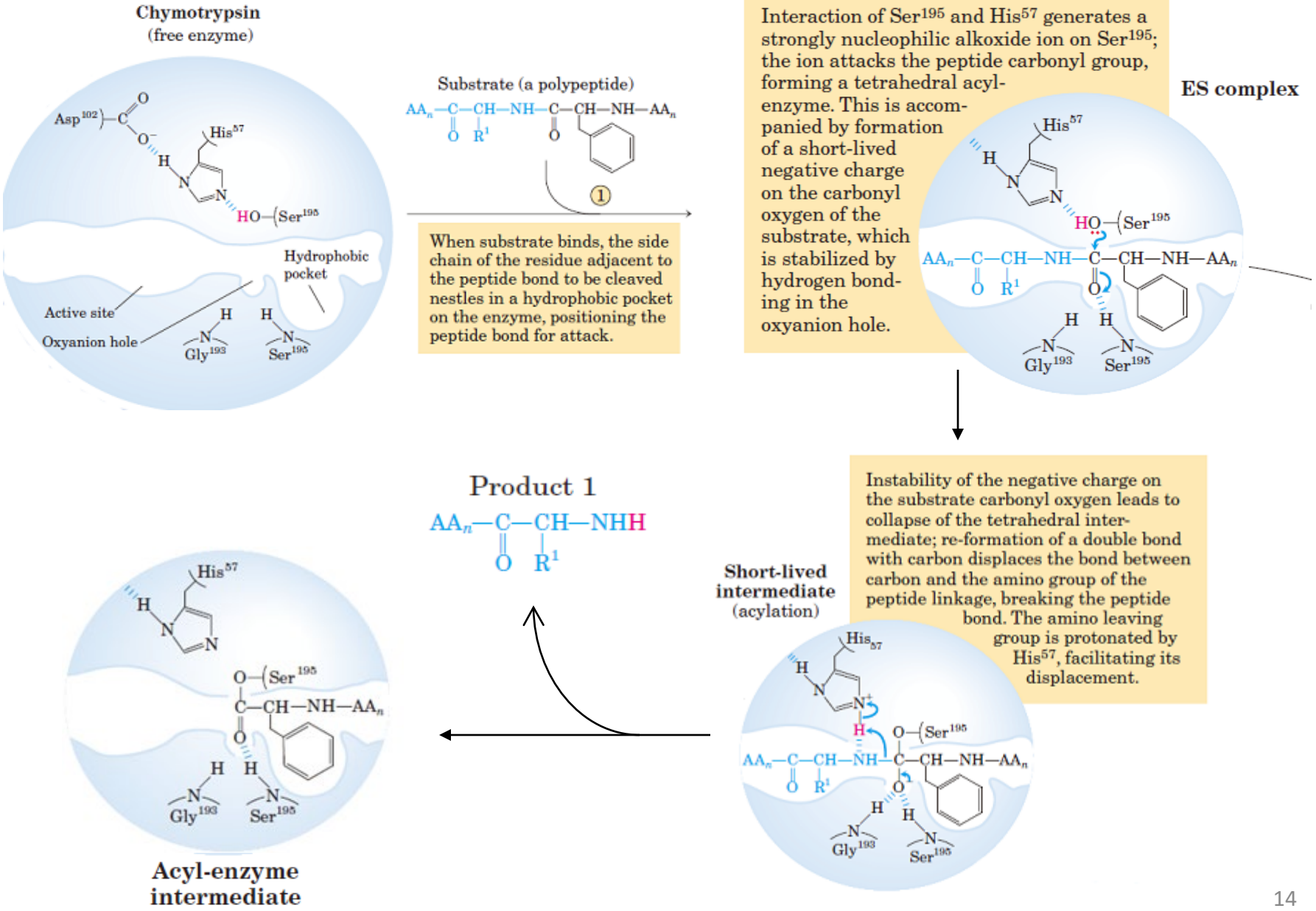
Chymotrypsin 胰凝乳蛋白酶

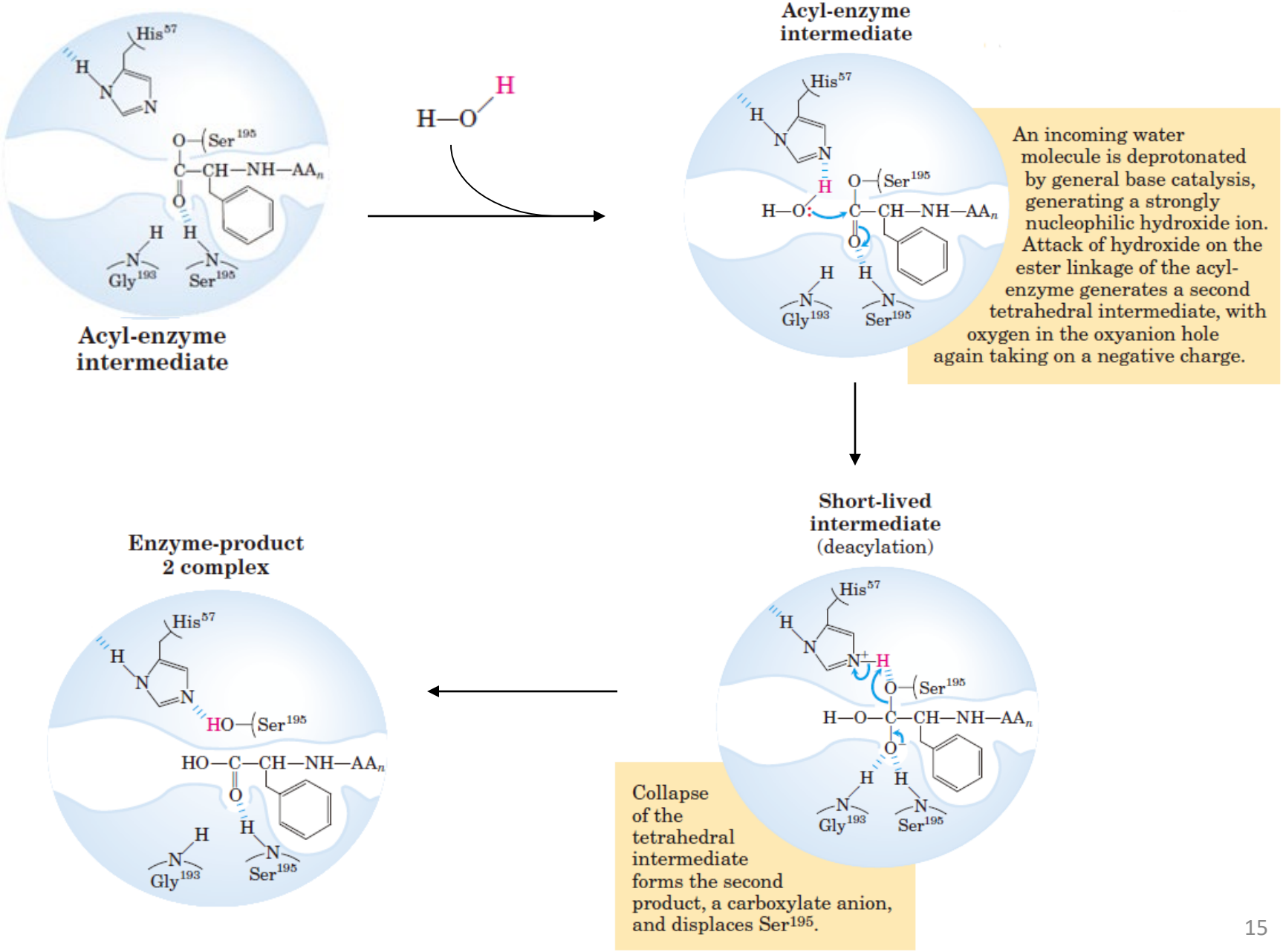


Chymotrypsin 胰凝乳蛋白酶

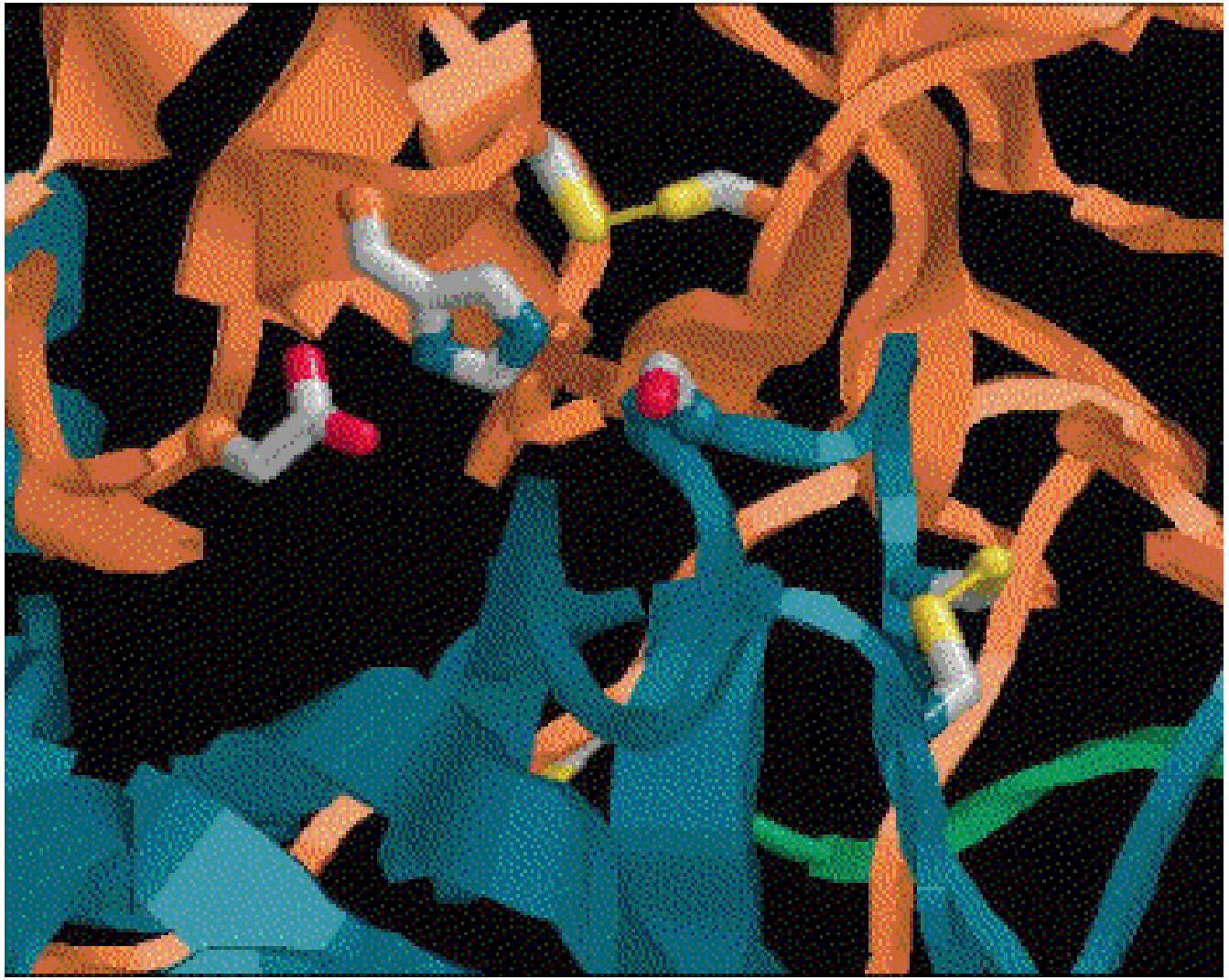


(juang.bst.ntu.edu.tw/BCbasics/Animation1.htm)


Chymotrypsin
(free enzyme)
Asp102
His57
HO—Ser195
Hydrophobic pocket
Active site
Oxyanion hole
Gly193
Ser195
Substrate (a polypeptide)
AAn—C—CH—NH—C—CH—NH—AAn
1
When substrate binds, the side chain of the residue adjacent to the peptide bond to be cleaved nestles in a hydrophobic pocket on the enzyme, positioning the peptide bond for attack.
Interaction of Ser195 and His57 generates a strongly nucleophilic alkoxide ion on Ser195; the ion attacks the peptide carbonyl group, forming a tetrahedral acyl-enzyme. This is accompanied by formation of a short-lived negative charge on the carbonyl oxygen of the substrate, which is stabilized by hydrogen bonding in the oxyanion hole.
ES complex
Instability of the negative charge on the substrate carbonyl oxygen leads to collapse of the tetrahedral intermediate; re-formation of a double bond with carbon displaces the bond between carbon and the amino group of the peptide linkage, breaking the peptide bond. The amino leaving group is protonated by His57, facilitating its displacement.
Short-lived intermediate
(acylation)
Product 1
AAn—C—CH—NHH
Acyl-enzyme intermediate


Acyl-enzyme intermediate
His57
Ser195
Gly193
Ser195
H—O
H
Acyl-enzyme intermediate
An incoming water molecule is deprotonated by general base catalysis, generating a strongly nucleophilic hydroxide ion. Attack of hydroxide on the ester linkage of the acyl-enzyme generates a second tetrahedral intermediate, with oxygen in the oxyanion hole again taking on a negative charge.
Short-lived intermediate (deacylation)
Collapse of the tetrahedral intermediate forms the second product, a carboxylate anion, and displaces Ser195.
Enzyme-product 2 complex

Chymotrypsin 胰凝乳蛋白酶



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International classification of enzymes

No.	Class	Type of reaction catalyzed
1	Oxidoreductase 氧化还原酶	Transfer of electrons
2	Transferase 转移酶	Group transfer reaction
3	Hydrolase 水解酶	Hydrolysis reaction
4	Lyase 裂合酶	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerase 异构酶	Transfer of groups within molecules to yield isomeric forms
6	Ligase 连接酶	Bond formation coupled with ATP hydrolysis

Serine endopeptidase:	Chymotrypsin	EC 3.4.21.1
	Trypsin	EC 3.4.21.4
	Subtilisin	EC 3.4.21.62
	……	

A → P

First order reaction $v = k[\mathrm{A}]$

Zero order reaction $v = k$

A + B → P

Second order reaction $v = k[\mathrm{A}][\mathrm{B}]$

A → P

$$v = -\frac{d[\mathrm{A}]}{dt} = \frac{d[\mathrm{P}]}{dt}$$

$$= k[\mathrm{A}]$$

$v : {Mol}/{L \cdot s}$

$k : {1}/{s}$

$$\frac{d[\mathrm{A}]}{[\mathrm{A}]} = -k\, dt$$

$$\ln[\mathrm{A}] = -kt + a = -kt + \ln[\mathrm{A}]_0$$

$$[\mathrm{A}] = [\mathrm{A}]_0 \cdot \mathrm{e}^{-kt}$$

A → P

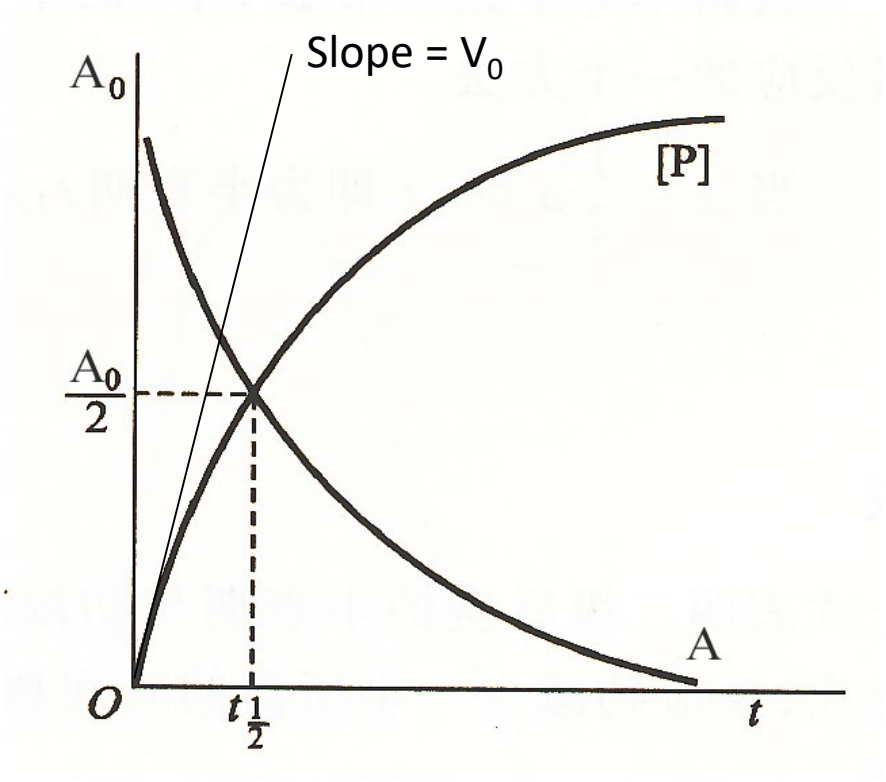
$$v = -\frac{d[\mathrm{A}]}{dt} = k[\mathrm{A}]$$

When $[A] = [A]_0$, $v = V_0$

V_0: initial velocity/rate（初速度）

When $[A] = [A]_0/2$, $t = t_{1/2}$

$t_{1/2}$: half-life time（半衰期）

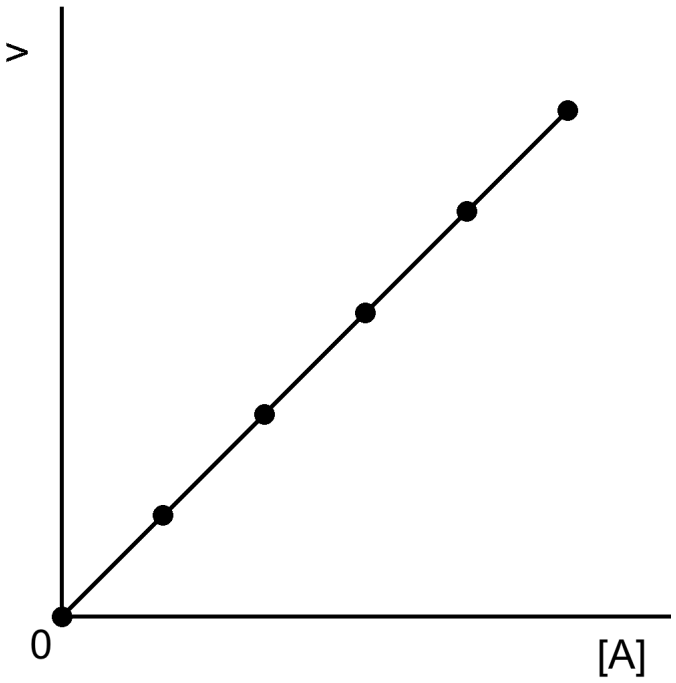


Radioactive isotope decomposition:

^{32}P $t_{1/2} \approx 14$ days; ^{125}I $t_{1/2} \approx 60$ days.

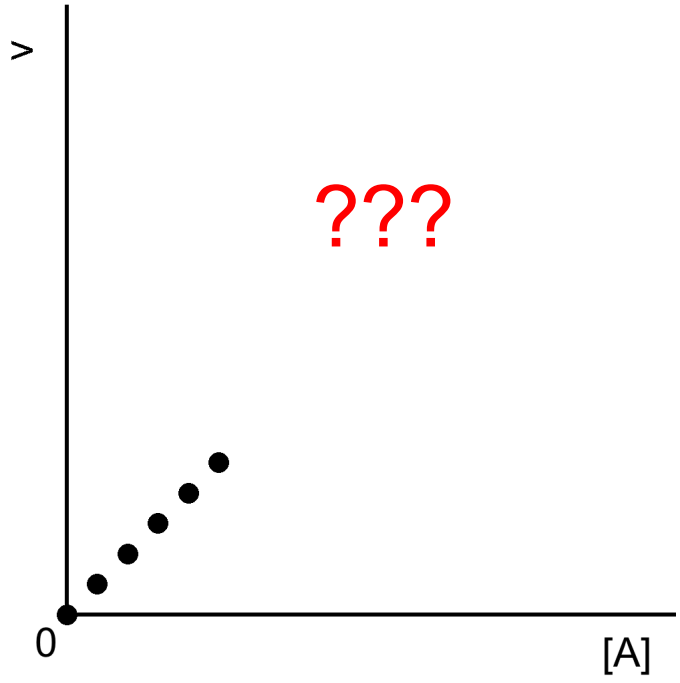
A → P

$$v = \frac{d[\mathrm{P}]}{dt} = k[\mathrm{A}]$$



A $\xrightarrow{\text{Enzyme}}$ P

$$v = \frac{d[\mathrm{P}]}{dt} = ??[\mathrm{A}]$$



Next time:

Michaelis-Menten Equation.