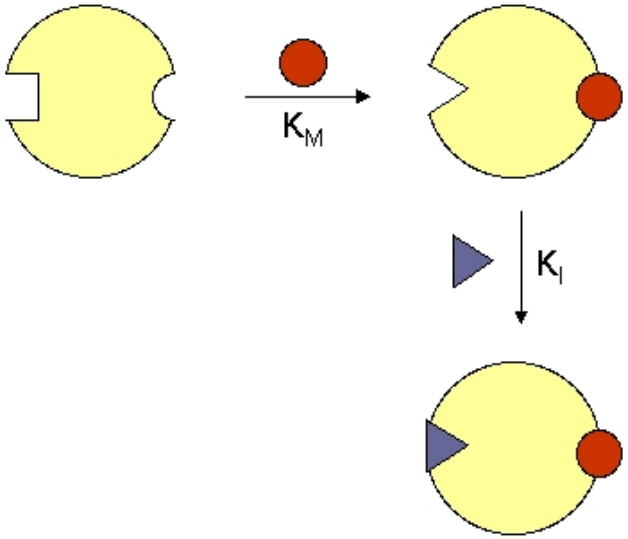
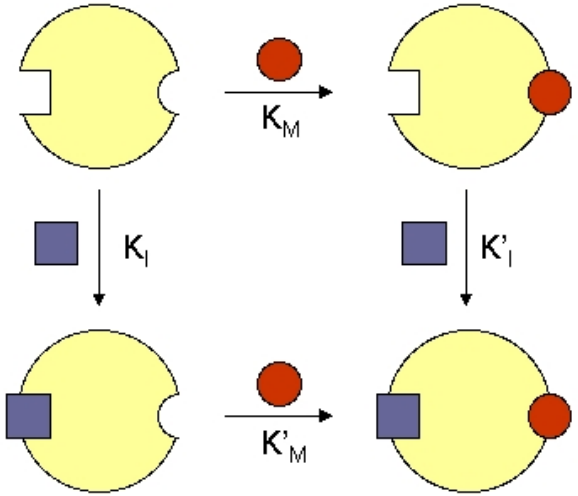
Other inhibition models



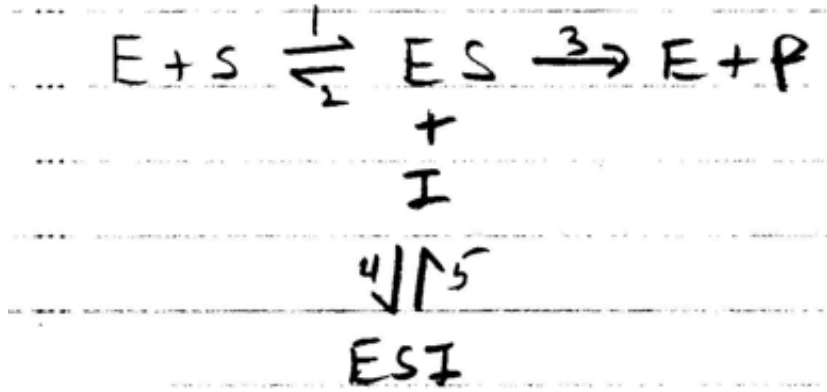


Uncompetitive inhibition

Non-competitive inhibition

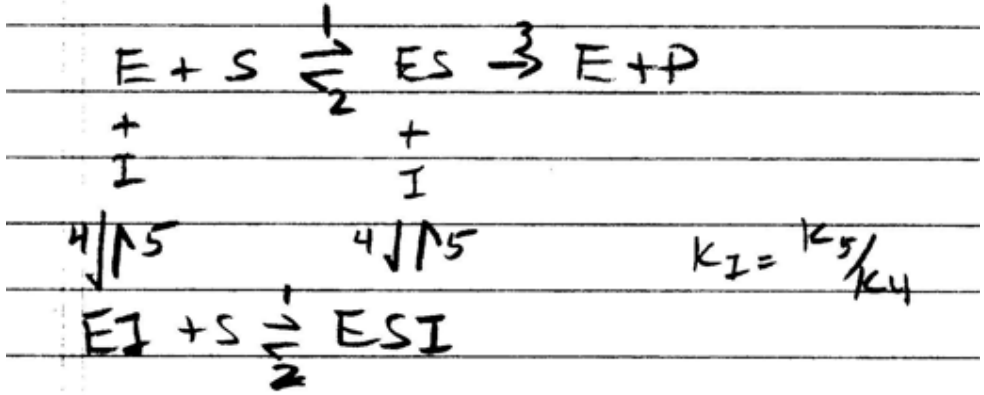
Binding of inhibitors changes binding of substrate

Uncompetitive inhibition



$K_I = \frac{k_5}{k_4}$

Non-competitive



General Inhibition Model

General Model

$$\begin{array}{l} \qquad K_M \quad k_2 \\ E+S \Leftrightarrow ES \Rightarrow E+P+I \qquad K_M = [E][S]/[ES] \\ + \qquad + \\ I \qquad I \qquad\qquad K_I = [E][I]/[EI] \\ K_I \Updownarrow \alpha K_I \Updownarrow \qquad\qquad \alpha K_I = [ES][I]/[ESI] \\ EI \Leftrightarrow EIS \Leftrightarrow E+P+I \\ \quad \alpha K_M \quad \beta K_2 \end{array}$$

General Inhibition Model

$v = V_f[S]/(K_f + [S])$ $\quad V_f = f_v V_M$

$K_f = f_K K_M$

$\alpha = \infty, \beta = 0$ Competitive inhibition

$f_v = 1, f_k = 1+[I]/K_I$ $\quad v = V_M[S]/\{[S]+ K_M(1+[I]/K_I)\}$

$\alpha = 1, \beta = 0$ Non-competitive inhibition

$f_v = 1/(1+[I]/K_I), \ f_k = 1$ $\quad v = V_M \{1/(1+[I]/K_I)\}[S]/\{[S]+ K_M\}$

Substrate Inhibition Model

General Model

$$\begin{array}{ccccc} & & K_M & k_2 & \\ E & + S & \Leftrightarrow ES & \Rightarrow & E + P \\ + & & + & & \\ S & & S & & \\ K_S \Updownarrow & & K_S \Updownarrow & & \\ SE & + S & \Leftrightarrow SES & & \\ & & K_M & & \end{array}$$

$K_M = [E][S]/[ES]$

$K_S = [E][S]/[SE]$

$$v = V_M/(1+K_M/[S] + [S]/K_S)$$

Examples of types of inhibitors

- Covalent/suicide inhibitors
  - TPCK (alpha-N-p-toluenesulfonyl-L-phenylalanine chloromethyl ketone) binds to the active site of chymotrypsin
  -
- Macropolyions
  - Nucleic acids, protamines (anionic polymer)
  - Bind positively charged proteins

- Antibodies (antienzymes)
  - Gamma globulins (precipitation)

- Protease inhibitors
  - Trypsin inhibitors, phaseolamine

- Organic substrate analogs
  - Synthetic substrate mimics
  - Cofactor analogs

Enzyme Kinetics References

- Handouts posted on Blackboard
- Comprehensive Biological Catalysis: A Mechanistic Reference, M. Sinnott, ed., Academic Press, 1998
- A Study of Enzymes, Vol. I Enzyme Catalysis, Kinetics, and Substrate Binding, S. A. Ruby, 1991
- Source Book of Enzymes, J. S. White and D. C. White, CRC 1997