

# Enzyme reactivity and inhibition

# Today's goal

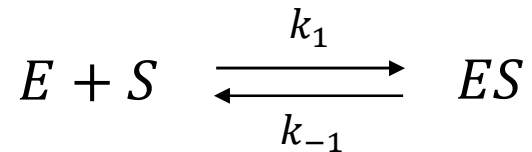
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- Look further into the Michaelis-Menten eq.
- Effect of (reversible) inhibitions on the rate of enzyme reactions
- Understand how biochemical mechanisms can be represented by mathematical models

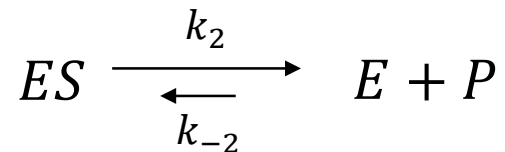
# Modeling enzyme reactions

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Step 1: The free enzyme (E) reacts with substrate (S) to form an enzyme-substrate complex (ES)



Step 2: The enzyme-substrate complex (ES) breaks down to form free enzyme and products (P)



## **Assumptions**

- 1) *The total concentration of enzyme ( $[E]_{total}$ ) in the system is constant*
- 2) *Step 2 is essentially irreversible*
- 3)  *$[ES]$  does not change over time (pseudo-steady state)*

**Use assumption 2) & 3):**

rate of ES-producing reactions = rate of ES-consuming reactions

$$k_1[E][S] = k_{-1}[ES] + k_2[ES] \quad \rightarrow \quad [E] = K_M \frac{[ES]}{[S]}$$

where  $K_M = \frac{k_{-1} + k_2}{k_1}$

**The rate of enzyme reaction ( $v$ )**

**= The rate of the reaction to produce "P"**

$$v = k_2[ES]$$

(step 2 forward reaction)

**Maximum "v" achievable in the system ( $v_m$ ):**

$$v_m = k_2[E]_{total}$$

**Mass balance for enzyme in the system**

$$[E]_{total} = [E] + [ES]$$

$[E]_{total}$  is constant by assumption 1)

**Compare  $v$  and  $v_m$ :**

$$\frac{v}{v_m} = \frac{[ES]}{[E]_{total}} = \frac{[ES]}{[E] + [ES]} = \frac{[ES]}{K_M \frac{[ES]}{[S]} + [ES]} = \frac{[S]}{K_M + [S]}$$

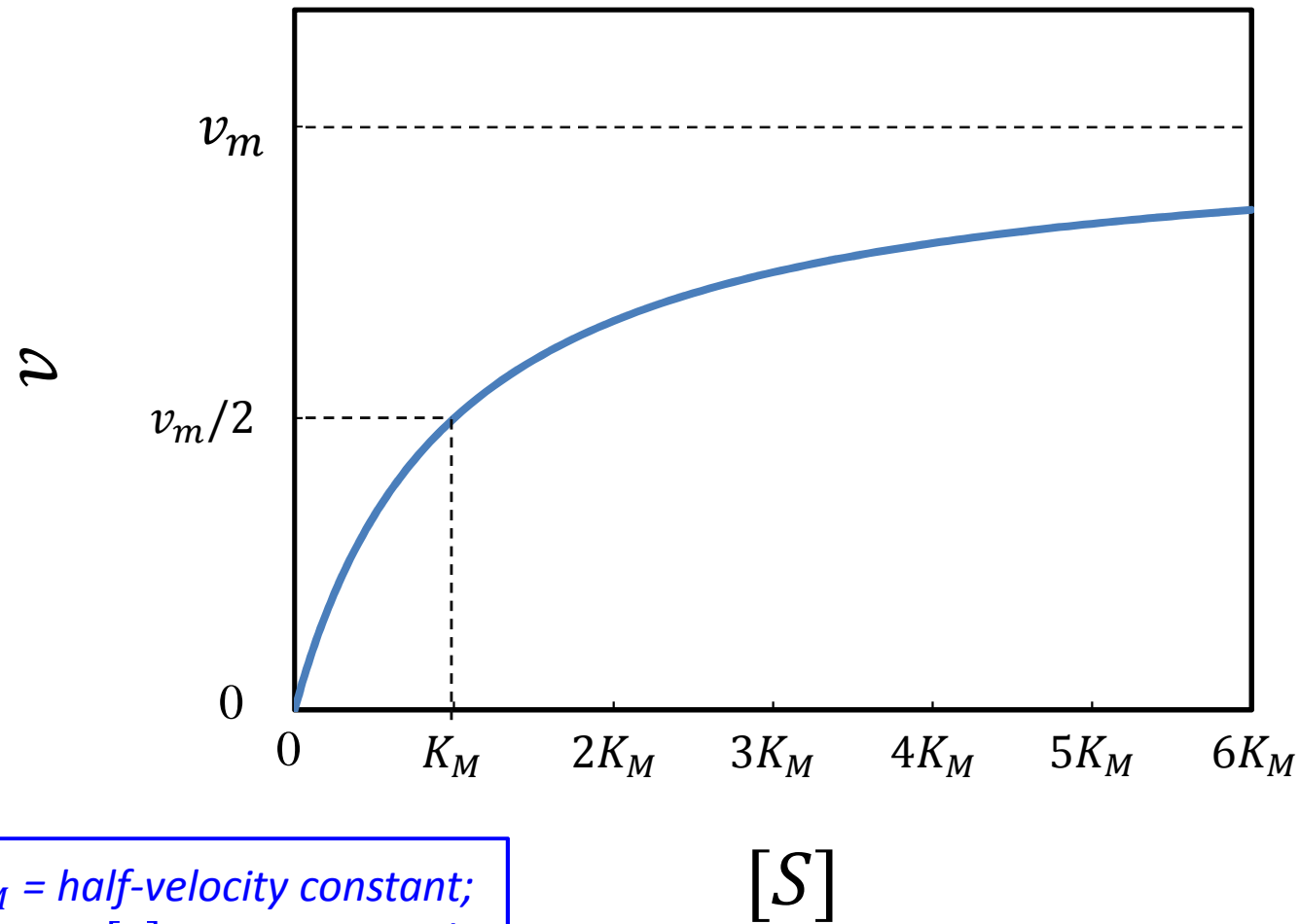
**Finally we get:**

$$v = v_m \frac{[S]}{K_M + [S]}$$

***Michaelis-Menten equation***

# M-M eq.: $[S]$ vs. $v$

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$K_M = \text{half-velocity constant};$   
value of  $[S]$  to achieve  $v_m/2$

$[S]$

# Inhibition of enzyme reactions

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- Chemical agents can reduce the activity of an enzyme by binding to it
- Reversible vs. irreversible inhibition
  - Reversible inhibition
    - An inhibitor binds to enzymes with non-covalent interactions
    - The effect of inhibition disappears when the inhibitor is removed
  - Irreversible inhibition
    - An inhibitor binds to enzymes with covalent interactions
    - The enzymes are made permanently inactive

# Reversible inhibitions

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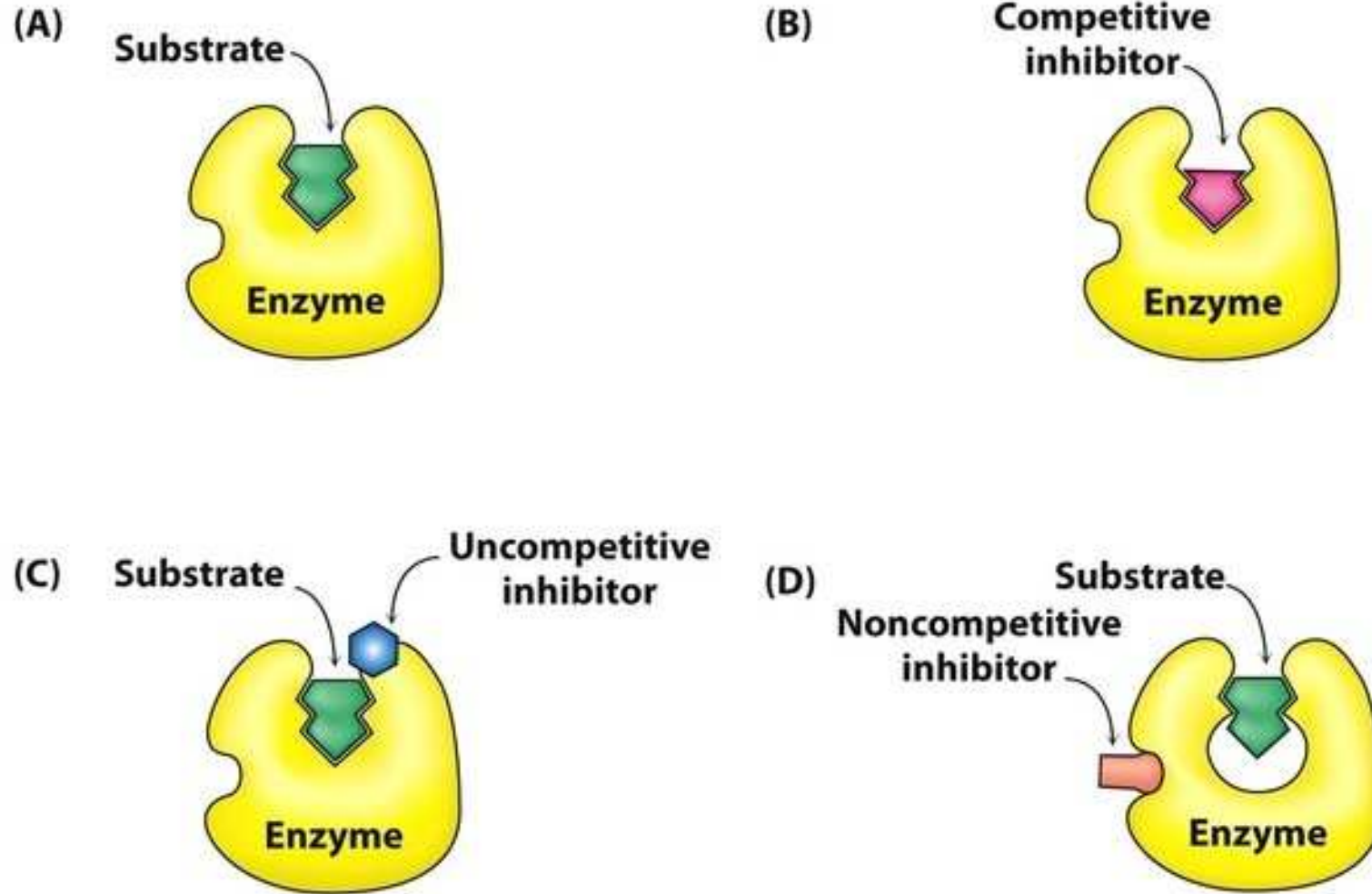


Figure 8.14  
Biochemistry, Seventh Edition  
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# Types of reversible inhibition (1)

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## 1) Competitive inhibition

- **E** (free enzyme) binds to **I** (inhibitor)
- max. velocity unchanged; half-saturation const. increased

## 2) Uncompetitive inhibition

- **I** binds only to **ES** (enzyme-substrate complex)
- max. velocity decreased; half-saturation const. decreased

# Types of reversible inhibition (2)

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## 3) Noncompetitive inhibition

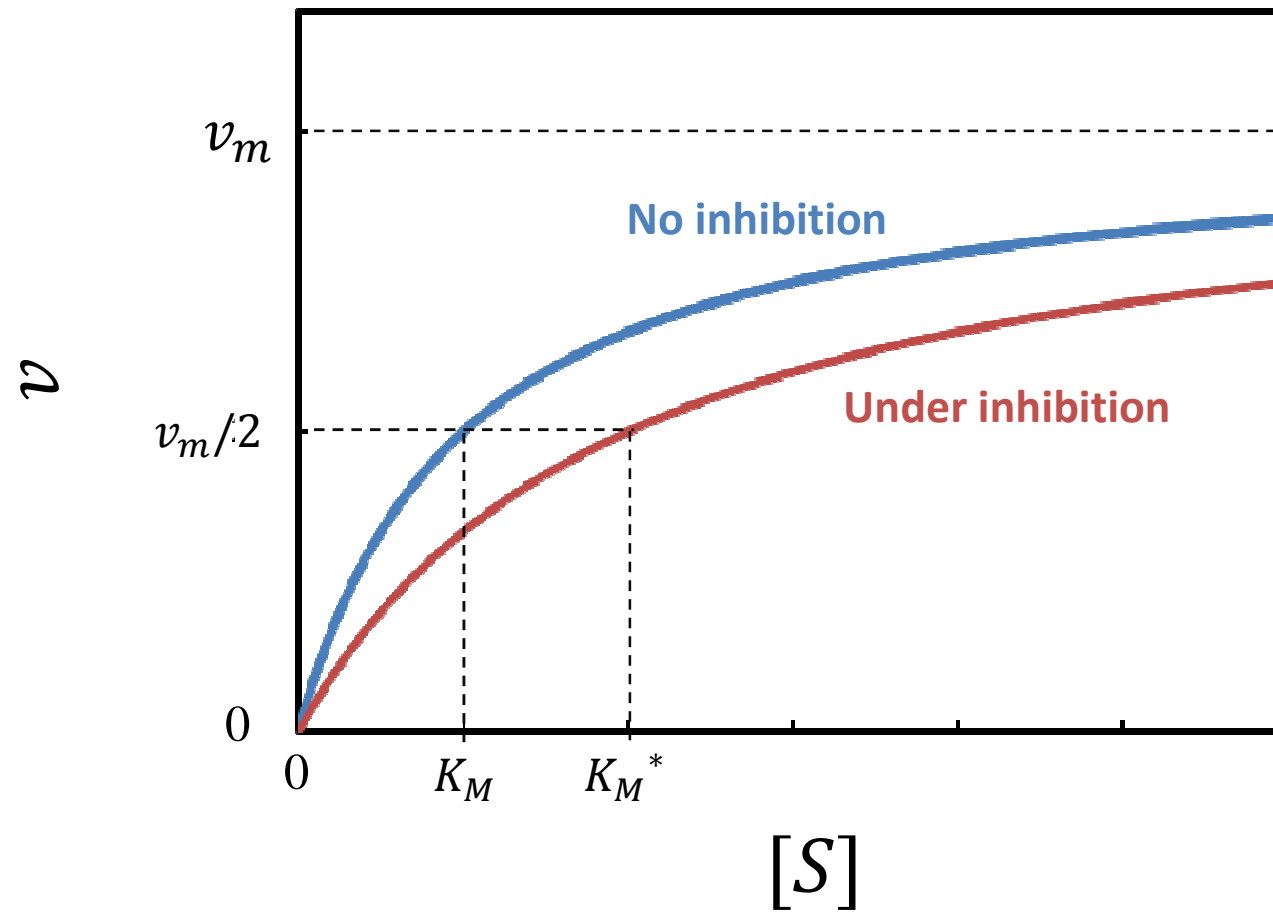
- **I** binds to both **ES** and **E**
- max. velocity decreased; half-saturation const. unchanged

## 4) Product inhibition

- **P** (product) binds to **ES**
- ( )

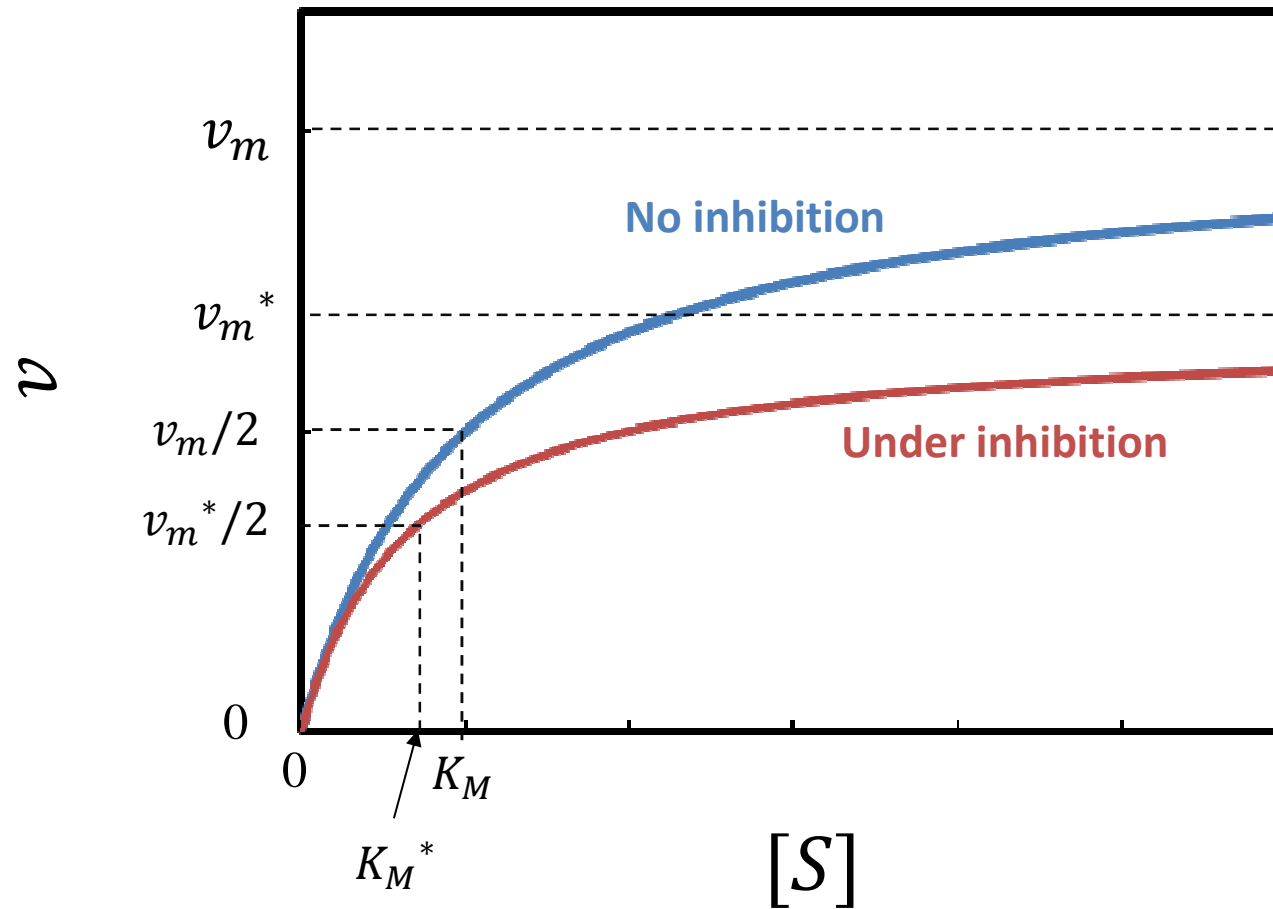
# Effect of competitive inhibition

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# Effect of uncompetitive inhibition

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# Effect of noncompetitive inhibition

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