INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Fundamentals of Medicinal and Pharmaceutical Chemistry

FUNCHEM.26 Catalysts and Enzymes

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DATE: 20th December 2024

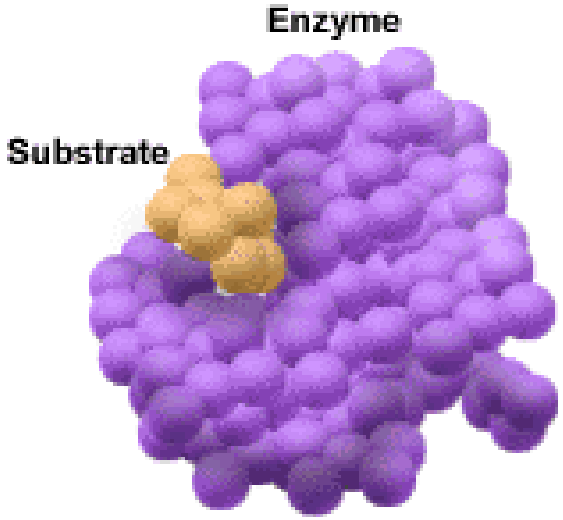
Learning Objectives

Catalysis and enzymes

- Define catalysis with the aid of an appropriate energy profile diagram.
- Distinguish between the ‘lock and key’ theory and ‘induced fit’ theory.
- Explain why enzymes are temperature and pH dependent.
- Recall the Michaelis-Menten equation, clearly defining all parameters.
- Draw a graph of rate of enzyme-catalysed reaction versus substrate concentration, (where enzyme:substrate is in a 1:1 ratio) clearly labelling Vmax, Vmax/2, KM.
- Apply the Michaelis-Menten equation to interpret how enzyme activity is affected by substrate concentration. Clearly differentiate between the rate of an enzyme-catalysed reaction at low substrate versus high substrate concentration.

Biological Catalysts: Enzymes

100 or more chemical reactions may take place at any one time in a single cell.



These chemical reactions would not occur at body temperature at a high enough rate to sustain life.

The body produces **ENZYMES** to allow reactions to occur at body temperature.

Enzyme abnormalities are connected to many diseases.

Enzyme Characteristics

Enzymes are globular proteins with an active site contained in their 3-D structure

Enzymes are very **specific** to a particular reaction or type of reaction

Like all catalysts, enzymes **increase the rate** of a reaction

Enzymes are required in very small amounts – they are **effective** catalysts.

Rate of Enzyme-Catalysed Reactions

Reactions with enzymes are up to 10 billion times faster than those without enzymes.

Enzymes typically react with between 1 and 10,000 molecules per second.

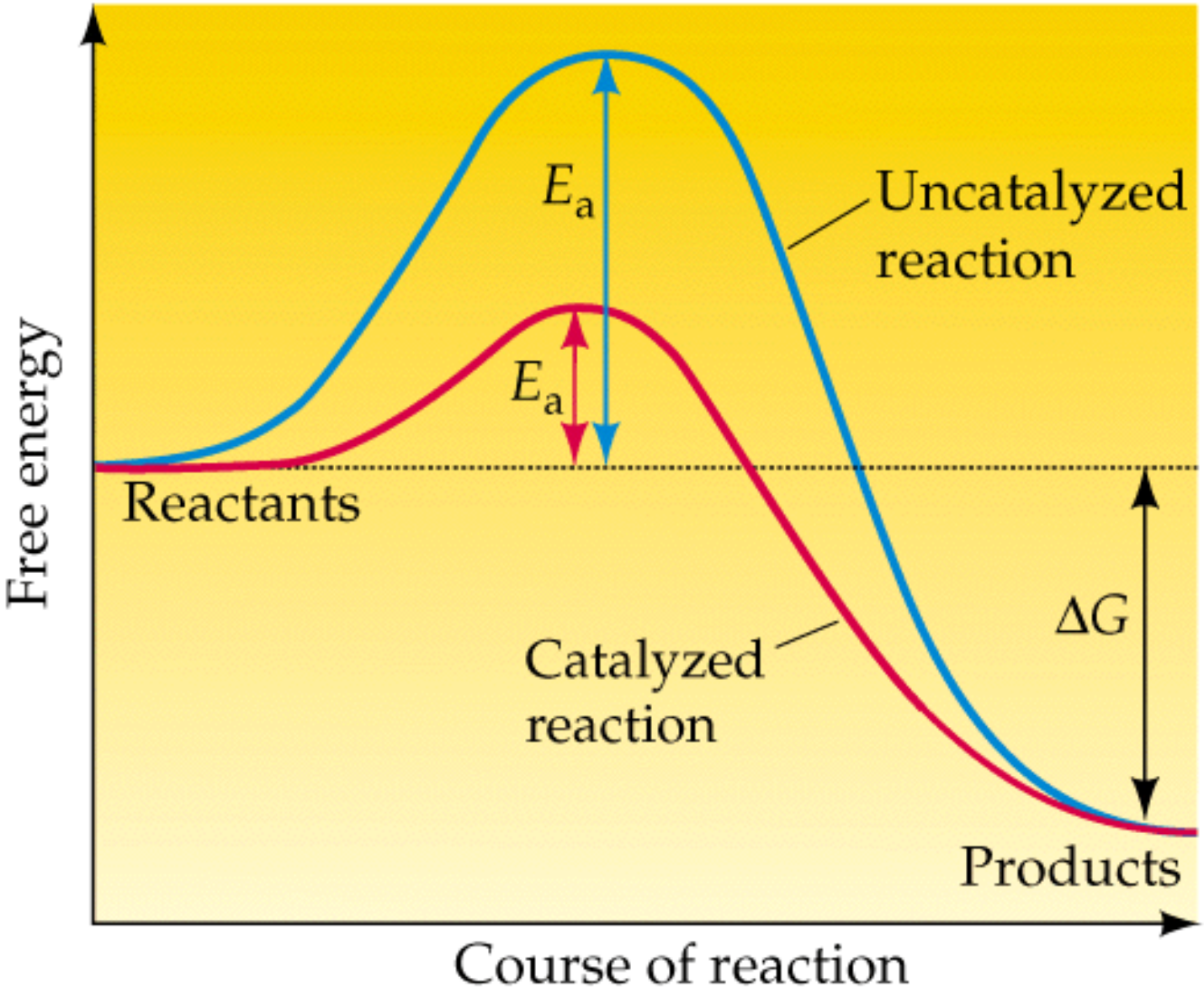
Substrate concentration, enzyme concentration, temperature, and pH affect the rate of enzyme reactions.

Enzymes as Catalysts

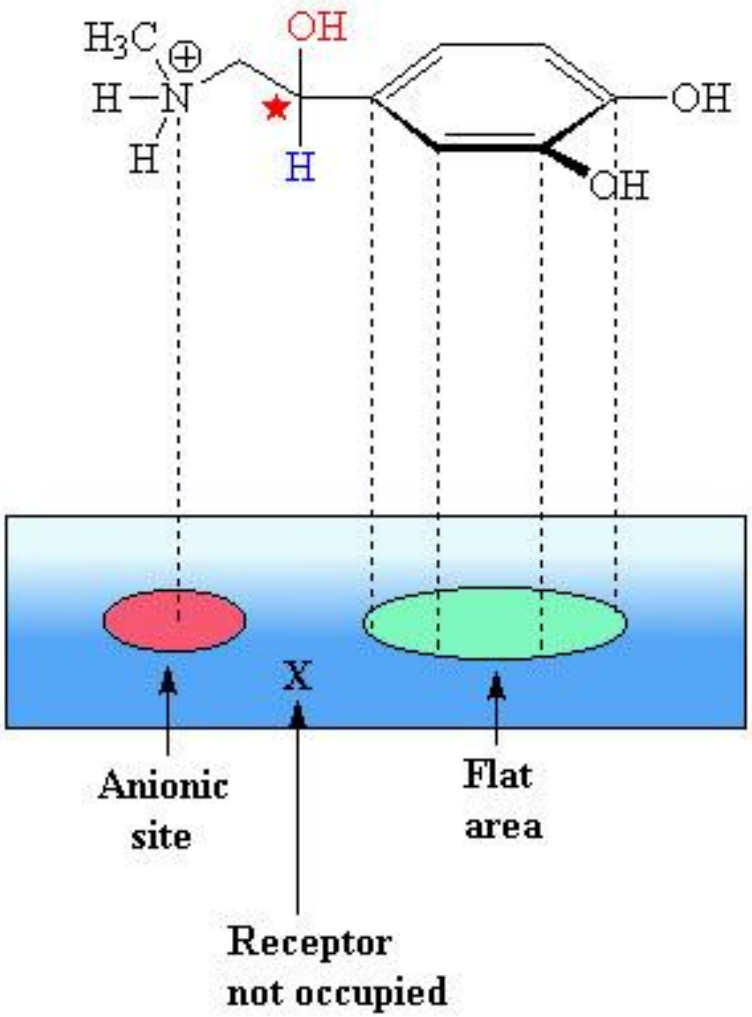
A catalyst is a substance that increases the rate of a chemical reaction without being consumed in the reaction.

- Lowers the activation energy
- A greater proportion of the colliding molecules will achieve the minimum energy needed to react
- Rate of product formation will be increased.

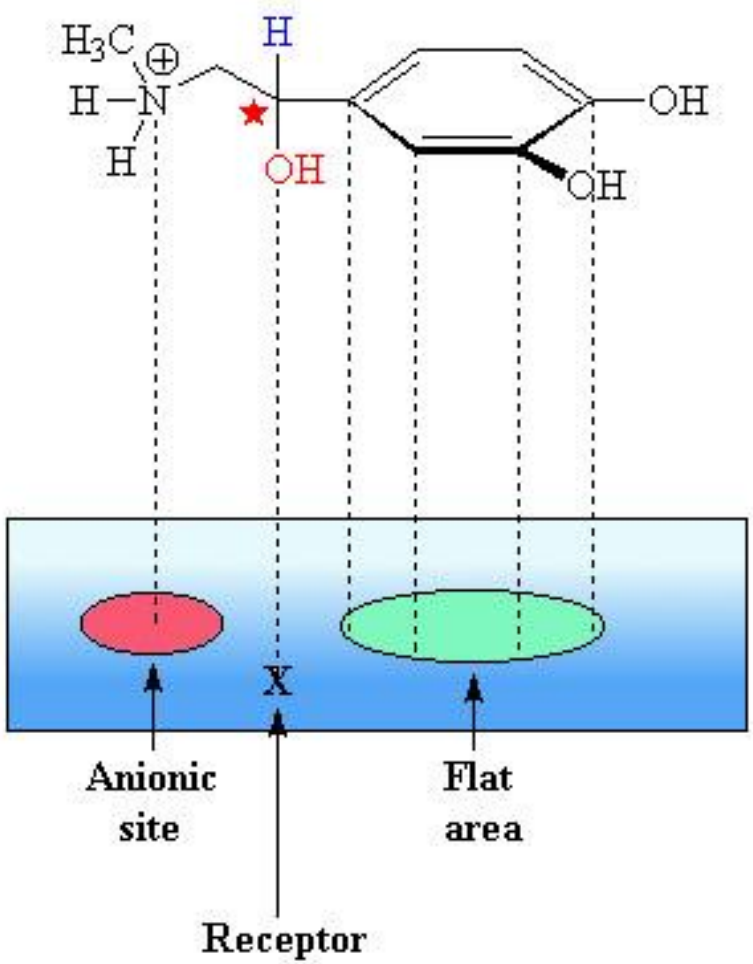
Enzymes as Catalysts



Enzymes are Chiral



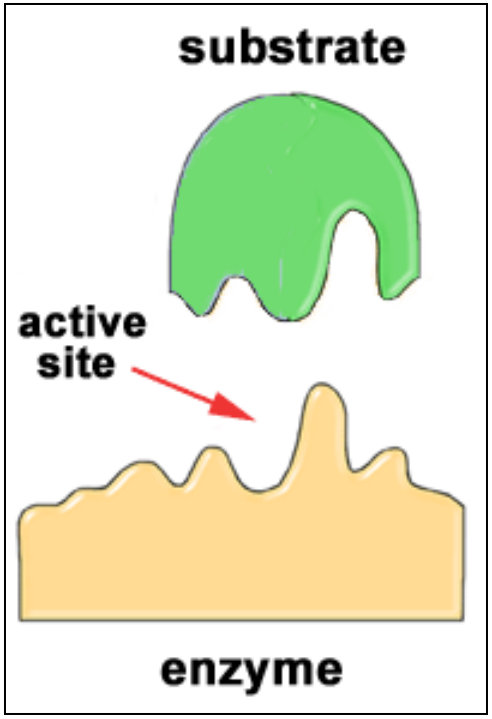
(+) **Epinephrine** - less active



(-) **Epinephrine** - more active

Enzymes as Catalysts

The functional groups in the active site of enzymes assist in balancing the bond breaking (energy needing) parts of a mechanism with the bond making (energy releasing) parts.



The placement of the functional groups **(also called prosthetic groups)** is a result of the folding of the enzyme's chain (secondary, quaternary and tertiary structure).

Anything that disrupts this structure will reduce the enzyme's catalytic power.

Enzymes as Catalysts: Lock & Key Theory

Enzymes catalyse reactions by lowering the activation energy needed for a reaction to take place.

Substrate + Enzyme → Enzyme/Substrate Complex

↓

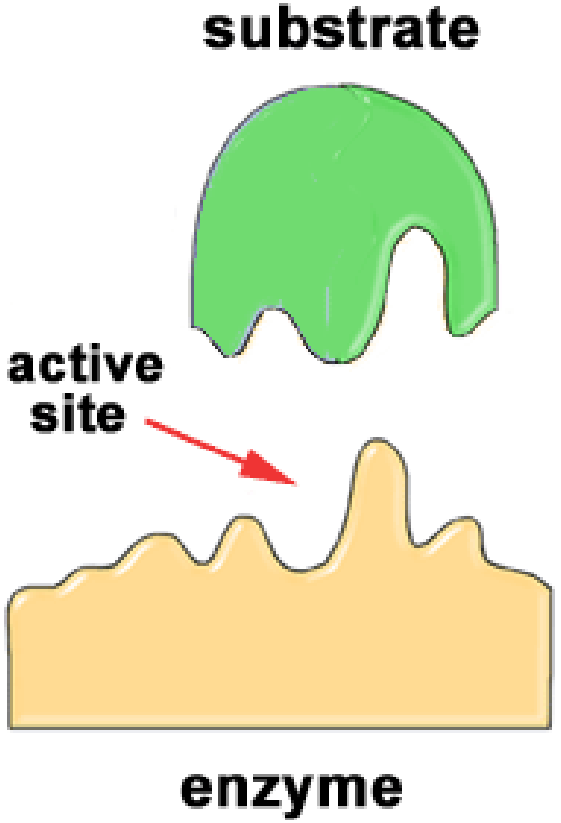
Enzyme + Products

Enzymes as Catalysts: Lock & Key Theory

Active site within structure of each enzyme.

It may involve only a small number of amino acids.

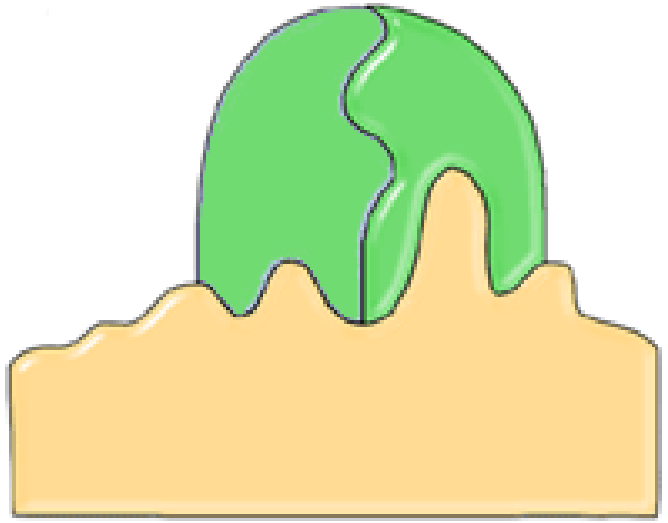
It has a specific shape, which gives each enzyme its specificity, as only one type of substrate will fit into the site or gap.



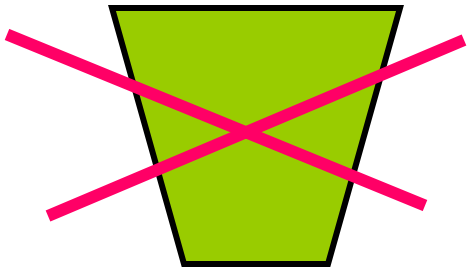
Enzymes as Catalysts: Lock & Key Theory

Enzymes are high specific:

There is a difference between the shape of the enzyme substrate and another biological molecule. Only a molecule of the right shape can be a substrate for the enzyme.



enzyme-substrate

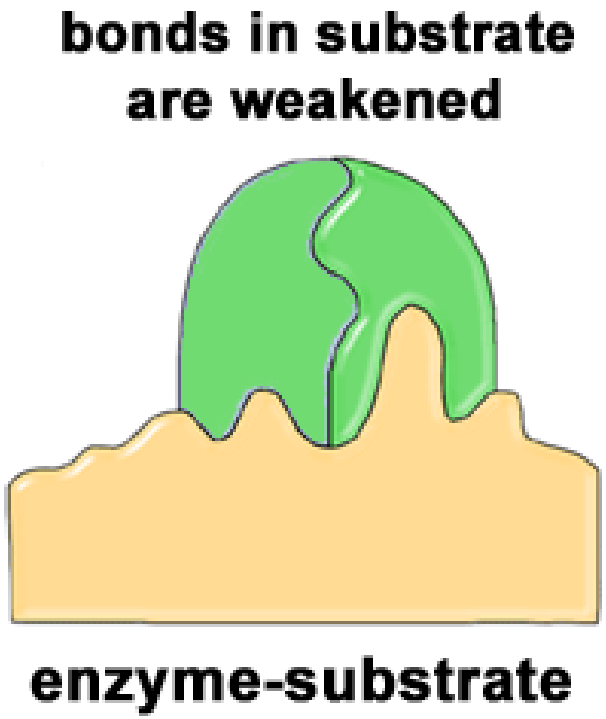


Enzymes as Catalysts: Lock & Key Theory

The enzyme & substrate slot together to form a complex, as a key fits into a lock.

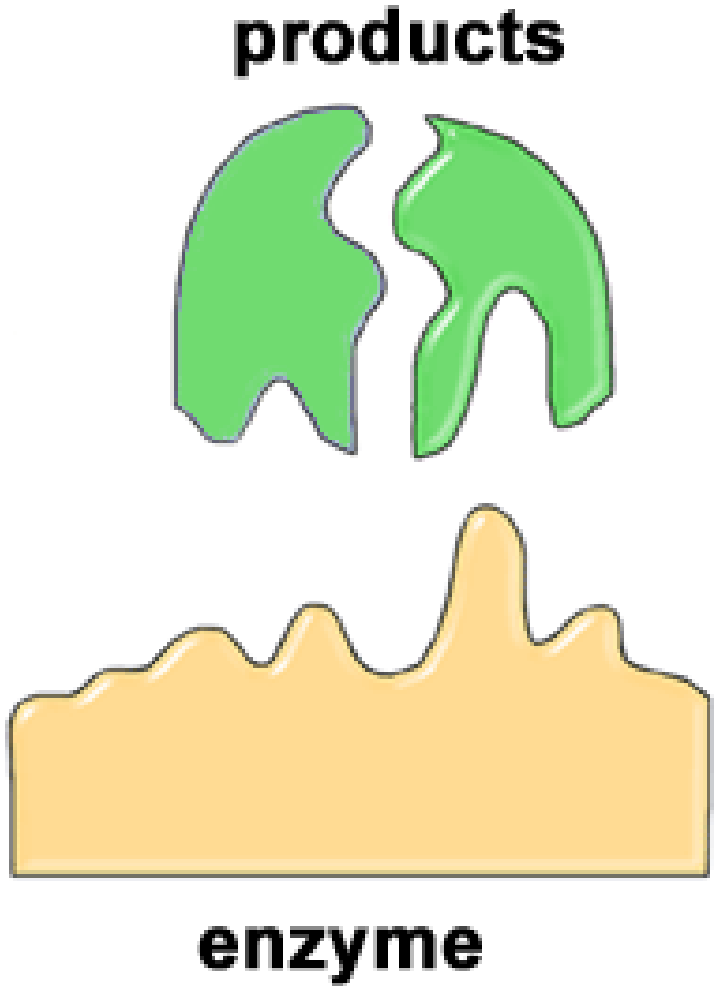
In this complex the substrate reacts at a lower activation energy.

This may be due to bonds within it being deformed & stressed in the complex, so making them more likely to react.

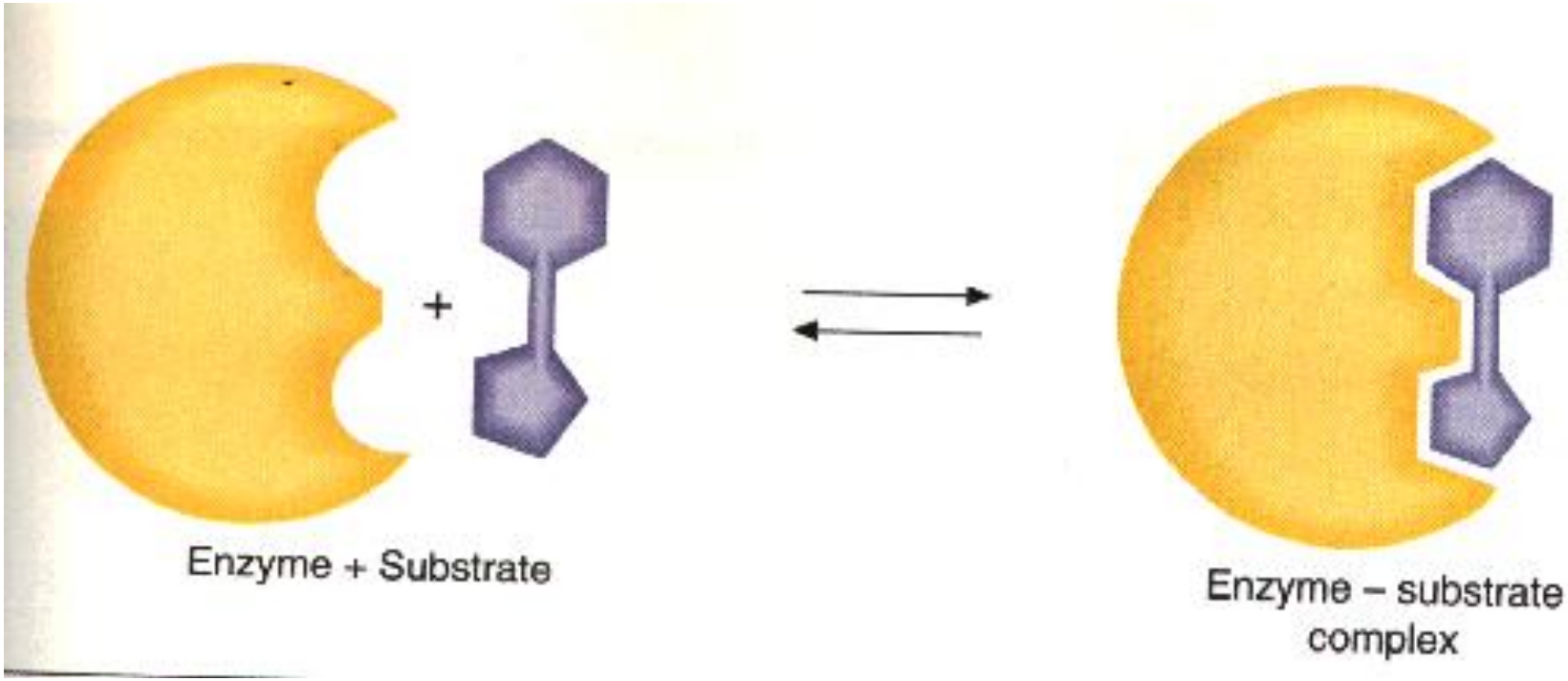


Enzymes as Catalysts: Lock & Key Theory

Once the reaction has been catalysed, the products are no longer the right shape to stay in the active site & the complex breaks up, releasing the products & freeing the enzyme for further catalytic action.



Enzymes as Catalysts: Induced-Fit Theory



Enzymes as Catalysts: Induced-Fit Theory

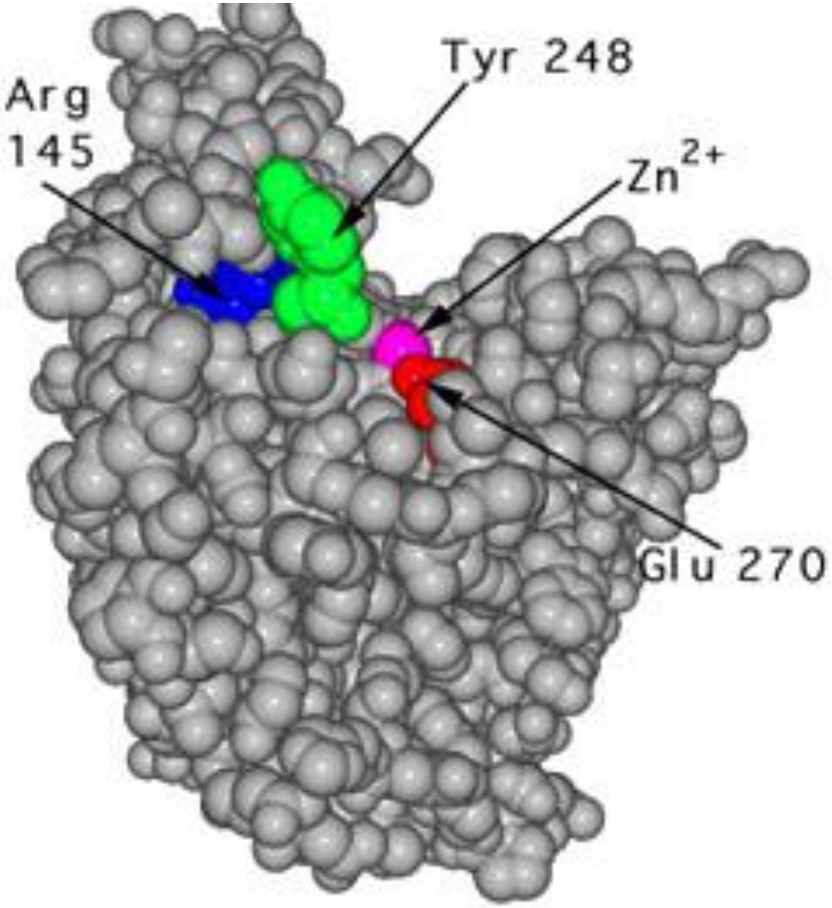
Enzyme undergoes conformational change as the substrate approaches and starts to bind.

We know that proteins are flexible molecules, whose overall structure is maintained by weak intermolecular interactions.

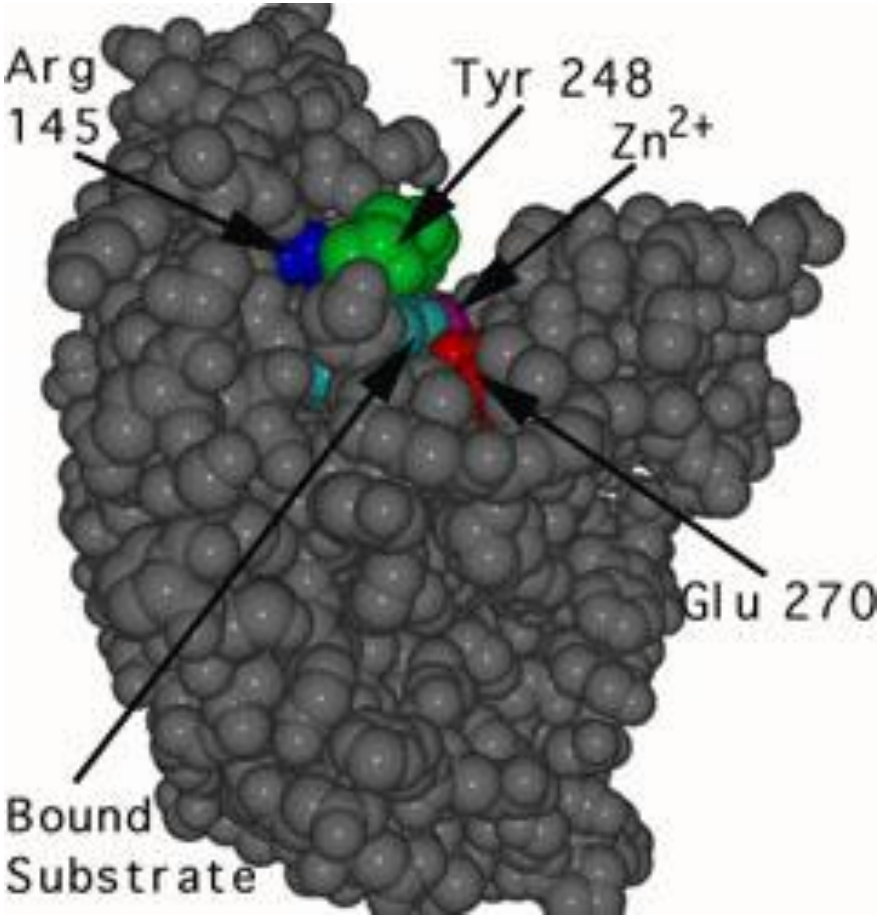
At any given time, these can be disrupted by small changes in their vicinity. The approach of the substrate is viewed as such a disruption.

The enzyme and substrate must still have complementary surfaces.

Enzymes as Catalysts: Induced-Fit Theory

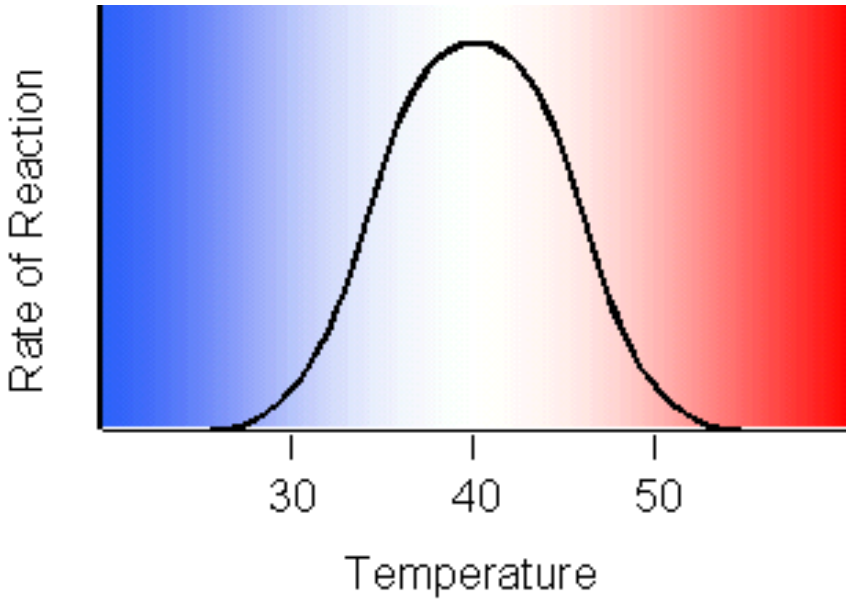


Carboxypeptidase A



Carboxypeptidase A with substrate bound

Enzymes are temperature dependent



Increasing temperature

– increase reaction rate until a point is reached when the enzyme starts to unfold.

WHY?

Hydrophobic bonds and salt bridges break as the increase in temperature causes the enzyme's structure to ‘wiggle’ around.

Enzymes are pH dependent

Salt bridges depend on ionic charges for their ‘bonding’ power.

Anything which neutralises such a charge will destroy the salt bridge and make the folded structure of enzyme less stable.

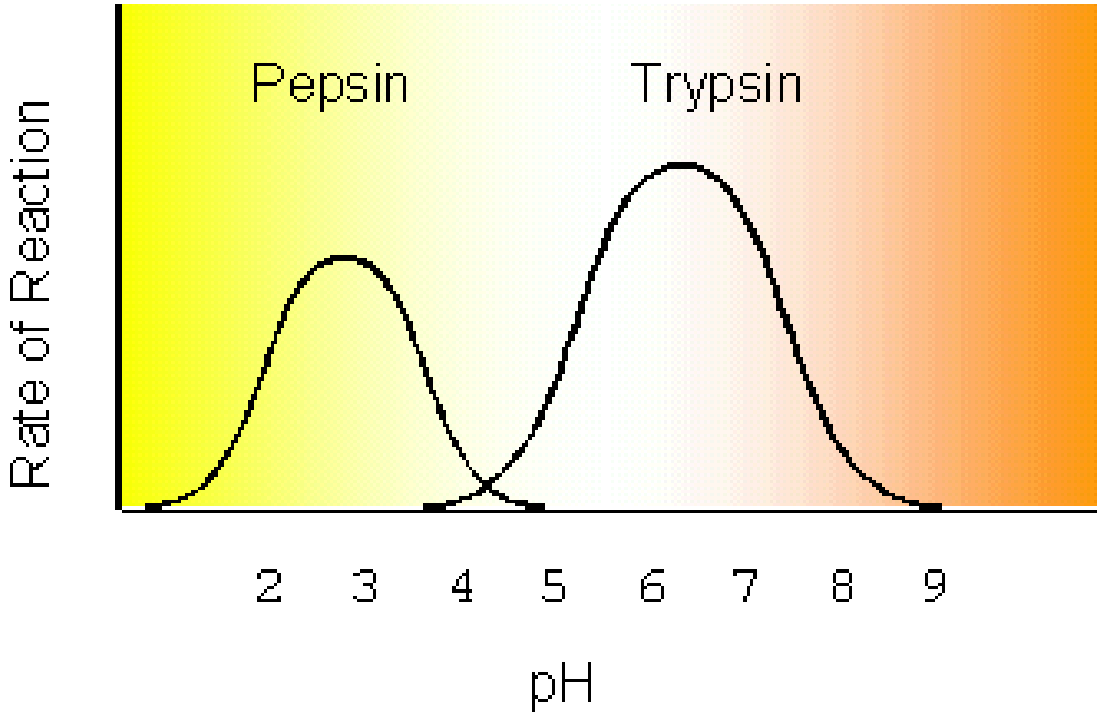
Increase of pH (more basic) will take an H^+ from an NH_3^+ group and neutralise its charge.

Similarly, **decrease in pH** will put an H^+ on a COO^-.

This means that each enzyme has an optimum pH at which its folded (active) structure is most stable.

It has its maximum catalytic power at that pH.

Enzymes are pH dependent



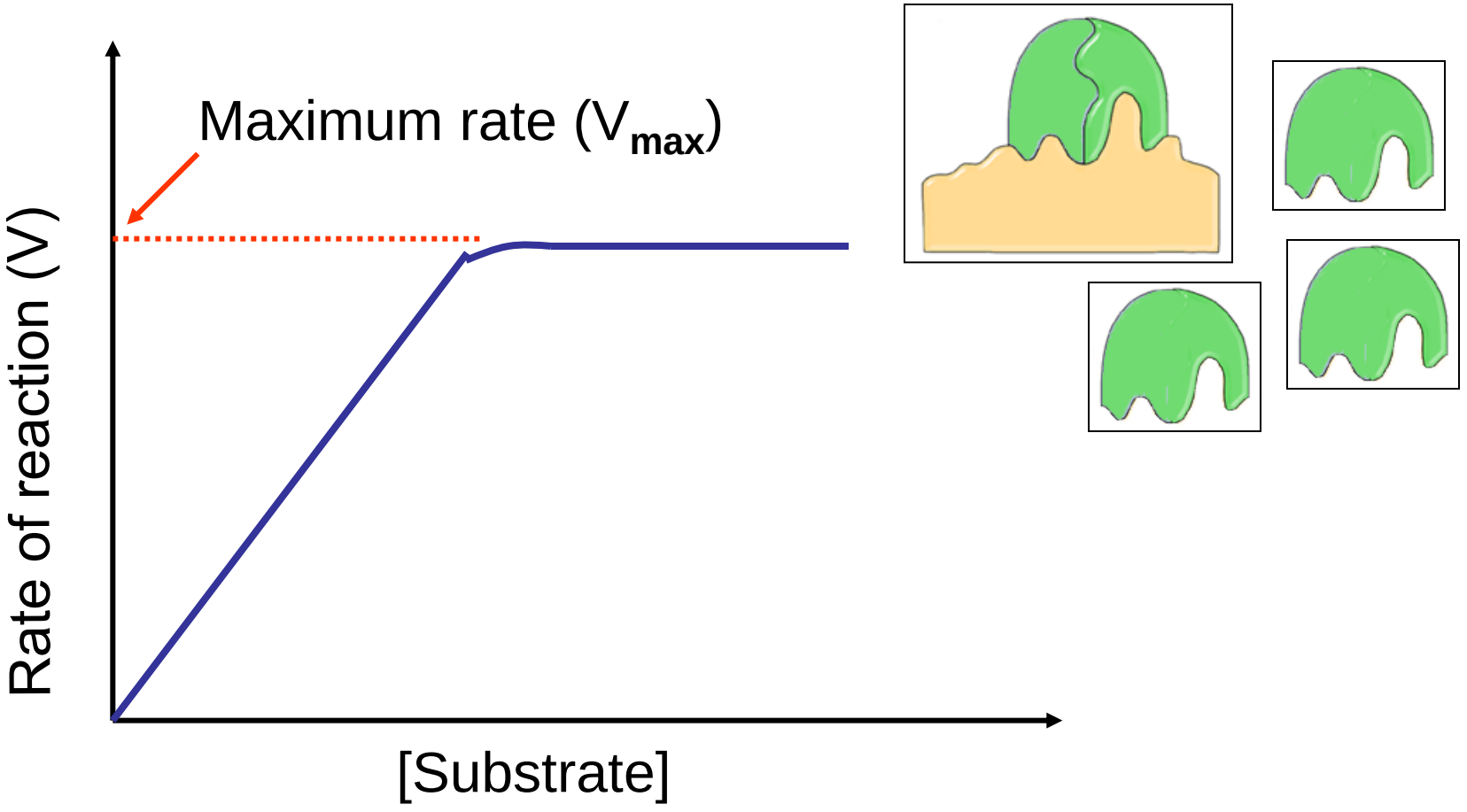
Pepsin functions best under acidic conditions

(found in stomach)

Trypsin functions best in neutral range

(found in duodenum)

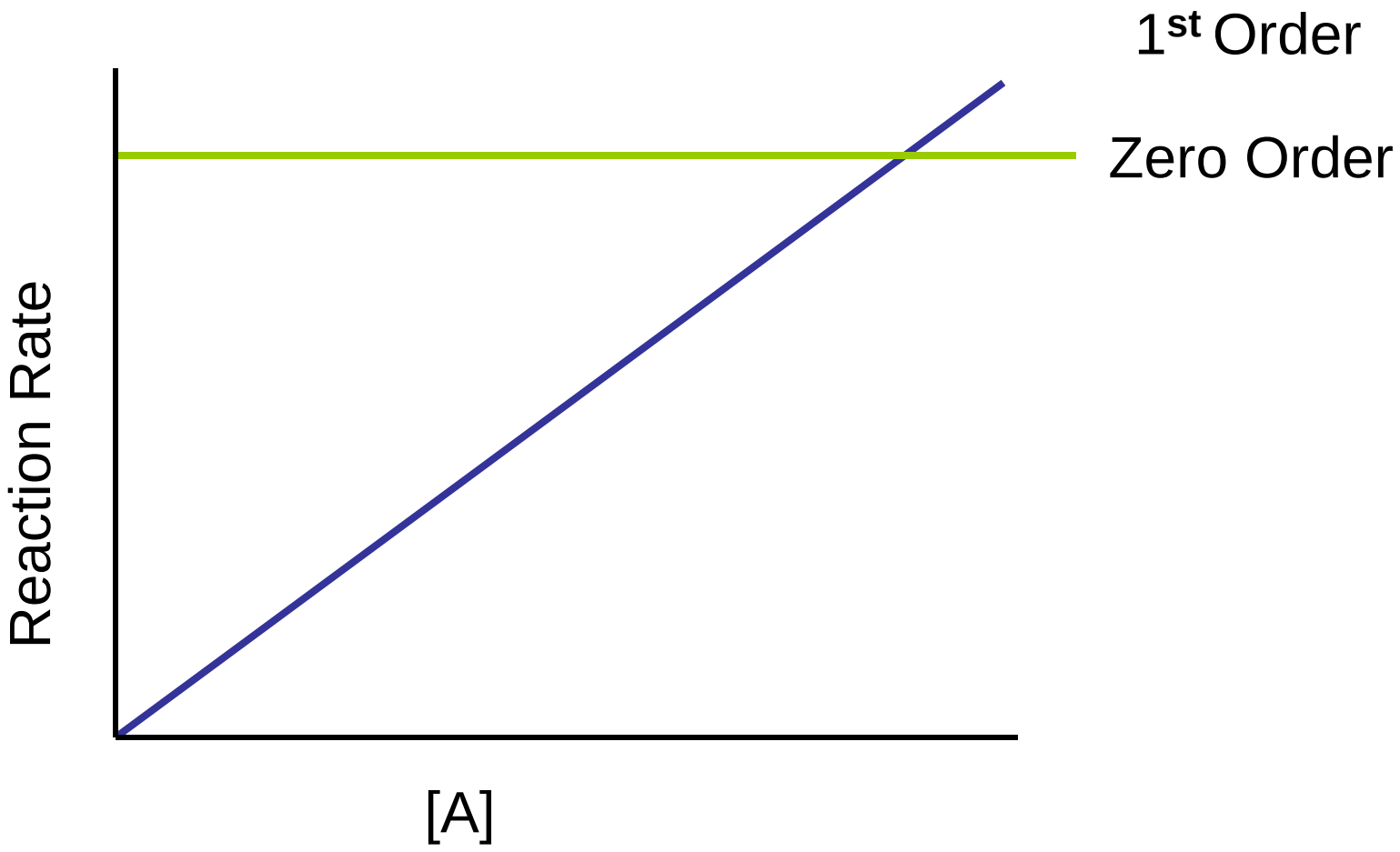
How is enzyme activity affected by SUBSTRATE CONCENTRATION (reactant concentration)?



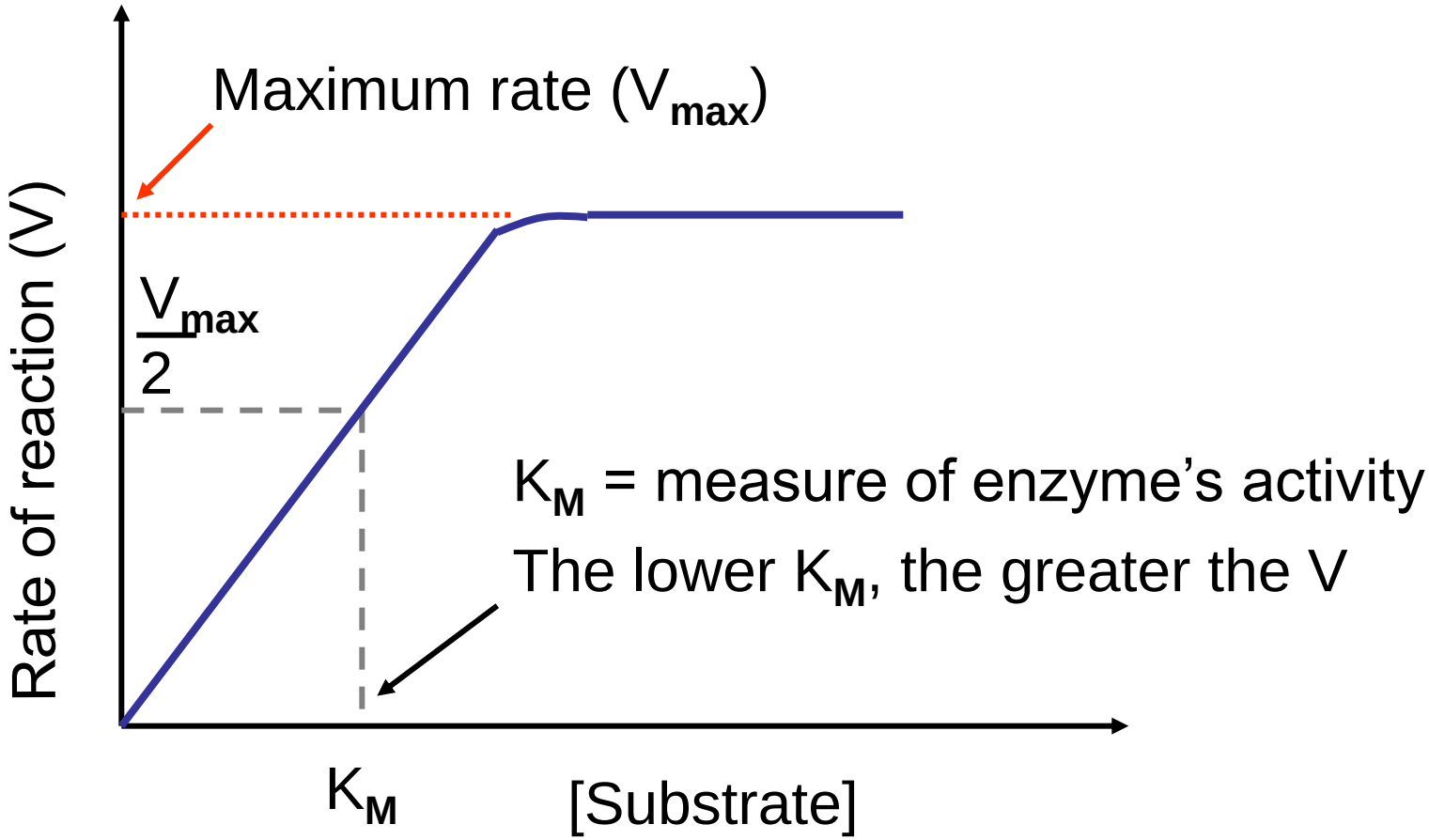
(assume enzyme:substrate = 1:1)

Enzyme Activity

Recall!



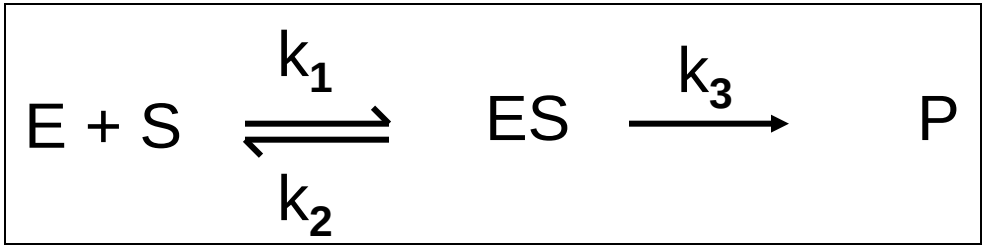
Enzymes and [Substrate]



Low [S] : Rate α [S] **(1st- order)**

High [S] : Rate independent of [S] **(zero-order)**

Enzymes and [Substrate]



Enzyme combines with substrate to form ES complex **(k_1)**

ES complex has 2 possible fates:

Dissociate to E + S **(k_2)**

Proceed to form product **(k_3)**

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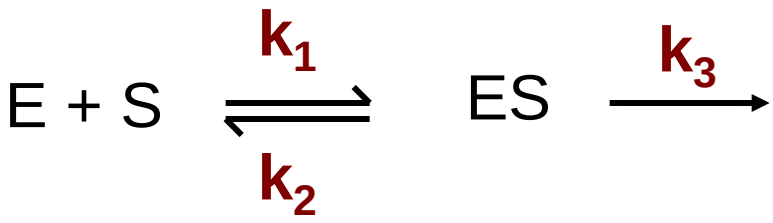
Michaelis – Menten Equation

(relates rate of enzyme catalysed reaction to [S])

Enzymes and [Substrate]: Michaelis – Menten Equation

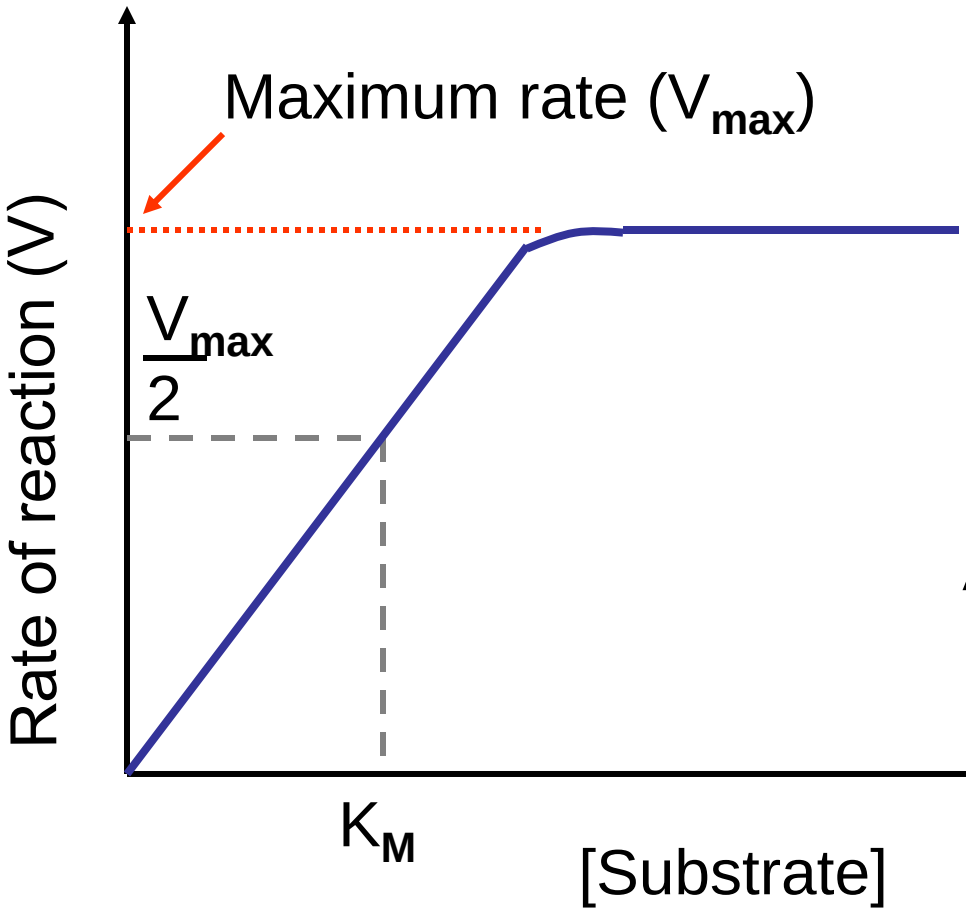


$$K_M = \frac{k_2 + k_3}{k_1}$$

$$\text{RATE} = \frac{V_{max}\ [S]}{K_M + [S]}$$

EQUATION EXPLAINS SHAPE OF CURVE

Enzymes and [Substrate]



$$K_M = \frac{k_2 + k_3}{k_1}$$

$$\text{RATE} = \frac{V_{max}\ [S]}{K_M + [S]}$$

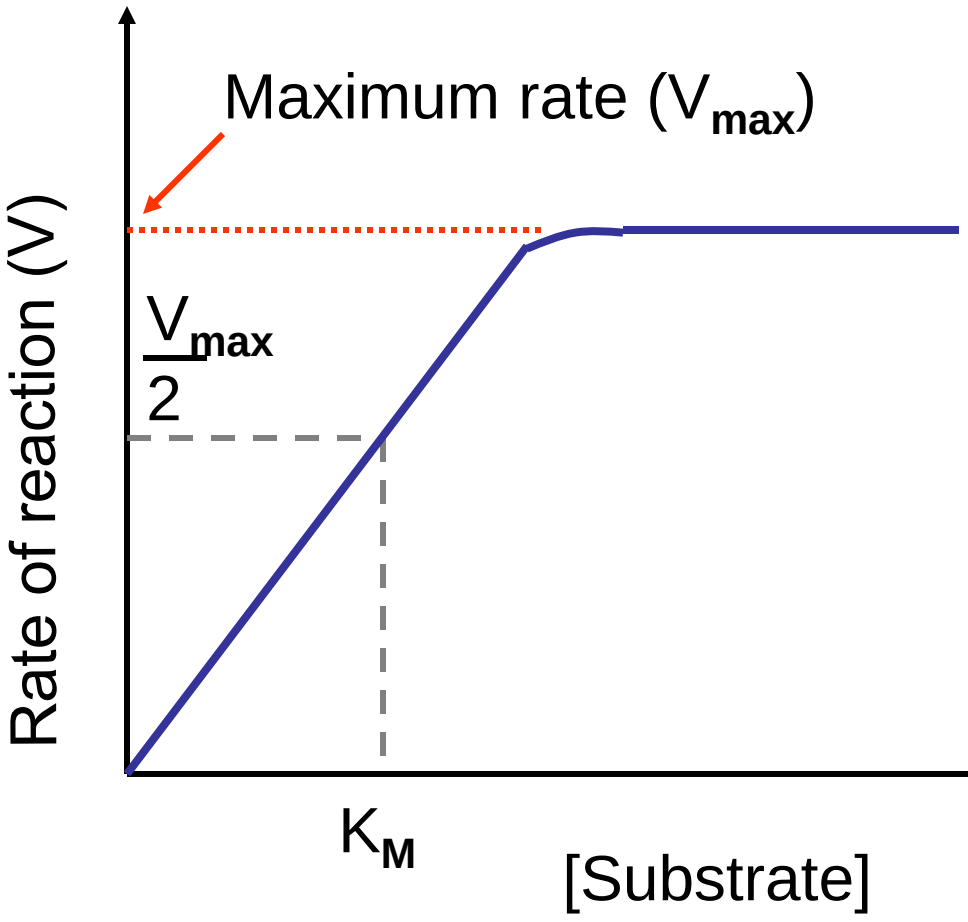
At low [S] : $[S] << K_m$

$$\text{Rate} = \frac{V_{max}\ [S]}{K_M}$$

Rate α [S]

First Order Reaction

Enzymes and [Substrate]



$$K_M = \frac{k_2 + k_3}{k_1}$$

$$\text{RATE} = \frac{V_{max}\ [S]}{K_M + [S]}$$

At high [S] : [S] > > > K_m

$$\text{Rate} = \frac{V_{max}\ \cancel{[S]}}{\cancel{[S]}}$$

Rate = constant

Zero Order Reaction

Summary of Chemical Kinetics

Reaction Rate Factors and Rate Equation

Reaction Order: Zero, First, Pseudo- First, Second

Determination of Reaction Order:
Initial Rates Method
Graphical method
Half Life Method

Collision Theory: Molecular Orientation
Frequency of Collisions
Energy of Collisions

Reaction mechanisms and energy profile diagrams

Arrhenius Equation: Work out activation energy

Enzymes as catalysts and Michaelis-Menten model

Learning Objectives

Catalysis and enzymes

- Define catalysis with the aid of an appropriate energy profile diagram.
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