Johns Hopkins Engineering

Molecular Biology

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Module 4 / Lecture 1

Enzymes

Enzyme structure

- Enzymes are **proteins**
- They have a **globular** shape
- A complex **3-D** structure

Human pancreatic amylase

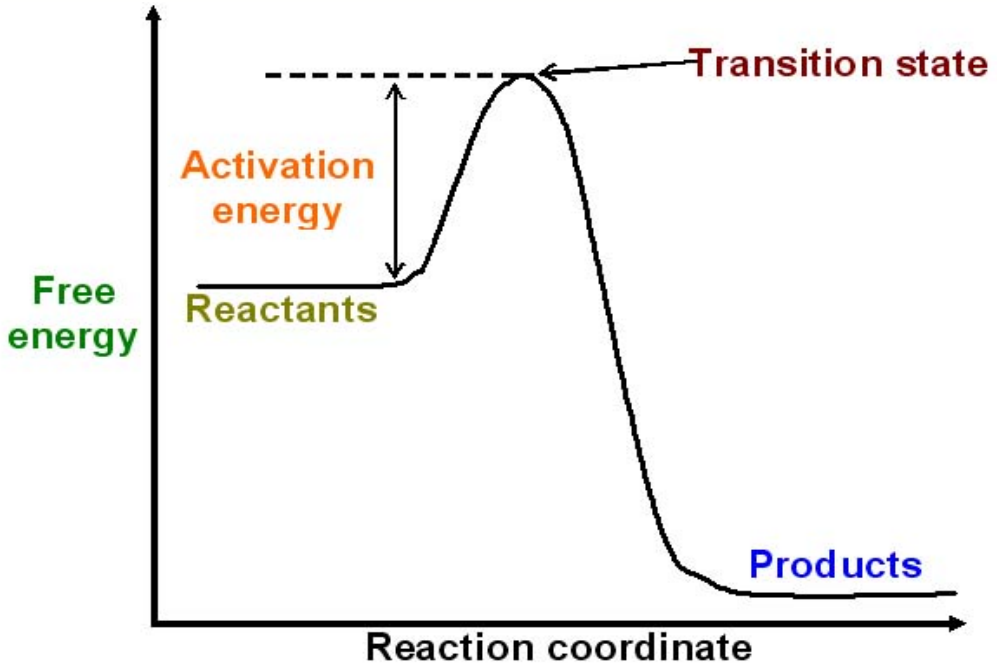
Enzymes make reactions proceed faster

- Increasing the temperature make molecules move faster
- Biological systems are very sensitive to temperature changes
- Enzymes can increase the rate of reactions without increasing the temperature
- They do this by lowering the activation energy
- They create **a new reaction pathway** “a short cut”

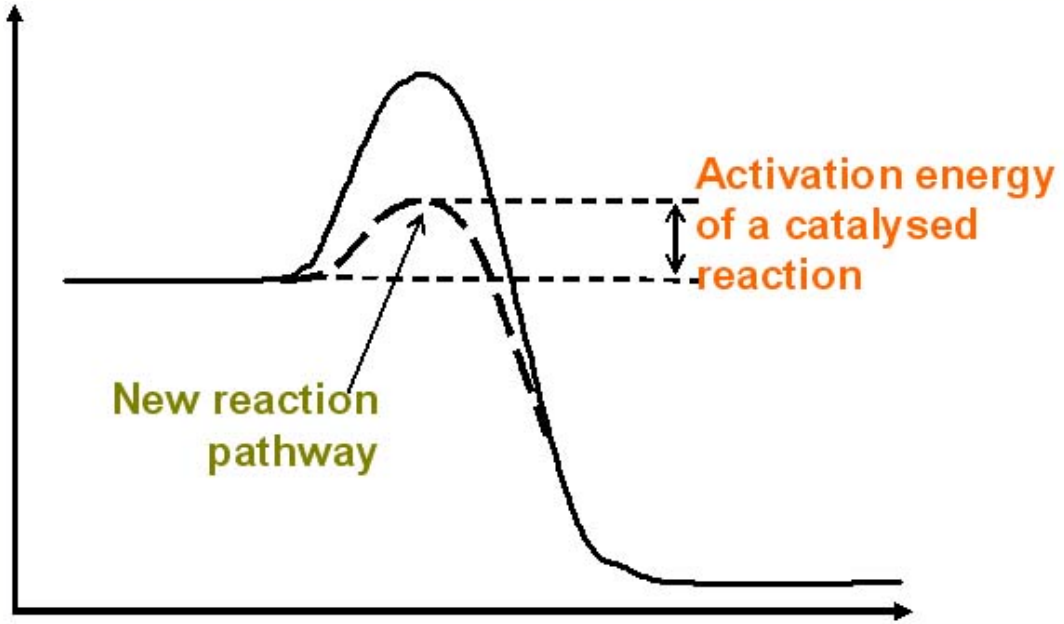
Enzyme catalysis

- Virtually all cellular reactions or processes are mediated by protein (or, in certain cases, RNA) catalysts called **enzymes**.
- The only reactions that occur at any appreciable rate in a cell are those for which the appropriate **enzymes** are **present** and **active**.
- **Enzymes** spell the difference between "can go" and "will go" for cellular reactions.
- In this module, we will explore enzymes and their catalytic properties to understand how reactions that are energetically feasible actually take place in cells and how the rates of such reactions are controlled.

A reaction pathway



An enzyme controlled pathway



- Enzyme controlled reactions proceed 108 to 1011 times faster than corresponding non-enzymatic reactions.

Reaction sequence with and without catalyst

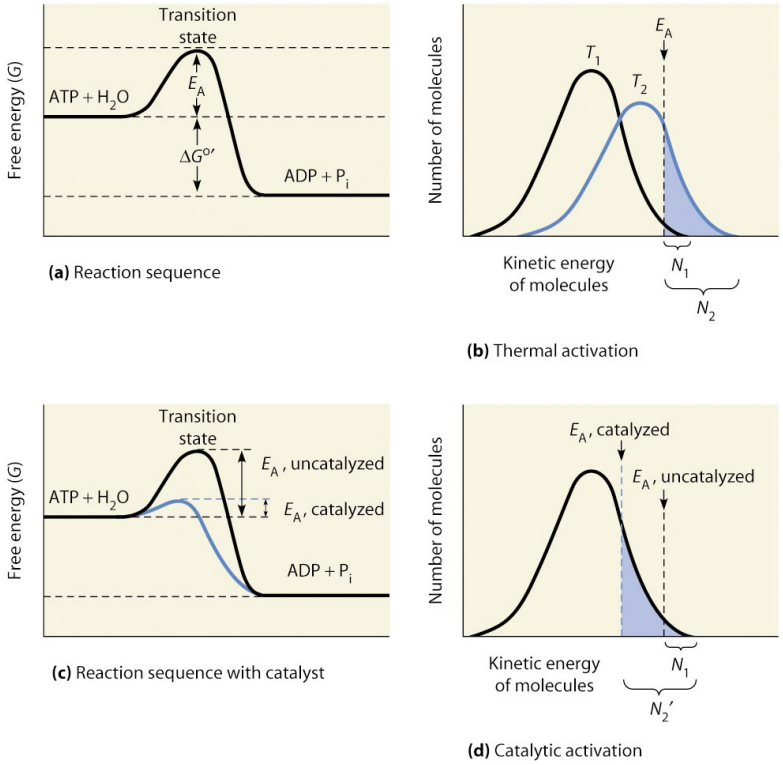


Figure 6-1

Effect of catalysis on activation energy and number of molecules capable of reacting

(a) The activation energy E_A is the minimum amount of kinetic energy reactant molecules (here ATP and H_2O) must possess to permit collisions leading to product formation.

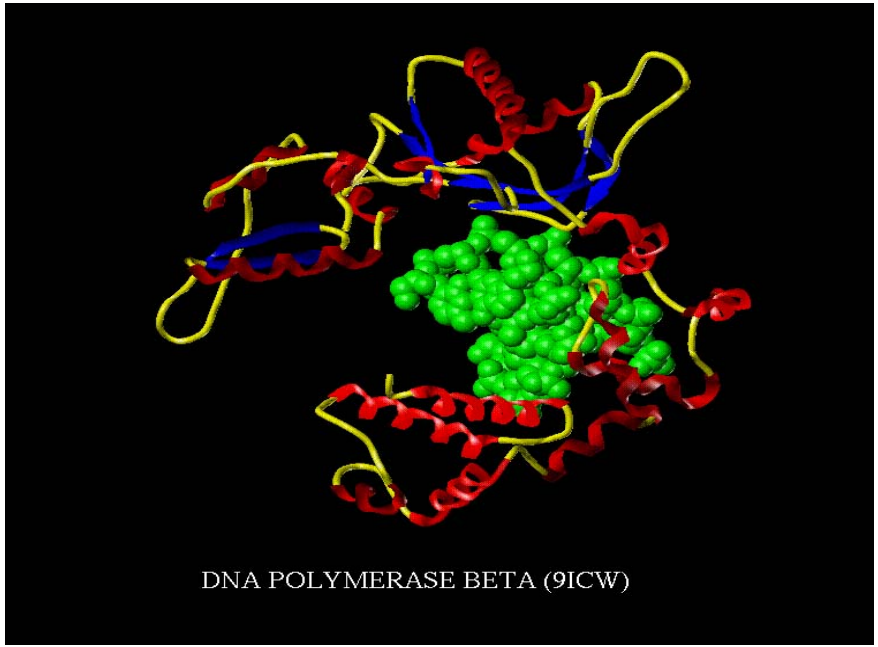
After reactants overcome the activation energy barrier and enter into a reaction. The products have less free energy by the amount $\triangle G^o$.

(b) The number of molecules N_1 that have sufficient energy to exceed the activation energy barrier (E_A) and collide successfully can be increased to N_2 by raising the temperature from T_1 to T_2.

(c) Alternatively, the activation energy can be lowered by a catalyst.

(d) increasing the number of molecules from N_1 to N_2.

The active site



- One part of an enzyme, **the active site**, is particularly important
- The **shape** and the **chemical environment** inside the active site permits a chemical reaction to proceed more easily.

The substrate

- The substrate of an enzyme are the **reactants** that are activated by the enzyme.
- Enzymes are **specific** to their substrates.
- Specificity is determined by the **active site.**

An enzyme, substrate and active site

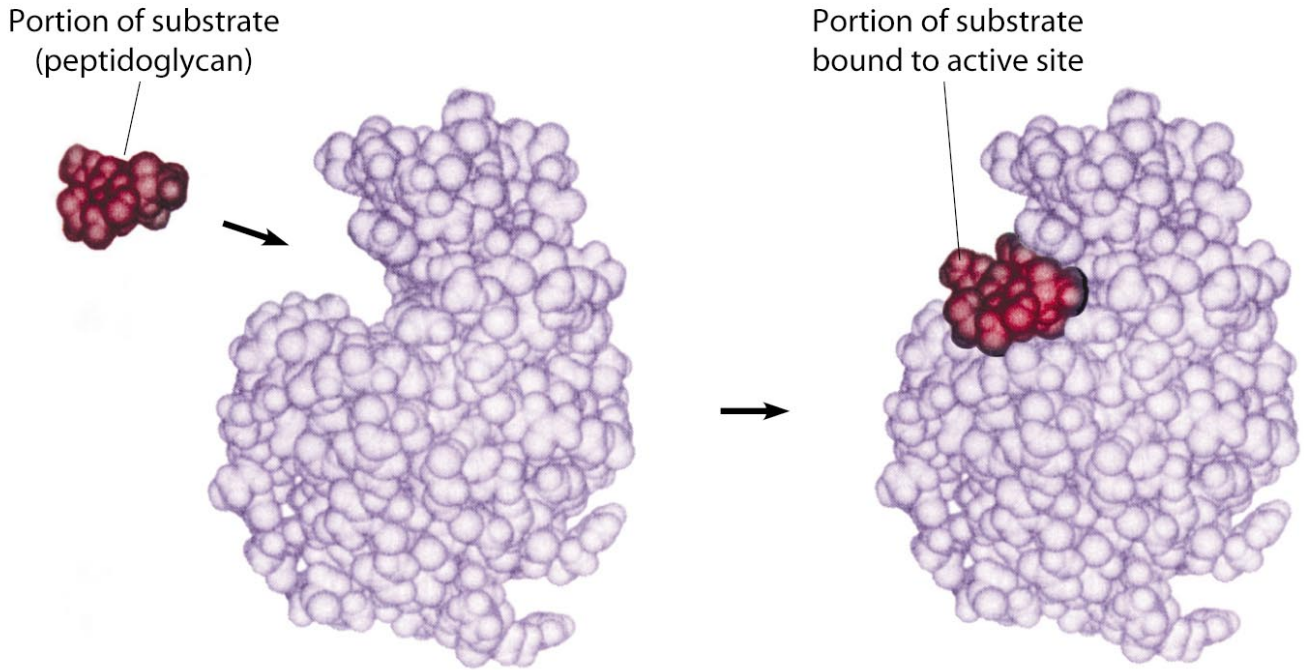
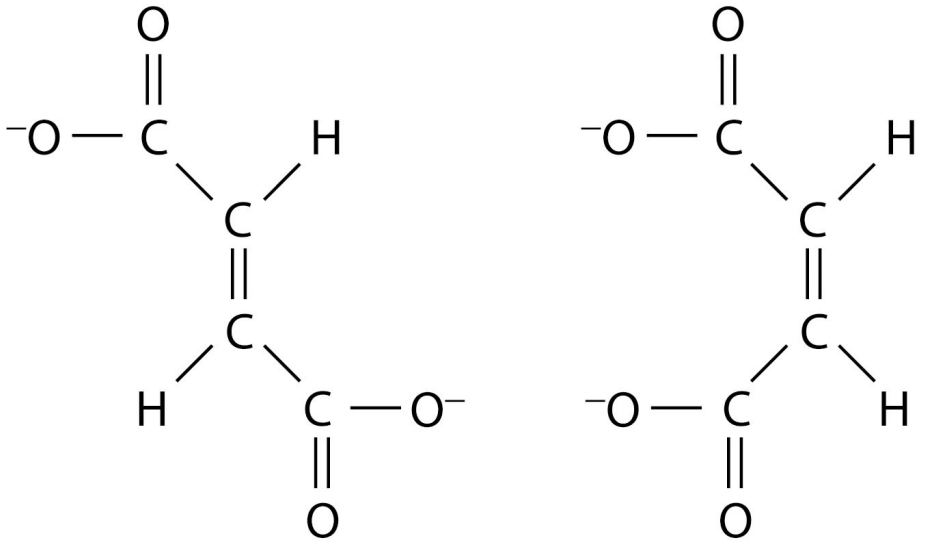


Figure 6-2

The specificity of enzyme reactions



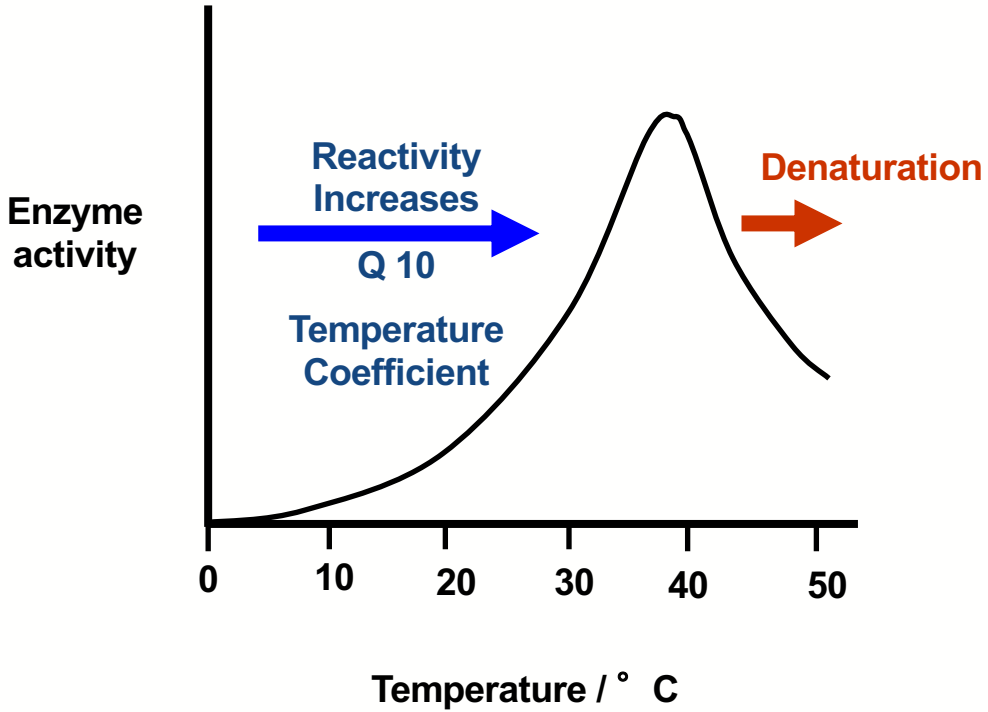
(a) Fumarate **(b)** Maleate

Dehydrogenase will not add or subtract hydrogens from any compounds except for fumarate. It will not even recognize maleate, a stereoisomer of fumarate.

Factors affecting enzymes

- substrate concentration
- pH
- temperature
- inhibitors

The effect of temperature



The effect of temperature

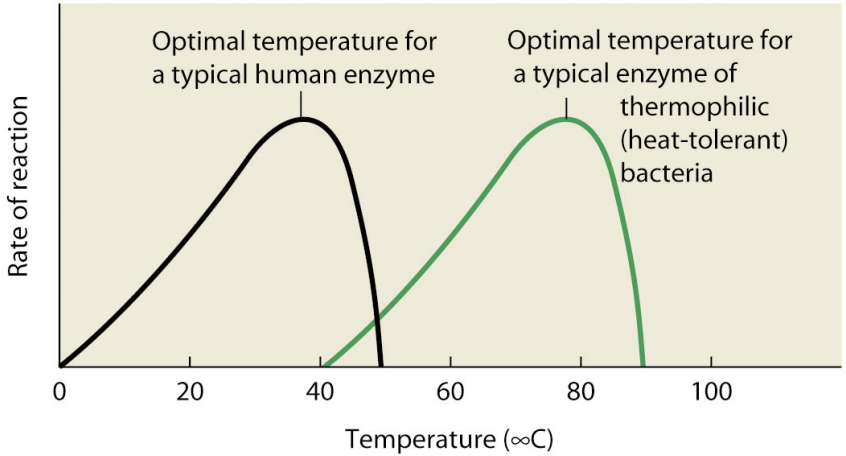
- For **Q10** (**the temperature coefficient**), the increase in reaction rate doubles with each 10° C rise in temperature.
- Enzyme-controlled reactions follow this rule as they are chemical reactions.
- BUT at high temperatures proteins **denature.**
- The optimum temperature for an enzyme controlled reaction will be a balance between the **Q10** and denaturation.

The effect of temperature

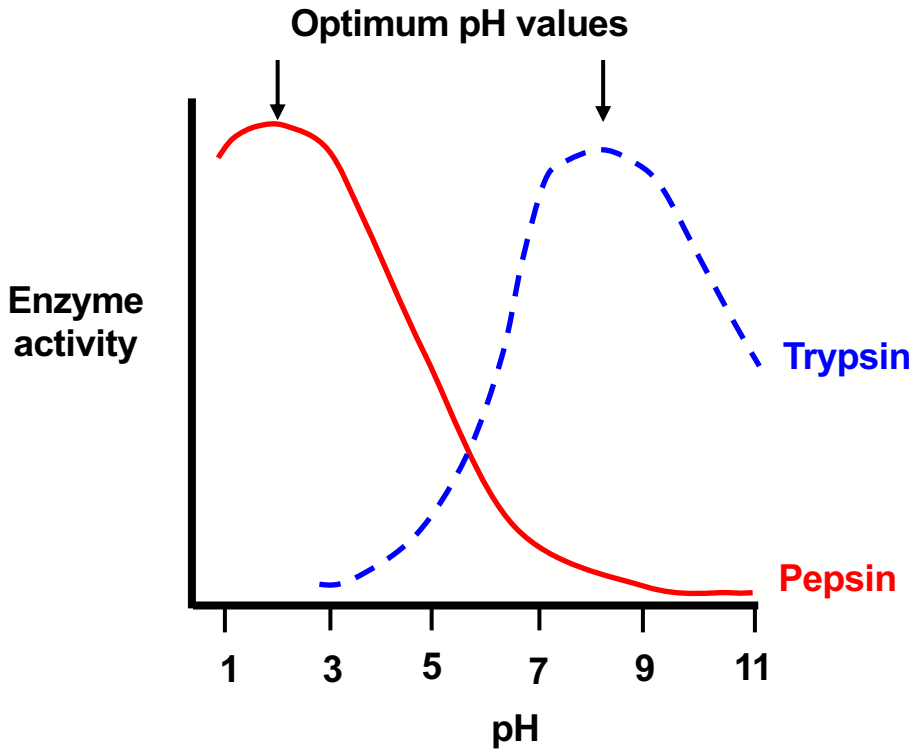
- For most enzymes, the optimum temperature is about 30° C.
- Many are a much lower, cold water fish will die at 30° C because their enzymes denature.
- A few bacteria have enzymes that can withstand very high temperatures up to 100° C.
- Most enzymes, however, are fully denatured at 70° C.

Temperature dependence of different species

(a) Temperature dependence. This panel shows how reaction rate varies with temperature for a typical human enzyme (black) and a typical enzyme from a thermophilic bacterium (green). The reaction rate is highest at the optimal temperature, which is about 37∞C (body temperature) for the human enzyme and about 75∞C (the temperature of a typical hot spring) for the bacterial enzyme. Above the optimal temperature, the enzyme is rapidly inactivated by denaturation.



The effect of pH



The effect of pH

(b) pH dependence. This panel shows how reaction rate varies with pH for the gastric enzyme pepsin (black) and the intestinal enzyme trypsin (red). The reaction rate is highest at the optimal pH, which is about 2.0 for pepsin (stomach pH) and near 8.0 for trypsin (intestinal pH). At the pH optimum for an enzyme, ionizable groups on both the enzyme and the substrate molecules are in the most favorable form for reactivity.

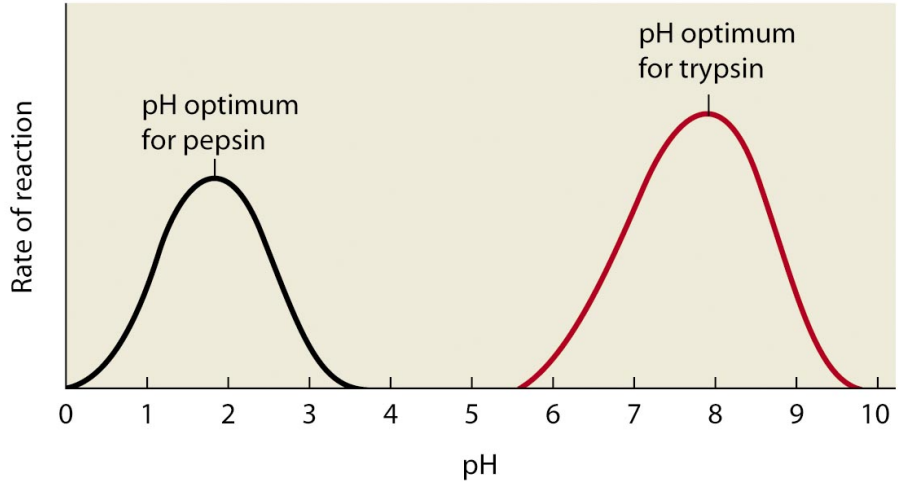


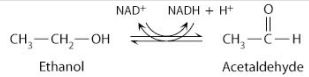
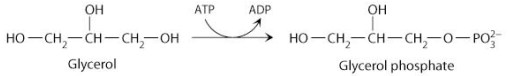
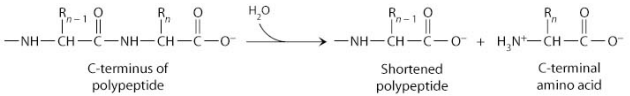
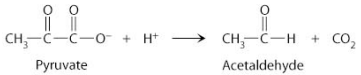
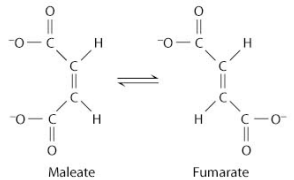
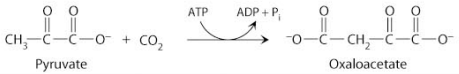
Figure 6-4b

The effect of pH

- Extreme pH levels will produce **denaturation**.
- The structure of the enzyme is changed.
- The active site is distorted and the substrate molecules will no longer fit in it.
- At pH values slightly different from the enzyme's optimum value, small changes in the **charges** of the enzyme and it's substrate molecules will occur.
- This **change in ionisation** will affect the binding of the substrate with the active site.

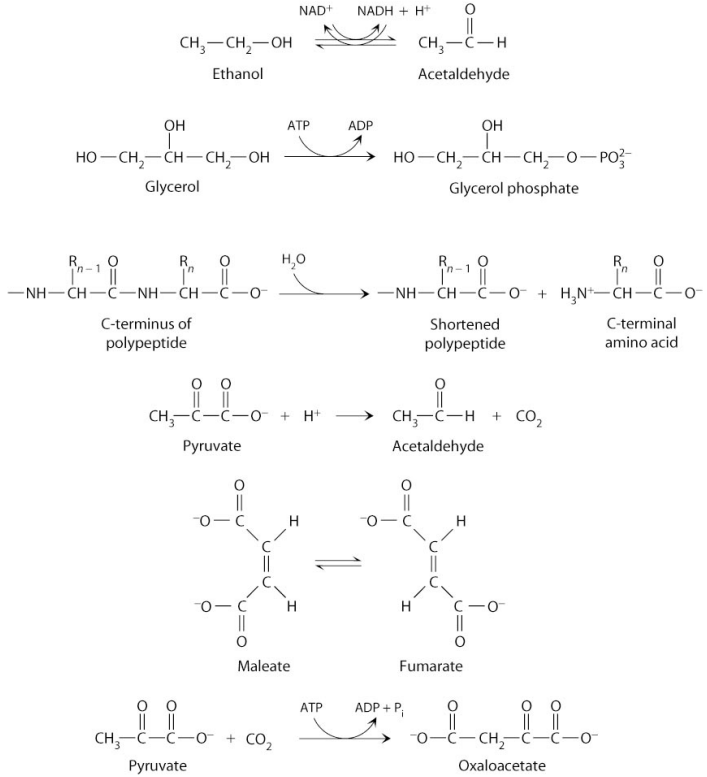
Major classes of Enzymes

Table 6-1 The Major Classes of Enzymes with an Example of Each

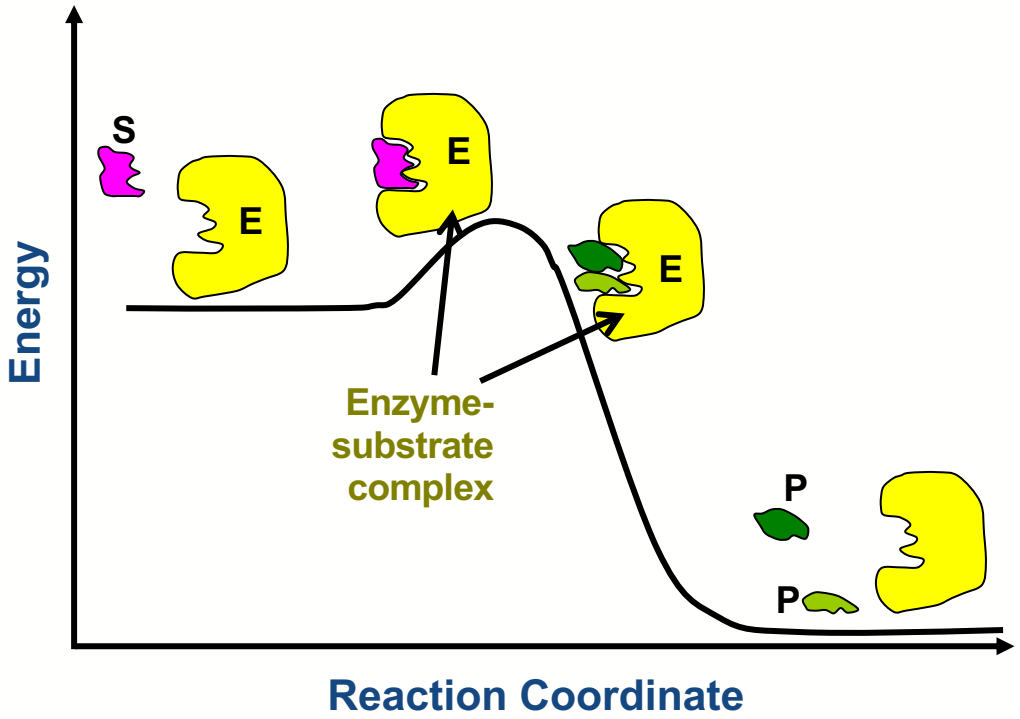
Class	Reaction Type	Example: Enzyme Name	Example: Reaction Catalyzed
1. Oxidoreductases	Oxidation-reduction reactions	Alcohol dehydrogenase (oxidation with NAD^+)	
2. Transferases	Transfer of functional groups from one molecule to another	Glycerokinase (phosphorylation)	
3. Hydrolases	Hydrolytic cleavage of one molecule into two molecules	Carboxypeptidase A (peptide bond cleavage)	
4. Lyases	Removal of a group from, or addition of a group to, a molecule with rearrangement of electrons	Pyruvate decarboxylase (decarboxylation)	
5. Isomerases	Movement of a functional group within a molecule	Maleate isomerase (*cis-trans* isomerization)	
6. Ligases	Joining of two molecules to form a single molecule	Pyruvate carboxylase (carboxylation)	

- Enzymes are divided into six major classes based on their
- general functions, with subgroups used to define their functions more precisely.
- The six major classes are oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases.
- Table 6-1 provides an example of each class, using enzymes that catalyze reactions.

Table 6-1-1

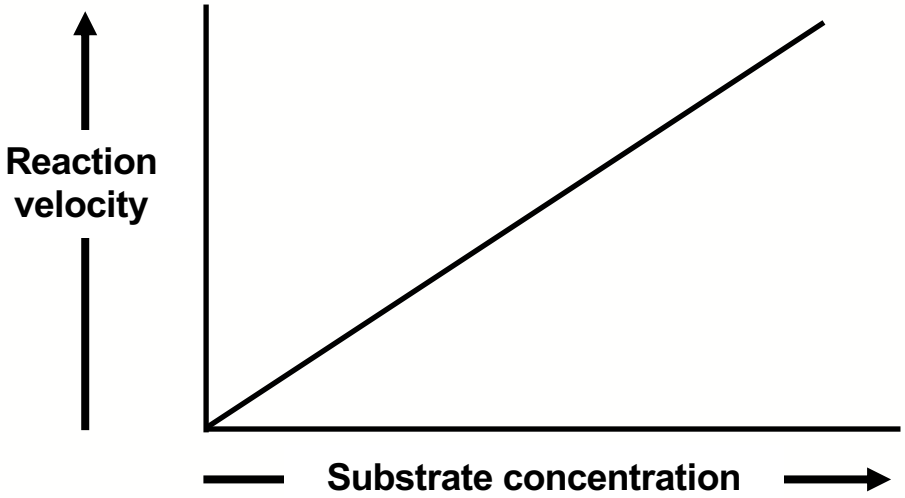


Progress of an enzyme reaction



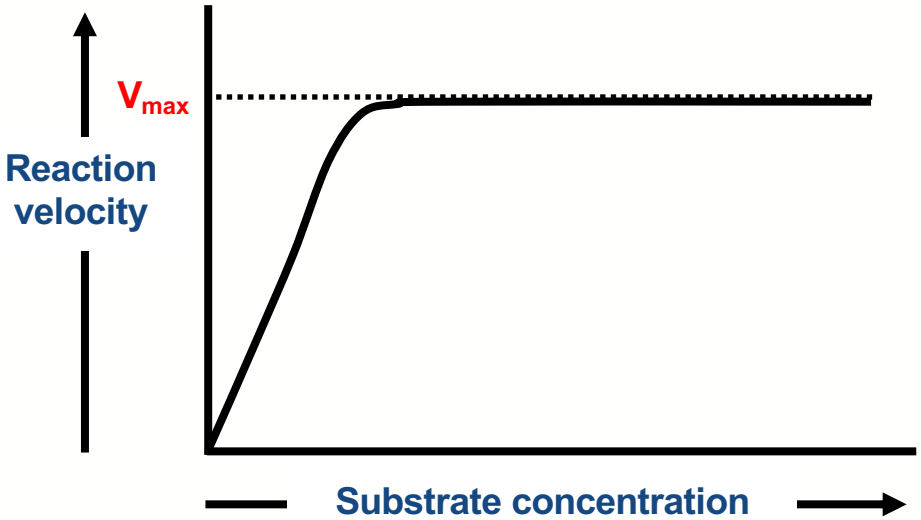
Enzymse can be used again

Substrate concentration: non-enzymatic reactions



The increase in velocity is proportional to substrate concentration!

Substrate concentration: enzymatic reactions



Reaction velocity reaches a saturation point when all the enzyme molecules are occupied.

If you alter the concentration of the **enzyme** then **V_{max}** will change too.