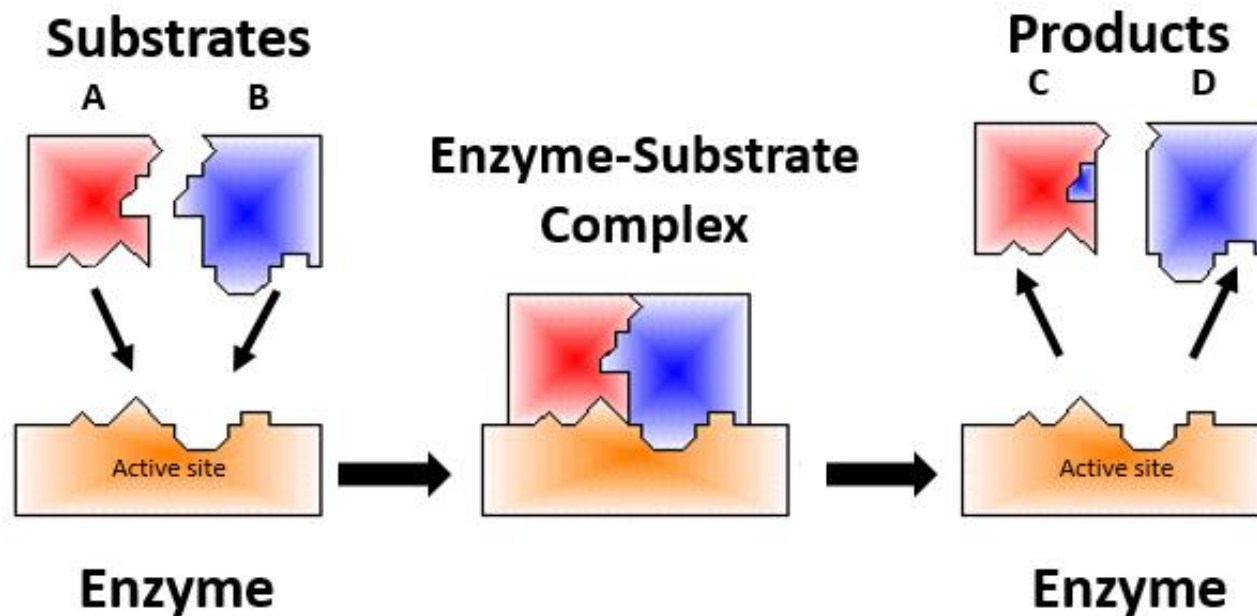


Enzymes are Proteins that act as Biological Catalyst

They **speed up** rate of chemical reactions w/out being consumed in process.

The **active site** on the enzyme is where the substrates bind.

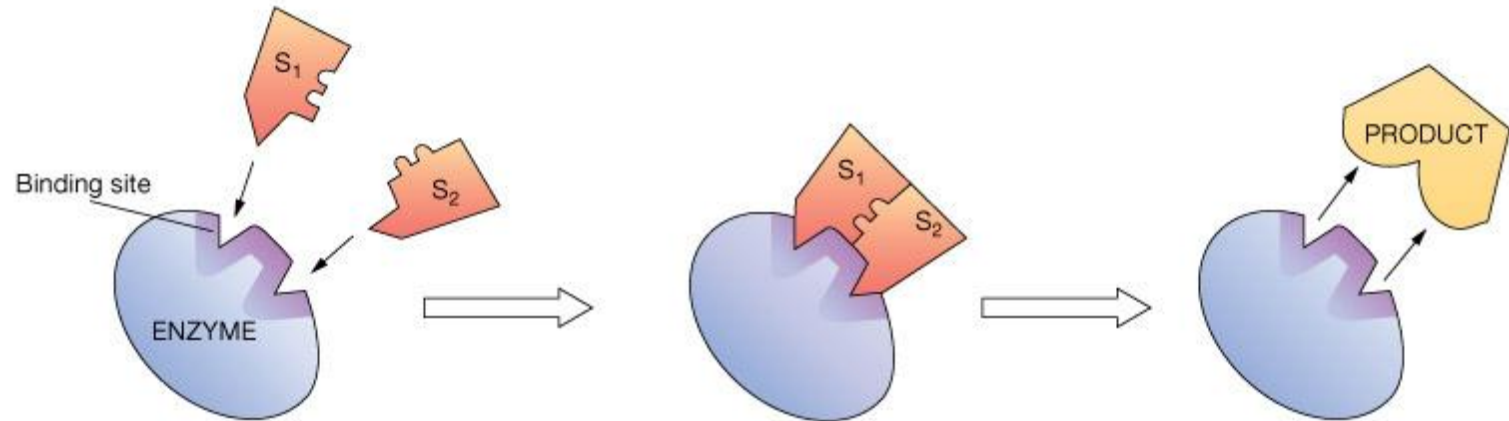
Substrates are the *reactants* in a chemical reaction requiring enzymes.



Specificity: a) lock and key or b) induced fit.

(a) Lock-and-key model

In this older model, the enzyme binding site was an exact match for the substrates.



Naming of Enzymes

Most enzymes end with **ase** and typically their name indicates their function or the substrates they bind. Some important examples:

kinase - adds phosphates to molecules;

phosphatase - removes phosphates from molecules;

dehydrogenase - removes Hydrogens;

hydrolase - adds H₂O;

synthase - dehydration synthesis reactions;

carbonic anhydrase - removes H₂O from carbonic acid;

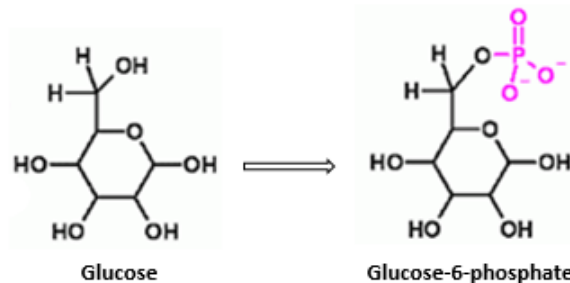
amylase - digests starch;

lipase - digests lipids;

protease - digests proteins.

Enzyme Specificity - ability of enzyme to catalyze only certain reactions. Some are *very* specific, such as **glucokinase**.

It catalyzes this reaction:



*Other enzymes have broader specificities,
e.g. *peptidases break all peptide bonds*.

The type and amount of enzymes in the body can vary.

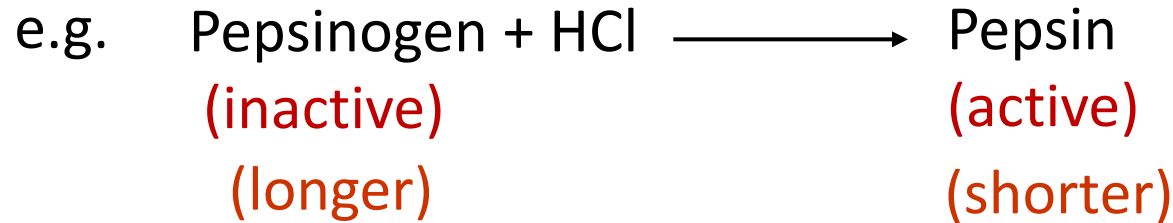
e.g., **alcohol dehydrogenase** removes H's from ethanol ('alcohol') thereby reducing its toxic effects.

Q: Is everyone's ability to "handle" alcohol the same?

Enzyme Activation

Some enzymes exists in an ***inactive*** state, need to be ***activated***.

1) Proteolytic Activation:



Other Examples of Proteolytic Activation:

Fibrinogen - > becomes...

Thrombinogen -> becomes...

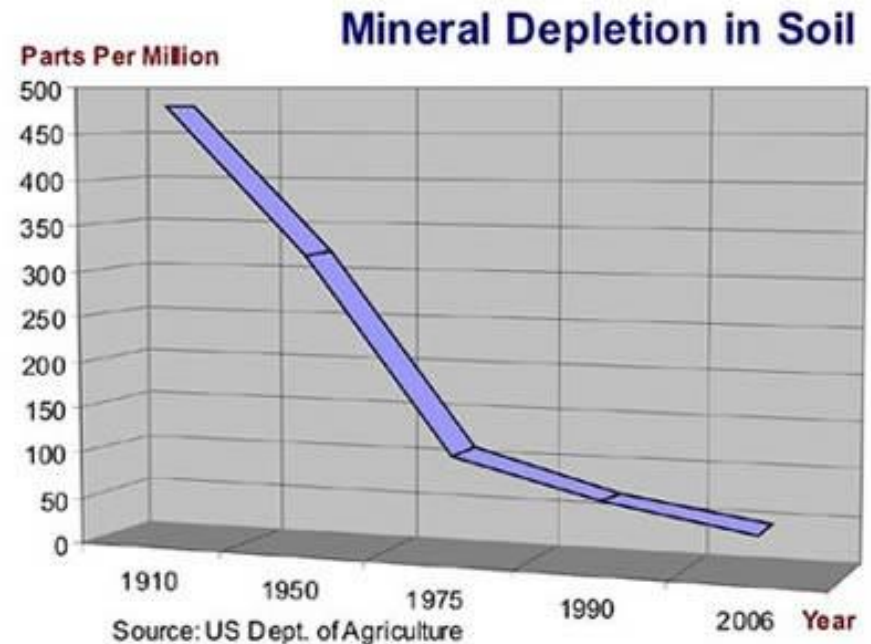
Angiotensinogen -> becomes ...

Enzyme Activation

2) Co-factors: Inorganic components required for substrate binding at the *active site*.

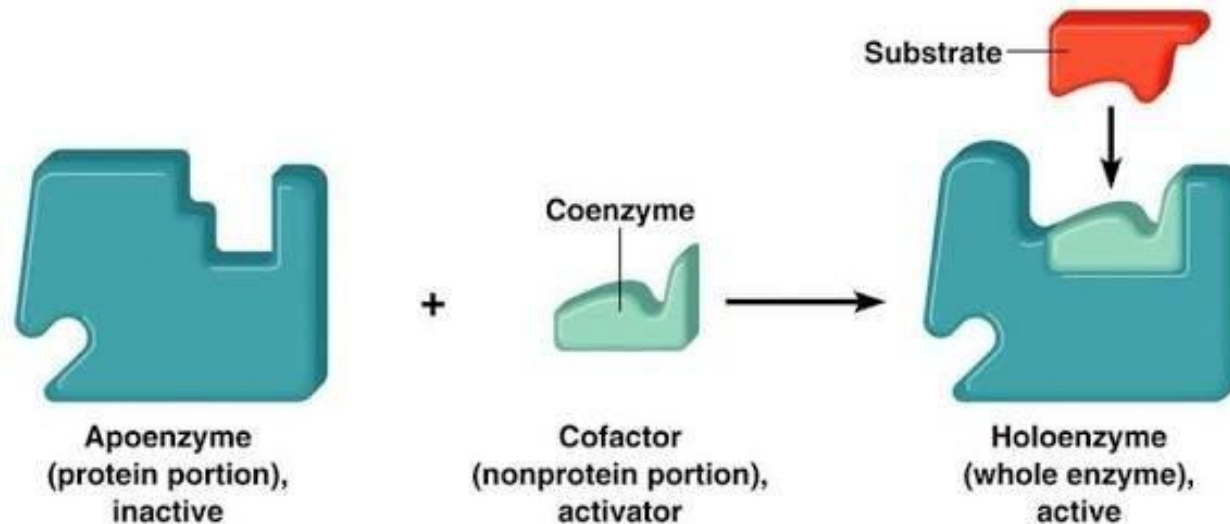
e.g., Zn^{2+} Ca^{2+} , Mg^{2+} or Cu^{2+} (conformational changes).

Cofactor	Example Enzymes
Zn^{2+}	carbonic anhydrase
Zn^{2+}	alcohol dehydrogenase
Cu^{2+}	cytochrome oxidase
K^{+} and Mg^{2+}	pyruvate phosphokinase



3) Co-enzymes: Small organic molecules to accept and transfer electrons (e^- s) from different enzymatic reactions.

Bind loosely to an enzyme at active site to help catalyze reactions.
Usually vitamins, vitamin derivatives, or from nucleotides.



Apoenzyme - an inactive enzyme that requires cofactor/coenzyme.

Holoenzyme - a complete and catalytically active enzyme because it has its cofactor/coenzyme.

e.g., Co-enzyme NAD^+ shuttles e^- s in glycolysis

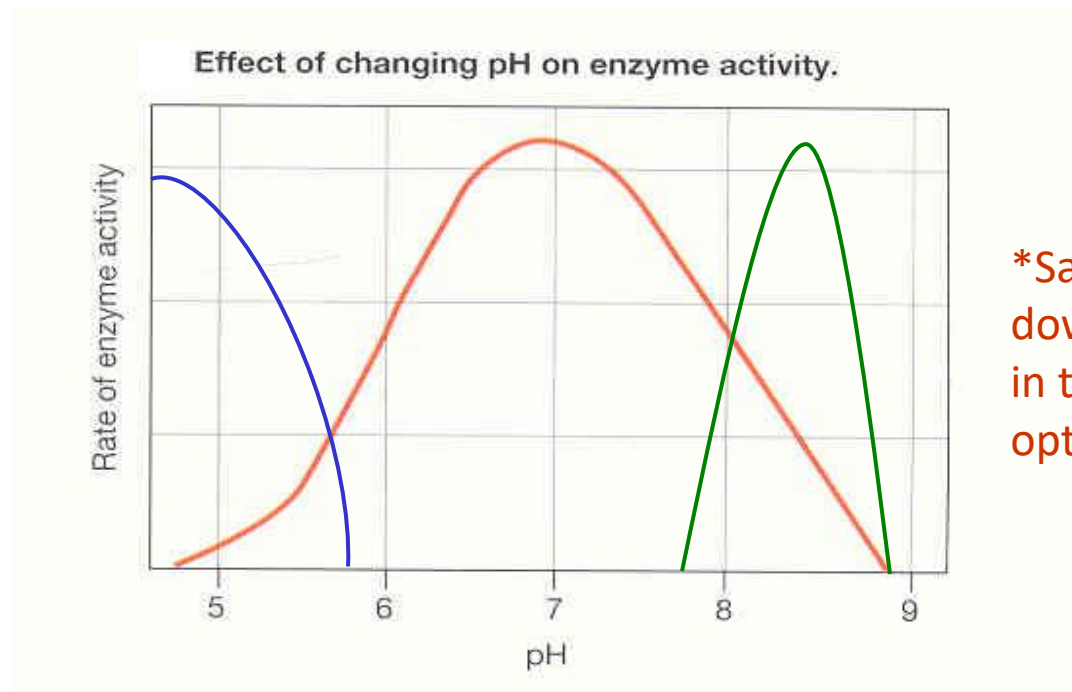
Factors that Effect Enzyme Activity

Once an enzyme is active, several factors can modulate (change) their activity.

1. pH (Acidity/Alkalinity)

Enzymes function within certain pH ranges. Changes in pH alter 3^o structure. Beyond a critical level (outside its optimal pH range), the enzyme is **denatured**.

e.g., compare enzymes of mouth, stomach and small intestine.

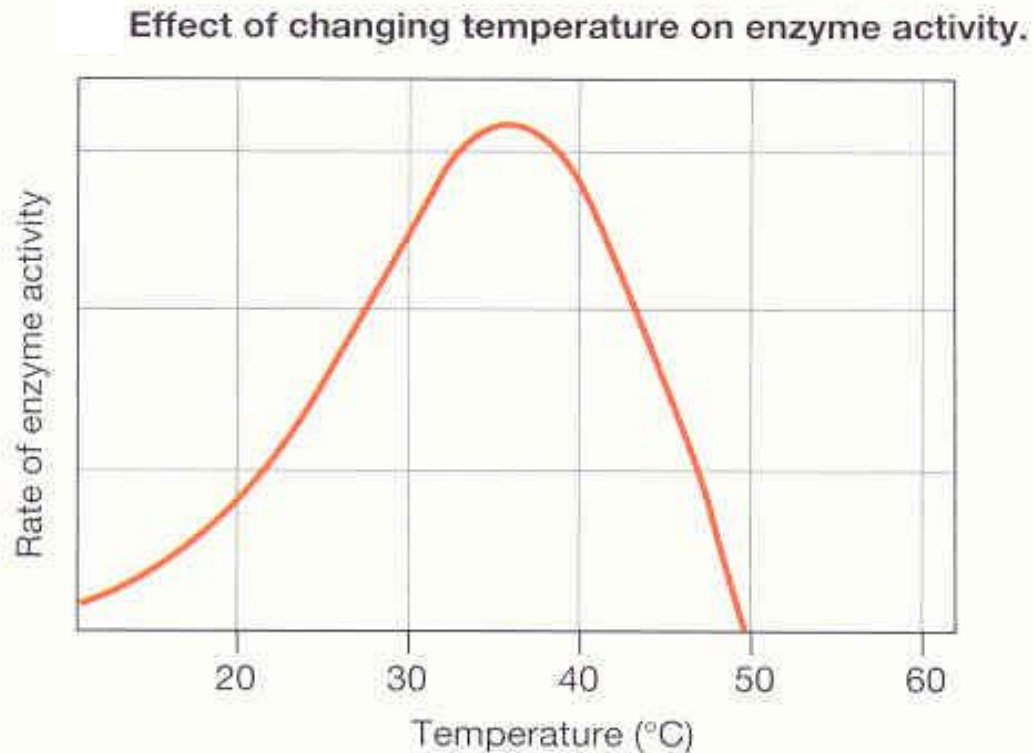


*Salivary amylase breaks down starch to maltose in the mouth, has an optimum pH 6.7 to 7.0.

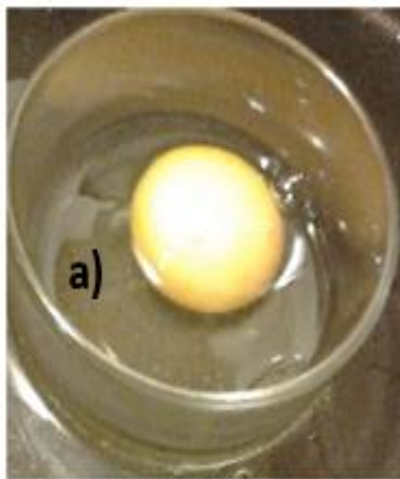
2. Temperature

Enzymes function within certain and temperature ranges. Most human enzymes are optimal at $\sim 36^{\circ}\text{C}$. Again, beyond a critical level, enzymes are **denatured**.

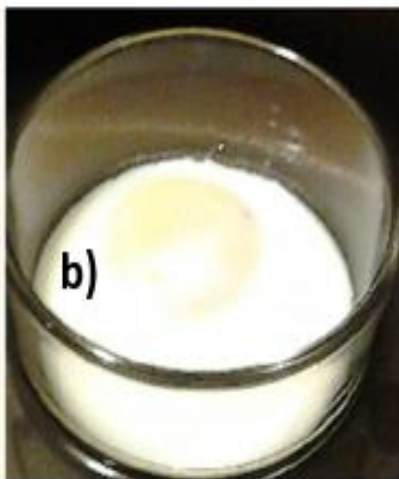
e.g., think of the effects of a fever on enzymes in the body.



**Functional
protein**

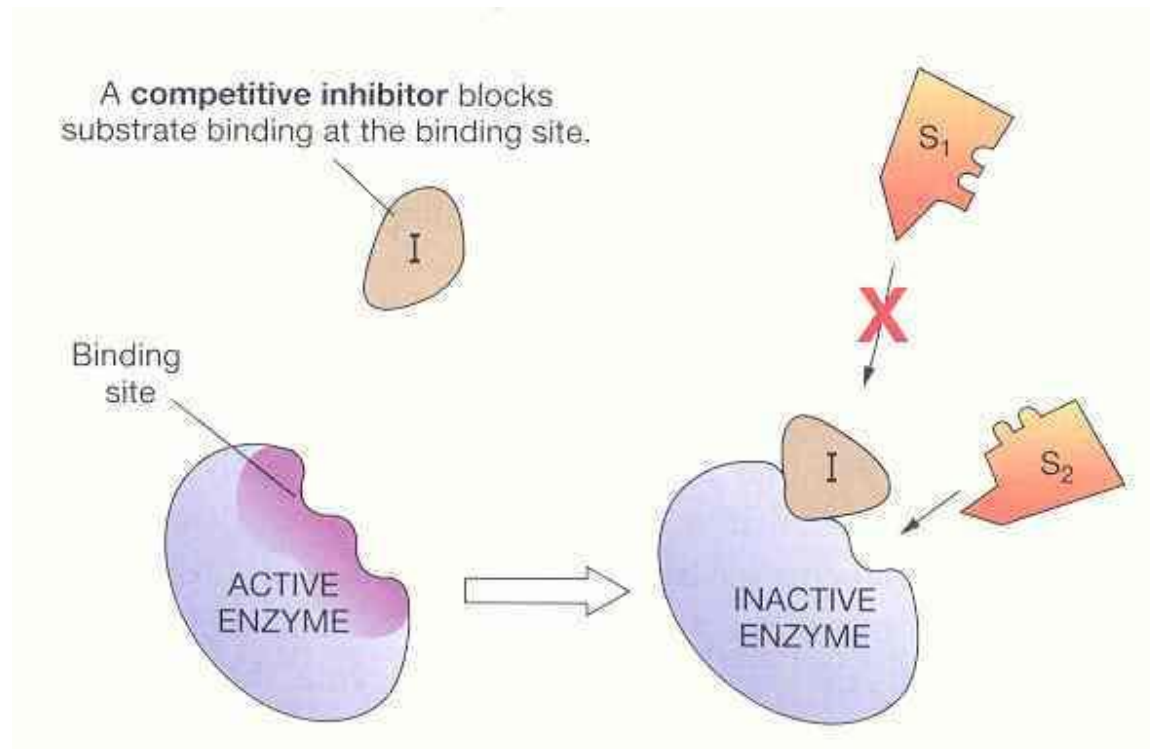


**Denatured
(destroyed) protein**



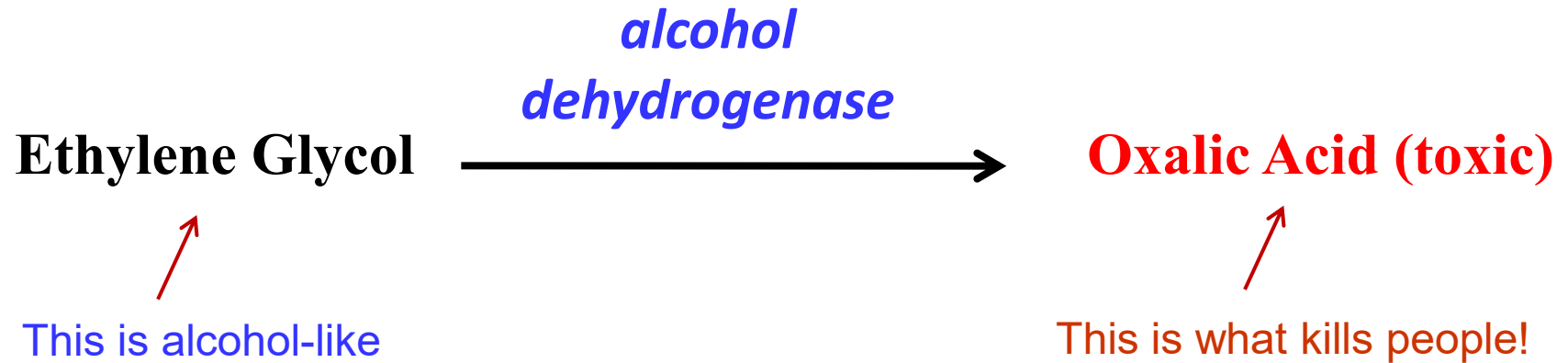
3. Inhibitors - Molecules that bind to enzymes and inhibit true substrate from binding

A) Competitive Inhibitors bind to the *active site* without being acted on, thus reducing reaction rate of true substrate(s). In other cases, the competing molecule is acted on by the enzyme, but again, inhibits reaction with natural substrate.



An interesting example of Competitive Inhibitors:

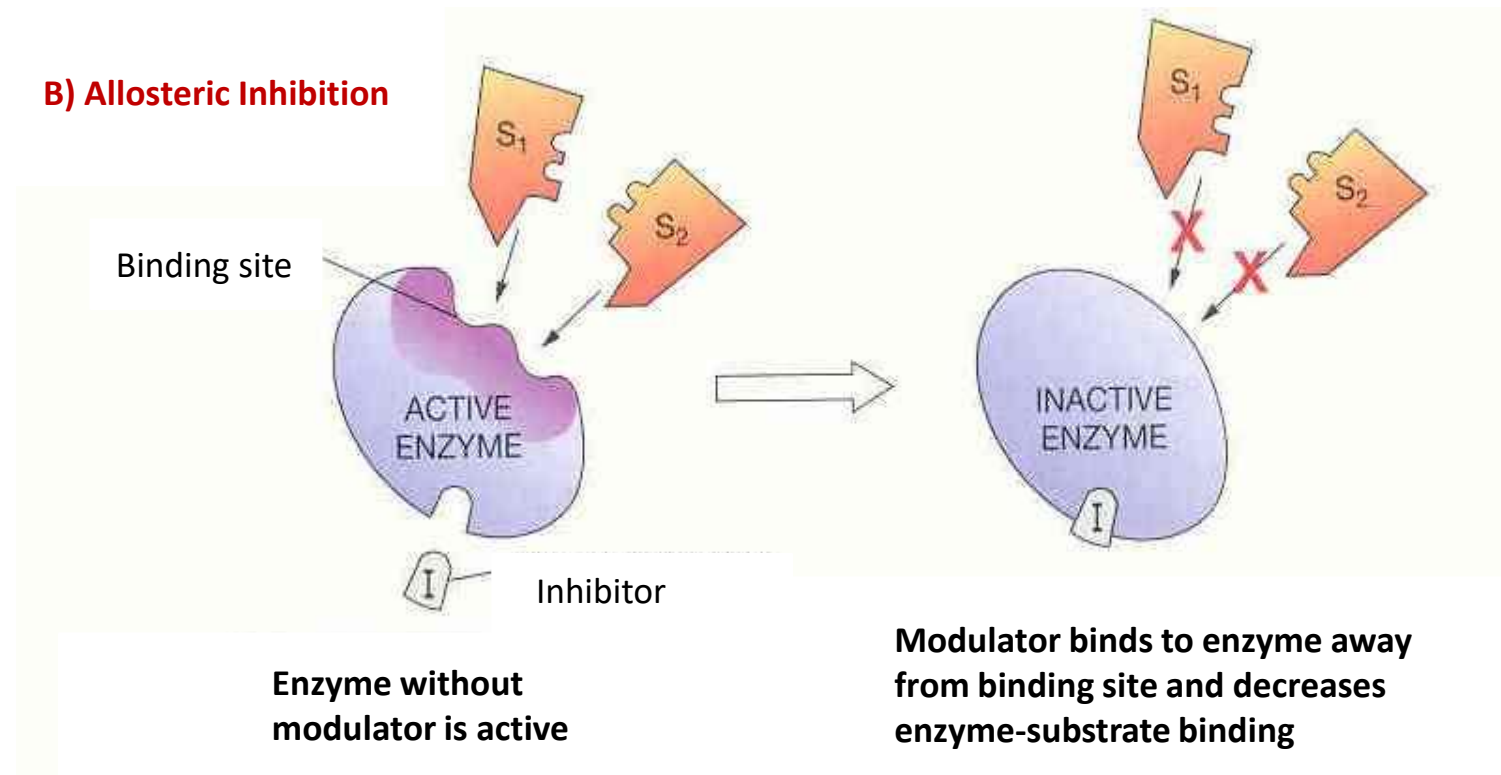
Ethylene glycol (antifreeze) is a poison which can kill people if ingested! This is what happens in the body:



What is one of the best treatments
for ethylene glycol poisoning?

B) Non-Competitive Inhibitors bind *at some site other than the active site*. They do not affect enzyme-substrate binding but inhibit the enzyme from catalyzing the reaction. Some act by binding to the cofactors of enzymes.

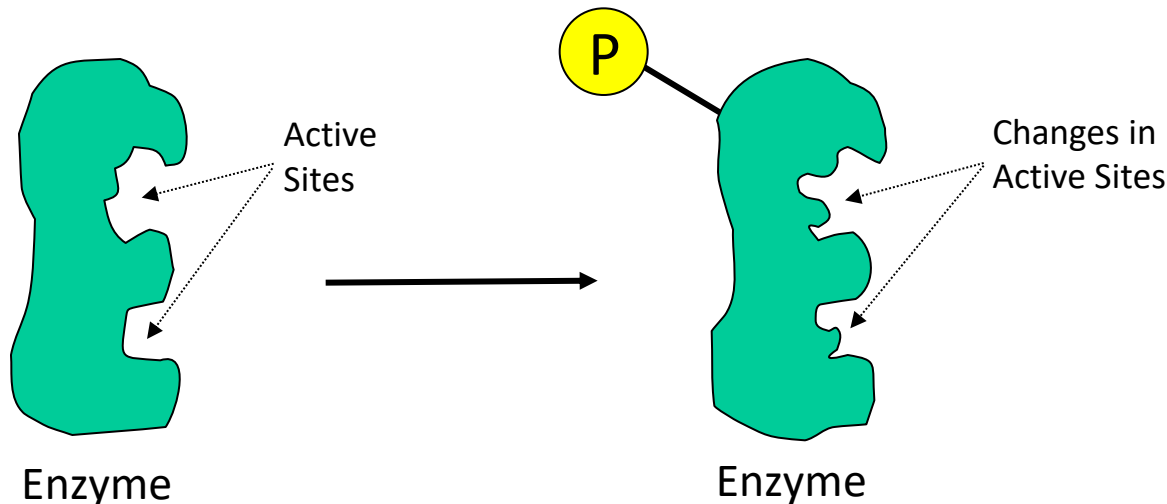
B) Allosteric Inhibition



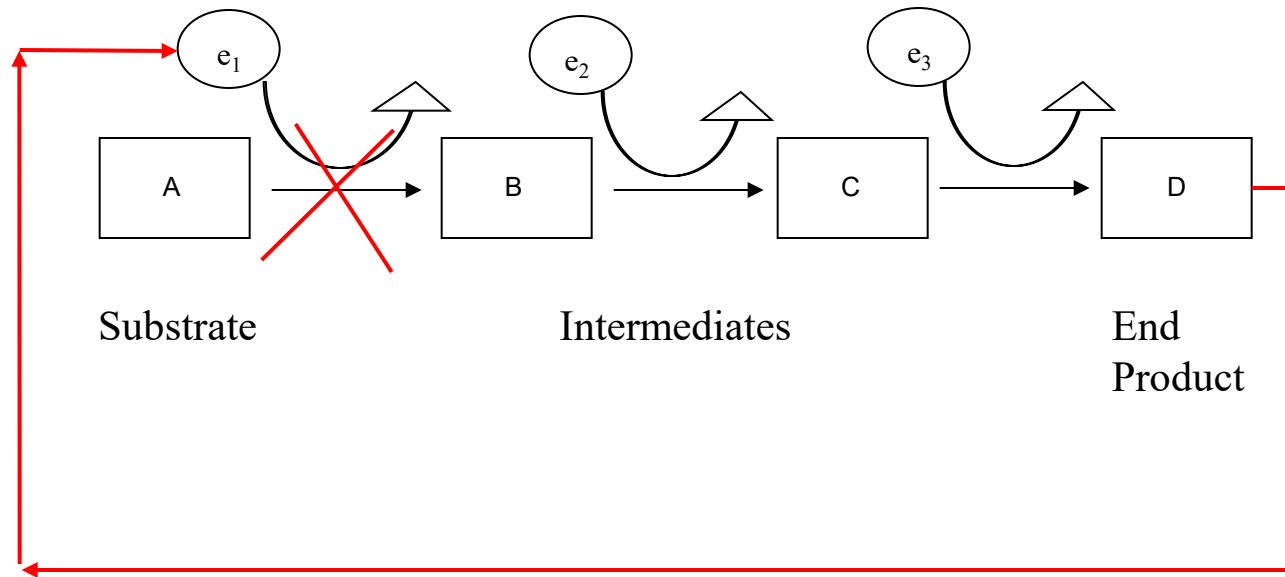
***Allosteric Modulators** - these bind away from active site but in doing so alter the shape of the active site. This can *increase* or *decrease* enzyme affinity for substrates.

Covalent Modulators - bind covalently to enzyme away from the active site, change the shape, thus function of the enzyme.

e.g., Phosphate groups are one of the most common and important covalent modulators in the human body.



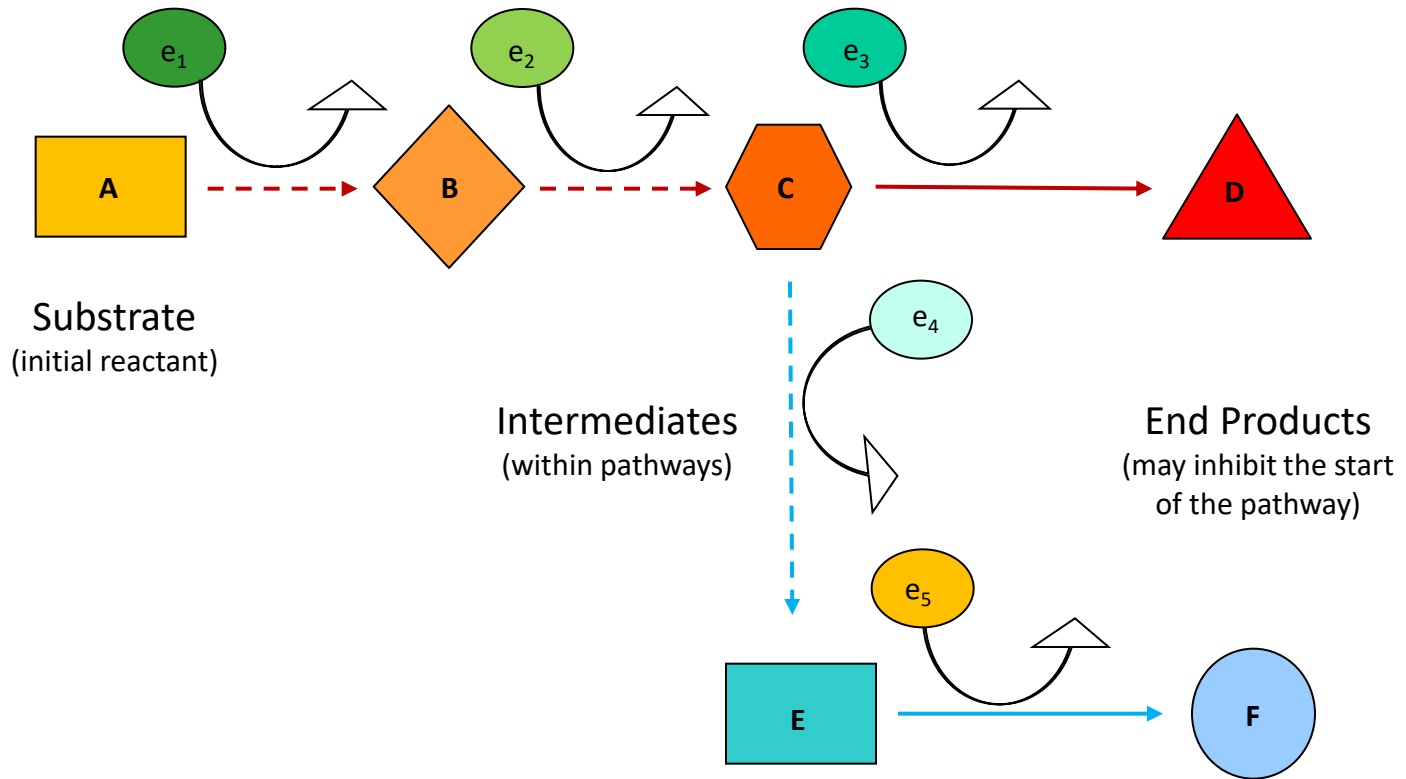
Enzymes control metabolic pathways:



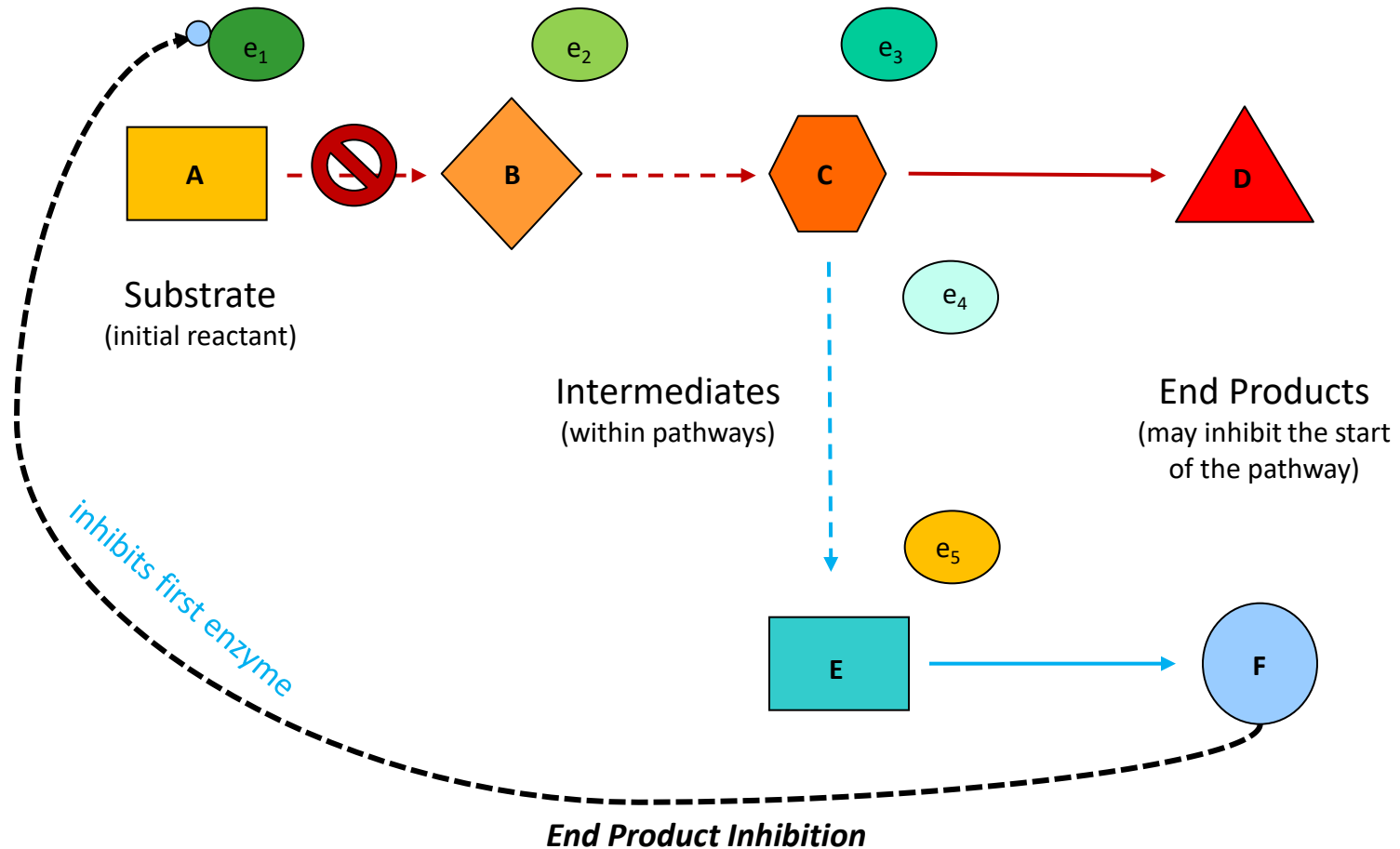
Allosteric Inhibition – substances bind away from the active site, changing the shape and thereby function of the enzyme.

In the case above, this can also be called “***End Product Inhibition***”.

Enzymes control metabolic pathways:



Enzymes control metabolic pathways:



Inhibiting one enzyme can stop multiple pathways

Enzyme & Substrate Concentration Affect Reaction Rate

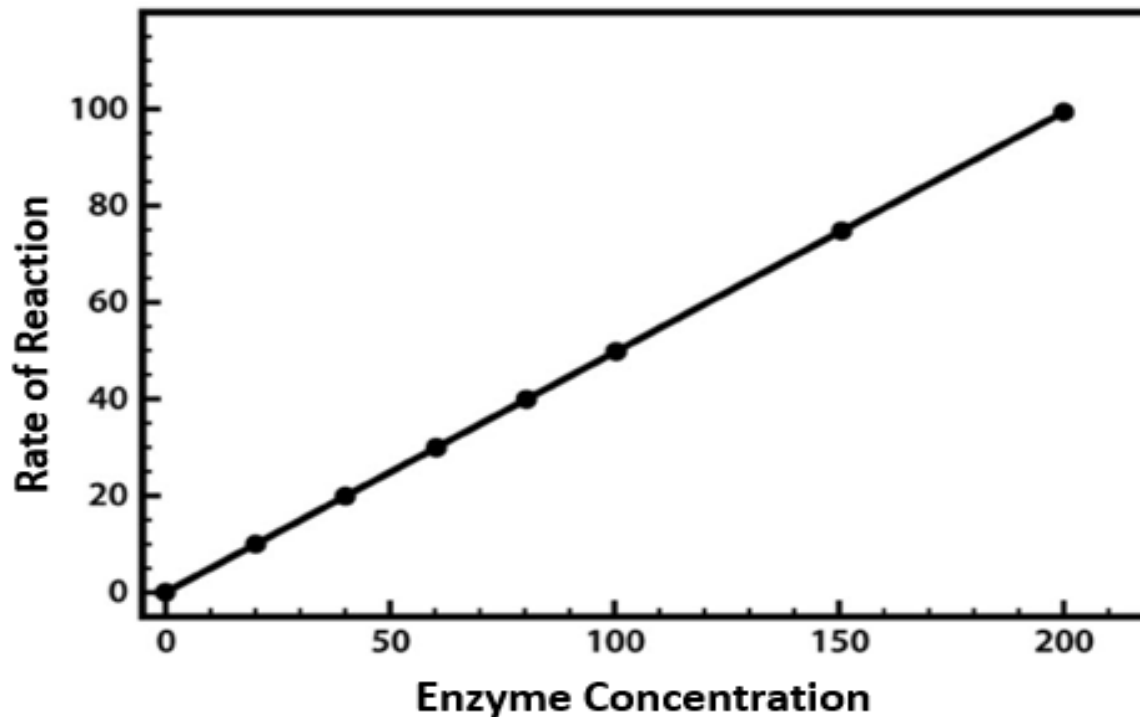
The rate of enzymatically catalyzed reactions assessed by measuring product synthesis (or substrate consumption).

Reaction Rate is:

1. Directly Related to the Amount of Enzyme Present.

If the substrate concentration ($[\text{substrate}]$) is kept constant, then the more enzyme that is present, the greater the rate of the reaction (i.e., the more product is produced).

1. Amount of Enzyme



2. Related to the Amount of Substrate Present and can Reach a Maximum.

If the enzyme concentration ($[\text{enzyme}]$) is held constant, the reaction rate will increase as $[\text{substrate}]$ increases but there is a limit to how fast a reaction can go.

2. Amount of Substrate

