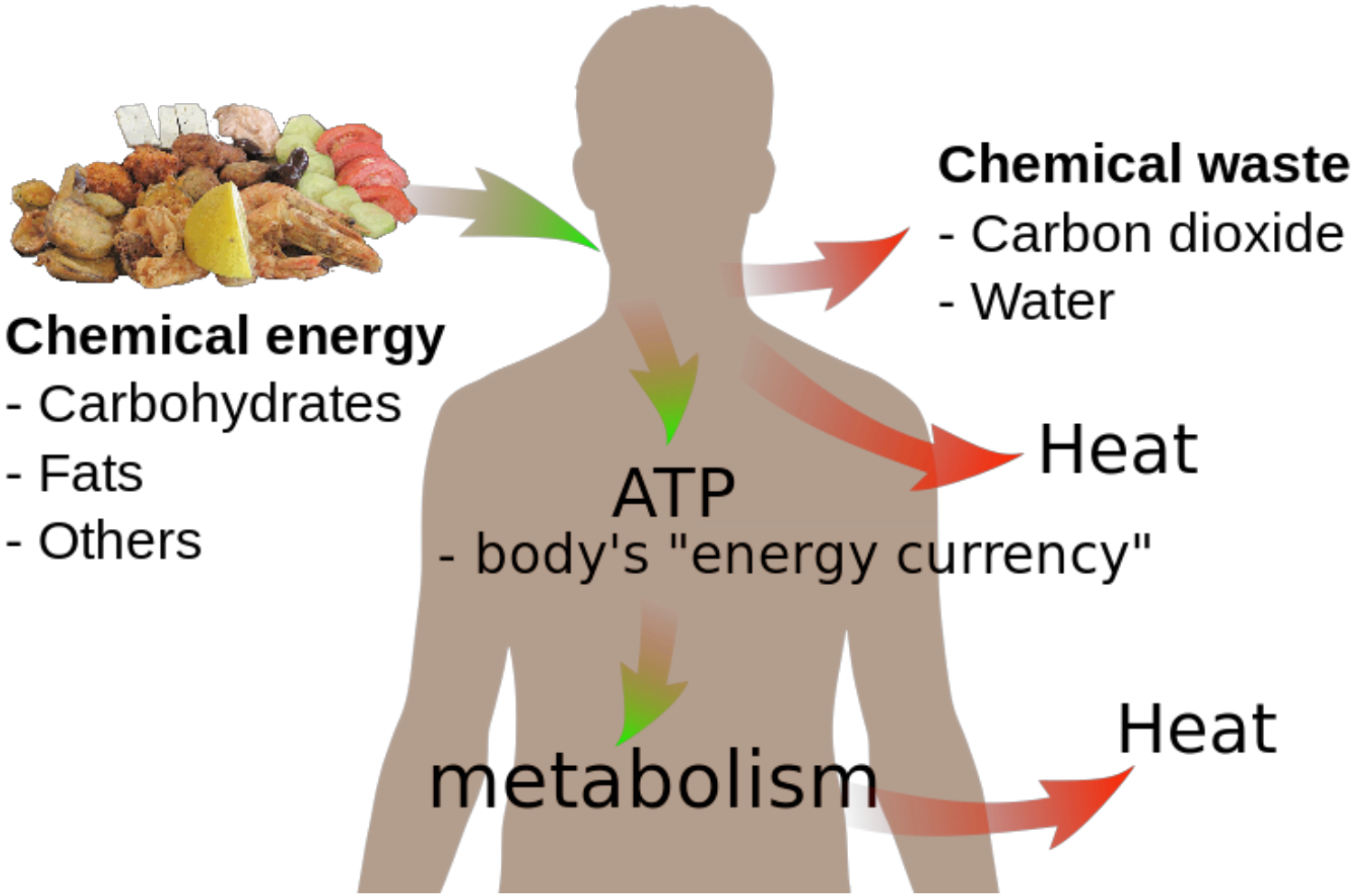
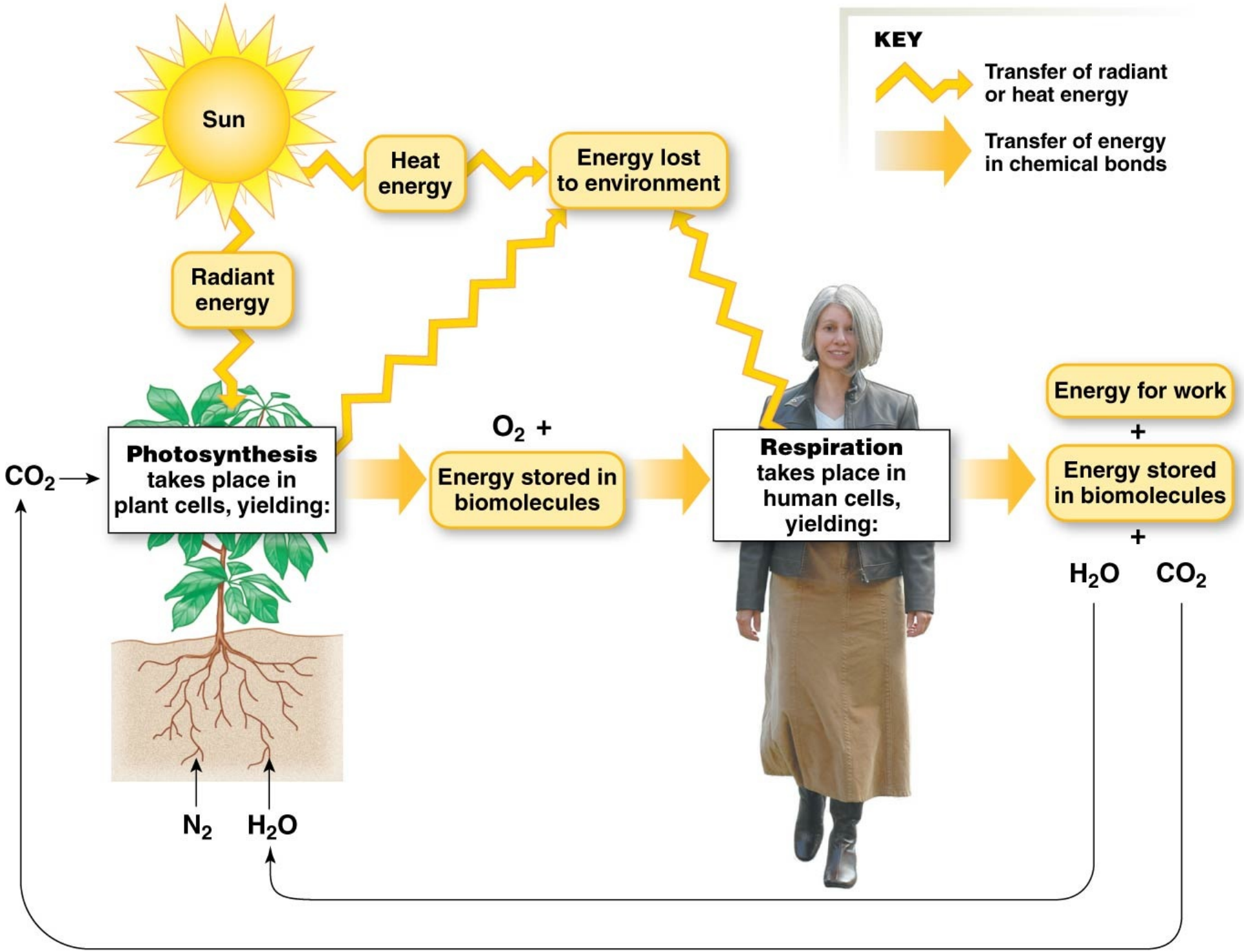
Enzymes and Energy





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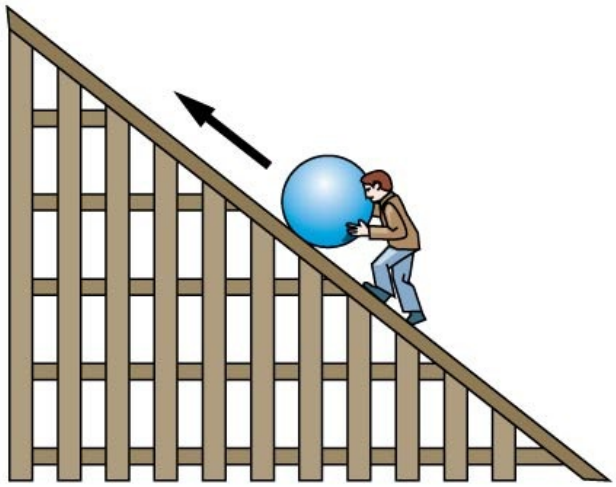
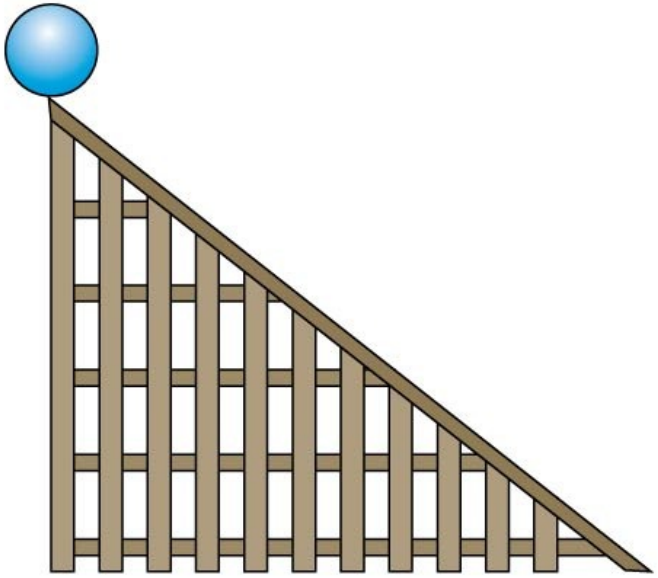
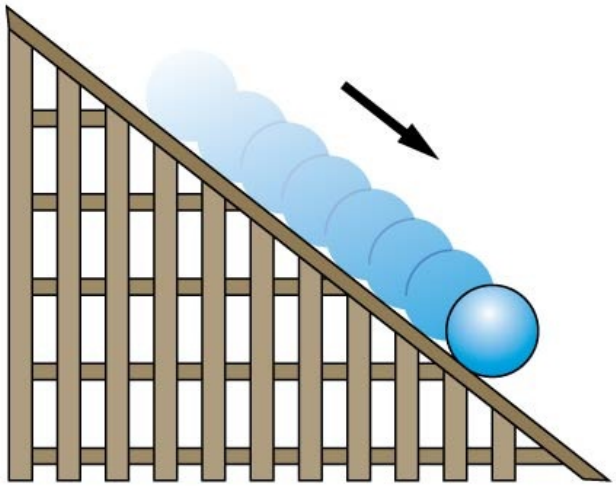
Types of Energy



(a) Work is used to push a ball up a ramp. Kinetic energy of movement up the ramp is being stored in the potential energy of the ball's position.



(b) The ball sitting at the top of the ramp has potential energy, the potential to do work.



(c) The ball rolling down the ramp is converting the potential energy to kinetic energy. However, the conversion is not totally efficient, and some energy is lost as heat due to friction between the ball, ramp, and air.

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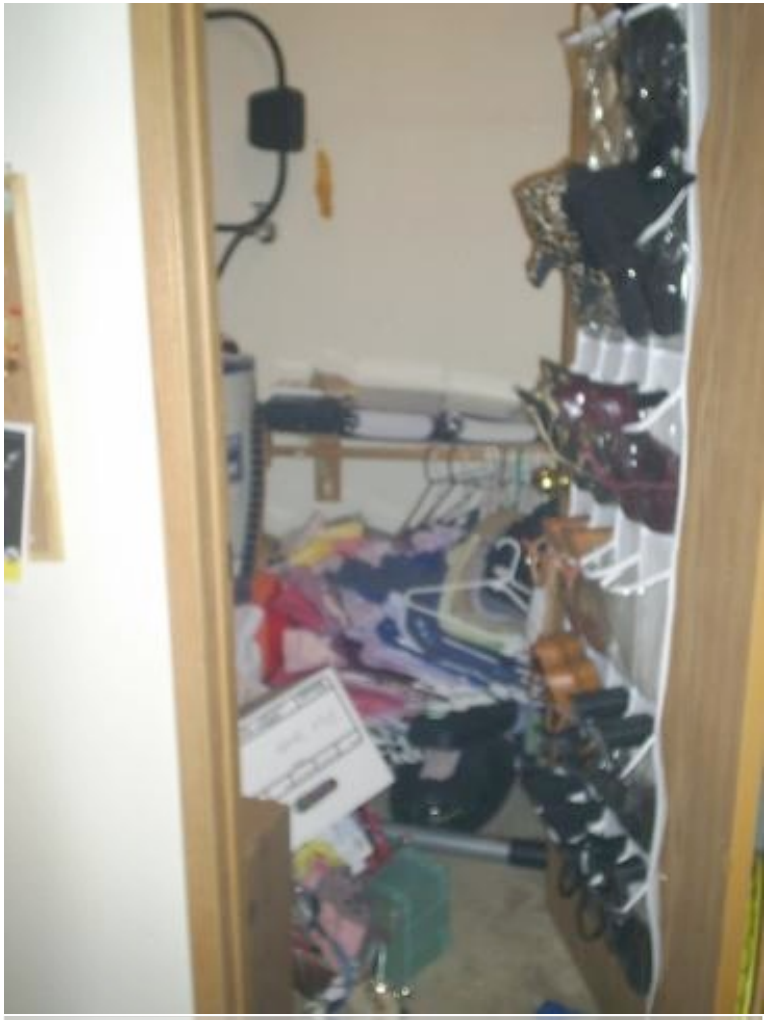
ENERGY LAWS

- First Law of Thermodynamics: Energy cannot be _____
- Second Law of Thermodynamics: Law of increasing _____

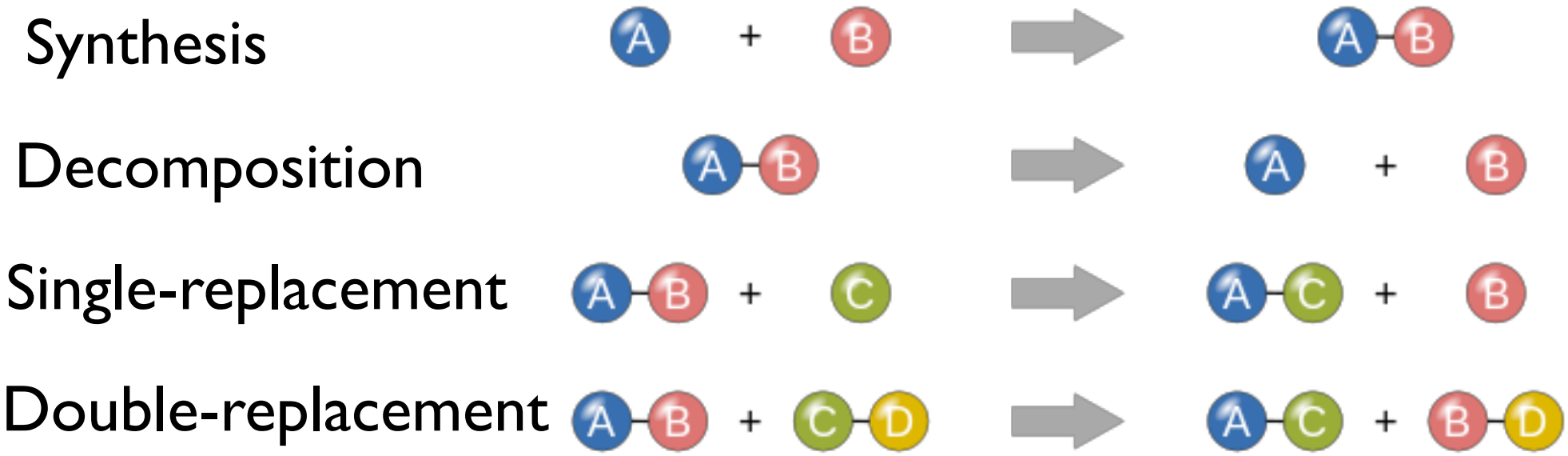


Chemical Reactions

The transformation of one set of chemical substances to another.

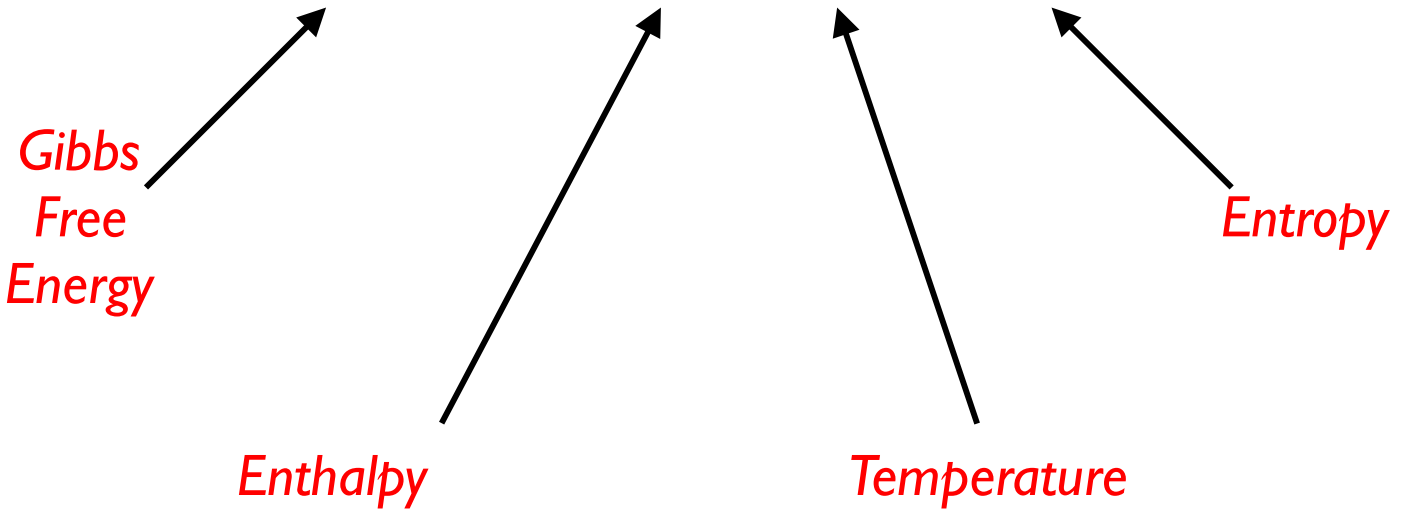
Reactants Products

Basic Types of Chemical Reactions

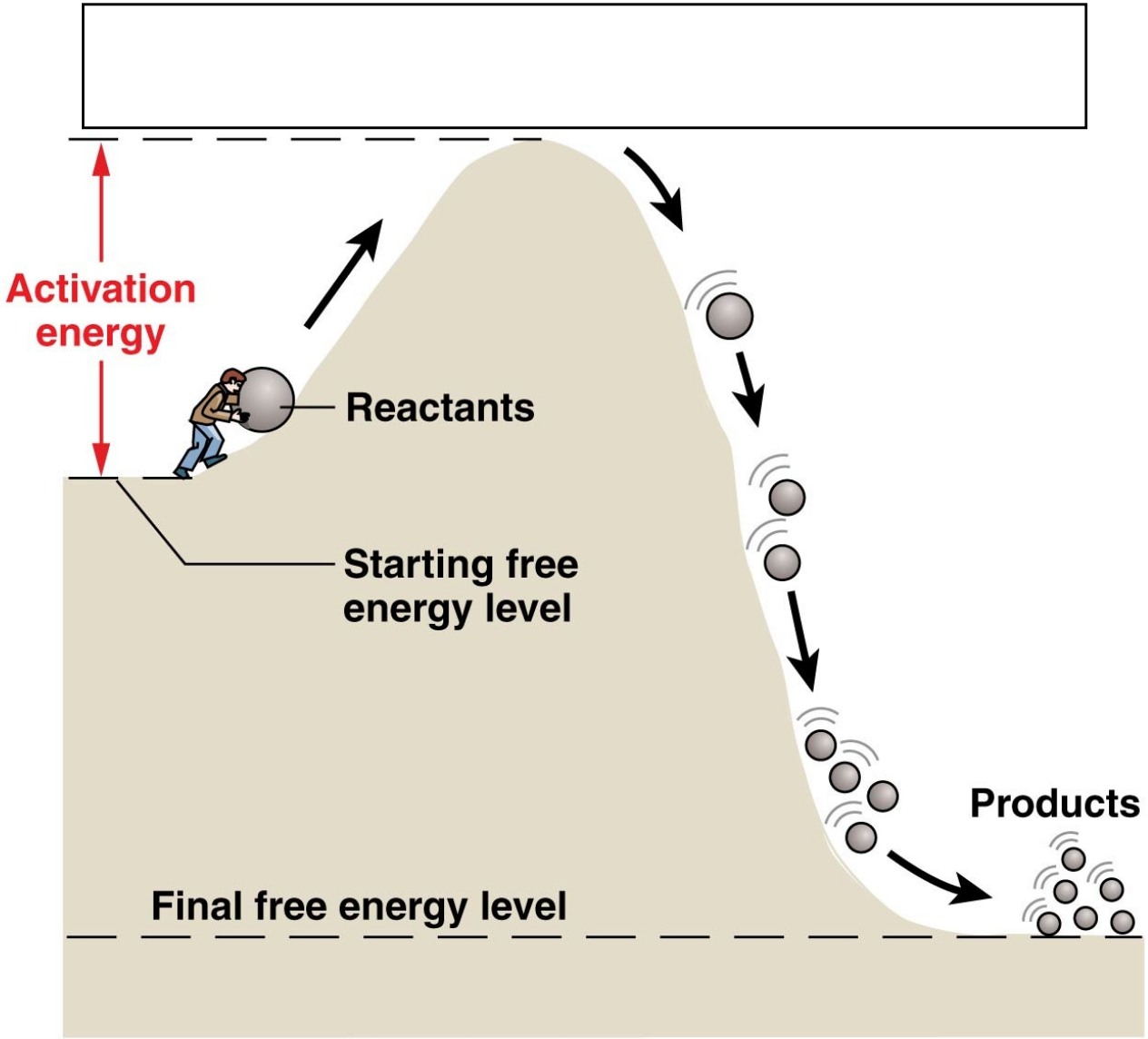


Thermodynamics in Chemical Reactions

$$\Delta G = \Delta H - T \cdot \Delta S$$



Chemical Reactions Require



(a) Activation energy is the "push" needed to start a reaction.

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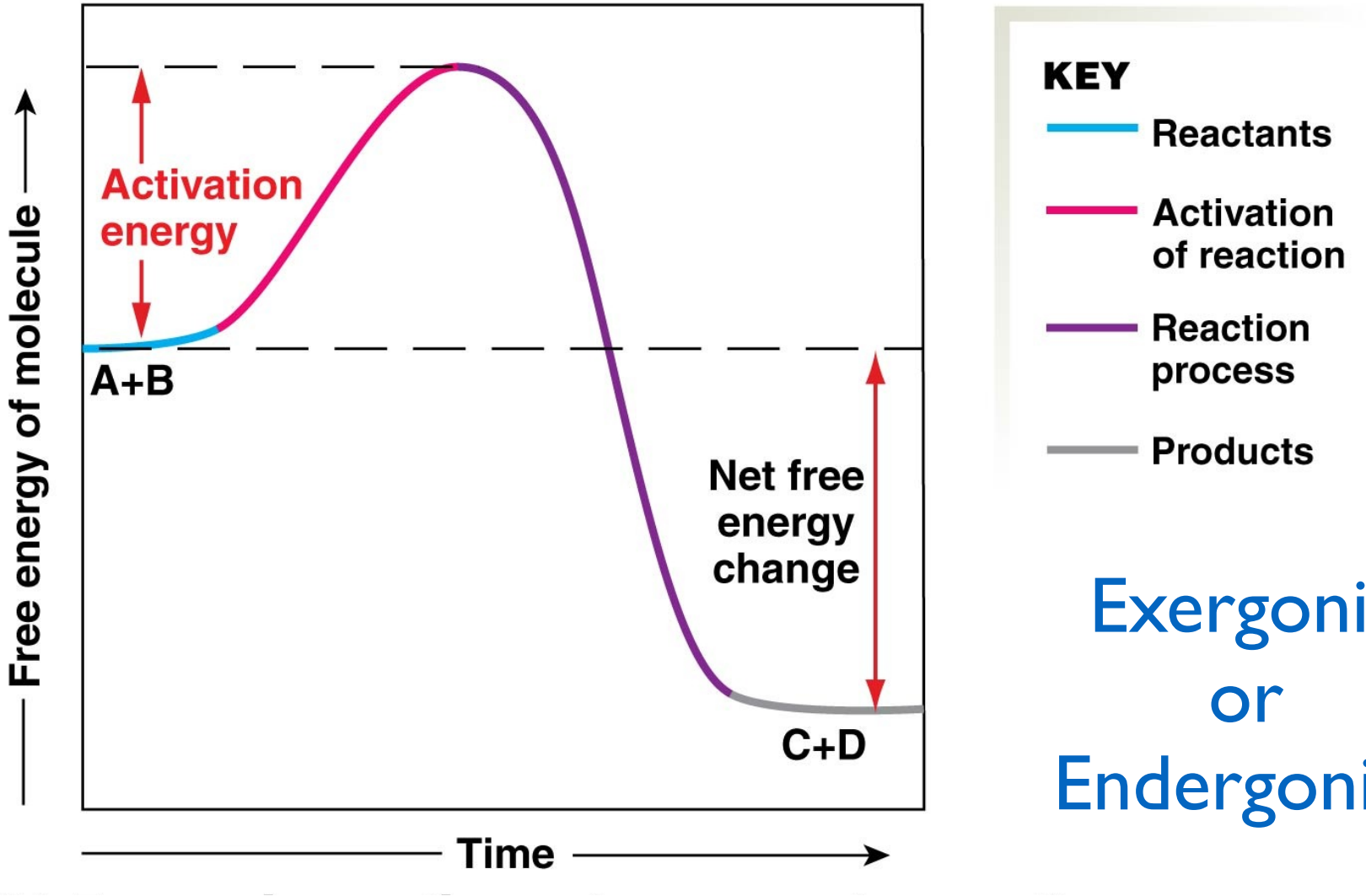
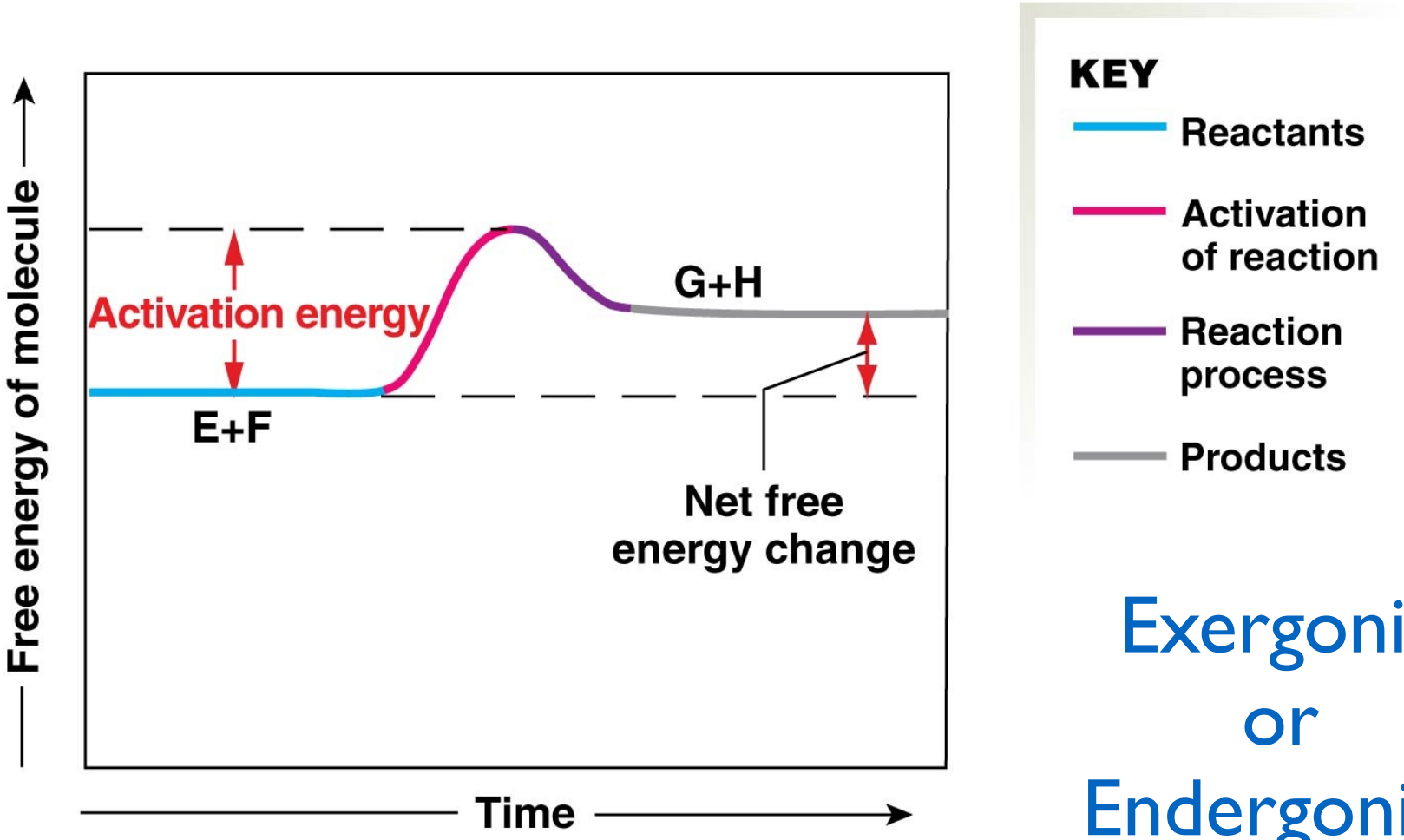
Chemical Reactions Store or Release Energy



Exergonic or Endergonic?

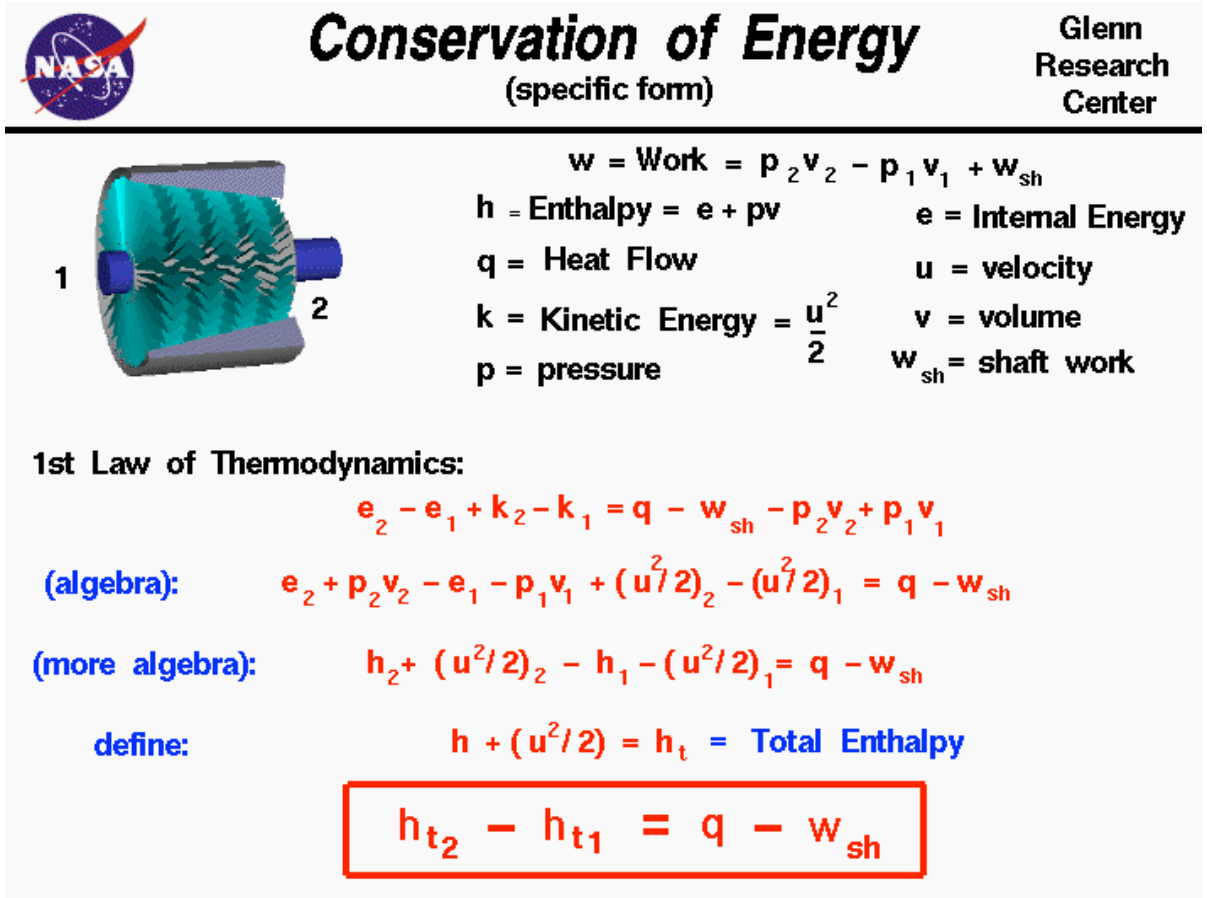
Chemical Reactions Store or Release Energy

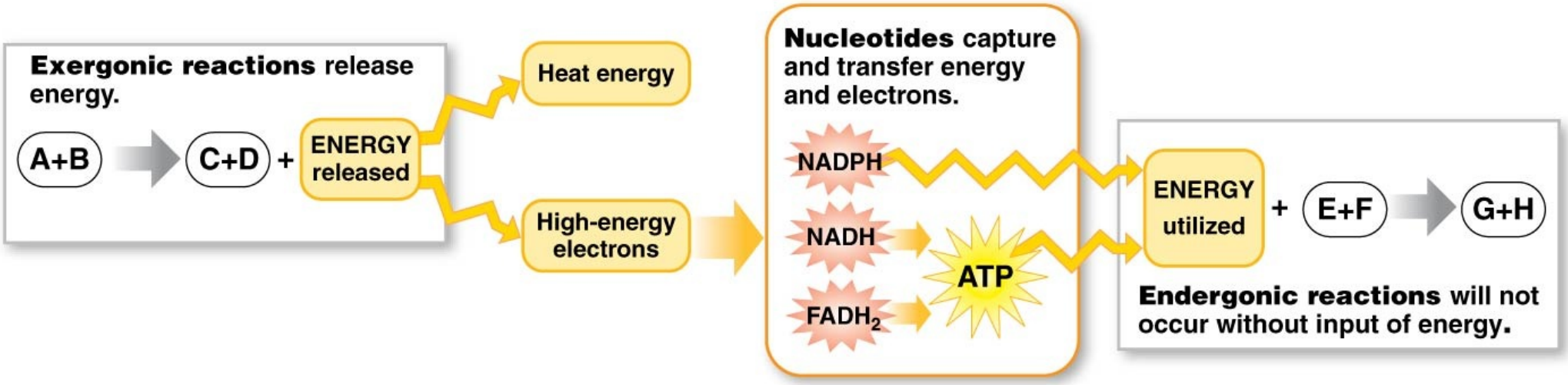


Exergonic or Endergonic?

Wait a Second!

- Isn't all that a VIOLATION of the First Law of Thermodynamics?





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Enzymes

Classification of Enzymatic Reactions — Table 4.4

Reaction Type	What Happens	Representative Enzymes
1. Oxidation-reduction	Add or subtract electrons	**Class:*** oxidoreductase
(a) Oxidation	Transfer electrons from donor to oxygen	Oxidase
	Remove electrons and H^+	Dehydrogenase
(b) Reduction	Gain electrons	Reductase
2. Hydrolysis-dehydration	Add a water molecule	**Class:*** hydrolase
	Subtract a water molecule	
(a) Hydrolysis	Split large molecules by adding water	Peptidases, saccharidases, lipases
(b) Dehydration	Remove water to make one large molecule from several smaller ones	Dehydratases
3. Transfer chemical groups	Exchange groups between molecules	**Class:*** transferases
	Add or subtract groups	**Class:*** lyases
(a) Exchange reaction	Phosphate	Kinase
	Amino group	Transaminase
(b) Addition	Phosphate	Phosphorylase
	Amino group	Aminase
(c) Subtraction	Phosphate	Phosphatase
	Amino group	Deaminase
4. Ligation	Join two substrates using energy from ATP	**Class:*** ligases
		Synthetase

* Enzyme classes as defined by the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology, *www.chem.qmul.ac.uk/iubmb/enzyme*

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Diagnostically Important Enzymes

Table 4.3

Elevated blood levels of these enzymes are suggestive of the pathologies listed.

Enzyme	Related Diseases
Acid phosphatase*	Cancer of the prostate
Alkaline phosphatase	Diseases of bone or liver
Amylase	Pancreatic disease
Creatine kinase (CK)	Myocardial infarction (heart attack), muscle disease
Glutamate dehydrogenase (GDH)	Liver disease
Lactate dehydrogenase (LDH)	Tissue damage to heart, liver, skeletal muscle, red blood cells

*A newer test for a molecule called prostate specific antigen (PSA) has replaced the test for acid phosphatase in the diagnosis of prostate cancer.

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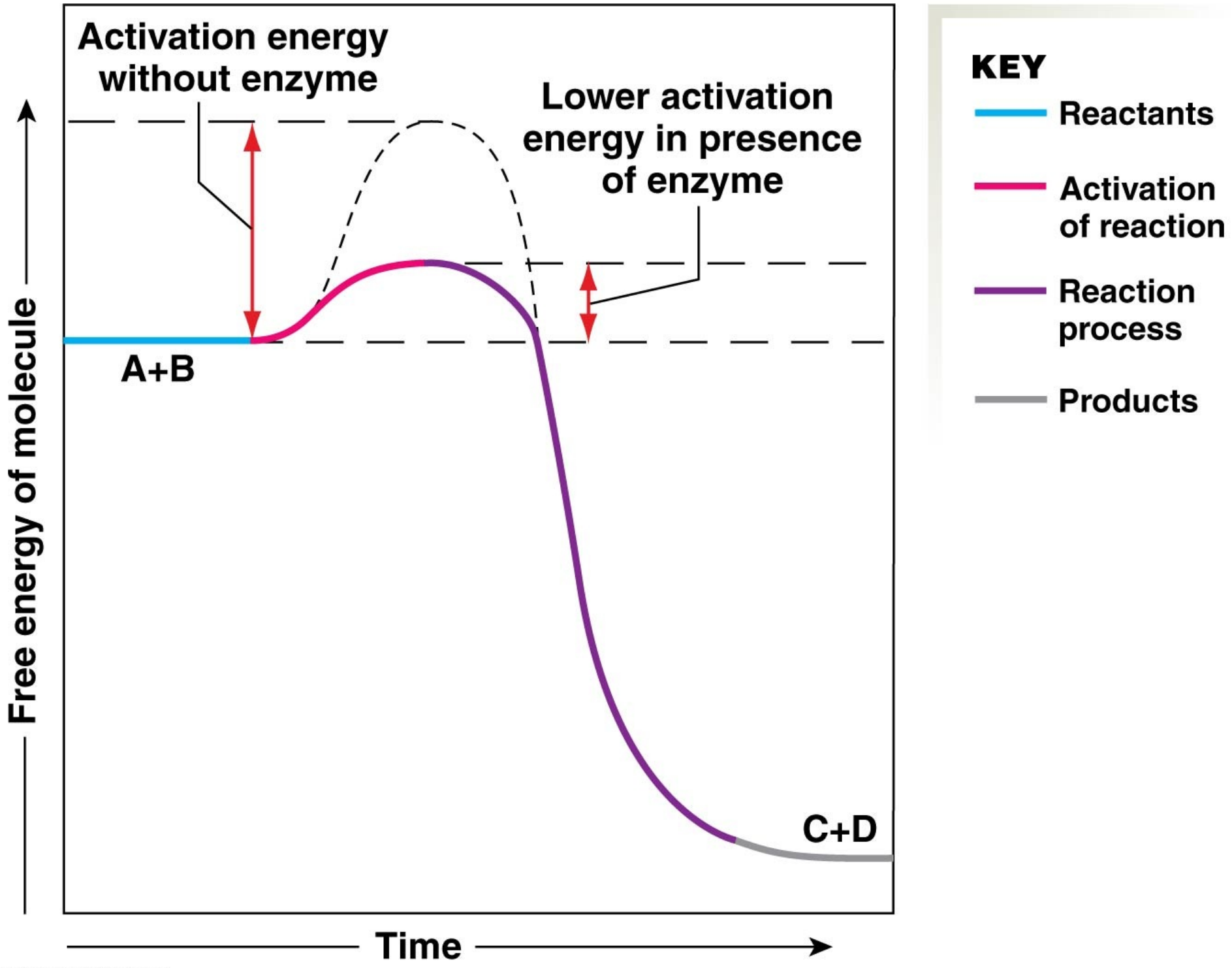
Enzymes are Catalysts

- An enzyme is a substance (usually a protein) that:
  - increases the [ ] of reaction
  - is not altered itself by the reaction
  - does not change the nature of the reaction or it's final result
- But HOW do they do it?



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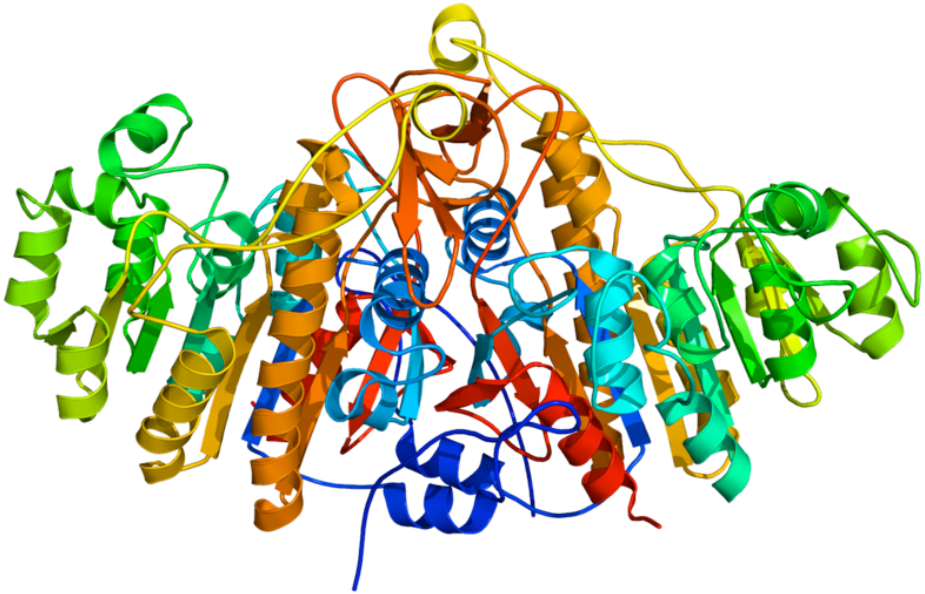
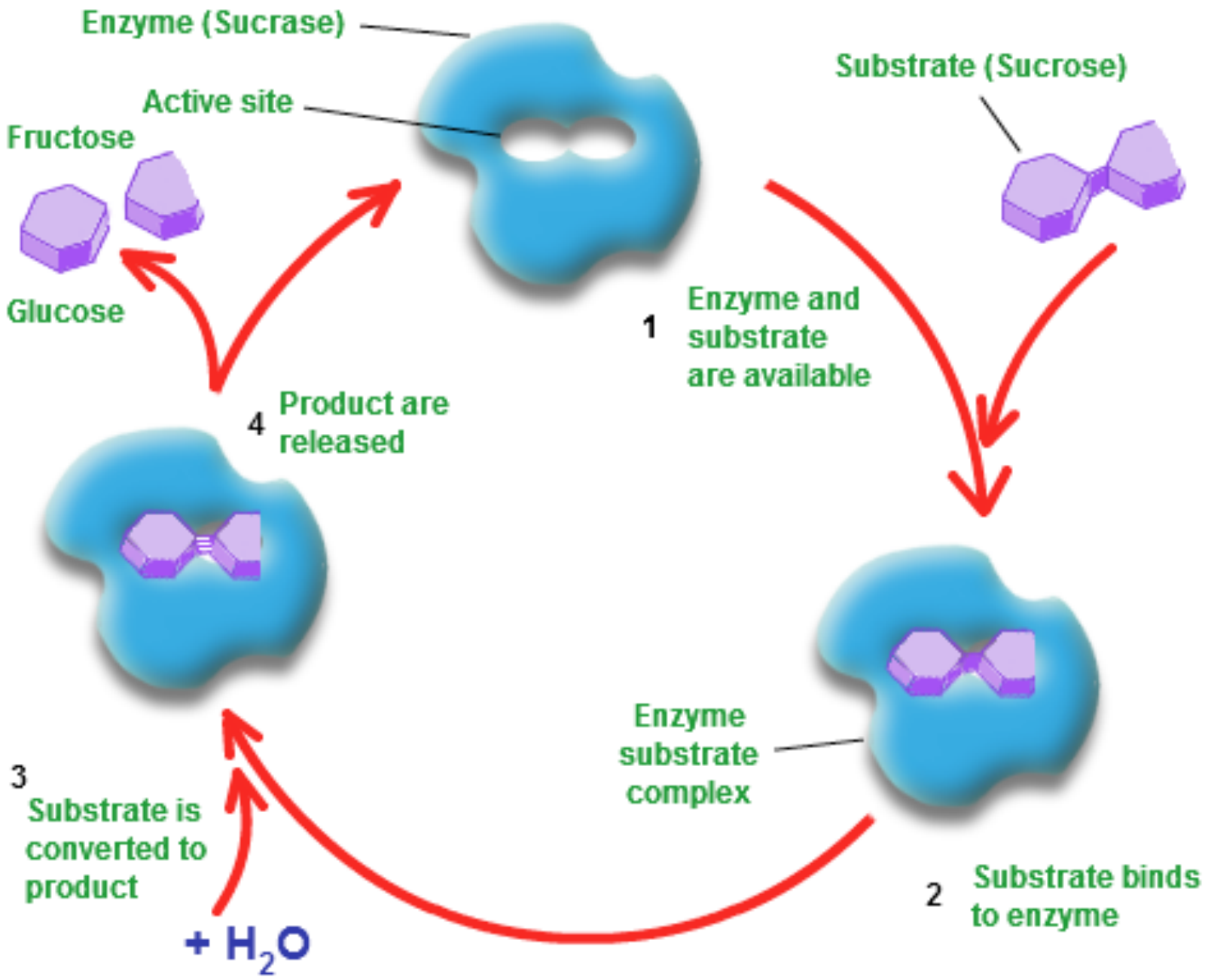
Terms:

- Substrate
- Enzyme
- [ ] (the place on the enzyme that interacts directly with the substrate)
- Affinity (how much the enzyme wants to bind the substrate)



alkaline phosphatase


Enzyme (Sucrase)
Active site
Fructose
Glucose
Substrate (Sucrose)
1 Enzyme and substrate are available
2 Substrate binds to enzyme
Enzyme substrate complex
3 Substrate is converted to product
+ H_2O
4 Product are released

Control of Enzyme Activity

Many things affect enzyme function

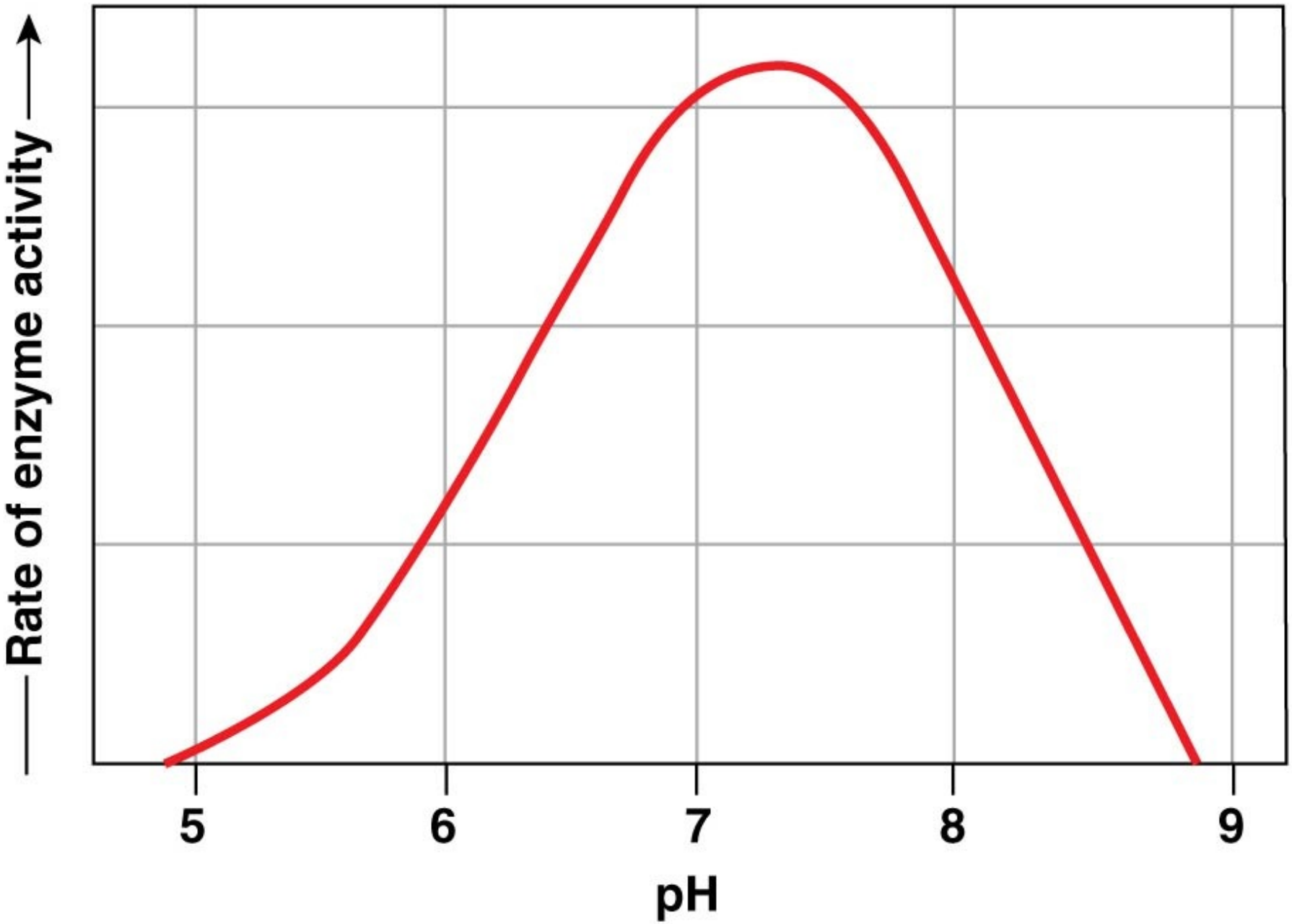
Reaction Rate = Costco Checkout Analogy

The Cellular Environment Affects Enzyme Activity

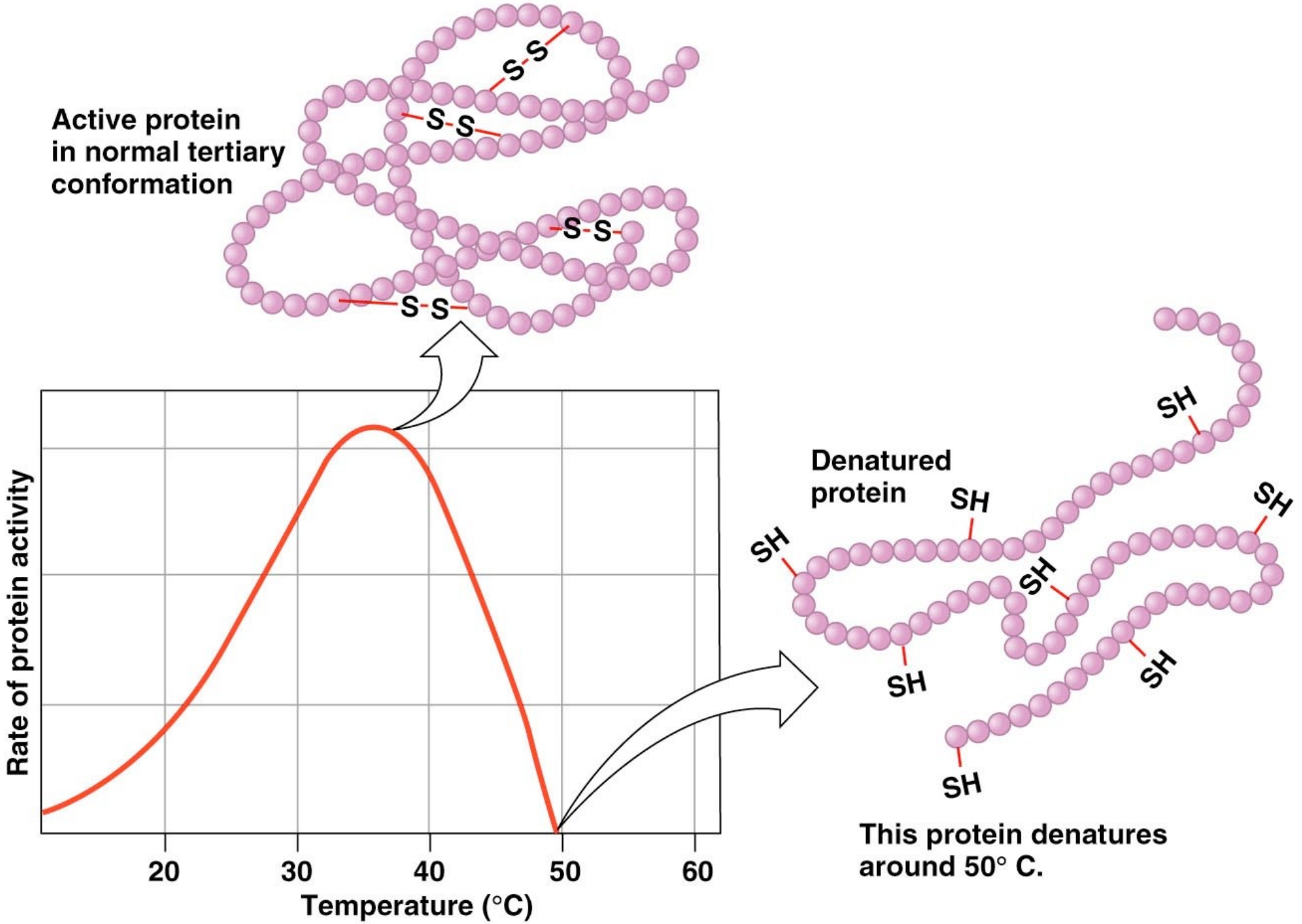
- The rate of reaction is affected by many factors:
  - [enzyme]
  - [substrate]
  - [helpers] (like [ ] and coenzymes)
  - feedback loops (products affect enzyme activity)

It's all about SHAPE

Remember the EGG!!



Most enzymes in humans have optimal activity near the body's internal pH of 7.4.



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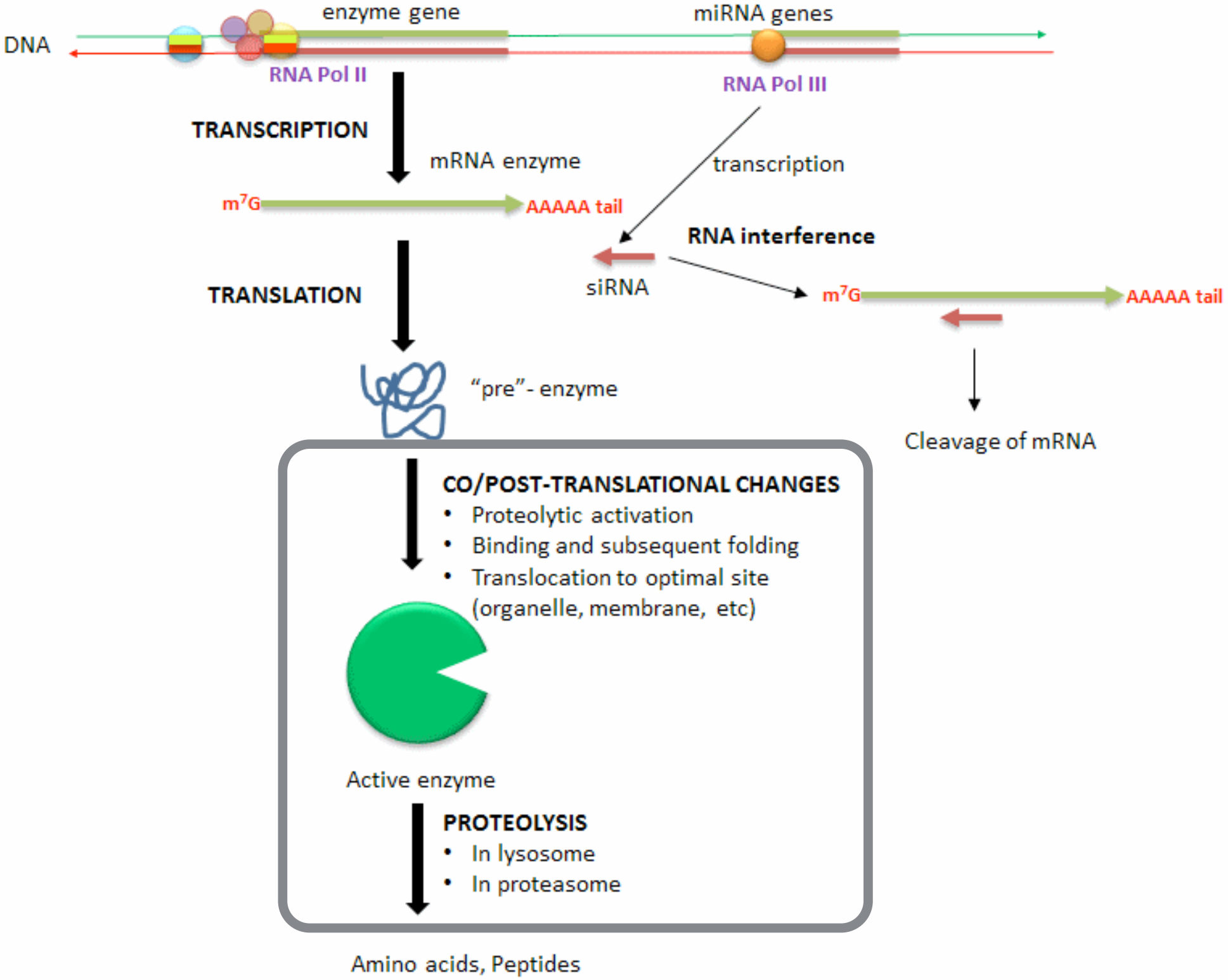
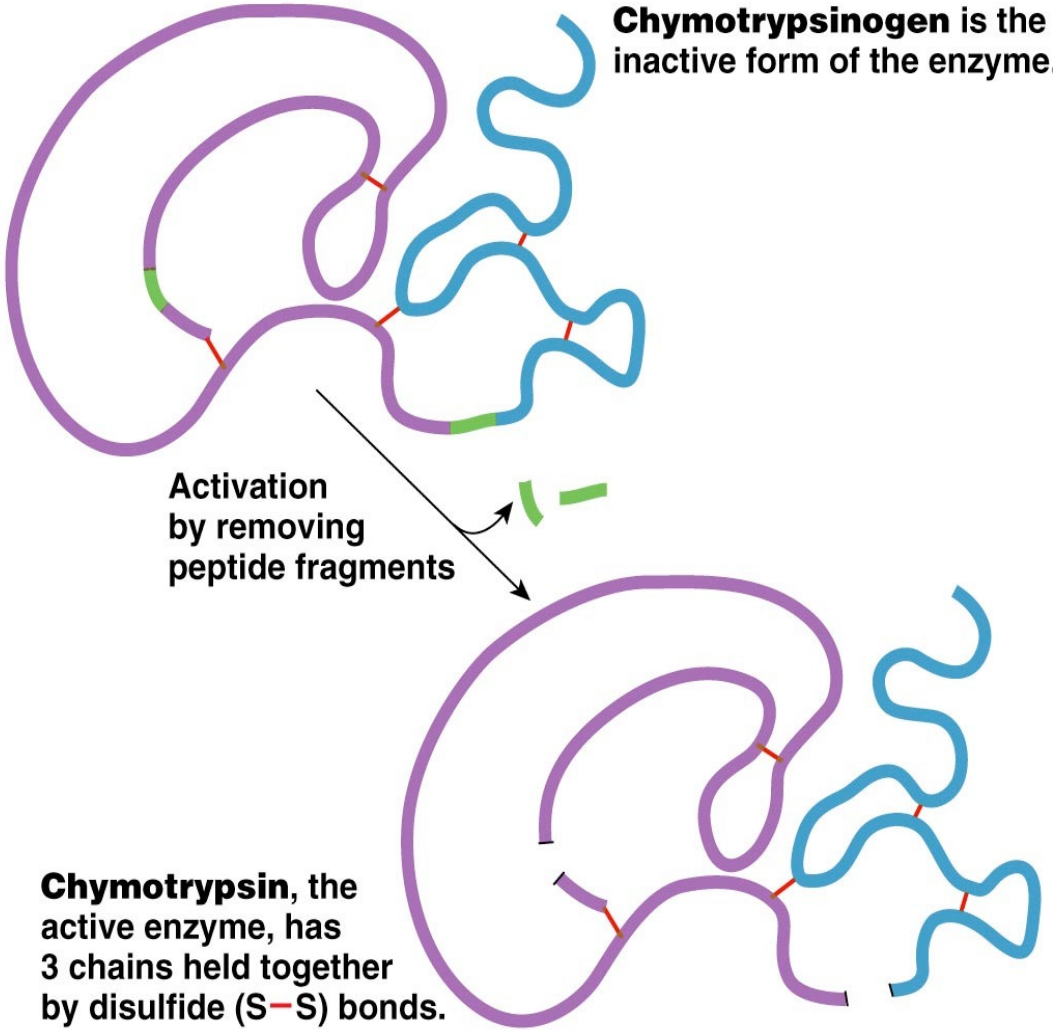
The Shape-Changing Nature of Enzymes Makes Them Easy to Control

- Enzymes can be up- or down-regulated:
  - Activators / Stimulators
  - Inhibitors
  -


DNA
enzyme gene
miRNA genes
RNA Pol II
RNA Pol III
TRANSCRIPTION
mRNA enzyme
transcription
m7G
AAAAA tail
RNA interference
TRANSLATION
siRNA
m7G
AAAAA tail
"pre"- enzyme
Cleavage of mRNA
CO/POST-TRANSLATIONAL CHANGES
• Proteolytic activation
• Binding and subsequent folding
• Translocation to optimal site (organelle, membrane, etc)
Active enzyme
PROTEOLYSIS
• In lysosome
• In proteasome
Amino acids, Peptides

Enzyme Activation

Enzyme Activation



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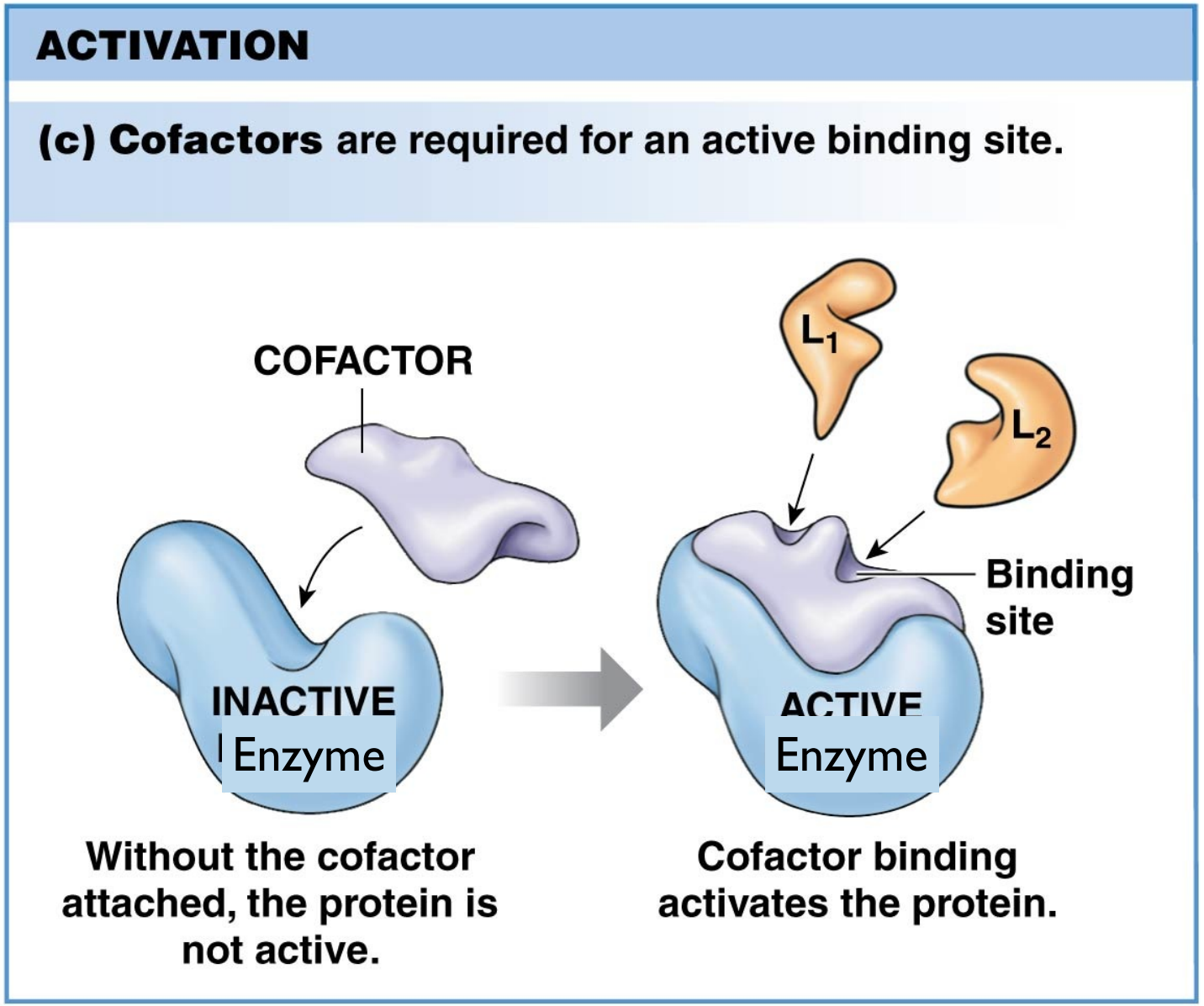
Enzyme Activation



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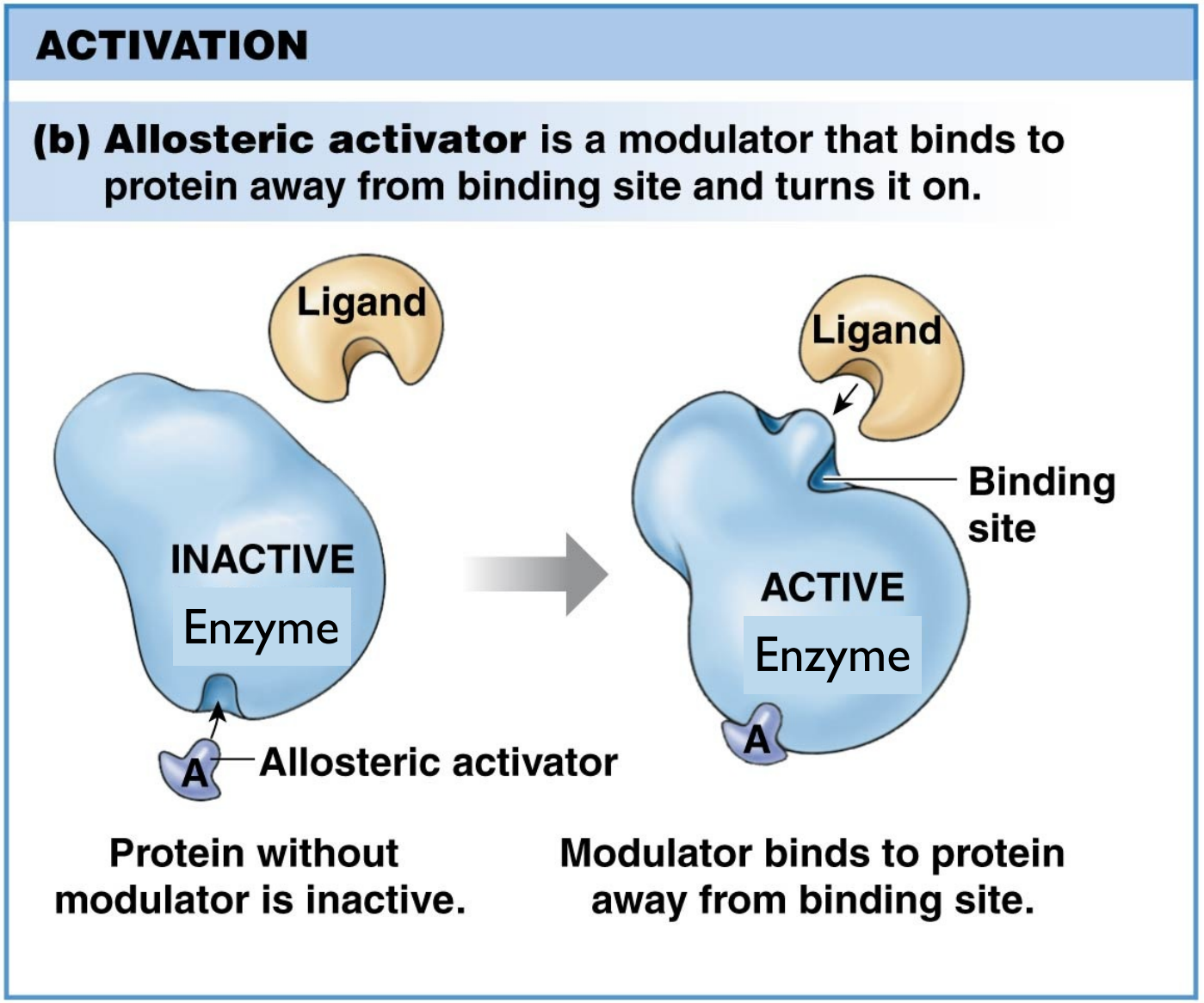
Enzyme Activation



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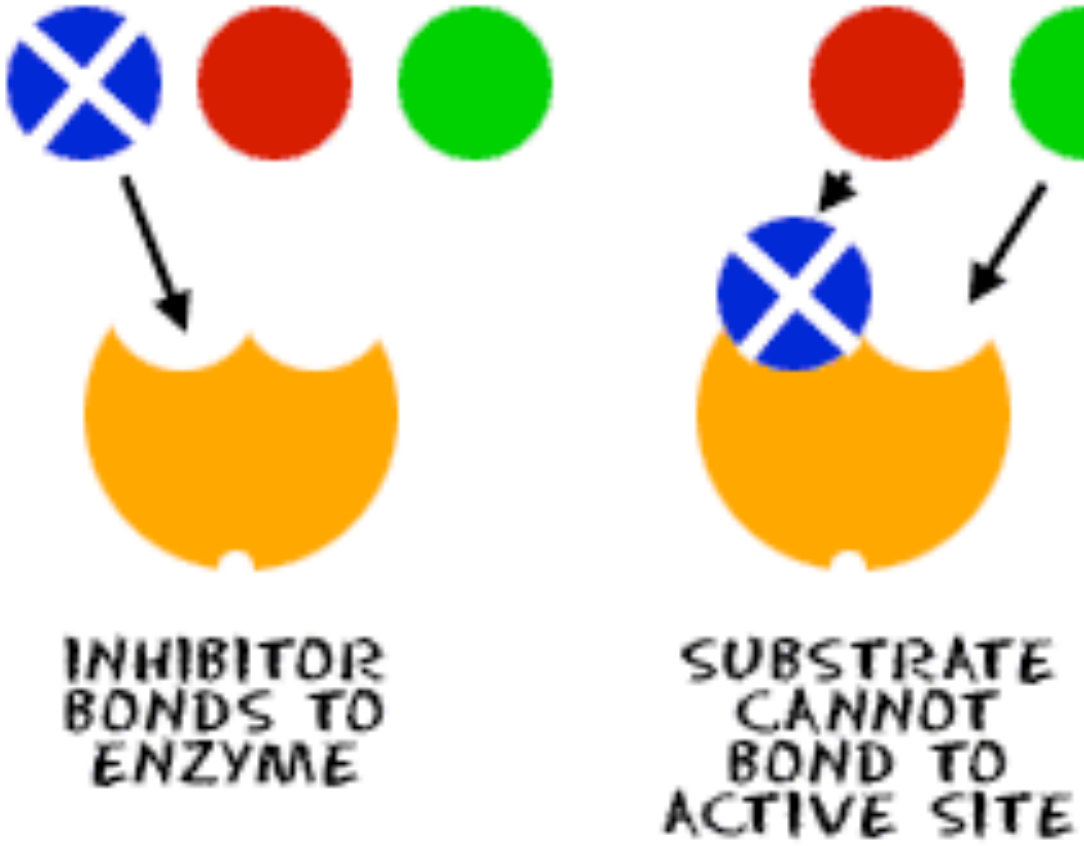
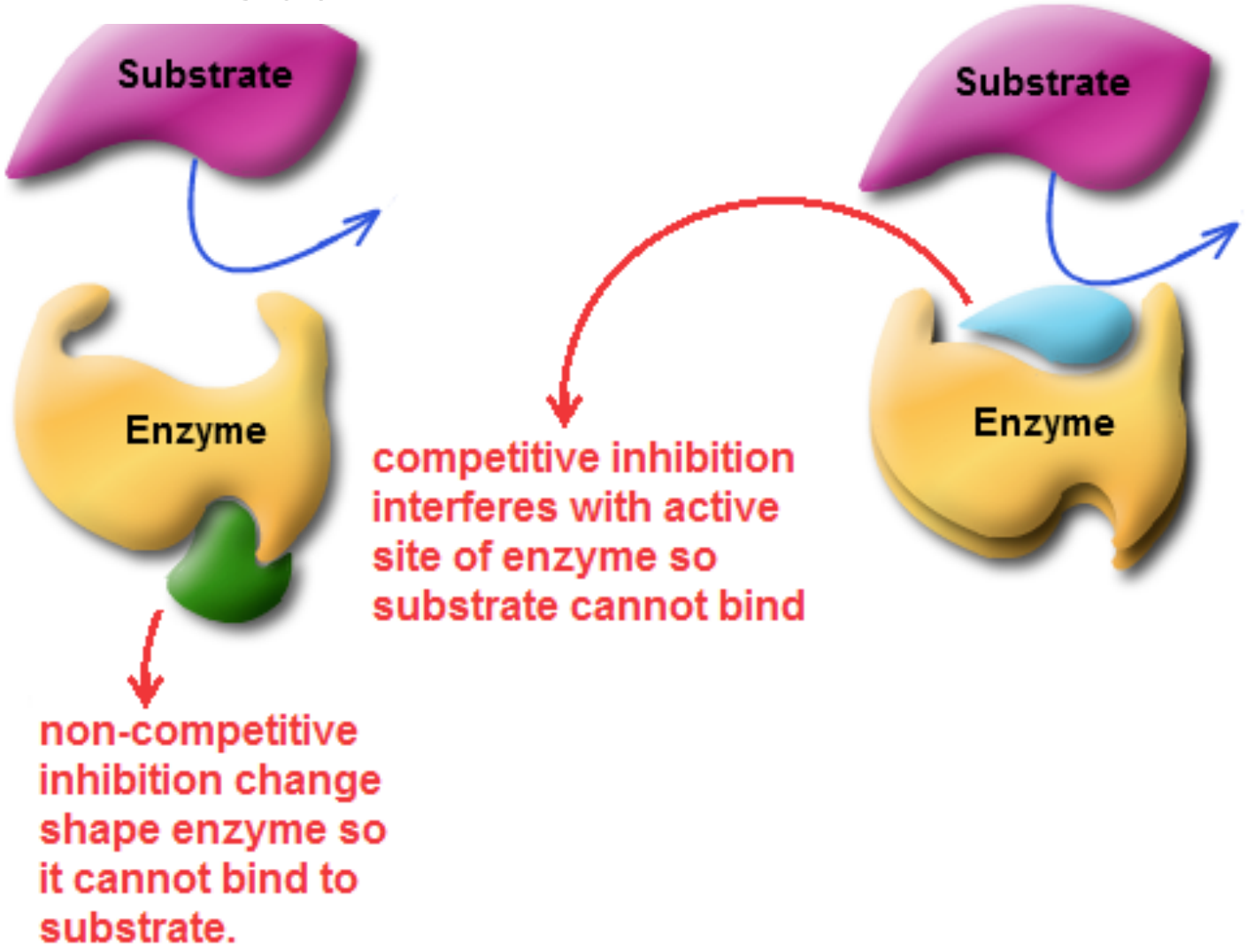
Inhibition


INHIBITOR BONDS TO ENZYME
SUBSTRATE CANNOT BOND TO ACTIVE SITE

Inhibition

Non-Competitive (Allosteric) Inhibition

Competitive (Inhibition)



(and enzyme)

Factors That Affect Protein Binding

Table 2.3

Essential for Binding Activity	
Cofactors	Required for ligand binding at binding site
Proteolytic activation	Converts inactive to active form by removing part of molecule. Examples: digestive enzymes, protein hormones
Modulators and Factors That Alter Binding or Activity	
Competitive inhibitor	Competes directly with ligand by binding reversibly to active site
Irreversible inhibitor	Binds to binding site and cannot be displaced
Allosteric modulator	Binds to protein away from binding site and changes activity; may be inhibitors or activators
Covalent modulator	Binds covalently to protein and changes its activity. Example: phosphate groups
pH and temperature	Alter three-dimensional shape of protein by disrupting hydrogen or S—S bonds; may be irreversible if protein denatures

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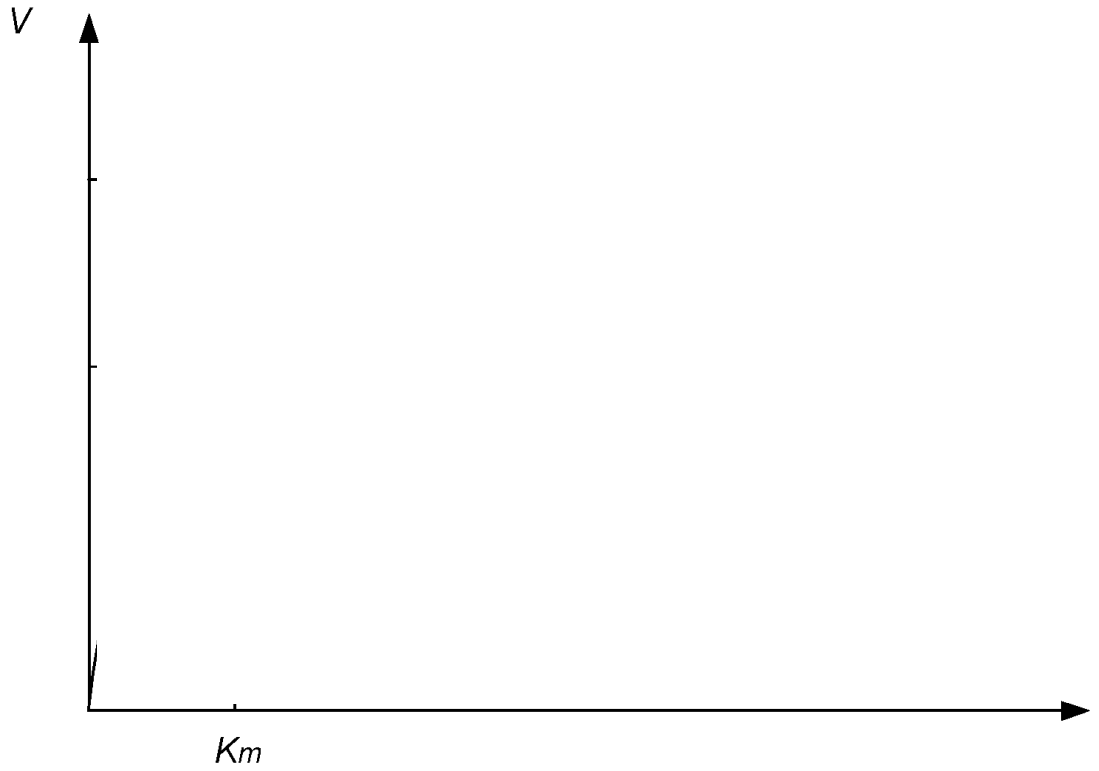
How Good Are Enzymes?

How fast can they catalyze reactions?
How much do they like their substrates?
How does one enzyme compare to another?

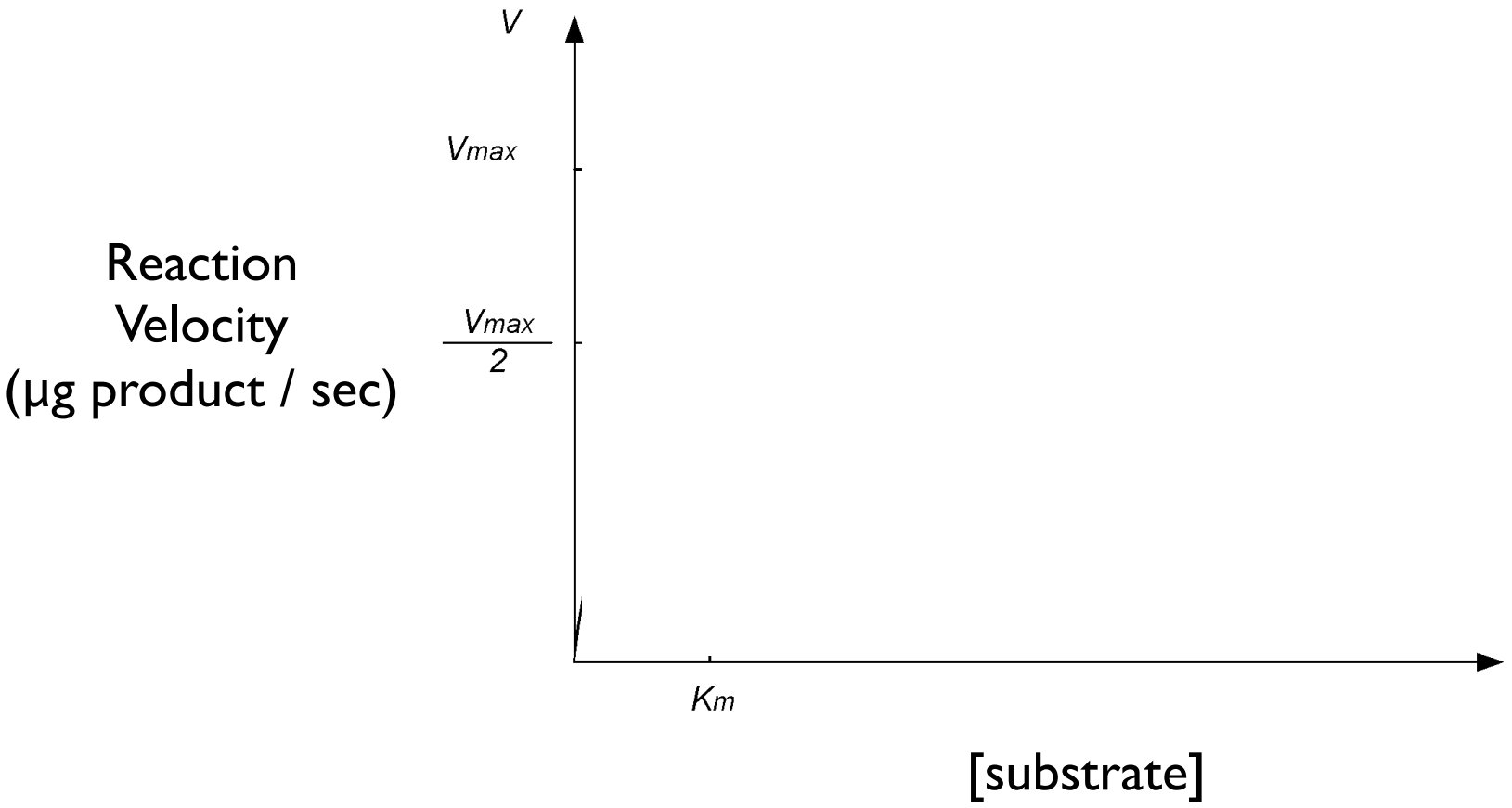
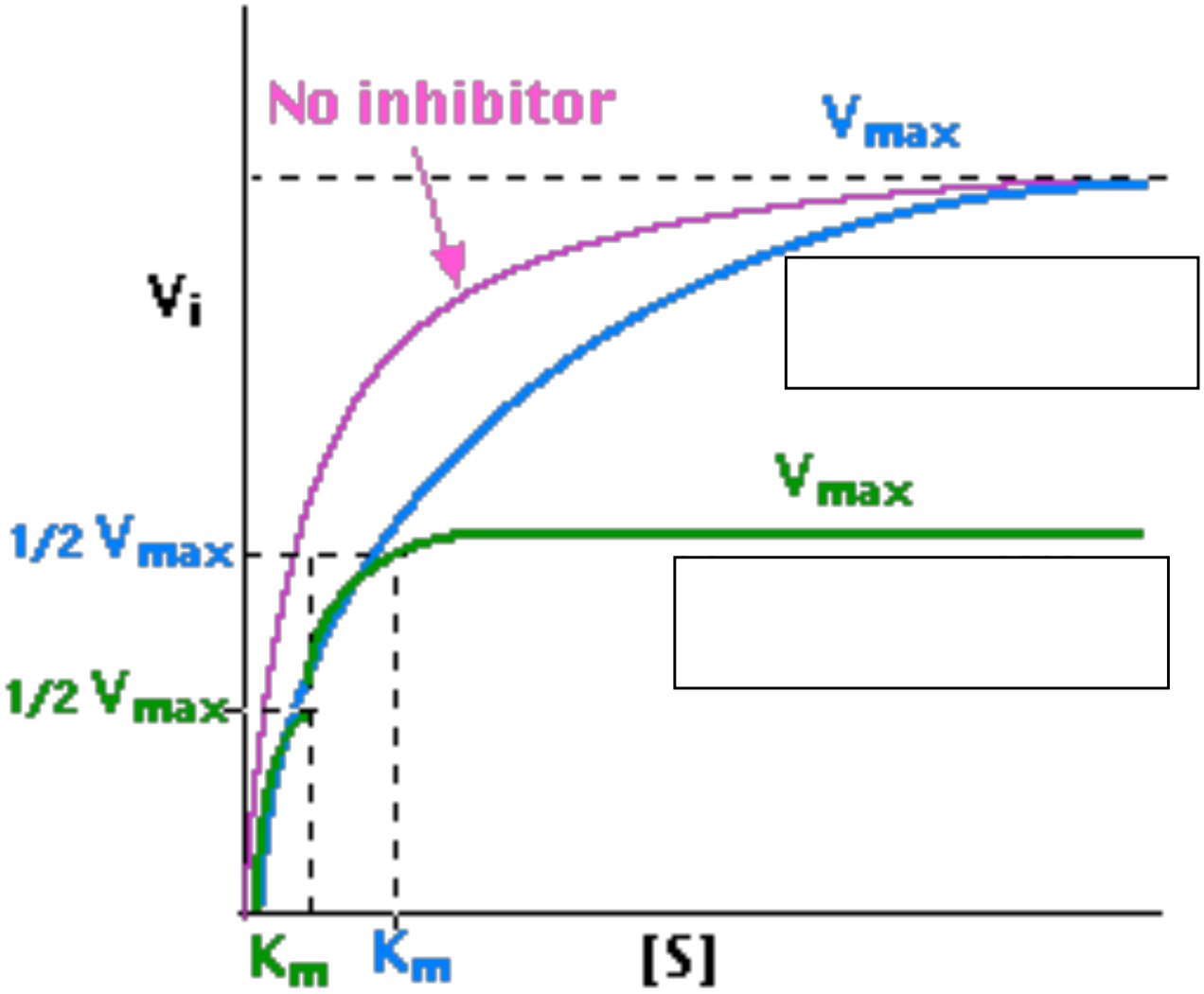
Kinetics

Check-Out Rate
(transactions / min)



[shoppers]

Enzyme Kinetics
(Michaelis-Menten Kinetics)



How Can You Tell What Kind of Inhibition Is Going On?