Chem 452 - Lecture 4
Enzymes
111017

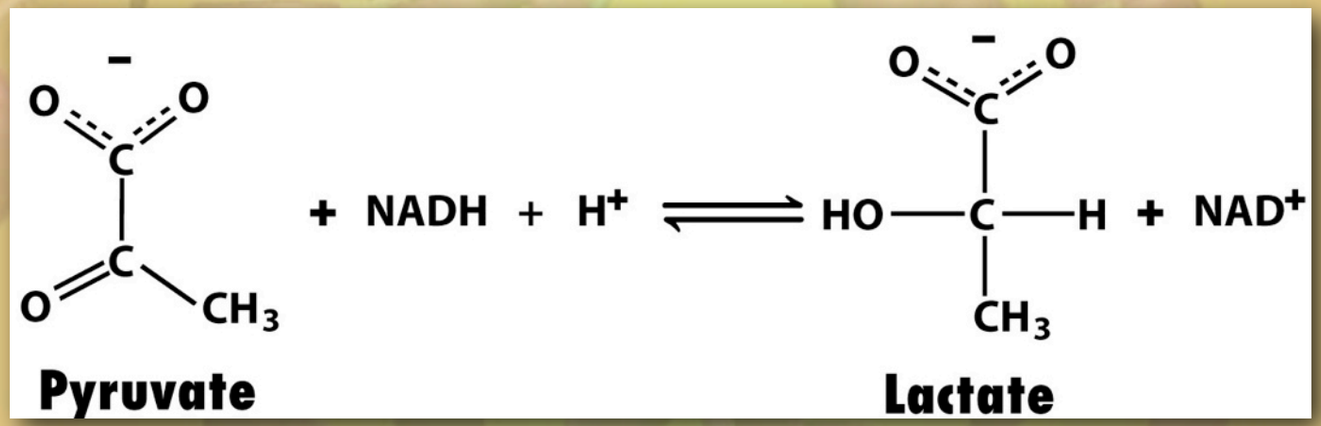
Enzymes are biological catalysts. Nearly every reaction that takes place in a living cell is catalyzed by an enzyme. Most enzymes are proteins. Beside their role in speeding up the rates of chemical reactions, enzymes also play an important role in controlling the flow of material through the myriad of metabolic pathways required to sustain a living cell.

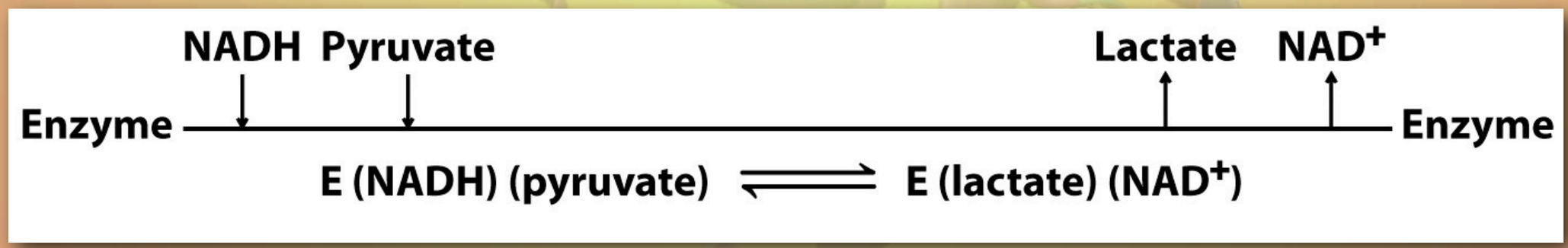
Enzyme Kinetics

- Most Reactions involve multiple substrates.
  - There are three different ways that the binding substrates can occur.
    - Ordered sequential
    - Random sequential
    - Double displacement (Ping Pong)

Enzyme Kinetics

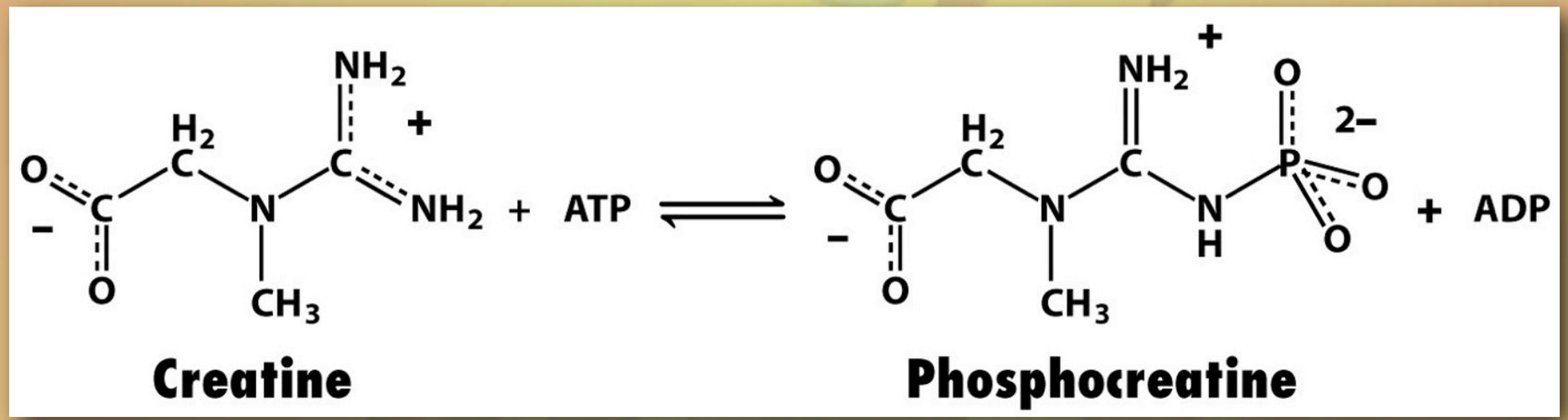
- Ordered sequential

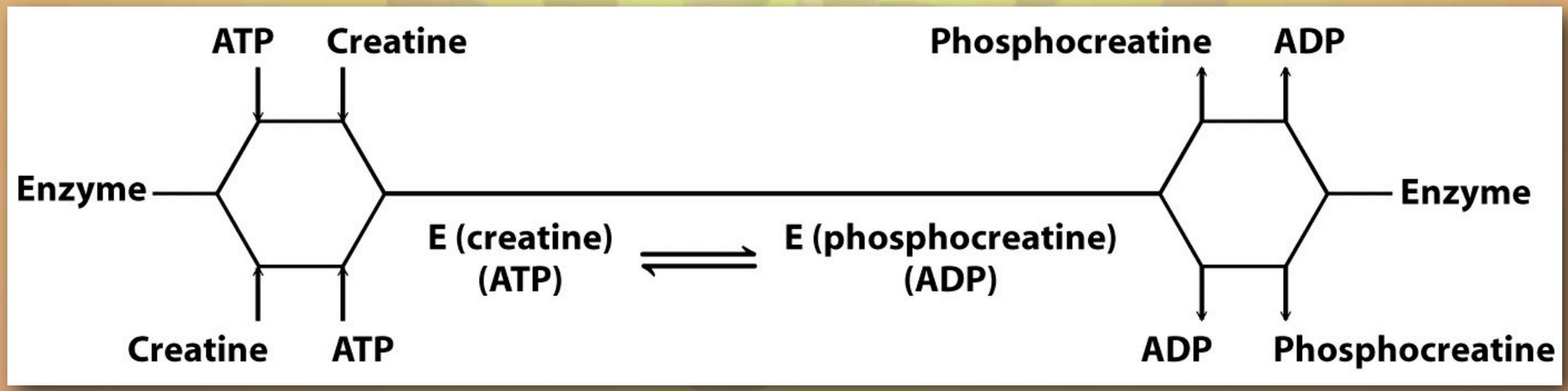




Enzyme Kinetics

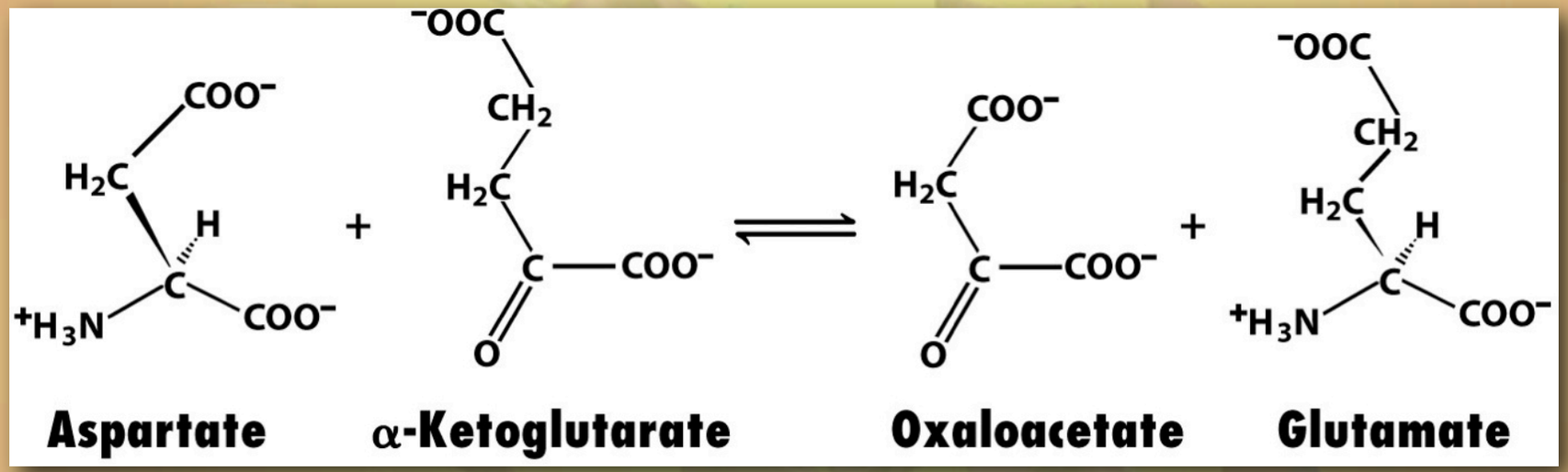
- Random sequential

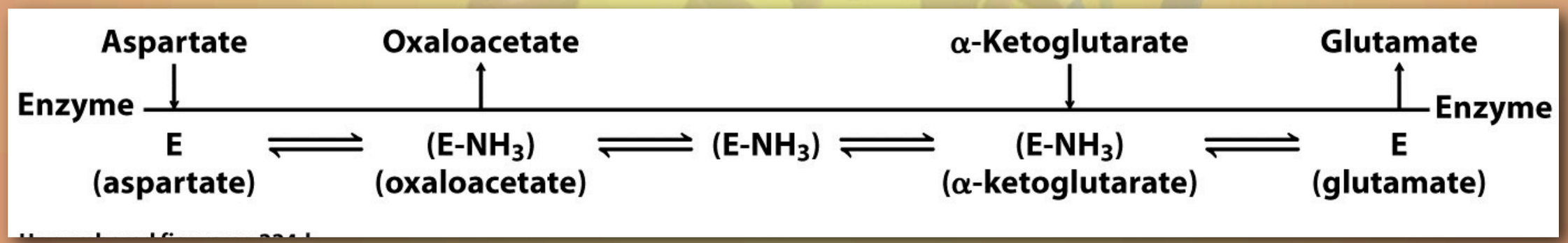




Enzyme Kinetics

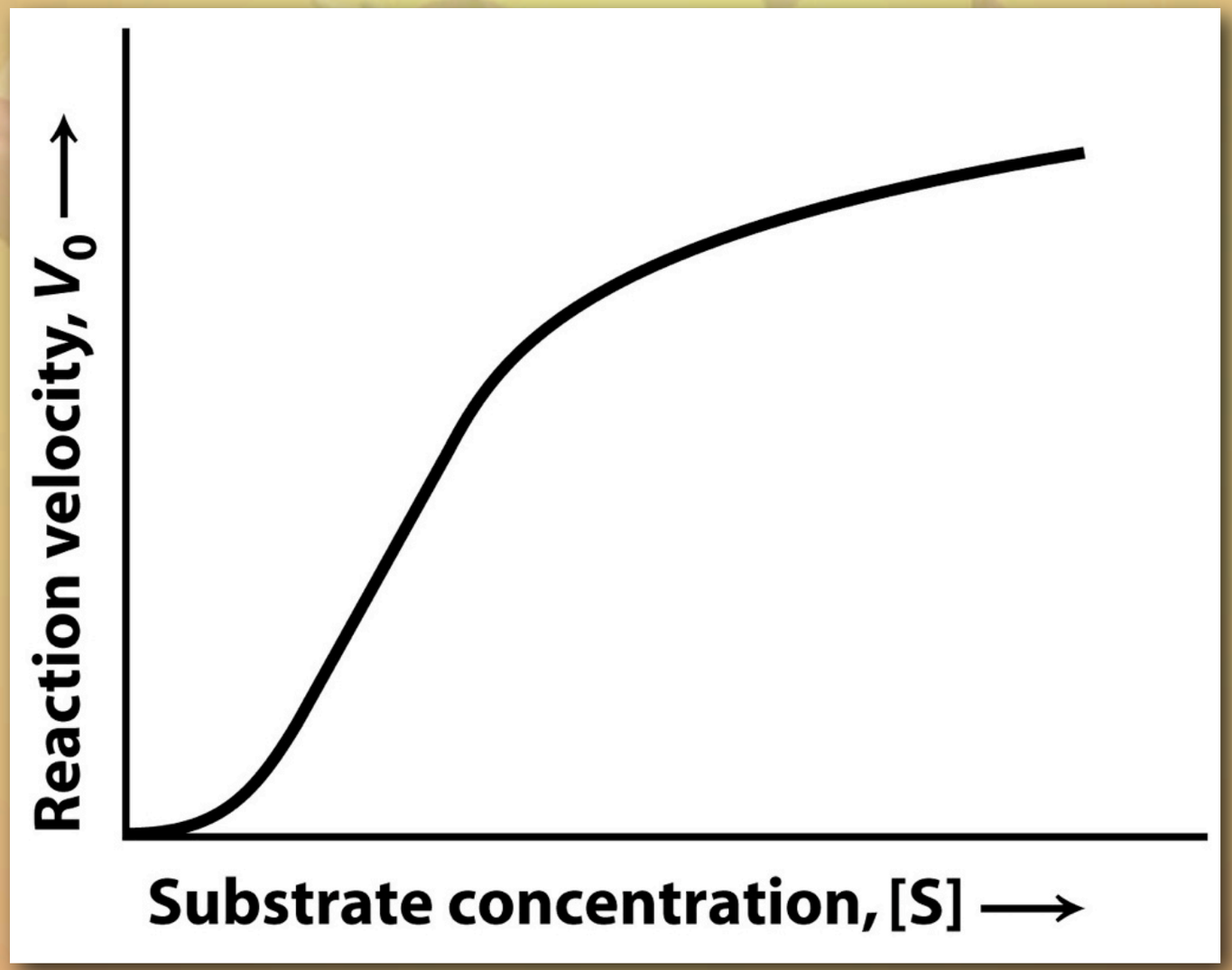
- Double displacement (Ping Pong)





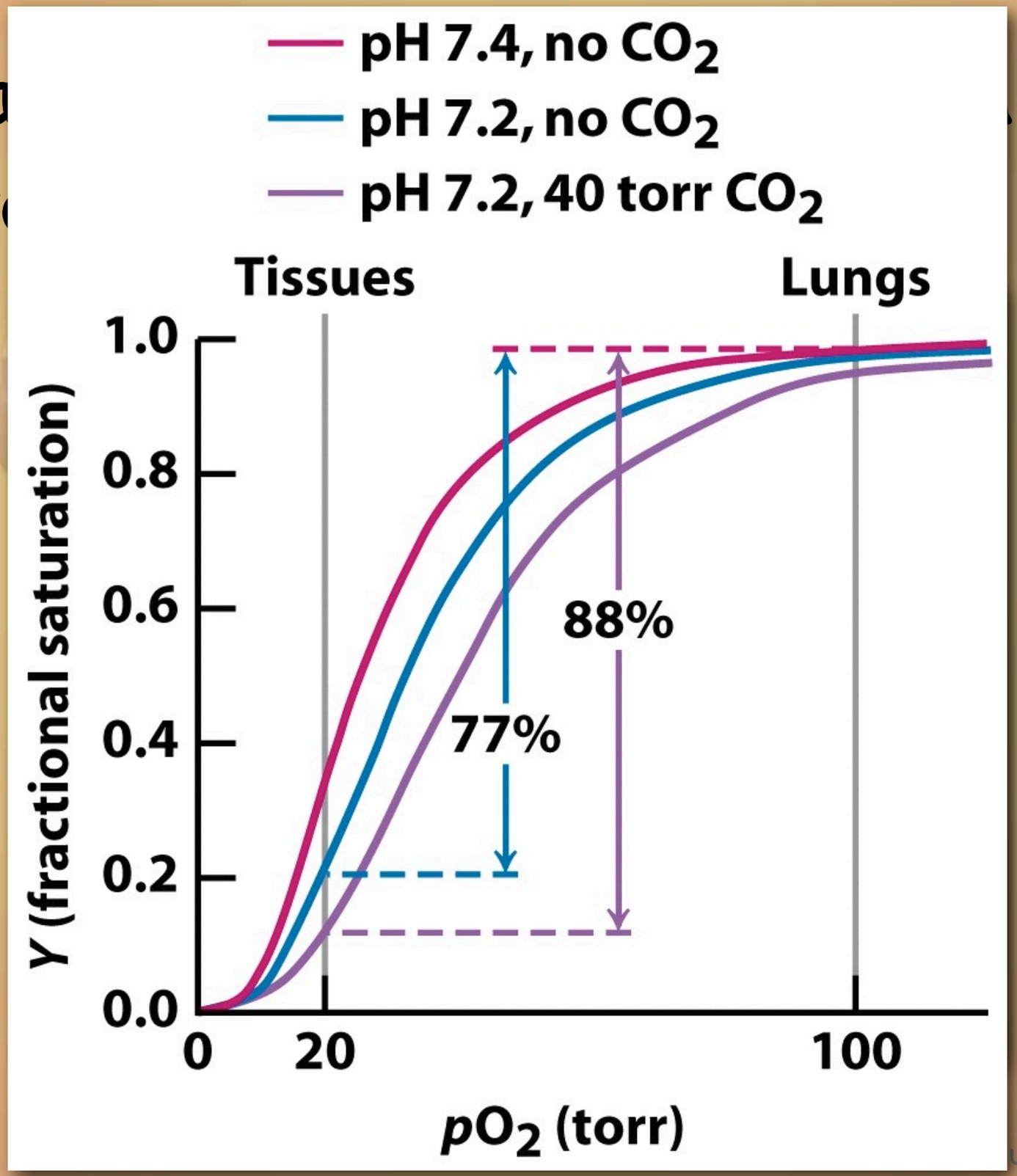
Enzyme Kinetics

- Not all enzyme obey the Michaelis-Menten model.



Enzyme Kinetics

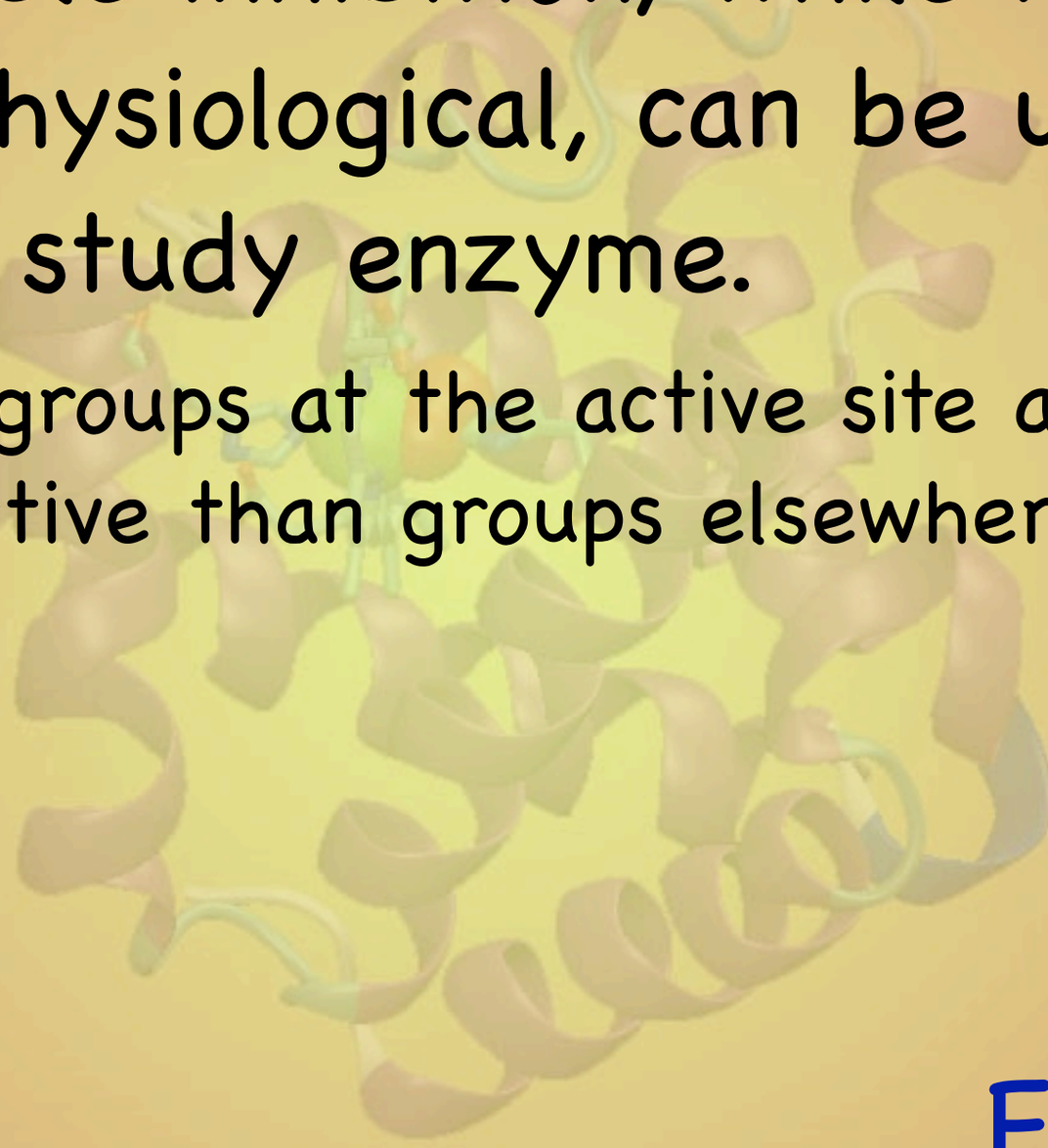
- Not a … elis–Ment…



Enzyme Inhibition

- The inhibition of enzyme activitity can be physiological or not.
  - It can be reversible or irreversible.
- Many drugs, pesticides and herbicides operate by inhibiting enzyme activity

- Irreversible inhibition, while not usually physiological, can be used as a tool to study enzyme.
  - Catalytic groups at the active site are often more reactive than groups elsewhere on the enzyme.



Enzyme Inhi

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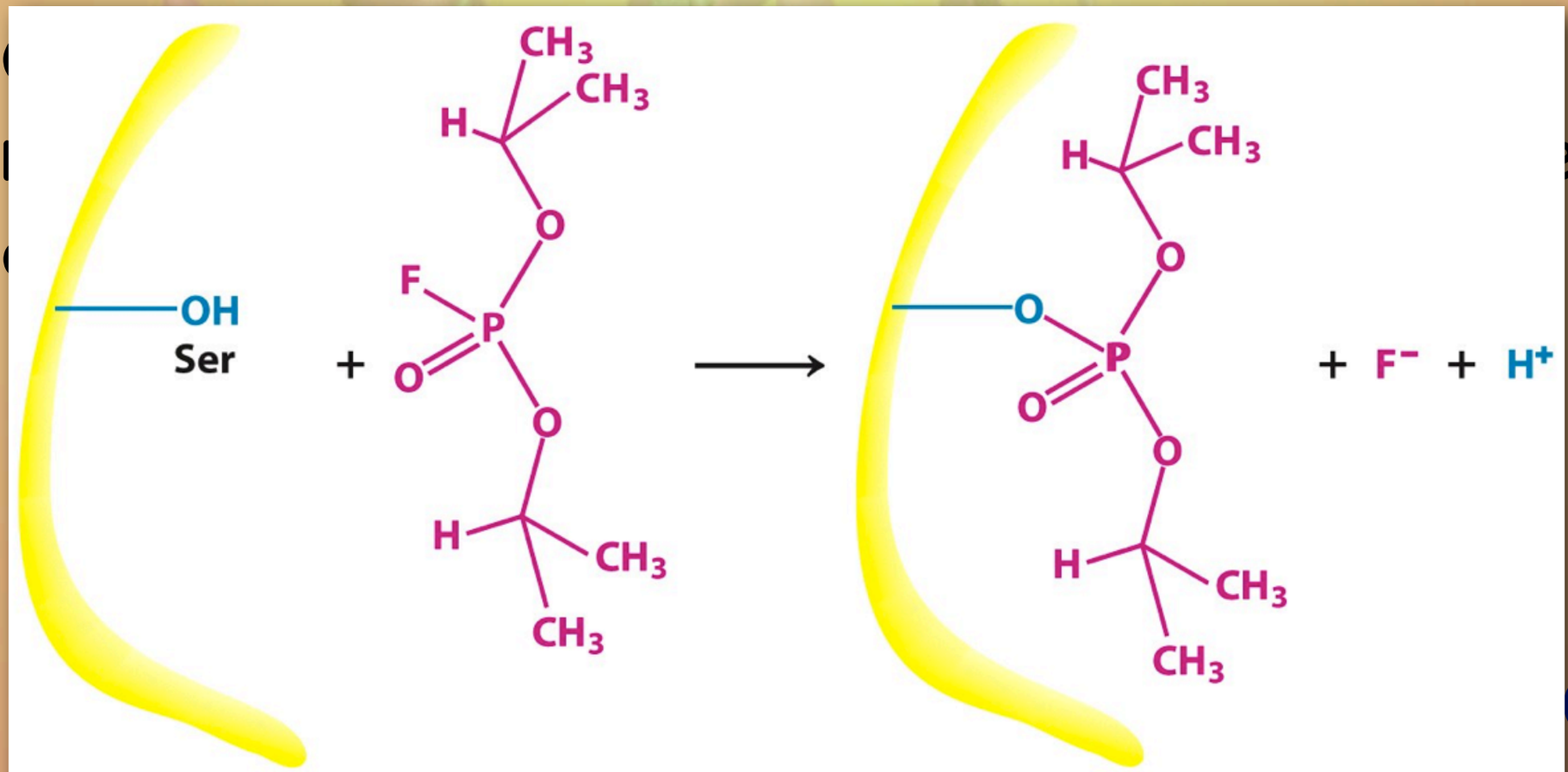

DIPF is a powerful nerve gas toxin

e Inhi

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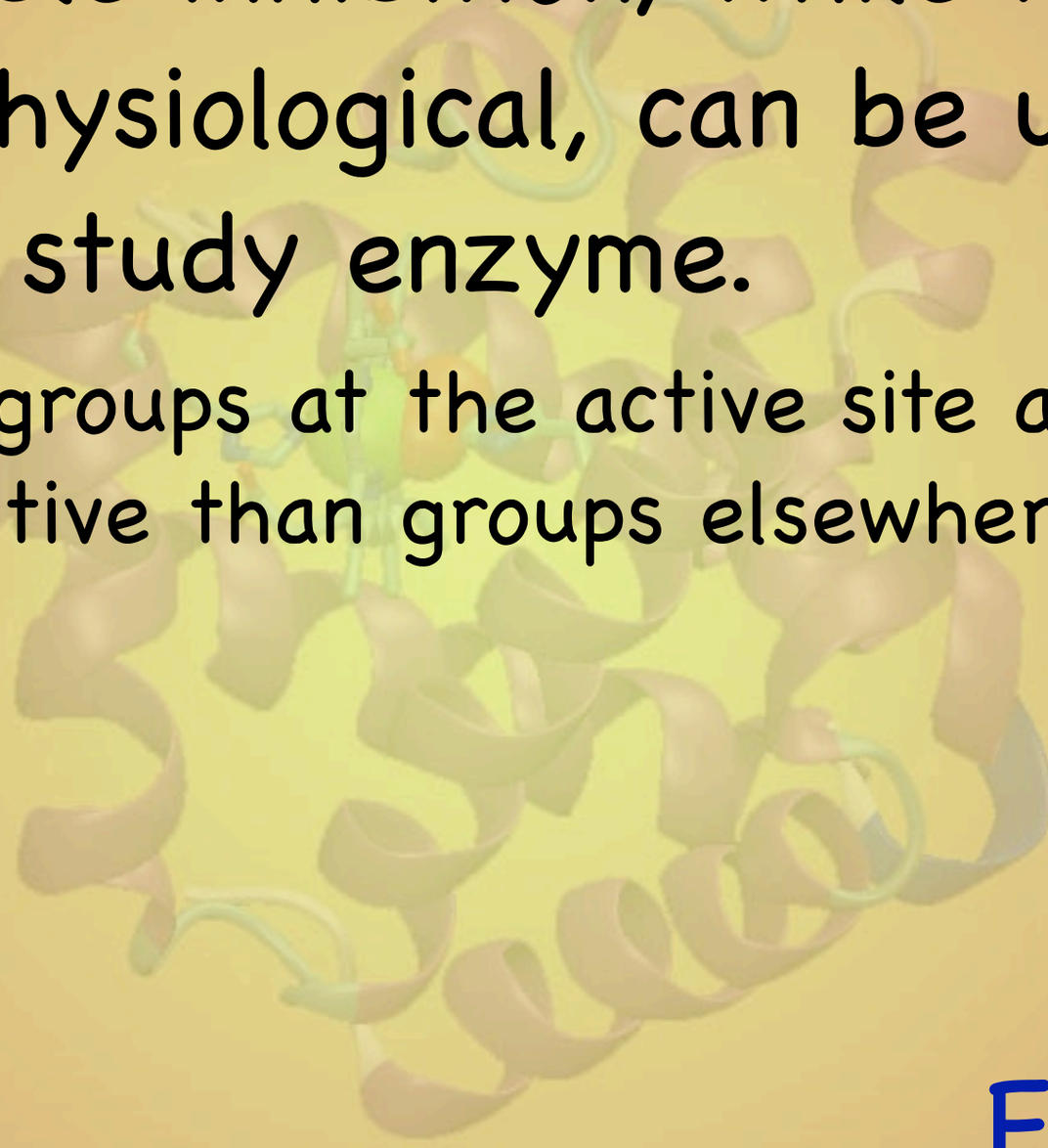

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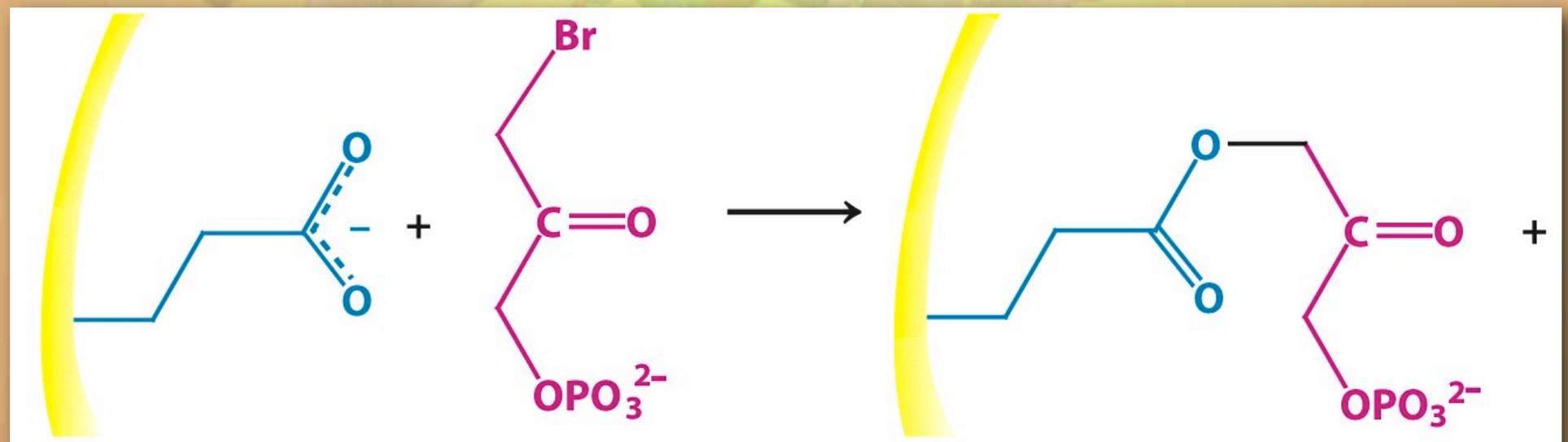

Bromoacetol phosphate is an affinity label which mimics the natural substrate for the enzyme triosephosphate isomerase

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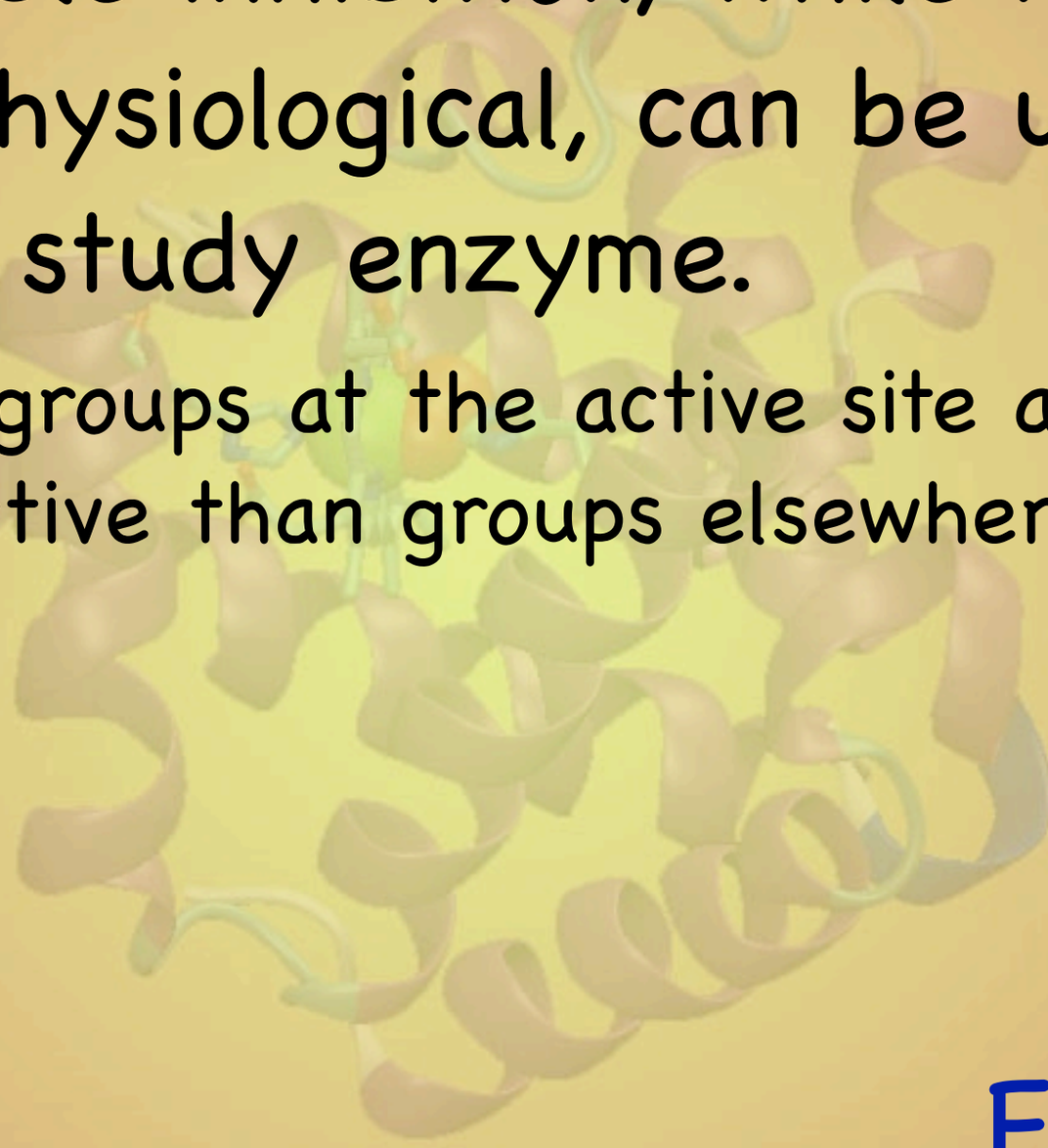
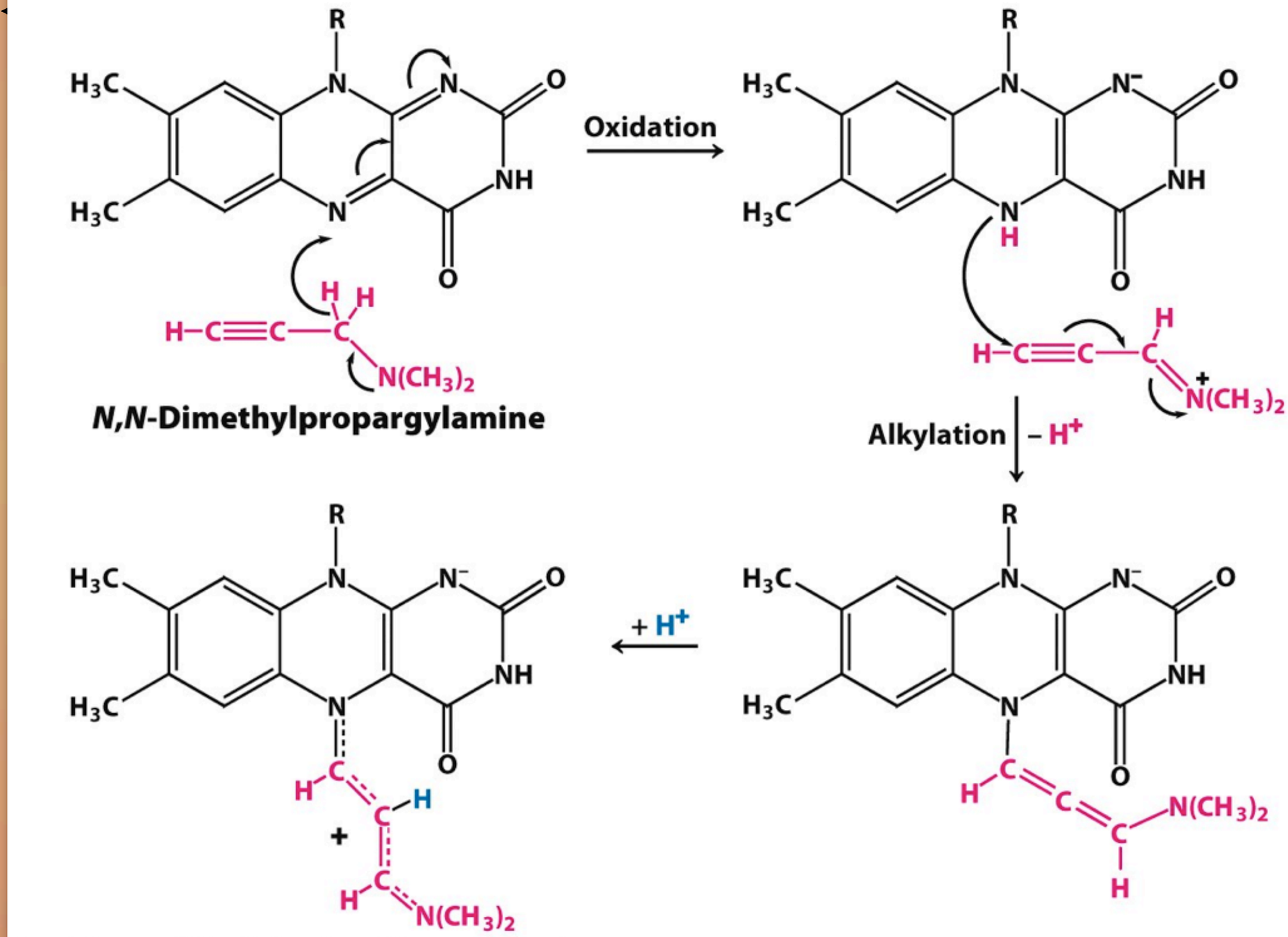


Enzyme Inhi

Suicide inhibitors of monoamine oxidase (MAO)



Inhi

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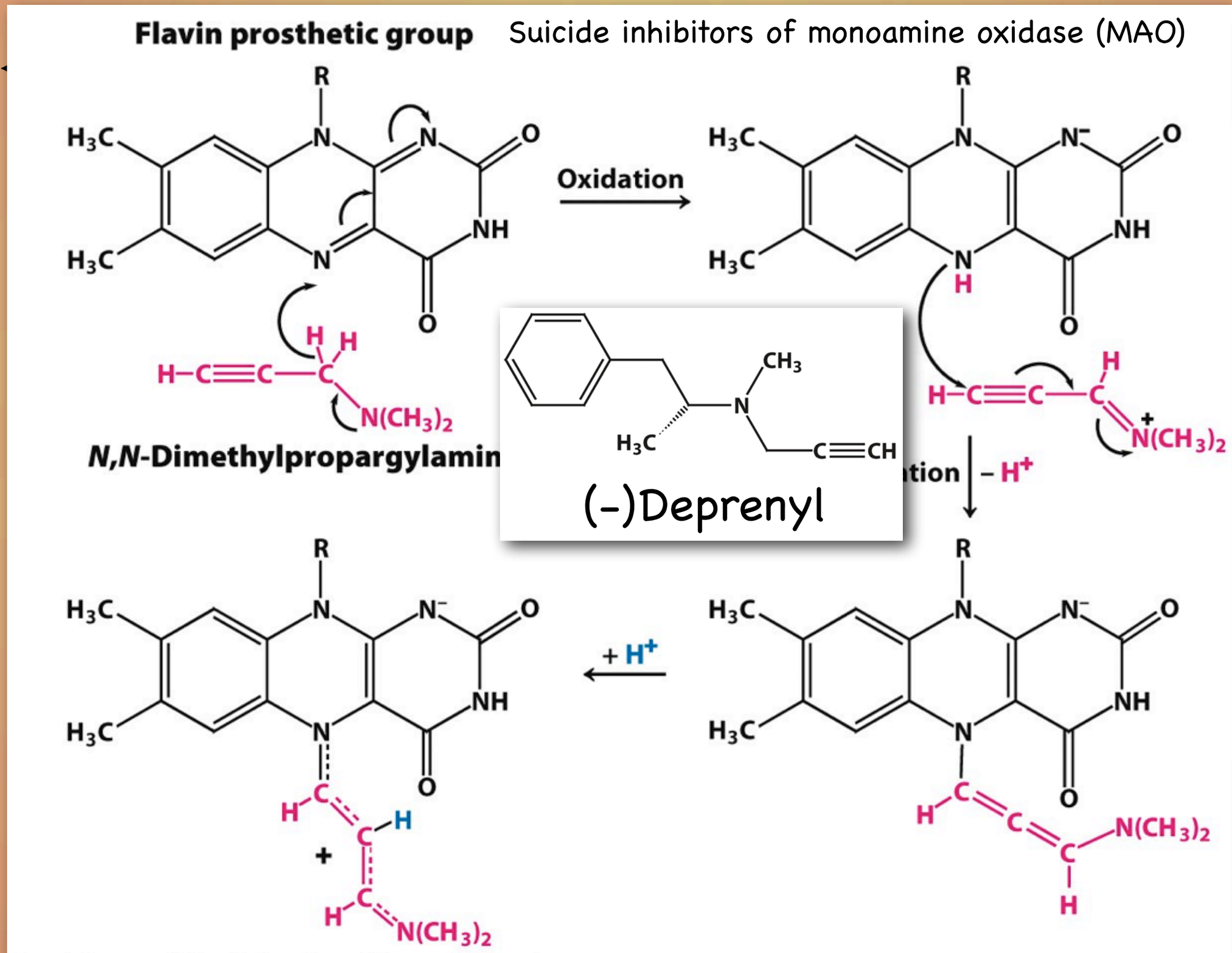

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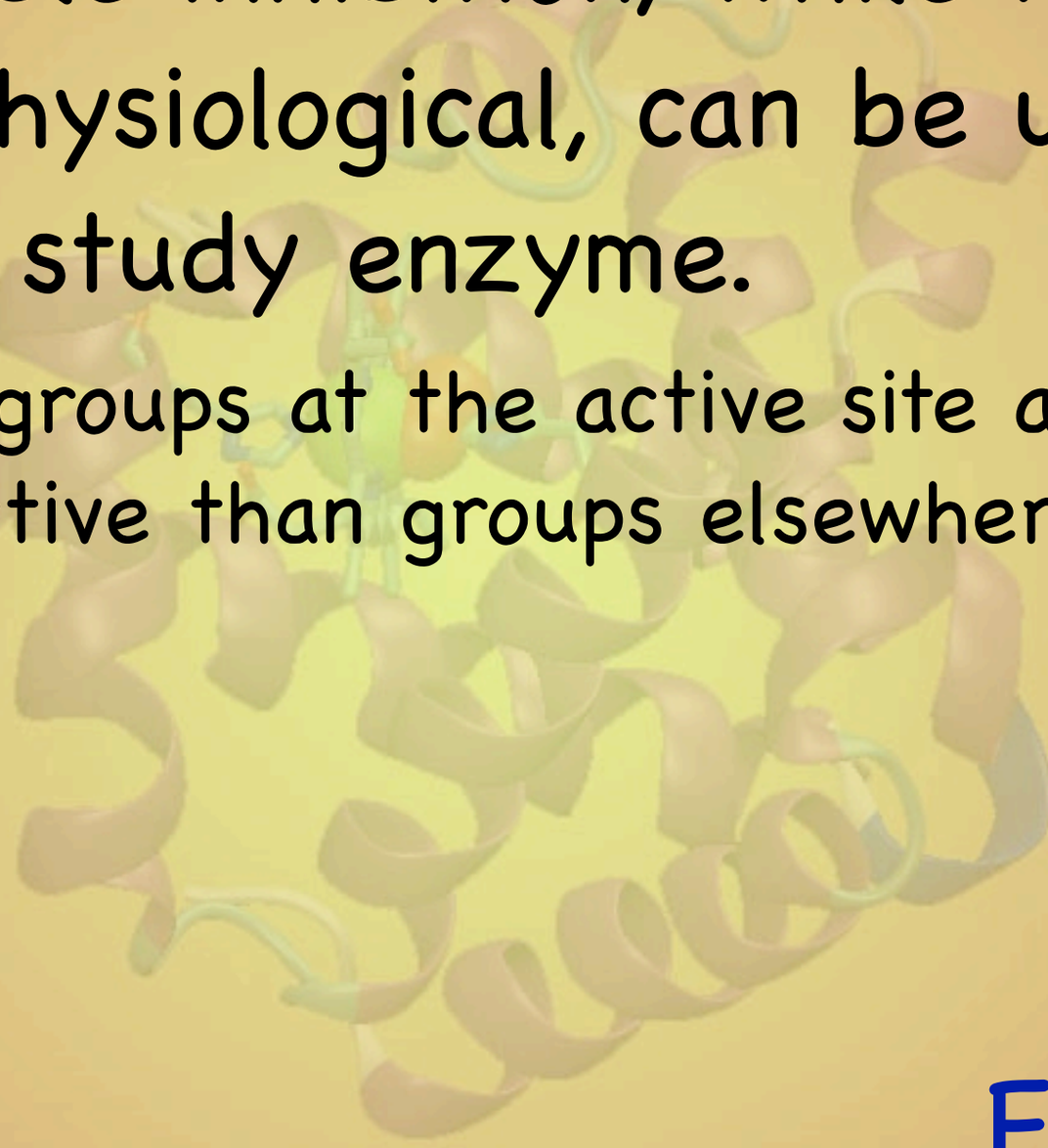


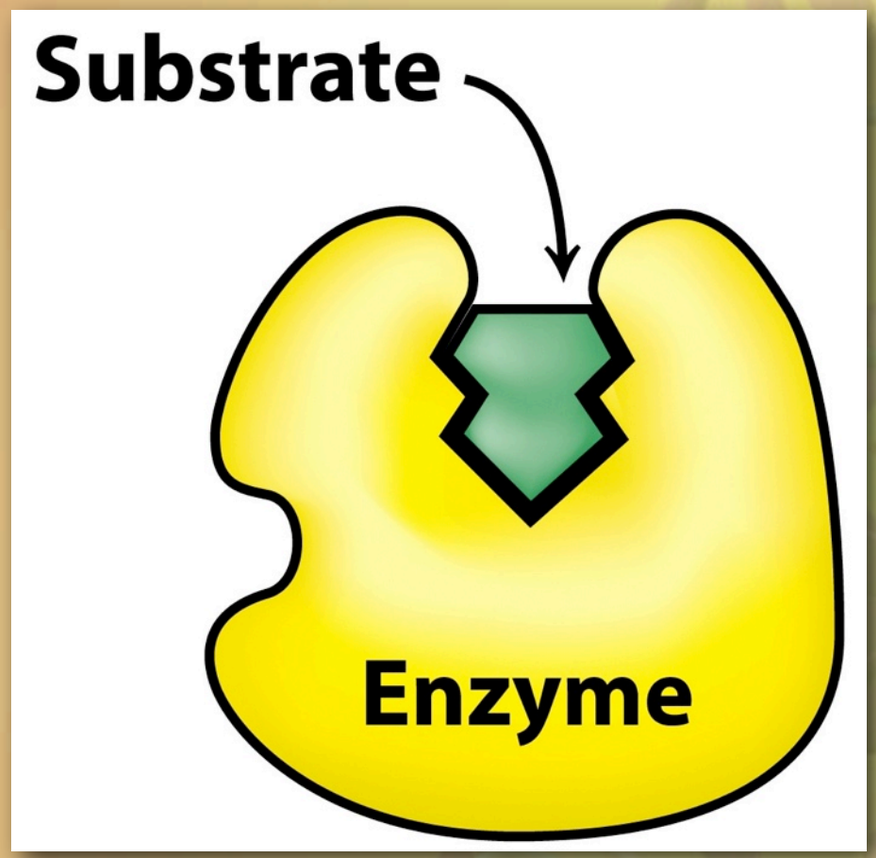
Enzyme Inhi

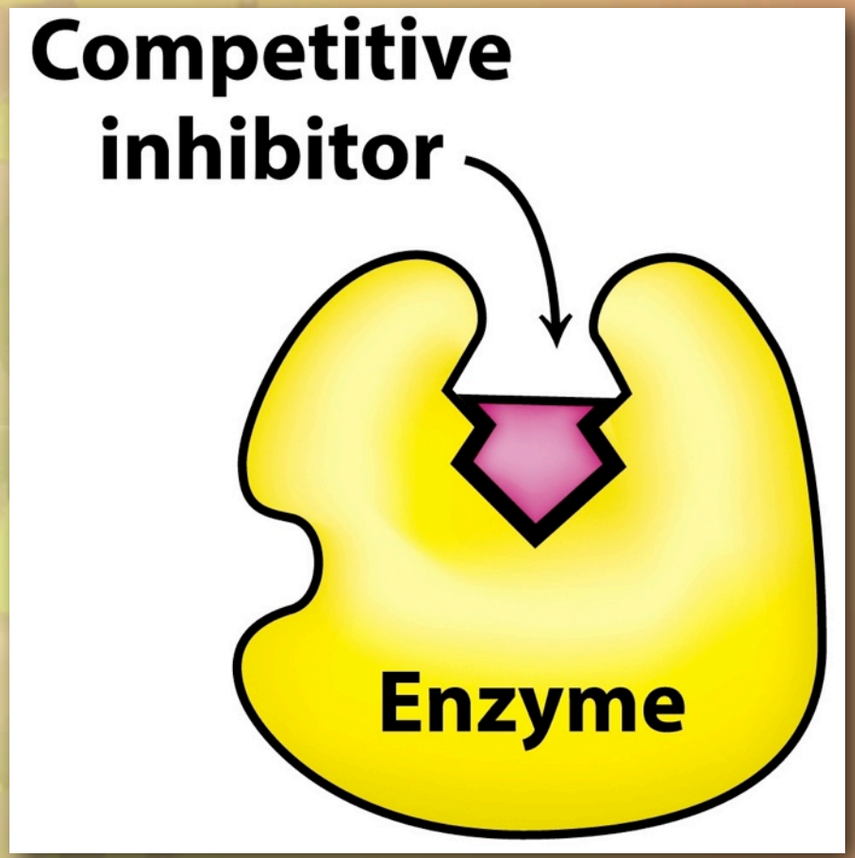
Enzyme Inhibition

- Reversible inhibition comes in three different forms.
  - Competitive
  - Noncompetitive
  - Uncompetitive
- Enzyme kinetics can be used to distinguish between these.

Enzyme Inhibition

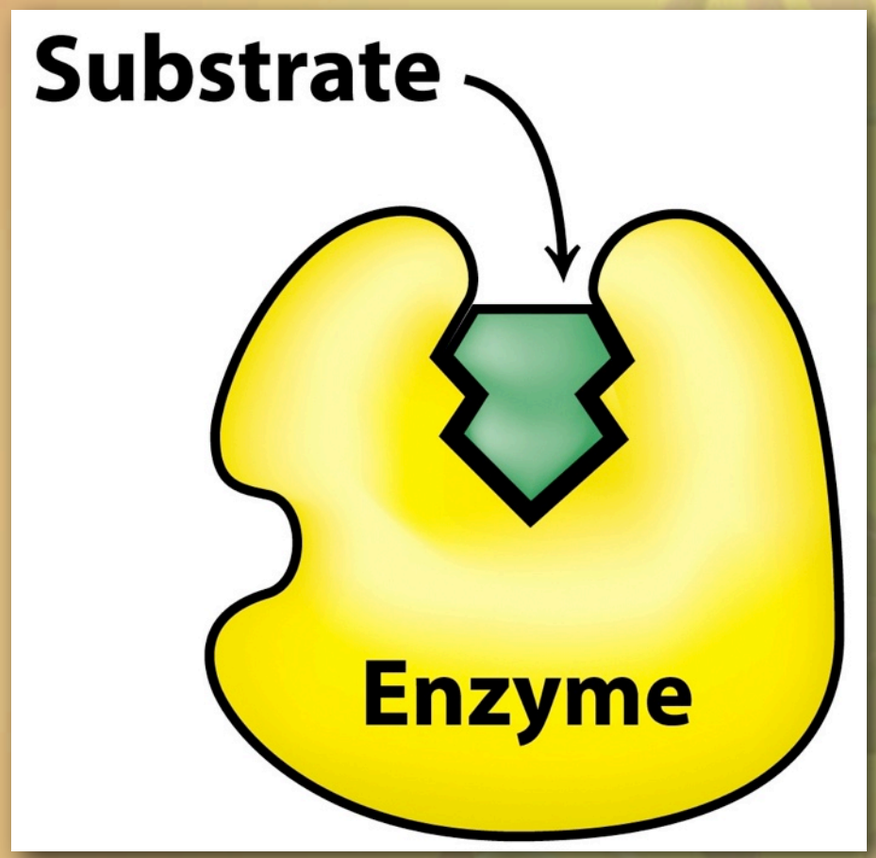
- Competitive Inhibition

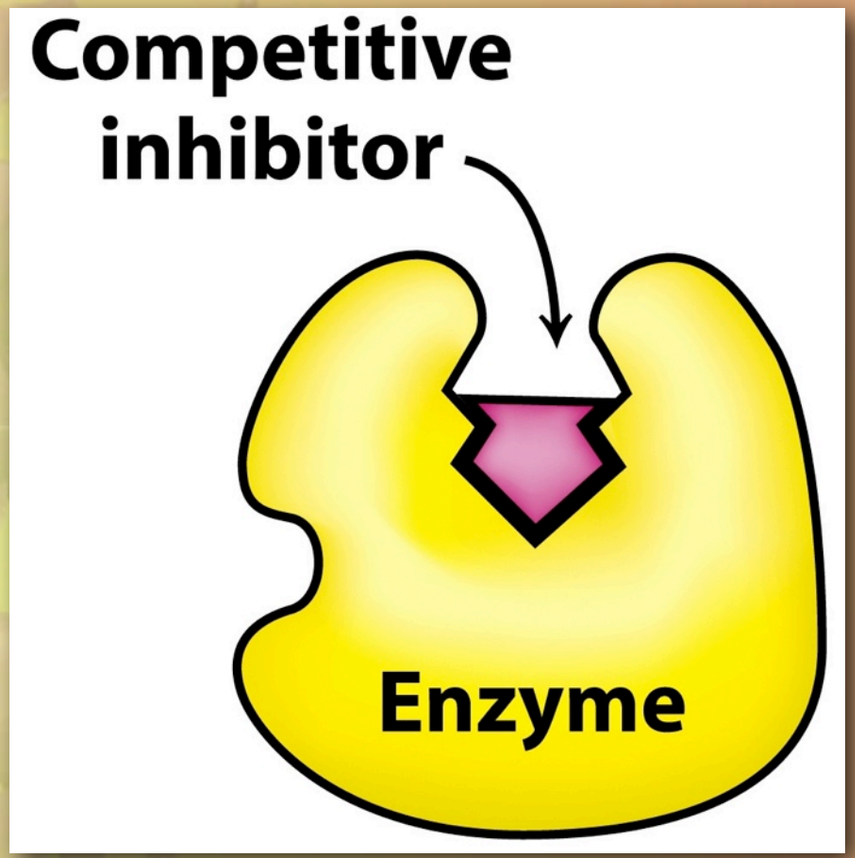




Enzyme Inhibition

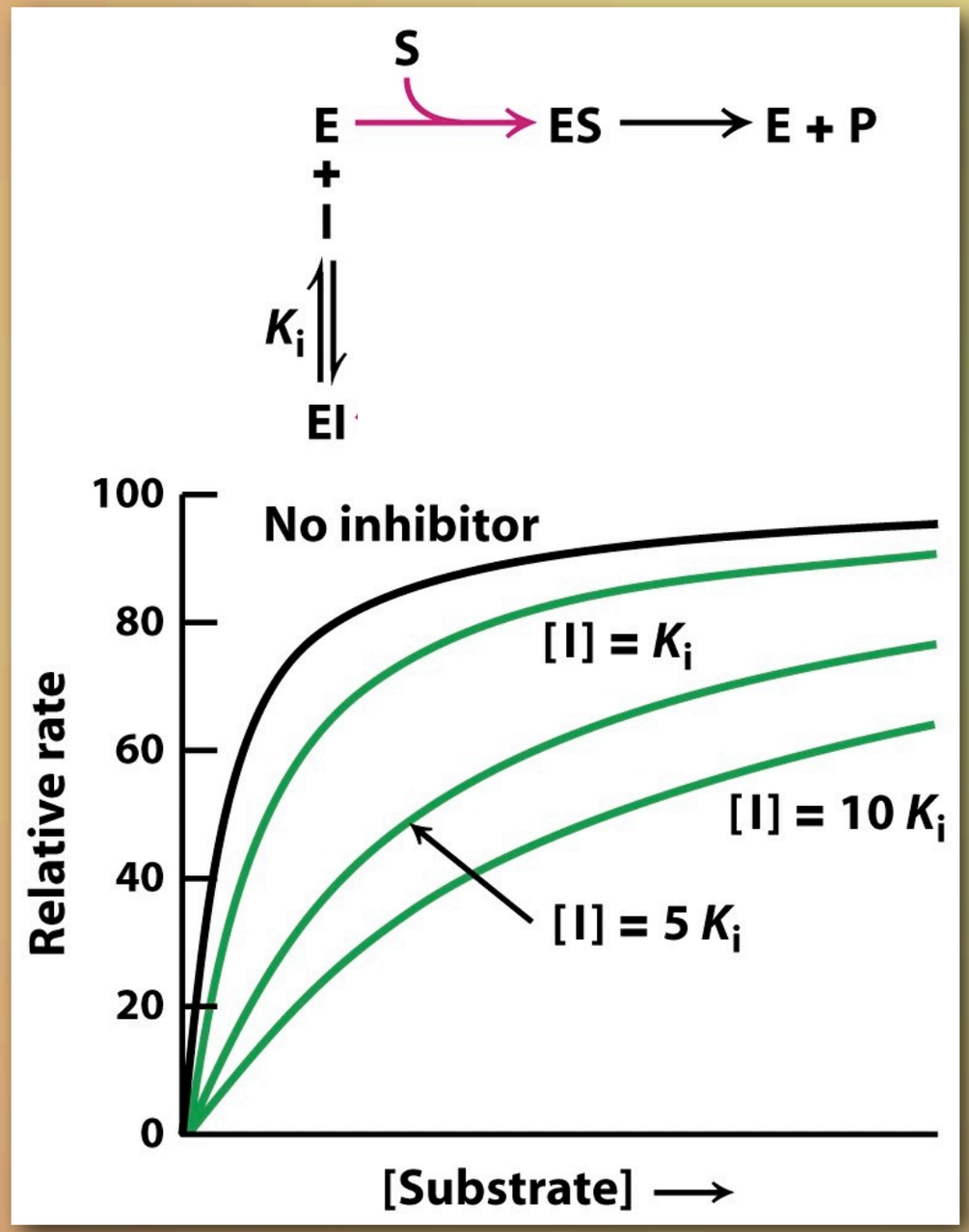
- Competitive Inhibition





Enzyme Inhibition

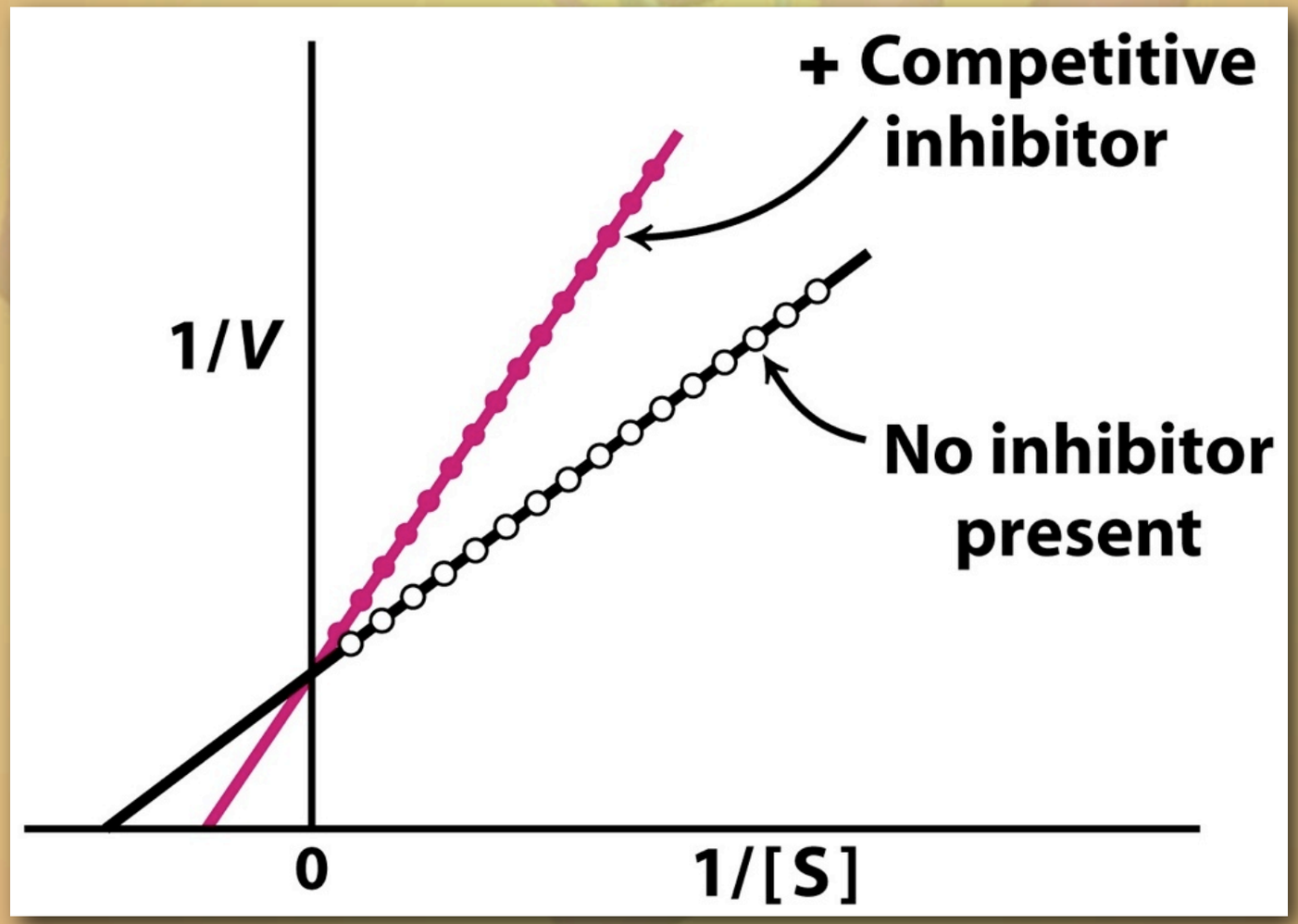
- Competitive Inhibition



$$K_M^{app} = K_M\left(1+\frac{[\mathrm{I}]}{K_I}\right)$$

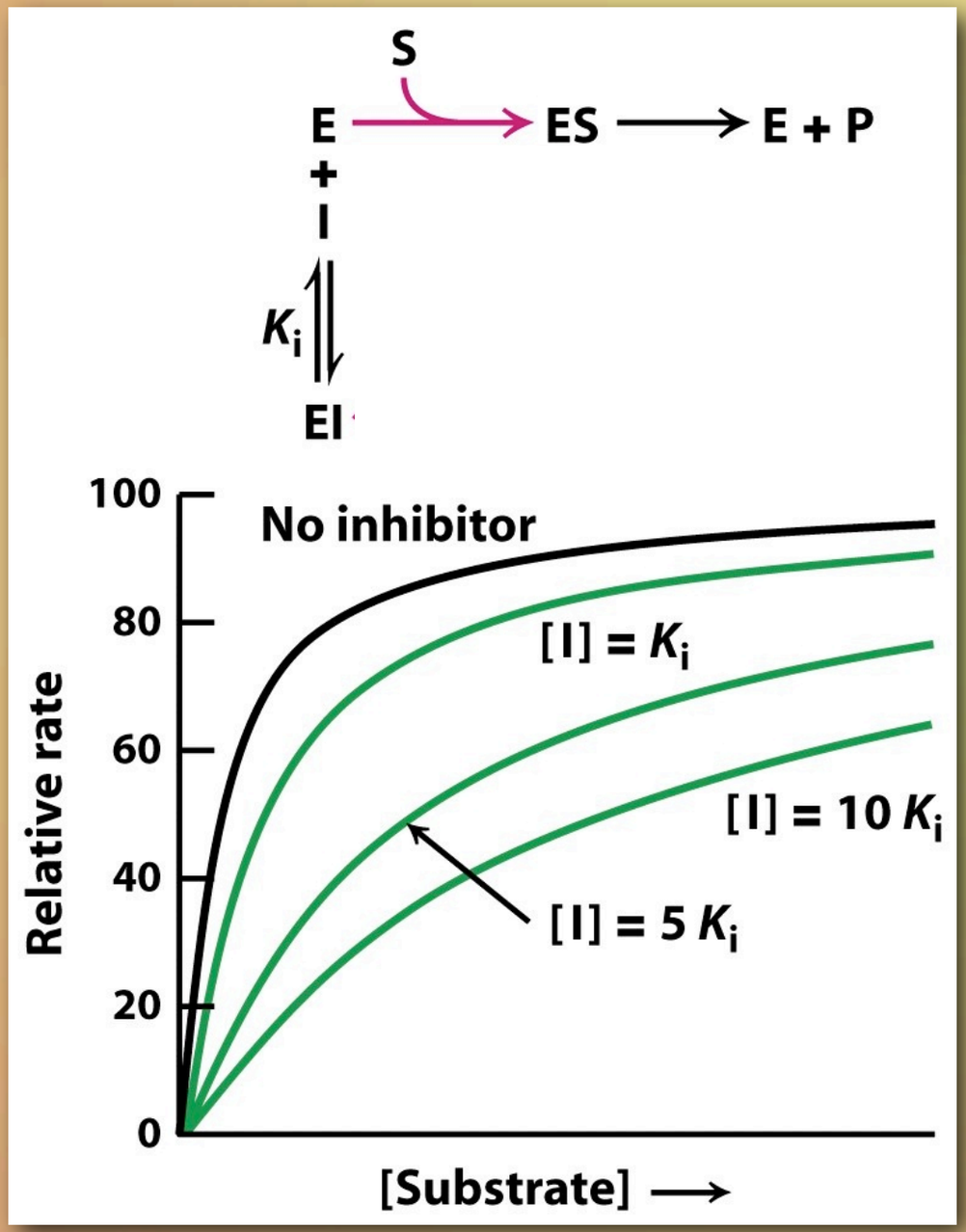
Enzyme Inhibition

- Competitive Inhibition



Enzyme Inhibition

- Competitive Inhibition



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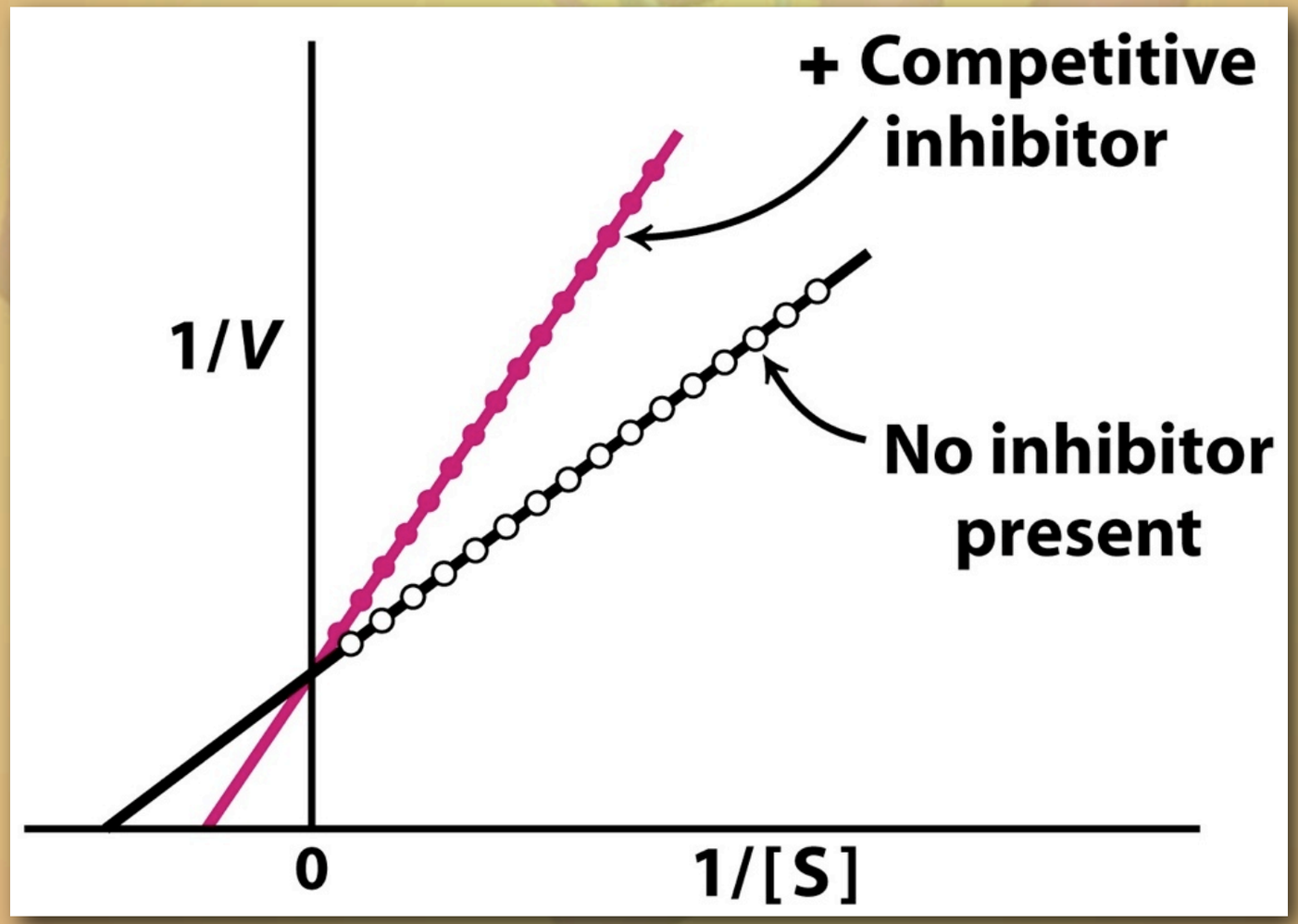
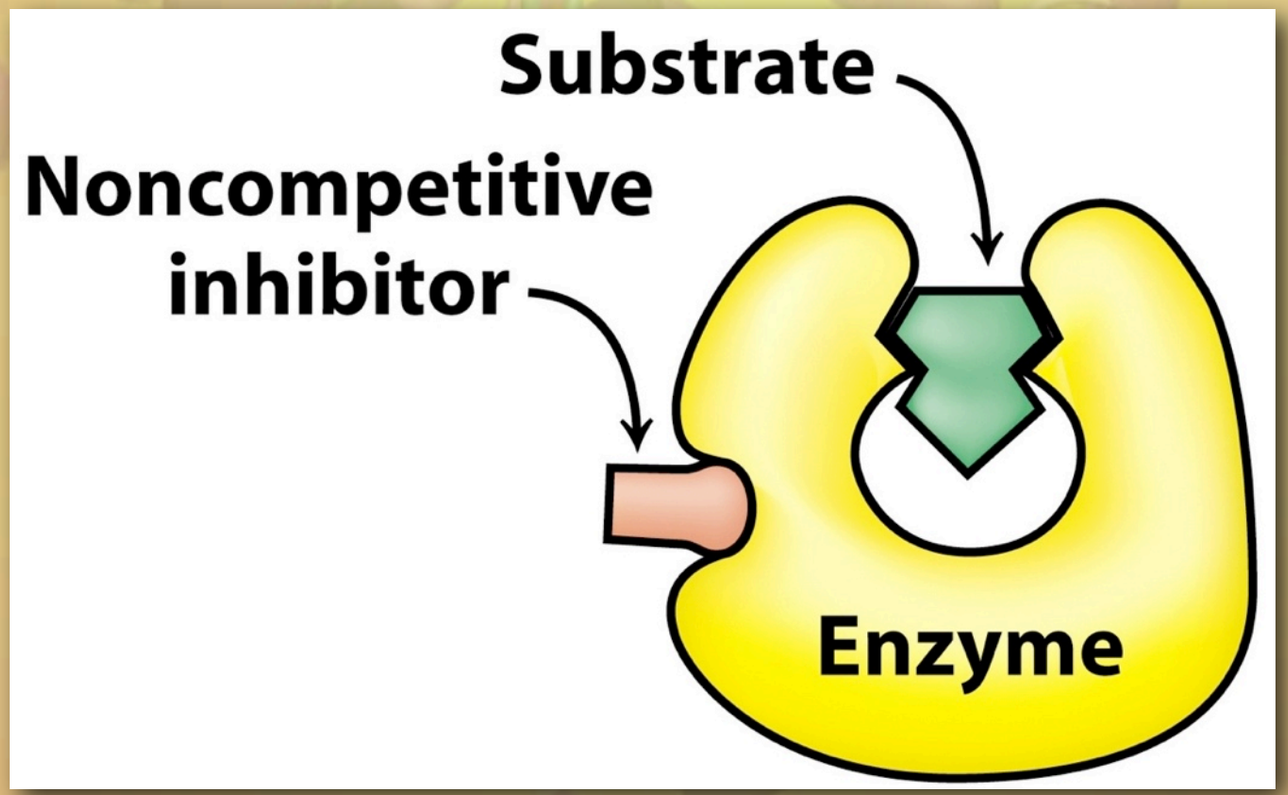
Enzyme Inhibition

- Competitive Inhibition



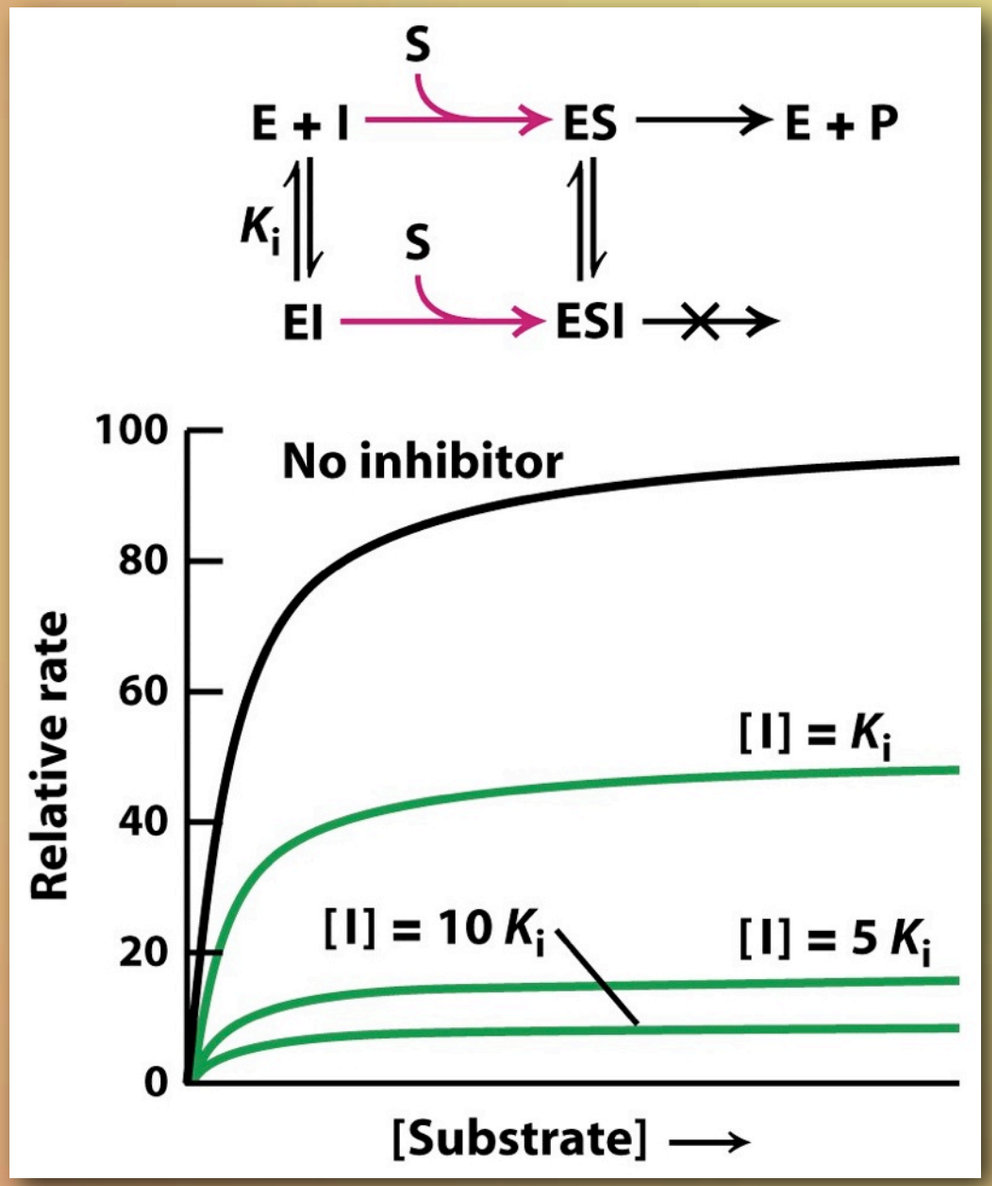
Enzyme Inhibition

- Noncompetitive Inhibition



Enzyme Inhibition

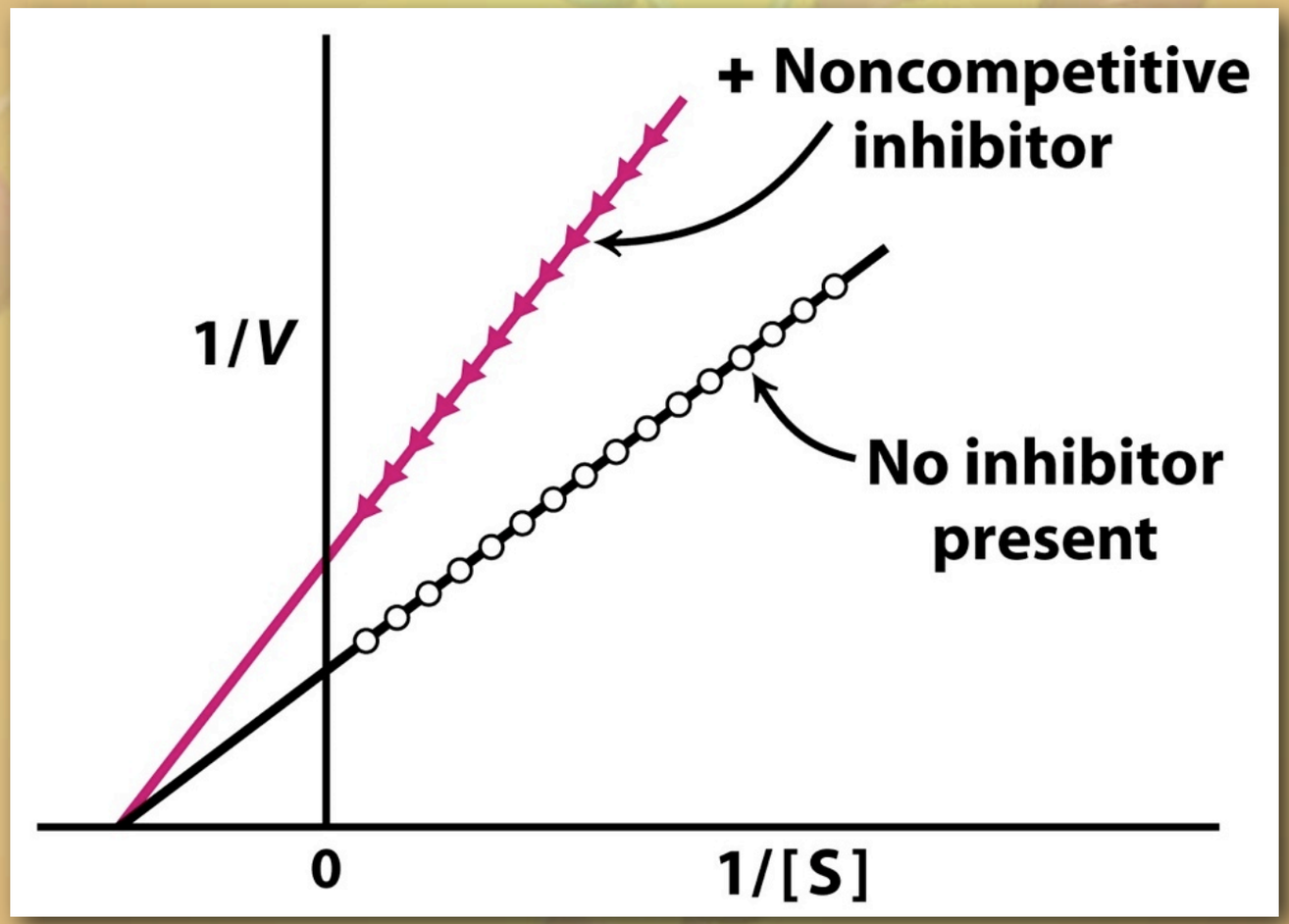
- Noncompetitive Inhibition



$$V_{MAX}^{app} = \frac{V_{MAX}^{app}}{\left(1 + \frac{[I]}{K_I}\right)}$$

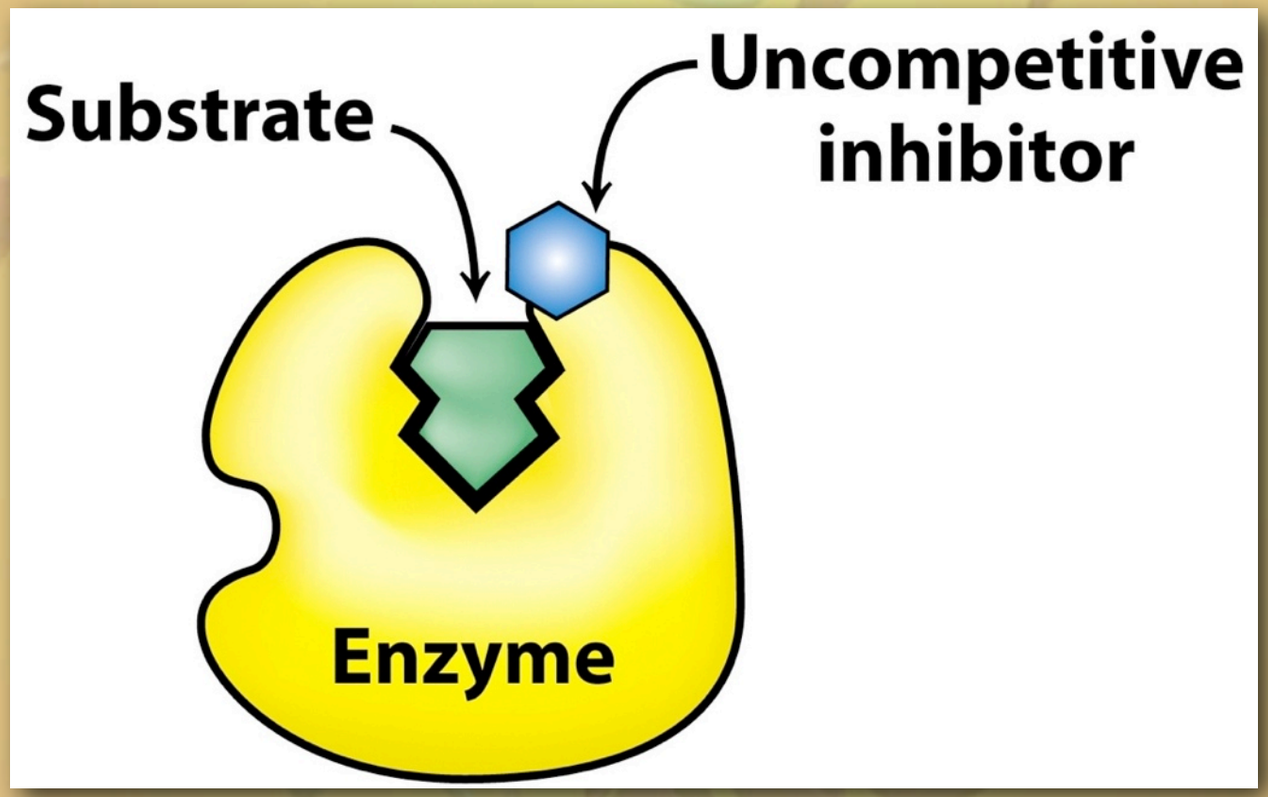
Enzyme Inhibition

- Noncompetitive Inhibition



Enzyme Inhibition

- Uncompetitive Inhibition



Enzyme Inhibition

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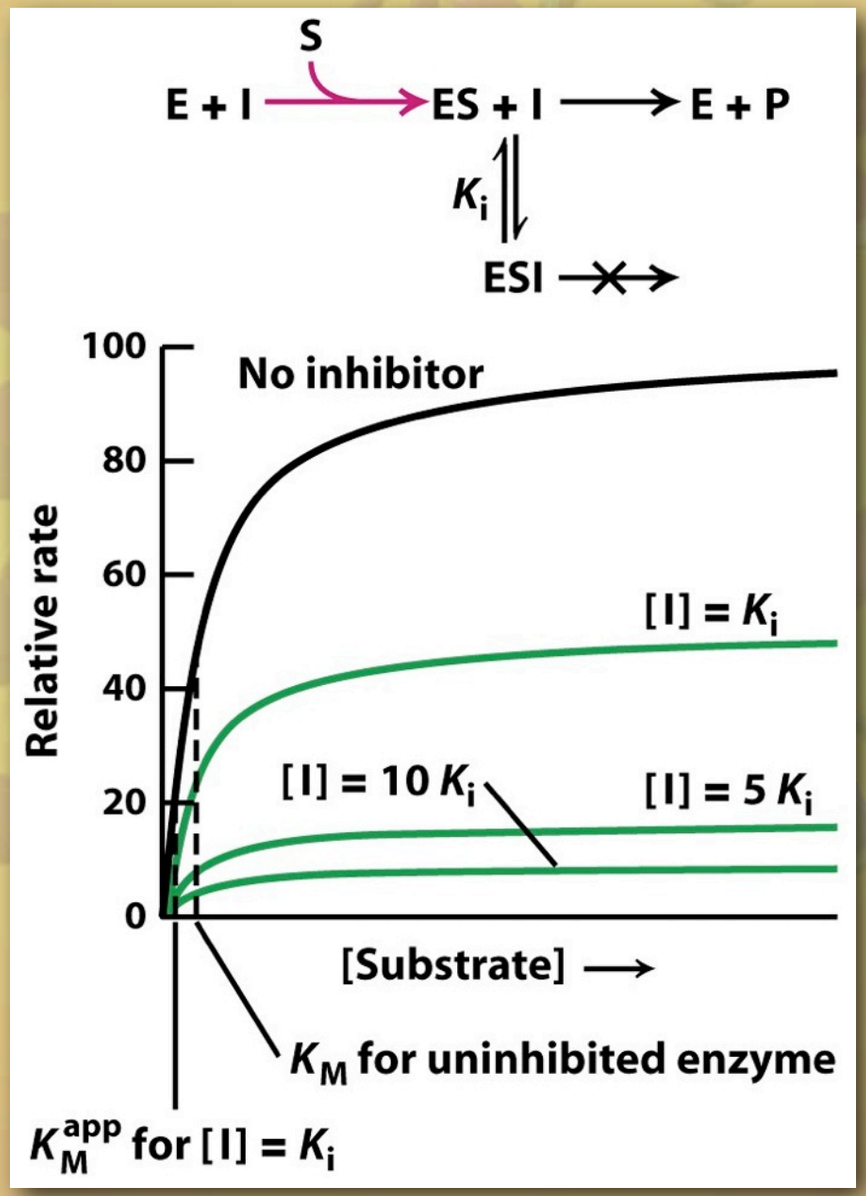
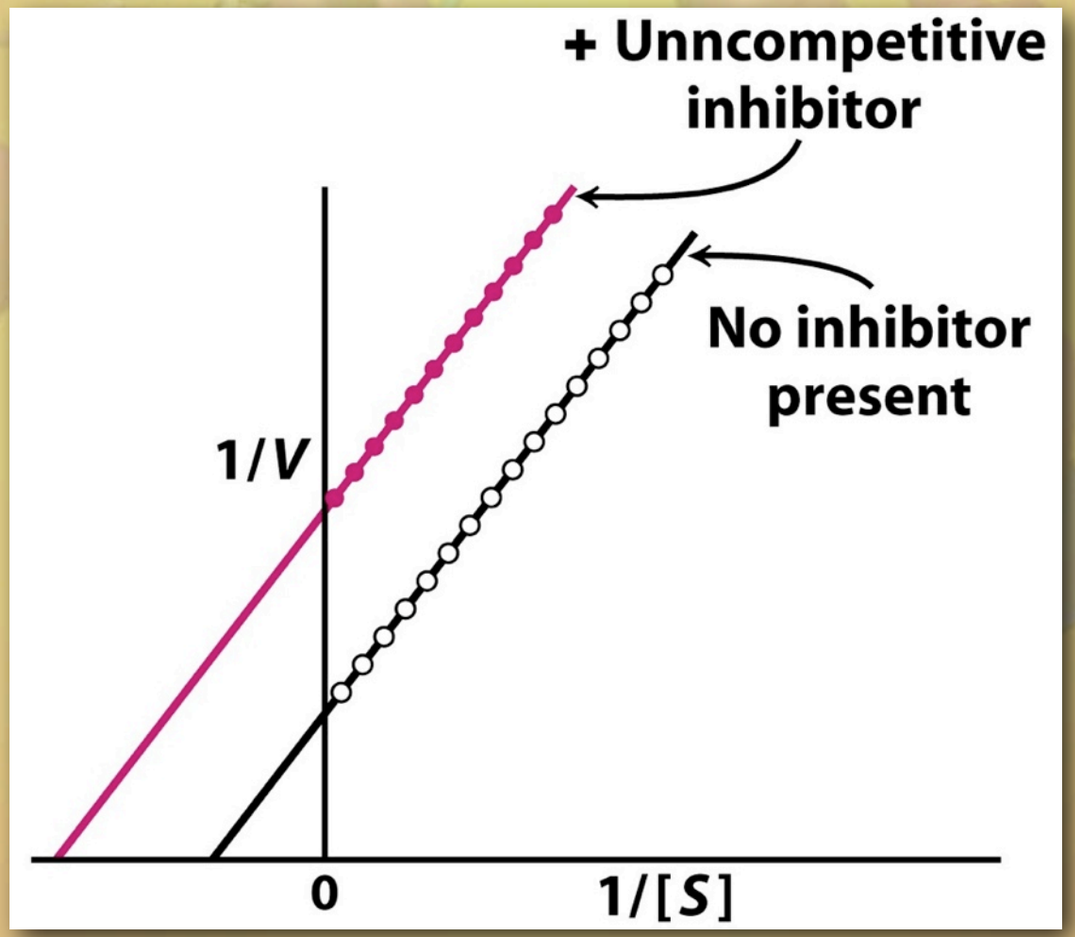


Enzyme Inhibition

- Uncompetitive Inhibition



Both K_M and V_{max} are affected to the same extent

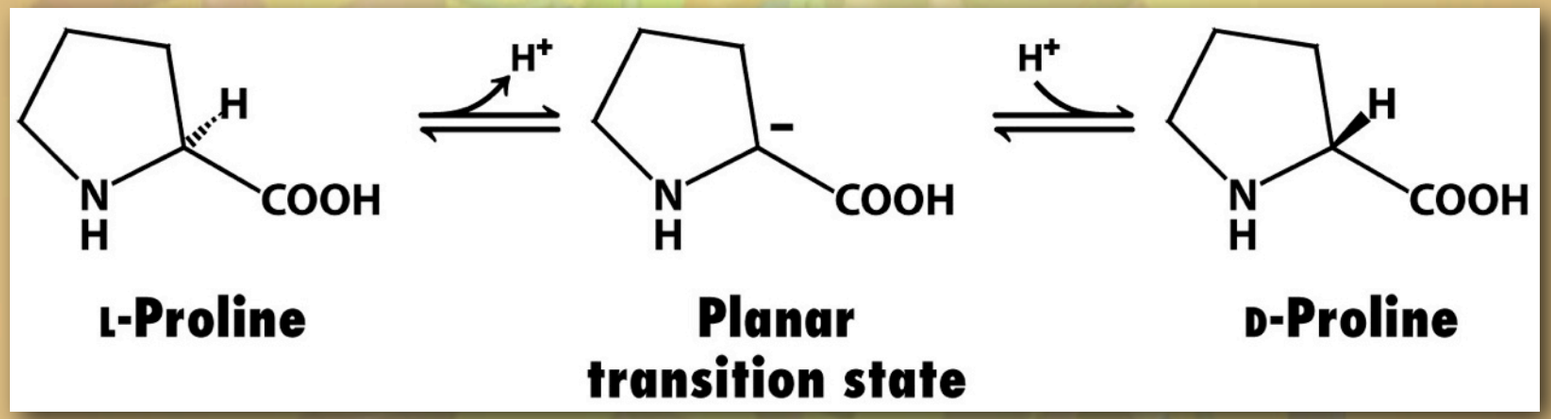
Problem

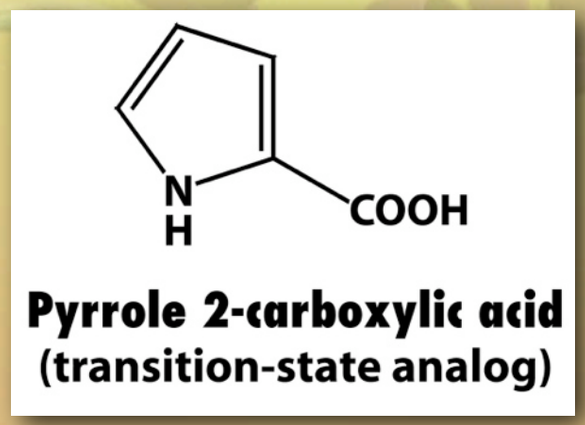
C) Ibuprofen is an inhibitor of the enzyme *prostaglandin endoperoxide synthase*. By inhibiting the synthesis of prostaglandins, ibuprofen reduces both inflammation and pain. Using the data below, determine the type of inhibition that ibuprofen exerts on prostaglandin endoperoxide synthase

[S] {mM}	v_o {mM/min}	v_o {mM/min} /w Ibuprofen
0.5	23.5	16.67
1	32.2	25.25
1.5	36.9	30.49
2.5	41.8	37.04
3.5	44	38.91

Enzyme Inhibition

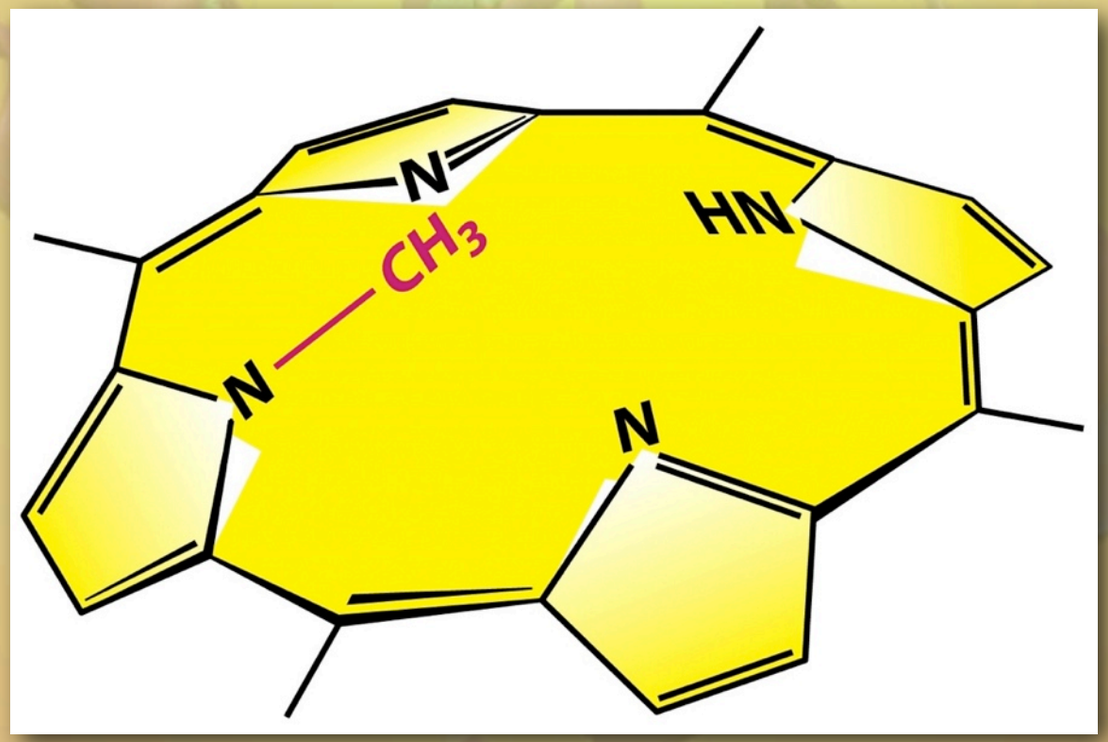
- Some inhibitors are transition state analogues instead of substrate analogues.





Synthetic Enzymes

- Antibody enzymes (Abzymes)
  - Antibodies raised to transitions state analogues exhibit enzymatic activity



Antibodies raised to this compound have ferrochelatase activity (≈2,500 x the uncatalyzed reaction)

Enzyme Classification

- Enzymes are classified based on the types of reactions they catalyze

TABLE 8.8 Six major classes of enzymes

Class	Type of reaction	Example	Chapter
1. Oxidoreductases	Oxidation–reduction	Lactate dehydrogenase	16
2. Transferases	Group transfer	Nucleoside monophosphate kinase (NMP kinase)	9
3. Hydrolases	Hydrolysis reactions (transfer of functional groups to water)	Chymotrypsin	9
4. Lyases	Addition or removal of groups to form double bonds	Fumarase	17
5. Isomerases	Isomerization (intramolecular group transfer)	Triose phosphate isomerase	16
6. Ligases	Ligation of two substrates at the expense of ATP hydrolysis	Aminoacyl-tRNA synthetase	30

Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB)

http://www.chem.qmul.ac.uk/iubmb/enzyme/

Next up

- Catalytic Strategies (Chapter 9)
  - Protease reaction (Hydrolysis rxn)
  - Carbonic anhydrase (Hydration rxn)
  - Restriction endonuclease (Hydrolysis rxn)
  - Myosin ATPase