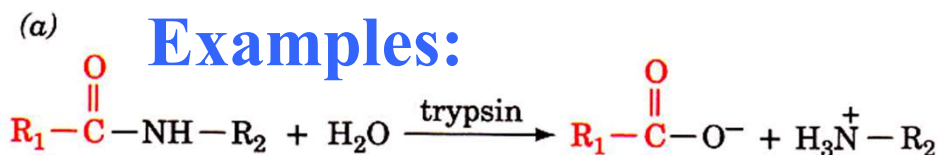
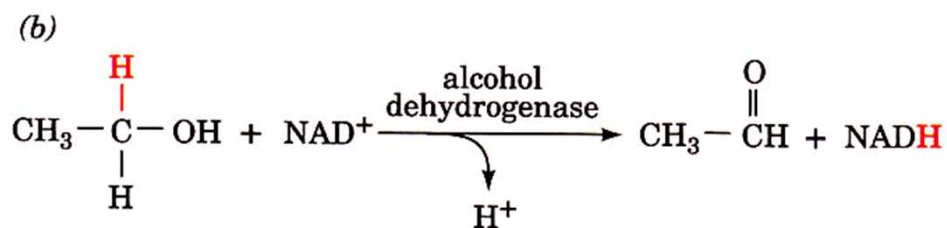


# What about two substrates? Sequential mechanisms



Polypeptide

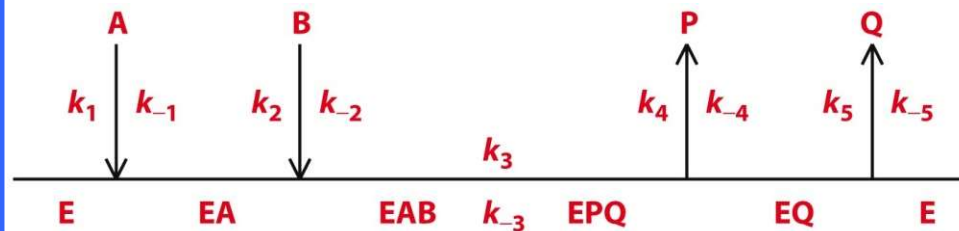


Nomenclature system by:



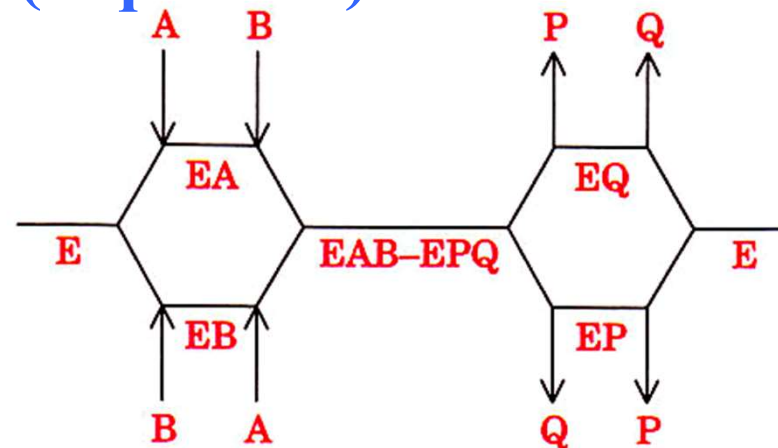
W.W. Cleland

## (sequential) Ordered Bi Bi:



Can be distinguished by  
product inhibition studies

## (sequential) Random Bi Bi:



# How to distinguish sequential mechanisms

Remember mixed inhibition?

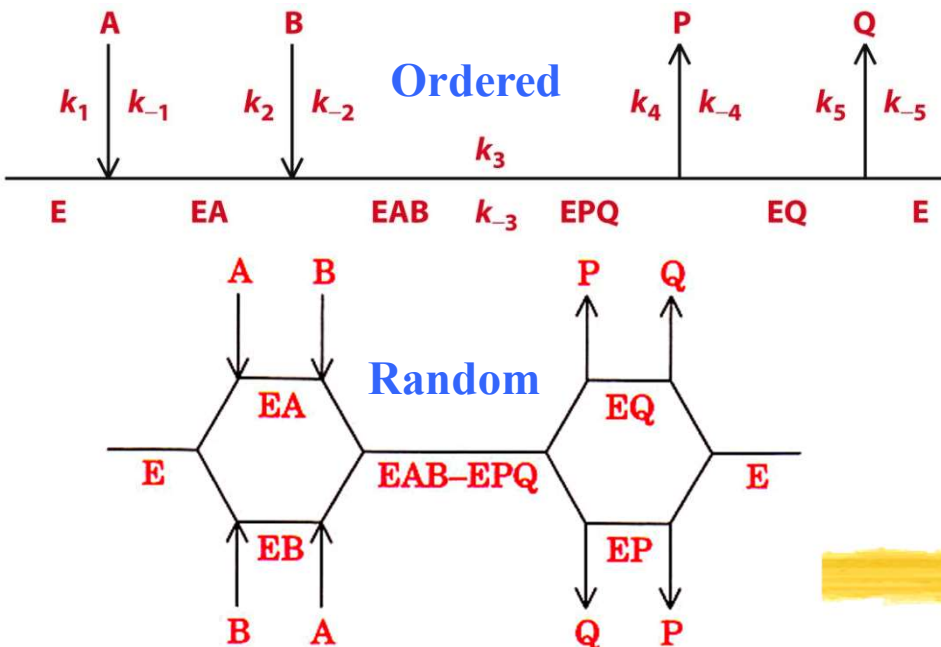
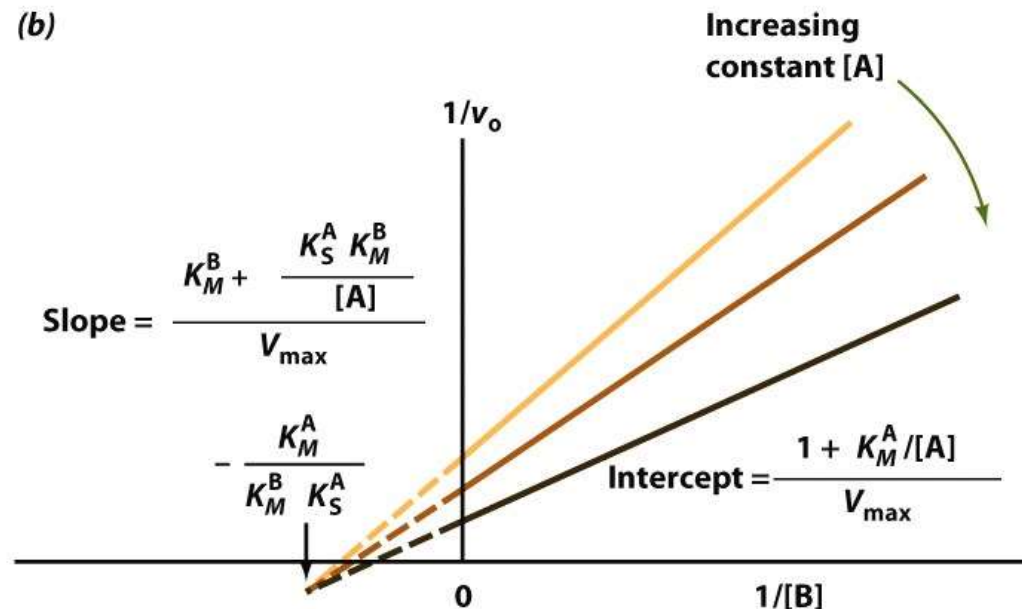
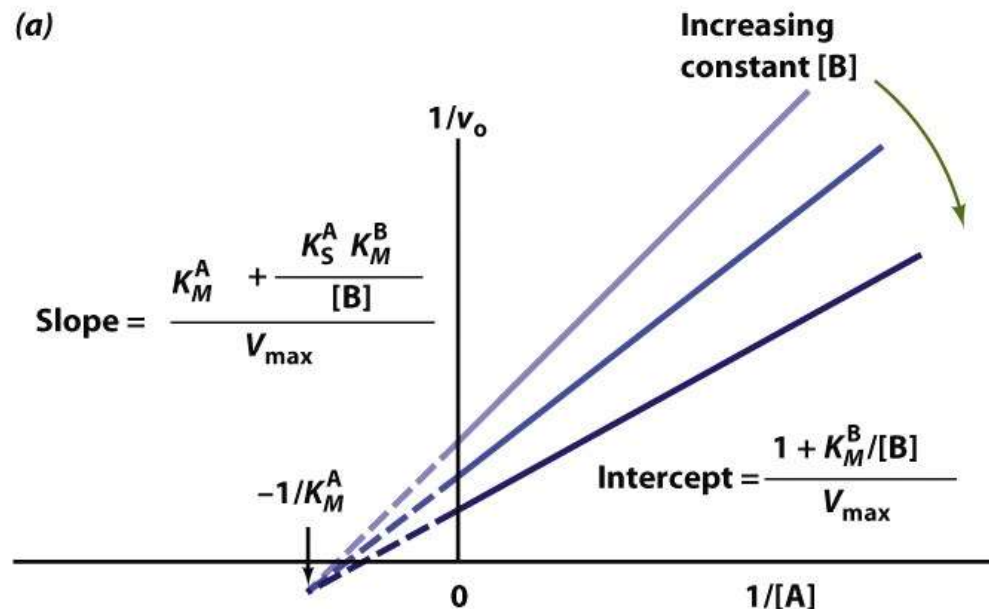
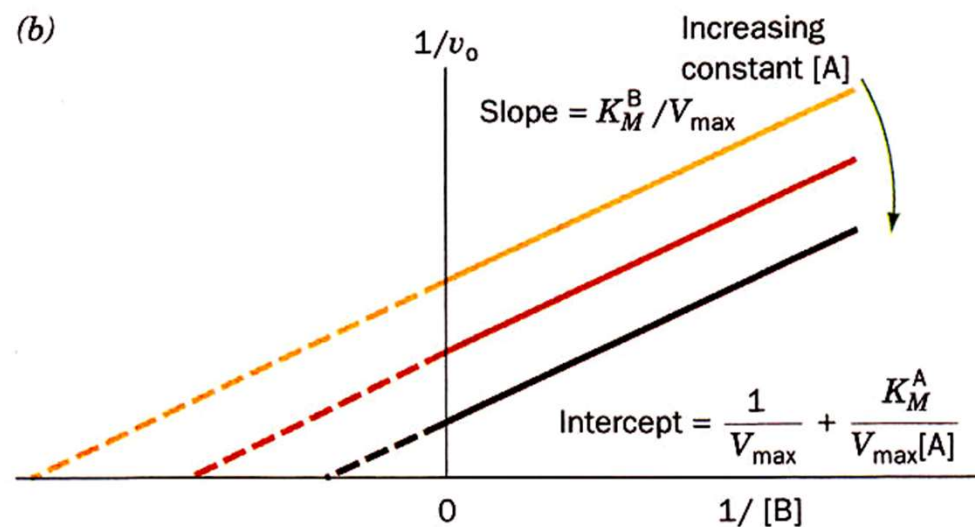
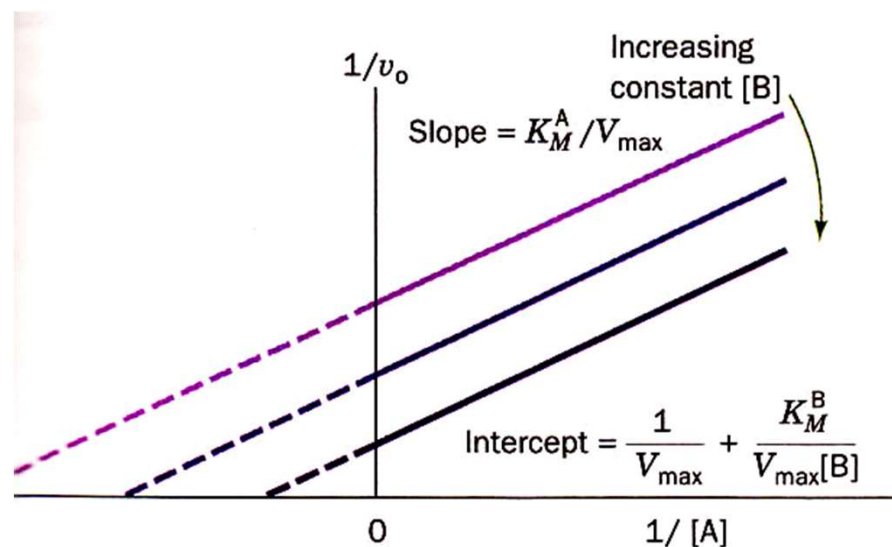
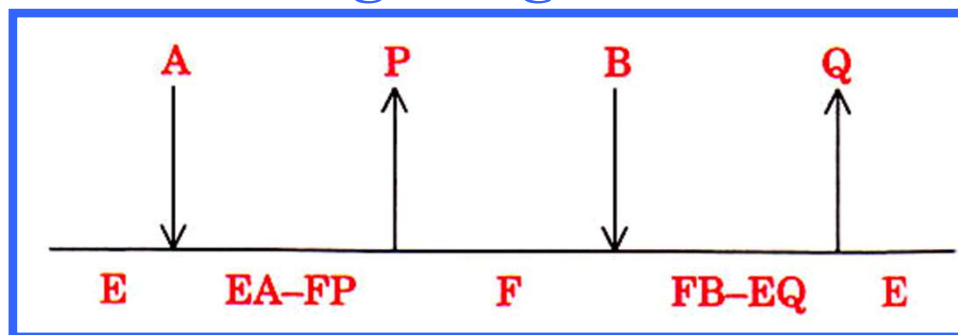


Table 14-3 Patterns of Product Inhibition for Sequential Bisubstrate Mechanisms

Mechanism	Product Inhibitor	[A] Variable	[B] Variable
Ordered Bi Bi	P	Mixed	Mixed
	Q	Competitive	Mixed
Rapid Equilibrium Random Bi Bi	P	Competitive	Competitive
	Q	Competitive	Competitive

# Two substrates that play ping-pong

## Ping Pong Bi Bi:



Remember uncompetitive inhibition?

# Enzyme Catalysis

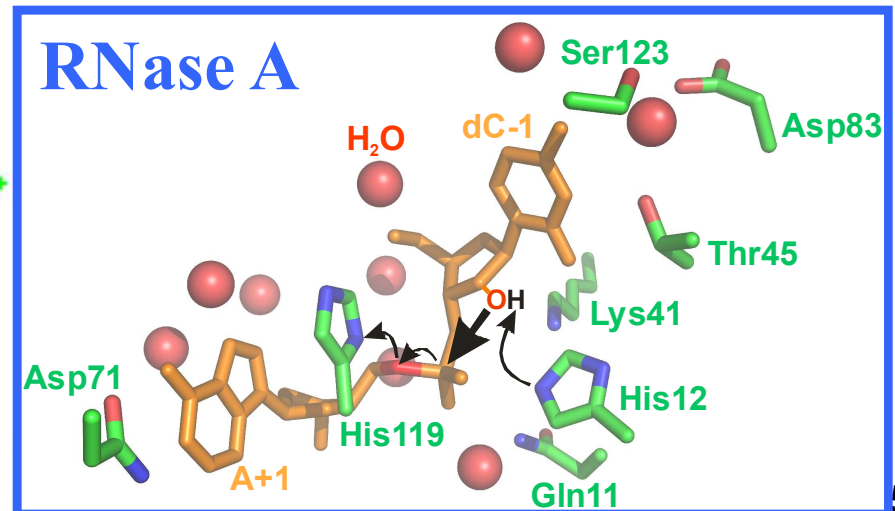
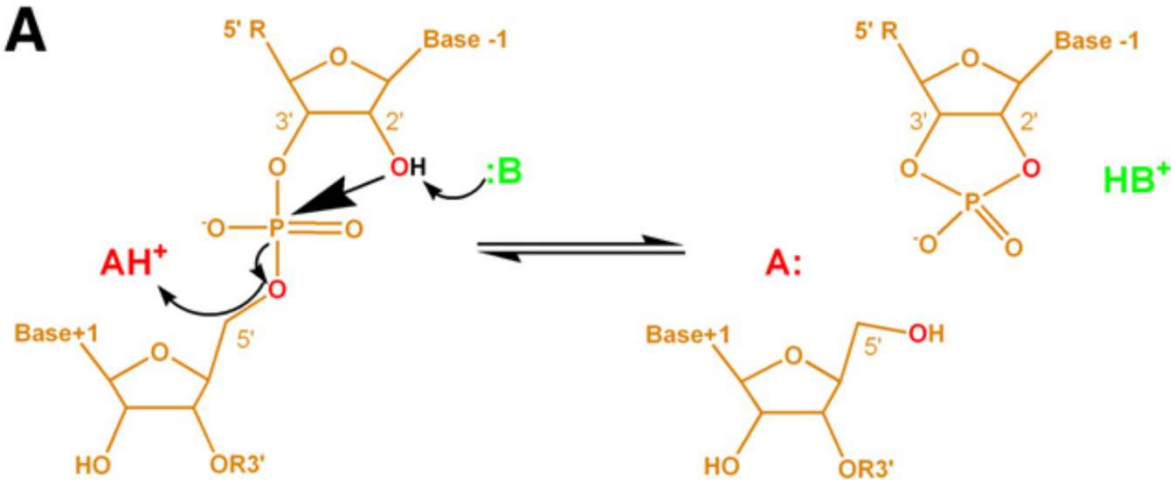
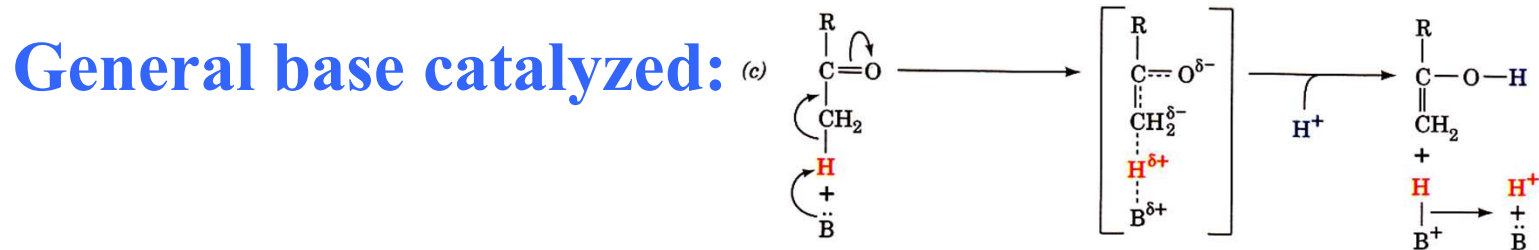
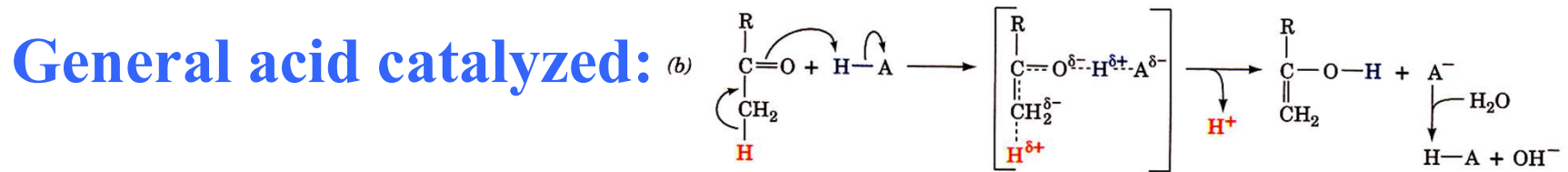
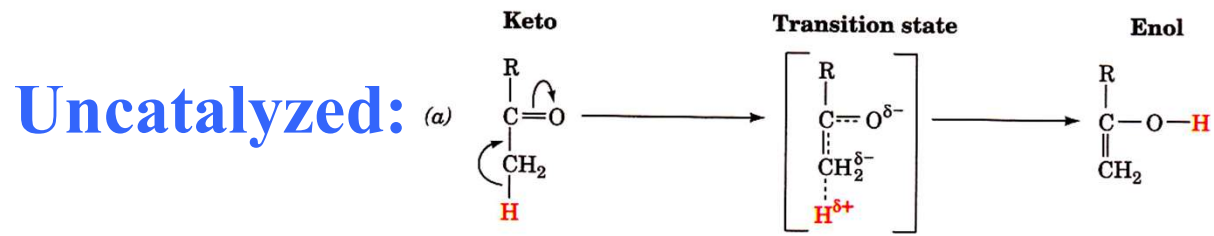
Voet & Voet, Chapter 15

Enzymes use a limited number of specific catalytic strategies:

- Acid-base catalysis
- Preferential binding of the transition state
- Electrostatic catalysis
- Metal ion catalysis
- Proximity and orientation effects
- Covalent catalysis

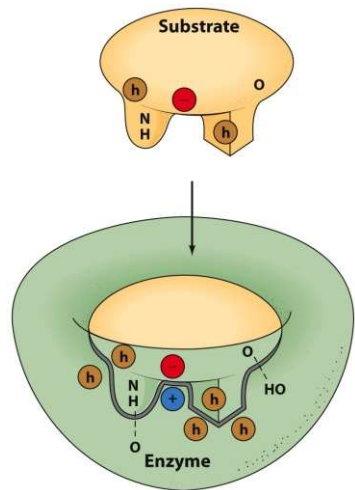


# Acid-base catalysis: Two examples

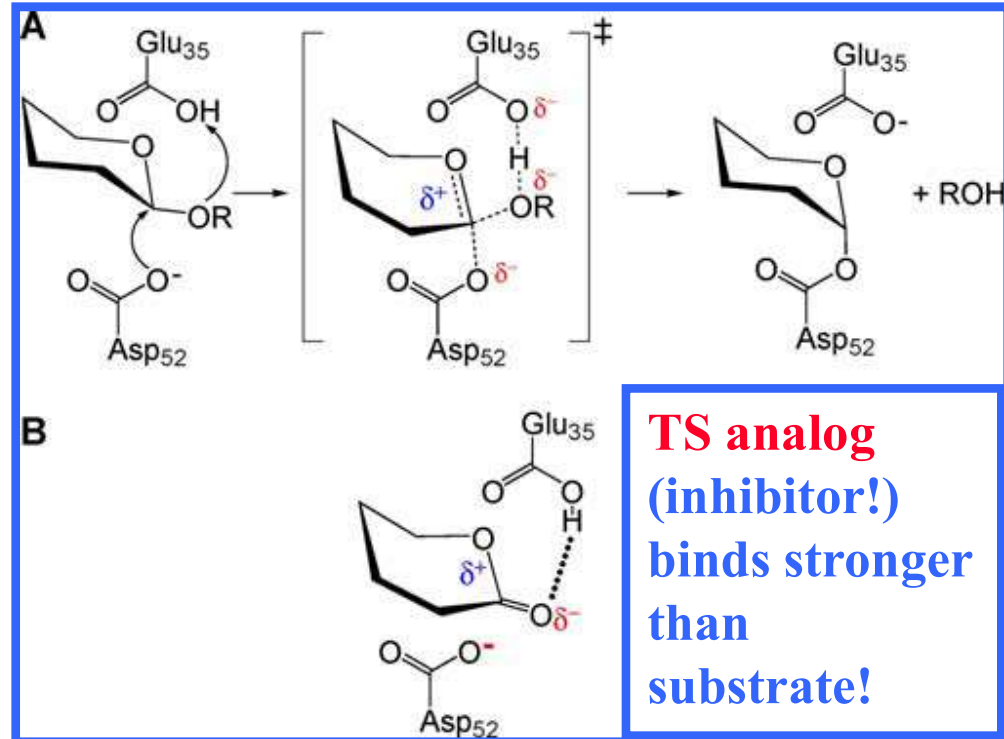
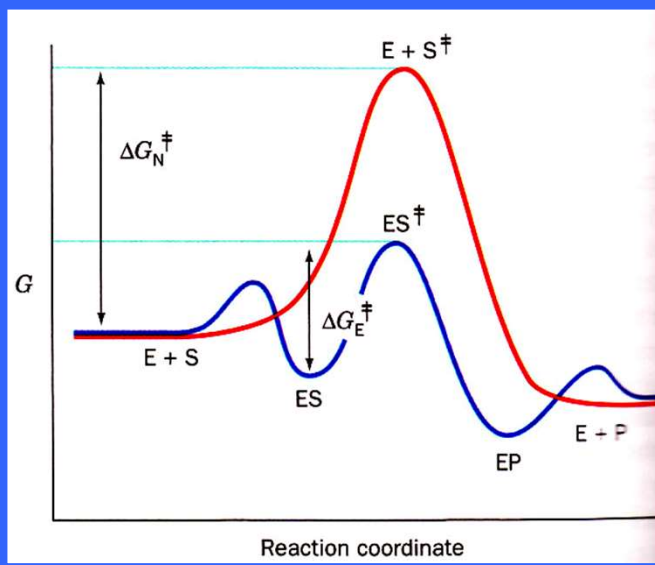




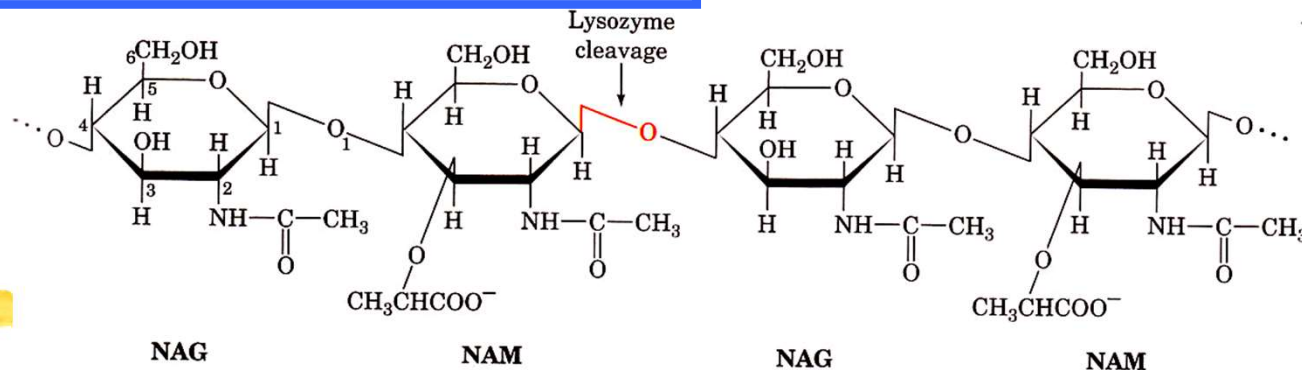
# Catalysis by preferential binding of the transition state (shape complementarity)



If TS better bound than GS:



Example: Lysozyme lyses bacterial cell wall

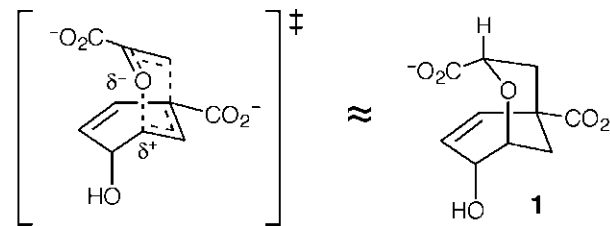
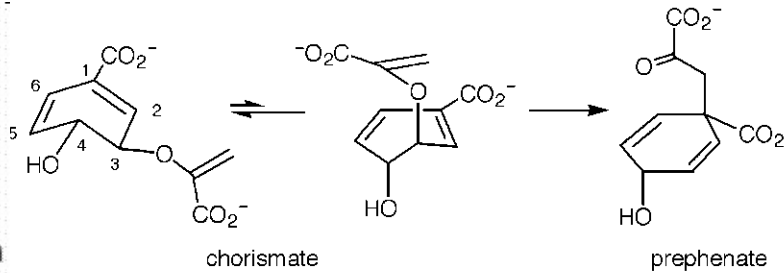
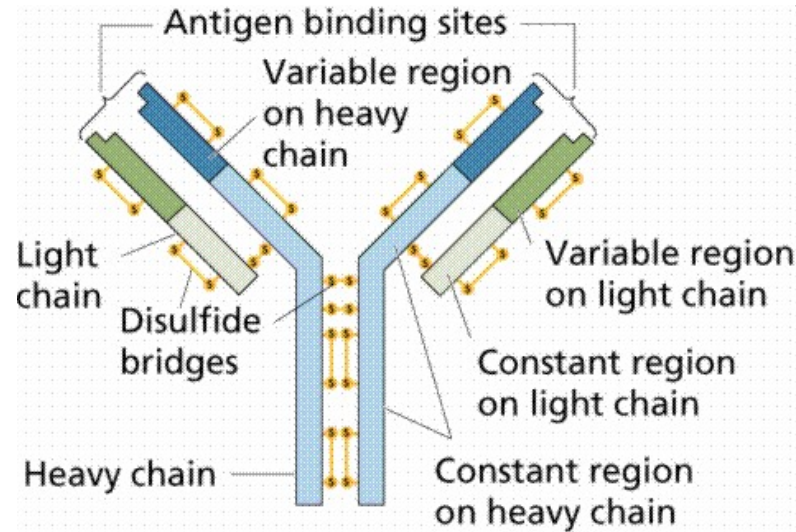


451

6

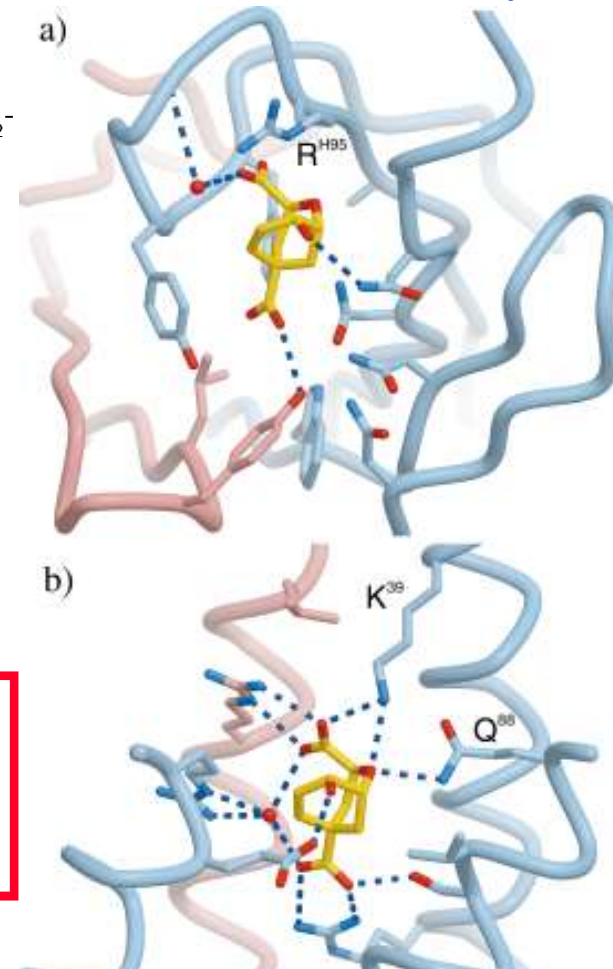
01/31/22

# Catalytic antibodies (abzymes)

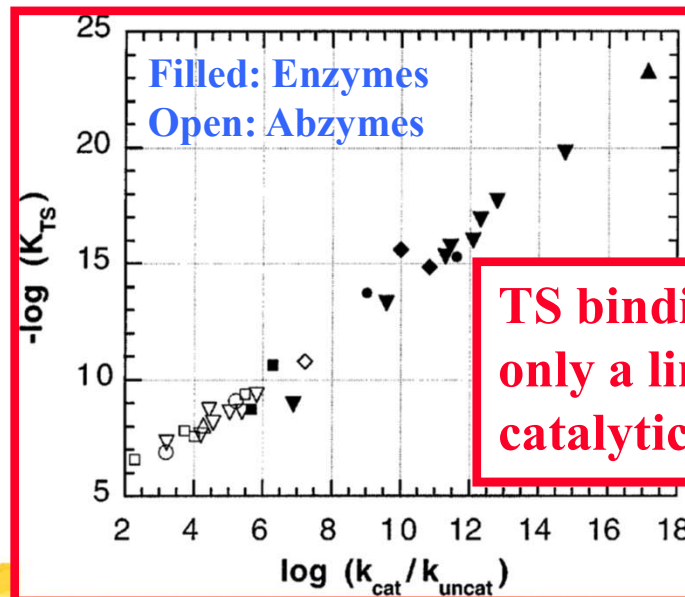
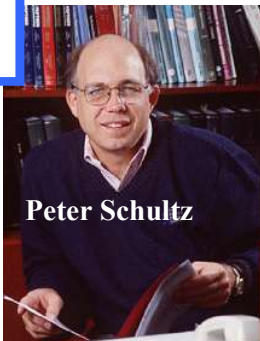


Claisen rearrangement

Active site of antibody 1F7



1986:

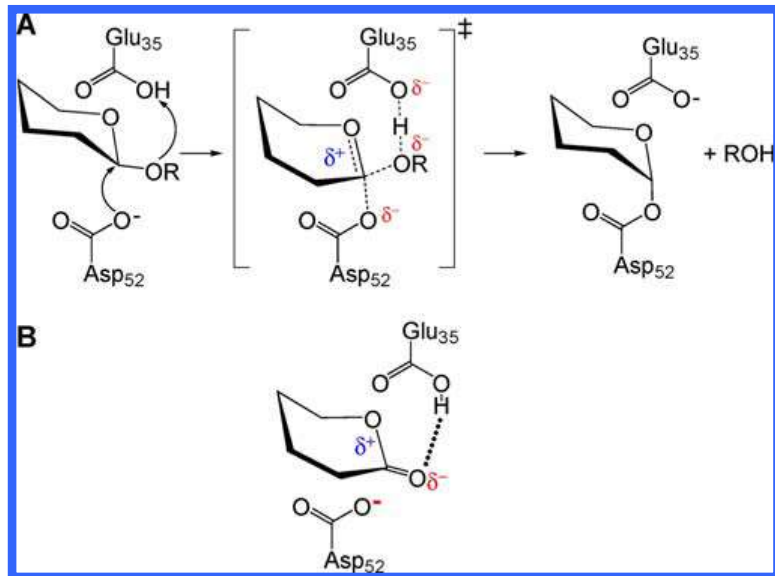


TS binding has only a limited catalytic effect!

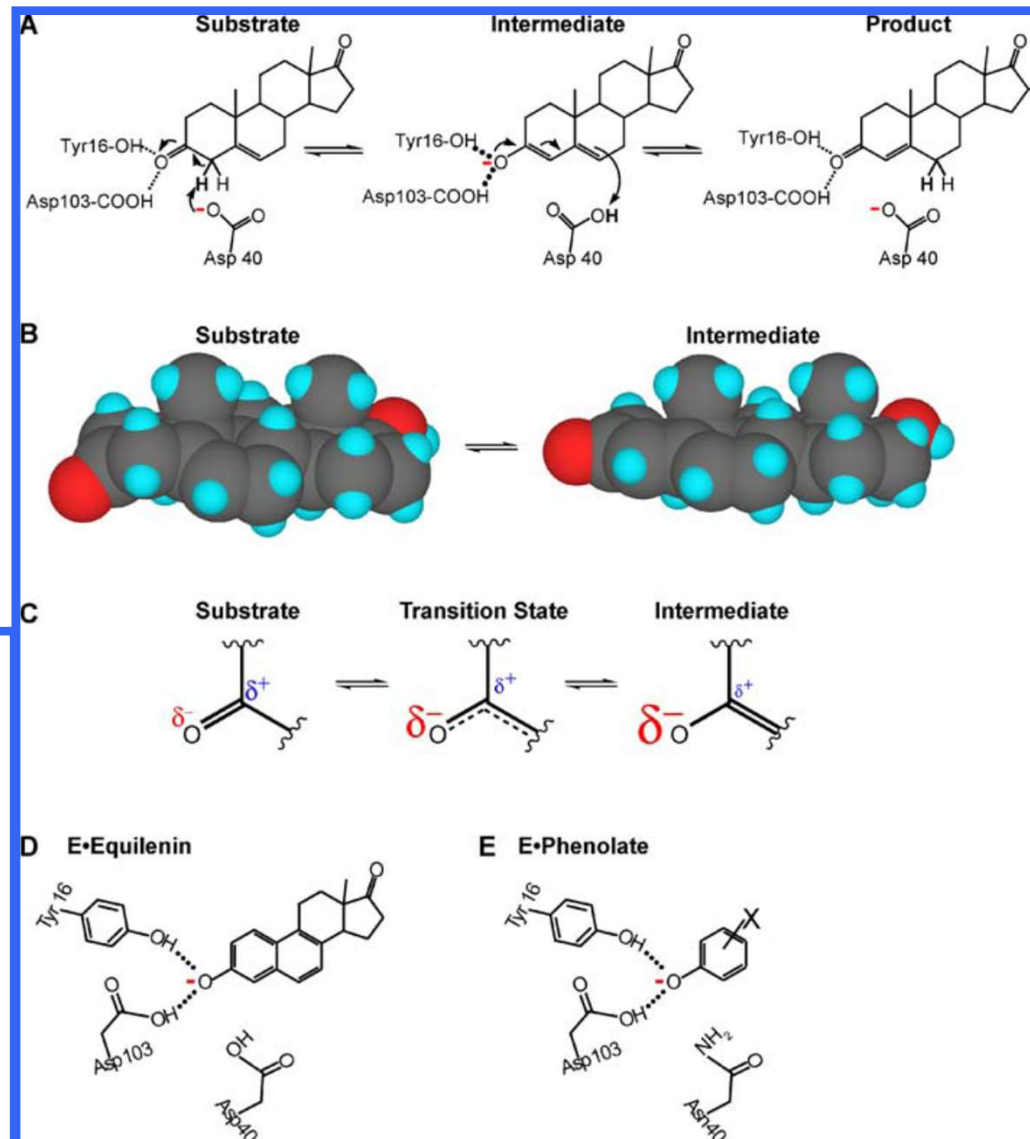
Nils Walter:

*E. coli* chorismate mutase 7

# Related: Electrostatic catalysis?



For Ketosteroid isomerase (KSI) a “...small effect of increased charge localization on affinity occurs... This shallow dependence of binding affinity suggests that electrostatic complementarity in the oxyanion hole makes at most a modest contribution to catalysis of ~300-fold. We propose that geometrical complementarity between the oxyanion hole hydrogen-bond donors and the transition state oxyanion provides a significant catalytic contribution, and suggest that **KSI, like other enzymes, achieves its catalytic prowess through a combination of modest contributions from several mechanisms rather than from a single dominant contribution.**”



Nils Walter: Chem 451

