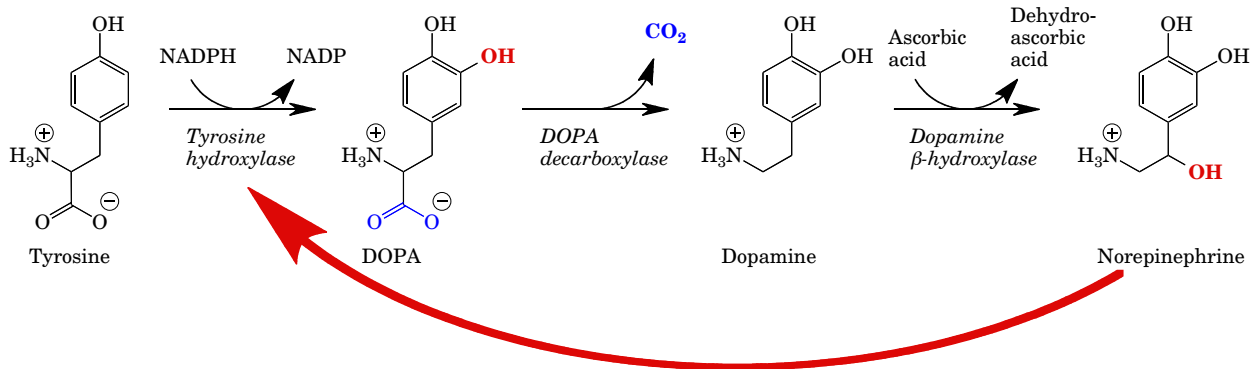
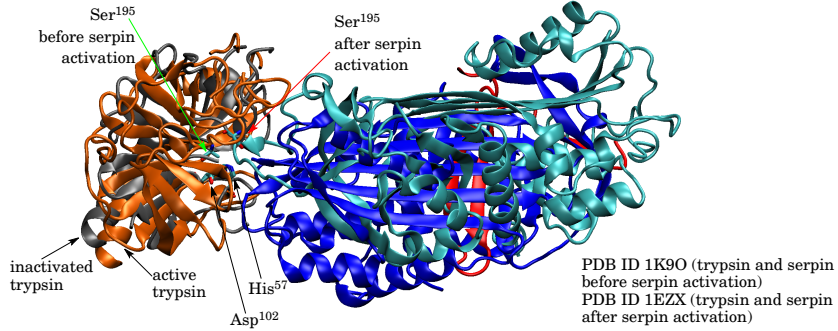


# Enzyme Inhibition

## Physiological processes -- Pathway regulation



## Physiological regulation -- Pancreatic trypsin inhibitor, serpins

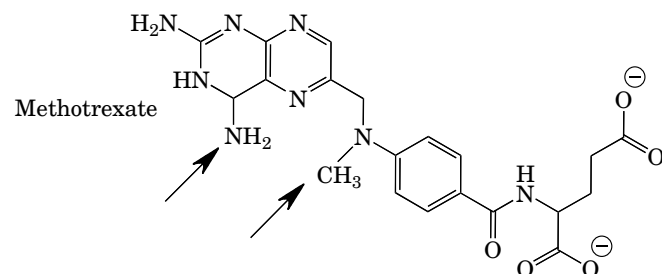
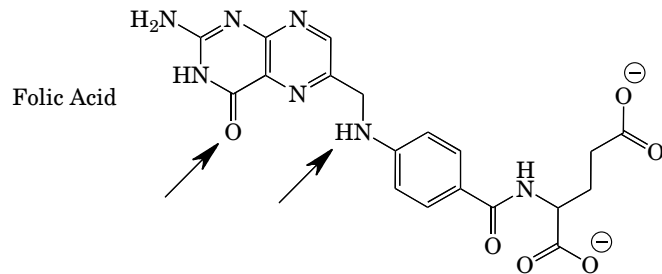
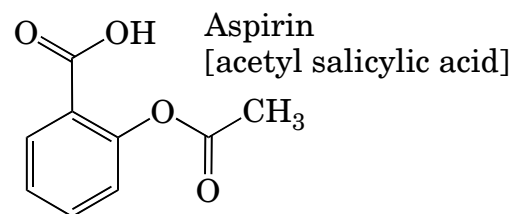
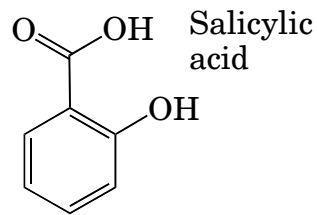


## Science

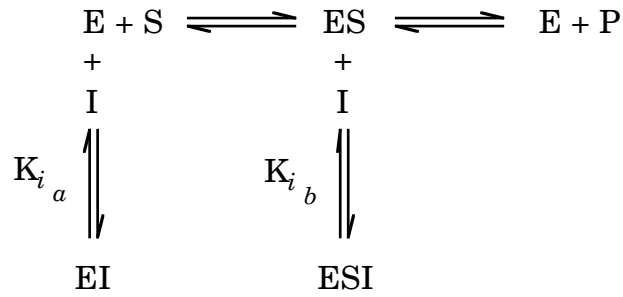
Enzyme mechanism probes

Probes for understanding metabolic pathways

## Therapy



## Reversible Inhibition

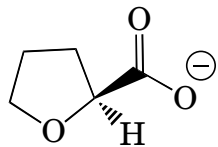
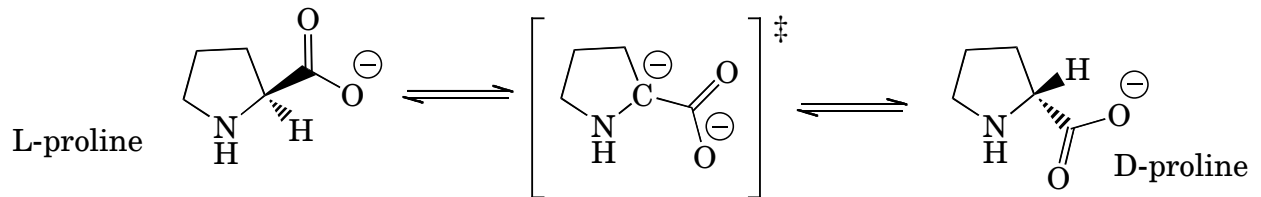


$$v = \frac{V_{max} [S]}{K_m \left( 1 + \frac{[I]}{K_{i_a}} \right) + [S] \left( 1 + \frac{[I]}{K_{i_b}} \right)}$$

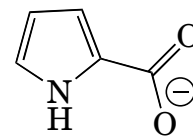
Type of Inhibition	$K_{m_{app}}$	$V_{max_{app}}$
<b>None</b>	$K_m$	$V_{max}$
<b>Competitive</b> (Inhibitor only binds to free enzyme)	$K_m \left( 1 + \frac{[I]}{K_{i_a}} \right)$	$V_{max}$
<b>Mixed</b> (Inhibitor binds E and ES)	$K_m \frac{\left( 1 + \frac{[I]}{K_{i_a}} \right)}{\left( 1 + \frac{[I]}{K_{i_b}} \right)}$	$\frac{V_{max}}{\left( 1 + \frac{[I]}{K_{i_b}} \right)}$
<b>Non-competitive</b> (Inhibitor binds E and ES with equal affinity)	$K_m$	$\frac{V_{max}}{\left( 1 + \frac{[I]}{K_{i_b}} \right)}$
<b>Uncompetitive</b> (Inhibitor only binds to ES complex)	$\frac{K_m}{\left( 1 + \frac{[I]}{K_{i_b}} \right)}$	$\frac{V_{max}}{\left( 1 + \frac{[I]}{K_{i_b}} \right)}$

## Substrate and Transition State Analogs

### *Proline racemase*



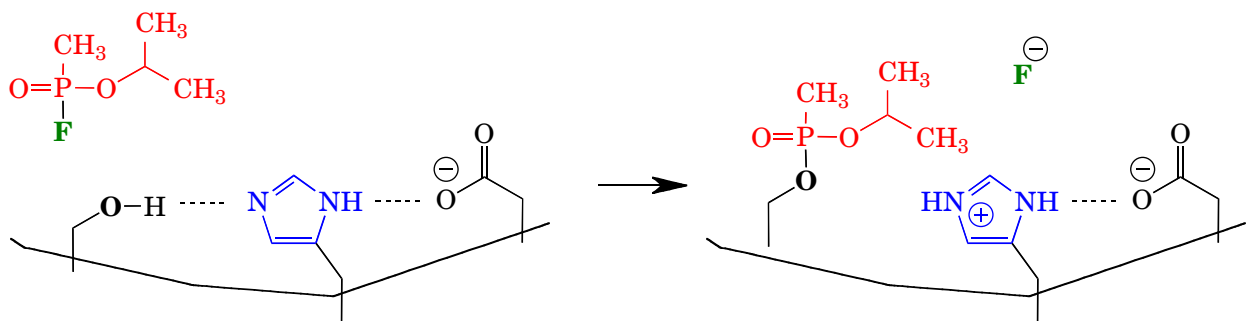
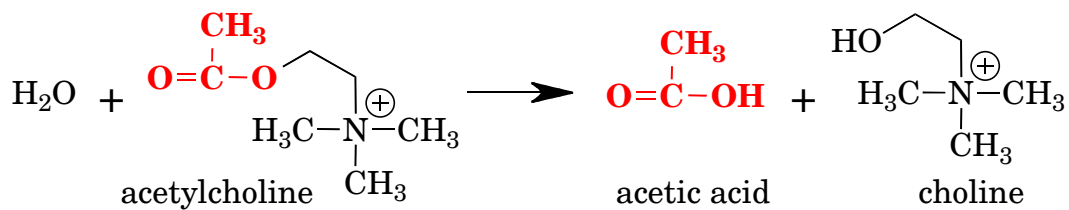
Tetrahydrofuran  
2-carboxylate

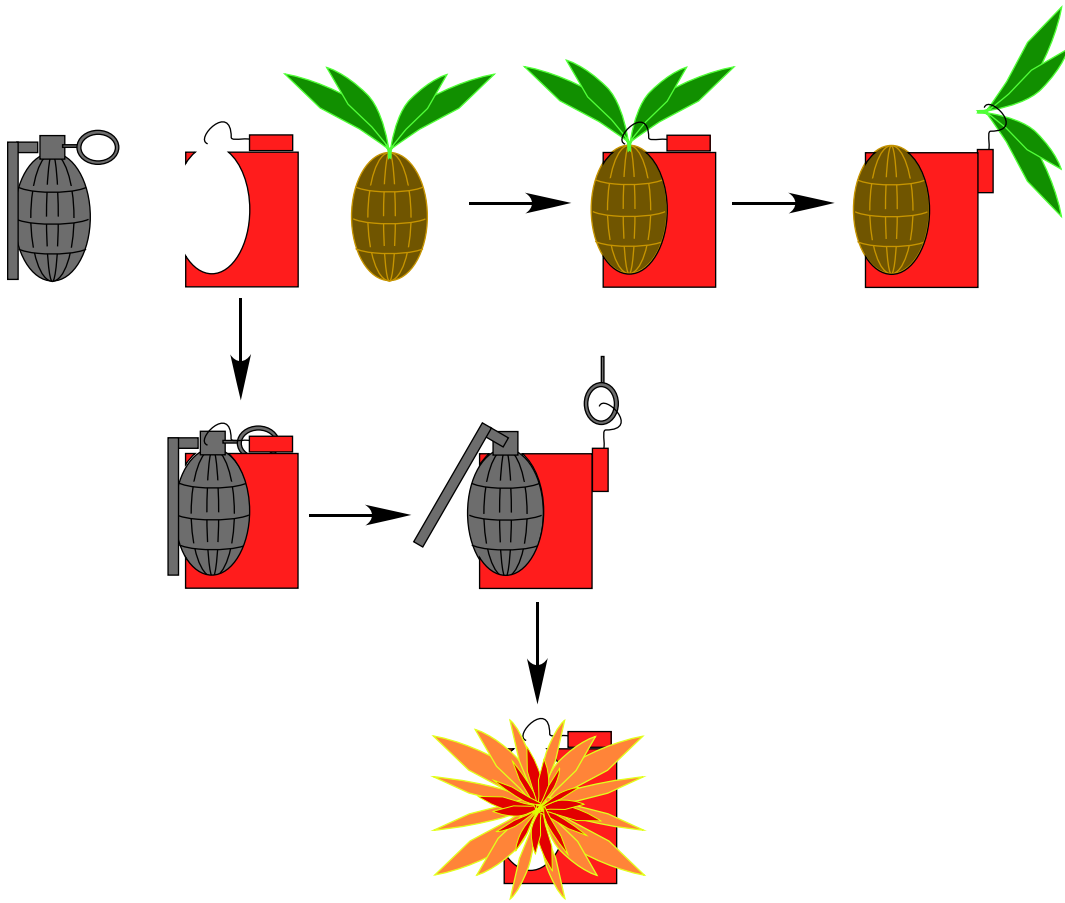


Pyrrole  
2-carboxylate

## Suicide Inhibition

### *Acetylcholinesterase*

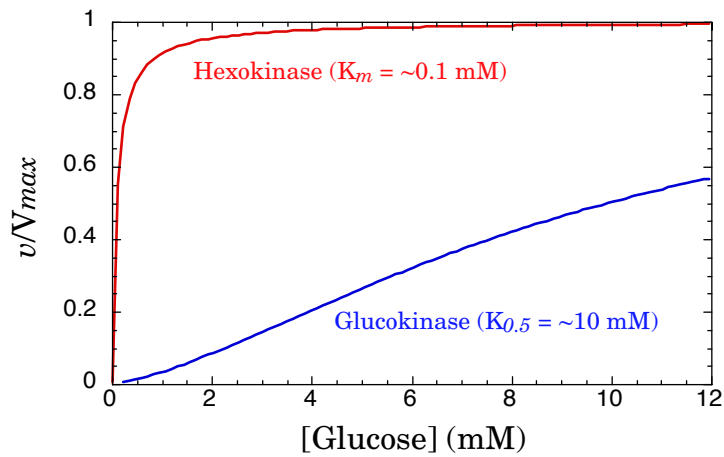
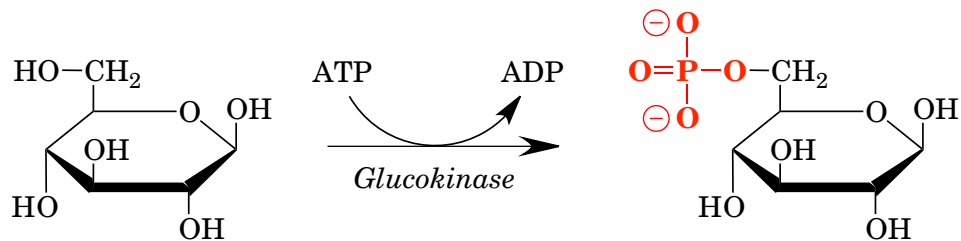
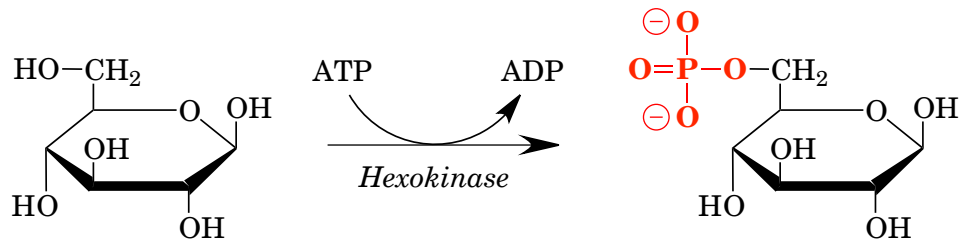




# Enzyme Regulation

## Genetic level control –

### Isozymes



### Control of existing enzymes

- 1.
- 2.
- 3.
- 4.

# Allosteric control

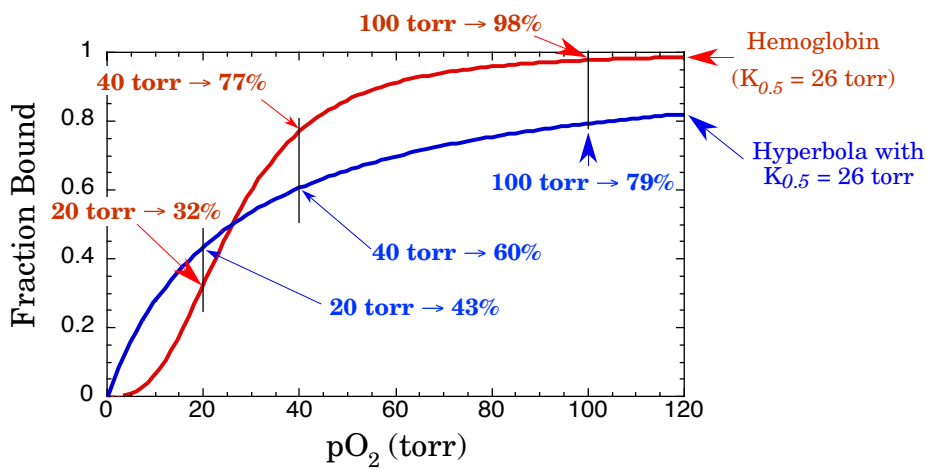
K-type

V-type

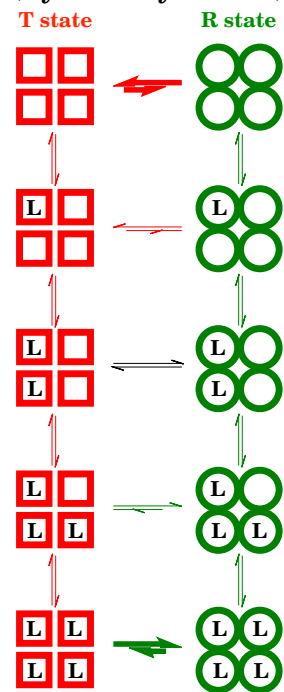
Cooperativity

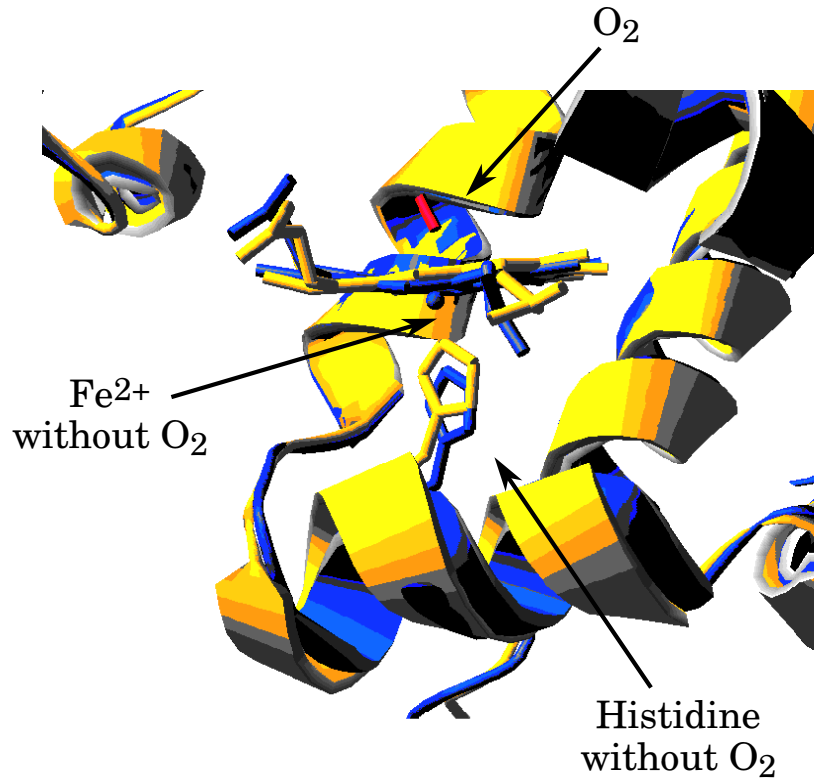
$$[B] = \frac{B_{\max} [F]}{K_d + [F]}$$

$$[B] = \frac{B_{\max} [F]^n}{K_{0.5}^n + [F]^n}$$



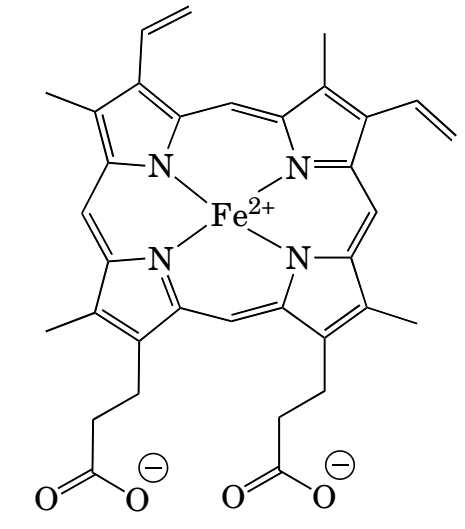
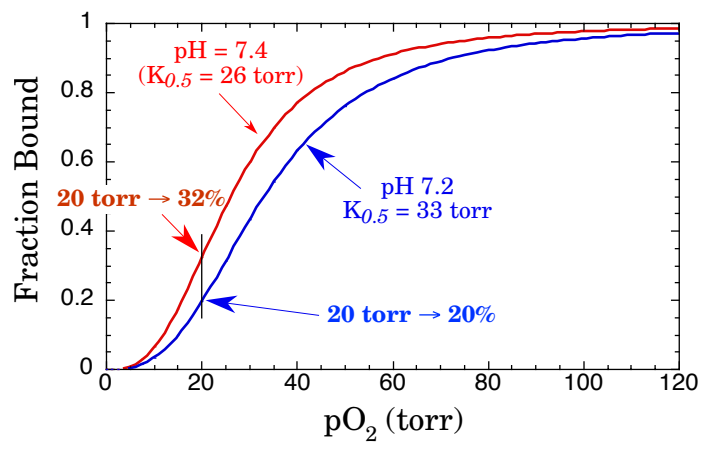
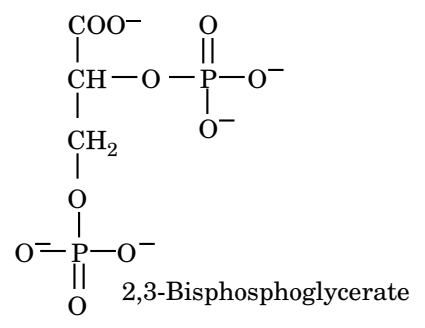
## Monod-Wyman-Changeux (Symmetry Model)





DeoxyHb

OxyHb



Heme *b*  
Iron-Protoporphyrin IX