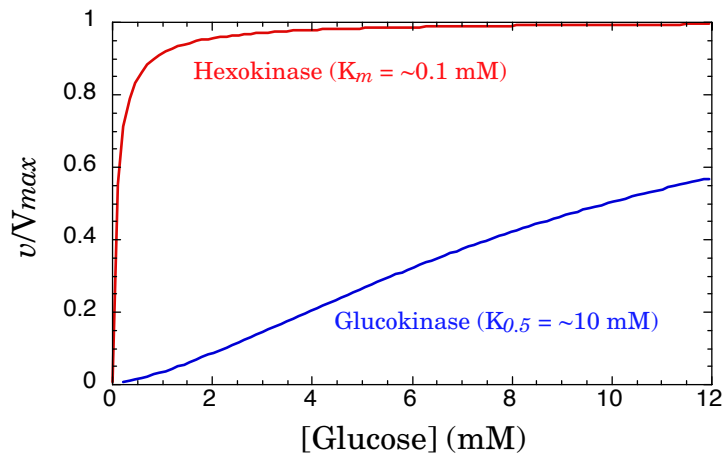
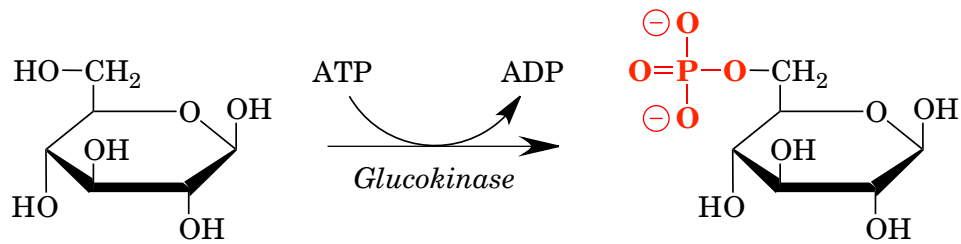
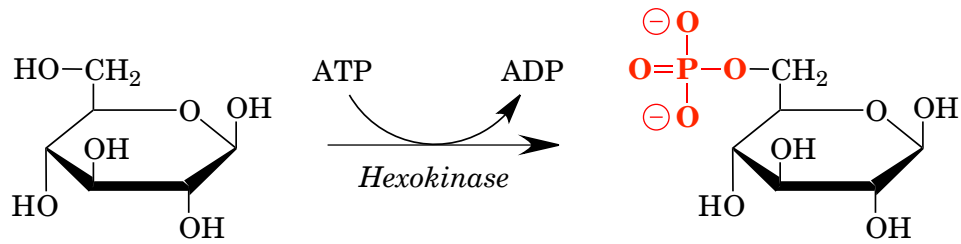


Enzyme Regulation

Genetic level control –

Isozymes



Control of existing enzymes

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

Allosteric control

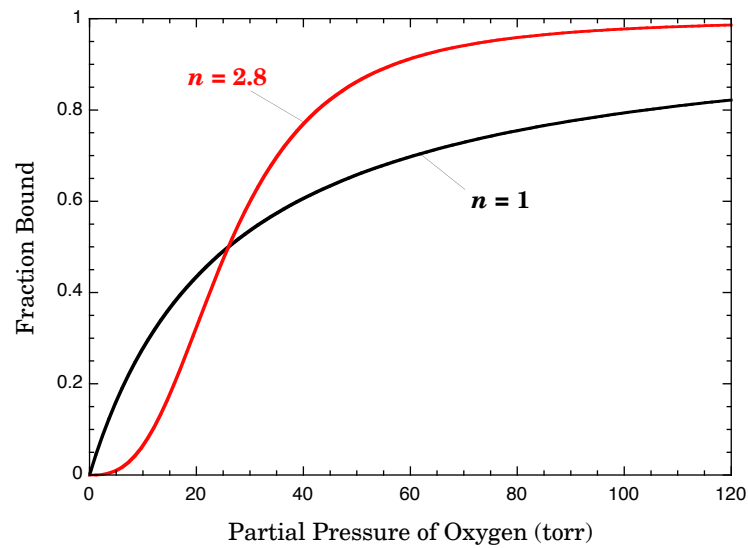
K-type

V-type

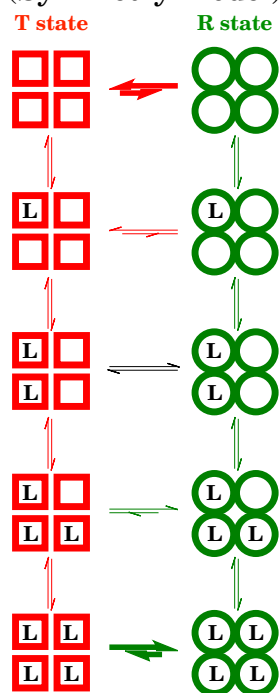
Cooperativity

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

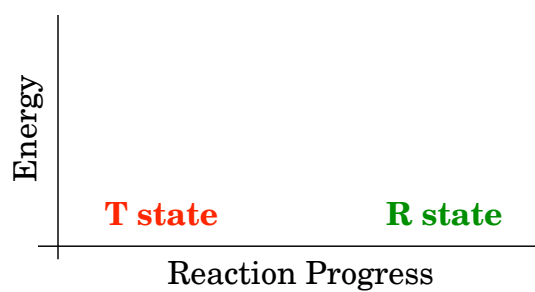
$$[B] = \frac{B_{\max} [F]^n}{K_{0.5}^n + [F]^n}$$



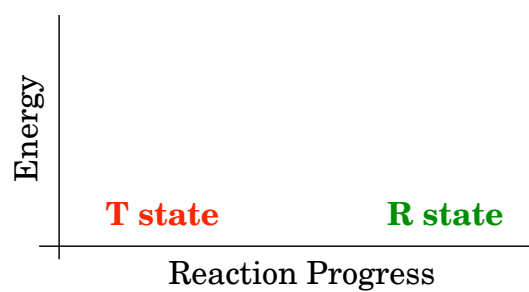
Monod-Wyman-Changeux (Symmetry Model)

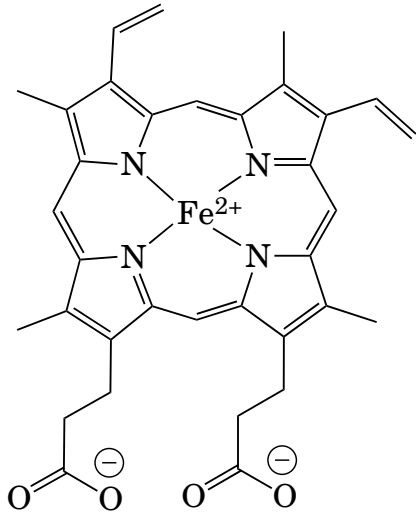


Without Ligand

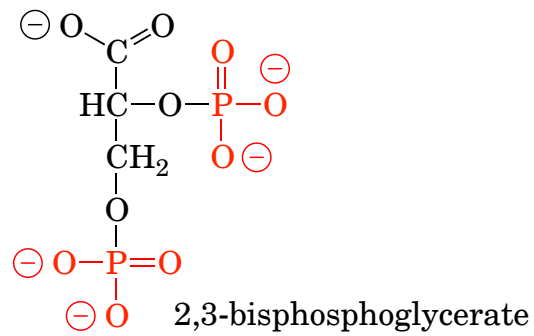
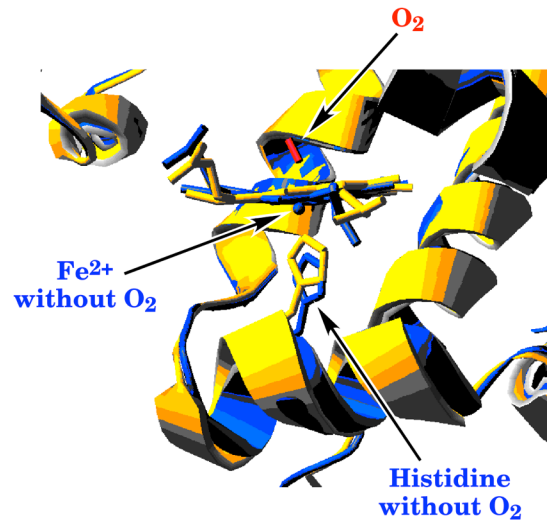


Ligand Bound

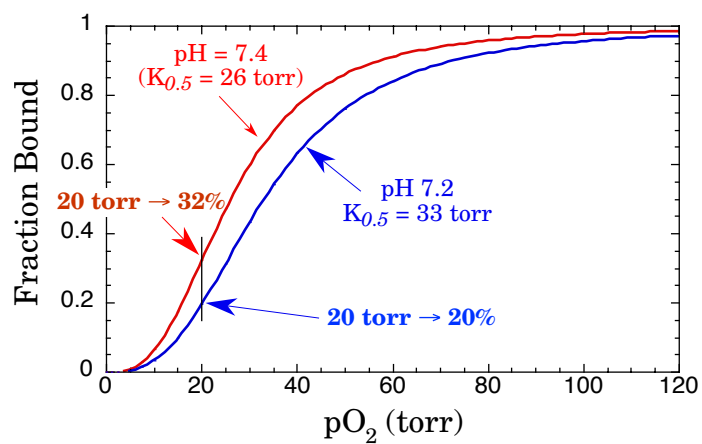




Iron-Protoporphyrin IX

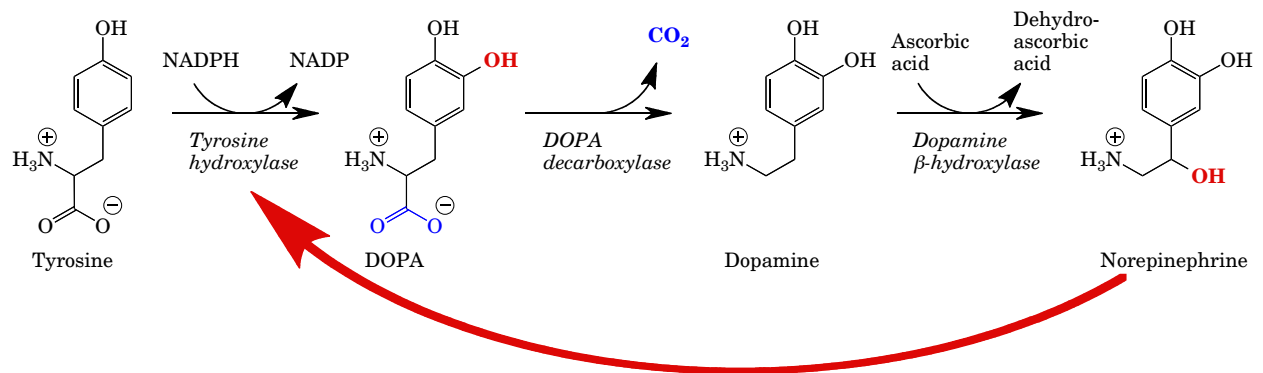


Bohr Effect:

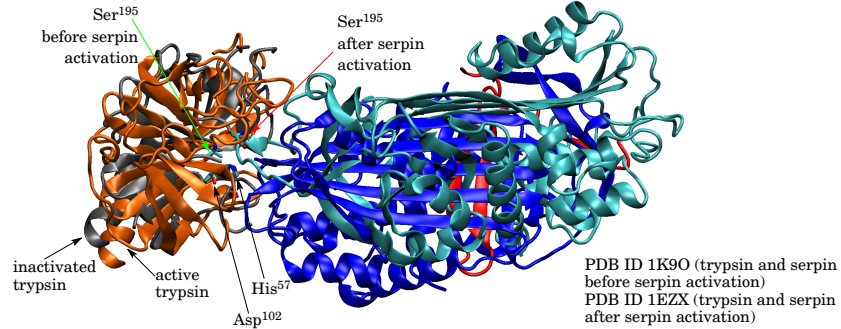


Enzyme Inhibition

Physiological processes -- Pathway regulation



Physiological regulation -- Pancreatic trypsin inhibitor, serpins

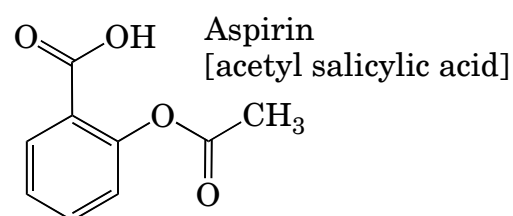
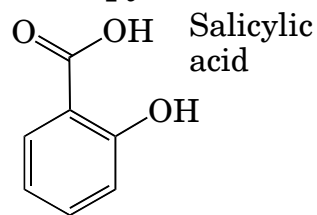


Science

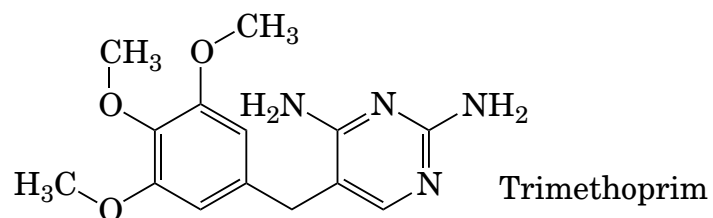
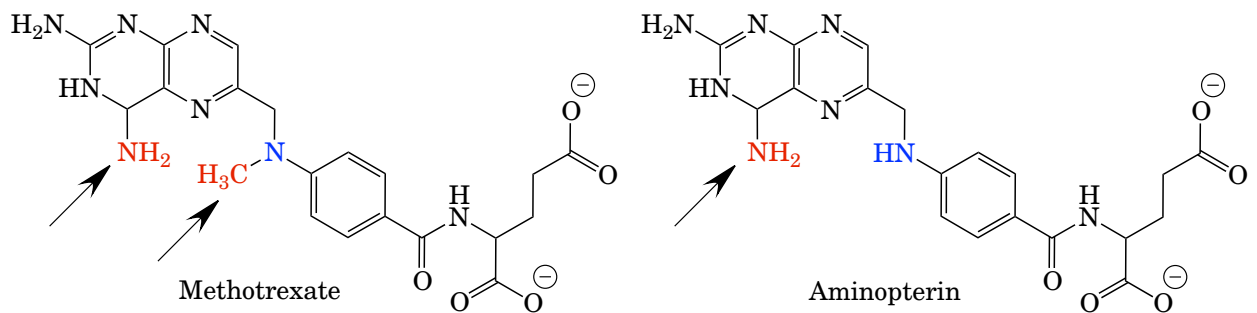
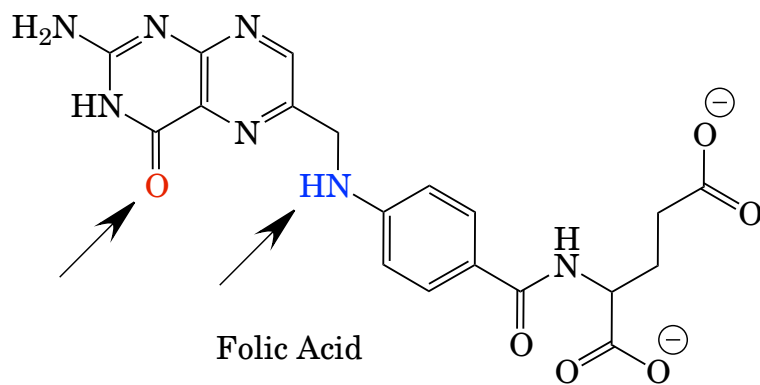
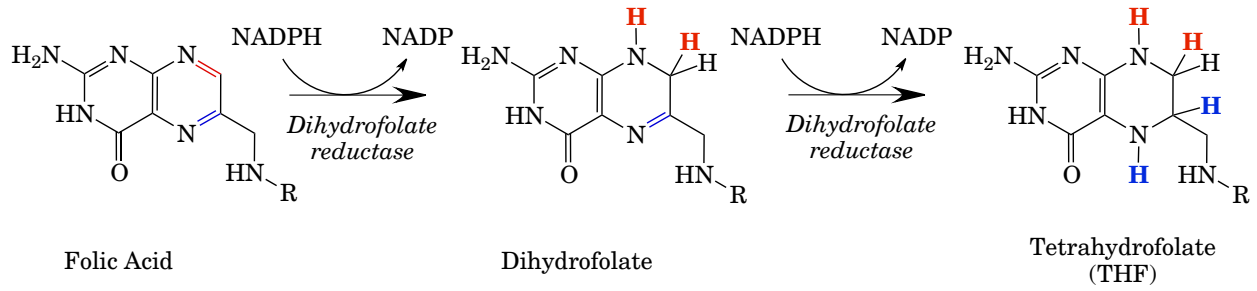
Enzyme mechanism probes

Probes for understanding metabolic pathways

Therapy

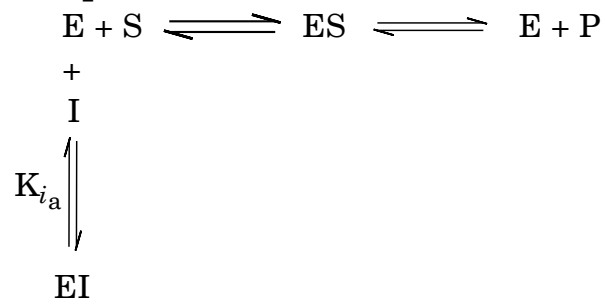


Therapeutic Inhibitors



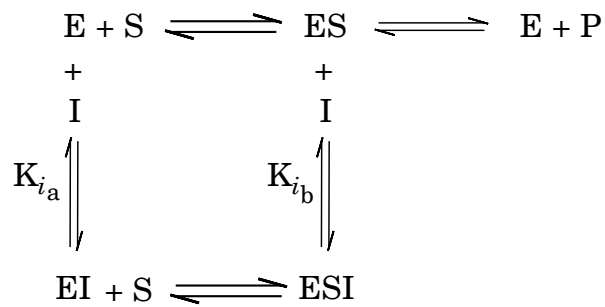
Reversible Inhibition

Competitive Inhibition



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

Mixed Inhibition



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

“Non-competitive” Inhibition

“Uncompetitive” Inhibition

Determining Inhibition Type

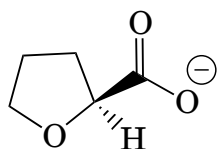
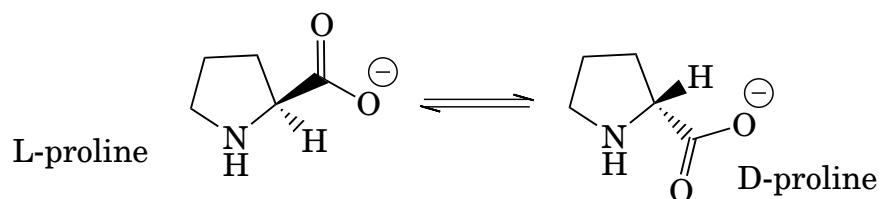
$$v = \frac{V_{max} [S]}{K_m + [S]}$$

$$v = \frac{V_{max_{app}} [S]}{K_{m_{app}} + [S]}$$

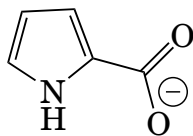
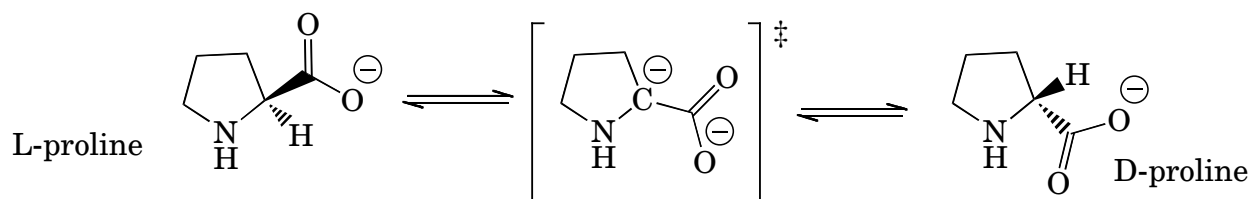
Type of Inhibition	$K_{m_{app}}$	$V_{max_{app}}$
None	K_m	V_{max}
Competitive (Inhibitor only binds to free enzyme)	$K_m \left(1 + \frac{[I]}{K_{i_a}} \right)$	V_{max}
Mixed (Inhibitor binds E and ES)	$K_m \frac{\left(1 + \frac{[I]}{K_{i_a}} \right)}{\left(1 + \frac{[I]}{K_{i_b}} \right)}$	$\frac{V_{max}}{\left(1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

Introduction to Inhibitor Design

Proline racemase

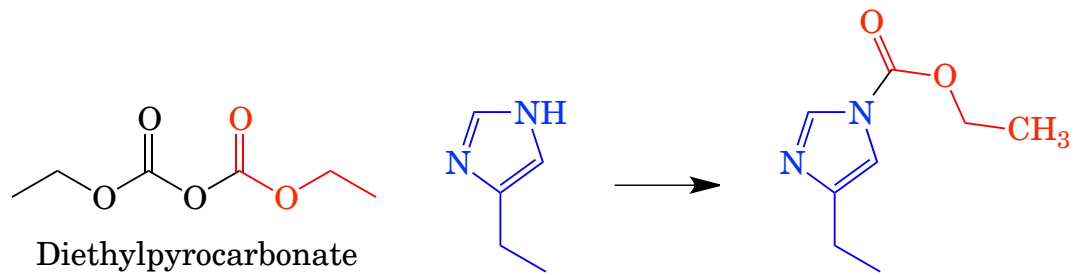


Tetrahydrofuran
2-carboxylate



Pyrrole
2-carboxylate

Irreversible Inhibition



Suicide Inhibition

Acetylcholinesterase

