

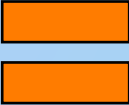
# Enzyme kinetics - Inhibition and Regulation

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# Inhibitors - Kinetics

## Competitive


- Bind SAME SITE

•  $V_{max}$  

•  $K_m$  

## Non-competitive

- Bind DIFFERENT SITE

•  $V_{max}$  

•  $K_m$  

# Inhibitors - Kinetics

## Competitive

- Effect on plot
  - Intersect on Y-axis unchanged
  - **X-axis point moves closer to 0**
- E.g. Statin drugs
  - HMG-CoA reductase
- E.g. Beta-blockers
  - Receptor-inhibitors

## Non-competitive

- Effect on plot
  - Intersect on X-axis unchanged
  - **Intersect on Y-axis increased**
- E.g. Heavy metal ions (Lead)

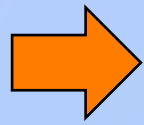
# Suicide inhibitors

- Irreversible inhibition of enzymes
- Bind active site by ***covalent bonds***
- Examples:
  - Aspirin – binds COX-1 and COX-2
    - Inhibits PGs and TXA synthesis → Reduced inflammation
    - Adverse effect: irritation of gastric mucosa

# Regulation

- Allosteric regulation
  - Effectors (positive/negative) bind noncovalently
  - Homotropic: Substrate = effector
    - E.g. O<sub>2</sub> for Hb
  - Heterotropic: Substrate ≠ effector
    - Feedback inhibition
    - E.g. 2,3-BPG for Hb
- Covalent modification
  - Most frequently: Phosphorylation/dephosphorylation

# Allosteric control of enzyme activity requires:



- A conformational change in an enzyme that changes its conformational activity
- The conversion of one form of the enzyme to another by the action of proteolytic enzymes
- A metal ion
- A cofactor derived from a vitamin
- An effector that is the product of an enzymatic reaction and which competes for the active site of the enzyme