# Notes 11/5

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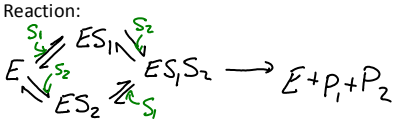
Monday, November 05, 2007
9:58 AM

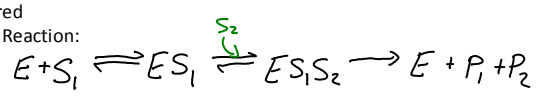
Notes 115

Audio recording started: 10:01 AM Monday, November 05, 2007

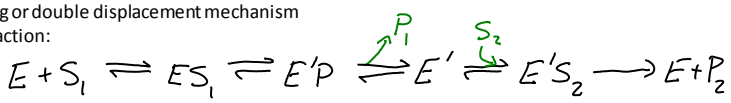
- **Slide 1: Enzymes: Regulation**
  - Nov. 5, 2007
- **Slide 2: Announcements**
  - Extra Credit
  - VOH
  - Office Hours
  - Midterm
    - 50 min
    - True false
    - Multiple choice
    - Fill in the blank
    - Draw something
    - Math
    - 6 pages long
    - Nonprogrammable calculator
    -
- **Slide 3: Bisubstrate reactions**
  - Hexokinase has 2 substrates
  - ATP + Glucose $\xrightarrow{\text{hexokinase}}$ ADP + glucose 6-phosphate
  - Mechanisms:
    - Ternary Complex
      - Random
        - Reaction:



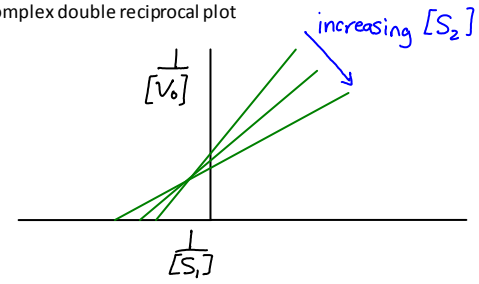
      - Ordered
        - Reaction:

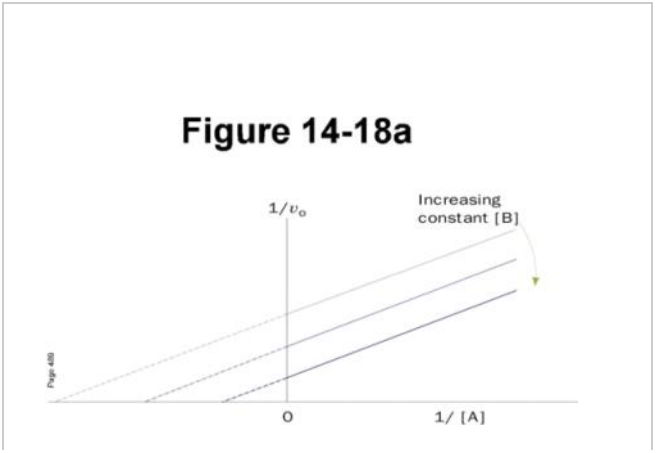


    - Ping-pong or double displacement mechanism
      - Reaction:



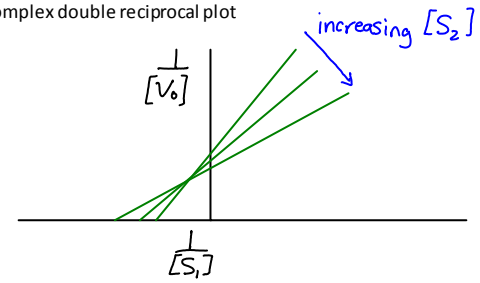
  - We use steady state kinetics and double reciprocal plots to determine the type of mechanism in a reaction
- **Slide 5: Figure 14-18a**
  - Graph
  - Ternary complex double reciprocal plot

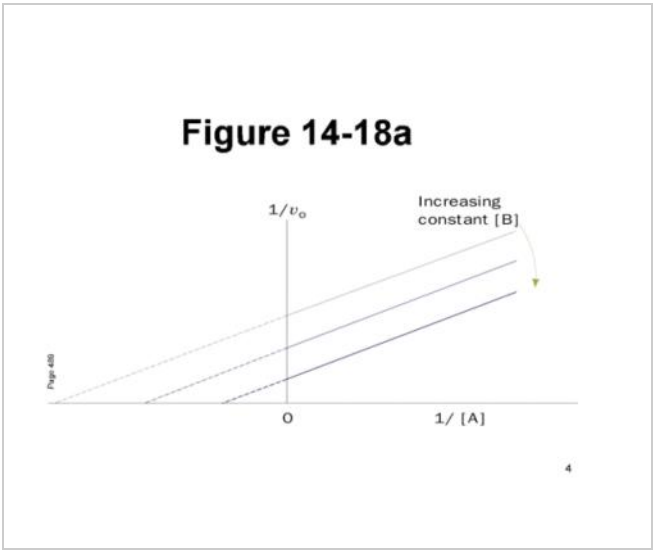



- **Slide 6: Enzymes are subject inhibition**
  - Enzyme inhibitors
    - molecular agents

- **Slide 5: Figure 14-18a**
  - Graph
  - Ternary complex double reciprocal plot




- **Slide 6: Enzymes are subject inhibition**
  - Enzyme inhibitors
    - molecular agents
    - Interferes with catalysis
      - Prevent reaction
      - Or slow down reaction
    - 2 Classes
      - Reversible inhibitors
        - Subclasses:
          - Competitive

$$E + S \rightleftharpoons ES \rightarrow E + P$$
$$+ I \Downarrow K_I \quad EI \qquad K_I = \frac{[E][I]}{[EI]}$$

$$V_0 = \frac{V_{max}[S]}{\alpha K_m + [S]} \qquad \alpha = 1 + \frac{[I]}{[K_I]}$$

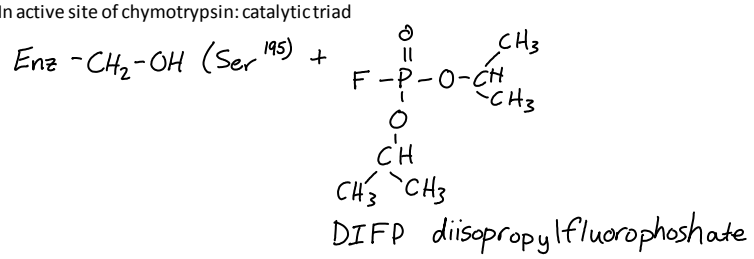
- Under competitive inhibition:
  - No effect on $V_{max}$
  - $K_m$ increases
  - When [S] is much greater than [I], normal Vmax

- Uncompetitive

- $E + S \rightleftharpoons ES \rightarrow EP$, $+ I \Downarrow K_I'$, $ESI$ $\qquad K_I' = \frac{[ES][I]}{[ESI]}$
- $V_0 = \frac{V_{max}[S]}{K_m + \alpha'[S]} \qquad \alpha' = 1 + \frac{[I]}{K_I'}$
  - At higher [S] $\quad V_0 = \frac{V_{max}}{\alpha'}$
  - lowers $V_{max}$
  - Decreases $K_m$

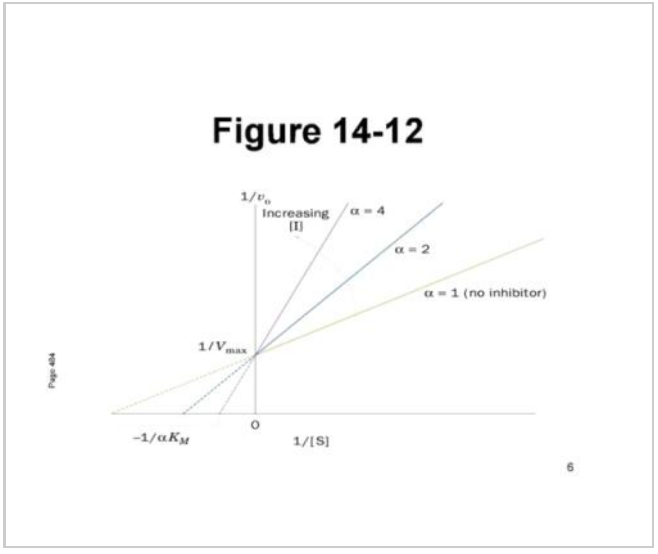
- Mixed
- $E + S \rightleftharpoons ES \rightarrow EP$, $+ I \Downarrow K_I$ on E, $+ I \Downarrow K_I'$ on ES, $EI + S \rightleftharpoons ESI$
- $V_0 = \frac{V_{max}[S]}{\alpha K_m + \alpha'[S]}$
  - $V_{max}$ is affected
  - $K_m$ is not affected

- Irreversible
  - Molecular agent
  - Will destroy catalysis
    - Bind to active site (usually covalently linked)
    - Change function group in active site
    - Irreversible inhibition with chymotrypsin
      - Synthesized in pancreas as inactive (zymogen)
      - Function: cleaves peptide bonds
      - In active site of chymotrypsin: catalytic triad

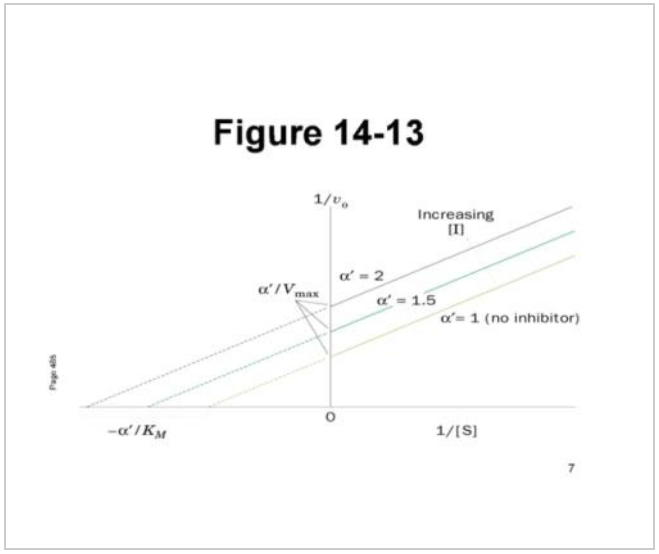



    - Suicide inactivator
      - Aka mechanism-based inactivators
      - Very important in drug design

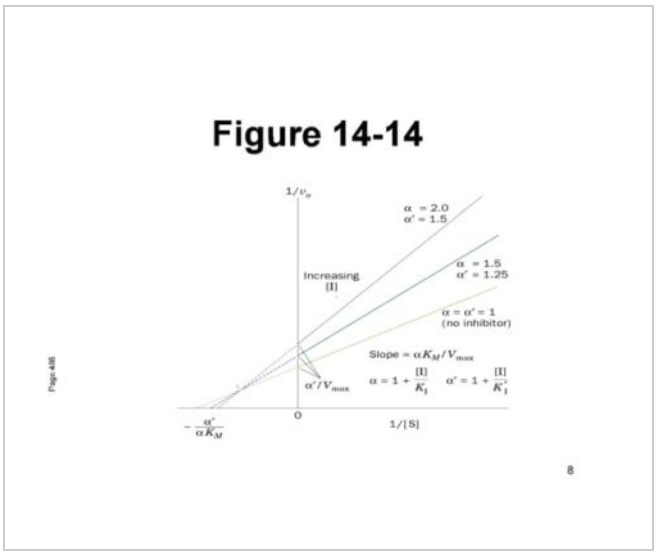
- **Slide 8: Figure 14-12**
  - Graph
    - Competitive inhibition



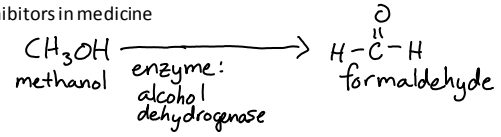

- **Slide 9: Figure 14-13**
  - Graph
    - Noncomptitive (parallel lines)
    - Do not mix up with ping pong

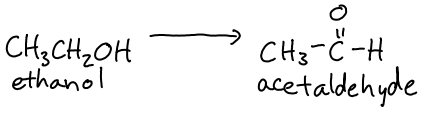



- **Slide 10: Figure 14-14**
  - Graph
    - Mixed




- Slide 11
  - Irreversible Inhibition
    - See outline above
  - Inhibitors in medicine




Example of competitive inhibition

  - Regulatory enzymes
    not enough time… did not cover