RATE LIMITING

$$E + S \stackrel{\mathrm{k}_1}{\rightleftharpoons} ES \stackrel{\mathrm{k}_2}{\rightleftharpoons} EP \stackrel{\mathrm{k}_3}{\rightleftharpoons} E + P \stackrel{\mathrm{k}_3}{\rightleftharpoons} E + P$$

- One of the steps will be rate limiting
 - ▶ Takes the longest amount of time to complete
- Typically in an enzyme catalyzed reaction, it is the conversion of the substrate to the product.
- Equilibrium must also be considered in these reactions
 - As first, a lot of enzyme will bind to the substrate
 - As the concentration of ES builds up (due to the rate limiting step) some of the ES will convert back to E+S
 - ▶ While this must also be considered for the presence of EP and E+P, the conversion of product back to the EP is minimal due to the low activation energy for its dissociation and because the product is often used immediately in another reaction in a cell.
 - ▶ The substrates high affinity for the enzyme also plays a role

K₂ = RATE DETERMINING STEP

$$E+S \stackrel{\mathrm{k}_1}{\rightleftharpoons} ES \stackrel{\mathrm{k}_2}{\rightleftharpoons} EP \stackrel{\mathrm{k}_3}{\rightleftharpoons} E+P \stackrel{\mathrm{k}_3}{\rightleftharpoons} E+P$$

- k_2 = Rate Determining Step
- k_2 = Rate of Catalysis ($k_2 = k_{cat}$)
- ▶ We get a build-up of enzyme-substrate complex (sitting there waiting to be used)
- The slowest step is the rate determining step
- ▶ The process of converting enzyme-substrate complex into enzyme + product = the rate determining step in Michaelis-Menten Kinetics
- In a Multi-Step Reaction, the slowest step or smallest reaction rate constant determines the overall reaction rate.