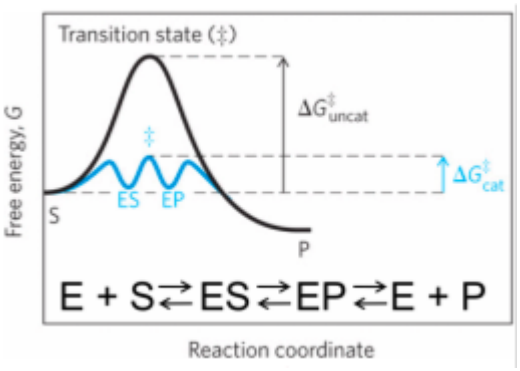
# Enzymes

Learning outcomes:
- Explain how enzymes speed up chemical reactions
- Discuss why enzymes are important in biology, medicine and industry
- Define the following terms: enzyme, active site, activation energy, transition state, initial state, steady-state kinetics, $K_m$, and $V_{max}$
- Explain how to experimentally determine $K_m$ and $V_{max}$
- Calculate the enzyme activity from the experimental data

**Enzymes:** biomolecules with distinctive 3-D structure which catalyzes reactions so a lower activation energy is needed to convert a substrate to a product
**Active site:**
**Activation energy:**
**Transition state:**
**Initial state:**
**Steady-state kinetics:**
**$K_m$:** [S] at ½ $V_{max}$
**$V_{max}$:**

How enzymes work

- Employ catalytic mechanisms such as weak interactions, acid-base, covalent & metal ion catalysis
- Provide specific environment in the active site for a reaction to proceed faster compared to the uncatalyzed or spontaneous reaction
- Active sites lined with functional group (amino acids) that binds to the substrate and catalyze the chemical transformation to the product
- Affect reaction rate but not equilibria
- Lowers activation energy required to convert substrate to product and perform this with a high degree of specificity
- Form complex with substrate (ES)
- Enzyme catalysis = stabilization of the transition state through tight binding to the enzyme -William P. Jencks (1975)
    - Transition state is unstable-metastable
    - It cannot be isolated and concentration cannot be measured
    - Enzyme works by stabilizing this transition state
    - It binds tightly due to specificity to the substrate and this lowers the activation energy- more stable= lower energy
    - Formation of bonds of substrate with enzymes lowers energy of the transition state
    - Rate of reaction depends on the height of the barrier, lower barrier means reaction is faster




## Importance of enzymes

- Disease is caused by imbalance of enzymatic activity (excessive or deficient)
- Example: Phenylketonuria (PKU)
    - Cause: deficiency in enzyme *Phenylalanine Hydroxylase*
    - Incidence: autosomal recessive, 1 in 8000-10 000 newborns
    - Clinical symptoms: severe mental retardation
    - Biochemical symptoms: increased concentrations of phenylpyruvate (keto acid of Phe) in blood and urine
    - Treatment: decrease phenylalanine in diet
- Drugs: target enzymes by either inhibiting or activating the enzyme target
    - Example: relenza (carbohydrate that binds with neuraminidase) inhibits neuraminidase enzyme in flu virus

## Common Types of Enzymes

- **Kinase (K)** - catalyzes phosphoryl transfer from one molecule (usually ATP) to another; eg. Hexokinase
    - Glucose + ATP -> Glucose-6-Phosphate + ADP
    - Phosphate from ATP transferred to glucose
- **Phosphorylase (P'Lase)** - catalyses covalent addition of inorganic phosphate (Pi) to a molecule;
  e.g. Glycogen Phosphorylase = attach phosphate to glucose molecules in glycogen, releasing glucose 1-phosphate molecules from glycogen
    - Inorganic phosphate, not ATP
    - Use phosphate to break bonds and chop off molecule
- **Phosphotase (P'Tase)** - Catalyzes cleavage of a phosphate to yield the dephosphorylated product and Pi; e.g. Glucose-6-Phosphatase
  G-6-P'Tase
    - G-6-P ----------→ Glucose + Pi
    - Opposite of enzyme kinase
    - Takes of phosphate