Enzymes - Basic Concepts and Kinetics I

OUTLINES
Enzymes as Catalysts
Enzyme rate enhancement / Enzyme specificity
Enzyme cofactors

Free Energy
G determines the direction a reaction proceeds
If G <0, the reaction proceeds forward as written
If G >0, the reaction proceeds backward as written
If G = 0, the reaction is at equilibrium
Note that equilibrium DOES NOT mean equal concentrations of reactants and products.
Rather, equilibrium means that the concentration of reactants and products does not change over time.

G0'
G0' is related to G. It is the same as G under standard conditions
Thus, the sign of G0' determines the direction of a reaction ONLY under standard conditions.
G determines the direction of a reaction under any conditions, including standard conditions.

Calculations
G = G0' + RT ln[Products]/[Reactants], w R is the gas constant and T is the temperature in Kelvin
At equilibrium, G = 0, so G0' = -RT ln[Products]/[Reactants] = -RT ln K'eq
Thus, G0' is related to the equilibrium constant for a reaction
Relation between G0' and K'eq at 25°C

Mechanisms
Enzymes speed reactions
Enzymes act by decreasing activation energy
Reaction velocity versus substrate concentration
Residues at active site / Hydrogen bonds with substrate
Fischer lock&key model of catalysis / Koshland induced fit model

Michaelis-Menten Model
Initial velocity determination
KM determination
LineWeaver-Burk plot
KM values of some enzymes / Turnover numbers
Substrate preferences of chymotrypsin
Diffusion-controlled enzymes

Multiple Substrate Reactions
Sequential displacement
Ordered example / Schematic
Random example / Schematic

Double displacement

Allosteric enzyme kinetics
Enzyme Inhibition

Uninhibited vs. Competitive vs. Uncompetitive vs. Non-Competitive
Methotrexate and Tetrahydrofolate
Kinetics of a competitive inhibitor (V vs. [S]) and (Lineweaver-Burk)
Kinetics of a non-competitive inhibitor (V vs. [S]) and (Lineweaver-Burk)
Serine modification by DIPF

Suicide inhibition
- Triose phosphate isomerase by bromoacetal phosphate
- Glycopeptide transpeptidase by penicillin

HIGHLIGHTS
Enzymes I

1. Enzymes are proteins that catalyze reactions. 
2. Enzymes are capable of speeding reactions quadrillions of times faster than the same reactions would occur in the absence of enzymes.
3. Substrate(s) are molecules that are affected by the catalysis of the enzyme
4. Substrates bind to a substrate binding site on an enzyme and this overlaps with the active site - the place on the enzyme where a reaction occurs.
5. Steps in catalysis include a) binding of the substrate(s) by the enzyme to form the ES complex; b) reaction between the substrate(s) at the active site (ES* complex); c) completion of the reaction (EP complex), and d) release of the product(s) by the enzyme.
6. The enzyme undergoes a change upon binding the substrate(s) and that is the key to the many fold enhancement of the reaction by the enzyme. (FLEXIBILITY)
7. Enzymes exhibit binding specificity - substrates have specific shapes and though a range of shapes may be accepted, the range is usually quite narrow.
8. Enzymes are flexible and their flexibility plays a major role in catalysis
9. Changes in enzyme shape and/or changes resulting from substrate binding affect/change the electronic environment of the enzyme and ultimately the active site.
10. Non-proteinaceous molecules that bind to enzymes and help the enzymes to catalyze reactions are called coenzymes.
11. Two models of enzyme action are a) the Fischer Lock and Key model and b) the Koshland Induced Fit model
12. The Fischer Lock and Key model states that a substrate fits into an enzyme like a key into a lock. It helps describe the specificity of substrate binding, but nothing of the mechanism of catalysis.
13. The Koshland Induced Fit model says that an enzyme changes substrate(s) into product(s) and that the substrate(s) transiently changes an enzyme, thus providing a mechanism of catalysis.
14. Changes in the enzyme on substrate binding create "tensions" or "stresses" that help to stimulate the catalytic process. These tensions can be electronic or mechanical in nature.
15. Chemical reactions require activation energy (I'll call it ΔG+) in order to get started. Catalysts (both enzymes and non-biological catalysts) act by lowering ΔG+. Catalysts DO NOT CHANGE ΔG. All they do is lower the energy required to activate the reaction. While enzymes speed reactions immensely, they therefore DO NOT CHANGE THE OVERALL REACTION CONCENTRATION AT EQUILIBRIUM. They simply allow the reaction to get to equilibrium faster.
16. Reactions catalyzed by enzymes are reversible.
17. At equilibrium, the concentration of reactants and products do not change. ONLY if \( \Delta G^\circ \) is zero can one say that \([A] = [B]\) for a reaction \( A \leftrightarrow B \).

18. Reactions can be a) single substrate - single product; b) single substrate - multiple product; c) multiple substrates - single products; and d) multiple substrates - multiple products.

19. Multiple substrate - multiple product reactions are of three types
a) ordered - order of binding of substrates required for reaction - lactate dehydrogenase example
b) random - order of binding of substrates not required for reaction - creatine kinase example
c) Ping-Pong - the enzyme flips between two different states in its catalytic action - transaminase example

19. For an enzyme reaction, \( E+S \leftrightarrow ES \leftrightarrow ES^* \leftrightarrow EP \leftrightarrow E+P \)

20. For a simple case of \( ES \to E+P \), then \( K_{cat} \) is the rate constant for the reaction and is what we aim to determine