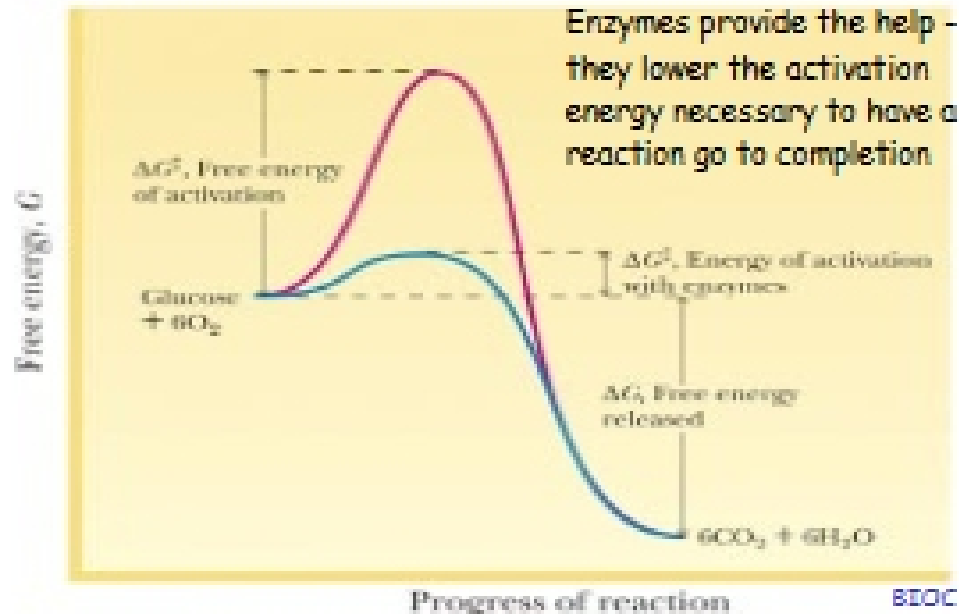


Lecture 12: Enzymes & Kinetics I

Introduction to Enzymes and Kinetics

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Fall 2003

THERMODYNAMIC POTENTIALITY: reaction is strongly exergonic; but doesn't occur under "normal" conditions. It needs help...



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ENZYMES: Why, what, when, where, how?
All but the who!

What: proteins that exert kinetic control over biological reactions

Why: We need to have chemical reactions occur on a biologically relevant time scale (recall the example from lecture 1)

When: At appropriate times during metabolic processes (brings us to the idea of biological regulation - lecture 16).

Where: Where ever chemistry needs to be accomplished in the body

How: Through the bringing together of reactive groups on the enzyme with the substrates that need to have chemistry performed on them.

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What is an enzyme?

General Properties

- Mostly proteins, but some are actually RNAs
- Biological catalysts
 - Higher reaction rates
 - Milder reaction conditions
- Great reaction specificity
- Capacity for regulation
- Not changed or used up after a reaction
- Nomenclature: frequently add -ase

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KEY FEATURES OF ENZYMES

CATALYTIC POWER: ratio of catalyzed reaction rate to uncatalyzed reaction rate; enzymes accelerate reactions as much as 10^{20} ; important to note that they do this under physiological conditions (pH 7, 37C, H₂O)

Table 3. Catalytic Power of Some Enzymes

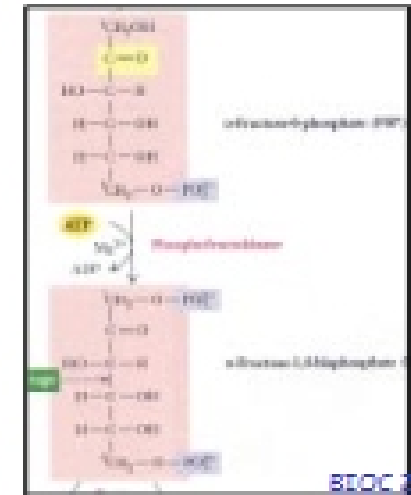
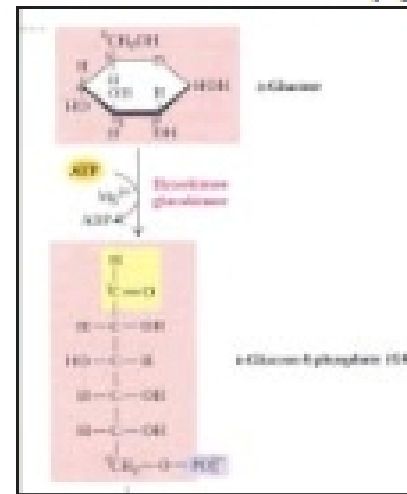
Enzyme	Noncatalyzed Reaction Rate (s ⁻¹)	Enzymatic Reaction Rate (s ⁻¹)	Rate Enhancement
Carbonic dehydratase	1.3×10^{-5}	1×10^7	7.7×10^{11}
Acetate kinase	2.6×10^{-13}	80	3.0×10^{15}
Acetylcholinesterase	4.3×10^{-9}	4500	1.0×10^8
Catalase	1.0×10^{-4}	178	1.8×10^{11}
Chloride	1.0×10^{-11}	60	6.0×10^{11}
Hexokinase	1.7×10^{-16}	95	5.6×10^{15}

see Table 3.1 of Molecular Biology of the Cell 6E (© Garland Science 2015)

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KEY FEATURES OF ENZYMES

SPECIFICITY: Enzymes are selective about their substrates (also called ligands, reactants) and the chemistry they carry out (active sites are specialized for both the reactant and the chemistry). There are no wasteful by-products.



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KEY FEATURES OF ENZYMES

REGULATION: Enzymes should only function when needed. They are exquisitely regulated at the level of DNA, by interactions with inhibitors and activators, by product feed-back inhibition.....

Glycogen Phosphorylase

1) Response to fuel needs:

High fuel state:

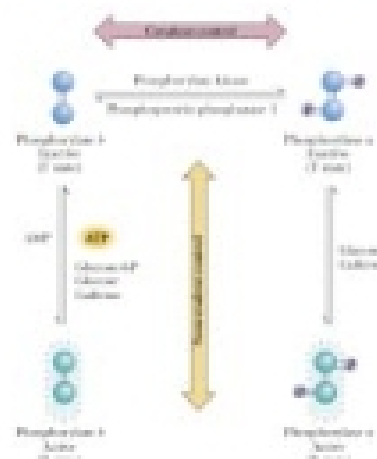
- Enzyme "off"
- high ATP
- high Glucose
- high G6P

Low fuel state:

- Enzyme "on"
- high AMP
- low ATP

2) Covalent modification:

- Stress situation
- Molecule on!



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Enzymes as Catalysts

the take home points

- Enzymes **DO NOT** change the equilibrium constant of a reaction
- Enzymes **DO NOT** alter the amount of energy consumed or liberated in a reaction (ΔH):
- Enzymes **DO** increase the rates of reactions that are otherwise impossible;
- Enzymes **DO** decrease the activation energy (ΔG^\ddagger):

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Enzymes

- Enzymes are protein catalysts
 - Bind the substrates
 - Lower the **activation energy**
 - Directly promote the catalytic events

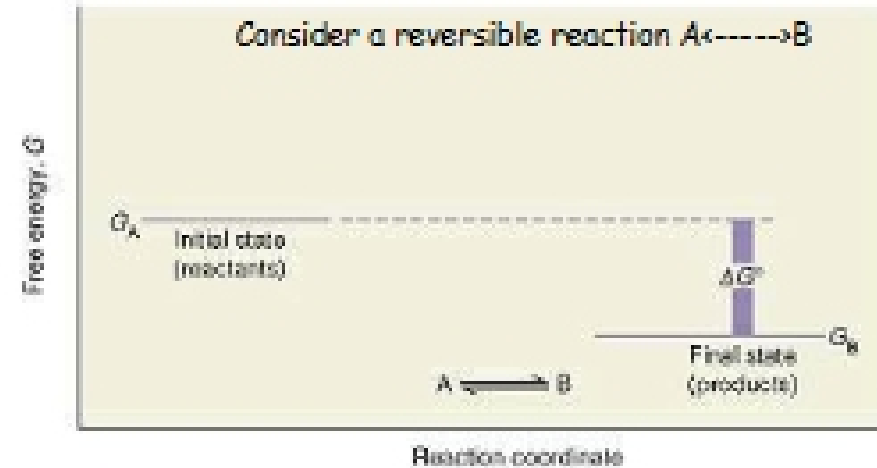
Catalyst enhancement	Rate
Non-enzymatic (metals)	$10^2 - 10^4$ fold
Enzymatic	up to 10^{20} fold

How much is 10^{20} fold?

- with a catalyst, the reaction takes place in 1 sec
- without a catalyst, 3×10^{12} years!

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Transition State and Free Energy

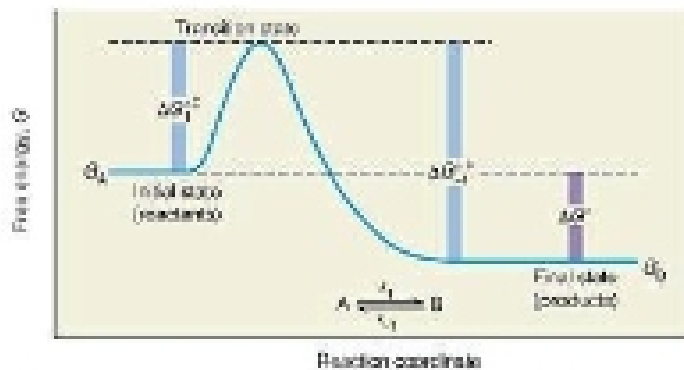


(a)

Thermodynamics tells it will proceed in the direction of B

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Transition State and Free Energy



Transition state theory provides information on ΔG^\ddagger and says that ΔG_{-1}^\ddagger is smaller than ΔG_{-2}^\ddagger , thus reaction favors formation of B

ΔG^\ddagger = Free Energy of Activation determines the rate of reaction

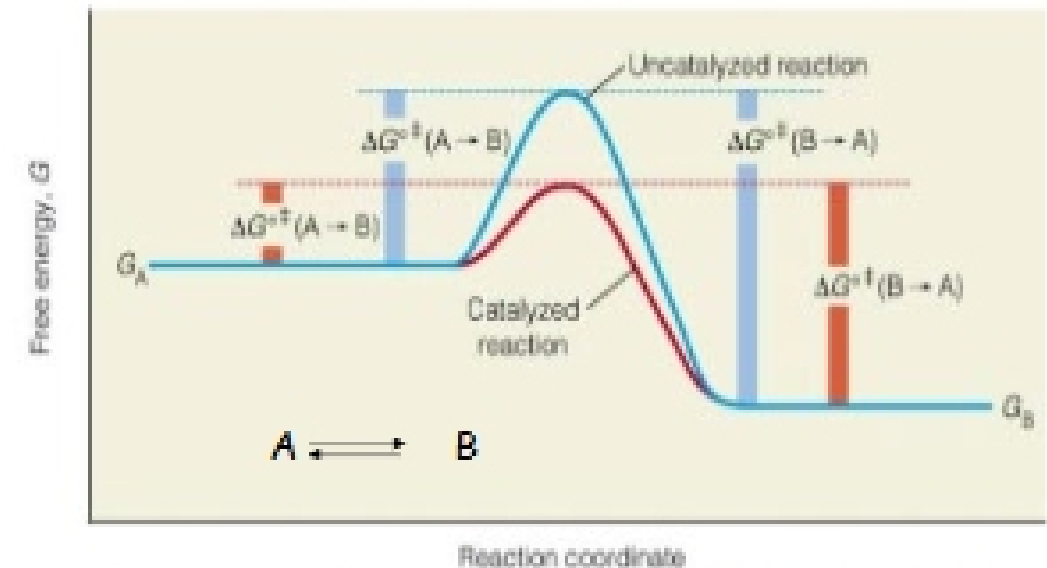
$$k = Ae^{-\Delta G^\ddagger/RT}$$

(Arrhenius Equation)

ΔG^\ddagger : rate is proportional to # of molecules that have this energy

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Catalytic Reactions



Do not raise energy of A
Catalysts (e.g. enzymes) act by **lowering the transition state free energy** for the reaction being catalyzed.

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