BIO 311C
Spring 2010

Your Exam 2 will be returned to you at the end of today's class period.

An answer key for Exam 2 will be posted before the end of today.

If you believe we have made any error in grading your Exam 2, please see Rebecca this week. We will not consider any requests for reconsideration of Exams 1 or 2 answers after 4:00 p.m. on Tuesday 30 March.

Lecture 21 – Monday 22 Mar.

Chemical Reactions in Living Cells

Definitions:

A chemical reaction that takes place within a living organism or within a living cell is called a <u>metabolic</u> <u>reaction</u>.

The sum of all chemical reactions that take place within a living organism or within a living cell is called the <u>metabolism</u> of the organism or of the cell.

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A chemical reaction might be written very simply as: $A \longrightarrow B$,

where A and B represent atoms, molecules or ions that participate in the reaction. Both A and B are then called substrates.

DEFINITION:
By convention, the substrate written on the left (A) is called a reactant, while the substrate written on the right (B) is called a product.

For the reaction written as: $W + X \longrightarrow Y + Z$,

W, X, Y and Z are all substrates,
W and X are reactants,
Y and Z are products.

Metabolic reactions operate under exactly the same set of chemical principles as reactions that take place in a chemistry laboratory.

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All chemical reactions are (in principle) reversible.

If the reaction: $A \longrightarrow B$ occurs,

then the reaction: $B \longrightarrow A$ can also occur,

In general it is possible to know the characteristics of any reaction by knowing corresponding characteristics of its reverse reaction.

Thus the reaction can be written more meaningfully as:

$$A \rightleftarrows B$$

A is the reactant while B is the product in the reaction as shown above, but the reaction could just as well have been written as $B \rightleftarrows A$, where B is shown as the reactant and A as the product.

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In this course we will consider two important aspects of chemical reactions, especially as they apply to metabolism.

1. **Today we will begin a consideration of energy changes that occur as reactions take place.**

   The study of changes in energy which occur during chemical reactions is a field of chemistry called <u>chemical thermodynamics</u>. These energy changes are called <u>chemical energetics</u>.

2. **Later we will consider the rates of chemical reactions and their relationships to mechanisms of reactions.**

   The study of these rates of chemical reactions is called <u>chemical kinetics</u>.

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Consider a chemical reaction in which substrate A is converted into substrate B:

$$A \rightleftharpoons B$$

Then do the following experiment:

1. Dissolve molecules of A, or molecules of B, or some mixture of the two, into a container of water under conditions that allow this reaction to occur. Maintain the temperature and other environmental factors under a standard set of condition (Temperature at 25°C, for example).

2. Wait until there are no more measurable changes in the concentrations of A or B with time. Then the reaction has come to equilibrium.

3. Calculate the equilibrium constant (abbreviated as K_{eq}) for the reaction after it has come to equilibrium as:

$$K_{eq} = \frac{[B]}{[A]}$$

where the brackets are read as "concentration of".

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For the reaction: $A \rightleftharpoons B + C$

$$K_{eq} = \frac{[B]\,[C]}{[A]}$$

For the reaction: $A + B \rightleftharpoons C + D$

$$K_{eq} = \frac{[C]\,[D]}{[A]\,[B]}$$

For a chemical reaction in general, K_{eq} can be written as:

$$K_{eq} = \frac{[\text{Products}]}{[\text{Reactants}]}$$

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The K_{eq} for a reaction is a measure of the tendency of the reaction to go in the forward or reverse direction.

Consider the reaction: $A \rightleftarrows B$, with $K_{eq} = \frac{[B]}{[A]} = 100$

Then this reaction will be at equilibrium when there is 100 times as much B as A in the solution.

Since there is more product than reactant at equilibrium, we could describe this reaction as "*having a tendency to go in the forward direction*".

This also could be expressed by stating that "*this reaction is spontaneous*".

It could also be expressed by stating that "*this reaction releases energy when it goes in the forward direction*" under a "standard" set of conditions.

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Consider the reaction: $A \rightleftarrows B$, with $K_{eq} = \frac{[B]}{[A]} = 100$

Then for the reverse reaction: $B \rightleftarrows A$, $K_{eq} = \frac{[A]}{[B]} = \frac{1}{100} = 0.01$

This reaction, regardless of which way it is written, will be at equilibrium when there is 100 times as much B as A in the solution. However, in the second way of showing the reaction, there is 100 times as much reactant as product at equilibrium.

When there is more reactant than product at equilibrium, we could describe this reaction as "*having a tendency to go in the reverse direction*".

This also could be expressed by stating that "*this reaction is endergonic*".

It could also be expressed by stating that "*this reaction requires an input of energy in order to go in the forward direction*" under a "standard" set of conditions.

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K_{eq} values have been determined for a large number of chemical reactions, including many metabolic reactions.

Example:

$$\text{D-glucose} \rightleftharpoons \text{D-fructose} \qquad K_{eq} = \frac{[\,\text{D-fructose}\,]}{[\,\text{D-glucose}\,]} = 0.8$$

This reaction has a K_{eq} value less than 1.0, so it tends to go in the reverse direction and would require an input of energy to go in the forward direction under the "standard" set of conditions. But the K_{eq} value is not much less than 1.0, which indicates it doesn't require very much energy input in order to go in the forward direction under standard conditions.

The K_{eq} value for a reaction predicts if it will go in the forward or the reverse direction, and it is related to the amount of energy that is released when a reaction occurs or is required in order to make a reaction occur.

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Consider the reaction: $A \rightleftharpoons B$ $K_{eq} = \frac{[B]}{[A]}$

Then consider the following hypothetical experiment:

1. Place exactly 1 M concentration of A and exactly 1 M concentration of B into a container, so that the reaction can start to occur.

2. Begin to add or remove A and B as soon as the reaction begins, such that each of their concentrations remains at 1 M as the reaction proceeds in the forward direction. Continue this process until exactly 1 mole of A has been converted to B. Depending on the value of K_{eq}, it may be necessary to apply energy in order to push the reaction in the forward direction, or else energy may be released as the reaction proceeds in the forward direction.

3. Measure the total amount of energy that must be added or that is released during this process. ΔG° is a quantitative measure of the amount of energy that must be supplied from an external source. ΔG° is related to K_{eq} as follows:

$$\Delta G^\circ = \underbrace{(-\ 5.7\ \text{kJ/mole})}_{\text{a constant}}\ (\log_{10} K_{eq})$$

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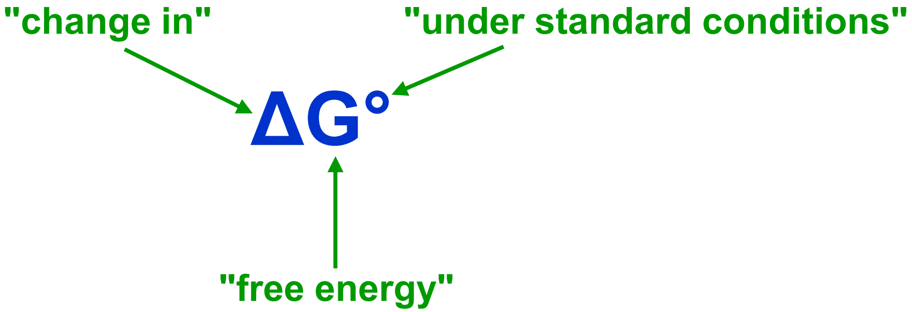
Definition of ΔG° for a specific chemical reaction:

The amount of energy <u>required</u> for the reaction to take place under a standard steady-state set of conditions.

How to read this symbol:



Standard conditions for measuring K_{eq} and ΔG° of a chemical reaction include a temperature of 25° C and one atmosphere of pressure. In addition, the standard steady-state condition that allows measurement of a ΔG° value for the reaction is the maintenance of 1 M concentration of substrates as 1 mole of reactant is converted to 1 mole of product.

Note: K_{eq} for a reaction is defined under equilibrium conditions and ΔG° for the reaction can be is defined under steady-state conditions.

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Consider the reaction: $A \rightleftharpoons B$, with $K_{eq} = 100$.

Then: $\Delta G° = (-5.7 \text{ kJ/mole}) (\log_{10} 100)$

$= (-5.7 \text{ kJ/mole}) (2)$

$= -11.4 \text{ kJ/mole}$

Thus, - 11.4 kJ of energy is required
(i.e. 11.4 kJ of energy is released)
for every mole of A that is converted to B
under standard conditions.

The equation for ΔG° shows that chemical reactions with a K_{eq} greater than 1 have a ΔG° value less than zero. Thus, reactions with a negative ΔG° value release energy and are exergonic (spontaneous). This can be illustrated for a reaction by showing the forward-direction arrow longer than the reverse-direction arrow.

$$A \mathrel{\substack{\xrightarrow{\hspace{4em}} \\ \xleftarrow{\hspace{2em}}}} B$$

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Consider the reaction:

D-glucose $\rightleftharpoons$ D-fructose $\quad K_{eq} = 0.8$

$$\Delta G° = (-\ 5.7\ \text{kJ/mole})\ (\log_{10}[0.8]) = (-\ 5.7\ \text{kJ/mole})\ (-\ 0.097)$$
$$= +\ 0.6\ \text{kJ/mole}$$

Thus, 0.6 kJ of energy is required from some outside source for every mole of D-glucose that is converted to D-fructose under standard conditions.

This reaction can be illustrated as endergonic by showing the reverse-direction arrow longer than the forward-direction arrow.

D-glucose $\overset{\rightarrow}{\longleftarrow}$ D-fructose

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The values of K_{eq} and $\Delta G°$ are constants for any given chemical reaction under defined standard conditions. These values are known for hundreds of metabolic reactions.

Although hundreds of reactions take place in the same cell at the same time, each chemical substance is maintained at approximately a constant concentration. This is one manifestation of homeostasis in living cells.

The steady-state concentrations of most substrates undergoing chemical reactions in living cells are maintained at much less than 1 M concentration, and in general they all differ from one another.

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Consider the endergonic reaction: $X \rightleftharpoons Y$, **with** $K_{eq} = 0.01$

Then: $\Delta G° = (-\,5.7\ \text{kJ/mole})\,(\log_{10} 0.01) = +\,11.4\ \text{kJ/mole})$

The reaction can be written: $X \overset{\longrightarrow}{\xleftarrow{\hspace{4em}}} Y$

Now suppose that within a living cell the steady-state concentration of X is 1,000 times higher than the steady-state concentration of Y. Under this <u>non-standard</u> set of conditions, the reaction is "pushed in the forward direction by the large excess of X over Y. The energy requirements under this non-standard set of conditions (ΔG) can be determined if the value of ΔG° (energy requirement under standard conditions) is known.

$$\Delta G = \Delta G° + (5.7\ \text{kJ/mole}) \left(\log_{10} \frac{[Y]_{actual}}{[X]_{actual}}\right)$$

For this reaction: $\Delta G = +\,11.4\ \text{kJ/mole} + (5.7\ \text{kJ/mole})\,(\log_{10} [1/1000]\,)$

$$= -\,5.7\ \text{kJ/mole}$$

Thus, a reaction can be changed from endergonic to exergonic by changing the relative steady-state concentrations of the substrates.

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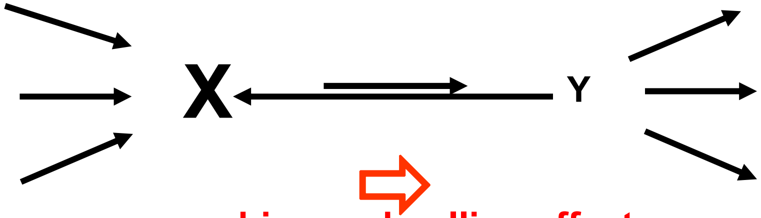
A reaction that tends to proceed in the reverse direction can be made to go in the forward direction in a cell by the cell’s appropriately adjusting the steady-state concentrations of substrates.

$$X \rightleftharpoons Y$$

endergonic reaction

Substrate X continually supplied by other reactions to keep its concentration high, thereby "pushing" this reaction



pushing and pulling effect

Substrate Y continually removed by other reactions to keep its concentration low, thereby "pulling" this reaction

A cell can sometimes push and pull a reaction in order to make it more exergonic. These pushing reactions that produce X as a product and pulling reactions that use y as a reactant are said to be coupled to the reaction X $\rightleftharpoons$ Y.

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By carefully considering the definitions and descriptions of K_{eq}, $\Delta G°$ and ΔG, the following should become evident:

If the reaction $A \rightleftharpoons B$ is exergonic (spontaneous),
Then the reaction $B \rightleftharpoons A$ is endergonic to the same extent.

The K_{eq} value of the reaction $A \rightleftharpoons B$ is the reciprocal of the K_{eq} value of the reaction $B \rightleftharpoons A$, and

The $\Delta G°$ value of the reaction $A \rightleftharpoons B$ is the negative of the $\Delta G°$ value of the reaction $B \rightleftharpoons A$.

A reaction that tends to proceed in one direction under a defined set of conditions can be made to go in the opposite direction by appropriately adjusting the steady-state concentration of substrates.

A reaction with a K_{eq} value of 1 (i.e., a $\Delta G°$ value of 0) does not have a tendency to proceed in either direction under standard conditions. (i.e. It is neither exergonic nor endergonic.)

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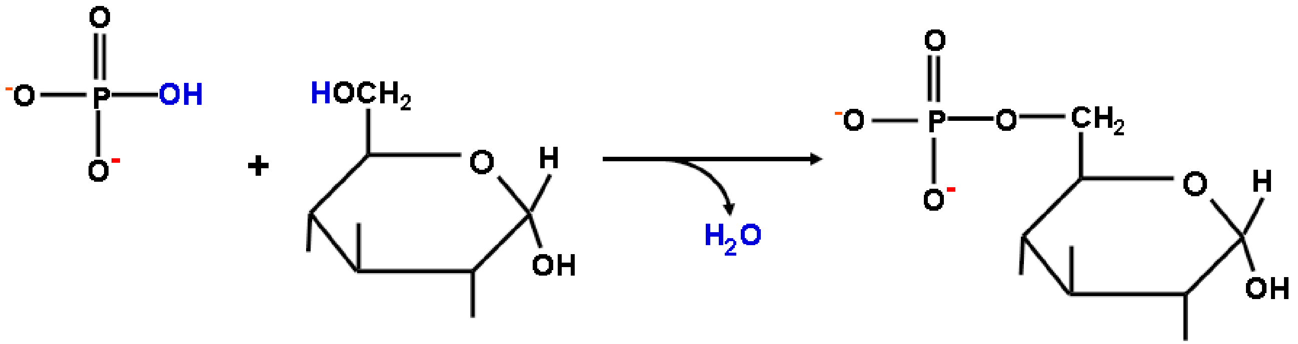
Consider the formation of glucose-6-phosphate from glucose and inorganic phosphate.



phosphate ester bond formation

$$\text{Glu} + P_i \xrightleftharpoons{\text{Dehydration rx.}} \text{Glu-6-}\textcircled{P} + H_2O \qquad \Delta G^\circ = +\,14\ \text{kJ/mole}$$

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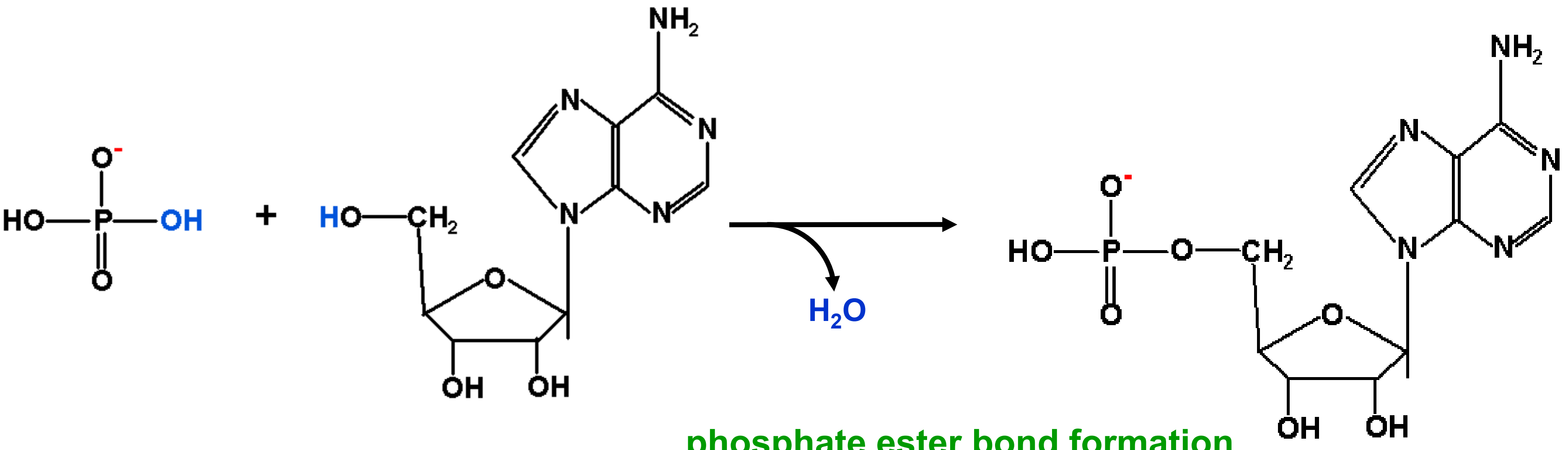
Consider the formation of AMP



phosphate ester bond formation

$$A + P_i \overset{\text{dehydration rx.}}{\rightleftharpoons} AMP + H_2O \qquad \Delta G° \approx +15 \text{ kJ/mole}$$

The formation of an ester from an alcohol and an acid in a dehydration reaction under standard conditions typically requires an input of approx. 15 kJ/mole of energy.

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