Medical Committee
The University of Jordan

SLIDE SHEET

LECTURE#: 6

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Biochemistry

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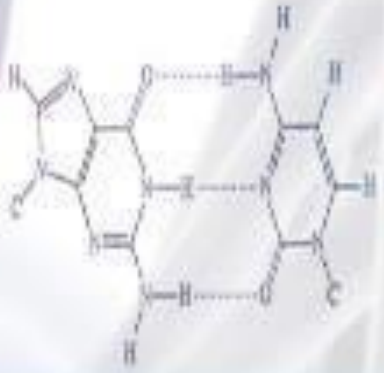


Majida Al-Foqaraa'

This sheet contains the last part of immunoglobulins and the introduction of bioenergetics, hoping that you will find this sheet smooth and easy, good luck ☺

Immunological memory

What does immunological memory means?

It means remembering the antigen determinants and repeated infections & repeated exposure to the same antigenic determent.

How does it occur?

What is the most common immunoglobulin in The GI tract?

IgA is the most common in secretions.

All immunoglobulins are close to each other in structure they all have a Y shape & they are close to each other in their constant regions and differ in their variable regions, most different in their hyper-variable regions.

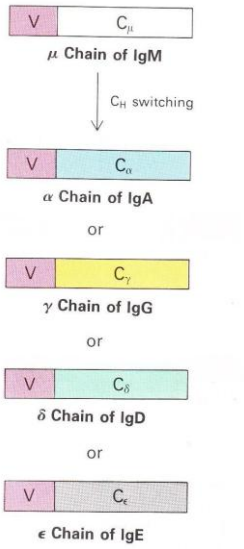
How can different immunoglobulins from different classes (IgG, IgA,IgM, IgD, IgE) recognize and bind the same antigen?

- For example, when an antigen enters the body, non-specific IgM bind initially to it, then specific IgM bind the antigen. To get a secondary immune response; specific IgG must bind the same antigen, but how can two different proteins from two different genes bind the same antigen?

This is done by class switching or isotype switching , what happens is that the constant gene synthesizes the constant region (heavy chain) which determines the class, and the variable gene synthesizes the variable region (these two genes are present in an immature B lymphocyte), so when your body recognizes the antigen, the plasma cells will start synthesizing for example IgM specific for this antigen , but to have IgG that can recognize the same antigen, you have to separate the constant gene from the variable gene, keep the variable gene that synthesizes the variable chain (to get the exact amino acid sequence of the variable region), then attach this variable gene to another constant gene (exchange between μ "for IgM" to gamma "for IgG" in our example).

So you will get 2 immunoglobulins that can recognize the same antigen.

Look at the figure below to understand the process clearly ☺



The most powerful immunoglobulin to fight against the antigens is the IgG; that's why we need the class switching in order to produce IgG for any antigen recognized by any other class of immunoglobulins.

Diseases

Myelomas: is increased production of anything considering immunoglobulins.

Multiple myeloma: is an increased production of one class of immunoglobulins or even an increase in the light chain production (not the whole immunoglobulin).

The increased light chain concentration will affect the urine, (its concentration in the urine will be high).

The 2 scientists who have discovered this are (bence & jones).

So when the concentration of the light chain is high we call it "bence & jones protein".

Multiple myeloma as a cancer affecting the plasma cells causes an increase in production of one class of immunoglobulins or even a light chain.

The question below is an exam question:

Multiple myeloma will result in increased production of which of the following:

A-haptoglobin

B-ceruloplasmin

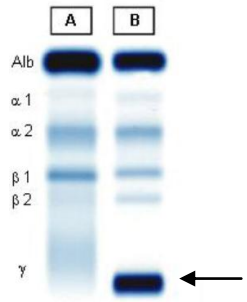
C-bence & jones protein

The answer is: C; increased production of a light chain

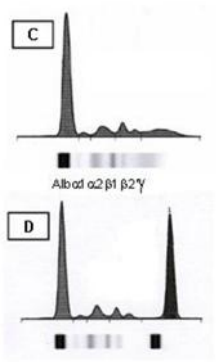
** Diseases can occur whether by an increase (plastic conditions; cancers) or decrease in the immunoglobulins concentration.

The decrease in concentration of immunoglobulins can be in one class or all classes, when the decrease of immunoglobulins is in all classes we call it "agammaglobulinemia", which means decreased production of all gamma globulins within the blood (-emia).

The figure (please **refer to slide # 38**) represents electrophoresis which shows an increase in gamma globulins concentration.



The densitometer representation also shows an increased production of the gamma band.



** Why it is sharp?

Because the increase was in only one class of the gamma globulins; if it is wide the increase will be for all globulins.

Bioenergetics

We will talk about energy metabolism, we have studied this topic in the summer semester, so we are almost familiar to everything in this subject ☺

Energy: is the ability or capacity to perform work.

Types of energy:

1-kinetic energy: energy in the process of doing work or energy of motion.

2-potential energy: energy content stored in a matter.

Why do reactions happen?

To reach a state of higher stability.

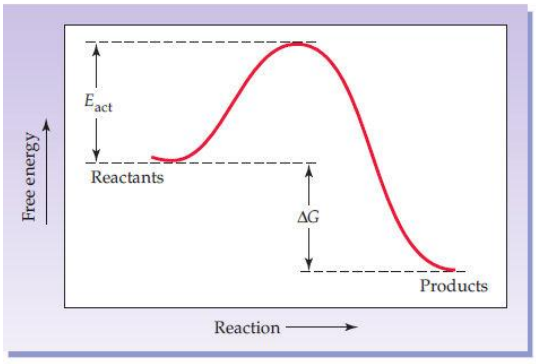
Are reactants stable?

Yes they are, but they undergo reactions to reach a higher stability.

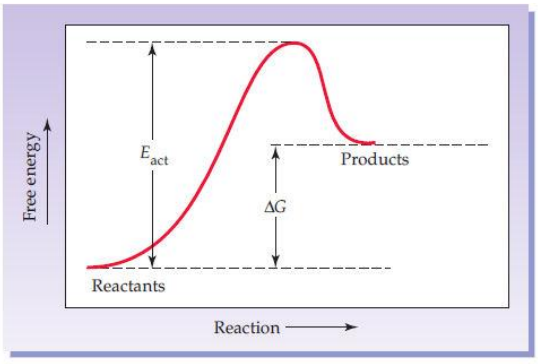
If the reactants are not reaching a higher stable state, why the reaction happens?

All reactions happen in a spontaneous manner (energy wise), which means the total energy of the reactants (inputs) should be higher than the products (outputs), so the reaction will occur, that's why when we see in figure (b) that the energy of the reactants is less than the products, we are achieving a less stable condition, what should we do??

This reaction is a non-spontaneous reaction, we give it more energy in the form of ATP at the beginning to make the total energy of reactants higher than the products, and then the reaction will occur.



(a) An exergonic reaction



(b) An endergonic reaction

Thermodynamics: the study of energy transformation that occurs in a collection of matter (studies the potential energy; not kinetic energy).

Bioenergetics: studying thermodynamics energy in living organisms.

First law of thermodynamics: energy cannot be created nor destroyed, but only converted to other forms. (Energy of the universe is constant)

Why do we care about this law?
To know where the difference in energy between the reactants and products had gone.

Second law of thermodynamics: all energy transformations are inefficient. This means that there is no machine in the world that is 100% efficient, always a certain amount of energy is lost during energy transformation.
The lost energy is mostly one of these two forms:

1- Heat.
2- Used in increasing the disorder of the system.

- Example on the increase of disorder:

You don't need any effort to make your room messy, but you need effort to clean it up. (Spontaneous systems tend to increase in their disorder)

Free energy change: the total energy change in a system with respect to its temperature.

$$\Delta G = \Delta H - T\Delta S$$

ΔG: free energy change (energy of products – energy of reactants), it tells you the bond energies within matter taking in consideration the disorder state of the matter.
ΔH: heat of reaction (heat of products – heat of reactants)
ΔS: entropy change.
T: temperature in Kelvin.

- ✓ The best example to understand disorder is *water states*:

Water can go into 3 states: solid, liquid, gas.
What's the difference between them?
They are all composed of H_2O.
The bond energies are the same (same length).
The difference is how water molecules are arranged around each other, in the solid state they are the most ordered out of the 3 states (crystallized

state), in the liquid state we are increasing the disorder so ΔS will increase, in the gas state the disorder is increasing more and more.

ΔG tells us if the reaction is spontaneous or not, favorable or not. (NOT ΔH)
If the energy of the reactants is higher than the products it results in a negative ΔG (spontaneous).

Any Δ is calculated by subtracting the final result from the initial result.

If ΔG is positive the reaction is non spontaneous (non-favorable).

+ΔG: endergonic
-ΔG: exergonic
+ΔH: endothermic
-ΔH: exothermic

Endothermic & exothermic "ΔH values" doesn't tell you anything about the spontaneity of the reaction; ΔG tells you about it because it takes in consideration the ΔS value.

- For example; ice melting is a spontaneous process, however it's an endothermic process.

Activation energy EA: the energy needed to convert the reactants (stable materials) to the transition state (unstable intermediates).

- Reactants are stable because we can deal with them.
- The transition state can either go back to form the reactants, or form the products.

ΔG°: the free energy difference at *standard conditions* , 25 C°, 1 atmospheric pressure, 1 molar concentration of reactants and products, ph= 7.

- ΔG° is the same as $\Delta G^{\circ}{}'$ (prime).

Why do we need to have standard conditions?
To be able to compare reactions together; it is easier to detect differences between reactions when they are at fixed conditions.
(having less variables)

ΔG: tells you if the reaction is spontaneous or not. NOT ΔG° , because it occurs at standard conditions.

ΔG depends on the initial and the final states only; it is not affected by the mechanism or the rate of the reaction.
If the reaction has a high negative ΔG value this does not mean that it is fast it means that it is spontaneous.

Thermodynamics is a predictable science, depends only on the initial and the final states, the kinetics deal with mechanisms and rates.

What is the effect of temperature on reactions?

We look at the reaction if it is endothermic or exothermic.

- **Exothermic** reactions produce heat, which means that heat is a product of the reaction, so if you are giving heat the reaction will go in the **backward direction**.
- If the reaction is **endothermic** the heat will be from the reactants, so upon adding energy to the reaction, you are encouraging the **forward reaction** to occur.

What is the effect of catalysts (enzymes)?

It has nothing to do for the favorability of the reaction.
Enzymes lowers the activation energy, they don't change the initial and the final states.

What is the reversible reaction?

It is a reaction that can go in both directions.
Theoretically all the reactions are reversible; sometimes the rate that gives products is much higher than the rate that gives the reactants, so we consider it as an irreversible reaction.

What is equilibrium?

The rate of forming products = rate of degrading products back to reactants.

- Example: suppose that you have 2 rooms, the first room's capacity is 150 students, and the second one's capacity is 100 students, so there is a difference in concentrations (suppose the 2 rooms have the same volume), we will have equilibrium when the number of students going out from the first room to the second room at a certain time is equal to the number of students going out from the second room to the first room at the same period of time, regardless of the content of the 2 rooms.(the concentration maybe higher, equal, lower but we don't care about it).

ΔG at equilibrium = 0

When the reaction is moving in the forward direction (reactants → products) spontaneously; the potential energy will be high to drive the rxn (less stable), but when the reaction reaches equilibrium; the rates of the two reactions (forward and backward directions) will be equal resulting in higher stability. So the reaction reaches highest stability at equilibrium.

What is the equilibrium constant K?

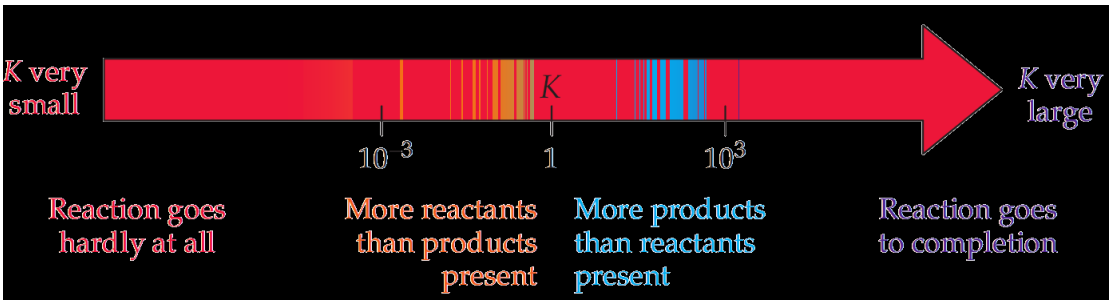
Concentration of products / concentration of reactants
*Noting that all concentrations are upped to the # of moles, and are measured at equilibrium

$$aA + bB + \cdots \rightleftharpoons mM + nN + \cdots$$

What equilibrium constant means?

- The K value helps us in predicting the direction the reaction needs to follow in order to reach the equilibrium state.

  - When the K value is 1 this means that at equilibrium the concentration of reactants = concentration of products at equilibrium.
  - When the value of K is 10 this means that the concentration of products is 10 times higher than the concentration of reactants at equilibrium, which means that the reaction should go in the forward direction to reach the equilibrium state if it had started with equal concentrations of both products and reactants.
  - When the value of K is higher than 1 this means that the reaction should go in the forward direction
  - When the value of K is lower than 1 this means that the reaction should go in the backward direction in order to reach the equilibrium state.
  - When the value of K = 1000 or more this means that the reaction is almost completed.
  - When the value of K is 10^{-3} or lower this means that the reaction is hardly going.



ΔG & K eq

A+B ⟺ C + D

ΔG = ΔG°' + RT ln((C) (D) / (A) (B))

ΔG at equilibrium = 0
ΔG°= -RTln(K eq)

This formula connects **ΔG with** K equilibrium

THAT'S IT!!
Sorry for any mistakes...
Good luck ☺