بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Metabolism | Lecture 1

Bioenergetic & Thermodynamics

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Energy and human life

1- Bioenergetics and Thermodynamics

Chemical energy

- Carbohydrates
- Fats
- Others

Chemical waste

- Carbon dioxide
- Water

Heat

ATP

- body's "energy currency"

DEFINITION

- The **quantitative study of the energy transductions** that occur in living cells and of the nature and function of the chemical processes underlying these transductions.

Why Do We Need Energy ??

We need energy for building up, Energy is required to build lipids ,proteins ,etc.

Anabolism: Building up molecules requires energy ▲

Catabolism: Breaking down molecules releases energy ▼

Bioenergetic Science

The branch of science that studies biochemical reactions from a thermodynamic perspective.

It predicts how energy flows in living systems.

Studying Biochemical Processes

We can study biochemical reactions in our body from two different perspectives:

(a) **Kinetic Theory**

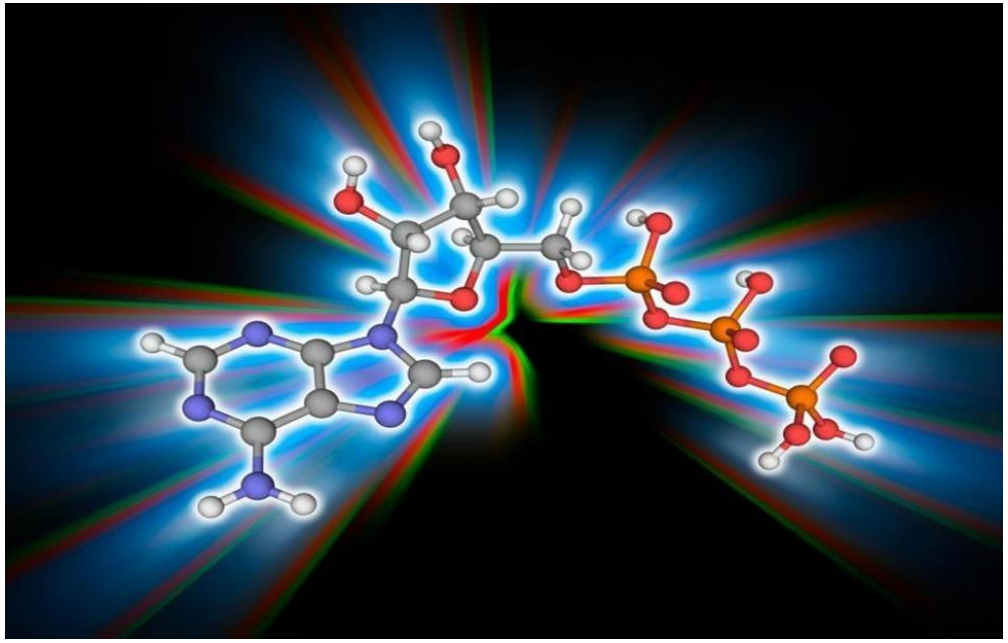
- Focuses on reaction rates and how fast reactions occur.
- Involves enzymes, which lower the activation energy (طاقة التنشيط)

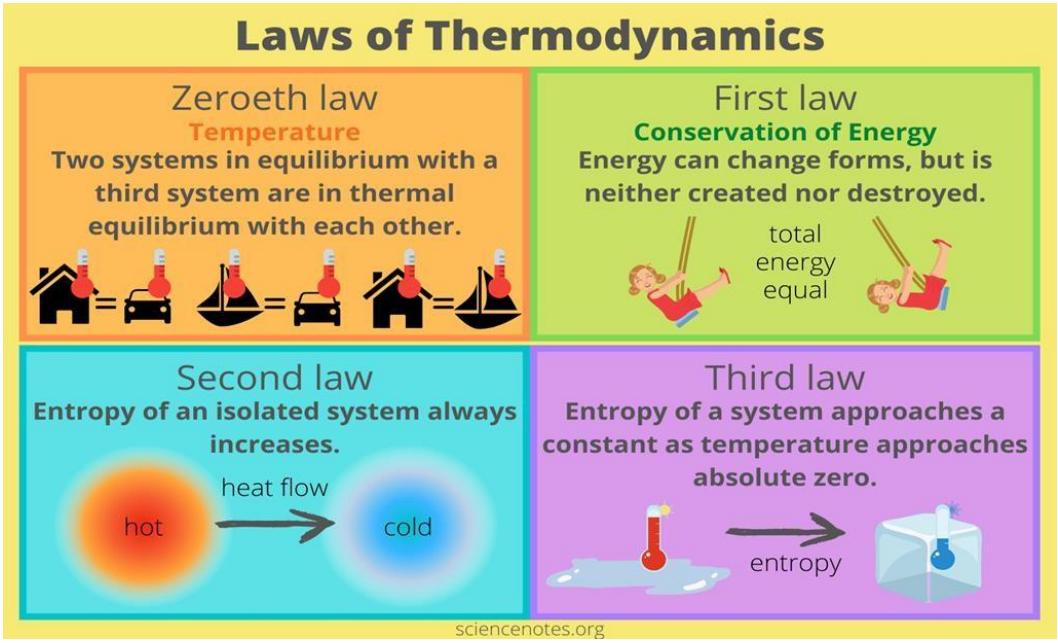
Example: Enzymes speed up biochemical reactions without being consumed.

(b) **Thermodynamic Theory**

- Concerned with the start and end points of reactions.
- It doesn't care about the path! only about energy changes between the start and finish.
- Studies whether a reaction can occur spontaneously or not.

LECTURE 1: THE LAWS OF ENERGY AND CELLULAR CURRENCY





THE CLINICAL STAGE: A CASE OF LETHARGY

Poor feeding → less nutrient intake → less ATP produced.
This leads to lethargy (الكسل أو الخمول)

Hypoglycaemia: Low blood sugar lack of glucose for energy.
Metabolic crisis: Failure of energy production

- Clinical Presentation
  - A 2-month-old infant presents with lethargy, poor feeding, and hypoglycemia indicating a metabolic crisis.
- Laboratory Findings
  - Initial labs reveal low blood glucose and mild metabolic acidosis, signaling disrupted metabolism.
- Biochemical Diagnostic Question
  - The clinical challenge is differentiating fuel deficiency from impaired energy utilization in the patient.
- Importance of Bioenergetics
  - Understanding bioenergetics is critical for diagnosing and managing metabolic crises in pediatric patients.

If the baby is actually eating well, we rule out bad feeding as the reason for his condition, which makes it easier to diagnose

BIOLOGICAL ENERGY TRANSFORMATIONS OBEY THE LAWS OF THERMODYNAMICS

The **1st** law (conservation of energy): for any change, the total amount of energy in the universe remains constant;

The **2nd** law of thermodynamics: the universe always tends toward increasing disorder (or); in all natural processes, the entropy of the universe increases.

Signs for spontaneous systems…

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

هذا السلايد مراجعة لمادة الصيفي

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

Gibbs Free Energy Equation

ΔG → Change in free energy (الطاقة الحرة)
ΔH → Change in enthalpy (الحرارة أو الطاقة الكلية للتفاعل)
TΔS → Effect of temperature × entropy change

The equation tells us whether a reaction will occur spontaneously or not.

If ΔG < 0, the reaction is spontaneous (occurs naturally, releases energy).
If ΔG > 0, the reaction is non-spontaneous (needs energy input).
If ΔG = 0, the system is at equilibrium.

ΔG° vs ΔG

ΔG° = Standard free energy change (under standard conditions: 25°C, 1 atm, 1 M concentration).

ΔG = Actual free energy change in the cell, which depends on the real concentrations of reactants and products.

ΔG°′ represents the standard free energy change under biochemical conditions (the energy change for a reaction at pH = 7)

ΔG is a state function, meaning it depends only on the initial and final states, not on the path.

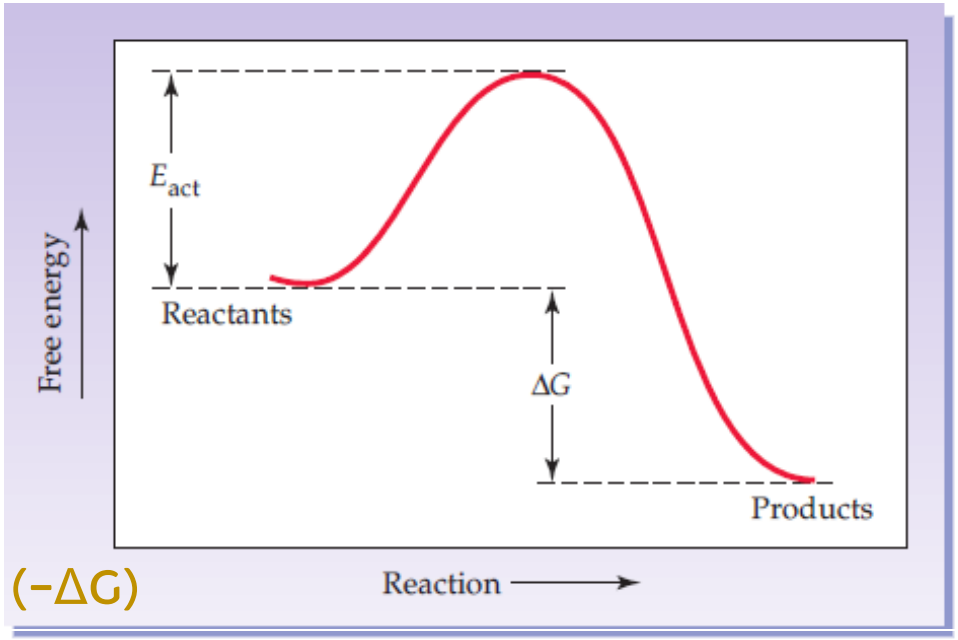
Example: Whether a reaction happens in one step or several steps, ΔG remains the same.

WHY DO CHEMICAL REACTIONS OCCUR?

- The concept of activation energy
- ΔG and ΔG^o

Activation Energy (E_a)

Every chemical reaction needs some activation energy to get started.
This is the energy barrier that must be overcome for reactants to turn into products.

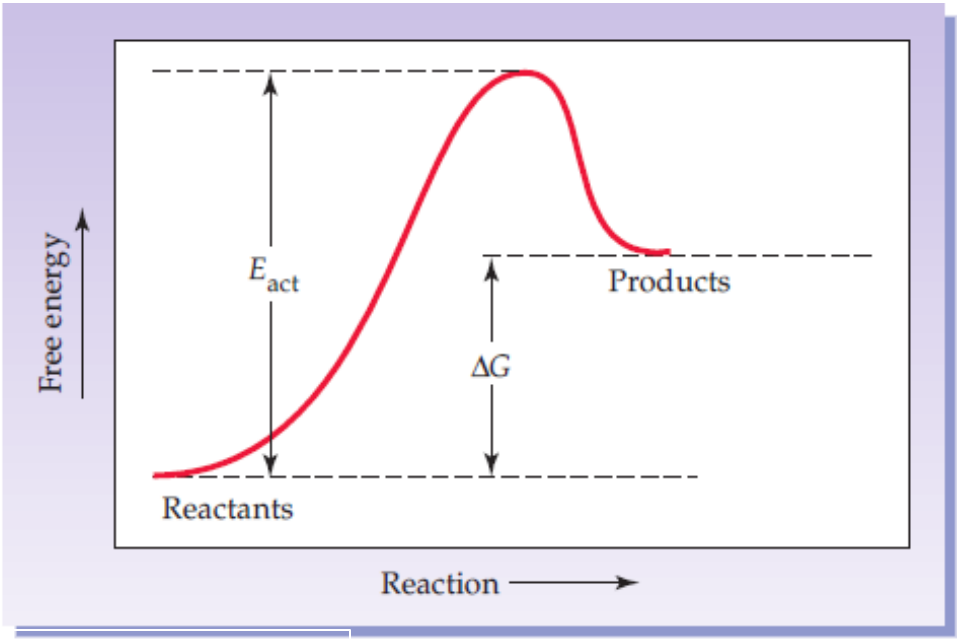


(a) An exergonic reaction

Negative ($-\Delta G$)

Releases energy

Spontaneous



(b) An endergonic reaction

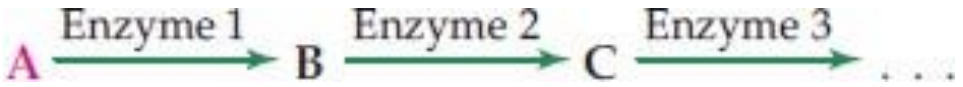
Positive ($+\Delta G$)

Absorbs energy

Non-spontaneous

ΔG IS A STATE FUNCTION?!

- **ΔG is not affected by the mechanism of the reaction**
- $A \rightarrow B \rightarrow C$



$\Delta G_{A \rightarrow B} = GB - GA$

$\Delta G_{B \rightarrow C} = GC - GB$

$GC - GA = \Delta G_{A \rightarrow C}$

- Combustion of glucose in calorimeter

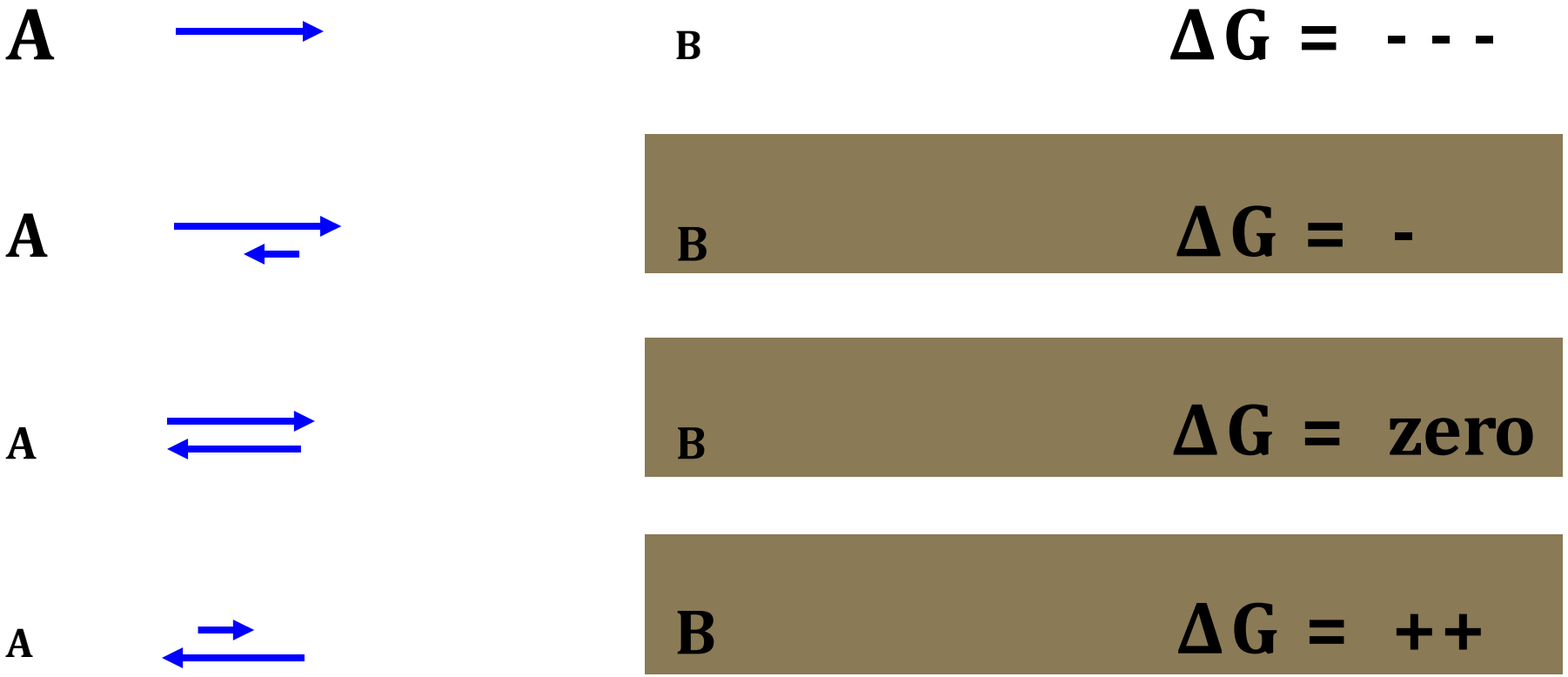
$Glucose + O_2 \rightarrow CO_2 + H_2O \qquad \Delta G = -680$ kcal/mol

In the cell

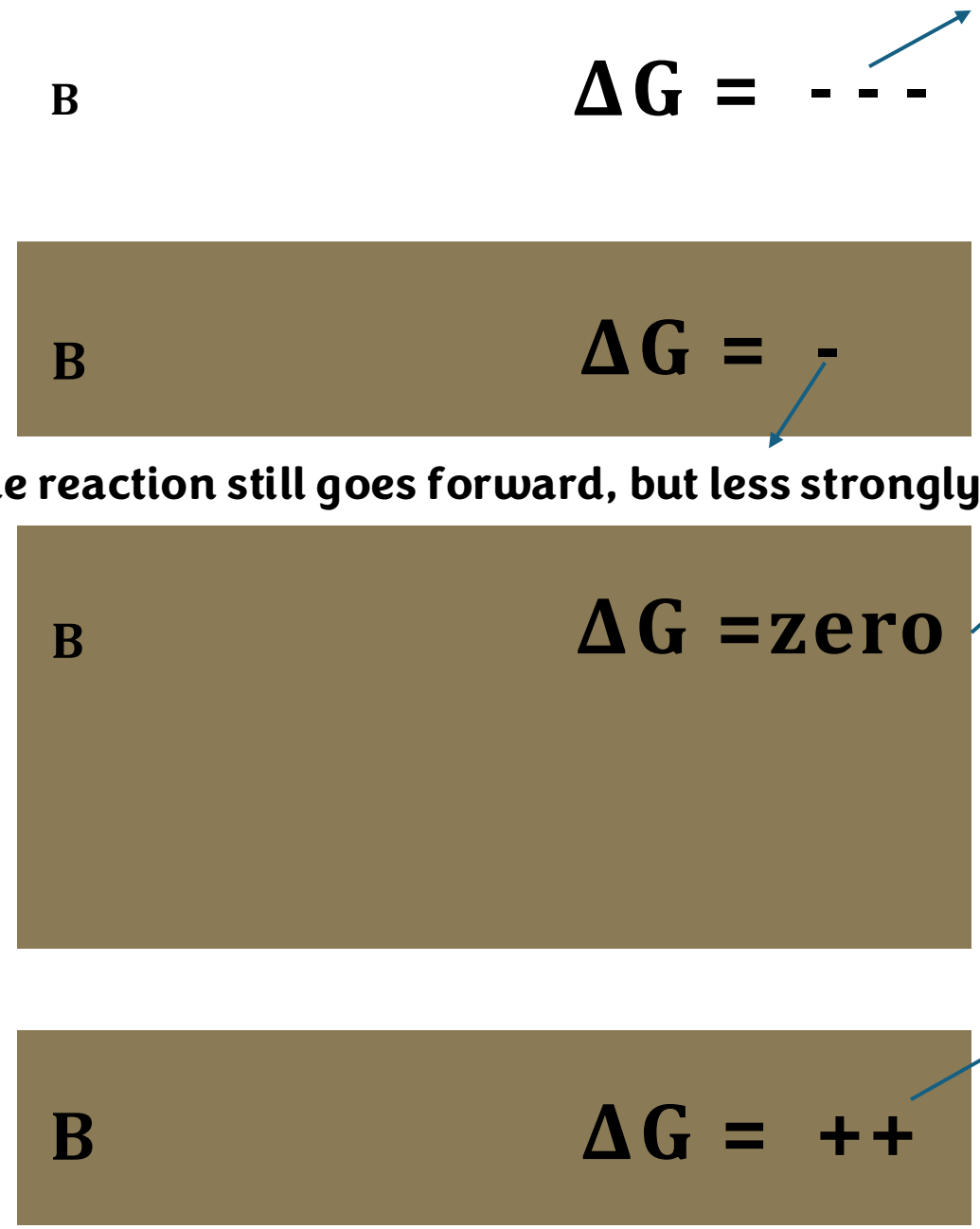
$Glucose \rightarrow\rightarrow\rightarrow\rightarrow\rightarrow CO_2 + H_2O \qquad \Delta G = -680$ kcal/mol

ΔG IS AFFECTED BY CONCENTRATION

Energy in glucose → energy in the bond, so can you calculate the energy in the bond? You should be.The energy should be affected by the concentration of products and reactants.



ΔG measures the tendency of a reaction to proceed towards equilibrium



There is a lot of A (reactant) and very little B (product). The reaction will go strongly forward because there are many reactants ready to react.

ΔG is very negative, meaning the reaction is spontaneous and releases energy

This means the reaction has reached equilibrium. The amount of A and B stays constant. ΔG = 0 means no net energy change; the reaction goes in both directions equally.

Now there is a lot of B (product) and very little A. ΔG becomes positive, so the reaction does not go forward. Instead, it tends to go backward to reach balance.

$$\Delta G = \Delta G^{o} + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$$

ΔG^{o} = standard free energy (constant, at 1M each)
ΔG = actual free energy (depends on concentrations)
Q = [Products]/[Reactants]

When [Reactants] are high, ΔG is negative → the reaction goes forward.
When [Products] are high, ΔG is positive → the reaction goes backward.
When [Reactants] = [Products], $\Delta G = 0$ → the reaction is at equilibrium.

HOW ΔG AND ΔG^o RELATE?

- Concentrations of reactants and products = 1 mole/L
- $\Delta G = \Delta G^o + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$
- $\Delta G = \Delta G^o + RT \; 2.3 \log \frac{[\text{Products}]}{[\text{Reactants}]}$

The free energy change (ΔG) depends on **concentrations** at any given moment.

If [Products] / [Reactants] = 1, then $\Delta G = \Delta G^{\circ\prime}$
→ reaction at standard conditions).

If [Products] / [Reactants] < 1, ΔG becomes more negative
→ reaction is more spontaneous (favorable).

If [Products] / [Reactants] > 1, ΔG becomes less negative or positive
→ reaction is less favorable (or reversed).

THE STANDARD FREE-ENERGY CHANGE IS DIRECTLY RELATED TO THE EQUILIBRIUM CONSTANT (Keq)

Equilibrium is reached at the end!

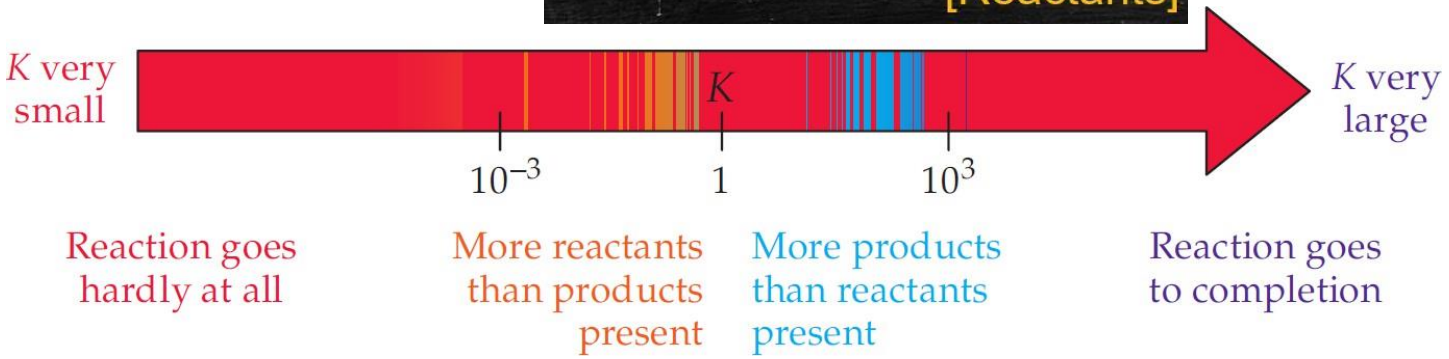
At equilibrium: concentration are fixed; rates are exactly equal

The concentrations define the equilibrium constant

$$aA + bB \rightleftharpoons cC + dD$$

$$K_{eq} = \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

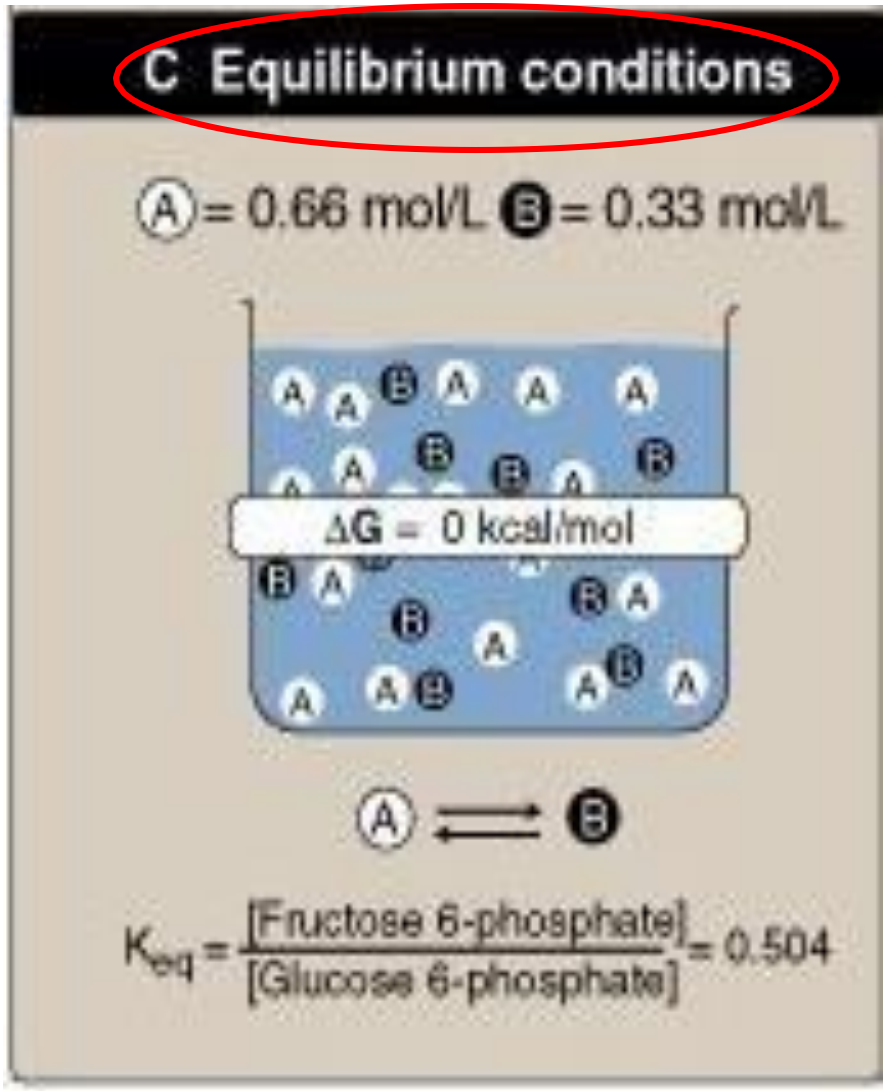
$$\Delta G = \Delta G^\circ + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$$



✓ The equilibrium constant (Keq) expresses the ratio of product to reactant concentrations at equilibrium

Glucose 6- phosphate ⇌ Fructose 6- phosphate

0.66 mol/L 0.33 mol/L

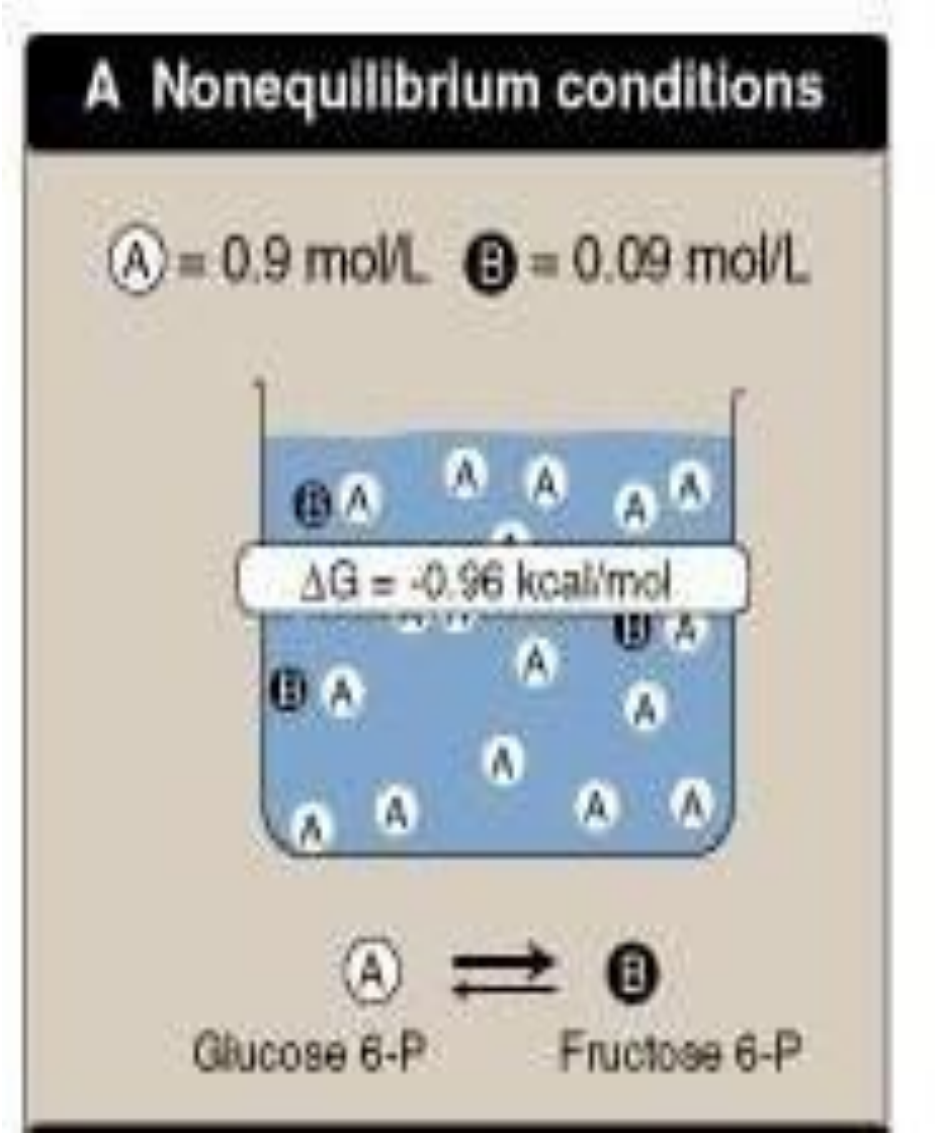


$\Delta G = \Delta G^{o} + RT\ 2.3 \log 0.33/\ 0.66$

$\Delta G^{o} = +\ 0.4$ kcal/mol

At equilibrium, ΔG = O because the reaction is balanced in **both** directions.
When substituting the concentrations into the equation, we find that ΔG° = +0.4 kcal/mol.
The positive value means the reaction is not spontaneous under standard conditions,

Glucose 6- phosphate ⇌ Fructose 6- phosphate



Constant

$\Delta G^{o} = + 0.4$ kcal/mol

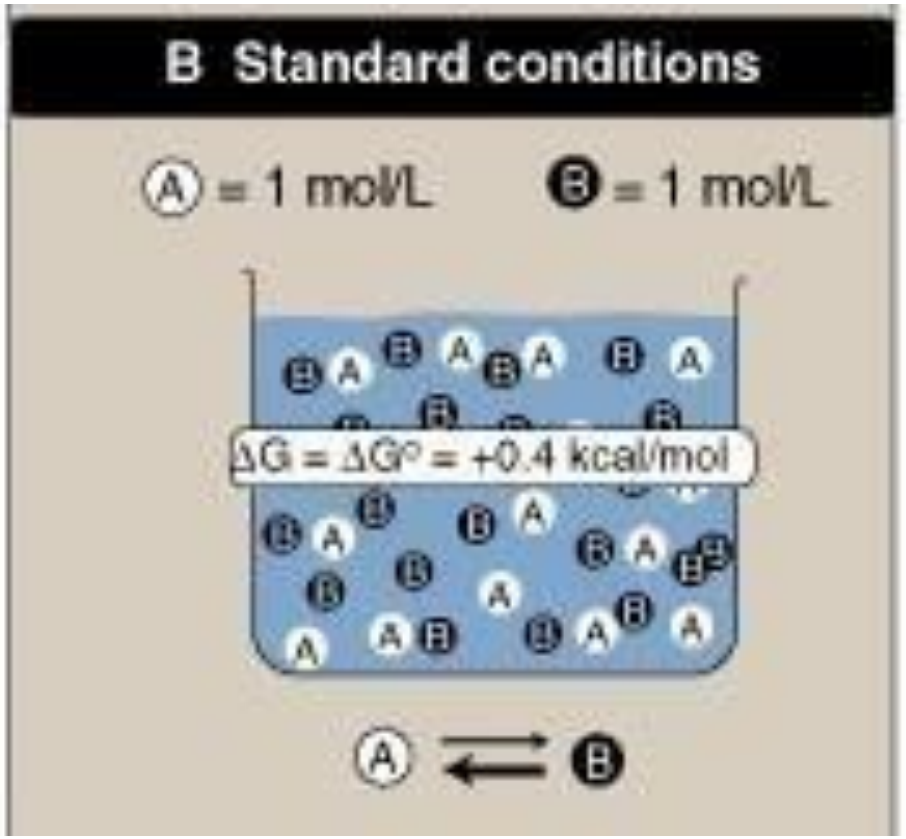
$\Delta G = \Delta G^{o} + RT\ 2.3 \log 0.09/0.9$

$\Delta G = - 0.96$

Since the ratio (0.09/0.9) is very small, the logarithm is negative, making ΔG negative. This means the reaction becomes spontaneous inside the cell, even though ΔG^{o} is positive.

Glucose 6- phosphate ⇌ Fructose 6- phosphate

1 mol/L 1 mol/L



$\Delta G = \Delta G^o + RT\ 2.3 \log 1/1$

$\Delta G = \Delta G^o$

Under standard conditions: all substances are at 1 mol/L, so the log term equals zero. Therefore, $\Delta G = \Delta G^o$, meaning the free energy change equals the standard free energy.

ΔG & K_{eq}

For a reaction $A + B \leftrightarrow C + D$

$$\Delta G = \Delta G^{o'} + RT \ln \frac{[C][D]}{[A][B]}$$

- At equilibrium, $\Delta G = 0$
- Can a reaction has a +ve ΔG^o & still be favorable?

K'_{eq}	$\Delta G^{o'}$ kJ/mol	Starting with 1 M reactants & products, the reaction:
10^4	- 23	proceeds forward (spontaneous)
10^2	- 11	proceeds forward (spontaneous)
$10^0 = 1$	0	is at **equilibrium**
10^{-2}	+ 11	reverses to form "reactants"
10^{-4}	+ 23	reverses to form "reactants"

$$\Delta G = \Delta G^{o'} + RT \ln \frac{[C][D]}{[A][B]}$$

$$0 = \Delta G^{o'} + RT \ln \frac{[C][D]}{[A][B]}$$

$$\Delta G^{o'} = -RT \ln \frac{[C][D]}{[A][B]}$$

defining $K'_{eq} = \frac{[C][D]}{[A][B]}$

$$\Delta G^{o'} = -RT \ln K'_{eq}$$

If keq =1 , it means that at equilibrium you have equal concentrations of reactants and products
If Keq is more than one : you have more products than reactants but there is no favourability, because we are at equilibrium and at equilibrium delta G is zero (theres no energy difference therefore no favourability)

For example: If Keq is 1000, it means that at equilibrium we have 1000 folds of products compared to reactants.
when you reach Keq of 1000 and more, the reaction is almost complete in one direction. If Keq is 10^-3: This means we have 1000 folds of reactants compared to the product. (For each 1000 reactant molecules we have one product molecule)
When you reach Keq of 10-3 and less the reaction is hardly going

ΔG° AND K_{eq}

ΔG° is negative, Keq > 1 → reaction is spontaneous (favors products).

When ΔG° is positive, Keq < 1 → reaction is nonspontaneous (favors reactants).

K_{eq}	ΔG°
10^{3}	- 4.08
10^{2}	- 2.72
10^{1}	- 1.36
1	0
10^{-1}	1.36
10^{-2}	2.72
10^{-3}	4.08

How much change in delta G compared to changes in Keq

If $K_{eq} = 1$, then $\Delta G^{\circ} = 0$

If Keq > 1, then $\Delta G^{\circ} < 0$

If Keq < 1, then $\Delta G^{\circ} > 0$

$$\Delta G = \Delta G^{\circ} + RT \ln \frac{[\text{Products}]}{[\text{Reactants}]}$$

ΔG & K_{eq}

رَبَّنَا ٱغْفِرْ لِى
وَلِوَٰلِدَىَّ وَلِلْمُؤْمِنِينَ
يَوْمَ يَقُومُ ٱلْحِسَاب

- ΔG is additive for multiple subsequent reactions
- K_{eq} is multiplicative for subsequent reactions

$$\text{Glucose} + P_i \longrightarrow \text{glucose 6-phosphate} + H_2O \qquad \Delta G'^\circ = 13.8 \text{ kJ/mol}$$

$$\text{ATP} + H_2O \longrightarrow \text{ADP} + P_i \qquad \Delta G'^\circ = -30.5 \text{ kJ/mol}$$

$$\begin{array}{ll} (1) & \text{Glucose} + P_i \longrightarrow \text{glucose 6-phosphate} + H_2O \\ (2) & \text{ATP} + H_2O \longrightarrow \text{ADP} + P_i \\ \hline \text{Sum:} & \text{ATP} + \text{glucose} \longrightarrow \text{ADP} + \text{glucose 6-phosphate} \end{array}$$

$$\Delta G'^\circ = 13.8 \text{ kJ/mol} + (-30.5 \text{ kJ/mol}) = -16.7 \text{ kJ/mol}$$

$$K'_{eq_1} = \frac{[\text{glucose 6-phosphate}]}{[\text{glucose}][P_i]} = 3.9 \times 10^{-3} \text{ M}^{-1}$$

$$K'_{eq_2} = \frac{[\text{ADP}][P_i]}{[\text{ATP}]} = 2.0 \times 10^{5} \text{ M}$$

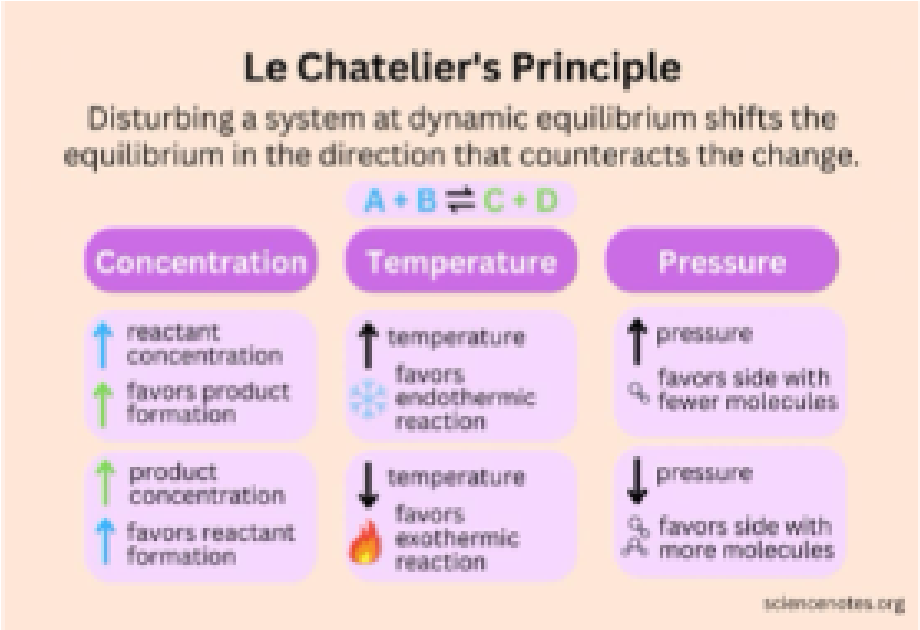
$$K'_{eq_3} = \frac{[\text{glucose 6-phosphate}][\text{ADP}][P_i]}{[\text{glucose}][P_i][\text{ATP}]}$$

$$= (K'_{eq_1})(K'_{eq_2}) = (3.9 \times 10^{-3} \text{ M}^{-1})(2.0 \times 10^{5} \text{ M})$$

$$= 7.8 \times 10^{2}$$

THE EFFECT OF CHANGING CONDITIONS ON EQUILIBRIA

- When a stress is applied to a system at equilibrium, the equilibrium shifts to relieve the stress
- Effect of Changes in Concentration
  - What happens if a reactant/product is continuously supplied/ removed?
  - Metabolic reactions sometimes take advantage of this effect
- Effect of Changes in Temperature
  - Endothermic/exothermic are favored by increase/decrease in temperature, respectively.
- Effect of a catalyst on equilibrium



Effect of a Catalyst

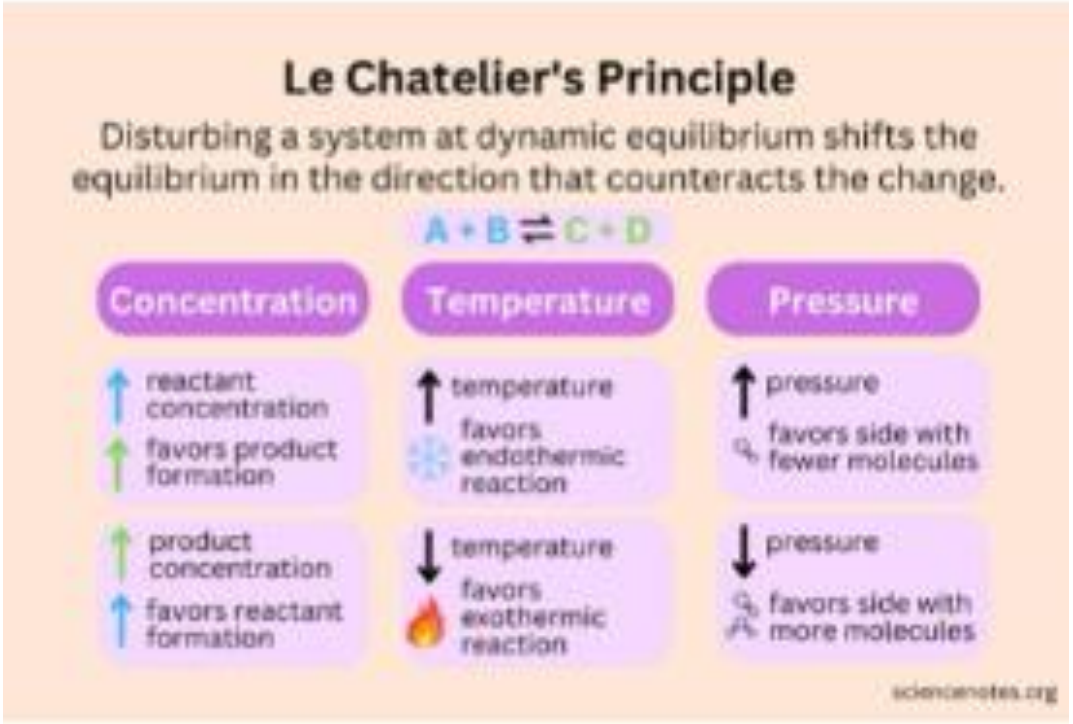
A catalyst speeds up both forward and reverse reactions equally.
It helps reach equilibrium faster but does not change the equilibrium position.

Le Chatelier's Principle:
When a system at equilibrium is disturbed (by changing concentration, temperature, or pressure), it shifts in a direction that counteracts the disturbance to restore equilibrium.

Effect of Concentration

If the concentration of a reactant increases, the equilibrium shifts to the right (toward products) to use up the extra reactant.

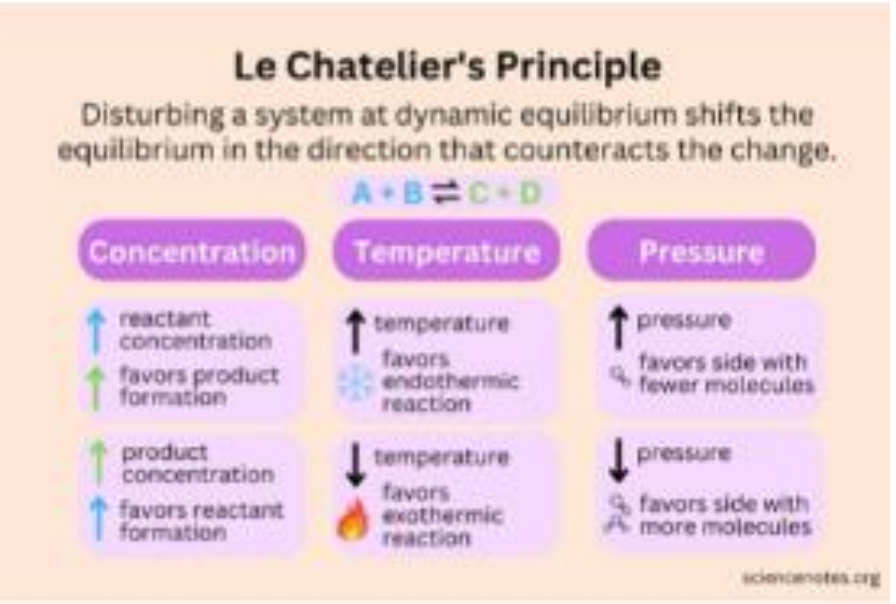
If the concentration of a product increases, the equilibrium shifts to the left (toward reactants) to reduce the product amount.



Effect of Pressure

Increase in pressure → equilibrium shifts to the side with fewer gas molecules.

Decrease in pressure → equilibrium shifts to the side with more gas molecules.



Effect of Temperature

The direction of the shift depends on whether the reaction is endothermic or exothermic.

↑ Temperature → favors endothermic reaction

(When the temperature increases, the equilibrium shifts toward the endothermic direction because it absorbs the extra heat.)

↓ Temperature → favors exothermic reaction

(When the temperature decreases, the equilibrium shifts toward the exothermic direction to produce more heat and compensate for the loss.)

We treat temperature as a reactant or product, for example :

Heat + N_2O_4 <-> 2NO

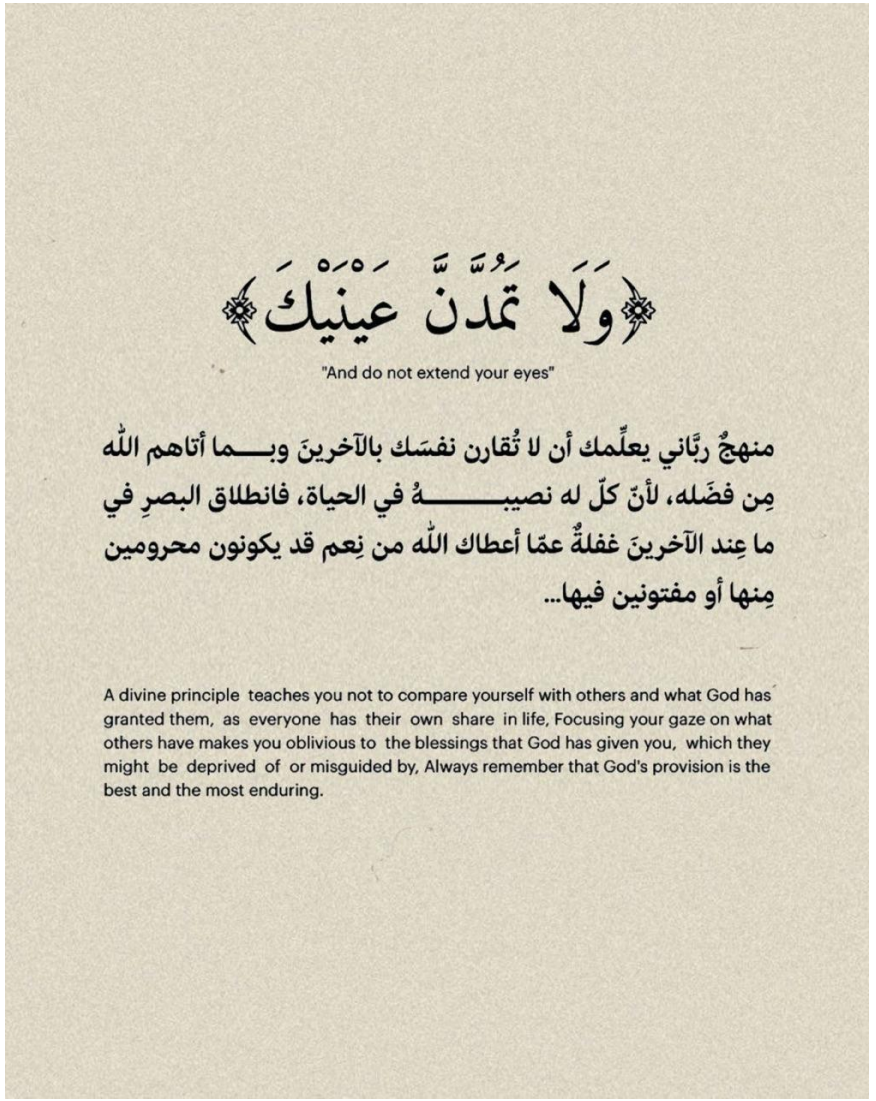
When heat increases it will drive the forward reaction in the endothermic perspective and the backward reaction from the exothermic perspective

Additional Resources:

رسالة من الفريق العلمي:

من لم يتعزَّ بعزاء الله تقطّعت نفسه حسرات، ومن يتّبع بصره فيما في أيدي الناس بطل حزنه، ومن ظنّ أنّ نعمة الله في مطعمِه ومشربه وملبسه فقد قلّ عمله وحضر عذابه .

- أبيّ بن كعب



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
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V1 → V2			