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Bioenergetics

Catabolism, breakdown, oxidation, exergonic, convergent

Metabolism

Anabolism, synthesis, reduction, endergonic, divergent

In addition to biosynthetic processes, the following are also endergonic: muscle contraction, active transport, nerve conduction, cell motility, thermogenesis.

In a living cell, exergonic and endergonic processes are coupled via ATP, the currency of energy in the cell.



The two terminal phosphate groups, β and γ , are called energy-rich or high-energy bonds. These phosphate groups are attached via phosphoanhydride bonds. In addition to ATP, other nucleotide triphosphates are also involved in specific endergonic processes. For example, GTP is the energy source for protein synthesis, UTP in glycogen synthesis and CTP in lipid synthesis. Again, ATP is the ultimate source of energy because synthesis of GTP, UTP, and CTP requires utilization of ATP.

Indicators of the energy level of the cell

 $\begin{array}{c} \text{ATP} \rightarrow \text{ADP} + \text{Pi} + \text{energy} \\ 2 \text{ ADP} \rightarrow \text{ATP} + \text{AMP} \\ \uparrow \\ \text{adenylate kinase} \end{array}$

Adenylate pool = [AMP] + [ADP] + [ATP]

In storing energy in the form of ATP, the cell is like an electric storage battery. The battery is fully charged if the adenylate pool consists only of ATP. It is fully discharged when the adenylate pool consists only of AMP.

When cellular energy is depleted, AMP accumulates. AMP activates a protein kinase, known as AMP-activated protein kinase (AMPK). This enzyme is a sensor of cellular energy status. AMPK stimulates mitochondrial biogenesis, so that cellular metabolism can be enhanced and ATP can be generated to bring back the cellular energy status to normal. AMPK stimulates energy-generating pathways and suppresses energy-utilizing pathways.

Bioenergetics and free energy

Bioenergetics is concerned with measurement of the energetic feasibility of a chemical reaction and predictions of the extent to which reactions will occur. It is not concerned with mechanisms or rates of reactions.

Free energy is that part of the energy in a system that is available for useful work. It is designated as G (The G is named after Gibbs).

In a chemical reaction: Reactants \rightarrow Products

Change in free energy of this reaction is called ΔG . $\Delta G = G_{\text{products}} - G_{\text{reactants}}$

The free energy of the reactants (G $_{reactants}$) becomes equal to the free energy of the products (G $_{products}$) at equilibrium.

i.e., At equilibrium, G reactants = G products

In other words, the change in free energy (Δ G) that occurs when the reactants are converted to the products is zero at equilibrium.

i.e., At equilibrium, $\Delta G = G_{\text{products}} - G_{\text{reactants}} = 0$

The change in free energy is described in two ways, ΔG and ΔG° . ΔG is the more general which indicates the change in free energy and hence the direction of a reaction at any specified concentration of products and reactants. In contrast, ΔG° indicates the change in free energy only at standard conditions in which the concentration of reactants and products is 1 M (mole/L). Therefore, ΔG is better than ΔG° in predicting the direction of a reaction, i.e. whether or not a reaction can occur spontaneously. However, ΔG° is useful in comparing the free energy changes of different reactions, because the concentration of reactants and products is kept constant at 1 M. In other words, ΔG° can predict the spontaneity of a reaction, but only under certain specified conditions.

 ΔG = free energy change ΔG° = standard free energy change

 ΔG is not related to the mechanism or rate of a reaction, but is related to the equilibrium constant.

For the following chemical reaction occurring under non-standard conditions

$$A \leftrightarrow B$$

$$\Delta G = \Delta G^{\circ} + RT \ln \frac{[B]}{[A]}$$

where R is the gas constant (1.987 cal/degree/mole) and T is the temperature in Kelvin units (273 + t° C).

At equilibrium, $\Delta G = 0$ and $K_{eq} = -\frac{[B]}{[A]}$

$$0 = \Delta G^{o} + RT \ln K_{eq}$$

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1.e.
$$\Delta G^{\circ} = -RT \ln K_{eq}$$

= -2.3 RT log K_{eq} = -1.36 log K_{eq} in kcal/mole (at 25°C)
= -5.69 log K_{eq} in kJ/mole
(1 kcal= 4.18 kJ)

The relationship between ΔG^{o} and K_{eq} indicates that

$$\Delta G^{o} = 0$$
 if $K_{eq} = 1$
 ΔG^{o} is negative if $K_{eq} > 1$
 ΔG^{o} is positive if $K_{eq} < 1$

For biological reactions, the standard free energy charge, ΔG° is used more frequently than the ΔG .

If ΔG° is negative, the reaction is spontaneous and is called exergonic. i.e, energy is released.

If ΔG° is positive, the reaction is not spontaneous and is called endergonic. i.e., energy has to be provided for the reaction to proceed.

 ΔG° of the forward reaction (e.g. A \rightarrow B) is equal in magnitude but opposite in sign to that of the backward reaction (i.e. B \rightarrow A).

Example: $A \rightarrow B$ $\Delta G^{\circ} = -x \text{ cal/mole}$ $B \rightarrow A$ $\Delta G^{\circ} = +x \text{ cal/mole}$

Since $\Delta G = \Delta G^{\circ} + 2.3 \text{ RT } \log \frac{\text{[Products]}}{\text{[Reactants]}}$

Whether ΔG for a reaction is larger than, smaller than or the same as ΔG° depends on the concentrations of the reactants and products. Even if ΔG° for a reaction is positive, it can be made to occur spontaneously by properly choosing the concentrations of the reactants and products.

For a metabolic pathway, e.g. $A \rightarrow B \rightarrow C \rightarrow D$

$$\Delta G^{o}{}_{A \to D} = \Delta G^{o}{}_{A \to B} + \Delta G^{o}{}_{B \to C} + \Delta G^{o}{}_{C \to D}$$

This means that as long as $\Delta G^{o}_{A \to D}$ is negative, the pathway is thermodynamically feasible, irrespective of the ΔG^{o} values for individual reactions.

In other words, chemical reactions with a positive ΔG° can be coupled to or driven by chemical reactions with a favorable negative ΔG° .

e.g. Glucose + Pi
$$\rightarrow$$
 Glucose-6-phosphate + H₂O $\Delta G^{\circ} = +4.0$ kcal/mole
ATP + H₂O \rightarrow ADP + Pi $\Delta G^{\circ} = -7.3$ kcal/mole

When combined

Glucose + ATP
$$\rightarrow$$
 Glucose-6-phosphate + ADP
 $\Delta G^{\circ} = -3.3$ kcal/mole

Therefore, when coupled with the exergonic ATP hydrolysis, the endergonic reaction of glucose phosphorylation can proceed.

e.g.	$A \rightarrow B$	$\Delta G^{o} = +1.2 \text{ kcal/mole}$
	$B + C \rightarrow D + E$	$\Delta G^{o} = -5.8 \text{ kcal/mole}$
	$D \rightarrow X$	$\Delta G^{o} = -1.1 \text{ kcal/mole}$
	$E \rightarrow Y$	$\Delta G^{o} = +4.6 \text{ kcal/mole}$
	$A + D \rightarrow B + X$	$\Delta G^{o} = + 0.1 \text{ kcal/mole}$
	$A + E \rightarrow B + Y$	$\Delta G^{o} = +5.8 \text{ kcal/mole}$

$B + C \rightarrow E + X$	$\Delta G^{o} = -6.9 \text{ kcal/mole}$
$B + C \rightarrow X + Y$	$\Delta G^{o} = -2.3 \text{ kcal/mole}$
$A + C \rightarrow X + Y$	$\Delta G^{o} = -1.1 \text{ kcal/mole}$

High-energy bonds

Phosphoenolpyruvate	– 14.8 kcal/mole			
Carbamoyl phosphate	– 12.3 kcal/mole			
1,3-Diphosphoglycerate - the	– 11.8 kcal/mole			
bond between -COOH and phosphate				
Acetyl phosphate	 – 10.3 kcal/mole 			
Creatine phosphate	 – 10.3 kcal/mole 			
Acetyl CoA	– 7.7 kcal/mole			
ATP γ-phosphodiester bond	– 7.3 kcal/mole			

Glucose-1-PO₄ (-5.0 kcal/mole), glucose-6-PO₄ (-3.3 kcal/mole) and glycerol-3-PO₄ (-2.2 kcal/mole) are examples for low-energy compounds.

High energy bond energy can be transferred from one compound to another in the presence of appropriate enzymes. In biological systems, the energy transfer occurs in the following way with ATP as the mediator.

High-energy compounds $\rightarrow ATP \rightarrow low-energy compounds$ e.g. Phosphoenolpyruvate + ADP \rightarrow Pyruvate + ATP Glucose + ATP \rightarrow Glucose-6-PO₄ + ADP

Caloric value of dietary substances

The caloric value of a dietary constituent depends upon ΔG° for complete oxidation of that particular constituent. For example, when glucose is oxidized to CO₂ and H₂O, ΔG° is -686 kcal/mole. This value translates to -3.8 kcal/g. The caloric value of glucose is then said to be 3.8 kcal/g.

Carbohydrates and proteins have a caloric value of about 4 kcal/g whereas lipids such as long-chain fatty acids and triglycerides have a caloric value nearly three times greater. Caloric value for palmitate, stearate, tripalmitin, etc. = approximately 9 kcal/g.

Alcohol (ethanol) has a caloric value of 7 kcal/g.

Caloric value of a dietary constituent depends upon the relative oxidized or reduced state of the constituent molecule. The more a molecule is in an oxidized state, the less is its caloric value. Carbohydrates and proteins contain more oxygen in relation to their carbon than lipids. Therefore, carbohydrates and proteins have less caloric value than lipids.

Fuel composition of the body

All of us carry stored supplies of fuel within our bodies. Fat is the primary fuel store and is made up of triacylglycerol stored in adipose tissue. Glycogen stored in the liver and muscle constitutes a relatively small energy store but is very important. Protein in muscle serves many important roles in the body and therefore is not solely a fuel store like fat and glycogen.

Adipose tissue is unique because its water content is very low (about 15% of the tissue weight). In contrast, liver and muscle contain about 80% water.

Fuel store in an average 70 Kg man:

Fat	15 Kg	135000 Kcal	(85%)
Protein	6 Kg	24000 Kcal	(15%)
Liver glycogen	0.08 Kg	320 Kcal	(0.2%)
Muscle glycogen	0.16 Kg	640 Kcal	(0.4%)

Kilocalorie and calorie are synonymous in nutrition.

Daily energy expenditure

If we want to stay in energy balance, neither gaining nor losing weight, we must, on average, consume an amount of food that meets our daily energy expenditure.

Daily energy expenditure = Basal metabolic rate (BMR) + Energy for physical activity

BMR is a measure of the energy required to maintain life in a resting person who has recently awakened in the morning after fasting for at least 12 hours.

Rough estimate of BMR = 24 x weight in Kg (calories/day)

Factors that affect BMR for a comparable body weight:

Gender (males higher than females) Body temperature (increased with fever) Environmental temperature (increased in cold climates) Thyroid status (increased in hyperthyroidism) Pregnancy and lactation (increased) Age (increased in childhood)

Weight gain and weight loss

Weight gain: Dietary calorie intake is greater than the daily energy expenditure

Weight loss: Dietary calorie intake is less than the daily energy expenditure

When we draw upon our adipose tissue to meet our energy needs, we lose approximately 1 lb whenever we expend 3500 calories more than we consume. Since the caloric value of fat is 9 cal/g and the water content of adipose tissue is 15%,

$$\frac{3500}{9} \times \frac{100}{85} = 458 \text{ g} (\sim 1 \text{ lb})$$

7,700 calories equal 1 Kg body weight (i.e., body fat)

Order of preference of fuels for use: glycogen > fat > protein

Fuel source for skeletal muscle during exercise

During vigorous exercise, ATP stores in the skeletal muscle are exhausted within 1-2 seconds. Similarly, the creatine phosphate energy buffer also gets exhausted within about 3-4 seconds. Then, the exercising muscle has to depend on glucose and glycogen as the energy source. Glycogenolysis (i.e., breakdown of glycogen into glucose 1-phosphate) itself does not generate any energy. It is the liberated glucose 1-phosphate that enters glycolysis to generate ATP.

During short bursts of muscle activity, glucose metabolism occurs in the presence of oxygen (aerobic glycolysis) in which glucose is completely oxidized into CO_2 . However, during continuous and vigorous exercise, glycolysis occurs mostly under anerobic conditions, generating lactate. If exercise is continued, muscle glycogen stores are depleted, and now the muscle depends on hepatic glucose (glycogenolysis and gluconeogenesis) and then on circulating fatty acids as the energy source.

100-meter race: Most of the energy comes from ATP, creatine phosphate, and glycolysis.

Marathon: Most of the energy during this activity comes from fatty acids because ATP, creatine phosphate, and glycogen stores are all exhausted at the early stages of marathon running.

Respiratory quotient is defined as the ratio of the amount of CO_2 produced to the amount of O_2 consumed. Measurement of RQ is known as indirect calorimetry to measure energy expenditure.

Direct calorimetry uses measurement of heat production.

RQ for glucose use for energy is 1; RQ for fat use for energy is 0.7.