Radical Processes in Cellular Structure

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Abstract

In biological objects, natural and foreign radicals are distinguished. It is known that foreign radicals have a negative effect on the cells of living organisms. Unlike foreign radicals, natural radicals predominate in biological objects, which play a key role in the processes of cell life, in the reactions of biosynthesis, oxidative phosphorylation, regulation of lipid metabolism, mitosis, metabolism, etc. Every day, each cell generates a huge number of compounds with a naturally radical nature, which then participate in biochemical processes associated with the donation or acquisition of electrons. A significant role in radical oxidation-reduction. The reactions of the cell are carried out by coenzymes NAD, NADP, FAD, FMN, and also CoQ, capable of forming intermediate radical structures and charge transfer complexes (CTCs) in biological membrane censoring the transfer of energy and the transport of electrons in the cell's polyenzyme complexes.

Keywords: radical processes in cells; radical transfer of protons and electrons; coenzyme radicals; carotenoid radicals; radicals and enzyme-cofactor complexes.

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1. Introduction

Radicals include atoms or molecules with an unpaired electron, which determines their high instability and activity associated with the desire of radicals to capture or give up an extra electron. In biological objects, natural and foreign radicals are distinguished. The emergence of foreign radicals is associated with the physical impact of radiation, ultraviolet irradiation, and the chemical effect of xenobiotics on cells. It is known that foreign radicals have a negative effect on the cells of living organisms, oxidize amino acids, proteins, damage and disorganize cellular structures and BM. The role of foreign free radicals in the development of diseases such as cancer, atherosclerosis, myocardial infarction, stroke, ischemia, diseases of the nervous and immune systems, lungs, liver, kidneys, blood, skin has been proven; they cause premature aging. To reduce the aggressive impact of radicals on the body of humans and animals, biological objects have specialized enzyme systems of antioxidant protection. This role is performed by enzymes - superoxide dismutase (SOD), catalase, glutathione-dependent peroxidase, transferase, which reduce the negative impact of radicals by removing organic peroxide compounds. A large number of phenolic compounds have been isolated that have antioxidant properties, for example, vitamins E (α-tocopherol), K1 (phylloquinone) and K2 (menaquinone), ubiquinone, tryptophan, phenylalanine, as well as a significant amount of plant and animal pigments: carotenoids, flavonoids, phenol carboxylic acids. Antioxidants interact with free radicals, resulting in chain termination and inhibition of free radical oxidation.

Unlike foreign radicals, biological objects are dominated by natural radicals that perform useful functions. Natural radicals are classified into primary – semiquinones CoQH-, superoxide ($\cdot O_2-$), nitroxide ($\cdot NO$), the formation of which is associated with the enzymatic oxidation-reduction reactions. Radicals play a key role in the processes of cell life, in the reactions of biosynthesis, oxidative phosphorylation, regulation of lipid metabolism, mitosis, metabolism, etc. The main biochemical processes occurring in cells are impossible without the formation and participation of free radicals. Every day, each cell generates a huge number of bioorganic compounds that have a naturally radical nature, which then participate in vital biochemical processes associated with the donation or acquisition of electrons. The proposed article discusses the possible mechanisms of photosynthetic and bioenergetic processes, the transfer of electrons and protons through some biological membranes (BM) with the participation of enzymes (E), coenzymes (Co), lipids (L), carotenoids (Car) and their radicals.

2. Materials and methods

The experimental studies used the enzyme alcohol dehydrogenase from horse liver (LADH), the coenzyme nicotinamide adenine dinucleotide (NAD). Purification of the enzyme - LADH and coenzyme -NADwas carried out by the sorption method, using carboxymethyl (CM) and diethylaminoethyl (DEAE) - cellulose, as well as Sephadex: G-100 and G-150. The concentration of the enzyme and coenzymes was determined spectrophotometrically on a SF56 spectrophotometer (Russia). The following reagents were used in the studies: mono- and disubstituted potassium phosphate; β-carotene, lipids: cardiolipin, lecithin of chemically pure grade.

Spectral oxidized, aminated, and hydrophobized carbons (fraction 0.200-0.315 mm), as well as aminated

carbochrome, were used as conductive sorbents for immobilization of the enzyme-cofactor system. The specific surface area of the sorbents was determined using a Thermo Scientific Surfer Gas Adsorption Porosimeter (Italy). Electrochemical studies were performed using potentiostat-galvanostat R-20X (Russia). The electrochemical properties of enzyme-cofactor systems were studied using a symmetrical electrochemical cell, the design of which is shown in Figure 1
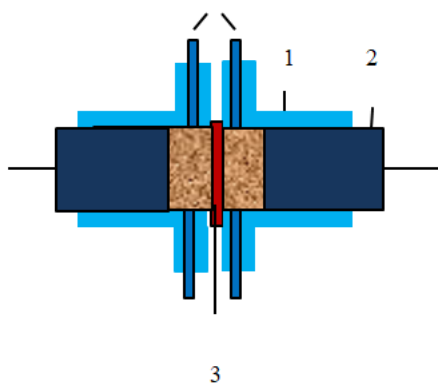

Figure 1: Design of a symmetrical electrochemical cell: A, B - half-cell chambers; 1 - electrochemical cell body; 2 - graphite electrode; 3 - cation-exchange membrane; 4 - capillaries for substrate circulation

The design of the electrochemical cell excluded the occurrence of side processes, which simplified the task of studying model systems. The reaction chambers (A and B) of the electrochemical cell were formed by a cationexchange membrane MK-40 (3) and carbon electrodes (2). Chambers A and B were loaded with conductive carbon sorbents with an immobilized enzyme-cofactor system of alcohol dehydrogenase - nicotinamide adenine dinucleotide (LADH-NAD). In both chambers, circulation of substrates in a 0.015 M phosphate buffer solution with pH = 8.2 containing 0.5 M sodium chloride was provided.

Experimental studies of the formation of a charge transfer complex (CTC) between β-carotene and the lipids cardiolipin and lecithin were carried out using a spectrophotometric method on a spectrophotometerSF-56 (Russia), the formation of micelles or liposomes was carried out using an ultrasonic homogenizer Bandelin Sonopuls HD 2070 (Germany).

3. Discussion of the research results

The carriers of protons and electrons in cells are coenzymes: NAD, NADP, FAD, FMN, CoQ. In many biochemical reactions, nicotinamide nucleotideNADAndNADPis reduced or oxidized with the addition or donation of electrons and protons. Enzymatic rThe reactions proceed through two one-electron steps, resulting in the formation of intermediate free radicals of the coenzymes NAD· or NADP·. The coenzymes FAD, FMN and their precursor - riboflavin (vitamin B2) have an isoalloxazine heterocyclic system, which also takes part in radical oxidationreduction enzymatic reactions. Thus, the reduction of the isoalloxazine ring occurs in two stages. In the first, as a result of electron transfer, a free radical is formed - semiquinone, which then attaches a second electron, passing into the reduced form of the coenzyme.

The coenzymes presented above are electron acceptors for one group of enzymes in polyenzyme complex and donors for another. In this case, the restoration and oxidation of metabolites is accompanied by cyclic enzymatic regeneration of coenzymes.

The most important role in the transport of electrons and protons in the BM mitochondria and chloroplasts is given to the mobile carrier-ubiquinone (CoQ). Ubiquinone (coenzyme Q6 and Q10) has a quinone structure and is localized in the mitochondrial BM. During the reduction process, coenzyme Q changes its chemical structure through the form of a free radical, semiquinone. Proton transfer is realized by CoQ, which accepts a redox equivalent, for example, from FAD, which changes its state from the oxidized, radical semiquinone to the reduced form. The conjugated enzymatic
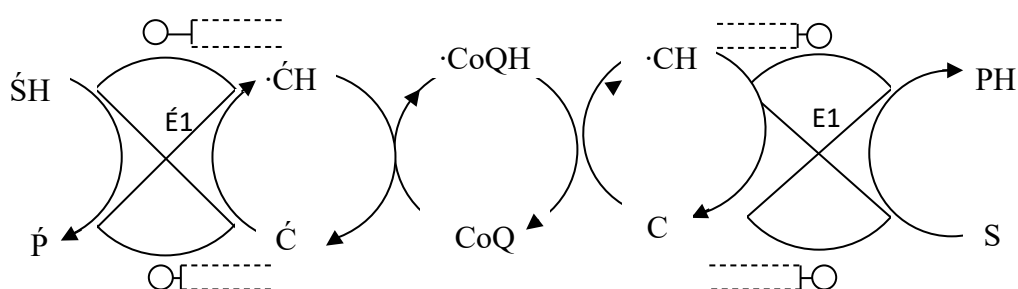

Figure 2: Proton transfer through BM with the participation of CoQ radicals.

É1 E1,-enzymes involved in the oxidation and reduction of substrates ŚH,S, respectively;·ĆH,·CoQH- ·CH-reduced coenzyme radicals; Ć, CoQ, C - oxidized forms of coffee compounds;RN,Ṕ -products of enzymatic reactions.

reactions occurring in the BM are possible due to the analogy of the catalytic clefts of the apoenzymes, as well as the similarity in the fixation of coenzymes in the active center and the strict orientation of the enzyme-cofactor complexes. According to the scheme in Fig. 1, the substrate ŚHas a result of an enzymatic reaction it is oxidized to Ṕ according to equation (1). In this case, the coenzyme radical ·CH is formed.

$$\text{É1}$$

$$\text{ŚH} + \text{C} \longrightarrow \text{Ṕ} + \text{·CH} \quad (1)$$
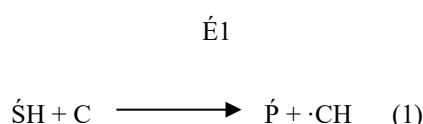
The coenzyme radical (·CH) transfers an unpaired electron and a proton to the coenzyme CoQ, which, having acquired them, is transformed into the reduced form of coenzyme Q, namely ·CoQH according to equation (2), while the oxidized form of the coenzyme (C) is regenerated

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$$\cdot CH + CoQ \longrightarrow C + \cdot CoQH \quad (2)$$
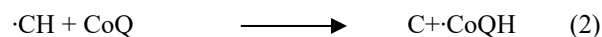
At the next stage, contact of the radical of the reduced form of the coenzyme occurs· CoQH with a cofactor of another biocatalytic system on the opposite side of the BM, which is accompanied by the transfer of an unpaired electron and a proton according to equation (3)

$$\cdot CoQH + C \longrightarrow CoQ + CH \quad (3)$$
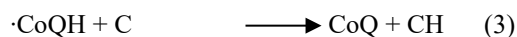
And finally, the process is completed by the enzymatic reaction (4) "pumping", storing energy in the form of a reduced form of the substrate, with the participation of the radical ·CH by reaction (4). It should be noted that the transmembrane, radical transfer of electrons and protons can also be realized in the opposite direction.

$$\cdot CH + S \xrightarrow{\quad E1 \quad} PH + C \quad (4)$$
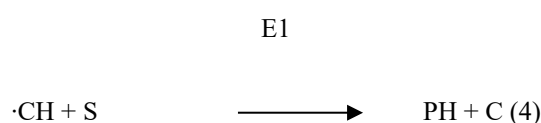
The group of energy and electron carriers that are widespread in the plant and living world includes natural organic pigments-carotenoids having a conjugated bond system. Carotenoids are mainly localized in the lipophilic region of the BM, where they form stable carotene complexes. Due to the presence of unsaturated conjugated bonds, carotenoids have an elongated light-sensitive, electron-conducting structure, due to which they perform the function of energy and electron carriers according to the scheme in Figure 3.
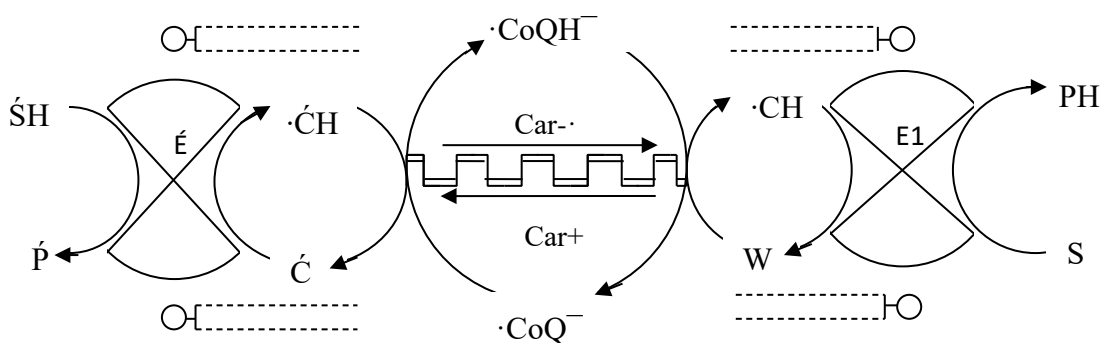

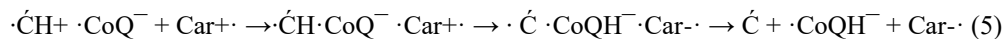**Figure 3:** Transfer of protons and electrons through BM with the participation of radicals.

According to the scheme substrate ŚHas a result of an enzymatic reaction it is oxidized to Ṕ according to equation (1). Then the process proceeds with the participation of the coenzyme radical CoQ and the cation-radical of carotene (Car+). The cation-radical of carotene (Car+) arises on one of the β-ionone rings during the

drain of electrons through the system of conjugated bonds to another β-ionone ring, where the anion radical (Car-) is formed. Another important element of the proposed model is the provision of electron transfer from the enzyme-cofactor system on the carotene molecule. Taking into account the above, the radical proton and electron transfer through the BM can be represented as a sequential transformation of radical complexes.

$$\cdot\acute{C}H + \cdot CoQ^- + Car+\cdot \rightarrow \cdot\acute{C}H\cdot CoQ^- \cdot Car+\cdot \rightarrow \cdot\,\acute{C}\,\cdot CoQH^-\cdot Car-\cdot \rightarrow \acute{C} + \cdot CoQH^- + Car-\cdot \quad (5)$$

At the same time, on the opposite side of the BM the following will flow:

$$C + \cdot CoQH^- + Car-\cdot \rightarrow \cdot C\cdot CoQH^-\cdot Car-\cdot \rightarrow \cdot CH\,\cdot CoQ^-\cdot Car+\cdot \rightarrow \cdot CH + \cdot CoQ^- + Car+\cdot \quad (6)$$
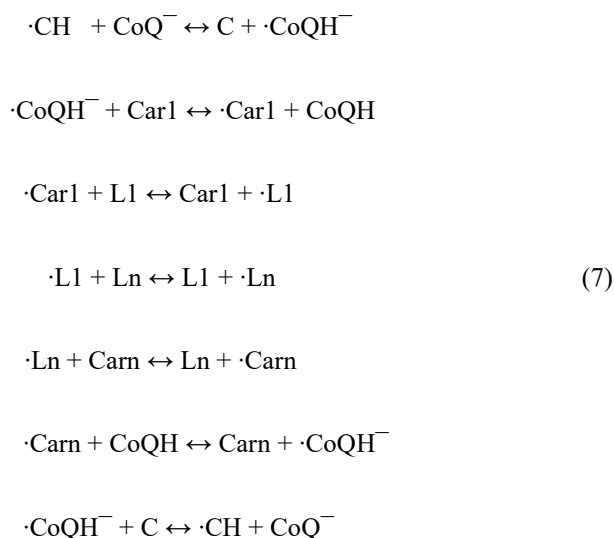
At the final stage, enzymatic reduction of the substrate can be observed according to equation (4).

An important place in the process of electron transfer is given to the formation of a charge transfer complex (CTC), accompanied by the appearance of a characteristic absorption band in the long-wave region associated with the transition of the complex from the ground to the excited state. The complete electron transfer in the CTC is accomplished from the ground state of the donor (D) to the excited state of the acceptor (A). The transition of the system from state D-A in D+-A- is accompanied by an increase in the dipole moment, which is the cause of large coefficients and also the expansion of the absorption band of the CPC. Charge transfer in the CPC increases significantly when it is excited by electromagnetic radiation, which is observed in the processes of photosynthesis. The main feature of the formation of the CPC is the maximum overlap of orbitals, according to which the minimum potential energy occurs if two molecules in the complex are oriented in such a way that the maximum possible overlap is achieved electron-donor and electron-acceptor orbitals. The above confirms that in the BM of cells, carotenoids form CTP with bioorganic compounds that acquire a free-radical form of quinone, formed in the cell during oxidationreduction reactions. Such bioorganic compounds include coenzymes FAD, FMN, which contain an isoalloxazine ring, the reduction of which occurs through a semi-reduced form with the formation of a radical structure of semiquine. Carotenoids are essential structural components of any photosynthetic membranes; in the form of complexes, they are part of chlorophyll-protein complexes, penetrate the membrane bilayer, forming an intermolecular bond with lipid molecules. Hydrocarbon chains of lipids can contain from 1 to 6 double bonds, and lipids of a number of plants, as well as carotenes, have a conjugated bond system. This gives grounds to assume that the energy and electron conductivity of biological membranes significantly depends on the quantitative content of polyunsaturated fatty acids in lipid membranes and the content of carotenoids. Thus, a highly organized system of packed molecules of carotenoids and lipids is capable of providing transmembrane electron transfer along the BM from one biocatalytic system to another. The radical formed in the enzymatic one-electron redox reaction is transferred as a result of a chain reaction along the lipid-carotenoid structure to neighbouring molecules, and this continues until the unpaired electron is captured by CoQ and transferred to other cofactors, such as FAD, which participates in the enzymatic radical redox reaction. The efficiency of electron transfer through the lipid-the carotenoid structure will increase significantly when exposed to light quanta, which can be observed in the processes of photosynthesis.

Radical electron transfer in biological membrane with the participation of coenzyme radicals (C, CoQ),

carotenoids (Car) and lipids L can be represented as sequential reactions.

$$\cdot CH \ + CoQ^- \leftrightarrow C + \cdot CoQH^-$$

$$\cdot CoQH^- + Car1 \leftrightarrow \cdot Car1 + CoQH$$

$$\cdot Car1 + L1 \leftrightarrow Car1 + \cdot L1$$

$$\cdot L1 + Ln \leftrightarrow L1 + \cdot Ln \qquad\qquad (7)$$

$$\cdot Ln + Carn \leftrightarrow Ln + \cdot Carn$$

$$\cdot Carn + CoQH \leftrightarrow Carn + \cdot CoQH^-$$

$$\cdot CoQH^- + C \leftrightarrow \cdot CH + CoQ^-$$

It is important to note that the absorption spectra of carotenoids have a close resemblance to the absorption spectra of flavoproteins, which gives grounds to conclude that the resonance energy of carotenoids and flavoproteins corresponds, due to which electron transfer from one molecule to another is possible practically without any significant energy costs.

In connection with the above, studies were conducted on the formation of the CTP between β-carotene and lipidcardiolipin. No absorption bands were detected for cardiolipin in the visible region of the spectrum, whereas βcarotene has characteristic bands at 425,450, 475 nm. Significant broadening (up to 100 nm) of the absorption band β-carotene in the long-wave region is observed during the formation of a complex of cardiolipin and β-carotene. A slight shift of absorption bands to the long-wave region up to 480 nm was obtained for the β complex-carotene-lecithin relative to the original length-450 nm. The experimental studies conducted have shown that the β system-carotenecardiolipin forms a CTP, through which electron transfer is possible lipid-carotenoid structure of BM. It can be assumed that carotenoids with heterocyclic rings are capable of forming CTP with coenzymes, while carotenoids without heterocyclic rings, provide electron transfer across the packaged lipid-carotenoid structure of BM. The mechanism of radical electron transfer was used in modelling a two-electrode enzymatic system [1,2].

Currently, extensive research is being conducted to find ways to use biocatalysts in electrochemical processes. The operation of the simulated electroenzymatic processes is based on the transformation of the initial substrates under the action of enzymes into electroactive components that enter into an electrochemical reaction on the electrodes. In this case, biocatalysts can be used both in a soluble and immobilized state. The prospects for obtaining heterogeneous biocatalytic systems are obvious, since it allows for the transfer of electrons between the conductive matrix and the active centre of biocatalysts. The principle of constructing such enzymatic systems was considered in [2] and practically implemented [3]. Immobilization of enzymes on conductive carriers currently does not cause any obstacles. A more complex task arises in the immobilization of cofactor-dependent biocatalysts, when the task is to bind apoenzymes and their coenzymes. In this case, it is important to

select a method that would provide the coenzyme with a certain degree of freedom for the purpose of its electrochemical regeneration on the conductive matrix.

Thus, the above-described type of heterogeneous biocatalyst should have a number of properties, in particular, provide more efficient electron transfer to the active centre of enzymes and maintain their high catalytic activity. The mechanisms of electron transfer to the active centre of biocatalysts are considered in a number of publications [1,4].

Enzyme-cofactor complexes immobilized on conductive carriers can be used in the development of various types of electroenzymatic systems, such as metabolite and toxicity analysers, fuel cells. Fig. 3 shows a model of a twoelectrode generator
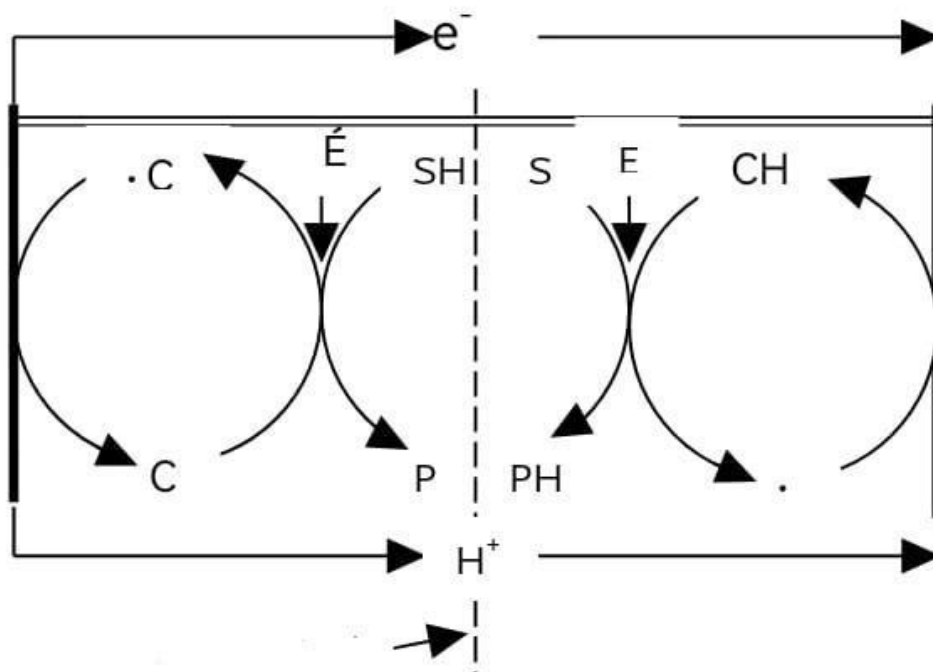
External chain

Figure 4: Schematic diagram of a biological current generator

current, the principle of operation of which is as follows. According to the diagram, the flow of electroenzymatic processes is accompanied by alternating oxidation and reduction of coenzymes. At the anode, as a result of the enzymatic reaction, a cofactor radical is formed (·CH H), which is then electrochemically oxidized to C. At the cathode, the enzymatic formation of the oxidized coenzyme and electrochemical "pumping" of its reduced form occurs. The magnitude of the voltage of the electrochemical cell (φ) in such a system can be determined by the equation:
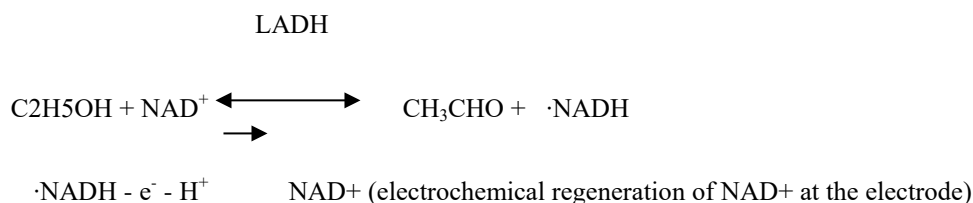
$$\varphi = \varphi_A - \varphi_K + iR = -\frac{2,3RT(pH_A - pH_K)}{2F} + \frac{RT}{2F} \ln \frac{[C]_A}{[CH \cdot H]_A} \frac{[CH \cdot H]_K}{[C]_K} + iR \ (7),$$

where φA and φK are the potentials at the anode and cathode, respectively; R is the universal gas constant; T is the absolute temperature; F is the Faraday number; pH_A and pH_K are the pH in the cathode and anode spaces; $[C]_A$, $[CH \cdot H]_A$, $[C]_K$, $[CH \cdot H]_K$ are the concentrations of both forms of the coenzyme at the anode and cathode; IR is the ohmic potential drop.
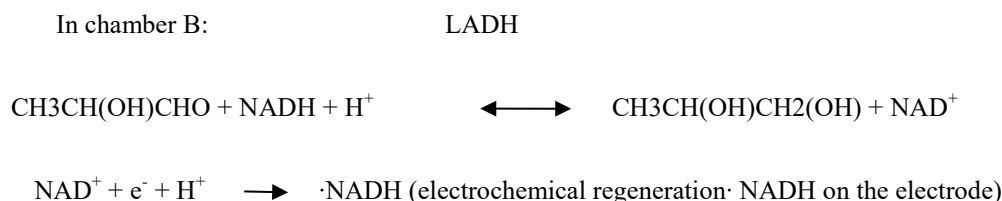
An enzyme complex was used as a model enzyme system. LADH-NAD, which was immobilized by the sorption method on a carbon conductive carrier. The latter was supposed to provide effective electron transfer to the active center of the biocatalyst. The design and diagram of the used biofuel cell are shown in Fig. 1 and 3, respectively. The chambers of the biological current generator were loaded with a carbon carrier with an immobilized enzyme-cofactor complex of LADH-NAD. An electrolyte of 0.015 M phosphate buffer solution with pH = 8.2, containing 0.5 M sodium chloride, was pumped through the chambers of the half-cells using a peristaltic pump. When ethanol was introduced into one chamber of the fuel cell, and lactaldehyde into the other, this resulted in an EMF of up to 87 mV and the generation of a stable current with a density of up to 0.58 μA/cm2. The system was tested to determine the nature of the current. There was no EMF or current in the system before the introduction of alcohol and lactaldehyde substrates into the half-cells, and the current value changed depending on the concentration of the substrates. When 5 μl of potassium cyanide with a concentration of 10-3 M was introduced into the electrolyte, the inhibitor completely stopped generating current.

The processes occurring in the semi-elements of a biological current generator can be represented as enzymatic and electrochemical reactions.

In chamber A:

LADH

$$C2H5OH + NAD^+ \rightleftharpoons CH_3CHO + \cdot NADH$$

$\cdot NADH - e^- - H^+ \qquad NAD+ \text{ (electrochemical regeneration of NAD+ at the electrode)}$

In chamber B: LADH

$$CH3CH(OH)CHO + NADH + H^+ \longleftrightarrow CH3CH(OH)CH2(OH) + NAD^+$$

$NAD^+ + e^- + H^+ \longrightarrow \cdot NADH \text{ (electrochemical regeneration} \cdot NADH \text{ on the electrode)}$

The conducted studies have shown that this system can operate for several days without loss of catalytic

activity. Increasing the rate of substrate recirculation leads to a significant increase in current, which is associated with the intensification of substrate transfer to the enzymatic system.

It has been established that when NAD^+ is reduced electrochemically [5] or under the influence of X-rays [6], a coenzyme with low or completely absent coenzyme activity is formed. This feature of the NAD coenzyme can be explained by the formation of an inactive dimer obtained during the interaction of two radicals, each of which gives its unpaired electron for general use, forming a chemical bond at the 4th position of the pyridine ring, which participates in the catalytic reaction. The observed stability of the biological current generator is due to the fact that the coenzyme radical is in a complex with an apoenzyme, which is immobilized on a carbon carrier, which significantly limits the mobility of the coenzyme and complicates the formation of a dimer.

The obtained experimental results confirm the radical single-electron nature of oxidation-reduction processes occurring in a living cell with the participation of coenzymes. The above explains the observed increase in carotenoid concentration in animal and human cells during hypoxia. At low partial oxygen pressure, energy supply to cells is intensified due to radical oxidation-reduction processes, the efficiency of which depends on the quantitative content of carotenoids. Significant accumulation of carotenoids in tissues of patients with atherosclerosis and ischemic heart disease [7] can be explained by oxygen deficiency, as a result of which the body is forced to compensate for this deficiency by enhancing the flow of radical oxidation-reduction reactions realized with the participation of carotenoids. It is also known that the tissues of marine animals and fish contain a large number of carotenoids, and their number increases significantly in deep-sea fish species, which solve the problem of energy supply to cells by using radical electroenzymatic oxidation-reduction reactions. Radical reactions are central to cell function The study shows that natural radicals (like semiquinones, superoxide, nitroxide) are vital for biosynthesis, oxidative phosphorylation, lipid metabolism, mitosis, and more. Cells produce these radicals daily to drive essential biochemical reactions involving electron and proton transfers. Coenzymes as radical carriers Coenzymes such as NAD, NADP, FAD, FMN, and CoQ participate in single-electron redox reactions, forming radical intermediates. These facilitate energy and charge transfer across biological membranes, particularly in mitochondria and chloroplasts. Carotenoids and lipids in electron transport Carotenoids, with their conjugated double bonds, serve as electron-conducting bridges. When combined with lipids like cardiolipin and lecithin, they form charge transfer complexes (CTCs) that support radical-mediated electron flow across membranes. Bioelectrochemical system demonstrated The research built a two-electrode system using immobilized LADH-NAD complexes on conductive carbon. When ethanol and lactaldehyde were added, the system generated a stable current (up to 0.58 µA/cm²) and an EMF of 87 mV, confirming the possibility of radical-based energy generation. Stability and efficiency The system remained catalytically active for days. Immobilizing the coenzymes helped prevent dimer formation, preserving activity and ensuring smooth electron transfer. Biological implications The study links higher carotenoid levels in hypoxic tissues to boosted radical activity. This may serve as an adaptive energy mechanism under low-oxygen conditions, such as in heart disease or deep-sea environments. Several foundational studies have established the dual nature of radicals in biological systems. For instance, research has shown that reactive oxygen species (ROS)—a type of free radical—are not only byproducts of metabolism but also key players in cell signaling and homeostasis. However, their overproduction leads to oxidative stress, damaging DNA, proteins, and lipids, and contributing to diseases like cancer and neurodegeneration. Earlier work by Shapovalov and Gladyshev (1985,

1987) laid the groundwork for understanding enzyme-cofactor systems in redox biology. They demonstrated that immobilized coenzyme-dependent oxidases could function in electroenzymatic systems, a concept your study builds upon by integrating LADH-NAD complexes into a bioelectrochemical generator.

Other studies have emphasized the role of protein-bound radicals in radical enzymes, highlighting how proteins stabilize these reactive intermediates to prevent side reactions. Additionally, the interaction between carotenoids and coenzymes in forming charge transfer complexes (CTCs) has been explored in the context of photosynthesis. Prior research has shown that these complexes can absorb light in the near-infrared region, enhancing energy transfer efficiency.

4. Constraints and Limitations

High reactivity of radicals Free radicals are extremely unstable and short-lived, making them difficult to isolate and study directly. Most conclusions rely on indirect measurements or the behavior of reaction by-products. Complexity of biological systems The radical processes described involve multiple interacting components—coenzymes, enzymes, lipids, carotenoids, and membranes. This complexity makes it challenging to attribute observed effects to a single factor or mechanism. Model system limitations The electrochemical cell and enzyme-cofactor systems used in the study are simplified models. While they mimic biological conditions, they may not fully replicate the dynamic environment of living cells. Immobilization effects Although immobilizing enzymes and cofactors improves stability, it may also restrict their natural conformational flexibility, potentially altering their activity compared to their native state. Scalability and practical application The bioelectrochemical system demonstrated promising results in a lab setting, but its scalability, long-term stability, and integration into real-world bioenergy or biosensing devices remain untested. Environmental sensitivity Radical-based processes are highly sensitive to pH, temperature, and oxygen levels. Small fluctuations in these parameters can significantly affect reaction efficiency and reproducibility. Potential for radical-induced damage While natural radicals are beneficial in controlled settings, their accumulation or misregulation can lead to oxidative stress and cellular damage. The balance between utility and toxicity must be carefully managed.

5. Conclusion

Physiological processes occurring in living nature are possible due to controlled, balanced single-electron processes. The balance of foreign and natural radicals present in biological systems constantly changes during the entire period of the life cycle. In childhood, natural radicals predominate, and in old age, there is a significant accumulation of foreign radicals, leading to disorder in the physiological processes of the cell and an increase in entropy. A change in the ratio of foreign and natural radicals is the cause of the suppression of the enzyme complex of radical protection of cells, which leads to a weakening of the bioenergetic processes of transformation and accumulation of energy, catabolism and anabolism, etc. and, as a consequence, to the manifestation of diseases and aging.

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