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Justification of the electrical scheme of biological tissue replacementunder the action of DC voltage

Abstract. The change in the impedance of biological tissue under the influence of voltage is used in the diagnosis and treatment of various diseases. Mathematical models describing physical and biological processes in biological objects are based on electrical substitution schemes. The subject of research of this work was the study of the change in the impedance of biological tissue in the transient process of ionization under the action of DC voltage. An analysis of the known substitution schemes was carried out, the shortcomings of their application were identified when the transient processes of ionization in the tissue under the action of direct current voltage were studied, and the substitution scheme with the introduction of additional resistance was substantiated, both analytically and experimentally. In the work, the bioimpedance method is applied when direct current voltage is applied to biological tissue, taking into account the law of commutation in transient ionization processes. An invasive measurement of the change in impedance with needle electrodes was carried out, and it was proved that the active component proportionally depends on the distance between the electrodes, while the capacitive component remains unchanged. It is shown that the ionization time constant is a criterion parameter and can be used in the diagnosis of the development of ischemic disease of muscle tissue, the change in the state of biological tissue when blood flow is stopped during the application of a tourniquet. It has been proven that the ionization time constant does not change with an unchanged ionic composition of the tissue and can be used in the analysis of the composition of the intercellular space. A simultaneous invasive measurement was performed in two identical places of different limbs, on one of which a hemostatic tourniquet was applied. The obtained results made it possible to conclude that a change in the constant time from 15% to 50% compared to two constant times allows for rapid diagnosis, within 2 minutes, of the state of biological tissue and can be used in the study of the development of diseases associated with ischemia. The results of the study can be used for rapid diagnosis of the state of a biological object and the creation of an inexpensive device for its use in surgery and research laboratories

Keywords: impedance; transient process; ionization process; cell resistance; capacitance; ionization time constant; diagnostics; ischemia

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INTRODUCTION

In diagnostic and medical practice, the bioimpedance method – a change in the complex resistance (impedance) of biological tissue under the action of voltage - has found wide application [1-3]. The effect of direct and alternating electric current on the electrical conductivity of biological tissue has been the subject of many scientific studies [4; 5].

The electrical resistance of biological tissue is one of the criteria for studying the processes of state change and detecting various diseases in a biological object [6; 7]. Resistance measurements are used to study limb ischaemia, diagnose the affected skin surface with haemangioma, and detect pathological changes in tissue in small volumes when diagnosing cancer, otorhinolaryngological, gynaecological, and other tumours [8-10].

The flow of direct current through living cells activates the movement of electrolyte ions and other charged particles. The mobility of these particles is different, so their redistribution occurs. Biological tissue for studying the effects of voltage is represented by an electrical substitution circuit. Depending on the object of study, different substitution circuits are used; simple ones consist of a capacitor and a resistor, complex ones of several resistors and capacitors. Depending on the objectives of the study, they are combined into different substitution schemes [4; 5; 11].

Both in scientific research and in the design of medical devices that use both direct and alternating currents, it is important to build a mathematical model that reliably describes the biophysical processes occurring in biological tissues.

The reliability of the mathematical model and the results obtained depends on the choice of the electrical scheme for replacing biological tissue.

The influence and application of direct current on the processes occurring in living organisms have been studied in [4; 12; 13]. Direct current is more often used in treatment as described in [7; 8; 13]. Current of variable frequency and amplitude is more commonly used in research. Papers [14; 15] investigated the effect of alternating current and alternating frequency from 10 to 44000 Hz on the change in biological tissue impedance using the frequencies of therapeutic intensities of drug penetration into cells. In these works [16-18], an electrical substitution circuit with a series connection of capacitance and active resistance was used to study the change in impedance under the action of alternating current. Using such a substitution scheme to study the effect of direct current on biological tissue would be incorrect. In steady-state mode, at zero voltage frequency, the capacitance is equal to infinity, and the current should be zero.

Papers [5; 8; 10] show the change in impedance under the influence of a variable frequency voltage. This paper also uses traditional substitution circuits with both series connection of the capacitive and active elements and parallel connection, and the expression of Ohm's law is given for these circuits.

In [3; 14], the use of the bioimpedance method was proved to study changes in the state of biological tissues and detect diseases. To build mathematical models that characterise changes in the properties of biological tissue, in [5; 6], various schemes applied to alternating current of different frequencies and amplitudes were analysed.

It should be noted that the above-mentioned scientific sources insufficiently investigated the impact of the choice of electrical circuit for biological tissue replacement on the study of the transient process of impedance change and the change in the ionisation time constant as an information and diagnostic criterion parameter in the diagnosis of various diseases. For example, the imperfection of the choice of electrical replacement circuits does not allow us to establish patterns of changes in electrical resistance and changes in tissue viability in partial and complete ischaemia. It should also be noted that equipment using direct current is less complex and cheaper.

The purpose of the study was to analyse existing electrical schemes for biological tissue replacement.

To achieve this goal, the following tasks were formulated: substantiation of a biological tissue replacement circuit with the introduction of an additional active resistance to study transient ionisation processes in biological tissue; development of a replacement circuit for a heterogeneous ionic composition of biological tissue from one to n types of ions; substantiation of changes in the time constant as a criterion for studying the dynamics of limb ischaemia and determining the time of ischaemia development when a tourniquet is applied.

MATERIALS AND METHODS

To achieve this goal, the bioimpedance method was used, which allows monitoring the change in the impedance of biological tissue in the transition period using invasive measurement of the electrical resistance of biological tissue under the influence of direct current voltage.

In the course of the research work, theoretical methods of approximation of experimental studies, laws of biophysics of cells and intercellular space of biological tissue were used to determine the change in biological impedance in the transient process under the influence of DC voltage.

The study was conducted at the Photonics Laboratory of Vinnytsia State Technical University. In Figure 1 shows a laboratory setup for measuring the electrical conductivity of biological tissue.

Materials: biological object (sexually mature guinea pigs – males weighing 500-600 g). Studies were performed under anaesthesia (composition: sodium thiopental 10 mg/ml – 3-4 ml). Anaesthesia was administered 30 minutes before the start of the study. Within 0.5 hours, premedication was performed with the following composition: dimedrol 1% ¬ 0.3 ml and analgin 50% ¬ 0.3 ml. When working with animals, the provisions of Article 26 of the Law of Ukraine No. 3447-VI of 16.10.2012 "On the Protection of Animals from Cruelty" [19], the "General Ethical Principles for Animal Experiments" approved at the First National Congress on Bioethics [20], the requirements of the European Convention for the Protection of Vertebrate Animals

Used for Research and Other Scientific Purposes [21], and the Declaration on the Humane Treatment of Animals [22] were followed.

Equipment: Figure 2 shows a block diagram of the equipment for measuring the conductivity of biological tissue.

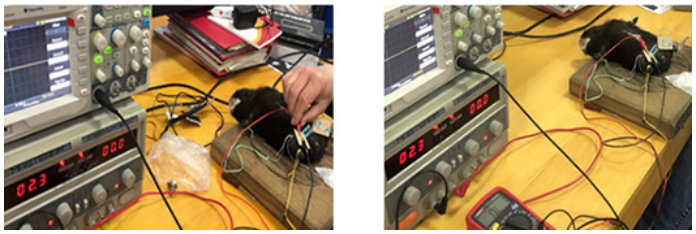

Figure 1. Laboratory setup for measuring the electrical conductivity of biological tissue

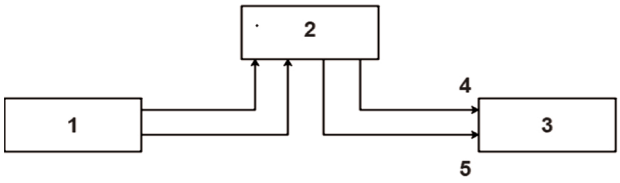

Figure 2. Block diagram of connection of equipment for measuring the conductivity of biological tissue, where indicated: 1 – DC voltage control unit; 2 – two-channel oscilloscope; 3 – biological object (guinea pig); 4 and 5 sensors for invasive conductivity measurement

DC power supply – voltage (0-50), current 10 A, voltage adjustment step 0.5 V, measurement error 1%. The oscilloscope is a Sony-Tektronix 314 two-channel portable storage oscilloscope with a bandwidth of 10 MHz. Medical needles (5 mm³ syringe) with stepwise adjustment of the distances between them were used as sensors for invasive measurement. The adjustment step is 1 cm. The needles are insulated with varnish, except for the tips with an open part that is inserted into the tissue, which is 5 mm.

To build mathematical models and analyse the impact of extraneous factors on biological tissue, electrical substitution schemes are used for both tissue sections and individual organs [7]. The criterion for choosing an electrical substitution scheme was to match the physical process in the biological environment that it describes.

RESULTS AND DISCUSSION

It is known from studie [3; 8] that the applied DC voltage to biological tissue causes the redistribution of free ions and the appearance of an electromotive force (EMF). Figure 3 shows a physical model of the electrical conductivity of biological tissue: the ionisation current directed against the current caused by the applied voltage depends on the number and types of ions.

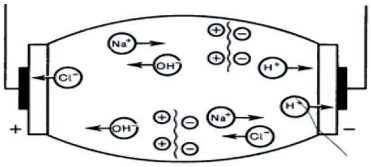

Figure 3. A physical model of the electrical conductivity of biological tissue

The heterogeneous structure of a biological object or tissue part, with its structural and physical features, constitutes the resistive characteristic of the object under study when exposed to an electric current. The structure of biological objects determines the total impedance (electrical resistance or electrical conductivity), which can vary depending on the current state of the object and the influence of an external factor, such as voltage, electromagnetic fields, etc.

A constant voltage applied to a biological object during the transient period causes electric currents, one of which is the current caused by the polarisation properties of the tissue. The total electrical resistance of a biological tissue is defined as:

$$R = \rho \frac{L}{S}, \quad (1)$$

$$R_c = \frac{1}{\omega C}. \quad (2)$$

Where indicated:

R – active component of tissue impedance; R_c – the capacitive component of tissue impedance; ρ – the specific component of biological tissue; L – the length of the current path; S – cross-section for current flow; C – the capacitance; ω – current frequency.

The total resistance in a current circuit is the impedance Z, which is defined by formula (3):

$$Z = \sqrt{R^2 + R_c{}^2}. \quad (3)$$

Electrical substitution circuits are constructed depending on the connection of active and capacitive resistances, which correspond to their mathematical model, which should reliably describe biophysical processes in biological

tissue. Traditional circuits are used to study the effect of voltage of different currents. Figure 4 shows the traditional electrical circuits for replacing biological tissue used in the above works.

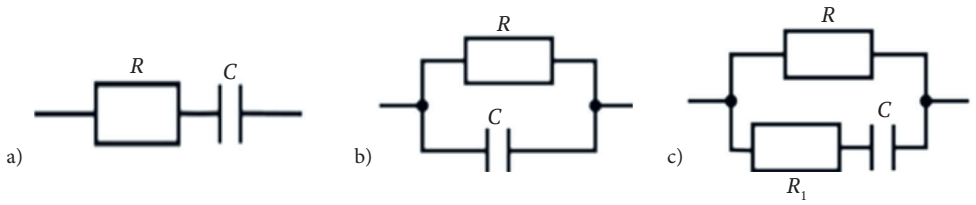

Figure 4. Traditional electrical circuits for biological tissue replacement, where R – active resistance in the intercellular space, R_1 – active resistance of tissue cells, C – capacitive component of the cell

Scheme A (Fig. 4a) is the simplest fabric replacement scheme. The input impedance – Z_{inp1} is given by formula (3). This scheme is not practically used in DC studies because, in the steady-state mode of the input current, I_{inp} tends to 0, since the impedance $Z_{inp1}\rightarrow\infty$. This, when using this substitution scheme, gives significant deviations and errors of experimental measurements from theoretically calculated ones.

$$Z_{inp2}=\frac{R\cdot R_c}{R+R_c}=\frac{R\frac{1}{\omega C}}{R+\frac{1}{\omega C}}. \quad (4)$$

Analysing expression (4), we see that at the initial time t=0, $R_c=\frac{1}{\omega C}\rightarrow\infty$,the input current I_{inp} tends to infinity $I_{inp},\rightarrow\infty$, since the active component of the impedance R is shunted. The use of this substitution scheme has significant deviations and errors from experimental measurements when studying the transient process of impedance change.

For the substitution scheme (Fig. 4c), the input impedance, Z_{inp3}, in the transient process has the form:

$$Z_{inp3}=\frac{R\cdot\sqrt{R_1^2+(\frac{1}{\omega C})^2}}{R+\sqrt{R_1^2+(\frac{1}{\omega C})^2}}. \quad (5)$$

Replacement scheme (Fig. 4c), is a common model for AC voltage studies, but when studying the transient process under the action of DC voltage at the initial switch-on (time point equal to zero t=0), given that the active component of the tissue cell impedance is less than the active component of the cell impedance $R<R_1$, the input current I_{inp} will be limited by the active component of the impedance $R_{inp3}=\frac{RR_1}{R+R_1}$, since $R_{inp3}<R<R_1$. The input current I_{inp} should exceed the steady-state value by several times, which is not observed in practice. In both schemes (Fig. 4b) and (Fig. 4c), at the initial moment of current flow, it causes the release of heat that can harm the tissue (local overheating [23]), which is not observed in practice. The use of a substitution scheme (Fig. 4c) also causes deviations and errors in experimental measurements from theoretically calculated ones.

To create a mathematical model that allows analysing transient ionisation processes under the action of DC voltage in tissues, the authors used the substitution scheme of Figure 5. Study of transient ionisation processes in tissues under the influence of DC voltage with different blood flow and different amounts of ions in the same volume, a tourniquet was applied to one paw of a guinea pig. The substitution scheme of Figure 5b corresponds to physicochemical processes with a reduced amount of ions, the simulation of ischemia is the scheme of Figure 5a, this scheme corresponds to the study of healthy biological tissue.

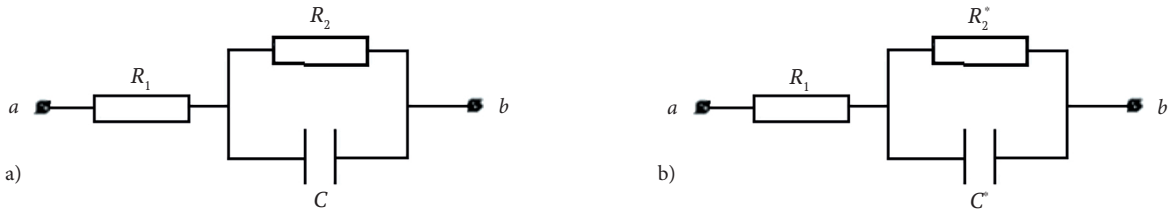

Figure 5. Electrical schemes of biological tissue replacement: a) without a tourniquet; b) with a tourniquet applied

In Figures 5a and 5b, R_1 is the active component of the impedance in the intercellular space, R_2 and R_2^* are the active components of the impedance of tissue cells without and with a tourniquet, C is the capacitive component of the impedance of tissue cells without a tourniquet, which characterises the process of ionisation in healthy biological tissue, and C^* is the capacitive component of the impedance with a tourniquet. At the initial switching on (time point t=0) (scheme of Fig. 5b), taking into account the switching law [24], is replaced by the equivalent scheme of Figure 6.

Figure 6 shows an equivalent replacement circuit to Figure 5a.

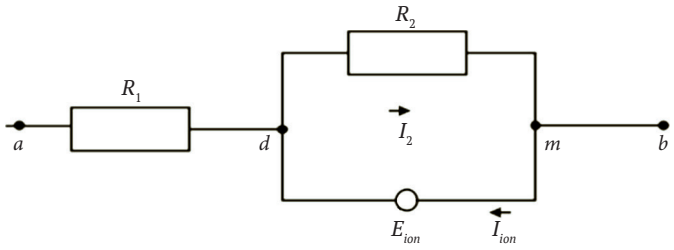

Figure 6. Electrical substitution scheme that takes into account the ionisation process

Note: E_{ion} is an electromotive force caused by the ionisation process, caused by the movement of free charged ions under the action of the source electric field. *a*, *d*, *m*, *b* are potential points. The voltage applied to the biological tissue is $U_{ab}=\varphi_a-\varphi_b$. φ_a and φ_b are the potentials at points *a* and *b*. The directional vector E_{ion} is opposite to the vector U_{ab}, I_2 is the current flowing in the area with the active impedance component R_2, I_{ion} is the current flowing in the area with the capacitance

According to the first Kirchhoff rule for the nodal connection at point d, Figure 6, the current balance is as follows:

$$I_{inp}+I_2-I_{ion}=0. \quad (6)$$

The voltage balance, according to Kirchhoff's second rule, looks like this:

$$U_{ab}=\Delta U_1+\Delta U_2. \quad (7)$$

Where ΔU_1, ΔU_2 – voltage drop on the active impedance components R_1 i R_2.

Equation (2), which characterises the change in E_{ion}, taking into account the boundary conditions, is written in the form:

$$\frac{dE_{ion}}{dt}+\left(\frac{1}{R_2\cdot C}\right)\cdot E_0, \quad (8)$$

where E_0 – is the value of the electromotive force of ionisation in steady state and is equal to $\Delta U_2=U_{dm}$.

$E_0=I_2\cdot R_2=I_1\cdot R_2$, worthy of the replacement scheme (Fig. 6), for the moment of time t=0, $I_2=I_1$.

The solution with respect to E_{ion} is known [24] and has the form:

$$E_{ion}=E_0\,(1-e^{-\frac{t}{\tau_{4.1}}}), \quad (9)$$

where $\tau_{4.1}$ – is the time constant of the ionisation process for the biological object under consideration and is equal to $\tau_{4.1}=C\cdot R_2$.

Let us write equation (2) in the form:

$$U_{ab}=\Delta U_1+E_0(1-e^{-\frac{t}{\tau_{4.1}}}). \quad (10)$$

According to equations (1), (4), (5), the input current is determined by the expression:

$$I_1=\frac{U_{ab}}{R_1+R_2(1-e^{-\frac{t}{\tau_{4.1}}})}=\frac{U_{ab}}{Z_{inp4}}, \quad (11)$$

where Z_{inp4} – is the input impedance of the biological tissue and is defined as:

$$Z_{inp4}=R_1+R_2(1-e^{-\frac{t}{\tau_{4.1}}})\cdot \quad (12)$$

It was verified the correctness of the choice of the electrical replacement circuit that describes the physical processes in the tissue and the obtained dependencies (10), (11), and (12) by transforming the diagram of Figure 6 for each boundary condition.

The first boundary condition is time t= 0, and, according to the law of switching in transients [25], E_{ion}=0, and $I_{ion}=I_1$.

The substitution scheme for this boundary condition t=0 (the initial moment of the transient) is shown in Figure 7.

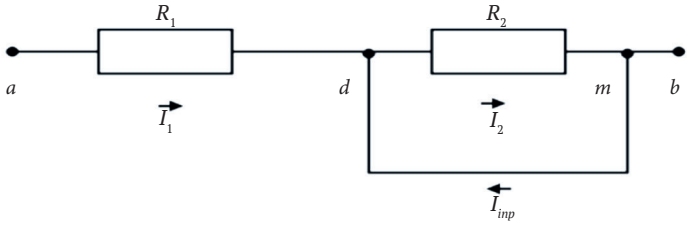

Figure 7. Scheme of biological tissue replacement for the first boundary condition

Note: I_2 is the current flowing in the active resistance R_2, I_2=0 since it is shunted, $I_1=I_{inp}$ is the input current for the first boundary condition

Thus, expression (12) is a mathematical model of the impedance change for the substitution Figure 5a). The input current is determined by expression:

$$I_1=I_{inp}=\frac{U_{ab}}{R_1} \quad (13)$$

and has a maximum value and is limited by R_1 – the active component of the impedance in the intercellular space. The second boundary condition at time $t\to\infty$ is the steady state, with, according to the law of switching in transients [25], I_{ion}=0, $E_{ion}=\Delta U_2=U_{dm}$.

Figure 8 shows the substitution scheme for the second boundary condition.

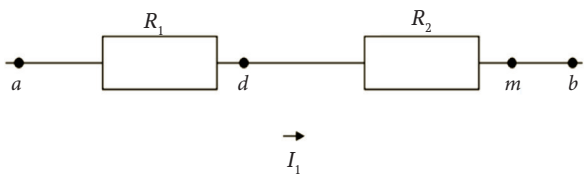

Figure 8. Scheme of biological tissue replacement for the second boundary condition, where $I_1=I_{inp}$

The input current is defined by the expression:

$$I_1 = I_{inp} = \frac{U_{ab}}{R_1 + R_2}. \quad (14)$$

Using the same calculation algorithm as for the replacement circuit in Figure 5a, it was obtained mathematical models of impedance change over time for the electrical replacement circuits shown in Figures 4a, 4b, 4c.

For the replacement circuit shown in Figure 4a, the mathematical model has the form:

$$Z_{inp1} = Re^{-\frac{t}{\tau_{11}}}, \quad (15)$$

where R is the total component of the active impedance resistance, which consists of the active impedances of cellular and intercellular connections.

τ_{11} – is the time constant determined by the formula $\tau_{11}=CR$.

The performance of the mathematical model of expression (15) is checked for the boundary conditions:

The moment of time is zero $t=0$, $Z_{inp1}=R$.

The moment of time is $t\to\infty$, $Z_{inp1}=0$.

The mathematical model meets the requirements of the boundary conditions.

Due to such regularities of impedance changes, this replacement scheme is not used in practice.

For the substitution scheme shown in Figure 4b, the mathematical model has the form:

$$Z_{inp2} = R(1 - e^{-\frac{t}{\tau_{2.1}}}), \quad (16)$$

where R is a component of the total active impedance resistance, which consists of the active impedances of cellular and intercellular connections.

$\tau_{2.1}$ – time constant – determined by the formula $\tau_{21}=C.R$.

The performance of the mathematical model of expression (16) is checked for the boundary conditions:

the moment of time is zero $t=0$, $Z_{inp.1}=0$,

the moment of time is equal to $t\to\infty$, $Z_{inp1}=R$.

The mathematical model meets the requirements of the boundary conditions.

To obtain the mathematical model, the substitution scheme shown in Figure 4c, it is advisable to use the electrical conductivity – $G_{inp3} = \frac{1}{Z_{inp3}}$.

For the substitution scheme shown in Figure 4c, the mathematical model is as follows:

$$G_{inp3} = \frac{1}{R} + \frac{1}{R_1}e^{-\frac{t}{\tau_{3.1}}}, \quad (17)$$

where $\tau_{3.1}$ – is the time constant determined by the formula $\tau_{3.2}=CR_1$. R and R_1 – correspond to the marks of the active resistance diagram of the substitution circuit Figure 4c.

The mathematical model was tested for boundary conditions:

the moment of time is zero $t=0$,

$$G = \frac{1}{R} + \frac{1}{R_1},\ Z_{inp3} = \frac{R \cdot R_1}{R + R_1};$$

the moment of time is equal to $t\to\infty$, $Z_{inp3}=R$.

The mathematical model meets the requirements of the boundary conditions.

To analyse the correspondence of the experimentally obtained results of the impedance change over time with the results obtained using mathematical models, formulas (12), (16), (17), and the substitution schemes shown in Figures 5a, 4a, 4b, 4c, we constructed graphs of the dependence $R=f(t)$, which are shown in Figure 9.

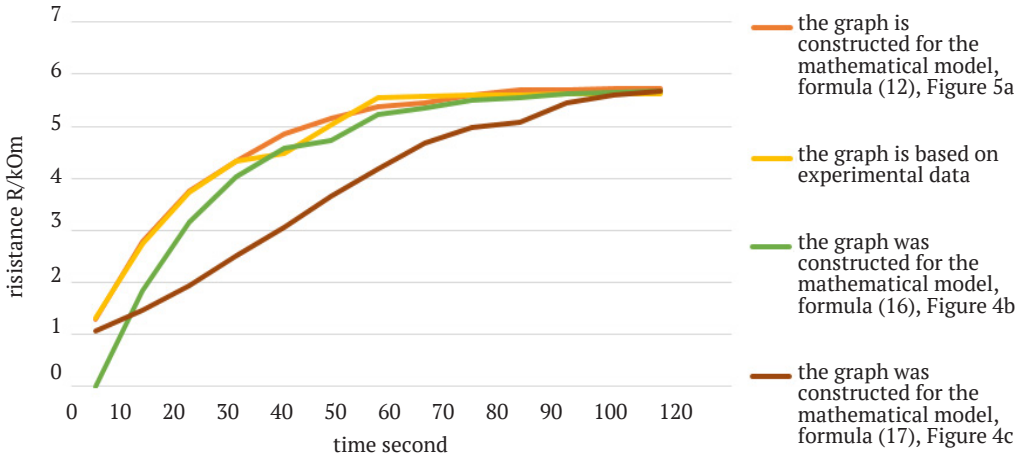

Figure 9. The graphs of the dependence R=f(t) for substitution schemes

To analyse the effect of the number of ions on changes in the conductivity of biological tissue, the scheme under consideration is shown in Figure 5b. The tourniquet applied to the guinea pig's paw stops blood flow in the tissue and prevents the flow of free ions. Such a study is important for determining the dynamics of ischaemia in the limbs and determining the time of the tissue's limiting state when a tourniquet is applied during domestic, industrial and military injuries

As is known from [8; 12], the main component of the biological tissue environment is blood, which is a solution of electrolytes. For example, blood plasma contains 0.32% NaCa, where the concentration of Na+ ions is 142 mmol/l, and K+ – 5 mmol/l. Current is a directed movement of positive and negative ions, which is defined for an electrolyte solution according to [4] as follows:

$$j_+=q_+\cdot n_+\cdot v_+;\ j_-=q_-\cdot n_-\cdot v_-, \tag{18}$$

where q_+ is the positive charge of the carrier, q_- is the negative charge of the carrier n_+, n_- are the number of positively and negatively charged ions, v_+, v_- are the concentration of positively and negatively charged ions, respectively.

The total current will be equal to: The total current will be equal:

$$G=j_++j_-=q_+\cdot n_+\cdot v_++q_-\cdot n_-\cdot v_-. \tag{19}$$

Expression (18) indicates that the electrical conductivity of biological tissue is proportional to n_+, n_- – the number of positively and negatively charged ions and v_+, v_- – the concentration of positively and negatively charged ions, respectively.

The rate of orderly movement of ions is directly proportional to Eion, which is caused by the movement of free charged ions under the influence of the source electric field and is defined:

$$V=g\cdot E_{ion}, \tag{20}$$

where g – coefficient of proportionality of media mobility.

The specific electrical conductivity δ for an electrolyte is written in the form:

$$\delta=\frac{1}{z}=b_+\cdot n_+\cdot v_++b_-\cdot n_-\cdot v_-+b\cdot n\cdot v. \tag{21}$$

The input impedance of the biological tissue for the scheme of Figure 5c with a limited number of ions, having carried out similar calculations as for the scheme of Figure 5a, is determined by the expression:

$$Z^*_{inp4}=R_1+R_2(1-e^{-\frac{t}{\tau^*_{4.1}}}), \tag{22}$$

where $\tau^*_{4.1}$ – is the time constant of the ionisation process for a biological object with a reduced number of ions and is equal to $\tau^*_{4.1}=CR_2$.

The analysis of expressions (20), (21), (22) shows that the ionisation process time constant $\tau^*_{4.1}=C\cdot R_2$ directly depends on the number of charged ions, their concentration in the biological tissue, the level of intensity E_{ion}, the composition of salts in the biological tissue and is a constant value characterising the course of this process.

Biological tissue is complex and heterogeneous in composition and environment. Tissue contains not only sodium and potassium, but also other ions. The introduction of new elements (active resistances and unities) into the substitution scheme will allow us to study biological tissue with any ion composition. Figure 10 shows a substitution scheme for a biological tissue with a heterogeneous composition of n ions.

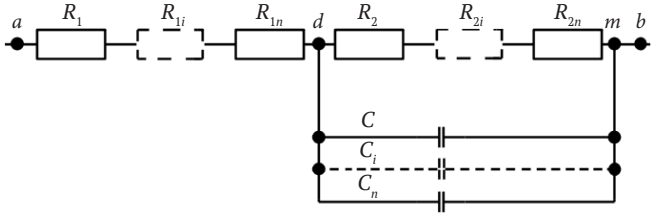

Figure 10. Scheme of replacement of biological tissue containing n-ions

Note: R_1, R_{1i}, R_{1n} – active components of impedance in the intercellular space, R_2, R_{2i}, R_{2n} – active resistance of tissue cells in a complex medium, C, C_i, C_n – capacitive component of impedance of tissue cells in a complex medium

Using the device, Figure 2, for invasive impedance measurement, data on changes in tissue impedance over time for different distances between needle electrodes were obtained, which are presented in Table 1.

Table 1. Results of studying the change in impedance over time depending on the distance between the needle electrodes

sec	0 kOm	10 kOm	20 kOm	30 kOm	40 kOm	50 kOm	60 kOm	70 kOm	80 kOm	90 kOm	100 kOm	110 kOm	120 kOm
L=1 cm	1.30	2.78	3.76	4.32	4.85	5.17	5.37	5.46	5.6	5.7	5.71	5.72	5.73
L=3 cm	1.65	3.16	4.10	4.65	5.16	5.42	5.67	5.86	5.99	6.13	6.34	6.34	6.42
L=5 cm	1.90	3.49	4.33	4.92	5.25	5.60	5.93	6.13	6.25	6.45	6.58	6.65	6.65

In Figure 11 shows the graphs of impedance changes in the transient period depending on the distance L between the needle electrodes, which were obtained experimentally. The studied biological object was not damaged after the completion of the research.

To investigate the use of the ionisation time constant as a diagnostic criterion, impedance changes were measured simultaneously invasively on two limbs in identical locations. A tourniquet was applied to one limb. Table 2 shows the results of the study.

In Figure 12 shows a graph of tissue impedance changes as a function of time. The tourniquet was applied to one paw, and the blood circulation was stopped for 30 minutes.

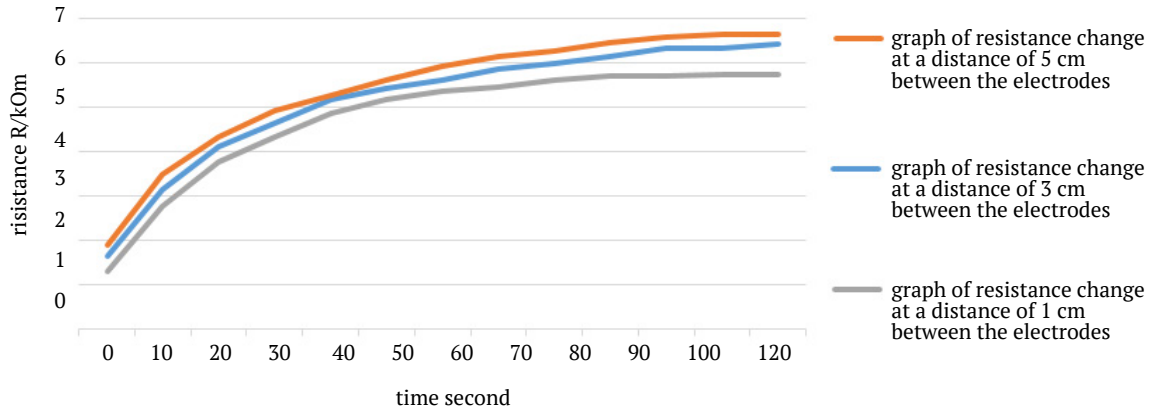

Figure 11. Dependence of the change in impedance $R=f(t)$, depending on the distance between the electrodes L=1 cm, L=3 cm and L=5 cm

Table 2. Impedance change measurement data over time

Time, sec	0	10	20	30	40	50	60	70	80	90	100	110	120
Limb without tourniquet	0.43	1.26	1.95	2.42	2.78	3.17	3.38	3.59	3.76	3.98	4.12	4.27	4.4
Limb from a tourniquet	1.1	2.89	3.82	4.53	5.12	5.65	6.06	6.50	6.79	7.17	7.46	7.69	7.98

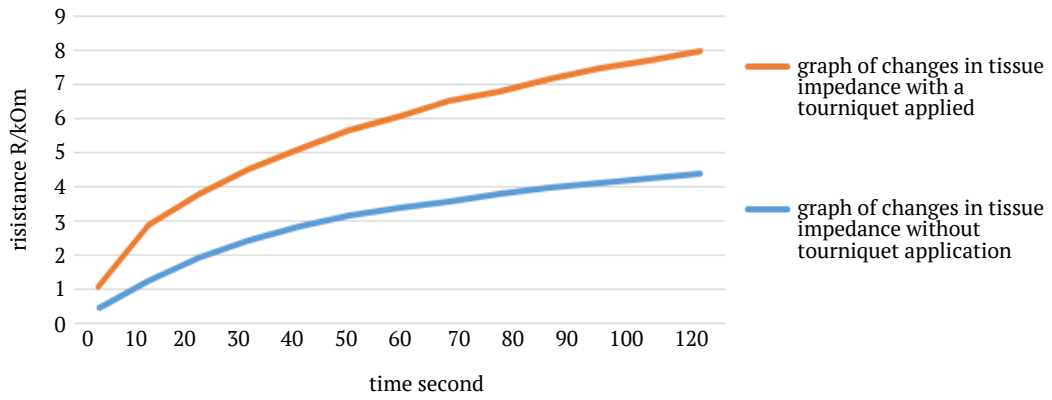

Figure 12. Graph of changes in tissue resistance depending on time, the tourniquet is applied to one paw for 30 minutes

Thus, this paper considers the issue of obtaining patterns of changes in the impedance of biological tissue under the influence of DC voltage in the transient process as an information parameter for the rapid diagnosis of limb muscle ischaemia. The authors proposed the introduction of an additional active resistance into the known electrical substitution circuit, which is traditionally used in AC voltage studies.

DISCUSSION

In well-known works, the issue of the influence of voltage of variable amplitudes and frequencies on biological tissue and the application of the obtained results for the diagnosis of a disease and its treatment is thoroughly studied. In [3; 9], the substitution scheme shown in Figure 4b. In [2; 6; 10], the substitution scheme shown in Figure 4c.

To substantiate the introduction of an additional active resistance in the proposed electrical substitution circuit, mathematical models for known substitution circuits were built and the change in $R=f(t)$ was analysed. Analysis of the results of the correspondence of the physiological process for the substitution schemes, Figure 4b and Figure 4c, and their corresponding mathematical models, expressions (15),

(16), and (17), with the substitution scheme proposed by the authors, Figure 5, and the mathematical model, expression (12), for the transient mode under the action of a DC voltage, was carried out by comparing the compliance coefficient - q, which is determined by Eq:

$$q = \left(1 - \frac{S_{ex}}{S_{inp\,i}}\right) \cdot 100\%, \qquad (23)$$

where S_{ex} – is the result of integration of the experimentally obtained function $Z=f(t)$, which is defined by the expression; $S_{ex}=\int_0^{100} Z_{inp\,i}dt$; $S_{inp\,i}$ – the result of integration of the function $Z=f(t)$ of each mathematical model. $S_{inp\,i}=\int_0^{100} Z_{inp\,i}dt$.

The numerical values used in the integration were obtained as a result of experiments, so the ionisation time constant is τ=25 seconds, the active components are R_1=1,3 kOm, R_2=4.43 kOm. The calculation results are shown in Table 3.

Table 3. The results of calculating the compliance ratio

	The proposed replacement scheme is shown in Figure 5	The substitution scheme is shown in Figure 4b, used in [5; 8; 10]	The substitution scheme is shown in Figure 4c, used in [3; 6; 14]
The value of the matching coefficient.	2.8%	13.8%	18.7%

The proposed electrical substitution scheme and its mathematical model have a convergence with experimental data of up to 3%, depending on the traditional substitution schemes, which have a convergence of 13% and higher.

Thus, the introduction of an additional active resistance in the electrical circuits of biological tissue replacement, under the action of a DC voltage, allows to study the transient ionisation process and increase the reliability of the results obtained in determining the impedance components with a reliability of ±3%. The field measurements of the impedance change during the transient process allowed us to confirm that the ionisation time constant is equal to $\tau = \frac{1}{4}T_{ion}$ with a probability (P=0.95), where T_{ion} is the transient time. This allows us to more reliably determine the capacitive component of the tissue under study. The capacitive component for the proposed substitution scheme is $C = \frac{25}{4{,}43} = 5{,}64 \cdot 10^{-3}\ F$, for the traditional substitution schemes $C = \frac{25}{5{,}73} = 4{,}16 \cdot 10^{-3}$F, and the difference is 35.5%.

An analysis of expressions (12), (15) and (16) and the graphs in Figure 9, shows that traditional substitution circuits should be used for studies under the action of voltage of variable frequencies and amplitudes, as well as in steady-state modes under the action of DC voltage. To study the transient process, it is necessary to use an adjusted electrical substitution scheme.

In the reviewed and analysed results of well-known works [5; 8; 10] and [3; 6; 14], the invasive method of measuring the impedance of biological tissue is not considered. The analysis of the obtained data of the impedance components by the invasive method, shown in the graph (dependence $R=f(t)$ for different distances between electrodes in Figure 10), shows that the active component of the impedance, both intercellular and cellular, varies according to a linear law depending on the distance between the electrodes, which corresponds to the pattern according to formula (1). The capacitive component, formula (2), which leads to the transient process caused by ionisation, does not change. The sensitivity of the needle sensor increases by (8-9)% when the distance between the electrodes is reduced by every ΔL=1 cm. To study the change in impedance in an invasive way, it is sufficient to have a distance of -1 cm between the needle electrodes, which makes the sensor compact and less traumatic.

The theoretically obtained dependence $R=f(t)$ according to expression (12) for the proposed replacement circuit shown in Figure 5 gives the right to assert that at the initial time (t=0), the resistance of biological tissue is not zero, which is confirmed by experimental data. The additional resistance of the replacement circuit corresponds to the active resistance of the intercellular space, which limits the initial input current, so the active resistance at the initial time (t=0) is within 1-2.0 kΩ.

The authors first proposed a method for diagnosing changes in the properties of biological tissue in case of blood flow disorders using a direct current voltage in the transient ionisation process. Papers [6; 16; 17; 27; 28] consider methods of using impedance changes to diagnose and determine the composition of biological tissue with subsequent treatment of deviations. Paper [26] presents a method for diagnosing skin myeloma. All of these methods use AC voltage and frequency, which requires sophisticated equipment and a certain amount of time for research. The article proposes a method of rapid diagnosis - the diagnostic period takes from 100s to 120s, which does not require sophisticated equipment.

The proposed method is based on the comparison of two simultaneously obtained integrated functions q of healthy and diseased tissue and the analysis of the relativity coefficient -q, which is determined by the formula $q = \left(1 - \frac{S_{ex}}{S^*_{ex}}\right) \cdot 100\%$·

Where S_{ex} – is the result of integrating the function $Z=f(t)$ without a tourniquet; S^*_{ex} – is the result of integrating the function $Z=f(t)$ with a tourniquet applied.

If the relativity coefficient is q=0±0.05%, this indicates unchanged properties of biological tissues in both limbs.

If the relativity coefficient varies – q=0.05% to 1, it indicates changes in the properties of biological tissues in both limbs.

At a value of q=0.5 and below, it indicates the presence of irreversible processes of ischaemia in muscle tissue.

The data presented in Table 2 and the graphs shown in Figure 12 show that the comparison of two integral

ionisation functions in biological tissue without a tourniquet and in tissue with a tourniquet is a criterion parameter for diagnosing the development of ischaemia.

CONCLUSIONS

Traditional electrical substitution circuits and their corresponding mathematical models should be used to study changes in biological tissue under the influence of alternating frequency voltage or in steady-state mode under the influence of direct current voltage. When using these substitution schemes to study the transient process under DC voltage, the error of the results obtained is 13% and higher. To study ionisation transients under DC voltage, it is necessary to use a corrected electrical substitution circuit with an additional active resistance. The introduction of an additional active resistance made it possible to obtain a convergence of the experimentally obtained measurements with the analytically obtained results up to ±3%, which indicates that the developed mathematical model is suitable for describing the transient process occurring in biological tissue under the action of a DC voltage.

It is analytically confirmed that the ionisation time constant can be determined with confidence (P=0.95) from the experimental data as $\tau = \frac{1}{4}T_{ion}$, where T_{ion} is the time of the transient process.

The mathematical model of the corrected electrical substitution scheme allowed us to obtain numerical values of the capacitive components of the impedance. The reliability of the determined capacitive component of the impedance compared to traditional substitution circuits and their corresponding mathematical models increased by 35%, which made it possible to determine and control the composition of biological tissue. Based on the results obtained, an electrical substitution circuit was developed for the complex composition of the biological environment.

Based on the results of the transient process study, a method for detecting changes in the properties of biological tissue in case of circulatory disorders was developed. The time of the transient process is 100s-120s, which allows for rapid diagnosis of ischemia of the patient's limb muscle tissue.

The method is based on the comparison of two simultaneously obtained integrated functions of healthy and diseased tissue and the analysis of the relativity coefficient -q, which is determined by the formula $q = \left(1 - \frac{S_{ex}}{S^*_{ex}}\right) \cdot 100\%$, where S_{ex} is the result of integrating the function Z=$f(t)$ without a tourniquet, S^*_{ex} is the result of integrating the function Z=$f(t)$ with a tourniquet. If the relativity coefficient is q=0±0.05%, this indicates that the properties of biological tissues in the two limbs are unchanged. If the relativity coefficient varies from 0.05% to 1, it indicates changes in the properties of biological tissues in both limbs. At the value of q=0.5 and below, it indicates the presence of irreversible processes of ischaemia development in muscle tissue. Thus, it was established that when simultaneously measuring the change in impedance in two identical limb areas, the ionisation time constant is a criterion parameter in the study of ischaemia development.

The obtained results of experimental and analytical studies have shown that, depending on the set tasks and goals of studying changes in biological tissues, electrical substitution schemes adequately describe the physiological processes of a biological object when corrected.

The development of rapid diagnostic methods based on data obtained in the transient processes of biological tissue ionisation requires further research together with the results of changes in tissue properties obtained by biopsy.

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Обґрунтування електричної схеми заміщення біологічної тканини при дії напруги постійного струму

Анотація. Зміна імпедансу біологічної тканини під дією напруги використовується в діагностиці та лікуванні різних захворювань. Математичні моделі, що описують фізико-біологічні процеси в біологічних об'єктах, засновані на електричних схемах заміщення. Метою цієї роботи було дослідження зміни імпедансу біологічної тканини в перехідному процесі іонізації під дією напруги постійного струму. В роботі застосовано біоімпендантний метод при впливі на біологічну тканину напруги постійного струму з урахуванням закону комутації у перехідних процесах іонізації. Було проведено аналіз відомих схем заміщення виявлені недоліки їх застосування при вивчені перехідних процесів іонізації в тканині при дії напруги постійного струму та обґрунтовано, як аналітично так і експериментально, схему заміщення із запровадженням додаткового опору. Було здійснено інвазійний вимір зміни імпедансу голчастими електродами, доведено, що активна складова пропорційно залежить від відстані меж електродами, а ємкісна складова залишається незмінною. Показано, що постійна часу іонізації є крітеріальним параметром та може використовуватись в діагностиці розвитку ішемічної хвороби м'язової тканини, зміна стану біологічної тканини при зупинці кровотоку під час накладання кровоспинного джгута. Доведено, що постійна часу іонізації не змінюється при незмінному іонному складу тканини і може використовуватися при аналізу складу міжклітинного простору. Було проведено одночасне інвазійне вимірювання у двох ідентичних місцях різних кінцівок, на однієї було накладено кровоспинний джгут. Отримані результати дозволили зробити висновки, що зміна постійної часу від 15 % до 50 % у порівнянні двох постійних часу дозволяє робити експрес діагностики, протягом 2 хвилин, стану біологічної тканини і може використовуватись при вивченні розвитку хвороби пов'язаних з ішемією. Результати дослідження можуть використовуватися при експрес діагностиці стану біологічного об'єкту та створенні не дорогого приладу для його застосування в хірургії та дослідних лабораторіях при вивчені розвитку ішемії

Ключові слова: імпеданс; перехідний процес; процес іонізації; опір клітини; ємність; постійна часу іонізації; діагностика; ішемія