ELECTRONICS AND ELECTRICAL ENGINEERING
ISSN 1392 – 1215 2009. No. 2(90)
ELEKTRONIKA IR ELEKTROTECHNIKA

AUTOMATION, ROBOTICS
T125
AUTOMATIZAVIMAS, ROBOTECHNIKA

Theoretical Evaluation of Space Constants of Electrotronic Decay in Resistive Anisotropic Media: Three-dimensional case

R. Veteikis
Institute for Biomedical Research, Kaunas University of Medicine
Eivenių str. 4, LT-50009 Kaunas, Lithuania, phone: +370 37 302966, e-mail: biof@kmu.lt

Introduction

Propagation of electric excitation wave in myocardium is conditioned by two principal factors: properties of the ionic currents (electrogenic membrane) and intercellular electrical contacts. Various physiological and pathological effects may evoke changes in passive electrical properties of myocardial tissue, that can lead to the electric excitation wave change and disorders in the mechanical activities of the heart. Therefore the investigations of various processes of excitation wave spreading in myocardium are very important. The intrinsic mechanisms are discovered not only experimentally but also by using various mathematical (biophysical) models.

For modeling of excitation wave spread in the myocardial tissue under normal and pathological conditions [1-3] the values of parameters of the passive electric properties of myocardium are used. Modeling makes sense only provided the used values of parameters are most precise. However, the electrical structure of myocardial tissue is rather complex and direct measurement of parameters of passive electrical properties in normal and various pathological conditions is not possible.

For finding these parameters the distribution of electrotonic potential in the cardiac tissue close to the current delivering electrode is measured and experimental space constants of electrotonic decay λ_{xe} and λ_{ye} (i.e. the distance at which the amplitude of electrotonic potential decreases by 2.71 times) are recording. Further analysis of experimental data by mathematical models of resistive (R) and resistive-capacitive (RC) media is performed [4, 5].

In our previous paper [6] the solution for the electrotonic potential distribution in myocardial tissue was obtained, when myocardium is modeling as three-dimensional anisotropic R-medium of finite thickness and the intracellular current is delivered by disk-shaped or cylindrical-shaped electrode. In the present study the dependencies of normalized values of experimental space constants of electrotonic decay along (L_x) and across (L_y) the fiber orientation in three-dimensional anisotropic medium upon the size of the current electrode, the degree of electrotonic anisotropy, medium thickness and the distance between the current electrode and the electrotonic potential recording site were obtained and the possible errors of the actual values of the space constants of electrotonic decay were estimated.

The results of computerized modeling of electrotonic potential distribution in three-dimensional resistive medium of finite thickness.

Computer programs were developed and the calculations of electrotonic potential distribution in surface of resistive medium ($z = 0$) were carried out by using the formula (18) of our previous paper [6]. We calculated the dependence of normalized experimental space constants of electrotonic decay ($L_x = \lambda_{xe} / \lambda_x$ and $L_y = \lambda_{ye} / \lambda_y$) on the size of the current electrode (radius r_o and altitude h), electrotonic anisotropy A_e ($A_e = \lambda_x / \lambda_y$), normalized distance between the recording point and the center of the current electrode in X and Y directions ($X = x/\lambda_x$, $Y = y/\lambda_y$), and normalized thickness of medium ($D = d/\lambda_z$). The calculation results were presented in Fig. 1 as families of curves.

The analysis of curves showed that with increase of normalized distance from the current electrode (*X* or *Y*), normalized experimental space constants of electrotonic decay (L_x and L_y) increase. When the normalized thickness of medium (*D*), the current electrode radius (r_o) and the normalized distance from the current electrode (*X* or *Y*) are fixed (Fig.1., a), with the increase of electrotonic anisotropy, L_x increases but L_y decreases. When values of electrotonic anisotropy (A_e) and radius of current electrode (r_o) are fixed, with bigger medium thickness (*D*), the corresponding values of normalized space constants of electrotonic decay (L_x and L_y) are smaller (Fig. 1., b). When D and A_e are fixed, with increasing r_o, L_x increases, but L_y decreases (Fig. 1., c). The great influence of the normalized altitude of cylinder-shaped current electrode H ($H = h/\lambda_z$) also is determined: with the increasing of H, L_x and L_y increase too. When $H \to \infty$ and $D \to \infty$, the case analogical to two-dimensional medium is obtained (Fig. 1., d). Besides, in all cases we assumed that λ_x = 1 mm.

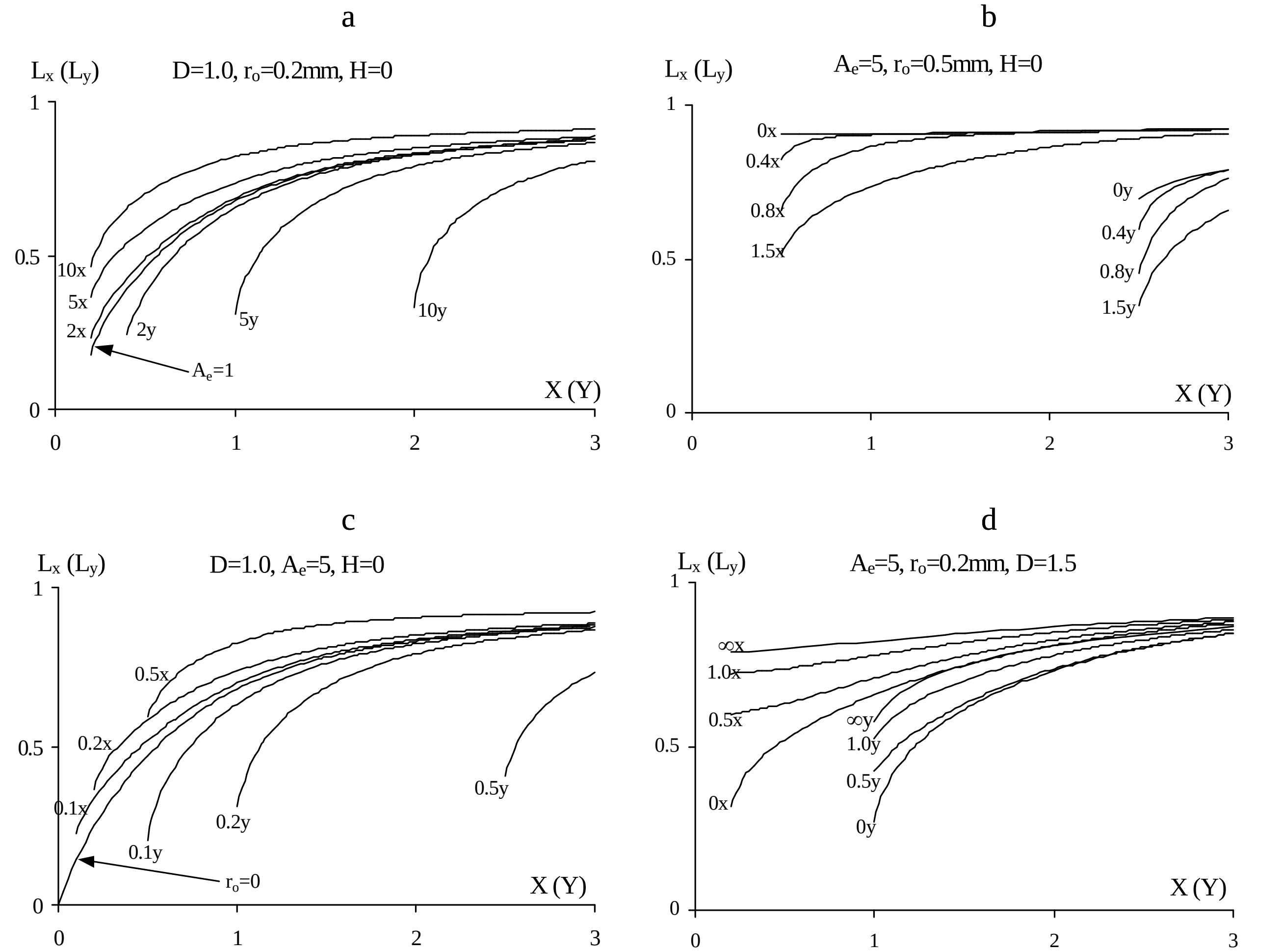

Fig. 1. Dependence of L_x and L_y on parameters of three-dimensional medium and a distance of recording site from a current electrode center (*X* or *Y*). "*x*" next to curves refers to the dependence of L_x on *X*, and "*y*" – the dependence of L_y on *Y*. In all cases $\lambda_x = 1.0$ mm. **a:** for all curves D = 1.0, r_o = 0.2mm, H = 0, and numbers – 1, 2, 5, 10 – are values of electrotonic anisotropy; **b:** for all curves $A_e = 5$, $r_o = 0.5$ mm, H = 0; the numbers – 0, 0.4, 0.8, 1.5 – are the normalized thickness (D) of the medium; **c:** for all curves D = 1.0, $A_e = 5$, H = 0; the numbers 0.1, 0.2, 0.5 – are radii of the current electrode in mm; **d:** for all curves D = 1.5, $A_e = 5$, $r_o = 0.2$ mm; the numbers 0, 0.5, 1.0 – are normalized altitudes (H) of cylinder-shaped current electrode; ∞ - refers to case when $H \to \infty$ and $D \to \infty$.

Errors of the evaluation of space constants of electrotonic decay

When the space constant of electrotonic decay is measured in experimental conditions, the parameters of anisotropic medium – normalized thickness of medium D, space constants of electrotonic decay λ_x, λ_y, the radius and the normalized altitude of cylinder-shaped current electrode r_o, H – are not known. So, which curve from families of curves (Fig. 1) is suitable for evaluation of true values of space constants of electrotonic decay (λ_x and λ_y) is not well-defined. Therefore for evaluation of true values of space constants of electrotonic decay (λ_x, λ_y) from experimentally measured λ_{xe} and λ_{ye}, the models of two-dimensional or three-dimensional finite thickness medium with point-shaped current source are applied. In cause of application of inadequate models the possibility of errors arises.

In Fig. 2 the calculation results are presented showing the errors that would be made if the measurements will be performed in three-dimensional medium of finite thickness with point-shaped current electrode (microelectrode), while for evaluation of true values of space constants of electrotonic decay (λ) the two-dimensional isotropic medium model or three-dimensional infinite medium model will be applied. As can be seen from the presented families of curves, bigger values of the space constants of electrotonic decay (λ_3) will be obtained if the model of three-dimensional infinite medium is used. The interpretation of measurements (calculations) performed close to the source of current shows that the obtained values of space constants of electrotonic decay (λ_3) are maximal: the errors may exceed 200%.

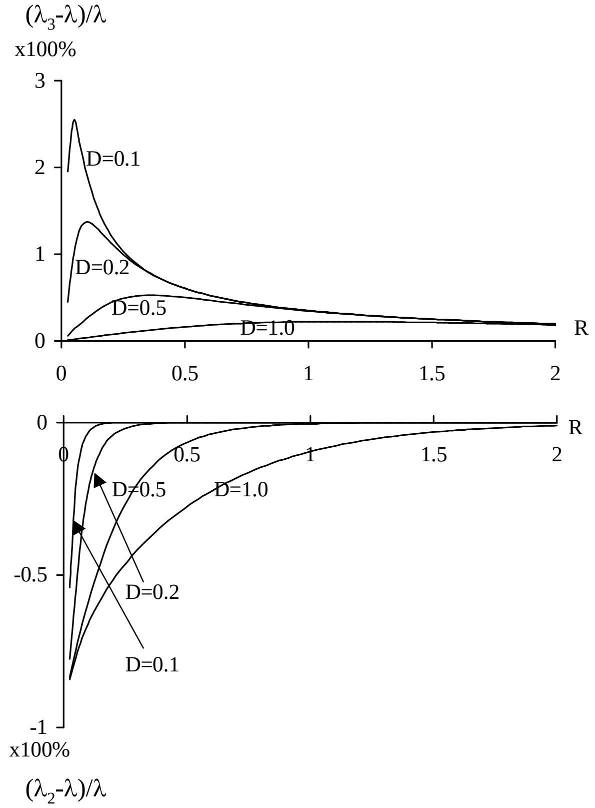

Fig. 2. Dependence of the errors of the space constants of electrotonic decay on the distance between the current electrode and the electrotonic potential recording site (*R*) in three-dimensional medium of finite thickness with point-shaped current electrode. λ_3 – the value of space constant of electrotonic decay obtained with aid of model of three-dimension infinite medium with point-shaped current electrode. λ_2 – the value of the space constants of electrotonic decay obtained with aid of the model of two-dimensional medium with point shaped current electrode. λ - the true value of space constant of electrotonic decay.

When in the same situation the model of two-dimensional medium is used, smaller values of space constants of electrotonic decay (λ_2) are obtained (see lower part of Fig. 2). The absolute magnitude of errors depends on medium thickness (*D*) and on distance at which the electrotonic potential is recorded (*R*).

In Fig. 3 the calculation results are presented showing the errors that would be made when the measurements of electrotonic potential distribution in three-dimensional anisotropic medium of finite thickness with cylinder-shaped current electrode will be made while for evaluation of true values of space constants of electrotonic decay (λ_x , λ_y) the two-dimensional medium model (dotted lines) or three-dimensional finite thickness medium model (continuous lines) with point-shaped current electrode will be used. When the model of two-dimensional isotropic medium is applied, the values λ_{2x} and λ_{2y} will be obtained, instead of true space constants of electrotonic decay λ_x and λ_y, while applying of model of three-dimensional finite thickness medium leads to the another values – λ_{3x} and λ_{3y}. When two-dimensional medium model with point-shaped current electrode is applied then the relative error (*RE*) of evaluation of space constant of electrotonic decay in X-axis direction is $RE = (\lambda_{2x} - \lambda_x)/\lambda_x$, while in direction of *Y*-axis – $RE = (\lambda_{2y} - \lambda_y)/\lambda_y$. In case of using three-dimensional medium model with point shaped current electrode, in *X*-axis direction the error of estimation of values of space constants of electrotonic decay is $RE = (\lambda_{3x} - \lambda_x)/\lambda_x$, and in *Y*-axis direction – $RE = (\lambda_{3y} - \lambda_y)/\lambda_y$. We can see that irrespective of model, with increasing of distance (*X* or *Y*), the errors of evaluation of space constants of electrotonic decay decrease. In almost cases of using of two-dimensional medium model, the relative errors of estimation of λ_x and λ_y are negative, i.e. the obtained values of λ_{2x} and λ_{2y} are smaller than its true values. In case of using of three-dimensional medium model of finite thickness (with point-shaped current electrode) the obtained λ_{3x} values are bigger, while the obtained λ_{3y} values are smaller, than its true values (λ_x and λ_y). The dependence of relative errors on medium/model parameters is more intricate. For fixed values of r_o , *H* and *D*, in case of two-dimensional medium model, in media of greater anisotropy the errors of evaluation of λ_x are smaller, while the errors of λ_y – bigger (Fig. 3., a). In aforementioned case with using the three-dimensional finite thickness medium model, for bigger values of A_e , both evaluation errors of λ_x , and λ_y are bigger: the obtained λ_{3x} values are bigger, while λ_{3y} values are smaller than its true values. With increasing of normalized altitude of cylinder-shaped electrode (Fig. 3., b), the relative errors increase, even in case of using of two-dimensional medium model the evaluated λ_{2x} values close to current electrode are greater than its true values (a case when $H = 0.5$). The modifying of the medium thickness (Fig. 3., c) also has a great influence upon relative errors with the exception of three-dimensional medium when the dependence of λ_x errors on *D* is weak (i.e. the difference between the curves for D = 0.4 and D = 1.5 is slight). The relative errors of λ_x and λ_y significantly depend on the radius of current electrode (Fig. 3., d).

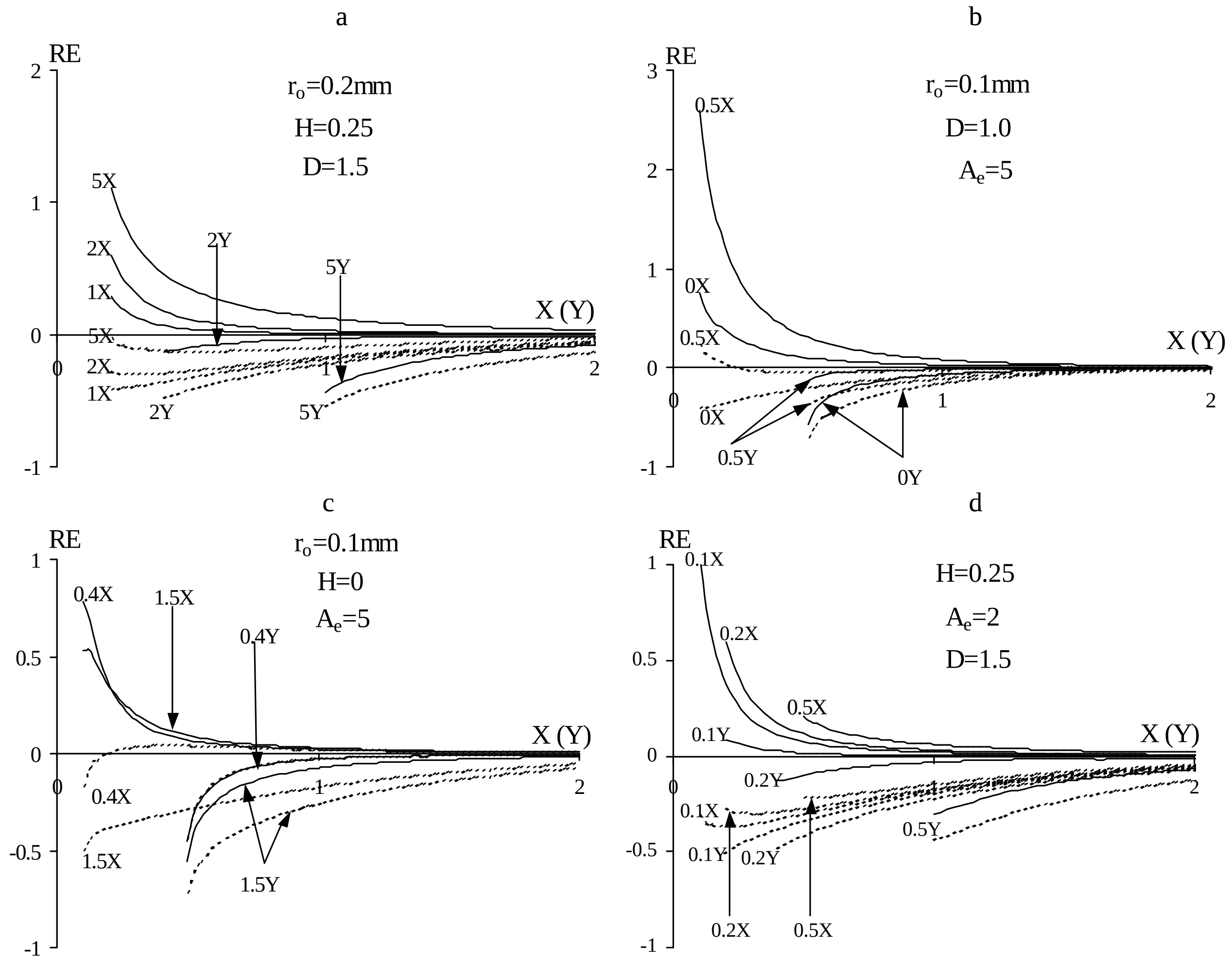

Fig. 3. Dependence of relative errors (*RE*) of λ_x and λ_y on parameters of anisotropic medium and on distance *X* (*Y*), when for evaluation of λ_x and λ_y two-dimensional medium (dotted lines) or three-dimensional medium of finite thickness (continuous lines) models with point-shaped current sources are applied. "*X*" next to curve refer to dependence of *RE* on *X*, "*Y*" – refer to dependence of *RE* on *Y*. **a:** for all curves r_o = 0.2mm, H = 0.25, D = 1.5, while numbers 1, 2, 5 next to curves are A_e values; **b:** for all curves r_o = 0.1mm, D = 1.0, A_e = 5, while numbers 0 and 0.5 next to curves are the values of H; **c:** for all curves r_o = 0.1mm, H = 0, A_e = 5, while numbers 0.4 and 1.5 next to curves are the values of D; **d:** for all curves H = 0.25, A_e = 2, D = 1.5, while numbers 0.1, 0.2 and 0.5 next to curves are the radius of current electrode in mm. In all cases (**a**, **b**, **c**, **d**) λ_x = 1.0mm.

Some aspects of resistive media models application for experimental data estimation

In the experimental conditions the distribution of electrotonic potential is measured in narrow stripes excised from the cardiac tissue that are several millimeters thick. In such cardiac stripes, only the superficial cardiac cells remain viable [7], whereas the deeper cells are under hypoxia. As the intercellular communication between the cells under ischemia is very weak [8], and the electric communication between the normal and hypoxic cells is disturbed [9], the cells remain viable only to the depth of 250 μm [7]. Therefore the equivalent electrical structure of the cardiac tissue *in vitro* is identical to that of the three-dimensional resistive medium of 250 μm thick.

In the experimental recordings of the electrotonic potential distribution in the myocardial tissue, as intracellular current source a circle-shaped suction electrode with internal perfusion of isotonic KCl [10] is applied. This current delivering method if compared to the microelectrode or camera partition method has advantages and drawbacks.

When microelectrode as the current electrode is applied, the amplitude of the electrotonic potential moving away from the current electrode abruptly decreases. In such experimental conditions it is impossible to measure precisely the electrotonic potential amplitude. The same is true when λ_x and λ_y values are being estimated with the aid of the resistive medium model.

A camera partition method for the measurement of the true space constants of electrotonic decay is applicable only for the cylindrical structures such as papillary muscle, trabeculae, and Purkinje fibers. Some authors tried to apply this method to thin cylindrical-shaped pieces of the tissue excised from myocardium [11–13]. Beyond doubt, in the cylindrical pieces excised from the tissue without prevalent cells' direction, as sinoatrial and atrioventricular nodes are, the longitudinal axis (the direction of excision) could vary from the best electrotonic potential spreading direction. When the electrotonic anisotropy of the tissue is big, the values of the measured true space constant of electrotonic decay strongly depend on the direction of excision.

By using a suction electrode as a current electrode, we avoid the above-mentioned drawbacks, but other problems arise. Due to the fact that the electrode current flows not only into intracellular space but in intercellular clefts too, furthermore, the ratio of these currents is unknown, we cannot adequately mathematically describe a current electrode electrical structure. Therefore, in the calculations we used the superposition principle according what the current electrode is divided into evenly distributed point-shaped sources, and a potential generated at some site of the medium is equal to the sum of the potentials generated by these point-shaped sources. However, due to the anisotropy of intracellular and extracellular space of the myocardial tissue [14], we cannot state that point-shaped sources are distributed evenly.

Let us assume that the resistive medium is anisotropic ($\lambda_x > \lambda_y$) and the current electrode is divided into sufficiently large number of point sources. For a single point-shaped source according to [15-16], the closer the source, the more rapidly the amplitude of electrotonic potential falls and the smaller space constants of electrotonic decay λ_{xe} and λ_{ye} are recorded. When the current electrode dimensions are fixed, closest point-shaped sources have the greatest influence on the fall of V_m. It follows from qualitative reasoning that the value of electrotonic potential amplitude V_m is influenced by the density of the point-shaped sources, its distance from calculation site, and by surface/volume into which the intracellular current is delivered.

Intercellular electrical communication and passive electrical parameters are rather widely explored in Purkinje fibers and papillary muscles when one-dimensional RC cable model is applied for the interpretation of experimental results [5]. In more complex anisotropic structures (SA, AV nodes, auricle, ventricles), intercellular electrical communication is investigated considerably less, and electrotonic potential distribution simulation tasks are also scarce. However, some authors [17] for the interpretation of the electrotonic potential distribution measurements apply the one-dimensional cable model and, therefore, obtain wrong parameters of the passive electrical properties. In conclusion, we can add that the application of various models in concrete experimental conditions gives us a possibility to evaluate more precisely passive electrical parameters of myocardium and to analyze excitation spread and mechanisms of arrhythmia genesis.

Conclusions

1. Using the superposition principle of electrostatics the three-dimensional resistive media models were created and analytical solutions of an electrotonic potential in respect to distance were obtained, when a current electrode is disk- and cylinder-shaped. Computer programs for the calculation of the normalized experimental space constants (L_x, L_y) and their evaluation errors were created.

2. When the distance between the current electrode center and the L_x, L_y recording site is fixed, then for greater current electrode radius and/or electrotonic anisotropy, L_x value is bigger and L_y value is smaller. When the distance between a current electrode and the potential recording site increases, L_x and L_y increases too. When the medium thickness increases, L_x and L_y decreases.

3. In cause of using inadequate theoretic model to the experimental conditions the estimation errors of L_x and L_y arise. When for three-dimensional anisotropic case a two-dimensional isotropic medium model is applied, the smaller values of space constants of electrotonic decay than its true values are obtained. When a three-dimensional isotropic finite thickness medium model is applied, the evaluated values of space constants of electrotonic decay are greater than its true values.

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Received 2008 06 12

R. Veteikis. Theoretical Evaluation of Space Constants of Electrotonic Decay in Resistive Anisotropic Media: Three-dimensional case // Electronics and Electrical Engineering. – Kaunas: Technologija, 2009. – No. 2(90). – P. 29–34.

The computer programs were developed for the calculation of electrotonic potential distribution in three-dimensional anisotropic resistive medium of finite thickness when a current electrode is point-, disk- or cylinder-shaped. The families of curves describing dependence of experimental constants of electrotonic decay on anisotropy, medium thickness, current electrode dimensions and a distance of recording site from a current electrode center were obtained. The errors of space constants of electrotonic decay were evaluated when for evaluation of space constant of electrotonic decay in anisotropic medium the model of isotropic medium is applied. Ill. 3, bibl. 17 (in English; summaries in English, Russian and Lithuanian).

Р. Ветейкис. Теоретическая оценка постоянных длины электротонического затухания в омических анизотропных средах: Случай трехмерной среды // Электроника и электротехника. – Каунас: Технология, 2009. – № 2(90). – С. 29–34.

Разработаны компьютерные программы для расчета распределения электротонического потенциала в трехмерной анизотропной проводящей среде конечной толщины, когда источник тока имеет форму точки, диска или цилиндра. Получены семейства кривых, описывающих зависимость нормализованных экспериментальных констант электротонического затухания от анизотропии, размеров токового электрода, а также от расстояния между точкой регистрации электротонического потенциала и электродом. Определены относительные погрешности постоянных длины электротонического затухания, когда в анизотропной среде для оценки постоянных длины электротонического затухания применяли модель изотропной среды. Ил. 7. библ. 17 (на английском языке, рефераты на английском, русском и литовском яз.).

R. Veteikis. Elektrotoninio gesimo konstantų teorinis įvertinimas anizotropinėse ominėse terpėse: trimatės terpės atvejis // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2009. – Nr. 2(90). – P. 29–34.

Sukurtos kompiuterinės programos, skaičiuojančios elektrotoninio potencialo pasiskirstymą trimatėje anizotropinėje ominėje baigtinio storio terpėje, kai srovės šaltinis taškinis, disko arba cilindro formos. Gautos kreivių šeimos, atvaizduojančios matuojamųjų normalizuotų elektrotoninio gesimo konstantų priklausomybę nuo anizotropijos, atstumo tarp potencialo registravimo vietos, terpės storio ir srovės šaltinio dydžio. Įvertintos elektrotoninio gesimo konstantų paklaidos, kai anizotropinėse terpėse elektrotoninio gesimo konstantoms įvertinti naudojami izotropinių terpių modeliai. Il. 3, bibl. 17 (anglų kalba; santraukos anglų, rusų ir lietuvių k.).