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LIVING CELL AS A RECEIVER OF MICROWAVE RADIATION

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Abstract. Threshold sensitivity of the living cell to external microwave radiation is estimated using microwave noise theory. Numerical modelling of electromagnetic wave propagation in multilayered tissue is applied for determination of the field level inside the body. Radiation density inside the body at the depth of 3 to 5 cm is from 10^{-5} to 10^{-6} times lower of the level near the surface, at 4500 MHz frequency. Fundamental electrical noise of living cells due to thermal and current carrier fluctuations is discussed. It is shown that the levels of thermal and shot noise at the cell membrane are comparable. Fluctuations caused by opening and closing of ionic channels can substantially increase the noise level and add excess noise. The threshold sensitivity of a typical cell is about 10^{-8} W/m^2 and equivalent radiation intensity at tissue surface 10^{-2} W/m^2.

Key words: radiation, cell, sensitivity, noise, microwave.

1. INTRODUCTION

Human physiological activity is based on electromagnetic phenomena [1]. From the other side, the external electromagnetic fields are known to interact with living systems and under certain circumstances may affect health [2,3]. For low-level microwave radiation, thermal effects can be neglected and mechanisms of interaction of the field with tissues can be examined. With low-level intensity, mechanisms of thermoregulation are not overwhelming and the physiological temperature can be maintained by regulatory mechanisms of the living system. Significant biological effects of the exposure of cells and animals to electromagnetic fields have been reported [2]. The low-level microwave effects are related to the direct interaction between the living tissue and electromagnetic field.

The quantum energy of the microwave radiation is below 0.001 eV and therefore too small to produce intramolecular changes or to break the intermolecular bond. No direct microwave-specific effects take place at molecular level. Sensitivity of living organisms to the electromagnetic field is related to the mechanisms at cellular, organ and system level. A physical model in which cells are considered as possible detectors of very weak electric fields has been proposed and discussed in [4]. In that model only influence of the thermal noise component on the membrane potential has been taken into account. The paradox is that, according to experimental data, much smaller fields can be detected than the calculated thermal noise limit.

Another problem that arises in connection with the microwave field interaction with cells inside a living tissue is the uncertainty of the field level at the cell location. The transfer function of the field from the body surface to the cell in the tissue has to be determined for estimation of the real electromagnetic sensitivity of cells inside the living tissue. The determination of the internal fields in biological media is a difficult problem due to heterogeneous material properties and shape irregularity. Analytical methods for calculation of the propagation and absorption of the electromagnetic radiation in homogeneous or inhomogeneous lossy medium, such as the methods of integral equations, plane waves, Fourier integrals, Green's function, and others, include always some approximation [5–7]. The direct finite difference time-domain (FDTD) method for solving Maxwell's field equations gives more reliable result [8].

The aim of this work is to develop a model of electrical noise for cell membrane potential taking into account thermal and shot noise, including the excess noise caused by conductance fluctuations due to stochastic opening and closing of ionic channels. Numerical calculations of the field distribution inside the three-layered tissue are used for the determination of the real level of radiation intensity inside the body and field level in the cell.

2. METHOD

The methods of microwave noise theory have been used. The process of registration of electromagnetic radiation by technical devices includes several steps:

– collection of electromagnetic energy from space or "switching" between electrical sensor and radiation, realized using antennas;

– interaction between electromagnetic field and current carriers, electrons and/or ions inside the sensor;

– detection of changes in the sensor current or field, limited by internal noise caused by stochastic movement of the carriers.

The sensors (semiconductor diodes, paramagnetic crystals and others) should be sensitive to the electromagnetic field. The sensitivity of the system to external electromagnetic radiation depends on the internal noise level of the system. The internal noise consists of different components: 1/f noise, thermal noise, shot noise, noise caused by fluctuations. The mechanisms of these noises have been thoroughly investigated for technical systems [9,10].

Electromagnetic interactions in living tissues are substantially more complicated than in technical systems. If we consider the cell as a microwave receiver, the following is to be taken into account:

– the cell is located inside inhomogeneous human tissue and the level of the field in it is different from the field at the tissue surface;

– the membrane of the cell has many different channels for different ions and the mechanisms of ionic currents are complicated;

– the threshold sensitivity is determined not only by the thermal noise, and the noise generation mechanisms related to current carriers are not clear yet.

The theory and experimental data about ionic channels of cellular membranes [11] permit the physical description of these processes. The first step of the theory of internal noise in living tissues can be exactly built up only at cellular level.

Following electrical model of the cell may be proposed. A number of current sources (ionic channels) are connected in parallel to the input of the receiving system (membrane). These sources are stochastically switching on and off and cause noise. The input of the receiving system has capacity C and resistance R that are equal to those of the membrane. These parameters determine the time constant of the system. The membrane resistance depends on the number of open channels and can vary for million times [11]. The time constant of the cell as a receiving system varies also strongly.

Let us suppose that the microwave field influences the velocity of ions passing the channel. This presumption has been approved by experimental data at least for calcium channels – the ion efflux has been shown to change under microwave exposure [12]. Thus we can consider the ionic channels as sensors. If we assume in this model that ionic channels act as sensors, then the threshold signal current caused by microwave radiation has stochastic character.

The internal noise of the receiver consists of the thermal noise of membrane resistance and current noise caused by ionic current of the channels. The noise of different origin may be presented as an equivalent current noise in ionic channels. The characters of the noise and threshold signal currents in ionic channels are similar. The time constant of the cell membrane causes integration of the radiation as well as noise currents inside equivalent receiving bandwidth of the system.

3. ELECTRICAL NOISE AT THE MEMBRANE

Two components of the electrical noise, thermal and shot noise, are fundamental and well described by a physical theory. The thermal noise δU due to random thermal fluctuations in electrical potential or voltage, predicted by Einstein, first observed by Johnson and explained by Nyquist, is expressed as

$$(\delta U)_{\mathrm{T}}^2 = 4RkT\Delta f, \quad (1)$$

where $T = 310$ K, k is the Boltzmann constant ($kT = 4.3\times10^{-21}$ J), and Δf is the frequency bandwidth.

The shot noise δI due to fluctuations of the current carriers is described by the Schottky formula

$$(\delta I)_{\mathrm{I}}^2 = 2eI\Delta f, \quad (2)$$

where I is mean value of the current and e is electron charge ($e = 1.6\times10^{-19}$ C).

Total level of the electrical noise of the system depends on the frequency bandwidth. The frequency bandwidth is determined by the time constant of the system. From the other side, the level of stochastic signals depends on the frequency bandwidth too. The equivalent noise bandwidth and signal averaging are determined by the same time constant. Therefore, in this case the signal-to-noise ratio does not depend on the frequency bandwidth. The spectral density of the noise power (or fluctuations spectrum) S is a better parameter to be used for comparison of noise of different origin and for estimation of threshold sensitivity than the integral noise power. The spectral parameter makes it possible to avoid additional uncertainty due to frequency bandwidth which is not constant for the membrane. In the following formulas unit frequency bandwidth is used.

For comparison of the thermal and current noise, the first one is presented as a fluctuation of the current. From Eq. (1) we can derive

$$(\delta I)_{\mathrm{T}}^2 = 4(kT/R)\Delta f. \quad (3)$$

In calculations of the noise for the living cell we have used typical numerical values for cell parameters: membrane resistance $R = 1\,\mathrm{M\Omega}$ and single channel current $I = 1$ pA [5]. Spectral density of the current noise due to thermal fluctuations according to Eq. (3) is 1.72×10^{-26} $\mathrm{A^2/Hz}$.

Spectral density of the noise due to current carrier fluctuations for a single channel according to Eq. (2), S_{I}, is 0.3×10^{-30} $\mathrm{A^2/Hz}$. The noise caused by current fluctuations in a single channel is substantially less than the thermal noise.

Nevertheless, the current carrier fluctuations take place in all open channels. The total noise at the cell membrane is caused by all of these fluctuations. Let us assume that the ion transfer processes in different channels are independent. In this case the level of total noise from N channels is described by

$$(\delta I)_{\Sigma\mathrm{I}}^2 = N(\delta I)_{\mathrm{I}}^2. \quad (4)$$

Spectral density of the current noise, when on average 10^4 channels are conducting, is $S_\Sigma = N\times S_{\mathrm{I}} = 0.3\times10^{-26}$ $\mathrm{A^2/Hz}$. This level of current noise at cell membrane corresponds to the model when all N channels are simultaneously open and the number of open channels is constant.

The channels are discrete molecules, gating stochastically. The number of open channels in any area of a membrane fluctuates even in equilibrium. The fluctuations of the opening, if the open state is chopped up by frequent closing, take also place. An excess noise arises due to these stochastic processes. The most convenient statistical parameter to describe the level of excess noise is the variance σ^2. If we assume that openings-closings of the channels are independent, the probability distribution of the process with excess fluctuations is binomial and without excess fluctuations – Poisson's distribution.

The variance of a single channel without excess noise that opens with probability p and passes the single-channel current $i = ne$ where n is the number of ions, is

$$\sigma_1^2 = np(1-p) + \sigma_n^2 p^2. \qquad (5)$$

In the case of the Poisson distribution of the current without excess noise, its variance σ_n^2 is equal to n and we have

$$\sigma_1^2 = np. \qquad (6)$$

The Schottky formula (2) is also based on the presumption of absence of excess noise [4].

Let us consider the case of N open channels with variance σ_N^2. If the single channel does not introduce excess noise, the total variance for opening of N channels is

$$\sigma_{N\Sigma}^2 = nNp(1-p) + \sigma_N^2 np^2. \qquad (7)$$

This is a general formula for variance in the case of N independent channels.

If excess noise is absent, the Poisson distribution of the opening of the channels is valid, the variance is equal to the mean number of open channels $\sigma_N^2 = N$, and the total variance is

$$\sigma_{N\Sigma}^2 = nNp. \qquad (8)$$

The presumption of absence of excess noise was also used in Eq. (4). We can see that Eqs. (4) and (8) determine the minimum possible level of current noise for a multichannel cell membrane. This is the level of fundamental physical noise.

The other mechanism of noise generation can create additional excess noise. The noise due to fluctuations, caused by opening and closing of the channels, is excess noise. For estimation of the level of current noise in the case of real binomial distribution of the opening of the channels, additional information about the variance of the number of open channels is needed. The variance σ_N^2 may have a value many orders higher than the average number of channels N. In technical systems the level of excess noise is usually substantially higher than the level of fundamental physical noise [4]. Unfortunately, this data for biological systems is not available. We can conclude from published experimental data [11] that the excess fluctuations of opening of the channels are quite significant. Therefore the level of the current noise may be substantially higher than shot noise calculated by the Schottky formula (2) or (4).

4. THRESHOLD SENSITIVITY OF THE RECEIVER

The sensitivity of the cell as an electromagnetic radiation receiver is determined by internal noise of the cell and its effective receiving area. The size (radius) of the cell a is substantially less than the wavelength of the radiation, therefore the cell can be considered to be an elementary antenna. The effective receiving area of the cell as an antenna is equal to its geometric area. For a typical mammalian cell the radius is about 10 μm, what is small by comparison with the wavelength of a microwave. The power of the electromagnetic radiation, collected by a cell, can be determined using the theory of antennas as

$$P_{\mathrm{r}} = \pi a^2 P, \tag{9}$$

where $P = (E^2 \varepsilon / 240)\pi$ is the intensity of radiation inside the body, E is the electric field of the radiation, and ε is the effective dielectric permeability of the tissue.

The spectral density of the noise power at the cell membrane is determined as

$$P_{\mathrm{n}} = [(\delta I)_{\mathrm{T}}^2 + (\delta I)_{\Sigma \mathrm{I}}^2] R. \tag{10}$$

We can obtain the simplest estimate of $P_{\min}$, the minimum intensity of the electromagnetic radiation to which a cell can respond, comparing P_{n} with the equivalent spectral density of the radiation P_{r}

$$\pi a^2 P = [(\delta I)_{\mathrm{T}}^2 + (\delta I)_{\Sigma \mathrm{I}}^2] R. \tag{11}$$

The sensitivity of the cell to the radiation is

$$P_{\min} = [(\delta I)_{\mathrm{T}}^2 + (\delta I)_{\Sigma \mathrm{I}}^2] R / \pi a^2 . \tag{12}$$

The calculated value of $P_{\min}$ for typical parameters of cells is about 10^{-7}–10^{-8} W/m^2. The minimum field to which a cell can respond depends on the dielectric permeability and is about 10^{-6}–10^{-7} V/m. This simplest approach provides absolute maximum of threshold sensitivity without taking into account the effect of radiation on the movement of ions through the channels.

5. TRANSFER FUNCTIONS FOR EXTERNAL RADIATION

The electromagnetic field inside a human body, exposed to a known external electromagnetic field, can be calculated by solving Maxwell's equations subject to given boundary conditions. Therefore the FDTD method was chosen and the program package MAFIA, based on this method, was used for this purpose [8].

In the calculation model the external field is considered to be a plane wave. Multilayered biological medium contains skin (thickness 2 mm), fat (thickness 3–10 mm), and muscle. The values of the dielectric constant ε and conductivity σ of different tissues for different frequencies are given in Table 1.

Table 1. Values of the dielectric constant ε and conductivity σ

	Frequency, MHz					
	450		900		4500	
	ε	σ	ε	σ	ε	σ
Skin	53	1.2	51	1.3	50 46*	4 2*
Fat	5.5	0.08	5.5	0.1	5.5	0.14
Muscle	53	1.2	51	1.3	50 46*	4 2*

* Two possible values were used in calculations.

The relative part of energy, absorbed in unit volume of the tissue, was calculated. Results of modelling of the absorption of microwaves in a multilayered biological tissue is shown in Fig. 1. The model consists of a waveguide at 40 deg inclination to the tissue. The tissue comprises three layers (skin, fat, muscle) with different dielectric properties. Figure 1 shows a slice in the middle of the waveguide perpendicular to its broad wall.

Modelling yields the following results:

– spatial distribution of the density of the absorbed field energy is highly nonuniform, in every layer there are several maxima; these maxima are located near boundaries of the layers and the absorbed energy level in these points is much higher than the average;

– high portion of the energy is dissipated in the skin;

– significant difference in the density distribution of the energy loss is caused by slight difference in electrical parameters of the tissue.

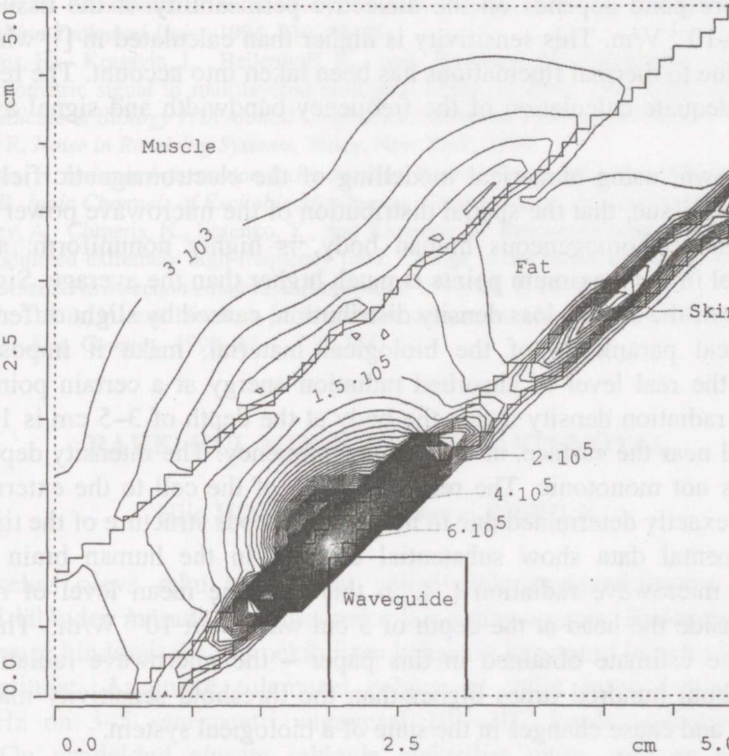

Fig. 1. Calculated distribution of absorbed microwave energy in a three-layered biological tissue, VA/m^3. Excitation power of the waveguide is 1 W.

The level of the radiation intensity inside the body at the depth of 3–5 cm is 10^{-5}–10^{-6} times lower than the level at the body surface, at frequency 4500 MHz. Due to nonhomogeneity of the microwave radiation distribution, in different body layers "hot spots" arise, especially near the boundaries of the layers. The intensity dependence on depth is not monotonic.

6. DISCUSSION AND CONCLUSIONS

The fundamental electrical noise of living cells is the noise due to thermal fluctuations, the Johnson noise, current carrier fluctuations, and shot noise. The levels of thermal and shot noise at cell membranes are comparable. The fluctuations caused by opening and closing of ionic channels can substantially increase the current noise and add excess noise. Therefore the current noise may become substantially stronger than the fundamental physical noise.

The threshold sensitivity of a typical cell is determined by fundamental physical noise and has a value of about 10^{-8} W/m^2. The minimum field to which a cell can respond depends on the dielectric permeability of the tissue and is about 10^{-6}–10^{-7} V/m. This sensitivity is higher than calculated in [4] where only the noise due to thermal fluctuations has been taken into account. The reason for that is inadequate calculation of the frequency bandwidth and signal averaging effects.

It is shown, using numerical modelling of the electromagnetic field in the multilayered tissue, that the spatial distribution of the microwave power density, absorbed in nonhomogeneous human body, is highly nonuniform: absorbed energy level in the maximum points is much higher than the average. Significant differences of the energy loss density distribution, caused by slight differences in the electrical parameters of the biological material, make it impossible to determine the real level of absorbed radiation energy at a certain point of the body. The radiation density inside the body at the depth of 3–5 cm is 10^{-5}–10^{-6} of the level near the surface, at 4500 MHz frequency. The intensity dependence on depth is not monotonic. The real sensitivity of the cell to the external field can not be exactly determined due to nonhomogeneous structure of the tissue.

Experimental data show substantial changes in the human brain activity caused by microwave radiation [13]. In this case the mean level of radiation intensity inside the head at the depth of 3 cm was about 10^{-6} W/m^2. These data agree to the estimate obtained in this paper – the microwave radiation with intensity about hundred times higher than the threshold sensitivity may effect ions efflux and cause changes in the state of a biological system.

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RAKK KUI MIKROLAINE VASTUVÕTJA

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Inimkehas oleva raku tundlikkust välise elektromagnetkiirguse suhtes on hinnatud lähtudes mürade teooriast mikrolaine diapasoonis. Elektromagnetvälja intensiivsuse hindamiseks mitmekihilises kehas on kasutatud lainelevi numbrilist modelleerimist. Arvutuste tulemusel selgus, et välja intensiivsus sagedusel 4500 MHz on 3–5 sentimeetri sügavusel 10^{-5}–10^{-6} korda väiksem kui keha pinnal. On vaadeldud elusate rakkude elektrilist müra, mis on põhjustatud soojuslikest fluktuatsioonidest, samuti voolukandjate fluktuatsioonidest tingitud haavelmüra. On näidatud, et soojusliku ja haavelmüra nivood raku membraanil on võrreldavad. Raku ioonkanalite avanemisest ja sulgumisest tingitud fluktuatsioonid võivad oluliselt tõsta müra nivood ja põhjustada lisamüra. Tüüpilise raku tundlikkus on umbes 10^{-8} W/m^2.