THEORETICAL ANALYSIS OF VOLTAGE-GATED MEMBRANE CHANNELS UNDER GSM AND DECT EXPOSURE

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Abstract

In this work the response of a theoretical model of voltage-dependent membrane channels is analyzed for EM fields used in GSM and DECT cellular phones. A comparison between the effects of the two different communication protocols is performed, as well as an evaluation of the response of the model to temperature variations. In the simulations the conditions of exposure to EM fields generated by GSM and DECT mobile equipments, has been set starting from existing safety standards. Microscopic effects are investigated at ionic channel's level inside cellular membranes.

The obtained results show that both GSM and DECT signals have an evident effect on the behaviour of ionic channels, and seem to induce non thermal effects. Maximum variations of around 30% in the open probability have been observed for Sodium and Potassium channels, and around 60% for Calcium. DECT signal seems to be more perturbing than GSM signal on Calcium channel.

1. Introduction

In the recent past an increasing attention is paid on environmental problems. A typical example is the evaluation of possible risks in the use of wireless communication systems due to effects of electromagnetic (EM) fields on human beings [1]. Safety standards have been proposed or are under evaluation [2, 3].

Bioelectromagnetic effects can be looked for both at macroscopic and at microscopic level. We focus on microscopic ones, and concentrate on a specific site of interaction: ionic channels inside cell membranes. They are considered as one of the most crucial sites, as well as of fundamental importance for all living processes [4]. They act as a gate, regulating current fluxes through cell membrane, thus ensuring biochemical equilibrium. Their polar nature makes them sensitive to EM stimulation, and their gating could be perturbed by EM exposure [4, 5]. A simple deviation, from the physiological behaviour of membrane channels at a microscopic level, could induce variations on metabolic processes at a higher level in the biological scale.

The complexity of appropriate experimental current recordings on single channels [6] compells researchers to set up appropriate models to evaluate EM effects on channel gating. A modelling technique, based on Markov finite-state machines, has been proposed by the authors both for voltage-dependent and ligand-dependent channels [7, 8].

In this work, we quickly summarize the modelling approach and describe how we customize our models for voltage-dependent channels (Potassium, Sodium, and Calcium) so that the effects of GSM and DECT phone signals can be simulated. A temperature sensitivity is included in the model parameters, in order to allow an evaluation of the changes in channel behaviour, as a function of thermal heating induced by an incident field. Results are given showing the perturbation induced on channel opening probability and comparing the effects of pulsed GSM and DECT signals with the effects of the possible thermal heating. Finally some conclusions end the work.

2. Models and Methodologies

The channel is considered as a finite-state Markov automaton, and its conductance an aleatory variable in a random process. Under the hypothesis of voltage-dependent channels, EM fields modify transition rates among the states, as they depend on transmembrane voltage [6]. Each state in the model represents a possible conformation for the channel (open or close), and transitions among states represent structural modifications, associated to energetical changes. More than one open or close state can exist for a single channel. If the channel is considered ohmic (experimentations confirm this with reasonable approximations [4]) the current flux through the channel in a certain instant is proportional to the probability that the system is in an open state. As the state probability is easily evaluated in a Markov models (MM) [9], they represent an appropriate way to study EM perturbations on channel currents. Details on this modelling approach are given in [7]. We show here the models used in this paper: in Fig. 1a the model for calcium channel is given, while Fig. 1b is for Potassium and 1c for Sodium.

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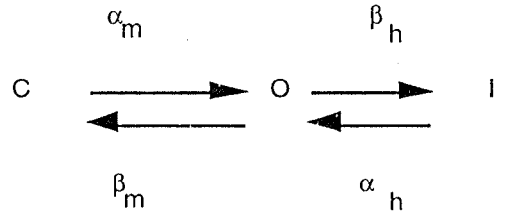


$$\alpha_m = \frac{10.0}{1.0 + 6671.6\, exp\,[-1.6\, log\,(V+50)]}\, T_f\ ;$$

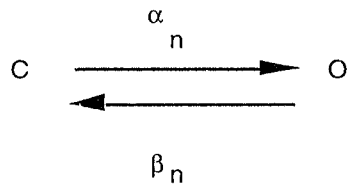
$$\beta_m = 0.06\,(V+50)\, exp\,[-0.03\,(V+50)]\, T_f\ ;$$

$$\alpha_h = [-0.075 exp\,[0.21\, log\,(V+50)] + 0.21]\, T_f\ ;$$

$$\beta_h = \frac{0.8}{1.0 + 374163.73\, exp\,[-2.8362\, log\,(V+50)]}\, T_f$$

$$T_f = 3^{\frac{(T-6)}{10}}$$

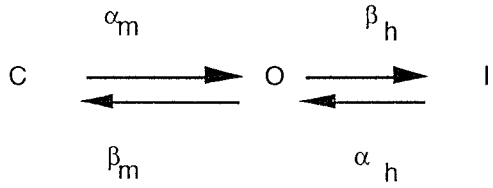
Fig. 1a - Calcium channel



$$\alpha_n = \frac{0.01\,(V+10)}{exp\left[\frac{(V+10)}{10}\right] - 1}\, T_f\ ;$$

$$\beta_n = 0.125 exp\left[\frac{V}{80}\right] T_f\ ; \qquad T_f = 3^{\frac{(T-6)}{10}}$$

Fig. 1b - Potassium channel



$$\alpha_m = \frac{0.1\,(V+25)}{exp\left[\frac{(V+25)}{10}\right] - 1}\, T_f\ ;$$

$$\beta_m = 4 exp\left[\frac{V}{18}\right] T_f$$

$$\alpha_h = 0.07 exp\left[\frac{V}{20}\right] T_f\ ;$$

$$\beta_h = \frac{1}{exp\left[\frac{(V+30)}{10}\right] + 1}\, T_f$$

$$T_f = 3^{\frac{(T-6)}{10}}$$

Fig. 1c - Sodium channel

EM field action is included by evaluating its effect on transmembrane voltage V(t). This can be done solving a boundary-value problem with some simplifying hypotheses on cell geometry [10, 11] or using more advanced methods, such as spherical transmission lines [12]. The dependence of transition rates on temperature is taken into account, and shown in the equations of the models.

In order to simulate the effects of GSM and DECT signals, their waveforms have been characterized [13, 14]; Fig. 2 sketches the waveform characteristics of the frames.

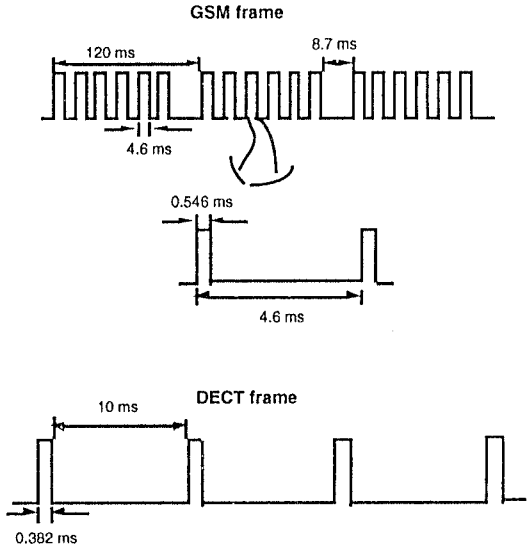


Fig. 2 - Waveform characteristics

"Pulsed" signals, as GSM and DECT can be considered, usually consists of a single frequency carrier (900 MHz for GSM and 1900 MHz for DECT), modulated by a digital waveform of lower frequency, generally in the range of ELF frequencies. The following simulations have been performed taking into account the only low-frequency contribution. This approach is based on the assumption that the cell behaves as a non-linear device, realizing a proper demodulation of the incident waveform.

3. Results and Discussion

As a first evidence of the effects of "pulsed" signals on the gating of voltage-dependent channels, we show in Fig. 3 the results of the exposure of Calcium channel to a GSM signal, varying both the values of the membrane voltage and the amplitude of the GSM signal (similar results have been obtained for DECT).

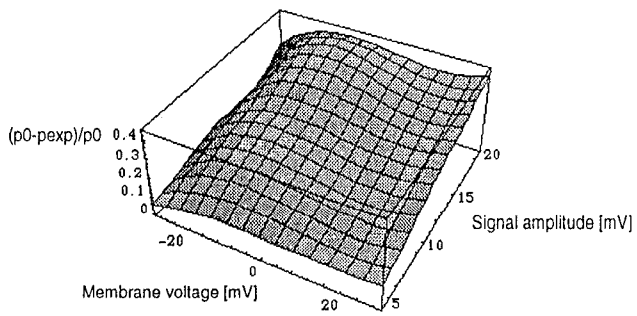


Fig. 3 - Calcium channel exposed to a GSM signal

On the z-axis the relative variation of the open probability p_o is shown (p_{oexp} is the open probability when the signal is on, p_o is the one at the specified membrane voltage). A global effect of reduction in the open probability of the channel can be seen. Furthermore for a fixed voltage clamp of -10 mV, for example, the intensity of the effect depends on the amplitude of the external signal. The effect of reduction in the open probability is stronger with "pulsed" signals than with continuous wave (CW) signals. In Fig. 4 this is demonstrated showing the values of open probability p_o for different amplitudes of the three external signals: GSM, CW at 8.3 Hz, and CW at 217 Hz (these frequencies are related to the burst repetition of the GSM signal). Data refer to Potassium channel.

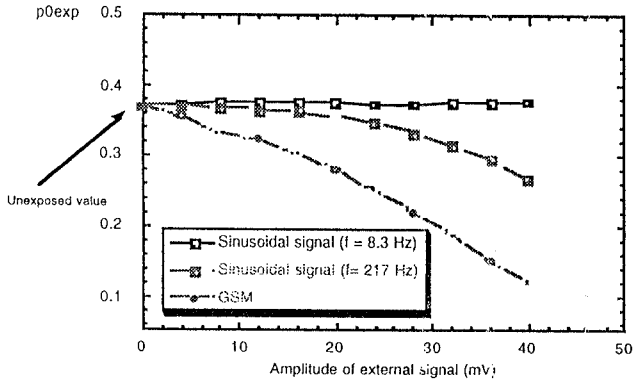


Fig. 4 - Comparison between a sinusoidal and a GSM stimulation

With similar results a DECT frame has been compared with a sinusoidal signal of 100 Hz. After these preliminary evaluations, in order to investigate furtherly the effect of GSM and DECT signals, more simulations have been performed. They were of two kinds. The former compares the effects of GSM and DECT signals of the same amplitude, with thermal effects, where a temperature variation is imposed perturbing the physiological conditions. The latter kind compares the GSM and DECT signals when they give the same amount of power to the tissue.

Thermal vs non thermal

In the former kind of evaluations the same value is used for the amplitude of the GSM and DECT signals, starting from dosimetric considerations on the values of the Specific Absorption Rate (SAR) in safety standards. For human beings the peak SAR value defined in the standards can not exceed 2 W/Kg, averaged over any 10 g of tissue (defined as a tissue volume in the shape of a cube [2]). The SAR is related to the internal electric field by means of the following relation:

$$SAR = \frac{\sigma E^2}{\rho} \qquad (1)$$

Therefore, considering instantaneous SAR values of 2 W/Kg, it is possible to know E on the cell membrane. The transmembrane voltage ΔV_m can then be calculated solving a simplified problem as described in [10]. The resulting ΔV_m , taking into account the presence of the EM field, becomes the amplitude induced on the cell by the GSM and DECT signals to be compared.

In the case where a temperature variation is imposed, the thermal stimulation has been taken into account using the following relationship:

$$SAR = c\frac{\Delta T}{\Delta t} \qquad (2)$$

in which the SAR is related to the temperature increase by means of the thermal conductivity c of the tissue. The temperature behaviour can therefore be described as:

$$T(t) = T_o + (\frac{SAR}{c})t \qquad (3)$$

where T_0 is assumed to be an initial temperature value.. The simulations have been performed for the three different channels. The results are reported in Fig. 5a,b for Sodium and Calcium channels as a function of membrane voltage.

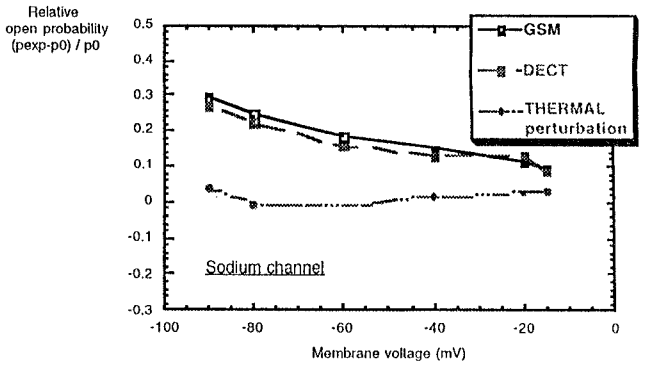


Fig. 5a - Comparison between "pulsed" signals and a thermal perturbation: sodium channel

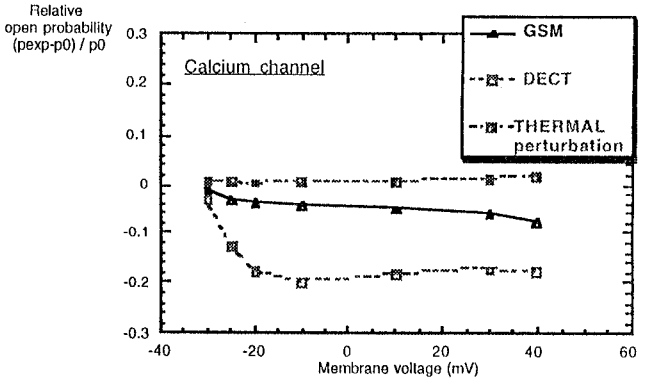


Fig. 5b - Comparison between "pulsed" signals and a thermal perturbation: calcium channel

In all the cases, a similar global behaviour can be observed. The non thermal effects are stronger than thermal ones. In Sodium (Fig. 5a) maximum variations in open probability are around 30 %, and the GSM effects are slightly more evident than the DECT ones. Similar results hold for Potassium channel, which has not been reported here. In Calcium channels (Fig. 5b) this trend is reversed, and the DECT signal induces a 20% variation larger than GSM one. In order to furtherly compare the two waveforms, some more results are shown in next subsection.

GSM vs DECT

From Fig. 6 it can be seen that in Calcium channels, GSM and DECT signals with the same amount of average power perturb the channel gating in a rather different way.

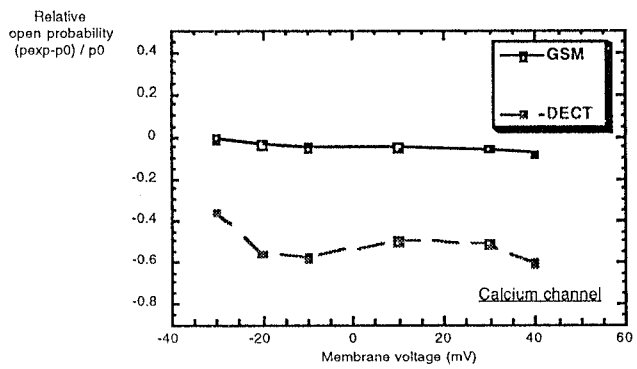


Fig. 6 - Comparison between GSM and DECT signals with an equal average power given to the tissue

In particular, DECT signals seem to induce stronger effects, confirming the observations of Fig. 5b. If we look at the waveforms in Fig. 2, more observations can be done. As the duty factors are substantially different, the DECT signal has a larger pulse-amplitude. This parameter is more important in the kinetical behaviour of the Calcium channel than other parameters (such as the burst frequency or number of pulses per burst). This is due to the strong non-linearity of the Calcium channel conductivity dependence on transmembrane voltage.

4. Conclusions

This work studies the microscopic effect of GSM and DECT signals on ionic channels inside cell membranes. It demonstrates that these fields induce non thermal effects more evidently than CW signals, perturbing the gating of the channels, and therefore causing modifications in the biochemical equilibrium of cells. Observed variations are around 30% in Sodium and Potassium channels, and 60% in Calcium one.

A rigorous model of a neuron based on experimental results has been developed in [15]: this model represents the behaviour of the whole membrane consisting of a certain number of channels. Including the results obtained in the present work in this macroscopic model [15] could represent the future development of this work

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