How the active and diffusional nature of brain tissues can generate monopole signals at micrometer sized measures

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We investigate mechanisms which could generate transient monopole signals in measuring current source density (CSD), as it had been indicated to occur in recent small volume experiments. A simple model is defined for this purpose. It is emphasized that the active nature of the neural biological activity, with its ability to generate ionic density imbalances, might be able to induce appreciable monopole signals in CSD detectors at micrometer scales. Thus, it follows that when both diffusive and ohmic transport are considered to be present in neural tissues, potential measures in micrometer regions can include appreciable electric monopole signals, for sufficiently small values of the ratio \( \frac{\sigma^2}{\varepsilon D} \), where, \( \sigma \) is the conductivity, \( \varepsilon \) is the dielectric constant, \( D \) is the diffusion constant and \( a \) is the linear dimension of the ionic charge densities generated by the neural processes. Ranges of possible magnitudes for these parameters in the considered experimental studies are estimated. The analysis indicates values for the ratio between the dipolar and monopole signals which are close to the ones measured in Pyramidal cells in recent experiments. The measured results for Spiny Stellate cells are also qualitatively described by the model by predicting a finite monopole signal in combination with vanishing dipolar and quadrupole ones.

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I. INTRODUCTION

The finding by Riera et al. in references [1, 3] about the possible existence of temporal unbalance in the extracellular ionic charge have generated a very intense theoretical debate with position divided in those that support it (See [2, 3]) and those that are opposed to it (See [4]). If monopole current sources can coexist transiently with dipolar ones at small physical scales, this coexistence may have a profound implication in the way we interpret current small-scale EEG and MEG data as well as in the models we employ today to simulate this type of brain data recordings.

In the present work we intend to argue that the inclusion of diffusion in the transport properties of the brain tissues, in addition to the consideration of the active properties of the membrane processes, could describe the above mentioned recent and surprising findings: namely, the evidences of non vanishing monopole components in the evoked potentials measured in mesoscopic portions of the brain tissues [1, 2]. It should be mentioned that the relevance of diffusion and other processes for the correct explanation of modern neurophysiology measurements had been discussed in detail in reference [2].

We start the presentation by reviewing the standard quasistatic approximation for the description of brain tissues, in which they are considered as perfect conductors [5]. Afterwards, the simple model in which the work is based will be defined. The main addition to the Ohmic conduction property of the brain tissues is the inclusion of the possibility of diffusion of the charges. The model assumes a single ionic component of the diffusion in order to simplify this starting analysis. The general Poisson equation describing the electric potential at the interior of the tissue medium is written. More complex situations can be treated with the help of the general discussions of diffusion effects in the literature (See [7]).

Next, the equations are considered for simple one dimensional (1D) models. A 1D model is constructed in which the cell interior is assumed to be the negative \( x \) axis, and the Ohmic and diffusional tissue fills the \( x > 0 \) region. A cell membrane was assumed to lay at the \( x = 0 \) point of the one dimensional model, which during some time interval was allowing the flow of positive ions to the \( x < 0 \) cell’s interior region. After that, the membrane was assumed to be blocked. Then, the equations for this 1D model were solved for the potential and densities as functions of the time and spacial variable \( x \). The solutions were found for two values for the single relevant parameter defining them \( \sigma^* = \frac{\sigma a^2}{\varepsilon D} \), where \( \sigma \) is the Ohmic conductivity of the tissue, \( a \) is the above defined linear length of the region being the support of the negative charges compensating the net ionic charges trapped within the cell interior. Further, \( \varepsilon \) is the dielectric constant of the tissue and \( D \) is the diffusion constant of the medium.
The 1D equations are exactly solved as Fourier integrals determined by the initial conditions. The solutions are firstly discussed for the zero conductivity limit value, in order to examine the case in which only diffusive transport is allowed. The results clearly illustrate how the diffusion is able to dissipate the initial cloud of negative charges located around the cells, by translating those charges to infinity, and then leaving the electric field generated by the charges inside the cell unscreened. Then, it follows that in this extreme unphysical limit, monopole charges can be "measured" at arbitrary faraway regions from the considered cell model. Next, a little more realistic family of solutions is discussed for a finite value of the unique parameter $\sigma^*$. The results show that in this case, the initial cloud of charges also starts to be dissipated by the combined conduction and diffusion currents, but now leading the negative charges to conform a distribution which stabilizes a 1D static Yukawa solution. At this configuration, the system stops to dissipate energy, because the total current vanishes at all the spatial points. It follows that the potential in the faraway regions always grows with the time, up to the value corresponding to the static Yukawa solution. However, this static configuration is clear that can not remain established for a long time, due to an additional physical process, not being taken into account in the present model. That is the slower, diffusion processes across the membrane, which tends to return the positive charges trapped within the cell to the tissue medium surrounding it. Therefore, the value of the Yukawa potential at some measuring electrode point can be considered as an estimate of the maximal signal arriving to this electrode from a firing cell. Then, we will adopt this potential values as giving a measure of these firing processes at the instant of their maximum. It should be noted, that this picture furnishes a qualitative explanation for the relevant times variations in the order of milliseconds shown by the CSD process in neural systems. This is the time scale of the membrane firings in the neurons and the consecutive ions return processes to the extra cellular medium. Next, it is argued that all the determined solutions of the 1D problem lead to corresponding solutions of the spherically symmetric 3D problem in which the radial distance $r$ coincides with the $x$ coordinate of the 1D problem. Further, the 3D potential and charge densities are equal to the 1D solutions after divided by $r$. In this mapping process the 1D static Yukawa solutions lead to corresponding 3D Yukawa field distributions. In these solutions the central point charge, models the positive ions being collected inside the cell after the diffusion through the membrane. The screening length associated with the Yukawa solution is defined by the square root of the above defined constant $\sigma^*$. The work continues by considering two models. The first one is for the firing of a spherically symmetric cells. It is basically described by the Yukawa solution at an instant in which the signal at the electrodes approaches its maximal value. The other one, is defined by a superposition of two spherically symmetric solutions, each of which is also described by Yukawa fields but corresponding to opposite charges which are displaced in a vector $\vec{r}$, corresponding to a similar length as the constant $a$. This is considered in the work as a simplified model for typical non-spherical CSD configurations. The Pyramidal cell action potential, and its physical description is reported in reference [1] and shows a more complex structure in which quadrupole components are also measured. In those experiments they also exhibit monopole and dipole components. The measured ratio between the dipolar and the monopolar signals will be taken here as a reference for a qualitative comparison between the predictions of the proposed model and the experimental results. The field configurations are employed for estimating the ratio between the potential at the electrodes created by the dipolar, $\phi_d(r)$, and monopolar, $\phi_m(r)$, components of the Pyramidal cell action potentials. The Spiny Stellate cells, in which CSD also demonstrate weak but non vanishing monopolar components as reported in [1]. The fact that the dipolar and quadrupolar components both vanish, can be estimated as indicating that the model reasonably describes the measurements associated to the Spiny Stellate neurons in that work. The range of values of the relevant parameter in cortical systems $\sigma^* = \frac{a}{\sqrt{3}}$ were estimated after considering the reported values for the brain tissue conductivities, the spatial dimensions $a$ and their typical separations $l$ of the charge densities in the action potentials of Pyramidal cells measured in [1]. The reported values of the diffusion constants in extra cellular media for the $N_a$ and $C_o$ ions, and the permeability values for the cortical tissues were employed.

The results allow for the extraction of a main conclusion of this work: for the experimental conditions reported in [1, 6], the presence of the surprising monopolar components in the estimated evoked potentials in mesoscopic regions of the brain tissues, can be justified after considering the active nature of the cell membrane processes in combination with the presence of diffusion in the intercellular brain medium.

It should mentioned that upon writing this article, we had been informed about the appearance of a work which independently underlines the relevance of the active and diffusional characters of the neural processes in the brain [6].

The exposition proceeds as follows: the basic ideas of the quasistatic model for the neural tissues are shortly reviewed in Section 2. In Section 3 the model for the transport equations including diffusion is introduced. Section 4 considers the solution of the equations for the density and the potentials, in the case of the simpler one dimensional systems. Section 5 is devoted to construct 3D solutions from the 1D solutions. The simple models for cell action potentials showing a spherically symmetric monopole and a cylindrical symmetric dipolar CSD are presented in Section 6. The estimates of the relative strengths of the two configurations, and the range for the experimental values for the parameter $\sigma^*$ are also described there.
II. THE QUASISTATIC MODEL FOR THE BRAIN TISSUE

In this initial section, we will review the elements of the volume conductor model for brain tissues. Let us consider a conductive tissue medium that can efficiently screen electric charge densities generated within it by the neurological system. The current and charge distributions associated with the conductive tissue will be, on one side, the Ohm conductivity current component
\[\vec{J}(\vec{x}, t) = \sigma(\vec{x})\vec{E}(\vec{x}, t)\]
and its associated charge density function \(\varrho(\vec{x}, t)\). In addition, the system will exhibit the so called impressed current and charge densities, generated by complex biological processes \(\vec{J}_{imp}(\vec{x}, t)\) and \(\varrho_{imp}(\vec{x}, t)\). The total current and charge densities in the conductor tissue will be defined as
\[
\varrho_T(\vec{x}, t) = \varrho(\vec{x}, t) + \varrho_{imp}(\vec{x}, t),
\]
\[
\vec{J}_T(\vec{x}, t) = \vec{J}(\vec{x}, t) + \vec{J}_{imp}(\vec{x}, t).
\]

The displacement field is given in the form
\[\vec{D}(\vec{x}, t) = \epsilon \vec{E}(\vec{x}, t),\]
in which the dielectric properties are assumed to be space independent. Thus, the Maxwell equations become
\[
\vec{\nabla} \times \vec{B}(\vec{x}, t) = \vec{J}_T(\vec{x}, t) + \frac{\partial}{\partial t} \vec{D}(\vec{x}, t),
\]
\[
\vec{\nabla} \cdot \vec{D}(\vec{x}, t) = \varrho_T(\vec{x}, t),
\]
\[
0 = \vec{\nabla} \cdot \vec{J}_T(\vec{x}, t) + \frac{\partial}{\partial t} \vec{\nabla} \cdot \vec{D}(\vec{x}, t) = \vec{\nabla} \cdot \vec{J}_T(\vec{x}, t) + \frac{\partial}{\partial t} \varrho_T(\vec{x}, t)
= \vec{\nabla} \cdot \vec{J}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho(\vec{x}, t) + \vec{\nabla} \cdot \vec{J}_{imp}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho_{imp}(\vec{x}, t).
\]

We will assume that both: the conductor and the current densities independently satisfy the local charge conservation condition. That is
\[
\vec{\nabla} \cdot \vec{J}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho(\vec{x}, t) = 0,
\]
\[
\vec{\nabla} \cdot \vec{J}_{imp}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho_{imp}(\vec{x}, t) = 0.
\]

Let us consider now a small region outside the neural system, that is, being inside the conductor tissue and assume that the conductivity, is a constant parameter. If it is also assumed that the impressed currents and charges vanish in this region, the charge conservation condition can be written as
\[
0 = \vec{\nabla} \cdot \vec{J}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho(\vec{x}, t)
= \frac{\sigma}{\epsilon} \vec{\nabla} \cdot \vec{D}(\vec{x}, t) + \frac{\partial}{\partial t} \varrho(\vec{x}, t)
= \frac{\sigma}{\epsilon} \varrho(\vec{x}, t) + \frac{\partial}{\partial t} \varrho(\vec{x}, t)
= \left(\frac{\sigma}{\epsilon} + \frac{\partial}{\partial t}\right) \varrho(\vec{x}, t).
\]

Thus, the tissue conductor charge density (working within the assumptions of this work) satisfies the simple equation
\[
\left(\frac{\sigma}{\epsilon} + \frac{\partial}{\partial t}\right) \varrho(\vec{x}, t) = 0,
\]
with the following solution:
\[
\varrho(\vec{x}, t) = c \exp(-\frac{\sigma}{\epsilon} t).
\]
In other words, if at a given time, the charge density in the tissue was forced to be non zero, it would decay with the time constant
\[
\tau = \frac{\varepsilon}{\sigma}.
\] (10)

For the cortex conductor tissue, the decay time is on the order of $1.66 \times 10^{-11} \frac{\varepsilon(f)}{\varepsilon_0}$ seconds (See reference \[2\]), where $\epsilon(f)$ is the frequency $f$ dependent relative dielectric constant. Note that only for values of $\epsilon(f)$ as high as $10^8$, the decay time $\epsilon(f)$ attains values of milliseconds. Thus, in very short periods of time the charges inside the cortex conductor tissues become screened. Below, we consider that the neural processes (diffusional, chemical, ....) producing the existence of impressed currents, have time periods very much longer than the screening time constant $\tau$.

In particular, in the situation where the interior of the region of the tissue does not contain any impressed currents, the mentioned rapid screening will enforce that the electric field satisfy the modified Poisson equation
\[
\nabla \cdot \overrightarrow{J}(\overrightarrow{x}, t) = \overrightarrow{\nabla} \cdot (\sigma(\overrightarrow{x}) \overrightarrow{E}(\overrightarrow{x}, t)) = \overrightarrow{\nabla} \cdot (\sigma(\overrightarrow{x}) \nabla \varphi(\overrightarrow{x}, t)) = 0.
\] (11)

On the another hand, considering that the impressed and Ohmic currents overlap in a given spatial region, and that the impressed current vanishes in the neighborhood of the boundary; the conservation condition
\[
\nabla \cdot (\overrightarrow{J}(\overrightarrow{x}, t) + J_{\text{imp}}(\overrightarrow{x}, t)) = \nabla \cdot (\sigma \nabla \varphi(\overrightarrow{x}, t) + J_{\text{imp}}(\overrightarrow{x}, t)) = 0,
\] (12)

after integration over the interior volume $V_n$ of the considered region leads to
\[
\int_{S_n} d\overrightarrow{s} \cdot \overrightarrow{J}(\overrightarrow{x}, t) = \frac{d}{dt} \int_{V_n} d\overrightarrow{x} (\varphi(\overrightarrow{x}, t) + \varphi_{\text{imp}}(\overrightarrow{x}, t)) - \frac{\sigma}{\varepsilon} Q_T(t) = \frac{d}{dt} Q_T(t),
\] (13)

where, $Q_T(t)$ is the total charge contained in the volume $V_n$, and the vectorial element of surface $d\overrightarrow{s}$ on the close surface $S_n$ surrounding the neural system, is oriented to the outside of the region $V_n$. The above relation simply expresses that the variation of the total charge inside any region of the conductor tissue tends to exponentially vanish with time. This vanishing monopole condition for the neural charge density is a direct consequence of the supposed rapid screening in the conductor tissue. This situation is usually assumed in most of the discussions regarding measuring of electrical activity in neural systems. Below we will argue that this conditions could result to be invalid for the description of the brain current measures being performed today in small spatial regions \[1\].

### III. A MODEL INCLUDING DIFFUSION AND ACTIVE PROCESSES

Let us again underline that within real neurological systems, impressed currents created actively by the biological system, can exist inside the conductor medium surrounding neuronal membranes and axons, with time variations in the millisecond range. The main observation in support of this view is that the time intervals for variations of the ionic currents leading to the neural impulses in axons and dendrites, are in the millisecond range. Thus, such impressed currents (and probably of diffusive nature) can be expected to exist in the close vicinity at the outside of the neurons volume. A support of this idea comes from the results of Ref. \[1\], which are compatible with a spatial distribution of impressed currents laying outside the structure of the pyramidal cell to which the reported distribution is associated. The natural blurring of the inverse methods employed to evaluate these distributions, however, does not allow for a clear definition of this point.

Figure 1 illustrates a simplified ”neuron” defined in the following way. Consider a region filled with a homogeneous conductor tissue and within it, suppose that a biological membrane encloses a region filled by the referred tissue or by another type of it. Let us suppose that by a given biological process, an amount of positive ions are assumed to be flowing into the interior of the membrane, leaving at the exterior a shell in which a deficit of positive ion exists. Note, that if the region is assumed to be spherical as well as the flux of positive ions, this initial state will show zero monopole component of the electric field.
FIG. 1: The figure illustrates a neuron in which a flux of positive ions is passing to the interior of the cell. The existence within the exterior tissue of a diffusional or chemical processes leading to the flow of ions in the cell, is indicated by the thin arrows within the exterior conducting tissue. The picture illustrates the following possibility: Assuming the flow of positive ions into the cell interior occurs during a time interval, a thin shell of negative compensating charges will remains close to the membrane given that the exterior tissue is a conductor sustaining only Ohmic ionic currents. However, if a diffusive nature is also assumed in the exterior tissue, such thin shell of negative charges tends to be strongly screened by external diffusion currents, which are proportional to the gradient of the density. Thus, positive charges are flowing into the vicinity of the cell up to some distances which depend on the parameters of the neural tissue. If such distances are large enough, they can create measurable signals in the small dimension CSD electrodes, and then monopolar structures could be detected in experiments.

Let us assume that the conductor tissue is constituted by a density $\rho$ of positive ionic charges which are mobile, and a compensating "jellium" of negative charges which are assumed to be static in order to simplify the further discussion by having only one dynamic charge density. The dynamics of the mobile ions are assumed to be given by a generalized diffusion equation in which the ohmic currents are also included.

$$-\nabla^2 \phi(\mathbf{x}, t) = \frac{1}{\varepsilon} \rho(\mathbf{x}, t),$$  

(14a)

$$0 = \frac{\partial \rho(\mathbf{x}, t)}{\partial t} + \frac{\sigma}{\varepsilon} \rho(\mathbf{x}, t) - D \nabla^2 \rho(\mathbf{x}, t),$$  

(14b)

$$J_T(\mathbf{x}, t) = -\left(\sigma \frac{\partial \phi(\mathbf{x}, t)}{\partial \mathbf{x}} + D \frac{\partial \rho(\mathbf{x}, t)}{\partial \mathbf{x}}\right),$$  

(14c)

$$\mathbf{E}(\mathbf{x}, t) = -\frac{\partial \phi(\mathbf{x}, t)}{\partial \mathbf{x}}.$$

(14d)

These equations constitute the general definition of the model. In what follows, we will search for particular explicit solutions of the equations which can be of help in discussing the possible relevance of monopolar structures. For the application to theses special problems, we will consider boundary conditions in the following simplifying way:

1) An explicit and simple form for the initial condition for the ionic charge density at all the spatial points will adopted for the model.

2) After the initial time $t = 0$, the membrane will be assumed to be closed not allowing the flow of ionic currents through it. Mathematically, this means that the total ionic current $J_T$ will be equal to zero at the membrane. This last constraint will avoid the rapid cancelation of the opposite charges existing at both sides of the membrane. After the action potential the neuron will be allowed to return to the standard charge balanced state.

It should be noted that the real processes in neural systems can be very much complex, implying, by example, multiple kind of positive and compensating negative ions. However, in this first discussion we intended to simplify the analysis by including one kind diffusive positive ionic component with the compensating charge assumed to be a "jellium" of fixed negative charges. In addition, a perfect non conductive state of the membranes during periods of time will be assumed, which is clearly a reasonable idealization for simplifying the finding of explicit solutions.

In next sections we will consider the system of equation and its solutions for the case of a spherical cell. However, before considering the spherical case, let us study the problem for a planar model in which the semi-space being at the right of a planar membrane is a conductor tissue and the left half semi-space is assumed to be formed by a medium which does not screen the entered positive charges and allows them to be mobile within a region near the membrane. This planar system will be qualitatively close to the real situation in cells, in which there is no possibility of creating
charges within the cell, in order to compensate for the positive ions entering the cell. Before the initial instant \((t = 0)\), it will be assumed that the membrane was open for a brief moment in which positive ions entered the left region forming the assumed initial ionic charge imbalance. After the initial times, the membrane is assumed to be closed for the flow of ions.

### IV. THE PLANAR VARIANT OF THE MODEL

As it was mentioned, in this section we will assume a simplified model of a cell formed by the membrane, and a right semi-space filled with conducting tissue. The left semi-space is assumed to be an empty region in which the ions having entered the intracellular space are mobile but held near the membrane. Therefore, the \(x\) coordinate is defined as measuring the distance from a point within the right semi-space to the membrane, \(x > 0\). Equations in this semi-space will have the form

\[-\frac{\partial^2}{\partial x^2} \phi(x, t) = \frac{1}{\epsilon} \rho(x, t),\]

\[0 = \frac{\partial \rho(x, t)}{\partial t} + \sigma \rho(x, t) - D \frac{\partial^2 \rho(x, t)}{\partial x^2},\]

\[\frac{\partial E(x, t)}{\partial x} = \frac{1}{\epsilon} \rho(x, t),\]

\[J_T(0^+, t) = -\left(\frac{\partial \phi(0^+, t)}{\partial x} + D \frac{\partial \rho(0^+, t)}{\partial x}\right) = 0,\]

\[J_T(x, t) = -\left(\frac{\partial \phi(x, t)}{\partial x} + D \frac{\partial \rho(x, t)}{\partial x}\right),\]

\[E(x, t) = -\frac{\partial \phi(x, t)}{\partial x}.\]

In the approximation under consideration, the problem is a one dimensional one in the vicinity of the membrane and the coordinate \(x\) has been chosen to be equal to zero at the membrane position. The one dimensional problem can be solved by taking the exponential Fourier transform with respect to time. Further, the spatial Fourier Transforms can be employed in order to expand the spatial dependence.

In order to complete the definition of the model, we need only to define a reasonable functional form for the ionic charge densities at the exterior and interior of the cell. The densities at the exterior will be specified as a function of the \(x\) coordinate at the initial time \(t = 0\) by the expression

\[\rho(x, t) = -\lambda x \Theta(a - x) \Theta(x) \equiv \rho_0(x),\]

where the constant \(\lambda\) has dimension of Coulomb over meters to the fourth power, in order to assure the dimension of \(\rho\) as Coulombs by cubic meter, \(\Theta(x)\) is the Heaviside step function and \(a\) is the width of the ionic charge distribution assumed to be created by some active biochemical processes. Note that an arbitrarily chosen strength for the density can be fixed since the equations are inhomogeneous, and the solution will be linearly dependent on the density function at the initial time. We will use this freedom to choose \(\lambda = 1\) \(\text{C/m}^4\). The solution for a specific charge density can be found by simply multiplying the resulting fields for \(\lambda = 1\), by the correct value of \(\lambda\).

The solution of the density equations for the chosen boundary condition was found in the following form. The charge density has the Fourier expansion:

\[\rho(x, t) = \int_{-\infty}^{\infty} dq \ c(q, x) \exp(-D q^2 + \frac{\sigma}{\epsilon} t) - \rho_0 \exp(-\sqrt{\frac{\sigma}{\epsilon D} x^2}),\]

where the function \(c(q, t)\) is a linear combination of the sine and cosine Fourier spatial modes as

\[c(q, x) = \sqrt{\frac{2}{\pi}} \left(\alpha s(q) \sin(qx) + \beta \left(\frac{a^2 \sigma}{\sqrt{2\pi(D \epsilon q^2 + \sigma)}} + c(q)\right) \cos(qx)\right).\]

The \(s(q)\) and \(c(q)\) expansion coefficients have the expressions

\[s(q) = \sqrt{\frac{2}{\pi}} \left(-q a \cos(a q) + \sin(a q)\right),\]

\[c(q) = \sqrt{\frac{2}{\pi}} \left(-1 + \cos(a q) + q a \sin(a q)\right).\]
In the expression $\alpha + \beta = 1$ and $\alpha$ is a constant which was determined in the process of constructing the solution of the problem. The above formula for the density is a superposition of waves, each one satisfying the homogeneous electro-diffusion equation for the density. The coefficients were fixed from the condition of reproducing the initial density profile at the right of the membrane. However, in this process we had added and substacted a particular solution of the equation for the density under the following reasoning. As the ionic flow is prohibited by the membrane, which is assumed to be closed after $t = 0$, it is clear that the electric field near the membrane at its outside will have a constant value defined by Gauss law. It should be noted that in this diffusional case, there can not exist a surface density of charge, because, in presence of diffusion this will be imply an infinite diffusional current density which is proportional to the time gradient of the ion density. In addition, the equation for the density has static modes which vary exponentially at infinity. This fact suggests the convenience of adding and subtracting to the found solution a static solution which directly solves the time independent problem. Since the static solution exponentially decays at faraway regions, the electric field should tend to zero at infinity. Therefore, after applying Gauss law, the charge of the system seen at infinite should be zero. This in turns, allows to determine the amplitude of the static solution from the condition of having a net charge of opposite sign but equal in magnitude to the positive ionic charge being at the left of the membrane. This solution corresponds to the last term in (22). Further, the subtracted term enforces that the solution minus this subtracted term, has a zero total charge in the whole axis at the beginning of the process. Now, since the static solution, by construction, has zero flux of particles at all points, in particular at the membrane, the subtracted solution (the first term in (22)) should also have zero flux at the membrane. But, precisely this condition can be directly satisfied, by choosing the value of the, up to now indefinite, parameter $\alpha$. This point can be understood after noting that for $\alpha = 0$ the expansion for the density is a pure cosine expansion. Therefore, the total current at the membrane of the solution vanishes. This property follows because the diffusional current is zero at the membrane as consequence of fact that the derivative of the density has a sine Fourier expansion vanishing at $x = 0$. Also, since the considered density has zero net charge on the whole axis, it also corresponds to a zero electric field at the membrane position.

The expression for the electric field after integrating the density from a point close to the membrane to an arbitrary one, can be written in the form

$$E(x,t) = \frac{1}{\varepsilon} \sqrt{\frac{2}{\pi}} \int_0^\infty dq \frac{1 - \cos(qx)}{q} \left( \frac{a^2}{\sqrt{2\pi(2\rho q^2 + \sigma)}} \right) + \frac{\beta}{\epsilon} \left( \frac{a^2\sigma}{2\pi(D\epsilon q^2 + \sigma)} + c(q) \frac{\sin(qx)}{q} \right) \exp(-D q^2 + \frac{\sigma}{\epsilon} t) +$$

$$\frac{a^2}{2\epsilon} - \frac{r_0}{\epsilon} \sqrt{\frac{\epsilon D}{\sigma}} (1 - \exp(-\sqrt{\frac{\sigma}{\epsilon D}})).$$

The value of the electric field at the membrane is given by Gauss law, which defines the constant $r_0$ by

$$E(0^+, t) = \frac{a^2}{2\epsilon} = \frac{r_0}{\epsilon} \sqrt{\frac{\epsilon D}{\sigma}}.$$

With the above relations for the density and the electric field the total ionic current flowing through the membrane at any point $x$, can be evaluated using the formula

$$J_T(x, t) = \sigma E(x, t) - D \frac{\partial \rho(x, t)}{\partial x}.$$

### A. New variables definitions

Let us discuss the properties of the above solution for the planar case. It can be noted that by a linear transformation of variables, the space coordinate $x$, the time variable $t$ and the electric field can be redefined to express the equations in the form

$$0 = \frac{\partial \rho^* (x^*, t^*)}{\partial t^*} + s \rho^* (x^*, t^*) - \frac{\partial^2}{\partial x^2} \rho^* (x^*, t^*),$$

$$\frac{\partial E^* (x^*, t^*)}{\partial x^*} = \rho^* (x^*, t^*) \Theta(x^*),$$

$$s = \sigma^* = \frac{\sigma a^2}{\epsilon D}.$$
This form is equivalent to a selection \( \epsilon = 1, D = 1 \) in the original equations. The starting values for the variables can be recovered by using the following relations

\[
x^* = \frac{x}{a}, \quad (32) \\
t^* = \frac{D}{a^2} t, \quad (33) \\
E^* = \frac{\epsilon}{a} E, \quad (34) \\
\rho^* = \rho. \quad (35)
\]

For \( N_a \) ions in extra cellular medium the diffusion constant \( D_{N_a} = 1.33 \times 10^{-5} \text{ cm}^2/\text{s} \) (as reported in references \[8, 10\]) and a charge density size \( a = 20 \mu\text{m} \), one unit of the newly defined time means \( a^2/D = 0.3 \) seconds. From now on, the variables to be employed will be those having an asterisk, but in order to simplify the notation, the asterisk will be omitted beyond this point.

**B. The vanishing conductivity limit**

Let us consider first the case in which the conductivity is assumed to vanish. This case is interesting, because it allows for the possibility that the electric field can be nonvanishing at infinity. It should be noted that a finite electric field at infinity and a finite conductivity implies infinite power dissipation by the system per any finite area of the membrane. This amount of power can not be delivered by the considered system, which has at the beginning a finite amount of energy per unit area of the membrane. However, if the zero conductivity case shows a monopole in a large finite volume, being comparable with the volume occupied by a nanometer array of detectors, then it will directly imply that at least for certain range of small values of the conductivity, the array could detect electric fields indicating a monopole component in the measured volume. Then, the explanation of the observed monopoles in Ref. [1], could be rationalized if the conductivity and diffusion constant of the experimental system have the appropriate ratio. The question about the experimental values for this ratio will be discussed in the last sections.

FIG. 2: The two top figures shows the plots of the ionic density as functions of the distance to the membrane for the zero conductivity solution. The top left figure contains the plots for the time values \( 0.1, 2, 3, \ldots, 10 \). In this time interval the initial peak in the density is damped. The top right figure shows the density plots for times in the interval 10 to 100 at larger times intervals of 10. In this period the negative density at the right of the membrane propagates to large distances. The two bottom figures show various plots of the electric field as function of the distance to the membrane for the zero conductivity case. The bottom left one contains the plots for times values \( 0.1, 1, 2, 3, \ldots, 10 \) ranging. In this time interval the electric field rapidly decreases with the spatial distances, but for larger times their values increases. The bottom right figure shows the electric field for times in the interval 10 to 100 at larger times intervals of 10. In this period the field continues to increase with time.
Figure 2a), shows the spatial dependence of the time dependent solution for ionic charge density as a function of the distance to the membrane for the zero conductivity case. The curves correspond to the times values (0.1, 1, 2, 3, ..., 10) in order to illustrate the starting period of the evolution. Then, figure 2b) next shows another set of ten curves corresponding to times ranging from 10 to 100 at intervals of 10, illustrating the later evolution. The plots illustrate how the charge density at the right side of the membrane decays with time. The curves for times increasing in figure 2a), show the disappearance of the initial triangular form of the ionic charge distribution. Figure 2b) illustrates that the diffusion is increasingly smoothing the spatial dependence of the density at all spatial points; this implies the tendency to vanish of the current flow at all spatial points. Figures 2c) and 2d), exhibit the values of the electric field as a function of the distance to the membrane, for the same corresponding sets of time values previously defined for figures 2a) and 2b). The results constitute an evidence of the ability of the considered planar model at vanishing conductivity, of showing a monopole charge densities at faraway regions from the membrane. This is directly implied by the non-vanishing values of the electric fields even in the large time limit for which the field tends to be constant in all space as generated by a monopole charge. This net charge is associated with ions which entered to the cell to the left of the membrane at the initial instant. This result, in the case of the vanishing conductivity assumed for the tissue, is allowed by the fact that the system is able to sustain an electric field in all space, showing a monopole, because there are not dissipation losses due to a finite electric conductivity.

C. The finite conductivity limit

Let us now present results for a non-vanishing value of the conductivity. We will consider the solution for the parameter value

$$\sigma^* = \frac{\sigma a^2}{\epsilon D} = 0.01,$$

in order to search for solutions retaining the property that the electric field shows appreciable values, at distances 10 times the initial size of the charge distribution a. The ionic charge density profiles for the same sets of time values chosen in the past section were evaluated.

Then, figures 3a) and 3b) present the results for the evolution of the time dependent component of the ionic charge densities at a set of instants. It should be recalled that this time dependent component of the density, is the value after subtracting the previously defined static part. For figure 3a) the times take the values (0.1, 1, 2, 3, ..., 10), for figure 3b) the time varies between 10 to 100 at intervals of 10. From figure 3a) it can be seen that the charge densities in the beginning, while the initial triangular distribution is being damped, also tends to rapidly decrease at large distances. Figures 3b) show that at larger times, the density tends to become homogeneous and the time decay of the field in this phase becomes slower.

The spatial behavior of the electric field is depicted in figures 3c) and 3d). For the same two sets of times instant, the field monotonically decays with the distance to the membrane and the field tends to grow with time at fixed spatial points as in the previous zero conductivity case. However, in the large time limit, the spatial behavior of the electric fields tends to be exponentially decaying as should be. For the parameters selected, it follows that at distances of the order of ten times the size of the initial charge density, the field (or what is the same, the monopole that a measuring system of electrodes situated inside the zone can measure) is an appreciable fraction of the charge trapped within the planar cell. This behavior leads to the interesting conclusion that at large distances (nearly ten times the width a of the initial ionic density) and longer periods of times, the amount of monopole at the membrane measured can be a relatively large fraction of the charge density of the initial distribution per unit area of the membrane. As the conductivity becomes larger this effect diminishes and the behavior at large times decays exponentially with distances of value 10 a.

The presented results could show relevance for the explanation of the measured monopoles in reference 1. This is possible in the case that the conductivity and diffusion parameters in the tissues containing the neurons in question show parameter values leading to measurable monopole signals. It is possible that the 3D situation could enhance the effect, since the diffusional charge dissipation is enhanced, and then allowing the monopole to be higher in proportion. One important point to note is that, assuming that the mechanism is valid, the important role taken by diffusion in the problem indicates, that the non-vanishing monopole measures presented in Ref. 1 becomes an notable effect due to the advanced and reduced size pioneering experiments done in that work. Finally one interesting point is that the effective conductivity $\sigma^* = \frac{\sigma a^2}{\epsilon D}$ includes the dielectric constant in the denominator, indicating that the high permittivity of the biological tissues can reduce the values of this quantity.

It can be recalled that the characteristic time $\tau^2$, when considered for charge distribution dimensions $a = 20 \mu m$ and the before cited value extra cellular diffusion constant of the ion $N_{a^+}$, takes a value close to $0.3 \ s$. Therefore,
Fig. 3: Figures 3a) and 3b) present the results for the time evolution of the time dependent component of the ionic charge densities at a set of instants for the finite conductivity solutions. It should be noted that the time dependent component of the density is the density after subtracting the previously defined static part. For figure 3a) the times take the values 0.1, 1.2, 3,..., 10, for figure 3b) the time varies between 10 to 100 at intervals of 10. From figure 3a) it can be seen the charge densities in the beginning, while the initial triangular distribution is being damped, also tend to rapidly decrease at large distances. Figures 3c) and 3d) depicts the electric field spatial behavior, of the finite conductivity system, for the same three sets of times instants. The field monotonically decays with the distance to the membrane, and tends to grow with the time at any fixed point as in the previous zero conductivity case. However, in the large time limit, the spatial behavior of the electric fields tends to be exponentially decaying it as should be. For the parameters selected, it follows that at distances of the order of ten times the size of the initial charge density, the field (or what is the same, the monopole that a measuring system of electrodes situated inside the zone can measure) is an appreciable fraction of the charge trapped with the planar cell. This behavior leads to the interesting conclusion that at large distances (nearly ten times the width of the initial ionic density) and large times, the amount of monopole at the membrane measured can be a relatively large fraction of the charge density of the initial distribution per unit area of the membrane.

after also recalling that for the cortical tissue the time constant $\frac{\varepsilon(f)}{\sigma}$ can show millisecond values (for high values of the relative dielectric constant $\frac{\varepsilon(f)}{\varepsilon_0}$ of $10^8$), the constant $\sigma^* = \frac{\sigma}{\sigma_0}$ can approximately get a value of $2 \times 10^2$. Thus, the chosen value in this section of $\sigma^* = 0.01$, for illustrative purposes results to be much smaller with respect to the values estimated for cortical tissues.

V. DERIVATION OF THE 3D SOLUTIONS FROM THE 1D ONES

In this section we will derive spherically symmetric 3D solutions of the equations (14) from the 1D solutions obtained in the previous section. For this purpose, let us rename the one dimensional variable $x$, giving the distance from the observation point to the planar membrane, in the way $r = x$. Next, let us define the new fields $\rho^d(r)$ and $\phi^d(r)$ in the forms
\[
\rho(x,t) = r \rho^d(r,t),
\]
\[
\phi(x,t) = r \phi^d(r,t).
\]
Then, it follows
\begin{align*}
\frac{d}{dx} \rho(x, t) &= \rho^d(r, t) + r \frac{d}{dr} \rho^d(r, t), \\
\frac{d^2}{dx^2} \rho(x, t) &= 2 \frac{d}{dr} \rho^d(r, t) + r \frac{d^2}{dr^2} \rho^d(r, t) \\
&= r \left( \frac{d^2}{dr^2} + \frac{2}{r} \frac{d}{dr} \right) \rho^d(r, t), \\
&= r \nabla^2 \rho^d(r, t) \tag{38}
\end{align*}

where \( \nabla^2 \) is the 3D Laplacian. In identical form for the electric potentials follows
\begin{align*}
\frac{d^2}{dx^2} \phi(x, t) &= r \nabla^2 \phi^d(r, t). \tag{40}
\end{align*}

The above relations allow us to write the equation of motion of the density and the potential, as written in the new dimensionless coordinates and times variables introduced before. The relations become
\begin{align*}
\frac{\partial \rho(x, t)}{\partial t} + s \rho(x, t) - \frac{\partial^2}{\partial x^2} \rho(x, t) &= r \left( \frac{\partial \rho^d(r, t)}{\partial t} + s \rho^d(r, t) - \nabla^2 \rho^d(r, t) \right) \tag{41} \\
- \frac{\partial^2}{\partial x^2} \phi(x, t) &= r \nabla^2 \rho^d(r, t). \tag{42}
\end{align*}

Therefore, after substituting in the equations, common factors can be canceled and the equations for the new fields turn to be
\begin{align*}
\frac{\partial \rho^d(r, t)}{\partial t} + s \rho^d(r, t) - \nabla^2 \rho^d(r, t) &= 0 \tag{43}, \\
- \nabla^2 \phi^d(r, t) &= \rho^d(r, t). \tag{44}
\end{align*}

Henceforth, the fields \( \rho^d \) and \( \phi^d \) satisfy the same equations but in the three dimensional space. Thus, all the solutions found for the 1D problem now define corresponding solutions of the 3D problem by performing the defined changes of variables. It will be helpful to underline some properties relating the two types of solutions:

1) The charge associated to the symmetry point \( r = 0 \) in the 3D solution is proportional to the linear density of the ionic charge which had passed to the interior of the cell in the 1D solution. This means that the whole cell in the 3D solution will be represented by the symmetry point \( r = 0 \), and its attached net charge.

2) A sphere of radial size \( a \) defines the region in which initial density of negative compensating charges were defined. These charges cancels the total positive charges inside the cell (represented by the physical point \( r = 0 \) in the 3D solution). At the initial time, \( (t=0) \), the region defined is analogous to that defined in the 1D solution where the compensating negative charge density resides in order to compensate for the positive ions that had entered the lipid bilayer. This defines the meaning to the parameter \( a \).

\section*{VI. TWO SIMPLE FIRING MODELS FOR THE SPINY STELLATE AND PYRAMIDAL CELLS}

In this section, we will apply the derived 1D and 3D solutions to qualitatively estimate the ratios between the signals produced outside the cells by two typical transient processes which we will model to occur in their vicinity. One of the processes will consider an initial density profile showing spherical symmetry. Such a configuration can qualitatively resemble the Spiny Stellate cells action potential showing a weak monopole moment and zero multipole moments in the experiments of reference [1]. The second process will be one in which two spherically symmetric configurations, will be superimposed at two spatial locations separated by a given vector \( \vec{L} \). These two configurations in this second process will be assumed to have initial density profiles which are identical but with oppositely signed charge densities. This model seems to reasonably resemble asymmetrical cell firing showing a dipole like structure.

It's clear that the detection of a non-vanishing signals in the electric detector, associated to the spherical spatial symmetry of the field in the first solution, will be identified as a monopole charge. Thus, in order to estimate the relative strength of the monopole signal, with respect to second "dipole" like signal, a tactic can be to compare the relative ratio of the potentials created at some observation point.

As it was seen from the solution for the one dimensional case, the time dependent solution of the initial value problems for the ionic density evolves in a way tending to approach a static exponential solution in which the internal
charge is screened without zero current density. That is, the Ohmic current density is exactly canceled by the diffusion current, to avoid energy dissipation. This behavior directly translates to the 3D counterpart solutions. Therefore, as mentioned before, we will take the values of such static solutions as a measure of the maximal signal at faraway regions at which the measuring electrodes will be assumed to be situated. This corresponds to a situation in which the transient solutions are assumed to decay in a very short time.

Further, it is assumed that these transient solutions could not be detected by a small bandwidth electric potential detector, or eventually, that they constitute the rising transient potentials leading to the peak action potential measured. Clearly, the measured decaying time evolution of the signals in the experiment should be directly attributed to the fact that the internal charges which passed to the internal region of the cell, will slowly return to the extra cellular medium, with the help of diffusion processes. These are recognized to exist, after the membranes becomes closed to the rapid flux of ions occurring during the neural impulse firings. Therefore, the potential of the spherically symmetric solution at far distances will be assumed to have the expression

\[ \phi_{\text{mon}}(r) = \frac{\phi_0}{r} \exp(-\sqrt{\sigma^*} r), \]  
\[ \sigma^* = \frac{\sigma a^2}{\epsilon D}. \]  

At this point it seems convenient to again describe the physical meaning of this Yukawa field as determined by its derivation within the model. Note that close to the symmetry point \( r = 0 \), the field is similar to the Coulomb one for a point charge. This point charge, as interpreted in the 1D variant of the model, describes the ionic charges that entered the cell through the membrane, which sits at the \( x = 0 \) coordinate value; which after the change of variables corresponds to the symmetry point. Thus, the net charge associated to the Yukawa solution can be naturally interpreted as the charge inside the cell, which in our model shows vanishing size. The parameter \( a \) was defined as the width of the zone in the 1D model in which the negative charges compensating the net positive ionic charge was assumed to be sitting at the initial instant of time. Therefore, after the change of variables defining the 3D solution in terms of the 1D solutions is done, the parameter \( a \) also describes the radius of the sphere at which the compensating charges are placed at the beginning of the 3D cell firing being modeled.

The physical process in the above written static Yukawa solution can be described in the following steps:

1) After the rapid "opening" of the membrane to the ionic flow, a net amount of positive ionic charges is assumed to diffuse through it at the \( x = 0 \) point of the 1D solution.

2) At this initial moment, and after interpreting the \( x \) coordinate of the 1D solution as the radial one for the 3D solution, and scaling the fields, in the 3D case, the situation in 3D can be viewed as corresponding to a net positive point charge concentrated at the symmetry point \( r = x = 0 \), surrounded by an sphere of radius \( a \) filled of negative charges. These charges exactly compensate the positive point charge at \( r = 0 \).

3) After that, assuming that the membrane becomes "closed" to the further flow of ions, the negative charges being within the sphere of radius \( a \) can not follow their natural tendency to enter the cell, and tend to diffuse away from the cell in a process which establishes the Yukawa solutions. The stability of this solution is assured by the fact that the Ohm currents are exactly canceled by the diffusion ones, leading to a non dissipative state in which the net current charge current vanishes. The tendency to enhance monopole components determined by the inclusion of diffusion processes in the model for the brain tissue, was seen in the previous sections in the limit of which the \( \sigma^* \) parameters becomes small. In this case the system tends to become a dielectric and the Yukawa solutions tends to approach the Coulomb solution in larger regions. Then, if the region is of the order of the similar size as the one associated to the array of detecting electrodes, the monopole components can become strong. As noted before, the non-vanishing measured potential determined by this solution can be interpreted as a monopole due to the spherical symmetry of its spatial distribution.

Let us now consider the second configuration, which might typically represent less spatially symmetrical processes occurring in neural systems. The aim will be to compare its strength with the previous one showing a monopole. For this purpose, as described before, assume a superposition of two spherically symmetric solutions, associated to two spherical membranes of identical sizes, which at the beginning have internal charges (and associated halos of opposite compensating charges of radius \( a \)) of equal magnitude, but different signs. The location of the spherical symmetry points of the two solutions will be supposed to be displaced in a vector \( \vec{l} \), whose length is assumed to be of order one. That is, corresponding in normal units to the same size of the radius "\( a \)". It will be also assumed that the two electro-diffusion processes can be approximately considered as non interacting. The initial charge density of the system will be less symmetrical than the previously discussed system. However, due to the transient screening processes the initial charge densities will be gradually evolving due to the diffusion and ohmic currents. The screening of the external charges outside the two points representing the cells is supposed to occur in short times, the inverse of these times is much larger than the signal bandwidth of the detector. In this situation, at points \( \vec{l} \) near the detector electrodes, the potentials created by the two cells systems can be approximately written by the difference between
the two Yukawa potentials created individually by each cell, in the following form

$$\phi^{\text{dir}}(\vec{r}) = \frac{\phi_0}{\sqrt{\vec{r}^2 + \vec{l}^2}} \exp(-\sqrt{\sigma^*} |\vec{r} + \vec{l}|) - \frac{\phi_0}{r} \exp(-\sqrt{\sigma^*} r)$$

$$\approx \vec{l} \cdot \vec{\nabla} \phi^m(r)$$

$$= - \vec{l} \cdot \vec{n}_r \left( \frac{1}{r} + \sqrt{\sigma^*} \right) \phi^m(r),$$

(47)

where $\vec{n}_r = \vec{r}/|\vec{r}|$, and it has been assumed that at the measuring distances $r \gg |\vec{l}|$.

Therefore, for this special model system the ratio between the signals at the detector will have the expression

$$\left| \frac{\phi^{\text{dir}}(\vec{r})}{\phi^m(r)} \right| = |\vec{l} \cdot \vec{n}_r \left( \frac{1}{r} + \sqrt{\sigma^*} \right)|.$$  

(48)

It should be noted that this quantity will be assumed to correspond to the maximal values of the detected potential at the electrodes, occurring precisely when the charge density halos of the cells had been annihilated by the diffusion process outside the cells. This process will translate the halos’s charges to conform the fields around the cells as the superposition of the Yukawa fields created by the ionic charges retained into the cells. After this period, the interior ionic charges will be assumed to slowly escape out from the cell’s interior thanks to slow returning diffusion mechanisms, which are known to allow for this decay in the millisecond region.

Note that in the considered systems of units, one unit of distance is equivalent to the size parameter $a$ which is of the order of the dimensions of the regions in which compensating charges appear around the cells. Thus, since the distance from the two cell system to the detector is at least ten times larger than the order of the dimensions of the regions in which compensating charges appear around the cells. Therefore, since the mechanisms, which are known to allow for this decay in the millisecond region.

Now, it can be noted that the deviation from a purely Ohmic behavior of the brain tissues implied by these measures should be associated with the diminishing of the ionic charges within the cells, due to slower diffusion mechanisms, which naturally tends to expulse the ionic unbalanced charges.

VII. THE $\phi_d/\phi_m$ - EXPERIMENTAL RANGES

Let us consider the peak (indicated by bottom arrow in Fig. 2 a) in Ref. 13 for an action potential fired by a pyramidal cell. This figure illustrates the time dependence of an Action Potential fired by a Pyramidal Cell (left) and the respective spatial distribution of current sources (top-right). The absolute values of the monopolar and dipolar electric currents measured in that work, are $I_m = 0.015 \mu A$ and $I_d = 0.070 \mu A$ mm respectively. Thus, these measures indicate a clear deviation of the system from a quasistatic fully Ohmic conductor behavior of brain tissues at the micrometer scales. We will assume that the instant signaled with the arrow in the figure at the left, indicates the moments in which transient diffusion processes lead to potential values at the electrodes, given by the static Yukawa field generated by the ionic charges concentrated in the cells. Afterwards, the time dependence of the measures should be associated with the diminishing of the ionic charges within the cells, due to slower diffusion mechanisms, which naturally tends to expulse the ionic unbalanced charges.

Now, it can be noted that the deviation from a purely Ohmic behavior of the brain tissues implied by these experiences is clearly indicated by equation (13). It directly determines that the monopole charge in a volume (whose boundary is fully included in a purely ohmic tissue) shows an exact exponential time decay of the form $e^{\frac{t}{\tau}}$. This kind of time evolution is incompatible with the repetitive time dependence exhibited by the monopole intensities $I_d$ measured in reference 1. Therefore, the experimental results seem to clearly indicate the limitation of the fully Ohmic nature of the charge transport in brain tissue. In what follows we will explore the implications of the discussions in the previous sections in which the role of the diffusion was included in a simplified model for the neural tissues.

Let us initially examine the prediction of our discussion for the $\phi_d/\phi_m$ ratio which can be estimated by the previously derived equation:

$$\frac{\phi_d(\vec{r})}{\phi_m(\vec{r})} = \frac{\vec{l} \cdot \vec{n}_r \left( \frac{1}{r} + \sqrt{\sigma^*} \right)}{\sqrt{\vec{r}^2}},$$

(49)
The vector parameter \( \mathbf{l} \) represents the direction and distance between the positive and negative charge clouds for the dipolar current source. Based on the preliminary data for the distribution of the current densities depicted at the right of figure 2 a) in Ref. [1], we assume this parameter ranges between 0 – 100 \( \mu m \). Let us assume that \( \mathbf{l} \) and \( \mathbf{r} \) are parallel and that the parameter \( l = |\mathbf{l}| = 1 \), that is, chosen to approximately coincide with \( a \) in the original units. This reflects the physical assumption that the separation between the ionic clouds of different signs should be similar to the size of such clouds, if they are associated to a common cell. Then, the ratio can be written in the form

\[
\frac{\phi_d(\mathbf{r})}{\phi_m(\mathbf{r})} = \left( \frac{1}{|\mathbf{r}|} \right) + \sqrt{\sigma^*}.
\]

The constant \( \sigma^* = \frac{\sigma^T}{\epsilon} \) is defined as a function of the tissue conductivity \( \sigma \), permittivity \( \epsilon \), width of ionic charge distribution \( a \) and ionic diffusion coefficient \( d \). We used experimental result for the electric permittivity and conductivity of the bovine’s gray matter reported in Ref. [11], to find lower and upper bounds for the conductivity and the permittivity both \( 0.05 \leq \sigma(\frac{\mu S}{m}) \leq 0.3 \) and \( 5 \times 10^5 \leq \frac{\epsilon_0}{\sigma} \leq 8 \times 10^7 \), in the frequency range for the electrophysiological recordings. Note that taking into account these bounds the time decay constant \( (\tau = \frac{1}{\epsilon d}) \) for gray matter could range from to 14.7 \( \mu s \) to 14.2 \( m s \).

![Figure 4](image.png)

**FIG. 4:** Dependency of \( \sqrt{\sigma^*} \) for the lower (blue) and upper (red) bounds, as functions of the parameter \( a \) measuring the size of the ionic charge clouds. The upper curve is obtained by using the maximal values of \( \sigma/\epsilon \) estimated for the neural brain tissues in conjunction with the minimal value of the diffusion constant of the normally involved ions. On the contrary the minimum value is evaluated by employing the minimal value of \( \sigma/\epsilon \) in common with the maximal value of the ionic diffusivity.

The quasi-static approach for the electromagnetic field has been based on the smallest values of this parameter. However, more complicated phenomena, like those discussed in this study, could emerge for the largest values of this decay constant. The lower and upper bounds for the diffusion coefficient were estimated based on the extracellular ionic profile existing in biological tissues, with sodium and calcium as the primary ions: \( d_{N++} = 1.33 \times 10^{-5} \ cm^2/s \) for the upper bound (See references [8, 10]) and \( d_{Ca^{2+}} = 0.45 \times 10^{-5} \ cm^2/s \), for the lower one (See reference [9]).

Based on these lower/upper bounds, we calculated the dependency of \( \sqrt{\sigma^*} \) with parameter \( a \) (See figure 4) and of \( \phi_d/\phi_m \) with respect to \( |\mathbf{r}| \) and \( a \) (See figure 5).

At this point, it should be noted the fact that well defined regions of values for \( \sigma^* \) and parameter exists which qualitatively match the experimental results for \( \phi_d/\phi_m \) predicted by the measures reported for Pyramidal cells in reference [1]. The plot of this ratio in figure 5 clearly provides evidence about the existence of a wide range of values for \( a \) which can produce a qualitative agreement with the ratios between dipolar and monopolar signals measured in reference [1], for the Pyramidal cells neuron action potentials. Specifically, for \( \sqrt{\sigma^*} \) values below the depicted horizontal line traced at the value 10 in figure 4 and simultaneously above the lower curve in this picture, this parameter, which approximately measures the relative strength between the dipolar and the monopolar signals, shows values between 10 and the unit. These are the magnitudes of the values shown by the experimental results for the ratios between the dipolar and monopolar signals, measured in reference [1].

Figure 6 illustrates in more detail the above comment. It plots the ratio between the dipolar and the monopolar signal as a function of the parameter \( a \) and the variable \( r \) (which as defined before is measured in units of the length \( a \)). The plot is associated to the minimal values of \( \sigma^* \) defined by the lower curve in figure 4. The value of the parameter...
FIG. 5: Dependency of $\frac{\phi_d}{\phi_m}$ as a function of the "radius of the ion clouds" $a$ and the distances $r$ from them to the measuring electrodes (given in units of $a$). The horizontal plane simply indicates a typical value close to 6, for the ratio $\frac{\phi_d}{\phi_m}$ as estimated from the results for Pyramidal cells of reference [1]. Note that the typical experimental value can be predicted by the model, for values of $a$ being close to $a = 20 \, \mu m$. This is valid up to large distances between the electrodes and the charge clouds of $r = 40$, that is, of $40 \, a = 800 \, \mu m$, after stating that $r$ is measured in units of $a$. This length is larger than the inter electrode separation of 200 $\mu m$ used in the experiments reported in reference [1]. The value parameter $l$ was fixed to coincide with $a$, reflecting that the separation between the ionic clouds of different signs should be similar to the size of these clouds, if they are associated to a common cell.

$l$ for the plot was fixed to one, which corresponds with a distance $a$ in normal units. This assumption is reflecting that the separation between the ionic clouds of different signs should be similar to the size of such clouds, if they are associated to a common cell. The depicted plane indicates a typical value for the ratio of dipolar to monopolar maximal signals reported in [1], whose value is approximately 6. Note that for reasonable values of the radius of the initial ionic clouds of 20 $\mu m$, the ratio between the dipolar and monopolar signal becomes close to the experimental values. Interestingly, this occurs at such large distances between the electrodes and the charge density sources of $r = 40$, which after recalling that $r$ is measured in units of $a$, corresponds to 800 $\mu m$. These distances are larger than the values of 200 $\mu m$ separating the electrodes in the experiments done in reference [1]. Finally, it should also be noted that the experiments for the Spiny Stellate cells reported in [1], which have an approximate spherical symmetry, are also in qualitative agreement with the discussion in this paper, since for these the measured monopole signal is the only non vanishing one, and the dipolar and quadrupole components results to be null.

Summary

In this work we investigated mechanisms which could generate transient monopole signals in measuring current source densities. A simple model was introduced for this purpose. It is concluded that the active and diffusive natures of the neural biological processes, might determine appreciable monopole signals in CSD detectors for experiments done at micrometer scales, due to the ability of the cell membranes and neural tissues to generate ionic density imbalances in the vicinity of the neurons. Therefore, it is argued that when both diffusive and Ohmic transport are considered to be present in neural tissues, electric potential measures in micrometer regions can include appreciable monopole signals. This might occur for sufficiently small values of the ratio of the parameter $\frac{\sigma l}{D}$, where $\sigma$ is the conductivity, $D$ is the diffusion constant and $a$ is the linear dimension of the ionic charge densities generated by the neural processes. Possible ranges of magnitudes for these parameters in the considered experimental studies are estimated. The analysis also predicts values for the ratio between the dipolar and monopolar signals, that are similar
to those measured in Pyramidal cells in recent experiments reported in [1]. This happens for feasible values of the tissue parameters. As for the measures in Spiny Stellate cells reported in this same work, the model also qualitatively reproduces them, by predicting a finite monopolar signal in combination with vanishing dipolar and quadrupolar signals. The discussion and results seem to be compatible with the conclusion of a recent work appeared in Ref. [6]. In this paper it is independently stressed the important role of the active and diffusional nature of the electromagnetic process occurring in the brain tissues.

The analysis also furnishes a qualitative explanation of the millisecond scales for the measured processes in the brain tissues. The active nature of the membrane processes appear in the picture as generating maximal signals at the detectors, that afterwards decay due to a slower returning of the trapped ions to the extra cellular medium. Both, the neuron membrane firings and the returning ionic currents, then constitute within the model, the "active" forces determining the millisecond periods of occurrence of the typical neuron firing detected in Ref. [1].

Several issues of interest remain to be investigated in connection with the present analysis. The generalization of the model to more properly include the presence of various types of ionic currents is one of the natural extensions. Another one is the study the uniqueness property of the model equations in connection with the determination of the sources as functions of the electric potentials. The adoption of the examined equations can imply modifications of the algorithms for the evaluation of the sources in terms of the measured electrode potentials. It is clear that, the possibility of "improving" the solution of the inverse problem at such micrometer sized experiments is suggested by the monopole measurability within the model, this constitutes a motivating factor for the further study of this question.

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