MODELING EXTRACELLULAR FIELD POTENTIALS
AND THE FREQUENCY-FILTERING PROPERTIES OF EXTRACELLULAR SPACE

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Running title:
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Abstract

Extracellular local field potentials (LFP) are usually modeled as arising from a set of current sources embedded in a homogeneous extracellular medium. Although this formalism can successfully model several properties of LFPs, it does not account for their frequency-dependent attenuation with distance, a property essential to correctly model extracellular spikes. Here we derive expressions for the extracellular potential that include this frequency-dependent attenuation. We first show that, if the extracellular conductivity is non-homogeneous, there is induction of non-homogeneous charge densities which may result in a low-pass filter. We next derive a simplified model consisting of a punctual (or spherical) current source with spherically-symmetric conductivity/permittivity gradients around the source. We analyze the effect of different radial profiles of conductivity and permittivity on the frequency-filtering behavior of this model. We show that this simple model generally displays low-pass filtering behavior, in which fast electrical events (such as Na$^+$-mediated action potentials) attenuate very steeply with distance, while slower (K$^+$-mediated) events propagate over larger distances in extracellular space, in qualitative agreement with experimental observations. This simple model can be used to obtain frequency-dependent extracellular field potentials without taking into account explicitly the complex folding of extracellular space.

Keywords

Computational models, Neurons, Local field potentials, LFP, Electroencephalogram, EEG
INTRODUCTION

Extracellular potentials, such as local field potentials (LFPs) or the electroencephalogram (EEG), are routinely measured in electrophysiological experiments. The fact that action potentials have a limited participation to the genesis of the EEG or LFPs was noted from early studies. Bremer (1938, 1949) proposed that the EEG is generated by non-propagating potentials, based on the mismatch of time course between EEG waves and action potentials. Eccles (1951) proposed that LFP and EEG activities are generated by summated postsynaptic potentials arising from the synchronized excitation of cortical neurons. Intracellular recordings from cortical neurons later demonstrated a close correspondence between EEG/LFP activity and synaptic potentials (Klee et al., 1965; Creutzfeldt et al., 1996a, 1996b). The current view is that EEG and LFPs are generated by synchronized synaptic currents arising on cortical neurons, possibly through the formation of dipoles (Nunez, 1981; Niedermeyer and Lopes da Silva, 1998).

The fact that action potentials do not participate to EEG-related activities indicate strong frequency-filtering properties of cortical tissue. High frequencies (greater than $\approx 100$ Hz), such as that produced by action potentials, are subject to a severe attenuation, and therefore are visible only for electrodes immediately adjacent to the recorded cell. On the other hand, low-frequency events, such as synaptic potentials, attenuate less with distance. These events can therefore propagate over large distances in extracellular space and be recordable as far as on the surface of the scalp, where they can participate in the genesis of the EEG. This frequency-dependent behavior is also seen routinely in extracellular unit recordings: the amplitude of extracellularly-recorded spikes is very sensitive to the position of the electrode, but slow events show much less sensitivity to the position. In other words, an extracellular electrode records slow events that originate from a large number of neighboring neurons, while the action potentials are recorded only for the cell(s) immediately adjacent to the electrode. This fundamental property allows to resolve single units from extracellular recordings.

However, little is known about the physical basis of the frequency-dependent attenuation of extracellular potentials in cortex. By contrast to intracellular events, which biophysical mechanisms have been remarkably well characterized during the last 50 years (reviewed in Koch, 1999), comparatively little has been done to investigate the biophysical mechanisms underlying the genesis of extracellular field potentials (see review by Nunez, 1981). The reason is that LFPs result from complex interac-
tions involving many factors, such as the spatial distribution of current sources, the spatial distribution of positive and negative electric charges (forming dipoles), their time evolution (dynamics), as well as the conductive and permittivity properties of the extracellular medium. One of the simplest and widely used model of LFP activity considers current sources embedded in a homogeneous extracellular medium (Nunez, 1981; Koch and Segev, 1998). Although this formalism has been successful in many instances (Rall and Shepherd, 1968; Klee and Rall, 1977; Protopapas et al., 1998; Destexhe, 1998), it does not account for the frequency-dependent attenuation and therefore is inadequate for modeling extracellular field potentials including spike activity.

In this paper, we would like to investigate possible physical grounds for the frequency-filtering properties of LFPs. We start from first principles (Maxwell equations) and consider different conditions of current sources and extracellular media. We delineate the cases leading to frequency-filtering properties consistent with physiological data. We show that the assumption of a resistive homogeneous extracellular medium cannot account for the frequency-dependent attenuation. It is necessary to take into account the inhomogeneous structure of the extracellular medium (in both permittivity and conductivity) in order to account for frequency-dependent attenuation. We next analyze a simplified representation of current sources in non-homogeneous media, and provide a simplified model which could be applied to simulate extracellular field potentials without using complex representations of extracellular space. We terminate by showing a concrete example of the genesis of extracellular LFPs from a conductance-based spiking neuron model.

MATERIAL AND METHODS

We will first develop a general formalism to express the temporal variations of extracellular potential, as well as a simple model in which most of the calculations can be done analytically (see Section General theory; see also Appendix 1 and 2 for details). We will next explore this simplified model numerically to illustrate its frequency-filtering behavior (Section Numerical simulations), in which we have performed two computations: (i) Calculate the impedance: the impedance is given by an integral, which was evaluated numerically by standard numerical integration routines. (ii) Convert time-dependent functions into frequency-spectra. These conversions were done via Fourier transformation (as well as its reverse transformation), which were carried out in C using standard numerical
To test this formalism, we also considered a simple biophysical model of a spiking neuron containing voltage-dependent and synaptic conductances (last part of Section Numerical simulations). A single-compartment neuron was constructed and included conductance-based models of voltage-dependent conductances and synaptic conductances. This model was described by the following membrane equation:

$$C_m \frac{dV}{dt} = -g_L(V - E_L) - g_{Na}(V - E_{Na}) - g_{Kd}(V - E_K) - g_M(V - E_K) - g_e(V - E_e),$$  

where $C_m = 1 \mu F/cm^2$ is the specific membrane capacitance, $g_L = 4.52 \times 10^{-5}$ S/cm$^2$ and $E_L = -70$ mV are the leak conductance and reversal potential. $g_{Na} = 0.05$ S/cm$^2$ and $g_{Kd} = 0.01$ S/cm$^2$ are the voltage-dependent $Na^+$ and $K^+$ conductances responsible for action potentials and were described by a modified version of the Hodgkin & Huxley (1952) model. $g_M = 5 \times 10^{-4}$ S/cm$^2$ is a slow voltage-dependent $K^+$ conductance responsible for spike-frequency adaptation. $g_e = 0.4 \mu S$ is a fast glutamatergic (excitatory) synaptic conductance. The voltage-dependent conductances were described by conventional Hodgkin-Huxley type models adapted for modeling neocortical neurons, and the synaptic conductance was described by a first-order kinetic model of neurotransmitter binding to postsynaptic receptors. These models and their kinetic parameters were described in detail in a previous publication (Destexhe and Paré, 1999). All numerical simulations were performed using the NEURON simulation environment (Hines and Carnevale, 1997).

**GENERAL THEORY**

In this section, we outline the main features of the model starting from first principles (Maxwell equations). We will consider a number of different special cases and derive a simplified model with radial (spherical) symmetry. In Section Numerical simulations, we will investigate numerically the behavior of this simplified model.

In Maxwell’s theory, the electric properties of a conductive medium are determined by two parameters, conductivity $\sigma$ and permittivity $\varepsilon$. While conductivity quantifies the local relation between the electric field and the current, permittivity characterizes the response of the system in terms of separation of opposite charges (polarisation) in the presence of an electric field. Maxwell’s theory of
electromagnetism allows one to compute electric and magnetic fields or potentials, for a given distribution of charges and electric currents. Because charges move very slowly in biological media, the effects of magnetic fields are very small compared to that of the electric field and will be neglected here.

One of Maxwell’s equations is *Gauss’ law*:

\[ \nabla \cdot (\varepsilon E) = \rho . \]  

(2)

Here \( E \) denotes the electric field, \( D = \varepsilon E \) is the called displacement and \( \rho \) is the charge density of the extracellular medium, also allowed to vary slowly in time.

The *continuity equation* relates the current density \( j \) to the charge density \( \rho \):

\[ \nabla \cdot j + \frac{\partial \rho}{\partial t} = 0 \]  

(3)

which states a balance between the electric flux into some volume and the change of the total charge in this volume. In other words, no charge will get lost.

Finally, there is *Ohm’s law*:

\[ j = \sigma E , \]  

(4)

which states that the relation between the local electric field and the local current density can be described by a single macroscopic parameter \( \sigma \). Here, we assume that the electric field and the current are parallel locally (i.e., at any given point in the medium). The coefficient relating \( E \) and \( j \), the conductivity \( \sigma \), is a scalar, which is justified by macroscopic measurements (Ranck, 1963).

Combining Eqs. 3 and 4 yields

\[ \nabla \cdot (\sigma E) + \frac{\partial \rho}{\partial t} = 0 . \]  

(5)

This equation describes charge conservation in differential form.

In the following, we assume that electric currents are distributed on the surface of the membrane (ionic currents), and that these currents are allowed to vary in time. We introduce the the electric potential \( V \) (also called extracellular potential) which obeys

\[ E = -\nabla V . \]  

(6)

Below, we successively consider different cases of increasing complexity, starting with a homogeneous extracellular medium, then going over to non-homogeneous media.
Homogeneous extracellular medium

Consider a membrane embedded in a homogeneous extracellular medium, with conductivity $\sigma$ and permittivity $\varepsilon$ being held constant in space and time. As shown in Appendix 3, using the assumption $\sigma = \sigma_0 = const., \varepsilon = \varepsilon_0 = const.$, we get for each spectral component

$$\nabla V_\omega \cdot \left( \frac{\nabla (\sigma + i\omega \varepsilon)}{(\sigma + i\omega \varepsilon)} \right) + \Delta V_\omega = \Delta V_\omega = 0. \quad (7)$$

Hence we find

$$\Delta V_\omega = -\frac{\rho_\omega}{\varepsilon} = 0. \quad (8)$$

Using the inverse Fourier transform, this yields

$$\Delta V(x, t) = -\frac{\rho}{\varepsilon} = 0. \quad (9)$$

One observes that the charge density $\rho$ vanishes at the exterior of the sources. The solution depends on the geometry considered, its symmetries and boundary conditions. We consider different cases below.

Spherical membranes

As a particular case, let us consider a spherical membrane obeying the conditions outlined above (homogeneous medium of constant conductivity and permittivity), in which the potential is allowed to vary as a function of time. There are two classic cases of boundary conditions, which yield unique solutions of the Laplace equation: (i) Specification of the potential on a surface (Dirichlet boundary condition) and (ii) Specification of the derivative of the potential normal to the surface (Neumann boundary condition). The latter is equivalent to specifying the normal component of the electric field. Due to Ohm’s law this means to specify the current density on the surface. In neurons, we consider the Neumann conditions in which current sources represent the ionic currents in the membrane. In this case, we have the following boundary conditions:

$$j(r = R) = j_0 n = \sigma E(r = R), \quad (10)$$

Here, we have assumed that the membrane is spherical of radius $R$ (which is also equivalent to consider a point current source). The current density on the surface of the sphere is is proportional to the unit vector $n$ normal to the surface of the sphere.
To analyze the behavior of the extracellular potential as a function of frequency, we perform a Fourier transformation with respect to time of the potential,

$$V_\omega(x) = \int_{-\infty}^{\infty} dt \, V(x, t) e^{i\omega t}.$$  \hspace{1cm} (11)

The potential $V$ satisfies the Laplace equation (11). Because the Fourier transform is linear, each Fourier component $V_\omega$ also satisfies (10). The solution, satisfying boundary conditions (Eq. 10), is given by

$$V_\omega(r) = \frac{I_\omega}{4\pi \sigma r},$$  \hspace{1cm} (12)

where $I_\omega = j_\omega/4\pi R^2$ is the total current for each frequency component. This shows that the potential is the same for all frequency components. Therefore, there is no frequency-dependence in this case.

Thus, the general expression for field potentials resulting from a set of $N$ current sources $\{I_j\}$ of spherical symmetry is:

$$V(x) = \frac{1}{4\pi \sigma} \sum_{j=1}^{N} \frac{I_j}{|x - x_j|},$$  \hspace{1cm} (13)

where $x$ is a point in extracellular space, $x_j$ is the location of the $j$th current source, and $|x - x_j|$ is the distance between $x$ and $x_j$. This expression is widely used to model extracellular field potentials (Nunez, 1981; Koch and Segev, 1998).

**Cylindric membranes**

Because neuronal processes (dendrites, axons) are closer to cylinders, we considered cylindric membranes as a second particular case. Here, the procedure is similar to the above, but the geometry and symmetries are different. If we assume that the membrane potential respects cylindric symmetry (ie, $V$ does not depend on the rotation angle around the cylinder axis), and is uniform on the surface of the membrane (isopotential compartment), then Eq. 9 can be solved for each component of the frequency spectrum and has a unique solution:

$$V_\omega(r) = V_\omega(R) + j_\omega(R) \frac{R}{\sigma} \ln (r/R),$$  \hspace{1cm} (14)

where $r$ is the distance perpendicular to the cylinder axis, while $j_\omega(R)$ and $V_\omega(R)$ are the $\omega$-frequency components of the current density and potential at the surface of the cylinder.
In this case again, the extracellular potential is independent of the frequency. The same conclusion applies to membranes of arbitrary geometries taken in the same conditions because the $\omega$-frequency component of the current density and potential obey Laplace equation. There is therefore no frequency dependence arising from single current sources in homogeneous media.

**Non-homogeneous extracellular medium**

We have shown above that, in a homogeneous medium with a current source of spherical or cylindric symmetry, the extracellular electric potential is the same for all frequency components, and therefore cannot display frequency-dependent properties. We now turn to a possible source of frequency-dependent attenuation, namely the presence of inhomogeneities in the conductivity of the extracellular medium.

*Stationary currents in spherically-symmetric non-homogeneous medium*

Before investigating the general case, let us first consider the case of a static spherical current source embedded in a medium where the conductivity $\sigma$ conserves spherical symmetry, but varies as a function of distance $r$ (as above we assume that $\sigma$ does not depend on time). We also continue to assume that permittivity $\varepsilon$ is homogeneous. If the total current flowing through the sphere of radius $R$ is denoted by $I$, then the radial dependence of the current density is given by

$$j(r) = \frac{I}{4\pi r^2} e_r.$$  

(15)

In this case, the charge density $\rho$ is non-zero and is given by

$$\rho = -\frac{\varepsilon}{\sigma} j \cdot \nabla \log \sigma.$$  

(16)

Then Ohm’s law implies for the spherically symmetric electric field

$$E(r) = \frac{I}{4\pi r^2 \sigma(r)} e_r.$$  

(17)

The spherically symmetric electric potential is the obtained by integrating the electric field, giving

$$V(r) = -\int_r^\infty dr' E(r') = \int_r^\infty dr' \frac{I}{4\pi r'^2 \sigma(r')}.$$  

(18)
Details of the calculation can be found in Appendix 1.

This equation shows that the potential may decrease or even increase, depending on the spatial variations of $\sigma$. An important consequence is that such net charge creates its own electric field (so-called secondary field), which will be analyzed in more detail below. What is the physical origin of this non-zero net charge? The current density behaves like $J \propto 1/r^2$, (Eq. 15), and the electric field like $E \propto 1/(\sigma(r)r^2)$, (Eq. 17). Consequently, there will be accumulations of charges in some regions of lower conductivity, similar to traffic jams. Consider a more realistic case in which the conductivity of the extracellular space is constant on average, but displays spatial fluctuations around this average. This could correspond for example to different processes and obstacles in the extracellular medium. In this case, the electric field, going like $1/r^2$ on average, fluctuates locally. This creates local areas of positive and negative charge, i.e. electric dipoles. Those dipoles also create a secondary electric field. However, to account for frequency dependence, time-varying current sources must necessarily be considered, in which case the situation is more complex, as analyzed in the next section.

**Time-varying currents in non-homogeneous medium**

Let us now consider the general case where both $\varepsilon$ and $\sigma$ are non-homogeneous in space, but constant in time. We assume that the current source is allowed to vary in time. The continuity equation implies that the charge density is also time-dependent. Ohm’s law implies that the electric field has a time-dependence as well, and so will also the extracellular potential. Due to the inhomogeneity of $\varepsilon$, the extracellular potential does no longer satisfy Poisson’s equation. To study the frequency-dependence of the extracellular potential, we perform a Fourier transform of the electric field, the potential and likewise of the charge density $\rho$.

$\rho_\omega$, the component of frequency $\omega$ of the temporal Fourier transform of the charge density $\rho$, satisfies

$$\frac{\partial}{\partial t} \rho_\omega = i\omega \rho_\omega.$$  \hspace{1cm} (19)

This equation expresses the differential law of charge conservation for a given Fourier component. Now we consider the Gauss’ law (Eq. 2), the law of charge conservation in differential form (Eq. 5), and carry out the Fourier transform with respect to time. Taking into account Eq. 19 yields

$$\Delta V_\omega = -\frac{(\nabla V_\omega) \cdot (\nabla (\sigma + i\omega \varepsilon))}{\sigma + i\omega \varepsilon} = -\nabla V_\omega \cdot \nabla \log (\sigma + i\omega \varepsilon).$$  \hspace{1cm} (20)
For details, see Appendix 2.

This equation is general and applies to any particular symmetries (under the assumption of scalar conductivity). We consider below a series of special cases, as well as special symmetries.

### Special cases

As a first special case, consider Eq 20 when permittivity is constant. Then Ohm’s law (Eq. 4) implies

\[
\Delta V_\omega = -\frac{\rho_\omega}{\varepsilon}.
\]

(21)

Constant permittivity also implies \(\nabla (\sigma + i\omega \varepsilon) = \nabla (\sigma)\). Hence Eq. 20 takes the form

\[
\Delta V_\omega = -\frac{\nabla V_\omega \cdot \nabla \sigma}{\sigma + i\omega \varepsilon} = -\frac{\rho_\omega}{\varepsilon}.
\]

(22)

We therefore observe the occurrence of a (complex) phase difference between the induced charge density \(\rho/\varepsilon\) and the current density \(j\) (recall: \(-\nabla V_\omega = E_\omega = j_\omega/\sigma\)). This effect depends on the frequency \(\omega\) of the Fourier component. Such phenomenon is well known from electric circuits of the RC type, where in general a phase difference between potential and current is observed. In particular, if the potential vanishes at some time \(t\), the electric charge density will not immediately go to zero.

Eq. 22 shows that for high enough frequency the induced charge density goes to zero. On the other hand, for low-frequency phenomena, the charge density will carry out large fluctuations and will be sensitive to spatial fluctuations of conductivity. This has important consequences for interpreting LFP activity (see Section Frequency-filtering properties of non-homogeneous media).

As another special case, consider Eq. 20 when the conductivity is constant. The law of charge conservation in differential form Eq. 5 then becomes

\[
\Delta V_\omega = \frac{1}{\sigma} \frac{\partial \rho_\omega}{\partial t}.
\]

(23)

Constant conductivity also implies \(\nabla (\sigma + i\omega \varepsilon) = \nabla (i\omega \varepsilon)\). Hence Eq. 20 takes the form

\[
\Delta V_\omega = -\frac{\nabla V_\omega \cdot \nabla i\omega \varepsilon}{\sigma + i\omega \varepsilon} = \frac{1}{\sigma} \frac{\partial \rho_\omega}{\partial t} = -\frac{1}{\sigma} \nabla \cdot j.
\]

(24)

This means in the limit of low frequencies that there are no current sinks or sources.

A third noteworthy special case is when both permittivity and conductivity are non-homogeneous, but have a fixed ratio:

\[
\frac{\varepsilon}{\sigma} = \text{const}.
\]

(25)
Under those circumstances one obtains
\[ \Delta V_\omega = -\frac{(\nabla V_\omega) \cdot (\nabla \sigma)}{\sigma} = - (\nabla V_\omega) \cdot (\nabla \log(\sigma)) \, . \] (26)

All frequency-dependence cancels out, the potential becomes frequency independent.

**Frequency-filtering properties of non-homogeneous media**

We now analyze the frequency-filtering properties of Eq. 20. Consider this equation in two limit cases: (i) \( \omega << \sigma/\epsilon \) (low frequency limit); in this case, \( \log(\sigma + i\omega\epsilon) \approx \log(\sigma) \), the solution becomes independent of the permittivity \( \epsilon \) and is determined only by the conductivity \( \sigma \). (ii) \( \omega >> \sigma/\epsilon \) (high frequency limit); in this case, \( \log(\sigma + i\omega\epsilon) \approx \log(i\omega\epsilon) \), and permittivity only determines the solution. These two cases will be considered in more detail below. The critical frequency around which this transition will occur depends on the relative values of \( \sigma \) and \( \epsilon \), and one can define the following critical frequency \( f_{cr} \)
\[ f_{cr} = 2\pi \omega_{cr}, \quad \omega_{cr} = \frac{\sigma}{\epsilon} \, . \] (27)

As an example, consider the value of average resistivity \( \rho_{res} \) (inverse of conductivity \( \sigma \)) measured in rabbit cerebral cortex (Ranck, 1963), giving \( \rho_{res} = 3 \, \Omega \, \text{m} \). Taking the permittivity of salt water (\( \epsilon = 7 \times 10^{-10} \, \text{F/m} \)), gives a critical frequency of \( f_{cr} \) of about \( 10^{10} \, \text{Hz} \). Thus, this analysis shows that the behavior will be similar for low and high frequency limits. However, if one evaluates \( 2\pi \sigma/\epsilon \) for a resting membrane (closed ion channels; \( \rho \simeq 10^9 \, \Omega \, \text{m} \) and \( \epsilon \simeq 10^{-10} \, \text{F/m} \)), one finds for the critical frequency a value in the range between 0 and 100 Hz. The phenomenon of induced charges will be likely to play a role in the frequency range of synaptic inputs in cerebral cortex (0 to 40 Hz). On the other hand, higher frequencies (> 100 Hz) — such as action potentials — are likely to cause negligible variations in charge density.

Further, we can compare Eq. 20 to cases where there is no frequency dependence (i.e., Laplace Eq. 9). At the limit of high frequencies, the left term of Eq. 20 vanishes and this equation becomes equivalent to Eq. 9 showing that for high frequencies, one recovers the same behavior as for a homogeneous medium. To have a low-pass filter, similar to what is observed from extracellular recordings, one must have a situation in which the attenuation of the potential at low frequencies must be less than for homogeneous media. Inspection of the left term of Eq. 20 shows that the attenuation can be either
less or more pronounced, resulting in low- or high-pass filters. The type of filter will depend on the behavior of the gradients of conductivity and permittivity. This behavior will be analyzed numerically in more detail later (see Section Numerical simulations).

**Time-varying currents in spherically-symmetric non-homogeneous medium**

In order to calculate the extracellular potential $V$ generated by time-varying currents in non-homogeneous media, Eq. 20 must be integrated by incorporating details about the particular geometry of current sources and extracellular properties. A general method for solving this problem is, e.g., finite-element analysis, which allows to explicitly incorporate the complex shape and composition of extracellular space around neurons. However, this approach requires to integrate complex morphological data and appropriate simulation tools. We defer this to a future study. In order to have a model of LFPs applicable to standard neuron models, we follow here a simpler approach, based on the following simplification: we consider that the variations of conductivity and permittivity have a radial symmetry in the vicinity of the current sources. This simplification allows us to obtain simpler expressions of the extracellular potential, still displaying frequency dependence, and apply this formalism using standard simulation tools.

Consider Eq. 20 for the case of a spherically-symmetric system. Then the potential obeys

$$\frac{d^2V_\omega}{dr^2} + \frac{2}{r} \frac{dV_\omega}{dr} + \frac{1}{\sigma + i\omega\varepsilon} \frac{d\left(\sigma + i\omega\varepsilon\right)}{dr} \frac{dV_\omega}{dr} = 0. \tag{28}$$

Integrating this equation gives the following relation between two points $r_1$ and $r_2$ in the extracellular space,

$$r_1^2 \frac{dV_\omega}{dr}(r_1) \left[\sigma(r_1) + i\omega\varepsilon(r_1)\right] = r_2^2 \frac{dV_\omega}{dr}(r_2) \left[\sigma(r_2) + i\omega\varepsilon(r_2)\right]. \tag{29}$$

This can be verified by differentiating this equation with respect to $r$, which then yields Eq. 28. Integrating Eq. 29 once more yields

$$V_\omega(r_1) = V_\omega(r_2) + \frac{dV}{dr}(r_2) \int_{r_2}^{r_1} \frac{r_2^2}{r^2} \left[\sigma(r_2) + i\omega\varepsilon(r_2)\right] \frac{dV}{dr}(r_2) \left[\sigma(r_1) + i\omega\varepsilon(r_1)\right]. \tag{30}$$

This can be seen most easily by differentiating Eq. 30 to yield Eq. 29. In particular, if $r_2 = R$, $-\frac{dV}{dr}(r_2)$ represents the electric field at the surface of the sphere of radius $R$, which by Ohm’s law is related to the current density at $R$, we obtain

$$V_\omega(r_1) = V_\omega(R) - \frac{I_\omega}{4\pi\sigma(R)} \int_{r_2}^{r_1} \frac{1}{r'^2} \frac{1}{\sigma(r_2) + i\omega\varepsilon(r_2)} \sigma(R) + i\omega\varepsilon(R). \tag{31}$$
If we assume that the extracellular potential vanishes at large distances \( V_\omega(\infty) = 0 \), we have:

\[
V_\omega(\infty) = V_\omega(R) - \frac{I_\omega}{4\pi\sigma(R)} \int_R^\infty \frac{1}{r'^2} \left( \frac{\sigma(R)}{\sigma(r')} + i\omega \epsilon(R) \right) \, dr'.
\] (32)

which allows to eliminate \( V_\omega(R) \) from Eq. 31, leading to:

\[
V_\omega(r_1) = \frac{I_\omega}{4\pi\sigma(R)} \int_{r_1}^\infty \frac{1}{r'^2} \left( \frac{\sigma(R)}{\sigma(r')} + i\omega \epsilon(r') \right) \, dr'.
\] (33)

This will be the main equation that forms the basis of our simplified model of LFP. Solving this equation for \( \sigma \) and \( \epsilon \) constant leads to the expression found above (Eq. 12) for homogeneous extracellular media. In the numerical part (Section Numerical simulations), we will solve this equation for different spatial profiles of \( \sigma \) and \( \epsilon \). To this end, it is useful to define the impedance:

\[
Z_\omega(r_1) = \frac{1}{4\pi\sigma(R)} \int_{r_1}^\infty \frac{1}{r'^2} \left( \frac{\sigma(R)}{\sigma(r')} + i\omega \epsilon(r') \right) \, dr'.
\] (34)

Then Eq. 33 becomes

\[
V_\omega(r_1) = Z_\omega(r_1) I_\omega.
\] (35)

The impedance is therefore the “filter” applied to the \( \omega \)-frequency component of the current source, to yield the corresponding frequency component of the extracellular potential. In the next section, we will examine the frequency-filtering properties of different extracellular media by calculating numerically the impedance for different cases of spatial inhomogeneities of conductivity and permittivity.

**NUMERICAL SIMULATIONS**

In this section, we use the expressions of the extracellular potential obtained above. In particular we analyze the behavior of the extracellular potential generated by a current source in a spherically-symmetric non-homogeneous medium (Eq. 33), and its associated impedance (Eq. 34). We investigated the frequency-filtering properties obtained for different cases of increasing complexity of the radial profile of \( \sigma \) and \( \epsilon \). The goal is to determine the conditions of spatial variations of conductivity and permittivity for which the frequency-filtering properties are consistent with physiological data. We terminate by an application of this model to calculating the LFP generated by a conductance-based spiking neuron model.
Parameters

Precise experimental data on the variations of permittivity $\varepsilon$ and conductivity $\sigma$ in the extracellular medium have not been measured so far. However, averaged values of these parameters are available from macroscopic measurements. A value for $\sigma$, averaged over large extracellular distances, $\sigma_{av}$, was measured by Ranck (1963) and was between $0.28 \, S/m$ and $0.43 \, S/m$, for 5 Hz and 5 kHz, respectively. The macroscopic frequency dependence of conductivity seems therefore relatively weak. However, the situation is different microscopically. As reviewed in Nunez (1981), the conductivity of the CSF fluid is $1.56 \, S/m$ while the typical conductivity of membranes is $3.5 \times 10^{-9} \, S/m$. This value was obtained from the resting (leak) membrane conductance of cortical neurons, typically around $4.5 \times 10^{-5} \, S/cm^2$, multiplied by the thickness of the membrane (7-8 nm; Peters et al., 1991). At microscopic scales, there is therefore approximately 9 orders of magnitude variations of conductivity.

Permittivity variations are not so dramatic. Fluids have higher permittivity, for example it is about $7 \times 10^{-10} \, F/m$ for sea water. Membranes have a permittivity of about $7.5 \times 10^{-11} \, F/m$. The latter value was derived from the specific capacitance of membranes, $C = 1 \, \mu F/cm^2$ (Johnston and Wu, 1997), and assuming a membrane thickness of 7.5 nm (Peters et al., 1991). Because those variations are small compared to the variations of conductivity, it is a good approximation to consider the permittivity as a constant. In the following, we will use the reference value of $\varepsilon = 10^{-10} \, F/m$.

In the following we will use normalized values for conductivity $\sigma(r)/\sigma(R)$ and permittivity $\varepsilon(r)/\sigma(R)$. Because the membrane is always surrounded by extracellular fluid, $\sigma(R) = 1.56 \, S/m$ and the normalized conductivity $\sigma(r)/\sigma(R)$ therefore varies between 1 and about $2 \times 10^{-9}$. Similarly, the normalized (constant) value of permittivity will be $\varepsilon(r)/\sigma(R) = 6 \times 10^{-11}$.  

**Frequency-filtering properties of spherically-symmetric media**

We calculated numerically the impedance (Eq. 34) for different cases of spatial variations of conductivity and permittivity. In all cases we assumed a current source with spherical geometry, characterized by radius $R$, and that $\sigma$ and $\varepsilon$ vary according to a radial (spherical) symmetry around this current source (see scheme in Fig. 1A). For each case, we represented the normalized impedance

$$\tilde{Z}_\omega(r) = Z_\omega(r)/Z_\omega(R) \, ,$$

(36)
which allows better comparison between the different cases. Because the value of impedance does not depend on the absolute value of permittivity and conductivity (dividing $\sigma$ and $\varepsilon$ by a constant factor does not change $Z_0(r)$ in Eq. 34), we used the normalized conductivity $\sigma(r)/\sigma(R)$ and the normalized permittivity $\varepsilon(r)/\sigma(R)$ defined above. It is also convenient to represent all distances in units of $R$, although we also considered absolute values of distances (see below).

We first investigated a simple case of smooth variations of those parameters, to illustrate the different types of frequency filtering that can be obtained in this model. The profiles of conductivity and permittivity are shown in Figs. 1B and C. These curves tend to the same asymptotic value for large distances. The corresponding impedance is shown as a function of frequency $f$ in Figs. 1D-F (see Appendix 3 for details of the method). When the ratio $\sigma/\varepsilon$ is kept constant (Fig. 1D-F, dotted line), there is no frequency dependence as analyzed above in Section Special cases. In the case of a decreasing conductivity with distance combined with constant permittivity, one has a high-pass filter (Fig. 1D-F, dashed line). By contrast, a low-pass filter is observed if an increasing conductivity with distance is combined with a constant permittivity (Fig. 1D-F, solid line). Thus, there is a clear frequency-dependent behavior when $\sigma$ and/or $\varepsilon$ vary as function of distance $r$, if the ratio $\sigma/\varepsilon$ is not constant. This also shows that low- and high-pass filters are both possible, depending on the exact form of the function $\sigma(r)$ and $\varepsilon(r)$. The impedance can also have a non-zero imaginary part, which means that beyond resistivity, the medium has also capacitive properties. In this case, there will be a phase difference between the potential and the current.

We next considered a case characterized by a localized drop of conductivity (Fig. 2A) while permittivity was kept constant (Fig. 2B). The resulting impedance measured at different distances from the source is shown in Fig. 2C-E as a function of frequency $f$. In this case, for distances around the conductivity drop, there is a moderate frequency dependence with low-pass characteristics (Fig. 2C-E, dotted and dashed lines). However, for larger distances, the imaginary part is zero and there is no frequency dependence (Fig. 2C-E, solid lines). This is explained by the fact that for large distances $\sigma(r) = \sigma(R)$ and $\varepsilon(r) = \varepsilon(R)$. This behavior can also be seen in the attenuation of the different frequency components illustrated in Fig. 2F. There is a different attenuation only for distances around the region where conductivity varies.

Because the extracellular space is composed of alternating fluids and membranes (Peters et al.,
1991), which have high and low conductivity, respectively, we have next considered the situation where conductivity fluctuates periodically with distance (Fig. 3). Considering a cosine function of conductivity (Fig. 3A) with constant permittivity (Fig. 3B) leads to a rather strong frequency-dependent attenuation (Fig. 3C-E) with low-pass characteristics. There was a strong attenuation with distance for all frequencies (Fig. 3F). Very similar results were obtained with other periodic functions (for example by replacing cos by sin in the function used in Fig. 3A), different oscillation periods, or even for damped oscillations of conductivity (not shown).

It could be argued that although fluids and membranes alternate in extracellular space, there is an efficient diffusion of ions only in the extracellular fluid around the membrane. For larger distances, diffusion becomes increasingly difficult because of the increased probability of meeting obstacles. In this case, conductivity would be highest around the source and progressively decrease to an “average” conductivity level for larger distances. This situation is illustrated in Fig. 4. We have considered that the conductivity is highest at the source, then decreases exponentially with distance with a space constant $\lambda$ (Fig. 4A; note that in this case, real distances were used). Permittivity was constant (Fig. 4B). The resulting impedance displayed pronounced frequency-filtering properties with low-pass characteristics (Fig. 4C-E). In particular, the attenuation with distance revealed strong differences between low and high frequencies of the spectrum (Fig. 4F). Similar results can be obtained with other decreasing functions of connectivity (not shown).

The above examples show that there can be a strong frequency-filtering behavior, with low-pass characteristics as observed in experiments. However, although these examples show a more effective filtering for high frequencies, it still remains to be shown that the high frequencies attenuate more steeply with distance compared to low frequencies. To this end, we define the quantity:

$$Q_{100} = \frac{Z_{100}(r)}{Z_1(r)},$$

where $Z_1$ and $Z_{100}$ are the impedances computed at 1 Hz and 100 Hz, respectively. This ratio quantifies the differential filtering of fast and slow frequencies as a function of distance $r$. Fig. 5A displays the $Q_{100}$ values obtained for some of the examples considered above. In the case of a localized drop of conductivity (Fig. 5A, *Drop*), there was an effect of distance for $r < 16R$, then the $Q_{100}$ remained equal to unity for further distances. This behavior is in agreement with the impedance shown in Fig. 2.
in which case there was no frequency filtering for \( r > 16R \). For oscillatory conductivities (Fig. S5A, Osc), the \( Q_{100} \) was always \(< 1\), consistent with the low-pass frequency-filtering behavior observed in Fig. 3. However, the \( Q_{100} \) oscillated around a value of 0.6 and did not further decrease with distance. Thus, in this case, although there was a clear low-pass filtering behavior, all frequencies still contribute by the same relative amount to the extracellular potential, regardless of distance. On the other hand, with exponential decay of conductivity, the \( Q_{100} \) monotonically decreased with distance (Fig. S5A, Exp). Thus, this case shows both low-pass filtering behavior (Fig. 4) and a stronger attenuation of high frequencies compared to low frequencies (Fig. S5A, Exp), which is in qualitative agreement with experiments. Analyzing exponentially-decaying conductivities of different space constants (Fig. S5B) revealed that the various patterns of distance dependence approximately followed the pattern of conductivity (Fig. S5C). This type of conductivity profile is relatively simple and plausible, and will be the one considered in the biophysical model investigated below.

**Biophysical model of the frequency-filtering properties of local field potentials**

We have applied the above formalism to model the frequency dependence of the extracellular field potentials stemming from a conductance-based spiking neuron model. The details about the model are given in the *Material and methods* section, while the details of the calculation of the extracellular LFP (general for any current source) is given in Appendix 3. The profile of conductivity and permittivity used is that of Fig. 4. We calculated the total membrane current generated by a single-compartment model of an adapting cortical neuron, containing voltage-dependent Na\(^+\) and K\(^+\) conductances for generating action potentials and a slow voltage-dependent K\(^+\) conductance responsible for spike-frequency adaptation. The model also contained a fast glutamatergic excitatory synaptic conductance, which was adjusted to evoke a post-synaptic potential just above threshold, in order to evoke a single action potential (Fig. 6A). The total membrane current (Fig. 6B) was calculated and stored in order to calculate its Fourier transform (power spectral density shown in Fig. 6C). The impedance of the extracellular medium (Fig. 6D) was calculated using absolute values of the parameters (Eq. 34).

This model was used to calculate the field potentials at different radial distances assuming the neuron was a spherical source (radius of 105 \( \mu \text{m} \)). The extracellular potential is indicated for 5, 100, 500 and 1000 \( \mu \text{m} \) away from the source (see Fig. 6E) and strong frequency filtering properties are
apparent: the fast negative deflection of extracellular voltage showed a steep attenuation and almost disappeared at 1000 µm (although it had the highest amplitude at 5 µm). In contrast, the slow positive deflection of the extracellular potential showed less attenuation with distance and became dominant at large distances (500 and 1000 µm in the example of Fig. 6E).

Thus, this simple example illustrates that the approach provided here can lead to a relatively simple model to calculate local field potentials with frequency filtering properties. The exact profiles of filtering and attenuation depend on the exact shape of the gradients of conductivity/permittivity as well as on the spherical symmetry inherent to this model.

**DISCUSSION**

In this paper, we have provided a model of extracellular field potentials in non-homogeneous media. We discuss here the validity of this model, how it relates to previous studies, and what perspectives are provided.

The theoretical analysis outlined in Section *General theory* shows that inhomogeneities of extracellular space (with respect to conductivity and/or permittivity) is a possible cause for frequency filtering. In general, non-homogeneous extracellular media will differently affect the attenuation of the various frequency components of the current sources, and can lead to high-pass or low-pass filters depending on the gradients of conductivity and permittivity. The composition of extracellular space is made from the alternance of fluids and membranes (Peters et al., 1991). Because these media have very different conductivity and permittivity, one may expect that the extracellular space is necessarily highly non-homogeneous. Therefore, the structural composition of extracellular space is very likely to be a main determinant of the frequency-filtering properties of LFPs. In addition, the conductivity of the extracellular fluid directly beneath the membrane depends on the ionic concentrations present. It turns out that the extracellular ionic concentrations may vary in time, in an activity-dependent manner (reviewed in Amzica, 2002). Therefore, it is also likely that there is an activity dependent contribution to the filtering properties of the extracellular medium. Here, we did not consider such time-dependent variations of conductivity, but this type of contribution is certainly worth to be considered by future theoretical work.

To correctly simulate the frequency-filtering behavior due to extracellular inhomogeneity, the ex-
tracellular potential should be calculated by a model incorporating details about the three-dimensional composition of the extracellular medium. Such type of simulations should use methods such as finite-element analysis. However, the complexity of this type of analysis, and of the data it requires, makes such simulations inaccessible to standard models. In addition, this requires orders of magnitude differences in computational power needs. For these reasons, we have considered the option of generating a simplified model under some approximation. We assumed that the geometry of extracellular inhomogeneities is spheric around the current source. In this condition, one can obtain relatively simple expressions of the extracellular potential such as Eq. 33. Not only this expression is amenable to theoretical analysis, but it is also sufficiently simple to be applied to current neuron models which do not have an explicit representation of extracellular space.

The drawback of this method is that it considers an un-realistic (radial) distribution of inhomogeneities in extracellular space, which will necessarily affect the frequency-filtering properties produced by the model. However, it should be possible to calculate the “average” radial variations of conductivity and permittivity by averaging the profiles of $\sigma$ and $\varepsilon$ in all directions emanating from neuronal membranes using three-dimensional reconstructions of the neuropil. Another direction would be to measure experimentally the profiles and distributions of $\sigma$ and $\varepsilon$, but such data are not currently available. Here, we have used “heuristic” profiles of conductivity and permittivity, which gives frequency-filtering properties in qualitative agreement with experiments. It should be easy to make this model more realistic by incorporating different radial functions of $\sigma$ and $\varepsilon$ when there will be better constraints by measurements.

The present results lead to several interesting perspectives for future work or extensions. First, as mentioned above, the simplified model could be enhanced by comparison with a more realistic model, for example based on three-dimensional reconstructions of extracellular space. The simplified model could be adjusted so that it fits as closely as possible the behavior of the more realistic model, yielding more optimal expressions of the radial profiles of conductivity and permittivity. A second possible direction is the “reverse” problem of estimating neuronal activity based on LFP measurements. By using data on the spatial and temporal variations of multisite LFPs and multi-unit activity, it should be possible to estimate what are the respective contributions of the natural frequency-filtering properties of extracellular space and the spatial coherence of neuronal sources in the different frequency com-
ponents. For example, it was shown that a consistent relation between LFP and cell firing extends to large cortical distances (>7 mm) for slow-waves but not for fast oscillations in the gamma (20-60 Hz) frequency range (Destexhe et al., 1999). A model of LFP is needed to evaluate whether this effect is really due to differences in the coherence of neuronal firing (as the single-unit data indicates), or if a large part could be explained by the low-pass filtering properties of the extracellular medium. A combination of experimental recordings and computational models will be needed to understand how neuronal activity translates into extracellular field potentials and vice-versa.

Acknowledgments

H.K. has been supported by the National Science and Engineering Research Council (NSERC, Canada). A.D. has been supported by the Medical Research Council (MRC, Canada) and the Centre National de la Recherche Scientifique (CNRS, France). Supplementary information is available at http://cns.iaf.cnrs-gif.fr
REFERENCES

1. Amzica, F. 2002. In vivo electrophysiological evidences for cortical neuron-glia interactions during slow (<1 Hz) and paroxysmal sleep oscillations. J. Physiol. Paris 96: 209-219.

2. Bremer, F. 1938. L’activité électrique de l’écorce cérébrale. Actualités Scientifiques et Industrielles 658: 3-46.

3. Bremer, F. 1949) Considérations sur l’origine et la nature des “ondes” cérébrales. Electroencephalogr. Clin. Neurophysiol. 1: 177-193.

4. Creutzfeldt, O., S. Watanabe, and H.D. Lux. 1966a. Relation between EEG phenomena and potentials of single cortical cells. I. Evoked responses after thalamic and epicortical stimulation. Electroencephalogr. Clin. Neurophysiol. 20: 1-18.

5. Creutzfeldt, O., S. Watanabe, and H.D. Lux. 1966b. Relation between EEG phenomena and potentials of single cortical cells. II. Spontaneous and convulsoid activity. Electroencephalogr. Clin. Neurophysiol. 20: 19-37.

6. Destexhe, A. 1998. Spike-and-wave oscillations based on the properties of GABA$_B$ receptors. J. Neurosci. 18: 9099-9111.

7. Destexhe, A., D. Contreras, M. Steriade. 1999. Spatiotemporal analysis of local field potentials and unit discharges in cat cerebral cortex during natural wake and sleep states. J. Neurosci. 19: 4595-4608.

8. Destexhe, A. and D. Paré. 1999. Impact of network activity on the integrative properties of neocortical pyramidal neurons in vivo. J. Neurophysiol. 81: 1531-1547.

9. Eccles, JC. 1951. Interpretation of action potentials evoked in the cerebral cortex. J. Neurophysiol. 3: 449-464.

10. Henze, D.A., Z. Borghegyi, J. Csicsvari, A. Mamiya, K.D. Harris, and G. Buzsaki. 2000. Intracellular features predicted by extracellular recordings in the hippocampus in vivo. J. Physiol. 84: 390-400.
11. Hines, M.L., and N.T. Carnevale. 2000. The NEURON simulation environment. Neural Computation 9: 1179-1209.

12. Hodgkin, A.L., and A.F. Huxley. 1952. A quantitative description of membrane current and its application to conduction and excitation in nerve. J. Physiol. 117: 500-544.

13. Johnston, D., and S. Wu. 1997. *Cellular Neurophysiology*. MIT Press, Cambridge MA.

14. Klee, M.R., K. Offenloch, and J. Tigges. 1965. Cross-correlation analysis of electroencephalographic potentials and slow membrane transients. Science 147: 519-521.

15. Klee, M., and W. Rall. 1977. Computed potentials of cortically arranged populations of neurons. J. Neurophysiol. 40: 647-666.

16. Koch, C. 1999. *Biophysics of Computation*. Oxford University Press, Oxford UK.

17. Koch, C. and I. Segev, editors. 1998. *Methods in Neuronal Modeling* (2nd ed). MIT Press, Cambridge MA.

18. Niedermeyer, E. and F. Lopes da Silva, editors. 1998. *Electroencephalography* (4th ed). Williams and Wilkins, Baltimore MD.

19. Nunez, P.L. 1981. *Electric Fields of the Brain. The Neurophysics of EEG*. Oxford University Press, Oxford UK.

20. Peters, A., S.L. Palay, and H.F. Webster. 1991. *The Fine Structure of the Nervous System*. Oxford University Press, Oxford UK.

21. Press, W.H., H.P. Flannery, S.A. Teukolsky and W.T. Vetterling. 1986. *Numerical Recipes. The Art of Scientific Computing*. Cambridge University Press, Cambridge UK.

22. Protopapas, A.D., M. Vanier and J. Bower. 1998. Simulating large-scale networks of neurons. In: *Methods in Neuronal Modeling* (2nd ed), C. Koch and I. Segev, editors. MIT Press, Cambridge MA. 461-498.

23. Rall, W. and G.M. Shepherd. 1968. Theoretical reconstruction of field potentials and dendrodendritic synaptic interactions in olfactory bulb. J. Neurophysiol. 31: 884-915.
24. Ranck, J.B., Jr. 1963. Specific impedance of rabbit cerebral cortex. Exp. Neurol. 7: 144-152.
APPENDIX

Appendix 1: Extracellular potential in non-homogeneous media with spherical symmetry

This Appendix refers to Section Stationary currents in spherically-symmetric non-homogeneous medium:

Recall $\sigma = \sigma(r)$, $\varepsilon = \text{const.}$ Then Gauss’ law becomes

$$\nabla \cdot E = \frac{\rho}{\varepsilon}. \quad (38)$$

The law of charge conservation becomes

$$-\frac{\partial \rho}{\partial t} = \nabla \cdot (\sigma E) = \sigma \nabla \cdot E + E \cdot (\nabla \sigma) = \frac{\sigma}{\varepsilon} \rho + E \cdot (\nabla \sigma). \quad (39)$$

Using Ohm’s law and assuming $\sigma \neq 0$, this becomes

$$-\frac{\partial \rho}{\partial t} = \frac{\sigma}{\varepsilon} \rho + j \cdot \nabla \log \sigma = \frac{\sigma}{\varepsilon} \rho + j \cdot \nabla \log \sigma. \quad (40)$$

We make the assumption that the current density $j$ is stationary, i.e. it does not explicitly depend on time. Also, by assumption $\sigma$ and $\varepsilon$ are time independent. Hence denoting $a = \frac{\sigma}{\varepsilon}$ and $b = j \cdot \nabla \log \sigma$, Eq. 40 takes the form

$$\frac{\partial \rho}{\partial t} = -a \rho - b = 0. \quad (41)$$

Consequently, the induced charge density (at steady-state) is given by

$$\rho = -\frac{b}{a}, \quad (42)$$

$$\rho = -\varepsilon E \cdot \nabla \log \sigma. \quad (43)$$

It shows that the net charge density is different from zero.

Electric field for spherical current source.

At the radius $r = R$, the electric field is given by the current

$$j|_{r=R} = \sigma(R) \ E|_{r=R}. \quad (44)$$
The total current passing through a sphere (surface $S$, radius $r$) is given by

$$I = \int_S dS \cdot j = S(r) \ j(r). \quad (45)$$

Thus the current density as function of radius $r$ behaves as

$$j(r) = j(r) \ e_r = \frac{I}{S(r)} \ e_r = \frac{I}{4\pi r^2} \ e_r. \quad (46)$$

Ohm’s law implies for the electric field

$$E(r) = \frac{1}{\sigma(r)} j(r) = \frac{I}{4\pi r^2 \sigma(r)} \ e_r. \quad (47)$$

Electric potential.

Because the electric field is radially symmetric, so is also the potential, which obeys

$$E(r) = -\frac{\partial}{\partial r} V(r). \quad (48)$$

Its solution is obtained from Eq. 47

$$V(r) = -\int_r^\infty dr' \ E(r') = \int_r^\infty dr' \frac{I}{4\pi r'^2 \sigma(r')} . \quad (49)$$

An independent check of this solution can be obtained by considering the law of charge conservation.

$$\nabla \cdot (\sigma E) = -\frac{\partial \rho}{\partial t}. \quad (50)$$

Because of the time-independent charge density, this becomes

$$\nabla \cdot (\sigma \nabla V) = (\nabla \sigma) \cdot \nabla V + \sigma \Delta V = 0. \quad (51)$$

Radial symmetry implies the following differential equation in the variable $r$,

$$(\partial_r \sigma(r)) (\partial_r V(r)) + \sigma(r) \left[ \frac{2}{r} \partial_r V + \partial_r^2 V \right] = 0. \quad (52)$$

A straightforward calculation shows that the potential, given by Eq. 49 is the solution of this differential equation for $V \to 0$ when $r \to \infty$. 
Appendix 2: Fourier component of the extracellular field potential

This Appendix refers to Section *Time-varying currents in non-homogeneous medium*:

Starting from Gauss’ law

\[ \nabla \cdot (\varepsilon \mathbf{E}) = \rho, \quad (53) \]

the inhomogeneity of \( \varepsilon \) implies

\[ \mathbf{E} \cdot (\nabla \varepsilon) + \varepsilon \nabla \cdot \mathbf{E} = \rho. \quad (54) \]

Then the electric potential obeys

\[ -(\nabla V) \cdot (\nabla \varepsilon) - \varepsilon \Delta V = \rho. \quad (55) \]

We recall that the potential \( V \) and the charge density \( \rho \) are time-dependent, while the permittivity \( \varepsilon \) is not. We define the Fourier transform of time-dependent function \( f(t) \) via

\[ f_\omega = \int_{-\infty}^{\infty} dt \ e^{i\omega t} f(t). \quad (56) \]

Now we perform a Fourier transform with respect to time of the potential \( V \) and the charge density \( \rho \) to obtain an equation for the Fourier components at frequency \( \omega \),

\[ (\nabla V_\omega) \cdot (\nabla \varepsilon) + \varepsilon \Delta V_\omega = -\rho_\omega. \quad (57) \]

Similarly, starting from the differential form of the law of charge conservation,

\[ \nabla \cdot (\sigma \mathbf{E}) = -\frac{\partial \rho}{\partial t}, \quad (58) \]

the inhomogeneity of \( \sigma \) implies

\[ \mathbf{E} \cdot (\nabla \sigma) + \sigma \nabla \cdot \mathbf{E} = -\frac{\partial \rho}{\partial t}. \quad (59) \]

Then the potential obeys

\[ (\nabla V) \cdot (\nabla \sigma) + \sigma \Delta V = \frac{\partial \rho}{\partial t}. \quad (60) \]

From the Fourier transform of \( \rho \) follows that a component at frequency \( \omega \) satisfies

\[ \frac{\partial}{\partial t} \rho_\omega = i\omega \rho_\omega. \quad (61) \]
The last two equations imply that the Fourier component at frequency $\omega$ of the potential obeys

$$(\nabla V_\omega) \cdot (\nabla \sigma) + \sigma \Delta V_\omega = -i \omega \rho_\omega. \quad (62)$$

Combining Eqs. 57 and 62 yields

$$(\nabla V_\omega) \cdot (\nabla (\sigma + i \omega \epsilon)) + (\sigma + i \omega \epsilon) \Delta V_\omega = 0. \quad (63)$$

**Appendix 3: Method to calculate the extracellular field potential from point current sources**

1. Compute the Fourier component $\omega$ of the impedance

$$Z_\omega(r) = \frac{1}{4\pi \sigma(R)} \int_r^\infty d'r' \frac{1}{r'^2} \left[ \frac{\sigma(R) + i \omega \epsilon(R)}{\sigma(r') + i \omega \epsilon(r')} \right], \quad (64)$$

where $\omega = 2\pi f$. This expression incorporates the values of the conductivity $\sigma(r)$ and permittivity $\epsilon(r)$ as a function of the distance $r$. It is also assumed that $V(\infty) = 0$.

This quantity is computed for each frequency component $\omega$ of the spectrum, and for each extracellular distance $r$ considered. It can be precalculated and stored in a matrix ($Z[f][r]$).

2. For each current source, compute the (complex) Fourier transform of the total membrane current, which we call here $I_\omega$.

3. For each current source, compute the Fourier component $\omega$ of the extracellular potential:

$$V_\omega(r) = Z_\omega(r) I_\omega. \quad (65)$$

4. For each current source, compute the extracellular potential by applying the (complex) inverse Fourier transform to Eq. 65.

5. Finally, combine the contributions from all current sources to yield the extracellular potential at a given position $x$ in the extracellular space.
FIGURES

Figure 1: Radial variations of conductivity and permittivity can induce frequency-filtering properties. A. Scheme of the current source in radial symmetry. The current source is assumed to be spherical (continuous line; radius $R$). The conductivity and permittivity vary in radial symmetry according to the distance $r$ from the center of the source. B. Conductivity $\sigma$ vs. radial distance $r$. Two cases are shown: (1) $\sigma(r)/\sigma(R) = 1 + \sqrt{r_0/r}$ and (2) $\sigma(r)/\sigma(R) = 1 - \sqrt{r_0/r}$, where $r_0 = 0.2025R$ ($R=1$ here). C. Permittivity $\varepsilon$ vs. radial distance $r$. The two curves shown are: (3) $\varepsilon(r)/\sigma(R) = 0.01$ and (4) $\varepsilon(r)/\sigma(R) = 0.01[1 - \sqrt{r_0/r}]$. D-F. Real part (D), imaginary part (E) and norm (F) of the impedance $Z_\omega(r=5R)$ vs. frequency $f$. Combining the profiles (1) and (3) in B-C leads to a high-pass filter (dashed line), whereas (2+3) gives low-pass characteristics (solid line). The combination (2+4) is such that $\sigma(r)/\varepsilon(r) = \text{const.}$, in which case there is no frequency dependence (dotted line).

Figure 2: Frequency-filtering properties obtained by a localized drop in conductivity. A. Profile of conductivity vs. distance. The conductivity was described by $\sigma(r)/\sigma(R) = 1 - 0.2\ (r - 6R)/R$ for $6R < r < 11R$, $\sigma(r)/\sigma(R) = -1 + 0.2\ (r - 6R)/R$ for $11R < r < 16R$, and $\sigma(r)/\sigma(R) = 1$ otherwise. B. Profile of permittivity. $\varepsilon(r)/\sigma(R)$ was constant and equal to 0.01. C-E. Real part (C), imaginary part (D) and norm (E) of the impedance as a function of frequency $f$. $Z_\omega(r)$ is shown for different distances $r$ away from the source. F. Attenuation of the impedance norm $|Z_\omega(r)|$ with distance. The different curves correspond to three different frequencies.
Figure 3: Frequency-filtering properties obtained from a periodically varying conductivity.
A. Oscillatory profile of conductivity vs. distance \( \sigma(r)/\sigma(R) = 0.501 + 0.5 \times \cos(2\pi(r-R)/2R) \). B. Profile of permittivity \( \varepsilon(r)/\sigma(R) = 0.01 \). C-E. Real part (C), imaginary part (D) and norm (E) of the impedance \( Z_\omega(r) \) vs. frequency \( f \). The different curves are taken at different distances \( r \) outside of the current source. F. Attenuation of the impedance norm \(|Z_\omega(r)|\) with distance. The different curves indicate the attenuation obtained at different frequencies.

Figure 4: Frequency-filtering properties obtained with exponential decrease of conductivity.
A. Profile of conductivity. \( \sigma(r)/\sigma(R) \) decays exponentially according to \( \sigma(r)/\sigma(R) = \sigma_0 + (1-\sigma_0) \exp[-(r-R)/\lambda] \), with a space constant \( \lambda = 500 \mu m \). B. Profile of permittivity. \( \varepsilon(r)/\sigma(R) \) was constant (0.01). C-E. Real part (C), imaginary part (D) and norm (E) of the impedance \( Z_\omega(r) \) vs. frequency \( f \). The different curves show the impedance calculated at different distances \( r \). F. Attenuation of the impedance norm \(|Z_\omega(r)|\) with distance. The different curves indicate the attenuation obtained at different frequencies.

Figure 5: Distance dependence of frequency-filtering properties
A. Ratio of impedance at fast and slow frequencies \( (Q_{100}) \) represented as a function of distance \( r \) (units of \( R \)). The \( Q_{100} \) ratios are represented for different profiles of conductivity. \textit{Drop}: localized drop of conductivity (short dash; same parameters as in Fig.3). \textit{Osc}: oscillatory profile of conductivity (solid line; same parameters as in Fig.3 the dotted line indicates a damped cosine oscillation). \textit{Exp}: exponential decrease of conductivity (long dash; same parameters as in Fig.4 except \( R = 1, \lambda=10R \)). B. Profiles of conductivity with exponential decay (same parameters as in Fig.4 space constants \( \lambda \) indicated in \( \mu m \)). C. \( Q_{100} \) ratios obtained for the conductivity profiles shown in B.
Figure 6: Frequency-filtered extracellular field potentials in a conductance-based model.
A. Membrane potential of a single-compartment model containing voltage-dependent Na$^+$ and K$^+$ conductances and a glutamatergic synaptic conductance. The glutamatergic synapse was stimulated at $t = 5 \text{ ms}$ (arrow) and evoked an action potential. B. Total membrane current generated by this model. Negative currents correspond to Na$^+$ and glutamatergic conductances (inward currents), while positive currents correspond to K$^+$ conductances (outward currents). C. Power spectrum of the total current shown in B. D. Impedance at 500 $\mu$m from the current source assuming a radial profile of conductivity and permittivity (as in Fig. 4). E. Extracellular potential calculated at various distances from the source (5, 100, 500 and 1000 $\mu$m). The frequency filtering properties can be seen by comparing the negative and positive deflections of the extracellular potential. The fast negative deflection almost disappeared at 1000 $\mu$m whereas the slow positive deflection was still present.
Figure 1
Figure 2
Figure 3
Figure 4
Figure 5
A
Membrane potential

B
Membrane current

C
Power spectrum

D
Impedance

E
Extracellular potential

Figure 6