Electrophysiology of living organs from first principles

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Abstract

Based on the derivation of the macroscopic Maxwell’s equations by spatial averaging of the microscopic equations, we discuss the electrophysiology of living organs. Other methods of averaging (or homogenization) like the bidomain model are not compatible with Maxwell’s theory. We also point out that modelling the active cells by source currents is not a suitable description of the situation from first principles. Instead, it turns out that the main source of the measured electrical potentials is the polarization charge density which exists at the membranes of active cells and adds up to a macroscopic polarization. The latter is the source term in the Laplace equation, the solution of which gives the measured far-field potential. As a consequence it is the polarization or dipole density which is best suited for localization of cardiac arrhythmia.

keywords: bioelectric sources, electrocardiography, cardiac action potential

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1 Introduction

Macroscopic measurements of the electrical activity of living organs are frequently employed to diagnose diseases. The main examples of bioelectric recordings are electrocardiography of the heart (ECG), electroencephalography of the brain (EEG) and electromyography of the muscles (EMG). The purpose of the present article is to describe the origin of the measured electrical potentials in these techniques. The basis of this description are the macroscopic Maxwell’s equations. Consequently, the physically well defined quantities appearing in these equations are the primary quantities to be used, and it is highly desirable to relate the measured potentials to them. Such a model-independent description of the electrical activity of the organ without ad hoc model assumptions (see below) has great clinical value, for example for the localization of cardiac arrhythmia as discussed at the end of sect.3.

In electrodynamics one has to make a clear distinction between Maxwell’s equation in the vacuum

\[
\begin{align*}
\frac{\partial \vec{B}}{\partial t} &= -\nabla \times \vec{E} \quad (1.1) \\
\nabla \cdot \vec{B} &= 0 \quad (1.2)
\end{align*}
\]

\[
\begin{align*}
\varepsilon_0 \frac{\partial \vec{E}}{\partial t} &= \frac{1}{\mu_0} \nabla \times \vec{B} - \vec{j} \quad (1.3) \\
\varepsilon_0 \nabla \cdot \vec{E} &= \rho \quad (1.4)
\end{align*}
\]

and the equations in matter (1.1) and (1.2) plus

\[
\begin{align*}
\frac{\partial \vec{D}}{\partial t} &= \nabla \times \vec{H} - \vec{j}_c \quad (1.5) \\
\nabla \cdot \vec{D} &= \rho_c. \quad (1.6)
\end{align*}
\]

Here we have used the standard notation with \(\vec{E}\) and \(\vec{H}\) being the electric and magnetic fields, \(\vec{B}\) and \(\vec{D}\) the magnetic induction and electrical displacement and \(\rho, \vec{j}\) the charge and current densities, respectively. \(\varepsilon_0\) is the dielectric constant of the vacuum and \(\mu_0 = 1/(\varepsilon_0 c^2)\) where \(c\) is the velocity of light. Two new fields \(\vec{D}\) and \(\vec{H}\) appear in (1.5) and (1.6) and \(\rho_c\) and \(\vec{j}_c\) are the charge and current densities, respectively, in contrast to the microscopic charge and current densities in (1.3) and (1.4). To have a closed system of equations for dead or living matter additional so-called constitutive relations are needed which take the structure of the matter into account. The simplest such relations are

\[
\begin{align*}
\vec{B} &= \mu \vec{H}, \quad \vec{D} = \varepsilon_0 \vec{E} + \vec{P} \quad (1.7)
\end{align*}
\]
where $\vec{P}$ is the electric polarization (see next section), and Ohm’s law

$$\vec{j}_c = \sigma \vec{E}. \quad (1.8)$$

However, on the atomic scale matter is vacuum with charged nuclei and electrons moving around. Consequently equations (1.1-4) are still true in dead and living matter, but $\varrho(t, \vec{x})$, $\vec{j}(t, \vec{x})$ vary rapidly in space and time. These rapid variations of the microscopic quantities are not observed in general. Instead a spatial average over many atoms or even many cells in the heart or brain, for example, is measured. That means the macroscopic Maxwell’s equations must be derived from the microscopic equations (1.1-4) by spatial averaging. In this derivation the meaning of the conduction charge and current densities $\varrho_c$, $\vec{j}_c$ and their properties are found.

This point of view is shared by all modern authors of textbooks, although it is sometimes a little hidden. For example Jackson in his most-cited book [1] treats the macroscopic averaging in Sect.6.7. But he considers the averaging of the charge density $\varrho$ only, leaving the more complicated current density $\vec{j}$ for “those readers who enjoy such challenges”. We are such readers, so we give the full derivation in the next section. This is also necessary in order to understand the properties of the different macroscopic currents. We here consider a living organ where the averaging must be performed over many cells. In this way we get a description of the electrical activity of the organ from first principles, i.e. from Maxwell’s theory.

On the other hand in physiology one often constructs models with quantities which have no direct relation to Maxwell’s theory. For example, in the bidomain model [2] one introduces at each point in space two electrical potentials $V_i$ and $V_e$ which refer to intra- and extracellular space. This does not follow from Maxwell’s theory: As we will see in the next section the averaging of the microscopic Maxwell’s equations gives one averaged electric field $\langle \vec{E} \rangle$ plus corrections which are represented by polarization $\vec{P}$ (see eq. (2.18) below). $\vec{P}$ has different properties than the gradient of the membrane potential $V_i - V_e$ in the bidomain model (see after eq. (3.6)). The intra- and extracellular currents that are introduced in the bidomain model are meaningful on the microscopic scale if one considers processes in single cells. As a consequence the model leads to some “mesoscopic” description of living tissue. Since we are interested in the measured far-field potential we need a true macroscopic description. The form of the macroscopic current and charge densities follows rigorously from the spatial averaging of the microscopic quantities (eqs. (2.16), (2.36) below) and so cannot be freely assumed. The macroscopic description of living tissue is given by the macroscopic Maxwell’s equations, and this is what is required for
ECG etc. The bidomain model on the other hand may be useful on some intermediate scale between single cell and macroscopic.

Another basic model in electrophysiology is the so-called volume conductor which goes back at least to R. Plonsey [3] (see also [4] [5]). The argument is the following: The total current density \( \vec{j} \) is written as the sum of the conduction current \( \vec{j}_c \) plus a so-called source current \( \vec{j}_s \)

\[
\vec{j} = \vec{j}_c + \vec{j}_s. \tag{1.9}
\]

This starting point makes sense if \( \vec{j} \) is the spatially averaged microscopic current \( \langle \vec{j} \rangle \) and \( \vec{j}_s \) is the polarization current plus further corrections found in the next section. Note that one is not free to add some “source current” to Maxwell’s equations because the equations govern the whole phenomenon, including the active cells (see next section). Then it is said that the displacement current \( \partial \vec{D}/\partial t \) can be neglected so that \( \vec{j} \) in (1.9) is equal to \( \text{curl}\vec{H} \) due to (1.5). But in equation (1.5) only the conduction current \( j_c \) appears, not \( \langle \vec{j} \rangle \). This misunderstanding has bad consequences: If the current is a curl, its divergence vanishes

\[
\nabla \cdot \vec{j} = 0 = \nabla \cdot (\sigma \vec{E}) + \nabla \cdot \vec{j}_s \tag{1.10}
\]

where Ohm’s law (1.8) has been used. Assuming a quasi-static situation where

\[
\vec{E} = -\nabla V \tag{1.11}
\]

one obtains the electric potential \( V \). For constant conductivity \( \sigma \) one arrives at the Laplace equation

\[
\nabla^2 V = \sigma \triangle V = -\nabla \cdot \vec{j}_s. \tag{1.12}
\]

Here a physicist protests: a current density cannot be the source of the electric potential. A static electric field must come from a charge density, a current density generates a magnetic field. The solution of (1.12) would be

\[
V(\vec{x}) = \frac{1}{4\pi\sigma} \int \frac{(\nabla \cdot \vec{j}_s(\vec{y}))}{|\vec{x} - \vec{y}|} d^3y. \tag{1.13}
\]

Now one sees that it is misleading to use Ohm’s law (1.8) to calculate the potential: for conductivity \( \sigma = 0 \) the potential would be infinite. But the whole argument would also apply to a completely isolating dielectrics in a condenser where \( V \) is always finite. Nobody knows which conductivity \( \sigma \) must be used in (1.13). If one says that \( \nabla \cdot \vec{j}_s/\sigma \) “models” the source of
the signals, then one makes fictitious physics and abandons Maxwell’s electrodynamics as first principle.

The correct treatment is given in Sect.3. We must use Gauss’ law (1.6) instead of Ohm’s law. The result is what everybody intuitively knows: the source of the electric field in electrophysiology is the polarization charge density at the membranes of the active cells. The conductivity plays no role here; if Ohmic currents are present they would weaken the measured potentials. We also discuss the consequences of our findings for the problem of analyzing cardiac activity.

2 Derivation of the macroscopic Maxwell’s equations

This derivation is of very general character. It is true for dead or living matter and does not depend on the structural details of the matter. To have a concrete picture we consider an organ (heart or brain for example) consisting of cells and extracellular space. We divide the extracellular space into “virtual cells” of approximately the same volume as the real cells, so that if we say “cells” we mean both types. The cells can move as for example in blood or ions in extracellular space.

Macroscopic measurements in electrophysiology give mean values over a length scale of, say $L \approx 10^{-3}$ m. Therefore, we average all microscopic quantities over a volume $L^3$. This averaging will be carried out by convolution with a positive function $a(\vec{x})$; we denote it by angular brackets

$$\langle \vec{E}(t, \vec{x}) \rangle \stackrel{\text{def}}{=} \int a(\vec{x} - \vec{x}') \vec{E}(t, \vec{x}') d^3x'. \tag{2.1}$$

The integral over $a(\vec{x})$ must be equal to

$$\int a(\vec{x}) d^3x = 1 \tag{2.2}$$

and otherwise we assume $a(\vec{x})$ to be smooth with a compact support of an extension of $L$, large compared with the dimension of the cells. Such spatial averaging is the only way to derive true macroscopic equations from microscopic ones.

Differentiating (2.1), we find

$$\frac{\partial}{\partial x_i} \langle \vec{E}(t, \vec{x}) \rangle = \int \frac{\partial}{\partial x_i} a(\vec{x} - \vec{x}') \vec{E}(t, \vec{x}') d^3x'$$

$$= \int a(\vec{x} - \vec{x}') \frac{\partial}{\partial x_i} \vec{E}(t, \vec{x}') d^3x' = \left\langle \frac{\partial \vec{E}(t, \vec{x})}{\partial x_i} \right\rangle, \tag{2.3}$$
where we have shifted the derivative from $\bar{x}$ to $\bar{x}'$ and performed an integration by parts. This means that averaging and spatial derivatives can be interchanged. The same is trivially true for partial derivatives with respect to $t$. Consequently, the homogeneous Maxwell’s equations (1.1) (1.2) are valid for the averaged fields, too,

$$\frac{\partial}{\partial t} \langle \vec{B}(t, \bar{x}) \rangle = -\nabla \times \langle \vec{E}(t, \bar{x}) \rangle \quad \text{(2.4)}$$

$$\nabla \cdot \langle \vec{B} \rangle = 0. \quad \text{(2.5)}$$

This was very cheap, but the inhomogeneous equations require much more work. The reason is that the averaged densities $\langle \rho(t, \bar{x}) \rangle$ and $\langle \vec{j}(t, \bar{x}) \rangle$ can no longer be assumed as given quantities as in microscopic electrodynamics. They usually depend on the local fields and on electrochemical processes, therefore, they must be worked out in detail, taking the cellular structure of the matter into account.

We write the microscopic charge density as a sum

$$\rho(t, \bar{x}) = \sum_i q_i(t, \bar{x}), \quad \text{(2.6)}$$

of the charge densities $q_i$ of the individual cells. Charge and current densities $\rho_i, \vec{j}_i$ of individual cells can change with time, therefore, arbitrary physical and chemical processes in living cells are included in the following derivation. The charge density $\rho_i$ of cell $i$ is concentrated at its position $\bar{y}_i(t)$. In the average

$$\langle \rho(t, \bar{x}) \rangle = \sum_i \int d^3x'[a(\bar{x} - \bar{x}')q_i(t, \bar{x}') \ d^3x' \quad \text{(2.7)}$$

$a(\bar{x} - \bar{y}_i + \bar{y}_i - \bar{x}')$ is slowly varying over the microscopic support of $\rho_i$. We therefore use a Taylor expansion and neglect quadratic and higher contributions:

$$\langle \rho(t, \bar{x}) \rangle = \sum_i \int d^3x' \left[ a(\bar{x} - \bar{y}_i) + \sum_k \frac{\partial a(\bar{x} - \bar{y}_i)}{\partial x_k} (y_{ik} - x'_{ik}) \right] q_i(t, \bar{x}')$$

$$= \sum_i q_i a(\bar{x} - \bar{y}_i) - \sum_i \bar{p}_i : \frac{\partial a(\bar{x} - \bar{y}_i)}{\partial \bar{x}}. \quad \text{(2.8)}$$

Here

$$q_i(t) = \int d^3x' \rho_i(t, \bar{x}') \quad \text{(2.9)}$$

is the total charge of the cell $i$, and

$$\bar{p}_i(t) = \int d^3x' (\bar{x}' - \bar{y}_i(t)) q_i(t, \bar{x}') \quad \text{(2.10)}$$
is its dipole moment with respect to the center \( \vec{y}_i \). Writing the first term on the r.h.s. of (2.8) as follows

\[
q_i a(\vec{x} - \vec{y}_i) = \langle q_i \delta(\vec{x} - \vec{y}_i) \rangle,
\]

we see that it represents the cells by point charges (monopoles) at the positions \( \vec{y}_i \) of the cells. The sum

\[
\sum_i q_i a(\vec{x} - \vec{y}_i) \overset{\text{def}}{=} \varrho_c(t, \vec{x})
\]

(2.12)
is the conduction charge density. Here only charged cells \( (q_i \neq 0) \) contribute, which explains the name “conduction charge”. The individual charges (ions and proteins) of neutral cells are not resolved, they add up to zero in the integral (2.9).

The dipole term in (2.8) can be written as follows

\[
\vec{p}_i \cdot \frac{\partial a(\vec{x} - \vec{y}_i)}{\partial \vec{x}} = \nabla_x \cdot \vec{p}_i a(\vec{x} - \vec{y}_i) = \nabla_x \cdot \langle \vec{p}_i \delta(\vec{x} - \vec{y}_i) \rangle.
\]

(2.13)

This represents a dipole moment at the position of the cell. The cells are represented by their lowest multipole moments. Summing over all cells, we get the so-called polarization charge density

\[
\sum_i \vec{p}_i \cdot \frac{\partial a(\vec{x} - \vec{y}_i)}{\partial \vec{x}} \overset{\text{def}}{=} \nabla \cdot \vec{P}(t, \vec{x}),
\]

(2.14)

where

\[
\vec{P} = \sum_i \langle \vec{p}_i \delta(\vec{x} - \vec{y}_i) \rangle
\]

(2.15)
is the electric polarization. Omitting higher multipole contributions, we obtain for the averaged charge density

\[
\langle \varrho \rangle = \varrho_c - \nabla \cdot \vec{P}.
\]

(2.16)

Then averaging of Gauss’ law (1.4) leads to

\[
\varepsilon_0 \nabla \cdot \langle \vec{E} \rangle = \varrho_c - \nabla \cdot \vec{P}.
\]

(2.17)

Introducing the new phenomenological field

\[
\vec{D} = \varepsilon_0 \langle \vec{E} \rangle + \vec{P},
\]

(2.18)

the macroscopic Gauss’ law assumes the same form as the microscopic one

\[
\nabla \cdot \vec{D} = \varrho_c.
\]

(2.19)
The field $\vec{D}$ is usually called the electric displacement, because the macroscopic electric field $\langle \vec{E} \rangle$ is displaced by the polarization $\vec{P}$ in (2.18). The source of $\vec{D}$ is only the conduction charge density $\rho_c$, not the total charge density (2.16).

In a similar manner we consider the current density

$$j(t, \vec{x}) = \sum_i j_i(t, \vec{x}), \quad (2.20)$$

where $j_i$ is the current density produced by the cell $i$. Charge conservation for the cell $i$ implies

$$\int d^3 x' \partial_t \rho_i = - \int \nabla \cdot j_i d^3 x' = - \int \vec{j}_i \cdot d\vec{\sigma} = 0, \quad (2.21)$$

where we have used Gauss' theorem and the vanishing of $\vec{j}_i$ at infinity. Similarly we treat the next moments

$$\int d^3 x' \partial_t \rho_i x_k' = - \int d^3 x' x_k' \nabla \cdot j_i =$$

$$= - \int d^3 x' \partial'q(x_k' j_k) + \int d^3 x' j_k = \int d^3 x' j_k \quad (2.22)$$

Now we are ready to expand the averaged current density

$$\langle \vec{j}_i \rangle = \int d^3 x' \left[ a(\vec{x} - \vec{y}_i) + \frac{\partial a(\vec{x} - \vec{y}_i)}{\partial \vec{x}} \cdot (\vec{y}_i - \vec{x}) \right] j(t, \vec{x}') \quad (2.24)$$

$$\text{def} = \vec{A}_i + \vec{B}_i, \quad (2.25)$$

By means of (2.22, 21), the first term $\vec{A}_i$ in (2.24) can be expressed by the dipole moment (2.10)

$$\vec{A}_i = a(\vec{x} - \vec{y}_i) \int d^3 x' \partial_t \rho_i(t, \vec{x}')(\vec{x}' - \vec{y}_i(t))$$

$$= a(\vec{x} - \vec{y}_i) \partial_t \vec{p}_i + a(\vec{x} - \vec{y}_i) q_i \partial_t \vec{y}_i$$

$$= \langle \partial_t \vec{p}_i \rangle \delta(\vec{x} - \vec{y}_i) \rangle + \langle q_i \partial_t \vec{y}_i \rangle \delta(\vec{x} - \vec{y}_i). \quad (2.25)$$

On the other hand, the time derivative of (2.15) yields

$$\partial_t \vec{P} = \sum_i \langle \partial_t \vec{p}_i \rangle \delta(\vec{x} - \vec{y}_i) \rangle + \sum_i \langle \vec{p}_i \partial_t \delta(\vec{x} - \vec{y}_i(t)) \rangle$$

$$= \sum_i \langle \partial_t \vec{p}_i \rangle \delta(\vec{x} - \vec{y}_i) \rangle - \frac{\partial}{\partial x_k} \sum_i \langle \vec{p}_i \partial_t \delta(\vec{x} - \vec{y}_i) \rangle \partial_t y_{ik}. \quad (2.26)$$
For the last term in (2.25) we introduce the conduction current density

\[ \vec{j}_c(t, \vec{x}) \overset{\text{def}}{=} \sum_i (q_i (\partial_t \vec{y}_i) \delta(\vec{x} - \vec{y}_i)). \]  

(2.27)

Then the sum of (2.25) over all cells yields

\[ \sum_i \vec{A}_i = \partial_t \vec{P} + \frac{1}{\partial x_k} \sum_i \langle \vec{y}_i \delta(\vec{x} - \vec{y}_i) \partial_t y_{ik} \rangle + \vec{j}_c. \]  

(2.28)

To compute the second term \( \vec{B}_i \) in (2.24), we decompose

\[ \int d^3x' (y_{ik} - x'_k) j_{il}(t, \vec{x}') = \]

\[ = \frac{1}{2} \left[ \int d^3x' (y_{ik} - x'_k) j_{il} - (y_{il} - x'_l) j_{ik} \right] \]

\[ + \frac{1}{2} \left[ \int d^3x' (y_{ik} - x'_k) j_{il} + (y_{il} - x'_l) j_{ik} \right] \]

(2.29)

into an antisymmetric and symmetric part. Using (2.22, 23) we get

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m + \frac{1}{2} \left[ y_{ik} \int d^3x' \partial_t q_i(x'_k - y_{ik})(x'_l - y_{il}) \right. \]

\[ \left. - \int d^3x' x'_lj_{il} + y_{il} \int d^3x' \partial_t q_i x'_k - \int d^3x' x'_lj_{ik} \right] = \]

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m + \frac{1}{2} \left[ y_{ik} \int d^3x' \partial_t q_i(x'_k - y_{ik})(x'_l - y_{il}) \right. \]

\[ \left. + \int d^3x' \partial_t q_i(x'_k - y_{ik}) \partial_t y_{il} \right] = \]

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m - \frac{1}{2} \partial_t q_{kl}^{(i)} - \frac{1}{2} [p_{il} \partial_t y_{ik} + p_{ik} \partial_t y_{il}], \]  

(2.30)

Here \( \vec{m}_i \) is the magnetic moment of cell \( i \) with respect to its center \( \vec{y}_i \), and the index \( m \) is such that \( k, l, m \) is a cyclic permutation of 1,2,3. The last term in (2.30) leads to the quadrupole moment

\[ q_{kl}^{(i)} = \int d^3x' q_i(x'_k - y_{ik})(x'_l - y_{il}). \]  

(2.31)

Then (2.30) yields

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m - \frac{1}{2} \int d^3x' (\partial_t \vec{q}_i)(x'_k - y_{ik})(x'_l - y_{il}) \]

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m - \frac{1}{2} \left[ \partial_t q_{kl}^{(i)} + \int d^3x' \vec{q}_i(\partial_t y_{ik})(x'_l - y_{il}) \right. \]

\[ + \int d^3x' \vec{q}_i(x'_k - y_{ik}) \partial_t y_{il} \right] = \]

\[ = -\frac{1}{\mu_0} (\vec{m}_i)_m - \frac{1}{2} \partial_t q_{kl}^{(i)} - \frac{1}{2} [p_{il} \partial_t y_{ik} + p_{ik} \partial_t y_{il}], \]  

(2.32)

where again the dipole moment (2.10) appears. According to (2.24), this result must be multiplied by the gradient of \( a(\vec{x} - \vec{y}_i) \)

\[ (\vec{B}_i)_I = -\frac{1}{\mu_0} \frac{\partial a}{\partial x_k} (\vec{m}_i)_m - \frac{1}{2} \frac{\partial a}{\partial x_k} (p_{ik} \partial_t y_{il} + p_{il} \partial_t y_{ik}) \]
\[
\frac{1}{\mu_0} \left( \nabla_x a(x - \bar{y}_i) \wedge \vec{m}_i \right)_l - \frac{1}{2} \frac{\partial a}{\partial x_k} (p_{ik} \partial_t y_{il} + p_{il} \partial_t y_{ik}).
\]

(2.33)

This gives the following result for the vector \( \vec{B}_i \):

\[
\vec{B}_i = \frac{1}{\mu_0} \nabla_x \times a(x - \bar{y}_i) \vec{m}_i - \frac{1}{2} \frac{\partial a}{\partial x_k} (p_{ik} \partial_t \bar{y}_i + \bar{p}_i \partial_t y_{ik}).
\]

(2.34)

Here we introduce the macroscopic magnetic moment density, or magnetization

\[
\vec{M} \defeq \sum_i a(x - \bar{y}_i) \vec{m}_i = \sum_i \langle \vec{m}_i \delta(\vec{x} - \bar{y}_i) \rangle.
\]

(2.35)

Then the total contribution of \( \vec{B}_i \) is equal to

\[
\sum_i \vec{B}_i = \frac{1}{\mu_0} \nabla \times \vec{M} - \frac{1}{2} \frac{\partial}{\partial x_k} \sum_i \left( \langle p_{ik} \delta(\vec{x} - \bar{y}_i) \partial_t \bar{y}_i \rangle + \langle \vec{p}_i \delta(\vec{x} - \bar{y}_i) \partial_t y_{ik} \rangle \right).
\]

The last term herein can be combined with the middle term in (2.28). We then obtain the following final result

\[
\langle \vec{j} \rangle = \vec{j}_c + \frac{\partial \vec{P}}{\partial t} + \frac{1}{\mu_0} \nabla \times \vec{M} + \vec{V},
\]

(2.36)

with

\[
V_l = \frac{1}{2} \frac{\partial}{\partial x_k} \left( \sum_i (p_{il} \partial_t y_{ik} - p_{ik} \partial_t y_{il}) \delta(\vec{x} - \bar{y}_i) \right).
\]

(2.37)

We notice that the divergence vanishes

\[
\nabla \cdot \vec{V} = \frac{\partial V_l}{\partial x_l} = \frac{1}{2} \frac{\partial^2}{\partial x_l \partial x_k} \langle \ldots \rangle = 0,
\]

because the sum in (2.37) is antisymmetric in \( k, l \), whereas the second derivative is symmetric.

Then the microscopic current conservation

\[
\partial_t \langle \rho \rangle + \nabla \cdot \langle \vec{j} \rangle = 0
\]

implies

\[
\partial_t \rho_c + \nabla \cdot \vec{j}_c = 0
\]

(2.38)

by means of (2.16) and (2.36). Hence, the conduction current alone is also conserved. For small velocities or small dipole moments, \( \vec{V} \) (2.37) can be neglected, as well as the higher order multipole contributions. Then the last macroscopic Maxwell’s equation, the macroscopic Ampère’s law assumes the following form

\[
\varepsilon_0 \frac{\partial \langle \vec{E} \rangle}{\partial t} = \frac{1}{\mu_0} \nabla \times \langle \vec{B} \rangle - \vec{j}_c - \frac{\partial \vec{P}}{\partial t} - \frac{1}{\mu_0} \nabla \times \vec{M}.
\]

(2.39)
Introducing the new field
\[ \vec{H} = \frac{1}{\mu_0} (\langle \vec{B} \rangle - \vec{M}) \] (2.40)
and using the electric displacement (2.18), we finally get
\[ \frac{\partial \vec{D}}{\partial t} = \nabla \times \vec{H} - \vec{j}_c. \] (2.41)

Unfortunately, the field \( \vec{H} \) is usually called “magnetic field” and \( \vec{B} \) magnetic induction, because it appears in the induction law (2.4). Of course, \( \vec{B} \) is the fundamental (microscopic) magnetic field and \( \vec{H} \) is derived from it (2.40). To avoid notational confusion, we will simply say \( \vec{B} \)-field and \( \vec{H} \)-field in the following.

As mentioned above (see (2.16)) this derivation of the macroscopic Maxwell’s equations is so general that it includes arbitrarily complicated electrochemical processes in living cells. Consequently, it is not possible to introduce additional terms by hand for such processes. For example, a "source current" density (1.9) must be identified with some term in (2.36), and one is not free in postulating properties of this quantity.

### 3 Application to electrophysiology

From now on all quantities are averaged macroscopic ones, so we omit the averaging brackets. It follows from the homogeneous Maxwell’s equations (2.4) and (2.5) that the \( \vec{E} \) and \( \vec{B} \) - fields can be expressed by the scalar and vector potentials
\[ \vec{B} = \nabla \times \vec{A}, \quad \vec{E} = -\nabla V - \frac{\partial \vec{A}}{\partial t}. \] (3.1)

In the applications to electrophysiology we are concerned with time-dependent electromagnetic fields in the frequency range 1-1000 Hz. The corresponding wavelengths \( \lambda \) are many kilometers. That means the distance of measurement \( r \) is always in the near zone \( r \ll \lambda \). Then the magnetic field \( \vec{B} \) can be neglected compared with the electric field \( \vec{E} \), so we set \( \vec{A} = 0 \) and we have the quasistatic approximation. Now using \( \vec{E} = -\nabla V \) in (2.19) we have
\[ -\varepsilon_0 \nabla^2 V + \nabla \cdot \vec{P} = \varrho_c \] (3.2)
or
\[ \Delta V = -\frac{1}{\varepsilon_0} (\varrho_{\text{pol}} + \varrho_c) \] (3.3)
where

\[ \varrho_{\text{pol}} = -\nabla \cdot \vec{P} \quad (3.4) \]

is the polarization charge density.

It is no surprise that we have again obtained Laplace’s equation for the electric potential. However, the source of the potential on the right-hand side of (3.3) is completely different from \( -\nabla \cdot \vec{j}/\sigma \) in (1.12). As already said the appearance of the conductivity \( \sigma \) in the denominator is misleading. Conduction current cannot be at the origin of the electrical potential in a living organ. On the contrary, Ohm’s current is a dissipative process, it would diminish the potential.

The main source of the potential is the polarization-charge density \( \varrho_{\text{pol}} \). As we have seen in the last section it is different from zero if a cell \( i \) has an electric dipole moment \( \vec{p}_i \) (2.10). Here is the point where living matter differs from dead matter: In dead matter the polarization is generated by passive response to an applied external electric field; in living matter an electric dipole moment can be produced actively by chemical processes. For example, a dipole moment is generated, if \( K^+ \) ions move through the membrane out of a cell, while the negatively charged proteins remain inside [5], the exact details are here not essential. The motion of the ions gives a conduction current which is not important for the electrical potential because it does not enter on the right-hand side of (3.3). What is important is the separation of positive and negative charges which generates a dipole moment and, hence, a polarization. If there remains a net charge in a cell, then it contributes to the charge density \( \varrho_c \). The total charge density \( \varrho_{\text{pol}} + \varrho_c \) is the source of the measured potential \( V \).

In infinite space the solution of Laplace’s equation (3.3) for a fixed time is given by

\[
V(\vec{x}) = \frac{1}{4\pi \varepsilon_0} \int d^3y \frac{(\varrho_{\text{pol}} + \varrho_c)(\vec{y})}{|\vec{x} - \vec{y}|}
\]

\[
= -\frac{1}{4\pi \varepsilon_0} \int d^3y \frac{(\nabla \cdot \vec{P})(\vec{y})}{|\vec{x} - \vec{y}|} + \frac{1}{4\pi \varepsilon_0} \int d^3y \frac{\varrho_c(\vec{y})}{|\vec{x} - \vec{y}|}. \quad (3.5)
\]

This solution can also be used in a nearly homogeneous situation as in the heart chamber, then \( \varepsilon_0 \) is the dielectric constant of the blood. The first term in (3.5) is the polarization potential \( V_{\text{pol}}(\vec{x}) \) which can be identified with the total transmembrane activation potential of the organ. This is the quantity of main clinical interest, so we concentrate on it in the following.

After partial integration we get

\[
V_{\text{pol}}(\vec{x}) = \frac{1}{4\pi \varepsilon_0} \int d^3y \vec{P}(\vec{y}) \cdot \frac{\partial}{\partial y} \frac{1}{|\vec{x} - \vec{y}|}. \quad (3.6)
\]
Following Frank (1954) [7] and Dotti (1974) [8] we assume that the polarization \( \vec{P} \neq 0 \) is located on a 2-dimensional surface \( S \) at a certain time and that the direction of \( \vec{P} \) is normal to \( S \); that means mathematically
\[
\vec{P}(\vec{x}) = \vec{n} d(\vec{x}) \delta_{S}(\vec{x}),
\] (3.7)
where \( \delta_{S}(\vec{x}) \) is the delta-function on \( S \). Such a surface of active cell membranes is also called a dipolar wavefront; \( d(\vec{x}) \) is the dipole density. Then the corresponding polarization potential is equal to the following surface integral over \( S \)
\[
V_{\text{pol}}(\vec{x}) = \frac{1}{4 \pi \varepsilon_0} \int_{S} d(\vec{y}) \frac{\partial}{\partial n} \frac{1}{|\vec{x} - \vec{y}|} d\sigma_y,
\] (3.8)
where \( \partial/\partial n \) is the derivative in the (outer) normal direction. The determination of the dipole density \( d(\vec{x}) \) from measured potential values \( V_i = V_{\text{pol}}(\vec{x}_i) \) is the so-called inverse problem.

In cardiology \( S \) is taken to be the endocardium. The potential measurements are performed either with a multielectrode balloon in the heart chamber or non-invasively by body surface measurements. In the first case the best localization of arrhythmia sources is achieved by contact mapping with a single electrode in contact with the endocardium. To understand this let the point \( \vec{x} \) of measurement in (3.8) move towards a point \( \vec{x}_S \) on the surface \( S \). Then the limiting potential value is given by [9]
\[
V(\vec{x}_S) = -2\pi d(\vec{x}_S) + \int_{S} d(\vec{y}) \frac{\cos \varphi_{xy}}{|\vec{x} - \vec{y}|^2} d\sigma_y,
\] (3.9)
where \( \varphi_{xy} \) is the angle between the vector \( \vec{x} - \vec{y} \) and the normal \( \vec{n} \). That means the measured potential \( V(\vec{x}_S) \) directly gives the desired dipole density \( d(\vec{x}_S) \) at the endocardium, apart from the second term which may be considered as a background.

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