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Equivalent dipole sources to estimate the influence of extracellular myocardial anisotropy in thin-walled cardiac forward models

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ABSTRACT

The extracellular domain of the heart is anisotropic, which affects volume conduction and therefore body surface potentials. This paper tests the hypothesis that when wall thickness is sufficiently small (such as in the atria), the effect of extracellular anisotropy can be estimated by modifying local dipole current sources. A formula based on the Gabor–Nelson equivalent dipole and on the reciprocity theorem is derived to compute a linear transformation of the dipole sources that approximates in an isotropic volume conductor the far-field of the actual sources in an anisotropic volume conductor. It involves solving three Poisson equation (once for all). The results obtained in an atrial model embedded in a boundary-element torso model suggest that when wall thickness is < 3 mm, simulated P waves are weakly altered by extracellular anisotropy during sinus rhythm: an anisotropy ratio of 4:1 typically reduced the longitudinal component of the dipole sources by $< 3\%$, increased the transverse component by $< 5\%$, and increased the transmural component by $\approx 25\%$ (which may be relevant in case of epicardial-endocardial dissociation). Due to uncertainty on experimental conductivity values, it is proposed that atrial extracellular anisotropy may be neglected when computing P waves.

1. Introduction

The forward problem of electrocardiography consists in computing the electric potential on the torso from the bioelectric current sources located within the myocardium. These potentials are affected by the volume conduction properties of the torso. Computer models have been developed to estimate the effects of the conduction inhomogeneities created by the heart, the blood and organs such as the lungs [1–10]. Most of these studies focused on the ventricles or neglected extracellular anisotropy in the atria.

The boundary element method [11] has been proposed and validated for computing the atrial contribution to the ECG [7,12,13]. This method can incorporate intracellular anisotropy but is not well adapted for taking into account extracellular anisotropy, so its applicability to the cardiac forward problem relies on the hypothesis that extracellular atrial anisotropy has a limited effect. The same question arises when computing atrial electrograms generated by an anisotropic tissue [14].

Due to the thinness of the atria, the effect of extracellular atrial myocardial anisotropy is expected to be small. The rationale is that, in the Henriquez et al. [15] theoretical model of plane wave propagation in a uniform slab of tissue (see also the subsequent paper by Tranquillo et al. [16]), the influence of myocardial extracellular properties on the potential in the surrounding bath disappears when tissue thickness tends to zero. In a more recent and more realistic simulation study by Keller et al. [10], the influence of cardiac extracellular properties on P wave morphology was found to be less important than that of blood, lungs, and skeletal muscles.

In this paper, we propose an approach for assessing not only the global influence of atrial extracellular anisotropy on the P wave as in previous works, but also for determining the type and location of bioelectric sources that may lead to increased errors, and how the sources could be modified to improve accuracy. The approach is inspired from Potse et al. [9] who adjusted the local dipole current sources in the ventricles in an attempt to reproduce cardiac anisotropy in a boundary-element torso model. Here a theoretical formula is provided to perform the local dipole optimization. The technique is studied as a function of tissue thickness in simplified and more realistic volume conduction models.

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2. Methods

2.1. Problem statement

Consider a current-dipole source $\mathbf{d}_0$ located at $\mathbf{x}_0$ within a region Ω (the myocardium) with inhomogeneous and anisotropic conductivity tensor $\boldsymbol{\sigma}(\mathbf{x})$. The rest of the space is assumed to be a uniform and isotropic volume conduction medium with conductivity σ_0. The potential field generated by this dipole at $\mathbf{y}$ in the unbounded (∞) inhomogeneous (i) medium is denoted by $\phi^{i,\infty}(\mathbf{y};\mathbf{d}_0)$. Note that through the application of a transfer matrix to this potential field, body surface potentials in a bounded, inhomogeneous volume conductor (for instance including lungs and blood cavities) can be derived [11]. Since the volume conduction problem is linear, the field $\phi^{i,\infty}$ can be expressed as $\mathbf{L}(\mathbf{y},\mathbf{x}_0)\cdot\mathbf{d}_0$. We are seeking a simple, approximate formula for the matrix $\mathbf{L}$.

The problem is to estimate the dipolar moment of an equivalent dipole $\mathbf{d}$ located at the same position $\mathbf{x}_0$ in a uniform (u) isotropic medium with conductivity σ_0 that would generate a potential field, denoted by $\phi^{u,\infty}(\mathbf{y};\mathbf{d})$, asymptotically similar to $\phi^{i,\infty}(\mathbf{y};\mathbf{d}_0)$ at large distances $\|\mathbf{y}-\mathbf{x}_0\|$. The objective is to derive a formula to compute $\mathbf{d}$ as a function of $\mathbf{d}_0$, the geometry and volume conduction properties.

2.2. Equivalent dipole estimation

In order to estimate the equivalent dipole, the problem in a bounded medium is first considered. A rectangular parallelepiped P containing Ω is constructed. The volume conduction properties remain the same inside P. The potential field generated by the dipole in the bounded (b) uniform medium and in the bounded inhomogeneous medium are respectively denoted by $\phi^{u,b}(\mathbf{y};\mathbf{d})$ and $\phi^{i,b}(\mathbf{y};\mathbf{d}_0)$.

The equivalent dipole may be approximated using the Gabor–Nelson theory [17], according to which the dipole moment is obtained as a surface integral over the outer surface P

$$\mathbf{d}=\sigma_0\int_P \phi^{i,b}(\mathbf{y};\mathbf{d}_0)\;\mathbf{n}\,\mathrm{d}S(\mathbf{y}), \tag{1}$$

where $\mathbf{n}$ is the normal vector. If the domain Ω was uniform with conductivity σ_0, the integral would give $\mathbf{d}=\mathbf{d}_0$. This approach has been previously used to derive vectorcardiographic transfer matrices [18].

The Green's function $G^{i,b}(\mathbf{y},\mathbf{x})$ is the potential in the bounded inhomogeneous medium generated at $\mathbf{y}$ by a point source located at $\mathbf{x}$, i.e. $\nabla_{\mathbf{y}}\cdot\boldsymbol{\sigma}\nabla_{\mathbf{y}}G^{i,b}(\mathbf{y},\mathbf{x})=-\delta(\mathbf{y}-\mathbf{x})$ with no-flux condition at the boundary of P. Therefore, the field generated by the dipole $\mathbf{d}_0$ can be written as:

$$\phi^{i,b}(\mathbf{y};\mathbf{d}_0)=\nabla_{\mathbf{x}}G^{i,b}(\mathbf{y},\mathbf{x}_0)\cdot\mathbf{d}_0, \tag{2}$$

where by definition the gradient is a row vector. Combining (1) and (2), the equivalent dipole is estimated as a linear transformation of the real dipole:

$$\mathbf{d}=\left(\sigma_0\int_P \mathbf{n}\cdot\nabla_{\mathbf{x}_0}G^{i,b}(\mathbf{y},\mathbf{x}_0)\,\mathrm{d}S(\mathbf{y})\right)\cdot\mathbf{d}_0=M(\mathbf{x}_0)\cdot\mathbf{d}_0, \tag{3}$$

The six faces of P are denoted by P_k^+ and P_k^- for $k=1,2,3$. Then, the matrix M can be expressed as

$$M(\mathbf{x}_0)=\sigma_0\sum_{k=1}^{3}\mathbf{e}_k\cdot\nabla_{\mathbf{x}_0}\left(\int_{P_k^+}G^{i,b}(\mathbf{y},\mathbf{x}_0)\,\mathrm{d}S-\int_{P_k^-}G^{i,b}(\mathbf{y},\mathbf{x}_0)\,\mathrm{d}S\right) \tag{4}$$

since $\mathbf{n}=\pm\mathbf{e}_k$ on $P_k^\pm$ if $\{\mathbf{e}_k\}$ forms the orthonormal basis associated with the parallelepiped P. After application of the theorem of reciprocity $G^{i,b}(\mathbf{y},\mathbf{x})=G^{i,b}(\mathbf{x},\mathbf{y})$, the term in parentheses, denoted by $\phi_k^{i,b}$, is written as

$$\phi_k^{i,b}(\mathbf{x}_0)=\int_{P_k^+}G^{i,b}(\mathbf{x}_0,\mathbf{y})\,\mathrm{d}S-\int_{P_k^-}G^{i,b}(\mathbf{x}_0,\mathbf{y})\,\mathrm{d}S \tag{5}$$

and is the solution to the volume conduction equation in the bounded inhomogeneous medium with distributed current source of intensity $+1$ on the face P_k^+ and intensity -1 on the face P_k^-.

The matrix $M(\mathbf{x}_0)$ can therefore be computed for every source location $\mathbf{x}_0$ in Ω by solving three Poisson problems to determine the fields $\phi_k^{i,b}$ and by inserting their gradient in the rows of the matrix M.

Note that if all conductivities are scaled by the same factor κ, then by the definition of the Green's function, $G^{i,b}$ is divided by κ while σ_0 is multiplied by κ, which means that the matrix M is invariant to such scaling (based on Eq. (4)).

If a sufficiently large parallelepiped P is used, the matrix M does not depend on P because $\phi_k^{i,b}(\mathbf{x})$ converges in Ω. Also, when P becomes large, $\phi^{i,b}\to\phi^{i,\infty}$ and $\phi^{u,b}\to\phi^{u,\infty}$ so that $\mathbf{d}=M(\mathbf{x}_0)\mathbf{d}_0$ provides a solution to the unbounded problem. As a result, an approximation for the far-field generated by a dipole $\mathbf{d}_0$ located at $\mathbf{x}_0$ in an inhomogeneous anisotropic medium is obtained as:

$$\phi^{i,\infty}(\mathbf{y};\mathbf{d}_0)\approx\phi^{u,\infty}(\mathbf{y};M(\mathbf{x}_0)\mathbf{d}_0)=\frac{(\mathbf{y}-\mathbf{x}_0)^T M(\mathbf{x}_0)\mathbf{d}_0}{4\pi\sigma_0\,\|\mathbf{y}-\mathbf{x}_0\|^3}. \tag{6}$$

The entries of the matrix M are non-dimensional and will be called correction factors. These components will be expressed in the local coordinate system associated with fiber orientation.

2.3. Tissue models

The approach was tested in 2D and 3D geometries in which tissue thickness was varied.

The first geometry was an annulus in 2D with a radius of 16 mm (mean of inner and outer radii) and a thickness between 1.5 and 10 mm. The annulus was embedded in a 50 by 50 mm conductive square region (the domain P). Fiber orientation was assumed to be tangent to the circles, so there were three extracellular conductivities: the radial conductivity σ_r, the tangential conductivity σ_θ, and the conductivity of the surrounding bath σ_0 (isotropic). Note that the non-dimensional matrix M depends only on the ratios σ_r/σ_0 and σ_θ/σ_0. To compute far-field potentials, the surrounding bath was then extended to 100 by 100 mm.

The second geometry was based on a 3D atrial model [13] in which atrial wall thickness δ was uniform and varied between 1.5 and 4 mm. For that purpose, the mid-atrial surface was extracted from the original model and the nodes within a distance of $\delta/2$ from the surface were included in the new geometry. Fast conducting bundles (including the pectinate muscles) were kept intact. The atria were embedded in a parallelepiped P that left at least 5 mm space between the epicardial surface and the boundary. To check convergence, the volume was extended by 5 mm on all six sides. Fiber orientation was assumed to be the same across atrial wall thickness. There were three extracellular conductivities: longitudinal (σ_l) and transverse (σ_t) conductivity, and that of the surrounding bath (σ_0).

The Poisson equation was discretized using a finite differences method [19] on a regular grid with 0.33 mm inter-node spacing. The linear systems were solved using a biconjugate gradient stabilized method with an incomplete LU preconditioner.

2.4. ECG computation

To evaluate the influence of atrial extracellular anisotropy on body surface potentials, P waves were computed. Sinus rhythm was simulated in the monodomain framework using the original