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Article

Formulation of the Transfer Matrix of the Invers Electrophysiology of the Heart Activation Inside Homogeneous and Inhomogeneous Volume Conductor

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Abstract

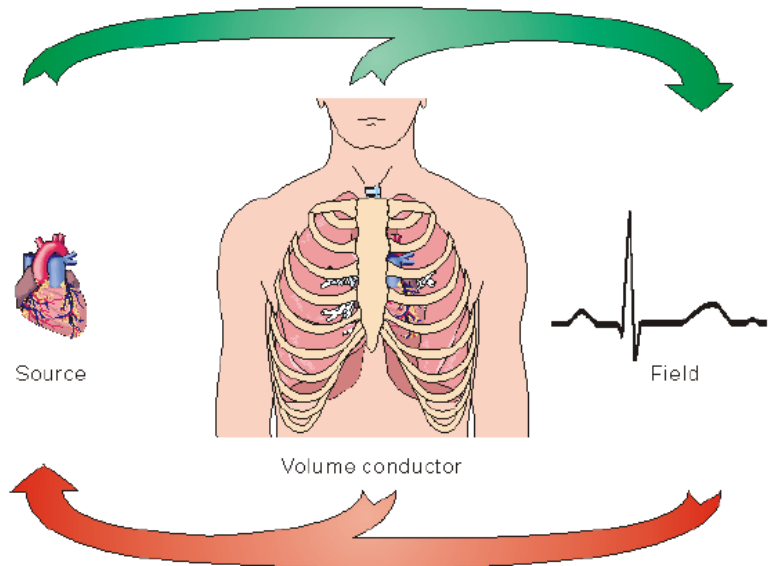
This work addresses the mathematical modeling of the Inverse Problem in cardiac electrophysiology. The Forward Problem aims to compute the potential field on the body surface generated by electrical sources within the heart, while the Inverse Problem seeks to reconstruct these internal sources based on body surface measurements. This research focuses on solving the Inverse Problem by formulating it in terms of transmembrane potentials (TMPs) rather than current density vectors, which significantly reduces the solution domain and computational cost. Three modeling scenarios are explored: an isotropic volume source in an infinite homogeneous volume conductor, an anisotropic source in a homogeneous medium, and an anisotropic source in an inhomogeneous medium. Each scenario leads to a different lead field transfer matrix formulation, ultimately enabling the reconstruction of cardiac TMPs from body surface potential maps (BSPMs). The linearity of the resulting system validates the application of advanced linear regularization methods.

Keywords: cardiac electrophysiology; inverse problem; transmembrane potential (TMP); body surface potential map (BSPM)

1. Introduction

There are two problems in modeling the electrophysiology of the heart: the Forward Problem and the Inverse Problem [1]. The heart Forward Problem involves designing a model that is capable of determining the field on the surface of known body (conductor) that is generated by electrical-sources inside the heart. Solving the Forward Problem requires the development of electrical models which are capable of describing the bioelectrical criteria of the heart and the body (Figure 1).

To determine the FIELD from the known source and conductor is called the
FORWARD PROBLEM



To determine the SOURCE from the known field and conductor is called the
INVERSE PROBLEM

Figure 1. The Forward and the Inverse Problems of the heart electrophysiology [1].

The Inverse Problem of the heart electrophysiology aims to recover the electrical-sources locations in the heart from a measured field on the body surface [1]. These electrical activities are represented as current dipoles (volume source) inside the body (volume conductor).

Formulating the Inverse Problem requires identifying the configuration of the volume source. The heart can be considered as one dipole source that generate the field as introduced in [2 – 4], where in Cartesian coordinates, six parameters are required to identify that source; three for location and three for direction. One of the most used source models is the potential distribution on the Epicardium surface from the body surface reading as described in [5 – 19]. This will provide an indication about the source distribution inside the heart. Finally, the most recent models use the multiple pole source distribution, where it is required to identify the distribution of electrical sources in the heart volume directly [20 – 27]. Instead of formulating the Inverse Problem in terms of current densities distributions as demonstrated in other research, the formulation of the problem in this research will be in terms of transmembrane potentials.

Formulating the problem in terms of TMP reduces the solution domain size to the 1/3 of the current density solutions, as each location inside the heart will be represented as one variable instead of the three variables for each component of the current density vector. Some operations (matrix multiplication and matrix inversion) of the Inverse Problem solutions are of cubic complexity, $O(N^3)$, and so reducing the solution domain size will decrease the computation cost.

Moreover, reducing the solution domain size will reduce the ‘underdeterminity’ of the system since providing fewer unknowns (independent variables) to the regularization process with the same number of results (dependent variables) will lead to a better solution.

The stages of the Inverse Problem solution are performed as shown in Figure 2, where the heart model [28 – 34] and the body model [35] are used to build the lead field transfer matrix and the BSPM (the output of the Forward Model solution) [36] is used as the dependent variables vector.

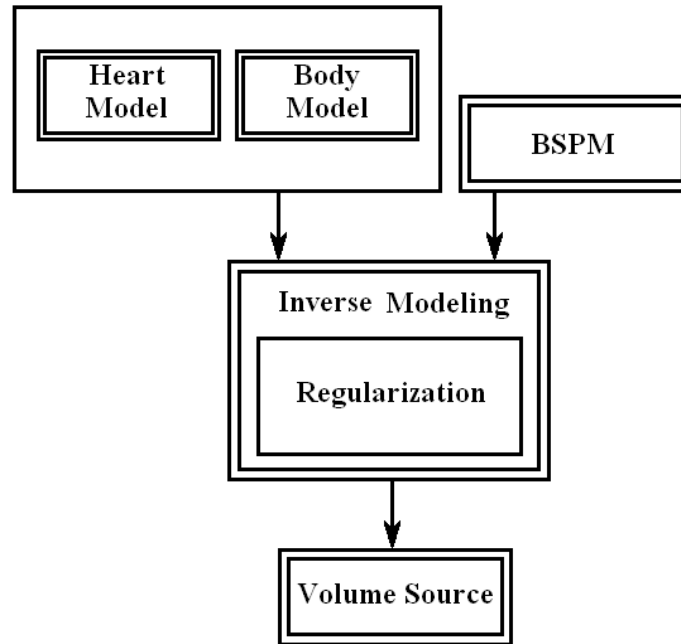


Figure 2. Block diagram of Inverse Problem solution.

The main objective here is to build a transfer matrix A that maps the transmembrane potentials x to the body surface potential b such that

$$b = Ax \quad (1)$$

where A is $M \times N$ transfer matrix, b is $M \times 1$ body surface reading vector, and x is $N \times 1$ TMP vector.

Formulation of the Inverse Problem is introduced for both homogeneous and inhomogeneous volume conductor and the volume source conductivity-tensor can be either isotropic or anisotropic, leading to different lead field transfer matrices. Three settings are introduced in this research, isotropic volume source in infinite homogeneous volume conductor, anisotropic volume source in infinite homogeneous volume conductor and anisotropic volume source in inhomogeneous volume conductor. The first is the simplest setting which requires the least information about the volume source and the volume conductor, but it is also the most inaccurate model among the three models.

2. Transfer Matrix of Isotropic Volume Source in Infinite Homogeneous Volume Conductor

Consider the equation of calculating the potential in an infinite homogenous volume conductor:

$$\phi_0 = \frac{-1}{4\pi\sigma_0} \int_v \frac{\sigma_i \nabla V_m \cdot r}{|r|^3} dv \quad (2)$$

where σ_0 is the homogeneous volume conductor conductivity, σ_i is the volume source conductivity tensor, V_m is the transmembrane potential, and r is the observation point to source point vector.

By assuming isotropic conductivity-tensor of the source and equal to the conductivity of the volume source medium then equation (2) can be written as

$$\phi_0 = \frac{-1}{4\pi} \int_v \frac{\nabla V_m \cdot r}{|r|^3} dv \quad (3)$$

and then

$$\phi_0 = \frac{-\delta_v}{4\pi} \sum_{i=1}^N \frac{\nabla V_{m_i} \cdot r_i}{|r_i|^3} \quad (4)$$

where N is the number of sources and δ_v is a unit volume. The gradient of transmembrane potential and the vector r can be written in Cartesian coordinates as

$$\nabla V_m = \frac{\partial V_m}{\partial x} \bar{X} + \frac{\partial V_m}{\partial y} \bar{Y} + \frac{\partial V_m}{\partial z} \bar{Z} \quad (5)$$

$$r = r_x \bar{X} + r_y \bar{Y} + r_z \bar{Z} \quad (6)$$

then

$$\frac{\nabla V_m \cdot r}{|r|^3} = \frac{\partial V_m}{\partial x} \frac{r_x}{|r|^3} + \frac{\partial V_m}{\partial y} \frac{r_y}{|r|^3} + \frac{\partial V_m}{\partial z} \frac{r_z}{|r|^3} \quad (7)$$

using Taylor's theorem

$$\frac{\partial V_m}{\partial x} \frac{r_x}{|r|^3} = \frac{V_{m(x+1,y,z)} - V_{m(x-1,y,z)}}{2h_x} \frac{r_x}{|r|^3} \quad (8)$$

Then in the X direction, the current element will contribute by $\frac{-\delta_v}{4\pi} \left[\frac{r_x}{2h_x |r|^3} \right]$ to the next element and by $\frac{-\delta_v}{4\pi} \left[\frac{-r_x}{2h_x |r|^3} \right]$ to the previous element, and so on for Y and Z directions.

Finally, each element in the transfer matrix A can be built as

$$A_{(i,j)} = \frac{-\delta_v}{4\pi} \left[\begin{aligned} &\frac{r_{x1}}{2h_x |r_1|^3} - \frac{r_{x2}}{2h_x |r_2|^3} + \frac{r_{y3}}{2h_y |r_3|^3} - \frac{r_{y4}}{2h_y |r_4|^3} \\ &+ \frac{r_{z5}}{2h_z |r_5|^3} - \frac{r_{z6}}{2h_z |r_6|^3} \end{aligned} \right] \quad (9)$$

where these elements represents the six orthogonal neighbors of the current node with respect to an observation point in the Cartesian coordinate system. Then, for M body-surface locations, the forward solution of the infinite homogeneous volume conductor can be written as

$$b_0 = A_0 x \quad (10)$$

where b_0 is the vector of the dependent variables, x is the vector of the independent variables, and A_0 is the lead field transfer matrix.

3. Transfer Matrix of Anisotropic Volume Source in Infinite Homogeneous Volume Conductor

The approach is taken as the previous section, but the conductivity tensor of the source is considered here to be anisotropic. Due to orthogonality of the conductivity tensor, the calculations can be in terms of the principal direction (first eigenvector) of the tensor. Equation (11) shows the equation in terms of principal direction e as

$$\phi_0 = \frac{-\sigma_t}{4\pi\sigma_0} \int_v \frac{\nabla V_m \cdot r}{|r|^3} dv + \frac{-(\sigma_l - \sigma_t)}{4\pi\sigma_0} \int_v \frac{ee^T \nabla V_m \cdot r}{|r|^3} dv \quad (11)$$

where e is the tensor's principal direction vector, e^T is the transpose of this vector, and σ_l and σ_t is the longitudinal and traverse conductivities, respectively. The term $\frac{ee^T \nabla V_m \cdot r}{|r|^3}$ can be written in the

X coordinate as

$$\frac{\partial V_m}{\partial x} [e_x e_x + e_x e_y + e_x e_z] \frac{r_x}{|r|^3} = \frac{V_{m(x+1,y,z)} - V_{m(x-1,y,z)}}{2h_x} [e_x e_x + e_x e_y + e_x e_z] \frac{r_x}{|r|^3} \quad (12)$$

Finally, each element in the transfer matrix $A_{(i,j)}$ can be built as

$$A_{(i,j)} = \frac{-\delta_v}{4\pi\sigma_0} \left\{ \left[\frac{r_{x1}}{2h_x |r_1|^3} - \frac{r_{x2}}{2h_x |r_2|^3} \right] \cdot [\sigma_t + (\sigma_l - \sigma_t)(e_x e_x + e_x e_y + e_x e_z)] + \right. \\ \left. \left[\frac{r_{x1}}{2h_x |r_1|^3} - \frac{r_{x2}}{2h_x |r_2|^3} \right] \cdot [\sigma_t + (\sigma_l - \sigma_t)(e_x e_y + e_y e_y + e_y e_z)] + \right. \\ \left. \left[\frac{r_{x1}}{2h_x |r_1|^3} - \frac{r_{x2}}{2h_x |r_2|^3} \right] \cdot [\sigma_t + (\sigma_l - \sigma_t)(e_x e_z + e_y e_z + e_z e_z)] \right\} \quad (13)$$

and the forward solution will be the same as equation (10)

4. Transfer Matrix of a Volume Source in Inhomogeneous Volume Conductor

The equation that calculates the potential field at any point inside an inhomogeneous volume conductor is defined as [Ref_102]:

$$\phi = \phi_\infty + \frac{1}{4\pi\sigma_0} \left[\sum_{k=1}^L \int_{S_k} \left(\frac{(\sigma_k'' - \sigma_k') \phi(r_k) r_k' \cdot \vec{n}_k}{|r_k'|^3} \right) dS_k \right] \quad (14)$$

where ϕ_∞ is the potential of the infinite homogeneous volume conductor (eq. 2), k is the organ's number, L is the number of organs, S_k is the surface of the organ, σ_k'' and σ_k' are the conductivities just inside and just outside the organ's boundary, $\phi(r_k)$ is the equation (2), r_k is the displacement vector from primary source to a point on the organ boundary, r_k' is the displacement vector from boundary surface (secondary source) to body surface and $\vec{n}_k$ is the normal vector on the organ's boundary surface and it points to the outside of the organ. Then, for an observation point W , ϕ_∞ and $\phi(r_k)$ can be written as in equation (10) as the following

$$\begin{aligned} \phi_\infty &= A_{0W} x \\ \phi(r_1) &= A_{1W} x \\ \phi(r_2) &= A_{2W} x \\ &\vdots \\ \phi(r_L) &= A_{LW} x \end{aligned} \quad (15)$$

such that A_{kT} represents the row of elements (a vector transpose) belonging to the observation point W in the matrix A of the organ k . For any point W on the body surface, equation (14) can be written as

$$\begin{aligned}
\phi &= A_0 x + \frac{1}{4\pi\sigma_0} \left[\sum_{k=1}^L (\sigma_k'' - \sigma_k') \int_{S_k} \left(\frac{(A_{kW} x) r_{kW}' \cdot \vec{n}_k}{|r_{kW}'|^3} \right) dS_k \right] \\
&= A_0 x + \frac{1}{4\pi\sigma_0} \left[\sum_{k=1}^L (\sigma_k'' - \sigma_k') \sum_{j=1}^{P_k} \left(\frac{\delta_{S_{kj}} (A_{kW} x) r_{kWj}' \cdot \vec{n}_{kj}}{|r_{kWj}'|^3} \right) \right] \\
&= \left\{ A_0 + \frac{1}{4\pi\sigma_0} \left[\sum_{k=1}^L (\sigma_k'' - \sigma_k') \sum_{j=1}^{P_k} \left(\frac{\delta_{S_{kj}} A_{kW} r_{kWj}' \cdot \vec{n}_{kj}}{|r_{kWj}'|^3} \right) \right] \right\} x \quad (16)
\end{aligned}$$

where P_k denotes the number of surfaces in the organ k , δ_s is a surface element area, r is the vector from an observation point W to a point on the surface of an organ k , and n is the normal vector at this point. Then for each organ, the partial transfer matrix will be

$$\overline{A}_w = \frac{(\sigma'' - \sigma')}{4\pi\sigma_0} \sum_{j=1}^P \left(\frac{\delta_{S_j} A_w r_{wj}' \cdot \vec{n}_j}{|r_{wj}'|^3} \right) = \sum_{j=1}^P \left(A_w \frac{\delta_{S_j} (\sigma'' - \sigma') r_{wj}' \cdot \vec{n}_j}{4\pi\sigma_0 |r_{wj}'|^3} \right) \quad (17)$$

Building the partial transfer matrix using equation (17) can be performed as follows

- 1- Compute the transfer matrix A of the organ or the body torso to all sources inside the heart using Equation 13. (Equation 9 can be used also in case of no information about fibers directions).
- 2- Tessellate the organ's surface into triangular elements and calculate the normal vectors on each surface element done by cross product of any two edges of the triangle in anti-clock-wise direction and calculate the area of the triangle element can be derived from the dot product of two these edges.

$$\text{Normal} = \vec{n} = AB \times AC = [n_x \quad n_y \quad n_z]^T$$

$$\text{Area} = \delta_s = \frac{1}{2} \sqrt{|AB|^2 |AC|^2 - (AB \cdot AC)^2}$$

- 3- From each point on the body surface, compute the vector r to a point on an organ surface element.

$$r = [rx \quad ry \quad rz]^T$$

- 4- Compute the scalar

$$U = \frac{\delta_s (\sigma_k'' - \sigma_k') [n_x r_x + n_y r_y + n_z r_z]}{4\pi\sigma_0 |r|^3}$$

- 5- Multiply the last scalar by the corresponding row (the row of the current observation point) in the corresponding A matrix, and add this row in a new matrix $\overline{A}$.

When applying these steps to all organs, Equation 16 becomes

$$\phi = [A_0 + \overline{A}_1 + \dots + \overline{A}_k] x \quad (18)$$

which can be written as

$$\phi = Ax \quad (19)$$

or in the form of equation (1)

$$b = Ax \quad (20)$$

Then this proves a linear relation between the body surface potential readings and the transmembrane potential which is the necessary condition for using any linear regularization methods such as MN, WMN [37 – 39] and LORETA [40].

5. Conclusions

This research develops a comprehensive framework for modeling and solving the cardiac Inverse Problem using transmembrane potentials. By reformulating the problem in terms of TMPs instead of current densities, the solution space is reduced by two-thirds, resulting in significant computational efficiency and improved system conditioning. The study derives and constructs lead field transfer matrices under three increasingly complex biophysical conditions: isotropic-homogeneous, anisotropic-homogeneous, and anisotropic-inhomogeneous conductors. The final formulation maintains linearity, ensuring compatibility with established linear regularization techniques such as MN, WMN, and LORETA. This approach provides a robust foundation for accurate non-invasive cardiac source imaging, potentially enhancing clinical diagnosis and treatment planning in electrophysiology.

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