ESTIMATING CURRENT DENSITY IN THE HEART USING ECG/MCG SPATIO-TEMPORAL ANALYSIS

Aleksandar Jeremić and *Arye Nehorai*

EECS Department (M/C 154)
The University of Illinois at Chicago
851 S.Morgan Street
Chicago, Illinois 60607-7053

ABSTRACT

The inverse problem of electrocardiography can be defined as the determination of the information about the electrical activity of the heart from measurements of the body-surface electromagnetic field. The solution to this inverse problem may ultimately improve the ability to detect and treat cardiac diseases early. In this study, we present an algorithm for estimating the current density of the heart using electrocardiography (ECG) and magnetocardiography (MCG) sensor arrays. We model the electrical activity of the heart using current density represented by a set of spatio-temporal basis functions. In order to solve the corresponding Fredholm equation we apply the element-free Galerkin method and compute the measurements as a function of the torso geometry and cardiac source. Then, we maximize the likelihood function to estimate the unknown parameters assuming a presence of spatially correlated Gaussian noise with unknown covariance matrix.

1. INTRODUCTION

The intrinsic electrical activity of the heart gives rise to an electro-magnetic field within the volume of the thorax and upon the torso surface. This field arise from individual cardiac cells receiving current from neighboring cells and responding with a local membrane action potential. The latter cells then inject excitatory current into their neighboring cells that are not yet excited thus generating an electric "pulse" that propagates through the heart. This electrical activity, the excitation of the heart, is interdependent with its mechanical activity [1] since the active tension developed in the cardiac muscle is proportional to the excitatory current intensity. Furthermore, in addition to excitation-contraction coupling, there is an evidence that there exists also a feedback pathway, whereby the electrical characteristics of the myocardium are altered by the mechanical state of the tissue, see [2]. However, in spite of these relations, there have been only few attempts to model the combined electromechanical system [1].

We have recently proposed a method for estimating *both* the active (contraction related) and passive (relaxation related) mechanical properties of the heart using dynamic modeling and tagged MR images [3]. Our ultimate goal is to develop a computational framework for estimating the electro-mechanical properties of the heart using a coupled model. As a first step, in this paper we present an inverse model of cardiac electric activity which can be coupled with our aforementioned mechanical model of the heart.

The inverse problem of electro-cardiology may be construed as determining of information about the heart from measurements of body-surface potentials. It is well known that this inverse problem is ill-posed since the intervening volume conductor consisting of the thorax implies that the electrical/magnetic potentials measured on the torso surface (ECG/MCG) are spatially very smooth projections of the electrical current sources associated with the cardiac activation [4]. In particular, the measured torso data is related to the desired image via a linear operator whose inverse is discontinuous. In principle, an image can be obtained from applying the inverse operator to the data - but the operator's discontinuous nature implies that any noise entering the process of measurement and modeling will be amplified in the solution in an unknown and uncontrolled fashion.

One point of view on how to make this ill-posed imaging problem better posed is to use a set of constraints on the solution which will sufficiently restrict the admissible class of solutions, so that the operator defined on the restricted set will have a continuous inverse [4]. In addition, these constraints can be related to the physiology and thus have physical mean-

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ing. We will impose these constraints implicitly in the formulation of the problem through our definition of the cardiac source. Most of the existing inverse electrocardiology solutions are obtained in terms of equivalent heart sources such as single or multiple (fixed or moving) dipoles or epicardial potentials. The source model determines the type of electrical information that can be deduced from the body-surface electrical measurements and the range of applicability of the inverse solution.

We model the spatio-temporal density of currents using a set of *a priori* known basis functions and unknown coefficients. Using this model and element-free Galerkin method we derive expressions for the electromagnetic field on the torso surface and corresponding measurement model for an ECG/MCG sensor array. The element-free Galerkin (EFG) method is based on moving least-squares interpolants for the test and trial functions and does not require any element connectivity data but can be imbued with the generality of a finite element method [5]. In addition, EFG does not seem to exhibit any volumetric locking even with the linear basis functions, and its rate of convergence can exceed that of finite elements significantly. The usefulness of the EFG method for analysis of bioelectric activity is demonstrated in [6]. We also derive a parametric statistical model for the array's measurements as a function of the basis functions coefficients in the presence of unknown spatially correlated Gaussian noise and derive a maximum likelihood (ML) estimator for the unknown parameters. Our use of spatially correlated noise should improve robustness with respect to perturbations such as noise, inhomogeneity, etc.

2. FORWARD MODEL

The forward problem in electro-cardiology is to calculate the electric potential $\phi(\boldsymbol{r},t)$ and magnetic field $\boldsymbol{B}(\boldsymbol{r},t)$ at a location $\boldsymbol{r}$ on the torso surface at time t from a given primary current distribution $\boldsymbol{J}(\boldsymbol{r}',t)$ within the heart. We use a piecewise homogeneous torso model consisting of the following surfaces: the outer torso, inner torso, lungs, epicardium and blood masses (left and right ventricles). Therefore, we model the heart as a volume G of M homogeneous layers separated by closed surfaces $S_i, i=1,\dots,M$. Let σ_i^- and σ_i^+ be the conductivities of the layers inside and outside S_i respectively. We will denote by $\{G_i\}$ the regions of different conductivities, and by G_{M+1} the region outside the torso, which behaves as an insulator. Therefore, in our model $\sigma_{M+1}^- = \sigma_M^+ = 0$.
It has been shown that in the case of a piecewise homogeneous torso model and using quasi-static assumption the magnetic field at a location $\boldsymbol{r}$ and time t is [7]

$$\begin{aligned}\boldsymbol{B}(\boldsymbol{r},t) &= \boldsymbol{B}_0(\boldsymbol{r},t) + \\ &+\frac{\mu_0}{4\pi}\sum_{i=1}^{M}(\sigma_i^- - \sigma_i^+)\int_{S_i}\phi(\boldsymbol{r}',t)\frac{(\boldsymbol{r}-\boldsymbol{r}')}{\|\boldsymbol{r}-\boldsymbol{r}'\|^3}\times \mathrm{d}S(\boldsymbol{r}'),\\ \boldsymbol{B}_0(\boldsymbol{r},t) &= \frac{\mu_0}{4\pi}\int_G \frac{\boldsymbol{J}(\boldsymbol{r}',t)\times(\boldsymbol{r}-\boldsymbol{r}')}{\|\boldsymbol{r}-\boldsymbol{r}'\|^3}\mathrm{d}^3r'. \end{aligned} \tag{1}$$

Similarly, the potential $\phi(\boldsymbol{r},t)$ is given by [7]

$$\begin{aligned}\frac{\sigma_k^- + \sigma_k^+}{2}\phi(r,t) &= \phi_0(\boldsymbol{r})(\sigma_k^- - \sigma_k^+) + \\ &+\frac{1}{4\pi}\sum_{i=1}^{M}(\sigma_i^- - \sigma_i^+)\int_{S_i}\phi(\boldsymbol{r}',t)\frac{(\boldsymbol{r}-\boldsymbol{r}')}{\|\boldsymbol{r}-\boldsymbol{r}'\|^3}\cdot \mathrm{d}S(\boldsymbol{r}'),\\ \phi_0(\boldsymbol{r},t) &= \frac{1}{4\pi}\int_G \frac{\boldsymbol{J}(\boldsymbol{r}',t)\cdot(\boldsymbol{r}-\boldsymbol{r}')}{\|\boldsymbol{r}-\boldsymbol{r}'\|^3}\mathrm{d}^3r' \end{aligned} \tag{2}$$

In order to solve the integral equations (1) and (2) we utilize the element-free-Galerkin method [5]. The essential idea of the EFG method is that the moving least-squares (MLS) interpolants are used for the trial and test functions with a variational principle for describing the MLS. The EFG method does not require any element connectivity data and does not suffer much degradation in accuracy when the nodal arrangements are very irregular. It is particularly useful in dynamic modeling since it does not require mesh generation.

To construct the MLS interpolants using orthogonal basis functions, we first consider an arbitrary point $\boldsymbol{r}'$ within thorax and a region around this point. In the region containing $\boldsymbol{r}'$ and $\boldsymbol{r}$, the function $\phi(\boldsymbol{r},t)$ can be locally approximated by

$$\tilde{\phi}(\boldsymbol{r},t) = \sum_{i=1}^{n_\mathrm{b}} u_i(\boldsymbol{r},\boldsymbol{r}')c_i(\boldsymbol{r}',t), \tag{3}$$

where $\tilde{\phi}(\boldsymbol{r},t)$ denotes the approximation of $\phi(\boldsymbol{r},t)$, n_b is the number of basis functions, $\{c_i(\boldsymbol{r}',t)\}$ are the coefficients, and $\{u_i(\boldsymbol{r},\boldsymbol{r}')\}$ are the basis functions satisfying the following orthogonality condition

$$\sum_{j=1}^{l} w(\boldsymbol{r}_j-\boldsymbol{r}')u_k(\boldsymbol{r}_j,\boldsymbol{r}')u_j(\boldsymbol{r}_j,\boldsymbol{r}') = \delta(j-k), \tag{4}$$

where l is the number of points in the neighborhood of $\boldsymbol{r}'$ for which

$$w_j(\boldsymbol{r}') \equiv w(\boldsymbol{r}_j-\boldsymbol{r}') \neq 0. \tag{5}$$

Consider a mesh consisting of m nodes located at $\boldsymbol{r}_i, i=1,\dots,m$. It has been shown [5] that using Schmidt orthogonalization the MLS approximation (3) can be written as

$$\tilde{\phi}(\boldsymbol{r},t)=\sum_{i=1}^{n_{\mathrm{b}}}\psi_i(\boldsymbol{r})\phi(\boldsymbol{r}_i,t), \quad (6)$$

where $\psi_i(\boldsymbol{r})$ is a shape function defined by

$$\begin{aligned}\psi_i(\boldsymbol{r}) &= w_i(\boldsymbol{r})\sum_{j=1}^{n_{\mathrm{b}}}\gamma_{i,j}(\boldsymbol{r}),\\ \gamma_{i,j}(\boldsymbol{r}) &= \frac{u_j(\boldsymbol{r},\boldsymbol{r})u_i(\boldsymbol{r}_i,\boldsymbol{r})}{\sum_{j=1}^{l} w_i(\boldsymbol{r}')u_j^2(\boldsymbol{r}_j,\boldsymbol{r}')}. \quad (7)\end{aligned}$$

It is possible to start the orthogonalization process using any complete polynomial basis. For example, in 3D analysis for a quadratic basis we would use $\{1,x,y,z,x^2,y^2,z^2,xy,xz,zy\}$.

The numerical implementation of EFG method is completed by choosing the weight functions. We propose to use the exponential weight functions given by

$$\begin{aligned}w_i(d_i) &= \begin{cases}\frac{\mathrm{e}^{-(d_i/c)^2}-\mathrm{e}^{(-d_0/c)^2}}{1-\mathrm{e}^{(-d_0/c)^2}} & \text{if } d_i\le d_0\\ 0 & \text{if } d_i>d_0\end{cases} \quad (8)\\ d_i &= \|\boldsymbol{r}-\boldsymbol{r}_i\|, \quad (9)\end{aligned}$$

where c is a constant that controls the relative weights and d_0 is the support for the weight function. This domain where $w_i(\boldsymbol{r})$ is non-zero is called the domain of influence of the node $\boldsymbol{r}_i$.

Source Model

We assume that the electrical activity of the cardiac sources is approximately periodic i.e. that $\boldsymbol{J}(\boldsymbol{r},t)=\boldsymbol{J}(\boldsymbol{r},t+kT_{\mathrm{c}})$ where $k=0,1,\ldots$, and T_{c} is the time length of the heart cycle during which the measurements are obtained. By using repeated measurement we are able to decrease signal-to-noise ratio (SNR). In addition we assume that the current density orientations are fixed in time. The latter constraint has been proposed in [8] in order to compensate for the non-physiological nature of the free-moment solutions.

Using this assumption, the current density can be written as Fourier series

$$\boldsymbol{J}(\boldsymbol{r},t)=\sum_{i=1}^{p}\boldsymbol{J}_i^{\mathrm{c}}(\boldsymbol{r})\cos(i\omega_{\mathrm{c}}t)+\boldsymbol{J}_i^{\mathrm{s}}(\boldsymbol{r})\sin(i\omega_{\mathrm{c}}t), \quad (10)$$

where $\omega_{\mathrm{c}}=2\pi/T_{\mathrm{c}}$ and p is the number of temporal basis functions.
We propose to model the spatial variability of $\boldsymbol{J}_i^{\mathrm{c}}(\boldsymbol{r})$ and $\boldsymbol{J}_i^{\mathrm{s}}(\boldsymbol{r})$ using

$$\boldsymbol{J}_i^{\mathrm{c}}(\boldsymbol{r}) = \sum_{i=0}^{q}c_{i,j}^{\mathrm{c}}\boldsymbol{\lambda}_i^{\mathrm{c}}(\boldsymbol{r}), \quad (11)$$

$$\boldsymbol{J}_i^{\mathrm{s}}(\boldsymbol{r}) = \sum_{i=1}^{q}c_{i,j}^{\mathrm{s}}\boldsymbol{\lambda}_i^{\mathrm{s}}(\boldsymbol{r}), \quad (12)$$

where $\{\boldsymbol{\lambda}_i^{\mathrm{c}}\}$ and $\{\boldsymbol{\lambda}_i^{\mathrm{s}}\}$ the spatial basis functions of current densities, q is the number of basis functions, and $\{c_{i,j}^{\mathrm{c}}\}$ and $\{c_{i,j}^{\mathrm{s}}\}$ are the coefficients.

$$\begin{aligned}\Lambda^{\mathrm{c}}(\boldsymbol{r}) &= [\boldsymbol{\lambda}_0^{\mathrm{c}}(\boldsymbol{r})\cdots\boldsymbol{\lambda}_q^{\mathrm{c}}(\boldsymbol{r})]^T,\\ \Lambda^{\mathrm{s}}(\boldsymbol{r}) &= [\boldsymbol{\lambda}_1^{\mathrm{s}}(\boldsymbol{r})\cdots\boldsymbol{\lambda}_q^{\mathrm{s}}(\boldsymbol{r})]^T, \quad (13)\\ \boldsymbol{g}(t) &= [\cos(\omega t),\ldots,\cos(p\omega t)]^T,\\ \boldsymbol{h}(t) &= [\sin(\omega t),\ldots,\sin(p\omega t)]^T. \quad (14)\end{aligned}$$

Then, we can rewrite our source model as

$$\boldsymbol{J}(\boldsymbol{r},t)=\Lambda^{\mathrm{c}}(\boldsymbol{r})\Theta_{\mathrm{c}}\boldsymbol{g}(t)+\Lambda^{\mathrm{s}}(\boldsymbol{r})\Theta_{\mathrm{s}}\boldsymbol{h}(t). \quad (15)$$

where Θ_{c} and Θ_{s} are the matrices of unknown basis functions coefficients $\{c_{i,j}^{\mathrm{c}}\}$ and $\{c_{i,j}^{\mathrm{s}}\}$, respectively.

Using (15) we can now solve the potential integral equation (2) in terms of the source parameters Θ_{c} and Θ_{s}. Introduce

$$\begin{aligned}\bar{\phi}_0(\boldsymbol{r},t,\Theta_{\mathrm{c}},\Theta_{\mathrm{s}}) &= \frac{1}{4\pi}\sum_{i=1}^{p}\sum_{j=1}^{q}\Big(c_{i,j}^{\mathrm{c}}\cos(j\omega_{\mathrm{c}}t)\cdot\\ &\cdot\int_G\frac{\lambda_i^{\mathrm{c}}(\boldsymbol{r}')\cdot\boldsymbol{d}_r}{\|\boldsymbol{d}_r\|^3}\mathrm{d}^3\boldsymbol{r}'+c_{i,j}^{\mathrm{s}}\sin(j\omega_{\mathrm{c}}t)\int_G\frac{\lambda_i^{\mathrm{s}}(\boldsymbol{r}')\cdot\boldsymbol{d}_r}{\|\boldsymbol{d}_r\|^3}\mathrm{d}^3\boldsymbol{r}'\Big),\\ \vartheta_l(\boldsymbol{r}) &= \frac{\sigma_k^-+\sigma_k^+}{2}\psi_l(\boldsymbol{r})-\\ &-\frac{1}{4\pi}\sum_{i=1}^{M}(\sigma_i^--\sigma_i^+)\int_{S_i}\psi_l(\boldsymbol{r}')\frac{\boldsymbol{d}_r}{\|\boldsymbol{d}_r\|^3}\mathrm{d}S(\boldsymbol{r}'),\end{aligned}$$

where

$$\boldsymbol{d}_r=\boldsymbol{r}-\boldsymbol{r}'. \quad (16)$$

Then equation (2) becomes

$$\sum_{l=1}^{n_{\mathrm{b}}}\vartheta_l(\boldsymbol{r})\phi(\boldsymbol{r}_i,t)=\bar{\phi}_0(\boldsymbol{r},t,\Theta_{\mathrm{c}},\Theta_{\mathrm{s}}). \quad (17)$$

We can form a system of n_{b} linear equations

$$\begin{aligned}\sum_{l_1=1}^{n_{\mathrm{b}}}\int_G\vartheta_{l_1}(\boldsymbol{r})\vartheta_{l_2}(\boldsymbol{r})\phi(\boldsymbol{r}_i,t)\mathrm{d}\boldsymbol{r} &=\\ &=\int_G\bar{\phi}_0(\boldsymbol{r},t,\Theta_{\mathrm{c}},\Theta_{\mathrm{s}})\vartheta_{l_2}(\boldsymbol{r})\mathrm{d}\boldsymbol{r}\\ l_2=1,\ldots.,n_{\mathrm{b}}, \quad (18)\end{aligned}$$

with $n_{\rm b}$ unknowns, namely $\{\phi(\boldsymbol{r}_i,t)\}$ which can be solved for a given $\Theta_{\rm c}$ and $\Theta_{\rm s}$. Using matrix notation, equation (18) becomes

$$\begin{aligned} H\tilde{\boldsymbol{\phi}}(t) &= \tilde{\boldsymbol{\phi}}_0(\Theta_{\rm c},\Theta_{\rm s},t), \\ H_{i,j} &= \int_G \vartheta_i(\boldsymbol{r})\vartheta_j(\boldsymbol{r})\mathrm{d}\boldsymbol{r}, \\ \tilde{\boldsymbol{\phi}}(t) &= [\phi(\boldsymbol{r}_1,t),\ldots,\phi(\boldsymbol{r}_n,t)]^T, \\ \tilde{\boldsymbol{\phi}}_0(\Theta_{\rm c},\Theta_{\rm s},t) &= \int_G \phi_{0,\Theta_{\rm c}\Theta_{\rm s}}(\boldsymbol{r},t)\boldsymbol{\vartheta}(\boldsymbol{r})\mathrm{d}\boldsymbol{r}, \\ \boldsymbol{\vartheta}(\boldsymbol{r}) &= [\vartheta_1(\boldsymbol{r}),\ldots,\vartheta_{n_{\rm b}}(\boldsymbol{r})]^T. \end{aligned} \quad (19)$$

Then, using $\boldsymbol{\phi}(\boldsymbol{r}_i,t)$ we can compute the magnetic field (1).

3. STATISTICAL MODEL

Consider a bimodal array of $n_{\rm b}$ MCG and $m_{\rm E}$ ECG sensors. Let $m = s_{\rm B} + m_{\rm E}$. Then, the measurement model for this array is

$$\boldsymbol{y}(t) = \boldsymbol{f}(\Theta_{\rm c},\Theta_{\rm s},t) + \boldsymbol{e}(t), \quad (20)$$

where $\boldsymbol{y}(t) = [\boldsymbol{y}_{\rm B}^T(t),\boldsymbol{y}_{\rm E}^T(t)]^T$ is the measurement vector, $\boldsymbol{f}(\Theta_{\rm c},\Theta_{\rm s},t)$ is the m-dimensional array vector response , and $\boldsymbol{e}(t) = [\boldsymbol{e}_{\rm B}^T(t),\boldsymbol{e}_{\rm E}^T(t)]^T$ is additive noise. The subscripts B and E correspond to the magnetic and electric components of the measurement vector (noise) respectively. The array vector response is derived using the quasi-static approximation of Maxwell's equations and meshless FE model as described in the previous section.

We assume that the measurements are obtained using m sensors located at $\boldsymbol{r}_i$, $i = 1,\ldots,m$ and that time samples are taken at uniformly spaced time points $t_j, j = 1,\ldots,N$. In addition, we assume that the data acquisition is repeated K times during several heart cycles in order to improve the signal-to-noise (SNR) ratio. In the kth cycle ($k = 1,\ldots,K$), N temporal data vectors $\boldsymbol{y}_k(1),\boldsymbol{y}_k(2),\ldots,\boldsymbol{y}_k(N)$ are collected. We refer to the matrix $Y_k = [\boldsymbol{y}_k(1)\cdots\boldsymbol{y}_k(N)]$ as the data matrix.

It can be shown that using (1), (15) and (19) the measurement model can be written as

$$\boldsymbol{y}_k(t) = B_{\rm c}\Theta_{\rm c}\boldsymbol{g}(t) + B_{\rm s}\Theta_{\rm s}\boldsymbol{h}(t) + \boldsymbol{e}_k(t), \quad (21)$$

where $B_{\rm c}$ and $B_{\rm s}$ denote *spatial* matrices obtained from $\Lambda^{\rm c}(\boldsymbol{r})$ and $\Lambda^{\rm s}(\boldsymbol{r})$, and $\boldsymbol{e}_k(t)$ denotes the noise, which is assumed to be zero mean with unknown spatial covariance Σ and uncorrelated in time and between different cycles. The noise is mainly due to incorrect modeling, more precisely, the basis functions approximation which creates spatial and temporal correlation (within a cycle). However, it has been shown [12] that the temporal correlation can be removed asymptotically by applying discrete Fourier transform (DFT). In the remainder of the paper we will assume that the data has already been temporally pre-whitened. The noise covariance matrix Σ is assumed to be positive definite and constant in time and across all cycles.

4. PARAMETER ESTIMATION

The model (21) can be written as

$$\boldsymbol{y}_k(t) = B\Theta\boldsymbol{a}(t) + \boldsymbol{e}_k(t), \quad (22)$$

where

$$\begin{aligned} B &= [B_{\rm c}\,, B_{\rm s}]\,, \\ \Theta &= \begin{bmatrix} \Theta_{\rm c} & 0_{p\times q-1} \\ 0_{p\times q} & \Theta_{\rm s} \end{bmatrix}, \\ \boldsymbol{a}(t) &= \begin{bmatrix} \boldsymbol{g}(t) \\ \boldsymbol{h}(t) \end{bmatrix}, \end{aligned} \quad (23)$$

where $0_{p\times q}$ is $p \times q$-dimensional matrix of zeros.

The model (23) then can be treated as a growth-curve model [9]–[11]. Applying ML estimation to (23), yields a constrained optimization problem since some of the entries in Θ are identically equal to zero. Since fewer parameters are always preferred and to avoid constrained optimization we propose to use the same spatial basis functions for modeling $\boldsymbol{J}_i^{\rm c}$ and $\boldsymbol{J}_i^{\rm s}$ i.e. $\boldsymbol{\lambda}_i^{\rm c}(\boldsymbol{r}) = \boldsymbol{\lambda}_i^{\rm s}(\boldsymbol{r})$ for $i = 1,\ldots,p$. Observe that the generality of the model is not affected as long as the coefficients $c_{i,j}^{\rm c}$ and $c_{i,j}^{\rm s}$ are different. In addition we choose $\boldsymbol{\lambda}_i^{\rm c}(\boldsymbol{r})$ so that the matrix $B_{\rm c}$ has a full rank.

Using these assumption we can rewrite the model (21) as

$$Y_k = B_{\rm c}\Theta_{\rm c}G + B_{\rm s}\Theta_{\rm s}H + E_k, \quad (24)$$

where

$$\begin{aligned} B_{\rm s} &\subset B_{\rm c}, \\ G &= [\boldsymbol{g}(t_1)\cdots\boldsymbol{g}(t_N)], \\ H &= [\boldsymbol{h}(t_1)\cdots\boldsymbol{h}(t_N)], \\ \boldsymbol{E}_k &= [\boldsymbol{e}_k(t_1)\cdots\boldsymbol{e}_k(t_N)]. \end{aligned} \quad (25)$$

To estimate the unknown coefficients we use the ML estimator which maximizes the likelihood function

$$\begin{aligned} f(\Theta,\Sigma) &= \frac{1}{(2\pi)^{1/2mNK}|\Sigma|^{1/2NK}} \cdot \\ &\quad \cdot\exp\left\{-\frac{1}{2}\mathrm{tr}\left[\Sigma^{-1}CC^T\right]\right\}, \\ C &= \tilde{Y} - \tilde{B}_{\rm c}\Theta_{\rm c}\tilde{G} - \tilde{B}_{\rm c}\Theta_{\rm s}\tilde{H}, \end{aligned} \quad (26)$$

where $\tilde{Y} = [Y_1 \cdots Y_k]$ is the stacked measurement matrix of size $m \times NK$. Similarly we stack the spatial and temporal basis function matrices B_c, B_s, G, H into $\tilde{B}_c, \tilde{B}_s, \tilde{G}, \tilde{H}$.

To compute the ML estimates, we first maximize (26) with respect to Θ_c for a fixed Θ_s and once we obtain Θ_c we maximize again but with respect to Θ_s. For measurements from several cycles it can be shown that the ML estimates of Θ_c, Θ_s and Σ are given by

$$\begin{aligned}
\hat{\Theta}_c &= [\tilde{B}_c^T S^{-1} \tilde{B}_c]^{-1} \tilde{B}_c^T S^{-1} (\bar{Y} - \tilde{B}_s \hat{\Theta}^s \tilde{H}) \tilde{B}_c^T (\tilde{B}_c B_c^T)^{-1}, \\
\hat{\Theta}_s &= [\tilde{B}_s^T \bar{S}^{-1} \tilde{B}_s]^{-1} \tilde{B}_s^T \bar{S}^{-1} \bar{Y} Q \tilde{G}^T (\tilde{G} Q \tilde{G}^T)^{-}, \qquad (27) \\
\hat{\Sigma} &= (\bar{Y} - \tilde{B}_c \hat{\Theta}^c \tilde{G} - \tilde{B}_s \hat{\Theta}^s \tilde{H})(\bar{Y} - \tilde{B}_c \hat{\Theta}^c \tilde{G} - \tilde{B}_s \hat{\Theta}^s \tilde{H})^T,
\end{aligned}$$

where $-$ denotes the pseudo-inverse and

$$\begin{aligned}
Q &= I - \tilde{G}^T (\tilde{G}\tilde{G}^T)^{-1} \tilde{G}, \\
\bar{S} &= \bar{Y} Q \Big[I - \tilde{H}^T (\tilde{H} Q \tilde{H}^T)^{-1} \tilde{H} \Big] Q \bar{Y}^T, \\
S &= (\bar{Y} - \tilde{B}_s \hat{\Theta}_s \tilde{H}) Q (\bar{Y} - \tilde{B}_s \hat{\Theta}_s \tilde{H})^T. \qquad (28)
\end{aligned}$$

Modeling the currents by linear combination of *a priori* known functions allows us to exploit prior information on the spatio-temporal evolution which improves the estimation accuracy. It has been shown that the temporal behavior of the heart's electric activity can be approximated well with less than 10 harmonics, however it has to be validated if *a priori* known basis functions can model the spatial variability of the currents. Therefore, it may be desirable to test if this model is indeed applicable.

5. CONCLUSIONS

We developed a maximum likelihood method for estimating the current density in the heart using a combination of ECG and MCG arrays, assuming spatially correlated noise with unknown covariance. We derived the forward model using element-free Galerkin method which is computationally efficient technique that does not require mesh generation, We modeled the spatio-temporal activity of the cardiac electric source using a set of *a priori* known basis functions and unknown coefficients. We estimated these coefficients using the maximum likelihood method which asymptotically has optimal accuracy. Future research will include testing the proposed method using real data, developing a coupled inverse model which will enable simultaneous estimation of the heart's electro-mechanical properties, etc.

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