A Bioelectromagnetic Inverse Problem

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1. INTRODUCTION

In neuroscience, we are often interested in the distribution of electrical sources in the brain, and wish to test for significant source activity in a region of the brain. The electrical sources are not directly observable. Instead, what are observable are electrical potentials recorded, say, at M locations on the scalp. For example, in a typical event related potential (ERP) measurement, an experimental subject is presented with numerous repetitions of a stimulus where each repetition is referred to as a sweep. For each sweep the scalp electrical or magnetic activity can be sampled periodically before and after the stimulus; and response differences can then be obtained. Based on many repetitions of these extracranial (electro- or magneto-encephalographic, EEG or MEG, respectively) measurements $\mathbf{v}$, a M-vector, we'd like to infer the neuronal current distribution $\mathbf{j}$ at N locations within the brain that gave rise to the observations. The neuronal currents are primary currents, as opposed to the secondary currents which flow ohmically through the volume conductor of the body in response to the primary current generators. Thus, $\mathbf{v}$ and $\mathbf{j}$ may be represented as real vectors in *signal space* and *source space*, respectively. Since there are many more (unknown) primary currents than there are measurements, the problem is ill-posed, and the solution depends on the construction of a source model.

[1]This joint work was initiated by Raz a few days before he passed away in 2000.

2. SOURCE MODEL

Our source model (**??**) below is motivated from the quasi-static classical electromagnetics for a continuous domain:

$$v(\mathbf{r}') = \int_{\Omega_s} \mathbf{K}(\mathbf{r}, \mathbf{r}') \cdot \mathbf{j}(\mathbf{r}) \ \ d\Omega \tag{1}$$

where $v(\mathbf{r}')$ is an electric or magnetic measurement at some location $\mathbf{r}'$, and $\mathbf{K}(\mathbf{r}, \mathbf{r}')$ and $\mathbf{j}(\mathbf{r})$ are vector fields (the lead field and the primary current field, respectively) over the source region $\Omega_s \in \mathcal{R}^3$. The kernel $\mathbf{K}(\mathbf{r}, \mathbf{r}')$ can be derived from solutions to Maxwell's equations for the physical medium of the brain.

A source model can then be obtained when the source region Ω_s is discretized as a source lattice, $\mathcal{L}_s$. Typically $\mathcal{L}_s$ may represent either the intracranial volume (i.e. the volume interior to the skull) or the surface of the cerebral cortex. When $\mathcal{L}_s$ represents the intracranial volume, each lattice point may be associated with a 3d-space of primary currents. When $\mathcal{L}_s$ represents the cortical surface, each lattice point may be associated with a 1d-space of primary currents, since the currents are constrained to be radial to the cortical surface. By restricting the primary currents to the lattice points, we may represent equation (1) in matrix form as $\mathbf{v} \approx \mathbf{Kj}$, where $\mathbf{v} \in \mathcal{R}^M$ and $\mathbf{j} \in \mathcal{R}^N$ are the signal and source vectors, and $\mathbf{K}$ is the lead field matrix. Let ϵ be a random vector representing equipment noise and any other noise unrelated to brain electrical activity that is represented by $\mathbf{j}$. It is then reasonable to assume a statistical source model:

$$\mathbf{v} = \mathbf{Kj} + \epsilon. \tag{2}$$

Here $\mathbf{v}$ is a $M \times 1$ data vector for a particular sweep (or average of sweeps) and a particular sample (time point); $\mathbf{j}$ be the unknown $N \times 1$ source vector, where N is the number of lattice points (locations). In general, $N > M$; $\mathbf{K}$ has rank M; and that $\mathbf{j}$ may be assumed to have a $N(\mathbf{\Theta}, \mathbf{\Sigma_j})$ distribution (denoted by $\mathbf{j} \sim N(\mathbf{\Theta}, \mathbf{\Sigma_j})$) and that $\epsilon \sim N(0, \mathbf{\Sigma}_\epsilon)$ is independent of $\mathbf{j}$.

If $N < M$, the model in (**??**) is a typical Factor Analysis model. The solution of $\mathbf{j}$ can then be computed using the Principle Factor Analysis. The distribution of $\mathbf{j}$ can be easily estimated based on many repetitions of $\mathbf{j}$, computed from the Principle Factor Analyses.

3. SOLUTIONS

Here we consider the interesting case that $N > M$.

Solution 1. This solution ignores the unidentifiability problem when $N > M$ and simply constructs a "suitable" generalized inverse matrix of K. Since the columns of $\mathbf{K}$ span $\mathcal{R}^M$, there exists $\mathbf{p} \sim N(0, \mathbf{\Sigma}_p)$ such that $\epsilon = \mathbf{Kp}$. Define $\mathbf{s} = \mathbf{j} + \mathbf{p}$. We can rewrite the statistical model (**??**) as:

$$\mathbf{v} = \mathbf{Ks} \tag{3}$$

where $\mathbf{s} \sim N(\mathbf{\Theta}, \mathbf{\Sigma_s})$ and $\mathbf{\Sigma_s} = \mathbf{\Sigma_j} + \mathbf{\Sigma_p}$. Thus, $\mathbf{v} \sim N(\mathbf{K\Theta}, \mathbf{\Sigma_v})$ with $\mathbf{\Sigma_v} = \mathbf{K\Sigma_s K^T}$. A simple estimator of $\mathbf{\Theta}$ is of the form

$$\hat{\mathbf{\Theta}} = \mathbf{K}^{+}\mathbf{v} \tag{4}$$

where $\mathbf{K}^{+}$ is an appropriate $N \times M$ generalized inverse matrix of $\mathbf{K}$. A typical example is

$$\mathbf{K}^{+} = \mathbf{W^{-1}K^T}(\mathbf{KW^{-1}K^T} + \mathbf{S_b})^{-1}$$

where $\mathbf{W}$ is an optional biasing matrix (e.g. the discrete Laplacian operator) and $\mathbf{S}_b$ is the background signal space covariance estimated in the absence of brain signals of interest. $\mathbf{S}_b$ represents the inherent correlation between the sensors imposed by the physical medium.

The estimator $\hat{\mathbf{\Theta}}$ has an N-dimensional singular normal distribution with mean vector $\mathbf{K}^{+}\mathbf{K\Theta}$ and singular covariance matrix $\mathbf{\Sigma}_{\hat{\mathbf{\Theta}}} = \mathbf{K}^{+}\mathbf{\Sigma_v}\mathbf{K}^{+\mathbf{T}}$. Since $\mathbf{K}^{+}\mathbf{K}$ is not equal to the identity matrix, $\hat{\mathbf{\Theta}}$ is a biased estimator of $\mathbf{\Theta} = (\theta_1, \ldots, \theta_N)$.

Solution 2. To solve the unidentifiability problem, we "impute" $\mathbf{v}$ values at each location $\mathbf{r}$ based on a spline model:

$$v(\mathbf{r}) = f(\mathbf{r}) + \eta(\mathbf{r}) \tag{5}$$

where f is the mean of the signal v, which can be approximated by a linear combination of spline basis functions, and that $\eta = v - f$ has zero mean and the same covariance as v. This idea is related to Shepp and Zhang (2000), and Bookstein (1997). Shepp and Zhang used Wavelets for fast functional magnetic resonance imaging and Bookstein applied thin spline basis for finding landmarks in a brain.

Specifically, we take $f(\mathbf{r}) = \mathbf{B}(\mathbf{r})^T\boldsymbol{\beta}$, where for each $\mathbf{r}$, $\mathbf{B}(\mathbf{r})$ is a $m \leq M$ dimensional known vector function (constructed from spline basis functions) and $\boldsymbol{\beta}$ is a m dimensional unknown vector. Based on *signals* at M locations, we have from (**??**) that

$$\mathbf{v} = \mathbf{B}\boldsymbol{\beta} + \boldsymbol{\eta}$$

where

$$\mathbf{B} = \begin{pmatrix} \mathbf{B}(\mathbf{r_1})^T \\ \ldots \\ \mathbf{B}(\mathbf{r}_M)^T \end{pmatrix}_{M \times m}, \quad \boldsymbol{\eta} = \begin{pmatrix} \eta_1 \\ \ldots \\ \eta_M \end{pmatrix}.$$

This leads to an estimate of $\boldsymbol{\beta}$ of the form $\hat{\boldsymbol{\beta}} = [\mathbf{B}^T\mathbf{W}^{-1}\mathbf{B}]^{-1}\mathbf{B}^T\mathbf{W}^{-1}\mathbf{v}$ and an estimate of $f(\mathbf{r})$ of the form

$$\hat{f}(\mathbf{r}) = \mathbf{B}(\mathbf{r})^T\hat{\boldsymbol{\beta}} = \mathbf{B}(\mathbf{r})^T[\mathbf{B}^T\mathbf{W}^{-1}\mathbf{B}]^{-1}\mathbf{B}^T\mathbf{W}^{-1}\mathbf{v}.$$

Since we can compute $\hat{f}(\mathbf{r})$ for every $\mathbf{r}$, we can then enlarge M in (**??**) to $M' > N$ by imputing additional v values and then solve for $\mathbf{j}$ based on the Principle Factor Analysis.

4. Significant Activity

To test for significant source activity at these N points of the brain, we consider the problem of testing null hypothesis concerning $\theta_1, \ldots, \theta_N$; or equivalently, we will obtain simultaneous confidence intervals for these θ_i's. A key idea in our procedure is *connect* $\theta_1, \ldots, \theta_N$ to a random field in a continuous domain in $\mathcal{R}^3$ (or $\mathcal{R}$ in 1d case) and then build simultaneous confidence intervals based on the ideas in Naiman (1986+), Sun (1993) and Worsley et al (2000) etc. Some tweaking is necessary to tailor these into specific domains, to accommodate the singularity in solution 1 and imputation in solution 2, and to consider response differences within individuals as well as within groups.

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RESUME

For the data from electro or magneto-encephalographic measurements, we are often interested in uncovering the distribution of currents within the neurons of brain. This is an ill-posed bioelectromagnetic inverse problem. In this talk, we present two solutions to the inverse problem and provide a new method for simultaneously comparing many responses to stimuli and background. Here the noises (to signals) may be inhomogeneous.

Un problme inverse bioelectromagnetique

En étudiant les données venant des mesures électro- ou magnéto-encéphalographiques, ou les courants dans les neurones du cerveau, nous sommes souvent intéressés par un problème inverse bioelectromagnetique mal-posé. Dans cette conférence, nous prsentons deux solutions au problème inverse et fournissons une nouvelle méthode pour comparer simultanément plusieurs réponses a des stimuli et bruits de fond. On admet ici des bruits qui ne sont pas homogènes par rapport aux signaux.