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Comparison of methods for optimal choice of the regularization parameter for linear electrical impedance tomography of brain function

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Abstract
Electrical impedance tomography has the potential to provide a portable non-invasive method for imaging brain function. Clinical data collection has largely been undertaken with time difference data and linear image reconstruction methods. The purpose of this work was to determine the best method for selecting the regularization parameter of the inverse procedure, using the specific application of evoked brain activity in neonatal babies as an exemplar. The solution error norm and image SNR for the L-curve (LC), discrepancy principle (DP), generalized cross validation (GCV) and unbiased predictive risk estimator (UPRE) selection methods were evaluated in simulated data using an anatomically accurate finite element method (FEM) of the neonatal head and impedance changes due to blood flow in the visual cortex recorded in vivo. For simulated data, LC, GCV and UPRE were equally best. In human data in four neonatal infants, no significant differences were found among selection methods. We recommend that GCV or LC be employed for reconstruction of human neonatal images, as UPRE requires an empirical estimate of the noise variance.

Keywords: electrical impedance tomography, regularization parameter, linear inverse problem

1. Introduction

1.1. Electrical impedance tomography of brain function
Electrical impedance tomography (EIT) is a portable non-invasive imaging technique that, by injecting current and measuring voltage at the boundary of the domain, or vice versa,
provides a volume conductivity map of the body. EIT for medical applications has been successfully employed to image gastric emptying (Mangall et al 1987), gastric acid secretion and lung ventilation (Metherall et al 1996, Harris et al 1988). Other potential applications include lung water detection, imaging breast cancer with EIT spectroscopy, using multiple frequencies (Ostermana et al 2000), detecting intraperitoneal fluid (Sadleir and Fox 2001), cerebral ischaemia (Holder 1992a, 1992b), or blood flow changes in the brain related to evoked activity (Tidswell et al 2001). Other applications have been reviewed in Brown (2001) and Holder (2005).

EIT of brain function could be based on one of the two major mechanisms: (1) fast brain activity, which occurs over milliseconds due to opening of ion channels during nerve action potentials or synaptic depolarization (Gilad et al 2004). (2) Slow changes over seconds or tens of seconds due to blood volume changes and cell swelling which occur in epilepsy, acute ischaemia and haemorrhage, or normal brain activity. Until now, most studies have recorded the latter slower and larger changes, as in EIT during evoked physiological activity, where a decrease of cortical impedance on the scalp is related to a decrease of regional cerebral blood volume (rCBV) in the stimulated cortical area (Ranck 1963).

Predominant impedance decreases of several per cent over seconds during functional activity have been observed in animal studies using intracortical (Adey and Didio 1962) or subdural (Holder et al 1996) electrodes, which are probably due to changes in blood volume. These results are in agreement with PET studies where increases of regional cerebral blood flow were seen during different brain stimulations (Mazziotta and Phelps 1984). In humans with recording with scalp electrodes, a finite element method (FEM) study found a decrease between one or two orders of magnitude less than this, for the effect of cerebrospinal fluid and skull will attenuate the changes (Horesh et al 2005). During visual stimulation on adults, an impedance decrease of 0.4% was observed with recording with scalp electrodes (Tidswell et al 2001). Although the raw scalp impedance changes were consistent, localization of conductivity changes in the reconstructed images was unsuccessful. Similar but slightly larger changes of about 1% have been recorded in neonates, which was probably due to lesser attenuation by the skull, which has a higher conductivity than adult skull because it is not calcified and is mainly formed by cartilaginous tissue (Tidswell 2002).

Applications have divided EIT into three different modes: absolute (static), dynamic and multifrequency imaging. Of these, absolute imaging, which aims for the recovery of absolute conductivity, is the most affected by systematic and experimental errors. When mismodelling errors are significant, but where there is no reference image, multifrequency imaging has been proposed in which changes across frequency are more significant than those given by static imaging (Holder 2005, chapter 4). For applications for which a reference image is available and for which the expected conductivity change is only of the order of a few per cent, dynamic imaging has been widely preferred. This is the case considered herein, for the application of dynamic EIT to epilepsy or assessment of brain development on newborn infants, for which a reference from an earlier time is available.

1.2. EIT forward model and image reconstruction algorithms

In contrast to hard field modalities, like CT or MRI, EIT is a soft field modality, because the applied current diffuses throughout the whole imaged object. The propagation of electrical fields therefore depends on the electrical properties of the whole domain, so that it is a priority to have an accurate model of the imaged object (Natterer 2001, Polydorides 2002). In EIT, a current of a few milliamperes is applied across a pair or several electrodes and the resulting voltage is recorded across other electrodes. Multiple combinations of electrodes are
recorded, usually serially, which usually provide a set of a few hundred independent voltage measurements that are nonlinearly related to the body conductivity.

Image reconstruction methods map boundary voltages into conductivity, for which the forward problem is first constructed with the use of a model of the imaged object; the boundary voltages are calculated for a given current injection and conductivity guess. This is achieved by solving Laplace’s equation. The potential drop across electrodes may also be modelled using complete electrode model (CEM) equations as the boundary condition (Isaacson et al 1990, Paulson et al 1992). For complex geometries like the human head, for which an analytical solution does not exist, this is usually done numerically, using a method such as the FEM. A generic mesh considering a four shell model has been used for EIT of brain function (Bagshaw et al 2003), obtained from a structural imaging technique like MRI or CT (Bayford et al 2001, Tizzard et al 2005). Recently, a FEM solution for anisotropic media has been proposed (Abascal et al 2007), and used to study the effect of modelling anisotropic conductivity on the forward and linearized inverse solutions for brain imaging (Abascal et al 2008). In this work, one assumes an isotropic medium.

Once a realistic model mapping conductivity into boundary voltages is achieved, conductivity can be then reconstructed using iterative methods (Arridge 1999), by linearly updating the conductivity at each step from the first derivatives or Jacobian of this map. Although theoretically there is a unique absolute conductivity that satisfies the boundary voltages (Kohn and Vogelius 1984, 1985, Sylvester and Uhlmann 1987), the nonlinearity, incomplete data due to partial sampling of the domain, and ill-posedness of the inverse problem, make boundary measurements more sensitive to boundary shape, electrode–skin contact impedance, electrode position errors and errors in the data than to conductivity [28].

Dynamic EIT based on time difference images has been widely used when a reference from an earlier time is available (Barber and Seagar 1987, Bagshaw et al 2003), as it reduced the effect of mismodelling errors and instrumentation noise (Holder 1993, chapter 4) (Barber and Brown 1988). Let \( \tilde{d} \in \mathbb{R}^m \) be a vector of the measured boundary voltage during the brain function stimulation period, \( \tilde{d}_{\text{ref}} \in \mathbb{R}^m \) the reference boundary voltage (in the absence of stimulation), where \( m \) is the number of measurements, and \( F(\tilde{x}) \in \mathbb{R}^m \) and \( F(\tilde{x}_0) \in \mathbb{R}^m \) be the respective voltages as predicted by the model for target and reference conductivities \( \tilde{x} \in \mathbb{R}^n \) and \( \tilde{x}_0 \in \mathbb{R}^n \), where \( n \) is the number of finite elements. The inverse problem in the dynamic mode can be formulated as the minimization of a least squares functional of the difference between the measured and model relative data plus a Tikhonov regularization term that penalizes large solution norms,

\[
\min_{\tilde{x}} \left\{ \frac{1}{2} \left\| \frac{F(\tilde{x}) - F(\tilde{x}_0)}{F(\tilde{x}_0)} - \frac{\tilde{d} - \tilde{d}_{\text{ref}}}{\tilde{d}_{\text{ref}}} \right\|_2^2 + \alpha \frac{1}{2} \left\| \tilde{x} - \tilde{x}_0 \right\|_2^2 \right\},
\]

where \( \alpha \) controls the amount of regularization and division by data is understood to be done measurement by measurement. This can be solved by using a nonlinear iterative approach (Arridge 1999, Schweiger and Arridge 2004, Horesh et al 2006).

### 1.3. Linear EIT image reconstruction approaches

For a conductivity change of a few per cent localized in the brain, the boundary data \( F(\tilde{x}) \) may be modelled by a linear approximation

\[
F(\tilde{x}) \simeq F(\tilde{x}_0) + \tilde{J}(\tilde{x}_0)(\tilde{x} - \tilde{x}_0),
\]
where $J \in \mathbb{R}^{m \times n}$ is the Jacobian and second-order terms have been neglected. Substitution of (2) into (1) leads to the linear inverse problem

$$\min_x \left\{ \frac{1}{2} \left\| \frac{\tilde{J}(\tilde{x}_0)}{F(\tilde{x}_0)} (\tilde{x} - \tilde{x}_0) \right\|^2_2 - \frac{\tilde{d} - \tilde{d}_{\text{ref}}}{\tilde{d}_{\text{ref}}} \right\} + \frac{\alpha}{2} \left\| x - \tilde{x}_0 \right\|^2_2. \tag{3}$$

The linear approximation (3) to (1) can be justified by comparison of the percentage error between the boundary data and the linear approximation (2) with the size of the relative data (see section 2.2). It can be solved by standard numerical methods with the regularization functional corresponding to a linear filter (Hansen 1992). Previous reconstruction of brain function data has been undertaken with truncated singular value decomposition (SVD), which corresponds to a low-pass step filter. In general many filtering or regularization techniques are possible, depending on our knowledge of the a priori information (Borsic 2002, Borden 2002).

Notation is simplified as $x = \tilde{x} - \tilde{x}_0$ for a change of conductivity, $d = \tilde{d} - \tilde{d}_{\text{ref}}$, and $J = \text{diag}(F(\tilde{x}_0)^{-1}) \tilde{J}$ for the so-called row normalized Jacobian. Solution to the linear inverse problem (3) is explained in the statistical framework as the maximum a posteriori (MAP) estimator (Vogel 2002, chapter 4), where the conductivity $x$ is assumed to be a random variable that follows a normal distribution centred at $x_0$ and with the covariance matrix $C_x \in \mathbb{R}^{n \times n}$, that is, $x \sim \mathcal{N}(x_0, C_x)$; and the boundary data $d \sim \mathcal{N}(Jx, C_\eta)$, where $\eta \in \mathbb{R}^m$ represents additive noise in the data, considered as a Gaussian random variable with mean zero and covariance matrix $C_\eta$. A generalized version of the linear inverse problem (3) is then given by

$$\min_x \left\{ \left\| Jx - d \right\|^2_{C^{-1}_\eta} + \alpha \left\| x - x_0 \right\|^2_{C^{-1}_x} \right\}. \tag{5}$$

Previous EIT applications have used a white noise model ($C_\eta = I$). Estimation of the off-diagonal components of the noise covariance requires a large number of measurements (Krzanowoski and Marriott 1994), or a robust procedure such as the shrinkage estimator (Schäfer and Strimmer 2005) or probabilistic principal component analysis (Tipping and Bishop 1999). A simpler model is to consider a diagonal covariance ($C_\eta$), for which difference data are divided by the mean of the baseline, which is equivalent to considering a diagonal covariance whose elements are the reciprocal of the data. With these assumptions, we may use the Tikhonov–Phillips solution for under-determined systems, which finds a minimizer to (5) given by

$$x_{\alpha} = J^+_\alpha d, \tag{6}$$

where $J^+_\alpha$ is the regularized Tikhonov inverse of $J$ given by

$$J^+_\alpha = J^T (JJ^T + \alpha I)^{-1}. \tag{7}$$

and depending on the selection of the regularization parameter $\alpha$.

Whatever the linearized filter is, one needs to select the filter truncation or its corresponding regularization parameter. Standard methods are divided into two types: those that require prior knowledge of the noise such as the discrepancy principle (DP), due to Morozov, or the unbiased predictive risk estimator (UPRE); others do not need a priori information such as the L-curve (LC) or generalized cross validation (GCV) (Wahba 1977, Vogel 2002, chapter 7). Other standard methods such as the quasi-optimality criterion can be found in Hansen (1992). For
Optimal choice of the regularization parameter for linear EIT of brain function

TSVD, a new method based on the mean-squared error (MSE) has been claimed to provide a better estimator in terms of the MSE and biases than the L-curve, which (over)stabilized ill-posed problems (Xu 1998). Iterative methods have been applied in other applications, which simultaneously converge to an optimum regularization parameter and regularized solution in a few steps; in image restoration, assuming white noise (Kang and Katsaggelos 1995); and in PET, based on iterative approximated computations of the L-curve (Kaufman and Neumaier 1996). A comparison of several regularization methods, for inverse helioseismology and 2D deconvolution, gave the best results, in decreasing order, for the LC, GCV, quasi-optimality and DP (Hanke and Hansen 1993). The authors emphasized, nevertheless, that their results were specific for their models, but were likely to differ for different inverse problems and other authors have confirmed the need for the comparison of selection methods for a specific application (Vogel 2002, chapter 7). In earlier experimental applications, the truncation level was chosen ad hoc by means of localization in phantom data (Tidswell et al 2001, Bagshaw et al 2003), and the authors suggested that an objective way of finding an optimum regularization parameter would be desirable (Bagshaw et al 2003). From a different perspective, although Hanke proved nonconvergence for the L-curve (Hansen and O’Leary 1993), Hansen (1992) suggested a distinguishable corner could be identified objectively for the L-curve, providing the noise followed a standard normal distribution. Otherwise, they suggested a general Gauss–Markov linear model for modelling a well-conditioned general covariance matrix of the noise (Zha and Hansen 1990).

1.4. Objective and study design

The goal in this paper is to establish the best choice for selecting the regularization parameter for linear EIT of brain function. Thus, we compared four methods: LC, GCV, UPRE and DP. The effect on image quality resulting from these methods were formally evaluated with respect to the particular clinical problem of imaging brain function in the neonatal head. As the skull is not calcified, it was assumed that the conductivity within the imaged region was homogeneous (Tidswell 2002). Images were reconstructed for computer simulated data and human neonatal data during a visual stimulus paradigm.

2. Methods

2.1. Model and forward solution

A realistic neonatal head-shaped FEM mesh of 36,000 tetrahedra was produced by segmentation of the outer surface of a neonatal MRI scan and meshing of the domain using IDEAS (Tizzard et al 2005) (figure 1). The forward solution was solved using a modified version (Horesh 2006, chapter 4, Horesh et al 2006) of the EIDORS-3D toolkit (Polydorides and Lionheart 2002), which modelled the CEM for the first-order tetrahedral finite elements, and provided boundary voltages and the Jacobian matrix. The Jacobian was computed assuming homogeneous conductivity as the product of the forward and adjoint fields (Polydorides and Lionheart 2002)

\[ \tilde{J} = - \int dV(\nabla u)^T \nabla u^* , \]

where \( u \) is the electrical voltage and \( u^* \) is the voltage solved by considering the measurement electrodes as current injecting electrodes (adjoint forward solution), and for simplicity we have assumed unit current.
Figure 1. A realistic neonatal head-shaped FEM mesh was created from a structural MRI scan of a neonate, segmented and meshed using IDEAS. Thanks to Andrew Tizzard, Middlesex University.

2.2. Image reconstruction

Justification of the linear approximation was done by comparison of the linear direct solution (6) to an iterative nonlinear reconstruction of (1) which produced no appreciable difference (results not shown). This can be seen by comparison of the percentage error between the boundary data and the linear approximation (2),

$$\frac{100 \left| F(\tilde{x}) - J(\tilde{x}_0)(\tilde{x} - \tilde{x}_0) \right|}{F(\tilde{x})},$$

with the size of the relative data (4) (as a percentage); this error was two orders of magnitude smaller than the size of the data where $\tilde{x}$ was the conductivity corresponding to 1% conductivity change in the occipital lobe with respect to a reference conductivity $\tilde{x}_0$ (figure 2).

The conductivity difference was reconstructed by the regularized Tikhonov solution (6) for 20 logarithmically equally spaced parameters $\alpha$, in the range $10^{-5}$ to $10^2$, that corresponded to a truncation level of 120 and 1 singular values. These different samples of $\alpha$ were used for the regularization parameter selection procedure described in the following section.

2.3. Computation of the selection method functionals

Selection method functionals were computed as follows (Vogel 2002, chapter 7). The GCV estimator minimized

$$\frac{1}{m} \left[ \frac{1}{m} \text{trace} \left( I - J J^T \right) \right]^2.$$

The LC is based on a plot of the solution norm $X = \|x_a\|_2^2$ versus the residual norm $Y = \|J x_a - d\|_2^2$. In principle, a trade off between fitting the data and regularization of
the solution provides a L-curve shaped graph whose corner corresponds to the optimum regularization parameter. First implemented regarding LS problems, the L-curve optimum corner can be obtained as the point on the curve with maximum curvature, where the curvature
\[ \kappa = \frac{\left(\log Y_\alpha\right)' - \left(\log X_\alpha\right)'}{\left(\left(\log Y_\alpha\right)'\right)^2 + \left(\left(\log X_\alpha\right)'\right)^2} \]

where prime (') means differentiation with respect to $\alpha$.

The DP estimator sought $x_\alpha$ that yielded an upper bound for the residual norm (Hansen 1992)

\[ \| J x_\alpha - d \|_2 \geq \| \eta \|_2, \]

where $\| \eta \|_2$ is the norm of the noise vector $\eta$.

The UPRE estimator minimized

\[ \frac{1}{m} \| J x_\alpha - d \|_2^2 + \frac{2\sigma^2}{m} \text{trace}(J J'_\alpha) - \sigma^2, \]

where $\sigma^2$ is the variance of the noise.

Estimates of the noise norm, for DP, and of the noise variance, for UPRE, are required. Let $\eta$ be the noise vector whose components follow $\eta_i \sim \mathcal{N}(0, \sigma_i^2)$, the estimation of the 2-norm $\| \eta \|_2$ is related to the measurement variance as

\[ E[\| \eta \|_2^2] = E[\eta_1^2 + \cdots + \eta_m^2] = \sum_{i=1}^m \sigma_i^2. \]

(13)

For simulated data, where $\eta$ was known, the noise norm was directly computed as $\| \eta \|_2^2 = \eta_1^2 + \cdots + \eta_m^2$; the noise variance was approximated from the noise norm, using (13), as the mean of the measurement variance

\[ \sigma^2 = \frac{1}{m} \sum_{i=1}^m \sigma_i^2 \simeq \frac{1}{m} \| \eta \|_2. \]

(14)
For real data, firstly, the variance of the \(i\)th measurement \(\sigma_i^2\) was estimated from the baseline period, and then the variance was approximated as the mean of the measurement variance; the noise norm was estimated from the variance by using the previous relation (14).

2.4. Data sets

2.4.1. Simulated data. Simulated difference data were employed for testing methods in the ideal case where the only difference between data and the model was additive noise. The situation of an impedance change due to increased blood volume in the occipital cortex of a neonate during visual evoked responses was simulated. Difference data were the subtraction between the data corresponding to a local conductivity perturbation and the data corresponding to homogeneous conductivity. A change in conductivity of 1% was simulated in the region of interest (RoI), here the visual cortex region, with radius 14% of the neonatal head axial diameter. The primary visual cortex, as fMRI indicates, has a volume in the range 8–14 cm\(^3\) (Andrews et al. 1997), which roughly corresponds to a range between 12% and 13% of the axial diameter of the adult head. It is located in the occipital part of the brain cortex at the height of the eyes.

Although we used only a diagonal covariance for the inverse problem, the forward problem was modelled with a full covariance matrix in order to provide a more realistic test. Let \(e\) be a pseudo-random vector (white noise) and \(C_\eta\) the covariance matrix, correlated noise was simulated as \(\eta = Be\), where \(B\), such that \(C_\eta = \text{cov}(\eta) = B^T B\), was determined here using the eigenvalue decomposition. White noise was computed by changing two parameters: five different states of a pseudo-random generator; and five different SNR in the range 2–20 dB, for each of the previous state. In total, there were 25 data sets. The general covariance matrix \(C_\eta\) was estimated from one of the neonatal data set period preceding the stimulation.

2.4.2. Neonatal data. Impedance measurements were acquired using the Mark 1b UCLH EIT system (Yerworth et al. 2002). It comprises a head box, set of electrodes, base unit and notebook PC. The head box containing the current source and multiplexer was connected by a 3 m lead to the base unit, which consisted of the power supply, measurement circuits and 8-bit microprocessor. The head box was attached to the neonate by a set of 21 silver/silver chloride EEG electrodes, of 1 cm diameter, whose positions were based on the 10–20 EEG electrode location protocol (Binnie et al. 1982). Individual measurements were made with four electrodes: two electrodes injected an alternating current of 5 mA at 38.4 KHz and two different ones to measure electrical impedance; 187 electrode combinations were collected in 0.25 s with the use of a multiplexer. Measurements, of tens of millivolts, were amplified to a range of \(\pm 5\) V, and then converted to a 12-bit digital signal by an analogue to digital converter. As fewer electrodes can be practically used on a neonatal head than in adults, a protocol of 21 electrodes (Tidswell 2002) was adapted from one previously employed with 31 electrodes (Bayford et al. 1996).

Neonates were recruited from the neonatal unit at University College London, being approved by the Joint UCL/UCLH Committees on the Ethics of Human Research (Tidswell 2002). They were exposed to a visual excitation using LED photic stimulation at 8 Hz (figure 3). The intensity of the flash produced was sufficient to be seen clearly through closed eyelids. Continuous recording during 12 min allowed 15 repetitions of the same experiment, where an experiment consisted of a stimulus period of 25 s in between two baseline periods of 20 s each. Each electrode combination was corrected for linear baseline drift and normalized to the initial value. Electrode combinations were eliminated when their standard deviation (SD) during the baseline exceeded the mean of the 10 largest measurements during the stimulus
period or if the mean SD of all measurements during baseline was larger than 1%. Before the reconstruction, each data set was averaged across experiment repetitions, and then averaged across the stimulus period. Consequently, the data for the reconstruction consisted of four data sets, where each one was a vector \( d \in \mathbb{R}^m \) with \( m \) electrode measurements corresponding to the normalized impedance averaged across experiments and stimulus period.

2.5. Comparison of methods

The different methods were evaluated in terms of the solution error norm, for simulated data, and in terms of the SNR of the largest change in the image, for neonatal data.

The solution error norm was computed as

\[
\| x_\alpha - x_{\text{true}} \|^2, \tag{15}
\]

where \( x_{\text{true}} \) was the simulated conductivity change and \( x_\alpha \) was the reconstructed conductivity change for each regularization parameter.

Image SNR was computed as the ratio between mean conductivity at full width half-maximum (FWHM), \( E[x_{\text{FWHM}}] \), for a manually identified peak, and the standard deviation of the background conductivity, \( \sigma(x_{\text{background}}) \), that is,

\[
\frac{E[x_{\text{FWHM}}] - E[x_{\text{background}}]}{\sigma(x_{\text{background}})}.
\]

For the statistical comparison, one way analysis of variance (ANOVA) was applied to 25 different noise vectors, for simulated data; four neonatal data sets; and the four predictors the LC, GCV, DP and UPRE against the dependent variable, the solution error norm for simulated data and the image SNR for neonatal data. In addition, a multicomparison test, Tukey’s honestly significant difference criterion, was employed to determine the rank of changes if significant. This was implemented as the ‘multcompare’ function in MATLAB (http://www.mathworks.com). Results are presented as mean \( \pm \) SD.

**Figure 3.** Neonate exposed to visual excitation using LED goggles with flash light of frequency 8 Hz. Thanks to Tom Tidswell, UCL.
Table 1. Solution error norm for simulated data.

<table>
<thead>
<tr>
<th>Method</th>
<th>Error Norm</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC</td>
<td>0.0898 ± 0.0003</td>
</tr>
<tr>
<td>GCV</td>
<td>0.0898 ± 0.0003</td>
</tr>
<tr>
<td>DP</td>
<td>0.0905 ± 0.0002</td>
</tr>
<tr>
<td>UPRE</td>
<td>0.0898 ± 0.0003</td>
</tr>
</tbody>
</table>

Table 2. SNR of the largest SNR of the largest change in the reconstructed images for neonatal data.

<table>
<thead>
<tr>
<th>Method</th>
<th>SNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>LC</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>GCV</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>DP</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>UPRE</td>
<td>4 ± 1</td>
</tr>
</tbody>
</table>

3. Results

First, for simulated data, the solution error norms were compared in order to verify that the selection methods converged to the optimum solution, under the influence of white noise. Then, the different methods for simulated and neonatal data were compared.

3.1. Example of results—simulated data with 100% white noise

In order to illustrate the method and results, we present the solution for a single data set for which 100% white noise has been added. The effects of continuously varying regularization are shown in figure 4. For small \( \alpha \), that is, little regularization, the residual norm was low (figure 4(b)), but the solution norm was large (figure 4(a)), which suggested that the solution was amplified by high-frequency noise components. In contrast, for large \( \alpha \), the solution was excessively smooth and the model poorly fitted the data. The four predictors were then computed in order to estimate the optimum regularization. The four predictors were computed as an estimate of an optimum trade off between fitting the noise and smoothing the solution. The LC, GCV and UPRE agreed on the prediction of the regularization parameter that corresponded to 37 singular values (figures 4(d)–(f)); DP estimated a cut off of 25 singular values (figure 4(g)). The LC curvature had a local maximum, which was present in other examples and had the potential to produce a misleading solution (figure 4(c)). The solution error norm minimized for 25 singular values (figure 4(h)), which, in this particular case, agreed with the DP and was closed to the LC, GCV and UPRE predictions.

Consequently, the four selection methods successfully predicted an optimum regularization parameter, among the given 20, in terms of minimizing the solution error norm.

3.2. Simulated data

The DP had a larger error while no difference was found among the other three methods (table 1) (reconstructed images for a particular data set in figure 5).

3.3. Neonatal data

On inspection, one image set presented the highest change over the visual cortex in the posterior part of the head; the others had dominant changes anteriorly over the frontal lobes (figure 6). No significant differences were found among methods for the four neonatal
data sets according to the SNR (table 2). Nevertheless, a qualitative comparison of images yielded specific differences among methods. The DP and UPRE provided smoother images...
Figure 4. (Continued.)

Figure 5. Sagital view, throughout the middle of the neonatal head, of the simulated conductivity change (first column) and the reconstructed conductivity images (rest of columns) for simulated data. This is a single example of SNR 1.8 dB out of the 25 simulations.

(columns 3 and 4 in figure 6), and LC and GCV gave similar images (columns 1 and 2 in figure 6).

4. Discussion

EIT of brain function has previously used a fixed regularization parameter for linear inversion. Here, we provided a methodology for optimizing the regularization parameter by comparing the LC, GCV, DP and UPRE methods. For simulated data, LC, GCV and UPRE were equally good in terms of minimizing the solution error norm. For real human neonatal data, there was no significant difference among any of the methods, presumably because of the variability across subjects. However, similar images were found between LC and GCV, and between DP and UPRE methods. Overall, therefore, selection of the regularization parameter yielded an optimum solution, but it was not possible to determine the best selection method from human data.
Selection of the regularization parameter relies on the assumption that the only difference between the model prediction and the data can be explained by a white noise distribution; therefore, we aimed to test the methods against deviation from a white distribution and real data, where other physiological activity is present. For simulated data, we tested whether all methods converged under the appropriate assumptions and coped with correlated noise. However, simulated correlated noise may have been biased to a specific correlation matrix, which was estimated from a particular neonatal data set.

Similarities between DP and UPRE images, for real data, may be due to the fact that both methods require a single estimate of the variance of the noise while measurements had different empirical variance estimates. Therefore, modelling of the off-diagonal elements of the covariance of the noise, which can be estimated with a robust method (Schäfer and Strimmer 2005, Tipping and Bishop 1999), may improve results.

Theoretically, UPRE has the best convergence and the LC lacks of convergence. In other published studies, the LC was found to be more robust to correlated errors than the GCV, while in this work the GCV and LC showed no differences. It was found that the GCV did not converge for correlated data (Wahba 1977); similar results were found for a low number of data sets (Karjalainen et al 1999). Moreover, a comparison of several regularization methods, for inverse helioseismology and 2D deconvolution, gave best results, in decreasing order, for the LC, GCV, quasi-optimality and DP (Hanke and Hansen 1993); where the performance of the DP agreed with our simulated study. Nevertheless, it was emphasized those results to be best for that specific model, yet likely to differ for different inverse problems.

In this work, one has assumed some simplifications in the model. A generic finite element mesh was used for reconstruction of all neonatal data. As the skull is not calcified, it was assumed that the conductivity within the imaged region was homogeneous (Tidswell 2002). In previous results on simulated and experimental tanks, it was found that considering a head-
shaped model distinguishing scalp, skull, cerebrospinal fluid, and skull had a significant effect in image quality, yet dynamic linear reconstruction with more simplistic conductivity models like homogeneous and spherical was possible (Tidswell et al 2001, Bagshaw et al 2003). The effect of other modelling inaccuracies, like mismodelling of electrodes and conductivities, has been assessed for brain imaging, being more relevant for applications such as stroke for which a time reference image is not available (Horesh 2006).

In the reconstruction of neonatal data, a predominant change was found over the frontal area rather than on the visual cortex. While there is possibility that other physiological mechanism are present, recent studies suggest that measurement accuracy and noise may be an issue caused by the small signal after shielding effect of the skull (Fabrizi et al 2006, 2007). In addition, anisotropy of the skull and scalp may decrease the signal further (Abascal et al 2008). Solved some of the measurement limitations, one expect that optimum regularization for a given model and data set would provide a significant improvement.

Given that no large differences were found among selection methods and the added complication for estimating the variance for UPRE, our recommendation for human scalp data in general, therefore, is to use the GCV or LC curve. However, this is based on this limited testing for neonatal visual evoked responses and a homogeneous head model, and so needs verification in other situations of current interest, such as in epilepsy or adult evoked response EIT, in which a four shell model (scalp, skull, cerebrospinal fluid and brain) is preferred.

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