A new general linear model (GLM) beamformer method is described for processing magnetoencephalography (MEG) data. A standard nonlinear beamformer is used to determine the time course of neuronal activation for each point in a predefined source space. A Hilbert transform gives the envelope of oscillatory activity at each location in any chosen frequency band (not necessary in the case of sustained (DC) fields), enabling the general linear model to be applied and a volumetric $T$ statistic image to be determined. The new method is illustrated by a two-source simulation (sustained field and 20 Hz) and is shown to provide accurate localization. The method is also shown to locate accurately the increasing and decreasing gamma activities to the temporal and frontal lobes, respectively, in the case of a scintillating scotoma. The new method brings the advantages of the general linear model to the analysis of MEG data and should prove useful for the localization of changing patterns of activity across all frequency ranges including DC (sustained fields).

Keywords: MEG; General linear model; Beamformer; Spatial filter; Cortical oscillatory power; Scintillating scotoma; ERD/ERS

Introduction

In recent years, beamformer techniques have been used to improve spatial localization in magnetoencephalography (MEG). See, for example, Dziwars et al. (2003), Gaetz and Cheyne (2003), Hashimoto et al. (2001a,b), Herdman et al. (2003), Hirata et al. (2002), Ibara et al. (2003), Ishii et al. (1999, 2002, 2003), Iwaki et al. (1999), Kamada et al. (1998), Ploner et al. (2002), Robinson and Vrba (1999), Robinson et al. (2002), Sekihara et al. (2001, 2002), Taniguchi et al. (2000), Ukai et al. (2002), van Drongelen et al. (1999), van Veen et al. (1997), Xiang et al. (2001, 2003), Hall et al. (2004), Hillebrand and Barnes (2003), Fawcett et al. (2004), and Furlong et al. (2004). In essence, a beamformer is a collection of spatial filters, each optimally tuned to a particular image voxel (Van Veen et al., 1997). Raw MEG data are projected through these spatial filters to obtain an estimate of electrical activity at each voxel. Some metric can then be applied to assess task-related change in electrical activity and, by applying it to all voxels, a spatial map of task-related change can be generated.

Typically, metrics comprise simple two-sample tests that compare the source power between predefined active and passive time–frequency windows (Barnes and Hillebrand, 2003; Vrba 2002). A widely used nonlinear beamformer method in MEG is synthetic aperture magnetometry (SAM) (Robinson and Vrba, 1999). SAM can be used to create statistical parametric maps (SPMs) showing the spatial distribution of cortical power change. This is achieved by integrating power in specified frequency bands over active and passive time windows. By subtracting source power in the passive time window from source power in the active time window and dividing the result by an estimate of noise magnitude, a pseudo $T$ statistic may be obtained (Robinson and Vrba, 1999; see also Discussion) for each vertex in a 3D lattice stretching across the source space. These pseudo-$T$ statistics can then be used to create 3D volumetric images of power change across the brain. This use of SAM has greatly enhanced the potential of MEG as a functional brain imaging technique. In addition, a recent SAM study (Singh et al., 2002) has demonstrated that a striking similarity exists between the spatial distribution of oscillatory power change and the fMRI BOLD response.

Despite these successes, simple two-sample tests do not allow for complex experimental designs where, for example, the hypothesis involves the covariation of oscillatory power with some physiological metric (such as galvanic skin response). Nor does it allow for investigation of covariant temporal behavior in different frequency bands (Friston, 2000). Also, despite recent reports (Forss et al., 2001; Lammertmann and Lutkenhoner, 2000) demonstrating that low-frequency sustained field effects are observable in MEG studies, spatially mapping such fields using
SAM has proved difficult. In this study, we generalize the beamformer methodology through application of the formalism of the general linear model (GLM) (Friston et al., 1996; Seber, 1977; Worsley and Friston, 1995). We demonstrate the method using simulations, showing that it can be used to obtain the spatial distribution of both low-frequency sustained fields as well as changes in oscillatory electrical activity. We go on to show the utility of the technique using experimental data through the identification of linear modulation in gamma oscillations in a scintillating scotoma study (Hall et al., 2004).

Theory

The nonlinear beamformer

The nonlinear beamformer approach requires that for any particular source location, the projected power must be minimized subject to the linear constraint that the filter maintains a unity passband at the location itself (Robinson and Vrba, 1999; Van Veen et al., 1997). Briefly, this involves the computation of data covariance over a predefined time–frequency window, known as the covariance window. The minimization of projected variance ensures the suppression of energy from all active sources at locations other than that selected, while the linear constraint ensures that energy arising from an active source at the location of interest will remain in the projected data. The nonlinear beamformer problem may be solved mathematically using the method of Lagrange multipliers. The choice of time–frequency covariance window completely determines the spatial filter or weight vector for any location (Barnes and Hillebrand, 2003). In this paper, we take the calculation of the weight vector as a given and investigate methods to statistically test the changes in electrical activity at each voxel as a result of stimulus presentation.

Mathematically, the electrical source strength \( y_h(t) \) at time \( t \) is given by:

\[
y_h(t) = W_y^T m(t)
\]

where \( W_y \) is the weight vector for location \( \theta \) and \( m(t) \) is the instantaneous column vector of field measurements at all MEG sensors at time \( t \). A single column vector of weights exists for each target voxel in the source space (i.e., the brain). By applying Eq. (1) to each instantaneous field measurement, it is possible to reconstruct a vector \( y_h \) giving estimated source strength at position \( \theta \) as a function of time. Time courses such as these are called virtual electrodes (VEs). Note however that this estimate contains a component of uncorrelated sensor noise whose amplitude increases with depth (Van Veen et al., 1997). Typically, this is factored out by taking a ratio of projected signal to projected noise (Robinson and Vrba, 1998; Van Veen et al., 1997). Application of the GLM renders this correction unnecessary (see Discussion).

The Hilbert transform and analytic signal

The key problem addressed in this paper is that of identifying known time–frequency signatures in virtual electrode data. To characterize the spatial distribution of these known patterns across the brain, a technique for identifying the modeled pattern at each virtual electrode \( y_h \) is required. This problem has been previously identified and solved in functional magnetic resonance imaging, and the most generally applicable method is the general linear model (GLM) (Worsley and Friston, 1995). The GLM allows its user to model temporal effects of interest that may occur in raw data. By doing this at each virtual electrode within the source space, the spatial distribution of such effects may be obtained. So, for example, if a sustained field effect was expected, one could model this as a Top-Hat function (defined mathematically as:

\[
f(t) = \begin{cases} 
0 & \text{if } t - A < - \tau/2 \\
1 & \text{if } - \tau/2 \leq t - A \leq \tau/2 \\
0 & \text{if } t - A > \tau/2
\end{cases}
\]

where \( \tau \) represents the width of the Top-Hat and \( A \) represents its temporal offset and assess its spatial distribution using the GLM. However, the application of the GLM to model effects at higher frequency (i.e., a gain or loss of oscillatory power in some frequency band of interest) is less clear. Because change in oscillatory power is generally time locked but not phase locked to an applied stimulus, it is difficult to model measured oscillatory behavior in a virtual electrode using the GLM. Such non-phase locked effects are far more suited to short-term Fourier and wavelet analyses (see Nikouline et al., 2000 or Furlong et al., 2004 for example). However, it is possible to use the GLM to model temporal modulation in oscillatory power in a frequency band of interest, the problem then being to ascertain an envelope of this modulation from the virtual electrode trace. For simple cases, this could be achieved by percentage synchronization and desynchronization calculations (see Pfurtscheller and Lopes da Silva, 1999); however, a more temporally resolved method of detecting such changes involves the use of the continuous Hilbert transform. The continuous Hilbert transform (Blackledge, 2003; Byron and Fuller, 1970) and associated analytic signal have previously been used to describe cortical synchronization and desynchronization in EEG (Clochon et al., 1996) and in other related areas (see Liang et al., 2000 for an example). Computation of the analytic signal for any given oscillatory signal will yield the envelope of the oscillatory activity. Such an envelope can then be modeled using the GLM.

We represent the time course of a single virtual electrode by \( y_h(t) \) dropping (for the purposes of this discussion) the vector notation previously introduced. The corresponding analytic signal \( z_h(t) \) is given by:

\[
z_h(t) = y_h(t) + iH(y_h(t))
\]

where \( H(y_h(t)) \) represents the Hilbert transform of \( y_h(t) \) and is given by:

\[
H(y_h(t)) = P \int_{-\infty}^{\infty} \frac{y_h(u)}{t - u} du
\]

\( P \) denotes the Cauchy principal value of the integral and is used to take account of the singularity at \( t = u \). This integral effectively represents a convolution of \( y_h(t) \) with \( 1/\pi t \). If \( F(y_h(t)) \) denotes the Fourier transform of \( y_h(t) \) and \( F(z_h(t)) \) denotes the Fourier transform of \( z_h(t) \), then

\[
F(z_h(t)) = F(y_h(t)) + iF(H(y_h(t)))
\]

Expressing \( H(y_h(t)) \) as a convolution:

\[
F(z_h(t)) = F(y_h(t)) + iF\left(\frac{y_h(t)}{\pi t}\right)
\]
The Fourier transform of $1/\tau t$ is $-i\text{sgn}(\omega)$, where

$$\text{sgn}(\omega) = \begin{cases} 1 & \text{if } \omega > 0 \\ 0 & \text{if } \omega = 0, \text{ thus} \\ -1 & \text{if } \omega < 0 \end{cases}$$

$$F(z(t)) = F(y(t))[1 + \text{sgn}(\omega)] \quad (7)$$

and so

$$F(z(t)) = \begin{cases} 2F(y(t)) & \text{if } \omega > 0 \\ F(y(t)) & \text{if } \omega = 0 \\ 0 & \text{if } \omega < 0 \end{cases} \quad (8)$$

The analytic signal may be obtained by inverse Fourier transformation of Eq. (8). The magnitude of the analytic signal is defined in Eq. (9) and gives the envelope of the measured activity in $y(t)$:

$$E(y(t)) = \sqrt{(y(t))^2 + (H(y(t)))^2} \quad (9)$$

In general, a single virtual electrode trace $y(t)$ (now written as a vector) may contain any number of independent oscillatory signals in various frequency bands (alpha, beta, etc.), each modulated in a different way. The application of a band pass filter followed by envelope detection using the Hilbert transform will yield an envelope showing this modulation of oscillatory power in the frequency band selected by the band pass filter. This low frequency envelope can then be mapped spatially using the GLM. Thus, in this context, the Hilbert transform can be thought of as a mathematical tool to convert oscillatory activity into a simple sustained effect such that it can be modeled using the GLM.

Application of the general linear model

The GLM beamformer method to be described is based on that of Worsley and Friston (1995) which when applied to the envelope of any one virtual electrode $E(y(t))$ states that:

$$E(y(t)) = G\beta + e \quad (10)$$

where $G$ is the design matrix, which contains a single column for each temporal effect modeled. These effects can include expected temporal modulation of a frequency band of interest as well as any predictable confounding effects. The vector $\beta$ comprises a single parameter representing the magnitude of each of the modeled effects. The vector $e$ represents deviations from the model caused by scanner or physiological noise that cannot be incorporated into the model (i.e., random noise). In the special case of the effect of interest being a sustained field and not an oscillatory response, the application of the Hilbert transform is irrelevant and $E(y(t))$ in Eq. (10) and all subsequent equations should be replaced with $y(t)$.

In using the GLM, it is assumed that elements of $e$ are unbiased, have constant variance, are uncorrelated, and follow a Gaussian distribution (Seber, 1977). However, confounding effects may exist in MEG data that do not meet with these assumptions. These confounding effects consist of aspects of spontaneous brain activity that can cause noise autocorrelation after projection through the beamformer. Common MEG artifacts such as eye blinks, cardiovascular, respiration, and muscular effects from the body as well as noise from the local environment should be suppressed by the beamformer because they do not originate from the source space. However, some of these effects may leak through the spatial filter, again causing autocorrelation in virtual electrode data. Such effects cause the elements of the vector $e$ to become correlated such that application of the GLM becomes impractical. This problem has again been identified and solved in fMRI, as the simplest solution involving application of a temporal smoothing kernel (Worsley and Friston, 1995). In general, temporal autocorrelation is not thought to be as great a problem in MEG as in fMRI, as MEG provides a direct measure of neural activity. However, application of a temporal filter to MEG data produces a known autocorrelation and hence allows for the accurate prediction of the degrees of freedom in the smoothed $E(y(t))$. This is a great advantage, particularly in the spatial characterization of low frequency effects, as it enables calculation of the statistical quantities associated with the GLM.

To perform temporal smoothing, a Gaussian smoothing kernel was designed of the form:

$$F(t) = \frac{1}{\sigma \sqrt{2\pi}} e^{-t^2/2\sigma^2} \quad (11)$$

where $\sigma$ represents the width of the smoothing kernel and is chosen based on the temporal scale of the modeled effects. It can be thought of as a low pass filter, but in the GLM is applied as a convolution in time using a convolution matrix $K$, whose rows represent temporally shifted versions of the smoothing kernel (Eq. (11)). After filtering, Eq. (10) becomes:

$$K E(y(t)) = G^* \beta + e \quad (12)$$

where $G^* = KG$ and represents the smoothed design matrix. $e = KE$ and represents the residual error between the model and the smoothed data. The GLM can now be applied as described in Worsley and Friston (1995) to compute $b_0$, an estimator of $\beta$ where:

$$b_0 = (G^* G^*)^{-1} G^* K E(y(t)) \quad (13)$$

The appropriate parameter in vector $b_0$ is used, together with its associated variance (Seber, 1977), to produce a single $T$ statistic for each voxel. So for example, if we wish to spatially map the effect modeled by the $i$th column of the design matrix, then

$$T = \frac{b_0(i)}{\sqrt{\text{var}(b_0(i, i))}} \quad (14)$$

where

$$\text{var}(b_0) = \tilde{\sigma}^2 \left( (G^* G^*)^{-1} G^* VG^*(G^* G^*)^{-1} \right)$$

if $V = K K^T$ and

$$\tilde{\sigma}^2 = \frac{r^2}{\text{trace}(RV)} \quad (16)$$

where $r = R K E(y(t))$ is a vector of residuals derived using the residual forming matrix $R = I - G^* G^* G^* - I$ and $I$ is the identity matrix. (For a complete description of this method, see Worsley and Friston, 1995.) $T$ scores calculated using Eq. (14) can indicate the presence or absence of any effect encompassed within the design matrix. By applying this technique to all virtual electrodes in the volume of interest, a statistical parametric map can be made showing the spatial distribution of the effect modeled.
Methods

Simulation of data

Initially, simulated data were used to examine the accuracy of the GLM beamformer method. For all simulations, the third order gradiometer configuration of a 151 channel Omega system (CTF Systems Inc., Port Coquitlam, Canada) was used. The source space was based on a subject’s head shape measured from an anatomical MRI scan. Two separate sources were positioned on the cortical surface, which had also been extracted from the subject’s anatomical MRI scan. The orientation of each source was defined to be perpendicular to the local cortical surface; positions were chosen pseudo-randomly and independently and are shown in Fig. 2A. The sources were dipolar, of strength 2 nAm, with additive uncorrelated noise of amplitude 1 nAm. For the solution to the forward problem, the best fitting sphere to the subject’s head shape was used as a volume conductor model. The forward solution itself was based on the derivation by Sarvas (1987). Ten epochs of data were created for both sources, each epoch being 2 s long, and comprising 0.5 s baseline followed by 1.1 s activation and a further 0.4 s baseline. The first source was a Top-Hat function (see Eq. (2) where for a single epoch $\tau = 1.1$ s and $\Delta = 1.05$ s). The second source was a sinusoid of 20 Hz, modulated by a Top-Hat function (where again for a single epoch $\tau = 1.1$ s and $\Delta = 1.05$ s). White noise was added to the simulated data at each MEG sensor.

![Diagram](image-url)

**Fig. 1.** Schematic showing the steps involved in the GLM beamformer methodology.
with an rms amplitude of 90 fT (10 fT/√Hz with an 81-Hz bandwidth).

The covariance window and band pass filtering

The application of the GLM beamformer method requires the choice of a time–frequency covariance window over which the weight vectors are calculated. The use of a large covariance window is advantageous because it minimizes the problem of suppression of correlated sources commonly associated with beamformer techniques (Barnes and Hillebrand, 2003; Van Veen et al., 1997) (because the sources are less likely to remain correlated over a larger temporal window). For this reason, weight vectors should ideally be calculated over a covariance window encompassing all time samples and as large a frequency window as possible. The choice of covariance window should not be confused with the choice of frequency band over which the Hilbert transform and GLM are applied. Choice of this second window can be made based on the expected activation (i.e., for experimental data, one may choose the alpha band, beta band, and so on). In practice, the choice of frequency band used in the covariance window and the band pass filter are matched. This is so that the rms noise levels are consistent for both the calculation of the weights vector and application of the GLM. This has the unfortunate effect of narrowing the covariance window (in frequency) and increasing the risk of suppression of correlated sources, thus effectively introducing a trade off between frequency sensitivity and source suppression. However, because the covariance window still encompasses all time samples, source correlation is minimized and is thus not thought to represent a major limitation to the method. The choice of pass band is trivial for simulated data because both sources lie at known frequencies. Two frequency bands were used for both the covariance window and band pass filter (0–2 and 18–22 Hz), each encompassing a single source. The detection algorithm is described below and shown schematically in Fig. 1.

Source detection

The source space was divided into a regular 3D cubic grid of 0.5 cm side length (Fig. 1A). A nonlinear beamformer using optimal source orientation (in the tangential plane) was used to create the lead field for each position in the source space. These lead fields were then used together with the MEG data, filtered using the covariance window, in the calculation of the weight vectors \( \mathbf{w}_g \). The best fitting sphere to the subject’s head shape (defined using the anatomical MRI) was used as a volume conductor model in the forward solution to be consistent with the data simulation.

After calculation of the weight vectors, the raw MEG data were band pass filtered using a second order Butterworth filter to retain only the frequency band of interest (Fig. 1B). Note that, to save computational time, this can be done before the construction of virtual electrodes because it is a linear operation, as is the projection of data through the weight vectors. The choice of the filter itself is not critical; a simple band pass filter can be used although ringing may be a problem for narrow pass bands. A zero-phase filter may also be used to construct a set of virtual electrodes (Fig. 1C), one for each voxel in the source space. For the oscillatory (20 Hz) signal, the magnitude of the analytic signal, defined using the Hilbert transform, was taken for each virtual electrode to give the envelope of observed oscillatory activity in the frequency band of interest (Fig. 1D). For the case of our sustained field (Top-Hat function), the application of the Hilbert transform was not necessary and so was omitted. The convolution matrix was then applied \((\sigma = 0.3 \text{ s})\) as per Eq. (12) to smooth temporally the Hilbert transformed data in the case of the 20-Hz source and the virtual electrode data in the case of the sustained field (Fig. 1E). A design matrix was constructed with the effect of interest modeled by a simple Top-Hat function (identical to that used for simulation of the Top-Hat source), smoothed as per the filter in Eq. (11). The design matrix was fitted to both the Hilbert transformed data (in the case of the 20-Hz source) and the virtual electrode data (in the case of the sustained field) (Fig. 1F). Volumetric images of \( T \) scores were determined as per Eq. (14) and thresholded for display at an uncorrected \( P \) value of 0.001.

Statistical testing of the GLM beamformer method

To demonstrate that the methodology developed results in a statistically valid test, that is, given the case where no signal is present at a virtual electrode, the false-positive rate is equal to or below the chosen significance level over many realizations, a Monte Carlo simulation was used. For 10 different \( P \) values (0.01 through 0.1 in steps of 0.01), 1000 virtual electrodes consisting of Gaussian random data were modeled. Because the projection of raw MEG data through the weights vector is linear, this is equivalent to creating 1000 sets of raw MEG data and projecting each of them through the same weights vector. Each modeled virtual electrode was band pass filtered using a 2nd order Butterworth filter with an 18- to 22-Hz pass band, and the Hilbert transform was then taken to obtain the analytic signal, which was smoothed using a Gaussian temporal smoothing kernel \((\sigma = 0.3)\). The GLM was used to fit a Top-Hat function to the filtered, transformed, smoothed, random data. For each of the 1000 iterations of this process, the total number of resulting \( T \) statistics that corresponded to a \( P \) value equal to or less than the selected threshold was counted and the percentage of false positives plotted against the \( P \) threshold.

Collection and analysis of experimental data

The experimental data were recorded using a 151-channel Omega system (CTF Systems Inc.) with a third order
gradiometer configuration and a sample rate of 625 Hz. The recording was taken continuously over a 20-min period from a patient experiencing a scintillating scotoma, a visual disturbance associated with migraine first described by Hubert Airy in 1854. These data were previously presented as a MEG case study (Hall et al., 2004) but are used here to illustrate the application of the GLM beamformer technique. For this purpose, only the final 400 s of the data was used, during which a strong increase in gamma band activity was noted in the temporal lobe that was coupled to decreasing gamma activity in the frontal lobe (Hall et al., 2004).

As with the simulated data, the source space was divided into a regular 3D cubic grid of 0.5 cm side. A weight vector \( \mathbf{W}_b \) was calculated for each vertex of the grid using the nonlinear beamformer technique and a covariance window encompassing the full duration and frequency window of 50–60 Hz. Hall et al. (2004) examined gamma band (30–200 Hz) activity, finding a peak in the range 50–60 Hz. This frequency window was therefore chosen to gain maximum signal sensitivity to the effect of interest while still keeping the duration over which the weight vector was calculated as wide as possible to minimize correlation effects. For accurate localization of the effect, a multiple sphere head model was taken as a volume conductor (Huang et al., 1999). Before calculation of the weight vector, all data were frequency filtered between 50 and 60 Hz using a second-order Butterworth filter to obtain maximum sensitivity to the gamma frequency band and to be consistent with the selected covariance window. The frequency-filtered data were projected through the spatial filter and the envelope of activity in this band determined using the Hilbert transform. To remove high frequency noise, the envelope was smoothed using a Gaussian smoothing kernel \( \sigma = 4 \) s.

Previously published results (Hall et al., 2004) have shown that both the increase in gamma activity in the temporal lobe and the decrease in gamma activity in the frontal lobe are, to a first approximation, linear. For this reason, the envelope of these gamma band effects was modeled using a simple straight line in the design matrix. This is represented by Eq. (17), which refers to a single virtual electrode and is a specific case of Eq. (10). (In Eq. (17), the location subscript \( \theta \) has been omitted for clarity.)

\[
\begin{bmatrix}
y_1 \\
y_2 \\
\vdots \\
y_N 
\end{bmatrix} = \begin{bmatrix} t_1 & 1 \\
t_2 & 1 \\
\vdots & \vdots \\
t_N & 1 
\end{bmatrix} \begin{bmatrix} \beta_1 \\
\beta_2 \\
\vdots \\
\beta_N 
\end{bmatrix} + \begin{bmatrix} e_1 \\
e_2 \\
\vdots \\
e_N 
\end{bmatrix}
\] (17)

Here, \( y_i \) represents the data and \( t_i \) represents time. The gradient of the straight line representing a linear increase in gamma band activity is given by the unknown parameter \( \beta_1 \) and the ‘steady state’ activity by \( \beta_2 \). Using Eq. (13), estimates of the unknown parameters were obtained \( (b_1 \) and \( b_2 \)), a \( T \) statistic was defined based on the gradient of the straight line for each voxel in the source space using Eq. (14), and a \( T \) statistical volumetric image was constructed and thresholded using an uncorrected \( P \) value of 0.001 to show focal areas of maximal effect. To confirm the accuracy of the GLM beamformer technique, this volumetric image may be compared to the original image produced by Hall et al. (2004) using the standard nonlinear beamformer implementation (Robinson and Vrba, 1999). Virtual electrodes were also constructed for areas of interest to show the temporal effect located by the GLM beamformer method.

**Results**

Fig. 2B shows the localization of the simulated DC source using the GLM beamformer method. The green marker shows the position of the Top-Hat source. The red overlay shows the volumetric \( T \) statistic image. The discrepancy between the peak of the volumetric image and the actual source position was found to be \( 9.7 \pm 5 \) mm. Fig. 2C shows the localization of the 20-Hz source. Again, the green marker shows the position of the 20-Hz source and the red overlay shows the corresponding volumetric \( T \) statistic image. In this case, the discrepancy between the peak position and the actual source was found to be \( 3.4 \pm 5 \) mm. To determine the size of the localization errors with respect to the maximal possible resolution of the beamformer (for this data set), we assessed the intrinsic smoothness of the beamformer due to the correlations between neighboring weight vectors (Barnes and Hillebrand, 2003). We found the FWHM of the DC and 20-Hz peaks to be 27.0 and 13.8 mm, respectively. These values are determined purely by the weights (and hence data covariance) and are independent of any subsequent GLM statistical manipulation. That is, the discrepancies observed between simulated and reconstructed source locations are of the same order as the intrinsic image smoothness in these regions. Judicious selection of the width of both covariance and band pass filter windows would enable these errors in peak location to be reduced.

Fig. 3 compares the simulated sources and the time courses of the virtual electrodes corresponding to the maxima of the volumetric \( T \) statistic images. Fig. 3A shows the simulated Top-Hat source time course averaged across all 10 trials; Fig. 3B shows the associated virtual electrode time course, again averaged across trials. Fig. 3C gives the average time course of the envelope of the simulated 20-Hz source and Fig. 3D shows the associated envelope of the 15- to 25-Hz virtual electrode signal. The envelopes for both the simulated source (Fig. 3C) and virtual electrode (Fig. 3D) were obtained by band pass filtering the associated time course (15–25 Hz using a second-order Butterworth filter) and computing the trial averaged analytic signal. Note that the raw 20-Hz signal cannot be shown as it is non-phase locked, and thus cannot be averaged across trials. (The noise added to the simulated data is such that the 20-Hz carrier is not visible in a single trial.) These plots show the strong temporal agreement between the simulated dipole time courses and the virtual electrode trace obtained using the GLM beamformer.

Fig. 4 shows the result of the Monte Carlo simulations. The data points show the relationship between the percentage of false positives and \( P \) threshold derived from the Monte Carlo simulations. The solid line shows the theoretically expected relationship. There is good agreement between the theoretical and experimental results (given the limitations of the Monte Carlo test), implying that the GLM beamformer method can provide accurate and valid statistical results.

Fig. 5 shows the volumetric \( T \) statistic image for the experimental data, showing localization of changes in gamma band activity. Increasing gamma activity is shown in red and occurs in the temporal lobe. Decreasing gamma activity is shown in blue and occurs in the frontal lobe. Both effects are associated with the scintillating scotoma (Hall et al., 2004). To confirm the success of
the technique using experimental data, virtual electrodes were placed at the peak of the activation foci and the non-normalized time courses of these electrodes are plotted in the figure together with the 3D rendered image. The locations of the maxima of the increase and decrease of gamma band activity as defined here agree closely with those published in the original study (Hall et al., 2004).

Discussion

The GLM beamformer method that we describe is accurate in a wide variety of applications, however because the method rests heavily on the nonlinear beamformer, the problems intrinsic to such techniques are still present in our approach. In particular, it has been shown (Van Veen et al., 1997) that use of the beamformer technique causes spatially separate but covariant sources to be suppressed. However, using a larger time window means that there is less chance of covariance between source time courses, and so this effect can be minimized by calculating the covariance matrix over a large temporal window (Barnes and Hillebrand, 2003). Uncorrelated sensor noise is projected nonuniformly throughout the source space such that noise increases with increasing depth into the brain (Van Veen et al., 1997). In the original implementation of the linearly constrained minimum variance (LCMV) beamformer technique (Van Veen et al., 1997), these nonuniform noise distributions were corrected by dividing the projected source power by an estimate of projected noise power to give a ‘neural activity index’ (Van Veen et al., 1997) or ‘pseudo-z-statistic’ (Robinson and Vrba, 1999). In the GLM beamformer method, no such noise correction is required. This is because, due to the unity pass band constraint employed by the beamformer, source amplitude in any given virtual electrode will be correct, despite the noise scaling with virtual electrode position. The $T$ statistical maps presented are derived using Eq. (14), where the numerator is representative of the amplitude of the modeled effect and the denominator is representative of the residuals left over after subtracting the model from the data. For these reasons, the

Fig. 3. The temporal correspondence of the simulated sources and the virtual electrode time courses for an averaged epoch. (A) The simulated Top-Hat source time course averaged over 10 trials. (B) The associated virtual electrode time course taken from the maximum in the volumetric $T$ statistic image and averaged over 10 trials. (C) The time course of the envelope of the simulated 20-Hz source averaged over 10 trials. The envelope was taken by band pass filtering the source time course (15–25 Hz using a second order Butterworth filter) and computing the trial averaged analytic signal. (D) The associated envelope of the 15- to 25-Hz signal measured in a virtual electrode placed at the maximum in the volumetric $T$ statistic image. Again, the envelope was taken by band pass filtering the source time course (15–25 Hz using a second order Butterworth filter) and computing the trial averaged analytic signal.

Fig. 4. The percentage false-positive count plotted against $P$ threshold. Results from the Monte Carlo simulation (circular data points) compared to the theory (solid line).
numerator will only be non-zero when the effect of interest is present at a given virtual electrode site, and hence noise correction is not a requirement for accurate localization (in practice, it can be shown that noise correction has no effect on $T$ statistical probability maps). The residuals in the denominator will scale with noise amplitude, and therefore position within the source space. As a consequence, given a series of uniformly distributed sources, the GLM beamformer technique would be less sensitive to deep sources than to shallow sources. This is an intrinsic problem associated with MEG itself, not the beamformer methodology, and reflects the increased detectability, and hence statistical significance of shallow sources (Hillebrand and Barnes, 2002).

The GLM beamformer method generates a $T$ statistic image that enables statistical quantities associated with the GLM to be calculated (e.g., a $P$ value may be derived for each image voxel). The derivation of these statistical quantities involves consideration of the temporal smoothing applied to the data via the convolution matrix $K$. As stated above, the number of degrees of freedom in a vector time series is dependent on the degree of autocorrelation in that time series. The application of a band pass filter coupled with the use of the Hilbert transform and analytic signal increases the degree of autocorrelation in the data and therefore reduces the degrees of freedom. If the value of $\sigma$ (the width of the Gaussian smoothing kernel) is not sufficiently large, the application of the temporal filter may have no effect on the degree of autocorrelation in the analytic signal. If this were the case, the degrees of freedom, predicted using only the temporal smoothing kernel, would be overestimated leading to artificially small $P$ values and an increase in the false-positive rate above that expected from the $P$ threshold.

$T$ statistics calculated using the GLM beamformer method refer only to the voxel (or virtual electrode) in question and in the current study uncorrected $P$ values are quoted. The problems inherent to the uncorrected $P$ value are apparent in Fig. 2C, where a single false peak is observed forward of the genuine 20-Hz peak. The maximum $T$ score in the false peak is less than that in the

Fig. 5. Spatial localization of the temporal effects associated with a scintillating scotoma. A linear increase in gamma band activity in the temporal lobe identified using the GLM beamformer method is shown in red. A linear decrease in gamma band activity in the frontal lobe is shown in blue. The image has been thresholded at an uncorrected $P$ value of 0.001 (78 degrees of freedom). Virtual electrode traces from the foci of maximum linear increase and decrease in gamma band activity are also shown.
genuine peak and thus could be eliminated simply by decreasing the $P$ threshold of the image. To avoid such problems, the ideal solution would be to calculate a corrected $P$ value. However, the inherent smoothness in the beamformer image rules out a simple Bonferroni correction (i.e., dividing the $P$ threshold by the number of virtual electrodes) because the number of spatial degrees of freedom is unknown. For these reasons, other methods are required if a corrected $P$ value is to be applied and false positives eliminated. For single subjects, Barnes and Hillebrand (2003) have outlined a method based on the assessment of spatial smoothness that can be used to correct for multiple comparisons across a volume. This method could be readily applied to the GLM beamformer technique. Alternatively, Singh et al. (2003) have outlined nonparametric statistical methods with which to develop robust, multiple comparison-corrected, group statistics. Again, this method could also be readily applied to the GLM beamformer technique to look at statistical significance of modeled effects across a group. We anticipate that the GLM beamformer method, when used in conjunction with such techniques to obtain corrected $P$ values, will enable the design of more complex experiments in MEG, allowing for the detection of multiple effects of interest, paralleling studies already undertaken using PET and fMRI. A simple method for achieving this is by construction of contrast of parameter estimates (Worsley and Friston, 1995). Such contrasts may be used to test differential effects or interactions between any number of experimental conditions or independent components described in the GLM design matrix.

**Conclusion**

The GLM beamformer method that we introduce in this paper shows how the Hilbert transform and general linear model can be applied to MEG beamformer data to identify the spatial distribution of known temporal effects. Our initial simulation demonstrates the accuracy of the technique locating low-frequency effects that are time and phase locked to external stimuli. Potentially, the GLM beamformer method can therefore be used to locate the auditory sustained field (Lammertmann and Lutkenhoner, 2001) or the sustained electrical effects that have been noted in somatosensory cortex (Forss et al., 2001). The 20-Hz source simulation shows that time locked but non-phase locked event-related synchronization (ERS) or desynchronisation (ERD) (Pfurtscheller and Lopes da Silva, 1999) can also be localized using the GLM beamformer method. This may be put to use in the identification of areas of ERD/ERS if specific modulation of the oscillatory effects is present. The success of the GLM beamformer method in finding both the temporal and frontal lobe sources in the scintillating scotoma study confirms its accuracy and sensitivity in an experimental situation and suggests that it will prove a useful method for the localization of changing patterns of both sustained activity (DC effects) and oscillatory phenomena.

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**References**


