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Spatial Resolution and the Neural Correlates of Sensory Experience

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Abstract Freeman and Baird [5; Freeman WJ, Baird B. Behav Neurosci 1987;101:393–408] recorded from the surface of the brain in waking rabbits and found spatial patterns of voltage that covaried with sensory experience. We simulate mathematically the electric fields produced by radial dipoles in cortical gyri and show that patterns with the spatial frequencies observed by Freeman and Baird could be produced by cortical dipoles spaced 3 mm apart. We further calculate that to resolve the patterns produced by such dipole arrays, it is necessary to record less than 2.5 mm above the surface of the cortex. High-pass spatial filters increase this distance to 4.5 mm. Since the human scalp is 15–16 mm above the brain, we conclude that spatial patterns of voltage covarying with sensation are unlikely to be detectable in scalp records. If such patterns do exist in humans, dural or sub-dural electrode arrays, with an inter-electrode spacing of 1 mm or less, will be necessary to record them.

Keywords Neural correlates of consciousness · Spatial resolution · EEG · ECoG · Sensory experience

Introduction

The question of what methodology to use when searching for the neural correlates of conscious sensation is a vexed one. Some investigators feel that single cell recording is the way to go, in some cases concentrating on the pattern of activity over a large number of single cells (e.g. [2, 14]). These approaches have had some success. Both electromagnetic and imaging measurements on a much larger spatial scale have also produced correlations between reported sensation and neural activity (e.g. [17]; for review see Ref. [15]). However, it is probably fair to say that to date, no consensus has been reached on a particular kind or pattern of neural activity which can be said to constitute the neural correlate of consciousness.

One view which has so far not received much attention is that, rather than looking for patterns on either a microscopic or a macroscopic spatial scale, it might be more productive to look for mesoscopic [3] patterns [13]. Some empirical support for this view is provided by a series of seminal papers from Walter Freeman and colleagues [4–7]. These papers show that it is possible to tell whether or not a rabbit is experiencing a particular olfactory, auditory or visual sensation by examining, on a mesoscopic scale, the spatial pattern of voltage recorded at an array of electrodes on the surface of the rabbit's brain. While the authors of this work never claim that the patterns they observe constitute neural correlates of consciousness (NCC), it seems a good bet that such patterns may at least stand in some lawful relationship with NCCs. Thus it is likely that interesting results will come from a repetition of Freeman's experiments using human subjects.

However, while it is relatively easy to record from grids on the surface of the brain in rabbits, there are considerable ethical and logistic difficulties associated with recording from the surface of the awake human brain. It would be much easier if the patterns in question could be recorded non-invasively, from the scalp. In the present paper we assume for the sake of argument that patterns like those recorded by Freeman and Baird [5] do exist in humans, and ask whether or not it would be possible to record them from the scalp.

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Materials and methods

The general approach adopted was to proceed in stages, as follows:

(1) A mathematical model was constructed to describe the electric potentials produced by dipoles of appropriate size and orientation to represent columns of pyramidal cells in the cerebral cortex (Kandel et al. 1991), as recorded by a linear electrode array on the surface of the brain.
(2) The mathematical model was validated using actual recordings of potentials generated by known dipoles in a homogeneous medium with conductivity similar to that of brain.
(3) The validated model was interrogated to determine what sort of dipole separation would produce patterns with the spatial frequency recorded by Freeman and colleagues (approximately 0.2 cycles/mm).
(4) The model was further interrogated to determine how far above arrays of dipoles with this separation one could record and still resolve the spatial pattern seen in records taken immediately above the dipoles.

Mathematical modelling

We chose initially to use a very simplified ‘‘flat-head’’ model, which treats the head–air interface as a planar surface rather than a spherical or more complicated, realistically curved surface. We did this because simple analytical solutions could then be employed, and the essential features bearing on resolution of dipole sources could be clearly exemplified. Since the depth of dipoles below the surface in our model was approximately 15 mm, which is considerably less than the approximate radius of the head (100 mm), it seemed likely that the ‘‘flat-head’’ model would be a reasonable approximation to actual conditions. In the event, the results this simple model produced with regard to dipole resolution were extremely striking, and we concluded that although increasing the sophistication in the model would clearly lead to some improvements in accuracy, it would in no way change the overall outcome.

In the simple model, the brain was treated as a homogeneous medium with a conductivity of 0.33 S/m [18], open to the air at its upper surface. Neural activity was simulated by introducing either radial dipoles orientated orthogonally to the surface of the medium to simulate activity in gyri, or tangential dipoles oriented parallel to the surface of the medium to simulate activity in sulci. All dipoles had an inter-pole distance of 2 mm, which is about the width of the cerebral cortex.

Because there was a free surface at the upper boundary, the medium could not be treated as infinite. Thus the method of images was used to generate the dipole fields: i.e. a mirror image dipole was simulated above the free surface, and its field was added to that of the actual dipole below the surface of the medium.

For one radial dipole, the general mathematical model was derived as:

$$\phi_T = \frac{Id}{4\pi\sigma}\left(\left((H-h)(H-h)^2+s^2+x^2\right)^{-3/2} + \left((H+h)(H+h)^2+s^2+x^2\right)^{-3/2}\right)$$

and for one tangential dipole:

$$\phi_T = \frac{Idx}{4\pi\sigma}\left(\left((H-h)^2+s^2+x^2\right)^{-3/2}+\left((H+h)^2+s^2+x^2\right)^{-3/2}\right)$$

where I is the injection current of the dipole; d is the distance between the two poles of the dipole; σ is the conductivity of the medium; H is the distance from the dipole to the free surface; h is the distance from the electrode array to the free surface; s is the horizontal distance from dipole to array; x is the distance of each electrode along the array.

For three adjacent radial dipoles, the model was:

$$\phi_T = \frac{Id}{4\pi\sigma}\left(\frac{H-h}{r_{11}^3}+\frac{H+h}{r_{12}^3}+\frac{H-h}{r_{21}^3}+\frac{H+h}{r_{22}^3}+\frac{H-h}{r_{31}^3}+\frac{H+h}{r_{32}^3}\right)$$

where
$r_{11} = \left((H-h)^2+s^2+x^2\right)^{1/2}$;
$r_{12} = \left((H+h)^2+s^2+x^2\right)^{1/2}$;
$r_{21} = \left((H-h)^2+s^2+(x-m)^2\right)^{1/2}$;
$r_{22} = \left((H+h)^2+s^2+(x-m)^2\right)^{1/2}$;
$r_{31} = \left((H-h)^2+s^2+(x-2m)^2\right)^{1/2}$;
$r_{32} = \left((H+h)^2+s^2+(x-2m)^2\right)^{1/2}$; and
m is the distance between dipoles.

The models were implemented in Matlab and the results displayed as plots of the voltage seen at each electrode in a linear array along the x axis. In some cases, a Laplacian filter (implemented by subtracting from the voltage at each electrode the average of the voltages at the two adjacent electrodes) was used to filter out low spatial frequencies and sharpen the image.

Experimental validation of the model

The mathematical model was validated using real dipoles immersed in a saline solution. Dipoles were constructed from pairs of 1 mm diameter copper or stainless steel rods, with short lengths of 1 mm diameter silver wires soldered to the tip of each rod to minimize polarization. Each rod was insulated from its partner and both members of the pair were insulated from the medium using heatshrink, leaving only a 2 mm length of the silver tips exposed. The distance between tips in a pair was 2 mm. For tangential dipoles, the exposed tips were side-by-side. For radial dipoles, one of the silver tips was bent in a partial S shape so that its exposed portion was directly below the tip of the other rod. The saline bath was a circular glass dish, 200 mm wide (roughly the width of a human head) filled to a depth of approximately 100 mm with a solution of 0.15% NaCl in water. The saline solution had a measured conductivity of 0.32 S/m at 40 Hz. Sinusoidal signals of either 30 or 40 Hz were produced by a Wavetek 191 signal generator and connected to the dipoles via an isolating transformer, so that the bath was floating with respect to ground. Current delivered to each dipole was monitored and adjusted to 5.7 μA. Single rows of electrodes with various inter-electrode distances were constructed either from sintered Ag/AgCl pellets or electrolytically chlorided Ag wires insulated to the tip. The dipoles were positioned approximately 5 mm to the side of the centre electrode in the row, with the exposed tips of the dipoles at the same depth below the surface of the saline as the exposed tips of the electrodes. Voltages were recorded between each electrode in the row and a distant reference electrode, using battery powered amplifiers that incorporated neither high nor low pass filters because the 20 bit ADCs sampled at 1 kHz [1]. Mains pickup was eliminated by recording in a Faraday cage. Electrodes distant from the dipole sometimes recorded sine waves with peak to peak voltages of less than 20 μV and in these cases, because no averaging was used, signal measurements were somewhat affected by instrumentation noise. Signal amplitude was therefore estimated using a Matlab routine that fitted a sinusoid to the data in each channel. When measuring the effects of tangential dipoles, signal polarity was taken into account by measuring the amplitude of the sinusoid at a fixed time after the start of data acquisition.

Results and discussion

In our mathematical model, brain activity is represented as a series of spatially independent but synchronously active cortical dipoles similar to those depicted by Kandel et al. [10]. The first problem was to determine whether or not the model accurately predicts the electric field patterns generated by such dipoles, as recorded between electrodes at the surface of the medium in which the dipoles are positioned and a distant reference electrode. Figure 1 shows a comparison between patterns predicted by the mathematical model and patterns measured experimentally, firstly for radial dipoles (representing activity in gyri) and secondly for tangential dipoles (representing activity in sulci), with the tangential dipoles positioned either parallel or orthogonal to the recording array. Good agreement is seen between the output of the model and the experimental measurements in all cases. This validates the mathematical model as producing an adequate simulation of the fields generated by dipoles like those widely accepted as occurring in the neocortex [10, pp. 783–784], when those dipoles are situated just below the free surface of a conductive medium that might reasonably be taken as simulating a segment of brain from which the overlying skull has been removed.

Thus validated, the model is then used to produce an electromagnetic pattern having roughly the same spatial frequency as the patterns measured at the surface of rabbit brains by Freeman and colleagues. Following the methods of Freeman and Baird [5], the electrodes in this simulation are spaced 0.57 mm apart and the electrode array is positioned at the surface of the medium, 0.5 mm above the dipoles. The top panel in Fig. 2 shows that in this simulation, a spatial pattern with a frequency of approximately 1 cycle/5 mm (0.2 cycles/mm), which is in the middle of the range of spatial frequencies that characterized the patterns found by Freeman and colleagues, is produced by three radial dipoles spaced 3 mm apart.

As pointed out by Szentagothai [16] both the anatomical types of neuron in the brain and the diameter of the columnar unit of cortico-cortical afferent terminations remain roughly the same over a wide range of species. In general, larger animals do not have larger anatomical units, just more of them. While few hard and fast rules have been discovered with respect to the size, function and relationship of cortical columns, microcolumns, macrocolumns, hypercolumns and modules [8], it is clear that in the human, ocular dominance columns are about 1 mm wide [9]. Thus, on the premise that some variety of anatomical column probably underlies the disposition of electric dipoles in the cortex, it seems reasonable to suppose that a spatial electromagnetic pattern generated by dipoles approximately 3 mm apart might occur in humans.

Given this, the next question is whether or not it would be possible with human subjects to detect the spatial patterns produced by radial dipoles spaced 3 mm apart by recording not from the surface of the brain, but from the scalp. Far from being 0.5 mm above the cortex, the surface of the human scalp is an average of 15 or 16 mm above the cortex, depending on the brain area over which measurements are taken [11]. Can the spatial electromagnetic pattern produced by dipoles 3 mm apart still be detected if the recording array is positioned 15 mm above the dipoles? The middle and bottom panels of Fig. 2 show that it cannot. With unfiltered simulated data, the recording array has to be less than 2.5 mm above the dipoles for the pattern diagnostic of dipoles spaced 3 mm apart to be detected

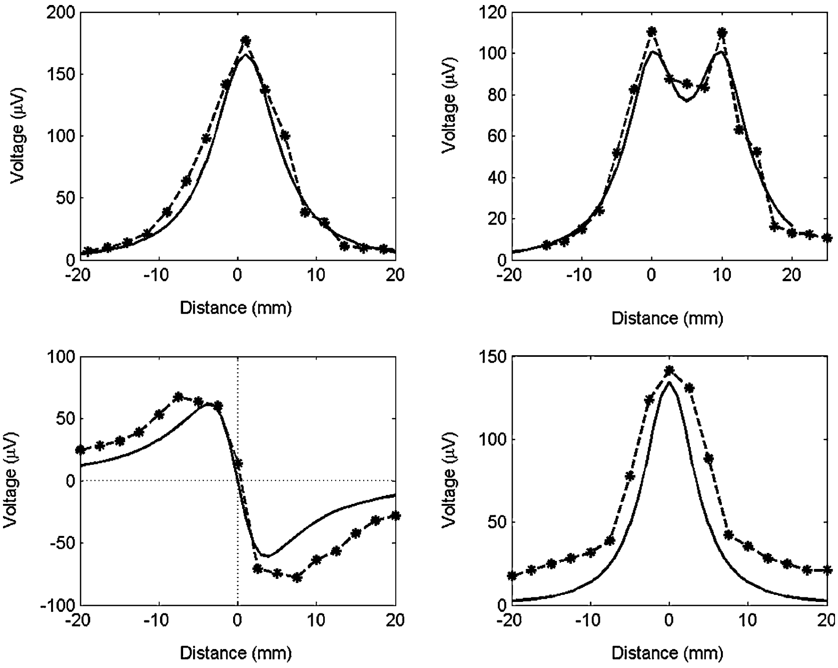


Fig. 1 Comparison of experimental data with predictions of model. Dotted lines experimental data, solid lines mathematical predictions. For experimental data, electrodes are spaced 2.5 mm apart and electrode arrays are approximately 5 mm away horizontally from the near edge of the dipoles. Top left: two radial dipoles 2 mm apart. Top right: two radial dipoles 10 mm apart. Bottom left: one tangential dipole parallel to electrode array. Bottom right: one tangential dipole orthogonal to electrode array, positive pole closer to array

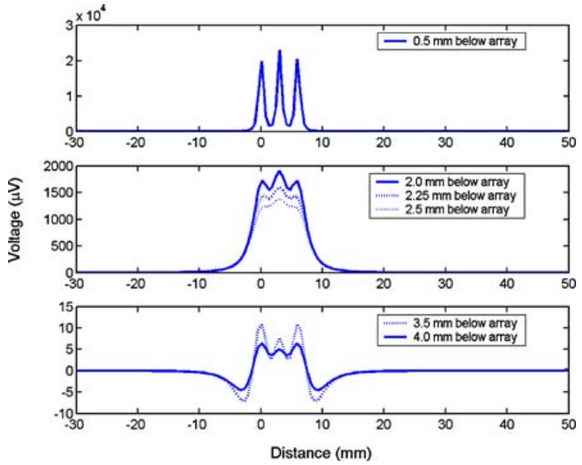


Fig. 2 Predicted measurements at different distances from three radial dipoles separated by 3 mm. Electrodes in these simulations are spaced 0.5 mm apart. Top panel: electrodes 0.5 mm above dipoles. Middle panel: electrodes 2, 2.25 and 2.5 mm above dipoles. Bottom panel: electrodes 3.5 and 4 mm above dipoles, Laplacian filter employed. This filter improved the resolution of the dipoles, provided greater resolution from 4.0 mm above the dipoles (bottom panel) than from 2.5 mm without (middle panel)

(middle panel). Even using a spatial filter to reduce the blurring effects of volume conduction, the recording array has to be less than 4.0 mm above a triplet of dipoles separated by 3 mm before it can be resolved that there are three dipoles, not one (bottom panel of Fig. 2).

What does this mean in anatomical terms? According to our measurements (Fig. 3), the average thickness of the human skull is 4.1 ± 0.6 mm over the temporal cortex, 6.3 ± 0.9 mm over the motor cortex, 5.9 ± 0.9 mm over the prefrontal cortex and as much as 9.1 ± 1.5 mm in the ridge of thick bone called the frontal crest, which marks the fusion of the frontal suture over the prefrontal cortex (all measurements given as mean ± SD, $n = 11$). Subtracting these measurements from the 15 to 16 mm cortex-scalp distance reported by McConnell et al. (11), it can be calculated that the distance from the surface of the cortex to

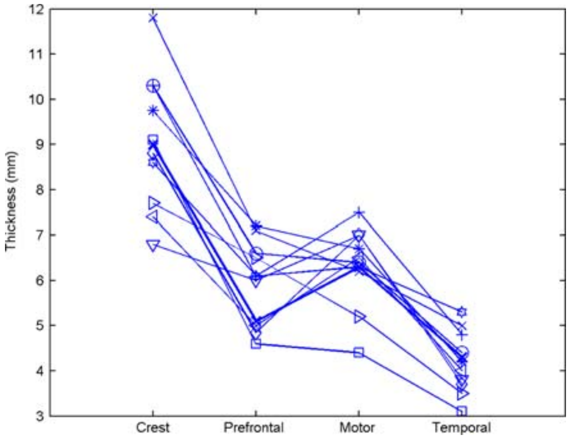


Fig. 3 Skull thickness in different regions. This scatter plot displays the relationship between thickness measured in the prefrontal crest and other prefrontal regions, and over the motor and temporal cortices, for each of 11 different skulls. Each symbol indicates the mean of three measurements in the relevant area of one skull. Measurements were made using a dial test indicator (Mitutoyo No. 2050F) mounted over a fixed stainless steel rod. Note that although there is a tendency for thickness over the motor cortex to be greater than over either temporal or prefrontal cortex, this relationship is not universal for all subjects

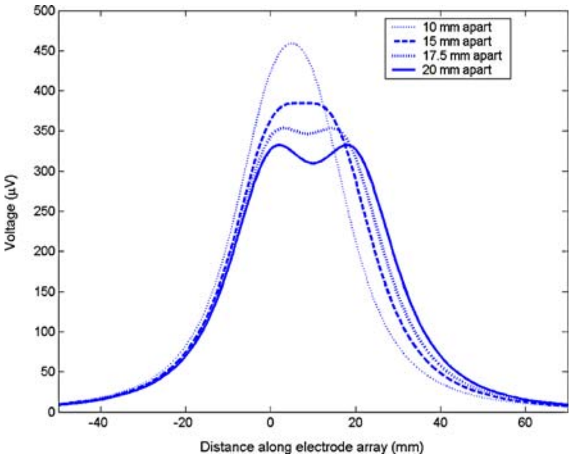


Fig. 4 Simulations of measurements taken 15 mm above a pair of dipoles separated by various distances. Simulated electrodes are 1 mm apart. Distances between dipoles is shown on this figure

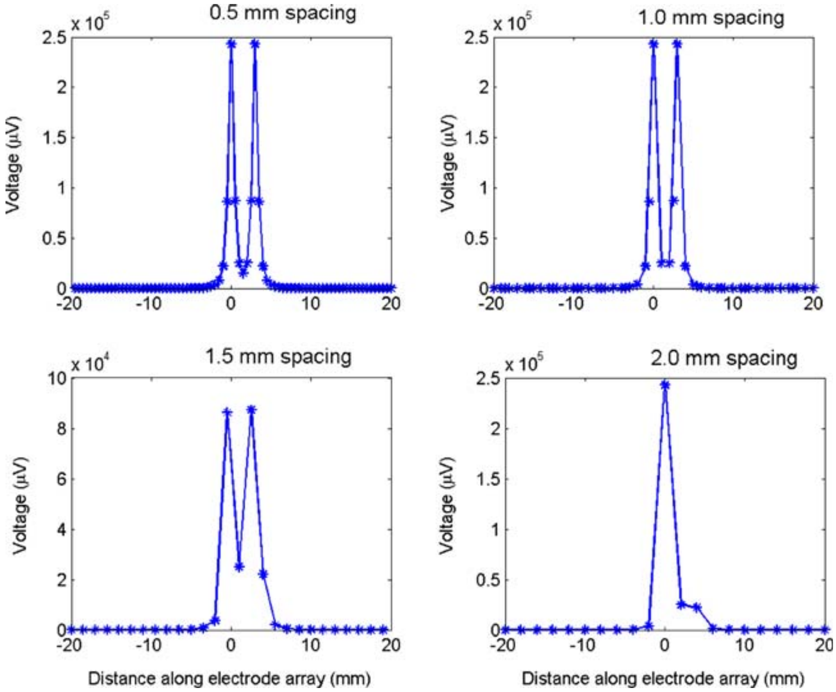
the inner surface of the skull varies from about 6 mm to about 12 mm, depending on location. In normal circumstances the tough dural membrane adheres fairly closely to the inner surface of the skull, which means that under most regions of the skull, the dura is of the order of 10–12 mm above the cortex. Our model shows that even with spatial filtering, the electrode array cannot be more than 4.0 mm above the surface of the cortex in order for the sorts of patterns we are looking for to be resolved. This means that in most areas, the sub-dural and sub-arachnoid spaces would have to collapse to a considerable extent when the skull was opened in order for these patterns to be detected even from the surface of the dura.

Figure 4 shows that even if one ignores the extra blurring effect of the low conductivity of the skull and uses only the simple model described here, two radial dipoles in a cortical gyrus have to be at least ~18 mm apart before they can be resolved in records taken from the closest section of scalp. Considering the fact that the simulations conducted here essentially represent a best-case scenario and that the skull (which has a conductivity about 1/80 that of brain) would almost certainly make the situation with regard to real scalp recordings significantly worse than the predictions of the present model, it seems highly likely that whatever deblurring methods were used, two cortical dipoles spaced 3 mm apart could never be resolved in scalp recordings. The conclusion seems inevitable that if patterns like those recorded by Freeman and Baird [5] do occur in humans, dural or sub-dural recording will be necessary to detect them.

The final question we address concerns the maximum electrode spacing that would suffice to detect such patterns even in dural or sub-dural recordings. Menon et al. [12] recorded from the surface of the brain in human subjects and concluded that if patterns covarying with perceptual categorization do occur, detection of them using ECoG would require electrode spacings under 5 mm. The simulations depicted in Fig. 5 of the present paper reduce this figure to 1–1.5 mm. This means that standard, clinically available, sub-cranial electrode grids, which have an inter-electrode spacing of 1 cm, will be of little or no use.

Our main conclusion is that, if electromagnetic patterns with spatial frequencies similar to those found by Freeman and colleagues in rabbits do occur in human brains, the

Fig. 5 Maximum inter-electrode spacing necessary to resolve two dipoles 3 mm apart, recording array 0.5 mm above dipoles. This simulation shows that even with a recording array positioned as close as 0.5 mm above the dipoles, the electrodes have to be spaced 1.5 mm or less apart in order to resolve two dipoles 3 mm apart



only way to detect them would be to record electrocorticograms from the surface of the brain. This conclusion may have some bearing on the question of what methodology would best facilitate the search for neural correlates of consciousness.

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