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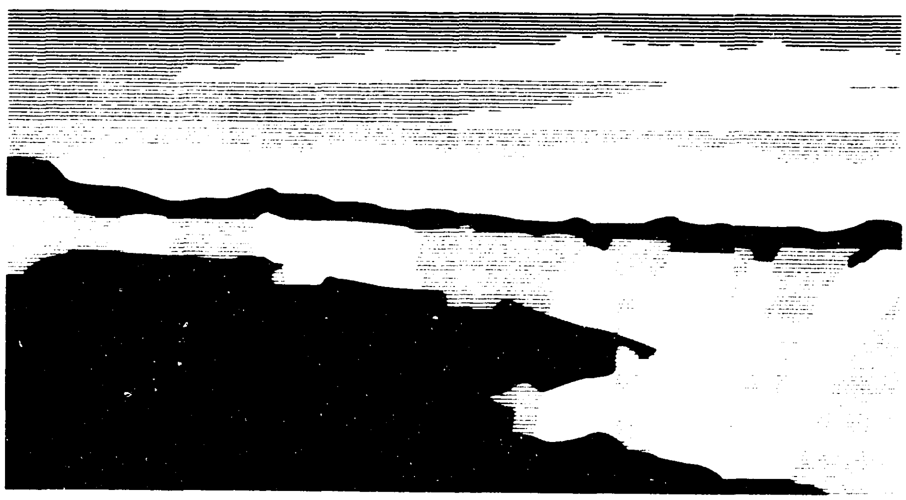

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STRATEGIES FOR SOURCE SPACE LIMITATION IN TOMOGRAPHIC INVERSE PROCEDURES

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INTRODUCTION

The use of magnetic recordings for localization of neural activity requires the solution of an ill-posed inverse problem: i.e. the determination of the spatial configuration, orientation, and timecourse of the currents that give rise to a particular observed field distribution. In its general form, this inverse problem has no unique solution; due to superposition and the existence of "silent" source configurations, a particular magnetic field distribution at the head surface could be produced by any number of possible source configurations. However, by making assumptions concerning the number and properties of neural sources, it is possible to use numerical minimization techniques to determine the source model parameters that best account for the experimental observations while satisfying numerical or physical criteria.

In this abstract we describe progress on the development and validation of inverse procedures that produce distributed estimates of neuronal currents. The goal is to produce a temporal sequence of 3-D tomographic reconstructions of the spatial patterns of neural activation. Such approaches have a number of advantages, in principle. Because they do not require estimates of model order and parameter values (beyond specification of the source space), they minimize the influence of investigator decisions and are suitable for automated analyses. These techniques also allow localization of sources that are not point-like; experimental studies of cognitive processes and of spontaneous brain activity are likely to require distributed source models.

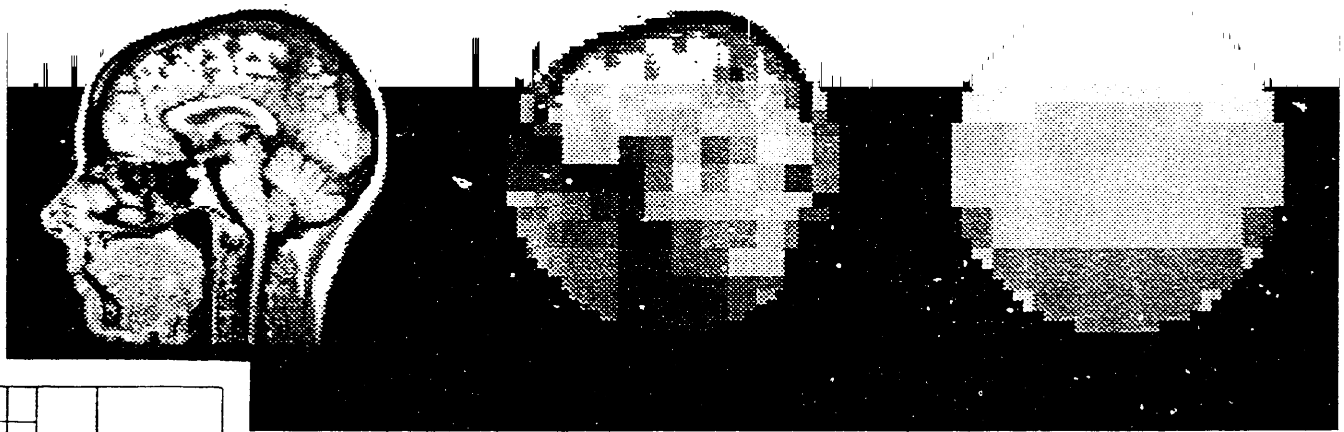
Most distributed current reconstruction procedures exploit the fact that the forward field calculation is linear with respect to current strength and orientation, though nonlinear with respect to source location. Field distributions scale with current strength, and any vector orientation at a given location can be decomposed into a linear combination of orthogonal unit vectors. The forward calculation for a set of dipoles at known locations can therefore be formulated as an operation on a basis matrix that defines the field associated with each elemental current vector in the reconstruction space. Such a basis matrix can account for exact measurement geometry and can easily incorporate high resolution models of head and brain conductivity without computational penalty. Given inherent limitations on spatial frequency of measured fields and of neural population current distributions, reconstruction on a discrete grid can be equivalent to a continuous solution.

A general formulation of the distributed inverse problem is typically highly underdetermined. Given the spatial frequency of field distributions measured a few centimeters from the source, an optimal magnetic sensor array for "full head" measurements will probably consist of a few hundred channels. However, a model of the full cortical volume at 2 mm^3 resolution contains ~40K voxels and ~80k unit currents. To combat this parameter explosion, we have explored both algorithmic and knowledge-based strategies to limit the effective reconstruction space: variable resolution hierarchical models; anatomical constraints on the reconstruction volume; iterative procedures that effectively eliminate putative source locations that are not relevant to the specific reconstruction; and methods that consider an evolving subspace of the reconstruction volume.

INVERSE PROCEDURES

Hierarchical Reconstructions: Following an initial reconstruction on a coarse grid, the resolution of the reconstruction grid can be increased systematically in a region suggested to be a source location, to improve the match between the resolution of reconstruction space and the actual source distribution. (Okada and Huang, 1990). We have implemented procedures for representing the basis matrix as an *octree*. This data structure allows the resolution of the reconstruction grid to be expanded locally to arbitrary limits. We have used this methodology to estimate the limits of spatial resolution of neuromagnetic reconstruction in a 3-D volume. For each voxel in the grid, we expanded the octree until a singular value decomposition (SVD) of the basis vectors of the daughter nodes produced singular values that were below the noise level. This was a symmetrical analysis in X,Y, and Z, and the expansion stopped whenever any singular values fell through the noise floor, even though we expect better resolution at a given depth than through depth.

Figure 1 illustrates the results of one such analysis. The simulated sensor array consisted of 11 by 11 sensors positioned 10 degrees apart in a rectangular array. Peak signal to noise ratio of 8:1 was assumed. The left panel illustrates an anatomical magnetic resonance image (MRI) acquired at 1 mm resolution in plane. The right panel is a schematic diagram of the resolution achievable with the given signal to noise ratio, as determined by the SVD procedure described above. The gray scale represents 3-D resolution values of 1.5 mm^3 (white), 3.0 mm^3, to 24 mm^3 (darkest gray). Note that a substantial region under the sensor array can be resolved at < 3.0 mm^3. The center panel illustrates the anatomical MR image convolved with a variable resolution filter to match the maximum resolution of current reconstruction from MEG data alone. This figure assumes a sensor array positioned over the vertex, as might be used for somatosensory or motor experiments. The use of a variable resolution reconstruction space allows reduction of the number of voxels that must be considered in a tomographic reconstruction, increasing the efficiency of calculations and helping to alleviate problems associated with the underdetermined linear system. Hierarchical reconstruction techniques of this sort should prove useful for a variety of inverse procedures employing a basis matrix.



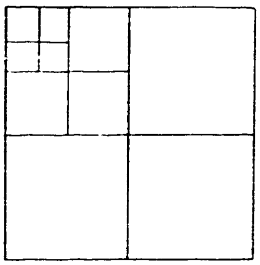


Figure 1. Hierarchical reconstruction strategies
Above: Resolution achievable with a variable resolution reconstruction, assuming SNR of 8:1
Left: Schematic representation of a quadtree (a 2-D octree).

Anatomical Constraints: Linear estimator procedures based on the Moore-Penrose pseudoinverse provide a useful, general methodology for underdetermined problems, finding the least squares solution of minimum Euclidean norm (Hamalainen and Ilmoniemi, 1984). In unconstrained three-dimensional reconstructions from simulated data, minimum norm procedures placed most of the current in the most shallow grid planes, even when the actual dipole location was deeper. However, when the reconstruction was implemented slice by slice through the depth of the volumetric model, there was a qualitative difference in the resulting distributions (current density was most focal) as the procedure moved through the proper source plane (Kullman et al., 1989). This observation prompted us to explore the performance of linear estimator procedures when the reconstruction volume was constrained to the surface of cortex by limiting which grid points were added to the basis matrix.

Simulations employed a 32^3 volumetric model containing a sphere with grooves in the surface representing cortical sulci. The minimum norm reconstruction was restricted to a one-voxel thick region along the surface of the model. In general, the solutions obtained for sources buried within sulci were more diffuse and more superficial than the target current distribution. Less diffuse solutions were achieved if the orientation of the current at each voxel was restricted to be normal to the local surface. We also applied the pseudoinverse procedure constrained by cortical geometry estimated from MRI to reconstruct magnetic sources observed in response to visual stimulation While the peak current elements in the reconstruction were more superficial than those estimated through multiple dipole fitting, the number and configuration of apparent sources were similar. Although anatomical constraints generally improved the fidelity of reconstructions, such reconstructions typically suffered some of the same problems observed with the unconstrained algorithms (George et al., 1991).

Basis Matrix Normalization: Minimum norm solutions tend to produce superficial current distributions due to the physical and mathematical nature of the underlying model. Magnetic fields measured with a gradiometer drop off strongly as a function of distance; a nearby source can account for more power in a field distribution with less current than a more distant source. However, in order to minimize chi-square, it is often necessary to produce a diffuse distribution of superficial currents to exactly match an observed map. In an attempt to defeat these undesirable tendencies, we have explored methods to compensate for the distance dependence of the magnetic field strength. To compensate exactly would require an element by element change of the basis matrix. Instead, we apply an average compensation to each column of the basis matrix, normalizing the set of basis vectors associated with each source voxel by their matrix norm. Such weighting is equivalent to compensation based on the average distance from the particular voxel to all the sensors, and essentially changes the strength of the unit vector without changing the shape of the field distribution. There are caveats associated with this method; unconstrained weights based on the matrix norm can introduce unwanted biases toward voxels far from the sensor array or near the center of the head. In general, the normalized minimum norm solution was not superficial and was more focused than the standard pseudoinverse solution, though reconstructions typically were more distributed than the point dipoles simulated.

The left hand panels illustrate the method used for basis matrix normalization. In these simulations, a 2-D planar reconstruction space was utilized, corresponding to a slice through a 3-D volume. Only sensors positioned within the slice plane are utilized, producing a linear sensor array. All current vectors were normal to the slice plane. This geometry preserves the most troublesome features of the 3-D problem while allowing more efficient computational investigation and simpler visualization of results. The upper panel illustrates the crescent-shaped reconstruction volume utilized in these simulations. Filled circles indicate the locations of sensors.

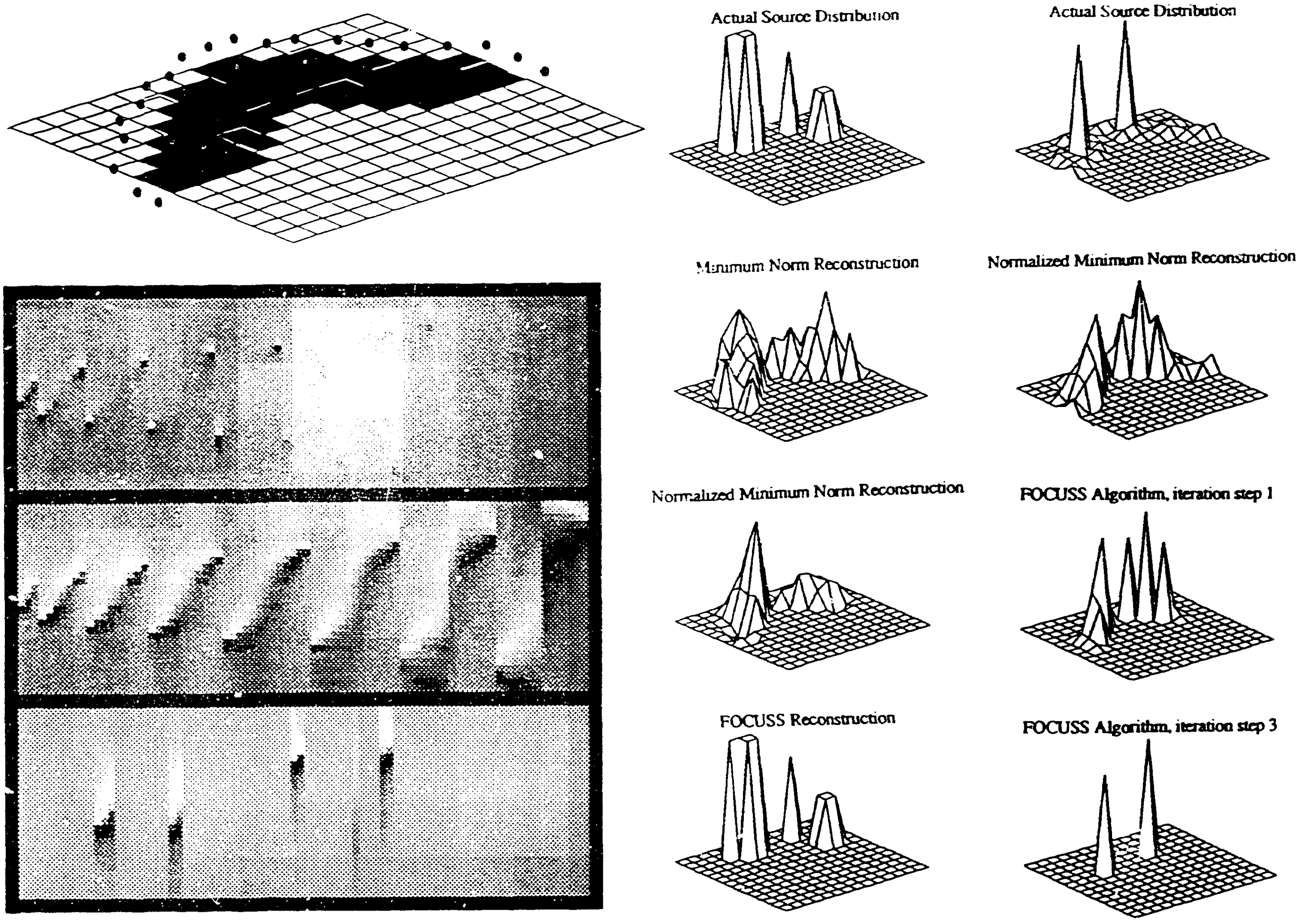


Figure 2. **Basis matrix weighting and the FOCUSS algorithm**
Upper left: Simulation and reconstruction geometry used in these examples.
Lower left: Several forms of the basis matrix associated with the reconstruction geometry.
Middle column: FOCUSS reconstruction of a complex source distribution containing point and clustered sources.
Right column: FOCUSS reconstruction of two point sources in the presence of additive noise.

The lower panel illustrates several forms of the basis matrix associated with this geometry. Each column represents the basis vector describing the field measurements over all sensors for a unit vector current at a particular voxel. Columns are ordered by systematically traversing the reconstruction space, left to right, top to bottom. The upper panel clearly demonstrates the distance dependance of the magnetic field measurements. Only the field contributions from the voxels closest to the sensor array are apparent in this grayscale mapping. The middle panel shows the effects of the column-wise normalization described above; this manipulation allows interior voxels to play a larger role in the weighted pseudoinverse reconstruction.

FOCUSS: The improvements in source reconstruction associated with basis matrix normalization motivated us to explore alternative weighting procedures. We have developed a new algorithm, FOCUSS (FOCal Underdetermined System Solution) which can accurately resolve the depth and extent of sources, including point sources (Gorodnitsky et al., 1992). The essence of the algorithm is the iterative application of weights derived from the previous reconstruction. The process is started by finding the normalized minimum norm solution. We have successfully employed procedures in which the weight vector is replaced by the new solution, where the existing weight vector is multiplied by the new solution, or where the normalized basis matrix is multiplied by the new solution. The method concentrates the solution around the true sources until they are resolved. However, in simulations with distributed sources the algorithm did not always converge to punctate source distributions. In typical simulations the algorithm converged when the rank of the weighted basis matrix dropped below the number of measurements. Accuracy of the FOCUSS algorithm was good, particularly when the desired reconstructions were sparse. The algorithm failed on certain difficult source distributions when the initialization was inappropriate. A similar algorithm was described by Ioannides et al. (1990) for 2-D reconstructions, but failed to resolve the sources accurately. The size of the iterative FOCUSS calculation is dictated by the size of the original reconstruction space. This and other observations suggest the potential merit of *basis matrix truncation* strategies in which a progressively smaller subset of the normalized basis matrix is considered at each step, according to some heuristic based on the previous iterative solution.

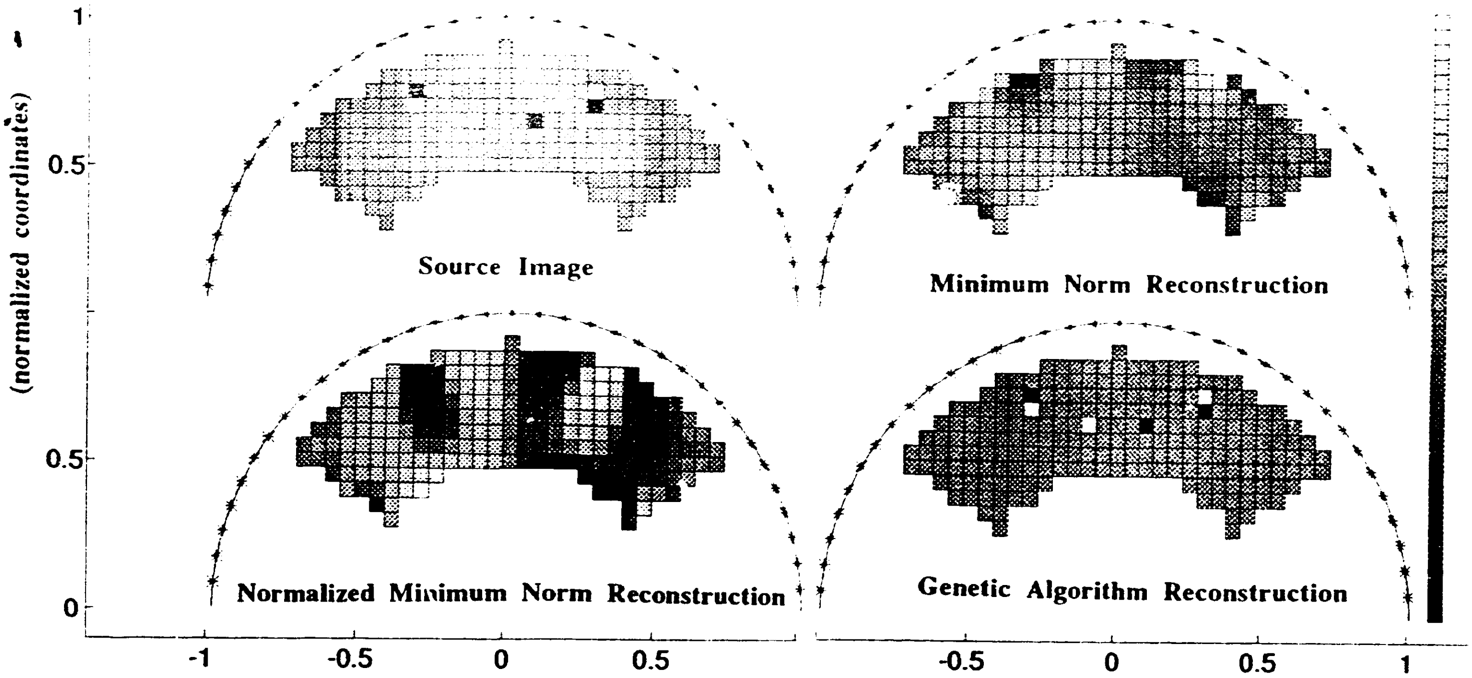


Figure 3. Genetic Algorithm Reconstructions

The second and third columns of figure 2 illustrate representative results obtained with the FOCUSS algorithm. The second column shows a FOCUSS reconstruction of a rather complex source distribution containing both distributed and point sources. In this case the reconstruction was exact. The bottom left panel of figure 2 shows the final form of the basis matrix after the iterative application of weighting. Note that only a few voxels remain strongly represented. The third column illustrates a FOCUSS reconstruction in the presence of noise, using an SVD truncation strategy similar to that described by Szinger and Kuc (8th International Conference on Biomagnetism,1991) to stabilize the solution.

Genetic Algorithms: We have recently achieved encouraging results by explicitly limiting the reconstruction space at each step so that the inverse problem is always well conditioned. Using a genetic algorithm, we specify a number of distinct subsets of the full reconstruction space using strings consisting of ones and zeros. At each step a metric is evaluated for the best linear reconstruction over the subspace specified by each string. This metric takes into account both the goodness of fit, and the number of active voxels in the reconstruction. Depending on this measure of "fitness" the string is either retained or removed from the evolving population of strings. New strings are produced by piecewise recombination of older strings. Under some conditions new "genetic material" is introduced into the population by stochastic processes.

Figure 3 illustrates a genetic reconstruction of a source distribution, including a pair of two-voxel clusters. The genetic algorithm was able to correctly reconstruct the simulated distribution. A number of issues are presently under active investigation, including optimal procedures for initialization of the algorithm and appropriate stopping criteria. Genetic algorithms appears to hold particular promise for the neuromagnetic inverse problem because effectively independent source domains can exist in this problem. Once a suitable subspace configuration has evolved to account for such a domain, it will tend to be preserved, and combined with other partial solutions.

CONCLUSIONS

Although distributed source reconstructions have a number of desirable properties, they are typically highly underdetermined in the general formulation. Algorithmic and knowledge-based approaches to source space limitation can substantially improve the performance of distributed current reconstruction procedures by recasting the problem in a mathematically more tractable form and by selecting for clustered sources and sparse distributions expected on the basis of physiological knowledge.

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