SENSOR ARRAYS IN THE MICRO-ENVIRONMENT OF THE BRAIN

David J. Anderson[1,2], Karim G. Oweiss[1] and Steven M. Bierer[2]
Departments of Electrical Engineering and Computer Science[1] and Biomedical Engineering[2]
University of Michigan, Ann Arbor, MI
(dja,koweiss,sbierer)@umich.edu

ABSTRACT

Technology for recording action potentials from the nervous system has changed in recent years from single or at most two or three neurons to tens of neurons recorded from geometrically precise arrays of recording sites. To fully exploit these research opportunities, signal delivery and processing are key factors. We desire not only sort the array input into neural channels but locate neurons with respect to the array so they can be later identified in histology and serve to further decode the activity of each neuron. The distribution of a neuron's signal across the sensor array is predictive of the cell location at least in projection onto the array but also in the dimension above the array. To achieve 3-dimensional locating power, careful estimation of signal strength at each site must be achieved taking into account the distance and the field distortion for all anticipated source positions. Achieving this independent of source strength appears to be feasible.

1. INTRODUCTION

The technology surrounding recording single neuron activity from the nervous system has given the electrophysiologist opportunities that can change the field. This trend has been accomplished by various technologies spanning from multi-wire hand built systems to complex micro-fabrication processes requiring advanced facilities. Each technology is a union of six basic critical knowledge components shown in Figure 1. This new access to recording technology has prompted neurophysiologists to explore new opportunities for increasing the information yield from animal experiments and has brought neuroprosthesis systems closer to reality. The new applications and the realization of what can be done has driven designs and packaging of devices to new levels. Many of the issues are outlined in [1]. Electrodes are now being produced and distributed to neuroscientists by the University of Michigan Center for Neural Communication Technology that record up to 96 channels with integrated buffering, deliver pharmaceuticals within 10μm of a recording site [2], have integrated cables [3] and multi-plane 3-D systems [4]. Other electrodes with more complex electronics have been designed and used in our laboratory [5] but have not been distributed to our collaborators. The objective of this paper is to introduce the close spaced neural recording array and the special signal processing challenges and opportunities it offers. There are three clear objectives associated with the use of these probes:

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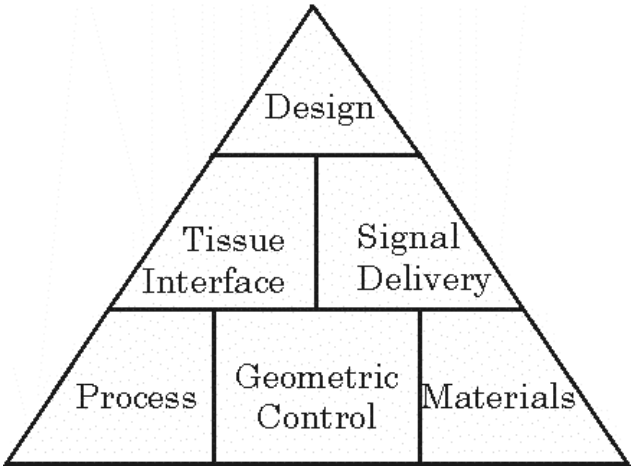

Fig 1. A successful multichannel electrode is a complex interactive combination of the above elements.

1. To detect and classify neural discharges observed over the array using information from wave-form shape and a signal's distribution across the many contact sites which make up the array
2. Determine the position of the identified neurons over the array with sufficient accuracy such that at the experiment's conclusion, each neuron can be located using histological methods
3. Correlated noise sources can be located with respect to the array thus yielding new physiological information about the global function of the surrounding neural tissue volume.

Solution to the source localization in the brain facilitates the understanding of the relationships among cells in a small volume and there are some practical advantages. It is known that some types of electrodes migrate randomly or systematically in a small range within the brain. Good source localization also allows tracking of electrode motion without losing continuous recording of individual cells. We are exploring signal processing structures for accomplishing this such as optimized linear combiners, wavelet decomposition with spatial decorrelation combined with denoising [6,7]. While we have obtained powerful results with our methods when we can provide a dedicated data path off the structure for each element of the array, available communication channels and limited bandwidth are additional challenges, particularly for chronically instrumented animals and eventually for neuroprosthesis systems. Vast savings in communication load can be achieved if these algorithms can be performed with minimal supervision on the implant system itself. The on going neural

activity can be reduced to time stamps, geometric position and information on discharge wave-shape.

2. RECORDING DEVICE TECHNOLOGY

Several technologies are now available for recording signals from multiple neurons in-vivo and in-vitro. Our interests are in-vivo studies in the sub-layers of surface structures such as cortex and brainstem, deep structures such as hippocampus, spinal cord and peripheral nerves. The multi-channel probes used to collect the data that have stimulated the organization of this paper are silicon substrate probes that are fabricated from single crystal silicon using thin-film techniques and the dissolved wafer process. The dissolved wafer process allows virtually any shape and a range of substrate thickness from $5\mu m$ to $15\mu m$. The ability to modulate the thickness allows us to fabricate sharp tips for tissue penetration and integrate flexible cables with the sensor system. For added strength, thicknesses up to $50\mu m$ can be obtained by burying channels in the probe making a 'box' beam like structure. The detail in the thin-film portion of the probe can be defined to about $3\mu m$ on a routine and down to $1.5\mu m$ for special applications. Substrate shape and site spacing also depend on the application. Figure 2 shows a small sampling from the several designs we have produced. that have electrode sites spaced closely enough

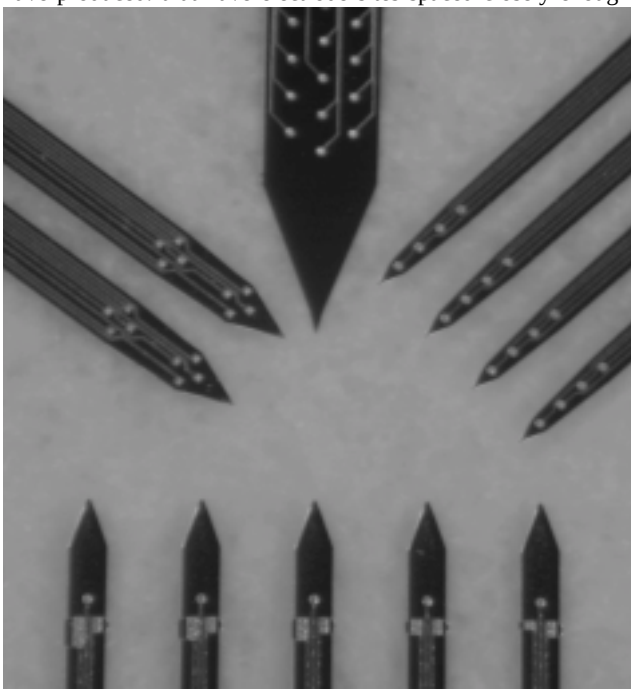

Fig 2. Neural recording probes fabricated with the dissolved wafer process are shaped by a diffusion process and therefore have smooth under surfaces. The thin-film layers on the top of the probe provide electrical isolation of the conducting lines from the media and the silicon substrate.

that several sites record electrical activity from a single neural source. As a practical matter this means spacing of 50 to $75\mu m$ and inter-shank spacing of about $100\mu m$. An example of this type of probe is shown in the layout shown in figure 3. The adja-

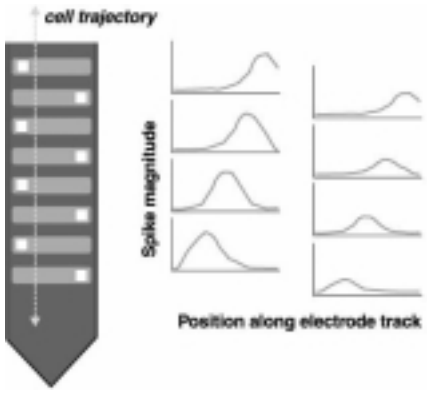

Fig 3. The probe design is one of several being used to collect data that support 3-dimensional reconstruction studies.

cent sites are within the voltage spread of single units and several sites are covered by synchronous neural sources. This probe is used for acute experiments specifically designed to determine the spread function of neurons it passes. The interface with the nervous system depends on a conductive pathway between the neural structure and the electrode surface. Electrically imaging cells with multichannel probes is possible because of spread of signals over sites. Figure 4 below shows data recorded from 4 sites. The

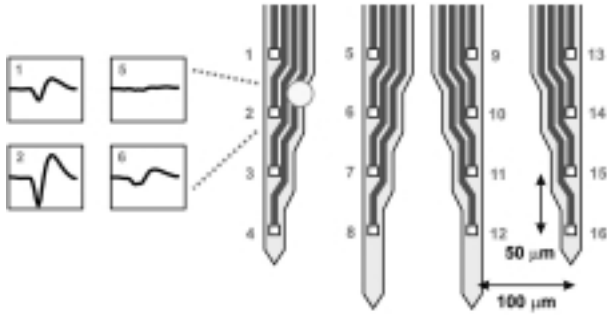

Fig 4. The average waveforms from a neural source appearing on 4 of the 16 channels are used to estimate the position of the neuron projected on to the plane of the array.An estimate of the z-location above the plane is sometime attempted when the potential is spread to more than 4 sites.

waveforms demonstrate that the influence from a single cell spreads over the array to allow some localization. Additional and more closely spaced sites gives a better estimation of the profile and better resolution of position.

3. THE TISSUE INTERFACE

There are two major components to the electrode-tissue interface. One, the few microns immediately surrounding each electrode site and two, the properties of the tissue volume containing sensor array and the neurons being observed.

3.1 The electrode site interface

The exposed metal or polymer that forms the tissue interface have projected areas between $50\mu m^2$ and $4000\mu m^2$ depending on the application. The real area can be many times that for materials have convoluted or porous surfaces. Depending on the appli-

cation, commonly used interface materials are gold, irridium (native or activated), TiN, and various conductive polymers. Irridium and conductive polymers have redox reactions that facilitate charge transfer in stimulation applications. The models for transfer of charge from an ion carrier system to an electron carrier system have been described by Roberson [8] and have been analyzed for several materials by Weiland [9]. The material used on the interface site is application specific. Activated Irridium has very large charge delivery capacity achieved by its redox reaction yielding a transfer function having fractional powers of s characteristic of distributed parameter systems such as cables. TiN is a purely capacitive transfer function and is very fast. Conductive polymers are important because they both have a redox reaction and can be carriers of bioactive chemicals that release into the tissue. For imaging applications it is very important that the sites be very consistent. Variation in the observed signal due to impedance imbalance between sites can distort the spacial profile of the recording.

3.2 The Surrounding Media

For the purpose of this paper the tissue media through which signals pass from the source to the electrode array is modeled as a homogenous resistive conductor with no space charge.

$$\nabla \cdot (\varepsilon \nabla V) = 0$$

The reality of the controlling equation is not know completely but there certainly are various membranes which isolate intracellular compartments from extra-cellular compartments and probably influence the flow of current. Two dimensional finite element method (FEM) simulations were performed using the MATLAB PDE toolbox to demonstrate some of the principles important to the formulation of this interesting sensor problem.The substrates

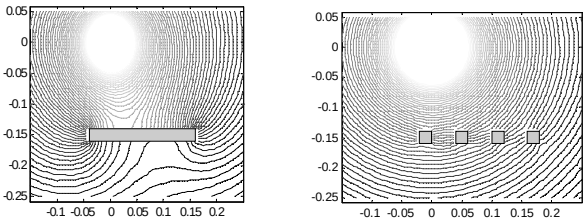

Fig 5. Distortions of he electrical field produced by a monopole source occur in the presence of a non-conductive object such as a silicon substrate probe. The panel on the left represents a wide probe could carry several sites across its width and the right panel is the cross-section of a multi-tine probe.

are modeled as non-conductors. FEM solutions shown in figure 5 demonstrate the field lines and how they are distorted by the substrates of our recording electrode. The substrate is doped silicon but is assumed to have a poor interface to the tissue because of the Helmholtz double layer. The only efficient conductors are the sensor sites themselves. The substrate interferes with the flow of current from a source to a sink surrounding the field of interest. One important phenomenon that can be explained directly from the appearance of the field is that the substrate acts as an amplifier for the observed signal particularly near the center of the substrate. This effect is illustrated in Figure 6. When attempting to make an estimation of the source location at an altitude above the

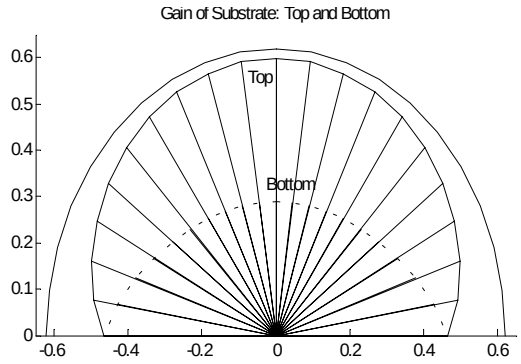

Fig 6. The gain of a site at the center of the substrate is highest when the probe faces the cell and lowest when the cell is on the other side of the probe. At the probe tilts to be edge on to the source, gains of the top and bottom centers are the same. If the gain followed concentric to the outside solid line, tilt would not be a factor.

array, it is not sufficient to assume the roll-off follows a simple $1/r$ or $1/r^2$ law. The roll-off is more gentle near the substrate. The increase in the signal is useful for recording a cell's potential but if the objective is to calculate the location of a cell from the profile of cell's potential across the substrate, the substrate amplification factor as a function of the source position and the location on the substrate becomes important. The FEM model was used to calculate the profiles of potentials across a one dimensional array for a 6x6 grid of cell positions with respect to the array. There were two substrate types used in the computational experiment, the single wide substrate and the multitine substrate. The six profiles shown below in figure 7 are from a continuous

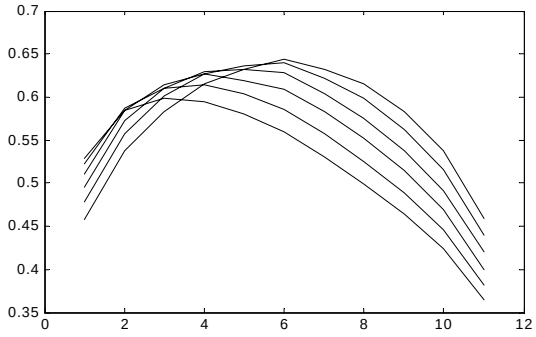

Fig 7. Six profiles across the substrate obtained from all shifts about half way up the height dimension. Note that, due to the amplification effect, the left end of the profile is never the maximum even when it is the point closest to the source.

substrate where the central values tend to be greater that the undistorted field and the data from the edges of the probe tend to be reduced by the high current density streaming around the edges.

4. RECONSTRUCTION OF THE GRID

After the FEM simulation for each point in the grid, we have the one dimensional point spread function for the source on the substrate for different altitudes and shifts of the source above the

substrate. As a heuristic choice of useful functions, the moments of each voltage profile across the probe surface were calculated to the third order. An approximation to a grid over the electrode was derived from the moments.

$$\tilde{G}(x, y) = A(m_1, m_2, m_3)$$

$\tilde{G}$ is the approximation grid and A is a linear matrix operator. A first attempt at the problem found that the pseudo inverse of a matrix (M) containing all three moments and their cross products up to the third power were used to create a matrix that maps the moments to the grid with sufficient accuracy.

$$a = M^{\dagger}G$$

The results for both second and third order systems are shown below in figure 8. The dotted grid was obtained with only second

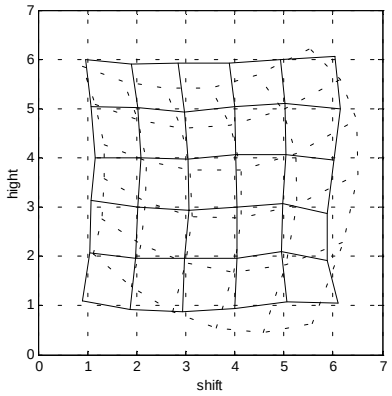

Fig 8. The accuracy of location reconstruction improves with the number of moments and products of moments used. The dotted grid is the all second order and below and the solid lines are all third order and below. Each profile used was normalized so source size was not a factor.

order moments, the solid grid is obtained with 3rd order moments. The data shown are for the continuous substrate and are very similar to the multi-tine case. Susceptibility to noise is high and will require obtaining the representation of discharges across the several sites to high accuracy. Figure 9 below shows the smearing of cell location resulting from about 44dB signal-to-noise ratio. It is clear from computational experiments that the continuous substrate case has better resolution of position probably because of the larger amplification factor. The locator matrix (a) was very similar in both cases.

5. CONCLUSIONS

The close spaced neural recording array promises to open new opportunities for neural circuit analysis. Not only will neurobiologists be able to simultaneously observe neurons that are cooperating in processing information flowing in the electrode region but will be able to locate them with respect to the array for histological analysis. The method for using spatial distribution functions of the several signals to do 3 dimensional location is feasible but requires application of more modern methods of estimation and the use of signals with high signal-to-noise ratios. This can only be achieved by paying the closest attention to

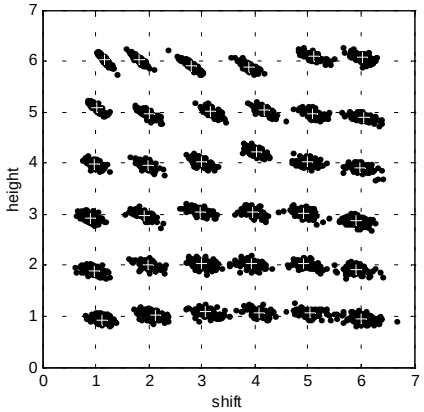

Fig 9. Adding Gaussian noise to the signal profile across the substrate smears the location of the cells on the grid. The distributions above result from 44dB S/R. A typical signal might have a 20 dB signal-to-noise ration thus requiring averaging of up to 200 waveforms to achieve par with the illustration.

coherent noise sources in particular. The complexity of these methods also place a stress on the communication and signal processing power required to take advantage of such methods an difficult behavioral environments.

6. REFERENCES

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