

RECORDING ADVANCES FOR NEURAL PROSTHETICS

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Abstract— An important challenge for neural prosthetics research is to record from populations of neurons over long periods of time, ideally for the lifetime of the patient. Two new advances toward this goal are described, the use of local field potentials (LFPs) and autonomously positioned recording electrodes. LFPs are the composite extracellular potential field from several hundreds of neurons around the electrode tip. LFP recordings can be maintained for longer periods of time than single cell recordings. We find that similar information can be decoded from LFP and spike recordings, with better performance for state decodes with LFPs and, depending on the area, equivalent or slightly less than equivalent performance for signaling the direction of planned movements. Movable electrodes in microdrives can be adjusted in the tissue to optimize recordings, but their movements must be automated to be a practical benefit to patients. We have developed automation algorithms and a meso-scale autonomous electrode testbed, and demonstrated that this system can autonomously isolate and maintain the recorded signal quality of single cells in the cortex of awake, behaving monkeys. These two advances show promise for developing very long term recording for neural prosthetic applications.

Keywords—Neural Prosthetics, LFP, Movable Electrodes

INTRODUCTION

A major challenge for cortical prosthetics is to acquire meaningful data from a large number of channels over a long period of time. This is particularly challenging if only single cell activity is used since typically only a fraction of the electrodes in an implanted electrode array will have isolated cells, and the action potential on these channels are difficult to maintain over very long periods of time. Also the signal quality degrades after implantation. This paper describes two new methods for improving the recording yield and recording time.

Local field potentials (LFPs) offer one method to improve yield and longevity. These signals are the averaged local activity of cells a small distance from the electrode tip. Since the “listening sphere” for LFPs is larger than that for single cells, LFP signals are present even if an electrode does not pick up the activity of a single cell. In our experience, the longevity of LFP recordings exceeds that of cells (Fig 1c). Also the larger listening sphere appears to protect the LFP recordings from the effects of local scarring around the electrode tips. However, LFPs have not been used routinely in neuroprosthetics research, perhaps because it is assumed that much less information can be extracted from averaged activity compared to single cell activity. This paper describes experiments indicating that, with the appropriate analysis tools, LFP recordings can provide similar information and decode performance to spike recordings.

Autonomously moving probes are another method to improve yield and longevity of recording. “Chronic” recording experiments, required for neural prosthetics applications, use arrays of electrodes that are implanted in a single surgery and cannot be moved. This “shot gun” approach to sampling cells is not optimal, since electrodes may not be positioned near cells, and there is no flexibility in targeting specific cell types or receptive field positions (for tiling a space). It would be advantageous to be able to move the electrodes once they are implanted in order to select individual cells, optimize cell recording quality, and adjust for cell migration effects.

In addition to optimizing cell yield and selection, autonomously moving probes could also improve the signal quality, stability and longevity of chronic recordings. The reported success of chronic array recordings vary widely across different animals, cortical areas, and array designs. While some arrays continued to record some signals for periods of up to a few years [1, 2], the quality of single cell activation in most channels of fixed-geometry implanted electrode arrays noticeably degrades after a few months [3]. Among the factors contributing to this deleterious loss of signal include reactive gliosis [4, 5] resulting from electrode movement in the tissue or bio-incompatibility of the electrode’s surface material [6, 7]. Movement of the electrodes, to follow the drift of cells by tissue movement, or the possibility of breaking through scars to fresh tissue, may improve the longevity of cell recording.

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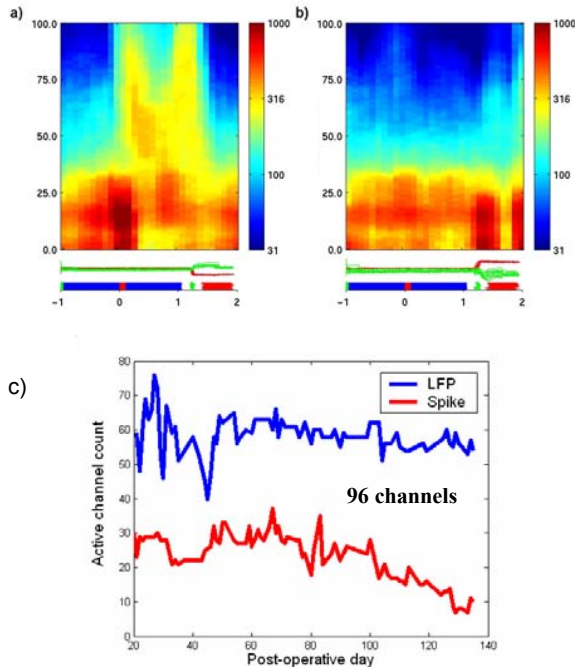


Fig 1 A) B) LFP spectrogram from a single recording site in area LIP. A) The monkey plans an eye movement in the preferred direction for this site and B) in the opposite direction. Modified from Pesaran et al.2002. C) Number of channels with LFP and spike activity for the same 96 electrode array in PRR and area 5.

There are some systems that allow movement of the electrodes [8-12]. However, these systems are all manually operated, and, with permanent implants of large numbers of electrodes, such manual adjustment would be tedious and impractical for patients. This is especially true considering that the electrodes would have to be moved throughout the lifetime of the implant to maintain longevity of recording. Automated movable probes would overcome these limitations. Below we describe the development of automated positioning algorithms and a positioner with very small piezoelectric motors which have been used successfully in monkeys to automatically isolate and hold signals from single cortical neurons.

COGNITIVE BASED NEUROPROSTHETICS

Before describing the new recording methods, we outline the type of neural prosthetic we are developing for use with these new techniques. Prior studies have focused primarily on deriving command signals from motor cortex [13-15]. Recordings from multiple cortical neurons are “decoded” to control the trajectories of a robotic limb or a cursor on a computer screen. We refer to this approach as *motor-based*. We have been developing another approach which uses high-level cognitive signals recorded from single cells or LFPs. This *cognitive-based* approach decodes the goals and intentions of the subject, rather than the instructions on how to obtain those goals. The lower-level

instructions are envisioned to be managed by smart output devices, such as robots, computers or vehicles, using supervisory control systems.

Cognitive control signals can be derived from many higher cortical areas related to sensory-motor integration in the parietal and frontal lobes. The primary distinction is not the place from which recordings are made. Rather it is the type of information that is being decoded, and the strategy for using these signals to assist patients. In monkeys we have focused on the posterior parietal reach region (PRR), but similar approaches can be used for interpreting cognitive signals from other brain areas. It is likely that some areas will be better than others depending on the cognitive signals to be decoded and the parts of the brain that are damaged.

Experiments have recently been performed in monkeys in which reach intentions are decoded from PRR activity in real time, and used to position a cursor on a computer screen [16]. Reach goals were decoded from activity present when the monkeys were planning the reach movements, but otherwise were sitting motionless in the dark, and were not making eye movements. Thus the cognitive signals in the brain control task were free of any sensory or motor related activity.

Signals related to reward prediction could also be decoded from the PRR activity. PRR cells were found to be more active and better tuned when the animal expects a bigger or more probable reward at the end of a successful trial where the monkey is controlling cursor position with his neural activity. Rather remarkably, PRR cell activity also reflects reward preference, being more active prior to the expected delivery of a preferred citrus juice reward than a neutral water reward. In fact, the goal *and* expected value could be read out simultaneously in the brain control task. These experiments show that multiple cognitive variables can be decoded at the same time.

LOCAL FIELD POTENTIALS

We recently discovered that the local field potentials recorded in the posterior parietal cortex of monkeys carry information regarding the animals’ movement intentions. In area LIP, the eye movement area adjacent to PRR, the magnitude of the gamma band (approximately 25-90 Hz) oscillations in the LFPs were good predictors of the direction of monkeys’ planned eye movements (Fig 1 a, b) [17]. The beta band, centered at around 20 Hz, carried different information. The oscillatory activity in this band was not direction tuned, but rather indicated the behavioral state of the subject. When the animal was planning a saccade, the magnitude of the signal slowly increased (planning state), while at the time of the eye movement the signal magnitude dramatically decreased (execution state) [17].

A direct comparison was made of the ability to decode intentions using the spikes and LFPs obtained from recordings made in LIP [17]. A linear discriminant analysis

was used to predict, from single trials, the direction of a planned eye movement. The performance for prediction of direction was similar for spikes and LFPs. The decoding performance for behavioral state was also examined; in this case, whether the monkey was planning or executing a movement. The LFPs were better for predicting the behavioral state of the animals [17]. The better performance of the LFP for state decoding may reflect the activity due to circuits within LIP or inputs to LIP from external sources.

We have also recently characterized the temporal properties of LFPs in PRR [18]. The gamma band activity in PRR is direction tuned for the spikes and LFPs, but the peak power in the spatially tuned frequency band is 10 to 20 Hz lower in PRR as compared to LIP [19]. The decoding of behavioral state from PRR activity was better when using LFPs compared to spikes, similar to the result found for LIP. Thus the LFPs provide the most reliable indication of changes in behavioral state for both areas. In motor cortex, LFPs evoked by limb movements have been decoded to predict reach movement directions, with similar performance to spike decodes [20].

Recent experiments from our lab indicate that LFP activity at single sites in PRR can be used in brain control tasks to decode the planned direction of reach movements. The performance is again comparable to that seen with spikes. Finally, it has been our experience that LFP activity is maintained for much longer periods of time than spikes. Fig 1c shows that the number of channels whose LFP power exceeds a fixed threshold remains approximately constant over months while the number of channels with spiking activity declines.

AUTOMATED, MOVABLE PROBES

We have developed movable electrode control algorithms for automated isolation and tracking of neural signals. These algorithms are based on a *cell isolation curve*, which relates electrode displacement to recorded signal quality. Such curves are the norm in neural recordings [21]. The electrode position control algorithm is based on the interpretation of the cell isolation curve as a regression function. To autonomously position the electrode, the control algorithm uses a stochastic optimization method to reliably find the peak of the isolation function, with small modifications that smooth the electrodes' movements and prevent excessive dithering. The control algorithm has been used successfully to control a microdrive to automatically isolate and maintain extracellular signal activity in monkey PRR [22]. An example of an automated isolation session is shown in Fig 2c. The blue trace shows the electrode's automated movement sequence while the red trace represents the smoothed isolation curve, and the bottom traces show the average waveform at each position (Fig 2c). The microdrive was built using small piezoelectric motors that allowed many millimeters of electrode movement, with sub-micron resolution.

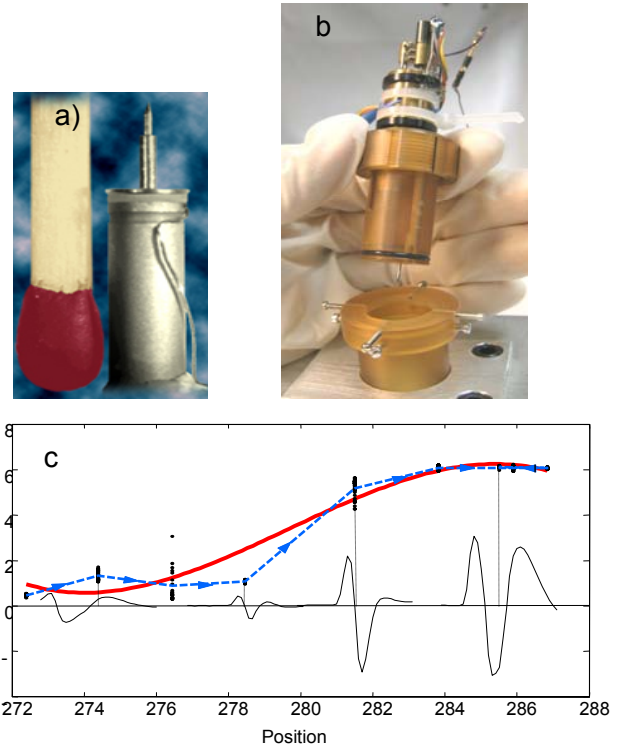


Fig 2 A) Small piezoelectric motor and B) assembled microdrive containing four motors. This microdrive can independently position 4 electrodes. C) Automated isolation of a PRR neuron. Shown is the peak to peak amplitude of the signal as a function of electrode position.

The eventual goal is to use micro-electro-mechanical systems (MEMS) technology to produce a movable electrode array implant (Fig 3). One promising method we are developing is to use electrolysis techniques to move and lock the probes in place [23-26]. The movement is accomplished by passing electrical current within small bellows-chambers filled with fluid. The gas generated by electrolysis increases pressure within the bellows and moves the electrode. The electrodes can be moved in the opposite direction by reversing the current flow and using a catalyst. Advantages of this electrolysis technique are relatively low driving voltage, low heat dissipation, the ability to lock electrodes in place without the need for continuous power dissipation, the ability to generate very high forces, and the ability to provide hundreds of microns of electrode displacement. Fig 3 shows an example of this system, in which linear arrays of these electrolysis actuators would be inserted into cortex through a small skull burr hole and duratomy. The electrodes would "float"; that is, they would not be rigidly connected to the skull and would move with the tissue [27].

CONCLUSION

In this paper, we outlined two new strategies for improving the yield and increasing the lifetime of recordings for neural prosthetics applications. One strategy is to utilize

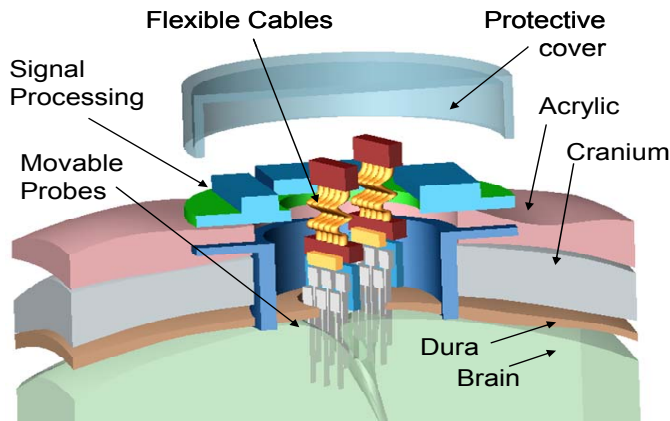


Fig 3. Schematic of MEMS based actuators and electrodes for cortical implantation.

LFPs. Because of the ease and longevity of the LFPs, and the recently discovered wealth of detail that can be decoded from these signals, they represent an interesting avenue of future exploration. The second is an engineering advance, which enables the automatic advancement of electrodes [22, 28]. Automated movable probes will allow neural prosthetics to increase the yield of recorded signals and to select specific cell types to enable the best tiling of cognitive spaces. These algorithms will also facilitate the increased quality and stability of signals for long term chronic recordings.

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REFERENCES

- [1] N. Jai, H.-X. Qi, and J. H. Kaas, "Long-term chronic multichannel recordings from sensorimotor cortex and thalamus of primates," in *Advances in Neural Population Coding. Progress in Brain Research*, vol. 130, M. A. L. Nicolelis, Ed. New York, NY: Elsevier, 2001.
- [2] M. A. L. Nicolelis, A. A. Ghazanfar, C. R. Stambaugh, L. M. O. Oliveira, M. Laubach, J. K. Chapin, R. J. Nelson, and J. H. Kaas, "Simultaneous encoding of tactile information by three primate cortical areas," *Nature Neuroscience*, vol. 1, pp. 621-630, 1998.
- [3] P. J. Rousche and R. A. Normann, "Chronic recording capability of the Utah Intracortical Electrode Array in cat sensory cortex," *Journal of Neuroscience Methods*, vol. 82, pp. 1-15, 1998.
- [4] J. N. Turner, W. Shain, D. H. Szarowski, M. Andersen, S. Martins, M. Isaacson, and H. Craighead, "Cerebral astrocyte response to micromachined silicon implants," *Experimental Neurology*, vol. 156, pp. 33-49, 1999.
- [5] P. Bovolenta, F. Wandosell, and M. Nietosampedro, "Cns Glial Scar Tissue - a Source of Molecules Which Inhibit Central Neurite Outgrowth," *Progress in Brain Research*, vol. 94, pp. 367-379, 1992.
- [6] S. Schmidt, K. Horch, and R. Normann, "Biocompatibility of Silicon-Based Electrode Arrays Implanted in Feline Cortical Tissue," *Journal of Biomedical Materials Research*, vol. 27, pp. 1393-1399, 1993.
- [7] D. J. Edell, V. V. Toi, V. M. McNeil, and L. D. Clark, "Factors Influencing the Biocompatibility of Insertable Silicon Microshafts in Cerebral-Cortex," *IEEE Transactions on Biomedical Engineering*, vol. 39, pp. 635-643, 1992.

- [8] J. D. Kralik, D. F. Dimitrov, D. J. Krupa, D. B. Katz, D. Cohen, and M. A. L. Nicolelis, "Techniques for Long-Term Multisite Neuronal Ensemble Recordings in Behaving Animals," *Methods*, vol. 25, pp. 121-150, 2001.
- [9] J. G. Keating and G. L. Gerstein, "A chronic multi-electrode microdrive for small animals," *J. Neuroscience Methods*, vol. 117, pp. 201-206, 2001.
- [10] S. N. Baker, N. Philbin, and e. al., "Multiple single unit recordings in the cortex of monkeys using independently moveable microelectrodes," *J. Neuroscience Methods*, vol. 94, pp. 5-17, 1999.
- [11] R. C. deCharms, D. T. Blake, and M. M. Merzenich, "A multielectrode implant device for the cerebral cortex," *J. Neuroscience Methods*, vol. 93, pp. 27-35, 1999.
- [12] B. P. Vos, M. Wijnants, S. Taeymans, and E. De Schutter, "Miniature carrier with six independently moveable electrodes for recording of multiple single-units in the cerebellar cortex of awake rats," *Journal of Neuroscience Methods*, vol. 94, pp. 19-26, 1999.
- [13] M. D. Serruya, N. G. Hatsopoulos, L. Paninski, M. R. Fellows, and J. P. Donoghue, "Instant neural control of a movement signal," *Nature*, vol. 416, pp. 141-142, 2002.
- [14] D. M. Taylor, S. I. H. Tillery, and A. B. Schwartz, "Direct cortical control of 3D neuroprosthetic devices," *Science*, vol. 296, pp. 1829-1832, 2002.
- [15] J. Wessberg, C. R. Stambaugh, J. D. Kralik, P. D. Beck, M. Laubach, J. K. Chapin, J. Kim, J. Biggs, M. A. Srinivasan, and M. A. L. Nicolelis, "Real-time prediction of hand trajectory by ensembles of cortical neurons in primates," *Nature*, vol. 408, pp. 361-365, 2000.
- [16] S. Musallam, B.D. Corneil, B. Greger, H. Scherberger, and R.A. Andersen, "Cognitive control signals for neural prosthetics," *Submitted*, 2004.
- [17] B. Pesaran, Pezaris, J., Sahani, M., Mitra, P.M., and Andersen, R.A., "Temporal structure in neuronal activity during working memory in Macaque parietal cortex.," *Nature Neuroscience*, vol. 5:805-811., 2002.
- [18] H. Scherberger, M. Jarvis, and R.A. Andersen, "Cortical local field potential encodes movement intentions," *Submitted*, 2004.
- [19] H. Scherberger, C.A. Buneo, M. Jarvis, and R.A. Andersen, "Local field potential tuning in the macaque posterior parietal cortex during arm-reaching movements," *Society of Neuroscience Abstracts*, vol. 29, 2003.
- [20] R. J. Mehring C., Vaadia E., de Oliverira S.C., Aertsen A. and Rotter S., "Inference of hand movements from local field potentials in monkey motor cortex," *Nat Neurosci*, vol. 6, pp. 1253-1254, 2003.
- [21] M. Abeles and M. H. Goldstein, "Multi-Spike Train Analysis," *Proceedings of the IEEE*, vol. 65, pp. 762-773, 1977.
- [22] J. G. Cham, E. Branchaud, Z. Nenadic, R.A. Andersen, and J.W. Burdick, "A semi-chronic microdrive and control algorithm for autonomously optimizing and maintaining extracellular action potentials.," *Submitted*, 2004.
- [23] C. G. Cameron and M. S. Freund, "Electrolysis Actuators: Alternative, high-performance, material-based devices.," *Proc. Natl. Acad. Sci. USA*, vol. 99, pp. 7827-7831, 2002.
- [24] J. Xie, Q. He, Y.-C. Tai, J. Liu, and T. Lee, "Integrated Electrospray Chip for Mass Spectrometry," in *mTAS 2002*. Nara, Japan, 2002, pp. 709-711.
- [25] J. Xie, Q. He., C. Pang, Y. C. Tai, Y. Miao, and T. D. Lee, "An Integrated LC-ESI Chip wit Electrochemical-based Gradient Generation," presented at IEEE MEMS Conference, Maastricht, Netherlands, 2004.
- [26] J. Xie, Q. He, Y. C. Tai, J. Liu, and T. D. Lee, "Electrolysis-Based On-chip Dispensing System for ESI-MS," presented at IEEE MEMS Conference, Kyoto, Japan, 2003.
- [27] D. R. Kipke, R. J. Vetter, J. C. Williams, and J. F. Hetke, "Silicon-substrate intracortical microelectrode arrays for long-term recording of neuronal spike activity in cerebral cortex," *IEEE Trans Neural Syst Rehabil Eng*, vol. 11, pp. 151-5, 2003.
- [28] Z. Nenadic, and J.W. Burdick, "Spike Detection using the Continuous Wavelet Transform.," *IEEE J of Biomedical Engineering (in press)*, 2004.