Brain-Control Interfaces for Sensory and Motor Prosthetic Devices

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ABSRACT

Injury and disease to the central nervous system often leaves patients with full cognitive ability but a loss of communication between the brain and sensorimotor systems of the rest of the body. During the past 30 years there has been tremendous progress in the development of prosthetic devices that stimulate peripheral nerves and muscles to restore movement of paralyzed limbs in these patients. However, control systems for these prosthetic devices that interface directly with brain signals carrying information about the intent to move and methods for returning sensory feedback to the brain are just beginning to be developed. We present a ceramic-based, multi-site electrode system capable of 1) recording from large numbers of neurons across several brain regions 2) stimulating neural tissue to restore sensory feedback and 3) measuring local concentrations of neuromodulators. Preliminary data from the rat suggest that this system can be used to record neural signals carrying information about the intent to move and restore sensory perception. Issues relating to interfacing with the brain's hierarchical and distributed information processing systems will be discussed.

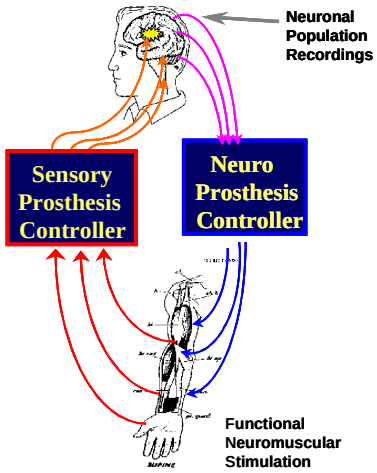

Fig. 1. Closed loop neuroprosthetic device that derives its command signals from neuronal population recordings. Neural activity is recorded from motor centers in the brain and transformed by the controller into appropriate signals for stimulating nerves and muscles of the limb. Sensory signals recorded in the limb are transferred back to the sensorimotor areas of the brain for fine-grained control of movements.

1. INTRODUCTION

The possibility of interfacing the nervous system with electronic devices has long fascinated scientists, engineers and physicians. In general, an ability to expand the bandwidth of communication between brain and machine would provide many interesting possibilities, ranging from faster human-computer interfaces to direct remote control of robotic devices. In medicine, the field of neuroprosthetics has grown rapidly to include a variety of devices for stimulating peripheral nerve tissue [1] through functional electrical stimulation (FES). Several of these devices are now available commercially. However, these devices are generally controlled through an on-off (or open/close for grasping) type of switch. Directly obtaining motor command signals from motor control regions of the brain and transforming them into electronic signals suitable for controlling an FES device and designing a closed loop system with sensory feedback would provide for more fine-grained temporal and spatial control of neural prosthetic devices (Fig. 1.).

Notwithstanding these futuristic scenarios, neural prostheses are rapidly becoming viable therapies for a broad range of patients with injury or disease of the nervous system. For example, over 30,000 auditory prostheses have been successfully implanted in deaf patients [2] and over 150 devices for FES that restore grasping have been implanted in patients who have suffered loss of function in their upper extremities. The primary motor cortex (MI), in the precentral gyrus of the human cerebral cortex, has long been known to be important for the control of voluntary limb movements. It is therefore conceivable that one could record commands for arm movement in the MI cortex and use those signals to directly drive a robotic arm or to control FES to a limb. We have recently demonstrated the feasibility of such "neurorobotic" control in rats [3], and similar studies are ongoing in monkeys.

However, these studies were performed with traditional chronic microwire array type of electrodes that are capable of recording neural signals for less than one year from a single site at the tip of the wire. We have developed a hybrid circuit device with multiple recording sites capable of recording single neurons and stimulating neural tissue safely. We present preliminary data on our ceramic-based, multi-site (CBMS) electrode. These electrodes have been used to record single neuron action potentials and stimulate neural tissue as well as record local concentrations of neurotranmitters in real time. Work is underway to improve the capability of these electrodes and enhance the duration and sensitivity of recordings.

2. BMI DEVELOPMENT

The initial design for the electrode included four recording sites, spaced 200 microns apart at the tip of the electrode. The end-recording site was 60 microns from the tip. Each recording site was 22 x 80 microns. The conducting lines were 8 microns wide and all features (recording sites, conducting lines and bonding pads) were separated by at least 5 microns. This electrode design was patterned onto ceramic substrates, 99.6% alumina. These substrates were polished to a thickness of 0.0015 – 0.002 inches. The recording sites, conducting lines and bonding pads were patterned directly onto the ceramic substrate using reverse photolithography.

2.1 Metalization process

Using reverse photolithography, the wafer is prepared with appropriate resist features that define the electrode. The metal was applied to the wafer completely covering the exposed regions and the resist features. The metal conductor chosen for these electrodes was platinum because it has been shown to cause the least histological damage for long-term implants. The metal was deposited onto the wafer and resides directly on the wafer surface where the resist had been developed away. The negative sidewall angle from the reverse photolithography process resulted in a thinner layer of metal at the step from wafer surface to resist. The unwanted metal, along with the underlying photoresist was then removed using standard lift-off procedure. The metal left behind defined the recording sites, conducting lines and the bonding pads of the electrode.

2.2 Insulation procedure

Ion-beam assisted deposition (iBAD) was used to deposit an insulating layer of alumina over the conducting lines of the electrode. The insulation procedure is similar to the metalization procedure. A second photomask was used that leaves only the recording sites and the bonding terminals exposed. Photoresists were applied over the entire circuit and developed using this photomask so that the terminals and bonding pads are protected. The entire substrate was then layered with alumina using iBAD effectively encasing the conducting lines in ceramic. Finally the resist over the recording sites and bonding terminals was subsequently removed, exposing the recording sites.

Individual electrodes were then released from the substrate by laser cutting. To complete the assembly, the bonding terminals were then attached to second stage recording equipment. The integrity of these bonds affects the recording capability of the entire electrode. For simplicity the electrodes were connected to a rigid connector using ultra-sonic wire bonding. However, it is likely that connection to a flexible cable is better and will allow the electrode to 'float' in the neural tissue and move with the brain inside the skull cavity. Testing of this type of floating connection is currently being done. After final assembly, a layer of polyimide was coated onto the electrodes as an added layer of insulation protection.

3. EXPERIMENTAL DESIGN

Our novel CBSM electrodes were used in three different preparations to test the feasibility of using them as a neuroprosthetic device. First, chronic electrophysiological recordings were made from rats chronically implanted with CBMS electrodes. Second, the electrodes were used to stimulate spinal tissue to induce movement of the limb and to stimulate somatosensory neurons in the cortex. Lastly, in-vitro recordings were made to evaluate the ability of these electrodes to record micromolar concentrations of neurotransmitters.

3.1 Stimulation of motor systems

To test the ability of these electrodes to record and stimulate neurons in the spinal cord we used an acute frog preparation. Frogs were anesthetized and an incision was made in the skin along the midline of the back to expose the spinal vertebrae. Vertebrae were removed to expose the spinal cord. Using a stereotaxic frame, a four site CBMS electrode was lowered into the dorsal roots of cauda equina of the spinal cord. Neural signals recorded from the electrode, including those recorded chronically as described in the next section, were filtered, amplified and displayed on a computer screen for further analysis using a multi-neuron acquisition program (MNAP) from Plexon, Inc. (Dallas, TX). A National Instruments data acquisition board (NI-DAQ PCI-6071E) was used to digitize the signals of interest and store them in data files on a PC. A constant current stimulator (A-M Systems, Inc) was used to apply current across two of the four recording sites to stimulate the neurons.

3.2 Interface with tactile systems in the rat

Arrays of CBMS, four-site electrodes were chronically implanted into the barrel region of the somatosensory (SS) cortex of adult rats. This region of the cortex is responsible for processing signals from the rat's whiskers, their main tactile organ. Rats use their whisker to navigate through their environment and to discriminate objects, much like monkeys and humans use their hand. The rats were placed in a stereotaxic frame and an incision was made in the skin on the top of the head to expose the skull. Holes were drilled in the skull above the SS cortex large enough to insert the electrode (approximately 0.5 mm diameter). Four screws were embedded in the skull. Electrodes were lowered into the SS cortex. Placement

was verified physiologically. The electrodes were secured to the skull using dental cement to create an electrode cap. Rats were allowed three days to recover from the surgery.

3.3.Neurochemical detection

Chronoamperometry was used to test the ability of these electrodes to record local concentrations of neurotransmitters. We tested the ability of these electrodes to detect dopamine, a neurotransmitter whose cell bodies reside in the hindbrain and project to the reward centers of the brain via the medial forebrain bundle and project to the basal ganglia where they contribute to motor control. The loss of this pathway, from hindbrain to basal ganglia, has been implicated in Parkinson's disease. Voltammograms of dopamine in-vivo show an irreversible, two electron oxidation wave with an $E_{1/2}$ of 0.12 V. A dramatic increase in the concentration of electroactive species associated with this wave occurs following administration of drugs such as amphetamine, which increase the concentration of dopamine, further verifying that dopamine is the electroactive species being recorded.

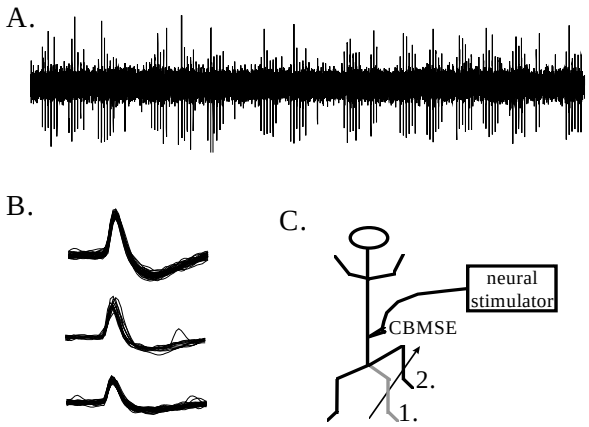

Fig. 2. Results of using CBMS electrode to record and stimulate in the acute frog preparation. A. Neural signals recorded from one site of a four site electrode. Multiple neurons can be recording from a single electrode. B. Three single neurons discriminated from the signal recorded in A. C. Schematic representation of the movement of the frogs hind limb when motor neurons were stimulated. By stimulating the ceramic based multi-site electrode (CBMSE) with the neural stimulator, the hind limb of the frog was moved from position 1 to a more contracted position, position 2.

4. RESULTS

4.1. Spinal cord recording and stimulation

Single neurons were recorded from the spinal cord of anesthetized frogs (Fig. 2). Trains of action potentials from multiple neurons were recorded from a single recording site (Fig. 2a). Fig. 2b shows three separate neurons discriminated from the signal recorded in Fig. 2a. When the recording site was stimulated, the hindlimb moved from a relaxed position (1) to a contracted position (2) (Fig. 2c.)

4.2. Chronic recording from multiple, single neurons

Stable recordings were made from four-site CBMS electrodes chronic implanted in the rat cortex for 3 months (Fig. 3.). The electrodes were placed in the somatosensory (SS) cortex of the rat and cells responsible

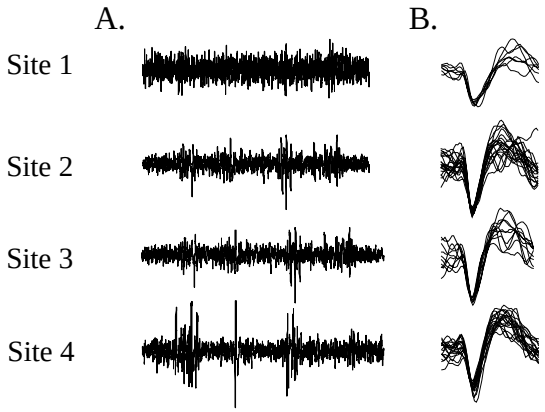

Fig. 3. Neural activity recorded from four sites of a single CBMS electrode simultaneously. The electrode was placed in a single cortical barrel. Neurons within this cortical barrel respond to movement of the same whisker. Spacing between recording sites was 200 μm. A. Neural signals recorded simultaneously from each of the four recording sites. More than one single neuron action potential can be seen on each channel. The individual neurons were discriminated based on their waveform shape. B. Single action potentials discriminated from the neural recording in A.

for processing tactile stimuli from the rat's whiskers were recorded. By moving the whisker, action potentials could be elicited from cells recorded on all four of the recording sites simultaneously. The ability to simultaneously elicit action potentials from cells on all four sites after moving a single whisker confirmed that the electrode was properly placed. Proper placement of the electrodes is essential for a working tactile prosthetic device. These results suggest that the CBMS electrode can be used to record neural signals from the brain for at least 3 months. Experiments are currently being performed to increase the duration of these recordings.

To test the ability of these electrodes to elicit tactile sensation, the rats with CBMS electrodes implanted into the SS cortex were trained to discriminate different

patterns of stimulation. The stimulus elicited action potentials in neurons known to respond to tactile stimulus of the whiskers. Rats routinely use their whiskers to navigate though their environment. When stimulated on the right, rats were trained to turn to the right. When stimulated on the left, rats were trained to turn to the left (Fig. 4). Rats could successfully be controlled while moving through a maze. As the rat approached an opening in the maze that allowed it to go right or left, a stimulus was passed to the right or left SS cortex. In 95% of the trials, the rat would turn in the direction indicated by the stimulus. These results, combined with the previous chronic single neuron recordings suggest that these electrodes can be used as the basis of a neuroprothetic device for the restoration of sensorimotor function.

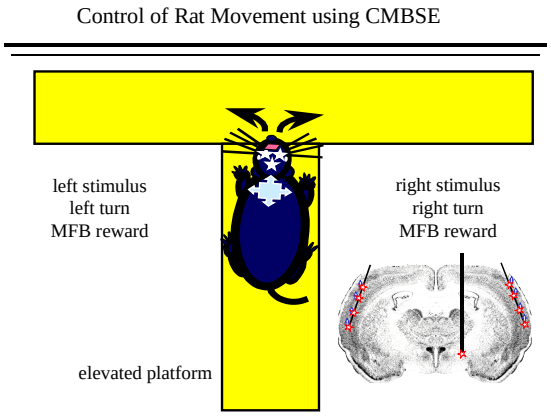

Fig. 4. Schematic representation of tactile stimulation experiment. CBMS electrodes were implanted bilaterally into the somatosensory cortex of rats. A stimulating electrode was implanted into the medial forebrain bundle for reward stimulus. When the left somatosensory cortex was stimulated, the rat learned to turn to the left. When the right somatosensory cortex was stimulated, the rat was trained to turn to the right. These results suggest that it might be possible to restore tactile using these CBMS electrodes as part of a neuroprosthetic device.

4.3. Detection of dopamine

These electrodes could successfully detect varying concentrations of dopamine using chronoamperometry. However, the sensitivity of the CBMS electrodes for the detection of dopamine was 5 times less effective than traditional carbon fiber electrodes. Current studies are being conducted to modify the recording sites to improve detection limits. It is most likely that the small size of the recording sites reduced the sensitivity of these electrodes. Increasing the surface area of the recording sites comparable to the size of recording sites of traditional carbon fiber electrodes will likely improve the sensitivity. In addition, platinum may not be the ideal metal interface for electrochemical detection. Therefore, sputter coating the surface of the recording sites with carbon to improve detection limits.

The ability of these electrodes to simultaneously recording single neuron activity as well as the local concentration of neurotransmitters will make them an invaluable tool for further study of diseases as well as provide a prototype for the development of brain pacemaker devices for alleviation of the symptoms of diseases such as Parkinson's disease. For example, by simultaneously recording local concentrations of dopamine and neural activity in the basal ganglia, proper medication can be titrated to patients for effective treatment.

5. DISCUSSION

Our CBMS electrode can be used to record neurons in the spinal cord and stimulate motor neurons to produce limb movement. In addition, the same electrode can be used for recording single neuron activity in the cortex of chronically implanted rats for at least 3 months. Stimulation of neurons in the somatosensory cortex through these electrodes can be perceived by the animal and used by the rat in a discrimination task. Lastly, these electrodes have been shown to be able to detect nanomolar concentrations of neurotransmitters such as dopamine.

These results suggest that this electrode can be used as the basis of a brain-machine interface device capable of restoring sensorimotor function. The CBMS electrode is capable of recording large numbers of single neurons chronically from the brain, which has been suggested to be necessary for reproducing smooth motor output encoded by these neurons.

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