# Revolutionizing Prosthetics: Devices for Neural Integration

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*Interfacing with the human body to extract signals that capture a subject's intent can be done in many ways but can in general be categorized into three different approaches that relate to how the signals are extracted: invasively, non-invasively, and minimally invasively. Over the course of three phases, the Revolutionizing Prosthetics team has explored a wide variety of devices capable of acquiring electrical signals at their source locations: nerves and neuronal cells. To accomplish this, we investigated invasive devices, which are intended to be implanted within the human body. Specifically, the Revolutionizing Prosthetics program focused much of its efforts on evaluating the state of these devices as well as advancing the state of the art of a select few that were found to have the best chance of being transitioned for human use. This article provides a summary of our efforts to identify optimal devices for neural signal acquisition.*

## INTRODUCTION

The main goals of the Revolutionizing Prosthetics (RP) effort focus on the development of high-dexterity upper-limb prostheses and controlling the prostheses by decoding signals expressing the intent of a prosthesis user. The injury suffered by the prosthesis user ultimately defines the source of these biological signals. For example, long transradial amputation patients (a below-elbow amputation) still have all of their forearm muscles, which are responsible for flexing and extending each individual finger. In this case, electromyography (EMG) electrodes (electrodes that capture electrical activity from the muscles) placed on the surface of the forearm can be used to acquire the myoelectric activity, which can in turn be processed, decoded, and transmitted for real-time control of the prosthesis. In the case of a shoulder disarticulation patient, the technique is similar but is implemented differently. This is because shoulder disarticulation subjects typically undergo a surgical procedure known as targeted muscle reinnervation.[1] The RP project has been at the forefront of these procedures, which were led by Dr. Todd Kuiken of the Rehabilitation Institute of Chicago.

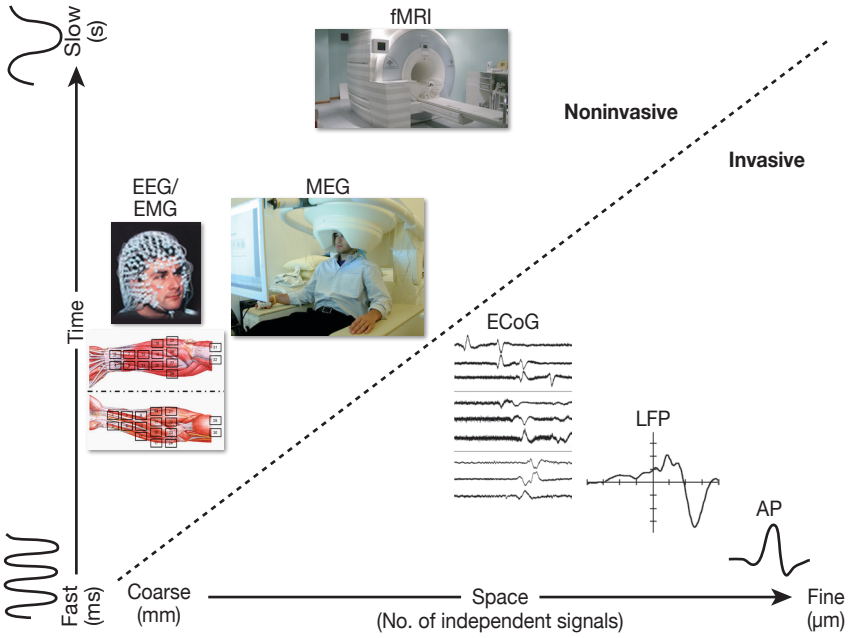


**Figure 1.** Spatial and temporal scales of neural activity. AP, action potentials; fMRI, functional magnetic resonance imaging; LFP, local field potentials; MEG, magnetoencephalography. Note that fMRI and MEG acquisition systems are not portable and hence were not examined in the course of the RP program.

In general, as shown in Fig. 1, EMG signals are characterized by their fast temporal response times (<100 ms) but poor spatial resolution (many underlying muscle signals are captured by a single electrode). Nonetheless, studies have shown that it is possible to use EMG signals to control flexion and extension movements of each individual finger in transradial amputees (corresponding to 5 degrees of freedom[2,3]).

Conversely, high spinal cord injury patients or patients affected by tetraplegia typically have fully or partially severed nerves, which prevents communication of the subject's intent signals from the central nervous system (CNS) to the peripheral nervous system (PNS). In these cases, the intent signals can be captured only from within the CNS. Noninvasive electroencephalography (EEG) systems, similar in functionality to EMG-based systems, have been shown to allow control of up to three separate degrees of freedom by learning to map unrelated "thoughts" to each degree of freedom.[4] Considering that the human upper limb has 27 degrees of freedom, this approach provides functional albeit rudimentary control. Additionally, the unintuitive mapping requires significant training to become effective. A more invasive approach involves the use of penetrating electrodes capable of recording activity from individual neurons at very fast sampling rates (up to 30 kHz). Although invasive, these devices provide the highest spatial and temporal resolutions of any recording system.

Over the course of its three phases, the RP program was tasked to look into increasingly invasive methods that allow control over a larger number of degrees of freedom in a natural, intuitive control paradigm. The main constraint was that the acquisition devices were to be portable and/or implantable, thus excluding neural acquisition systems such as magnetic resonance imaging and magnetoencephalography.

In Phase 1 of the program, we cast a wide net to evaluate the state of the art of invasive devices, which were characterized by their immediate proximity to the signal sources. Specifically, we evaluated and tested implantable myoelectric sensors (IMES)[5] and different types of cortical microelectrode arrays,[6,7] as well as peripheral nerve electrodes.[8] Additionally, an important purpose of these efforts was to develop, implement, and test technology suitable for creating fully integrated wireless neural interfaces for recording neural action potentials as well as aggregate neuronal signals and for stimulating neural tissue. Wireless neural interfaces, in fact, have the benefit of reducing the risk of infection, the electrical noise, the tethering forces, and the breakage all inherently associated with transcutaneous lead wires, thereby enhancing array viability, biocompatibility, and cosmetics. For use in human trials, all of these invasive devices present significant technological and regulatory challenges because of the high degree of invasiveness associated with them. In fact, for any neural integration strategy to be applied, the intended user as well as the Food and Drug Administration (FDA) must have a reasonable level of confidence in the level of safety afforded by the devices (backed up by rigorous scientific data) and, to a lesser extent, that there will be some benefit as a result of using neural interface devices and that this benefit will last a reasonable period of time.

Once the program identified these novel, modular, multimodal cortical and peripheral interfaces, Phase 2 consisted of selecting the devices that were best suited to carrying out the task of reliably and robustly controlling a prosthetic upper limb with multiple degrees of freedom and that have a reasonable chance of being approved or cleared for human use. The strategy therefore included verification in parallel, simultaneous, multi-institution, nonhuman primate experiments and under good laboratory practices provisions to demonstrate that these new neural interface devices were safe and robust.

In the next sections, we present the different devices that were examined: those that interface to muscles,

those that interface to nerves in the PNS, and those that interface to cortical neurons. We explain the inner-workings of the selection process that ultimately led to the devices used in the third phase of the program and summarize the current state of the devices and the experiments that are part of Phase 3.

## MYOELECTRIC INTERFACES AND PERIPHERAL NERVE INTERFACES

Myoelectric interfaces are the least invasive interfaces available on the market today. These interfaces extract information by being placed in contact with the skin and over muscle tissue. The skin itself acts as a noisy low-pass spatial and temporal filter—the extracted myoelectric signal has a reduced response time with respect to that of the underlying signal it seeks to record (muscle activation), and the spatial resolution is such that the signal is a dampened weighted sum of a number of underlying muscles. Extracting information from the underlying peripheral nerves, although more invasive, provides a more reliable measurement of the subject's intent. The advances in techniques and devices provided by the RP program are described in the following section.

### Targeted Muscle Reinnervation

Targeted muscle reinnervation is a procedure that provides improved motor and sensory information for control of motor prosthetic devices.[1] This technique reroutes the peripheral nerves that in able-bodied subjects innervate the upper-limb muscles to intact pectoral muscles. This novel type of surgery was the focus of much attention in RP efforts because it provided a noninvasive method of controlling upper limbs. For example, in shoulder disarticulation amputees, myoelectric sensors are placed over the *pectoral* muscles to provide the mapping between the newly innervated muscles and the perceived upper-limb muscles and to provide the control signals for the upper-limb prosthesis.

Using the same technique, residual sensory nerves can be transferred to the skin surrounding the intact muscle group, providing sensory reinnervation. When this reinnervated skin is touched, it feels as though one is touching the missing limb. This provides an intuitive way to provide pressure, thermal, and vibratory feedback to the patient.

### Multimodal Peripheral Nerve Interface Device

Interactions with the PNS are coordinated by a multimodal peripheral nerve interface device (multi-PID). The device was dubbed *multimodal* because it was to be composed of many devices capable of interacting with (i.e., recording from and stimulating) the PNS. This strategy increases the longevity and quality of signals extracted from the residual limb and nerves by using redundant interfaces to the PNS. The multi-PID and its CNS counterpart, the multimodal brain interface device (multi-BID) (see the *Multimodal Brain Interface Device* section), process the source data described in the next sections using a multimodal control unit (MCU) and a neural fusion unit (NFU) shared with the multi-BID. A schematic representation of the data acquisition and processing units that make up the multi-PID and multi-BID is shown in Fig. 2.

The MCU and NFU, designed and developed here at APL as part of Phase 2 efforts, are responsible for processing the data to decode user intents and encode sensory information for feedback to the brain (cortical MCU) or peripheral nerve (peripheral MCU). The implanted devices that were considered as candidate sources for the multi-PID during Phase 1 of the program are shown in Fig. 3. Neural and physiological data are simultaneously gathered from many sources including efferent (motor control signals that originate in the CNS) and afferent (sensory signals that originate in the PNS) peripheral nerve action potentials, peripheral nerve field potentials, electroneurograms, epimysial electromyograms, intramuscular electromyograms, residual limb/muscle motion, and optical tissue health monitors. Although some of these efforts were not included as part of Phase 3 research, for which a final round of device down-selection was required to help ensure the devices

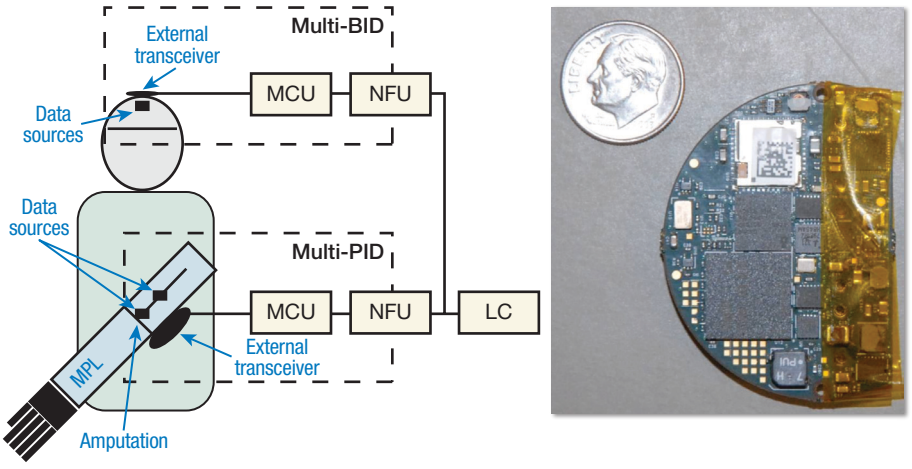


**Figure 2.** (Left) Closed-loop, fully cortical control of the Modular Prosthetic Limb (MPL). The multimodal interface devices, the MCU, the NFU, and the limb controller (LC), all have a form factor that allows them to fit within the MPL itself. (Right) Photograph of an NFU, which is part of both the multi-BID and the multi-PID.

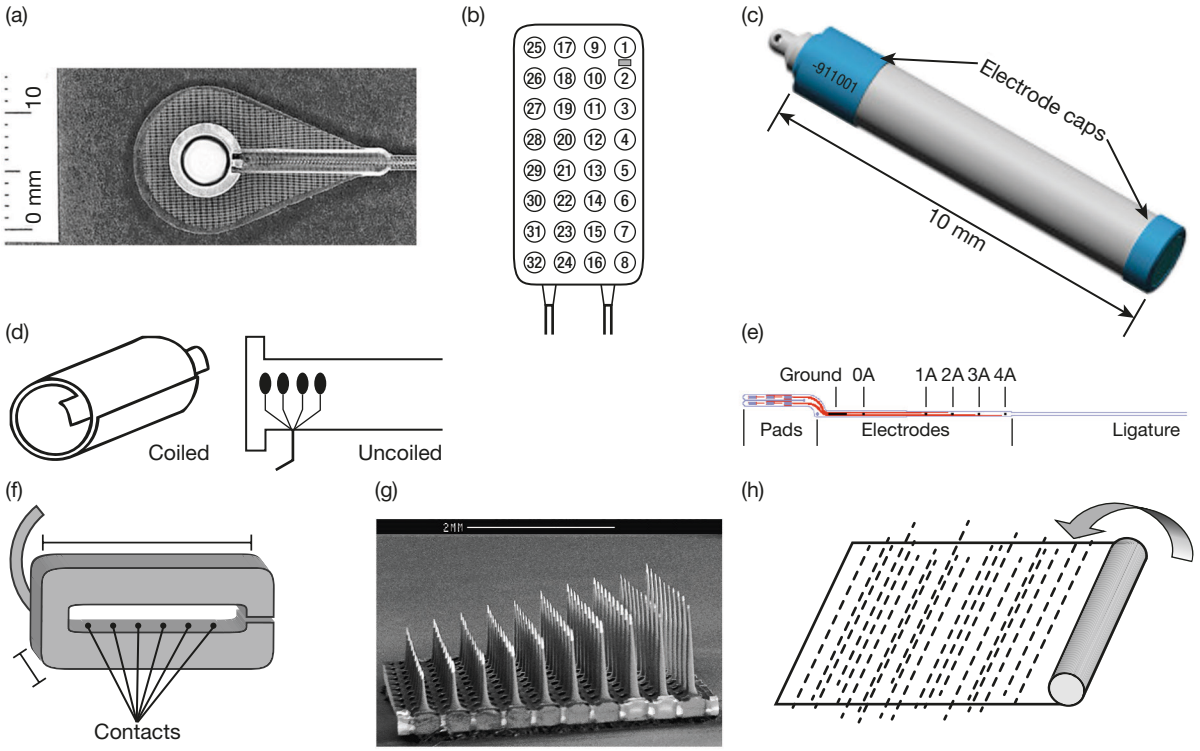


**Figure 3.** Candidate electrode technologies for the multi-PID. The degree of invasiveness increases from left to right and from top to bottom. (a) Epimysial electrode for subdermal EMG.[9] (b) Drawing of an envisioned epimysial electrode array.[10] (c) IMES. (d) Self-sizing spiral cuff electrode.[11,12] (e) Thin-film longitudinal intrafascicular electrodes.[13] (f) Flat interface nerve electrode.[14] (g) Utah Slanted Electrode Array[8] with lengths ranging from 0.5 to 1.5 mm. (h) Drawing of an envisioned biodegradable multiwalled resection interface electrode.[15]

could and would be used for human patients, we do provide an overview of some of these devices, many of which are now closer to actual implementation thanks to the program's efforts.

### *Implantable Myoelectric Sensors*

The IMES (Fig. 3c) were developed at the Rehabilitation Institute of Chicago and Sigenics, Inc., and are partly based on the A. E. Mann Foundation's "BION" stimulator. The IMES and BION share the same exterior packaging system but the IMES have a different set of electronics in the interior to allow recording of electrical muscle activity. Significantly, the BION module has already been used extensively, including in human clinical studies, and found to be safe.[16,17] The use of recording electronics, instead of BION's stimulating electronics, inside the hermetically sealed package does not affect the device's safety, making the IMES system also amenable to human use. The IMES/BION package (see Fig. 3c) is a ceramic cylinder ~15.6 mm long and 2.5 mm in diameter. The IMES electrodes are powered by an external power/telemetry coil system, which also sends and receives the telemetered commands and data. EMG data are transmitted at both a relatively low frequency (60 samples per s; band one) and at a higher frequency (1500 samples per s; band two) that is more suitable for EMG.

### *Extraneural and Intraneural Interfaces*

Cuff electrodes are extraneural electrodes that typically surround the epineurium and record activity from a large number of fibers simultaneously. These electrodes have been investigated in animal studies for more than 30 years (reviewed in Ref. 18), and one model was FDA approved for use in humans more than a decade ago (VNS Therapy System, Cyberonics Inc., Houston, Texas). More recently, Case Western Reserve University's self-sizing spiral nerve cuff electrode (Fig. 3d) received an FDA Investigational Device Exemption (which allows use of the device with human patients) for chronic stimulation of the axillary, suprascapular, radial, and musculocutaneous nerves in the upper arm to reanimate the upper limbs after spinal cord injury.[11] All of the human data obtained to date suggest that the electrode properties remain stable, and the stimulation remains effective, for extended periods of time. Consequently, cuff electrodes could provide a relatively low-risk, low-resolution, and highly reliable chronic interface to the PNS. The primary limitation of cuff electrodes is that their small number of contacts limits the resolution of both stimulation and recording to large populations of peripheral nerve fibers.

In contrast with the cuff electrodes described above, intraneural electrodes can be placed in close proximity

to individual nerve fibers, allowing for single- or multiunit recordings and selective stimulation of small groups of fibers within individual fascicles. An intraneural electrode technology that was evaluated in Phase 2 consisted of longitudinal intrafascicular electrodes (LIFEs; Fig. 3e). LIFEs are small-diameter electrodes that are inserted into a nerve fascicle and then oriented parallel to the fibers. In recent experiments, LIFEs were used to stimulate and record from median and ulnar nerves within the upper-limb stumps of human amputees.[19] These studies demonstrated that intrafascicular recordings could be used to decode motor intent and that intrafascicular stimulation could be used to encode sensory percepts, both of which are critical requirements of the proposed peripheral nerve interface in Phase 2. Although the standard metal LIFEs have not historically had good chronic performance, more recent flexible thin-film varieties have shown favorable biocompatibility and long-term stability of recording properties.[20] Thin-film LIFEs have the additional advantages of incorporating multiple recording sites on one substrate[13] and being potentially compatible with integrated electronics. Because LIFEs can be inserted into specific nerve fascicles, we believe that they may be useful as an intraneural counterpart to the relatively nonspecific recording locations provided by the Utah Slanted Electrode Array (USEA).

### *Utah Slanted Electrode Array*

USEA is a type of intraneural array of 100 electrodes of various lengths (Fig. 3g). Whereas the IMES electrodes had transceiving capabilities built into the device, the USEA [along with its cortical counterpart, the Utah Electrode Arrays (UEAs)] was retrofitted with one of two application specific integrated circuits that afforded the ability to record nerve action potentials (USEA-R) or stimulate the nerve fibers (USEA-S) *wirelessly*. Although details of these chips are provided in the *Recording: the UEA-R* and *Stimulation* sections, some of the results obtained with these devices are detailed here.

Neural command and signal data traveling to and from the chip were wirelessly transmitted and recovered from an array implanted in cat sciatic nerve. The chip provided thresholded neural signals acquired from the USEA. These signals were then compared with those recorded using a commercial Cerebus system (Blackrock Microsystems, Salt Lake City, Utah), a signal acquisition unit to which each individual electrode is connected through a custom cable. The multipeak waveforms recorded by the two systems were equivalent (different filters were applied), although the noise level was somewhat higher for the wireless recording system, as shown in Fig. 4. To prove that the waveform that was transmitted and recovered with the wireless system indeed represented neural discharges, the firing rates in the

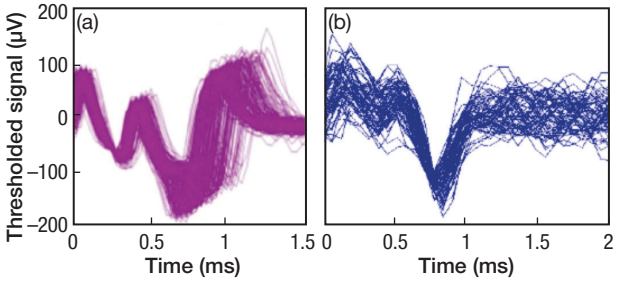


**Figure 4.** Recording of cat sciatic nerve action potentials using (a) an external tethered neural signal processor (Cerebus system) and (b) wireless transmission from an application specific integrated circuit flip-chip mounted to the backside of the USEA.

presence and absence of a hand-delivered stimulus (toe squeeze and possible plantar flexion) were compared. This comparison, using 15 trials each, yielded stimulus-driven firing rates (9.4 ± 0.8 Hz) that were statistically higher than the no-stimulus baseline firing rate (0.8 ± 0.1 Hz; $t_{1,28} = 10.77$, $p < 0.0001$). Comparable results were obtained when the unit was recorded with the Cerebus neural signal processing system.

## INTERFACES WITH THE CNS

Interfacing with the CNS, as shown in Fig. 1, is the most invasive methodology for decoding a patient's movement intent. In some cases, such as in high spinal cord injuries, it is also the only methodology possible. Throughout its phases, the RP program significantly advanced the microelectrode array technology for wirelessly interfacing with the CNS. Many types of microelectrode arrays as well as less invasive electrocorticography (ECoG)-grid arrays (less invasive because they do not penetrate the surface of the brain) were evaluated before commencing the development of fully integrated wireless recording and stimulating arrays. Here, we review the devices that were used for interfacing with the CNS and the pros and cons of each. Finally, we illustrate the technology that was developed to produce the wireless interfaces.

### Multimodal Brain Interface Device

Signal acquisition and processing of activity to and from the CNS is coordinated by a multi-BID. The multi-BID includes a MCU (cortical MCU, see Fig. 2) that coordinates activities from the devices implanted in the CNS and an NFU (shared with multi-PID) that decodes user intent and sends control signals to the virtual or actual upper-limb prosthesis. Therefore, the multi-BID allows different types of electrodes to be implanted depending on the user's degree of disability, the amount of function retained by the residual limb, and the user's tolerance for invasive technologies such that all users will obtain a high level of functionality from the MPL

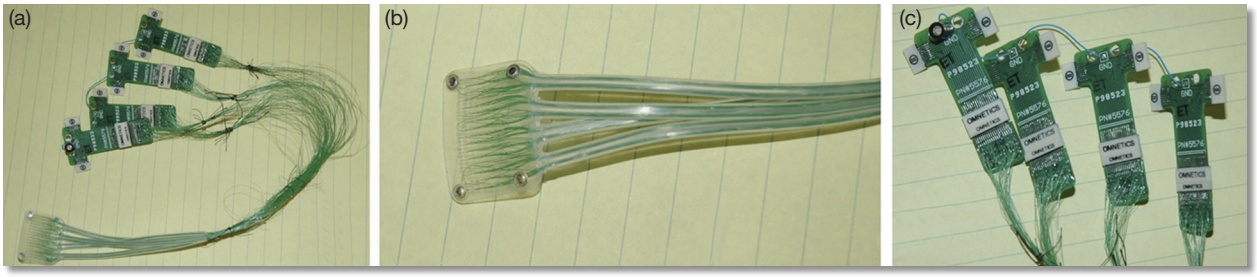


**Figure 5.** Plexon ECoG grid prior to implantation.

(for more information about the MPL, see the article by Johannes et al. elsewhere in this issue).

Primary motor and somatosensory "large field" coverage is provided by electrodes that are spaced 5 mm apart and compose the ECoG grid. Local field potentials and unit activity from higher cortical areas are recorded by UEAs. Microelectrode arrays with longer shanks, such as those from Caltech or Duke, are also used for recording/stimulation but penetrate deeper than the UEAs. This multiplicity of sources increases the robustness of the overall system thanks to its inherent redundancy.

### ECoG Grids

ECoG grids have historically been used to record neural activity in epilepsy patients. The focus in this project was for the ECoG grids to provide broad coverage of the cortex. Figure 5 depicts a 128-electrode ECoG grid that was developed for the program and intended for nonhuman primate implantation. The grid has 128 contacts in an 8 × 16 array, and each contact is at the end of a microwire that is 50 μm in diameter. Contacts spaced 1.5 mm apart afforded a contact area of 10.5 × 22.5 mm.

## PENETRATING MICROELECTRODE ARRAYS

Figure 6 presents four different types of microelectrode arrays that were examined during the RP program. Ultimately, however, only MicroProbes' floating microelectrode array (FMA) and the UEA were used during the course of the program because of their more advanced phase of development and testing.

### Floating Microelectrode Arrays

FMAs are typically made up of a matrix of 16 or 32 electrodes arranged in a four-by-four or four-by-eight grid, respectively. They are characterized by the fact that they have sufficient flexible cabling that allows the arrays to "float" with the brain while one end of the cable remains tethered. The shaft length can reach up to 7 mm (as shown in Fig. 6b), which allows access to deep cortical areas. For example, using long microwires, Schieber[21] showed that neurons that encode movements of each individual finger are located deep within the primary motor cortex (M1) hand region. These electrodes were used in various experiments as part of RP, in the Andersen Lab at Caltech, and at the University of Rochester Medical Center's Schieber lab. The experiments in these labs were designed to collect sufficient data to help make the case to the FDA that the devices are safe to use in human studies. These data are still being collected as part of Phase 3 efforts in hopes that the devices will be approved for use in human patients in 2012.

Importantly, these arrays were used in Dr. Marc Schieber's lab at the University of Rochester Medical Center in an effort to produce the first fully cortical closed-loop brain–computer interface experiments. The arrays were placed on either side of the central sulcus of a rhesus monkey (*Macaca mulatta*). Ten FMAs were implanted in the hand region of the primary motor cortex (M1). The arrays in this region were used to decode 3-D arm trajectory. In addition, five FMAs were implanted in the hand region of the somatosensory cortex (S1). These

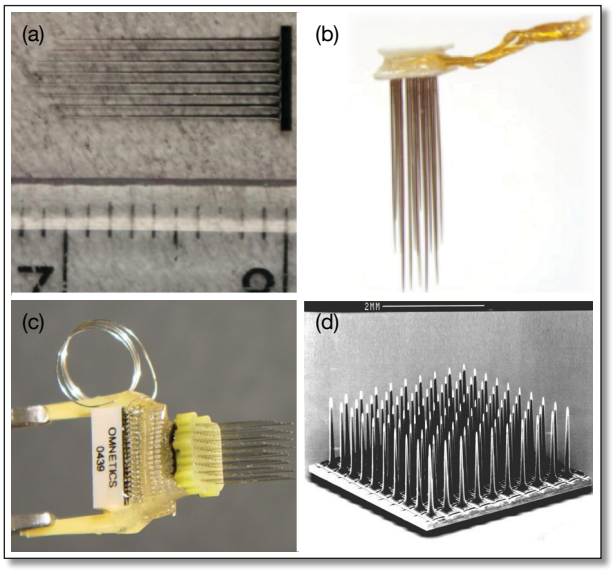


**Figure 6.** Select penetrating microelectrode array architectures investigated over the course of the first two phases of the program. (a) Caltech silicon probes. (b) MicroProbes for Life Science FMAs. (c) Nicolelis 64-channel multielectrode array. (d) Blackrock Microsystems NeuroPort Array (UEA).

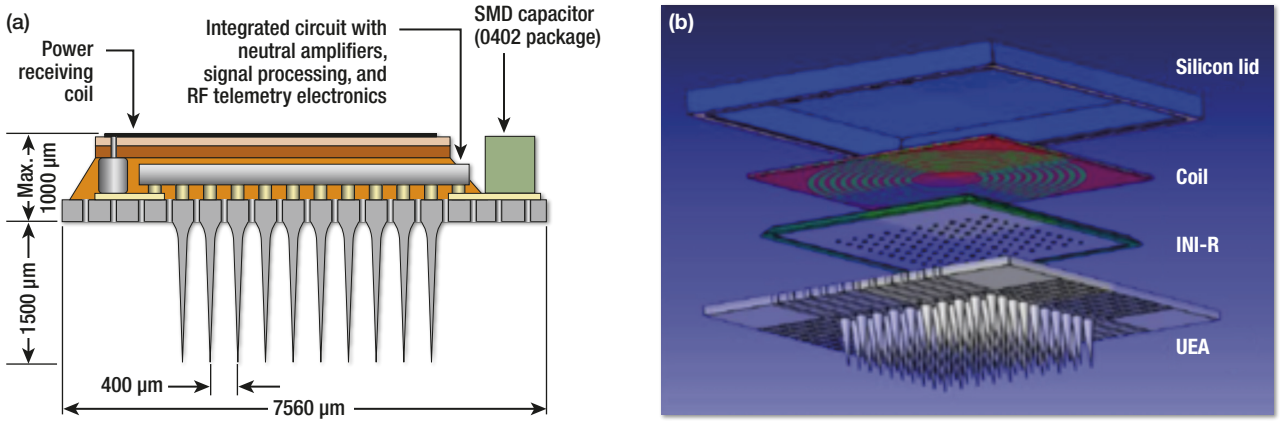


**Figure 7.** (a) Schematic of the integrated UEA-R, with approximate dimensions. (b) Exploded view of the lidded version of the UEA-R, showing the stack hierarchy.

arrays were used to convey vibratory percepts from the monkey's hand in order to alter the trained primate's behavior as a function of the electrical stimulation.

## Utah Electrode Array

The UEA is currently the only penetrating array that is cleared by the FDA for temporary (<30 days) use in human patients for recording electrical activity in the brain. This feature, combined with preliminary efforts at the University of Utah aimed at producing the first wireless modules for the array, made the UEA the best candidate to build upon and to use in developing the technology needed to produce the next generation of fully integrated wireless implants.

### *Recording: the UEA-R*

The UEA-R consists of two main subsystems: the UEA (Fig. 6d) and the integrated neural interface for recording (INI-R) chip developed in collaboration with the University of Utah.[22] The UEA-R device can be used for chronic, wireless recording of neural signals, specifically action potentials and local field potentials, from the cortex. Figure 7a presents a schematic view of the components of the UEA-R and how they are arranged, and Fig. 7b presents an exploded view of the UEA-R's components, which include the UEA, the INI-R, and the power/signal coil.

Rerouting metallization, which is sputter deposited on the backside of the UEA, is used to interconnect the discrete electrical components (SMD capacitors) and the INI-R chip.

The INI-R chip has multiple responsibilities. As shown in Fig. 8, it rectifies and bandpass filters the signals using two-stage amplifiers; it digitizes an analog channel through an analog-to-digital converter for monitoring/threshold selection of a specific channel; and it allows temperature monitoring as well as the unregulated power supply voltage. Most importantly, the chip can

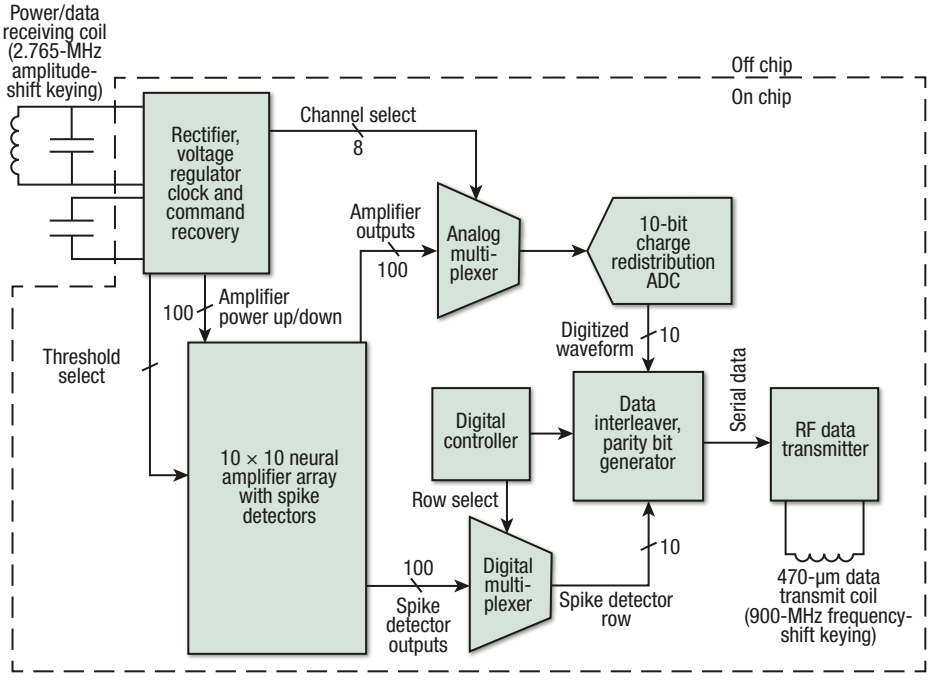


**Figure 8.** System-level block diagram of INI-R chip.

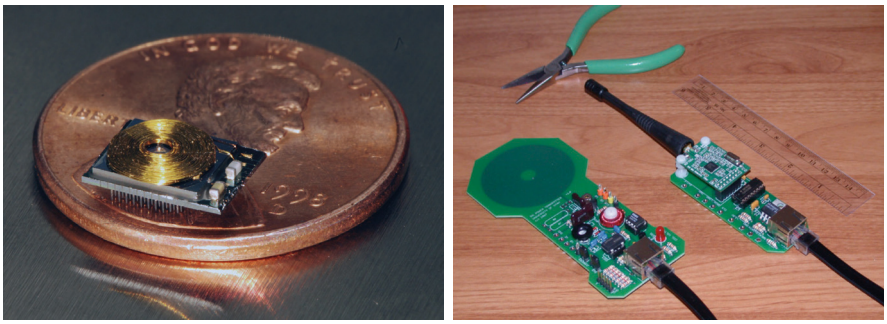

**Figure 9.** Photographs of an unlidded UEA-R wireless recording array (left) and external power and telemetry modules (right). (Left) Fully integrated UEA-R: the electrode tips can be seen on the bottom, the interposer module is the interface between the array and the chip, and the chip itself can be seen beneath the coil. (Right) Interface boards for the INI system. On the left is the power and command transmitter with integrated printed circuit board coil (diameter = 5.2 cm). The coil is driven at 2.765 MHz to provide power and a clock signal to the UEA-R; the amplitude of this signal is modulated to send commands to the chip. On the right is the RF telemetry receiver. The board receives wireless data from the chip in the 902- to 928-MHz industrial, scientific, and medical band at a data rate of 345.6 Kbps.

be programmed to individually select a spike-detection threshold on each electrode, which is the information that ultimately is transmitted to an external receiver for further processing and decoding of user intent. Finally, the chip allows configuration of the 900-MHz industrial, scientific, and medical band, frequency-shift keying RF telemetry transmitter.

The UEA-R is ultimately encapsulated in Parylene C and tested in saline solution under accelerated conditions (57°C as opposed to 37°C) to verify the device's long-term mechanical and dielectric stability; the device would be sterilized prior to implantation.

The dimensions of the device are 7.56 × 5.16 × 2.5 $mm^3$. Figure 9 (left) shows the fully integrated device. In order to power/transmit data to the device as well as receive data from it, two printed circuit boards were developed and tested at the University of Utah (Fig. 9, right).

### *Stimulation*

The UEA-S is similar to the UEA-R in architecture but different in functionality. The purpose of the UEA-S is to deliver charge-balanced, biphasic current pulses to areas of the somatosensory cortex that are capable of being perceived and eliciting behavioral responses. The functionality of the UEA-S is implemented in the device's integrated neural interface for stimulation chip (INI-S), of which a system-level block diagram is shown in Fig. 10. At its core, the INI-S is characterized by a finite state machine that allows configuration of the stimulation parameters of each electrode. As shown in Fig. 11, the finite state machine allows control over the pulse amplitudes, pulse widths, interphasic delay, and the pulse repetition rate.

## RP PHASE 3 DEVICES

The first two phases of the program were responsible for paving the path toward the next generation of neuroprosthetic technologies, occasionally without being able to bring these paths to their natural conclusions. In many instances, this was due to regulatory considerations: the devices that were developed are significant technological improvements compared with implanted devices that are currently approved or cleared by the FDA. Specifically, the FDA had only cleared for acute use (less than 30 days) a standard UEA (known as NeuroPort array).

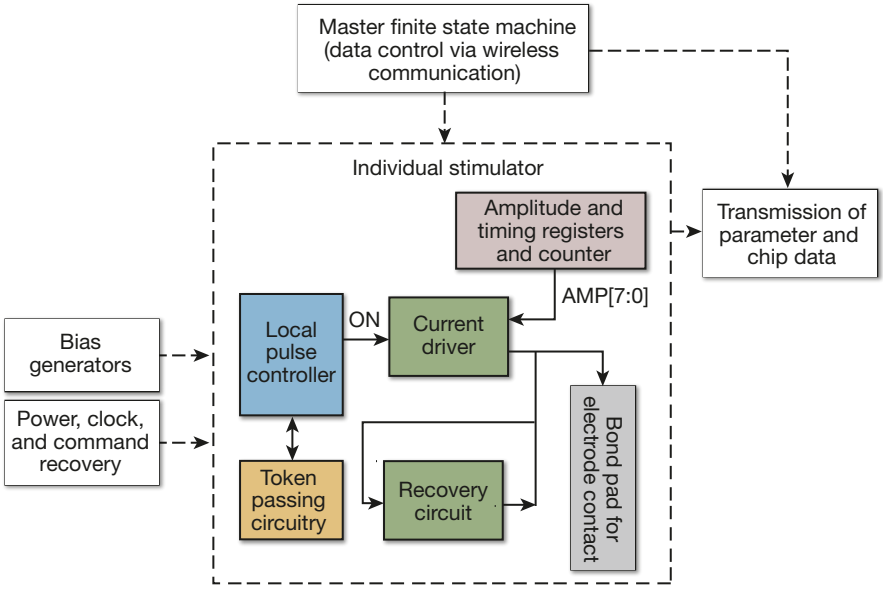


**Figure 10.** System-level block diagram of the INI-S chip.

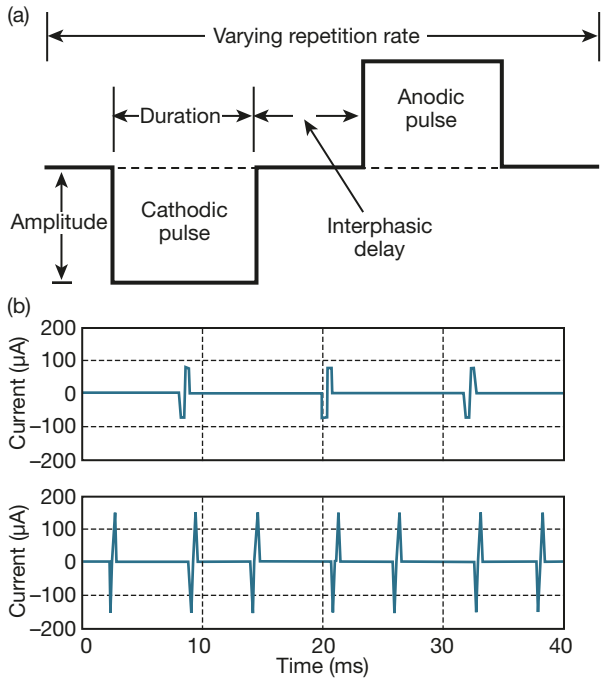


**Figure 11.** (a) Diagram of biphasic current pulse produced by the INI-S chip. (b) Stimulation pulses programmed with repetition rates of 88 Hz (upper) and 166 Hz (lower).

This is in contrast with the devices developed during Phase 2, which had silicon chips mounted on the backside of the arrays and communicated *and were powered* wirelessly to the external modules. These considerations were at the foundation of the approach taken with the Phase 3 devices, which have a much larger emphasis on their potential for regulatory approval and significantly leverage the technologies developed over the course of the first two phases.

In particular, the device shown in Fig. 12, known as the *active UEA for recording*, leverages much of the development of the UEA-R, the main difference between the two being that the array is *wired* and that the application specific integrated circuit flip-chip mounted on the backside of the UEA multiplexes the 96 analog channels such that the surgical operation requires merely 16 wires to be routed through the pedestal per device. As shown in Fig. 12 (right), this allows many recording electrodes (96 per array and two arrays) as well as stimulating electrodes (96) to be connected to a single pedestal, thus simplifying the surgical procedure while not increasing the risk of infection, which would be greater if multiple pedestals were used. This device, or a minor variation of it, is intended to be implanted in a human tetraplegic patient. This paradigm will be a major breakthrough in neuroprosthetics because it will be the first device capable of neurally closing the motor-sensory control loop. In other words, the recording arrays will provide the control signals for the MPL, whose sensors will record percepts that will be transmitted back to the brain through the stimulation array.

Subsequently, we intend to leverage these technological breakthroughs by using a similar framework to develop an *active UEA for stimulating* in an effort to ultimately provide wireless power and communication to a chest-implanted module that allows two-way communication with the implanted arrays.

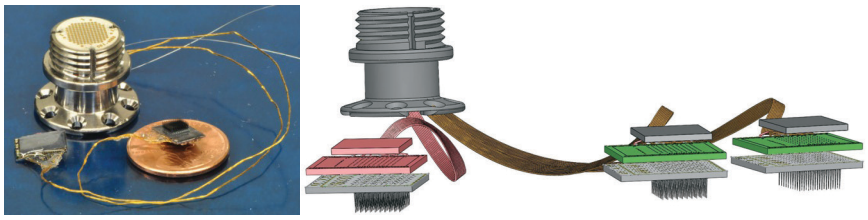

**Figure 12.** (Left) Active recording arrays connected to a single pedestal. (Right) Schematic depiction of three-array solution (two recording, one stimulating) connected to a single pedestal.

## CONCLUSIONS

The first two phases of the program investigated many paths toward achieving a fully neural closed-loop brain–machine interface for amputees and tetraplegic patients alike. The third phase focuses specifically on tetraplegic patients for whom a brain–machine interface that allows them to intuitively control many of the degrees of freedom provided by the prosthetic limb required a huge spark of innovation that resulted in the devices described in the *RP Phase 3 Devices* section. Many questions still remain to be answered by the program. For example, it is uncertain how many neural units are required to control a specified number of degrees of freedom. Hochberg et al.,[23] for example, showed that tetraplegic patients implanted with a single UEA are capable of reliably controlling 2 degrees of freedom. While that is a far cry from the 17 degrees of freedom afforded by the MPL, it is not clear how many degrees of freedom will be made controllable by doubling the number of recording electrodes, as will occur during Phase 3. Importantly, however, the stimulation part of the Phase 3 experiments will allow the first fully neural closed-loop brain–machine interface in human subjects and will help spur new advances aimed at the full rehabilitation of completely paralyzed patients. Specifically, the stimulation/feedback side of the loop will constitute a groundbreaking step in prosthetics because for the first time, humans will be able to *tell us* what they are feeling and experiencing when different stimulation pulses are delivered to different electrodes of the stimulating array.

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