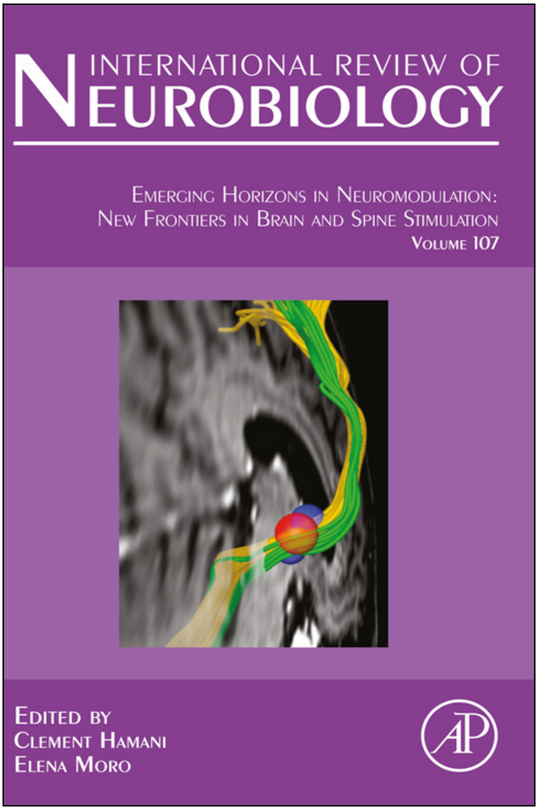

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CHAPTER SEVEN

Current Challenges to the Clinical Translation of Brain Machine Interface Technology

Charles W. Lu[*], **Parag G. Patil**[*,†,1], **Cynthia A. Chestek**[*]
[*]Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, USA
[†]Department of Neurosurgery, University of Michigan Health System, Ann Arbor, Michigan, USA
[1]Corresponding author: e-mail address: pgpatil@med.umich.edu

Contents

Abstract

Development of neural prostheses over the past few decades has produced a number of clinically relevant brain–machine interfaces (BMIs), such as the cochlear prostheses and deep brain stimulators. Current research pursues the restoration of communication or motor function to individuals with neurological disorders. Efforts in the field, such as the BrainGate trials, have already demonstrated that such interfaces can enable humans to effectively control external devices with neural signals. However, a number of significant issues regarding BMI performance, device capabilities, and surgery must be resolved before clinical use of BMI technology can become widespread. This chapter reviews challenges to clinical translation and discusses potential solutions that have been reported in recent literature, with focuses on hardware reliability, state-of-the-art decoding algorithms, and surgical considerations during implantation.

1. INTRODUCTION AND MOTIVATION

Neural prosthetic devices have the potential to provide treatment for many different neurological conditions. As this technology matures, it becomes increasingly relevant to a number of clinical applications. "Input" devices that stimulate the nervous system, in particular, have been especially

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successful in achieving therapeutic effects. Cochlear prostheses, for example, have been implanted in over a hundred thousand people, enabling many profoundly deaf individuals to comprehend spoken language (Fayad & Elmiyeh, 2009). Similarly, deep brain stimulators (DBSs) are the preferred surgical treatment for late-stage Parkinson's disease (Benabid, Chabardes, Mitrofanis, & Pollak, 2009). However, there are also many potential applications for output systems, which record and decode neural signals from the brain. Output systems are commonly used to localize seizures in cases of intractable epilepsy (Kelly & Chung, 2011) and for target guidance of DBS electrodes (Chen et al., 2006; Snellings, Sagher, Anderson, & Aldridge, 2009). In recent years, research has focused on recording neural signals directly from motor cortex to predict motor movements in order to restore movement to individuals with paralysis or amputation.

Paralysis is a widespread problem, common to many disorders such as spinal cord injury, muscular dystrophy, stroke, cerebral palsy, and amyotrophic lateral sclerosis (ALS) (Donoghue, Nurmikko, Black, & Hochberg, 2007). According to the Christopher Reeve Foundation, nearly 6 million individuals in the United States are affected by some form of paralysis, including over a million who are victims of spinal cord injury. Figure 7.1 shows a breakdown of the various causes. Older studies have estimated that there are closer to a quarter million spinal cord injury victims in the United States (Lasfargues, Custis, Morrone, Cars well, & Nguyen, 1995). In either case, however, this represents a large potential demand for implantable brain–machine interfaces (BMIs). The average annual cost of treatment per affected individual ranges from \$40,000/year, for incomplete motor function, to over \$170,000/year, for high tetraplegia (National Spinal Cord Injury Statistical Center, 2012). The use of neural interfaces to bypass dysfunctional neural pathways may significantly offset such costs and improve patients' lives by restoring their ability to interact with their surroundings, via improved communication, control of a motor prosthesis, or other assistive technologies. In a 2008 survey of spinal cord injury patients (Anderson, Friden, & Lieber, 2009), 44% of respondents indicated willingness to undergo tendon transfer surgery to obtain a 30% increase in elbow-extension strength and 66% indicated willingness to gain a 50% improvement in pinch function. Such a procedure can be associated with a long recovery time of 6–12 weeks (Gupta, 2011; Wolford & Stevao, 2003). A BMI system may be able to provide similar or greater benefit with a less invasive surgical procedure.

A number of neural signal sources have been used to generate motor control signals, most notably electroencephalography (EEG), electrocorticography

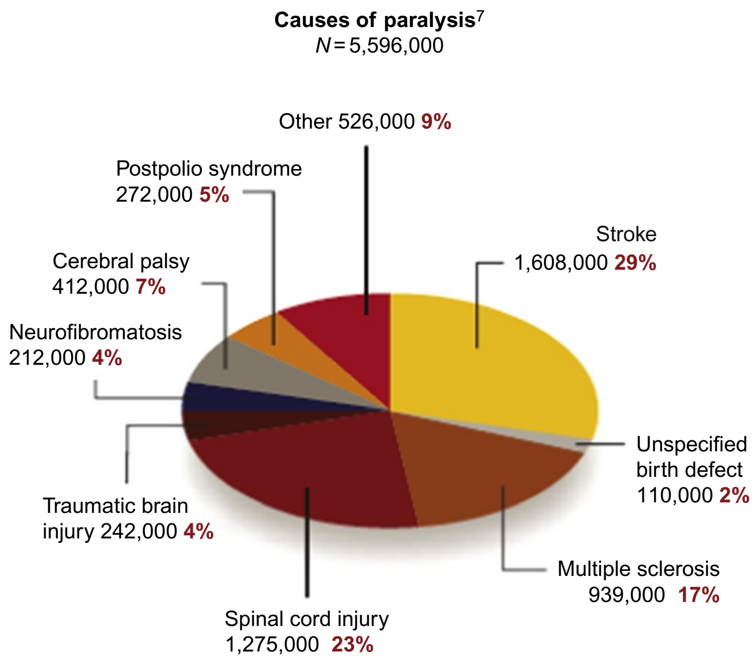

Figure 7.1 Causes of paralysis in the United States. $N = 5{,}596{,}000$. *Reeve Foundation. Paralysis facts and figures.*

(ECoG), and intracortical microelectrode arrays (Schwartz, 2004; Wolpaw, Birbaumer, McFarland, Pfurtscheller, & Vaughan, 2002). All three methods typically record from the cerebral cortex, due to its accessibility and high involvement in both motor and sensory processes. EEG and ECoG detect summed field potentials via surface electrodes, placed on the scalp and cortical surface, respectively (Schwartz, Cui, Weber, & Moran, 2006). EEG systems have been able to reach a communication speed of ~0.5 bps (Wolpaw et al., 2002), which may be useful to patients who are otherwise unable to communicate, except through eye movements (Krusienski et al., 2006). ECoG signals in able-bodied epilepsy patients have shown promise decoding 1 of 5 finger movements with an accuracy of ~80% (Kubánek, Miller, Ojemann, Wolpaw, & Schalk, 2009; Wang et al., 2009). Future higher density ECoG arrays may provide even better performance (Kellis et al., 2010). However, since neural signals fall off in magnitude as the distance to the neurons increases, the highest theoretical information density can be obtained by recording from many individual neurons in the motor cortex, using penetrating high impedance electrode arrays. The exposed tips of these wires can be positioned near individual neurons, providing high spatial and temporal resolution and allowing for single-unit recordings, as shown in Fig. 7.2. This review focuses on BMIs utilizing penetrating microelectrode arrays, though similar device and performance challenges exist for other signal sources as well.

Correlation between single-unit activity and motor control was established as early as 1966, by Evarts, who found that certain arm movements in monkeys could be predicted from the firing rate of individual pyramidal tract neurons, measured using an intracortical electrode. Four years later, Humphrey, Schmidt, and Thompson (1970) showed that accurate, real-time predictions of wrist movements could be made using a small population of recorded cells. In the following decades, development of improved decoding algorithms and recording techniques led to animal models capable of controlling external devices, such as a computer cursor (Carmena et al., 2003; Musallam, Corneil, Greger, Scherberger, & Andersen, 2004; Serruya, Hatsopoulos, Paninski, Fellows, & Donoghue, 2002; Taylor, Tillery, & Schwartz, 2002). The first report of a neural-controlled robotic arm was published by Chapin, Moxon, Markowitz, and Nicolelis (1999), in which rats were successfully trained to position a robotic arm in one dimension to obtain water. Similar results were produced in monkeys 1 year later, by Wessberg et al. (2000), achieving

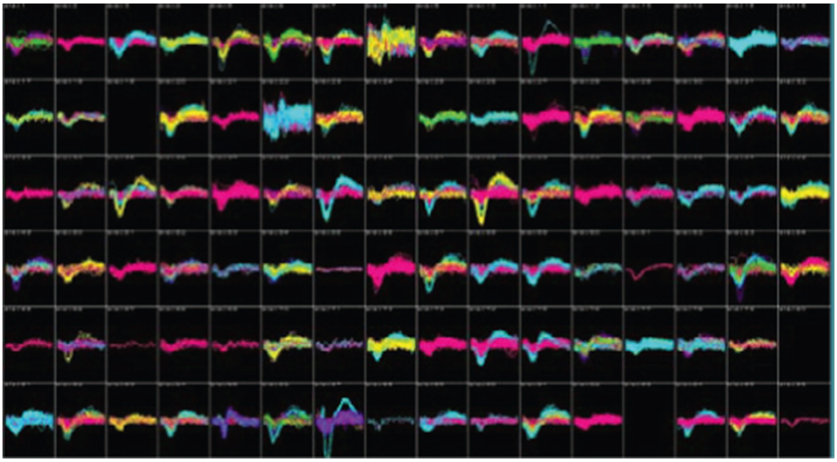

Figure 7.2 Single-unit recordings from the human temporal cortex, 5 days postimplant (Normann et al., 2009). Recordings such as these, from multielectrode arrays, can be used to grant cortical control of external devices.

both one- and three-dimensional manipulation of a robotic arm. In 2008, Velliste et al. presented a groundbreaking achievement in which a monkey was able to feed itself using a cortically controlled prosthetic arm. The success of this project demonstrated a BMI capable of effectively interacting with the physical environment and firmly established the potential of BMIs in prosthetic applications.

The first human trial of intracortical output BMIs was performed by Kennedy and Bakay (1998), in which a patient with severe ALS was able to produce binary on/off indications by controlling neural activity. Since then, several other individuals have participated in intracortical BMI trials, dubbed BrainGate and BrainGate2. This clinical trial's primary objective is to establish safety of the implant. However, experiments have demonstrated some success replicating animal model results in humans. In 2005, one subject became the first person to control a computer cursor and prosthetic hand with a BMI (Hochberg et al., 2006). Most recently, a BrainGate2 subject with tetraplegia successfully used a neural prosthetic arm to drink from a bottle (Hochberg et al., 2012), setting a new milestone in BMI accomplishments.

Despite the success of recent human trials, there remain a number of technological and procedural obstacles to overcome before BMIs are adopted as a routine clinical treatment for paralysis, and these will be the subject of this review. First, there does not yet exist a wireless, implantable, many-channel device that can provide reliable neural signals for many years. Second, systems must have sufficient performance to significantly improve users' quality of life. And third, a standardized surgical protocol must be established prior to widespread use. The following sections describe the current state of the art in these areas and highlight ongoing work to overcome these challenges. Adequately addressing these issues could lead to the first BMI system for clinical use.

2. DEVICE HARDWARE

A clinical BMI system requires an electrode array that can record from many channels in the cortex across many years. Currently, the state-of-the-art device for long-term recording is the Utah array (Nordhausen, Maynard, & Normann, 1996). This array consists of 100 narrow silicon shanks protruding 1.5 mm from a flat rectangular base, as shown in Fig. 7.3 (Normann, Maynard, Rousche, & Warren, 1999). It can be fabricated using wafer scale processes (Bhandari, Negi, Rieth, Normann, & Solzbacher, 2009). Recording sites are located on the shank tips. The flat base enables a one-step pneumatic

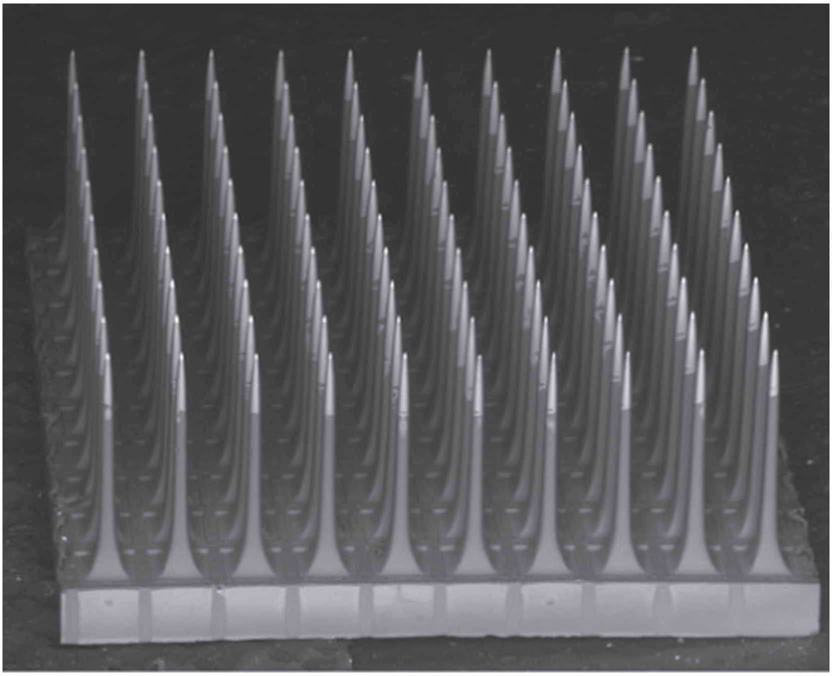

Figure 7.3 The "Utah" array, used in the human BrainGate trials, is capable of simultaneously recording from the tip of each of its 100 electrodes. Stiff shanks allow for precise targeting and positioning of recording sites in a target cortical layer (Bhandari et al., 2010).

insertion of all 100 electrodes. The Utah array has been used in the BrainGate clinical trials (Hochberg et al., 2006) and research with epilepsy patients (Normann et al., 2009; Truccolo et al., 2011). This is the only many-channel cortical array that has been FDA approved for long-term human BMI studies. However, there still exist broad challenges to using such a device in a clinical system, most notably: maintaining signal stationarity, extending device longevity, and eliminating transcutaneous wires.

Over periods longer than several hours, significant variations in the neural signal across time, often referred to as "nonstationarities," can become apparent (Chestek et al., 2011). Action potential waveforms change shape, as illustrated in Fig. 7.4, potentially due to array or neuron movement (Gilletti & Muthuswamy, 2006; Santhanam et al., 2007). Factors such as behavioral shifts (Chestek et al., 2007) or learning (Ganguly & Carmena, 2009; Jackson, Mavoori, & Fetz, 2006) may also contribute to changes in signal.

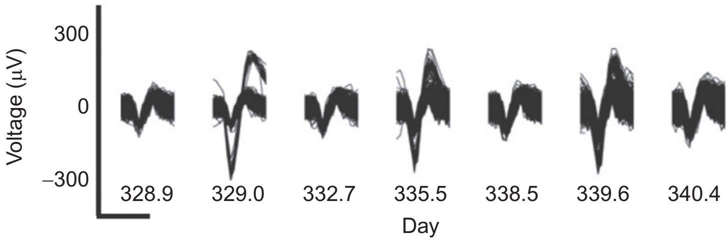

Figure 7.4 Example waveforms across days. A single unit is regularly visible across the recording period, but its waveform changes in shape and can occasionally disappear (Chestek et al., 2011).

In laboratory experiments, changes can be addressed by daily recalibration. Such frequent maintenance, however, is not practical in a clinical setting.

Most approaches to increasing recording longevity have focused on minimizing the gliosis that is an immune response to electrode penetration. The resulting proliferation of astrocytes and dead neurons at the insertion site form a sheath around the electrode, distancing and insulating the electrode from active neurons (He, McConnell, & Bellamkonda, 2006; Polikov, Tresco, & Reichert, 2005; Szarowski et al., 2003; Turner et al., 1999; Zhong & Bellamkonda, 2005). Various methods to mitigate immune response have been investigated, including modification of electrode geometry and modulus (Gandhi, Rousche, Das, Saggere, & Krishnan, 2001; Keefer, Botterman, Romero, Rossi, & Gross, 2008; Kim et al., 2010; Kozai & Kipke, 2009; Szarowski et al., 2003) and insertion technique (Edell, Toi, McNeil, & Clark, 1992; Kozai et al., 2010; Normann et al., 1999). Microwire designs (Lehew & Nicolelis, 2008) may be important in future clinical systems, as very small microwires (<25 μm) elicit minimal immune response from the brain (Kozai et al., 2010; Seymour & Kipke, 2007; Skousen et al., 2011). In such systems, electrodes are driven longitudinally into the cortex for recording and can theoretically be repositioned postsurgery to compensate for electrode movement (Jackson, 2010; Jackson & Muthuswamy, 2009; Wolf et al., 2009). However, it is interesting to note that the glial scar may be stable after a period of weeks (Szarowski et al., 2003) and may not be an important source of signal decline at multiple years.

Various electrode designs have attempted to stabilize neural signals by integrating electrode surfaces with the surrounding neurons. Cone electrodes developed by Kennedy (1989), for example, consist of microwires encased in a small glass cone. Neurotrophic factors within the cone encourage neighboring neurons to grow into the glass cone, establishing close and long-term proximity to the recording electrodes. Such electrodes have potential recording lifetimes of years or longer (Kennedy, 1989; Kennedy, Mirra, & Bakay, 1992). A number of groups have also experimented with biocompatible coatings, which have been shown to improve cell adhesion to recording surfaces (Cui et al., 2001; Cui, Wiler, Dzaman, Altschuler, & Martin, 2003; Green, Lovell, & Poole-Warren, 2009; Kam, Shain, Turner, & Bizios, 2002; Lu, Bansal, Soussou, Berger, & Madhukar, 2006; Olbrich, Andersen, Blumenstock, & Bizios, 1996). Other approaches to mitigating the effects of signal nonstationarities include adaptive algorithms, user adaptation (see Section 3), and simply recording from a greater number of channels. Local field potentials may also provide an alternative source of control signals while maintaining greater stability (Blakely, Miller, Zanos, Rao, & Ojemann, 2009; Chao, Nagasaka, & Fujii, 2010; Hwang & Andersen, 2009; Scherberger, Jarvis, & Andersen, 2005).

Signal nonstationarities from unit recording can also be addressed algorithmically, by learning the statistical properties of the day-to-day signal changes (Bishop et al., 2012; Dickey, Suminski, Amit, & Hatsopoulos, 2009; Nuyujukian et al., 2012) or iteratively updating the model (Hwang & Andersen, 2009; Li, O'Doherty, Lebedev, & Nicolelis, 2011; Otto, Vetter, Marzullo, & Kipke, 2003). Nonstationarities need not be completely eliminated, as small signal changes can be corrected by the user online with subtle adaptations in behavior (Chase, Schwartz, & Kass, 2009; Nuyujukian, Fan, Kao, Ryu, & Shenoy, 2011). It is also important to note that anything that reduces the information content of the signal can worsen nonstationarity in end-effector control. For example, if an electrode lands in a bad location, such as the wrong cortical layer or the wrong somatotopic area, the recorded units will be only weakly tuned to the training movement. Users would then have to generate very precise patterns of activity to achieve particular trajectories, and small behavioral changes can substantially lower performance. A small change of posture or visual stimuli in such a scenario could generate changes in firing rate and cause a strong bias for unexpected movement directions.

Beyond short-term signal changes, a second important issue for clinical devices is longevity. The Utah array has demonstrated the longest neural decoding capability so far, showing high performance several years postimplantation in both human (Simeral, Kim, Black, Donoghue, & Hochberg, 2011) and nonhuman primate models (Chestek et al., 2011;

Fraser, Chase, Whitford, & Schwartz, 2009). During this time period, single-unit waveform height can substantially decline, though it is slower than reported declines for microwire arrays (Williams, Rennaker, & Kipke, 1999). Fortunately, the signal-to-noise ratio of the remaining multiunit activity remains sufficiently high that performance can be maintained for years (Chestek et al., 2011; Fraser et al., 2009). One novel microwire approach has also demonstrated recording capability across 7 years (Krüger, 2010). Even greater longevity, however, may be required for a clinical device.

Another limitation to recording longevity is hardware failure, particularly involving mechanical failures in device encapsulation due to the biological environment. Intracortical devices have traditionally been coated and sealed by biocompatible polymers such as Parylene, Teflon, and silicones (Bae et al., 2010; Borton et al., 2009; Hsu, Rieth, Normann, Tathireddy, & Solzbacher, 2009; Hsu, Tathireddy, Rieth, Normann, & Solzbacher, 2007; Loeb, Walker, Uematsu, & Konigsmark, 1977). Such coatings, however, still experience significant corrosion after chronic exposure to electrolytic environments (Sharma, Rieth, Tathireddy, Harrison, & Solzbacher, 2010) and eventually lead to the failure of electronic components over a timescale of months or years. The current standard for protecting electronics in implantable biomedical devices, used in pacemakers and DBSs, is a welded titanium can with hermetically sealed connections to electrodes. There is currently no simple way to achieve the same standard for cortical BMI implants, which typically have many more channels than a conventional hermetic feed-through. A few groups, however, have made significant progress toward the realization of such a device (Borton, Yin, Aceros, & Nurmikko, 2012; Kelly et al., 2009; Rizk et al., 2009).

Another clinically challenging aspect of current BMI devices is the use of transcutaneous leads, which are vulnerable to infection. For this reason, many groups are working to develop wireless interfaces to the electrodes. Currently, transcutaneous devices are limited by the number of channels on the connector and by the electrical noise picked up by the cables. Both of these problems could be solved by amplifying and digitizing the data close to the electrodes with the use of integrated circuits. The Michigan-style array is an example of an electrode with active electronics. It consists of one or more planar silicon shanks with recording sites spaces along its length (Johnson, Franklin, Gibson, Brown, & Kipke, 2008; Wise, Anderson, Hetke, Kipke, & Najafi, 2004) as shown in Fig. 7.5. A number of microchips have also been developed for neural signal processing that

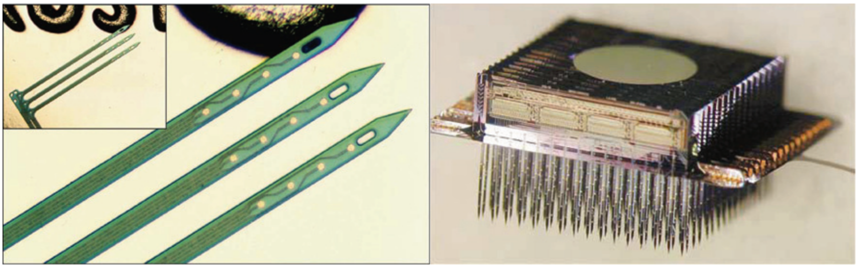

Figure 7.5 Left: Individual shanks of a "Michigan"-style array. Individual recording sites are spaced along a planar silicon shank. The probe is juxtaposed with the "TRUST" on a US penny. Right: A high-density Michigan-style array with 1024 recording sites. Each of the 128 silicon shanks supports 4 independent sites. While not used *in vivo*, this provides a proof of concept for achieving higher channel counts through active electronics (Wise et al., 2004).

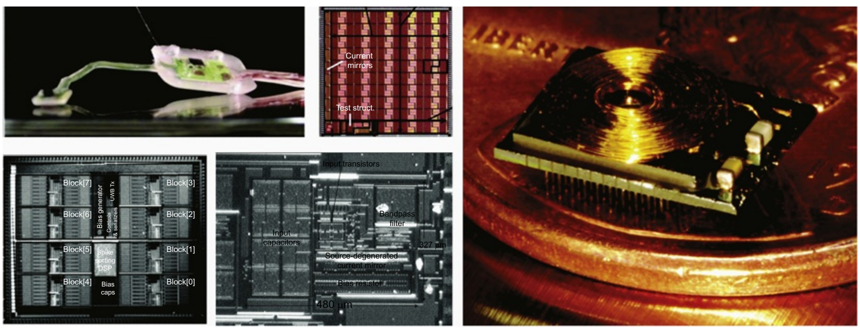

Figure 7.6 There exist a wide variety of microchips developed for neural signal processing. Some, like the device shown right (Harrison et al., 2009; Sharma et al., 2011), are integrated with an electrode array. Clockwise from top-left: Borton et al. (2009), Chae et al. (2009), Gao et al. (2012), Sharma et al. (2011), and Wattanapanitch, Fee, & Sarpeshkar (2007).

could theoretically be integrated with an electrode array (Bae et al., 2010; Borton et al., 2009; Chae, Yang, Yuce, Hoang, & Liu, 2009; Gao et al., 2012; Gregory et al., 2009; Nurmikko et al., 2010; Rizk et al., 2009; Sarpeshkar et al., 2007; Sharma et al., 2011; Sodagar, Perlin, Yao, Najafi, & Wise, 2009) as shown in Fig. 7.6. Such systems generally operate using ultralow power amplifiers and can be powered and controlled via inductive connections to external devices. One system has been integrated directly on the back of the Utah array (Chestek et al., 2009; Harrison et al., 2009; Tathireddy et al., 2011).

3. PERFORMANCE

If an appropriate device were available, what level of BMI performance would justify its surgical implantation? In a 2004 survey of tetraplegics by Snoek, Ijzerman, Hermens, Maxwell, and Biering-Sorensen (2004), over 70% of participants responded that restoration of hand control was important or very important to improving their quality of life. This finding was affirmed in a survey by Andersen (Andersen et al., 2004; Anderson, 2009), in which tetraplegics overwhelmingly ranked arm and hand function as the most effective way to improve their quality of life. These could theoretically be provided using cortical BMI control over a prosthetic limb or reanimation of the existing paralyzed limb using functional electrical stimulation (Peckham & Knutson, 2005). However, in a laboratory setting, tasks of daily living are not easy to evaluate, particularly in nonhuman primates. Therefore, most prior research has focused on the control of computer cursors or other convenient abstractions.

Traditionally, tasks and algorithms can be categorized into two distinct control paradigms: discrete and continuous. Of the two, performance is easiest to evaluate for discrete systems, as it can be simply measured in bits per second. Discrete control algorithms allow users to make categorical selections from a number of available options. Commonly employed algorithms include Naive Bayes (Baker et al., 2009; Santhanam, Ryu, Yu, Afshar, & Shenoy, 2006), linear discriminant analysis (Ajiboye & Weir, 2009; Fazli et al., 2012; Pistohl, Schulze-Bonhage, Aertsen, Mehring, & Ball, 2012; Zhou et al., 2007), and support vector machines (Olson, Si, Hu, & He, 2005; Stark & Abeles, 2007; Wang et al., 2009). Discrete interfaces are particularly relevant for restoration of communication and can be implemented in the form of keyboards or menu selection. Also, many practical clinical prosthetic systems use discrete commands to control continuous devices, for example, in arm prostheses for amputees (Ohnishi, Weir, & Kuiken, 2007) or functional electrical stimulation systems (Peckham & Knutson, 2005). Classifiers can also provide a supporting role for continuous decoders that switch between various modes (Achtman et al., 2007; Kemere et al., 2008; Wu et al., 2004; Yu et al., 2009).

Currently, the fastest reported decoder achieved peak speeds of 6.5 bps (Santhanam et al., 2006), equivalent to about 15 words per minute (wpm).

For communication, this is already higher than typical composition speeds, on the order of 9 wpm (Pianko, 1979). It is also comparable to classification rates achieved by many advanced prosthetic arm controllers (Ajiboye & Weir, 2009; Kuiken, Dumanian, Lipschutz, Miller, & Stubblefield, 2004; Kuiken et al., 2007; Ohnishi et al., 2007; Zhou et al., 2007). However, cortical BMI results have come from nonhuman primate studies, and the same level of performance has not yet been demonstrated in human subjects. Also, as discussed above, this performance must be maintained across many days without recalibration to be practical.

In the case of continuous control of a computer cursor, performance can be more difficult to judge as tasks vary substantially between studies. However, performance can theoretically still be quantified in terms of bits per second using Fitts law (Fitts, 1954; Kim et al., 2006, 2007; Kim, Simeral, Hochberg, Donoghue, & Black, 2008; Soukoreff & MacKenzie, 2004). In this approach, the information content or "index of difficulty" of a reach is determined by ratio of the distance to the target over the size of the target and can be measured in bits. For example, Ganguly and Carmena (2009) used a difficulty of 2.4 bits, which is high compared to other BMI studies. One can normalize by the average prosthetic reach time (including the selection time) to estimate bits per second. One recent study demonstrated nearly 2 bps (Gilja et al., in press) (Fig. 7.7). This is 80% as fast as when the monkey was using its hand to perform the same task and is on par with some commercial computer input devices in terms of bit rate (Soukoreff & MacKenzie, 2004).

Many algorithms have been attempted over the years that have increased the overall level of performance. Early studies focused on linear decoders such

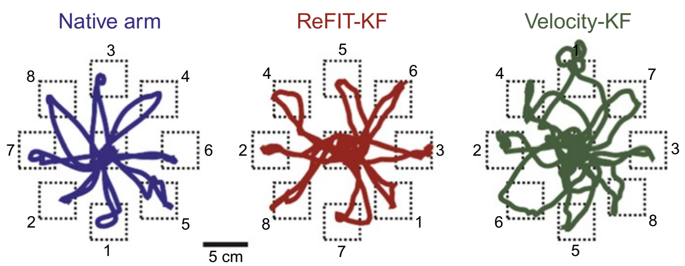

Figure 7.7 Traces of continuous center-out-and-back tasks. The left trace was performed with the monkey's native arm while the center and right traces were performed using cortical control via two different decoding algorithms. The center trace, using a recalibrated feedback intention-trained Kalman filter algorithm, approaches that of the native arm (Gilja et al., in press).

as Wiener filters (Carmena et al., 2003; Serruya et al., 2002) or population vectors (Georgopoulos, Schwartz, & Kettner, 1986; van Hemmen & Schwartz, 2008), which utilize a linear map between neural firing rate and endpoint position or velocity. Performance with such systems can be high, particularly when there is adaptation on the part of the user, or the algorithm, or both (Fetz & Baker, 1973; Ganguly & Carmena, 2009; Koyama et al., 2010; Serruya, Hatsopoulos, Fellows, Paninski, & Donoghue, 2003; Taylor et al., 2002). However, they do pass noise in neural firing rates directly through to the output. To mitigate this problem and increase the "controllability" of the cursor, several groups have improved performance using variations of Kalman filters (Gilja et al., in press; Kim et al., 2008; Wu, Gao, Bienenstock, Donoghue, & Black, 2006; Yu et al., 2009), which include a "trajectory model" that forces the cursor to act like a physical object with momentum. However, the Kalman filter still assumes a linear relationship between neural activity and endpoint kinematics. This could be improved by adding an appropriate nonlinearity at the output of a linear decoder (Pohlmeyer, Solla, Perreault, & Miller, 2007), or using a more general nonlinear decoder such as a neural network (Aggarwal et al., 2008; Sussillo et al., 2012).

Cursor control paradigms are important for establishing quantitative benchmarks for evaluating control schemes. However, they can only approximate hand and arm control in three-dimensional space. Just recently, a small number of studies have demonstrated such control using BMIs. Another demonstration was published by Velliste, Perel, Spalding, Whitford, and Schwartz (2008), in which a monkey could self-feed using a cortically controlled robotic arm. In 2012, similar accomplishments were achieved by a human subject in the BrainGate2 trials (Hochberg et al., 2012) as shown in Fig. 7.8. In terms of restoring control of an individual's own paralyzed limbs, Moritz, Perlmutter, and Fetz (2008) and Ethier, Oby, Bauman, and Miller (2012) demonstrated restored grasping in a temporarily paralyzed limb on a nonhuman primate by decoding EMG signals from cortical brain activity and stimulating the paralyzed muscles with a similar pattern. These landmark studies achieve restoration of movements that are relevant to activities of daily living, and may represent sufficiently high performance to motivate future clinical trials.

4. SURGICAL CONSIDERATIONS

With the exception of surface-mounted EEG, the creation of a usable BMI is likely to require surgery. Signals have been accessed from both the surface of the brain and deep brain structures. Other sources of neural signals

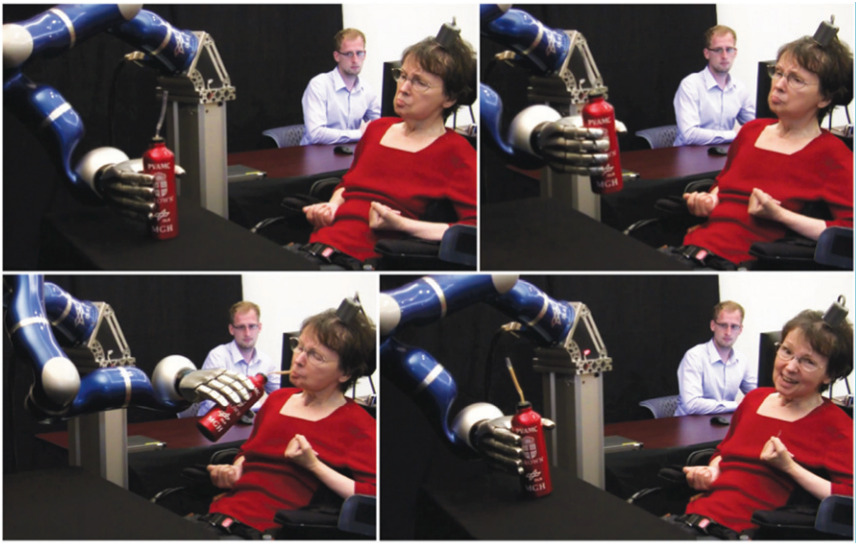

Figure 7.8 A BrainGate2 participant using a cortically controlled robotic arm to drink coffee from a bottle. Control of the robotic arm relies on both continuous and discrete control paradigms to dictate motion and grasping, respectively (Hochberg et al., 2012).

may include the spinal cord or peripheral nerves. State-of-the-art devices for restoration of communication and motor capabilities, however, have relied on the Utah array, requiring removal of a small section of skull.

Implantation of the Utah array into the motor cortex utilizes a high-speed pneumatic impactor system as shown in Fig. 7.9. Insertion is performed at 1–11 m/s in order to effectively penetrate the cortical surface (Rousche & Normann, 1992). Electrode tips are precisely positioned, often at layer 5 of the motor cortex. Placement of the array can be determined using an atlas and can be functionally confirmed with microstimulation. Once the array is implanted in the target location, wires must pass through a remaining opening in the skull. As discussed earlier, future BMIs will likely be without transcutaneous connections. Operating time is typically a few hours and recovery time is under 3 days (Normann et al., 1999; Rousche & Normann, 1992).

Comparable surgeries in widespread clinical use include ECoG and deep brain stimulation (DBS) surgery. Procedures such as these are safely and routinely performed for the treatment of epilepsy, the treatment of pain, and the mapping of brain tumors. Surgeries performed thus far for BMI implantation

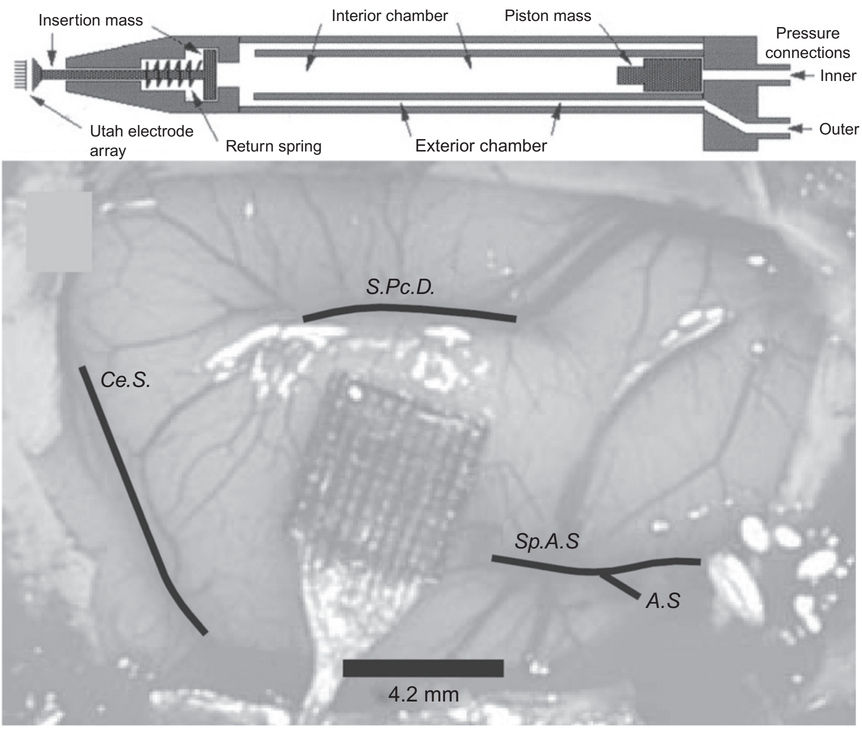

Figure 7.9 Top: Diagram of the pneumatic impactor used to implant the Utah array. The Utah array is located at the left end of the figure (Normann et al., 1999). Bottom: Placement of an electrode array in the dorsal aspect of the premotor cortex (Batista et al., 2007). Sulcal landmarks used to locate the recording site are hand-drawn on the image.

are less invasive than other commonly performed neurosurgical procedures for trauma, vascular lesions, and brain tumors (Chan et al., 2009; Lee et al., 2008; National Comprehensive Cancer Network, 2009). For the placement of subcortical electrodes, the techniques have also been already established for the precise placement of depth electrodes in the evaluation of epilepsy and the placement of DBSs for movement disorders (Chen et al., 2006; Snellings et al., 2009). These procedures are well within the reach of most well-trained neurosurgeons, and many have brief recovery times for the patient.

Alternative surgical interventions to restore motor function include tendon transfer and nerve grafts. Both, however, are feasible only for a selected subset of patients and often create a secondary defect. Tendon transfer requires a functioning muscle local to the affected area and typically results in the loss of another motor function (American Society for Surgery of the Hand, 2011).

Nerve grafts require functioning nerves above the C6 or C7 level and result in the loss of a less crucial function. Recovery for such surgeries is typically on the order of a few months, including a period of immobilization, prior to the start of physical therapy (Gupta, 2011; Wolford & Stevao, 2003).

In comparison to alternative treatments, output BMIs may offer a less invasive solution and broader applicability. Implantation of a Utah array is also less invasive than DBS surgery, while offering a potentially greater improvement in quality of life given the high level of disability in paralyzed individuals. This is not to say that BMI surgery is not without substantial technical challenges and potential for improvement. These arise from the need for accurate targeting of the region of the interface, adept placement of the BMI sensor, and implantation of a mechanism to transduce the electrical activity of the brain to transmissible signals. Current targeting techniques might be improved using anatomical imaging and fMRI, similar to other neurosurgical procedures (Chen et al., 2006; Snellings et al., 2009). Challenges arise both from our lack of understanding of where usable signals may be in the brain and also individual variability in the localization of these signals (Schieber, 2001). BMI surgeries are also likely to benefit from greater standardization of devices and protocols in BMI technology (Kubler, Mushahwar, Hochberg, & Donoghue, 2006). For example, the use of a common standard across the field could allow for mixing and matching of components to customize implants for individual needs.

5. CONCLUSION

With the success of recent human studies, output BMIs are on the cusp of providing a new avenue for paralyzed patients to regain communication and motor functions. Having achieved significant levels of performance with existing BMI technology, increased effort has been directed toward the establishment of a clinically viable device. Much of the field is now focused on steps toward translation, similar to those taken by now-widespread technologies such as pacemakers and DBSs. With an emphasis on collaboration and a concerted push for additional clinical trials, BMIs may one day substantially reduce the burden of disease associated with paralysis.

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