CHAPTER 2

Sensor Technology

Greg A. Gerhardt and Patrick A. Tresco

INTRODUCTION

This chapter deals with an overview of sensors used in the collection of data for Brain-Computer Interface (BCI) technology. For the purposes of this chapter, we divide sensor technologies into two basic categories. First, we discuss "invasive" technologies, which entail brain surgery procedures for implantation involving primarily multielectrode recordings from arrays of microelectrodes implanted directly into the brain to measure action potentials from single cells. This is a major growth area for sensor technologies and will be the major focus of this chapter. However, we caution that most of this technology is under development in animal models and is not yet approved for human use. In addition, measurements from subdural or epidural strips of electrode arrays used to record cortical potentials somewhat analogous to EEG-type recordings on the surface of the skull will be discussed, as this is currently the greatest application for use of these invasive electrodes in humans for (primarily) epilepsy surgery. However, this could help increase the growth of other BCI applications. Second, we discuss "noninvasive" technologies, which primarily involve multielectrode EEG recording arrays of "wet" silver (Ag) or gold (Au) conducting paste electrodes that are placed on the surface of the skull to record EEG activity. These electrodes are commercially available from a number of sources, but surprisingly, there has been limited growth in this area. We caution that "noninvasive" electrodes have largely been used acutely and may be more invasive to the scalp when used in future, more chronic, applications of BCI technology by humans at home or work. Additional tech-nology development in this area will be briefly discussed.

We do not discuss other types of recording electrodes such as EMG electrodes and associated electrodes, which are covered in other sources. In addition, we do not discuss deep-brain stimulation (DBS) technology, which is used extensively in patients with movement disorders (Kossof et al., 2004). This area, however, should be monitored as the chronic implantation of the stimulating electrodes for DBS is a

T.W. Berger et al., Brain-Computer Interfaces, 7–29.

clinical forum for development of long-lasting brain electrode technologies and a test bed for development of brain-compatible BCI devices (see Chapter 3).

Electrodes are enabling technologies to allow information from the brain to be encoded by computer algorithms to provide input and control of BCI devices. Without these devices we cannot transfer information from the brain that can be used to control BCI instrumentation. As such, it is too often assumed that the technologies surrounding sensors for BCI are fully worked out and that there is little room for improvement. In reality, there is a tremendous potential for growth of these devices and need for new types of both invasive and noninvasive electrode technologies to further pursue BCI applications. The major challenges are discussed at the end of this chapter.

The purpose of the present chapter is to review the current sensor technologies used for invasive and noninvasive BCI approaches throughout North America, Europe, and Asia. We have visited and/or interacted with key laboratories with expertise in these areas. Although not completely comprehensive, this chapter gives an overview of the major sensor technologies that are being developed for potential BCI applications.

We are pleased to acknowledge the extensive assistance of Jason J. Burmeister, our colleague at the University of Kentucky, for helping us prepare this chapter.

BCI SENSOR WORLD OVERVIEW

Most BCI science in North America involves “invasive” sensor technologies, i.e., multielectrode recordings from arrays of microelectrodes implanted directly into the brain. This is the greatest area of growth in sensor technology.

Most BCI science in Europe involves “noninvasive” sensor technologies, i.e., using multielectrode recordings from arrays of EEG electrodes mounted onto the surface of the skull. This sensor technology has experienced a very limited growth and requires substantial improvement. Certain BCI sites in Europe are capable of providing sensor technologies that could aid in the advancement of “invasive” sensor technologies; however, this is not their current plan.

Even with respect to noninvasive technologies, many European sites collaborate with, or utilize paradigms that were developed in the United States, such as at the Wadsworth Center in Albany NY.

In Asia, there is a clear emphasis on less expensive EEG BCI approaches. Reasons include the large population in China and the need for low-cost, noninvasive BCI technology for improved public healthcare there. Japan is also focused on noninvasive EEG-based BCI technologies. There is rapid economic growth and science spending in China and Japan that will propel all BCI technology development forward. In addition, there are clear indications that facilities are available and there is interest in invasive BCI technology in China. Overall, the panel believes Asia has the manufacturing facilities and infrastructure to drive

development of new invasive BCI technology development that could rival or exceed U.S. efforts in five to ten years.

MAJOR TYPES OF SENSORS FOR BCI TECHNOLOGY

History of Direct Implantable Electrodes

The history of implanting electrode arrays in the CNS (see Chapter 3 for historical references and additional papers) dates back to the early work of Hess in the 1930s with initial implants in felines. This set the stage for investigators in the 1950s, such as Heath and Olds (Heath et al., 1953; Olds et al., 1971; Baumeister, 2006), to use implantable electrodes primarily for electrical stimulation of the brain, but also for recording. In the late 1950s, Fischer and colleagues were the first to use a variety of different metal-type electrodes and single-wire electrodes and also started to investigate any pathology resulting from the effects of wire electrodes (see Chapter 3). However, the more modern adaptation of implantable electrodes occurred in the 1970s. Selman and Bach in the early 1970s started using coated microwires for electrophysiological recordings, and in the early 1980s Chapin and Woodward (1986) reported the development of 50 μm tungsten microwire arrays for multiple single-unit recordings. Basically, this type of technology is used today by many laboratories for the more routine multiple single-unit recordings and many applications of BCI in animals. However, some of the problems of multiwire arrays relate to precise control of the electrode recording sites and issues surrounding the viability of individual wires.

Between 1970 and 1975, Wise and Angell (Wise et al., 1970; Wise and Angell, 1975) introduced the concept of using integrated chip (IC) technology to develop microelectrodes. Over the next years, numerous papers were published, and in the 1980s the seminal work of BeMent and coworkers (BeMent et al., 1986; Drake et al., 1988) was the first development of a multisite microelectrode arrays from silicon. A few years later, in the early 1990s, the first silicon-based monolithic multishank electrode array was developed, which is now used by numerous laboratories and is even used for human BCI applications by Donoghue and coworkers (Hochberg et al., 2006). In general, microelectrodes can provide a means to electrically stimulate and record both electrophysiological activity and chemical activity of neurons in the brain and spinal cord (Hochberg et al., 2006; Burmeister and Gerhardt, 2006). There have been many reports too numerous to cite for this chapter of the design and use of microelectrodes for electrophysiological recordings (Anderson et al., 1989; Burmeister and Gerhardt, 2006; Cheung, 2007). In addition, in part we have discussed some of this technology in a recent chapter (Burmeister and Gerhardt, 2006).

Wire-Type Microelectrodes

Currently, the workhorse electrode for recording multiple single-unit action potential activity from the brains of animals is through the use of what are termed microwire array bundles. These generally involve the use of 13–200 μm-diameter, Teflon®-coated tungsten (W) or iridium (Ir) wires arranged in bundles of 16–64 or even hundreds of wires. Some of the longest BCI-type recordings for 1.5 years have been carried out with these types of electrodes (see also Chapter 3).

Most wire-type microelectrodes are constructed by sealing a metal (tungsten, gold, platinum, iridium, platinum-iridium, stainless steel) wire in an insulating material. The metal wires from the brain and the connections between the recording wires are insulated using Teflon or plastics. The microelectrode surface area is determined by cutting the exposed wire to a desired length. Typical wire electrodes range in diameter from 13–200 μm, with an exposed length of up to 1 mm. Wire electrodes are widely used for recordings in rats, monkeys, cats, and more recently, mice (see Table 3.1 in Chapter 3, Burmeister and Gerhardt, 2006; Ludvig, 2001; Chapin and Nicolelis, 2001; Chapin, 2004; Chiganos et al., 2006; Lin et al., 2006). Figure 2.1 shows an example of a high-density array and integrated microdrive for recordings from as many as 128 wires from freely moving mice (Lin et al., 2006). In addition, this microwire bundle incorporates a microdrive device so that the microwire electrodes can be repositioned for optimum performance during the recordings. Additional information about wire electrodes can be found in other sources (Burmeister and Gerhardt, 2006).

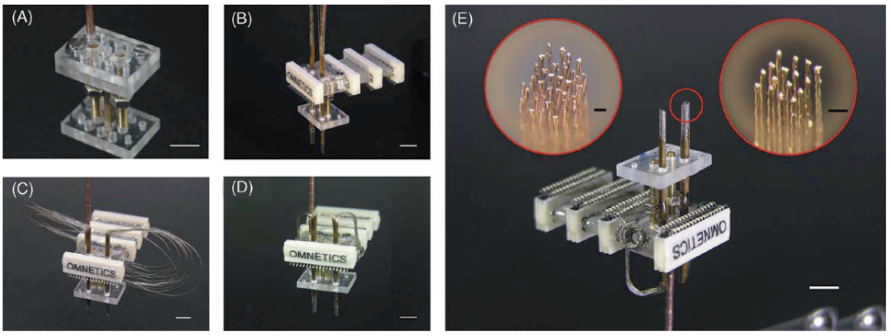

Figure 2.1. Construction of a high-density ensemble recording microdrive for mice. (a) is the base foundation for the microdrive; (b) indicates four 36-pin connector arrays positioned at the base of the microdrive in parallel (each bundle of 32 pieces—for stereotetrodes—or 16 pieces (for tetrodes) of polyimide tubing was glued to an independently movable screw nut on the microdrive base); (c) is a microdrive on the assembly stage (the free ends of electrode wires are wrapped around to adjacent connect pins); (d) is a fully assembled, adjustable 128-electrode microdrive; (e) indicates that 128 channels can be formatted with either tetrodes (right inset) or stereotetrodes (left inset) on each bundle. The tip of the two electrode bundles was shaped at a certain angle (10°–20°) to fit the contour of the dorsal CA1 cell layer. Black scale bars in red circles of (e) are 100 μm. White scale bars in (a–d) are 3 mm (Lin et al., 2006; © The Society for Neuroscience).

Traditional wire-type microelectrodes are still in wide use for several reasons. First, they can be purchased from several vendors or constructed from commercially available materials (Sugiyama et al., 1994; Williams et al., 1999; Rennaker et al., 2005; Lin et al., 2006; Burmeister and Gerhardt, 2006). Second, very small microelectrodes can be constructed (Lin et al., 2006; Burmeister and Gerhardt, 2006). Third, they are established in the field. However, traditional wire microelectrodes have disadvantages. Because they are handmade, large variability between individual microelectrodes with inconsistent geometries can result. Surface area variability resulting in altered response characteristics can be caused by irregularities in the cut tip and the junction between the metal and the insulating material. Because of the needed supplies and materials as well as the art of their production, many labs have difficulty assembling reproducible microelectrodes.

Mass-Fabricated Microelectrodes

Photolithographic methods employed in the microcircuit industry are used for the mass fabrication of microelectrodes (Burmeister and Gerhardt, 2006; Cheung, 2007). Recording surfaces as small as 5–10 μm can be routinely produced now, and in the future, surfaces as small as 0.1–4 μm will be developed using photolithography methods (Smith et al., 2004). This rivals or exceeds some of the smallest traditional microelectrode tips for intracellular recordings. However, less expensive screen-printing methods can be used to fashion features as small as 50–100 μm if very small microelectrode features are not required. In addition, multiple designs of microelectrodes can be patterned simultaneously on the same substrate, allowing for large numbers of microelectrodes to be simultaneously fabricated, reducing production costs. Also, micromachining procedures may be used to construct microelectrodes with multiple recording sites in well-defined spatial arrangements that may be used to record from layered brain structures. The microelectrodes can be designed to conform to brain structures. Improved quality of microelectrodes may be achieved by allowing experts in the semiconductor industry to fabricate the microelectrodes, thereby avoiding the inherent costs of setting up in-house microfabrication facilities (e.g., Thin Film Technologies, Inc.).

There are four basic layers to most microelectrodes constructed using thin-film techniques. The substrate is the first layer, which often is composed of silicon, ceramic, silicon, silica/glass, or polyimide. An insulating layer such as silicon nitride often covers the substrate when a silicon substrate is used. An adhesion layer of titanium or chromium may be applied to the substrate to allow the active metal to adhere to the substrate surface if needed. Photolithography or screen printing is used to lay out the microelectrode recording sites, connecting lines, and bonding pads using the desired noble metals such as Au, Pt, or Ir. An insulating layer such as polyimide, silicon nitride, or alumina is applied to the connecting lines (Burmeister and Gerhardt, 2006). After application of the insulating layer, only the recording

sites and bonding pads are exposed. Microelectrodes constructed using eight or more photomasks with very specialized layers have been reported (Anderson et al., 1989; Bai et al., 2000; Burmeister and Gerhardt, 2006; Najafi et al., 1990). Numerous microelectrodes can be formed on a single substrate at the same time using this approach. The final shape of the microelectrodes is achieved by chemical etching, laser cutting, or diamond saw procedures. Finally, the bonding pads of the individual microelectrodes are wire-bonded to a larger printed circuit board (PCB) holder or "paddle" that is more easily handled and connected to recording equipment.

Silicon-Based Microelectrodes

Silicon was the first substrate to be used to construct multisite, semiconductor-based microelectrodes, and there have been many reports of such microelectrodes for brain recordings and brain tissue stimulation (Anderson et al., 1989; Schmidt et al., 1993; Kovacs et al., 1994; Della Santina et al., 1997; Bai et al., 2000; Najafi et al., 1990; Yoon et al., 2000; Vetter et al., 2004; Kipke et al., 2003; Burmeister and Gerhardt, 2006). The option of using chemical etching is one of the desirable properties of silicon as a substrate. Individual microelectrodes can be formed from a single substrate simultaneously without the need for laser machining or sawing. Small features such as channels in the substrate can be constructed. Very thin microelectrodes may be fashioned by etching to reduce the substrate thickness. Substrates as thin as 6–15 μm have been reported (BeMent et al., 1986; Drake et al., 1988; Hetke et al., 1994; Burmeister and Gerhardt, 2006). However, a very thin silicon substrate is flexible and fragile. Flexibility is both desirable and a liability. Once implanted, flexible microelectrodes have the ability to move with the tissue and possibly minimize damage. However, one must caution that long, thin, flexible silicon electrodes can be difficult to implant. An insulating layer between the metal and the silicon substrate may be necessary to reduce electrical crosstalk between adjacent recording sites because silicon is a semiconductor (Moxon et al., 2004; BeMent et al., 1986; Drake et al., 1988; Hetke et al., 1994; Ensell et al., 2000; Burmeister and Gerhardt, 2006).

The semiconductor properties of silicon can be altered by doping. Also, silicon is very compatible with onboard circuitry. Silicon has many features that have made it widely used as the foundation for forming microelectrode arrays. Photographs of some silicon-based microelectrodes constructed at the Center for Neural Communication Technology at the University of Michigan, which is the home to some of the greatest contributions to BCI microelectrode technology, are shown in Figure 2.2 (Anderson et al., 1989, Bai et al., 2000, Najafi et al., 1990, BeMent et al., 1986, Drake et al., 1988, Hetke et al., 1994). These represent many of the current designs that have been used for BCI applications in rats and nonhuman

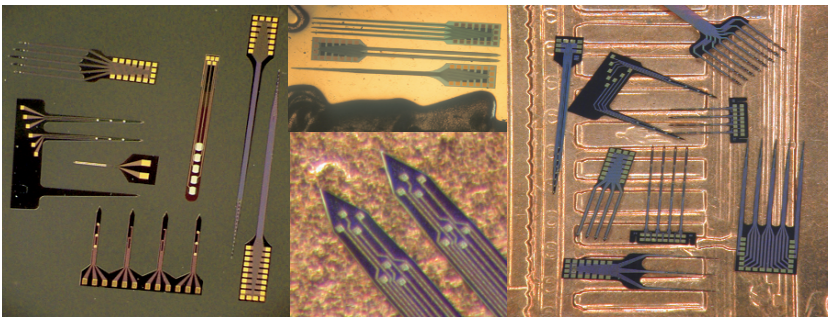

Figure 2.2. Photomicrograph of silicon-based microelectrode arrays constructed at the University of Michigan. Michigan probe photos were provided by David Anderson at the University of Michigan Center for Neural Communication Technology, an NIH/NCRR Resource Center. Used with permission, from *Encyclopedia of Sensors* (Burmeister and Gerhardt, 2006).

primates. In addition, this grouping of microelectrodes shows some of the versatile designs afforded by this approach. The option of chemical etching procedures is one of the greatest advantages silicon has as a substrate material. The micro-electrode thickness as well as shape can be altered using etching. Isotropic etchant (10% hydrofluoric acid, 90% nitric acid) is used for thinning of the substrate. An etch of ethylene-diamine-pyrocatechol water (EDP) is used to separate the individual microelectrodes from the silicon substrate (Burmeister and Gerhardt, 2006). A layer of silicon nitride patterned onto the silicon wafer can be used to define the intended microelectrode shape. Silicon nitride stops the etchant from reacting with the substrate. Alternatively, the etchant may also be stopped by selectively doping the substrate with boron (Bai et al., 2000; Najafi et al., 1990, Ensell et al., 2000).

A promising silicon-based electrode array design has been developed by the VSAMUEL consortium (European Union, grant IST-1999–10073 termed ACREO [ACREO AB, Sweden]) on microelectrode arrays (Jensen et al., 2006; Yoshida et al., 2001). These electrodes have one to eight recording shafts, are very versatile and flexible, and appear to have very promising insertion mechanics (Jensen et al., 2006). These also represent the major microelectrode manufacturing capabilities in the European Union, which strongly competes with the technologies being developed in the United States and Asia. Figure 2.3 shows representative designs.

Novel devices can be integrated onto the sensors using silicon-based microelectrodes. Holes have been etched into the substrate to aid in securing the microelectrode into brain tissue and to perhaps better integrate the electrode into the brain extracellular space (Kovacs et al., 1992, 1994; Della Santina et al., 1997; Burmeister and Gerhardt, 2006). Multiple flow channels for the delivery of chemicals/drugs, while performing electrophysiological recordings, have been etched into the silicon probe substrate (see Figure 2.4) (Chen et al., 1997; Rathnasingham et al., 2004; Burmeister and Gerhardt, 2006).

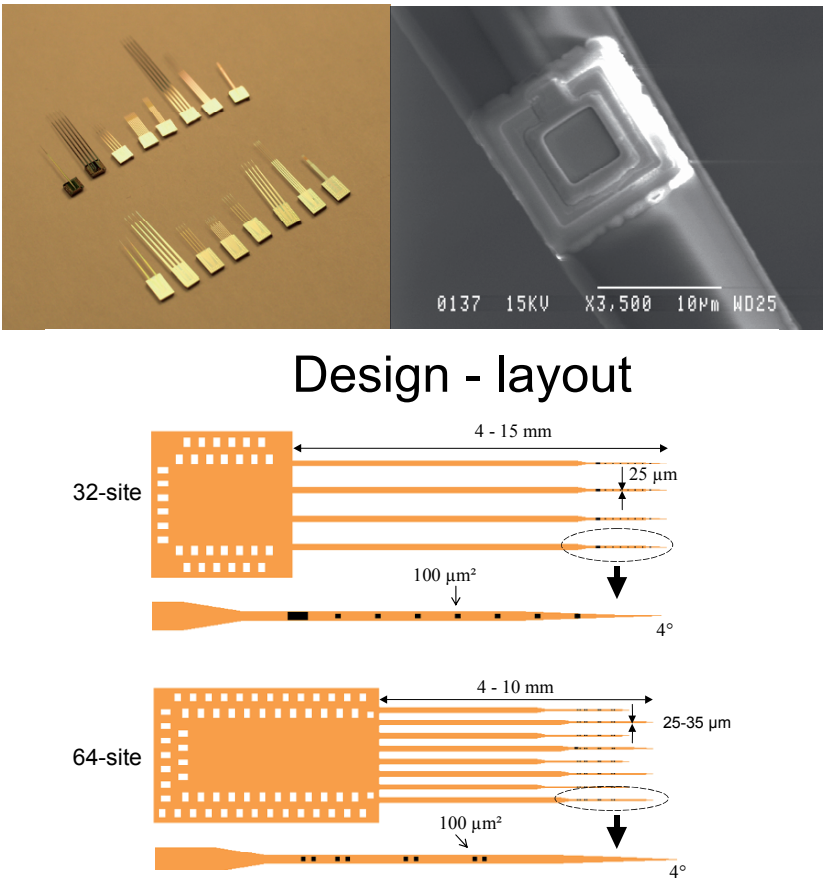

Figure 2.3. (Top-left) examples of silicon-based ACREO microelectrode arrays; (top-right) micrograph of an individual ACREO microelectrode recording site; (bottom) schematic of the ACREO microelectrode arrays (Photographs courtesy of ACREO AB, Sweden).

Integrated Ag/AgCl reference electrodes have been included on microelectrode arrays (Burmeister and Gerhardt, 2006; Pancrazio et al., 1998). Microdrives have been integrated into the microelectrode design for *in situ* adjustments after implantation (Burmeister and Gerhardt, 2006). An integrated polysilicon microheating device has been constructed (Chen and Wise, 1997). On-electrode amplification and signal processing may be achieved by including VLSI chips on the silicon substrate (see Figure 2.5 with integrated amplification) (Patterson et al., 2004; Bai and Wise, 2001; Pancrazio et al., 1998; Csicsvari et al., 2003). Silicon-based microelectrodes allow "hybrid" microelectrode designs to be manufactured.

Electrophysiological arrays with 100 recording sites have been developed to provide an interface for prosthetics, which is the foundation for the seminal work of Norman, Donoghue, and coworkers (Nordhausen et al., 1996; Hochberg et al.,

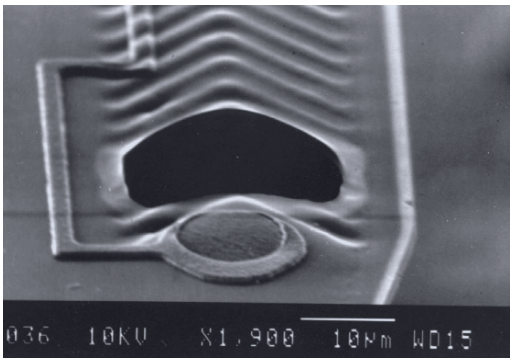

Figure 2.4. SEM of a microchannel on a silicon-based microelectrode for delivery of chemicals into CNS tissue. (Michigan probe photos provided by David Anderson at the University of Michigan Center for Neural Communication Technology, an NIH/NCRR Resource Center; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

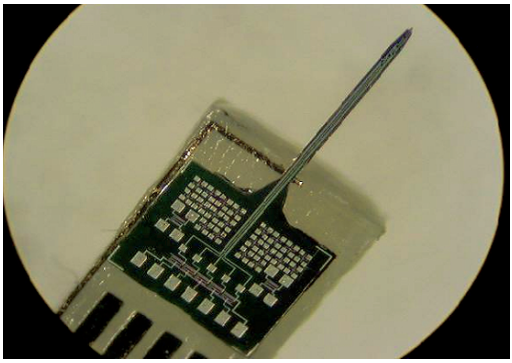

Figure 2.5. Photomicrograph of a silicon-based microelectrode for electrophysiological recordings with on-chip amplification is shown (photograph provided by Sung June Kim of Inter-University Semiconductor Research Center at Seoul National University, Korea; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

2006; Warren et al., 2001; Schmidt et al., 1993; Branner et al., 2004; Burmeister and Gerhardt, 2006). These designs are currently being used in humans and represent the first BCI microelectrode arrays that have been sterilized and used in both nonhuman and human primate trials. Individual microelectrode "shafts" extend 1.5 mm from the 10 ×10 mm planer substrate. The shaft tips are metalized with Pt over doped silicon for conduction down the shaft. The conducting doped silicon is insulated using glass and silicon nitride. Figure 2.6 shows a SEM of one of the "Utah" electrodes. Similar three-dimensional microelectrode arrays can be constructed by combining many planar silicon multishank microprobes (Hoogerwerf and Wise, 1994; Bai et al., 2000; Burmeister and Gerhardt, 2006), as shown in Figure 2.7. For brain-slice recordings, planar microelectrode arrays have been used to map neuronal communication (Borkholder et al., 1997; Burmeister and Gerhardt, 2006).

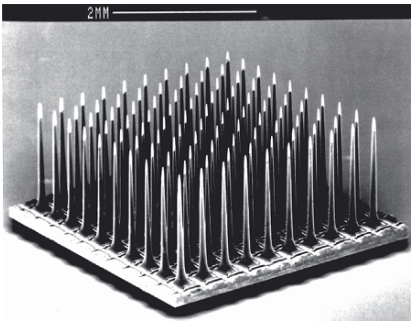

Figure 2.6. SEM of Utah Electrode Array (UEA) for visual prosthetics. The array consists of 100 individual microelectrode "shafts" that extend 1.5 mm from the 10 ×10 mm planar substrate (SEM provided by Richard A. Normann, Department of Bioengineering, University of Utah, Salt Lake City; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

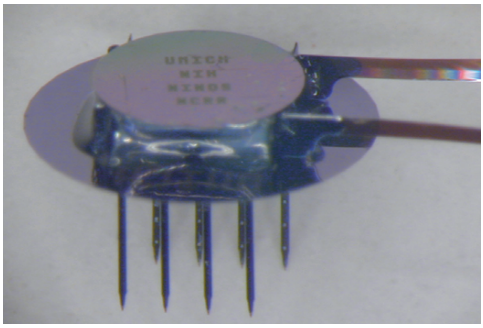

Figure 2.7. Photomicrograph of a multishank probe formed using several silicon-based microelectrodes. There are multiple recording sites on each shaft for recordings at different brain depths. (Michigan probe photos provided by the University of Michigan Center for Neural Communication Technology, an NIH/NCRR Resource Center; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

Ceramic-Based Microelectrodes

The insulator ceramic (alumina, Al_2O_3) has been used as a substrate to reduce crosstalk between adjacent connecting lines (Burmeister and Gerhardt, 2001, 2006; Burmeister et al., 2000). Ceramic is mechanically strong, allowing for development of microelectrodes that can access much deeper brain structures (up to 5–6 cm vs. 2–4 mm for silicon). Precise placement of the microelectrode in tissue without flexing or breaking can be achieved. Multisite microelectrodes on ceramic substrates for use in animal models have been constructed (Moxon et al., 2004; Burmeister et al., 2000).

Individual microelectrodes must be mechanically cut from the wafer because the ceramic is not compatible with standard etching procedures. Laser machining is the most flexible way to cut the microelectrodes from the bulk wafers enabling formation of complex shapes. However, due to the stepping of the laser, laser machining can produce rough edges that can cause potential problems with microelectrode insertion into tissues. Much smoother microelectrode edges may be formed using a diamond saw, which polishes as it cuts; thus unnecessary tissue damage may be avoided. Minimal CNS tissue damage is required to study the biology of the intact brain. When using a diamond saw it is more difficult to form complex shapes because saws generally cut in straight lines. Figure 2.8a is a photograph of a complex microelectrode shape cut by laser machining. Figure 2.8b is a simple ceramic substrate microelectrode shape formed by a computer-controlled diamond saw. Figure 2.8c is a magnification of this microelectrode's smooth edges. The use of excimer lasers may provide smoother edges than conventional laser machining. Thinner microelectrodes may be achieved by polishing the ceramic substrate (Moxon et al., 2004).

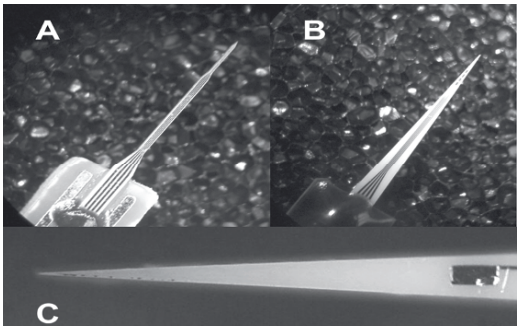

Figure 2.8. (a) Photograph of a complex ceramic substrate-based microelectrode shape cut by laser machining; (b) a less complex microelectrode shape formed by a computer-controlled diamond saw; (c) a magnification of the microelectrode's much smoother edge (Reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

Figure 2.9 shows microelectrodes assembled on ceramic substrates that have been polished to make them between 38 to 51 μm thick with a tip width of 60 μm. The alumina insulating layer is applied using ion-beam-assisted deposition. These 20 × 80 μm platinum recording sites with 200 μm spacing have been used to record single-neuron action potentials *in vivo* for up to 24 weeks.

Numerous four- and five-site Pt microelectrodes on ceramic substrates have been developed. The versatility of the lithographic methods can be seen in Figure 2.10. In general, recording sites are either grouped in side-by-side pairs or in a linear arrangement. Two recent designs configure the microelectrodes in a linear arrangement similar to the previously reported 50 × 50 μm microelectrodes (Burmeister et al., 2000). The new designs have larger Pt recording sites of 50 × 100 and

50 × 150 μm in order to investigate whether larger recording sites can record better single-unit activity or lower detection limits for chemical recordings.

Two other new designs have two sets of microelectrodes arranged side-by-side: 25 × 100 and 25 × 300 μm. Recording-site dimensions vary from 10 × 10 μm to 25 × 300 μm, depending on the application. Other designs (dimensions in μm) include 10 × 10 serial (200 spacing), 20 × 20 serial (200 spacing), 50 × 50 serial (200 spacing), 25 × 100 pairs (15 spacing), 50 × 100 serial (200 spacing), 50 × 150 serial (200 spacing), 25 × 300 pairs (15 spacing), 25 × 300 pairs (30 spacing), 50 × 50 serial (400 spacing), 15 × 300 "eliminator," and 15 × 300 "T-eliminator." This also shows the versatility of such microelectrode fabrication approaches. Although the ceramic-base, multisite microelectrodes were originally intended to be disposable (one-time use), a cleaning procedure has been developed to allow for multiple uses due to the durability of the materials *in vivo* (Burmeister et al., 2002).

Figure 2.11 shows several designs of 8-site "conformal" microelectrodes that are under development for different brain region recordings in rats and monkeys. The individual electrodes may be chosen based on the brain region(s) and type of recordings of interest. For instance, two or more recording sites placed toward the tip of the microelectrode are useful in studying thin layers of cells such as the Purkinje cells in the cerebellum or pyramidal cells in the hippocampus. Multiple measures can be accomplished in the brain region of interest by providing a large concentration of recording sites at the tip. By spreading out the recording sites over a larger vertical distance, layered and/or larger brain structures such as the hippocampus, cortex, and striatum may be studied. Various species of animals may require different sizes and features of the microelectrode. In addition, the recording site density of the ceramic-based microelectrodes can be increased by

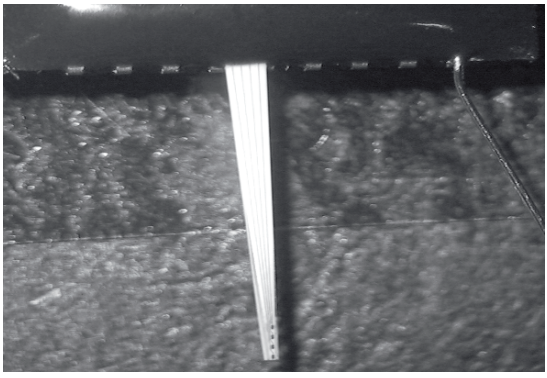

Figure 2.9. Photomicrograph of a ceramic-based microelectrode constructed on a thinner substrate with an alumina insulating layer. Alumina is applied using ion-beam-assisted deposition. The substrate thickness is between 38 to 51 μm with a tip width of 60 μm. The 20 × 80 μm platinum recording sites have been used to chronically record single-neuron action potentials *in vivo* for up to 8 weeks (Figure provided by Karen A. Moxon, Drexel University; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

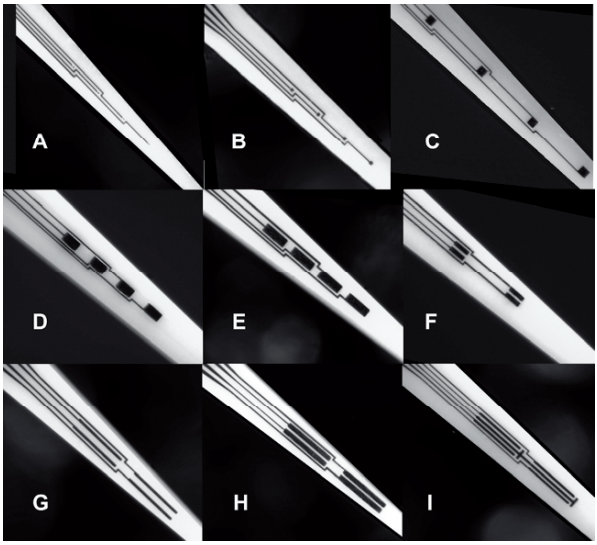

Figure 2.10. Photomicrographs of several ceramic-based multisite microelectrode designs. (a) 100 μm^2 serial—10 × 10 μm recording sites; (b) 400 μm^2 serial—20 × 20 μm recording sites; (c) 2,500 μm^2 serial—50 × 50 μm recording sites with 400 μm center-to-center spacing; (d) 5,000 μm^2 serial—100 × 50 μm recording sites; (e) 7,500 μm^2 serial—150 × 50 μm recording sites; (f) 2,500 μm^2 pairs—100 × 25 μm recording sites; (g) 4,500 μm^2 pairs—300 ×15 μm recording sites, 30 μm spacing; (h) 7,625 μm^2 pairs—305 × 25 μm recording sites; (i) 4,500 μm^2 eliminator—300 × 15 μm recording sites (Photographs are courtesy of Mr. Peter Huettl of the Center for Microelectrode Technologies University of Kentucky, Lexington, Kentucky; reprinted with permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

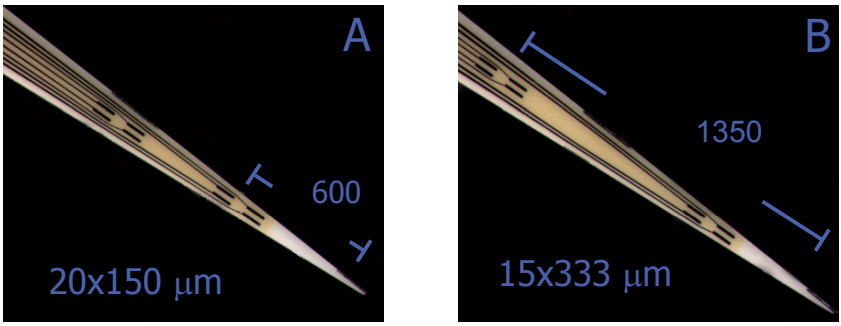

Figure 2.11. Layouts of ceramic-based "conformal" microelectrodes with eight recording sites. Parts (a) and (b) each have four pairs of 20 × 150 μm recording sites separated by 1,350 μm and 600 μm, respectively (Photographs courtesy of Mr. Peter Huettl at the Center for Microelectrode Technologies, University of Kentucky, Lexington, Kentucky).

forming sites on the front and back of the substrate. Finally, several recording sites in the array may be used to electrically stimulate, and the others can be used for electrophysiological or neurochemical recordings.

Polyimide-Based Microelectrodes

Polyimide films, trade name Kapton® (DuPont, Circleville, OH), have been used as a substrate as well as the top insulator for microelectrodes used for intracortical implantation Besides polyimide, the polyimide precursor Parylene (DuPont) can be spun onto surfaces as a liquid then polymerized at high temperatures (200°C). Microelectrodes less than 20 μm thick have been constructed (Rousche et al., 2001). Polyimide as a substrate is very structurally flexible. Figure 2.12 shows a photomicrograph of a three-dimensional multishank microelectrode designed for intracortical implantation. Although the flexibility of polyimide can make implantation difficult, a flexible microelectrode may in certain cases contribute to less tissue damage. Guide incisions in the neural tissue are often needed to prevent the micro-electrode shaft from buckling upon microelectrode implantation (Rousche et al., 2001). Polyimide microelectrodes have even been driven through tissue using surgical suture (Gonzalez and Rodriguez, 1997). The substrate may be folded to provide some rigidity (Takahashi et al., 2003).

As with other substrates, perforations or holes in the polyimide have been used to help secure the microelectrodes in place (Gonzalez and Rodriguez, 1997). Multiple layers can be used to construct useful microelectrodes. Wells may be constructed by simply leaving an open via in a polyimide layer (Rousche et al., 2001).

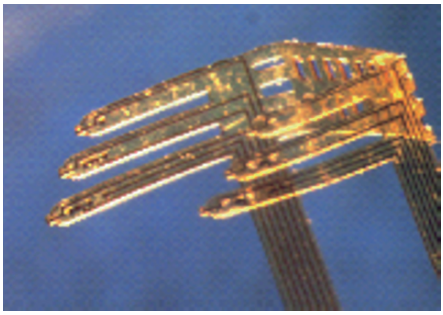

Figure 2.12. Photograph of a polyimide-based microelectrode array for intracortical implantation. The semitransparent polyimide substrate can be folded to achieve multishank arrays. The metal connecting lines are visible (Photograph provided by Daryl Kipke of the University of Michigan Center for Neural Communication Technology; reprinted by permission from *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

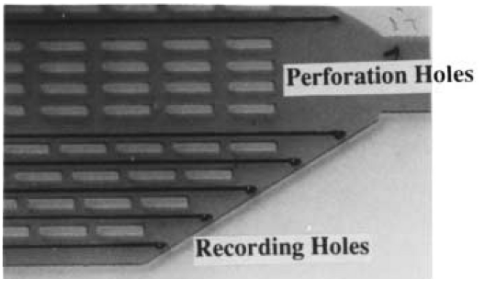

Figure 2.13. Magnification of several recording sites on a polyimide-based microelectrode with perforation holes to help secure the microelectrode in tissue (Used with permission from Elsevier Publishing; adapted from Gonzalez and Rodriguez. 1997; also in *Encyclopedia of Sensors* [Burmeister and Gerhardt, 2006]).

Connectors

Connecting microelectrodes to recording equipment is a major problem for microelectrode fabrication. Often, the microelectrode is secured to a PCB holder or "paddle." The recording sites are electrically connected to the holder by wire bonding from the pads on the microelectrode to pads on the connector. Metal lines (usually Au or Pt) run the length of the holder to pins, or some other type of connecting device. These may be connected to electronic equipment using dual-inline-pin (DIP) sockets or zero-insertion-force (ZIF) sockets.

Another approach to attach microelectrodes to recording equipment combines flexible polyimide ribbon and silicon ribbon cables (Hetke et al., 1994; Bragin et al., 2000; Akin et al., 1999; Kipke et al., 2003). The same photolithographic techniques and basic processes used to construct the silicon microelectrode probes are used to fabricate miniature, flexible, multi-lead silicon ribbon cables consisting of a long, thin, silicon substrate that supports multiple dielectrically encapsulated leads. The ends of the cable are thicker with exposed metal pads for bonding the cable either to a microelectrode or to a connector. The main cable itself can be electrically shielded with an outer barrier layer (typically Au or polysilicon) over the upper dielectrics. This layer makes contact to the silicon substrate so that the leads are electrically shielded as well as sealed, effectively making the cable a multilead "coaxial" structure. Because ribbon cables can be integrated into the microelectrode itself, the need for bonding, soldering, or encapsulation between the microelectrode and the interconnect system is eliminated. Ribbon cables as thin as 4–5 μm have been reported. Flexibility is maintained in all dimensions providing functionality for periods of at least one year (Hetke et al., 1994).

ECoG Strip Electrodes

A growing area of study involves the use of electrocorticographic (ECoG) recordings for BCI (Felton et al., 2007; Marzullo et al., 2005; Leuthardt et al., 2004). This technology grew out of clinical EEG recordings through the work of Jasper and Penfield in the 1930s through the 1950s. The technology has been primarily used by surgeons to record from cortical areas in patients with drug refractory epilepsy to determine the best surgical targets for transaction. We do not review this extensive area as applied to epilepsy surgery. Rather, we discuss the electrodes that are available for such recordings in humans as these electrodes, although invasive, may possess many of the features that make them ideal for BCI applications. First, the safety of the technology, at least acutely, has been tested in thousands of human subjects. Second, ECoG has higher spatial resolution than EEG (tenths of millimeters vs. centimeters) and newer electrode designs (see Figure 2.14) possess spatial resolution closer to that of direct penetrating electrode recordings. Third, the signals recorded from the surface of the brain exhibit higher amplitudes with broader band widths. Fourth, patients undergoing epilepsy surgery constitute a large test bed for investigating BCI technology that is starting to be investigated in the United States and Europe. Finally, such proven technologies may have better long-term stability *in vivo*, but this is still to be determined.
One of the largest manufacturers of ECoG electrodes for human recordings is Ad-Tech Medical Instrument Corporation (Racine, WI). It designs and manu-factures about 70% of the sterilized ECoG electrodes used throughout the world. Ad-Tech is an FDA- and ISO13485-registered manufacturer of high-quality medical devices. Ad-Tech, which successfully distributes its electrodes in more than 40 countries, has been active in the design, development, manufacture, and marketing of intracranial monitoring strip-type, grid-type, depth-type, and other related

Figure 2.14. Subdural ECoG microgrid for epidural recordings (Reprinted with permission from D. Moran).

electrodes for more than 22 years. These electrodes are used primarily by comprehensive epilepsy centers and major institutions/medical centers that provide brain mapping in their neurological programs. These electrodes are made of implant silicone or polyurethane with microconductors attached to stainless steel or platinum contacts (usually 7 or 10 mm disks) that populate the dielectric area.

Figure 2.15 shows numerous Ad-Tech ECoG strip electrodes ranging in size from 4 to 64 recording sites. Proprietary connectors/cables attach these electrodes to commercial monitoring equipment. More than 100 medical journal papers have been written on the use of Ad-Tech's products for the treatment of epilepsy and other neurological disorders and diseases (Kossoff et al., 2004; Pan et al., 2005; Ad-Tech [http://www.adtechmedical.com/articles.htm]).

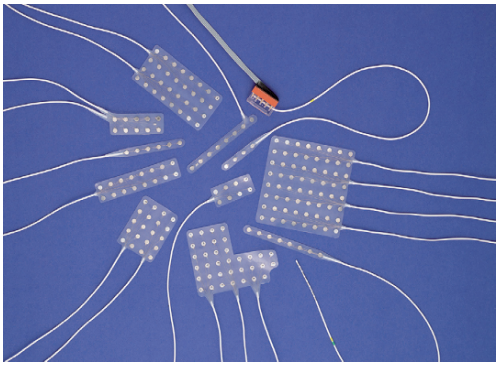

Figure 2.15. Four-to-64-site ECoG recording strip electrodes (Reprinted with permission from Ad-Tech Medical Instruments).

Noninvasive EEG Sensors for BCI

Nearly all BCI studies using noninvasive sensors involve the use of Ag or Au disk electrodes with conducting paste that are affixed to the skull using some type of head cap configuration to facilitate the application of the EEG electrodes. Limited progress has been made in improving these devices over the last two decades to rapidly and comfortably affix them to the skull of a BCI user. Head caps have been developed that aid in the measurement and placement of 64 to 256 EEG electrodes using the "International 10–20 grid system." Suppliers of head caps and electrodes are numerous and include g.tec (Guger Technologies OEG), Grass Technologies, BioSemi, and others. For a variety of BCI technologies, g.tec is a source of one of the best head caps used in the field involving wet electrode recordings, as shown in Figure. 2.16. Its unique head cap for EEG electrodes design allows for some of the best signal-to-noise achievable in the business from wet electrode technology. In particular, the electrode cap design requires extra time for attachment

of electrodes but achieves excellent signal-to-noise characteristics. This highly versatile design can be employed with other g.tec products and amplifiers, as well as other suppliers of such instrumentation.

A promising improvement is the 128- and 256-channel active "pin-type" Ag electrodes and head cap design distributed by BioSemi (Amsterdam, The Netherlands). This company's active electrode designs have potentially improved signal-to-noise capabilities without the need for Faraday-cage shielding for BCI recordings (see Figure 2.17). In addition, there are promising "dry-type" electrode configurations that have been under development using carbon nanotube electrodes and other dry-type sensor designs (Ruffini et al., 2006; Fonseca et al., 2007).

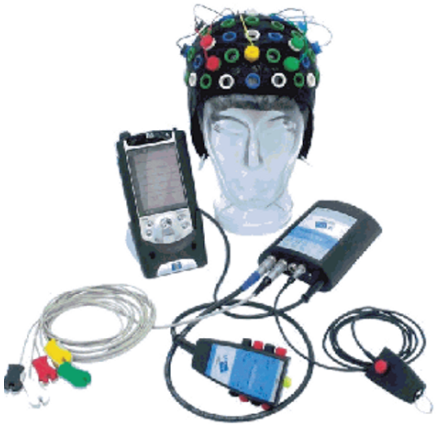

Figure 2.16. A g.tec head cap system for EEG recordings (Reprinted with permission from g.tec).

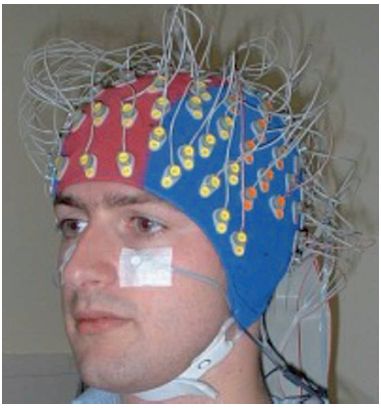

Figure 2.17. BioSemi 128-channel active EEG system (Courtesy of BioSemi).

The process of fitting individuals with EEG electrodes with head caps, however, is time consuming, requires testing of individual electrodes for their impedance, and results in a system that is not comfortable or practical for routine BCI use. There is a need for development of "dry electrodes," which could be used without the preparation required for the current designs. In addition, active electrode designs (such as sold by BioSemi) are needed to improve signal-to-noise ratios of such recordings in practical, real-world applications.

MAJOR CHALLENGES FOR PRODUCING BCI SENSORS

There are major questions that need to be addressed for the development of both noninvasive and invasive sensors that can be used for practical, real-world applications of BCI technology. These are as follows:

- How long do current sensors really last?
- How do we make dry EEG electrodes that allow for ease of application and use?
- How do we develop sensors that last for 5–20 years?
- How do we develop a systematic and scientific approach to developing "biologically-based," implantable microelectrodes and surface electrodes?

Perhaps the largest challenge in the area of implantable electrodes for BCI is the development of electrode arrays that will function for 5–20 years *in vivo*. By far the longest recordings from the CNS of individual unit activity with respect to the context of BCI technology have been achieved by the use of microwire arrays. In fact, more than one-and-a-half years of recording using microwire arrays in nonhuman primates was reported in 2003 (Nicolelis et al., 2003). Unfortunately, this has not been reliably achieved by methodology involving the silicon, ceramic, or polyimide-based multielectrode arrays that have many advantages for future recordings involving BCI technology. Dry EEG electrodes with improved signal-to-noise ratio and ease of use are also needed for noninvasive BCI applications.

In the context of multielectrode arrays, one of the groups that have achieved the greatest amount of success and the greatest following of investigators resides at the University of Michigan. In fact, the greatest number of silicon-based microelectrodes implanted in a nonhuman primate has been achieved at the University of Michigan. Here, Drs. Schwartz and Kipke have been able to record, for more than a year, 60 functional, silicon, microelectrode channels that were implanted in an awake monkey, resulting in more than 90 high-quality recording spikes. This is ground-breaking work that demonstrated the ability of the BCI to control a mechanical limb through recordings of the individual unit activity involving multiple single-unit array electrodes of the silicon type. These studies and the seminal work of Dr. John Donoghue and co-workers (Hochberg et al., 2006; Song et al., 2005) will help shape the development of reliable, long-lasting, tissue-compatible BCI sensors in the years to come (see Chapter 3).

SUMMARY AND CONCLUSIONS

The majority of BCI science in Europe involves "noninvasive" sensor technologies, i.e., multielectrode recordings from arrays of EEG electrodes mounted onto the surface of the skull. This sensor technology has experienced limited growth and needs substantial improvement. Even with respect to noninvasive technologies, many European sites collaborate with, or utilize paradigms that were developed in the United States (Wadsworth Center, Albany, NY).

In Asia, there is clear emphasis on inexpensive, EEG-BCI approaches as the population is large and there is a need for low-cost, noninvasive BCI technology for improved health care in China. In addition, Japan is also focused on noninvasive, EEG-based BCI technologies. However, there is rapid economic growth and

science spending in China and Japan that will propel BCI technology in Asia. In addition, there are clear indications that interest and facilities are available to pursue invasive, BCI-sensor technology in China. Asia has manufacturing facilities and infrastructure to drive development of new, invasive, BCI-sensor development that could rival or exceed the efforts in the United States in five to ten years.

REFERENCES

Akin, T., B. Ziaie, S.A. Nikles, and K. Najafi. 1999. A modular micromachined high-density connector system for biomedical applications. *IEEE Trans. Biomed. Eng.* 46(4):471–480.

Anderson, D.J., K. Najafi, S.J. Tanghe, D.A. Evans, K.L. Levy, J.F. Hetke, X.L. Xue, J.J. Zappia, and K.D. Wise. 1989. Batch-fabricated thin-film electrodes for stimulation of the central auditory system. *IEEE Trans. Biomed. Eng.* 36:693–704.

Bai, Q., and K.D. Wise. 2001. Single-unit neural recording with active microelectrode arrays. *IEEE Trans. Biomed. Eng.* 48:911–920.

Bai, Q., K.D. Wise, and D.J. Anderson. 2000. A high-yield micro assembly structure for three-dimensional microelectrode. *IEEE Trans. Biomed. Eng.* 47:281.

Baumeister, A.A. 2006. Serendipity and the cerebral localization of pleasure. *J. His. Neurosci.* 15(2):92–98.

BeMent, S.L., K.D. Wise, D.J. Anderson, K. Najafi, and K.L. Drake. 1986. Solid-state electrodes for multichannel multiplexed intracortical neuronal recording. *IEEE Trans. Biomed. Eng.* 33:230.

Borkholder, D.A., J. Bao, N.I. Maluf, E.R. Perl, and G.T. Kovacs. 1997. Microelectrode arrays for stimulation of neural slice preparations. *J. Neurosci. Meth.* 77(1):61–66.

Bragin, A., J. Hetke, C.L. Wilson, D.J. Anderson, J. Engel Jr, and G. Buzsaki. 2000. Multiple site silicon based probes for chronic recordings in freely moving rats: implantation, recording, and histological verification. *J. Neurosci. Meth.* 98(11):77–82.

Branner, A., R.B. Stein, E. Fernandez, Y. Aoyagi, and R.A. Normann. 2004. Long-term stimulation and recording with a penetrating microelectrode array in cat sciatic nerve. *IEEE Trans. Biomed. Eng.* 51(1):146–157.

Burmeister, J.J., and G.A. Gerhardt. 2001. Self-referencing ceramic based multisite microelectrodes for the detection and elimination of interferences from the measurement of l-glutamate and other analytes. *Anal. Chem.* 73:1037–1042.

Burmeister, J.J., and G.A. Gerhardt. 2006. Neurochemical arrays. In *Encyclopedia of sensors*, Vol. 6, Eds. C. Grimes, E. Dickey, and M.V. Pishko. Stevenson Ranch, CA: American Scientific Publishers, 525.

Burmeister, J.J., K. Moxon, and G.A. Gerhardt. 2000. Ceramic-based multisite microelectrodes for electrochemical recordings. *Anal. Chem.* 72:187–192.

Burmeister, J.J., F. Pomerleau, M. Palmer, B.K. Day, P. Huettl, and G.A. Gerhardt. 2002. Improved ceramic-based multisite microelectrode for rapid measurements of l-glutamate in the CNS. *J. Neuro. Meth.* 119:163–171.

Chapin J.K., and D.J. Woodward 1986. Distribution of somatic sensory and active-movement neuronal discharge properties in the MI-SI cortical border area in the rat. *Exp. Neurol.* 91(3):502–523.

Chapin, J.K., M.A.L. Nicolelis, 2001. Brain Control of Sensorimotor Prostheses. In *Neural prostheses for restoration of sensory and motor function*. Eds. Chapin, J.K., and K.A. Moxon. Boca Raton, FL: CRC Press, 235–261.

Chapin, J.K. 2004. Using multi-neuron population recordings for neural prosthetics. *Nat. Neurosci.* 7:452.

Chen, J., and K.D. Wise. 1997. A silicon probe with integrated microheaters for thermal marking and monitoring of neural tissue. *IEEE Trans. Biomed. Eng.* 44:770–774.

Chen, J., K.D. Wise, J.F. Hetke, and S.C. Bledsoe Jr. 1997. A multichannel neural probe for selective chemical delivery at the cellular level. *IEEE Trans. Biomed. Eng.* 44:760.

Cheung, K.C. 2007. Implantable microscale neural interfaces. *Biomed. Microdevices* Jan. 25 (epub), PMID: 17252207.

Chiganos, T.C., W. Jensen, and P.J. Rousche. 2006. Electrophysiological response dynamics during focal cortical infarction. *J. Neural Eng.* 3(4):15–22.

Csicsvari, J., D.A. Henze, B. Jamieson, K.D. Harris, A. Sirota, P. Bartho, K.D. Wise, and G. Buzsaki. 2003. Massively parallel recording of unit and local field potentials with silicon-based electrodes. *J. Neurophysiol.* 90:1314–1323.

Della Santina, C.C., G.T. Kovacs, and E.R. Lewis. 1997. Multi-unit recording from regenerated bullfrog eighth nerve using implantable silicon-substrate microelectrodes. *J. Neurosci. Meth.* 72(1):71–86.

Drake, K.L., K.D. Wise, J. Farraye, D.J. Anderson, and S.L. BeMent. 1988. Performance of planar multisite microprobes in recording extracellular activity. *IEEE Trans. Biomed. Eng.* 35:719.

Ensell, G., D.J. Banks, P.R. Richards, W. Balachandran, and D.J. Ewins. 2000. Silicon-based microelectrodes for neurophysiology, micromachined from silicon-on-insulator wafers. *Med. Biol. Eng. Comput.* 38(2):175–179.

Felton E.A., J.A. Wilson, J.C. Williams, P.C. Garell. 2007. Electrocorticographically controlled brain-computer interfaces using motor and sensory imagery in patients with temporary subdural electrode implants. Report of four cases. *J. Neurosurg*. 106(3):495–500.

Fonseca C., J.P., Silva Cunha R.E. Martins, V.M. Ferreira, J.P. Marques de Sa, M.A. Barbosa, and A. Martins da Silva. 2007. A novel dry active electrode for EEG recording. *IEEE Trans. Biomed. Eng.* 54(1):162–165.

Gonzalez, C., and M. Rodriguez. 1997. A flexible perforated microelectrode array probe for nerve and muscle tissues. *J. Neurosci. Meth.* 72:189–195.

Heath R.G., S.M. Peacock, Jr., and W. Miller, Jr. 1953. Induced paroxysmal electrical activity in man recorded simultaneously through subcortical and scalp electrodes. *Trans. Am. Neurol. Assoc.* 3:247–250.

Hetke, J.F., J.L. Lund, K. Najafi, K.D. Wise, and D.J. Anderson. 1994. Silicon ribbon cables for chronically-implantable microelectrode arrays. *IEEE Trans. Biomed. Eng.* 41:314.

Hochberg, L.R., Serruya, M.D, Friehs, G.M, Mukand, J.A., Saleh, M, Caplan, A.H., Branner, A., Chen, D., Penn, R.D., and Donoghue, J.P. 2006. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* 442:164–171.

Hoogerwerf, A.C. and K.D. Wise. 1994. A three-dimensional microelectrode array for chronic neural recording. *IEEE Trans. Biomed. Eng.* 41:1136–1146.

Jensen, W., K. Yoshida, and U.G. Hofmann. 2006. *In vivo* implant mechanics of flexible, silicon-based ACREO microelectrode arrays in rat cerebral cortex. *IEEE Trans. Biomed. Eng.* 53(5): 934–940.

Kipke, D.R., R.J. Vetter, J.C. Williams, and J.F. Hetke. 2003. Silicon-substrate intracortical microelectrode arrays for long-term recording of neuronal spike activity in cerebral cortex. *IEEE Trans. Neural Syst. Rehab. Eng.* 11(2):151–155.

Kossoff, E.H., E.K. Ritzl, J.M. Politsky, A.M. Murro, J.R. Smith, R.B. Duckrow, D.D. Spencer, and G.K. Bergey. 2004. Effect of an external responsive neurostimulator on seizures and electrographic discharges during subdural electrode monitoring. *Epilepsia* 45(12):1560–1567.

Kovacs, G.T., C.W. Storment, and J.M. Rosen, 1992. Regeneration microelectrode array for peripheral nerve recording and stimulation. *IEEE Trans. Biomed. Eng.* 39:893.

Kovacs, G.T., C.W. Storment, M. Halks-Miller, C.R. Belczynski Jr, C.C. Della Santina, E.R. Lewis, and N.I. Maluf. 1994. Silicon-substrate microelectrode arrays for parallel recording of neural activity in peripheral and cranial nerves. *IEEE Trans. Biomed. Eng.* 41:567.

Leuthardt, E.C., G. Schalk, J.R. Wolpaw, J.G. Ojemann, and D.W. Moran. 2004. A brain-computer interface using electrocorticographic signals in humans. *J. Neural Eng.* 1:63–71.

Lin, L., G. Chen, K. Xie, K.A. Zaia, S. Zhang, and J.Z. Tsien. 2006. Large-scale neural ensemble recording in the brains of freely-behaving mice. *J. Neurosci. Meth.* 155(1):28–38.

Ludvig, N. 2001. Drug deliveries into the microenvironment of electrophysiologically monitored neurons in the brain of behaving rats and monkeys. In *Neural prostheses for restoration of sensory and motor function*. Eds. Chapin, J.K., and K.A. Moxon. Boca Raton, FL: CRC Press, 263–283.

Marzullo T.C., J.R. Dudley, C.R. Miller, L. Trejo, D.R. Kipke. 2005. Spikes, local field potentials, and electrocorticogram characterization during motor learning in rats for brain-machine interface tasks. *Conf Proc IEEE Eng. Med. Biol. Soc.* 1:429–431.

Moxon, K.A., S.C. Leiser, G.A. Gerhardt, K.A. Barbee, and J.K. Chapin. 2004. Solid-state electrodes for multichannel multiplexed intracortical neuronal recording. *IEEE Trans. Biomed. Eng.* 51:647.

Najafi, K., J. Ji, and K.D. Wise. 1990. Scaling limitations of silicon multichannel recording probes. *IEEE Trans. Biomed. Eng.* 37:1.

Nicolelis, M.A., D. Dimitrov, J.M. Carmena, R. Crist, G. Lehew, J.D. Kralik, and S.P. Wise. 2003. Chronic, multisite, multielectrode recordings in macaque monkeys. *Proc. Natl. Acad. Sci. USA*, 100(19):11041–11046.

Nordhausen, C.T., E.M. Maynard, and R.A. Normann. 1996. Single-unit recording capabilities of a 100-microelectrode array. *Brain Res.* 726:129.

Olds, J., W.S. Allan, and E. Briese. 1971. Differentiation of hypothalamic drive and reward centers. *Am. J. Physiol*. 221(1):368–375.

Pan, J.W., J.H. Kim, A.A. Cohen-Gadol, C. Pan, D.D. Spencer, and H.P. Hetherington. 2005. Regional energetic dysfunction in hippocampal epilepsy. *Acta Neurol. Scand.* 111(4):218–224.

Pancrazio, J.J., P.P. Bey Jr., A. Loloee, S. Manne, H.C. Chao, L.L. Howard, W.M. Gosney, D.A. Borkholder, G.T. Kovacs, P. Manos, D.S. Cuttino, and D.A. Stenger. 1998. Description and demonstration of a CMOS amplifier-based system with measurement and stimulation capability for bioelectrical signal transduction. *Biosens. Bioelectron.* 13(9):971–979.

Patterson, W.R., Y.K. Song, C.W. Bull, I. Ozden, A.P. Deangellis, C. Lay, J.L. McKay, A.V. Nurmikko, J.D. Donoghue, and B.W. Connors. 2004. A microelectrode/microelectronic hybrid device for brain implantable neuroprosthesis applications. *IEEE Trans. Biomed. Eng.* 51:1845.

Rathnasingham, R., D.R. Kipke, S.C. Bledsoe Jr, and J.D. McLaren. 2004. Characterization of implantable microfabricated fluid delivery devices. *IEEE Trans. Biomed. Eng.* 51:138–145.

Rennaker, R.L., A.M. Ruyle, S.E. Street, and A.M. Sloan. 2005. An economical multichannel cortical electrode array for extended periods of recording during behavior *J. Neurosci. Meth.* 142(1):97–105.

Rousche, P.J., D.S. Pellinen, D.P. Pivin Jr, J.C. Williams, R.J. Vetter and D.R. Kipke. 2001. Flexible polyimide-based intracortical electrode arrays with bioactive capability. *IEEE Trans. Biomed. Eng.* 48:361–371.

Ruffini, G., S. Dunne, E. Farres, P.C.P. Watts, E. Mendoza, S.R.P. Silva, C. Grau, J. Marco-Pallares, L. Fuentemilla, and B. Vandecasteele. 2006. ENOBIO: First tests of a dry electrophysiology electrode using carbon nanotubes. In *Proceedings of the 28th IEEE EMBS Annual International Conference*, New York City, Aug 30–Sept 3, 2006. Piscataway, NJ: IEEE Engineering in Medicine and Biology Society (EMBS), 1826–1829.

Schmidt, S., K. Horch, and R. Normann. 1993. Biocompatibility of silicon-based electrode arrays implanted in feline cortical tissue. *J. Biomed. Mater. Res.* 27(11):1393–1399.

Smith, S.L., J.W. Judy, and T.S. Otis. 2004. An ultra small array of electrodes for stimulating multiple inputs into a single neuron. *J. Neurosci. M.* 133:109–114.

Song, Y.K., W.R. Patterson, C.W. Bull, J. Beals, N. Hwang, A.P. Deangelis, C. Lay, J.L. McKay, A.V. Nurmikko, M.R. Fellows, J.D. Simeral, J.P. Donoghue, and B.W. Connors. 2005.

Development of a chipscale integrated microelectrode/microelectronic device for brain implantable neuroengineering applications. *IEEE Trans. Neural Syst. Rehab. Eng.* 13:220.

Sugiyama, K., W.K. Dong, and E.H. Chudler. 1994. A simplified method for manufacturing glass-insulated metal microelectrodes. *J. Neurosci. Meth.* 53:73.

Takahashi, H., T. Ejiri, M. Nakao, N. Nakamura, K. Kaga, and T. Herve. 2003. Microelectrode array on folding polyimide ribbon for epidural mapping of functional evoked potentials. *IEEE Trans. Biomed. Eng.* 50(4):510–516.

Vetter, R.J., J.C. Williams, J.F. Hetke, E.A. Nunamaker, and D.R. Kipke. 2004. Chronic neural recording using silicon-substrate microelectrode arrays implanted in cerebral cortex. *IEEE Trans. Biomed. Eng.* 51:896.

Warren, D.J., E. Fernandez, and R.A. Normann. 2001. High-resolution, two-dimensional spatial mapping of cat striate cortex using a 100-microelectrode array. *Neuroscience* 105:19.

Wise K.D., and J.B. Angell. 1975. A low-capacitance multielectrode probe for use in extracellular neurophysiology. *IEEE Trans. Biomed. Eng.* 22(3):212–219.

Wise K.D., J.B. Angell and A. Starr 1970. An integrated-circuit approach to extracellular microelectrodes. *IEEE Trans. Biomed. Eng.* 17(3):238–247.

Williams, J.C., R.L. Rennaker, and D.R. Kipke. 1999. Long-term neural recording characteristics of wire microelectrode arrays implanted in cerebral cortex. *Brain Res. Brain Res. Protoc*. 4:303–313.

Wilson, J.A., E.A. Felton, P.C. Garell, G. Schalk, and J.C. Williams. 2006. An ECoG-based brain-computer interface using multimodal control. *IEEE Trans. Neural Syst. Rehab. Eng.* 14(2):246–250.

Yoon, T.H., E.J. Hwang, D.Y. Shin, S.I. Park, S.J. Oh, S.C. Jung, H.C. Shin, and S.J. Kim. 2000. A micromachined silicon depth probe for multichannel neural recording. *IEEE Trans. Biomed. Eng.* 47:1082.

Yoshida, K., W. Jensen, P. Norlin, M. Kindlundh, and U.G. Hofmann. 2001. Characterization of silicon microelectrodes from the EU VSAMUEL project. *Biomediinische Technik* 446.