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Vision Research 39 (1999) 2577–2587

Vision Research

A neural interface for a cortical vision prosthesis

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Received 11 August 1998; received in revised form 7 December 1998

Abstract

The development of a cortically based vision prosthesis has been hampered by a lack of basic experiments on phosphene psychophysics. This basic research has been hampered by the lack of a means to safely stimulate large numbers of cortical neurons. Recently, a number of laboratories have developed arrays of silicon microelectrodes that could enable such basic studies on phosphene psychophysics. This paper describes one such array, the Utah electrode array, and summarizes neurosurgical, physiological and histological experiments that suggest that such an array could be implanted safely in visual cortex. We also summarize a series of chronic behavioral experiments that show that modest levels of electrical currents passed into cortex via this array can evoke sensory percepts. Pending the successful outcome of biocompatibility studies using such arrays, high count arrays of penetrating microelectrodes similar to this design could provide a useful tool for studies of the psychophysics of phosphene perception in human volunteers. Such studies could provide a proof-of-concept for cortically based artificial vision.

Keywords: Neuroprosthetics; Artificial vision; Electrode arrays; Multielectrode recordings; Biocompatibility

1. Introduction

The concept of cortically based artificial vision had its origins in studies of the functional architecture of the cerebral cortex. Wilder Penfield observed the behavioral consequences of electrically stimulating various regions of cerebral cortex and noted that there was a rational map of visual space onto the primary visual cortex (Penfield & Rasmussen, 1950). He observed that electrical stimulation of the surface of the visual cortex generally evoked the perception of points of light (called phosphenes) at specific regions in space. These observations have led a number of investigators to propose that electrical stimulation of visual cortex via arrays of electrodes might provide the profoundly blind with a limited form of functional vision. Subsequent experiments in the late sixties and early seventies by Brindley (Brindley & Lewin, 1968), Dobelle (Dobelle & Mladejovsky, 1974), Pollen (Pollen, 1975), and their co-workers demonstrated that a field of individual phosphenes could be evoked by stimulating visual cortex with an array of electrodes implanted subdurally over its surface. These studies showed that currents in the milliampere range were required to evoke individual phosphenes, and that currents passed through groups of electrodes that were spaced too close to neighboring electrodes produced highly non-linear interactions between the evoked phosphenes. It became clear from these experiments that stimulating visual cortex via an array of surface electrodes would not be an effective means to produce a useful visual sense in individuals with total blindness.

Recent experiments by Schmidt et al. (1996) have caused renewed interest in cortically based visual prosthetics. They stimulated visual cortex of a profoundly blind human volunteer with groups of microelectrodes that were designed to penetrate the cortex to the level of its normal thalamic input. Neural stimulation via penetrating electrodes has been long known to occur with electrical currents that are much smaller than those used to excite neurons via surface stimulation. Schmidt and his coworkers demonstrated that phosphenes could be evoked with currents that were orders of magnitude lower than those used with surface stimulation, and that simple patterned perceptions could be

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0042-6989/99/$ - see front matter

PII: S0042-6989(99)00040-1

evoked by current stimulation via small groups of these microelectrodes. Unfortunately, the electrode arrays used by Schmidt et al. were too sparse to allow them to answer the key question upon which a cortical approach to artificial vision must be based: does patterned electrical stimulation via a high electrode count electrode array evoke discriminable patterned percepts, or nondiscriminable blobs of light? If this psychophysical experiment can be performed, and the former result maintains, cortically based artificial vision could become a reality.

In order to answer this critical question (and many others associated with phosphene psychophysics), researchers need a new class of tools: arrays of microelectrodes that can be safely implanted into the visual pathways, and that will allow periodic injections of electrical currents at many closely spaced sites. Such arrays could eventually also form the cornerstone of visual neuroprosthetic systems. It therefore is clear that progress in cortically based artificial vision systems is directly linked to progress in the development of high electrode count microelectrode arrays.

Over the past few years, the research efforts of an increasing number of laboratories around the world have been committed to the development of such arrays. Work has been focused mainly on arrays that will interface to neurons of the retina (Humayun et al., 1995; Wyatt & Rizzo, 1996; Chow & Chow, 1997; Eckmiller 1997; Zrenner et al., 1997) or to neurons of the visual cortex (Wise & Najafi, 1991; Jones et al., 1992; Schmidt et al., 1996), although a recent study has described phosphene generation via optic nerve stimulation (Veraart et al., 1998a,b). Because of the importance of the neural interface in a visual prosthesis, much of this paper will focus on one example of such a penetrating cortical electrode array: the Utah electrode array. We will discuss considerations that were used in its design, how the array can be implanted in the visual cortex, and its biocompatibility as revealed by histological and electrophysiological experiments. The immediate motivation behind much of what we have developed at the University of Utah has not been to create vision neuroprosthetic systems (not enough is known about the human visual pathways to optimally design such a system today). Rather, we have been trying to create experimental systems that will allow researchers to better understand the vertebrate visual system though electrophysiological and behavioral experiments. When the long term biocompatibility of these experimental implant systems has been demonstrated, these systems could eventually be used in human experimentation to study the psychophysics of phosphene perception, and to establish the proof-of-concept that cortical stimulation may provide a limited, but useful visual sense to those with profound blindness.

2. A high electrode count, penetrating electrode array: design considerations

The cornerstone of a visual neuroprosthetic is the interface between the functioning neurons in the visual pathways, and implanted devices that can excite these neurons. This system must individually stimulate a very large number of neurons that have retained function even though more distal neurons have been irreparably damaged by the etiology of the blindness. This interface bypasses the malfunctioning distal components in the visual pathway and directly excites neural pathways that are proximal to the implant site. Recent work at the University of Utah (Jones et al., 1992), at the University of Michigan by Wise et al. (Hoogerwerf & Wise, 1994), and Stanford University (Kewley et al., 1997) has focused on the use of silicon as an electrode material from which high electrode count arrays can be fabricated. Silicon is highly biocompatible (Stensaas & Stensaas, 1978; Yuen et al., 1987; Schmidt et al., 1993), can be micromachined using standard microfabrication technologies, and can incorporate integrated electronics. The Michigan and Stanford electrode arrays have been built to take advantage of the planar photolithographic manufacturing techniques used in the semiconductor industry, while the Utah arrays were designed from the ground up to meet the needs of a neural interface. As such, new manufacturing techniques had to be developed in order to build this device. These techniques have been described elsewhere (Jones et al., 1992).

The Utah electrode array (UEA), shown in Fig. 1, provides a multichannel interface to the visual cortex. It has a large number of 1.5 mm long electrodes (typically 100 in a 10×10 square grid) that project out from a very thin (0.2 mm) substrate and that are separated from each other by 0.4 mm. The tips of the electrodes are metalized with platinum to facilitate electronic to ionic transduction. As the array's substrate must rest on the cortical surface, minimizing its thickness was an important design consideration: if it was too thin, it might break upon insertion, if it was too thick, the dura and the skull would produce a constant downward force on the array, tending to push it into the cortex.

The large number of penetrating electrodes in the UEA presents a very large surface area to the cortex and the implanted array tends to self anchor to the cortical tissues. Such an array has the strong advantage that it floats in the cortical tissues. As the cortex moves due to respiration and blood pumping, or to skeletal displacements, the array moves with it, thereby producing little or no relative motion between the electrode tips and the neurons near its active tips. This design feature should therefore, produce an extremely stable interface with the surrounding neurons.

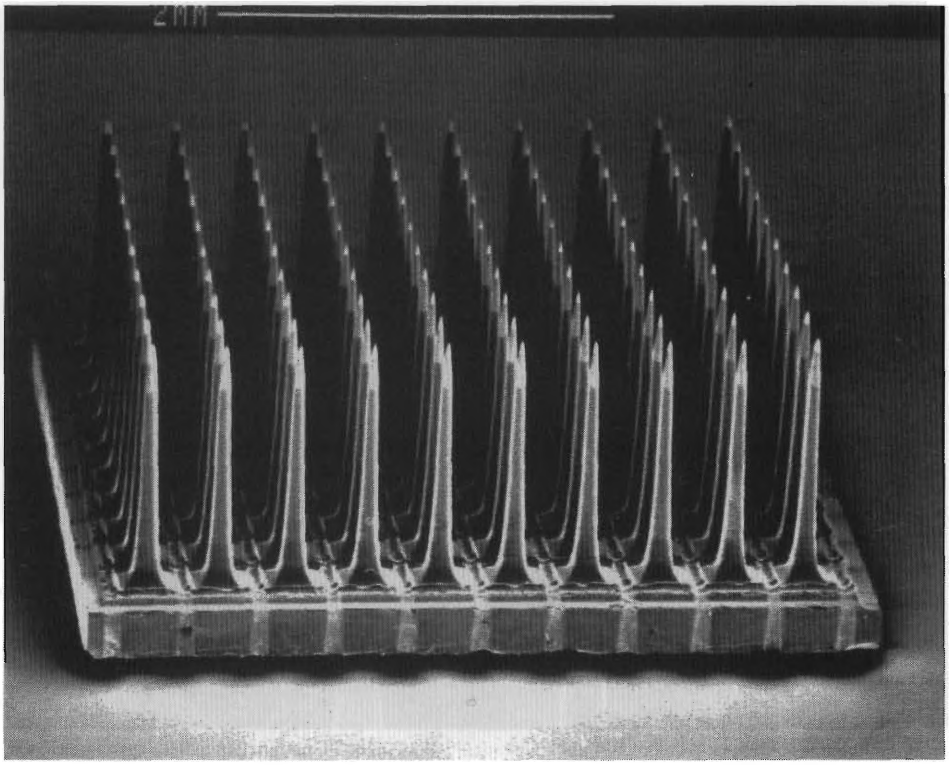

Fig. 1. A scanning electron micrograph of the 100 microelectrode, Utah electrode array (UEA).

The penetrating electrodes in an implanted array must compromise as little cortical volume as possible (ideally zero). Thus, each needle must be made as slender as possible yet retain sufficient strength to withstand the implantation procedure. Further, consistent with concept of blunt dissection used by neurosurgeons, these penetrating structures should displace the tissues they are inserted into rather than cut their way through them. Thus, the needle should have a cylindrical (or slightly conical) rather than a planar geometry. They must also be strong enough so that they are not deflected by the tissues they are inserted into. The needle electrodes in the UEA meet these criteria and are about 80–100 microns in diameter at their bases. They taper to a sharpened tip that has a radius of curvature of two to three microns. Fig. 2 shows an electron micrograph of the tips of these electrodes. Electrodes with these dimensions have been shown to be sufficiently strong to withstand insertion into materials that are considerably less compliant than cortical tissue (cork, balsa wood, even egg shell). As will be shown later, they do not bend during the insertion process, and they only displace about 4% of the cortical volume into which they are inserted.

Each electrode is electrically isolated from its neighboring electrodes with a moat of glass that surrounds the base of each electrode and each electrode has a bonding pad on the rear surface of the substrate. Conduction of signals along the length of the silicon needles is achieved by the use of doped silicon. The entire electrode array (with the exception of the platinum coated tips) is insulated with a 1 micron thick coat of silicon nitride. An electrical connection is made to each electrode by bonding an insulated 25 micron diameter wire to each bond pad, and connecting these wires to a percutaneous connector. The rear of the array (with bonded lead wires) is encapsulated with a silicone elastomer. Electrode impedances (measured with a 100 nA, 1 kHz sine wave current) are typically in the 100–300 kΩ range.

We have used both chronic and acute arrays in our experiments. The acute array has all 100 electrodes brought out to a small printed circuit board containing four, 26-pin IDC connectors. The chronic system has only 11 of the 100 potentially functional electrodes brought out to a Microtech connector via 11, 25 micron diameter, platinum–iridium lead wires. The connector is integrated into a titanium pedestal that is mounted with titanium bone screws to the cranium. Fig. 3 shows a photograph of the latest version of our chronic electrode assembly that uses a 20 micron thick, polyimide ribbon cable rather than 12 discrete lead wires to connect the array to the percutaneous connector.

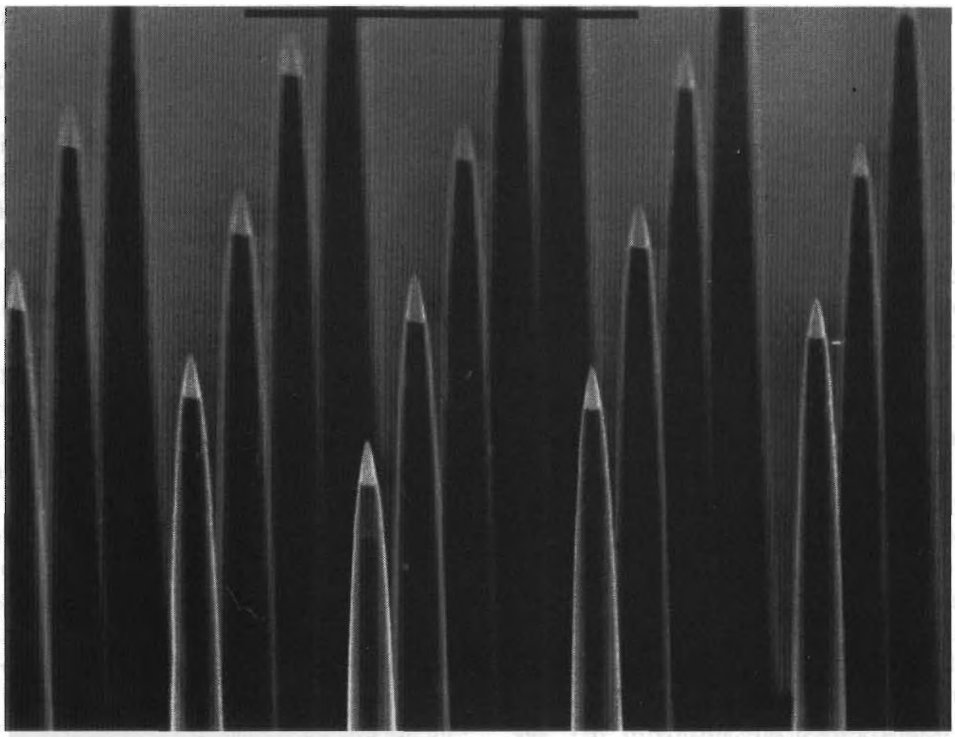

Fig. 2. A scanning electron micrograph of the platinum coated tips of the UEA electrodes. Scale bar = 0.5 mm.

3. Surgical issue: implanting high count electrode arrays

A visual prosthesis will be a highly invasive system that, eventually, must contain active integrated electronic circuitry. While relatively large electronic and mechanical systems have been implanted in the body (pacemakers, artificial joints, and the cochlear prosthesis), miniaturized devices of the mechanical and electronic complexity of the UEA have yet to be implanted on a long term basis in human volunteers. Whether the implant site is intended to be the cortex or the retina (or the optic nerve (Veraart et al., 1998a,b)), safe and effective surgical procedures that are cost-effective will have to be developed and validated in animal models before they are attempted in human volunteers.

The Utah researchers have developed new surgical techniques and tools that enable the UEA to be implanted in cortical tissues. Even though the individual electrodes of the UEA are extremely sharp, early attempts at implanting large numbers of them into the visual cortex only deformed the cortical surface and resulted in incomplete implantation. Further, the compression of the cortical surface produced by slow mechanical insertion can injure blood vessels, causing intracranial hemorrhage and cortical edema.

Because the brain is a viscoelastic material, it will behave in a much more rigid fashion if the electrodes can be inserted into the cortex at a very high velocity. We have developed a unique surgical instrument based upon this concept that appears to circumvent the above mentioned problems: a system that rapidly inserts the UEA into the cortex (Rousche & Normann, 1992). A drawing of the pneumatically actuated insertion tool we have developed is shown in Fig. 4. Array insertion is achieved by a transfer of momentum between an accelerated piston, and an insertion mass that rests against the back side of the electrode array which is to undergo implantation. When the momentum transfer takes place, the array is rapidly inserted into the cortical tissues in about 200 μs. The insertion is so rapid that the viscoelastic properties of the cortical tissues cause the cortex to experience only slight mechanical dimpling and the insertion is generally complete. Occasionally implantation of the UEA through surface vasculature is accompanied by a small amount of subpial bleeding, but this typically resolves itself, and single unit recordings of neural activity can often be made within hours after the surgical procedures are completed. The implantation of a chronic UEA in a cat takes typically about 4 h, and the surgical procedure has been described elsewhere (Maynard, Fernandez & Normann, 1999).

4. Biocompatibility of the Utah array

A neuroprosthetic system must be implanted into the nervous system and remain fully functional for periods that will eventually extend to many decades. This con-

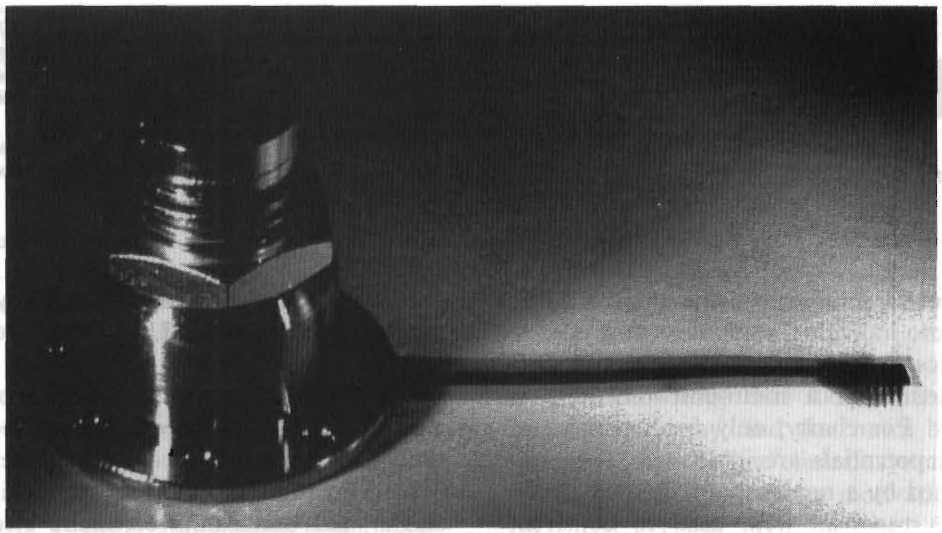

Fig. 3. A photograph of a chronic 25 electrode, UEA assembly that uses a 20 micron thick, polyimide ribbon cable to connect the array to a transdermal connector.

sideration places unique constraints on the architecture, materials, and surgical techniques used in the implementation of the neural interface. Inattention to these issues can result in chronic inflammatory responses around the implant site and generate a thick capsule surrounding each electrode. Because the UEA is a unique implantable structure, the consequences of its presence in the body for extended durations must be evaluated. We have studied its biocompatibility using histological and electrophysiological techniques.

4.1. Histological findings

The materials of which the UEA is built: silicon, silicon nitride, silicon dioxide, platinum, titanium, tungsten, and silicone are known to be well tolerated by the CNS (Stensaas & Stensaas, 1978; Edell et al., 1992; Schmidt et al., 1993). Our 6 month histological experiments support this notion. Fig. 5a and b show hematoxylin and eosin stained sections of such tissue. A thin capsule (2–5 microns thick) forms around each electrode track, but neuronal cell bodies are typically seen in close apposition to the electrode tracks. In fact, in sections where the tracks are similar in diameter to blood vessels, it is often difficult to tell a track from a vessel. Fig. 5 is an example of a particularly benign tissue response. We also have histological samples showing gliosis, buildup of fibrotic tissue between the array and the meninges, array displacement through the cortex, and bleeding in some tracks. It is clear that more work must be done to ensure that histological findings like those shown in Fig. 5 can be achieved on every implantation. These brief histological observations have been elaborated upon in a recent study by Maynard on the long term consequences of UEA implantation (Maynard, Fernandez & Normann, 1999).

4.2. Acute recording capability

An excellent index of the biocompatibility of a cortical implant is its ability to record single- and/or multi-unit activity from the neurons near the electrode tip for prolonged periods of time. If the materials used in the array, or the implantation techniques are not biocompatible, neuronal processes close to the electrode track will degenerate and it will not be possible to record single-unit activity. However field potential activity located far from the electrode tracks might still be recorded from functioning neurons, and such neurons may still be stimulated effectively in a neuroprosthetic application.

We have recorded responses from the UEA in both acute and chronically implanted animals to better understand its short and long term biocompatibility. Specimen responses with high, medium and low signal-to-noise ratios that were evoked by a bar of light moving across the receptive fields of visual cortical units are shown in Fig. 6. To generalize these findings, we have tabulated below the recording results of our past 17 acute cat implants. In this table, we classified responses on each electrode using the scale of Fig. 6 (Table 1).

In our best acute implantations in cat area 17, we have been able to record good single- and multi-unit responses from 68% of the electrodes (because of the curvature of the gyri in cat cortex, it is not possible to implant all 100 electrodes in a given gyrus and some electrodes end up in sulci). More typically, however, we are able to record good quality single- and multi-unit responses from 36% of the electrodes in a given array. Global field potentials, non-discriminable multi-unit responses, and an absence of responses are recorded from the remaining electrodes.

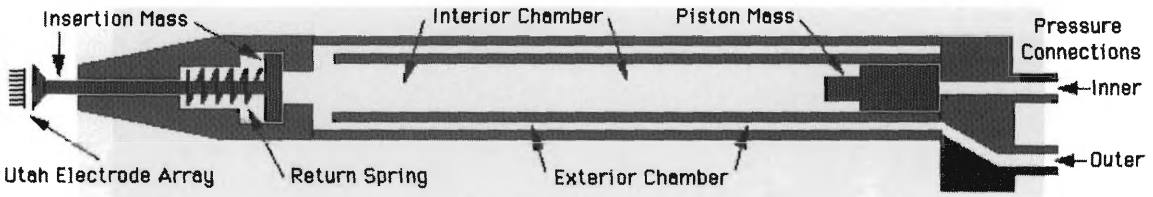

Fig. 4. A drawing of the high velocity, impact insertion tool used to implant the UEA into cortical tissues.

In many multi-unit responses, single-units can easily be discriminated into individual responses using criteria of response kinetics. An example of three single units that were recorded from a multi-unit recording is shown in Fig. 7A. For clarity, only five examples of each unit's action potentials are illustrated. These responses were evoked by a randomly modulated checkerboard, and the responses were used to construct receptive field plots for each unit (Fig. 7B).

4.3. Chronic recording capability

We have used chronic implantations of the UEA in cat visual and auditory cortex and monkey motor cortex to better monitor the stability and long term biocompatibility of the UEA. We have recorded multi- and single-unit evoked activity and identified single-units (based on response kinetics) on many of our electrodes. We have been able to record single- and multi-unit responses in cat and monkey cortex for over 3 years (the longest intervals studied). The presence of single- and multi-units on many electrodes, and the stability of these units over periods of months provides the most compelling evidence for the biocompatibility of the UEA.

5. Behavioral experiments

Useful function will be achieved in a visual neuroprostheses by injection of electrical currents into the visual pathways through large numbers of electrodes. Current injections can produce short term and long term complications depending upon the levels of the currents that are injected (McCreery et al., 1994) (or see Agnew, Chapter 6 for a review (Agnew & McCreery, 1990)). In order to determine the levels of current injections via the UEA that are required to evoke sensory percepts, we have conducted a series of behavioral experiments in cats (Rousche & Normann, 1999). Ideally, these experiments would be performed with implants in visual cortex, but, because of the ease of delivering auditory stimuli to a behaving cat, we

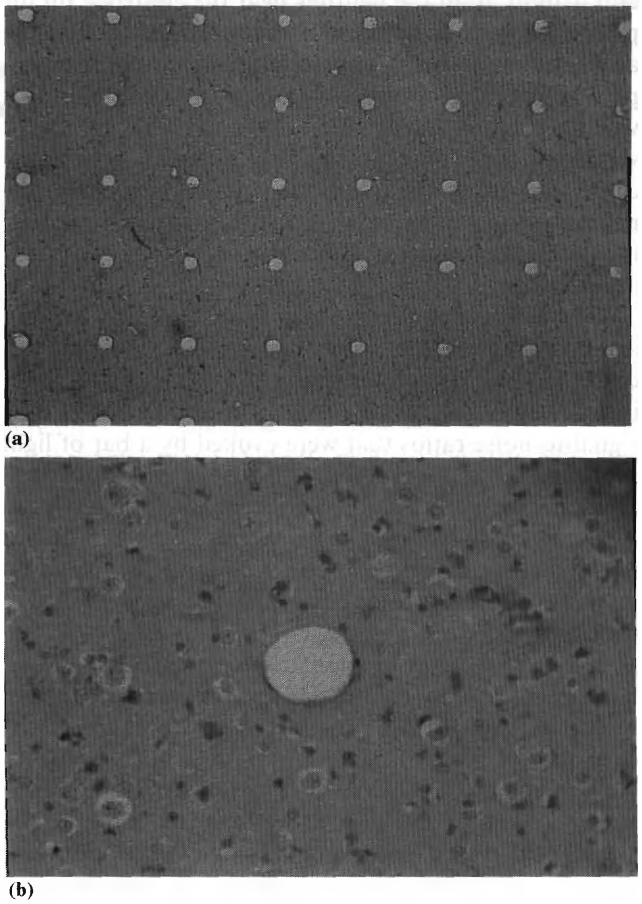

Fig. 5. (a) Hematoxylin and eosin stained sections of visual cortex implanted for 6 months with a UEA. Spacing between electrode tracks is 0.4 mm. (b) Higher magnification of one track.

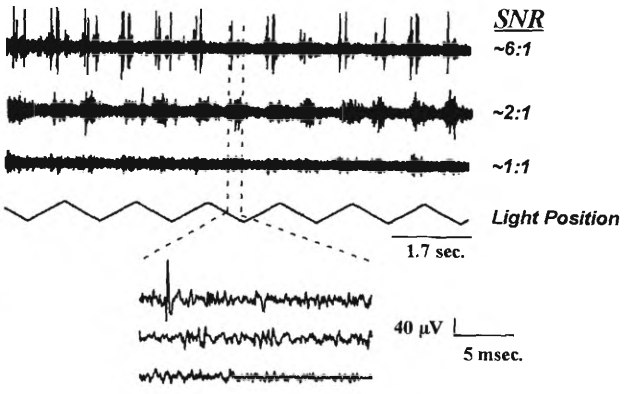

Fig. 6. Specimen responses evoked by a bar of light moving across the receptive fields of cortical units. The slow and fast time bases illustrate examples of high, medium and low signal to noise ratio recordings.

Table 1
Recording statistics from our past 17 acute implants illustrating the mean and standard deviation of the number of electrodes with high, medium and low signal-to-noise ratios for each of the arrays[a]

	High SNR > 3	Medium SNR 3 < med < 1.5	Low SNR < 1.5	Inactive (No discernable activity)	Useful SNR > 1.5
Minimum	1%	3%	0%	16%	10%
Maximum	53%	52%	35%	88%	68%
Mean ± S.D.	20 ± 15%	16 ± 13%	8 ± 9%	56 ± 23%	36 ± 19%

[a] Minimum and maximum are the lowest and highest number of electrodes with the indicated quality of recording on each of the arrays. Some arrays had a few broken electrodes, so data is presented as percent of potentially functional electrodes.

targeted the auditory cortex as our implant site and used auditory stimulation rather than visual stimulation.

Cats were trained over a 1–2 month period to lever press as a result of auditory stimulation, and auditory thresholds were measured. Trained cats that performed this task at 90% correct were chronically implanted with the UEA. Following implantation of the UEA, we interspersed current injections via the UEA and conventional auditory stimulation. Current injections that evoked auditory percepts should have resulted in a positive lever press in the trained animals. Results from a typical frequency of hearing experiment are shown in the psychometric function plots of Fig. 8A where the percentage of trials that evoked a lever press is plotted as a function of the current (charge per phase) that was passed into auditory cortex. In this example, eight frequency of hearing curves were measured from the same electrode over a 2 week interval, and the average 50% threshold was about 2 nC/ph.

The chronic percutaneous connectors used had limited pin counts and permitted access to a total of only 22 of the active electrodes in these three cats. Behavioral thresholds, measured on different electrodes in these three cats as the amount of charge injected per phase of stimulation, ranged from 1.5 nC/ph up to 26 nC/ph. The average threshold, measured in 71 sessions was 8.9 nC/ph. Fig. 8B shows the stability of four of these threshold measurements made in one cat over a 3 month period. Over the 100 days monitoring interval, thresholds varied by no more than 50%. This provides an additional index of the biocompatibility of the floating array design.

6. Conclusions

In this paper we have proposed that progress in cortically based visual prosthetics is closely linked to progress in electrode array development, and we have demonstrated a novel device, the UEA that could form the cornerstone upon which a cortically based visual prosthesis could be built. While the ultimate goal of our work has been the development of such a system, we fully acknowledge that such clinical systems are still many years away, and that much basic research must be performed before clinical systems may become a reality. A more immediate motivation for the creation of the UEA has been the need for a multichannel implant system that will expedite the conduct of this basic research.

The research performed by Brindley (Brindley & Lewin, 1968) and Dobelle (Dobelle & Mladejovsky, 1974), and more recently by Schmidt et al. (Schmidt et al., 1996) have provided us with a basic understanding of the psychophysics of single phosphenes: their perceptual aspects, the currents required to evoke them, and, to a lesser extent, their stability. While these researchers also had a goal of understanding how multiple phosphenes interact, their studies only slightly address this important question. It is this topic that will decide the ultimate feasibility of this technology as a means to provide a useful visual sense to the blind.

Schmidt et al. (1996) has demonstrated that safe levels of currents (McCreery et al., 1994) can evoke individual phosphenes when delivered via electrodes that penetrate the cortex. However, we don't know if patterned electrical stimulation via large numbers of electrodes will evoke discriminable patterned percepts, or merely generalized blobs of light. For example, can a trained subject discriminate the percept evoked by stimulation of a square pattern of electrodes from the percept evoked by a triangular pattern of electrodes? If so, is this a trivial discrimination to perform, or does it require considerable attention by the subject? What is the relation between current intensity and perceptual brightness, and how does a bright phosphene influence the perceived brightness and location of a neighboring dim phosphene? If patterned stimulation evokes patterned percepts, can a subject learn to associate these patterned percepts with objects in the physical world? If so, how much training will be required in order to make this association? These last issues are felt to be key to a successful visual prosthetic: the basic plasticity of the higher visual pathways may cause them to remodel with continued electrical stimulation to the point where the phosphene images of the user's environment

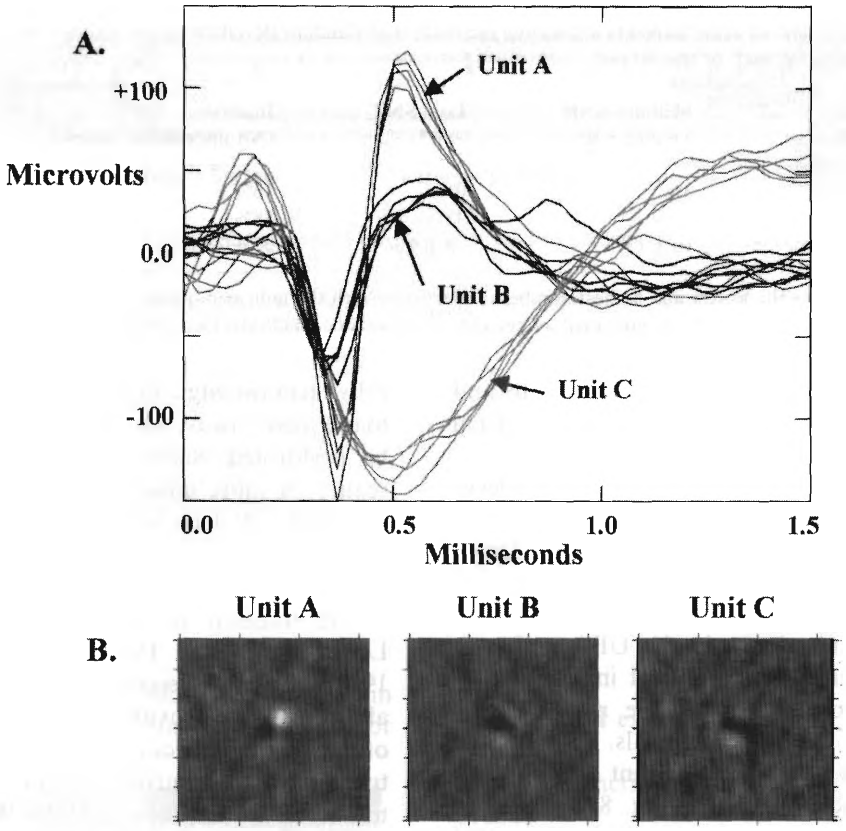

Fig. 7. (A) Example of three single-units that have been isolated from a multi-unit recording from one electrode. Stimulus was a randomly modulated checkerboard. (B) Plots of the receptive fields of the three single units of (A). The plots show 12 vertical by 16 horizontal degrees of visual angle. The gray scale intensity of the receptive field maps is in units of standard deviation of a zero mean, unit variance, normal distribution. White is +25 standard deviations and black is −15 standard deviations.

begin to become the defining features of the objects in the environment. These problems present new research opportunities and challenges for the neuroscientist.

The pursuit of these basic psychophysical questions, both in the cortex and in the retina, will provide insights into the functional organization of the human visual system and into mechanisms of memory, learning, and cognition. One tangible result from these studies will be the development of greatly improved design specifications that can be used to create future generation electrode arrays that may be better suited to a visual prosthesis. However, the first step in this new line of investigation into the psychophysics of phosphene perceptions will be the development and evaluation of new types of tools that will make this investigation possible. We feel that the Utah, Michigan and Stanford electrode arrays are examples of such tools.

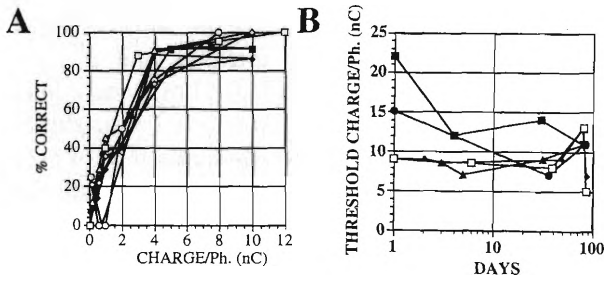

Fig. 8. (A) Psychometric function curves for a behavioral response to current injections into auditory cortex via the UEA. Curves were measured for a single electrode on 8 separate days over a 2 week period. (B) Stability of current thresholds for electrodes over a 100 day period.

Before these tools can be used in human experimentation, however, their safety and efficacy must be well documented in animal experiments. The experiments described briefly in this paper and more completely elsewhere have shown that the electrode arrays with considerable geometric complexity (such as the UEA) can be safely implanted in the cerebral cortex. Our physiological studies demonstrate that such arrays can be implanted for over 3 years with little pathological complications. However, we have yet to refine our surgical techniques to the degree that we can ensure that every UEA implantation can be achieved without histological complication.

Another significant limitation of the existing microelectrode array technology is connector technology. Because our chronic implant system uses a 12 pin

Microtech connector, electrical access to 89 potentially useful electrodes in a 100 electrode UEA is not provided (one pin is used for a reference connection). Higher pin count connectors are commercially available, but these devices are larger and have greater insertion and removal forces. New connector designs based on the compression of anisotropic conducting sheets between aligned contact pads offer a novel approach to this problem (Bioelectric Corp., Portland, OR), but these systems are not yet fully commercialized. A better approach to the problem would be to multiplex the signals going to and from the UEA, and such integrated circuits have been built (Ji & Wise, 1992; Jones & Normann, 1997, 1998), but these systems fail prematurely when implanted due to their high sensitivity to ion diffusion and to the lack of a hermetic seal to protect them from the ions of the extracellular space. Telemetry offers an even superior solution to this interconnection problem, but such systems that can support the high signal bandwidth and low power requirements of a 100 electrode array have yet to be built. These are challenges for the engineer.

6.1. Number of pixels needed for useful vision

The researchers developing these electrode arrays are not expecting to restore the panoramic visual sense enjoyed by sighted individuals. The long range goal of the Utah researchers has been to develop systems that will provide the profoundly blind with independent mobility in typical visual environments. Interestingly, the amount of visual input required to perform basic visually guided tasks is not as great as one might expect. In a series of psychophysical experiments conducted with a portable simulator of pixelized images, we suggest that a functional visual sense might be restored in those with profound blindness with arrays containing as few as 625 electrodes (Cha et al., 1992a,b,c). A total of 625 pixels of appropriate visual information (placed in a square grid, with a center-to-center spacing of 4 min of arc), can provide sufficient visual information to allow sighted volunteers to read at 2/3 the rate that they could read with normal vision. More importantly, 625 pixels allow volunteers to navigate complex visual environments with normal speed and good levels of confidence. This simulates the visual sense that could be provided by a 25×25 electrode array, with a 0.4 mm interelectrode spacing (under the incorrect presumption of perfectly conformal retinotopy). Such 625 electrode arrays have been built with the same techniques used to build the UEA. The possibility of providing some degree of functional vision with as few as 625 electrodes is encouraging to the Utah researchers.

6.2. Retinal versus cortical approaches to a vision prosthesis

Over the past few years, there has been considerable interest in developing a vision prosthesis based upon direct retinal stimulation with extrinsic currents. Two general approaches have been proposed: an epiretinal approach whereby the stimulating electrodes would be implanted on the retina's vitreal surface (Wyatt & Rizzo 1996; Eckmiller, 1997) and a subretinal approach where the electrodes would be implanted between the retina and the pigment epithelium (Chow & Chow, 1997; Zrenner et al., 1997). While these two competing retinal approaches have their adherents, there are clear advantages and disadvantages to a retinal versus a cortical approach, and these are summarized below.

6.2.1. Advantages of a retinal approach

- Could use existing physiological optics. If the photosensors can be placed in the plane of the retina, the optics of the eye could form optical images directly on these sensors.
- Less invasive and less severe consequences of infection. While the retina is central nervous tissue, a retinal infection has less severe consequences than a cortical infection.
- Closer to photoreceptors: easier spatial mapping. Remapping due to nonconformal retinotopy (Nordhausen et al., 1996) would be less of a problem the closer stimulating electrodes are to the photoreceptor level.
- As the implant is lower in the visual pathways, there is more opportunity for natural processing of the electrically stimulated images.

6.2.2. Problems with a retinal approach

- Retinotopy is dependent on stimulating ganglion cell (GC) bodies, not optic nerve fibers. If the injected electrical currents preferentially excite optic nerve fibers over GC bodies, the field of evoked phosphenes will not bear a rational relation to the distribution of electrodes.
- Hard to ensure chronic GC/electrode apposition. In order to ensure such apposition, the electrode array will likely have to be a structure that penetrates the retina to the level of the ganglion cell bodies.
- Encapsulation of the array will reduce GC/electrode apposition. If the array encapsulates, it could be expelled from the retina, thereby decreasing GC/electrode apposition.
- Multiple visual representations by ganglion cells. As ganglion cells encode spatial, chromatic, intensity and temporal information, it is not clear what features will be evoked by current injections via a retinal electrode array.

- High rotational accelerations associated with saccadic eye motions could dislodge array.
- Limited to outer retinal pathologies.
- Will patterned stimulation evoke discriminable patterned percepts or generalized blobs of light?

6.2.3. Advantages of a cortical approach

- The skull provides a more rugged housing for the implant.
- Penetrating arrays have been and can be simply inserted into visual cortex.
- Stable stimulation site.
- Successful long term animal studies.
- Provides a solution to pathologies not only of the outer retina, but to the entire retina, optic nerve, and thalamus.

6.2.4. Problems with a cortical approach

- Non-conformal retinotopic mapping may require extensive electronic remapping of visual inputs onto cortical electrode array.
- Multiple visual representations in cortex. Visual cortex encodes color, intensity, orientation, ocular dominance, and other spatial features. It is unclear what kind of percepts will be evoked by stimulation of large numbers of cortical units.
- Convoluted cortical anatomy can make implantation of large arrays or many small arrays difficult or impossible.
- Surgical complications. Meningeal infections can have very serious consequences on other cortical regions.
- Societal perceptions of brain implant. The negative perception of electronic implants in the brain will be mitigated to a large degree by the success of the implants in restoring visual function.
- Patterned stimulation may not produce patterned perceptions.

Both retinal and cortical approaches offer unique surgical challenges, and proponents of either approach often claim that one approach is surgically simpler than the other. These claims will have to be validated with future work.

The increased level of interest in visual prosthetics that has occurred over the past decade and the new tools that have been spawned by this interest is certain to generate new knowledge regarding the functional organization of the visual system. It is also clear that technological innovations that are made in new cortical implant systems will also facilitate developments in retinal implant systems and vice versa. Progress in both approaches will also expedite new neuroprosthetic solutions to problems in other parts of the nervous system. Disorders in other sensory modalities or in the motor system could be mitigated by such neuroprosthetic systems.

Successful cortical implant systems will not preclude the continued development and eventual use of retinal implant systems: both approaches are seen as being synergistic and each may have an appropriate set of pathologies best suited each implant system. The next few years will see these systems start to become applied in human experiments to provide proof of concept that microelectrode arrays can provide a safe and efficacious restoration of vision to the profoundly blind.

Acknowledgements

The authors want to thank John Donoghue at Brown University for the data on monkey motor cortex. We thank Vinh Ngo and Yanping Zhang for their help in building these microelectrode arrays. Research supported by the N.S.F. (grant # IBN 9424509), a State of Utah Center of Excellence grant, and donations from the W.M. Keck Foundation and John A. Moran.

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