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Penetrating multichannel stimulation and recording electrodes in auditory prosthesis research

David J. Anderson *

Electrical Engineering and Computer Science, Biomedical Engineering, Kresge Hearing Research Institute, University of Michigan, 1301 East Ann Street, Ann Arbor, MI 48109-0506, USA

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ABSTRACT

Microelectrode arrays offer the auditory systems physiologists many opportunities through a number of electrode technologies. In particular, silicon substrate electrode arrays offer a large design space including choice of layout plan, range of surface areas for active sites, a choice of site materials and high spatial resolution. Further, most designs can double as recording and stimulation electrodes in the same preparation. Scala tympani auditory prosthesis research has been aided by mapping electrodes in the cortex and the inferior colliculus to assess the CNS responses to peripheral stimulation. More recently silicon stimulation electrodes placed in the auditory nerve, cochlear nucleus and the inferior colliculus have advanced the exploration of alternative stimulation sites for auditory prostheses. Multiplication of results from experimental effort by simultaneously stimulating several locations, or by acquiring several streams of data synchronized to the same stimulation event, is a commonly sought after advantage. Examples of inherently multichannel functions which are not possible with single electrode sites include (1) current steering resulting in more focused stimulation, (2) improved signal-to-noise ratio (SNR) for recording when noise and/or neural signals appear on more than one site and (3) current source density (CSD) measurements. Still more powerful are methods that exploit closely-spaced recording and stimulation sites to improve detailed interrogation of the surrounding neural domain. Here, we discuss thin-film recording/stimulation arrays on silicon substrates. These electrode arrays have been shown to be valuable because of their precision coupled with reproducibility in an ever expanding design space. The shape of the electrode substrate can be customized to accommodate use in cortical, deep and peripheral neural structures while flexible cables, fluid delivery and novel coatings have been added to broaden their application. The use of iridium oxide as the neural interface site material has increased the efficiency of charge transfer for stimulation and lowered impedance for recording electrodes.

1. Introduction

The natural parallelism and stochastic principles of the nervous system have led neurophysiologists to aspire to interacting with multiple neurons simultaneously. Auditory system physiologists comprised one of the principal driving forces behind the cascade of technological developments that has led us to the present state where massive amounts of data from the nervous system may be processed without being excessively invasive.

Numerous advances in technology resulted from pursuing how precisely-timed neural discharges in auditory neurons, organized in exquisite tonotopic order through out the auditory pathways, code the acoustic environment. Advances in electrodes, amplifiers, waveform visualization tools and signal processing methods culminated in the development of specialized data acquisition equipment coupled with laboratory computers to achieve precise quantification of electrophysiological data. These advances were quickly assimilated. Auditory science demands precise timing of neural events because nowhere in the brain is timing more important than in the auditory system. In addition, few systems have such an easily observed organizational theme as the orderly distribution of the auditory spectrum at every nuclear level. Practitioners of auditory physiology were therefore involved in the earliest vision for multichannel recording technology because the next great challenge was understanding how neurons cooperated to extract information from the auditory environment. In the early 1960s laboratory computers were finding a perfect marriage with auditory neurophysiology. Forward thinking individuals were inspired to invent methods for study of multiple neurons recorded simultaneously. Moise Goldstein and Moshe Abeles pioneered ways to separate extracellular potentials recorded from single channel electrodes (Abeles and Goldstein, 1977), Perkel et al. (1967a,b) invented visualization and computational methods that could be used to extract information from multichannel data, and Starr et al. (1973) gathered colleagues at Stanford to exploit the

* Tel.: +1 734 763 4367; fax: +1 734 763 8041.
E-mail address: dja@umich.edu

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thin-film methods of the electronics industry to realize multichannel neural recording devices (Wise et al., 1970). The first results from recording in the auditory cortex with thin-film electrodes was reported shortly after the first fabrication process was developed (Starr et al., 1973). The effort at the University of Michigan to perfect the "Michigan probe" discussed below stemmed directly from Starr's initiative and Wise's technical skills. The advent of the auditory prosthesis in the early 1970s with its quick advance to an array of electrodes further inspired the need to electrically visualize the spatial organization of the system and later consider stimulation of the system at other more central centers. It is interesting, and probably a comparative advantage, that neurophysiologists with interests in the auditory system were early leaders in multisite electrode arrays and multichannel processing.

With the advent of the scala tympani auditory prosthesis, it was important to evaluate the response of the central nervous system (CNS) to this stimulation. Initially the work was done by passing single channel electrodes through a tonotopic region of the auditory system, usually the inferior colliculus (Merzenich and Reid, 1974). Stimulation of the peripheral auditory system became a vast and extremely successful clinical enterprise starting in the early 1970s. At the same time, little research related to stimulation in the auditory CNS was taking place. This is not surprising considering the peripheral stimulation success and the problems that would be faced in the CNS. Nevertheless, the same thin-film technology that was successful in recording can easily be applied to stimulation. Stimulation of the cochlear nucleus (CN) using silicon multichannel penetrating arrays started in the late 1980s (Anderson et al., 1989; Evans et al., 1989). More recently, these arrays have been more precisely evaluated for CN stimulation (McCreery et al., 2007), the inferior colliculus (Lim and Anderson, 2006), and the auditory nerve (Middlebrooks and Snyder, 2007).

Parallel efforts were being carried on in other brain areas with other technologies. While microwires (Nicolelis et al., 2003) and the Utah probe (Rousche and Normann, 1998) are not featured herein, they have made very significant contributions to neuroscience and multichannel recording and stimulation.

Progress in auditory systems neuroscience has been considerable in the last three decades but it has been a difficult science to scale up to study of the intact auditory system. Research on the code and coding mechanisms in the nervous system has remained an important subject but without tools to interrogate the massively parallel nature of the nervous system, progress will continue to be slow. Here we explore the thin-film multichannel electrode array, which is one of the devices that has shown some promise for accelerating the discovery process in auditory neurobiology by systematic multichannel recording and stimulation at several levels in the auditory pathway.

2. Micromachined multichannel electrode arrays

Scaling the monitoring of single neurons to whole populations of neurons has been a dream of neurobiology since the early discoveries made by recording from single cells with single metal and glass electrodes. The objective is to fabricate recording electrodes with communication electronics by the same precise methods used by the semiconductor industry to create integrated circuits such as the ubiquitous microprocessor. There are several forms of micromachined multichannel electrode arrays that utilize a variety of fabrication methods but we will focus on planar recording and stimulation arrays. The basic features of a successful electrode are the substrate, exposed metal, conductors, and dielectrics. The substrate provides the mechanical support and the shape of the electrode array. Exposed metals provide the localized interface to the nervous system and the interface to the instrumentation electronics. Conductors, thin-film traces in the case of the Michigan probe, provide the electrical communication within the device. Finally, the dielectrics isolate the internal conductors from the external conducting media and thus allow safe delivery of the signal along the probe. The first version of this probe was developed by Najafi et al. (1985) and soon after reported as a tool for neuroscience (BeMent et al., 1986; Drake et al., 1988). Demonstration for use as a stimulation device in the auditory system was reported later (Anderson et al., 1989). Each of the devices was engineered as they are today to endow individual electrodes with the structure, dimensions and electrical characteristics suitable for stimulation or extracellular recording in each specific application. There have been hundreds of electrode designs fabricated over the years. In addition, several extensions to the technology have become available such as integrated silicon and polymer cables (Hetke et al., 1994; Pang et al., 2005; Yao et al., 2007), fluidic channels (Chen et al., 1997), the implementation of electronic circuits for recording (Ji and Wise, 1992) and stimulation (Tanghe and Wise, 1992) and incorporation of 2D probes into 3D devices (Bai et al., 2000). These features vastly expand the design space of the electrode arrays. While not the only viable technology, our focus will be the Michigan probe which has been the subject or our developments for more than 20 years.

2.1. Fabrication process

The substrate upon which the thin-films are deposited is a matter of choice. Silicon (Wise and Angell, 1975; Edell, 1986), ceramic (May et al., 1979; Prohaska et al., 1986; Moxon et al., 2004) and polymer (Pickard et al., 1979; Rousche et al., 2001) have been used. There are positives and negatives to all of these technologies but silicon and polymer substrates have proliferated significantly. Silicon has the advantage of allowing electronics to be fabricated as part of the device as first demonstrated by Wise and Angell (1975). Our discussion will include the silicon substrate devices developed at the University of Michigan under NIH Neuroprosthesis Program (NPP) projects and the polymer substrate developed at Arizona State University. These probes are fabricated at the University of Michigan for distribution either for testing purposes through the NPP program prior to 1994, through the NIH sponsored Center for Neural Communication Technology (CNCT) from 1994 to 2004 and thereafter by NeuroNexus Technologies of Ann Arbor, Michigan. An extensive review of the silicon technology containing much of the detail was published in 2004 (Wise et al., 2004) and the polymer technology is discussed by Rousche et al., (2001). The advantages that make these devices useful and practical are batch fabrication, precision of relative site positions on the substrate, few limitations on planer substrate shape, a variety of tip configurations for different penetration needs, an integrated cable technology (Hetke et al., 1994), and strength sufficient to be inserted into the brain. The fabrication process for the Michigan probe is shown in Fig. 1. With extra fabrication steps, the arrays can be augmented with a hollow channel on the shanks (Chen et al., 1997). These can be used for either stiffening the substrate or delivery of pharmaceuticals.

Two key features of this fabrication process which make it so versatile for producing neural probes are selective silicon etching and the ability to pattern the surface features to submicron precision. Selectively etching of a silicon wafer is achieved by patterned boron doping of the wafer to a depth of 5–15 μm at the beginning of the process and the use of an etchant that preferentially etches undoped silicon vs. doped silicon at the end of the process. The pattern of the doping thus produces the gross shape of the device while the depth of the doping determines the thickness and thus the strength and flexibility of the probe. Probes which must penetrate into the brain are usually 15 μm thick while flexible cables