Development of Nanowire Arrays for Neural Probe

Jose K. Abraham, Jining Xie and Vijay K. Varadan
CENNESS/ HiDEC
Department of Electrical Engineering
University of Arkansas, Fayetteville, AR 72701

ABSTRACT

It is already established that functional electrical stimulation is an effective way to restore many functions of the brain in disabled individuals. The electrical stimulation can be done by using an array of electrodes. Neural probes stimulate or sense the biopotentials mainly through the exposed metal sites. These sites should be smaller relative to the spatial potential distribution so that any potential averaging in the sensing area can be avoided. At the same time, the decrease in size of these sensing sites is limited due to the increase in impedance levels and the thermal noise while decreasing its size. It is known that current density in a planar electrode is not uniform and a higher current density can be observer around the perimeter of the electrodes. Electrical measurements conducted on many nanotubes and nanowires have already proved that it could be possible to use for current density applications and the drawbacks of the present design in neural probes can be overcome by incorporating many nanotechnology solutions. In this paper we present the design and development of nanowire arrays for the neural probe for the multisite contact which has the ability to collect and analyze isolated single unit activity. An array of vertically grown nanowires is used as contact site and many of such arrays can be used for stimulating as well as recording sites. The nanolevel interaction and wireless communication solution can extend to applications involving the treatment of many neurological disorders including Parkinson's disease, Alzheimer's disease, spinal injuries and the treatment of blindness and paralyzed patients with minimal or no invasive surgical procedures.

Key Words: Neural implants; Gold nanowire; Nanowire array.

1. INTRODUCTION

Many modern biomedical devices have the potential to revolutionize the medicine because these systems can greatly improve human health and the current health care systems previously it was not thought possible. Nanotechnology and Nanoengineering involve the design, synthesis, characterization and application of materials and devices whose smallest dimensions are on the scale of a billionth of a meter. In biology and medicine, these materials and devices can be designed to interact with cells and tissues at a molecular or submolecular level with a high degree of functionality that allows integration between devices and biological systems that was not previously attainable.

Developments of many multichannel neural implants were possible due to the advancement of technologies in material science and microelectronics. The use of microelectrodes together with electronic recording and signal processing allow meaningful studies of the central nervous system. Reliable and long term monitoring of brain activities brought the perception of sound to thousands of deaf individuals by means of cochelear implant, which was the first success story in brain-machine interface. Attempts are also underway to provide images to the visual cortex and allow the brains of paralyzed patients to re-establish control of external environment. The brain-machine interface is a challenging job due to the complex nature of the brain. Implantable probes are also required for continuous monitoring, diagnosis and treatment of neurological disorders. Due to the biocompatibility as well as the well defined standard CMOS fabrication process, silicon has been most successful implantable material.

Early experiments using cutoff wire bundles [1] to record the nervous action simultaneously from many points had some success but were limited due to its geometry as well as reproducibility. Lithographic and silicon etching technologies were then developed to produce electrode arrays capable of simultaneously recording many points in the

Smart Structures and Materials 2005: Smart Electronics, MEMS, BioMEMS, and Nanotechnology,
edited by Vijay K. Varadan, Proceedings of SPIE Vol. 5763 (SPIE, Bellingham, WA, 2005)
0277-786X/05/$15 · doi: 10.1117/12.608131

tissue [2]. Development of prosthetic devices for the dead and blind started in 1960s using array of metal electrodes implanted in cochlea [3], auditory nerve [4], inferior colliculus [5] and visual cortex [6]. Initially, these experiments were find difficulty in exact placement of electrodes and in many cases, problems with leads, packaging and electronics were severe. Due to the emerging technologies and advancements in nanofabrication techniques today it could be possible over 70000 cochlear implants worldwide. Retinal implants have recently received great attention [7-8] and many efforts are underway.

In Parkinson's Disease (PD), the degeneration of neurons in a region of the brain, called substantia nigra, results in a shortage of the neurotransmitter, dopamine that is responsible for transmitting signals between the substantia nigra and the corpus striatum. Decreased dopamine in the striatum leaves patients unable to control their normal motor activities. Currently there is no cure for PD. When the symptoms grow severe, patients are usually prescribed levodopa (L-dopa), which helps to increase brain's dopamine levels. L-dopa, a dopamine precursor, is transformed into dopamine by neurons in the substantia nigra. The prescription of high dosages of levodopa was the first breakthrough in the treatment of PD. Unfortunately, patients may experience debilitating side effects such as uncontrolled arms and legs movement. In severely affected PD patients, a neurosurgical procedure known as pallidotomy (lesioning the globus pallidus of the corpus striatum) has been effective in reducing symptoms. Pallidotomy is a destructive procedure that uses heat from an implanted electrode to destroy neurons. Another type of neurosurgical procedure, in which healthy dopamine-producing tissue is transplanted into the brain, has shown little benefit to date.

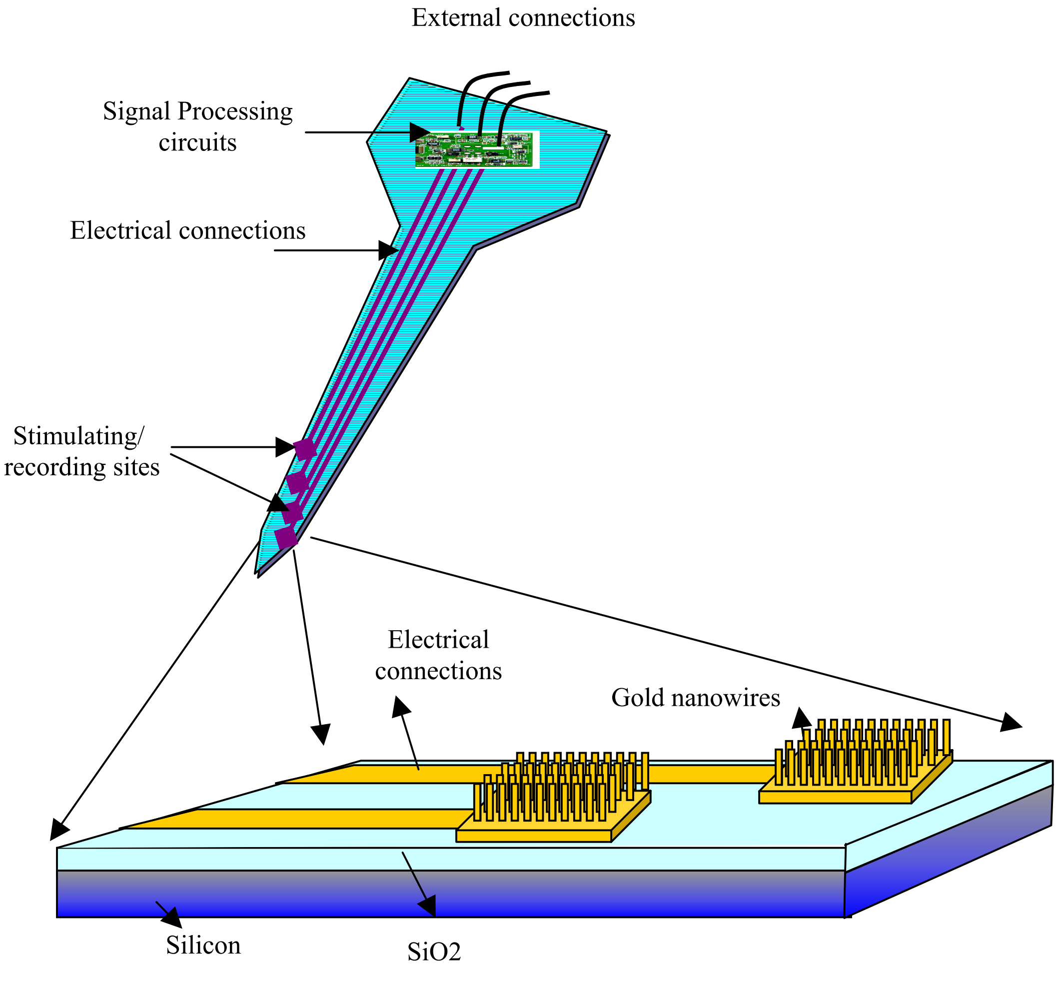

Figure 1. Schematic diagram of the micromachined silicon neural probe with gold nanowire array

The most widely accepted neurosurgical treatment for PD employs deep brain stimulator that deliver continuous high-frequency electrical stimulation to the thalamus or other parts of the brain that control movement [9]. The stimulator consists of implanted in the thalamus and connected to a pacemaker-like device in the chest that the patient can switch on or off as symptoms dictate. High frequency stimulation decreases neuronal firing in the vicinity of the electrodes, helping to rebalance control messages throughout the movement control centers in the brain. Deep Brain Stimulation (DBS) is useful for treating tremor, dyskinesias, and other motor dysfunctions of PD such as bradykinesia and rigidity. DBS requires a surgical procedure to place the electrode in the brain. The electrode is connected by wire to a battery source. The wire is implanted under the scalp and neck, and the battery is implanted in the chest wall just below the clavicle. A series of stimulation adjustments are required in the weeks following implantation. Most of the time the battery lasts for three to five years, then is replaced through an incision in the chest. The advantage of DBS over pallidotomy is that, instead of destroying neurons, the overactive cells that cause symptoms in PD are temporarily disabled.

2. SILICON MICROMACHENED NEURAL PROBES

Figure 1 presents typical schematic diagram of the silicon micromachined neural probe which is used for stimulation and recording of neural activities. The microprobes with four sites in-line shank edge have been the typical configuration and are appropriate for recording from cells with columnar organization. Microporbes with transverse sites can be used to record from adjacent cells in cell assemblies oriented to the principal probe axis [10-13]. These neural probes are typically sharpened pins of 5 to 50 μm in size which exposed to a recording area of 100 μm^2. The thickness of the silicon substrate can be controlled from few tenths of micrometers to 15μm or more and substrates as narrow as 5 μm can be achieved. The thin film external leads must connect to exposed stimulating / recording sites to sense and record the biopotentials generated by active neurons.

<u>2.1</u> <u>Stimulating and Recording Leads</u>: The sensing of the action potential generated by the neuron is done by using exposed metal sites as shown in figure 1. These sites should be small relative to the total special spread. Other wise the sites will read the average potential. The recording of the action potentials generated by the neurons within a group of cells is needed to study accurate nervous activities. The recording area can be increased by multiple recording sites. Multiple recording sites are precisely located on the silicon substrate with a special distribution of 20 to 300 μm. These recording sites consist of gold inlayed on conductors or polysilicon or tantalum with conducting electrical inter-connections. It is necessary to insulate the conductor above and below by multilayered dielectric materials such as SiO_2 and Si_3N_4. Gold, platinum and iridium oxide have been used for stimulating sites. Since charge stimulates the cellular activity, the selection of the material depends on the requirement of the amount of charge delivery in to the cellular region as well as it has to remain within the application window to avoid any local pH changes due to the evolution of oxygen or hydrogen.

<u>2.2</u> <u>Signal Processing Circuits:</u> The microprobes were mounted on to custom printed circuit boards which provide input to the buffer amplifier stages during the initial experiments [12]. Additional amplifier enhances the gain of the neural signals and is give to the recording system.

<u>2.3</u> <u>Probe Encapsulation:</u> The thin-film leads on the probe have to be connected with the recording sites as well as the signal processing circuits with proper insulation with biological medium. It is found that silicon dioxide and silicon nitride have performed well *in vivo* when deposited by LPCVD. The layer thickness ratios in such stacks need to be controlled so that any stress in the overall film is near neutral and the probe does not wrap. It is proved that leads formed from polysilicon with LPCVD oxide/ dielectric has produced stable impedance. However their performance over decades, consistent with prosthetic applications, is still unknown.

<u>2.4</u> <u>Polymer Materials:</u> Current microfabricated implantable electrodes are stiff enough to be inserted through the pia or dura without many problems and can have microfluidic channels for precise delivery solutions. However, the long term stability of silicon implants especially considering the induced strain due to the micromotion of the brain is not yet studied. Due to the concerns in long term safety and functional stability of the implanted devices, new designs were evolved in polymer based intracortical electrode array [15], neural implants with stiffness improvement [16].

These designs show many attractive features like flexible, biocompatible, and manufacturing easiness due to the compatibility in existing microfanrication. Due to the possibility of tissue damage due to micromotion of the brain, flexible implants are highly desirable.

3. NANOWIRE ELECTRODE NEURAL PROBES

The lack of adequate electrical contacts with neurons and the proper instrumentation is the biggest issues on today's implantable devices. Neural probes sense the biopotentials mainly through the exposed metal sites. These sites should be smaller relative to the spatial potential distribution so that any potential averaging in the sensing area can be avoided. At the same time, the decrease in size of these sensing sites is limited due to the increase in impedance levels and the thermal noise while decreasing its size. Typical site dimensions are ranging from 6 to 20 µm for recording with a geometrical area of 40 to 400 μm^2. The area of the stimulation site depends on the requirements in the amount of charge delivery to the neurons. Ziaie et. al. [17] reported a planar high current stimulating microelectrode system using iridium oxide. The test results show that it can be used for a current density of 2 µC of charge in an area of $0.3mm^2$ in 200µsec, which is equivalent of 3300 mA/cm^2. This is achieved due to using irridium oxide which has the highest know charge injection capability. It is known that current density in a planar electrode is not uniform and a higher current density can be observer around the perimeter of the electrodes. Electrical measurements conducted on many nanotubes and nanowires have already proved that it could be possible to use for current density applications and the drawbacks of the present design in neural probes can be overcome by incorporating many nanotechnology solutions. In this paper we report the design and development of nanowire arrays for the neural probe for the multisite contact which has the ability to collect and analyze isolated single unit activity. An array of vertically grown nanowires is used as contact site and many of such arrays can be used for stimulating as well as recording sites.

3.1. Development of Nanowire Electrodes: Many modern biomedical devices have the potential to revolutionize the medicine because these systems can greatly improve human health and the current health care systems previously it was not thought possible. Nanotechnology and Nanoengineering involve the design, synthesis, characterization and application of materials and devices whose smallest dimensions are on the scale of a billionth of a meter. At these scales, individual molecules and its interaction with macroscopic materials or devices becomes important since the nanomaterials are controlled manipulation of fundamental molecular structure of bulk material. In biology and medicine, these materials and devices can be designed to interact with cells and tissues at a molecular or submolecular level with a high degree of functionality that allows integration between devices and biological systems that was not previously attainable.

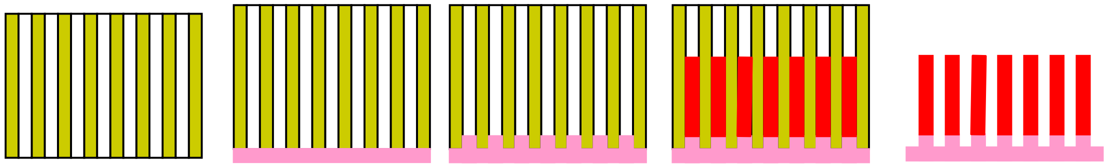

Figure 2: Schematic diagram of process steps of gold Nanowire electrode fabrication.

(a) Blank membrane (Anodic alumina)
(b) Backside contact formation (Ag)
(c) Electrodeposition (Ag)
(d) Electrochemical deposition of gold
(e) Template removal (NaOH etching)

3.2 Fabrication of Aligned Gold Nanowire Electrodes: Nanowire array is fabricated using a template of nanosize structures. Anodic aluminum oxide (AAO) and polycarbonate are two types of templates which are commonly used. Both of them have self-organized arrangements of neighboring pores in hexagonal arrays. Anodic alumina membranes are prepared by the anodic oxidation of aluminum in various electrolytes. By carefully controlling the anodic oxidation parameters, the diameter of nano-channels ranges from 4 to 200 nm. In this experiment, commercially available anodic alumina membranes with a nominal pore diameter of 200 nm and a thickness of 60 μm were used without any treatment.

Figure 2 presents the major steps involved for the fabrication of aligned gold nanowires by electrochemical deposition incorporated with a template. In the first step, an ion-milling machine was used to sputter a silver film on the backside of alumina membrane. In the second step, another silver film was deposited on the backside of membrane by electrochemical plating to cover most of the area on the backside of the membrane.

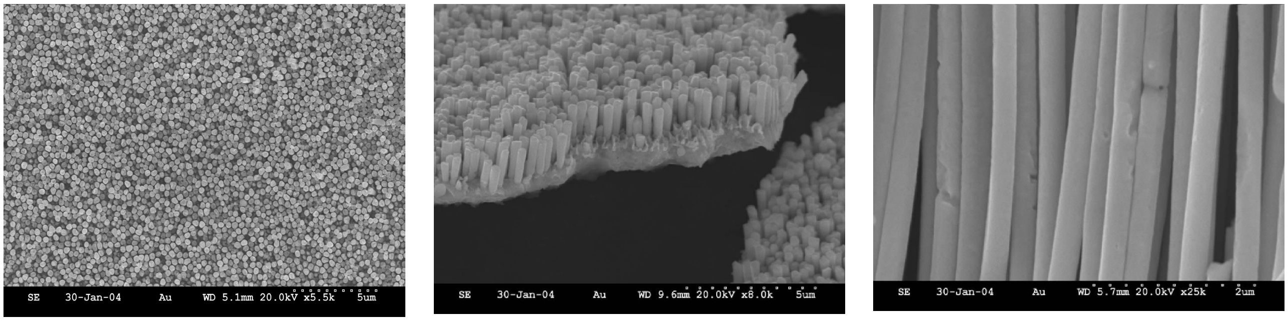

Figure 3. Photographs of the fabricated nanoelectrode array using template method

This silver film also functioned as the electrode for further electrodeposition steps. After this step, the final silver electrodeposition was performed on the front side of membrane to fill the gaps between the membrane and the silver film deposited in the first two steps. Then, gold was electrochemically deposited on top of the silver from the front side. As the final step, diluted NaOH was used to dissolve the never defined AAO template thus free gold nanowires.

One of the advantages of this template method is that the diameter and length of nanowires is easily controlled by adjusting the pore size of AAO template and electrodeposition time. To obtain better uniformity, a smooth nanowire surface, or even gold nanotubes, other deposition conditions, need to be carefully controlled, such as electrolyte concentration, electrochemical deposition current, surface modification of AAO template, etc. By this electrochemical deposition-template method, various conducting metal (e.g. Ag, Ni, Pt, Pd, Cu) or organic (polyaniline, polypyrrole) nanowires can be prepared. Figure 3 shows SEM photographs of the nanowire electrodes fabricated using the template method. The schematic diagram of the implantable nanowire electrode is shown in figure 1. The electrode is fabricated using silicon-on-insulator as the backbone with electrical connections and nanowire electrodes to deliver control pulses to the brain.

4. CONCLUSIONS

Functional electrical stimulation is an effective way to restore many functions of the brain in disabled individuals. The electrical stimulation can be done by using an array of electrodes. Neural probes stimulate or sense the biopotentials mainly through the exposed metal sites. These sites should be smaller relative to the spatial potential distribution so that any potential averaging in the sensing area can be avoided. At the same time, the decrease in size of these sensing sites is limited due to the increase in impedance levels and the thermal noise while decreasing its size. Typical site dimensions are ranging from 6 to 20 μm for recording with a geometrical area of 40 to 400 μm^2. The area of the stimulation site depends on the requirements in the amount of charge delivery to the neurons. For high current stimulating applications microelectrode system uses iridium oxide which can be used for a current density of 2 μC of charge in an area of $0.3 mm^2$ in 200μsec, which is equivalent of 3300 mA/cm^2. It is known that current density in a planar electrode is not uniform and a higher current density can be observer around the perimeter of the electrodes. Electrical measurements conducted on many nanotubes and nanowires have already proved that it could be possible to use for current density applications and the drawbacks of the present design in neural probes can be overcome by incorporating many nanotechnology solutions. In this paper we present the design and development of nanowire arrays for the neural probe for the multisite contact which has the ability to collect and analyze isolated single unit activity. An array of vertically grown nanowires is used as contact site and many of such arrays can be used for stimulating as well as recording sites.

REFERENCES

1. M. Verseano and K. Negishi, “Neuronal activity in cortical and thalamic networks”, J. Gen Physiol., vol 43, pp. 547-558, 1963.
2. K.E. Pertersen, “Silicon as a mechanical material”, Proc IEEE vol. 70 pp. 420-457, 1982.
3. W.F. House and K.I. Berliner, “Cochlear implants: From idea to clinical practice”, Cochlear implants: A practical guide, H cooper Ed., San Diego, Singular 1991.
4. F.B. Simmons, “Electroical Stimulation of the auditory nerve in man”, Arch. Otolaryngol., vol. 84, pp. 2-54, 1966
5. F.B. Simmons and C.J. Mongenon, W.R. Lewis and D.A. Huntington, “Electrical stimulation of acoustical nerve and inferior colliculus: Results in man”, Arch. Otolaryngol., vol. 79, pp.559-567, 1964.
6. G.S. Brindley and W.S. Lwein, “The sensations produced by electrical stimulation of the visual cortex”, J Physiol, vol. 196, pp. 479-493, 1968.
7. W. Lui, “Retinal implants: Bridging engineering and medicine”, Proc of IEEE Eng. Med. Biol, Mag., pp. 27-33, 1999.
8. E. Margalit, M. Maria, J.D. Weiland, R.J. Greenberg, G.Y. Fujii, “Retinal prosthesis for the blind”, Surv. Opthalmol., vol. 47, 4, pp. 335-356, 2002.
9. P.Limousin, P.Krack, P.Pollack, A. Bebazzouz, C. Ardouin, D. Hoffman and A. Benabid, “Electrical stimulation of the subthalamic nucleus in advanced Parkinson’s disease”, New Eng. J. Med, vol. 339, pp. 1105-1111, 1998.
10. K.D. Wise, J.B. Angell and A. Starr, “An integrated circuit approach to extracellular microelectrodes”, IEEE Tran Biomed Eng. vol. BME-17, pp. 238-247, 1970.
11. K. Najafi and K.D. Wise, “An implantable microelectrode array with on-chip signal processing”, IEEE Trans on Solid State circuits, vol.21, pp. 1035-1044, 1987.
12. K. Najafi and K.D. Wise, “A high-yield IC compatible multichannel recording array”, IEEE Trans Electron Devices, vol. ED-32, pp. 1206-1211, 1985.
13. K. Najafi and J.F. Hertka, “Strength characterization of silicon microprobes in neurophysiological tissues”, IEEE Trans Biomed Eng., vol. 37, pp. 474-481, 1990
14. R.H. Olsson, M.N. Gulari and K.D. Wise, “Silicon neural recording arrays with on-chip electronics for in-vivo data acquisition”, Proc of IEEE-EMBS Int Conf Microtechnology Medicine and Biology, 2002, pp. 237-240.
15. P.J. Roushe, D.S. Pellinen, D.P. Pivin, J.C. Williams, R.J. Vetter and D.R. Kipke, “Flexible polyimide-based intracortical electrode arrays with bioactive capability”, IEEE Trans Biomed Eng. vol. 48, 3, pp. 2001, 361-371.
16. K. Lee, A. Singh, J. He, S. Massia, B. Kim and G. Raupp, “Polyimide based neural implants with stiffness improvement”, Sensors and Actuators B 102, 2004, pp. 67-72.
17. B. Ziaie, J. von Arx and K. Najafi, “A micro-fabricated planar high current IrOx stimulating microelectrode”, IEEE Int conf. Engg Med and Biol., pp. 270-271, 1996.