An advantage of bio-MEMS is an improvement in treatment of medical problems due to better initial or continuous diagnosis and treatment options. Micro devices can perform minimally invasive procedures via catheter-like inspections and surgeries. An intelligent MEMS implant can perform interactive functions rather than just structural functions, and can communicate with other implants or controllers inside and outside the body. Human body applications for MEMS devices include blood and interstitial pressures, temperature, cardiac output, and chemical analysis. Functional implants include retinal and cochlear implants and neural stimulation. Electrical analysis of the brain (EEG), nerve conduction, and heart (ECG) are possibilities as well.

Traditional bio-electrodes are constructed or plated with noble metals such as platinum or gold to be minimally toxic. Proper material selection and construction must be addressed due to bio-fouling of devices, traumatic and inflammatory response of the body, packaging size, corrosion resistance, device life, and structural-mechanical properties. Metallic, ceramics, diamond-like coatings and polymer coatings all have certain advantages. They must also have a rough surface to decrease interface impedance and improve electrical potential stability. Thin film technology is of great importance to production of such electrodes. Thin film processes allow the production of sensors and devices on flexible substrates for use in implants.

One particular biomedical application of MEMS is thalamic stimulation. This deep brain stimulation is intended to help Parkinson’s disease patients by regulating brain signals normally transmitted from the thalamus and eliminate their physical tremors. Stimulation improves a number of aspects of motor function, particularly movement time and force production. In addition, quadripolar electrodes that allow examination of the therapeutic effects induced by stimulation are in development as well.

Medical Background

Parkinson's disease is a progressive disorder of the central nervous system affecting over one million people in the United States. Both men and women are affected and the frequency of the disease is considerably higher in the over 50-age group. Clinically, the disease is characterized by a decrease in spontaneous movements, gait difficulty, postural instability, rigidity and tremor. Parkinson's disease is caused by the degeneration of the pigmented neurons in the Substantia Nigra of the brain, resulting in decreased dopamine availability. An English physician, Dr. James Parkinson, who called it "Shaking Palsy", originally described the major symptoms of the disease in 1817. Only in the 1960's, however, were pathological and biochemical changes in the brain of patients identified, opening the way to the first effective medications for the disease. (http://apdaparkinson.com/)

Administration of the drug levodopa has been the standard treatment for Parkinson's disease. Once it reaches the brain, levodopa is converted to dopamine. Treatment with levodopa does not, however, prevent the progressive changes of the brain typical of Parkinson's disease. The drug may also produce side effects in some people, due to its change to dopamine before reaching the brain. The simultaneous administration with levodopa of substances inhibiting this change allows a higher concentration of levodopa to reach the brain and also considerably decreases the side effects. Some new drugs have recently been approved offering a wider choice of medications for the patient, while others are under investigation in this country and overseas in an effort to obtain better therapeutic results with fewer side effects. (Krack 2000)
Surgical interventions are also commonly used to help Parkinson’s patients. Thalamotomy is a type of brain surgery that involves making a lesion in the thalamus, the area of the brain that produces tremors. While this method has been shown to effectively reduce tremor in some patients, it is not frequently performed because of the risk of disabling and permanent side effects such as problems with balance, speech, and numbness. Pallidotomy, the surgical destruction of a portion of the globus pallidus, is done to improve the symptoms of rigidity, bradykinesia, tremor, and dyskinesia, but it may also result in serious, permanent side effects, especially when performed on both sides of the brain. This surgical approach is irreversible and may have to be repeated if symptoms recur. (Krack 1998)

Certain nerve cells become overactive in Parkinson’s patients to the point of causing uncontrollable muscle excitation in tremor patients, and electrical stimulation has been found to interfere with this abnormal activity. Benabid and colleagues, for the treatment of tremors with the ventral intermediate nucleus as the target, first proposed high-frequency deep brain stimulation in Parkinson’s disease in 1987. (Krack 1998) Medtronic has developed an implantable medical device, similar to a cardiac pacemaker, which uses mild electrical stimulation in the thalamus to block the brain signals that cause tremor. Researchers have found that the electrical pulses effectively block faulty brain signals that cause tremor. The electrical stimulation can be non-invasively adjusted to meet each patient’s needs.

In the remainder of this paper, we will examine current technologies and avenues of research in implantable neural electrodes for stimulation and recording.

Basic Engineering Requirements

![Figure 1: Model of implanted electrode. Resistance $R_w$ and Capacitance $C_w$ are due to material properties and geometry and Resistance $R_f$ is faradic resistance of electrolyte. (Wallman 1999)](image)

The electrode-electrolyte interface can be expressed as a serial capacitance and a serial resistance, together with a Faradic resistance. This is seen in Figure 1. For good signal coupling it is desired to have a large capacitance for recording electrodes and a small resistance for stimulation electrodes. (Wallman 1999)

An important feature of stimulation microelectrodes is the safe charge injection limit. Bucher reports that stimulation microelectrodes cannot exceed a certain current density or gas evolution of oxygen or hydrogen may occur. Polycrystalline electrodes are limited to 5mC/cm$^2$ while conventional TiN electrodes have a safe limit of 20mC/cm$^2$ and Au electrodes a limit of 3mC/cm$^2$. However, polycrystalline electrodes only caused evolution when a negative potential was applied, and thus demonstrate that they are well suited for the stimulation of electrogenic cells.

The use of thin film electrodes allows for the advantages of simultaneous stimulation of a large number of electrodes and thus a large number of cells (Bucher 1999). It is however, very important to achieve a low specific phase boundary impedance in order to gain effective charge transfer from the microelectrode device to cells.

No redox processes, i.e. faradic currents should be involved in the charge transfer, because tissue may be sensitive to the reaction products (Bucher 1999). Consequently there should be an exclusively capacitive coupling throughout the double
layer capacitance of the electrode (Bucher 1999). From the material science standpoint, many of the materials commonly employed for fabrication of thin film electrodes are incompatible to CMOS fabrication processes. This makes the chip expensive and limits the practical application in biomedicine and neural implants.

Substrate Selection / Production

Traditional gold and platinum single electrodes have not been micro-fabricated with thin-film lithographic processes. The desire for multiple electrodes on a small scale along with the supporting electronics requires MEMS fabrication technologies. Traditional gold and platinum electrodes have certain disadvantages by themselves and in addition are not compatible with CMOS production technologies.

To combat the problem of CMOS incompatibility, Bucher et al. analyzed the possibility of polycrystalline silicon thin-film electrodes since they can be fabricated with typical CMOS electronic components while the usual thin-film materials such as gold, platinum and iridium cannot (Bucher 1999). The use of polysilicon microelectrode arrays would thus lower costs and design complexity. Retina and fibroblast cells were also cultured on the polycrystalline micro-electrode arrays and no toxic influence or inhibition of adhesion was observed (Bucher 1999).

The polycrystalline silicon electrodes were made porous to increase their specific surface by anodic etching. Although increased surface area should reduce impedance, increased oxide growth countered the effect. This idea was tested by exposing the polycrystalline silicon electrodes with a native oxide layer (5-7 nm) and HF etched porous polycrystalline silicon electrodes (1-2 nm oxide remaining) to a physiological saline solution (PBS 0.9%) for 5 months at 37°C. No change in impedance was observed. Nor did any additional oxide layer growth or morphological changes within the surface layer occur. After five months, the impedance (1kHz in PBS 0.9%) of 20μm polycrystalline electrode still was about 500kΩ for the 5-7 nm SiO2 layer and 400kΩ for the 1-2 nm oxide layer. (Bucher 1999)

The use of doped silicon electrode arrays was investigated by Wallman et al. and illustrated in Figure 2. Nerve in-growth and insignificant tissue reactions were observed after implantation in rat specimens. They reported on the frequency dependent impedance of N-doped silicon electrodes and found that they had nearly the same magnitude of electrode-electrolyte impedance as the copper control group and traditional gold, silver and platinum electrodes. In addition, they reported that doped silicon demonstrated high capacitance values equivalent to copper and platinum, which are required for signal recording applications.

In medical applications, invasive diagnosis instruments are used once. Thus an inexpensive technique for batch processing of electrodes is desired. Van Gerwen et al. reported on a process where metal is deposited based on the anisotropy of the vacuum evaporation process. A micro-injection molded plastic substrate rather than a silicon wafer was used as a basis for a single step of metal deposition. The shadow zone (Figure 3) in valleys or behind hills allows for electrical insulation between adjacent electrodes and the connection of circuit elements. Advantages of this process include realization of
Current Deep Brain Stimulation Techniques

One of the newest and most promising techniques to control Parkinson’s induced tremor is deep brain stimulation (DBS). DBS involves inserting an electrode into the brain that is connected to a programmable stimulator. The device electrically stimulates either the subthalamic nucleus or the globus pallidus, depending on the placement of the electrodes. While this may seem like an unattractive alternative to drugs, it has been proven extremely reliable and does not exhibit the “wearing off” phenomena that drugs eventually do. It is also usually preferable than other alternatives: Pallidotomies or thalamotomies – removal of portions of the globus pallidus or thalamus, respectively. Unlike these procedures, DBS is reversible in that little damage is done to the brain when the electrode probes are removed. It is also adaptable in that if the patients need change, therapy can be adjusted with immediate results. Bilateral operations can also be performed with less risk of patient morbidity. (Marjana-Lyons 2000)

DBS systems are housed almost entirely below the skin, only a small portion of wire between the stimulator and the electrode is exposed. The stimulator is implanted in the trunk of the body, normally in the upper chest. The stimulator consists of a programmable board and signal generator encased in a hermetically sealed titanium housing. Connection wires are also imbedded and their terminal ends are exposed near the back of the neck. The probes are made of platinum/iridium wires and electrodes and nickel alloy connectors encased in a polyurethane sheath. Platinum/iridium was chosen because of its minimal toxicity and excellent conduction properties. A nonconductive material around the probe is necessary to prevent stimulation at unspecified sites. Unfortunately, these sheaths can sometimes break down to form neurotoxins. Electrodes are placed inside a burr hole made in the skull and held in place by a plastic cap on the scalp. The connection wires are run under the skin down the head and exposed at the back of the neck where they are attached to the wires from the stimulator.

Currently, very few DBS systems are available on the market. The most widely used and studied system belongs to Medtronic, Inc. Their Itrel neurostimulator is part of their Activa Tremor Control System. The Itrel stimulator, which is placed in the chest, measures 50mmx60mmx10mm, and is turned on and off by an external magnet controlled by the patient. It can be programmed to supply pulses to the neural probe that last between 60 μs and 450 μs at voltages between 0.1 V and 10.5 V. Device usage cannot be kept up for extended periods of time, however, and patients are cautioned to only turn the device on when necessary. A maximum of 135,000 stimulations per day is recommended.

The probes used in the Medtronic Activa system have quadripolar electrode tips that are 1.27 mm in diameter. The name quadripolar electrode refers to the fact that there are four stimulating electrodes at the tip of the probe. Each electrode is 1.5mm in length and they are spaced 0.5 mm apart. This is illustrated in Figure 6.

Other DBS systems may vary the type of electrode or type of signal generator, but all are very similar in function and structure. Besides the neurotoxicity mentioned above, the only major common problem is interference due to
electromagnetic instruments and diagnostic machines. There is currently no way to avoid this because of the location and type of the implant. If the implant was shielded, it would prevent the electrodes from stimulating the neurons in the thalamus and transmitting the correct neural signals to the rest of the body as it does normally. This is an area that requires further investigation.

Device Operating Parameters

In normal thalamic stimulation, the probe is placed inside a 15 mm burr hole anterior to the coronal suture and 25 mm from the midline inside the brain. Probes are chosen based on patient physiology. Stimulators do not vary patient to patient. Figure 4 shows an MRI of the implanted thalamus stimulator. Figure 5 displays dimensions of two current electrode options.

![Figure 4: Implanted DBS probe. (Koller 1997)](image)

Stimulation begins 1 day after surgery and the device is programmed to yield the greatest tremor suppression with the fewest side effects (Marjama-Lyons 2000).

![Figure 5: Medtronic Device Dimensions. (Medtronic Implant Manual)](image)

The therapeutic voltage ranges from 1 to 10 V with a frequency of 120 to 180 Hz. Duration of these pulses lasts 60-80 microseconds. Average therapeutic values from a study done by Koller et al. are shown in Table 1. (Koller 1997, Marjama-Lyons 2000)

<table>
<thead>
<tr>
<th></th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voltage (V)</td>
<td>3.07 ± 1.2</td>
<td>3.30 ± 1.1</td>
<td>3.38 ± 1.1</td>
</tr>
<tr>
<td>Frequency (Hz)</td>
<td>158.1 ± 29.1</td>
<td>160.6 ± 29.0</td>
<td>165.6 ± 23.5</td>
</tr>
<tr>
<td>Pulse Width (µsec)</td>
<td>107.0 ± 47.6</td>
<td>105.0 ± 41.5</td>
<td>117.5 ± 80.8</td>
</tr>
</tbody>
</table>

Table 1 Average values of operating characteristics. (Koller 1997)

Closing the Loop – Feedback Sensing

One major concern in bio-electrical systems is feedback. Feedback allows for closed loop control rather than open loop control that usually over stimulates in an attempt to be effective. Thus feedback systems would allow for more effective power consumption, increased safety for the patient, and a wealth of sensory information for physicians. (Hoffer 1996)

Hoffer placed a nerve cuff around a nerve in the ankle or wrist with a quadrupolar electrode. In a more invasive procedure, Wallman transected a nerve (Figure 6) and allowed it to regenerate through a perforated silicon membrane so that the nerve growth held the electrode stationary (Wallman 1999). The current reported research for the transecting electrode network has four poles and a
ground lead but Wallman projected that 20 electrode leads within the cross-section of a nerve will be necessary to accurately map the signals of the hand or foot and thus electrodes with higher spatial resolution are required to decipher the relative location of signals in nerve bundles. In the Central Nervous System (CNS) a similar technique be used by seeding the electrode with neural growth factor. The CNS neurons cannot be transected but would grow into the implant in a similar fashion.

![Figure 6: Transected nerve for localized stimulation and sensing of electrical signals. (Wallman 1999)](image)

**Conclusion**

Parkinson’s disease is a medical condition that affects millions of people in the United States every year. Current therapies include drugs that decrease in effectiveness after long time periods and highly invasive surgeries that remove portions of the patient’s brain. An emerging technology that shows promise is stimulation of the thalamus by a deep brain electrode implant. This procedure minimizes trauma experienced by the brain during implantation and provides long-term therapeutic effects.

Medtronic has developed a quadripolar electrode that has shown to have favorable clinical results. Their stimulator is versatile; patients can control the device settings for personalized therapeutic voltages, pulse widths and operating frequencies. The actual stimulating electrode is constructed using traditional photolithography techniques with gold and platinum.

Future versions of stimulating electrodes may employ a silicon substrate with polysilicon electrodes. This will enable engineers to interface the design with CMOS technology thereby minimizing both cost and the degree of fabrication complexity. This would also allow for the possibility of making the device significantly smaller and less damaging to surrounding neural tissues in the brain.

**References:**


