GBM8320
Dispositifs Médicaux Intelligents

Introduction
Part 1: History of smart medical devices
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GBM8320: Overview

1. Organization of the course

<table>
<thead>
<tr>
<th>Class</th>
<th>3 hr/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab works</td>
<td>(1.5 hr/week), Lab VLSI: L5904</td>
</tr>
</tbody>
</table>

2. Documents

- Course description
- List of references (articles)
- Program of the course
- Lab works / topics and Projects
- Web site
- Support for design tools & techniques.

GBM8320: Overview

3. Content of the course (Chapters)

- Introduction (6h):
  - History, physiology, regulation, biopotential, etc.
- Sensing interfaces (9h):
  - Bio-amplifiers & other building blocks
- Electrodes & sensors (8h):
  - Models, Electrodes, types of transducers
- Electrostimulation (12h):
  - Principle, stimulators & dedicated circuits.
- Projects (4 h):
  - Reports & presentations
- Others: Tools & design techniques.
4. Lab work & Projects
   - Two Labs & one Project: Lab #1 (2 weeks), Lab #2 (3 weeks).
   - Project (7 weeks):
     - Bioamplifier, Biotelemetry
     - Sensors & Interfaces to sensors: Temperature, pressure, etc.
     - Implantable Microstimulator
     - Data acquisition: EEG, EcoG, ENG
     - Ionic concentration sensor (ISFET)
     - Spectroreflectometer, Oxymeter
     - Neurotransmitter concentration: detection & measurement
     - Energy and data links for implantable medical devices.

Outline

1. History of implantable medical devices
2. Physiologic systems and applications
   - Central and peripheral nervous systems
   - Biopotentials, types of nerves, nerve conduction
   - Membrane model
3. Main applications
   - Auditory system: Cochlear implant
   - Vision system: Visual implants (Cortical, retinal)
   - Cardiovascular system: Pacemaker and defibrillator
   - Endocrine system, Gastrointestinal system: Chemical sensors and stimulators
   - Respiratory system: EMG, pressure, and chemical sensors.

Introduction

“Based on a foundation of fundamental science and empirical observation, engineering research and design has brought us into an era where it is no longer boastful to expect that the blind will see and the paralyzed will walk. WE ARE AT THE CUSP OF A TECHNOLOGICAL REVOLUTION...”


- Objective of smart medical devices: augment and ultimately replace organ function.
- Expected payoff: improved quality-of-life and functional restoration following stroke, spinal cord injury, and traumatic brain injury; with extension into deafness, blindness, paralysis, and movement disorders, and even some mental illness and seizure disorders.
- Impact of the associated industry: promises to be as dramatic as that of the development of antibiotics. We are entering an era in which the nervous system is replaceable and augmentable.
Introduction

Definitions

• **Functional electrical stimulation (FES):** Technique that uses voltage/currents to activate tissues innervating extremities affected by paralysis resulting from neurological disorders (spinal cord injury (SCI), head injury, stroke or other), restoring function in people with disabilities.
• **Electrostimulation:** Direct electrical stimulation of neuromuscular tissues.
• **Neurostimulation:** Direct electrical stimulation of neural tissues.
• **Neuromodulation:** Chronic electrical stimulation of the nervous system for functional disorders. Deep brain stimulation for movement disorders, psychiatric disorders and pain, and neurostimulation to prevent epileptic seizures are examples of devices using neuromodulation.
• **Neuroporsthethics:** This is a discipline related to neuroscience and biomedical engineering concerned with developing neural prostheses, artificial devices to replace or improve the function of an impaired nervous system. The neuroprosthetic seeing the most widespread use is the cochlear implant, with approximately 100,000 in use worldwide as of 2006.
• **Neural engineering:** Discipline that uses engineering techniques to understand, repair, replace, enhance, or treat the diseases of neural systems. Neural engineers are uniquely qualified to solve design problems at the interface of living neural tissue and non-living constructs.

The discovery of bioelectricity and electrical stimulation

• Electricity and the nervous system were intricately associated early on because the most sensitive electrical detector at the time was in fact the nervous system.
• The new phenomenon was quickly embraced by the medical field, and “cures” of paralysis and other ailments rapidly proliferated, yielding books from “electrotherapists” such as John Wesley the divine.
• By 1752, even Benjamin Franklin was using electrical stimulation for pain relief, and to treat a 24-year-old woman with convulsions, and various ailments.
• In 1791 Galvani stimulated inactive frog nerve-muscle tissue (Galvani’s stimulation)
• This event linked electricity and life and it was believed that electricity could restore life, a process called reanimation, which possibly contributing to the inspiration behind the Frankenstein myth.
The discovery of bioelectricity and electrical stimulation

- The first galvanic (direct-current) stimulator consisted of joined different metals in contact with electrolytic tissue fluids which, in the hands of Galvani (1791), resulted in contraction of muscles in the frog's leg.
- Much later, the works of Volta, Faraday and others resulted in the creation of batteries.

**History of implantable stimulators**

First stimulators: Capacitor-discharge stimulators

- The first electrical stimulator was the capacitor;
- A static electricity machine was used to charge the capacitor;
- The combination of a static electricity machine and the capacitor, which could store the charge, ushered in the quantitative study of electricity as well as providing the opportunity of delivering single stimuli of controlled intensity and duration to enable discovery of the law of stimulation;
- The Leyden jar (consisted of a phial filled with water into which an electrode dipped) was used as a capacitor.

http://physics.unl.edu/history/histinstr/electrostatics.htm
http://chem.ch.huji.ac.il/history/ramsden.html

First stimulators: Electrochemical cell

- The electrochemical cell developed by Volta (1800) and improved by his successors, was later used to charge the stimulating capacitor;
- Stack of dissimilar metals interspersed with thick paper are soaked in an electrolyte.
- The capacitor was charged to the desired voltage. Then it was connected to electrodes on the excitable tissue to stimulate it.
- Between the middle of the 18th century and the beginning of the 19th, Franklin experimented with stimulation unofficially.

Various types of cells and batteries. Wollaston's version of the voltaic pile (a), Daniell (b), Grove (c), Bunsen (a), and Leclanche (e) cells.
The First stimulators

- Faraday showed that a changing current in one coil (the primary), induced a voltage in a second coil (the secondary), which lay in the magnetic field produced by current in the primary.
- In 1833, Faraday’s law (magnetic induction) led to the development of the induction-coil stimulator (Inductorium) which than served as a basis for electrical stimulation of nerves.
- The Inductorium was very popular because it could provide single, as well as repetitive stimuli of easily controlled intensity (but not duration), thereby allowing the discovery of new properties of excitable tissues.
- The figure from 1871 illustrates “Faradization” being performed on a subject using a DC inductorium device. The unit shown is similar to those used previously by Benjamin Franklin.

First stimulators: Induction coil-stimulator

- Major physiologic discoveries with the Inductorium were tetanic (sustained) contraction of skeletal muscle, inhibition of the heart, the role of vasomotor nerves, and cortical localization.
- In the hands of clinicians, it was used to diagnose neuromuscular disease and to produce artificial respiration with body-surface electrodes.
- Du Bois Reymond's contribution (1850) was the addition of an electromagnetically driven current interrupter to the primary coil. In this way, a train of make and break (positive and negative pulses) stimuli could be generated.
- The output was derived from the secondary coil which could be slid over the primary coil, to control the stimulus intensity.
- Many different types of induction stimulators developed as alternating current generators started to appear in the mid 1800s.

The First stimulators

- By 1863, scientist G. Gaiffe, in Paris France, had constructed a transcutaneous electrical nerve stimulating (TENS) device.
- This box contains a complete stimulator. It is both a fascinating medical device as well as a work of art. The Gaiffe TENS unit is described in the 1871 Beard and Rockwell textbook of Medical and Surgical Electricity.
- This device, was the true precursor of the modern TENS unit featuring removable batteries, an inductorium, lead wires and skin electrodes. Its limitation was its low electrical output under load (about 3 mA as opposed to modern TENS units with 90 mA outputs).
First stimulators: Gaiffe’s stimulator

1) The TENS is compact. The red dots show the battery, blue dot the mercury sulfate (sic) vial, green dot the Faradic inductorium, and the yellow dot the wooden handle for the various skin electrodes. The lead wires for the electrodes lie next to the inductorium. The battery has two compartments which were filled with mercury sulfate. The covers were placed and the unit was inserted into the TENS unit.

2) This vial was purchased from “Mottershead & Co.”, Manchester, England. The small spoon ladle is shown next to the vial. Note the “POISON” label at the bottom of the vial.

3) Various pointed, brush, and roller skin electrodes are screwed into the wooden handle. The lead wires insert into the handle as well as the upper section of the cherry wood case.

4) Another model of the Gaiffe stimulator it was widespread used in the late part of the nineteenth century.

http://www.burtonreport.com/infspine/NSHistStimGaiffe.htm

Later, in 1882, Faraday’s techniques were broadcasted to the public with an advertisement in the Boston Globe newspaper, claiming the Faradic Electrifier as a cure for many diseases, including rheumatism, liver, stomach and lung problems, and paralysis.

http://www.sparkmuseum.com/quack.htm

The 1900s

- In 1919 Charles Willie Kent patented a TENS device, the “Electreat”, which competed with the Faradic Electrifier. About 250,000 Electreats were sold over 25 years.

- The Electreat was one of the very first high-output battery operated TENS units manufactured. Touted as the “Artificial Heart” its claims rivaled those of the Faradic Electrifier.

- Following passage of the Food, Drug and Cosmetic Act in 1938, Kent was prosecuted for unsubstantiated medical claims only pain relief was claimed.

http://www.burtonreport.com
**History of implantable stimulators**

**The 1900s**

- The first intracellular electrodes in the 1930s and the use of square pulses led to modern stimulators.
- Medtronic developed some of the early devices during the 1970s.
- Shown below are some of the TENS which were manufactured at Medtronic in Minneapolis during the 1970s.

[Image of TENS devices]

**A knowledge of the process by which excitable tissue is stimulated had to await the availability of electrodes small enough to be placed inside a single cell without damage to its enveloping membrane. Such electrodes were made by many investigators starting around 1930.**

- With such a microelectrode inside a cell, paired with an external electrode, the resting (trans)-membrane potential could be measured, as well as its excursion, which is the action potential. It was Hodgkin in 1939 who examined the change in membrane potential in response to single cathodal and anodal pulses of different intensities.


**Technological advances**

- The problem of stimulating neural structures deep in the body without the danger of infection that can accompany percutaneous leads was investigated by Loucks, Chaffee and Light in the 30s (in 1933 and 1934 respectively).
- Bardeen, Brattain, and Shockley invent the transistor at Bell Labs in 1947.
- Transistors were later incorporated into integrated circuits. These advances allow more sophisticated and compact circuit designs suitable for use in miniature implants.
- Further perfection of radio frequency induction techniques allows Glenn and Mauro to develop a totally implanted heart pacemaker in 1958-59.
- The first modern, patient-wearable TENS was patented in U.S.A. on 1974 (U.S. Patent 3,817,254) by Medtronic. It was used for chronic pain.
The cardiac pacemaker

- The invention of the electrocardiograph over the late 1800’s – early 1900’s had a major effect on the understanding of arrhythmias and hence on the development of specific therapy including pacing.
- Einthoven recorded the first human electrocardiogram in Europe on 1892 using the Lipmann capillary electrometer.

Early Einthoven ECG's

Einthoven's device in a box

- In 1932, American physiologist Albert Hyman, working independently, described an electro-mechanical instrument of his own, powered by a spring-wound hand-cranked motor. Hyman himself referred to his invention as an “artificial pacemaker”, the term continuing in use to this day.

Hyman's "artificial pacemaker"

- A number of innovators made smaller but still bulky transcutaneous pacing devices in the following years using a large rechargeable battery as the power supply.
- P. Zoll, a Boston cardiologist, is given credit for ushering in the modern era of clinical cardiac pacing. In 1951, he developed an external tabletop pacemaker that was successfully applied to the treatment of heart block.
- In 1957 Earl E. Bakken and co-founder of Medtronic Inc. produced the first battery-operated wearable pacemaker.

Zoll's external pacemaker

First wearable devices on patients (1958)
History of implantable stimulators

The cardiac pacemaker

- Senning and Elmqvist’s first implantable pacemaker used on a human (in Oct 1958). The entire unit consisted of 2 nickel-cadmium batteries (60mAh each), an electronic circuit and a coil recharging antenna. These were encapsulated in a new epoxy resin (Araldite) which had excellent biocompatibility.

- The pulse generator delivered impulses at an amplitude of 2 volts and a pulse width of 1.5 ms at a constant rate of 70 to 80 beats per minute. Transistors are used to design a stable and efficient blocking oscillator with small power consumption.

Diameter and thickness are of 55 mm and 16 mm respectively.

History of implantable stimulators

The cochlear implant

- Electrical stimulation of the acoustic nerve in a totally deaf human by direct application of an electrode in the inner ear was reported by Djourno and Eyrie in 1957.

- In 1961, W. House had devices made which he implanted into three patients. In 1969 he created the first wearable implant.

- Throughout the 1970s, devices to stimulate the cochlea at multiple points were developed. In 1978, Melbourne resident Rod Saunders was implanted with the first multi-channel cochlear implant with stunning successes. This marked the beginning of one of the most successful.

- In 1984, the Australian cochlear implant was approved by the FDA to be implanted into adults in the US. In 1990 the FDA lowered the approved age for implantation to 2 years, then 18 months in 1998, and finally 12 months in 2002.

Motor prostheses

- Neurovascular Stimulation for Control of Limb Movement

- Heel-switch triggered stimulator causing foot dorsiflexion, thus correcting drop foot are experimented in the 1960s.

- This simple device started a new area of advanced rehabilitation called functional electrical stimulation.


**History of implantable stimulators**

**Brain stimulation**

- 1983-1990: Recordings in the basal ganglia of monkeys provided the conceptual framework for movement disorders.
- 1993: The first report of deep brain stimulation (DBS) to treat Parkinson's Disease.
- 1997: FDA approval given for DBS in the thalamus.
- 2001: FDA approval given for DBS in the subthalamic nucleus.

**X-Ray image of a patient with Deep Brain Stimulation (DBS) leads inserted (Cleveland Clinic)**

**A firsthand account of DBS,Posted in Health & Medicine,Neuroscience, Parkinson’s Disease by MC on Feb. 2007**

**Brain stimulation nowadays**

- Various types of Electrodes for both recording and stimulation in the CNS.
  - Silicon or metallic based
  - Array of vectors...