Bioelectric Interface
The Metal-Electrolyte interface

Neuron

Electrolyte (Body)

Electrode
Neuron

Ion Channel

Electrolyte


Neural Prosthetic Engineering

Metal

Electrolyte

$V_m$

$C_m$

$E_{Na}$

$E_K$

$E_L$

$G_{Na}$

$G_K$

$G_L$

$I_m$

site

Top

Side

Insulation

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Capacitive Interface
Resistive Interface (Faradaic)

electrode surface

electron transfer

Mass transfer

double layer

give electron (e\textsuperscript{-})

take electron (e\textsuperscript{-})

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Partially Both. So a simple model may be

- Most metal electrodes have partial Faradaic, partial capacitive charge injections under the practical bias voltages.
A more complete model of Electrode Impedance $Z_e$ is,

- **Equivalent Circuit**

![Equivalent Circuit Diagram]

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_s$</td>
<td>solution resistance</td>
</tr>
<tr>
<td>$C_d$</td>
<td>double layer capacitance</td>
</tr>
<tr>
<td>$R_{ct}$</td>
<td>charge transfer resistance</td>
</tr>
<tr>
<td>$Z_w$</td>
<td>impedance to Mass transfer</td>
</tr>
</tbody>
</table>

Neural Prosthetic Engineering
Equivalent Circuit Modeling for Neural Recording

Optimum Conditions are achieved by the following, but some are difficult to achieve or have conflicting conditions with others:

- Smaller $Z_e$
- Smaller area of electrode
- Smaller $R_{spread}$
- Larger $R_{seal}$
- Larger $Z_{in}$ input of amplifier
Neural Probe

What is neural probe?
- Microstructure that connects neural tissue of brain and electronics

It is used to
- Record and/or Stimulate specific sites of the brain

Substrate Material
- Metal
- Silicon
- Polymer

Structure
- 2-dimensional
  - Single shank, multi channels
  - Multi shanks, single channel per a shank
- 3-dimensional
  - Multi shanks, multi channels per a shank


Neural Prosthetic Engineering

Neural Probe

Glass Micropipette Electrodes

• Glass micropipette electrodes can record current flowing through a single or multiple ion channels of cells. : Patch Clamp
• A glass micropipette containing electrolyte solution is tightly sealed onto the cell membrane and isolates a patch of cell membrane electrically.
• Currents through the ion channels in this patch flow into the micropipette and are recorded by an metal wire electrode.

http://www.leica-microsystems.com/science-lab/the-patch-clamp-technique/
https://en.wikipedia.org/wiki/Patch_clamp
Metal Wire Based Neural Probes

- **Metal wire**
  - less than 100μm in diameter
  - insulated except for a small exposed area at the tip which forms the recording or stimulation site.

- **Metal wire** : platinum, iridium, platinum-iridium, gold, stainless steel, and tungsten.

- **Insulation material** : quartz glass, teflon, polyimide, and parylene.

- 1 Metal wire = 1 Electrode site
- To make a multi channel electrode array, number of metal wires are linearly increased.

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Silicon Based Neural Probes

• Using silicon batch micromachining, microprobes with
  – well defined shanks
  – and precise placement of recording sites
  have been made with high accuracy and repeatability at low cost.

• Also, active probes have been made.
  – on-probe signal processing circuitry
  – integrated micro actuators driving the electrode shank

• The fabrication of silicon based neural probes includes
  – Deposition of a metal layer on an insulated substrate
  – Patterning the metal layer
    • recording sites, read-out pads for connecting to external circuitry, and interconnecting traces between them.
  – Additional insulating layer deposition over the whole structure
  – Opening of the recording sites and bonding pads
Michigan Probe

- **Michigan Probe**
  - A variety of neural electrodes including single-shaft, multi-shaft, and 3-D-stacked layouts
  - Integrated with microelectronic circuitry for signal processing
  - Typically involved anisotropic etching with ethylene diamine pyrocatechol (EDP) and using a boron-etch-stop.
    - The process is based on the fact that the etch rate for p-type silicon is much slower than for un-doped silicon.
    - Boron diffusion is first performed on silicon to define the shaft shape
    - EDP wet etching to release the probe shafts
    - Gold, platinum, or iridium metal is used for recording sites
    - The insulation on top of silicon substrate is made with triple layers of silicon dioxide, silicon nitride, and silicon dioxide.
    - Interconnection is made with a 4–5 μm thick polysilicon cables
      - weak cables and easy to break leading to lower yield for long lengths because of the high aspect ratio and lack of robustness.
  - Mechanical weakness of the probes causes the probes to crack and shatter and may cause severe damage and disturbance to the brain tissue during insertion.


Fabrication of Michigan Probe

- **Anisotropic wet etching for probe shaping**[^2]
  - reproducible and uniform probe dimensions

- high temperature boron diffusion and selective wet etch[^1]
  - hard to control thickness

Utah Probe

• Utah Probe (Utah electrode array)
  – Typically made from 1.83mm thick boron doped silicon substrates (resistivity of 0.01 Ω-cm) using diamond dicing saw.
    • A diamond dicing saw is used to create the electrode columns.
    • Acid etching smoothes the pillars and creates sharpened probe tips.
    • Probe tips are coated with metal for recording and stimulation. (Gold, platinum, and iridium)
    • Polyimide is used to coat the probes as the insulation layer with only the recording sites exposed.
    • Read-out pads: ultrasonically bonded on the back of the array to a set of aluminum.
      – The stiffness of the metal wires makes the probe unsuitable for chronic implantation.
    • Interconnections: polyimide insulated gold wires
  – Probe length limited by the silicon wafer thickness
    • The longest reported probe length: 1.5 mm.
  – Only one recording site can be made on each probe shank

Fabrication of Utah Probe

1. thermomigration

Fig. 1. Before the thermomigration process, aluminum pads are created on one side of an n-type silicon wafer. During the process a temperature gradient is applied to the silicon wafer which drives Si-Al eutectic droplets through the wafer. After the process, highly doped p⁺ silicon trials result from the eutectic droplet passage through the n-type substrate.

2. sawing

3. Dynamic etching (tip sharpening)

Multi-channel Utah probe

Electrodes for Neural Stimulation

- **Applications**
  - Visual prostheses, Auditory cortical prostheses, Intraspinal electrodes, etc.

- **Common challenges**
  - Chronic, safe, high degree of functional specificity.

- **Constraints (small tip area vs. charge density)**
  - **small tip area** - approaching the size of the surrounding neurons so that **selective stimulation of the neurons can be obtained.**
  - As the **surface area** of the exposed tip is **reduced**, the **charge density** (typically reported in mC/cm²) **increases** for constant stimulus charge (charge density limits).
  - → irreversible damage to the metal stimulation microelectrode inserted into the cortex. Near the tip of the electrode, neural stimulation takes place via current that passes from the electrode tip to the surrounding neurons. (Courtesy of Cyberkinetics, Inc.)

Neural Recording vs. Stimulation

• For Neural Recording, the Electrode Impedance is the most relevant parameter to show effectiveness of the electrode.
• For Neural Stimulation, however, the ability to deliver Charge, effectively and safely, to the Neuron, with small electrode surface area, is more relevant.
• Delivered Charge causes membrane potential change to excite neuron.
• In general, the larger the Effective surface area of the electrode is, the smaller the electrode impedance and the larger the charge delivery capacity.
• Effective surface area vs. Geometric surface area: The effective surface area considers actual 3-dimensional surface structure, while the geometric one is the 2-dimensional capture of such.
The distribution of charges and potentials

Active Electrode

Reference Electrode

Direction and strengths of the field vectors

Transmembrane potential ($V_m$) at resting condition

Voltage change induced by the external field ($\Delta V_m$)

Resulting transmembrane potential ($V_{m'}$)

$$V_{m'} = V_m + \Delta V_m$$
The capability of charge delivery of the electrode is expressed in CSC.

Charge storage capacity (CSC)
- Definition: The total amount of charge per unit geometric surface area (GSA) available from an electrode.

Cathodal charge storage capacity ($CSC_c$)
- Cathodic (negative) charges only
- Essential measure of the total amount of charge available for a stimulation pulse.
How to measure Charge storage capacity

- All electrodes are characterized *in vitro* immersed in phosphate buffered saline (PBS).
- Through Cyclic Voltammetric (CV) techniques at a proper scan rate (e.g. 50mV/s).
- A three electrode Potentiostat setup is used.
- Working electrode is the DUT.
- Reference electrode is where Triangular Voltage Waveform is applied.
- Current is measured from the Auxiliary (Counter) electrode - Working electrode Current Path.
- Plot potential versus current, and calculate the area of close loop line.
Charge storage capacity

- Ion concentration and CV plot

O-R ion concentration vs. voltage

Cyclic voltammogram

CSC

- Cathodal charge storage capacity \((CSC_C)\)
  - The **time integral** of the cathodic current during a potential sweep from 0.8 V and -0.6 V
  - **The area is directly proportional** to \(CSC_C\) because of the constant sweep rate.

- Example: CV plot of Pt and AIROF (Activated IrOx)
  - charge capacity of AIROF electrode is much higher than that of Pt electrode

- Water Window defines Safe region
  - the potential range over which no electrolysis of water

Neural Prosthetic Engineering

“Safe” neural stimulation

• The safe electrochemical window ("water window")
  - A voltage range that doesn’t induce Hydrolysis.
  - $-0.6V \sim 0.8V$.

• Electrode of large CSC should be used.
  - Large CSC can be achieved by
    (1) increasing the effective surface of the electrode
    (2) using appropriate electrode material with large CSC (e.g. Pt, IrO, TiN)

• Use balanced waveform to prevent charge accumulation (Biphasic Pulse)
**Current Pulse & Charge Injection Capacity**

- **Biphasic, charge-balanced current pulse**
  - To avoid damage to the electrode or surrounding tissue, net charge is zero by using two current phases.
  - Charge-balanced: \( Q_{\text{cathode}} = I_c \times t_c = I_a \times t_a = Q_{\text{anode}} \)

<table>
<thead>
<tr>
<th>( I_c )</th>
<th>Cathodic current</th>
<th>( 10 , \mu A \sim 10 , mA )</th>
<th>( t_a )</th>
<th>Anodic half-phase period</th>
<th>( 50 , \mu s \sim 10 , ms )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( t_c )</td>
<td>Cathodic half-phase period</td>
<td>( 50 , \mu s \sim 10 , ms )</td>
<td>( I_a )</td>
<td>Anodic current</td>
<td>( 10 , \mu A \sim 10 , mA )</td>
</tr>
<tr>
<td>( t_d )</td>
<td>Interphase dwell</td>
<td>( 0-1 , ms )</td>
<td>Pulse per second</td>
<td>( 10 \sim 250 , Hz )</td>
<td></td>
</tr>
</tbody>
</table>

- **The Maximum charge injection capacity**
  - the charge that can be injected without polarizing the electrode beyond the potentials for reduction or oxidation of water.
  - It depends to varying degrees on
    - the current density, the pulse frequency, and the relative magnitudes of \( I_c \) and \( I_a \).
    - The geometry, and porosity of the electrode also impact the uniformity and magnitude of the polarization.

<table>
<thead>
<tr>
<th>Material</th>
<th>Mechanism</th>
<th>Charge limit (mC/cm²)</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt and Pt-Ir alloys</td>
<td>Faradaic</td>
<td>0.05-0.15</td>
<td>Pacing, nerve cuff electrodes, DBS</td>
</tr>
<tr>
<td>Activated iridium oxide</td>
<td>Faradaic</td>
<td>1-3.5</td>
<td>Intracortical stimulation</td>
</tr>
<tr>
<td>Thermal iridium oxide</td>
<td>Faradaic</td>
<td>(~1)</td>
<td>Cardiac pacing</td>
</tr>
<tr>
<td>Sputtered iridium oxide</td>
<td>Faradaic</td>
<td>&gt;0.5</td>
<td>Limited to IDEs</td>
</tr>
<tr>
<td>Tantalum/Ta2O5</td>
<td>Capacitive</td>
<td>-0.5</td>
<td>Limited to animal studies</td>
</tr>
<tr>
<td>Titanium nitride</td>
<td>Capacitive</td>
<td>(~1)</td>
<td>Cardiac pacing</td>
</tr>
</tbody>
</table>

Polymer Based Neural Probes

- Recently, various polymeric materials have been studied to make neural probes because of their flexibility and compatibility with semiconductor processes.
  - Polyimide
  - Parylene
  - Liquid Crystal Polymer (LCP)

- However, polyimide and parylene are too flexible to be inserted into brain tissues.
  - Additional reinforcement structures or specific insertion methods are needed.
    - Hybrid with rigid material


Fabrication of Polyimide based Probe

Polyimide based probe

Fabrication

LCP- Based Neural Probes

- Liquid crystal polymer (LCP)-based neural depth probes are flexible, not easily broken, and do not require a guide tool for insertion.
  - Liquid crystal polymer
    - Thermoplastic polymer consisting of both a rigid and flexible monomer
    - Good biocompatibility
    - Low moisture absorption rates (~0.02%) and a low moisture permeability
    - Good long-term chemical resistance against most acids, bases, and solvents over a broad temperature range
  - Stiffness of the probe could be controlled by the thickness of the LCP film

<table>
<thead>
<tr>
<th>Property</th>
<th>Ideal depth probe</th>
<th>Micro-wire (metal)</th>
<th>Metal probe</th>
<th>Silicon or SOI probe</th>
<th>Polymer-based probes</th>
<th>Proposed LCP probe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Reproducible</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>Mass-fabricated</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Long-term durability</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Long-term neural recording</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Multi Electrode Array capability</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Probe length [mm]</td>
<td>&gt;10</td>
<td>Any</td>
<td>22</td>
<td>2-9</td>
<td>1-8.5</td>
<td>0.5-2.5</td>
</tr>
<tr>
<td>Mechanical reinforcement</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Au, Ni, Si</td>
<td>PEG, SU-8</td>
</tr>
<tr>
<td>Fractal characteristics</td>
<td>None</td>
<td>None</td>
<td>Rigid</td>
<td>Fracture</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Flexible</td>
<td>Rigid</td>
<td>Rigid</td>
<td>Flexible</td>
<td>Flexible</td>
<td>Flexible</td>
</tr>
<tr>
<td>References</td>
<td>[13]</td>
<td>[14]</td>
<td>[2]-[3], [9]</td>
<td>[3], [10], [15]</td>
<td>[5], [16]-[18]</td>
<td></td>
</tr>
</tbody>
</table>

- Partially reprinted from the reference [14].
Fabrication of LCP based probe

- **Liquid crystal polymer (LCP) based probe**[1]
  - Good biocompatibility
  - Low moisture absorption rates ($\sim$0.02%) and a low moisture permeability
  - Good long-term chemical resistance against most acids, bases, and solvents over a broad temperature range
  - Stiffness of the probe could be controlled by the thickness of the LCP film

- **Fabrication of LCP based probe** [2,3]

  ![Fabrication Diagram]

[1] S. Lee et al., TBME, 59 (7), 2085-2094, 2012
Reference

Reference