Mechanical considerations for designing neural implants

Applications in Neural Microsystems

Lecture 10
Source of interactions between device and tissue

- Surgical procedure: insertion (penetration)
- Repositioning of the device inside the tissue
- Oscillatory motions (Micromotions)

Significance

- Induces neuronal loss
- Contributes to structural failures of the device
Results of tissue trauma

Implanted device elicit foreign body response (encapsulation)

Marin, 2010
Device perspectives
Device properties influencing mechanical response

- Sensor geometry (structural design)
- Chemical and physical nature of boundary interfaces
- Bulk properties (Flexibility, softness, density)
- Packaging, interconnections

Other important variables:
- Implantation methods (device sterilization, insertion speed)
- Variability in biological properties of the target tissue
Mechanical loads during tissue-device interaction
Definitions in solid mechanics

Stress
(compressive, tensile)

\[ \sigma = \frac{F}{A} \quad [\text{N/m}^2] \]

Strain

\[ \varepsilon = \frac{l - l_0}{l_0} \quad [-] \]
Definitions in solid mechanics

$\sigma$ vs $\varepsilon$?

Linerar approximation:

Hooke’s law

$$\sigma = E \cdot \varepsilon$$

$E$ constant parameter

Elastic modulus

Young’s modulus $[N/m^2]$

In crystalline structures:

$E$ is anisotropic

Silicon as mechanical carrier of neural probes is particularly sensitive to the direction of load
Mechanical loads during insertion

Bending

- Tangential forces during insertion
- Lateral forces after insertion

Buckling

- Normal forces during penetration

Fracture

- Thin film or substrate
Bending

\[
\frac{x}{r} = \frac{dx}{y} \quad \rightarrow \quad \varepsilon = \frac{dx}{x} = \frac{y}{r},
\]

\[
\sigma = E \varepsilon = \frac{E}{r} y
\]

\[
F = \int_A \sigma \, df = \frac{E}{r} \int_A y \, df = 0,
\]

\[
\int_A y \, df = 0.
\]

Neutral axis goes through the center of mass. Neutral axis is less prone to the change in bending/buckling force.
Bending

How to calculate bending radius?

\[ \sigma = E \varepsilon = \frac{E}{r} y \]

\[ M = \int_A y \sigma \, df = \frac{E}{r} \int_A y^2 \, df \]

\[ \frac{1}{r} = \frac{M}{EI} \]

where \( I = \int_A y^2 \, df \) - second moment of area depends on cross-section only!
Second moment of inertia for various cantilever cross-sections in MEMS

\[
I_x = \frac{bh^3}{12}, \quad I_y = \frac{b^3h}{12} \quad [4]
\]

\[
I_x = \frac{\pi r^4}{4}, \quad I_y = \frac{\pi r^4}{4} \quad [1]
\]

\[
I_x = \frac{\pi}{4} (r_2^4 - r_1^4), \quad I_y = \frac{\pi}{4} (r_2^4 - r_1^4) \quad [1]
\]

Functional components integrated in the substrate of neural probes (e.g. microfluidics, waveguides etc) alters $I$. 
Thin probes are prone to deflection without external forces

Technology to thinning: etching-before grinding

Residual stress!

(Herwik, 2011)

Fekete, 2015
Reason for inherent deflection: Residual stress

Reason: high-temperature processes/annealing
- mismatch in CTE (coefficient of thermal expansion)

Example: SiO$_2$ is deposited on a 4” Si wafer at 700 °C ($\alpha_{Si}=3\times10^{-6}$ 1/K, $\alpha_{SiO2}=0.6\times10^{-6}$ 1/K)

$\Delta L = \alpha \ast L_0 \ast \Delta T$  \hspace{1cm} $\Delta L_{Si} < \Delta L_{SiO2}$  \hspace{1cm} Compressive stress is built up!

$\Delta L = \alpha \ast L_0 \ast \Delta T$  \hspace{1cm} $\Delta L_{Si} < \Delta L_{SiO2}$

Thermal strain: $\varepsilon_{therm} = \Delta T \ast \Delta \alpha \sim 0.2mm$

Stress management is an essential part of technology design!
Residual stress depends on deposition parameters

Examples

Silicon dioxide

Silicon-nitride

Lang, 1992

Open.edu

What parameters determines intrinsic stress?
Process temperature, precursor (gas) ratio, annealing profile, initial CTE of materials
Effects of intrinsic stress on cantilever deflection

1. No stress gradient along z-direction

2. Higher tensile stress near top surface of cantilever before release from substrate

3. Higher compressive stress near top surface of cantilever before release from substrate
How to compensate thin film stress?
How to measure residual stress?

Residual stress typical of a deposition step can be derived from wafer (substrate) curvature

**Radius of Curvature of warpage**

\[
 r = \frac{E_s \times t_s^2}{(1-v)_s \times 6 \times \sigma_f \times t_f}
\]

**“Stoney Equation”**

- \( t_s \): substrate thickness
- \( t_f \): film thickness
- \( E \): Young’s modulus of substrate
- \( n \): Poisson’s ratio of substrate
Optimal location of thin film elements to reduce failure due to bending stress

Recommended composition for flexible probes:

Polymer  Metal  \( X_1 = X_2 \)

Result: no change in electrical behaviour of flexible implants with brittle conductive layers (Pt, ITO etc)
Buckling

Unlike bending, it's a failure mode! (structural damage is induced if occurs)

\[ P_{CR} = \frac{\pi^2 EI}{L^2} \]

Euler’s Equation

- \( P_{CR} \) = critical or maximum axial load on the column just before it begins to buckle.
- \( E \) = modulus of elasticity for the material
- \( I \) = least moment of inertia of the column’s cross-section
- \( L \) = unsupported length of the column, whose ends are pinned
Fracture

- External axial forces above the critical buckling force may lead to fracture.
- The overall stress during buckling leads to fracture when approaching the ultimate tensile strength.

Ultimate tensile strength: maximum stress that a material can withstand while being stretched or pulled before breaking. (7000 MPa).

Silicon is hard, but brittle.

Thin films have usually lower tensile strength. (Signal quality may predict device failure)
Application perspective
Device insertion (biomechanics)

Trade-off between two fundamental aims:
- To avoid device failure
- To avoid tissue damage

Major biological barriers:
- Meninges (dura and pia mater)
- Gray and white matter

Rupture of this barrier initiate foreign body response (detailed in upcoming lecture)

Haines, 1991
Mechanical properties of meninges and tissue

Physical description by a hyperelastic model: strain-strain curve is non-linear

<table>
<thead>
<tr>
<th>Biological tissues</th>
<th>Mechanical properties</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young modulus (MPa)</td>
</tr>
<tr>
<td>Cranial dura</td>
<td>60</td>
</tr>
<tr>
<td>Spinal dura</td>
<td>100</td>
</tr>
<tr>
<td>Retina</td>
<td>0.02</td>
</tr>
<tr>
<td>Brain tissue</td>
<td>0.01</td>
</tr>
<tr>
<td>Bone</td>
<td>5,000-21,000</td>
</tr>
</tbody>
</table>

Maikos, 2008

Sharp, 2009
Penetration loads

- Significance: device should withstand penetration forces
- Possible loads: bending and buckling
- $F_{\text{penetration}} > F_{\text{crit}}$ leads to fracture!

Characteristic parts of force-distance curves:
- Penetration force (insertion)
- Dimpling (insertion)
- Rest force (tissue relaxation)
- Retraction force (explantation)

How to measure?
Neural probes mounted on a force gauge
Significance of dimpling

**Dimpling:** Indentation of superficial tissue layer before tissue rupture

Identification on force-distance curve: at maximum load

**Reason to minimize:** may lead to TBI (traumatic brain injury)

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*TBI may lead to secondary degeneration*

*TBI may lead to block in cerebral blood flow*

*Hayward, 2010*
Sensor geometry (structural design)
Probe geometry

**Significance:**
All forces are coupled to interfacial area, which in general should be reduced.

**Relevant design parameters:**
Length: depends on implantation target
Width: depends on integrated functionalities
Thickness: depends substrate thickness, post-processing technologies
Tip: depends on both layout and technology
Symmetry: depends on technology (wet or dry chemical etching)
Investigation of interfacial parameters during penetration

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Shaft length (mm)</th>
<th>Shaft width x thickness (µm x µm)</th>
<th>Tip angle (°)</th>
<th>Insertions per data points</th>
<th>Insertion speed (mm/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Force vs. Speed; Dimpling vs. Speed</td>
<td>30</td>
<td>200x200</td>
<td>30</td>
<td>8</td>
<td>1.2, 3, 5.2, 7.5, 10.5</td>
</tr>
<tr>
<td>Force vs. Cross-sections Dimpling vs. Cross-section</td>
<td>30</td>
<td>200x200, 200x400, 400x200, 400x400</td>
<td>30</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Force vs. Tip angle Dimpling vs. Tip angle</td>
<td>7</td>
<td>400x100</td>
<td>30, 60, 90</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Force vs. Sharpening</td>
<td>7</td>
<td>500x00</td>
<td>45</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Force vs. Age; Dimpling vs. Age</td>
<td>30</td>
<td>200x200, 400x400</td>
<td>30</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Fekete, 2015
**Effect of geometry on insertion**

<table>
<thead>
<tr>
<th>Shank thickness x width (µm x µm)</th>
<th>Penetration force (mN)</th>
<th>Dimpling (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 x 200</td>
<td>58 ± 8</td>
<td>1.06 ± 0.2</td>
</tr>
<tr>
<td>200 x 400</td>
<td>70 ± 10</td>
<td>1.19 ± 0.21</td>
</tr>
<tr>
<td>400 x 200</td>
<td>98 ± 11</td>
<td>1.56 ± 0.12</td>
</tr>
<tr>
<td>400 x 400</td>
<td>93 ± 12</td>
<td>1.70 ± 0.26</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tip angle (°)</th>
<th>Penetration force (mN)</th>
<th>Dimpling (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>27 ± 3</td>
<td>0.78 ± 0.08</td>
</tr>
<tr>
<td>60</td>
<td>72 ± 22</td>
<td>0.93 ± 0.11</td>
</tr>
<tr>
<td>90</td>
<td>112 ± 28</td>
<td>1.03 ± 0.08</td>
</tr>
</tbody>
</table>

Trends are in agreement with literature on retracted dura: Davis, 2004; Jensen, 2006; Sharp, 2009; Andrei, 2012;

First experimental data in the case of intact dura mater

*Fekete, 2015*
Improved technologies

Sharpening of the probe tip with multiple-step wet chemical etching (Grand, 2010)
Etching anisotropy in crystalline materials

Orientation of patterns determines the etch rate!

Underetching for Si with KOH

Vázsonyi, 2003

Vázsonyi, 2005
Performance of sharpened probes

Surface quality after deep reactive ion etching (DRIE) improved by subsequent wet etching in a mixture of NaOH:NaOCl

<table>
<thead>
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<th>Samples</th>
<th>Penetration force (mN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A0</td>
<td>49 ±13</td>
</tr>
<tr>
<td>A1</td>
<td>20 ± 6</td>
</tr>
<tr>
<td>A2</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>A_{ref}</td>
<td>5 ± 1.5</td>
</tr>
</tbody>
</table>

A0: DRIE probe with intact dura
A_{ref}: DRIE probe with retracted dura

Insertion forces can be substantially lowered even with dura mater on top.

Fekete, 2015
Chemical and physical nature of boundary interfaces
Interfacial load (shear stress)

Depends on the characteristic roughness of device surfaces.
Induced by insertion, repositioning and micromotions in tissue.
Concepts for repositioning recording depth

**Mechanical (for passive probes)**

- Stereotaxic holder
- Fibre optic
- Nano-Drive
  - 2 x 4 mm footprint
  - 0.5 grams
- Flex cable
- Stack additional probes here to make 3-D arrays
- Silicon neural probe
- Electrode arrays

**Electrical (for active probes)**

- Connector for data cable
- Headstage
- Detachable connector
- Flex cable
- Base
- Shank

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*Cambridge Neurotech*
Microdrives

Advantage: single units can be recorded at higher yield in spite of the ongoing glial encapsulation

Disadvantage: induces shear stress during vertical positioning along the probe track
Micromotions

Displacements caused brain movement modulated by physiological activity

Effects of vasculature and pulmonary activity

Cortical surface drift
Packaging, interconnections

How to mitigate mechanical coupling between microdevice and connectors?

Lecomte, 2017

Shander, 2018

Concept:
Formation a hybrid stiff-flexible device configuration
Reason for lateral displacement during insertion

Integrated MEMS components

3D config. or assembly methods

Tip symmetry

Son, 2015

Cui, 2003

Fekete, 2013

Grand, 2010
Interface stress

Reason: rough device surfaces (typically on sidewalls)

Approaches to mitigate:
- Parylene C coating (Andrei, 2012)
- Hydrogel coating (Spencer, 2017)
- PVA coating (Sridharan, 2015)
Dissolvable coatings vs interfacial stress


Dissolvable coatings can only influence short-term (acute) mechanical impact.
Bulk properties of the sensor
Softness

Device substrates are usually much stiffer than tissue.

Lecomte, 2017
Responsive neural interfaces

Device that alters their mechanical properties at physiological conditions (pH, temperature, liquid) may mitigate micromotion induced damage

*Cellulose nanocomposites*

*Shape memory polymers*

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*Zatonyi, 2019*

*Dunning, 2018*
Swelling

Phenomenon: increase in device volume if exposed to liquids (water)

To be considered for implants made of polymers, hydrogels, composite fibers!

**Advantage:** reduces density mismatch between device and tissue

**Disadvantage:** increase strain in swollen states
- may induce injuries in blood capillaries
- may lead to thin film cracks

*Dunning, 2014*
Surgical conditions
Ways to mitigate insertion forces?

- Low speeds result in low insertion forces, but have no effect on dimpling. Dimpling is influenced by interfacial area only.
- Increase in penetration force between cases of retracted and intact dura: one order of magnitude (!)

_Fekete, 2015_  
_Andrei, 2012_
Implantation time window

- Undefined for stiff implants
- To be carefully considered for responsive materials (e.g. shape memory polymers, cellulose nanocomposite)
- Shortest for chemoresponsive materials, longer for thermoresponsive materials >> induces elevated penetration forces due to large insertion speed

*Zatonyi, 2019
*Dunning, 2018
Effects on neural recording

Low insertion speed provides high yield in neural recordings

- Higher signal-to-noise ratio
- More clustered units
- No effect on spike amplitude
Effect of tissue conditions

Explanation: dura is getting thicker and less flexible by age

Similar results: Van Noort, 1981 (human dura)
Questions

1. List relevant device properties that have influence on device-tissue interactions.
2. List the main sources of mechanical interactions between device and tissue.
3. How does an integrated bulk component change response of needle-like implants to bending and buckling loads?
4. What is residual stress in MEMS devices and why it is important?
5. What is the relationship between buckling and fracture? What is the critical buckling force of a needle?
6. What is tissue dimpling during device penetration, and why it is important to be reduced?
7. What is the effect of device geometry on insertion forces and dimpling measured during implantation?
8. What is tethered and untethered probe configuration?
9. Describe micromotions inside the brain. What kind of forces are induced around the implants due to micromotions?
10. What is the relationship between insertion speed and penetration forces?
11. Describe the relevance of responsive neural implants regarding their mechanical properties.