Electrodynamic modeling of bacterial biofilm impedance sensing

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Bacterial Biofilms

• Prevalent in environment, healthcare
  – Common cause of persistent and implant-associated infections
  – Increase antibiotic resistance

History: Characterization & Treatment

Characterization
In-vitro Biofilm Systems

Micro-BOAT Platform
Kim, Hilton Head Workshop

Biofilm Sectioning Device
Meyer, J. Micromech Microeng

Valveless Bifurcation Sectioning
Subramanian, Transducers ‘15

An Integrated System
Subramanian, Biomed Microdevices

Flexible Impedance Sensor
Huiszoon, AVS ‘16

3D-printed Characterization Platform

Treatment
In-vivo Biofilm Systems

An Integrated Sensor-Treatment System

A Biofilm Treatment
Kim, NPJ Biofilms Microbiomes

An Integrated System
Kim, Sensor Actuat A-Phys
Catheter Biofilms

• Leading cause of nosocomial infections

• Initial formation detection key to improve patient outcomes


Cross section of a urinary catheter showing crystal encrustation and blockage due to biofilm colonization

Autonomous biofilm sensing and treatment microsystem

Parallel Electrodes

Flexible electrodes for biofilm monitoring and treatment in a catheter

Catheter Biofilm Impedance Sensing

Section of urinary catheter with flexible impedance sensor inserted

Biofilm Sensing Principle

Silicone catheter tube

Gold interdigitated electrodes

Flexible polyimide substrate

Biofilm grows on the surface of the IDEs, altering the electrical circuit, resulting in a measureable change in impedance
Biofilm Growth Modeling

- Complex material
- Stochastic growth process
  - Markov Chain Theory

Markov chain for the stochastic component of bacterial biofilm growth

Mosteller et al (2012), INCOSE International Symposium
Can we use commercial modeling software to predict the impedance sensor response in a cylindrical catheter geometry?
Electrodynamic Biofilm Modeling Parameters

- Define biofilm in terms of electrical properties
  - Cells, extracellular matrix, growth media

<table>
<thead>
<tr>
<th></th>
<th>Conductivity (S/m)</th>
<th>Relative Permittivity</th>
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</thead>
<tbody>
<tr>
<td>Cell cytoplasm</td>
<td>0.19</td>
<td>61</td>
</tr>
<tr>
<td>Cell membrane</td>
<td>$5 \times 10^{-8}$</td>
<td>10.8</td>
</tr>
<tr>
<td>ECM</td>
<td>0.68</td>
<td>60</td>
</tr>
<tr>
<td>LB media</td>
<td>0.754</td>
<td>78</td>
</tr>
</tbody>
</table>

These values correspond to the constituents, but not the biofilm.

Asami et al (1980), Biophysical Journal
Park et al (2011), Lab on a Chip
Korth et al (2015), Bioelectrochemistry
Biofilm Parameters

• Maxwell’s Mixture Theory
  – Yields effective permittivity and conductivity for biofilm layer

\[
\varepsilon^*_{biofilm}(\omega) = \varepsilon^*_{mat}(\omega) \frac{2(1 - \varphi)\varepsilon^*_{med}(\omega) + (1 + 2\varphi)\varepsilon^*_{eq}(\omega)}{(2 + \varphi)\varepsilon^*_{med}(\omega) + (1 - \varphi)\varepsilon^*_{eq}(\omega)}
\]

• Equivalent circuit for biofilm exposed to growth media
Planar Microsensor Model

- 100 Hz A/C potential between electrodes: 0.05V
- Biofilm layer of varying thickness
  - Remaining volume is growth media
- Results show trade-off between initial sensitivity and linear range

How will signal change at mm scale in a cylindrical geometry?

Subramanian et al (2017), ACS Appl. Mater. Interfaces (Submitted)
Cylindrical mm-scale Model

- D = 4.5 mm
- 0 – 0.5 mm biofilm
- 0.1 – 0.5 mm electrode width and spacing

Current Density (A/m²)
Z-Component
Planar mm-scale Model

- Same electrode surface area
- Same spacing, biofilm parameters

Current Density (A/m$^2$) Z-Component

Electrode 1  Electrode 2

LB Media  Biofilm
Percent Impedance Change

Planar Model

% Change in Z vs. Simulated Biofilm Thickness (mm)

- 0.1 mm Spacing
- 0.3 mm Spacing
- 0.5 mm Spacing

Cylindrical Model

% Change in Z vs. Simulated Biofilm Thickness (mm)

- 0.1 mm Spacing
- 0.3 mm Spacing
- 0.5 mm Spacing

100 µm spacing shows highest sensitivity to initial formation, but smaller linear range due to signal saturation

Minor differences between geometries due to similar volumes of material within range of electrodes at mm-scale
Can we use this physical model to evaluate different sensor electrode designs?
Parallel Electrode Model

- Electrodes parallel to catheter axis
- Same electrode surface area
- Same spacing, biofilm parameters
Each electrode arrangement shows similar impedance response
Conclusions & Future Work

- Modeled complex biofilm via accessible commercial software
- 100 µm electrodes: highest sensitivity to initial biofilm formation
- mm-scale geometries do not vary impedance response
- Confirm sensor response in *in vitro* catheter model
- Adapt electrodes to additional relevant geometries
Acknowledgements