

A CELLULAR AUTOMATA MODEL OF INFECTION CONTROL ON MEDICAL IMPLANTS

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Individual-Based Ecology of Microbes
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The Problem

Over 4 million people in the United States have long-term biomedical implants. However, many medical implants have to be removed because of infection or because their protein coating causes excessive inflammation and decrease in the immune system response.

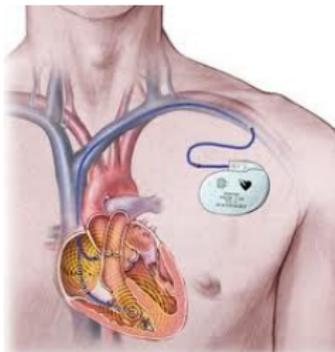


Figure: Medical Implant

Research Goals

To obtain:

- A protein coating mixture that will optimize the immune system reaction while minimizing implant rejection
- The amounts of antibiotics needed to avoid infections on any protein-coating mixture
- Find (if possible) other methods to decrease infections on medical implants

We will achieve this by:

- Modeling the immune system reaction to medical implants pre-coated with a mixture of two different proteins.

Biological Background

S. epidermidis: most common bacterial colonizers of the human skin.

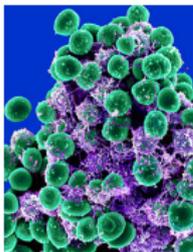


Figure: Staphylococcus epidermidis

Neutrophils: one of the most common white blood cells. Phagocytic cells that adhere to the surface of the implants and move towards bacterial formations.

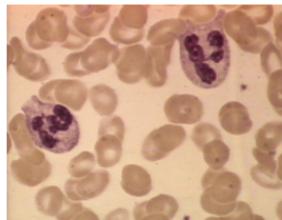


Figure: Neutrophil cells

Biological Background

Fibrinogen: common protein used on implant coatings.

- Recruits large amounts of *Neutrophils*
- Reduces the motility of *Neutrophils*

Albumin: different protein used on implant coatings.

- Allows free and fast motility of *Neutrophils*
- Lowers the amount of *Neutrophils*

Biological Background

Biofilms: slimy, slippery coat that guards communities of bacteria. The immune system has a hard time removing biofilms and most antibiotics are effective only against fast growing cells, so the slow growers within the biofilm tend to be spared.

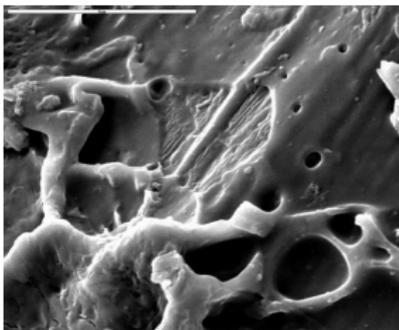


Figure: Biofilm on a catheter

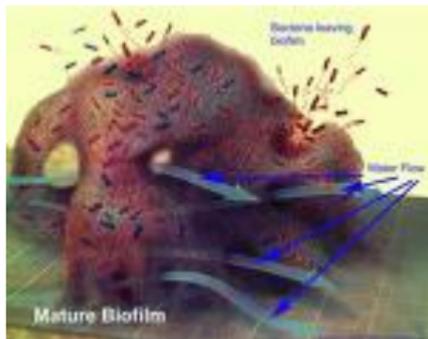


Figure: Biofilm on a catheter

Cellular Automata (CA) Model

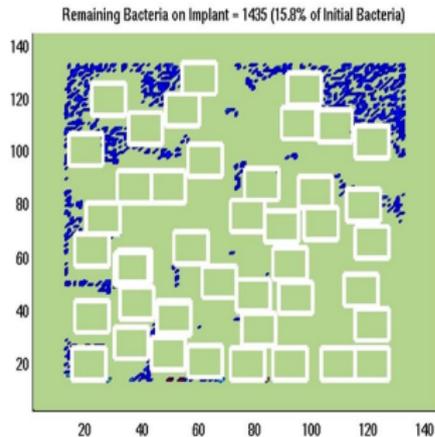
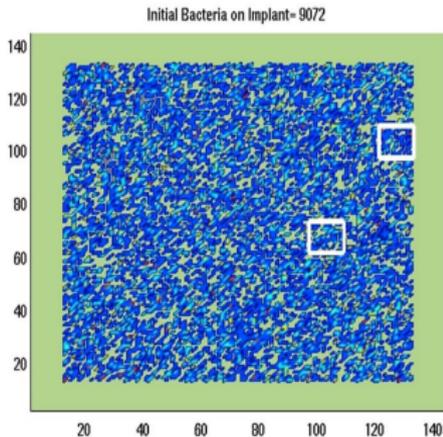
Cellular Automata consist of a regular 14400×14400 grid that has the following properties:

- every square can be in one of 4 possible states:
 1. be empty
 2. be covered by *S. epidermidis*
 3. be covered by part of a *Neutrophil* cell
 4. be covered by both *S. epidermidis* and part of a *Neutrophil* cell
- states are updated synchronously every 20 seconds and depend only on the current and neighboring squares

CA Simulations

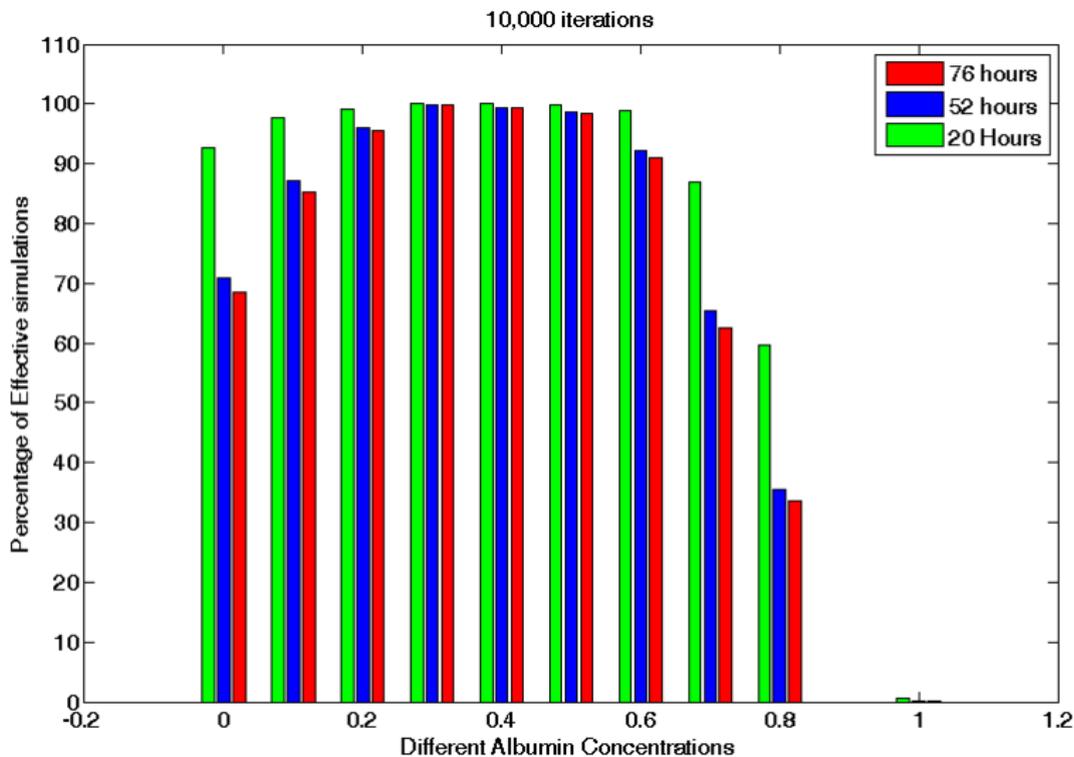
Snapshot of the initial (left) and final (right) state of the system in a 16 hour simulation with initial conditions:

- $A = 0.4$ (40% *Albumin* and 60% Fibrinogen)
- $b = 9072$ (62% of the implant area covered with bacteria)



(Cellular Automata Simulation)

Monte Carlo CA Results



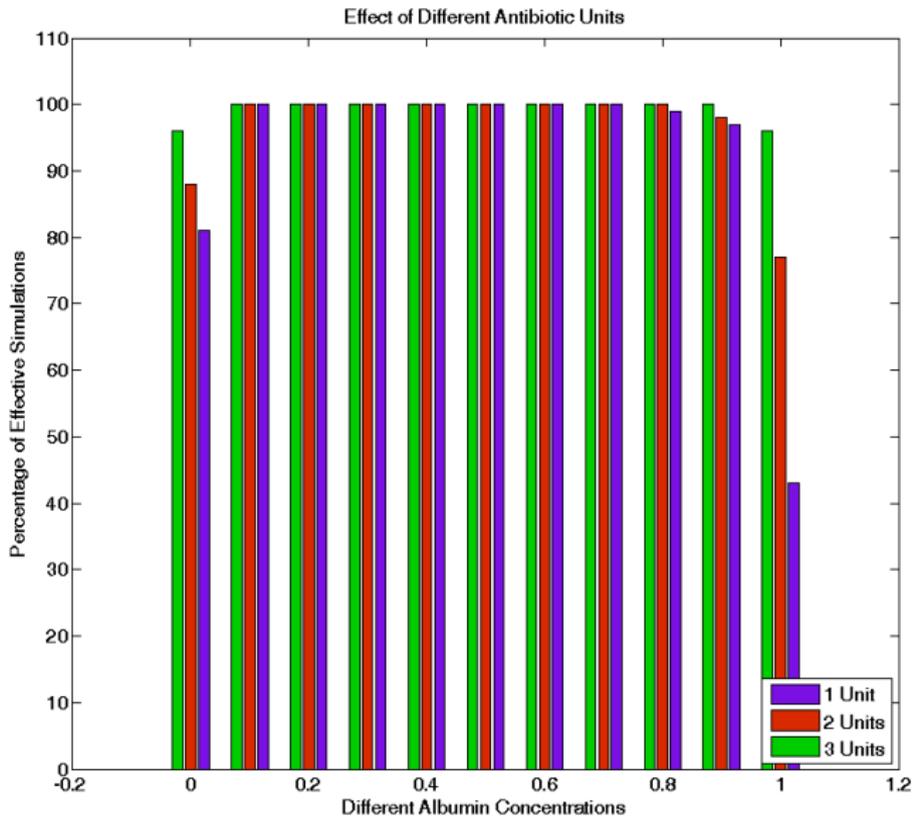
Treatment Alternatives

In order to improve the results for all *Albumin* and *Fibrinogen* percentages two strategies can be used:

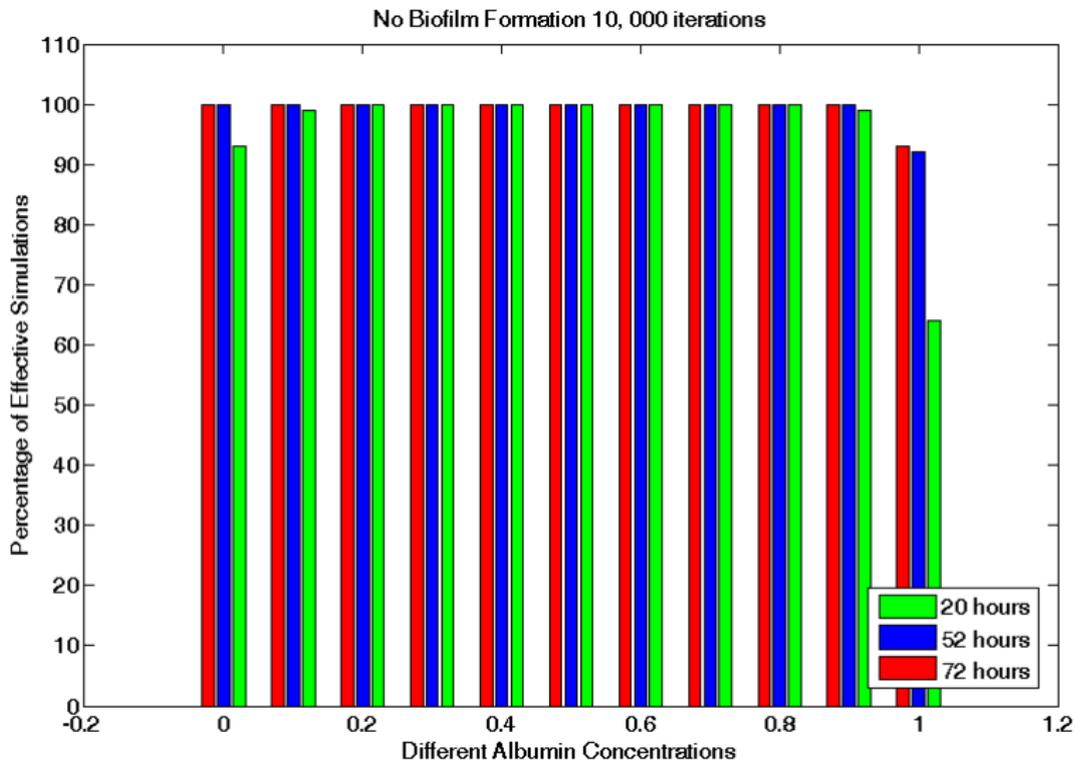
- Precoating implants with antibiotics
- "Block" cell signalling to avoid *biofilm* formation

The model was modified to include both alternatives.

Precoating with Antibiotics



Cell-Signal Blocking



References

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