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# Biofilm Growth Model towards Nano-scale Elucidation

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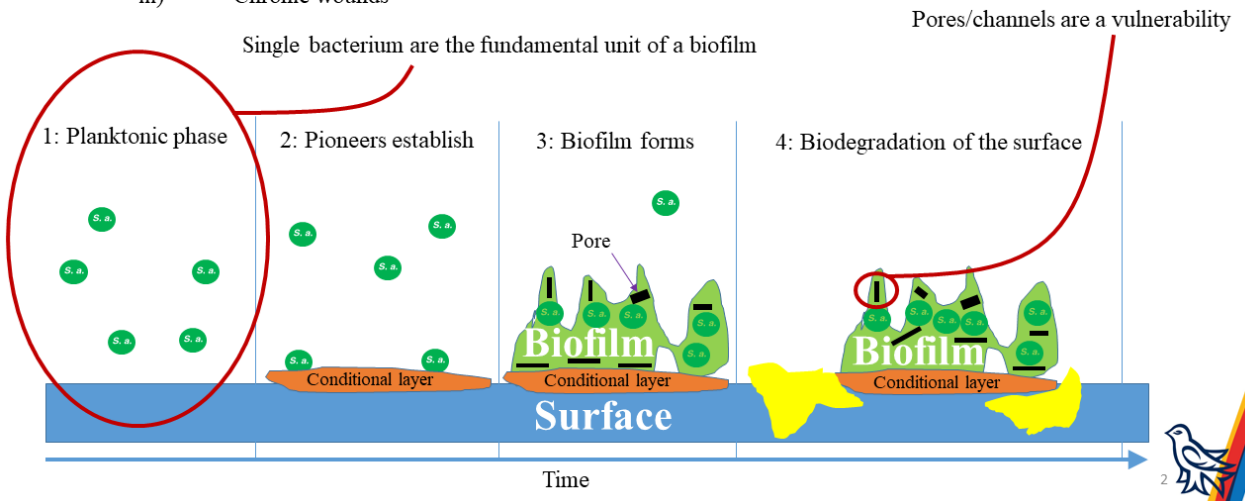
## Biofilms are Problematic

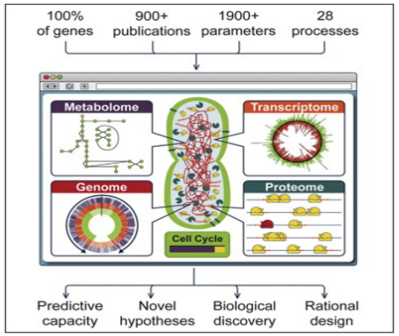
1. Biofilm = Micro-organismal communal colony.
   a) Heath Care complications
      i) Cystic Fibrosis
      ii) Dental plaque
      iii) Chronic wounds
   b) Membrane and surface fouling
      i) Desalination membranes
      ii) Aquatic vehicle hulls






## Bacterial and Biofilm Growth Simulation Schematic

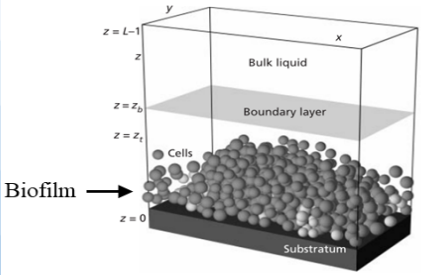
Step 1: Individual bacterium simulation




The Whole Cell Model (WCM) of *Mycoplasma Genitalium* [Karr et al., **2012**] is the foundation for the simulation of an isolated bacterium.

The rigorous detail of the WCM is distilled to probabilities of reactions and behavioral phenomena, which considerably simplifies the code while minimally sacrificing accuracy.

Step 2: Biofilm simulation




The probabilistic model of an isolated bacterium from Step 1 is programmed into a secondary simulation of biofilm propagation.

The biofilm simulation will explore the Cellular Automaton (CA) algorithm and the Individual-based Model [Kreft et al., **2001**] to recursively track chemical concentrations, cellular states, and biofilm structure through each timestep. The CA algorithm may more faithfully depict the nanostructures of channels and pores within a biofilms.

Step 3: Validation and refinement

- Validate:
  - Rates of bacterial replication
  - Rates of biofilm growth
  - Model assumptions
    - Instantaneous diffusion
    - Probabilistic biochemistry
    - Michaelis-Menten kinetics.
- Expand:
  - Pre-program a collection of different input files for simulation qualities
    - Bacteria
    - Initial solutions
    - Antibiotic exposure
    - Surface materials
    - User interface



## Currently in Step 1 = Python 3 Coding and Preliminary Assessments

- Preliminary trials of the simulation printed encouraging changes in chemical concentrations.
- Reactions, and thus chemical concentrations, are programmed via reversible Michaelis-Menten kinetics.
- A data mining script was successfully developed to transfer data from the MATLAB-based WCM to the Python-based biofilm simulation.
- Vectorization and other efficiencies were implemented to improve computational time by orders of magnitude.



## Future Scale-up to a Biofilm Simulation and Elucidated Nanostructures

1. The complete WCM must be encoded and reduced to probabilities.
   - The probabilistic simulation must be validated with the original simulation and with corresponding literature for pertinent rates and metabolic proportions, et cetera.
2. The WCM must be expanded for common biofilm-forming species like *Staphylococcus aureus* or *Pseudomonas aeruginosa.*
   - The *Mycoplasma genitalium of the WCM* is among the smallest and simplest known bacteria, and thus the unrepresented pathways in *M. genitalium* must be added.
3. Antibiotic effects upon bacterial biochemistry and importantly upon the formation of a biofilm must be quantified and parameterized into the simulation.
   - Antibiotic considerations may permit fundamental understanding of how treatments alter biofilm nanostructure and thereby degrade existing biofilms.
4. The simulation will be refined to approximate the composition and chemical characteristics of biofilms with increasing accuracy.
   - Existing biofilm growth models simplify biofilms to consist of only dead/alive bacterial cells and water, without consideration of proteins or microenvironments.


580 kb
525 genes

2.8 Mb
2600 genes