Dynamic Networks of Microbial Biofilms

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Big problem: Antibiotic resistance

WHO 2014 report reveals that antibiotic resistance is no longer a prediction for the future; it is happening right now
Bacteria bring together computation, communication, and control

This presentation puts the “network” at very center of this socio-microbiological perspective on pathogens

Intra-cellular networks
Quorum sensing modeling

Inter-cellular networks
Biofilm dynamics

Understanding and engineering “Molecular Tweeting” could hold the key to busting superbugs
What is quorum sensing (QS)?

- Bacteria use quorum sensing (QS) to monitor the environment and regulate their collective behaviors
  - Biofilm formation
  - Virulence expression

https://www.youtube.com/watch?v=be-mjOGi6qu


How to model QS?

LuxR-AI dynamics

\[ \frac{[C]}{dt} = \alpha [R][A] - \delta [C] \]

QS upregulates multiple virulence genes

\[ \frac{[A]}{dt} = -\alpha [R][A] + \delta [C] - b[R] + \frac{V[C]}{K + [C]} + r + \frac{d}{\rho} ([A_E] - [A]) \]

\[ \frac{[A_E]}{dt} = -d([A_E] - [A]) - b[A_E] \]

Gram-negative bacteria use largely homologous QS networks, where the AIs are detected and regulated via genetic circuits
Bacterial population dynamics is a complex problem. Direct wet-lab experimentation is costly and often impractical.

Experimenting with efficient GPU kernels using NVIDIA Thrust allows to achieve 100x acceleration with GTX980 GPUs.

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Applications
Network control

Understanding and engineering “Molecular Tweeting” could hold the key to busting superbugs.
Bacterial biofilm: Use Twitter-like metaphor to explain participants and network formation

(a) Intracellular network
(b) Intercellular network
(c) EPS/Virulence
(d) Signal molecule (molecular tweet)

@bacteria: generate public goods (EPS) or virulence

The structure and dynamics of the inter-cellular communication network is heavily influenced by its environment

Network formulation is based on the QS activity

\[ S_{ij} = Q \frac{I_{ij}}{\max(I)} \]

\[ R_{ij} = \frac{\log(S_{ij})}{D} \]
Network metrics

- **Clustering coefficient**: Measures the degree to which network nodes are clustered together. A high clustering coefficient means that the network nodes are not only highly active but also in close proximity to one another.

- **Communities**: Groups of nodes with high clustering coefficient. If the two cell groups have a large impact on one another (e.g., gene expression synchronization), then they are considered to belong to the same community.

Pure wild type (WT): All bacteria tweet and retweet the message of producing EPS

(300x300x500μm³)
Red: WT
Green: EPS
1/3WT, 1/3SB, 1/3SN: Bacteria communication enables social intelligence (“molecular tweeting”)

Dynamics of network evolution

- Biofilm Max Thickness
- Biofilm Roughness
- Number of Communities
- Network Diameter
- Clustering Coefficient
- Number of Links
- Wild-type %
- Networked Cells %
Do bacteria have a social life?

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<th>Category</th>
<th>Network</th>
<th>Type</th>
<th>Nodes</th>
<th>Links</th>
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<th>PathLength_avg</th>
<th>Clustering</th>
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</table>

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Effect of QSIs

QSI1: targeting LasR receptor
C-30 furanone (Al analog)

QSIs can effectively reduce the virulence

Consider only wild type cells

QSI1 targets LasR
QSI2 targets AI
QSI3 targets the gene which produces LasR
QSI strategies

Day 1
QSI1: signal reception

Day 5
QSI2: signal accumulation

Day 10
QSI3: signal generation

QSI combined

Summary

Intra-cellular networks
Quorum sensing modeling

Inter-cellular networks
Biofilm dynamics

Applications
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Contributors (in no particular order...)
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