How Quorum Sensing Interactions Affect Population Structure

02-712 Final Project

Sid Reed, Evan Trop, Neel Mehtani, Deepika Yeramosu, Sarah Wenger

Carnegie Mellon University

December 2, 2021

Background

Quorum-Sensing Systems

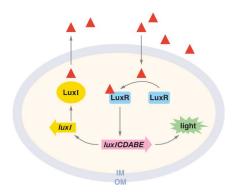


Figure 1: Qqs diagram

Signal-Receptor molecule pairs that modulate gene expression

Quorum-Sensing Systems

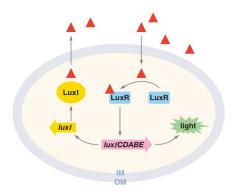


Figure 1: Qqs diagram

How Quorum Sensing Interactions Affect Population Structure

- ► Signal-Receptor molecule pairs that modulate gene expression
- Once threshold density is reached, enough signal is received to upregulated target genes

Quorum-Sensing Systems

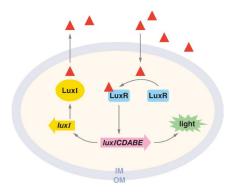


Figure 1: Qqs diagram

- Signal-Receptor molecule pairs that modulate gene expression
- ▶ Once threshold density is reached, enough signal is received to upregulated target genes
- Can lead to biofilms, antibiotic production etc.

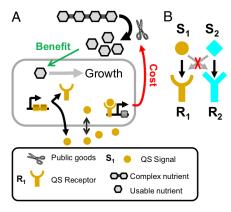


Figure 2: @eldar 2011

 When quorum is reached, bacteria produce a "public good"

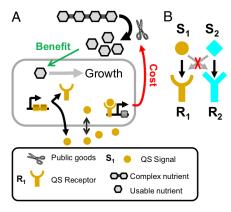


Figure 2: @eldar 2011

- When quorum is reached, bacteria produce a "public good"
- Everyone benefits from this even if they don't contribute

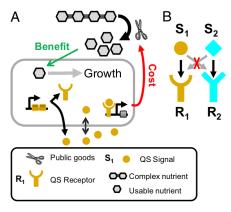


Figure 2: @eldar 2011

- When quorum is reached, bacteria produce a "public good"
- Everyone benefits from this even if they don't contribute
- Must produce the receptor, signal molecule and good to contribute

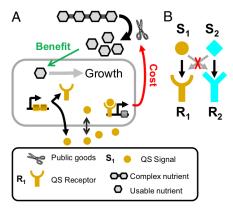


Figure 2: @eldar_2011

- When quorum is reached, bacteria produce a "public good"
- Everyone benefits from this even if they don't contribute
- Must produce the receptor, signal molecule and good to contribute
- Cheaters DO prosper (if you are a bacterium)

Who Cares?

▶ check the discussion from @eldar 2011 for references

Maintaining Freeloaders as a Diversity Reservoir

Who Cares?

▶ check the discussion from @eldar_2011 for references

Maintaining Freeloaders as a Diversity Reservoir

Kin Recognition for Strains

Who Cares?

▶ check the discussion from @eldar 2011 for references

Maintaining Freeloaders as a Diversity Reservoir

Kin Recognition for Strains

Designing Cheaters to Disrupt Pathogen Growth

Methods

Basic ODE Model

Social conflict drives the evolutionary divergence of quorum sensing

Avigdor Eldar¹

Department of Molecular Microbiology and Biotechnology, Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel

Basic ODE Model

Social conflict drives the evolutionary divergence of quorum sensing

Avigdor Eldar¹

Department of Molecular Microbiology and Biotechnology, Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel

Model Equations

$$\begin{split} \frac{dn_i}{dt} &= n_i (\frac{P_d}{P_d + 1} (1 - rf(R_i^{active})) - n_{tot} - \gamma_n) \\ \frac{dS_i}{dt} &= \beta_S (n_i - S_i) \\ \frac{dE}{dt} &= -\beta_E E + \sum_i f(R_i^{active}) n_i \\ \frac{dP_d}{dt} &= J_{P_d} + V_{max} E - \beta_{P_d} (\frac{P_d}{P_d + 1}) n_{tot} \end{split}$$

▶ The interaction term is defined as $R^{active} = \frac{K_{ac}\vec{S}}{K_{RS} + K_{ac}\vec{S}}$

- ▶ The interaction term is defined as $R^{active} = \frac{K_{ac}\vec{S}}{K_{RS} + K_{ac}\vec{S}}$
 - ⋄ assumes Michalis-Menten dynamics of signal-receptor binding (K_{RS} is a constant)

- ▶ The interaction term is defined as $R^{active} = \frac{K_{ac}\vec{S}}{K_{RS} + K_{ac}\vec{S}}$
 - assumes Michalis-Menten dynamics of signal-receptor binding (K_{RS} is a constant)
- ▶ K_{ac} represents all receptors-signal pairs (R_iS_i) produced in each strain

- ▶ The interaction term is defined as $R^{active} = \frac{K_{ac}\vec{S}}{K_{RS} + K_{ac}\vec{S}}$
 - ♦ assumes Michalis-Menten dynamics of signal-receptor binding (K_{RS} is a constant)
- ▶ K_{ac} represents all receptors-signal pairs (R_iS_i) produced in each strain
- $ightharpoonup K_{ac}$ is of dimension $|R| \times |S| = |n| \times |n|$

Facultative Cheaters

Matrix for 2 strains R_1S_1 and R_2S_2

$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Facultative Cheaters

Matrix for 2 strains R_1S_1 and R_2S_2

$$\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Obligate Cheater

Matrix for 2 strains R_1S_1 and R_0S_0

Facultative Cheaters

Matrix for 2 strains R_1S_1 and R_2S_2

Obligate Cheater

Matrix for 2 strains R_1S_1 and R_0S_0

$$\begin{bmatrix} 1 & 0 \\ 0 & 0 \end{bmatrix}$$

Custom Matrix

Matrix for 2 strains $R_1R_2S_1$ and R_2S_2

▶ Implemented in python using scipy.integrate.solve_ivp

- Implemented in python using scipy.integrate.solve_ivp
- \triangleright Generated different K_{ac} matrices and run simulations

- Implemented in python using scipy.integrate.solve_ivp
- \triangleright Generated different K_{ac} matrices and run simulations
 - \diamond Specific patterns and randomly generated K_{ac}

- Implemented in python using scipy.integrate.solve_ivp
- \triangleright Generated different K_{ac} matrices and run simulations
 - \diamond Specific patterns and randomly generated K_{ac}
- Examine population structure and model dynamics

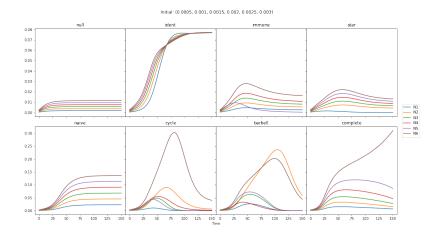
- Implemented in python using scipy.integrate.solve_ivp
- \triangleright Generated different K_{ac} matrices and run simulations
 - \diamond Specific patterns and randomly generated K_{ac}
- Examine population structure and model dynamics
- Simulate using gut microbiome data as initial state

- ▶ Implemented in python using scipy.integrate.solve_ivp
- \triangleright Generated different K_{ac} matrices and run simulations
 - \diamond Specific patterns and randomly generated K_{ac}
- Examine population structure and model dynamics
- Simulate using gut microbiome data as initial state
- ▶ All code/results easily available to use on Github

Sid Reed, Evan Trop, Neel Mehtani, Deepika Yeramosu, Sarah Wenger

Results

Comparing Different K_{ac} Matrices



How K_{ac} Sparsity Affects Population Structure

Simulating With Human Gut Microbiome Data

Discussion

Cheating works...

Cheating works...

(for bacteria)

Cheating works...

(for bacteria)

but cooperating is better!

Bibliography I