

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 1, 2021

Background

Quorum-Sensing Systems

- Signal-Receptor molecule pairs that modulate gene expression

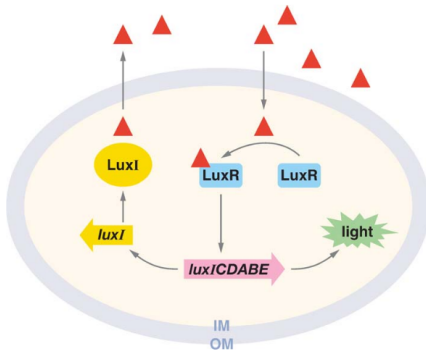
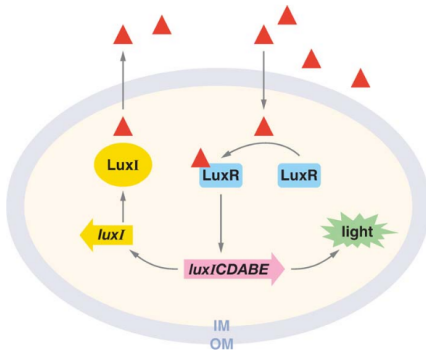


Figure 1: Waters and Bassler (2005)

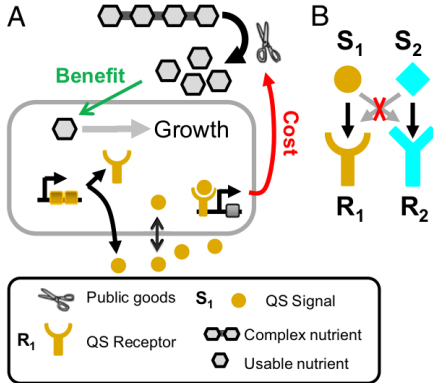
Quorum-Sensing Systems



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

Figure 1: Waters and Bassler (2005)

Public Goods and Cheating



- ▶ When quorum is reached, bacteria produce a “public good”

Figure 2: Eldar (2011)

Public Goods and Cheating

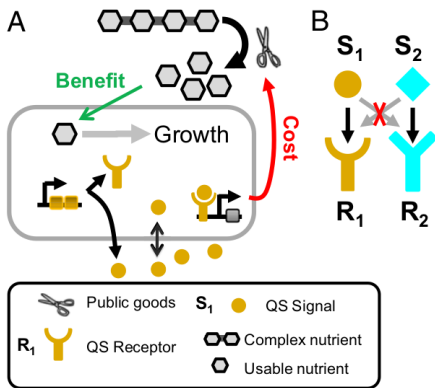


Figure 2: Eldar (2011)

- ▶ When quorum is reached, bacteria produce a “public good”
- ▶ Everyone benefits from this even if they don’t contribute

Public Goods and Cheating

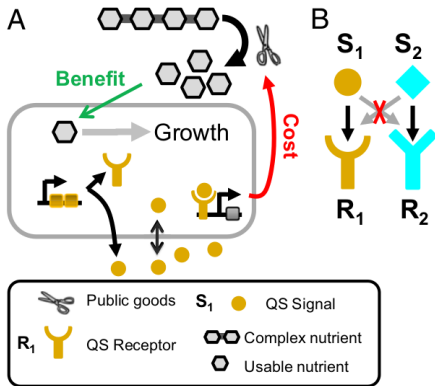


Figure 2: Eldar (2011)

- ▶ 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

Public Goods and Cheating

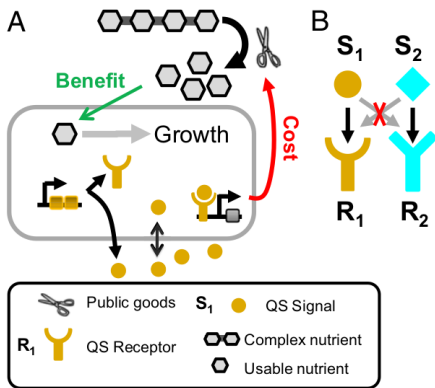


Figure 2: Eldar (2011)

- ▶ 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

$$\frac{dn_i}{dt} = n_i \left(\frac{P_d}{P_d + 1} (1 - rf(R_i^{\text{active}})) - n_{\text{tot}} - \gamma_n \right)$$

$$\frac{dS_i}{dt} = \beta_S (n_i - S_i)$$

$$\frac{dE}{dt} = -\beta_E E + \sum_i f(R_i^{\text{active}}) n_i$$

$$\frac{dP_d}{dt} = J_{P_d} + V_{\text{max}} E - \beta_{P_d} \left(\frac{P_d}{P_d + 1} \right) n_{\text{tot}}$$

Signal-Receptor Activation Matrix K_{ac}

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

Signal-Receptor Activation Matrix K_{ac}

- ▶ 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)

Signal-Receptor Activation Matrix K_{ac}

- ▶ 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 ($R_i S_i$) produced in each strain

Signal-Receptor Activation Matrix K_{ac}

- ▶ 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 ($R_i S_i$) produced in each strain
- ▶ 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

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

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

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

Custom Matrix

Matrix for 2 strains $R_1R_2S_1$ and R_2S_2

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

Our Work

- ▶ Implemented in python using `scipy.integrate.solve_ivp`

Our Work

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

Our Work

- ▶ Implemented in python using `scipy.integrate.solve_ivp`
- ▶ Generated different K_{ac} matrices and run simulations
 - ◇ Specific patterns and randomly generated K_{ac}

Our Work

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

Our Work

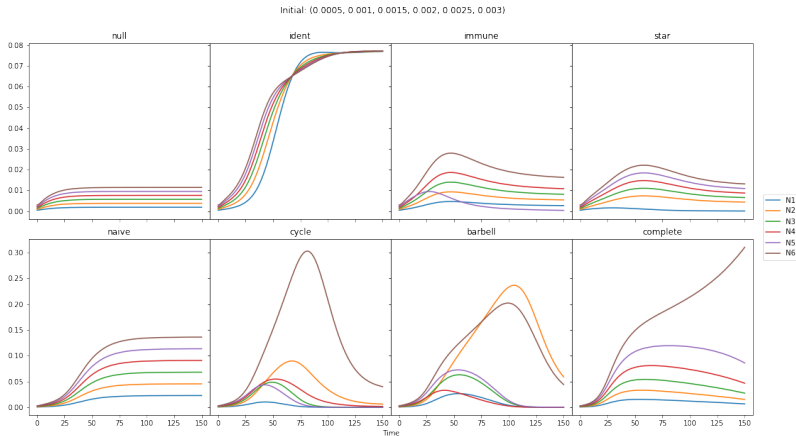
- ▶ Implemented in python using `scipy.integrate.solve_ivp`
- ▶ Generated different K_{ac} matrices and run simulations
 - ◇ Specific patterns and randomly generated K_{ac}
- ▶ Examine population structure and model dynamics
- ▶ Simulate using gut microbiome data as initial state

Our Work

- ▶ Implemented in python using `scipy.integrate.solve_ivp`
- ▶ Generated different K_{ac} matrices and run simulations
 - ◇ 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

Results

Comparing Different K_{ac} Matrices



How K_{ac} Sparsity Affects Population Structure

Simulating With Human Gut Microbiome Data

Discussion

Moral of the Study

Moral of the Study

Cheating works...

Moral of the Study

Cheating works...
(for bacteria)

Moral of the Study

Cheating works...

(for bacteria)

but cooperating is better!

Bibliography I

Aggarwal, Surya D., Hasan Yesilkaya, Suzanne Dawid, and N. Luisa Hiller. 2020. "The Pneumococcal Social Network." *PLOS Pathogens* 16 (10). <https://doi.org/10.1371/journal.ppat.1008931>.

Calle, M. Luz. 2019. "Statistical Analysis of Metagenomics Data." *Genomics & Informatics* 17 (1).
<https://doi.org/10.5808/gi.2019.17.1.e6>.

Dimitriu, Tatiana, Frances Medaney, Elli Amanatidou, Jessica Forsyth, Richard J. Ellis, and Ben Raymond. 2019. "Negative Frequency Dependent Selection on Plasmid Carriage and Low Fitness Costs Maintain Extended Spectrum Beta-Lactamases in *Escherichia Coli*." *Scientific Reports* 9 (1).
<https://doi.org/10.1038/s41598-019-53575-7>.

Bibliography II

Eldar, A. 2011. "Social Conflict Drives the Evolutionary Divergence of Quorum Sensing." *Proceedings of the National Academy of Sciences* 108 (33): 13635–40.

<https://doi.org/10.1073/pnas.1102923108>.

Pérez-Escudero, Alfonso, and Jeff Gore. 2016. "Selection Favors Incompatible Signaling in Bacteria." *Proceedings of the National Academy of Sciences* 113 (8): 1968–70.

<https://doi.org/10.1073/pnas.1600174113>.

Bibliography III

Pollak, Shaul, Shira Omer-Bendori, Eran Even-Tov, Valeria Lipsman, Tasneem Bareia, Ishay Ben-Zion, and Avigdor Eldar. 2016.

“Facultative Cheating Supports the Coexistence of Diverse Quorum-Sensing Alleles.” *Proceedings of the National Academy of Sciences* 113 (8): 2152–7.

<https://doi.org/10.1073/pnas.1520615113>.

Waters, Christopher M, and Bonnie L. Bassler. 2005. “Quorum Sensing: Cell-to-Cell Communication in Bacteria.” *Annual Review of Cell and Developmental Biology* 21: 319–46.

<https://doi.org/10.1146/annurev.cellbio.21.012704.131001>.