How Quorum Sensing Interactions Affect Population Structure

02-712 Final Project

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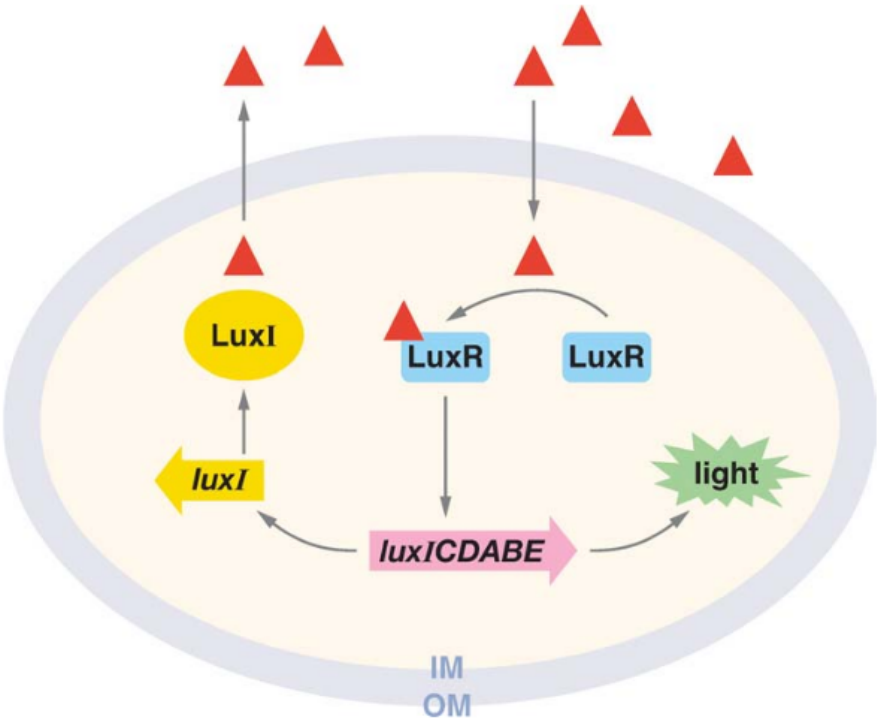
Background

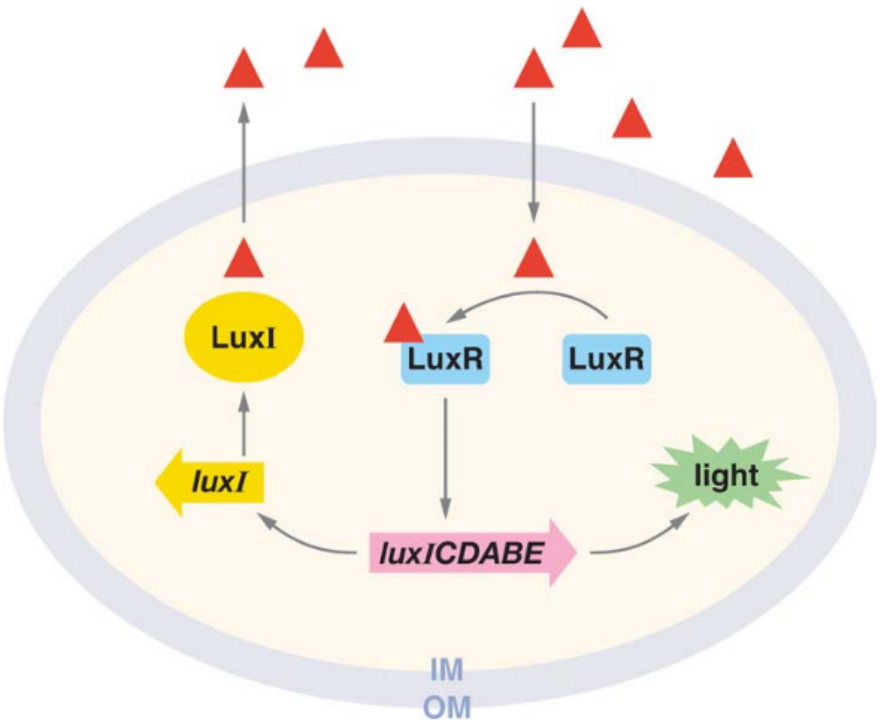
Quorum-Sensing Systems



- Signal-Receptor molecule pairs that modulate gene expression

Figure 1: Waters and Bassler (2005)

Quorum-Sensing Systems



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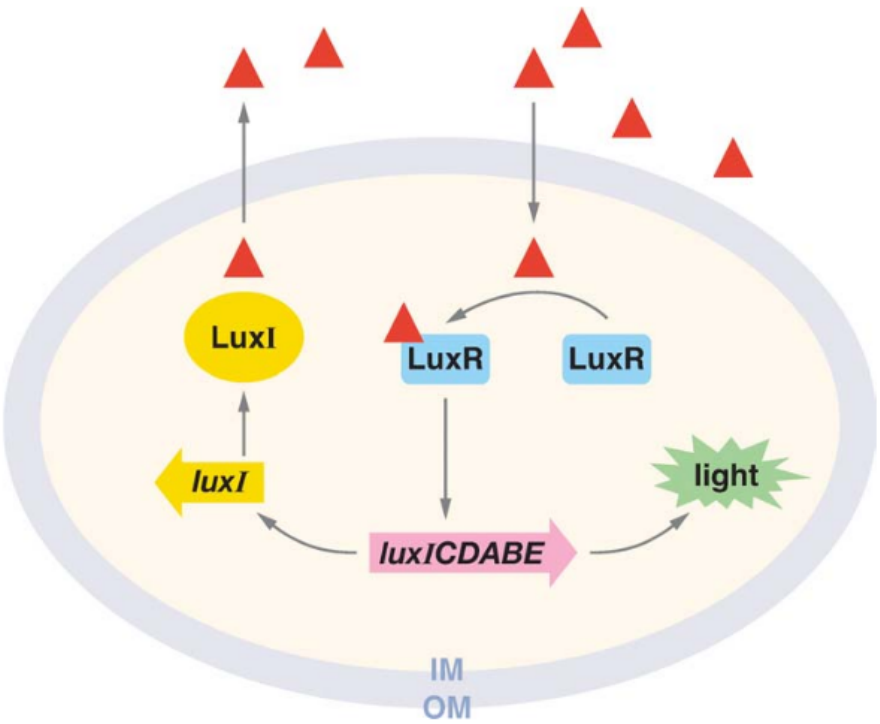

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- Signal-Receptor molecule pairs that modulate gene expression
- Once threshold density is reached, enough signal is received to upregulated target genes
- Can lead to biofilms, antibiotic production etc.

Public Goods and Cheating

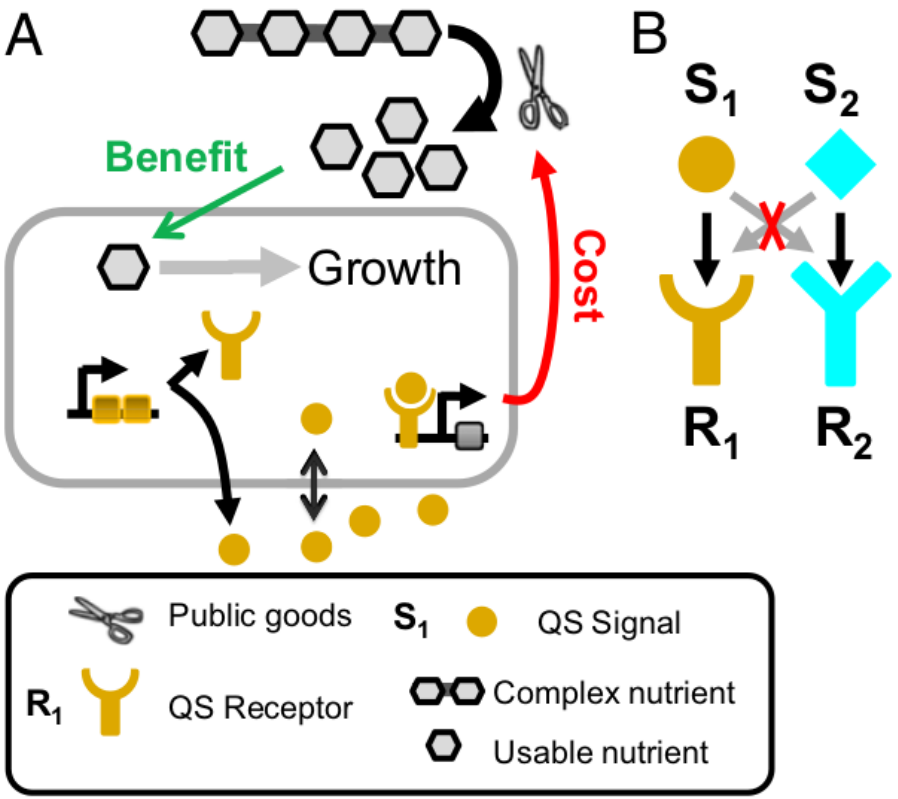
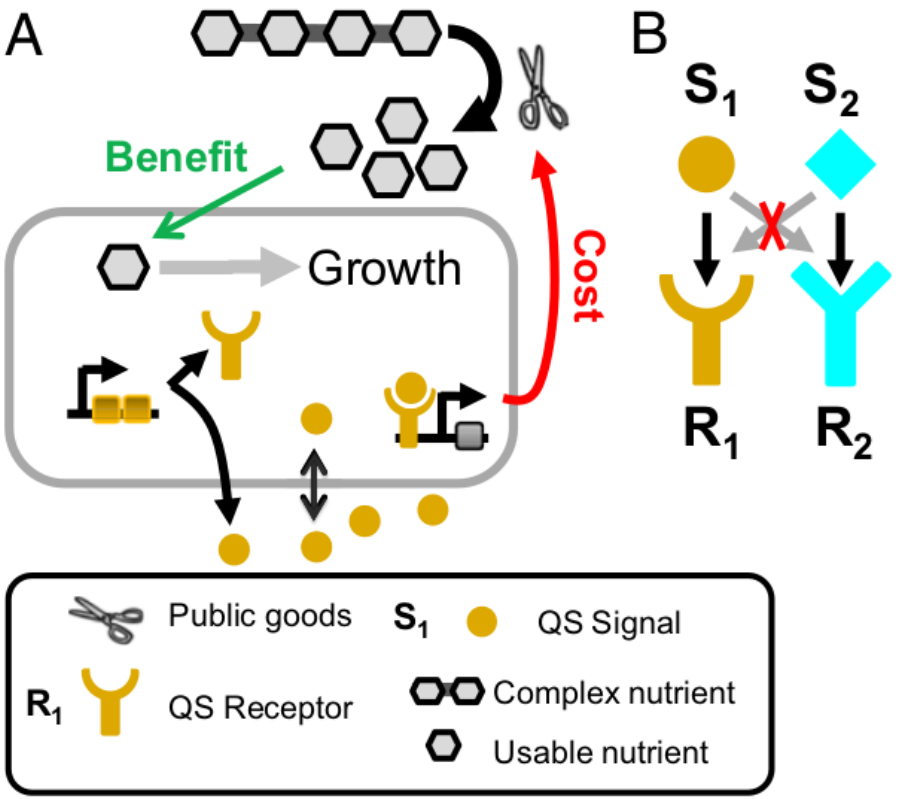


Figure 2: Eldar (2011)

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

Public Goods and Cheating



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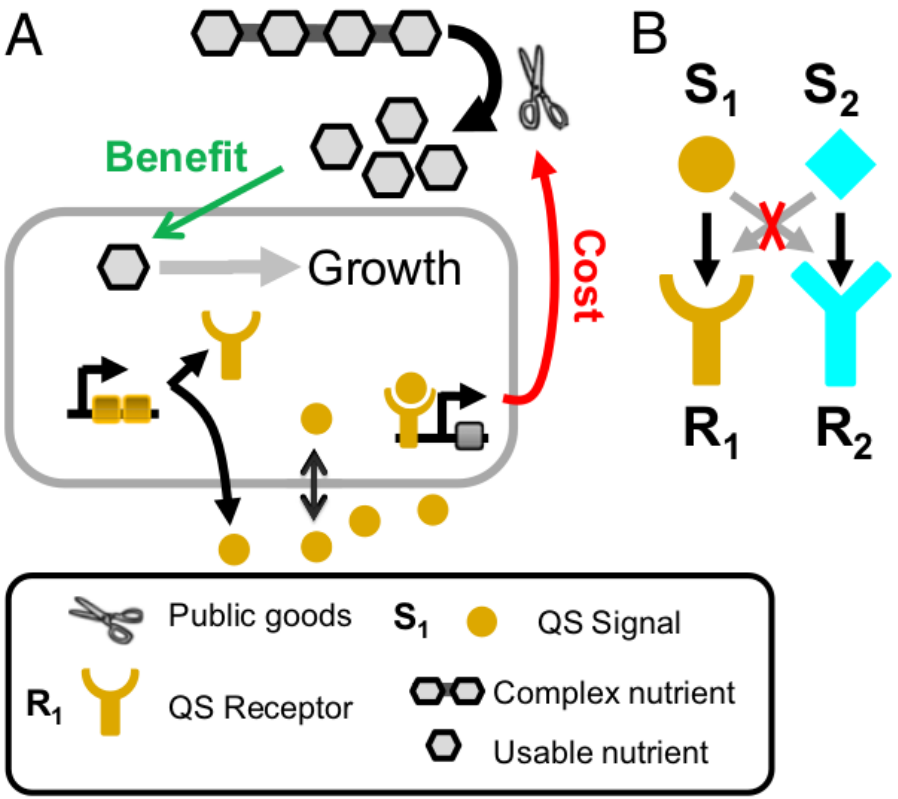

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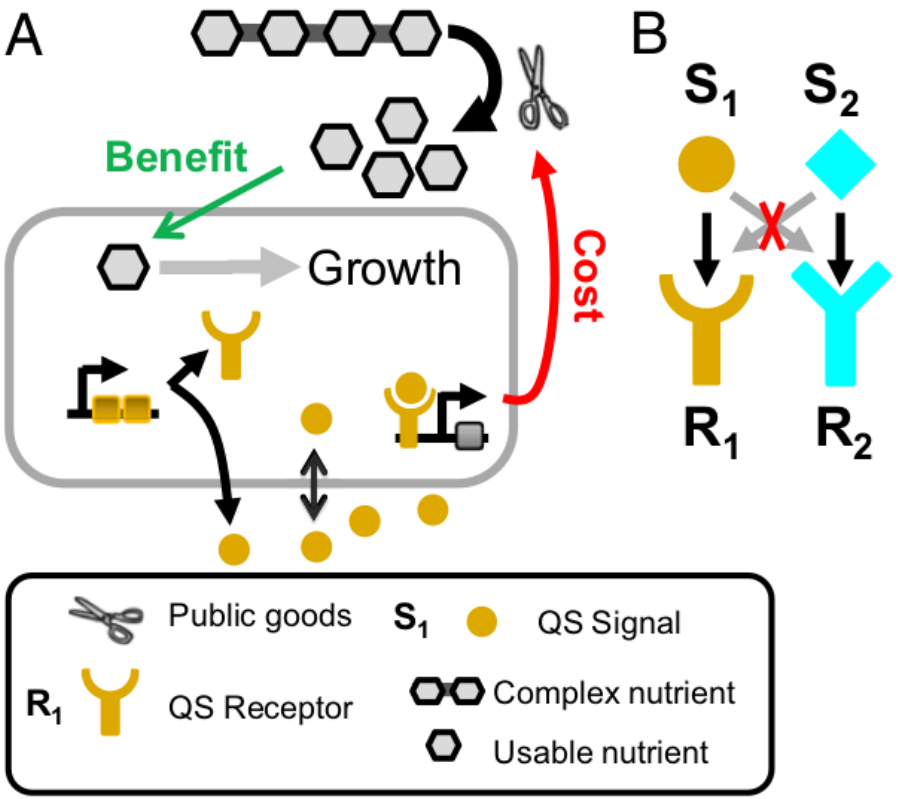

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- When quorum is reached, bacteria produce a "public good"
- Everyone benefits from this even if they don't contribute
- Must produce the receptor, signal molecule and good to contribute
- Cheaters DO prosper (if you are a bacterium)

Who Cares?

- check the discussion from Eldar (2011) for references

Maintaining Freeloaders as a Diversity Reservoir

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Kin Recognition for Strains

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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 Eldar[1]

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Model Equations

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

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

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

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

Signal-Receptor Activation Matrix K_{ac}

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

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  - 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
- K_{ac} is of dimension $|R| \times |S| = |n| \times |n|$

Facultative Cheaters

Matrix for 2 strains R_1S_1 and R_2S_2

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

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Obligate Cheater

Matrix for 2 strains R_1S_1 and R_0S_0

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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 the ODE in python using `scipy.integrate.solve_ivp` (RK45)

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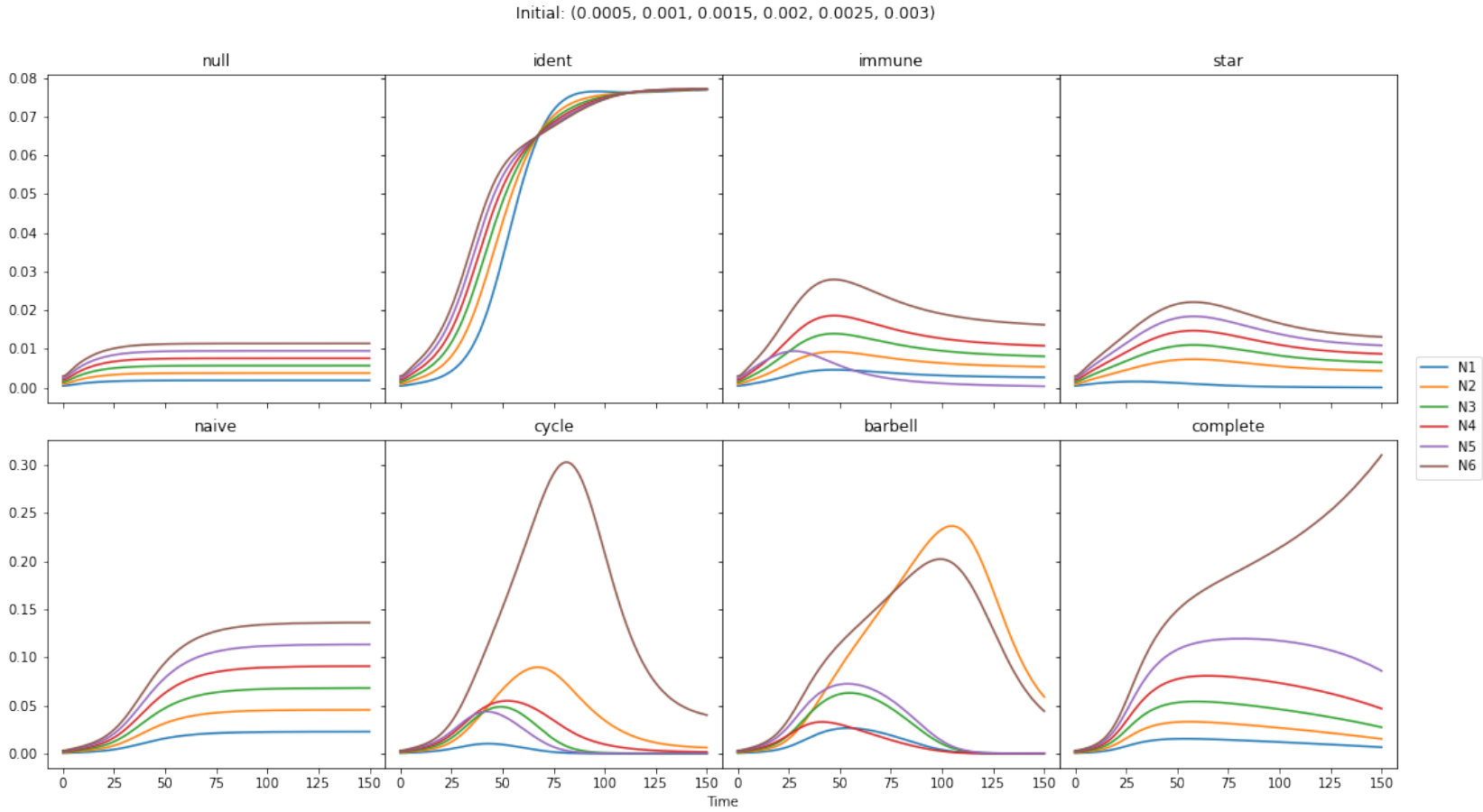
- Implemented the ODE in python using `scipy.integrate.solve_ivp` (RK45)
- Generated different K_{ac} matrices and run simulations
- Examine population structure and model dynamics

Results

Comparing Different K_{ac} Matrices



How K_{ac} Sparsity Affects Population Structure

Simulating With Human Gut Microbiome Data

Discussion

Moral of the Study

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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 &Amp; 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.