A mathematical model for the quorum sensing system in Sinorhizobium meliloti

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Quorum sensing in bacteria

- For bacteria, it is important to sense the environment
- Quorum sensing/Diffusion sensing/Efficiency sensing
- Here: Sin-system of *S. meliloti*, nitrogen-fixing soil bacterium, found in the root nodules of leguminous plants

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The molecular basis of the Sin system
A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The positive feedback

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The negative feedback

Medium

Cell

\[ \text{ExpR} \rightarrow \text{AHL} \rightarrow \text{ExpR} \]

\[ \text{SinR} \rightarrow \emptyset \]

\[ \text{SinI} \rightarrow \emptyset \]

\[ \text{AHL} \rightarrow \emptyset \]

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The molecular basis of the Sin system

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The full dynamical system

\[
\text{SinR: } \frac{dR}{dt} = \alpha_1 \frac{1}{\beta_3 C + 1} - \gamma_1 R
\]

\[
\text{SinI: } \frac{dI}{dt} = \alpha_2 \frac{\beta_1 R}{\beta_1 R + 1} \left(1 + \alpha_5 \frac{\beta_2 C}{\beta_2 C + 1}\right) - \gamma_2 I
\]

AHL inside cell: \[
\frac{dA_i}{dt} = \alpha_3 I - \delta_1 A_i + \delta_2 A_o - \alpha_4 A_i (\bar{E} - C) - \gamma_3 A_i + \gamma_4 C
\]

AHL outside cells: \[
\frac{dA_o}{dt} = B (\delta_1 A_i - \delta_2 A_o) - \gamma_3 A_o
\]

:= number of cells

Complex ExpR/AHL: \[
\frac{dC}{dt} = \alpha_4 A_i (\bar{E} - C) - \gamma_4 C
\]

:= ExpR + ExpR/AHL constant

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The initial phase (no QS); $B$ small

\[ \text{SinR: } \frac{dR}{dt} = \alpha_1 - \gamma_1 R \]

\[ \text{SinI: } \frac{dI}{dt} = \alpha_2 - \gamma_2 I \]

\[ \text{AHL inside cell: } \frac{dA_i}{dt} = \alpha_3 I - \delta_1 A_i \]

\[ \text{AHL outside cells: } \frac{dA_o}{dt} = B \delta_1 A_i - \gamma_3 A_o \]

\[ \text{Complex ExpR/AHL: } \frac{dC}{dt} = 0 \]

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
The positive feedback; $B$ moderate

\[
\text{SinR: } \quad \frac{dR}{dt} = \alpha_1 - \gamma_1 R
\]

\[
\text{SinI: } \quad \frac{dI}{dt} = \alpha_2 \left( 1 + \alpha_5 \frac{\beta_2 C}{\beta_2 C + 1} \right) - \gamma_2 I
\]

\[
\text{AHL inside cell: } \quad \frac{dA_i}{dt} = \alpha_3 I - \delta_1 A_i + \delta_2 A_o
\]

\[
\text{AHL outside cells: } \quad \frac{dA_o}{dt} = B \left( \delta_1 A_i - \delta_2 A_o \right) - \gamma_3 A_o
\]

\[
\text{Complex ExpR/AHL: } \quad \frac{dC}{dt} = \alpha_4 A_i \left( \tilde{E} - C \right) - \gamma_4 C
\]

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The negative feedback; $B$ large

\[
\begin{align*}
\text{SinR: } & \quad \frac{dR}{dt} = -\gamma_1 R \\
\text{SinI: } & \quad \frac{dI}{dt} = -\gamma_2 I \\
\text{AHL inside cell: } & \quad \frac{dA_i}{dt} = -\delta_1 A_i + \delta_2 A_o \\
\text{AHL outside cells: } & \quad \frac{dA_o}{dt} = B \left( \delta_1 A_i - \delta_2 A_o \right) - \gamma_3 A_o \\
\text{Complex ExpR/AHL: } & \quad \frac{dC}{dt} = \alpha_4 A_i \left( \underbrace{\overline{E}}_{\text{ExpR+ExpR/AHL constant}} - C \right) - \gamma_4 C
\end{align*}
\]
Introduction

The mathematical system

Data and simulations

Comparison

Outlook

Summary of analysis

- System has both, positive and negative feedback
- Quorum sensing means that autoinducers from other bacteria enter a cell
- Within cell, chemical system is not bi-stable
- Degradation rates of SinR and SinI high $\rightarrow$ fast reactions of the system to environment changes are possible
- System highly sensitive to amount of available ExpR (ExpR low: no negative feedback possible)

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
Data

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
Simulation results

SinR and SinI are sensitive to expression of ExpR

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
Simulation results

AHL inside and outside of cells show the same behavior

A mathematical model for the quorum sensing system in Sinorhizobium meliloti
Comparison with model from Müller et al (2006)

- QS Model e.g. for *Vibrio fischeri*
Comparison with model from Müller et al (2006)

- Only positive feedback modeled by

AHL inside cell: \[
\frac{dA_i}{dt} = \alpha + \beta \frac{A_i^n}{A_i^n + x_*} - \delta_1 A_i + \delta_2 A_o
\]

AHL outside cells: \[
\frac{dA_o}{dt} = \delta_1 A_i - \delta_2 A_o - \gamma_3 A_o
\]

- Bi-stable system, but no dependence on number of cells \( B \)!
Outlook

- Stochastic aspects to fluctuations in number of ExpR
- Downstream mechanisms: EPS production, ...
- Heterogeneity in bacterial population