A mathematical model for the quorum sensing system in Sinorhizobium meliloti

Peter Pfaffelhuber
University of Freiburg

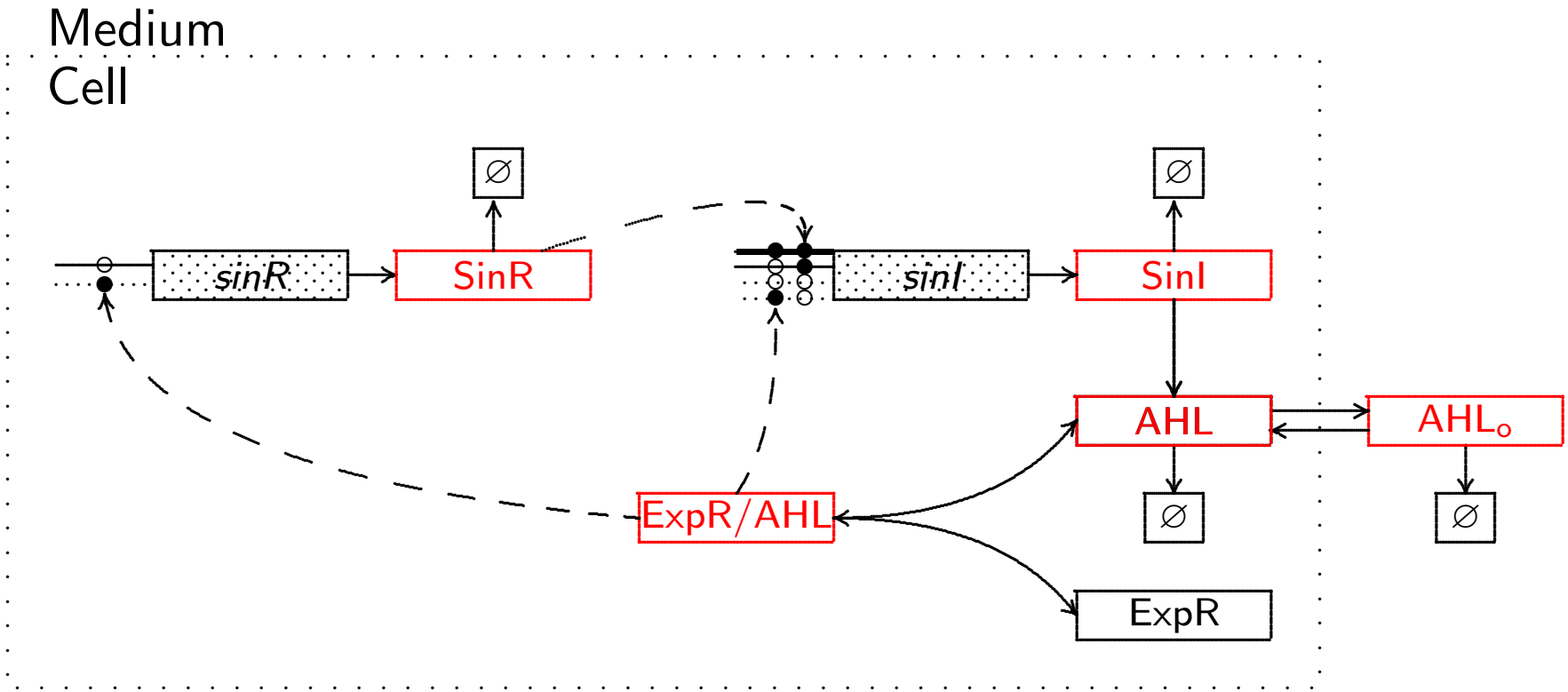
Joint work with Peter Czuppon, Matthew McIntosh, Anke Becker

June 29th, 2012

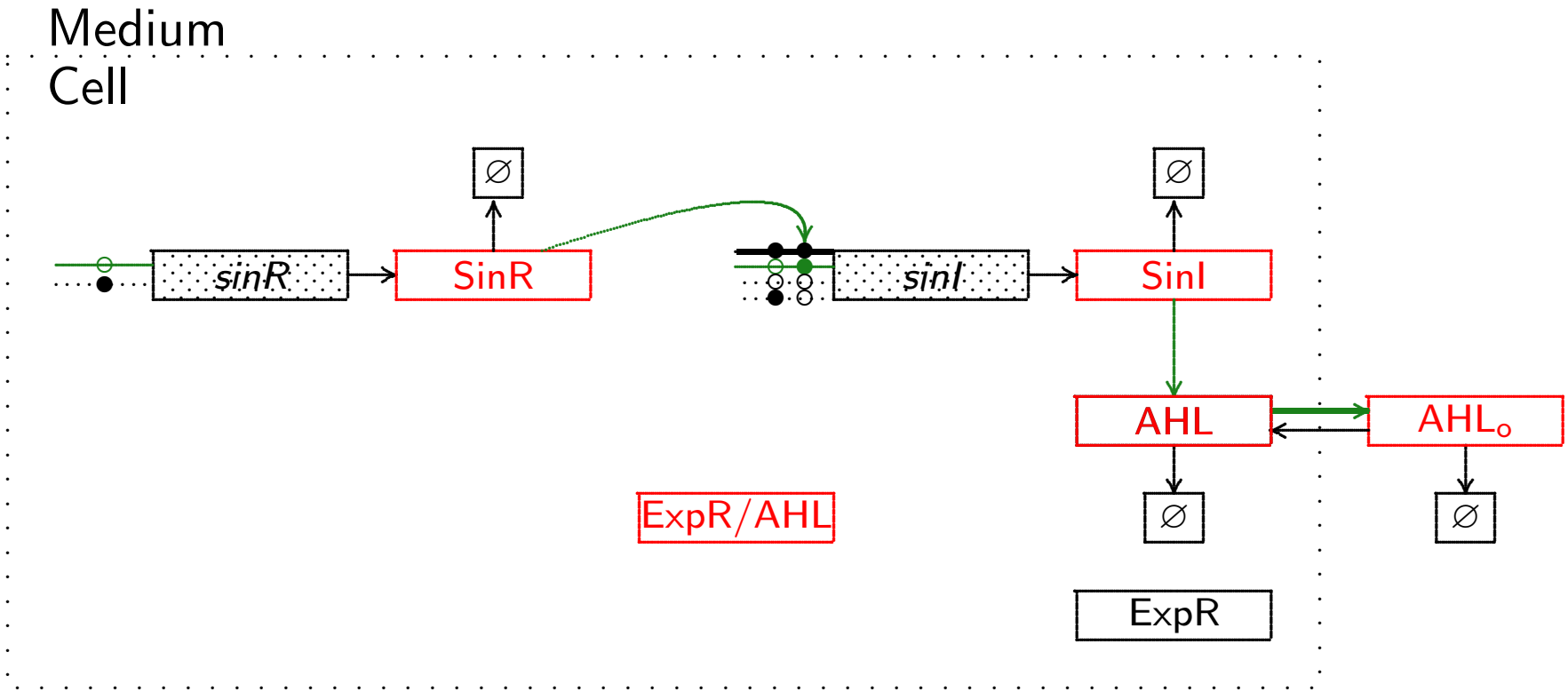
Quorum sensing in bacteria

- 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

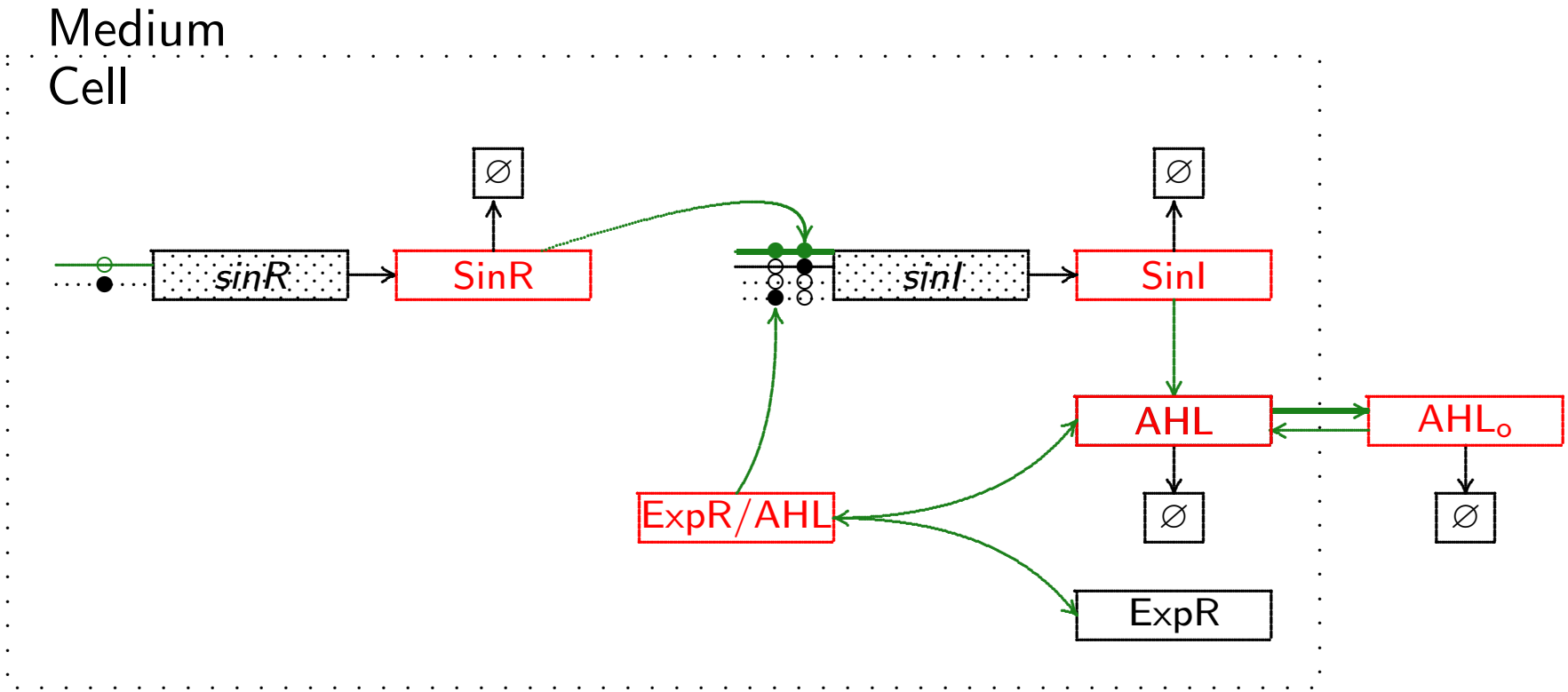
The molecular basis of the Sin system



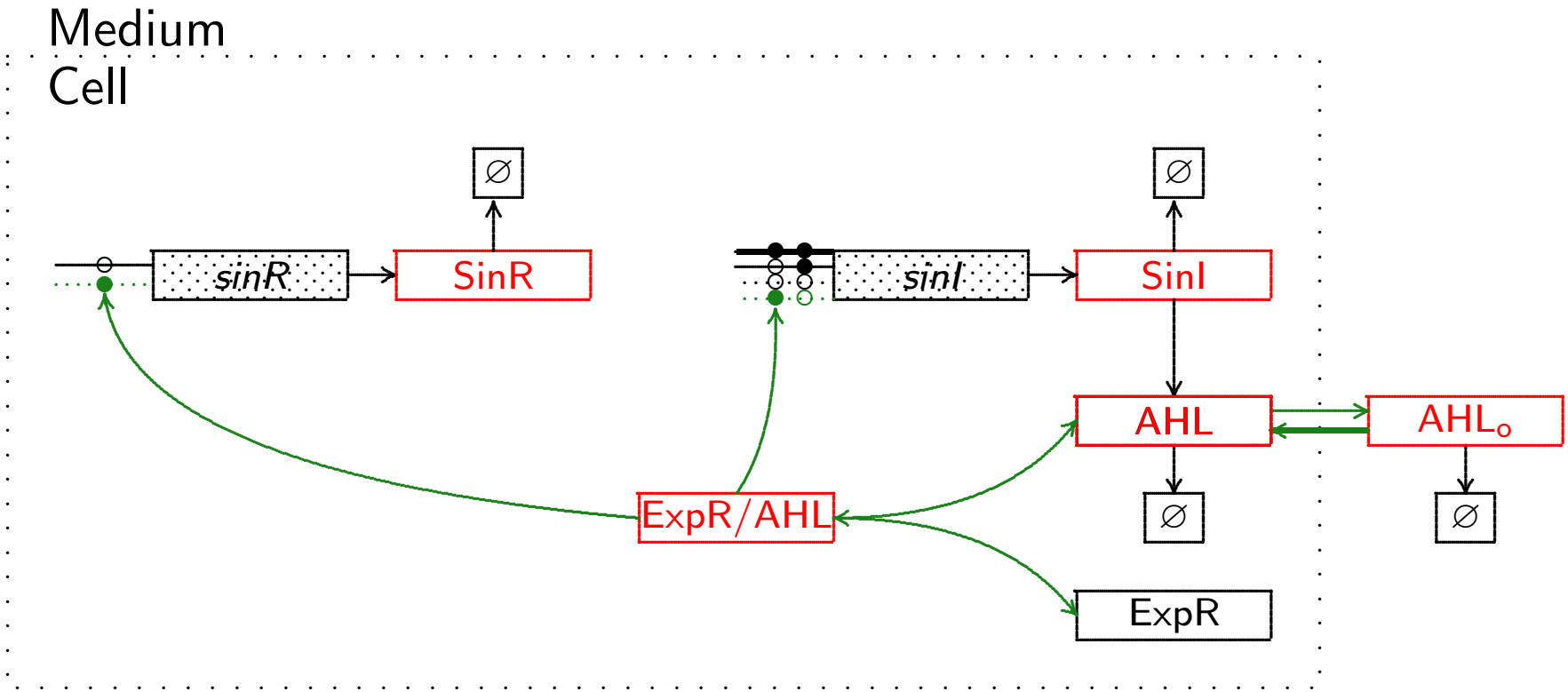
The initial phase (no QS)



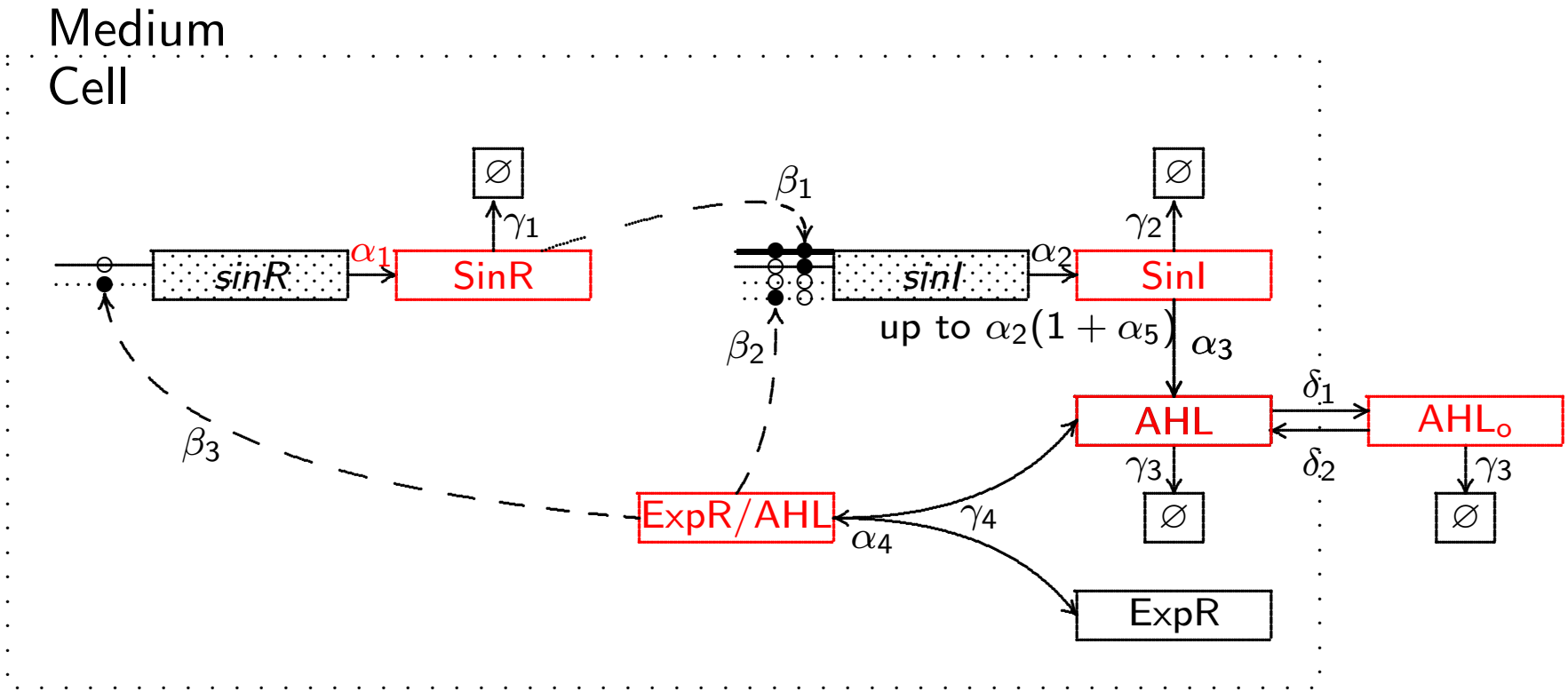
The positive feedback



The negative feedback



The molecular basis of the Sin system



The full dynamical system

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

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 outsice cells:
$$\frac{dA_o}{dt} = \underbrace{B}_{:= \text{number of cells}} \left(\delta_1 A_i - \delta_2 A_o\right) - \gamma_3 A_o$$

Complex ExpR/AHL:
$$\frac{dC}{dt} = \alpha_4 A_i(\underbrace{\bar{E}}_{:=ExpR+ExpR/AHL \text{ constant}} - C) - \gamma_4 C$$

The initial phase (no QS); B small

SinR: $$\frac{dR}{dt} = \alpha_1 - \gamma_1 R$$

SinI: $$\frac{dI}{dt} = \alpha_2 - \gamma_2 I$$

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

AHL outsice cells: $$\frac{dA_o}{dt} = \underbrace{B}_{:= \text{number of cells}} \delta_1 A_i - \gamma_3 A_o$$

Complex ExpR/AHL: $$\frac{dC}{dt} = 0$$

The positive feedback; B moderate

SinR:
$$\frac{dR}{dt} = \alpha_1 \qquad - \gamma_1 R$$

SinI:
$$\frac{dI}{dt} = \alpha_2 \qquad \left(1 + \alpha_5 \frac{\beta_2 C}{\beta_2 C + 1}\right) - \gamma_2 I$$

AHL inside cell:
$$\frac{dA_i}{dt} = \alpha_3 I - \delta_1 A_i + \delta_2 A_o$$

AHL outsice cells:
$$\frac{dA_o}{dt} = \underbrace{B}_{:= \text{number of cells}} \left(\delta_1 A_i - \delta_2 A_o\right) - \gamma_3 A_o$$

Complex ExpR/AHL:
$$\frac{dC}{dt} = \alpha_4 A_i (\underbrace{\bar{E}}_{:=ExpR+ExpR/AHL \text{ constant}} - C) - \gamma_4 C$$

The negative feedback; B large

$$\text{SinR:} \quad \frac{dR}{dt} = -\gamma_1 R$$

$$\text{SinI:} \quad \frac{dI}{dt} = -\gamma_2 I$$

$$\text{AHL inside cell:} \quad \frac{dA_i}{dt} = -\delta_1 A_i + \delta_2 A_o$$

$$\text{AHL outsice cells:} \quad \frac{dA_o}{dt} = \underbrace{B}_{:= \text{number of cells}} \left(\delta_1 A_i - \delta_2 A_o\right) - \gamma_3 A_o$$

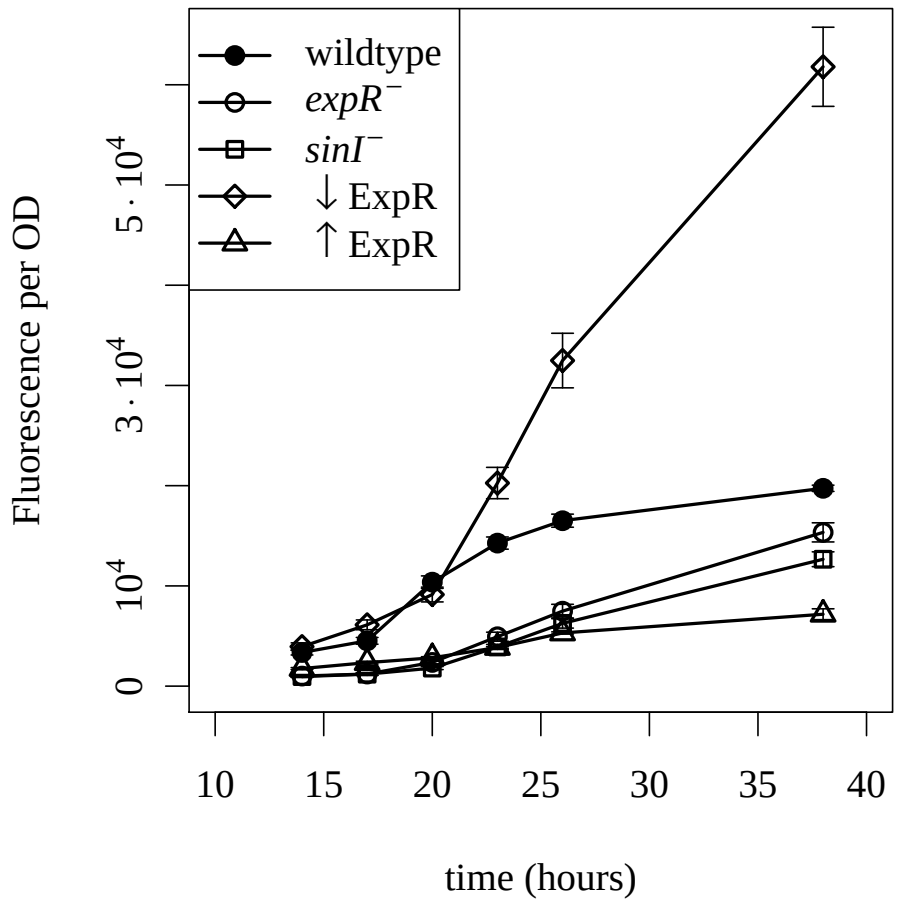
$$\text{Complex ExpR/AHL:} \quad \frac{dC}{dt} = \alpha_4 A_i \Big(\underbrace{\bar{E}}_{:=ExpR+ExpR/AHL \text{ constant}} - C \Big) - \gamma_4 C$$

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

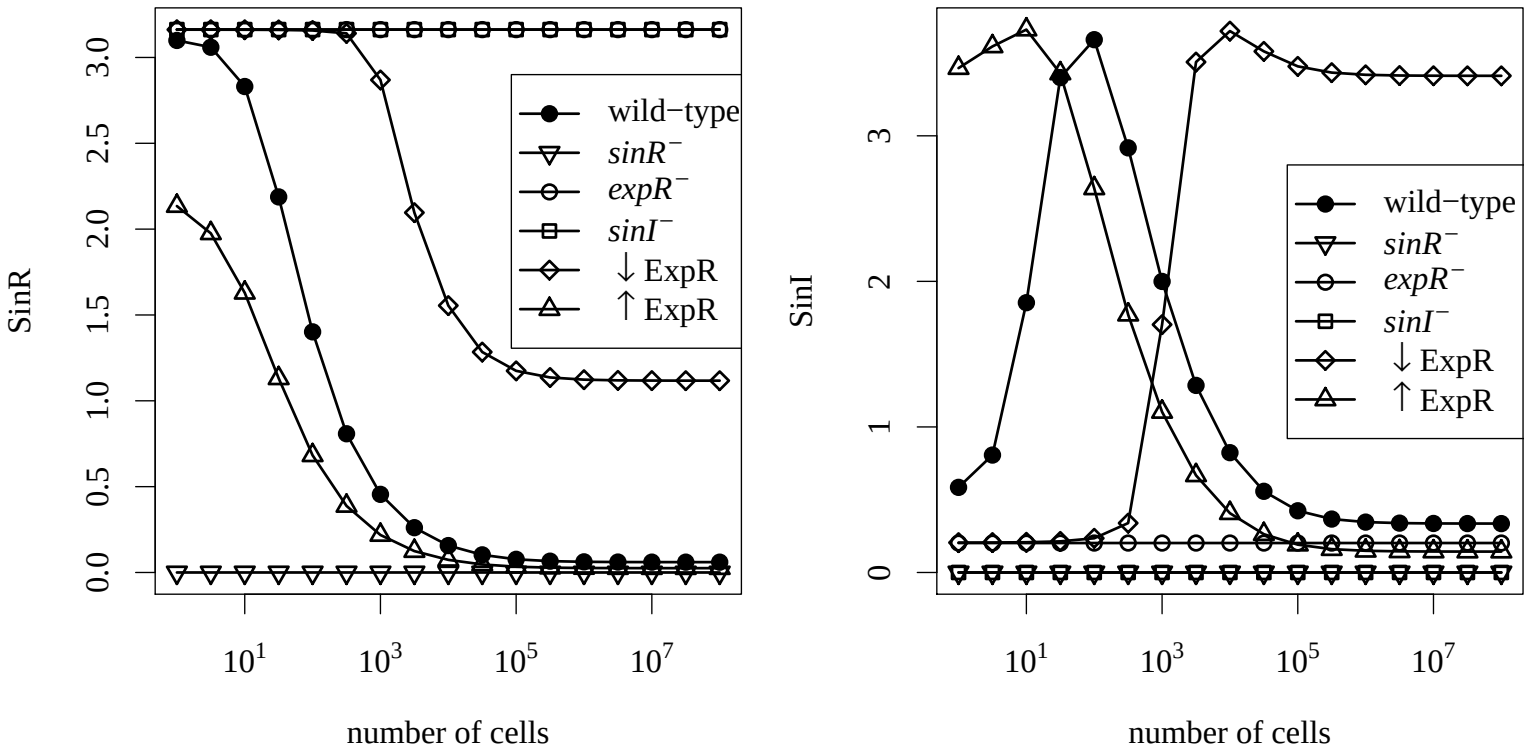
- Degradation rates of SinR and SinI high $\rightarrow$ fast reactions of the system to environment changes are possible
- System highly sensitive to amount of available ExpR (ExpR low: no negative feedback possible)

Data


wildtype
expR⁻
sinI⁻
↓ ExpR
↑ ExpR
Fluorescence per OD
0
10^4
3 · 10^4
5 · 10^4
10
15
20
25
30
35
40
time (hours)

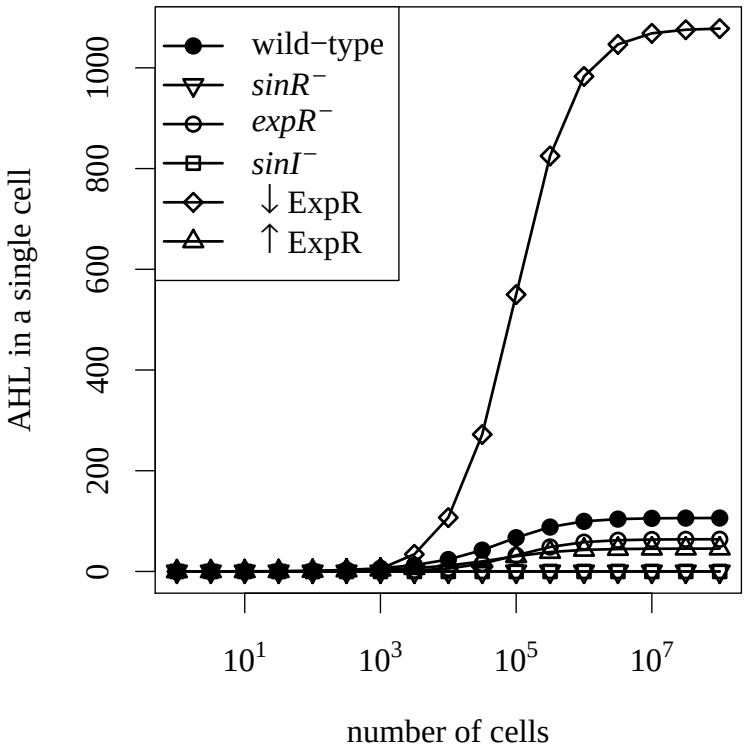
Simulation results

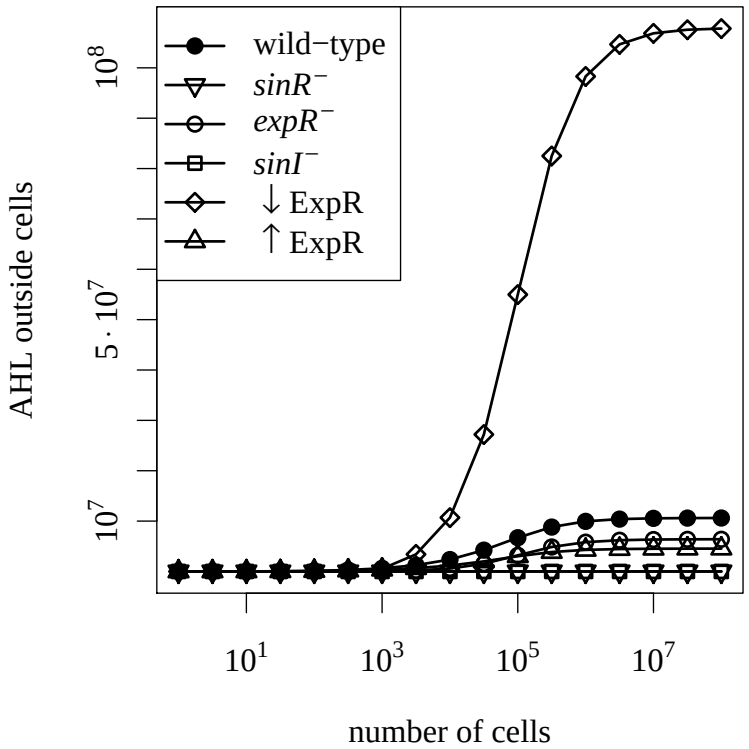
SinR and SinI are sensitive of expression of ExpR



Simulation results

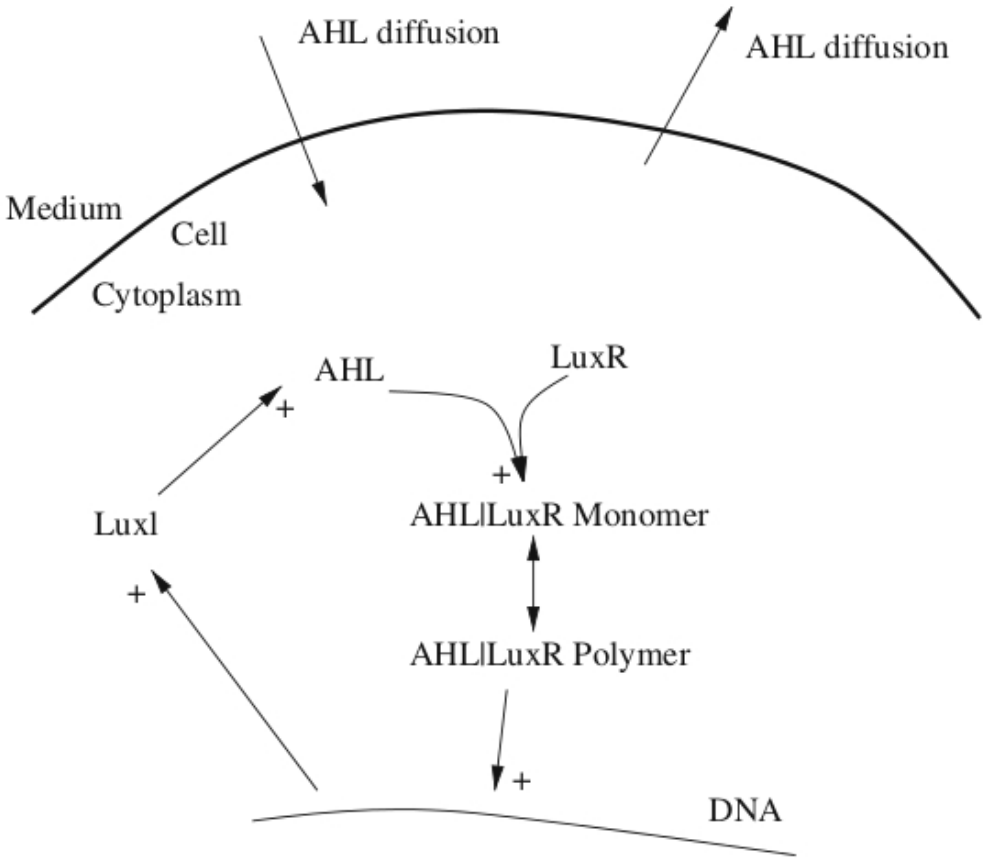
AHL inside and outside of cells show the same behavior





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

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

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

- 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