DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

PON project

C·T·S·B CONTROL THEORY & SYSTEMS BIOLOGY

ETH zürich

A Control Perspective on Antimicrobial Resistance Inhibition: from Systems to Synthetic Biology

Ph.D. candidate: **Chiara Cimolato**

Supervisor: **Luca Schenato**, Full Prof.

Co-supervisor: **Massimo Bellato**, Assist. Prof.

External Supervisor: **Mustafa Khammash**, Full Prof.

People

SynthBio@unipd
Study centre

Prof. Luca Schenato

Prof. Massimo Bellato

Prof. Mustafa Khammash

ETH zürich

Prof.ssa Barbara Di Camillo

Prof. Simone del Favero

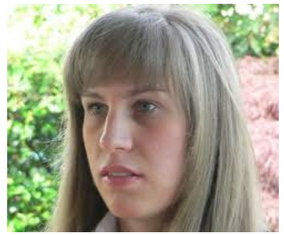
Prof. Morten Gram Pedersen

DIPARTIMENTO DI INGEGNERIA DELL'INFORMAZIONE

Prof.ssa Paola Brun

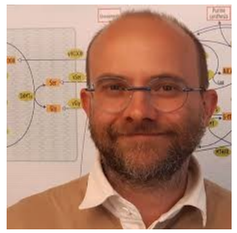
Prof. Ignazio Castegliuolo

DMM



Prof.ssa Giulia Giordano

UNIVERSITÀ DI TRENTO

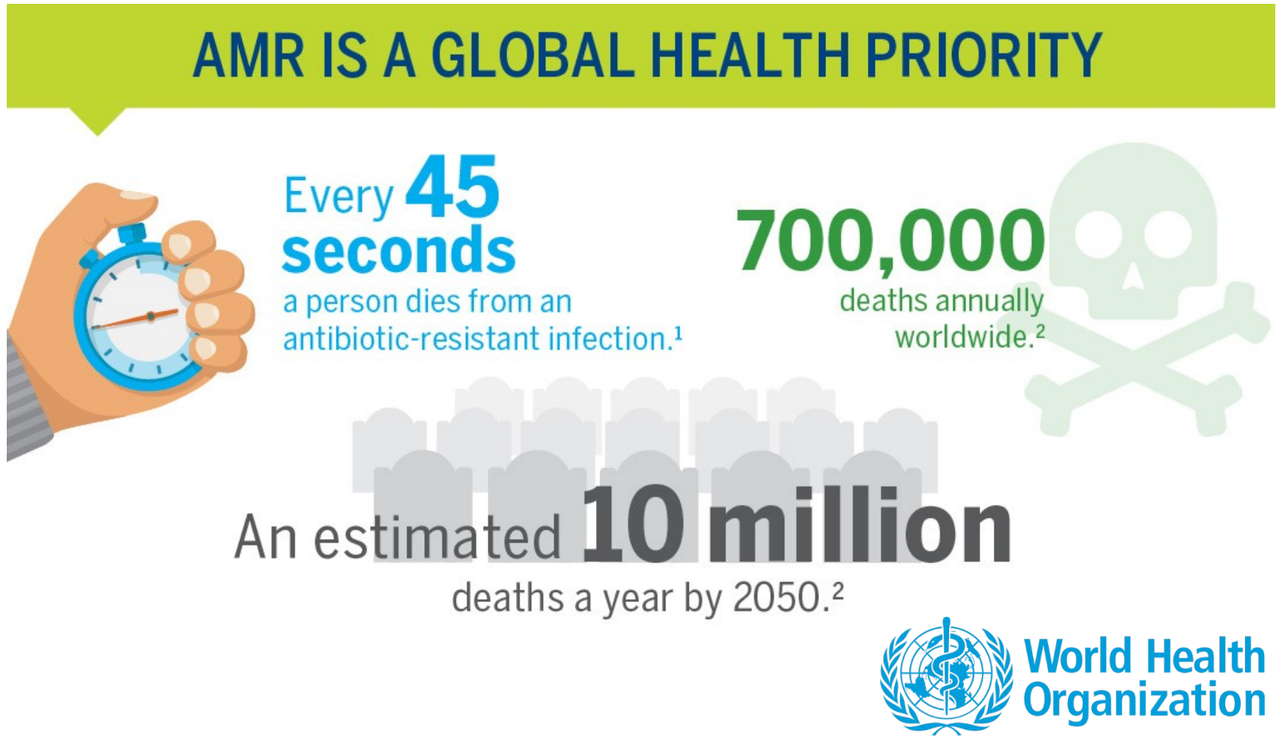


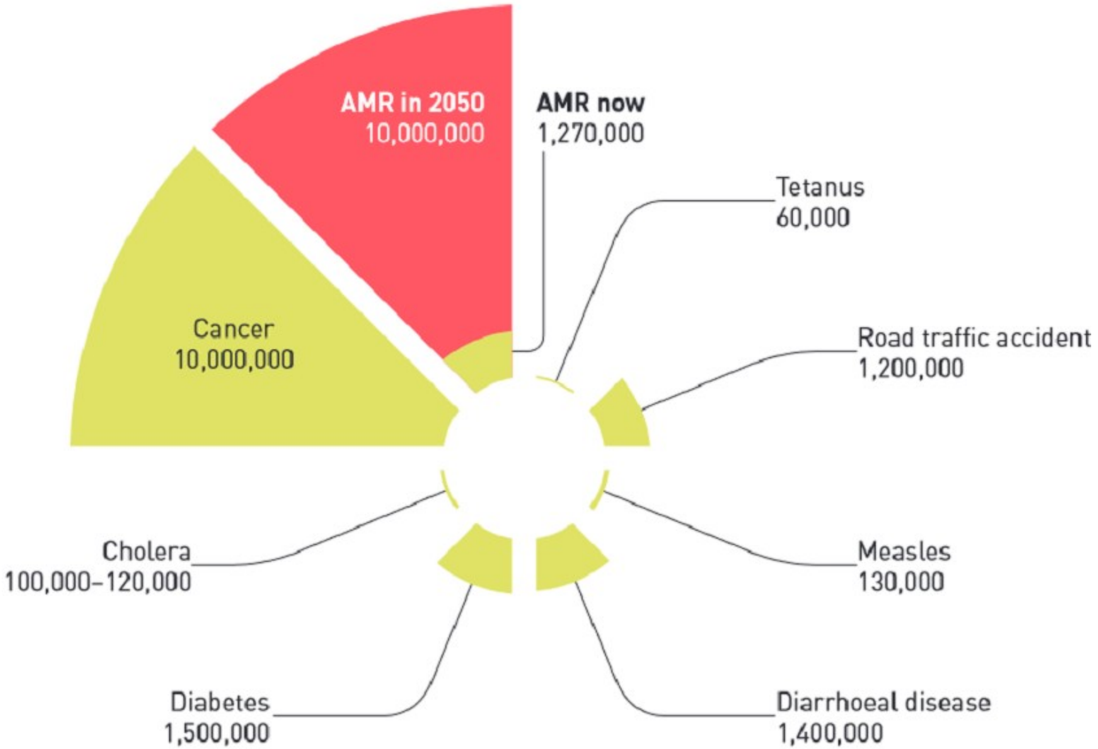
Prof. Luca Marchetti

COSBI

1. Problem of Antimicrobial Resistance (AMR)

AMR in numbers





1. Problem of Antimicrobial Resistance (AMR)

AMR abroad

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theguardian

news opinion sport arts lifestyle

UK UK politics education media society law scotland wales northern ireland

Drug resistance The Observer

‘Antibiotic apocalypse’: doctors sound alarm over drug resistance

The terrifying prospect that even routine operations will be impossible to perform has been raised by experts alarmed by the rise of drug-resistant genes

AMR in Italy

G Salute & benessere

IL GAZZETTINO

65%

97%

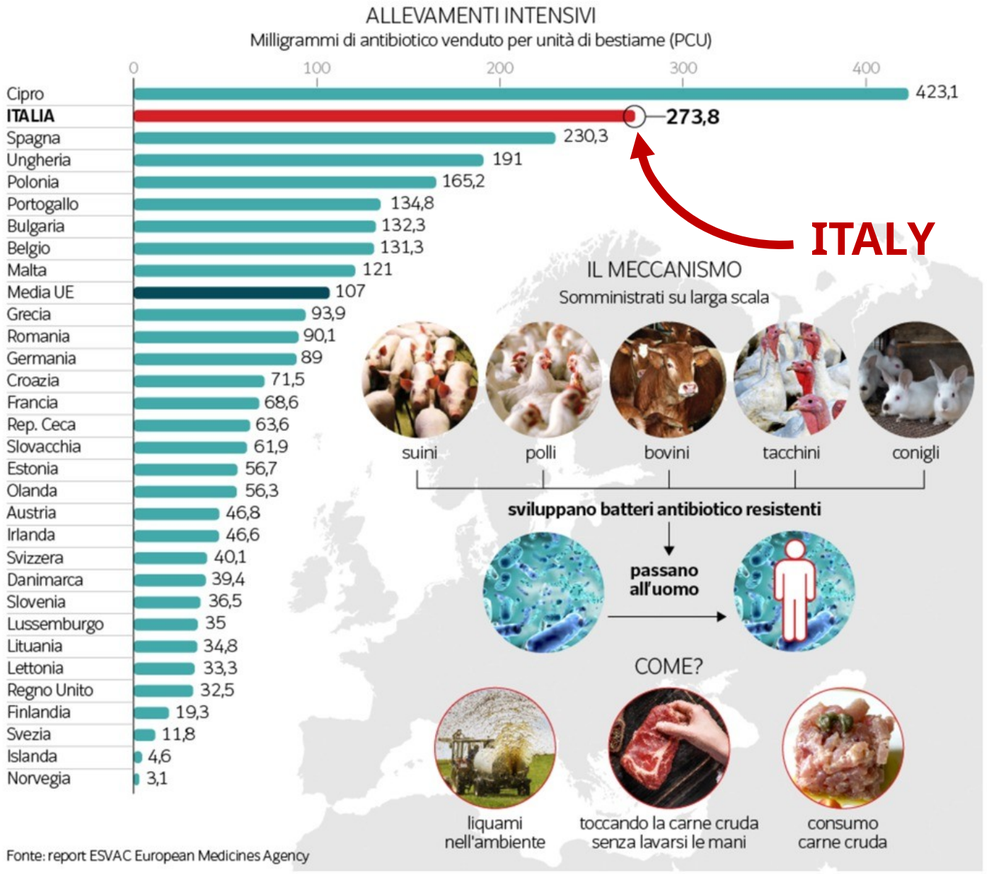
86%

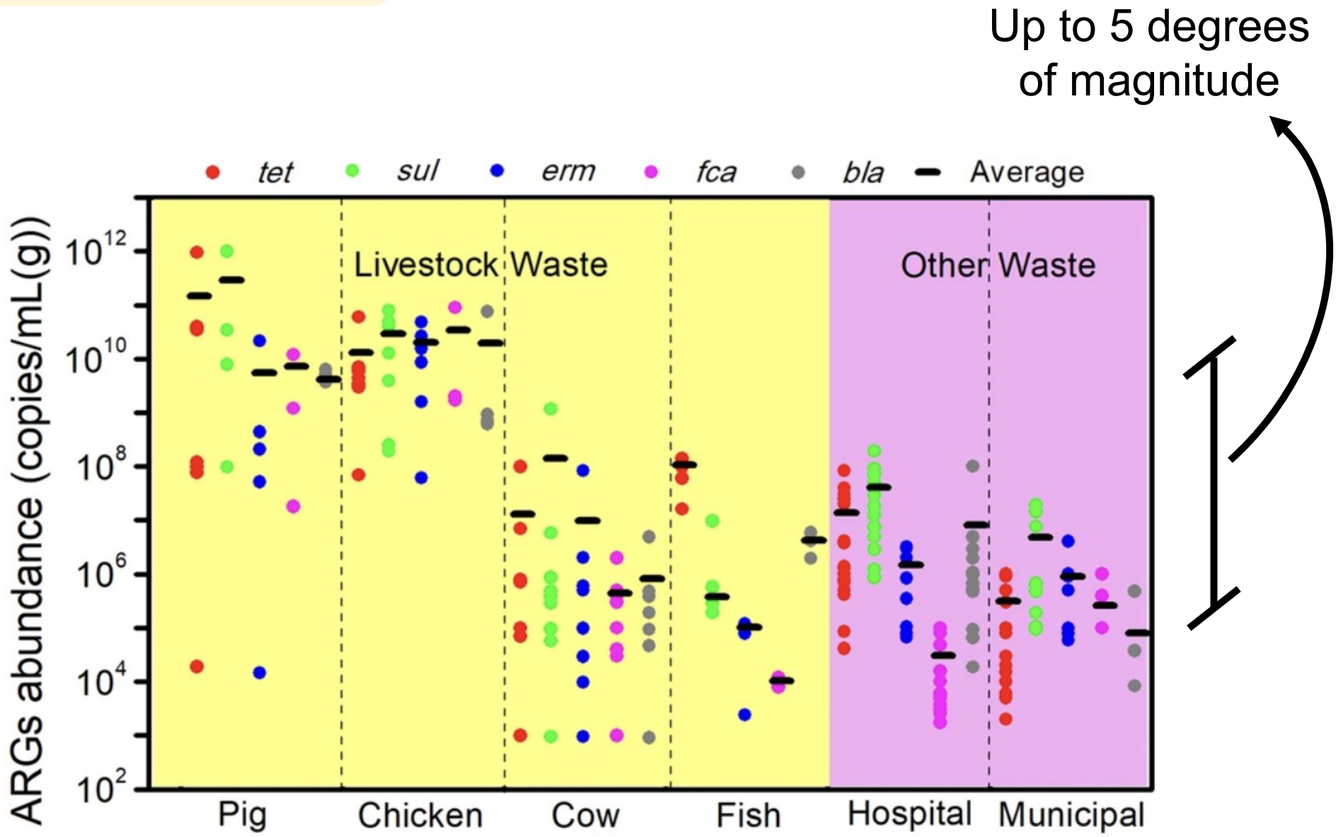
In Italia record di morti da antibiotico-resistenza

Allarme allergie, lattice nelle siringhe dei vaccini

1. Problem of Antimicrobial Resistance (AMR)

The One Health Approach





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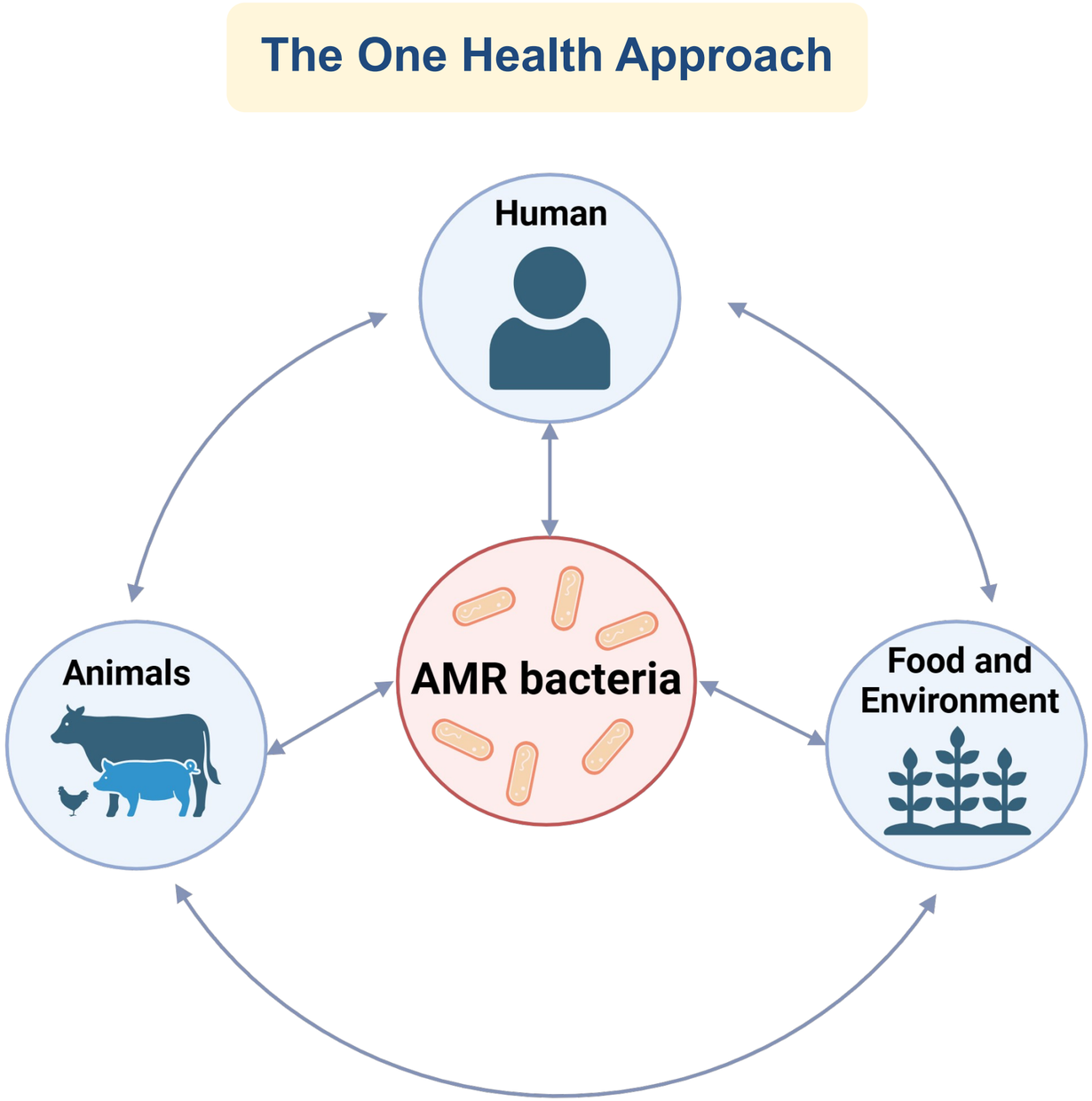
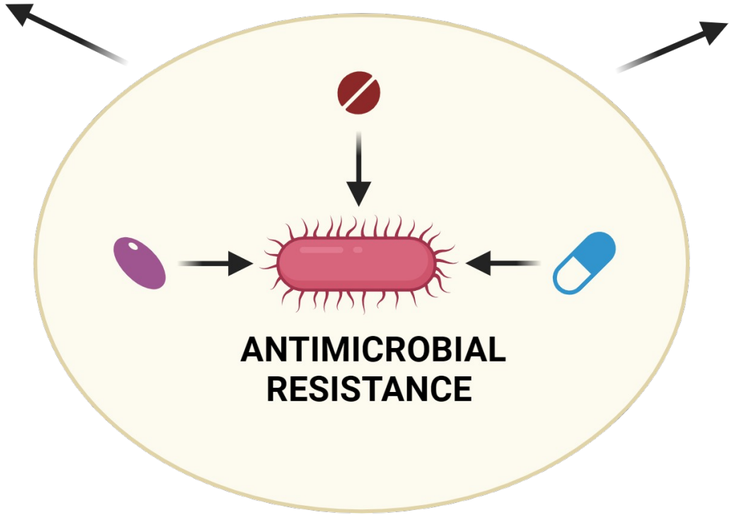


1. Problem of Antimicrobial Resistance (AMR)

CHALLENGES

- **Complexity** of Resistance Mechanisms
- **Mutations** and **horizontal gene transfer**
- Off-target Effects and **Safety** Risks



CUTTING-EDGE TRENDS

- Identify **novel drugs**
- Edit genetic material with **CRISPR** → Geeta Ram et al., ***Nature Biotechnology,*** 2018.
- **Bacteriophages**, that can kill the bacteria → ***"Center for Innovative Phage Applications and Therapeutics",*** first phage therapy center in US
- Interefere with **Quorum Sensing** → P. Piewngam et al., ***Nature,*** 2018.

1. Problem of Antimicrobial Resistance (AMR)

CHALLENGES

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- **Mutations** and **horizontal gene transfer**
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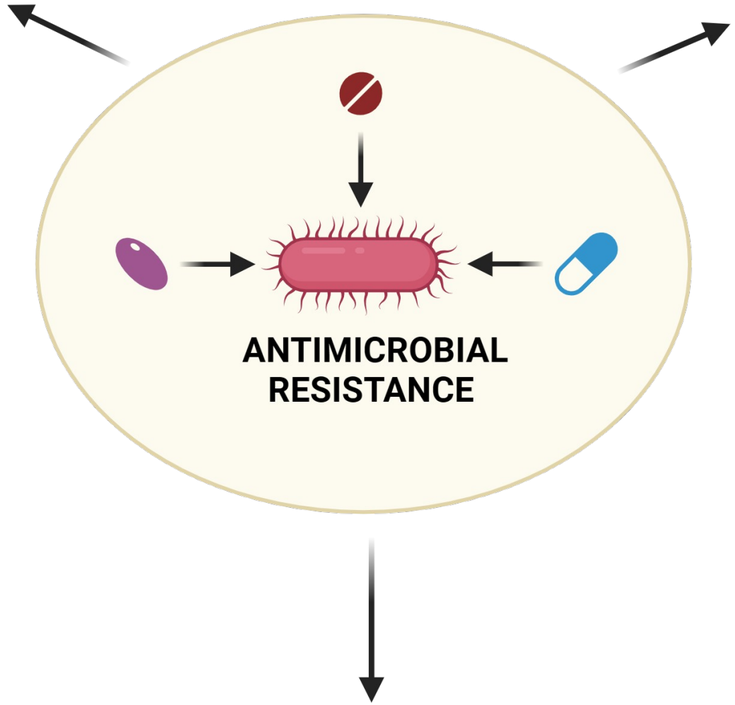


CUTTING-EDGE TRENDS

- Identify **novel drugs**
- Edit genetic material with **CRISPR**
- **Bacteriophages**, that can kill the bacteria

First Strategy

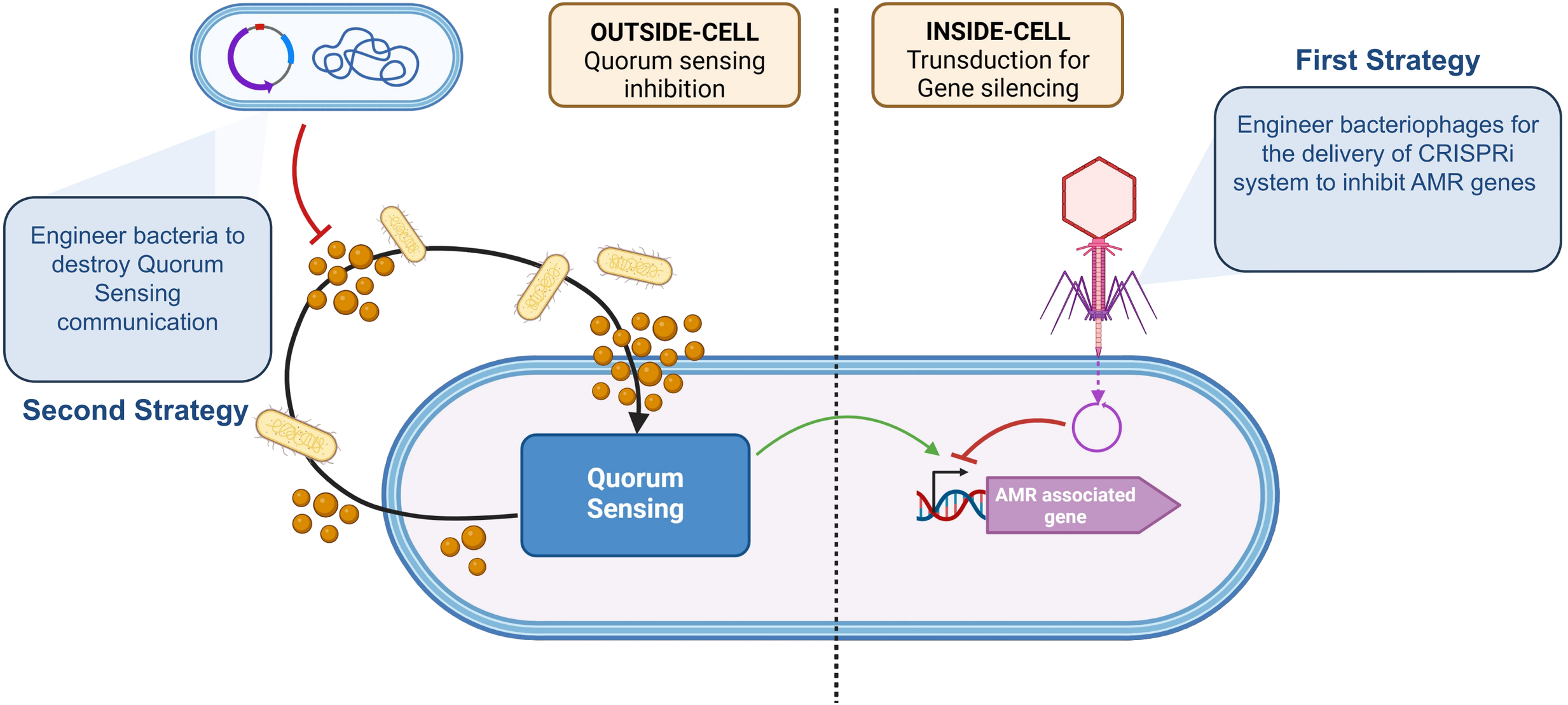
- Interefere with **Quorum Sensing**

Second Strategy

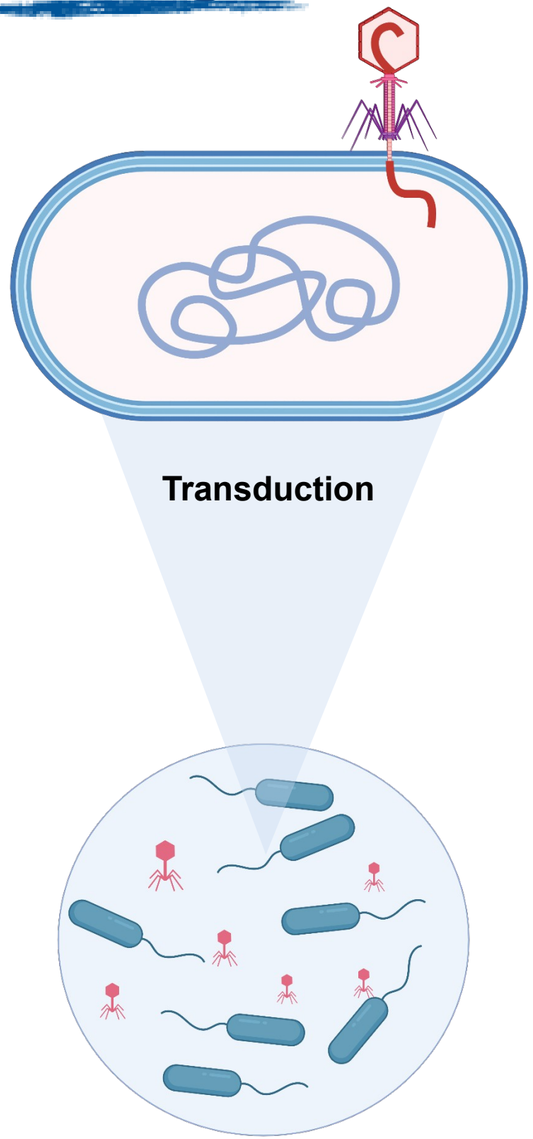
OUR OBJECTIVE

Exploit Synthetic Biology to **restore sensitivity on antibiotics** with a **twofold approach**

1. Antimicrobial Resistance Mechanisms



2. Phage-Mediated CRISPRi System



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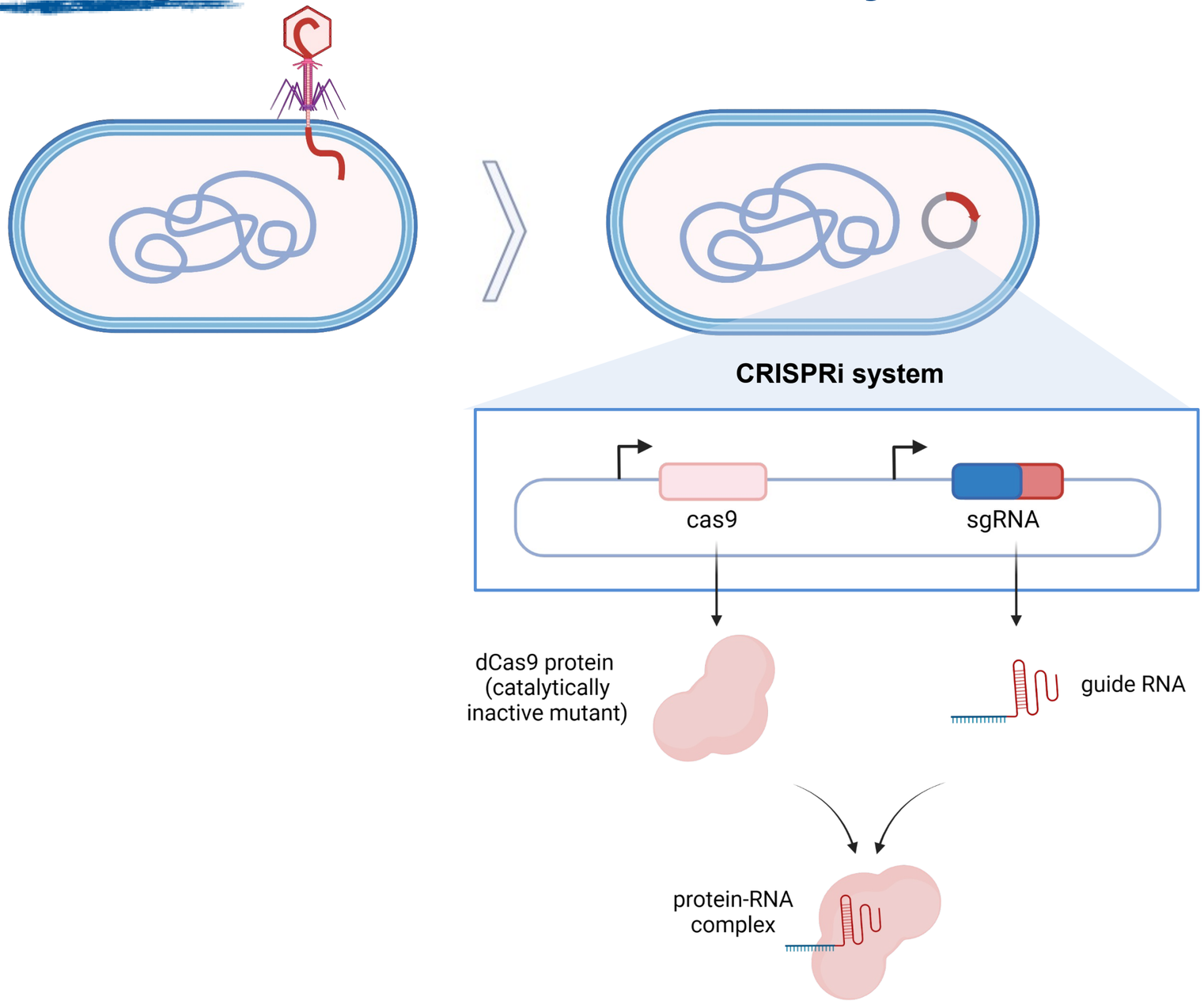

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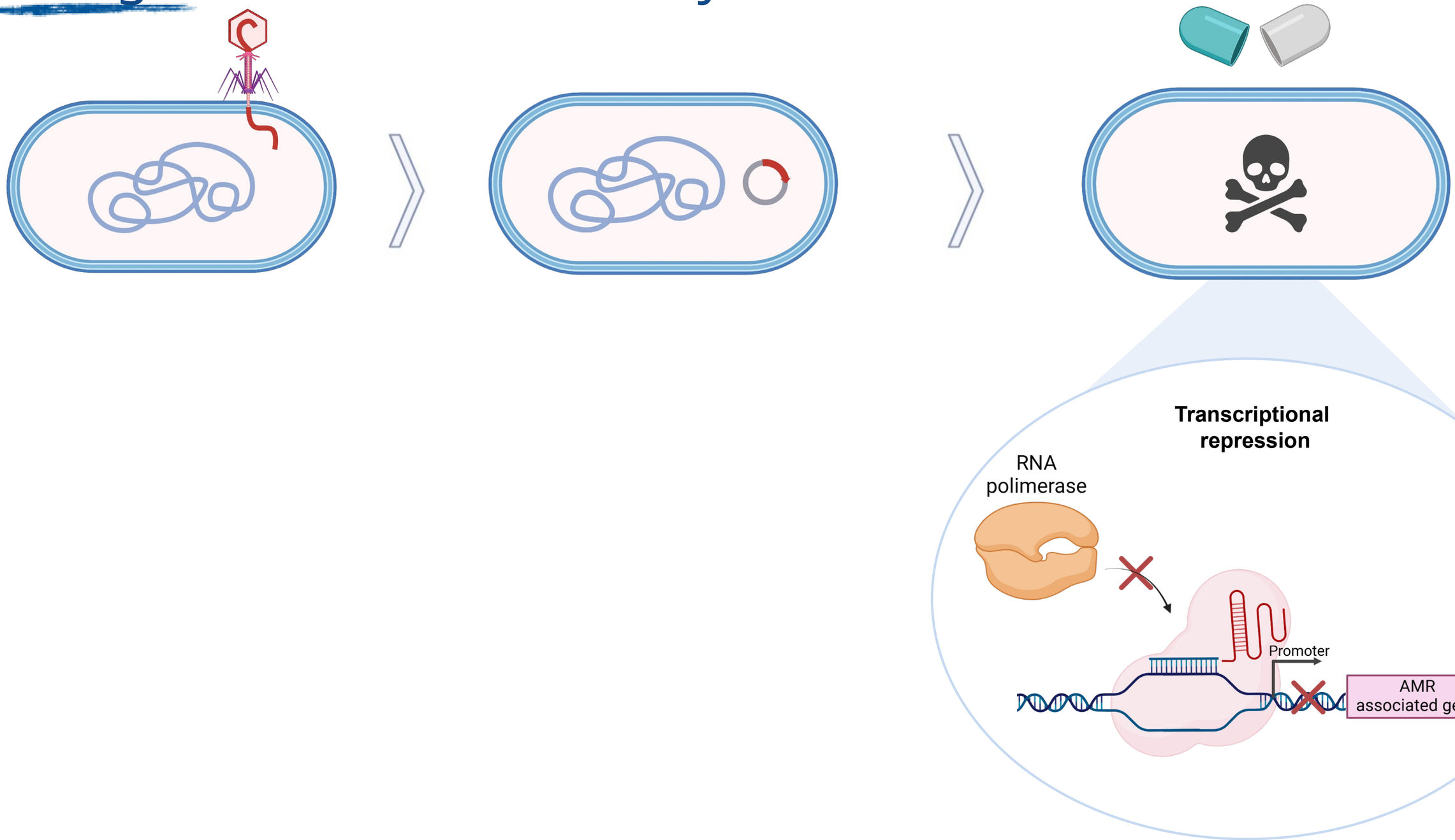

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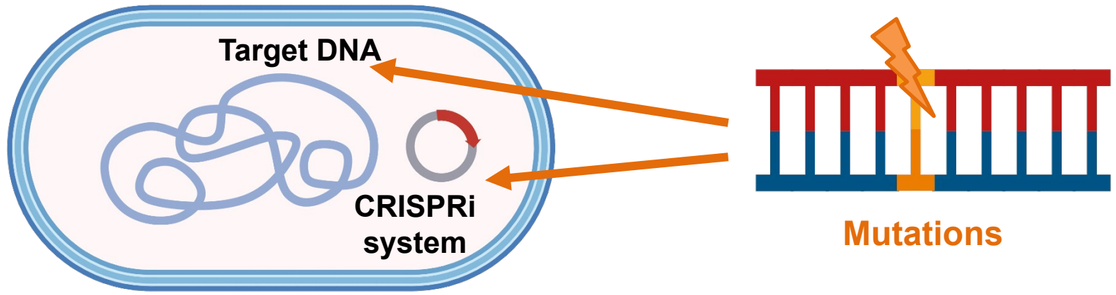
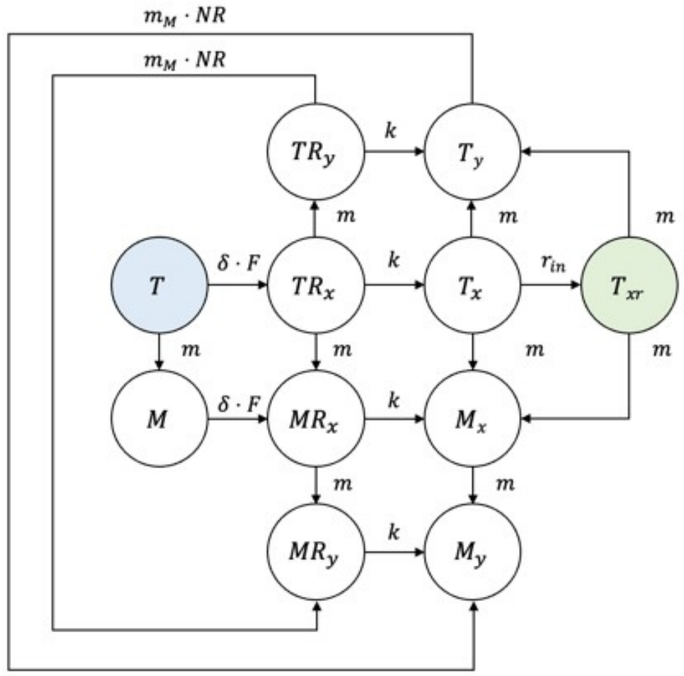


Transit compartmental model



$$\frac{dT}{dt} = -\delta \cdot F \cdot T - m \cdot T + [\lambda - w] \cdot T$$
$$\frac{dM}{dt} = -\delta \cdot F \cdot M + m \cdot T + [\lambda - w] \cdot M$$
$$\frac{dTR_x}{dt} = +\delta \cdot F \cdot T - (k + 2m) \cdot TR_x + [\lambda - w] \cdot TR_x$$
$$\frac{dTR_y}{dt} = +m \cdot TR_x - (k + m) \cdot TR_y + [\lambda - w] \cdot TR_y$$
$$\frac{dMR_x}{dt} = +\delta \cdot F \cdot M + m \cdot TR_x - (k + m) \cdot MR_x + [\lambda - w] \cdot MR_x$$
$$\frac{dMR_y}{dt} = +m \cdot MR_x + m \cdot TR_y - k \cdot MR_y + [\lambda - w] \cdot MR_y$$
$$\frac{dT_x}{dt} = +k \cdot TR_x - (r_{in} + 2m) \cdot T_x + [\lambda - w] \cdot T_x$$
$$\frac{dT_y}{dt} = +k \cdot TR_y + m \cdot (T_x + T_{xr}) - m \cdot T_y + [\lambda - w] \cdot T_y$$
$$\frac{dM_x}{dt} = +k \cdot MR_x + m \cdot (T_x + T_{xr}) - m \cdot M_x + [\lambda - w] \cdot M_x$$
$$\frac{dM_y}{dt} = +k \cdot MR_y + m \cdot T_y + m \cdot M_x + [\lambda - w] \cdot M_y$$
$$\frac{dT_{xr}}{dt} = +r_{in} \cdot T_x - 2m \cdot T_{xr} + [\lambda - w] \cdot T_{xr} - A \cdot T_{xr}$$
$$\frac{dF}{dt} = -\delta \cdot (T + M) - w \cdot F$$

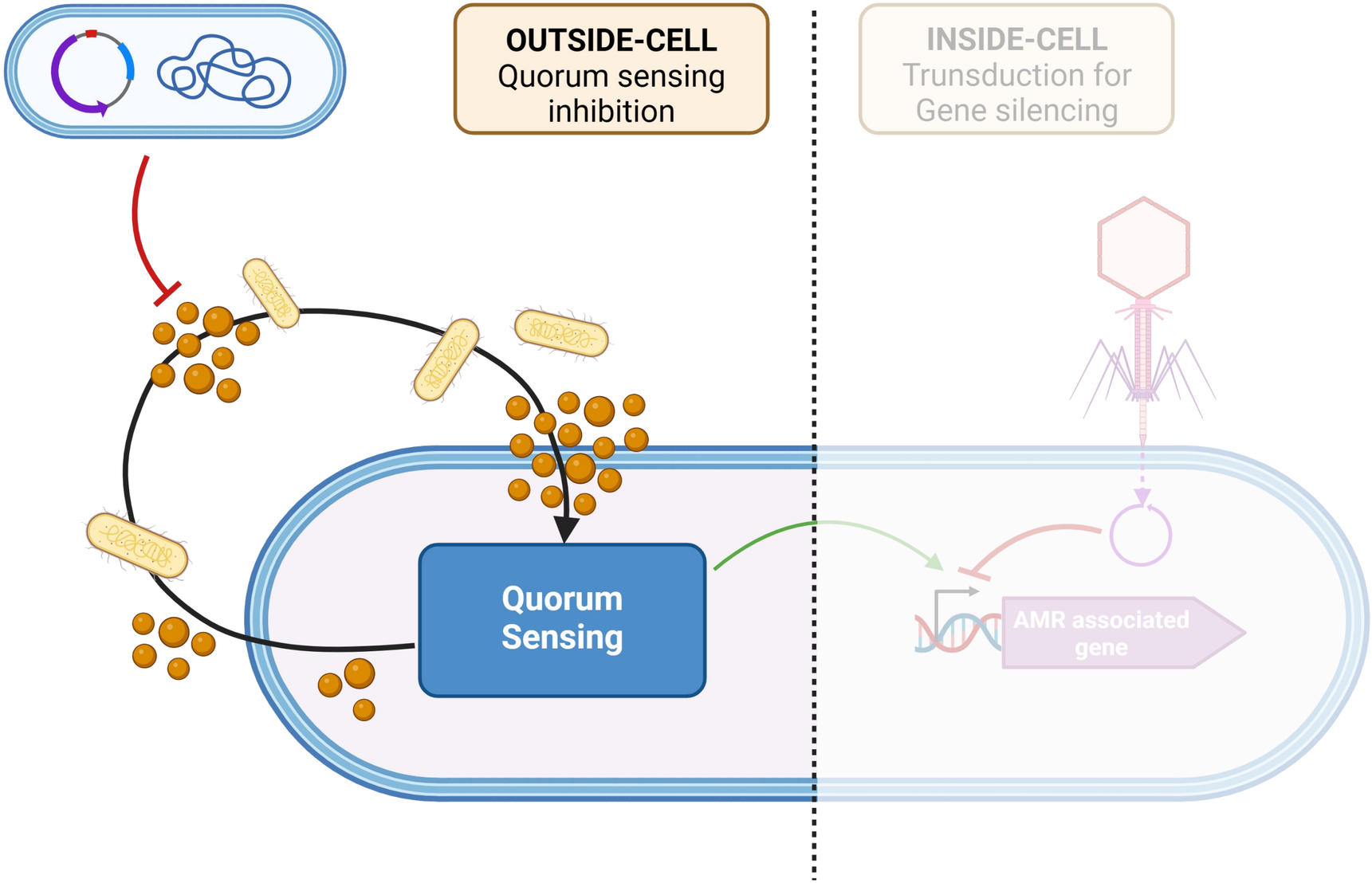
CONTRIBUTION

Develop a mathematical model of the phage-mediated CRISPRi system, with specific **focus** on the **mutations dynamics**

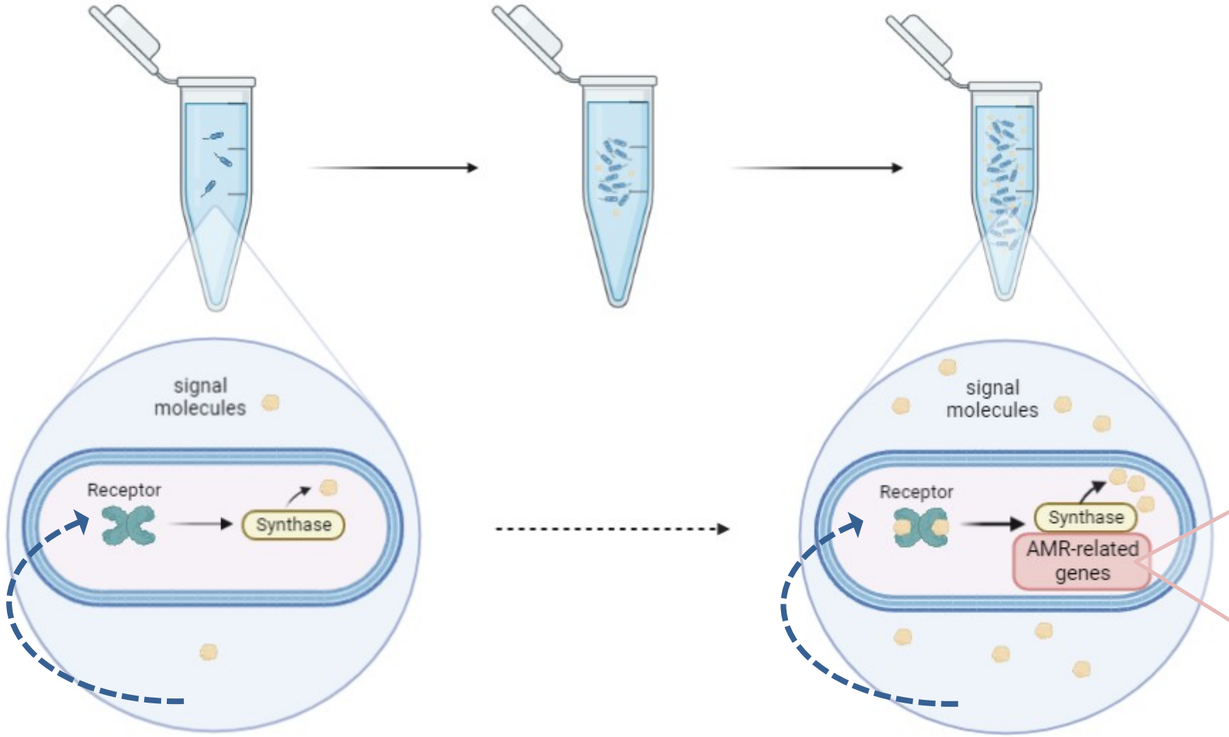
[1] M. Bellato, **C. Cimolato**, S. Letrari, L. Schenato, BBCC 2024

[2] S. Letrari, **C. Cimolato**, et al., 2023 International Conference on Microbiome Engineering

3. Antimicrobial Resistance Mechanisms

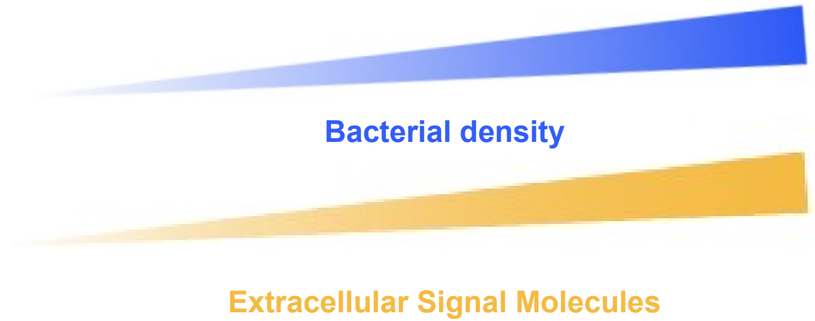


3. Quorum Sensing in Gram Negative bacteria

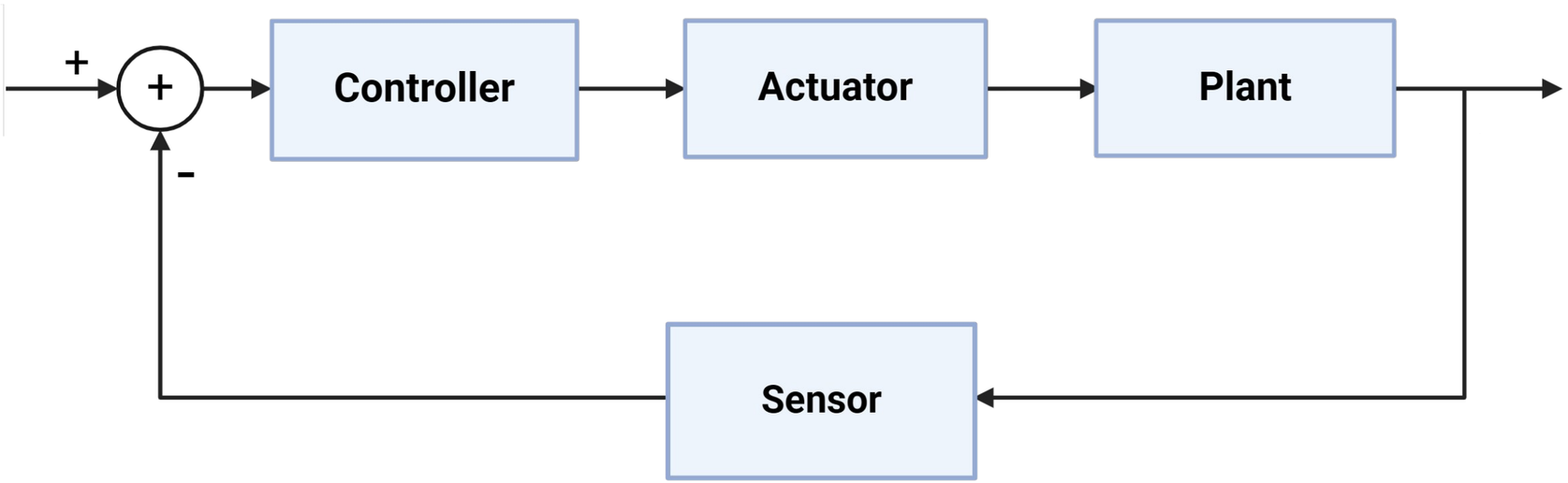


QS-regulated processes:

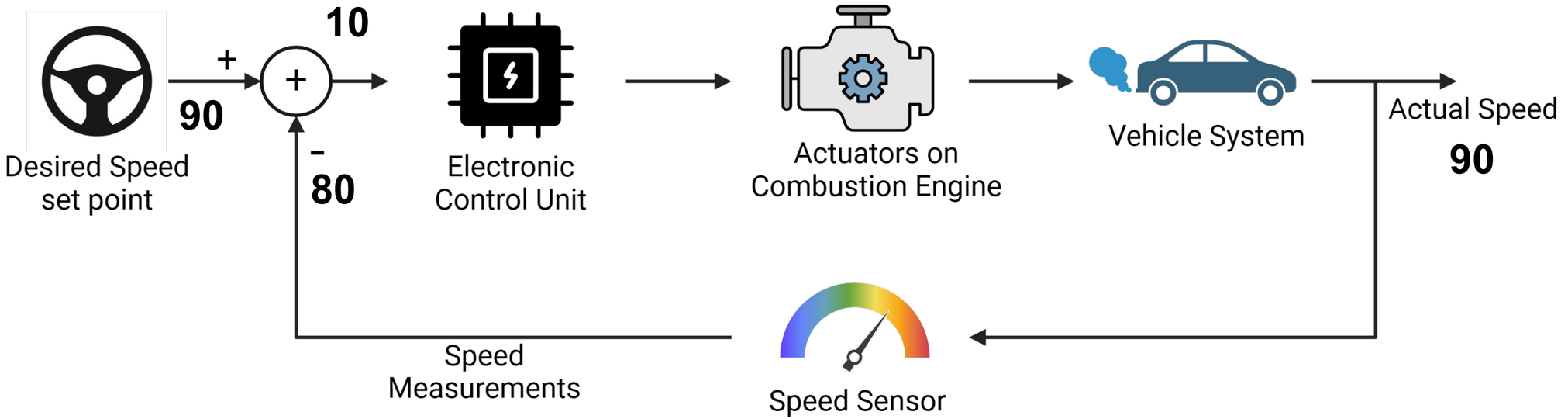
- **Biofilm formation**
- Horizontal gene transfer
- Production of extracellular polysaccharides, enzymes, antibiotics, etc.



3. A control perspective

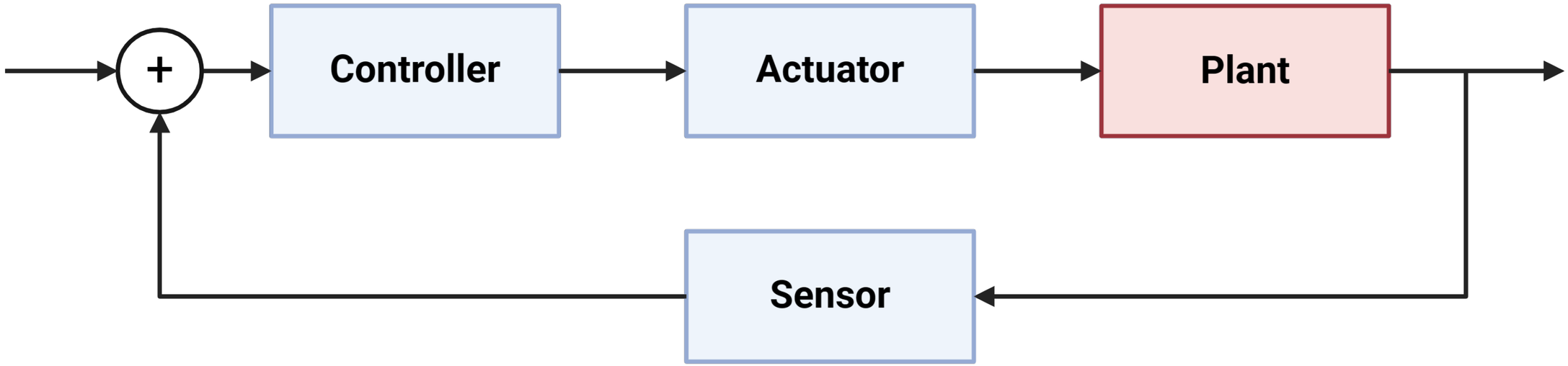


3. A control perspective



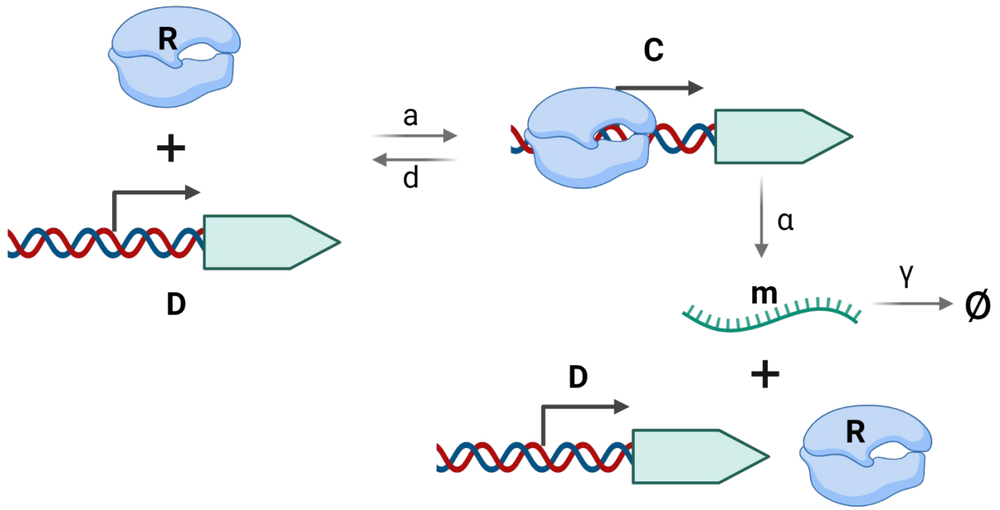
Cruise control system

3. Modelling of the Plant



3. From biology to mathematical models

Biology



Kinetic reactions

$$\mathrm{D} + \mathrm{R} \underset{\mathrm{d}}{\overset{\mathrm{a}}{\rightleftharpoons}} \mathrm{C}$$

$$\mathrm{C} \xrightarrow{\alpha} \mathrm{m} + \mathrm{D} + \mathrm{R}$$

$$\mathrm{m} \xrightarrow{\gamma} \emptyset$$

Conservation of mass

$$D^{TOT} = D + C$$

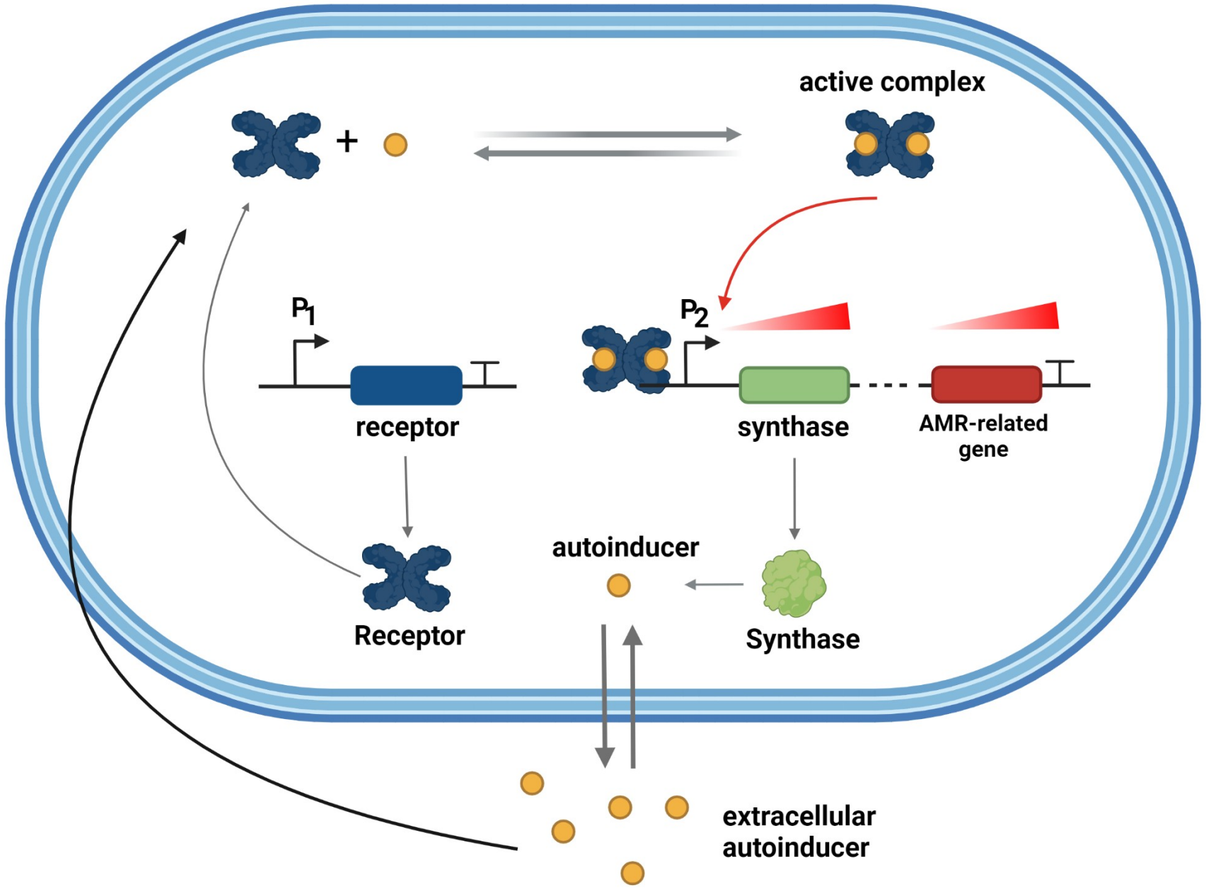
$$R^{TOT} = R + C$$

Dynamic model

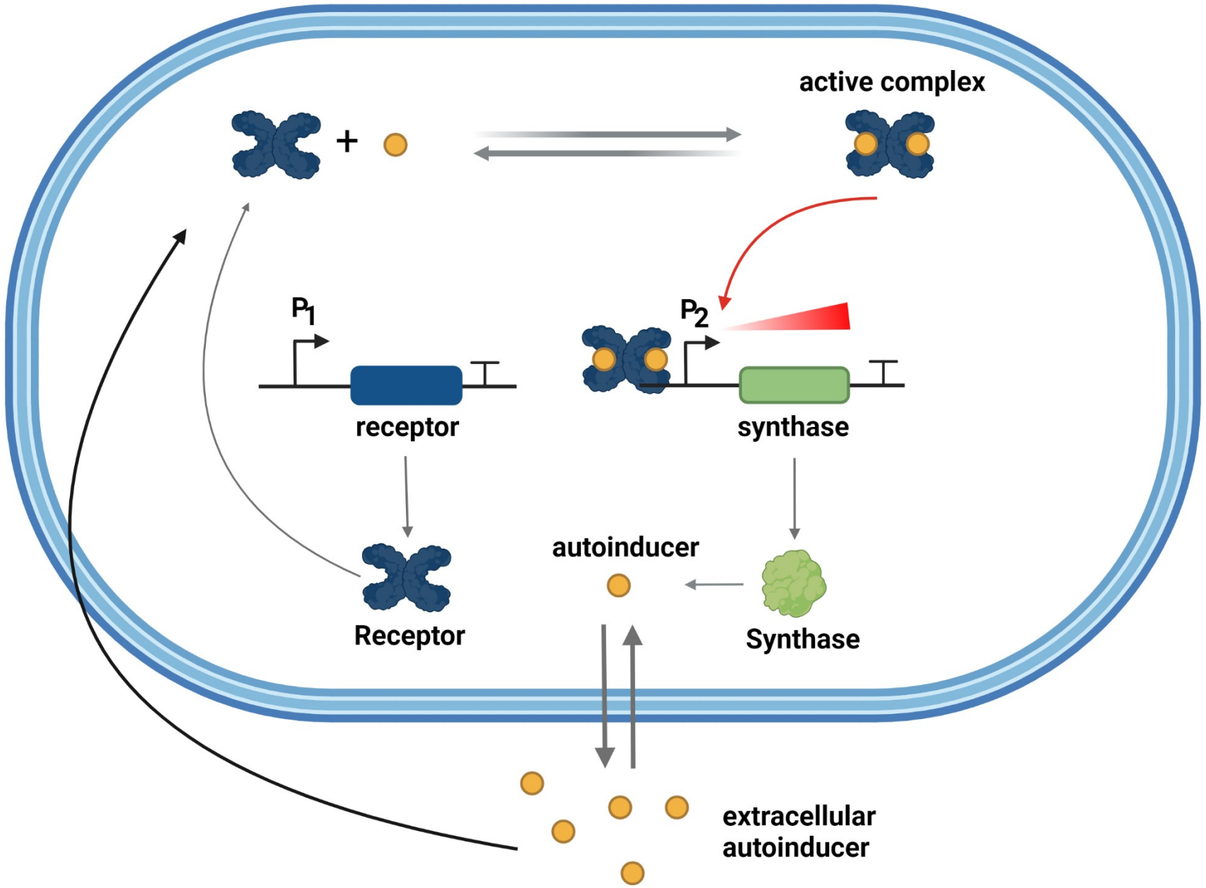
$$\begin{aligned}
\frac{dC}{dt} &= aDR - dC - \alpha C \\
\frac{dm}{dt} &= \alpha C - \gamma m \\
\frac{dR}{dt} &= -aDR + dC + \alpha C \\
\frac{dD}{dt} &= -aDR + dC + \alpha C
\end{aligned}$$

Mechanical derivation (*Systems Biology*, MS class DEI)

3. Single feedback QS system



3. Single feedback QS system



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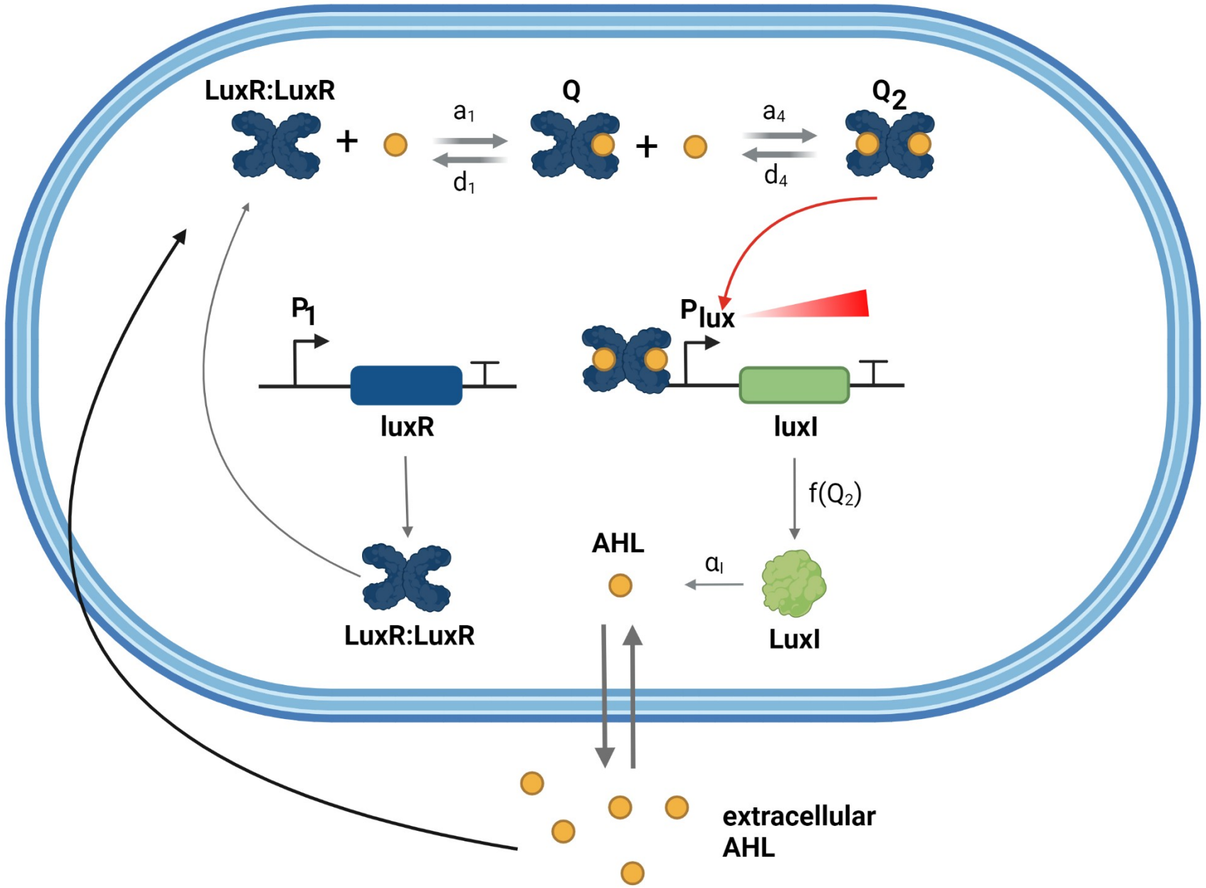
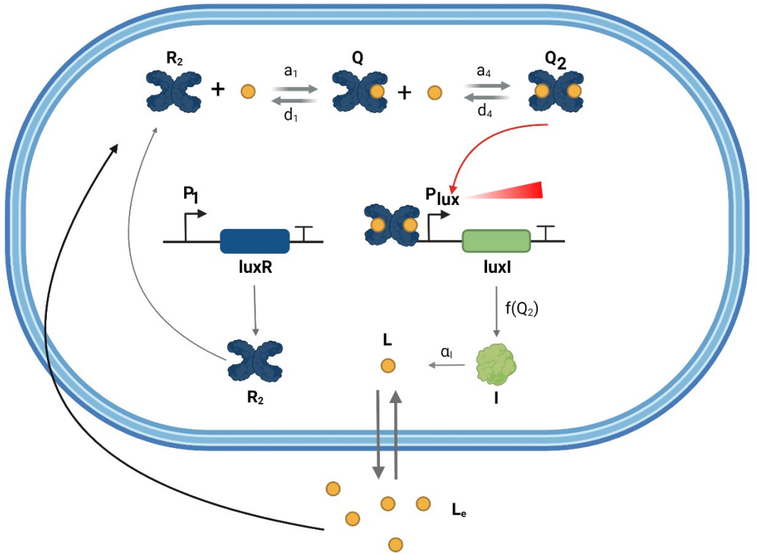


3. Single feedback QS system



Reactions

$$R_2 + L \underset{d_1}{\overset{a_1}{\rightleftharpoons}} Q$$

$$Q + L \underset{d_4}{\overset{a_4}{\rightleftharpoons}} Q_2$$

$$\emptyset \xrightarrow{f(Q_2)} I$$

$$I \xrightarrow{\alpha_I} L + I$$

$$I \xrightarrow{\gamma_I} \emptyset$$

$$L \xrightarrow{\gamma_L} \emptyset$$

$$L_e \xrightarrow{\gamma_{Le}} \emptyset$$

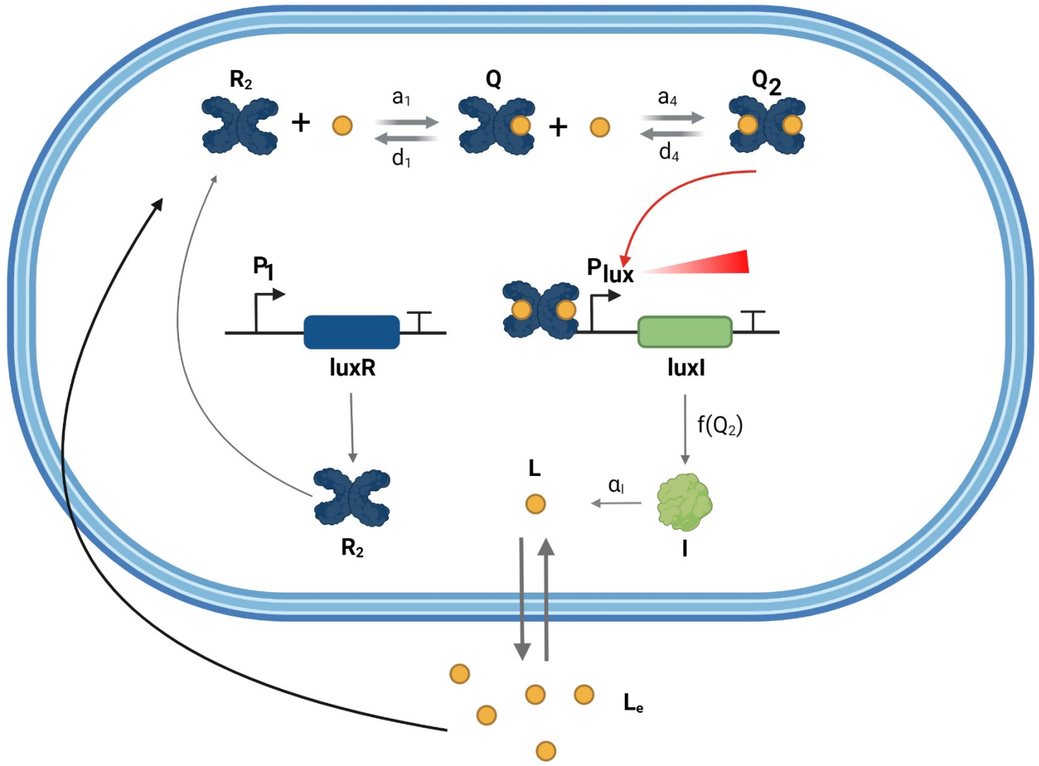
Conservation of mass

$$\begin{aligned} R_2^{TOT} &= R_2 + Q + Q_2 = R_2^{TOT}(0) \\ L^{TOT} &= L + Q + 2Q_2 \end{aligned}$$

Model

$$\begin{aligned}
\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I \\
\frac{dL}{dt} &= \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L) \\
\frac{dL_e}{dt} &= K_{15} \frac{N V_I}{V - N V_I}(L - L_e) - \gamma_{L_e} L_e \\
\frac{dR_2}{dt} &= d_1 Q - K_1 d_1 R_2 L \\
\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 \\
\frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2
\end{aligned}$$

3. Single feedback QS system



Reactions

$$R_2 + L \underset{d_1}{\overset{a_1}{\rightleftharpoons}} Q$$
$$Q + L \underset{d_4}{\overset{a_4}{\rightleftharpoons}} Q_2$$
$$\emptyset \xrightarrow{f(Q_2)} I$$
$$I \xrightarrow{\alpha_I} L + I$$
$$I \xrightarrow{\gamma_I} \emptyset$$
$$L \xrightarrow{\gamma_L} \emptyset$$
$$L_e \xrightarrow{\gamma_{Le}} \emptyset$$

Conservation of mass

$$R_2^{TOT} = R_2 + Q + Q_2 = R_2^{TOT}(0)$$
$$L^{TOT} = L + Q + 2Q_2$$

Model

$$\frac{dI}{dt} = \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I$$

$$\frac{dL}{dt} = \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L)$$

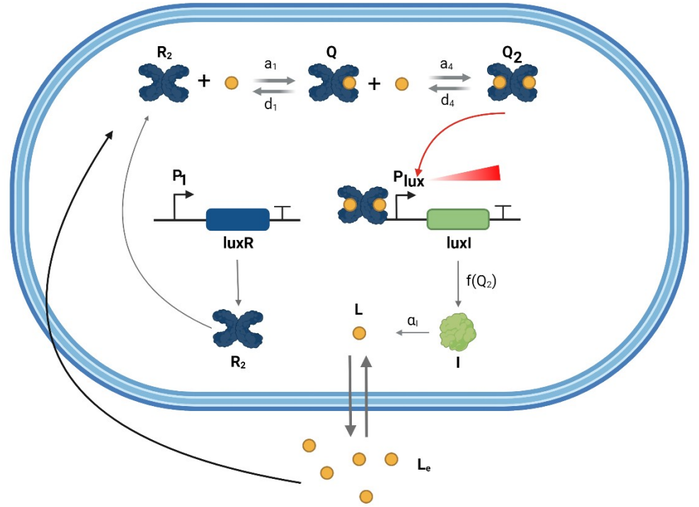
$$\frac{dL_e}{dt} = K_{15}\frac{NV_I}{V - NV_I}(L - L_e) - \gamma_{Le} L_e$$

$$\frac{dR_2}{dt} = d_1 Q - K_1 d_1 R_2 L$$

$$\frac{dQ}{dt} = K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2$$

$$\frac{dQ_2}{dt} = K_4 d_4 Q L - d_4 Q_2$$

3. Single feedback QS system



Quasi steady state approximation

$$\begin{aligned}\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 = 0\\ \frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2 = 0\end{aligned}$$

Conservation of mass

$$\begin{aligned}R_2 &= \frac{1}{1+K_1 L+\frac{K_1^2}{4}L^2} R_2^{TOT}\\ Q &= \frac{K_1 L}{1+K_1 L+\frac{K_1^2}{4}L^2} R_2^{TOT}\\ Q_2 &= \frac{\frac{K_1^2}{4}L^2}{1+K_1 L+\frac{K_1^2}{4}L^2} R_2^{TOT}\end{aligned}$$

Simplified model

$$\begin{aligned}\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux}-\beta_{lux}}{1+\frac{K_{lux}}{Q_2}} - \gamma_I I\\ \frac{dL}{dt} &= \alpha_I I - \gamma_L L + K_{15}(L_e - L)\\ \frac{dL_e}{dt} &= K_{15}\frac{NV_I}{V-NV_I}(L-L_e) - \gamma_{L_e} L_e\\ Q_2 &= \frac{\frac{K_1^2}{4}L^2}{1+K_1 L+\frac{K_1^2}{4}L^2} R_2^{TOT}.\end{aligned}$$

3. Equilibria Analysis

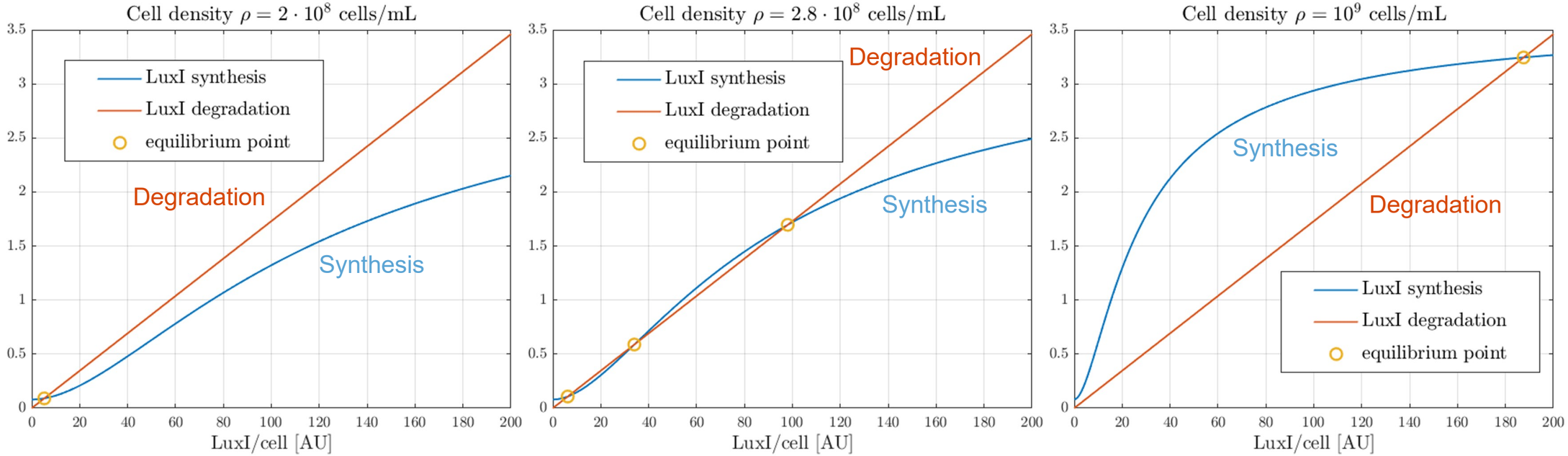
intr. autoinducer
synthase
$_2$ = receptor

$$\frac{dI}{dt} = \underbrace{\beta_{lux} + (\alpha_{lux} - \beta_{lux}) \frac{(\frac{K_1}{2}\chi I)^2}{(\frac{K_1}{2}\chi I)^2 + \frac{K_{lux}}{R_2^{TOT}}(1 + \frac{K_1}{2}\chi I)^2}}_{=synt_I} - \underbrace{\gamma_I I}_{=deg_I} = 0$$

where $\chi = \frac{\alpha_I(\frac{K_{15}\rho V_I}{1-\rho V_I} + \gamma_{L_e})}{(\frac{K_{15}\rho V_I}{1-\rho V_I} + \gamma_{L_e})\gamma_L + K_{15}\gamma_{L_e}}$

$L \propto I$

ρ = cell density



Low cell density **ρ**

Threshold cell density **ρ**

High cell density **ρ**

3. Bifurcation Diagram

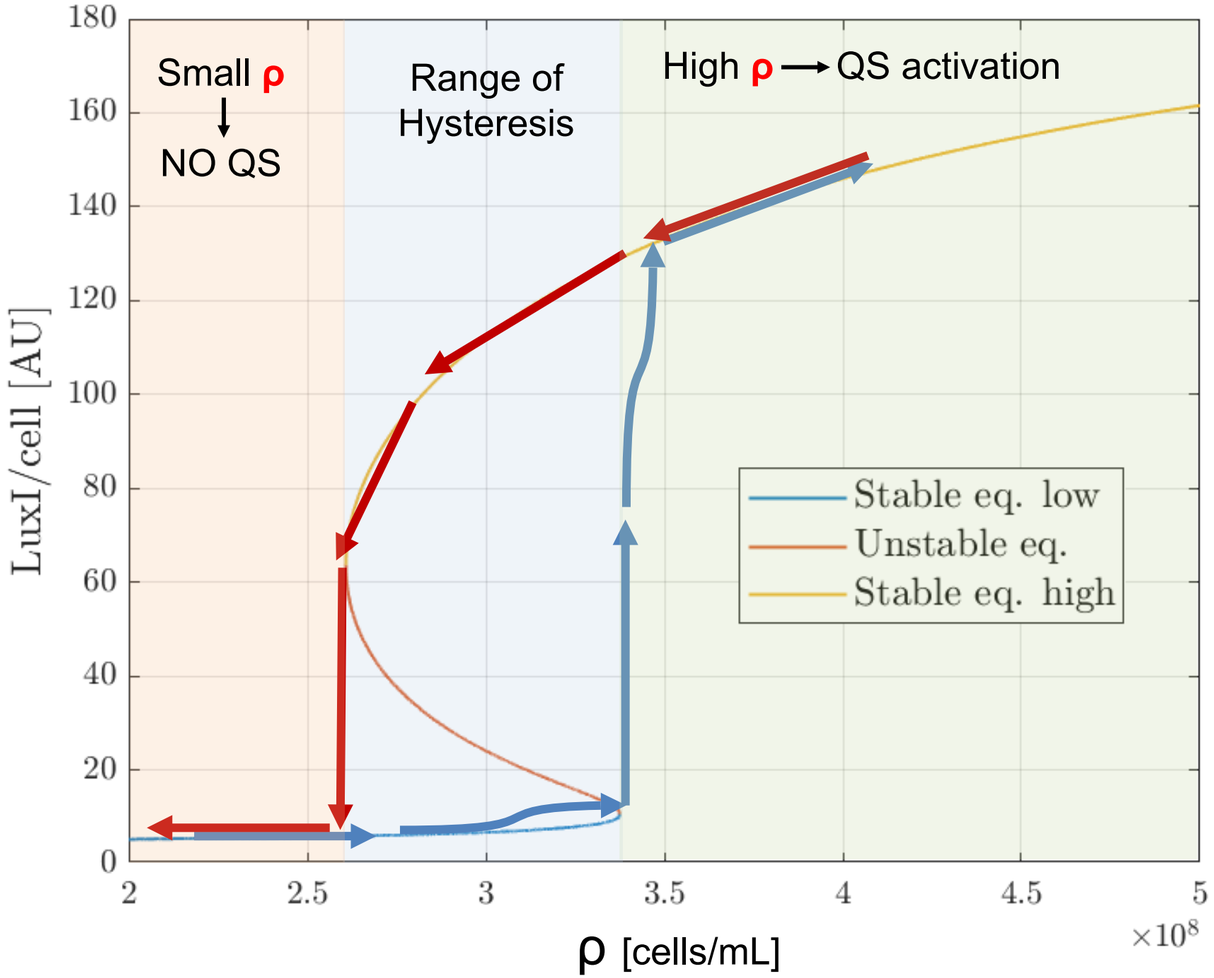
$$\frac{dI}{dt} = \underbrace{\beta_{lux} + (\alpha_{lux} - \beta_{lux})\frac{(\frac{K_1}{2}\chi I)^2}{(\frac{K_1}{2}\chi I)^2 + \frac{K_{lux}}{R_2^I OT}(1+\frac{K_1}{2}\chi I)^2}}_{=synt_I} - \underbrace{\gamma_I I}_{=deg_I} = 0$$

where

$$\chi = \frac{\alpha_I(\frac{K_{15}\rho V_I}{1-\rho V_I} + \gamma_{L_e})}{(\frac{K_{15}\rho V_I}{1-\rho V_I} + \gamma_{L_e})\gamma_L + K_{15}\gamma_{L_e}}$$

$L \propto I$

ρ = cell density



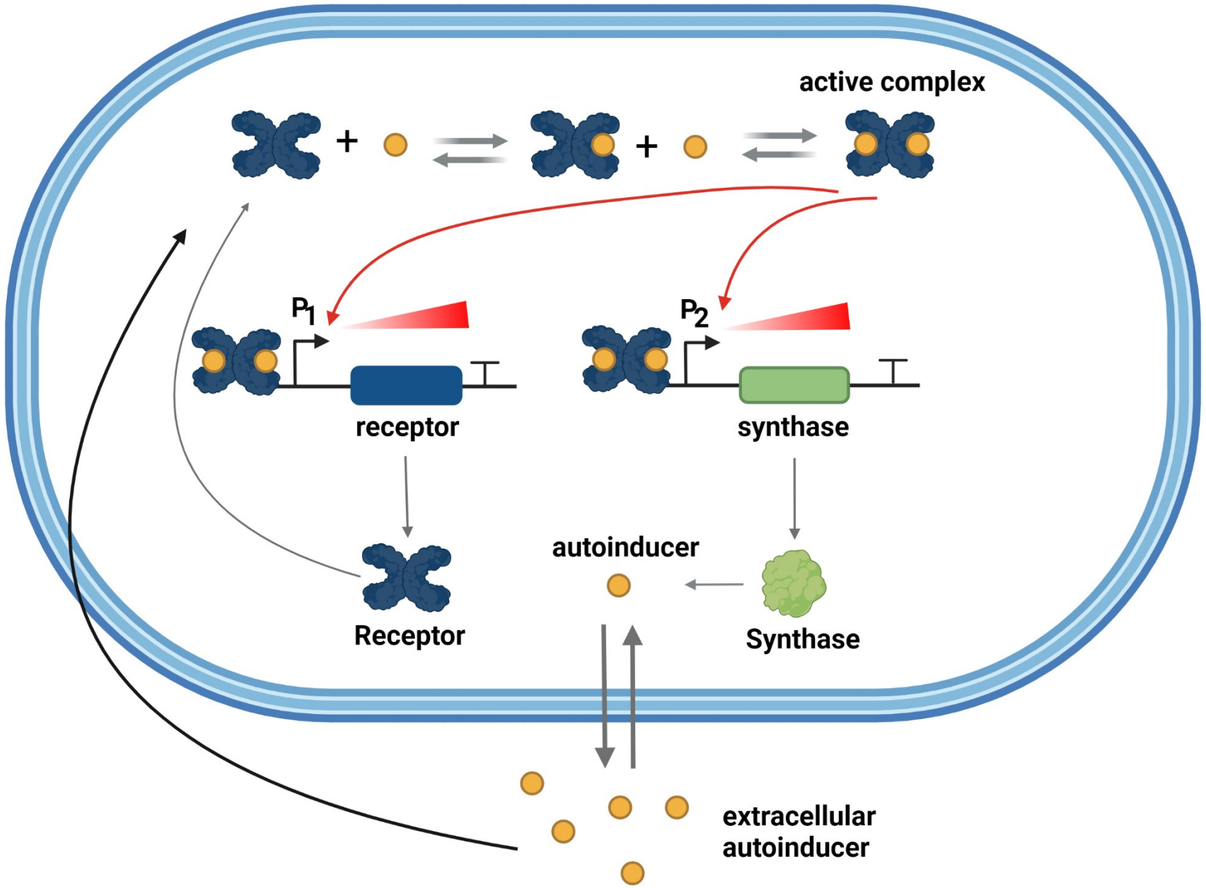
RESULTS

- ✓ **Bistability**
- ✓ **Hysteretic behavior**

↓

- History dependent
- Disturbance rejection
- **Robustness**

3. Two interlocked Feedbacks



3. Double-feedback Model

Reactions

$$R_2 + L \underset{d_1}{\overset{a_1}{\rightleftharpoons}} Q$$

$$Q + L \underset{d_4}{\overset{a_4}{\rightleftharpoons}} Q_2$$

$$\emptyset \xrightarrow{f(Q_2)} I$$

$$I \xrightarrow{\alpha_I} L + I$$

$$\emptyset \xrightarrow{g(Q_2)} R_2$$

$$I \xrightarrow{\gamma_I} \emptyset$$

$$R_2 \xrightarrow{\gamma_R} \emptyset$$

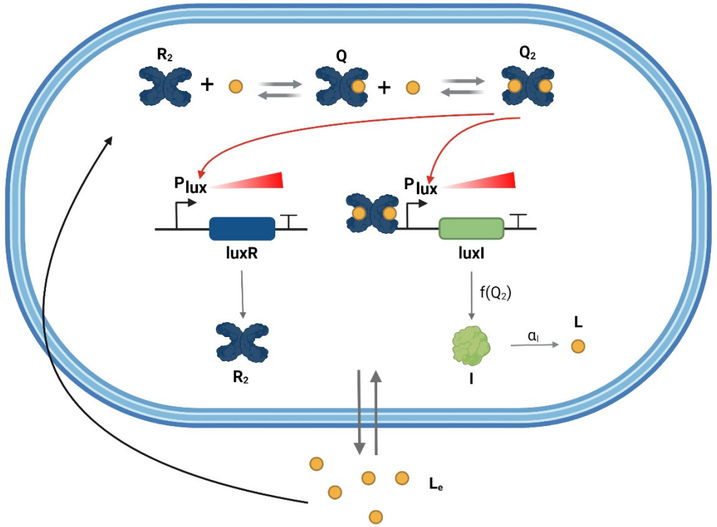
$$L \xrightarrow{\gamma_L} \emptyset$$

$$L_e \xrightarrow{\gamma_{L_e}} \emptyset$$

Conservation of mass

$$R_2^{TOT} = R_2 + Q + Q_2$$

$$L^{TOT} = L + Q + 2Q_2$$



Model

$$\frac{dI}{dt} = \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I$$

$$\frac{dR_2}{dt} = \beta_R + \frac{\alpha_R}{1 + \frac{K_R}{Q_2}} - \gamma_R R_2 + d_1 Q - K_1 d_1 R_2 L$$

$$\frac{dL}{dt} = \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L)$$

$$\frac{dL_e}{dt} = K_{15} \frac{N V_I}{V - N V_I}(L - L_e) - \gamma_{L_e} L_e$$

$$\frac{dQ}{dt} = K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2$$

$$\frac{dQ_2}{dt} = K_4 d_4 Q L - d_4 Q_2$$

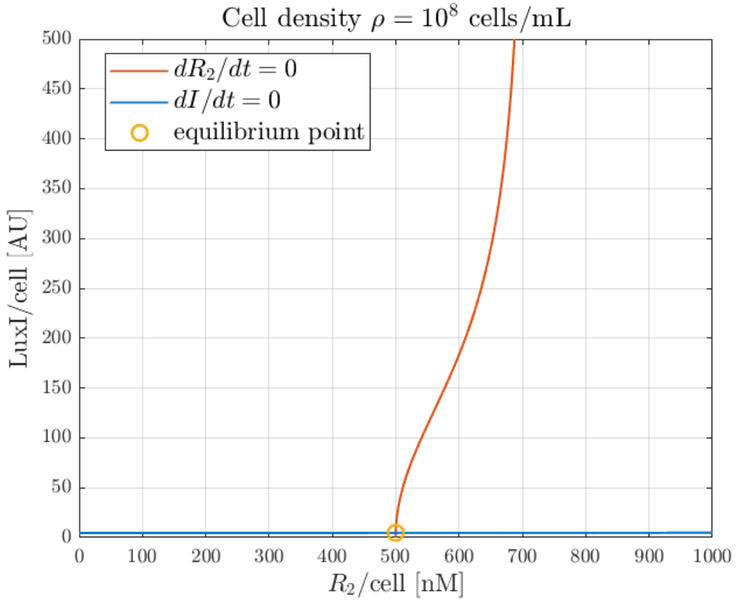
3. Equilibrium analysis

$$\frac{dI}{dt} = \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{4K_{lux}}{K_1^2 \chi^2 I^2 R_2}} - \gamma_I I = 0$$

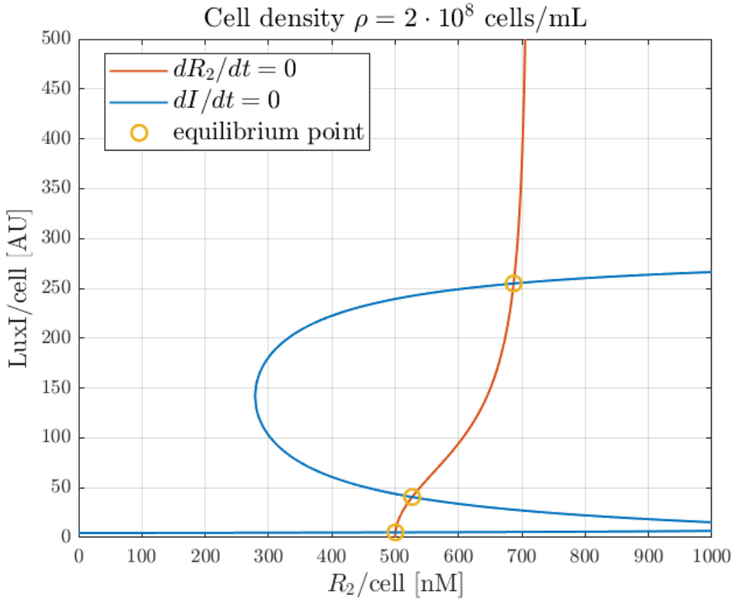
$$\frac{dR_2}{dt} = \beta_R + \frac{\alpha_R}{1 + \frac{4K_R}{K_1^2 \chi^2 I^2 R_2}} - \gamma_R R_2 = 0$$

intr. autoinducer synthase

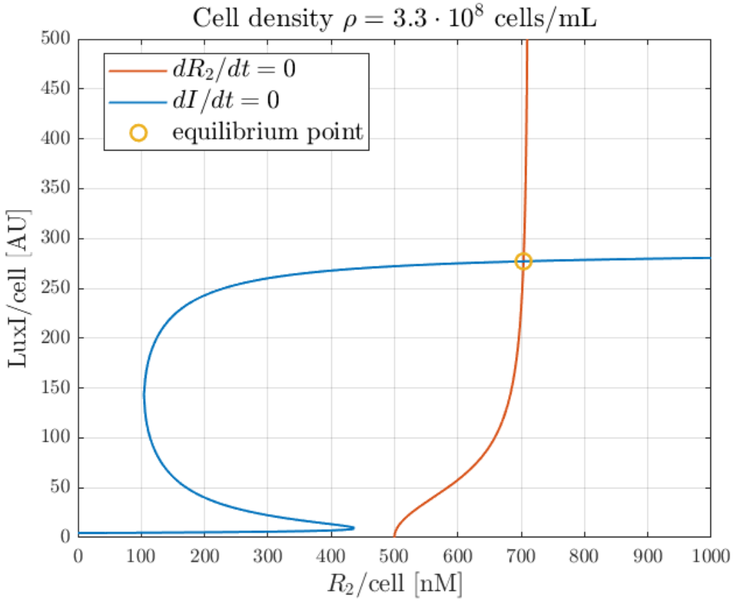
$_2$ = receptor



Low cell density

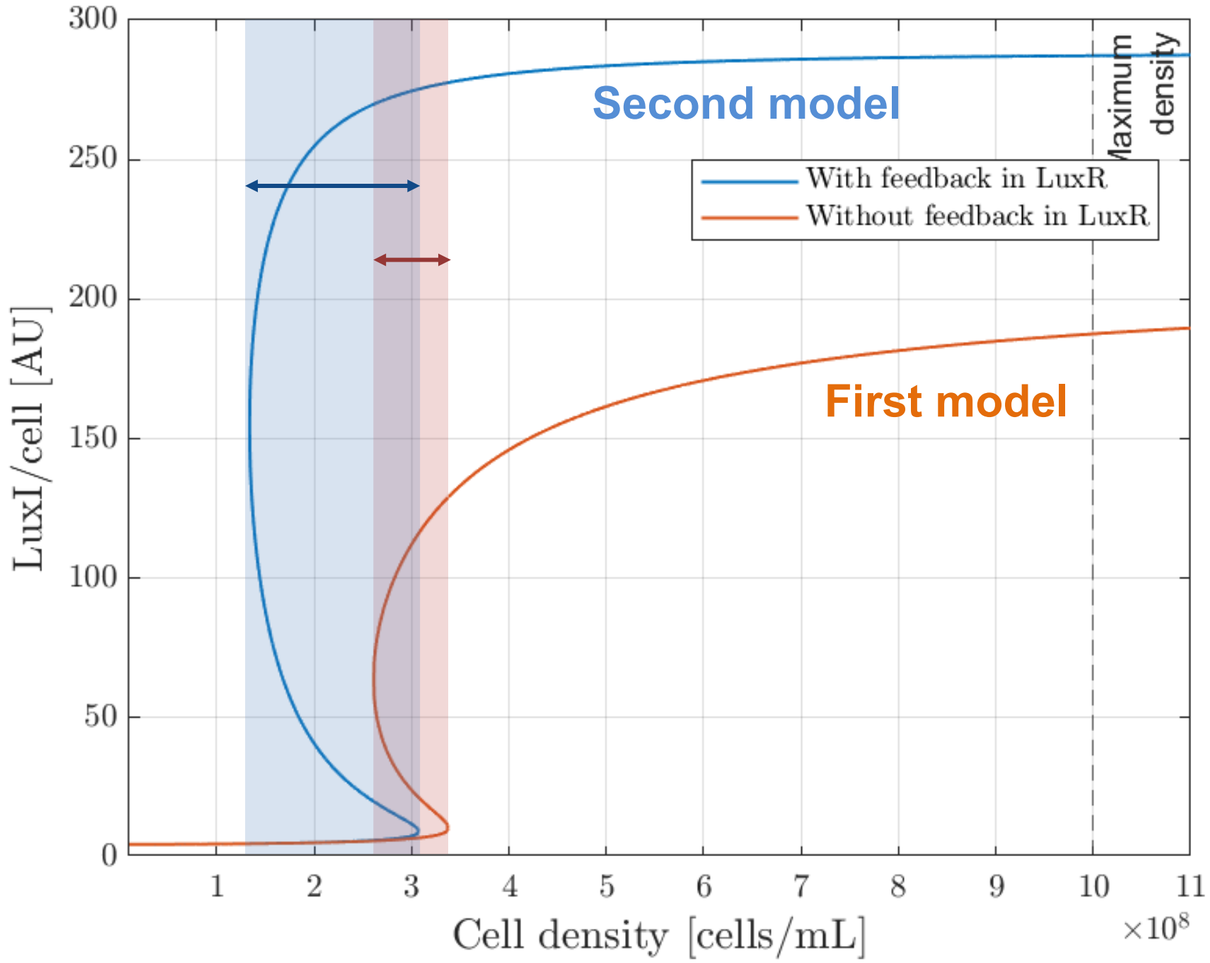


Threshold cell density



High cell density

3. Bifurcation Diagram



$$\frac{dI}{dt} = \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{4K_{lux}}{K_1^2 \chi^2 I^2 R_2}} - \gamma_I I = 0$$

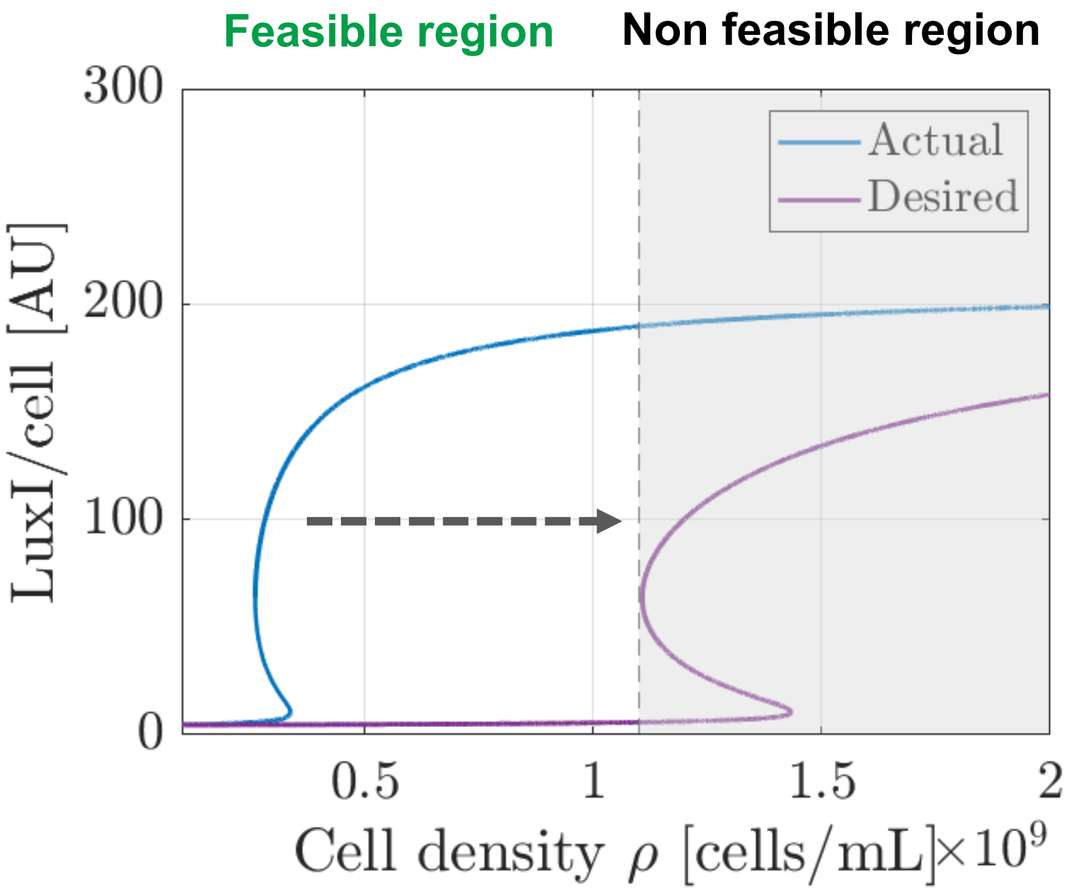
$$\frac{dR_2}{dt} = \beta_R + \frac{\alpha_R}{1 + \frac{4K_R}{K_1^2 \chi^2 I^2 R_2}} - \gamma_R R_2 = 0$$

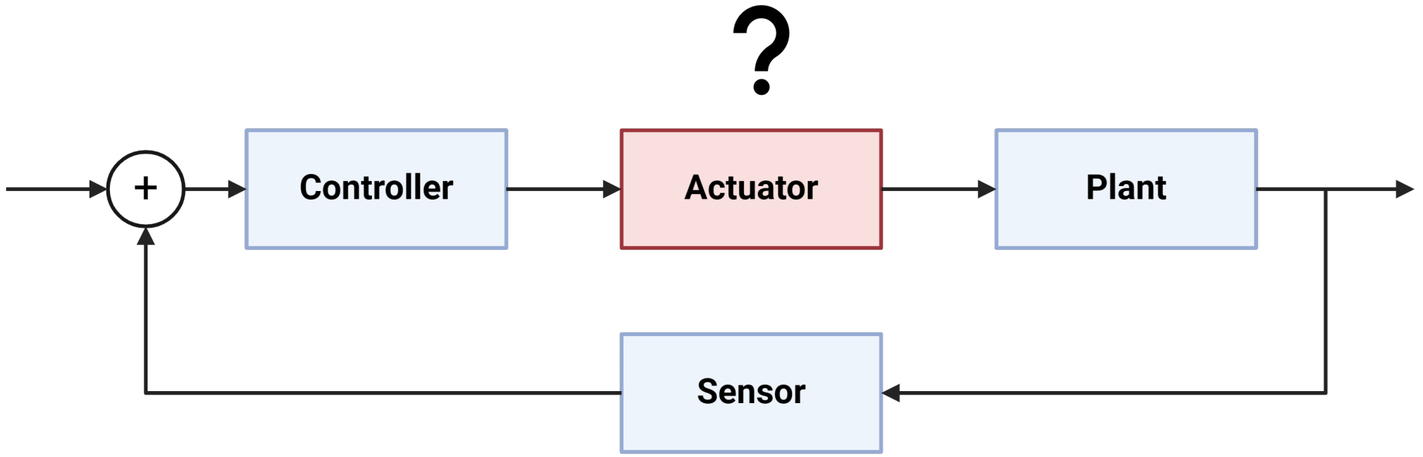
RESULTS

- ✓ **Robustness** increases due to enhance of the range of hysteresis
- ✓ Maximum steady state value increases
- ✓ Early activation of QS

C. Cimolato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato, M. Bellato, IEEE TMBMSC (under review).

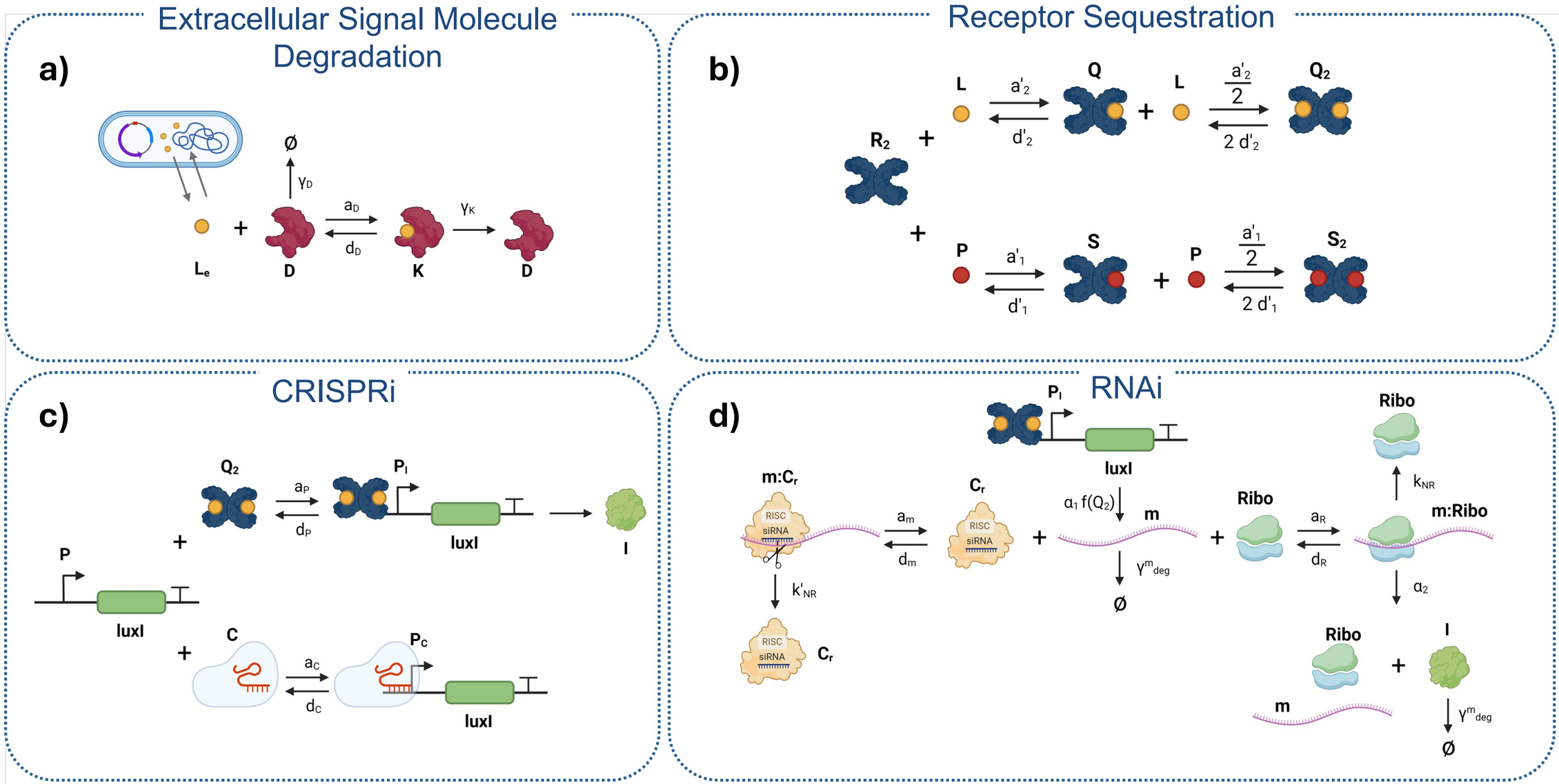
3. From Systems to “Feedback Control”





C. Cimolato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato, M. Bellato, IEEE TMBMSC (under review).

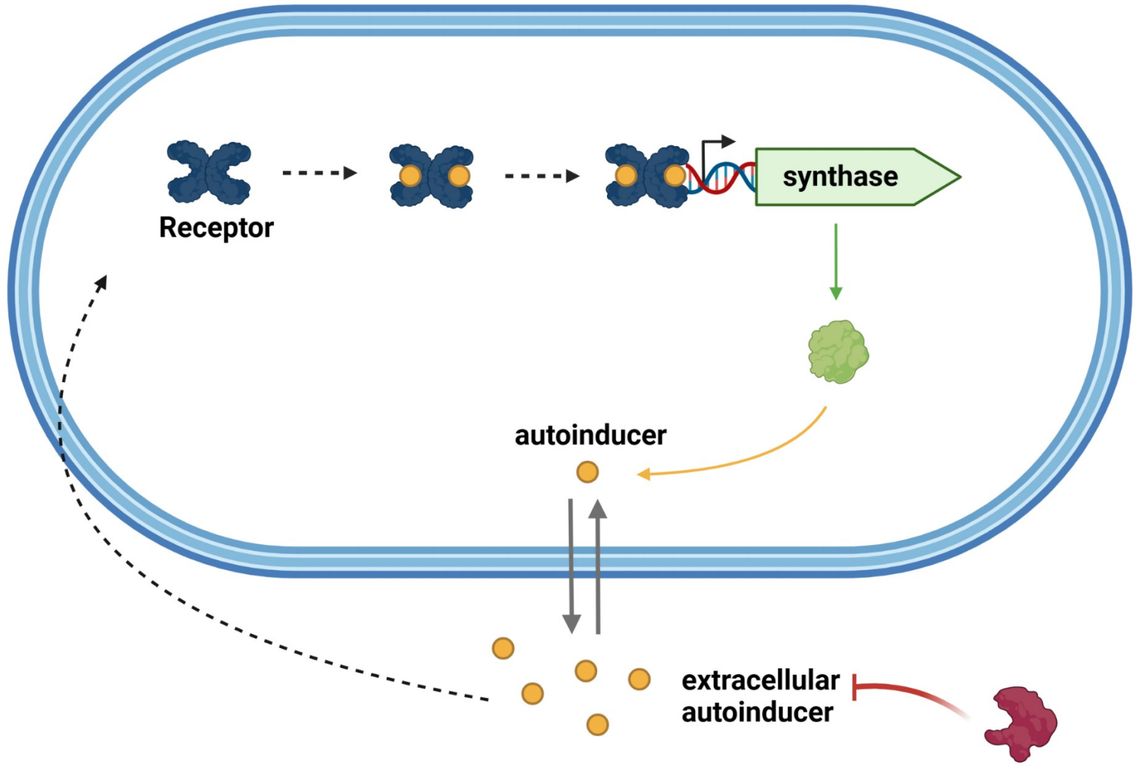
4. QS Inhibition: Actuators



C. Cimolato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato, M. Bellato, IEEE TMBMSC (under review).

4. QS Inhibition

1. Extracellular Signal Molecule Degradation

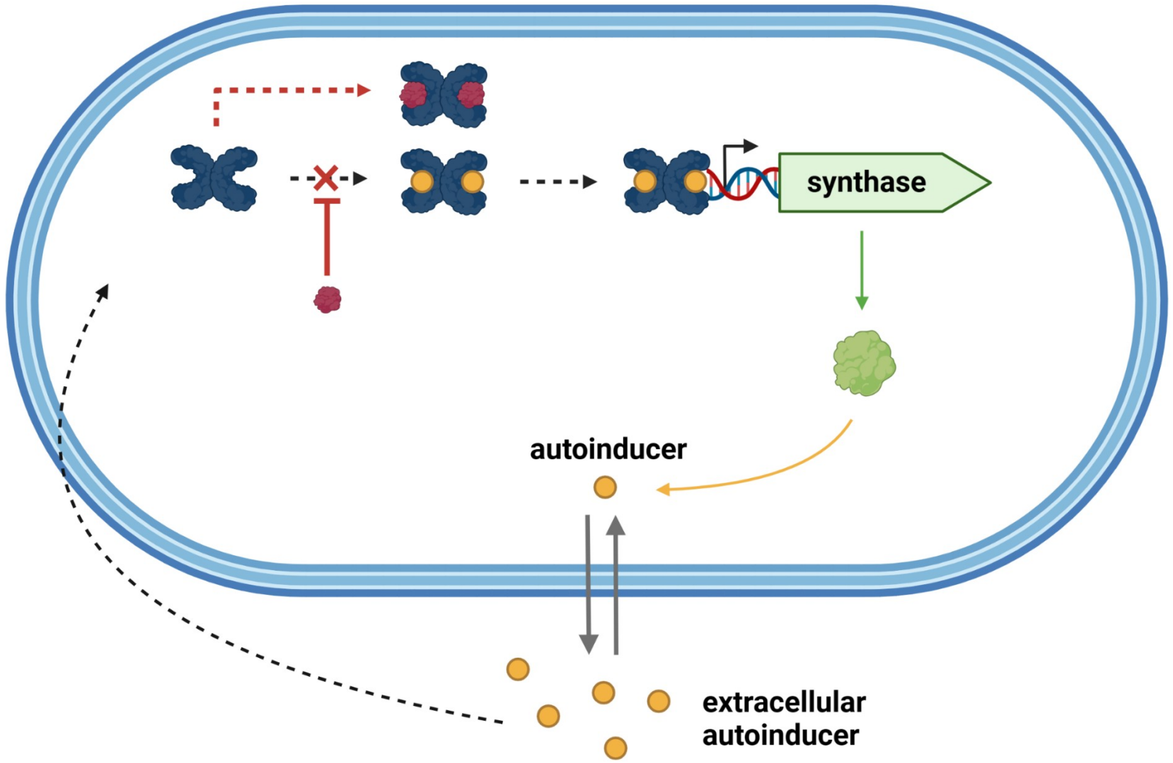


Increase of degradation rate of extracellular autoinducer

$$
\begin{aligned}
\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I \\
\frac{dR_2}{dt} &= \beta_R + \frac{\alpha_R}{1 + \frac{K_R}{Q_2}} - \gamma_R R_2 + d_1 Q - K_1 d_1 R_2 L \\
\frac{dL}{dt} &= \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L) \\
\frac{dL_e}{dt} &= K_{15}\frac{NV_I}{V - NV_I}(L - L_e) - \gamma_{L_e} L_e \\
\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 \\
\frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2
\end{aligned}
$$

4. QS Inhibition

2. Receptor Sequestration

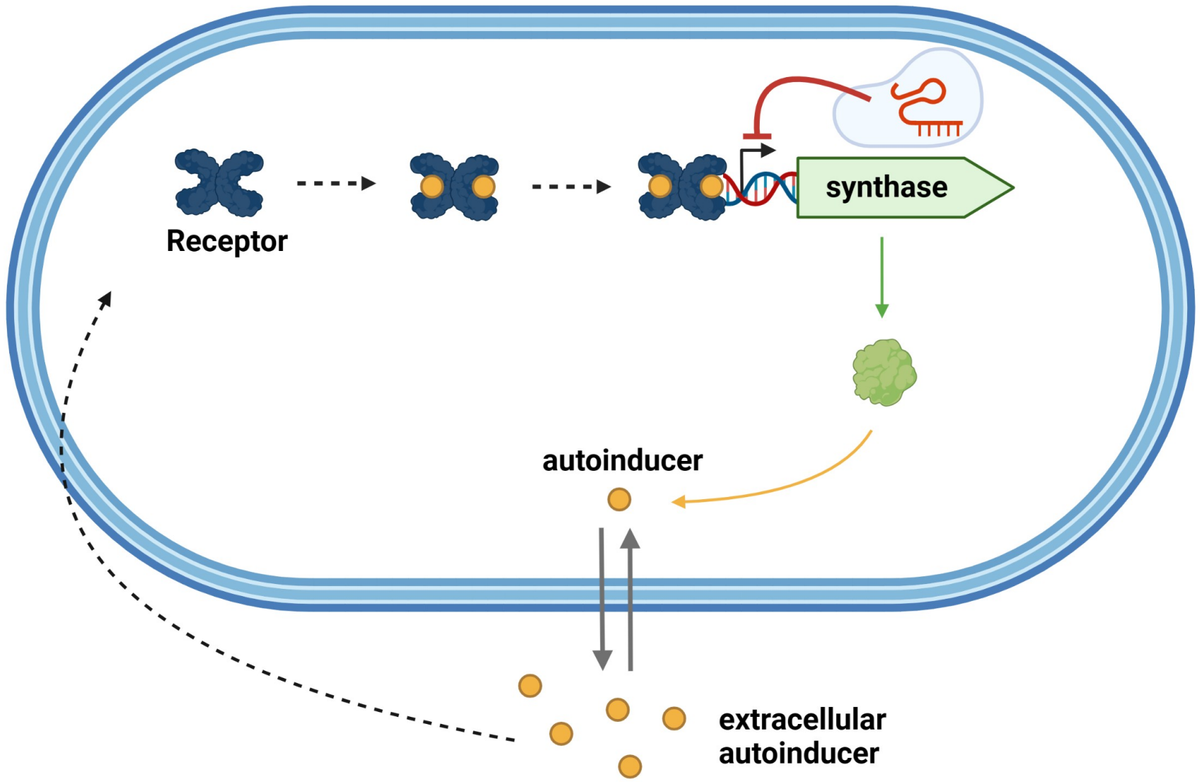


Decrease the association rate among the receptor and the autoinducer

$$
\begin{aligned}
\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I \\
\frac{dR_2}{dt} &= \beta_R + \frac{\alpha_R}{1 + \frac{K_R}{Q_2}} - \gamma_R R_2 + d_1 Q - K_1 d_1 R_2 L \\
\frac{dL}{dt} &= \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L) \\
\frac{dL_e}{dt} &= K_{15} \frac{N V_I}{V - N V_I}(L - L_e) - \gamma_{L_e} L_e \\
\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 \\
\frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2
\end{aligned}
$$

4. QS Inhibition

3. Synthase synthesis reduction - CRISPRi

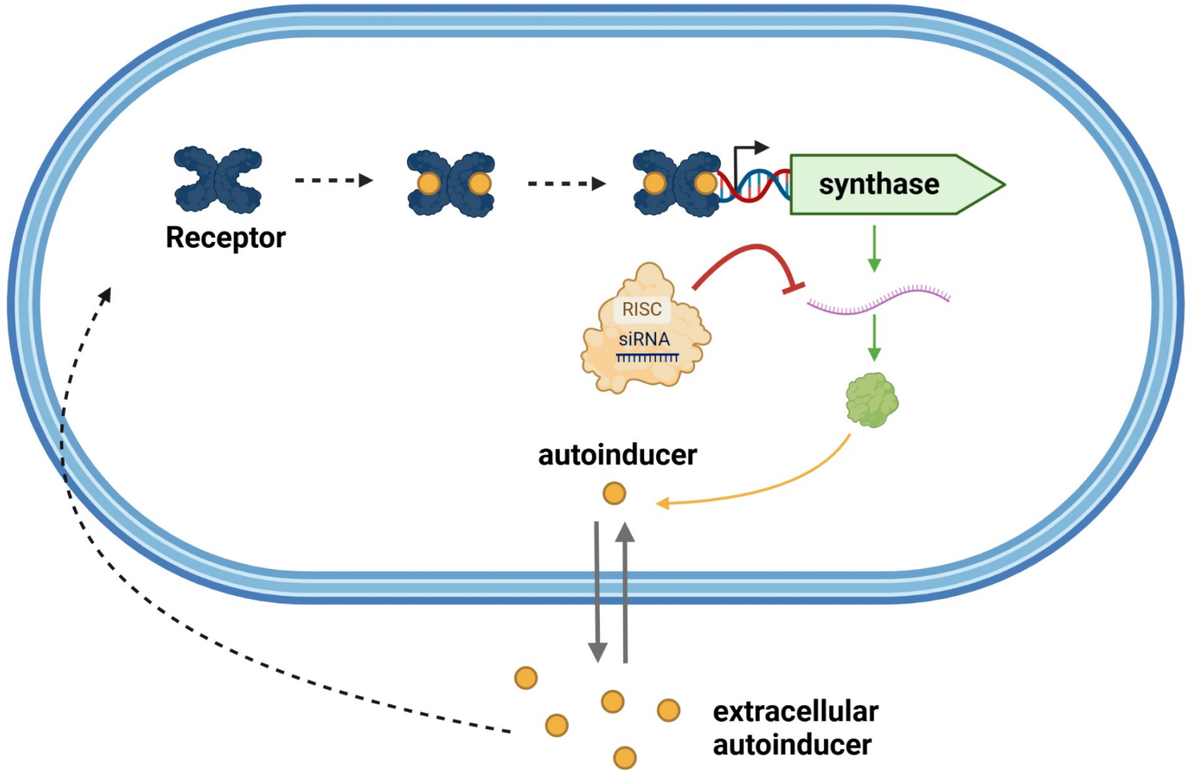


Reduce

$$
\begin{aligned}
\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I \\
\frac{dR_2}{dt} &= \beta_R + \frac{\alpha_R}{1 + \frac{K_R}{Q_2}} - \gamma_R R_2 + d_1 Q - K_1 d_1 R_2 L \\
\frac{dL}{dt} &= \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L) \\
\frac{dL_e}{dt} &= K_{15} \frac{N V_I}{V - N V_I}(L - L_e) - \gamma_{L_e} L_e \\
\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 \\
\frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2
\end{aligned}
$$

4. QS Inhibition

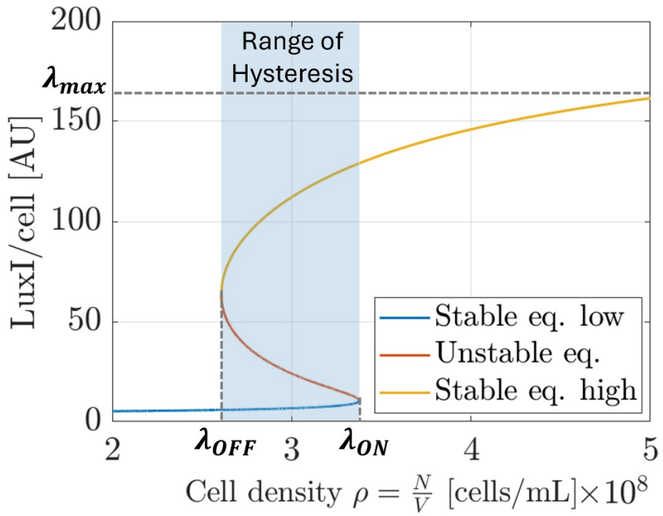
4. Post-transcriptional interference - RNAi

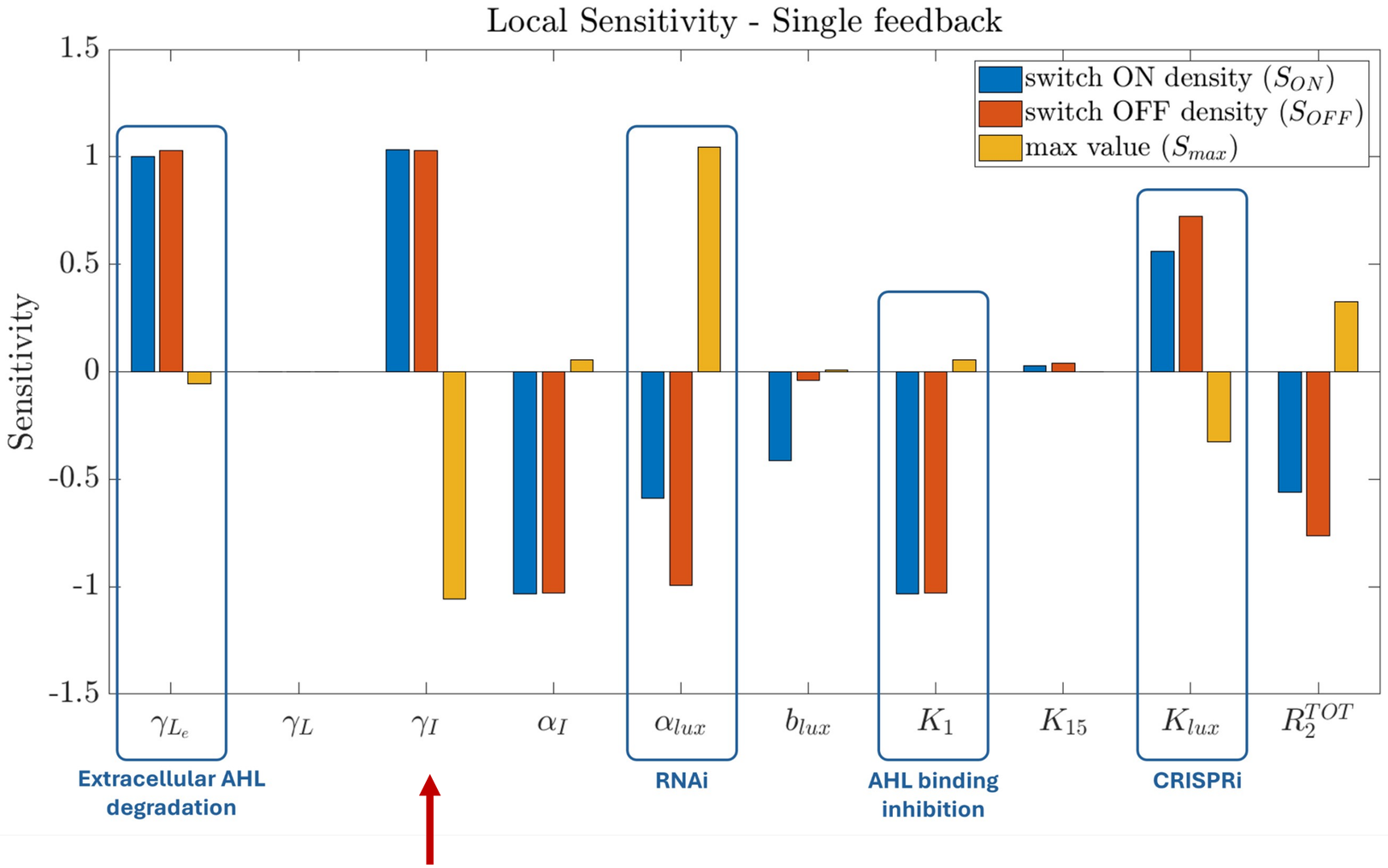


Reduce the synthesis rate of synthase

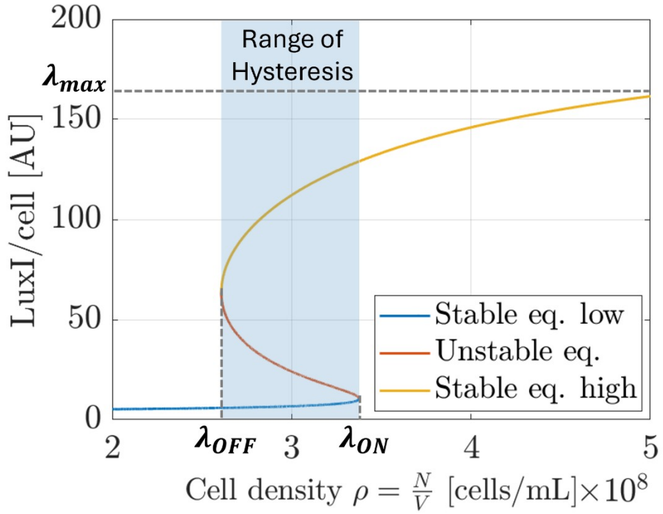
$$
\begin{aligned}
\frac{dI}{dt} &= \beta_{lux} + \frac{\alpha_{lux} - \beta_{lux}}{1 + \frac{K_{lux}}{Q_2}} - \gamma_I I \\
\frac{dR_2}{dt} &= \beta_R + \frac{\alpha_R}{1 + \frac{K_R}{Q_2}} - \gamma_R R_2 + d_1 Q - K_1 d_1 R_2 L \\
\frac{dL}{dt} &= \alpha_I I - \gamma_L L + d_1 Q - K_1 d_1 R_2 L + d_4 Q_2 - K_4 d_4 Q L + K_{15}(L_e - L) \\
\frac{dL_e}{dt} &= K_{15} \frac{N V_I}{V - N V_I}(L - L_e) - \gamma_{L_e} L_e \\
\frac{dQ}{dt} &= K_1 d_1 R_2 L - d_1 Q - K_4 d_4 Q L + d_4 Q_2 \\
\frac{dQ_2}{dt} &= K_4 d_4 Q L - d_4 Q_2
\end{aligned}
$$

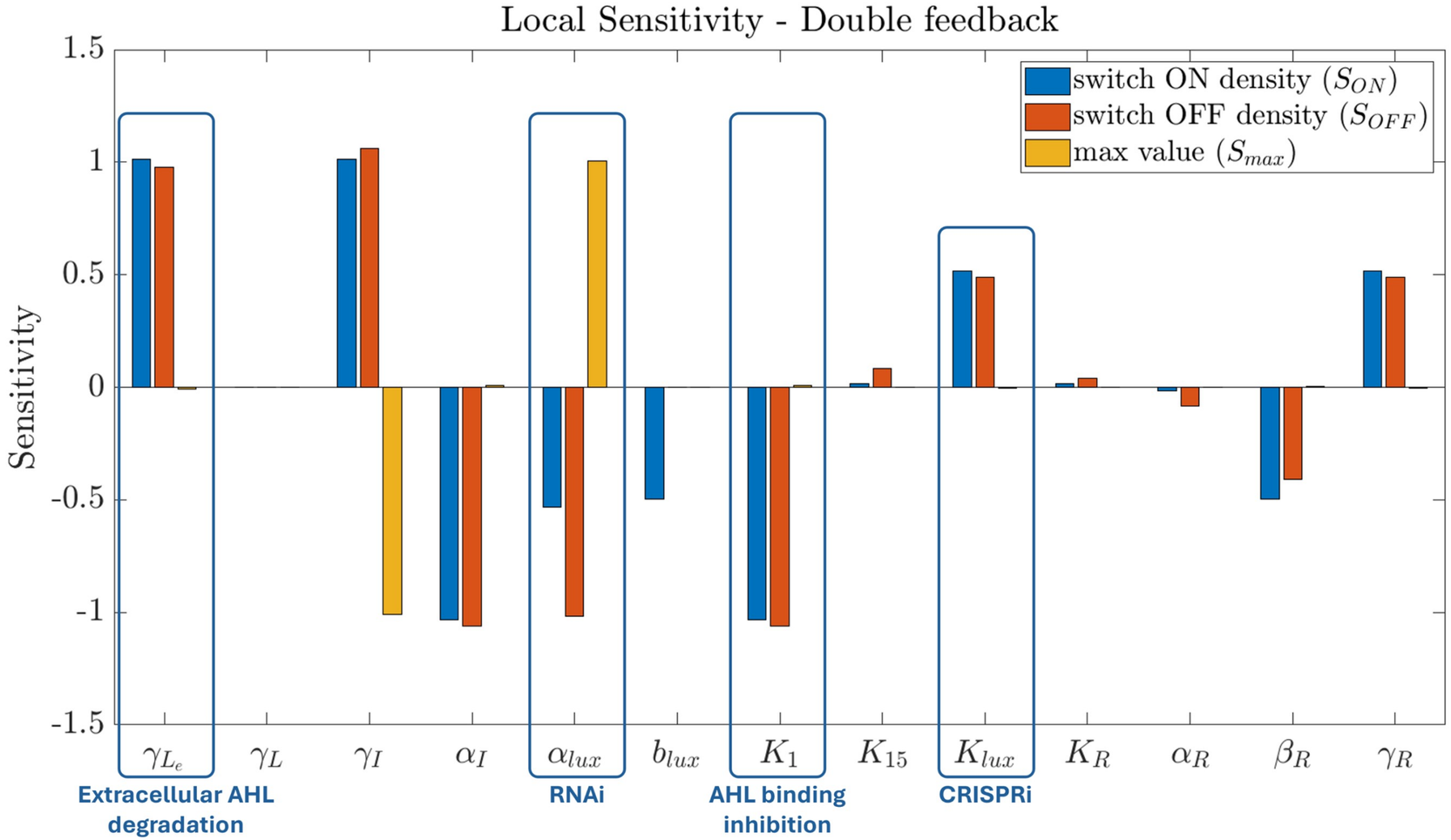
4. Sensitivity analysis – Single Feedback





4. Sensitivity analysis – Double Feedback





4. QS Inhibition

Inhibition strategies

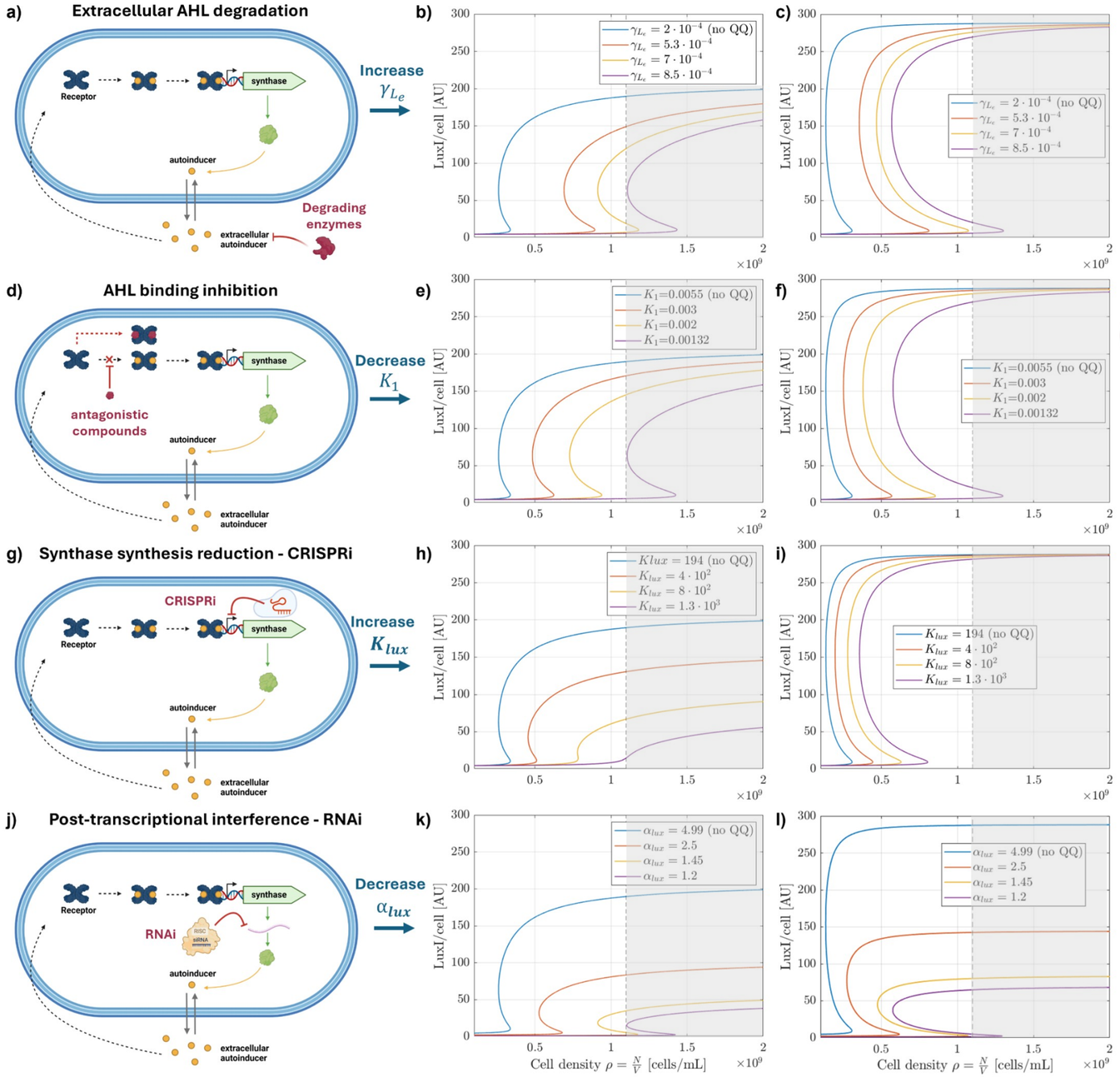
1. Extracellular autoinducer degradation

2. AHL binding inhibition via antagonistic compounds

3. Synthase synthesis reduction CRISPRi

3. Post-transcriptional interference - RNAi

Single-feedback **Double-feedback**

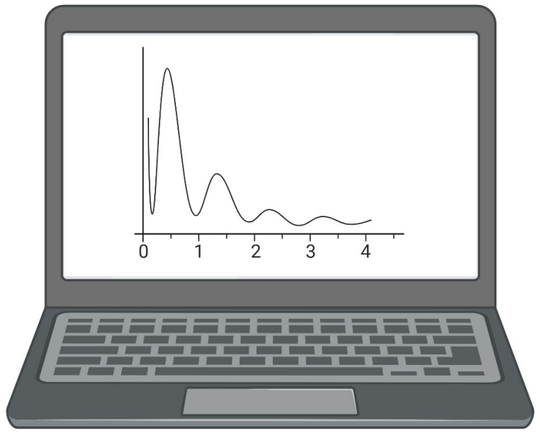


CONTRIBUTION

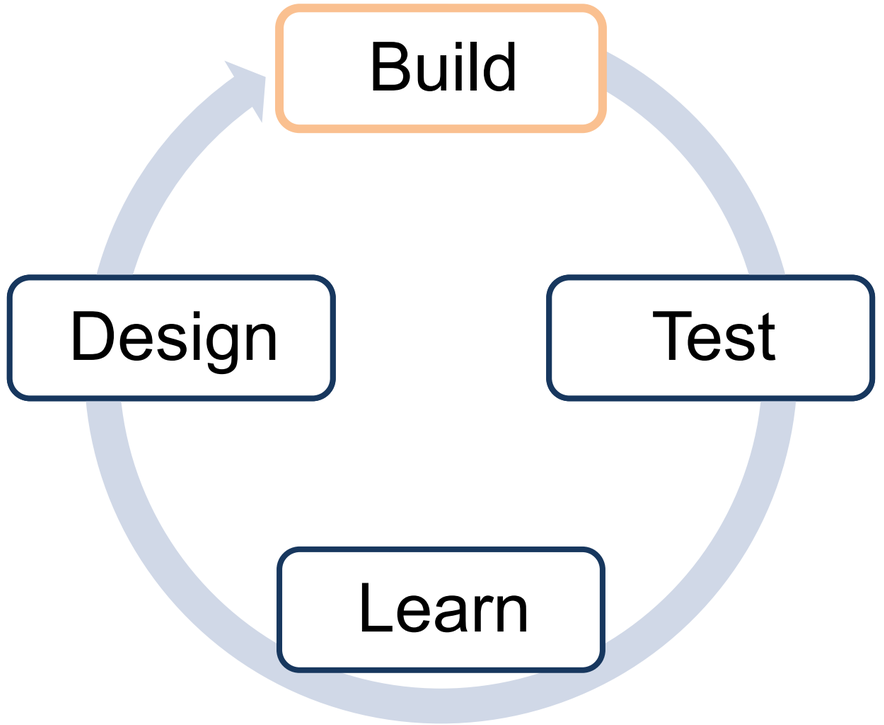
Comprehensive, model-driven evaluation of QS inhibition strategies to identify optimal QQ approaches

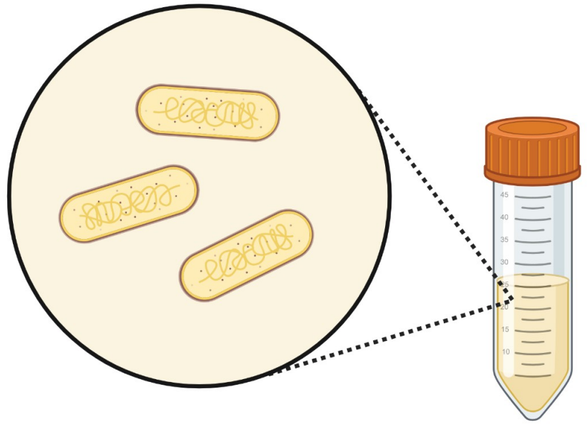
C. Cimolato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato, M. Bellato, IEEE TMBMSC (under review).

5. From simulation to experiments



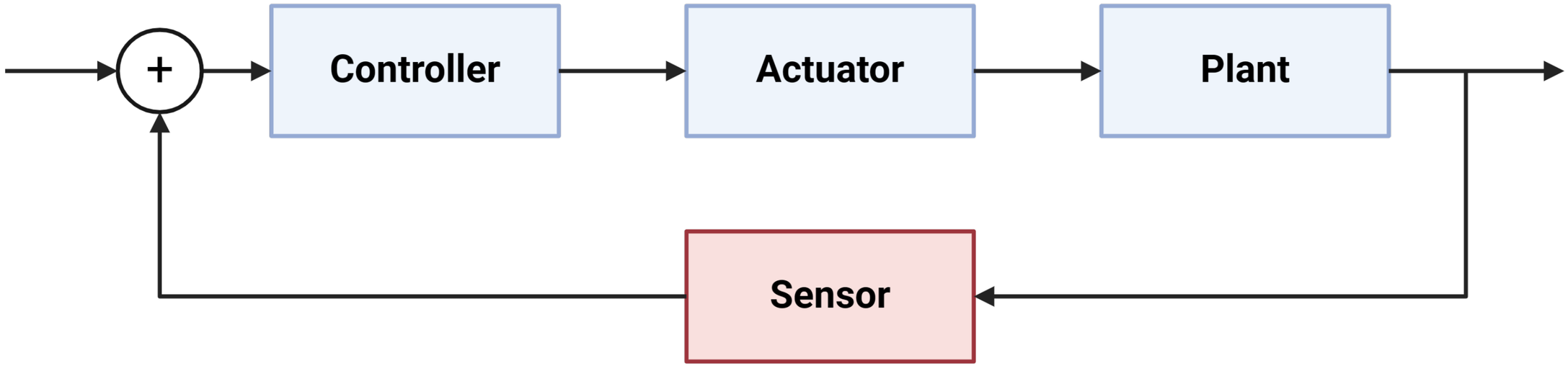
Systems biology



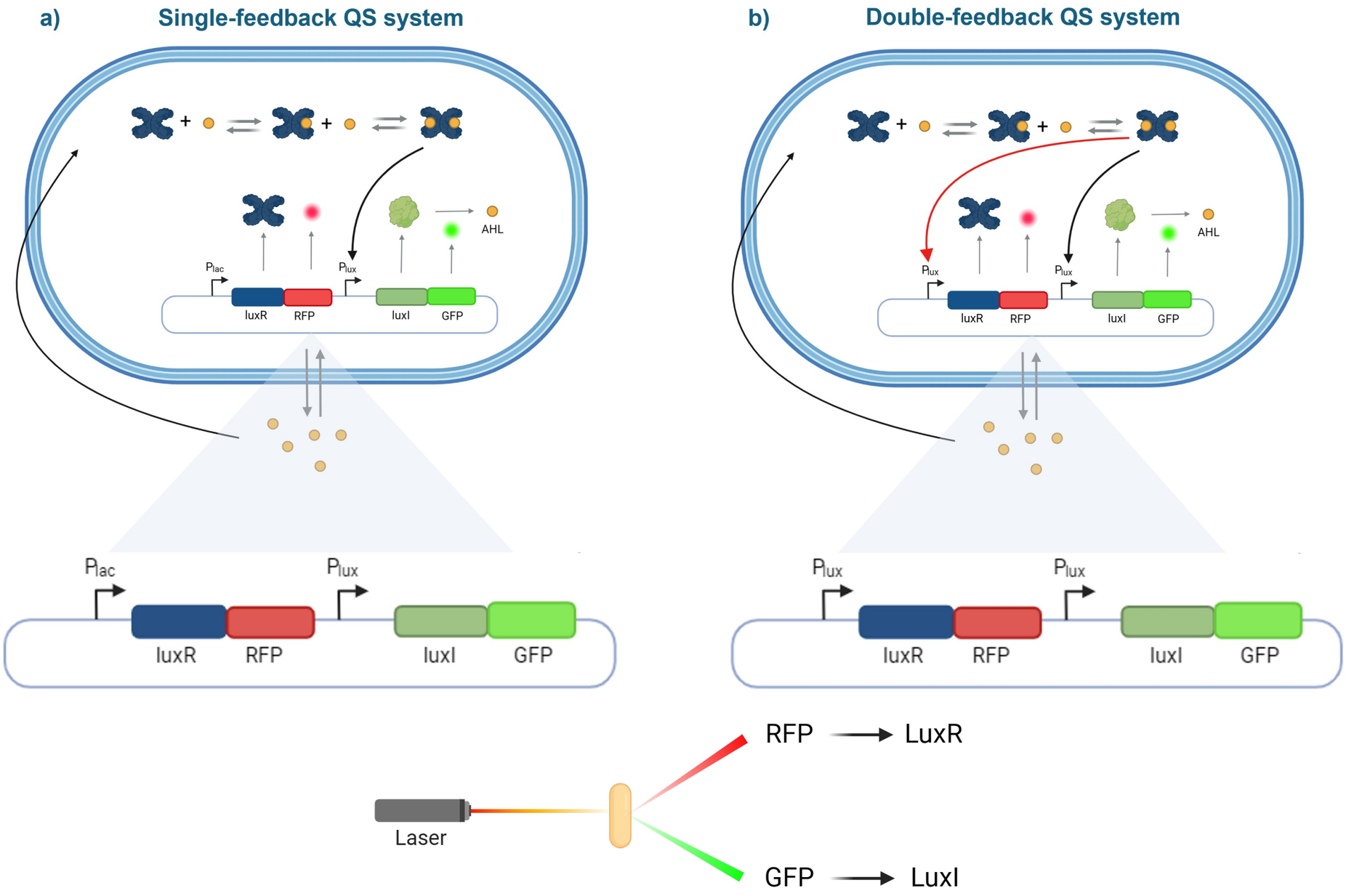


Synthetic biology

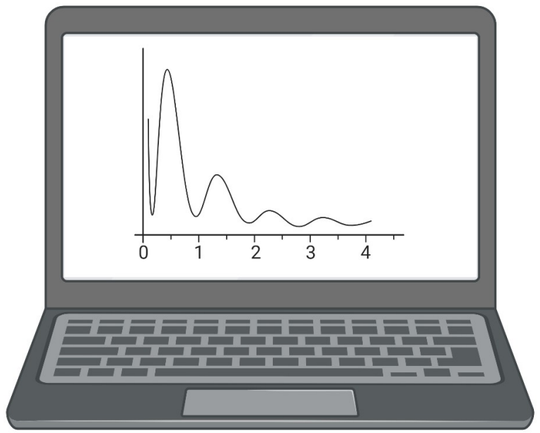
5. Engineering QS bacterial strains: Sensor



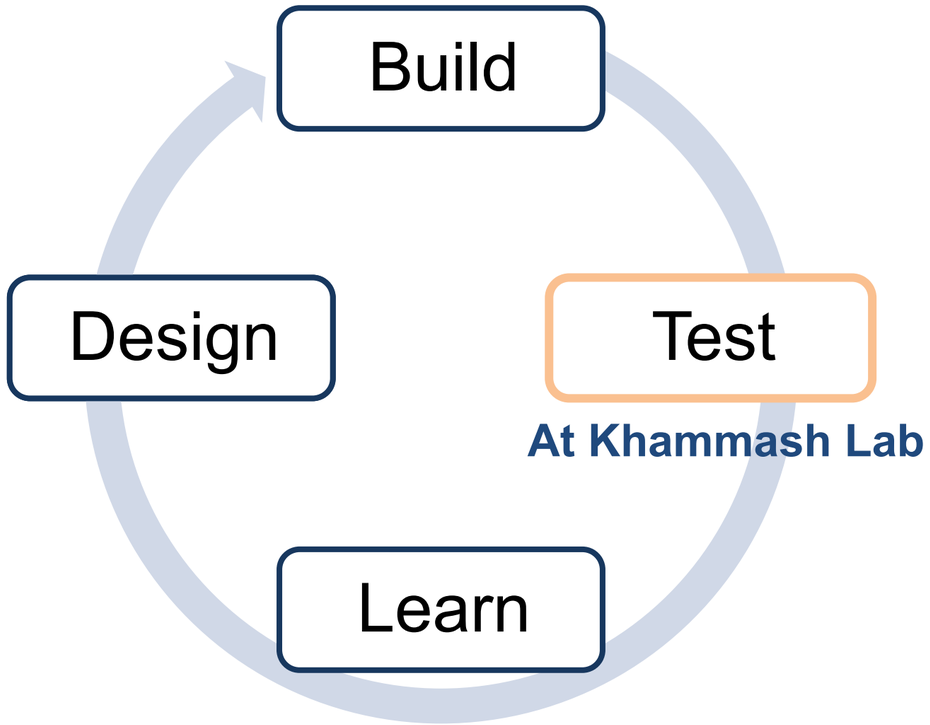
5. Engineering QS bacterial strains



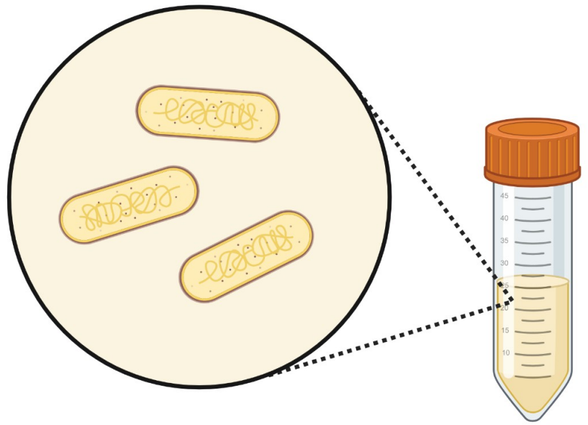
5. Future Perspectives



Systems biology



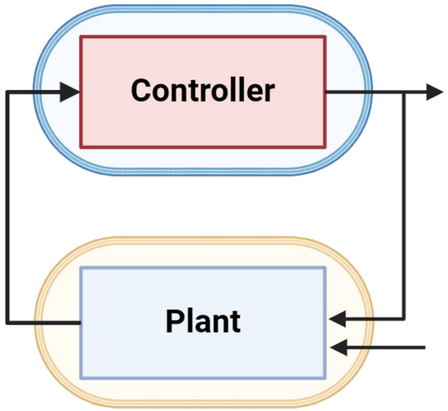
At Khammash Lab



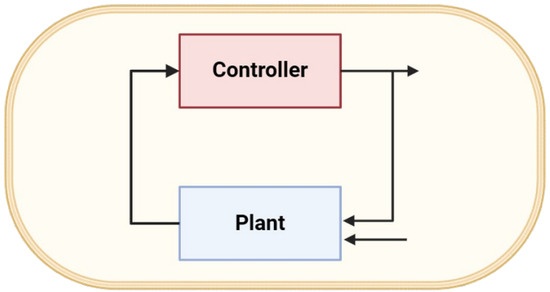
Synthetic biology

6. Future Perspectives

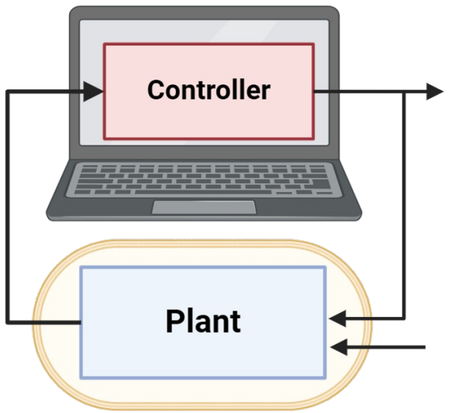
- **Feedback control** on the QS communication system



Out-cell

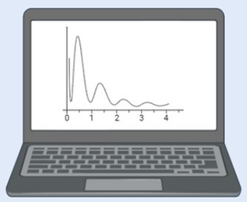


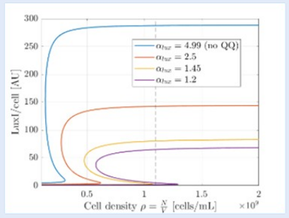
In-cell



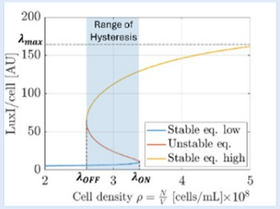
Cyber in the loop

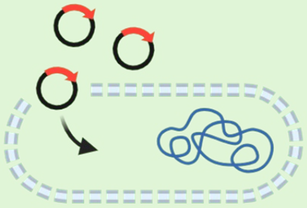
6. Summarizing

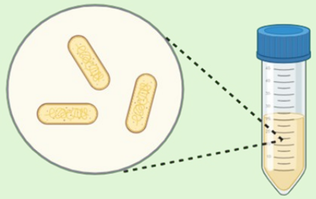




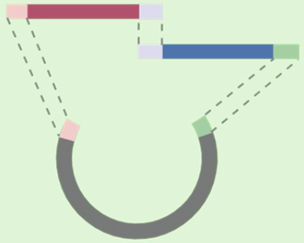
Modelling







Part assembly



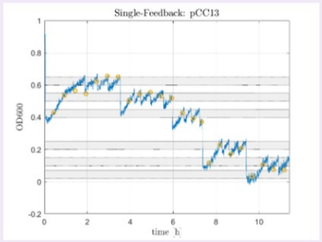
DESIGN

BUILD

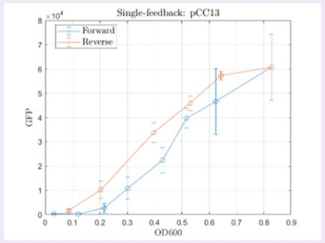
DBTL cycle

LEARN

TEST



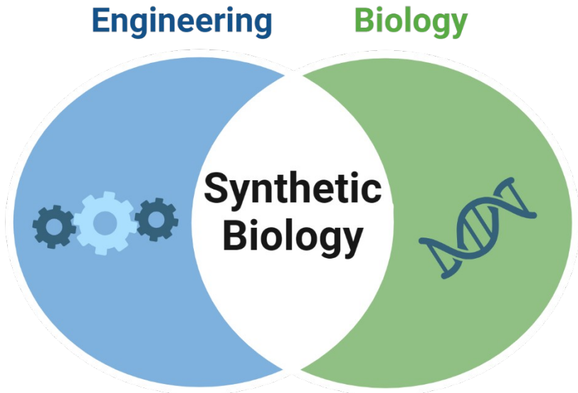
Data analysis and Optimization



Experiments

CONTRIBUTION

1. **Model** of the phage-mediated CRISPRi system with **mutations dynamics.**
2. **Model-driven evaluation of QS inhibition strategies**
3. **First experimental validation of the hysteretic behavior of QS** as function of bacterial cell density



Conference and Journal papers

1. C. Cimolato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato, M. Bellato. “*Quorum Sensing Model Structures Inspire the Design of Quorum Quenching Strategies*”, IEEE Transactions on Molecular, Biological, and Multi-Scale Communications (under review).

2. M. Bellato, C. Cimolato, S. Letrari, L. Schenato, “*Mathematical Modeling of Phage-Mediated CRISPRi System for Inhibiting Antibiotic Resistance*”, BBCC 2024, Napoli, Italy.

3. C. Cimolato, M. Bellato, G. Selvaggio, L. Marchetti, G. Giordano, L. Schenato “*Model Driven Design of Bacterial Communication Inhibition: from Quorum Sensing to Quorum Quenching*”, Automatica.it 2024, Bolzano.

4. Sara Letrari, Chiara Cimolato, Mahmoud Elsayed Mossad Shalata, Claudia Del Vecchio, Veronica Zatta, Giulia Bernabé, Paola Brun, Luca Schenato, Ignazio Castagliuolo and Massimo Bellato, "*Exploiting Synthetic Biology and Phage Delivery Technologies to Tackle Antimicrobial Resistance*". 2023 International Conference on Microbiome Engineering (ICME23)

5. C. Cimolato, M. Bellato, G. Selvaggio, L. Marchetti, L. Schenato. “*Controlling bacterial communication: uncovering quorum sensing and quenching structural properties via a systems biology approach*”, Automatica.it 2023, Catania.

6. C. Cimolato, G. Selvaggio, M. Bellato, L. Marchetti, L. Schenato. “*Uncovering quorum sensing and quenching structural properties: a systems biology approach*”, VIII Congress of the National Group of Bioengineering (GNB), 2023.

7. E. Gaetan, C. Cimolato, L. Schenato, M. Bellato. “*Modeling metabolic overload effects in bacterial growth rate in synthetic biology*”, VIII Congress of the National Group of Bioengineering (GNB), 2023.

DIPARTIMENTO
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DELL'INFORMAZIONE

ETH zürich
C·T·S·B
CONTROL THEORY & SYSTEMS BIOLOGY

Prof. **Mustafa Khammash**

Thank you for your attention

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