Information Processing in Quorum-Sensing Circuits

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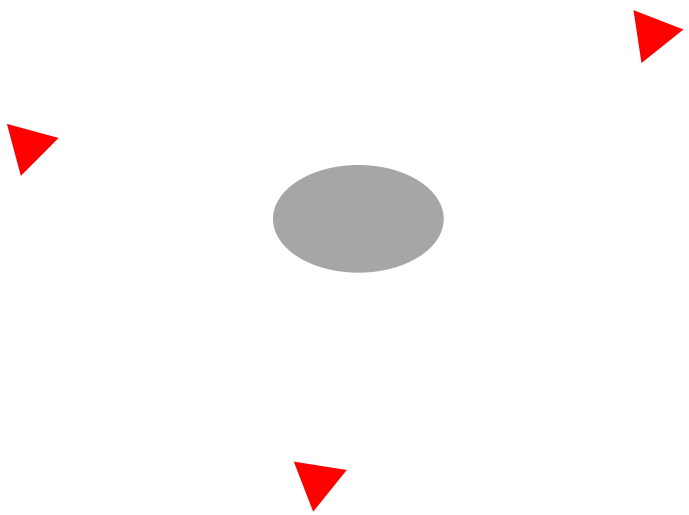
KITP Viral11, Jan 18, 2011

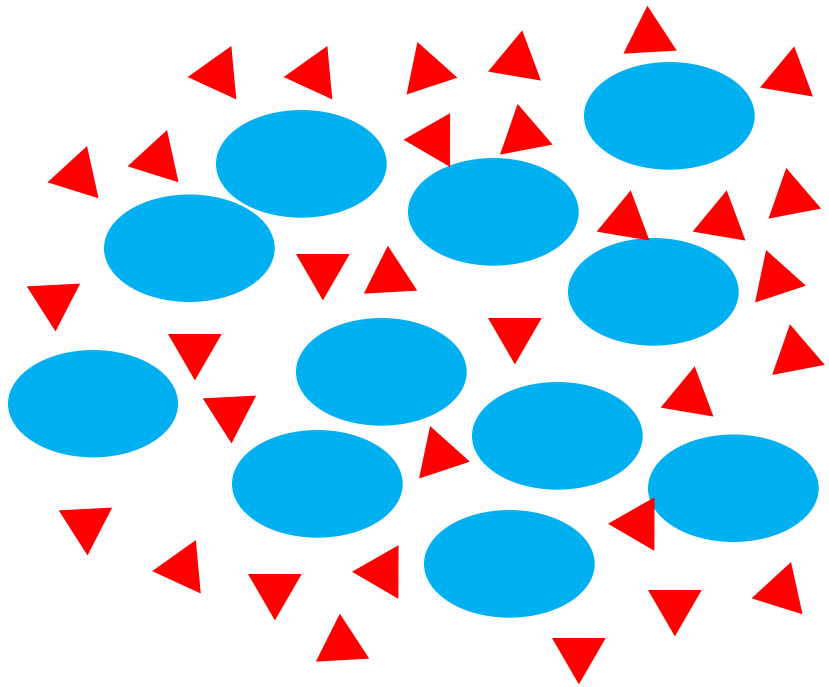
Quorum Sensing

Low Cell Density



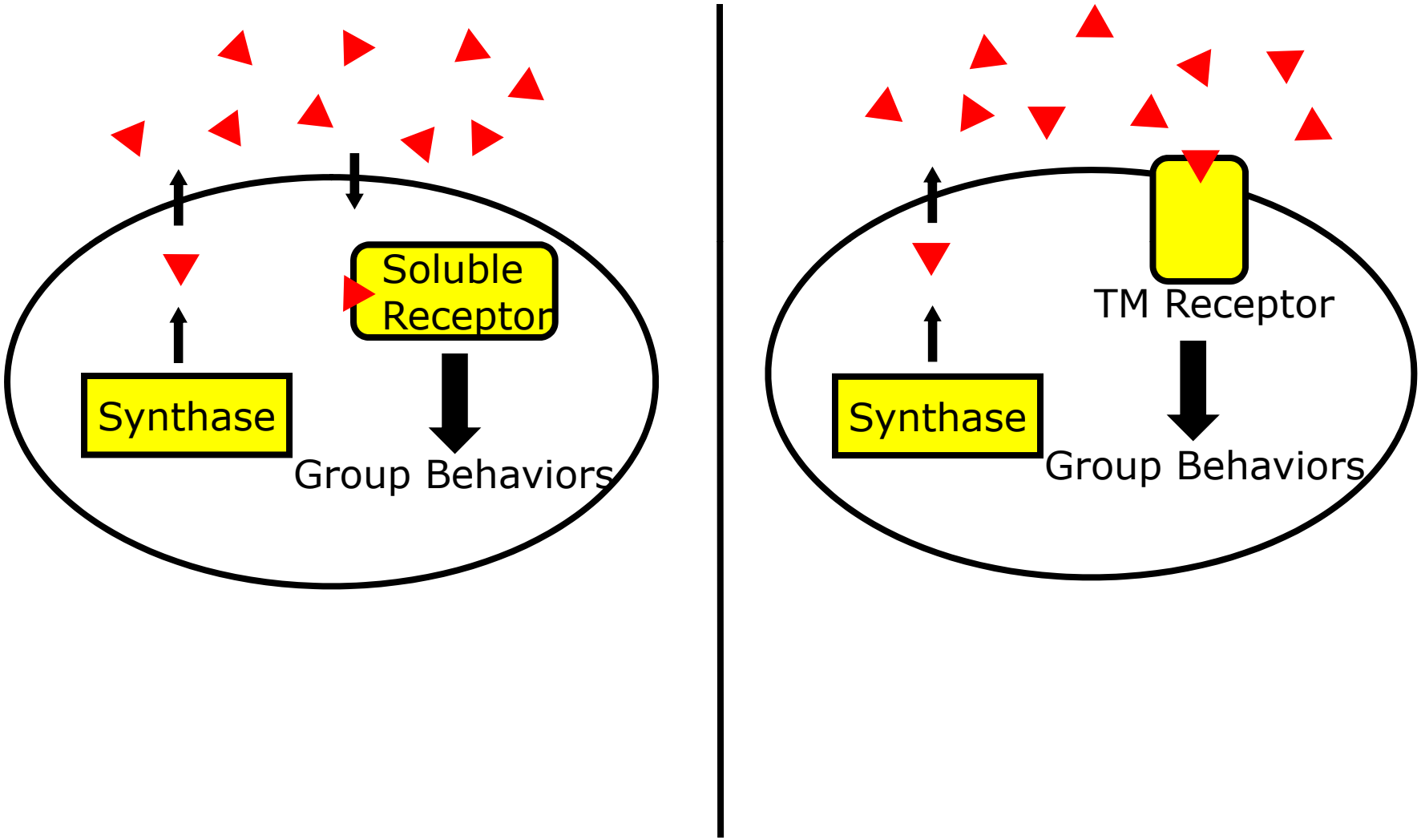
Individual Behaviors

High Cell Density



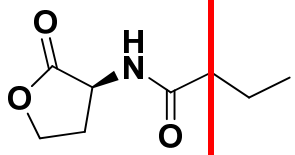
Group Behaviors

Signal Transduction

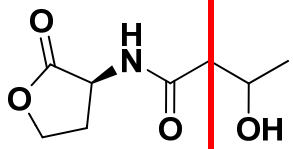


Homoserine Lactone Autoinducers

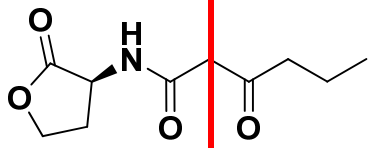
Serratia marcesens



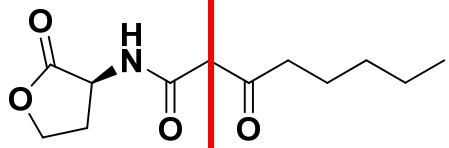
Vibrio harveyi



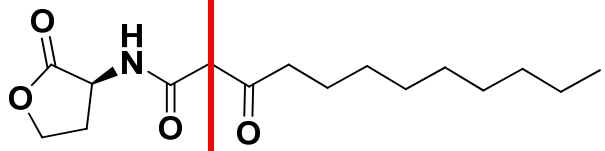
Vibrio fischeri



Agrobacterium tumefaciens



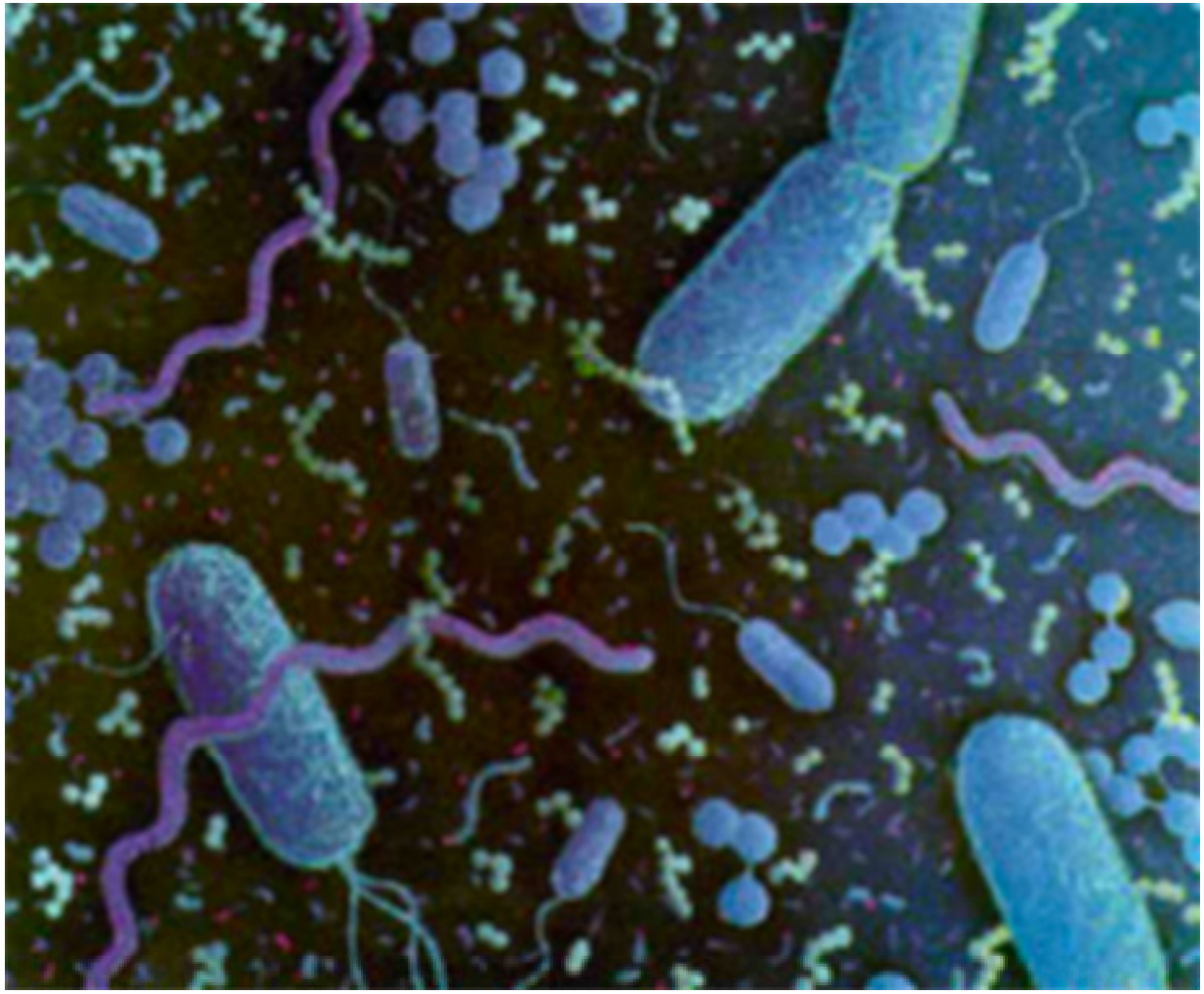
Pseudomonas aeruginosa



Quorum-Sensing Behaviors

V. fischeri	Bioluminescence
P. aeruginosa	Virulence Factors, Biofilms
E. carotovora	Virulence Factors, Antibiotics

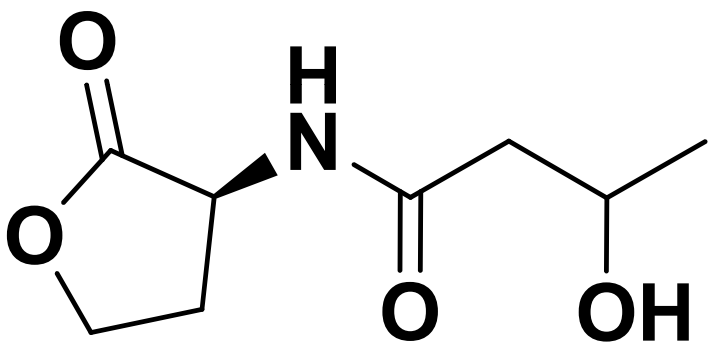
Bacterial Communities



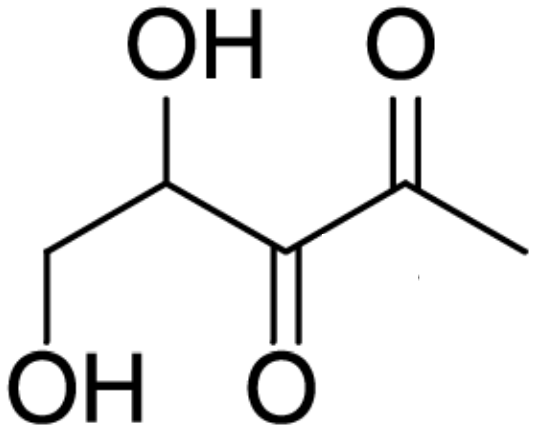
V. harveyi Output

Two Types of Molecules

AI-1



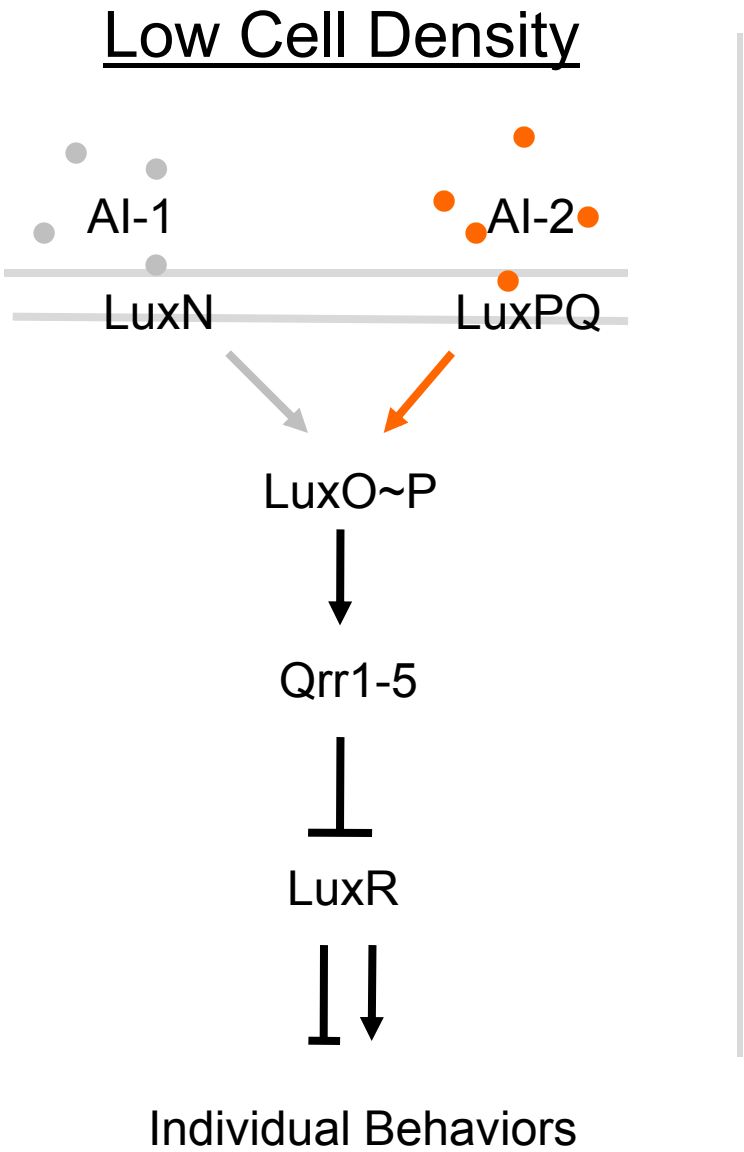
AI-2



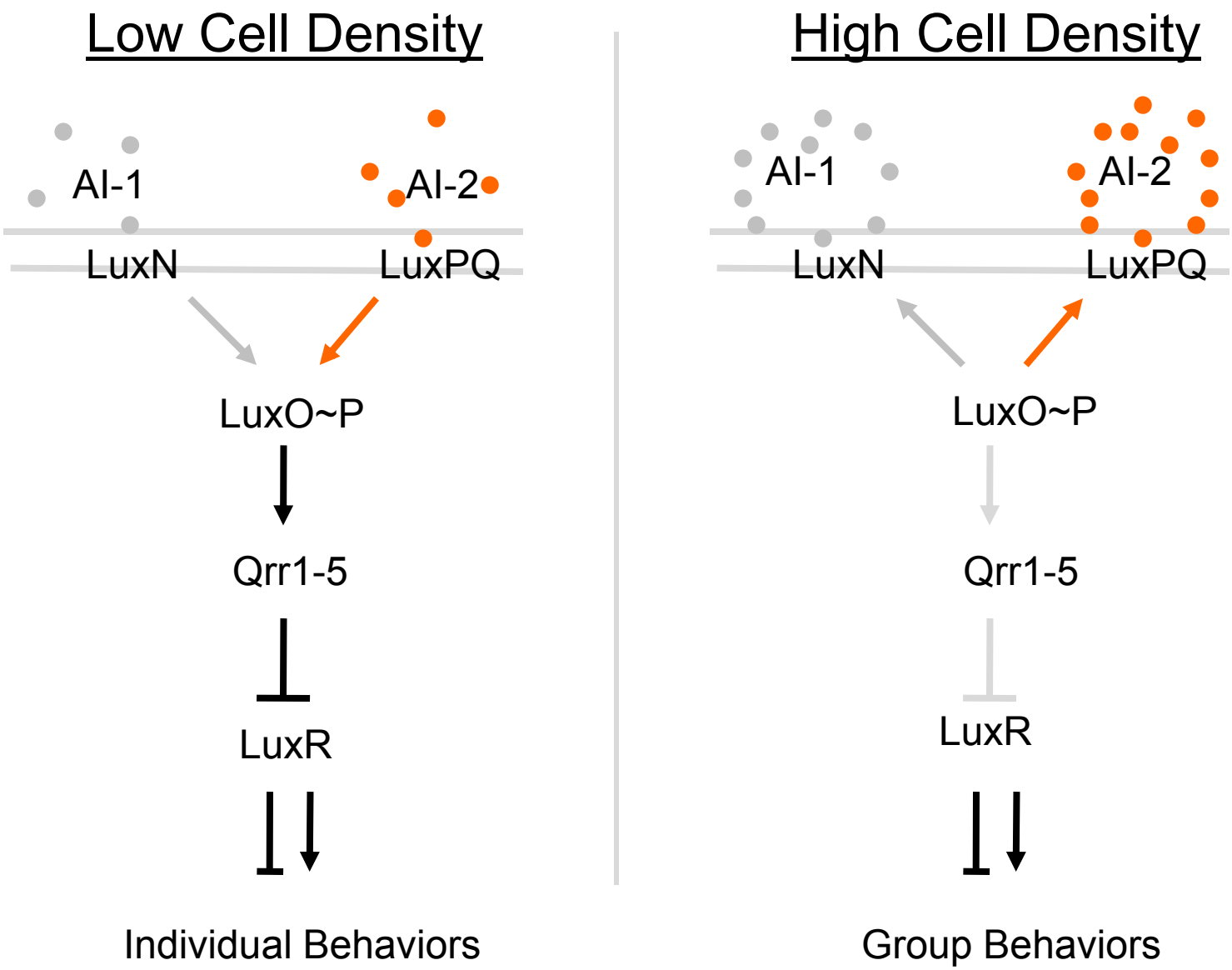
Self

Other

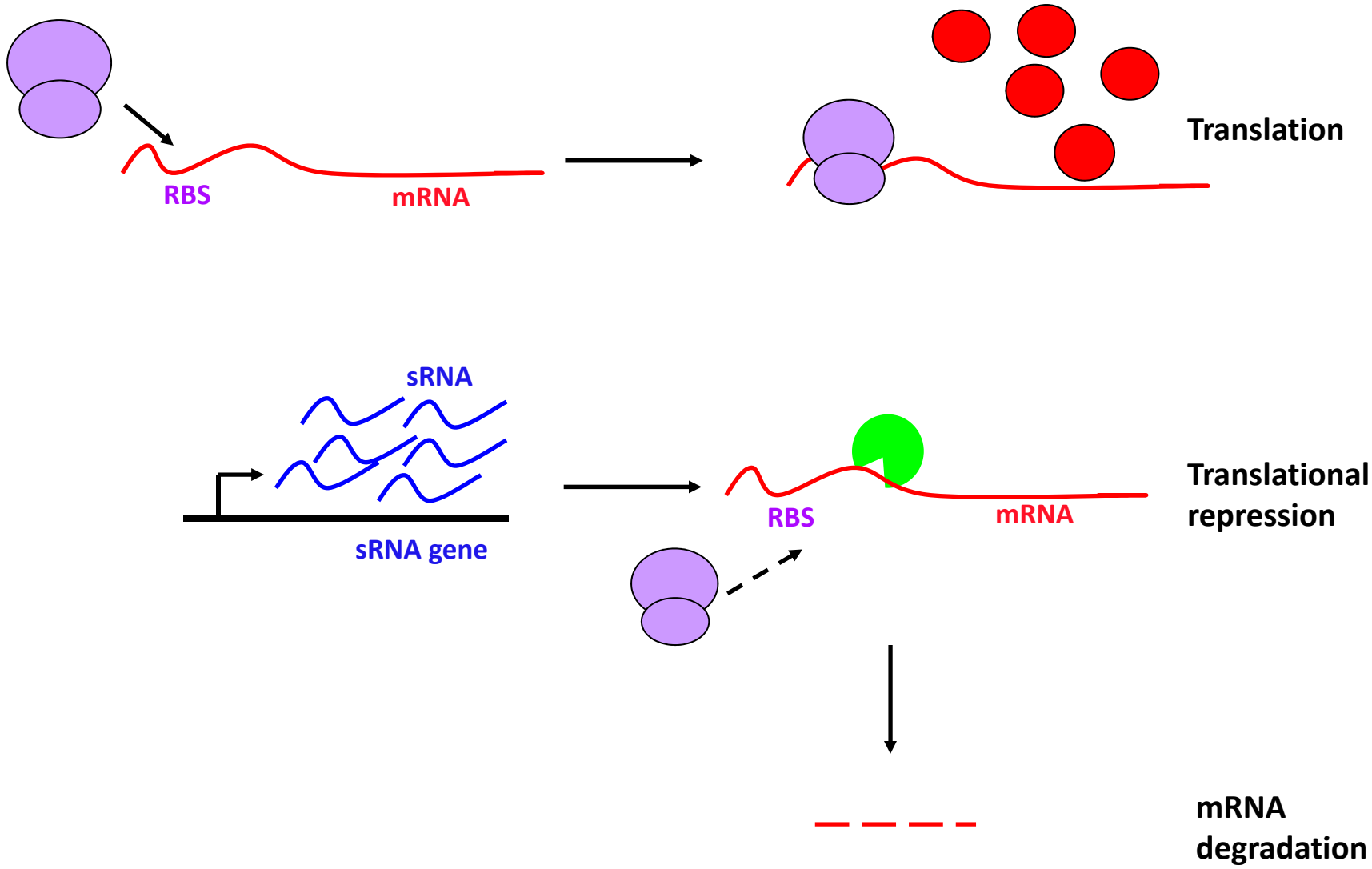
The *V. harveyi* Quorum-Sensing Network



The *V. harveyi* Quorum-Sensing Network



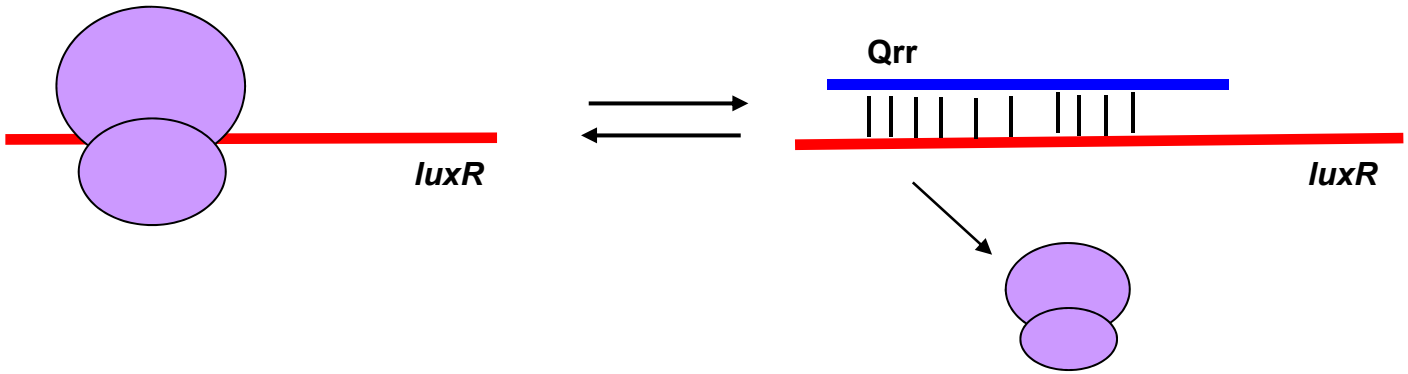
sRNA Regulation in Bacteria



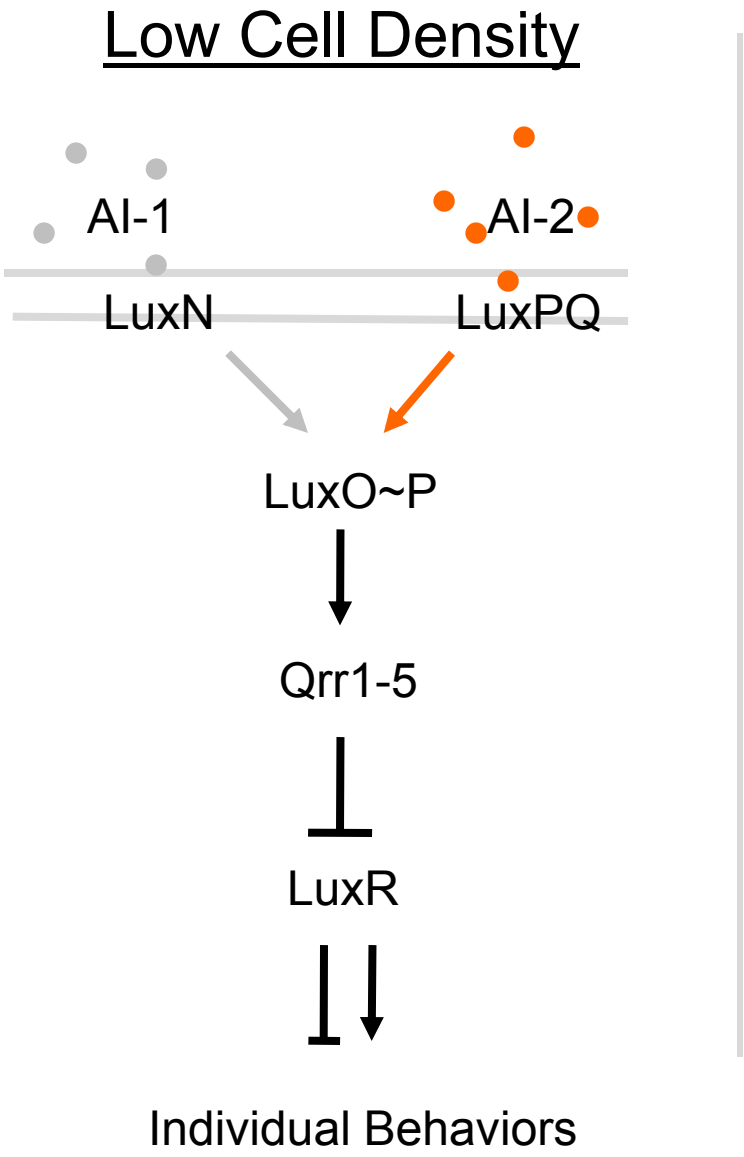
Qrrs-LuxR:Stoichiometric Binding

```
          Start        RBS
luxR      CAUAUUUCUUUUUCCUUGCCAUUUGA-GUUGAUGUUUUGGGGAUAAUCCCCUAA--
Qrr1      -------GGGUCACCUAUCCAACUGACGUUGUUAGUGAACG-ACA-U-GUUCACAG
Qrr2      -------GGGUCACCUAGCCAACUGACGUUGUUAGUGAAUACACA-UUGUUCACA-
Qrr3      -------GGGUCACCUAGCCAACUGACGUUGUUAGUGGACUCGAAUUUGUUCACA-
Qrr4      -------GGGUCACCUAGCCAACUGACGUUGUUAGUGAAUACACA-UUGUUCACA-
Qrr5      -------GGGUCACCUAGCCAACUGACGUUGUUAGUGAACCCAA--UUGUUCACA-
```

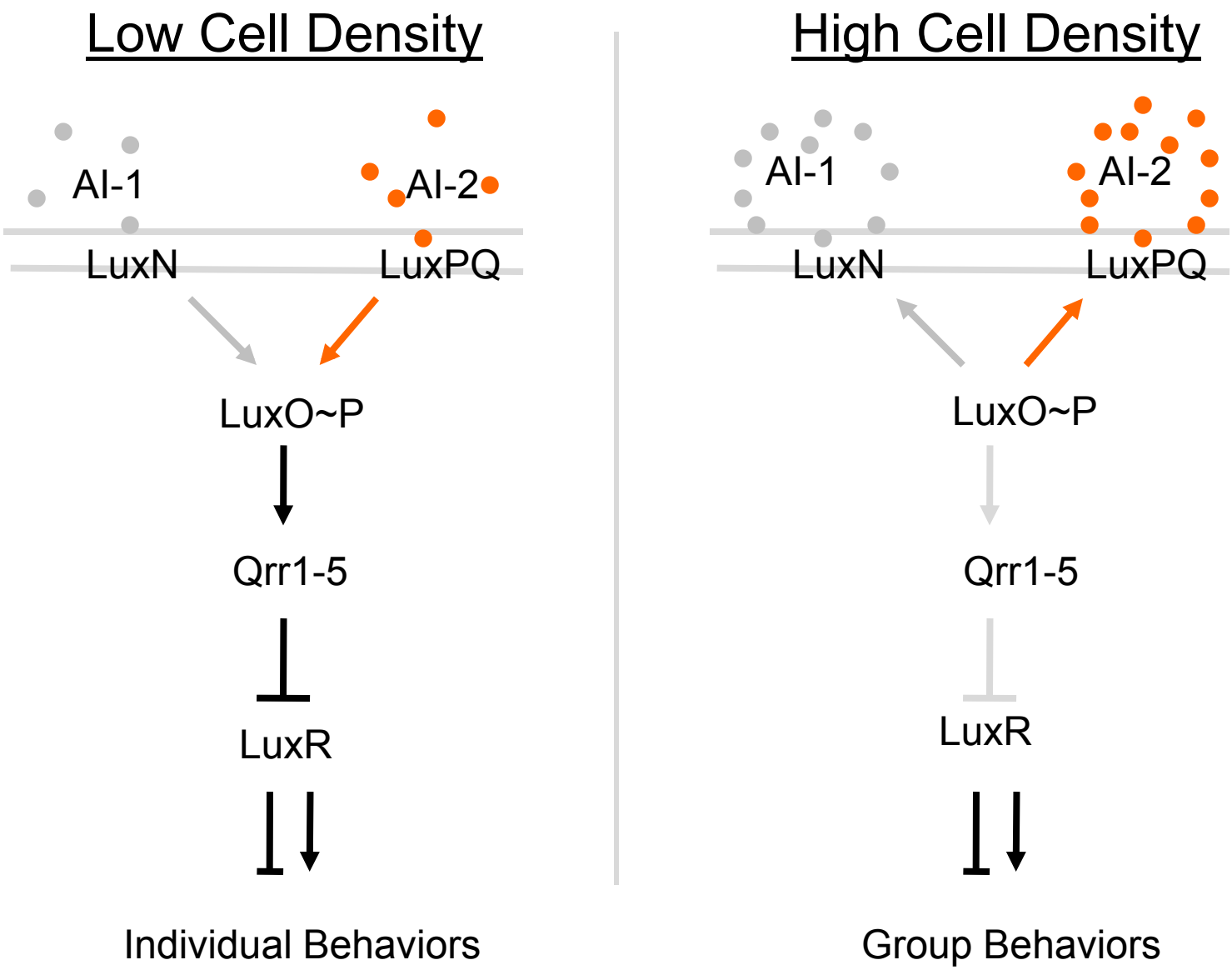
mRNA



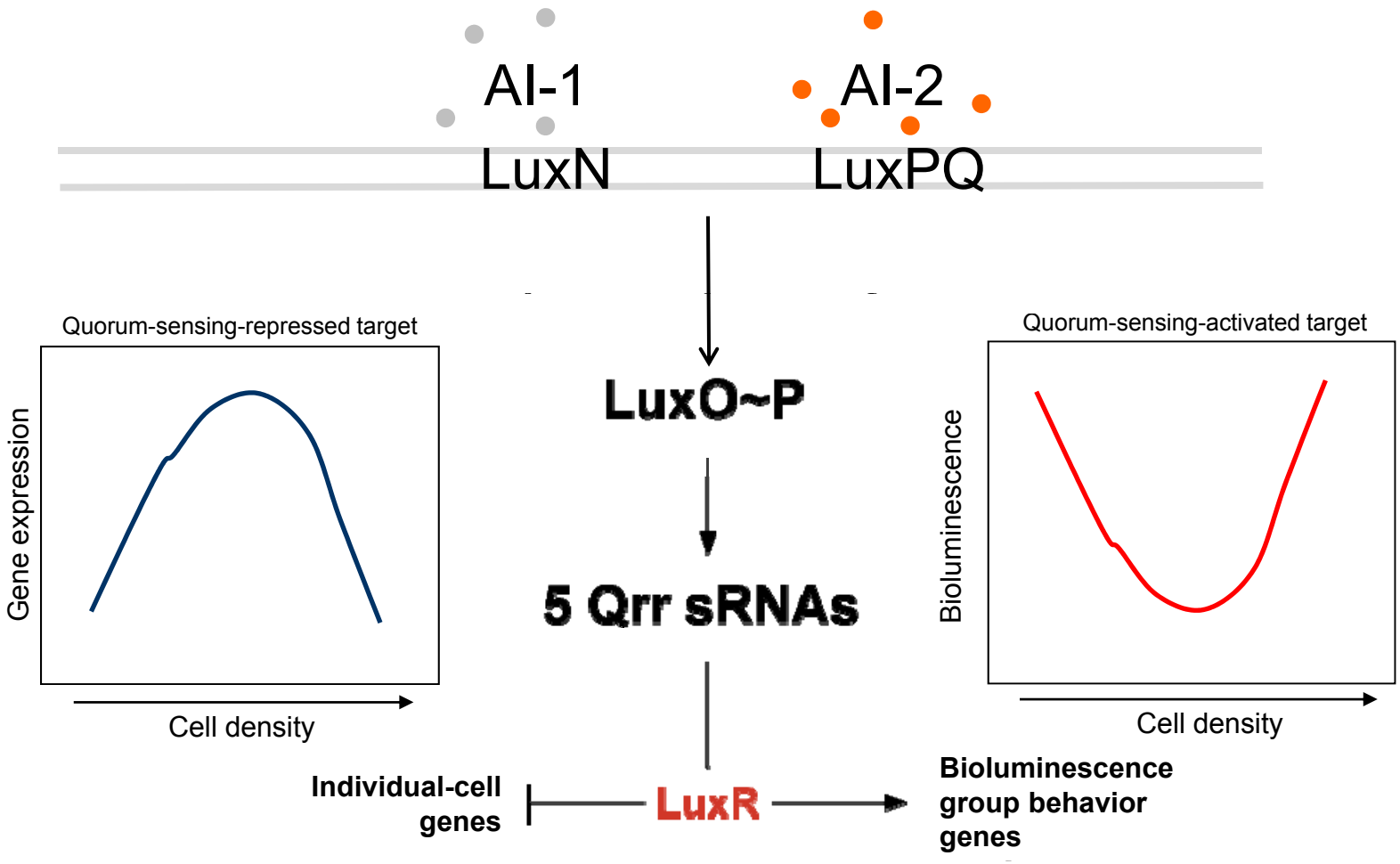
The *V. harveyi* Quorum-Sensing Network



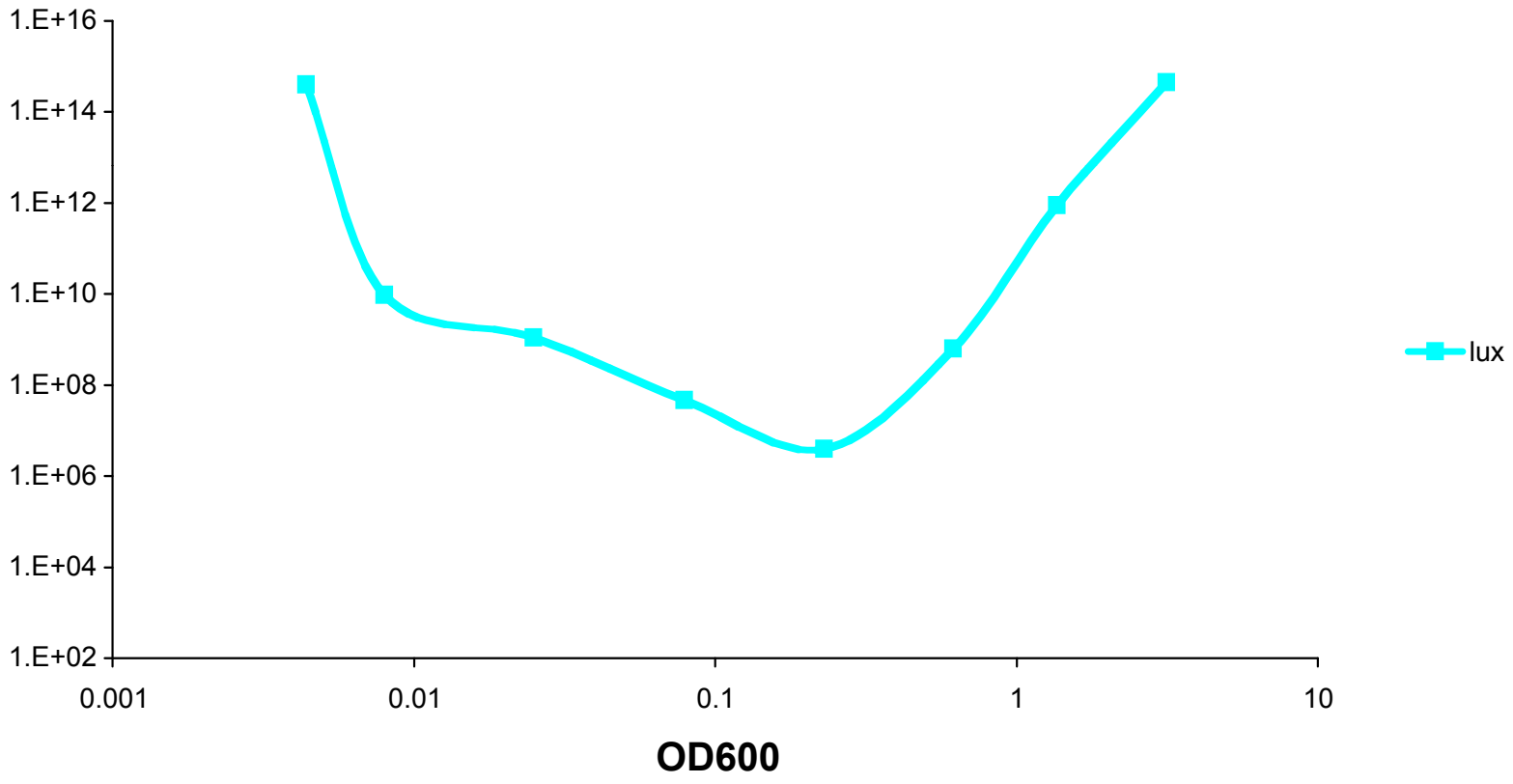
The *V. harveyi* Quorum-Sensing Network



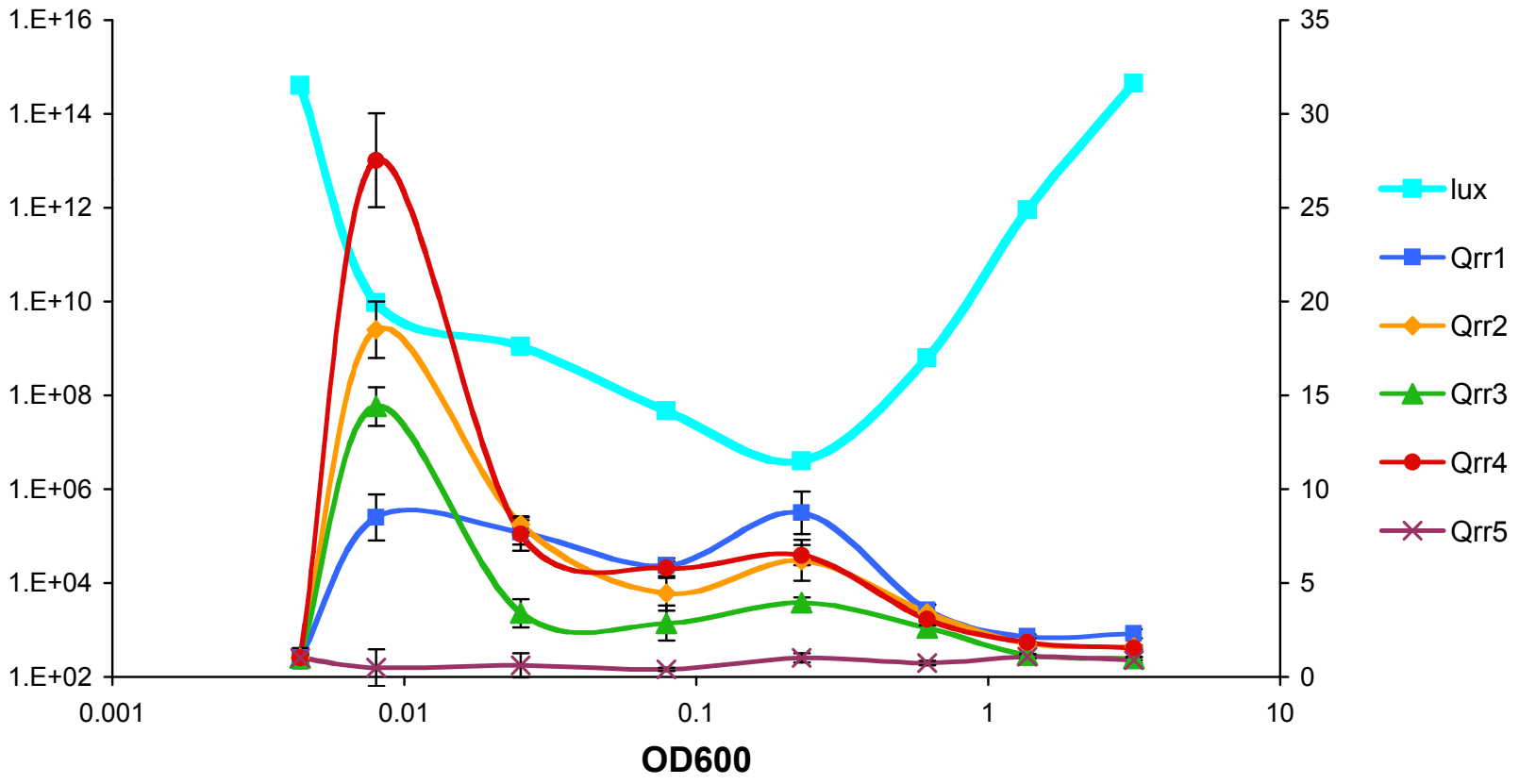
V. harveyi Quorum Sensing



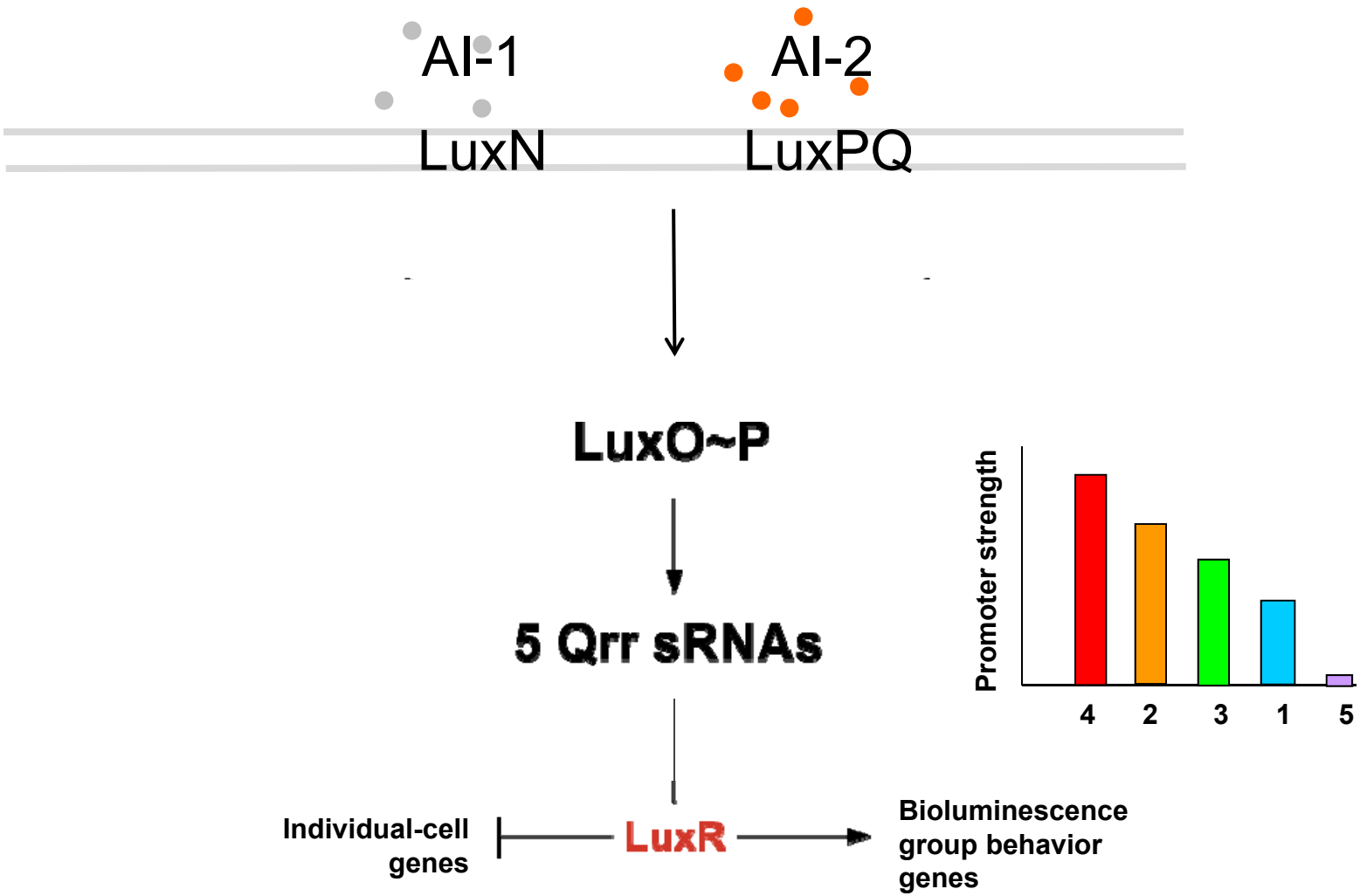
Differential Regulation of Qrr sRNAs



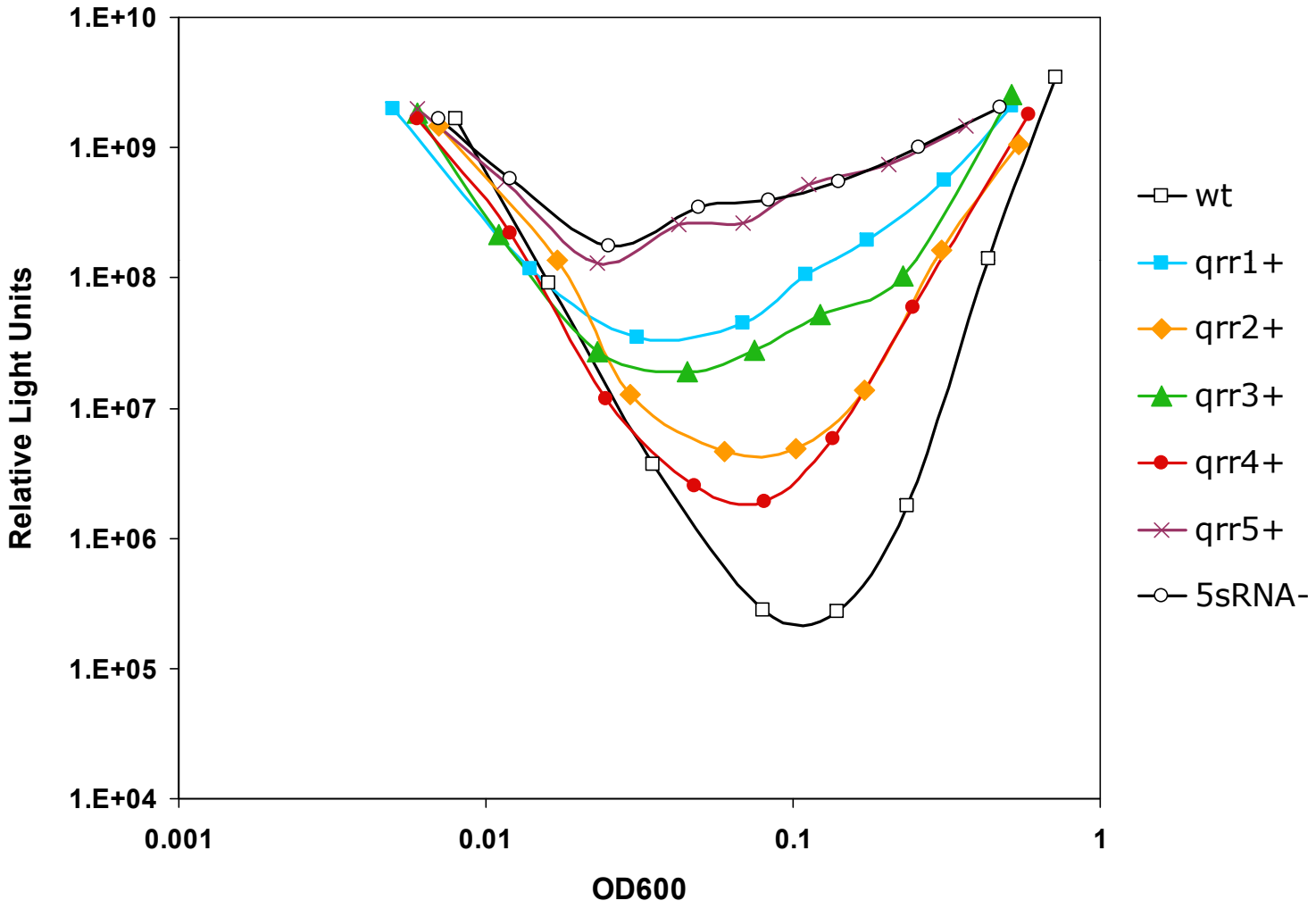
Differential Regulation of Qrr sRNAs



V. harveyi Quorum Sensing



The Qrrs Function Additively



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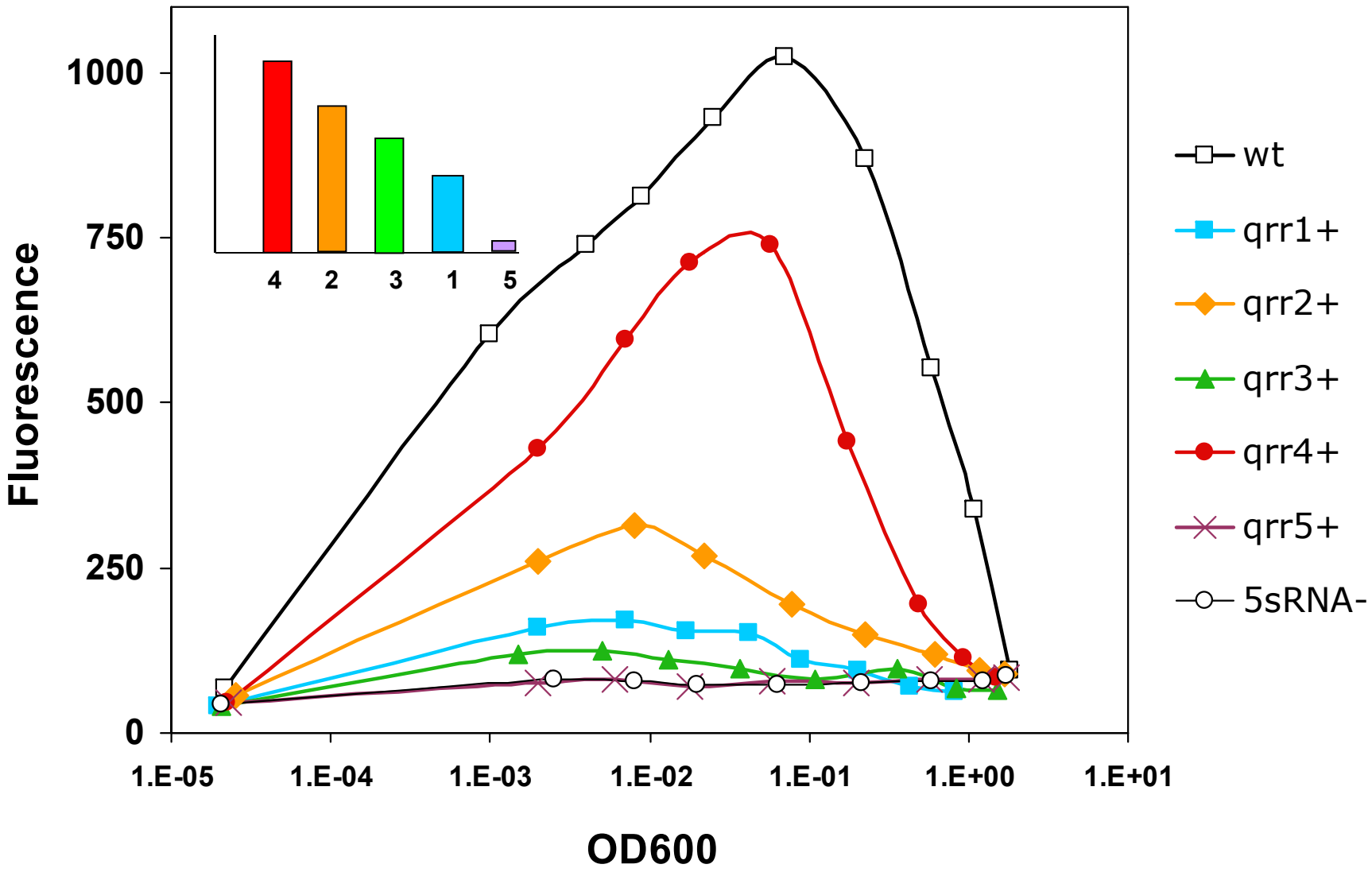
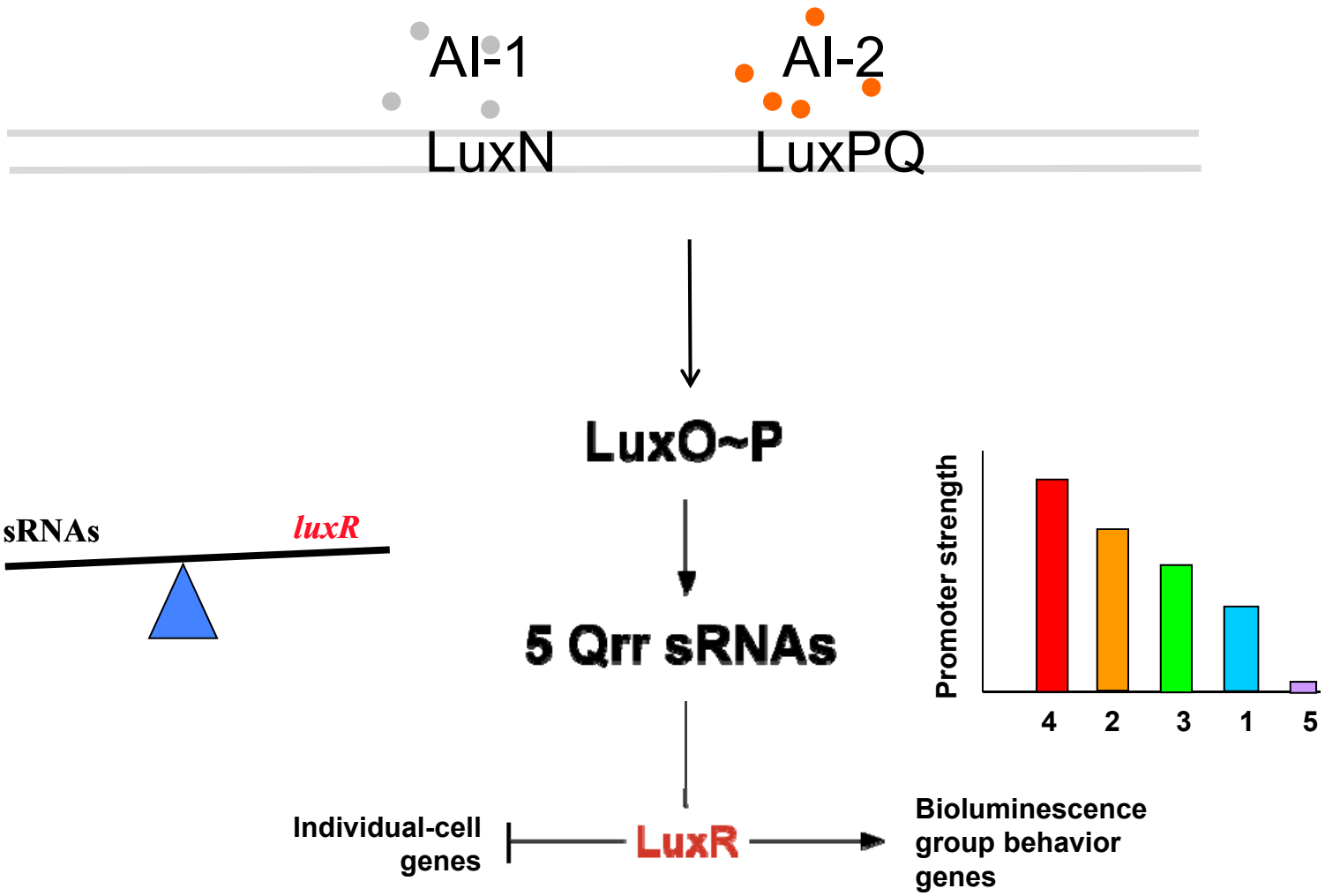
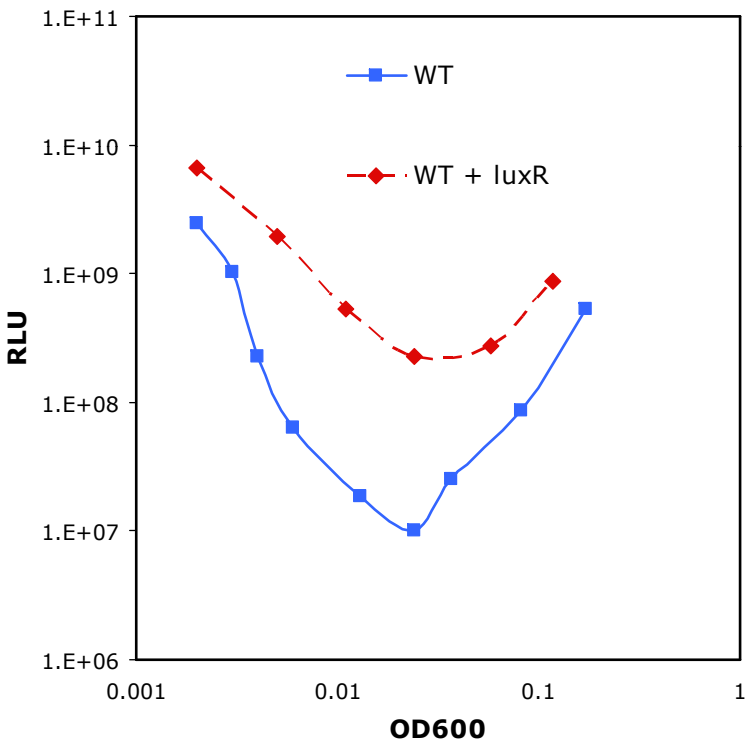
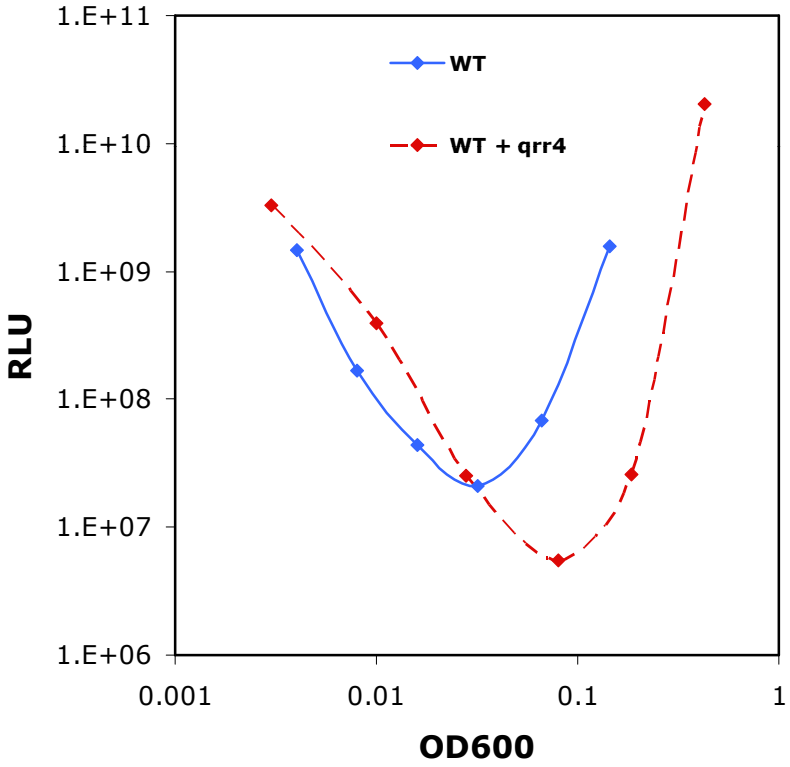


V. harveyi Quorum Sensing

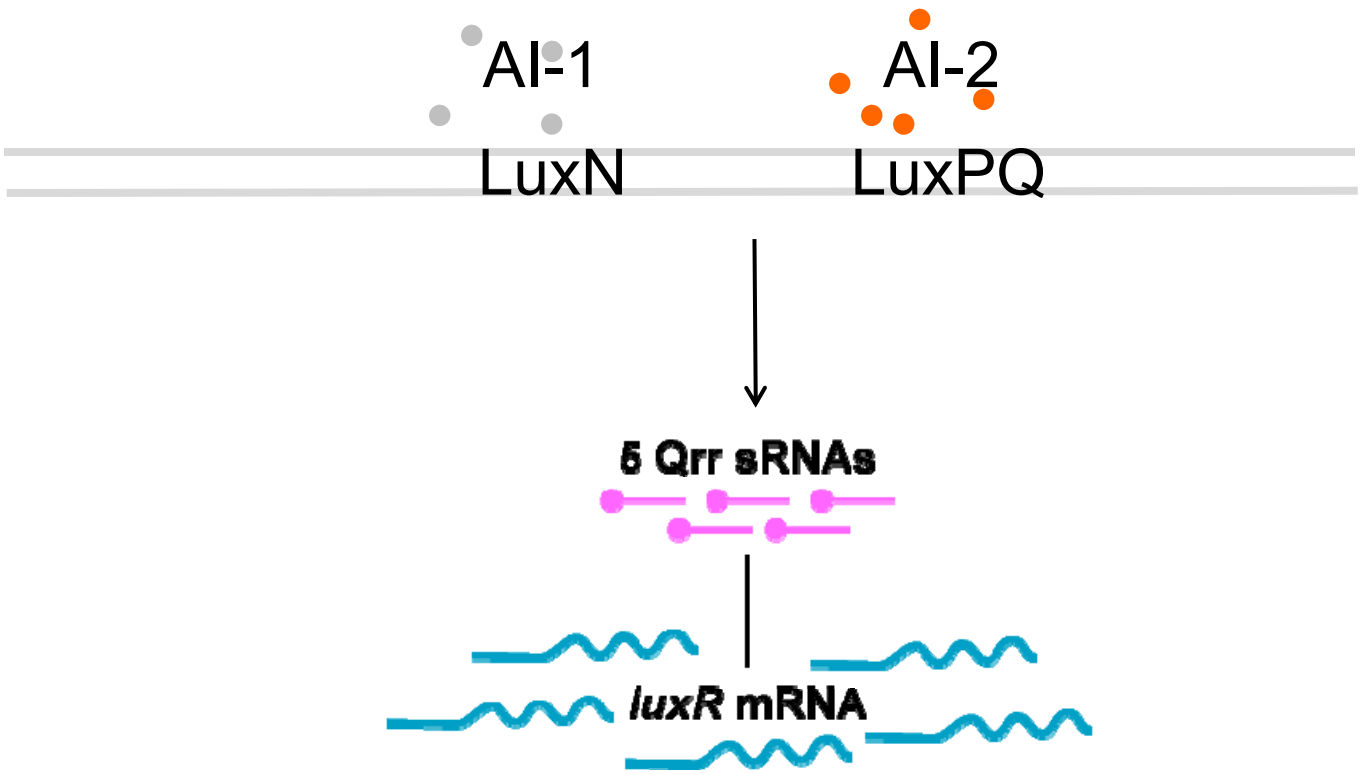


Titration Model: Balance of Qrrs and LuxR

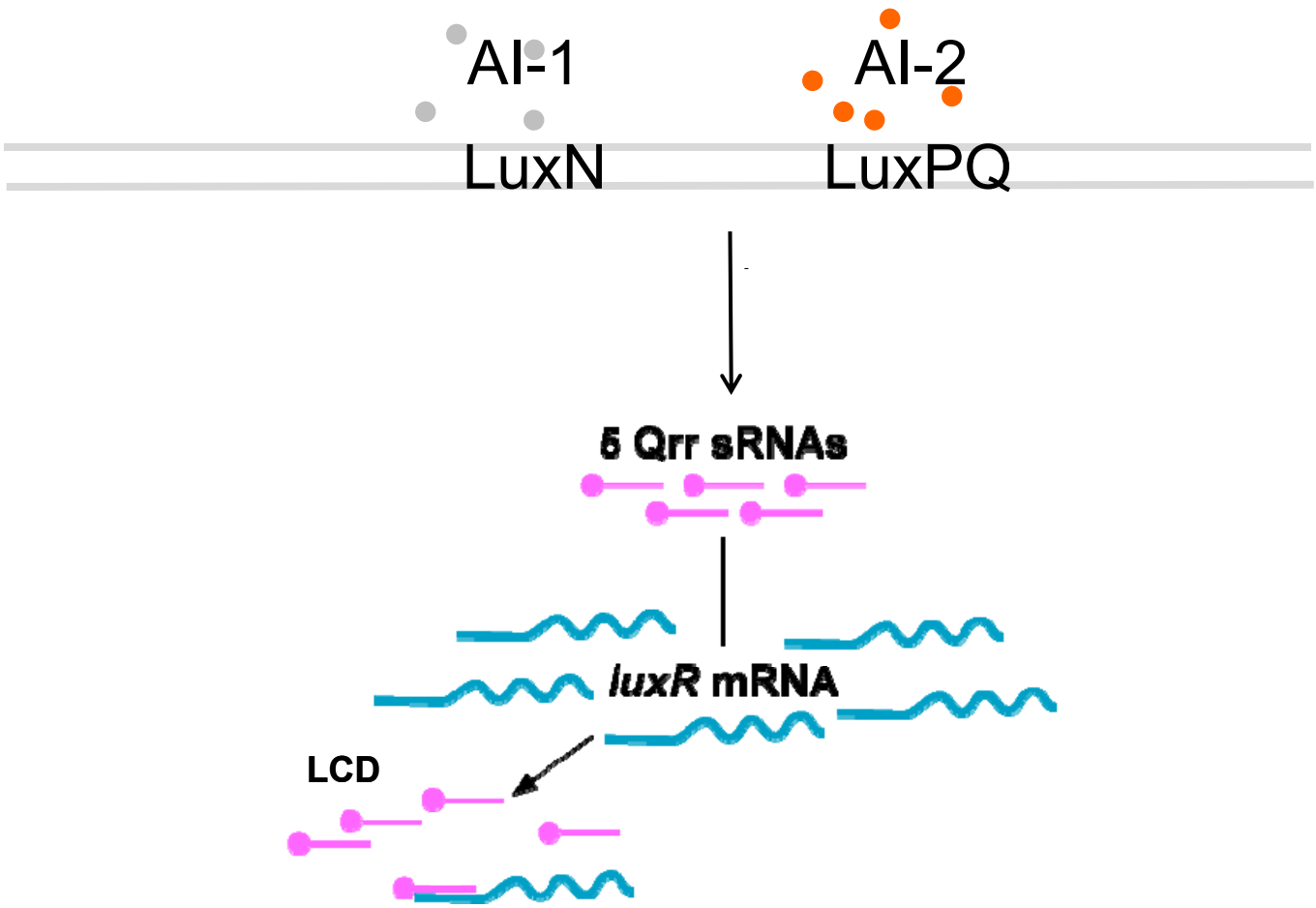




Precise Regulation of Gene Expression



Precise Regulation of Gene Expression



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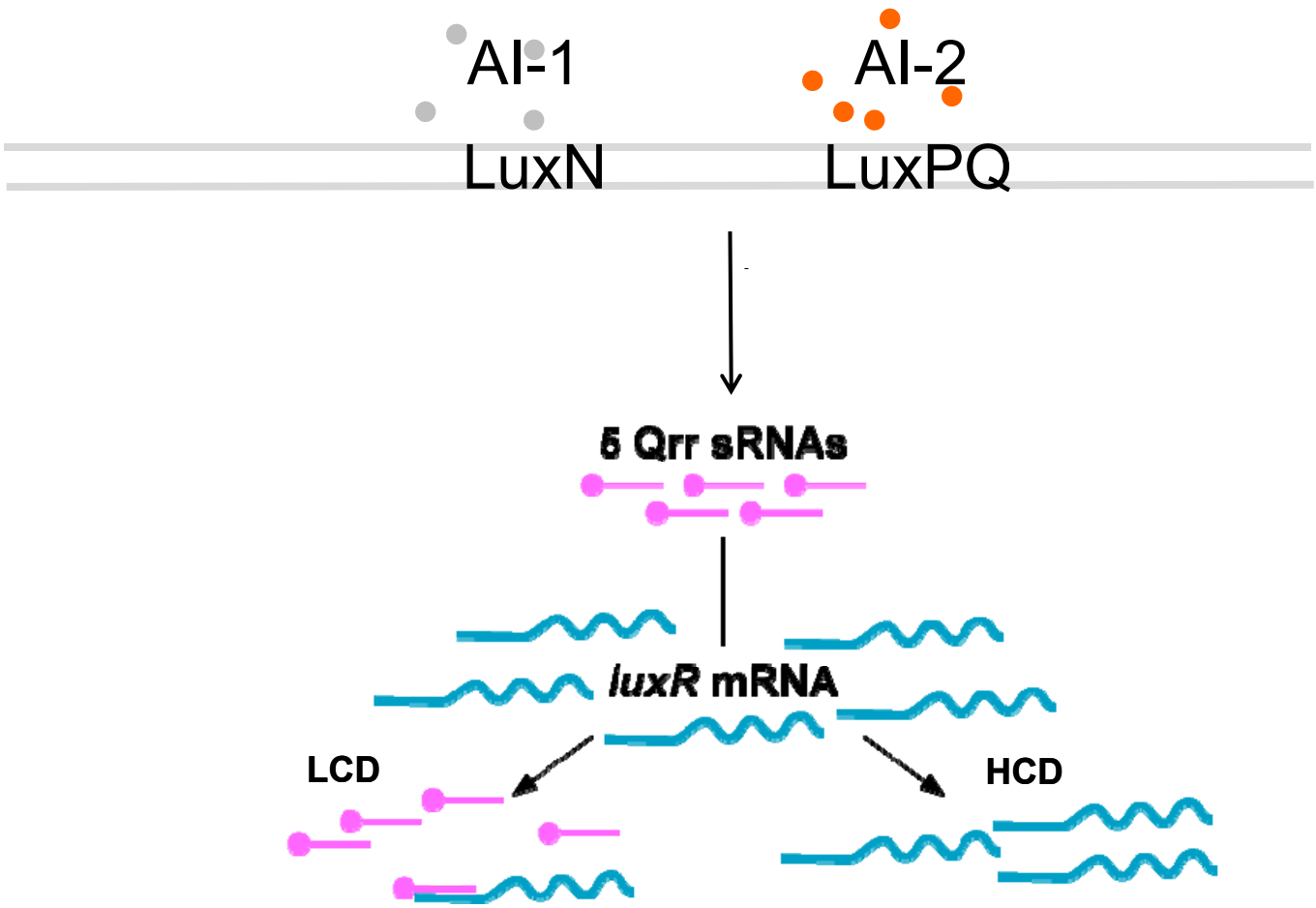
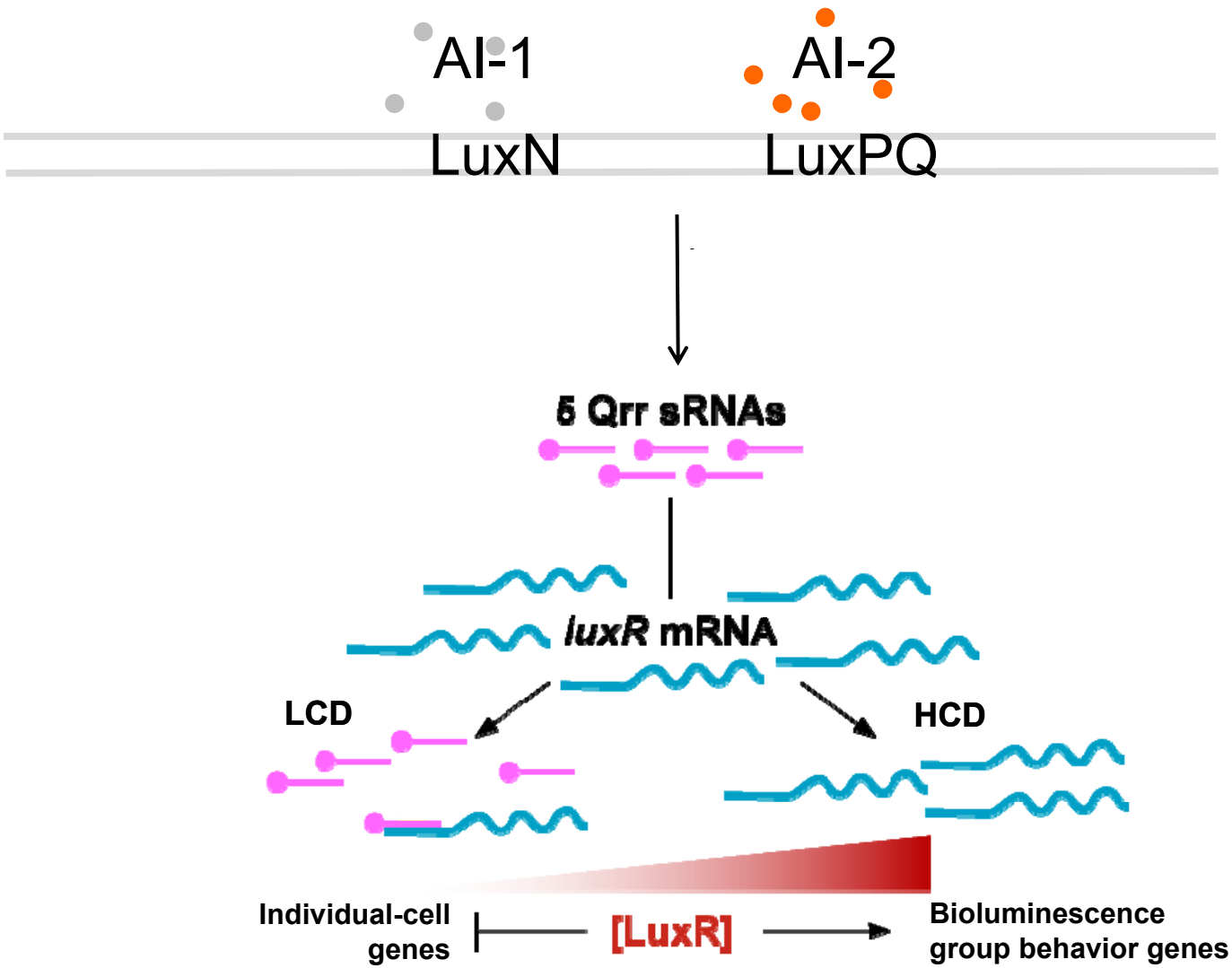
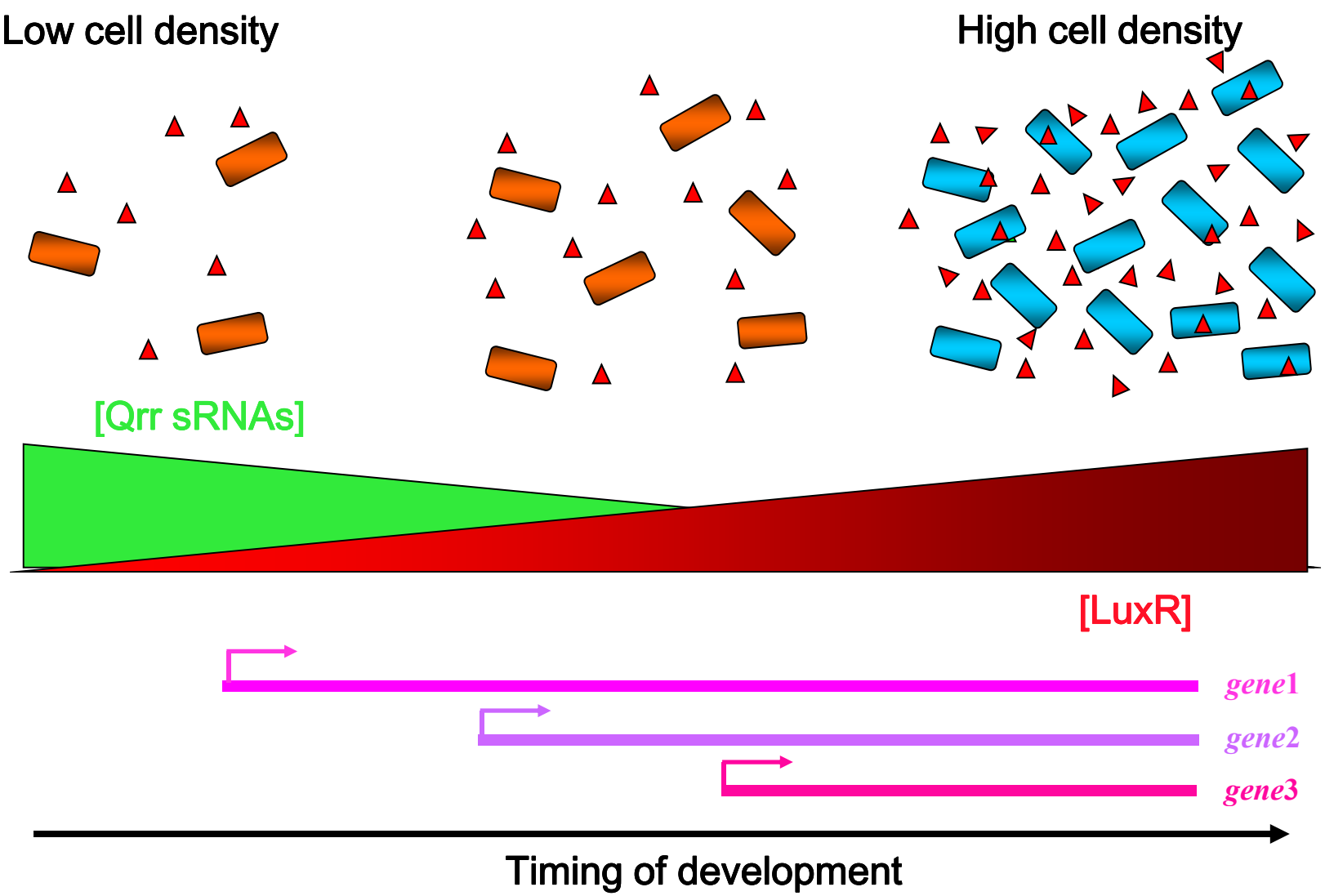


Precise Regulation of Gene Expression

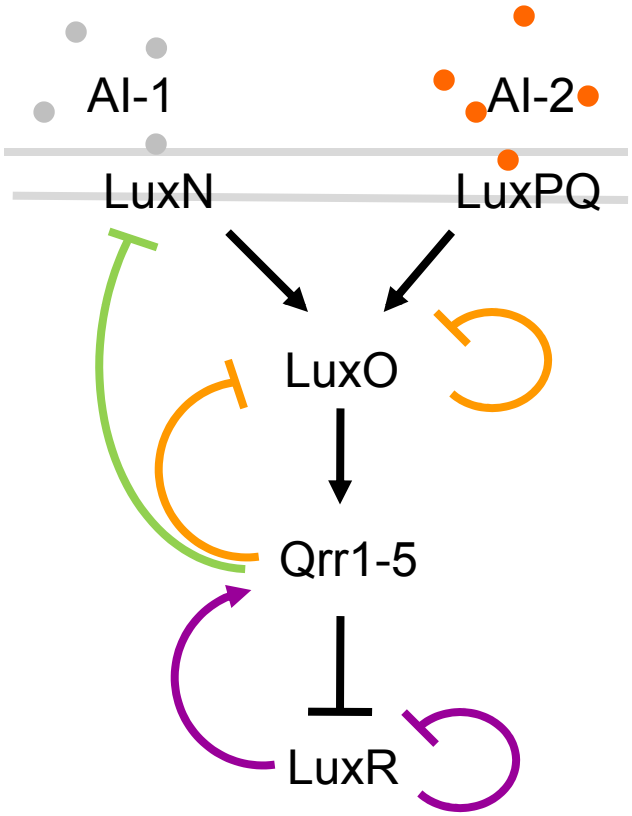


V. harveyi Quorum Sensing

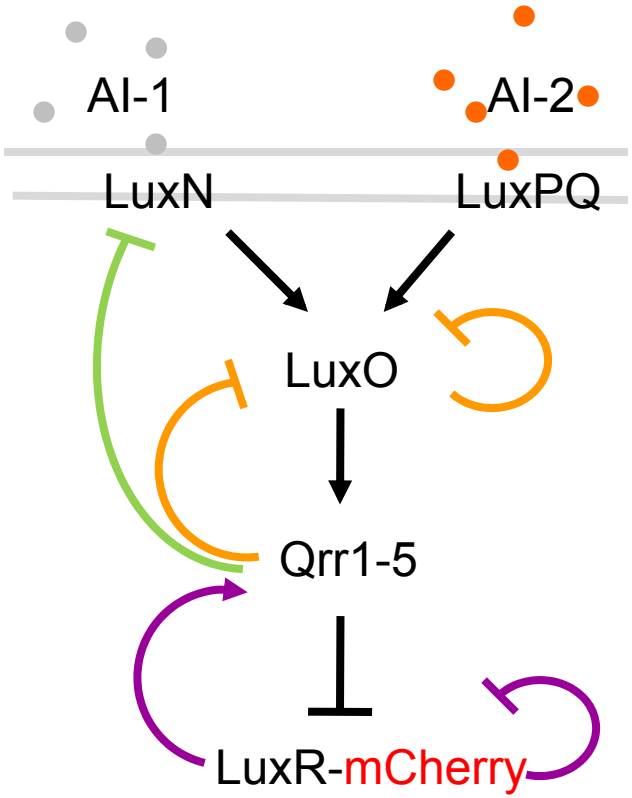


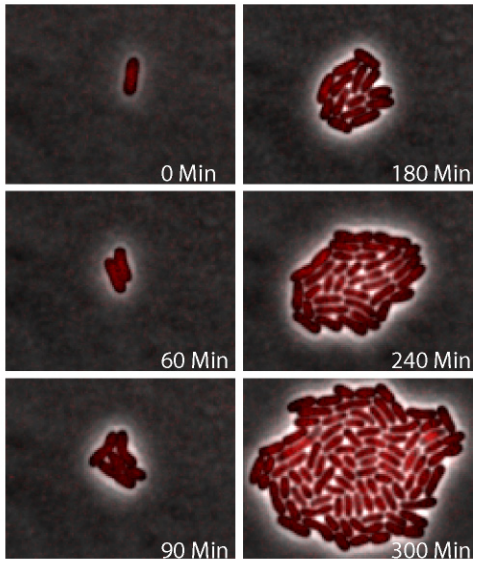
Feedback in the Circuit

Feedback Loops in the Network

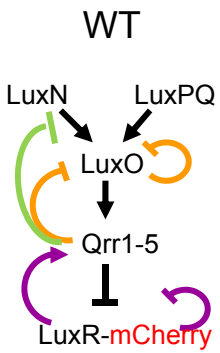


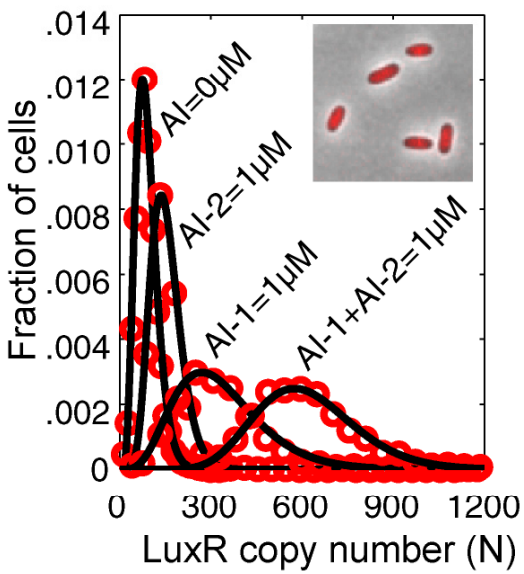
LuxR-mCherry Protein as the Output

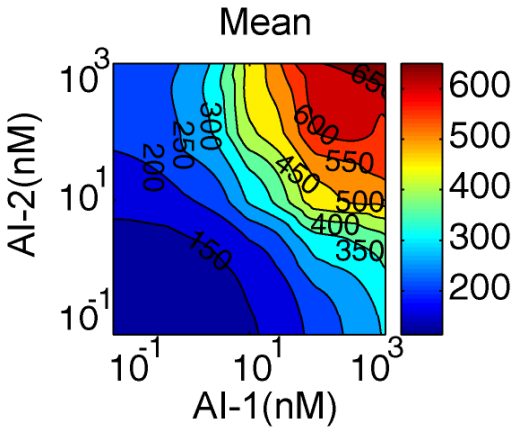




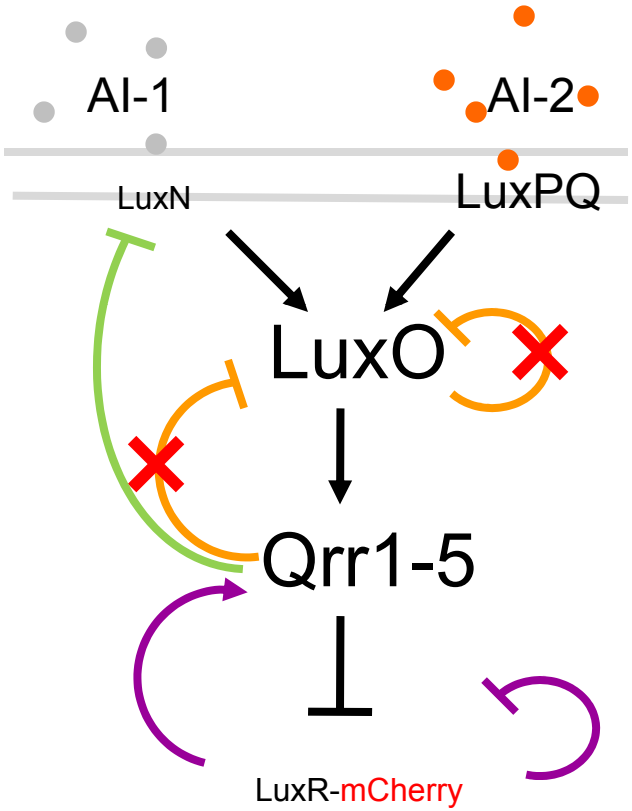
Wild-type Input-Output Relation

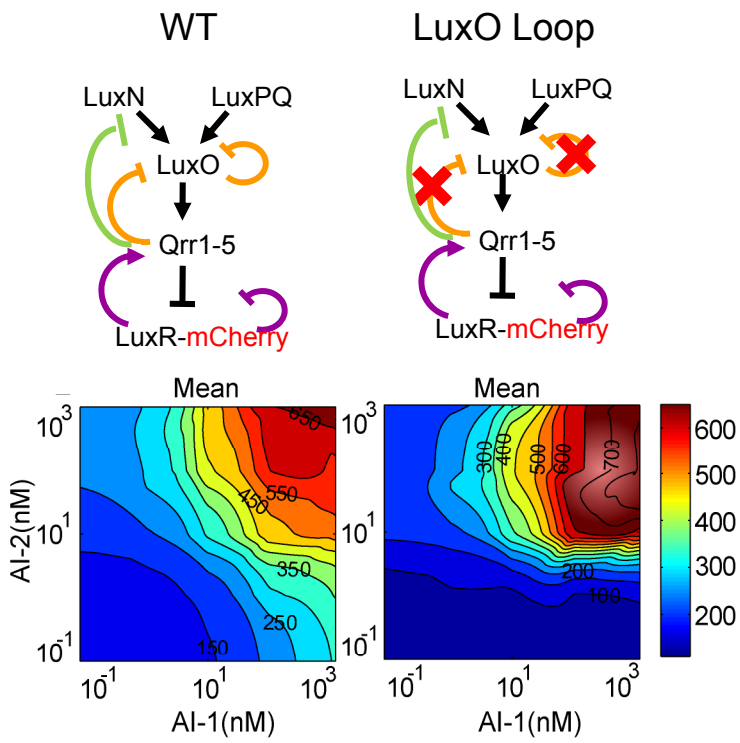




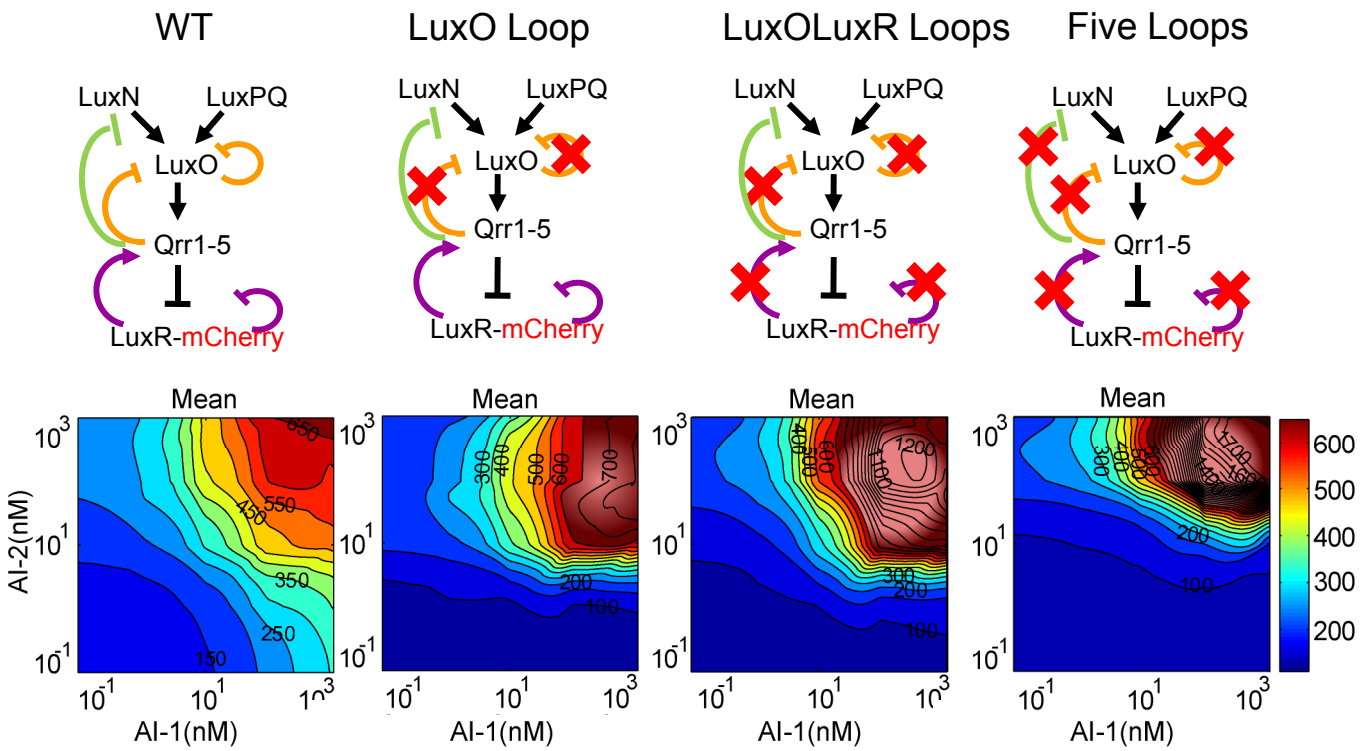


Effect of LuxO Feedback on Output





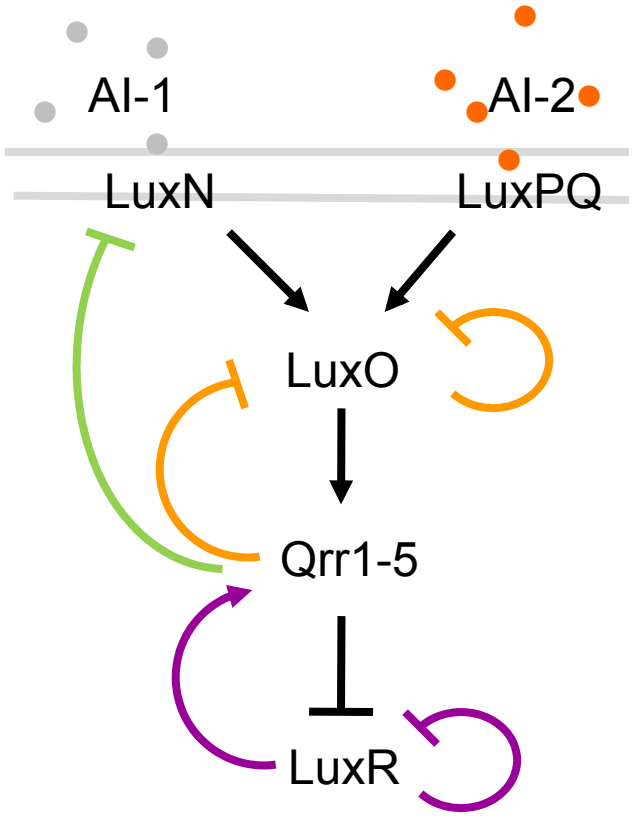
Effects of Feedback Loops on Output



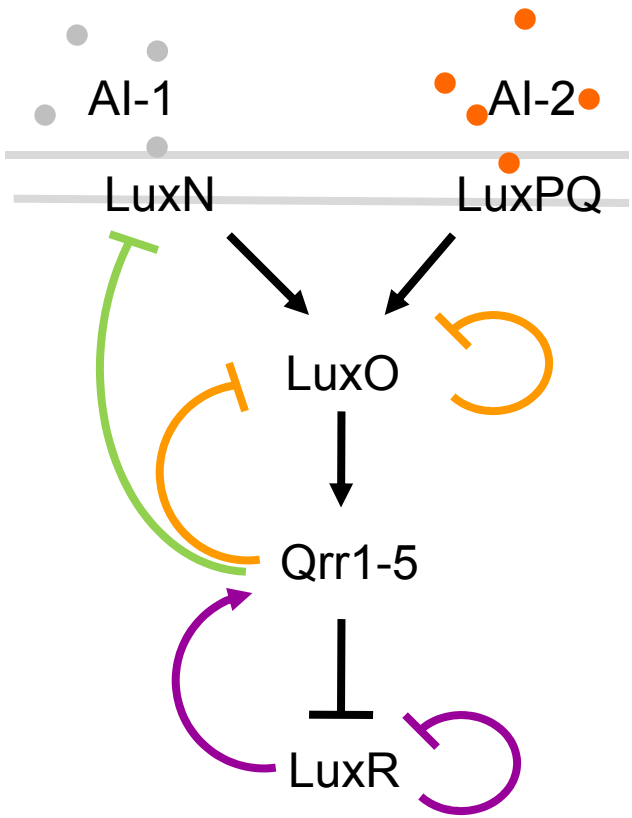
The circuit is designed to detect a large input dynamic range

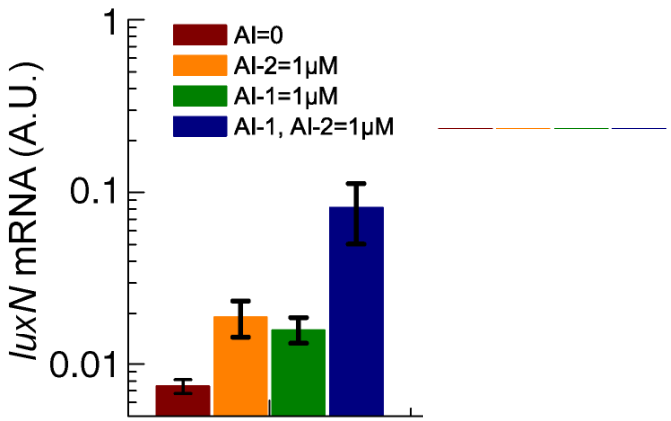
The circuit is designed to restrict the output dynamic range

A Feedback Loop to the LuxN Receptor



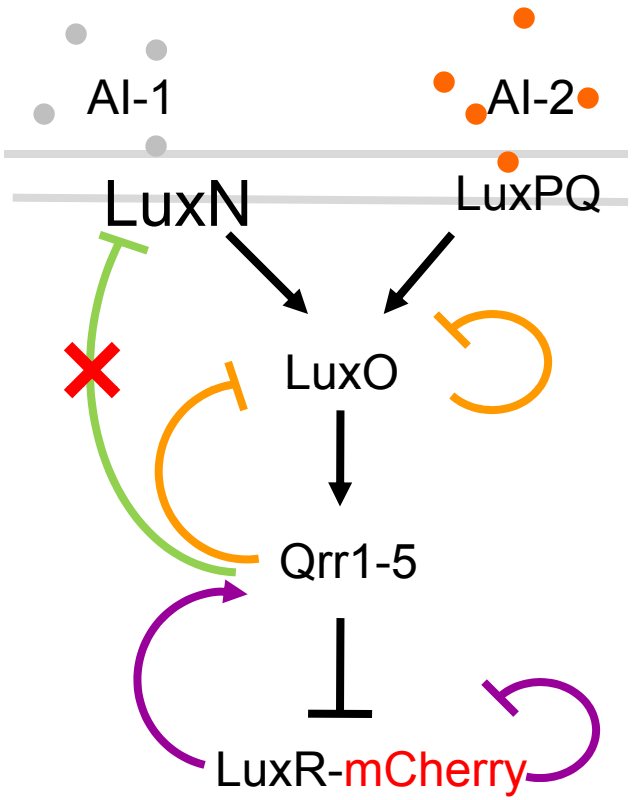
Cells Regulate Receptor Ratios

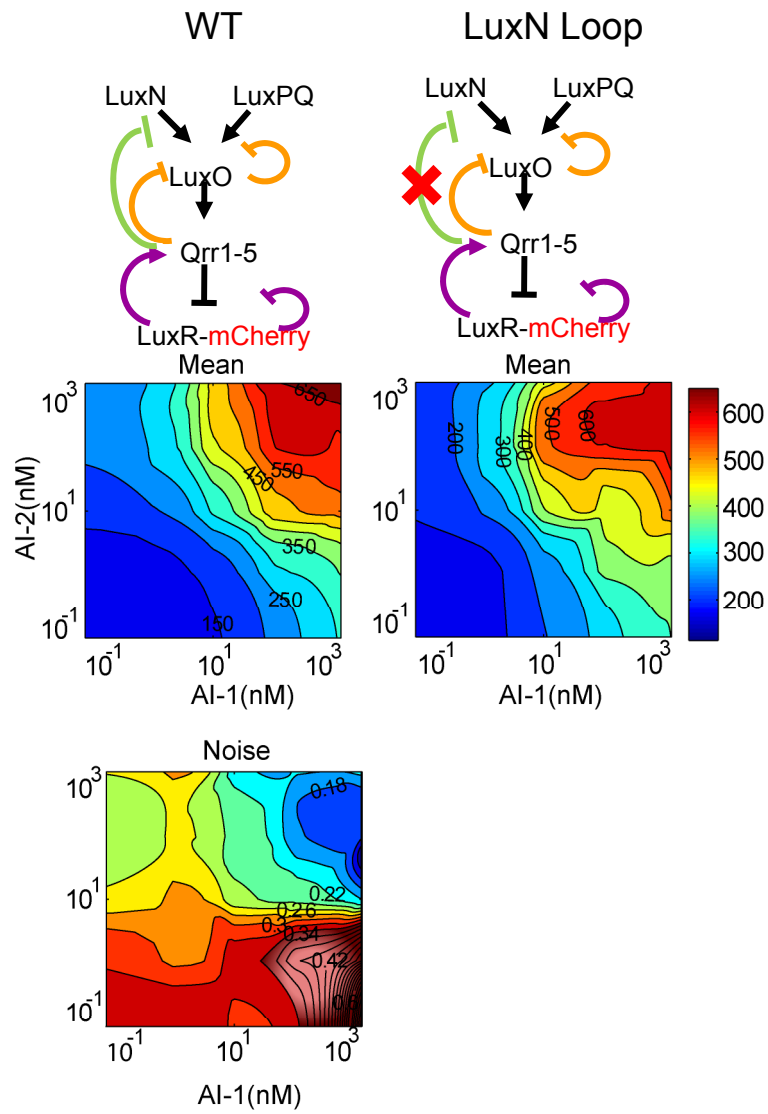




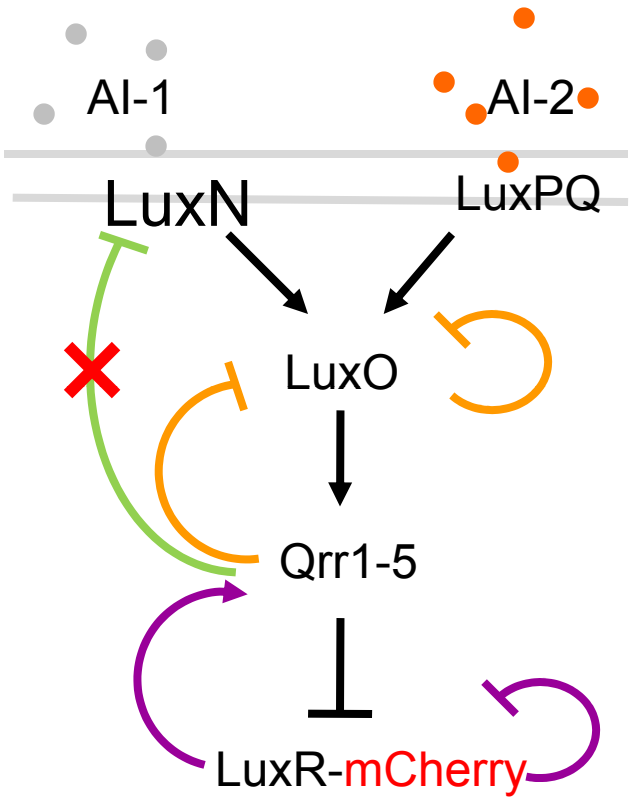
LuxN Receptor Level

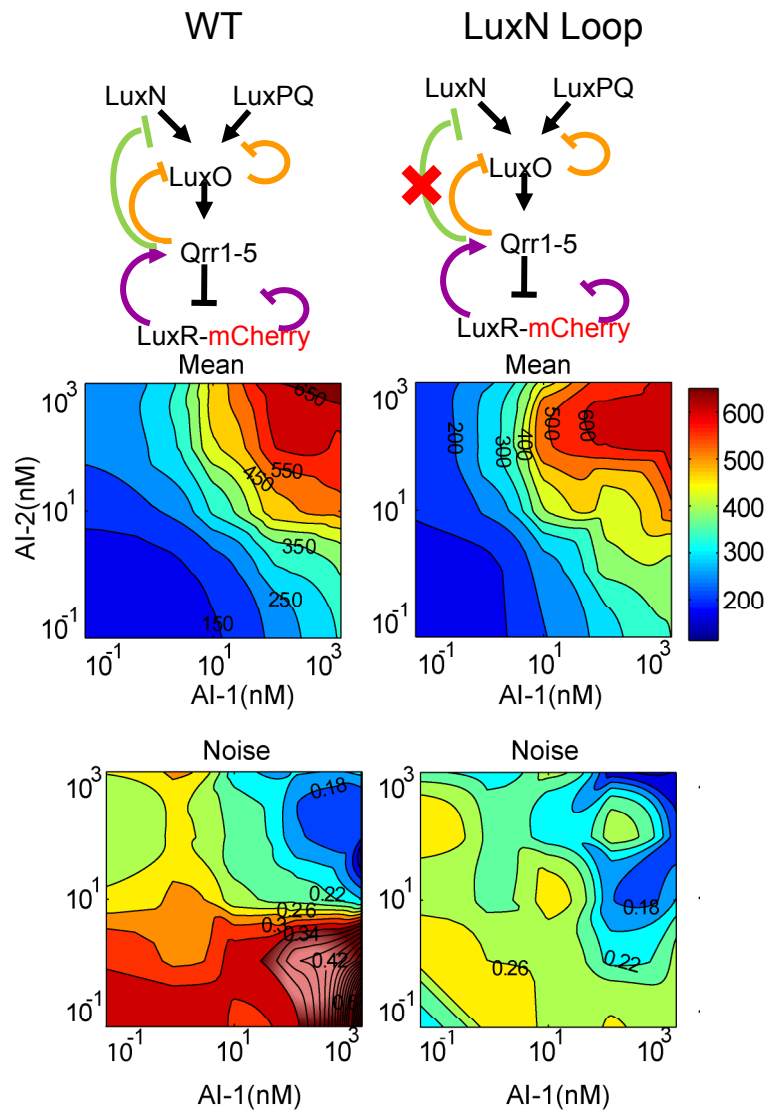
Eliminating Receptor Ratio Regulation





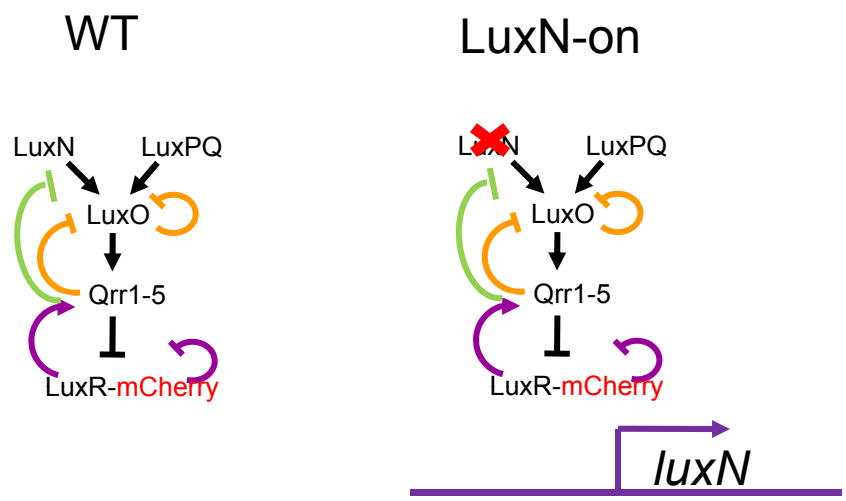
Eliminating Receptor Ratio Regulation

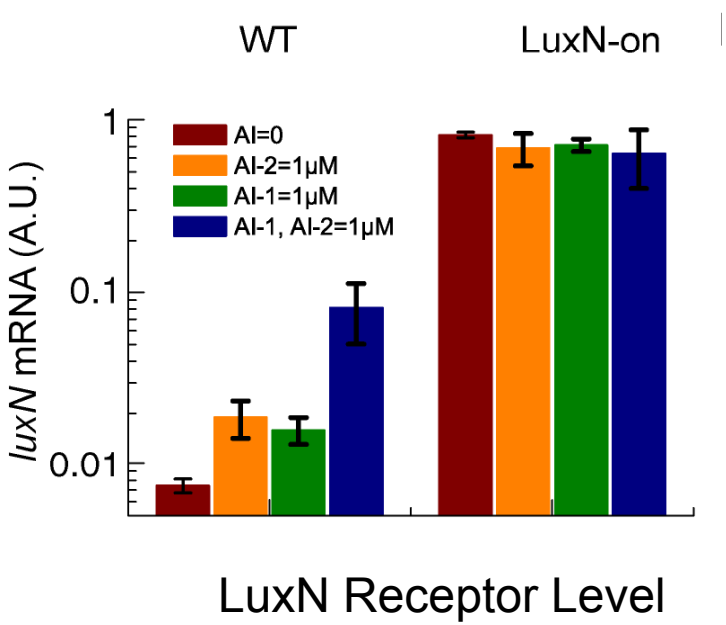




The LuxN Feedback Loop Adds Noise

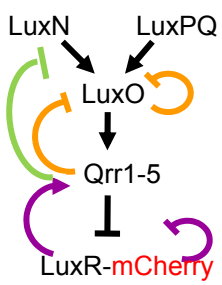
Extra LuxN to Alter Receptor Ratios



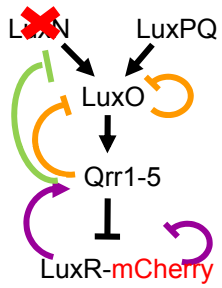


Adding Extra LuxN to Alter Receptor Ratios

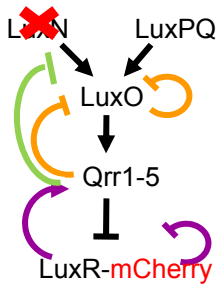
WT



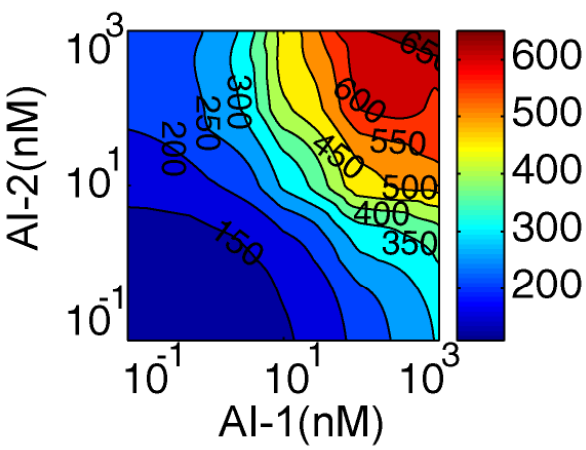
ΔLuxN

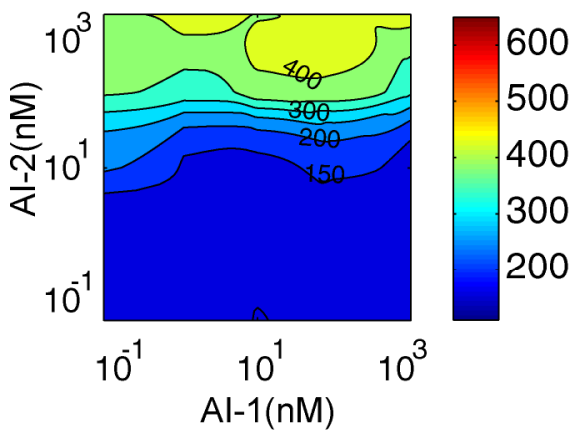


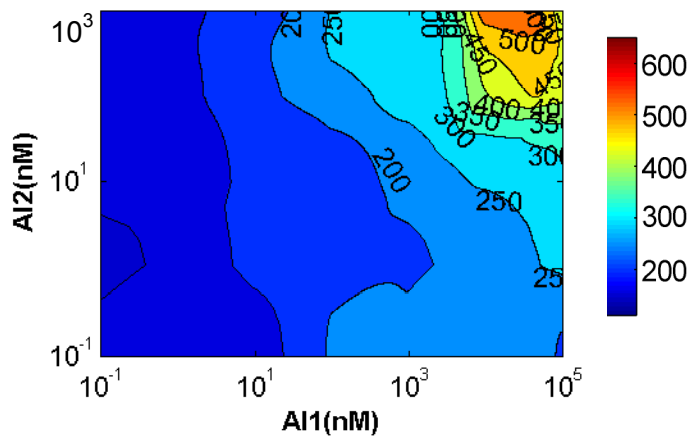
LuxN-on



Mean

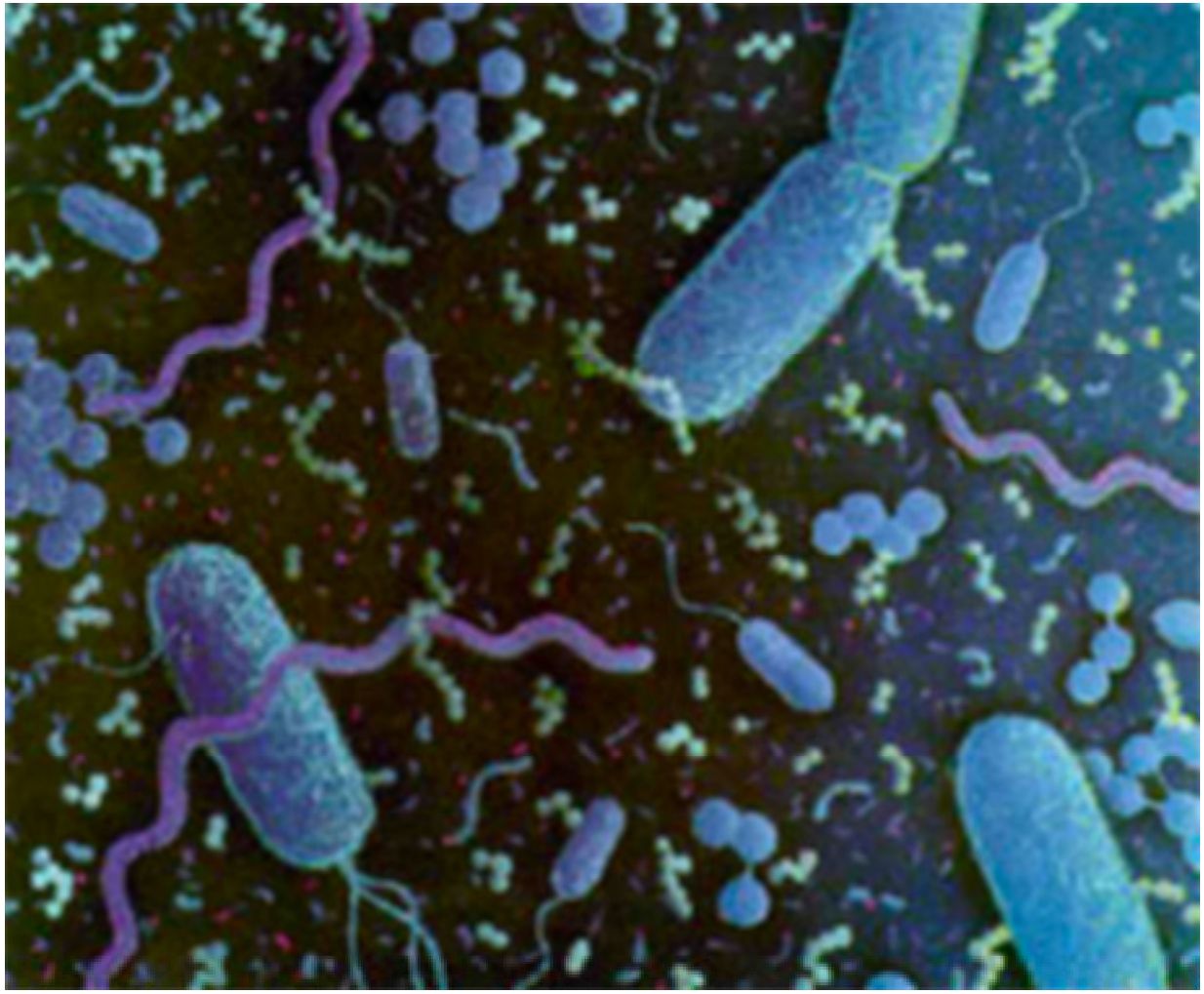






Why Regulate Receptor Ratios?

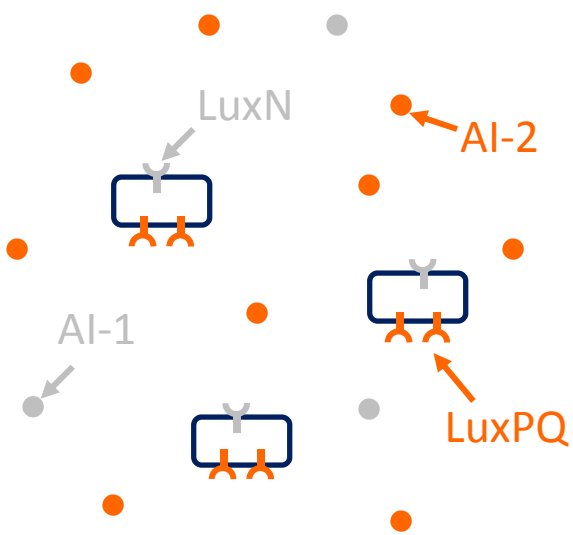
Bacterial Communities



Why Regulate Receptor Ratios?

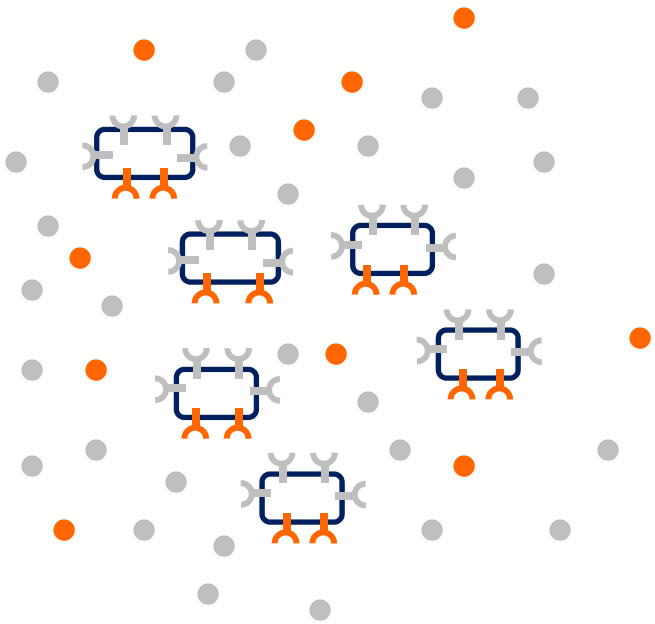
Low Cell Density

LuxN is repressed
Pay attention to AI-2
Filter out AI-1 fluctuations



High Cell Density

Increased LuxN is produced
Pay attention to AI-1
Filter out AI-2 fluctuations



Reminder: AI-1 means “Self” and AI-2 means “Other”

Ongoing Experiments

Precisely alter receptor ratios and monitor circuit function.

Control and regulate the input signal temporal profile using microfluidics.

Examine if the input dynamic range affects fitness.

Quorum Sensing In Bacteria

Bacteria talk to each other

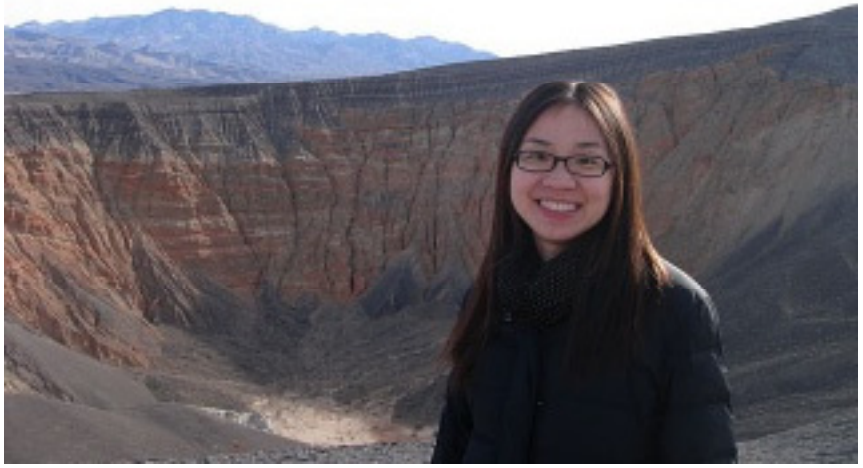
Bacteria are multi-cellular

Bacteria can distinguish self from other

Receptor regulation allows signal discrimination

Feedback loops control input range, output range and noise

Shu Wen Teng



Kim Tu

Long time Collaborator: Ned Wingreen