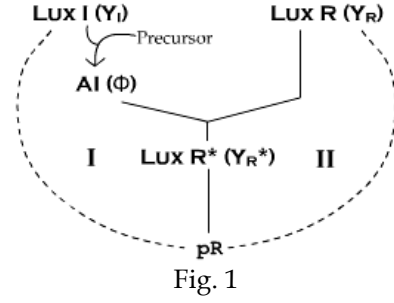


Mathematical Model

In this section, we present the differential equations used in the mathematical model of our synthetic *Vibrio* quorum sensing system. Fig. 1 is a schematic representation that outlines the important components of the system. The following dynamical variables are involved,

- Y_R : concentration of LuxR
- Y_I : concentration of LuxI
- ϕ_i : concentration of autoinducer (AI) inside the cell
- ϕ_e : concentration of AI in the surrounding medium
- ρ : cell number density



LuxI is the enzyme involved in the production of autoinducer, AI from a precursor that is constitutively expressed in the cell. LuxR*, the active form of LuxR formed on binding with AI, is the transcriptional regulator of the pR promoter. By placing either of the two proteins, LuxI and LuxR under the control of pR, we obtain a positive-feedback system.

I. LuxI in feedback:

$$\begin{aligned}
 \text{i. } \quad & \frac{dY_R}{dt} = \alpha_o \lambda_R - \gamma_R Y_R - \gamma_c Y_R \\
 \text{ii. } \quad & \frac{dY_I}{dt} = \alpha_1 \left(\beta_1 + \frac{(1 - \beta_1) Y_R^{*n}}{K_R^n + Y_R^{*n}} \right) \lambda_I - \gamma_I Y_I - \gamma_c Y_I
 \end{aligned}$$

where,

$\alpha_o \rightarrow$ number of luxR transcripts

$\alpha_1 \rightarrow$ maximal expression of luxI

$\lambda_R \rightarrow$ translational rate of LuxR

$\lambda_I \rightarrow$ translational rate of LuxI

$\gamma_R \rightarrow$ degradation rate of LuxR

$\gamma_I \rightarrow$ degradation rate of LuxI

$\gamma_c \rightarrow$ dilution factor (as cells divide, concentration of LuxR decreases)

$\alpha_1 \beta_1 \rightarrow$ basal expression of luxI

$Y_R^* \rightarrow$ concentration of LuxR*

$n \rightarrow$ Hill coefficient

$K_R \rightarrow$ half saturation constant

Here, we have assumed that the expression of a gene from a regulated promoter has a sigmoidal form.

II. LuxR Feedback Loop:

$$\text{iii. } \frac{dY_I}{dt} = \alpha_o \lambda_I - \gamma_I Y_I - \gamma_c Y_I$$

$$\text{iv. } \frac{dY_R}{dt} = \alpha_1 \left(\beta_1 + \frac{(1 - \beta_1) Y_R^{*n}}{K_R^n + Y_R^{*n}} \right) \lambda_R - \gamma_R Y_R - \gamma_c Y_R$$

Here, $\alpha_o \rightarrow$ number of luxI transcripts
 $\alpha_1 \rightarrow$ maximal expression of luxR

For both the topologies (I and II), the differential equations governing the other dynamical variables are as follows.

$$\bullet \quad \frac{d\phi_i}{dt} = \eta(\phi_e - \phi_i) - \gamma_c \phi_i - \gamma_i \phi_i + k_1 Y_I$$

where, $k_1 \rightarrow$ rate constant determining the production rate of autoinducer due to LuxI
 $\eta \rightarrow$ diffusion rate of autoinducer across the cell membrane

The above equation can be arrived at using diffusion theory. The derivation for the same is available under the link [AI Derivation](#).

$$\bullet \quad \frac{d\phi_e}{dt} = \rho v_c \left[\eta(\phi_i - \phi_e) + \gamma_c \phi_e \right] - \gamma_e \phi_e$$

where, $v_c \rightarrow$ volume of individual cell

- Due to growth of cells in the medium, the volume fraction occupied by the cells increases with time. This is represented by the following differential equation,

$$\frac{d(\rho v_c)}{dt} = \gamma_c (\rho v_c)$$

- LuxR* is a complex that is obtained by the binding of autoinducer molecules to LuxR. The formation of LuxR* is very fast as compared to transcription, translation and cell growth. Hence, we assume LuxR* to be in quasi-equilibrium with LuxR. The concentration of LuxR* can be expressed as,

$$Y_R^* = Y_R \left(\frac{\phi_i^{n_1}}{K_\phi + \phi_i^{n_1}} \right)$$

where, $K_\phi \rightarrow$ half saturation constant
 $n_1 \rightarrow$ Hill coefficient

This equation has been derived using elementary rate kinetics. The derivation can be found under the link [LuxR* Derivation](#).

Dimensional Analysis

In order to facilitate computation and choose effective parameters, we rescale our set of differential equations and convert each dynamical variable into a dimensionless quantity. To do this, we first define the following quantities,

$$Y_I = \bar{Y}_I \tilde{Y}_I$$

$$Y_R = \bar{Y}_R \tilde{Y}_R$$

$$t = \bar{t} \tilde{t}$$

$$\phi_i = \bar{\phi}_i \tilde{\phi}_i$$

$$\phi_e = \bar{\phi}_e \tilde{\phi}_e$$

Here, the barred terms are constant scaling factors and the tilde terms are the required dimensionless variables.

In order to draw effective parameters, we set the scaling factors as follows,

$$(i) \bar{t} = \frac{1}{\gamma_c}$$

$$(ii) \frac{\alpha_1 \lambda_I}{\gamma_c \bar{Y}_I} = 1 \Rightarrow \bar{Y}_I = \left(\frac{\alpha_1 \lambda_I}{\gamma_c} \right)$$

$$(iii) \frac{\alpha_1 \lambda_R}{\gamma_c \bar{Y}_R} = 1 \Rightarrow \bar{Y}_R = \left(\frac{\alpha_1 \lambda_R}{\gamma_c} \right)$$

$$(iv) \bar{\phi}_i = \bar{\phi}_e = \bar{\phi} = K_\phi$$

We then set time units by setting: $\gamma_c = 1$

Substituting the above values in the equations greatly simplifies them. Additionally, a combination of certain parameters gives rise to the following effective parameters.

$$\alpha = \frac{\alpha_o}{\alpha_1}$$

$$k_\phi = \frac{k_1 \alpha_1 \lambda_l}{K_\phi}$$

Thus, our final equations in the rescaled dimensionless form are as follows,

I. LuxI in feedback:

$$\frac{dY_R}{dt} = \alpha - (1 + \gamma_R)Y_R$$

$$\frac{dY_I}{dt} = \left(\beta + (1 - \beta) \frac{(\alpha_1 \lambda_R)^n Y_R^n \left(\frac{\phi_i^{n_1}}{1 + \phi_i^{n_1}} \right)^n}{K_R^n + (\alpha_1 \lambda_R)^n Y_R^n \left(\frac{\phi_i^{n_1}}{1 + \phi_i^{n_1}} \right)^n} \right) - (1 + \gamma_I)Y_I$$

II. LuxR in feedback:

$$\frac{dY_I}{dt} = \alpha - (1 + \gamma_I)Y_I$$

$$\frac{dY_R}{dt} = \left(\beta + (1 - \beta) \frac{(\alpha_1 \lambda_R)^n Y_R^n \left(\frac{\phi_i^{n_1}}{1 + \phi_i^{n_1}} \right)^n}{K_R^n + (\alpha_1 \lambda_R)^n Y_R^n \left(\frac{\phi_i^{n_1}}{1 + \phi_i^{n_1}} \right)^n} \right) - (1 + \gamma_R)Y_R$$

$$\frac{d\phi_i}{dt} = k_\phi Y_I + \eta(\phi_e - \phi_i) - (1 + \gamma_i)\phi_i$$

$$\frac{d\phi_e}{dt} = \rho v_c [\eta(\phi_i - \phi_e) + \phi_e] - \gamma_e \phi_e$$

$$\frac{d(\rho v_c)}{dt} = \rho v_c$$

Parameter ranges:

Parameters were drawn at random from certain ranges based on biological considerations and the model was simulated.

Parameter	Range	Reasoning
n, n_1	linspace (2,4)	reasonable range of values for Hill coefficients
α	logspace (-1, 0)	we set maximum rate of gene expression as 1 and basal 0.1
β	logspace (-2,-1)	we set basal rate of gene expression from the pR promoter as 0.01 to 0.1 times α
$\gamma_R, \gamma_I, \gamma_i, \gamma_e$	logspace (-1, 0)	we set degradation rates of proteins as 0.1 to 1 times the rate of dilution, $\gamma_c (=1)$
η	logspace (1, 2)* K_ϕ	based on our analysis that η must be $>10^* K_\phi$ to ensure that the rate of diffusion of AI is high enough such that the pR promoter is not turned on at the beginning of the simulation; hence we span from 10 times to 100 times K_ϕ
K_ϕ	logspace (3, 5)	based on our analysis that K_ϕ must be $> 10^3$ for pR promoter to be turned on within reasonable limits of cell density
K_R	logspace (-1, 1)	the half saturation coefficient must be of the same order as Y_R ; we go from 0.1 to 1 span the full range of characteristic curves