PART 1 Original Full Model

At our first step, we wanted to describe the system thoroughly without leaving out any seemingly unimportant actions and factors. As a result, the description of the system contains every possible mass actions as well as some hill kinetics, Henri-Michaelis-Menten. We came up a set of ODEs with 19 equations.

Construction of ODE equation

CELL I

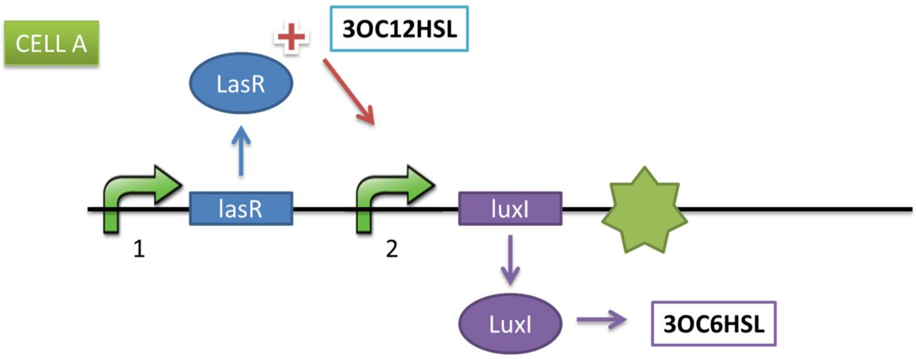

Figure 1 designed circuit of cell I

CELL II

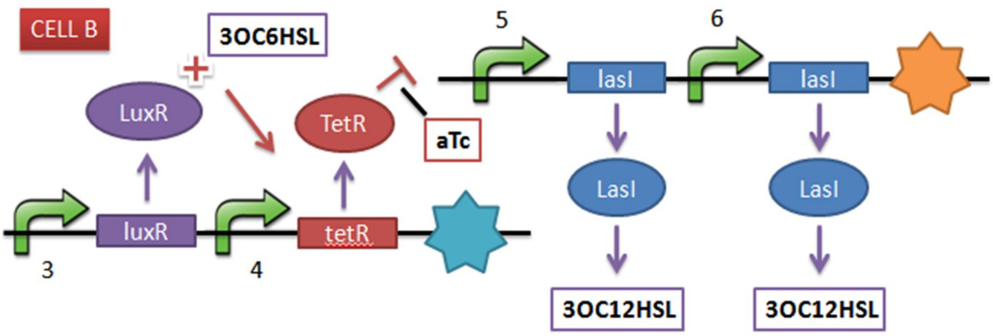

Figure 2 designed circuit of cell II

Promoter 1 and promoter 2 preceding lasR and luxR genes respectively are constant promoters, which will transcribe and translate into protein PlasR and PluxR. LA1 is the binding association of lasR and 30C12HSL(A2C1) and it can affect the subsequent promoter 2 which can be described by Hill Equation. The same goes to LA2. Gene luxI will be translated into protein PluxI which would generate 30C6HSL(A1C1) through enzymatic reaction. The AHL will diffuse through the membrane to the environment(A1e) and finally enter into Cell 2(A1C2). Protein PtetR which is translated from gene tetR represses promoter 5 which is responsible for transcription of gene lasI. Promoter 6 is constant for translation of protein PlasI. 30C12HSL(A2C2) is generated from Protein PlasI through enzymatic reaction. 30C12HSL in the environment is called A2e which will diffuse to Cell 1. aTc is added manipulatively to change the phase of oscillation by binding the protein PTetR. Therefore, we have these following ODEs:

$$\frac{dM_{lasR}}{dt} = v_{MlasR} - d_{MlasR} \times M_{lasR} \tag{1}$$

$$\frac{dM_{luxI}}{dt} = k_{MluxI} \times [\beta_{MluxI} + (1 - \beta_{MluxI}) \times \frac{LA1^{n1}}{K_{M1}{}^{n1} + LA1^{n1}}] - d_{MluxI} \times M_{luxI} \tag{2}$$

$$\frac{dP_{lasR}}{dt} = k_{TL1} \times M_{lasR} - d_{PlasR} \times P_{lasR} - k1 \times A1_{c1} \times P_{lasR} + k2 \times LA1 \tag{3}$$

$$\frac{dP_{luxI}}{dt} = k_{TL2} \times M_{luxI} - d_{PluxI} \times P_{luxI} \tag{4}$$

$$\frac{dLA1}{dt} = k1 \times A1_{c1} \times P_{lasR} - k2 \times LA1 \tag{5}$$

$$\frac{dA1_{c1}}{dt} = -k1 \times A1_{c1} \times P_{lasR} + k2 \times LA1 + \gamma \cdot (A1_e - A1_{c1}) \tag{6}$$

$$\frac{dA2_{c1}}{dt} = \lambda_1 P_{luxI} + \gamma \cdot (A2_e - A2_{c1}) \tag{7}$$

$$\frac{dM_{luxR}}{dt} = v_{MluxR} - d_{MluxR} \times M_{luxR} \tag{8}$$

$$\frac{dM_{TetR}}{dt} = k_{MTetR} \times [\beta_{MTetR} + (1 - \beta_{MTetR}) \times \frac{LA2^{n2}}{K_{M2}{}^{n2} + LA2^{n2}}] - d_{MTetR} \times M_{TetR} \tag{9}$$

$$\frac{dM_{lasI}}{dt} = k_{MlasI} \times [\beta_{MlasI} + (1 - \beta_{MlasI}) \times \frac{K_{MT}{}^{n3}}{K_{M3}{}^{n3} + TetR^{n3}}] - d_{MlasI} \times M_{lasI} \tag{10}$$

$$\frac{dP_{luxR}}{dt} = k_{TL3} \times M_{luxR} - d_{PluxR} \times P_{luxR} - k3 \times A2_{c2} \times P_{luxR} + k4 \times LA2 \tag{11}$$

$$\frac{dP_{lasI}}{dt} = k_{TL4} \times M_{lasI} - d_{PlasI} \times P_{lasI} \tag{12}$$

$$\frac{dP_{TetR}}{dt} = k_{TL5} \times M_{TetR} - d_{PTetR} \times P_{TetR} - k5 \times P_{TetR} \times aTc + k6 \times TetR^* \tag{13}$$

$$\frac{dLA2}{dt} = k3 \times A2_{c2} \times P_{luxR} - k4 \times LA2 \tag{14}$$

$$\frac{dA2_{c2}}{dt} = -k3 \times A2_{c2} \times P_{luxR} + k4 \times LA2 + \gamma \cdot (A2_e - A2_{c2}) \tag{15}$$

$$\frac{dTetR^*}{dt} = k5 \times P_{TetR} \times aTc - k6 \times TetR^* \tag{16}$$

$$\frac{dA1_{c2}}{dt} = \lambda_2 P_{lasI} + \gamma \cdot (A1_e - A1_{c2}) \quad (17)$$

$$\frac{dA1_e}{dt} = -\gamma \frac{1 - p \cdot (1 + n_{12})}{p \cdot n_{12}} \cdot (A1_e - A1_{c1}) - \gamma \cdot \frac{1 - p \cdot (1 + n_{12})}{p} \cdot (A1_e - A1_{c2}) - \mu A1_e \quad (18)$$

$$\frac{dA2_e}{dt} = -\gamma \frac{1 - p \cdot (1 + n_{12})}{p \cdot n_{12}} \cdot (A2_e - A2_{c1}) - \gamma \cdot \frac{1 - p \cdot (1 + n_{12})}{p} \cdot (A2_e - A2_{c2}) - \mu A2_e \quad (19)$$

Parameters

The parameters are inherent factors determining the behaviors, properties of a system. We selected the quantities thoughtfully from previous iGEM teams and some others were found from published papers.

Parameter Name	Value	Description	Reference
n_1	2	Parameters of hill equation	Assumption
n_2	2	Parameters of hill equation	Assumption
n_3	2	Parameters of hill equation	Assumption
K_{M1}	40nM	Parameters of hill equation	Assumption
K_{M2}	40nM	Parameters of hill equation	Assumption
K_{M3}	40nM	Parameters of hill equation	Assumption
k_{MluxI}	5.25nM/min	Strength decide by R0079	Peking 2009
k_{MTetR}	5.25nM/min	Strength decide by R0062	
k_{MlasI}	5.25nM/min	Strength decide by R0040	
k_{TL1}	42	Translation rate, connecting with strength of RBS(tunable)	All tunable for test Just estimate as standard
k_{TL2}	42	Translation rate, connecting with strength of RBS(tunable)	
k_{TL3}	42	Translation rate, connecting with strength of RBS(tunable)	
k_{TL4}	42	Translation rate, connecting with strength of RBS(tunable)	
k_{TL5}	42	Translation rate, connecting with strength of RBS(tunable)	
v_{MlasR}	5.25nM/min	Transcription rate(tunable)	Peking 2009
v_{MluxR}	5.25nM/min	Transcription rate(tunable)	Peking 2009
β_{MluxI}	0.01	Basal expression in hill equation	Assumption
β_{MTetR}	0.01	Basal expression in hill equation	Assumption
β_{MlasI}	0.01	Basal expression in hill equation	Assumption
γ	$2.5min^{-1}$	Diffusion rate of AHL through membrane.	published paper

λ_1	0.06	Generation rate of 30C6HSL	published paper
λ_2	0.06	Generation rate of 30C12HSL	published paper
d_{MlasR}	$0.0173 min^{-1}$	Degradation constant of mRNA	published paper
d_{MluxI}	$0.0173 min^{-1}$	Degradation constant of mRNA	published paper
d_{MluxR}	$0.0173 min^{-1}$	Degradation constant of mRNA	published paper
d_{MTetR}	$0.0173 min^{-1}$	Degradation constant of mRNA	published paper
d_{PluxR}	$2.31 \times 10^{-2} min^{-1}$	Degradation constant of luxR protein.	2010 MIT
d_{PluxI}	$1.67 \times 10^{-2} min^{-1}$	Degradation constant of luxI protein.	2010 MIT
d_{PlasI}	$0.01 min^{-1}$	Degradation constant of lasI protein.	2010 MIT
d_{PlasR}	$1.88 \times 10^{-2} min^{-1}$	Degradation constant of lasR protein.	published paper
d_{PtetR}	$1.67 \times 10^{-2} min^{-1}$	Degradation constant of tetR protein.	assumption
k1	$9.6 \times 10^{-3} nM^{-1} min^{-1}$	Rate constant of binding reaction between LasR and 30C12HSL	published paper
k2	$15 min^{-1}$	Rate constant of dissociation reaction between LasR and 30C12HSL	published paper
k3	$0.14232 nM^{-1} min^{-1}$	Rate constant of binding reaction between LuxR and 30C6HSL	2008 KULeuven
k4	$60 min^{-1}$	Rate constant of dissociation reaction between LuxR and 30C6HSL	2008 KULeuven
k5	$0.06 nM^{-1} min^{-1}$	Rate constant of binding reaction between tetR and aTc	published paper
k6	$50 min^{-1}$	Rate constant of dissociation reaction between tetR and aTc	published paper
p	0.2	Ratio of cell2 volume to total volume	For test
n_{12}	1	Ratio of cell1 volume to cell2 volume	For test
μ	$10 min^{-1}$	Dilution rate of C12 and C6 in environment (tunable)	For test

Table 1 Parameters of ODEs

Results

We simulated this system by SIMBIOLOGY, a toolbox embedded in MATLAB. However, unaware of the key parameters to which the system is sensitive, we felt difficult to control or adjust properly, and the simulation result of the system came into a damped oscillation. We ascribed the inability of our model to the fact that the precise descriptions contain too many equations and parameters and we felt obliged to establish a simplified model in place of the precise one for simulation and further analysis.