# Reaction-Diffusion Ising model (RDIM) - ODEs and Parameters

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# 1 Chemical reactions involved in the system

The chemical reactions below depict the entire dynamics of the synthetic genetic circuit. These reactions were simplified where specified, in order to reduce the number of equations and parameters of the model.

- LuxR and LasR dynamics

  The complete chemical reactions leading to the formation of the dimerized LuxR protein with the 3-oxo-C6 HSL molecules consists of the interaction of LuxR and C6 to form a monomer, and afterwards the interaction between two LuxR-C6 monomers to form a dimer, which is the active form of the transcriptional activator. LasR dynamics are analogous to the ones previously described, differing only in that the interaction is between LasR and 3-oxo-C12 HSL. The constitutive production of the LuxR and LasR proteins (equations 1 and 2) is represented by the constitutive production term $\alpha$, which is derived from the quasi-steady state assumptions of mRNA and protein dynamics.

$$\emptyset \underset{\delta_p}{\overset{\alpha}{\rightleftharpoons}} \mathrm{R} \tag{1}$$

$$\emptyset \underset{\delta_p}{\overset{\alpha}{\rightleftharpoons}} \mathrm{S} \tag{2}$$

$$\mathrm{R} + \mathrm{C_6} \underset{\mathrm{kr_{RC6}}}{\overset{\mathrm{kf_{RC6}}}{\rightleftharpoons}} \mathrm{RC_6} \xrightarrow{\delta_p} \emptyset \tag{3}$$

$$\mathrm{S} + \mathrm{C_{12}} \underset{\mathrm{kr_{SC12}}}{\overset{\mathrm{kf_{SC12}}}{\rightleftharpoons}} \mathrm{SC_{12}} \xrightarrow{\delta_p} \emptyset \tag{4}$$

$$\mathrm{RC_6} + \mathrm{RC_6} \underset{\mathrm{kr_{RC6_2}}}{\overset{\mathrm{kf_{RC6_2}}}{\rightleftharpoons}} [\mathrm{RC_6}]_2 \tag{5}$$

$$\mathrm{SC_{12}} + \mathrm{SC_{12}} \underset{\mathrm{kr_{SC12_2}}}{\overset{\mathrm{kf_{SC12_2}}}{\rightleftharpoons}} [\mathrm{SC_{12}}]_2 \tag{6}$$

- LuxI and LasI enzyme production

  The production of the LuxI and LasI enzymes is under control of the pLT and pLL promoters respectively, which depend on the amount of transcriptional activators and the amount of repressors. Assuming that the cell contains saturating amounts of the precursors for the HSL molecules, we can write the following chemical reactions:

$$\emptyset \underset{\delta_p}{\overset{(\phi_{\mathrm{pLT}}+\beta_{\mathrm{pLT}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}}{\rightleftharpoons}} \mathrm{LuxI} \xrightarrow{\mathrm{k_{LUX}}} \mathrm{C_{6}}_i \xrightarrow{\delta_{\mathrm{HSL_i}}} \emptyset \tag{7}$$

$$\emptyset \underset{\delta_p}{\overset{(\phi_{\mathrm{pLL}}+\beta_{\mathrm{pLL}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}}{\rightleftharpoons}} \mathrm{LasI} \xrightarrow{\mathrm{k_{LAS}}} \mathrm{C_{12}}_i \xrightarrow{\delta_{\mathrm{HSL_i}}} \emptyset \tag{8}$$

  Where $\phi_{\mathrm{pLT}}$ and $\phi_{\mathrm{pLL}}$ correspond to the activity functions for the pLuxTet and the pLasLac promoters respectively (derived in the following section).

- TetR and LacI repressor production

  The production of the TetR and LacI repressors is also under the control of the pLL and pLT promoters (respectively), therefore we can write the following chemical reactions. Also, the repressors carry a degradation tag, so that their degradation is faster than that of the one for other proteins in the system, which we arbitrarly chose a 3 times the mean degradation rate for stable proteins:

$$\emptyset \xrightleftharpoons[3\,\delta_p]{(\phi_{\mathrm{pLT}}+\beta_{\mathrm{pLT}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}} \mathrm{LacI} \tag{9}$$

$$\emptyset \xrightleftharpoons[3\,\delta_p]{(\phi_{\mathrm{pLL}}+\beta_{\mathrm{pLL}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}} \mathrm{TetR} \tag{10}$$

- C6 and C12 AHL dynamics

  The AHL lactone molecules can freely diffuse across the membrane with diffusion coefficient $Dm_{HSL}$, and considering there are few differences between the membrane diffusion coefficients of the two lactones, we assume they have the same $Dm_{HSL}$, leading to the following reactions:

$$\mathrm{C}_{6i} \xrightleftharpoons[\mathrm{D}_{m\,\mathrm{HSL}}]{\mathrm{D}_{m\,\mathrm{HSL}}} \mathrm{C}_{6e} \xrightarrow{\delta_{\mathrm{HSL_e}}} \emptyset \tag{11}$$

$$\mathrm{C}_{12i} \xrightleftharpoons[\mathrm{D}_{m\,\mathrm{HSL}}]{\mathrm{D}_{m\,\mathrm{HSL}}} \mathrm{C}_{12e} \xrightarrow{\delta_{\mathrm{HSL_e}}} \emptyset \tag{12}$$

- RFP and GFP reporter production

  The production of the reporter proteins of the circuit depends on the amount of transcriptional activators and the amount of transcriptional repressors present, giving the following reactions:

$$\emptyset \xrightleftharpoons[\delta_p]{(\phi_{\mathrm{pLT}}+\beta_{\mathrm{pLT}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}} \mathrm{RFP} \tag{13}$$

$$\emptyset \xrightleftharpoons[\delta_p]{(\phi_{\mathrm{pLL}}+\beta_{\mathrm{pLL}})\cdot\frac{\mathrm{k_{tr}k_{tx}}}{\delta_{\mathrm{mRNA}}}} \mathrm{GFP} \tag{14}$$

### 1.0.1 Simplification of the system from LuxR and C6 to the binding of the TFs to the promoters

- Starting from the original full model

  If we start the assumptions of steady states from the original model of LuxR binding to HSL and then the dimerization of this species, we can write it down as follows:

$$\frac{d[R]}{dt} = \underbrace{\frac{k_{tx}k_{tr}}{\delta_m}}_{\alpha_R} + k_{r1}[RC6] - [R](\delta_p + k_{f1}[C6_i]) \tag{15}$$

$$\frac{d[RC6]}{dt} = k_{f1}[R][C6_i] + 2k_{r2}[RC6_2] - [RC6](\delta_p + k_{r1} + 2k_{f2}[RC6]) \tag{16}$$

$$\frac{d[RC6_2]}{dt} = k_{f2}[RC6]^2 - k_{r2}[RC6_2] \tag{17}$$

  If we assume steady state for the three equations above, we can then derive the following:

$$0 = \frac{d[R]}{dt} + \frac{d[RC6]}{dt} + \frac{d[RC6_2]}{dt} \tag{18}$$

  From the above, replacing the terms of the derivatives with the ones we have, we can derive an expression of $[R]$:

$$0 = \alpha_R - \delta_p[R] - \delta_p \underbrace{[RC6]}_{K_1[R][C6]} \tag{19}$$

  Expanding and factorizing common terms:

$$0 = \alpha_R - \delta_p[R](1 + K_1[C6]) \tag{20}$$

$$[R]_{SS} = \frac{\frac{\alpha_R}{\delta_p}}{1 + K_1[C6]} \tag{21}$$

  From the steady state assumption, we derive equilibrium constants for the rest of the species in the system:

$$K_1 = \frac{[RC6]}{[R][C6]} \tag{22}$$

  Replacing the expression obtained for $[R]$:

$$[RC6]_{SS} = K_1[R][C6] = K_1\frac{\frac{\alpha_R}{\delta_p}}{1 + K_1[C6]}[C6] \tag{23}$$

  And also, for the dimer term we have:

$$K_2 = \frac{[RC6_2]}{[RC6][RC6]} \tag{24}$$

And replacing the term for the LuxR/C6 obtained before:

$$[RC6_2]_{SS} = K_2[RC6]^2 = K_2\left(K_1\frac{\frac{\alpha_R}{\delta_p}}{1+K_1[C6]}[C6]\right)^2 \tag{25}$$

The final expression we obtain is as follows (after expanding the power and re-grouping terms):

$$[RC6_2]_{SS} = \frac{K_2{K_1}^2[C6]^2(\frac{\alpha_R}{\delta_p})^2}{1+2K_1[C6]+K_1^2[C6]^2} \tag{26}$$

This term can be replaced in a hybrid Hill function used for describing the promoter activity. We replace the AHL dimer term in the equation with this expression and we can obtain a Hill function dependant only on the HSL concentration and the repressor concentration.

- Simplification using the full chemical reaction system from LuxR, C6 HSL and Promoters. The following reactions are involved in the full pathway which leads to the transcription factor bound to the promoter site on DNA.

$$\emptyset \underset{\delta_{\mathrm{R}}}{\overset{\frac{\mathrm{k_{tx}k_{tr}}}{\delta_{\mathrm{mRNA}}}}{\rightleftharpoons}} [\mathrm{R}] \tag{27}$$

$$[\mathrm{R}] + [\mathrm{C_6}] \underset{\mathrm{k}_{r1}}{\overset{\mathrm{k}_{f1}}{\rightleftharpoons}} [\mathrm{RC_6}] \xrightarrow{\delta_p} \emptyset \tag{28}$$

$$[\mathrm{RC_6}] + [\mathrm{RC_6}] \underset{\mathrm{k}_{r2}}{\overset{\mathrm{k}_{f2}}{\rightleftharpoons}} [\mathrm{RC_6}]_2 \tag{29}$$

$$[\mathrm{RC_6}]_2 + [\mathrm{P}] \underset{\mathrm{k}_{r3}}{\overset{\mathrm{k}_{f3}}{\rightleftharpoons}} [\mathrm{P}\cdot[\mathrm{RC_6}]_2] \tag{30}$$

$$[\mathrm{P}\cdot[\mathrm{RC_6}]_2] \xrightarrow{\frac{\mathrm{k_{tx}k_{tr}}}{\delta_m}} [\mathrm{P}\cdot[\mathrm{RC_6}]_2] + \mathrm{sfGFP} \tag{31}$$

$$\emptyset \xrightarrow{\beta_0} \mathrm{sfGFP} \tag{32}$$

Following the same logic applied above, we can define a new equilibrium constant for the binding and unbinding of the RC6 dimer to the DNA (denoted as [P]) as $K_3 = \frac{k_{f3}}{k_{r3}} = \frac{[P\cdot[RC6]2]}{[P][RC6]_2}$. Considering the mass conservation principle, the amount of total DNA is equal to the sum of the free DNA and the DNA bound to transcription factors. This is equal to a constant and we are interested in the **probability of finding DNA bound to the transcription factor ($P_{\mathbf{bound}}$)**. Therefore, we can write down the following.

$$P_{\mathrm{bound}} = \frac{[P\cdot[RC6]_2]}{[P]+[P\cdot[RC6]_2]} \tag{33}$$

But from the equilibrium we know that $[P\cdot[RC6]2] = K_3[P][RC6]_2$. Replacing we can do the following:

$$P_{\mathrm{bound}} = \frac{K_3[P][RC6]_2}{[P]+K_3[P][RC6]_2} = \frac{K_3[RC6]_2}{1+K_3[RC6]_2} = \frac{K_3\frac{K_2{K_1}^2[C6]^2(\frac{\alpha_R}{\delta_p})^2}{1+2K_1[C6]+K_1^2[C6]^2}}{1+K_3\frac{K_2{K_1}^2[C6]^2(\frac{\alpha_R}{\delta_p})^2}{1+2K_1[C6]+K_1^2[C6]^2}} \tag{34}$$

We can multiply this expression by the quasi steady state approximation of transcription/translation to get a dynamic rate of expression for the protein of interest driven by this promoter only in terms of the HSL involved:

$$\frac{k_{tx}k_{tr}}{\delta_m}\left(\frac{\beta_0 + K_3\frac{K_2{K_1}^2[C6]^2(\frac{\alpha_R}{\delta_p})^2}{1+2K_1[C6]+K_1^2[C6]^2}}{1 + K_3\frac{K_2{K_1}^2[C6]^2(\frac{\alpha_R}{\delta_p})^2}{1+2K_1[C6]+K_1^2[C6]^2}}\right) \tag{35}$$

- Grouped term form for simpler curve fitting to experimental data

  We group the parameters we assume have a certain biological value together, for example, we cann group the production term and protein degradation ($\frac{\alpha_R}{\delta_p}$) into one constant value (here we set it to $c$, but we don't fit it during the curve fitting procedure since it is a constant number). We can also group the TF-DNA association constant with the TF dimerization constant ($K_3$ and $K_2$ respectively) into one single parameter $K_R$ or $K_S$ (depending on whether the data is LuxR or LasR). Assuming these simplifications, we are left with the following equation:

$$P_{\text{bound}} = \frac{\beta_0 + K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^n}{1 + K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^n} \tag{36}$$

This equation reprsents the probability of promoter activity in the presence of either the C6 HSL or the C12 HSL (depending on the promoter). For the full probability of activation AND repression, we have to multiply the probability of activity by the probability of repression by the corresponding repressor (TetR or LacI):

$$P_{\text{active}} = \frac{\beta_0 + K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^{n_{act}}}{1 + K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^{n_{act}}}\frac{1}{1 + (K_{\text{TetR}}[\text{TetR}])^{n_{rep}}} \tag{37}$$

However, we assume that due to the length of the synthetic promoter and the proximity between the activator and repressor binding sites, that there will be steric hinderance between the two, therefore the state where both an activator and a repressor are bound is unlikely to happen. Following this logic, the final form of the probablity of finding the promoter in its active state is given by the partition function:

$$P_{\text{active}} = \frac{\text{Active States}}{\text{Total States}} \tag{38}$$

And our final expression is:

$$P_{\text{active}}^{(\text{LuxR})} = \frac{\overbrace{\beta_0}^{\text{Leaky binding}} \quad \overbrace{+ K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^{n_{act}}}^{\text{Activator binding}}}{\underbrace{1}_{\text{Empty Promoter}} \quad \underbrace{+ K_R c^2(\frac{K_1[C6]}{1+K_1[C6]})^{n_{act}}}_{\text{Activator binding}} + \underbrace{(K_{\text{TetR}}[\text{TetR}])^{n_{rep}}}_{\text{Repressor binding}}} \tag{39}$$

And following a similar simplification for the LasR/C12 node:

$$P_{\text{active}}^{(\text{LasR})} = \frac{\underbrace{\beta_0}_{\text{Leaky binding}} + \underbrace{K_S c^2 \left(\frac{K_1[\text{C12}]}{1+K_1[\text{C12}]}\right)^{n_{\text{act}}}}_{\text{Activator binding}}}{\underbrace{1}_{\text{Empty promoter}} + \underbrace{K_S c^2 \left(\frac{K_1[\text{C12}]}{1+K_1[\text{C12}]}\right)^{n_{\text{act}}}}_{\text{Activator binding}} + \underbrace{(K_{\text{LacI}}[\text{LacI}])^{n_{\text{rep}}}}_{\text{Repressor binding}}} \tag{40}$$

- Final system of ODEs

  From the simplfications made, we are left with a system of 10 ODEs, describing the dynamics of: Intracellular C6 HSL, Intracellular C12 HSL, Extracellular C6 HSL, Extracellular C12 HSL, TetR repressor, LacI repressor, LuxI enzyme, LasI enzyme, RFP reporter protein, and GFP reporter protein

$$\frac{d[\text{C6}_i]}{dt} = k_{C6}[\text{LuxI}] + D_m([\text{C6}_e] - [\text{C6}_i]) - \delta_{HSLi}[\text{C6}_i] \tag{41}$$
$$\frac{d[\text{C12}_i]}{dt} = k_{C12}[\text{LasI}] + D_m([\text{C12}_e] - [\text{C12}_i]) - \delta_{HSLi}[\text{C12}_i] \tag{42}$$
$$\frac{d[\text{C6}_e]}{dt} = D_m([\text{C6}_i] - [\text{C6}_e]) - \delta_{HSLe}[\text{C6}_e] \tag{43}$$
$$\frac{d[\text{C12}_e]}{dt} = D_m([\text{C12}_i] - [\text{C12}_e]) - \delta_{HSLe}[\text{C12}_e] \tag{44}$$
$$\frac{d[\text{TetR}]}{dt} = P_{\text{LasLac}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{TetR}] \tag{45}$$
$$\frac{d[\text{LacI}]}{dt} = P_{\text{LuxTet}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{LacI}] \tag{46}$$
$$\frac{d[\text{LuxI}]}{dt} = P_{\text{LuxTet}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{LuxI}] \tag{47}$$
$$\frac{d[\text{LasI}]}{dt} = P_{\text{LasLac}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{LasI}] \tag{48}$$
$$\frac{d[\text{RFP}]}{dt} = P_{\text{LuxTet}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{RFP}] \tag{49}$$
$$\frac{d[\text{GFP}]}{dt} = P_{\text{LasLac}}\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p[\text{GFP}] \tag{50}$$

These equations were numerically integrated using the `numbalsoda` package in conjunction with `numba` for JIT compiling. The numerical integration was perfomed following the LSODA algorithm. These equations were also ported to Julia for use with the `ModelingToolkit.jl` and the `Catalyst.jl` packages, which were used to find the equilibrium points of the system. Of the 3 points that were found, 2 were stable equilibrium points and 1 was an unstable equilibria, confirming that our system behaves as a toggle switch with our chosen parameter values.

## 2 Extended system with external diffusion in 2D space

In many practical settings, the extracellular medium is not well-mixed, and the external HSL species diffuse through a two-dimensional domain (e.g., a 2D lattice or a thin biofilm layer). Hence, we extend the previous ODE model to include spatial diffusion for the external HSLs, $C6_e$ and $C12_e$, by introducing an external diffusion coefficient $D_e$. Concretely, we replace the ordinary differential equations for $[C6_e]$ and $[C12_e]$ with partial differential equations (PDEs) in 2D that include a Laplacian term, $\nabla^2(\cdot)$. The intracellular species remain well-mixed inside each cell and thus still follow ODEs.

- **Intracellular equations (well-mixed assumption):**

$$\frac{d[C6_i]}{dt} = k_{C6}[\text{LuxI}] + D_m\big([C6_e] - [C6_i]\big) - \delta_{HSLi}[C6_i], \tag{51}$$

$$\frac{d[C12_i]}{dt} = k_{C12}[\text{LasI}] + D_m\big([C12_e] - [C12_i]\big) - \delta_{HSLi}[C12_i], \tag{52}$$

$$\frac{d[\text{TetR}]}{dt} = P_{\text{LasLac}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{TetR}], \tag{53}$$

$$\frac{d[\text{LacI}]}{dt} = P_{\text{LuxTet}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{LacI}], \tag{54}$$

$$\frac{d[\text{LuxI}]}{dt} = P_{\text{LuxTet}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{LuxI}], \tag{55}$$

$$\frac{d[\text{LasI}]}{dt} = P_{\text{LasLac}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{LasI}], \tag{56}$$

$$\frac{d[\text{RFP}]}{dt} = P_{\text{LuxTet}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{RFP}], \tag{57}$$

$$\frac{d[\text{GFP}]}{dt} = P_{\text{LasLac}}\,\frac{k_{tx}k_{tr}}{\delta_m} - \delta_p\,[\text{GFP}]. \tag{58}$$

- **Extracellular equations (reaction-diffusion in 2D):**

  For the concentrations $[C6_e]$ and $[C12_e]$ in the external domain, we add the two-dimensional diffusion with coefficient $D_e$. The Laplacian in 2D is denoted $\nabla^2$. Hence, for each spatial location $(x, y)$:

$$\frac{\partial[C6_e]}{\partial t} = D_e\,\nabla^2\big[C6_e\big] + D_m\big([C6_i] - [C6_e]\big) - \delta_{HSLe}\,[C6_e], \tag{59}$$

$$\frac{\partial[C12_e]}{\partial t} = D_e\,\nabla^2\big[C12_e\big] + D_m\big([C12_i] - [C12_e]\big) - \delta_{HSLe}\,[C12_e]. \tag{60}$$

Thus, the overall reaction-diffusion system captures the intracellular production, degradation, and exchange of HSLs, while also accounting for the spatial diffusion of the external lactones in two dimensions. The model still involves 10 species, but now $[C6_e]$ and $[C12_e]$ obey PDEs, whereas the remaining 8 species (including the intracellular HSL pools, enzymes, repressors, and reporters) follow ODEs under a well-mixed assumption within each cell.

**Lattice size, stability conditions and numerical integration**

For most simulations we defined a lattice size of $256 \times 256$ cells, where each cell was considered to be a square of $1 \times 1\mu m$, i.e the lattice is defined with:

$$N_x = N_y = 256\mu m$$
$$\Delta x = \Delta y = 1\mu m$$

The system, with both the ODEs that describe internal biochemical processes as well as the PDEs describing the external diffusion of C6 and C12 lactones, was numerically integrated using the forward Euler method, with a fixed time step of $\Delta t = 1\text{e}^{-3}$, which satisfies the Von Neumann stability condition defined by:

$$\Delta t \leq \frac{\Delta x^2}{4kD_e} \rightarrow \frac{1\mu m^2}{4 \cdot 2 \cdot 100 \frac{\mu m^2}{min}} \rightarrow \Delta t \leq 0.00125 \text{ min}$$

We defined our largest tested diffusion coefficient as $D_e = 100 \frac{\mu m^2}{min}$. All simulations in the 2D lattice were perfomed with **periodic boundary conditions**.

| Symbol | Parameter | Value Used | Reference |
|---|---|---|---|
| $K_P$ | Association constant of RNA polymerase to DNA | 1 $\mu$ M $^{-1}$ | (Gouti et al., 2017) |
| $K_{AR}$ | Association constant of LuxR-C6 dimer to DNA | 10 $\mu$ M $^{-1}$ | (M. Weber & Buceta, 2013) |
| $K_{AS}$ | Association constant of LasR-C12 dimer to DNA | 10 $\mu$ M $^{-1}$ | (M. Weber & Buceta, 2013) |
| $K_{RTET}$ | Association constant of TetR to DNA | $10^3$ $\mu$ M $^{-1}$ | Estimated from (Kamionka et al., 2004) |
| $K_{RLAC}$ | Association constant of LacI to DNA | 10 $\mu$ M $^{-1}$ | Estimated from (Stamatakis & Mantzaris, 2009) |
| $w_{AR}$ | Cooperativity between activator and repressor | $R^+$ | (Sherman & Cohen, 2012) |
| $[ARNp]$ | Concentration of RNA polymerase | 1.8-3.5 $\mu$ M | (Müller-Hill, 2011) |

Table 1: Parameters used for the simulation of the thermodynamic assembly function.

| Symbol | Parameter | Value Used | Reference |
|---|---|---|---|
| $K_{DR}$ | Dissociation constant of LuxR-C6 dimer and DNA | 0.1 $\mu$ M | (M. Weber & Buceta, 2013) |
| $K_{DS}$ | Dissociation constant of LasR-C12 dimer and DNA | 0.1 $\mu$ M | (M. Weber & Buceta, 2013) |
| $K_{DT}$ | Dissociation constant of TetR repressor and DNA | $10^{-3}$ $\mu$ M | Estimated from (Kamionka et al., 2004) |
| $K_{DL}$ | Dissociation constant of LacI repressor and DNA | 0.1 $\mu$ M | Estimated from (Stamatakis & Mantzaris, 2009) |
| $n_T$ | Hill coefficient of TetR repressor | 2 | Derived from chemical reactions |
| $n_L$ | Hill coefficient of LacI repressor | 4 | Derived from chemical reactions |

Table 2: Parameters used for the simulation of the Hill function.

| Reaction | Description |
|---|---|
| $\emptyset \underset{d_R}{\overset{\alpha}{\rightleftharpoons}} [R]$ | Constitutive production and degradation of LuxR |
| $[R] + [C6_i] \underset{k_{r1R}}{\overset{k_{f1R}}{\rightleftharpoons}} [RC6_i] \rightarrow \emptyset$ | Association and dissociation of LuxR and 3-oxo-C6 AHL, forming LuxR-C6 |
| $[RC6_i] + [RC6_i] \underset{k_{r2R}}{\overset{k_{f2R}}{\rightleftharpoons}} [RC6_i]_2 \rightarrow \emptyset$ | Association and dissociation of two LuxR-C6 complexes, forming LuxR-C6 dimer |
| $[P_R] + [RC6_i]_2 \underset{k_{r3R}}{\overset{k_{f3R}}{\rightleftharpoons}} [P_R \cdot [RC6_i]_2]$ | Association and dissociation of LuxR-C6 dimer with pLux76Tet promoter |
| $\emptyset \underset{d_S}{\overset{\alpha}{\rightleftharpoons}} [S]$ | Constitutive production and degradation of LasR |
| $[S] + [C12_i] \underset{k_{r1S}}{\overset{k_{f1S}}{\rightleftharpoons}} [SC12_i] \rightarrow \emptyset$ | Association and dissociation of LasR and 3-oxo-C12 AHL, forming LasR-C12 |
| $[SC12_i] + [SC12_i] \underset{k_{r2S}}{\overset{k_{f2S}}{\rightleftharpoons}} [SC12_i]_2 \rightarrow \emptyset$ | Association and dissociation of two LasR-C12 complexes, forming LasR-C12 dimer |
| $[P_S] + [SC12_i]_2 \underset{k_{r3S}}{\overset{k_{f3S}}{\rightleftharpoons}} [P_S \cdot [SC12_i]_2]$ | Association and dissociation of LasR-C12 dimer with pLas81Lac promoter |

Table 3: Reactions of the LuxR-C6 AHL node involved in transcriptional regulation.

| Symbol | Parameter | Value Used | Reference |
|---|---|---|---|
| $\alpha$ | Constitutive transcription/translation | 20 uM/min | (Yáñez Feliú et al., 2020) |
| $k_{f1R}$ | Association rate of LuxR and C6 | 100 $\text{uM}^{-1}$ $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{r1R}$ | Dissociation rate of LuxR-C6 complex | 10 $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{f2R}$ | Association rate of two LuxR-C6 to form LuxR-C6 dimer | 50 $\text{uM}^{-1}$ $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{r2R}$ | Dissociation rate of LuxR-C6 dimer | 1 $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{f3R}$ | Association rate of LuxR-C6 dimer and DNA binding site | 66.7 $\text{uM}^{-1}$ $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{r3R}$ | Dissociation rate of LuxR-C6 dimer and DNA | 10 $\text{min}^{-1}$ | (M. Weber & Buceta, 2013) |
| $k_{f1S}$ | Association rate of LasR and C12 | 100 $\text{uM}^{-1}$ $\text{min}^{-1}$ | Estimated* |
| $k_{r1S}$ | Dissociation rate of LasR-C12 complex | 10 $\text{min}^{-1}$ | Estimated* |
| $k_{f2S}$ | Association rate of two LasR-C12 to form LasR-C12 dimer | 50 $\text{uM}^{-1}$ $\text{min}^{-1}$ | Estimated* |
| $k_{r2S}$ | Dissociation rate of LasR-C12 dimer | 1 $\text{min}^{-1}$ | Estimated* |
| $k_{f3S}$ | Association rate of LasR-C12 dimer and DNA binding site | 66.7 $\text{uM}^{-1}$ $\text{min}^{-1}$ | Estimated* |
| $k_{r3S}$ | Dissociation rate of LasR-C12 dimer and DNA | 10 $\text{min}^{-1}$ | Estimated* |
| $d_p$ | Degradation rate of LuxR, LasR, LuxR-C6, and LasR-C12 | 0.2 $\text{min}^{-1}$ | (Yáñez Feliú et al., 2020) |

Table 4: Parameters used for the simulation of the promoter activity using the simplified function.