Bio-Model Selection System (BMSS): Models Documentation

Inducible System **Constant Inducer** Single-equation Double-equation Double-equation with Protein Maturation Time Inducer with Degradation Single-equation Double-equation Double-equation with Protein Maturation Time Inducer with Delay Single-equation Double-equation Double-equation with Protein Maturation Time Inhibition at High Concentrations Constant Inducer Inducer with Delay response Combinational Effect Delay Degradation Degradation Delay

Constitutive System

Single-equation

Single-equation

Single-equation with Protein Maturation Time

Double-equation

- Double-equation
- Double-equation with Protein Maturation Time

Multiple Fixed RBS

- Multiple Single-equation Fixed RBS
- Multiple Single-equation Fixed RBS with Protein Maturation Time
- Multiple Double-equation Fixed RBS
- Multiple Double-equation Fixed RBS with Protein Maturation Time

Multiple Fixed Promoter

- Multiple Double-equation Fixed Promoter
- Multiple Double-equation Fixed Promoter with Protein Maturation Time

Figure 1: Libraries of models developed for the three gene regulatory systems: Inducible, Constitutive and Logic gates. Single-equation and double-equation models refer to the lumped protein expression kinetics and two-step process (transcription and translation) representations respectively. The protein maturation time feature accounts for the maturation step undergone by nascent fluorescent proteins to start fluoresce.

Logic Gates System

NOT gate

- NOT gate Single-equation
- NOT gate Single-equation with Protein Maturation Time
- NOT gate Doubleequation
- NOT gate Doubleequation with Protein Maturation Time

AND gate

- AND gate Doubleequation
- AND gate Doubleequation with Basal Leakiness at Input 1
- AND gate Doubleequation with Basal Leakiness at Input 2
- AND gate Doubleequation with Basal Leakiness at Output
- AND gate Doubleequation with Basal Leakiness at Input 1 and Output
- AND gate Doubleequation with Basal Leakiness at Input 1 and Output, with Protein Maturation Time

OR gate

- OR gate Double-equation
- OR gate Double-equation with Delay at Input 1
- OR gate Double-equation with Delay at Input 2
- OR gate Double-equation with Inducer Degradation at Input 1
- OR gate Double-equation with inducer degradation at Input 2
- OR gate Double-equation with Delay at Input 1 and Inducer Degradation at Input 2
- OR gate Double-equation with Inducer Degradation at Input 1 and Delay at Input 2
- OR gate Double-equation with Delay responses at Input 1 and 2
- OR gate Double-equation with Delay at Input 1 and Inducer Degradation at Input 2, and with Resources Competition
- OR gate Double-equation with Inducer Degradation at Input 1 and Delay at Input 2, and with Resources Competition
- OR gate Double-equation with Delay responses at Input 1 and 2, and with Resources Competition

Table 1: Mathematical Formulations for Inducible Promoter Systems

Model = 'ConstantInducer'

$$\begin{split} \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Inducer]^n}{[Inducer]^n + K_{ind}^{n}} \right) - deg_{mRNA}[mRNA] \\ &\frac{d[Pep]}{dt} = syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Model = 'ConstantInducerKMat'

$$\begin{split} \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Inducer]^n}{[Inducer]^n + K_{ind}{}^n} \right) - deg_{mRNA}[mRNA] \\ & \frac{d[Pep]}{dt} = syn_{Pep}[mRNA] - K_{mature}[Pep] \\ & \frac{d[Pep_m]}{dt} = K_{mature}[Pep] - deg_{Pep}[Pep_m] \end{split}$$

Model = 'DegradationInducer'

$$\begin{split} \frac{d[Ind]}{dt} &= -deg_{Ind}[Ind] \\ \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Ind]^n}{[Ind]^n + K_{ind}^{-n}} \right) - deg_{mRNA}[mRNA] \\ \frac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Model = 'DegradationInducerKMat'

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[mRNA]}{dt} = syn_{mRNA} \left(\frac{[Ind]^n}{[Ind]^n + K_{ind}^n}\right) - deg_{mRNA}[mRNA]$$

$$\frac{d[Pep]}{dt} = syn_{Pep}[mRNA] - K_{mature}[Pep]$$

$$\frac{d[Pep_m]}{dt} = K_{mature}[Pep] - deg_{Pep}[Pep_m]$$

Model = 'DelayInducer'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[Ind_i]}{dt} &= V_m \left(\frac{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) - deg_{mRNA}[mRNA] \\ \frac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Model = 'DelayInducerKMat'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[Ind_i]}{dt} &= V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) - deg_{mRNA}[mRNA] \\ \frac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - K_{mature}[Pep] \\ \frac{d[Pep_m]}{dt} &= K_{mature}[Pep] - deg_{Pep}[Pep_m] \end{split}$$

Model = 'SingleConstantInducer'

$$\frac{d[Pep]}{dt} = syn_{Pep} \left(\frac{[Inducer]^n}{[Inducer]^n + K_{ind}^n} \right) - deg_{Pep}[Pep]$$

Model = 'SingleDegradationInducer'

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[Pep]}{dt} = syn_{Pep} \left(\frac{[Ind]^n}{[Ind]^n + K_{ind}^n} \right) - deg_{Pep}[Pep]$$

Model = 'SingleDelayInducer'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[Ind_i]}{dt} &= V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[Pep]}{dt} &= syn_{Pep} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) - deg_{Pep}[Pep] \end{split}$$

Model = 'ConstantIndInhibition'

$$\frac{d[mRNA]}{dt} = K_{Leak} + syn_{mRNA} \left(\frac{[Inducer]^n}{[Inducer]^n + K_{ind}^n} \right) \left(1 - K_{inhmax} \left(\frac{[Inducer]^{n_{inh}}}{[Inducer]^{n_{inh}} + K_{inh}^{n_{inh}}} \right) \right) - deg_{mRNA}[mRNA]$$

$$\frac{d[Pep]}{dt} = syn_{Pep}[mRNA] - deg_{Pep}[Pep]$$

Model = 'DelayIndInhibition'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ &\frac{d[Ind_i]}{dt} = V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[mRNA]}{dt} &= K_{Leak} + syn_{mRNA} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) \left(1 - K_{inhmax} \left(\frac{[Ind_e]^{n_{inh}}}{[Ind_e]^{n_{inh}} + K_{inh}^{n_{inh}}} \right) \right) \\ &- deg_{mRNA}[mRNA] \\ \frac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Model = 'DelayDegradationInducer'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[Ind_i]}{dt} &= V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) - deg_{Ind}[Ind_i] \\ \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) - deg_{mRNA}[mRNA] \\ \frac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Model = 'DegradationDelayInducer'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -deg_{Ind}[Ind_e] - V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ &\frac{d[Ind_i]}{dt} = V_m \left(\frac{[Ind_e]^{n_{trans}}}{[Ind_e]^{n_{trans}} + K_{trans}^{n_{trans}}} \right) \\ \frac{d[mRNA]}{dt} &= syn_{mRNA} \left(\frac{[Ind_i]^n}{[Ind_i]^n + K_{ind}^n} \right) - deg_{mRNA}[mRNA] \\ &\frac{d[Pep]}{dt} = syn_{Pep}[mRNA] - deg_{Pep}[Pep] \end{split}$$

Table 2: Mathematical Formulations for Constitutive Promoter Systems

Model = 'ConstDouble'

$$rac{d[mRNA]}{dt} = syn_{mRNA} - deg_{mRNA}[mRNA] \ rac{d[Pep]}{dt} = syn_{Pep}[mRNA] - deg_{Pep}[Pep]$$

Model = 'ConstDoubleKMat'

$$egin{aligned} rac{d[mRNA]}{dt} &= syn_{mRNA} - deg_{mRNA}[mRNA] \ rac{d[Pep]}{dt} &= syn_{Pep}[mRNA] - K_{mature}[Pep] \ rac{d[Pep_m]}{dt} &= K_{mature}[Pep] - deg_{Pep}[Pep_m] \end{aligned}$$

Model = 'ConstSingle'

$$\frac{d[Pep]}{dt} = syn_{Pep} - deg_{Pep}[Pep]$$

Model = 'ConstSingleKMat'

$$\frac{d[Pep]}{dt} = syn_{Pep} - K_{mature}[Pep]$$
$$\frac{d[Pep_m]}{dt} = K_{mature}[Pep] - deg_{Pep}[Pep_m]$$

Model = 'MultiDoubleFixRBS'

$$\frac{d[mRNAX]}{dt} = syn_{mRNAX} - deg_{mRNA}[mRNAX]$$

$$\frac{d[PepX]}{dt} = syn_{Pep}[mRNAX] - deg_{Pep}[PepX]$$

$$for X = 1, 2, ... 6$$

Model = 'MultiDoubleFixRBSKMat'

$$\frac{d[mRNAX]}{dt} = syn_{mRNAX} - deg_{mRNA}[mRNAX]$$

$$\frac{d[PepX]}{dt} = syn_{Pep}[mRNAX] - K_{mature}[PepX]$$

$$\frac{d[PepX_m]}{dt} = K_{mature}[PepX] - deg_{Pep}[PepX_m]$$

$$for X = 1, 2, ... 6$$

Model = 'MultiSingleFixRBS'

$$\frac{d[PepX]}{dt} = syn_{PepX} - deg_{Pep}[PepX]$$

$$for X = 1, 2, ... 6$$

Model = 'MultiSingleFixRBSKMat'

$$\frac{d[PepX]}{dt} = syn_{PepX} - K_{mature}[PepX]$$

$$\frac{d[PepX_m]}{dt} = K_{mature}[PepX] - deg_{Pep}[PepX_m]$$

$$for X = 1, 2, ... 6$$

Model = 'MultiDoubleFixPromoter'

$$\frac{d[mRNAX]}{dt} = syn_{mRNA} - deg_{mRNA}[mRNAX]$$

$$\frac{d[PepX]}{dt} = syn_{PepX}[mRNAX] - deg_{Pep}[PepX]$$

$$for X = 1, 2, ... 6$$

Model = 'MultiDoubleFixPromoterKMat'

$$\frac{d[mRNAX]}{dt} = syn_{mRNA} - deg_{mRNA}[mRNAX]$$

$$\frac{d[PepX]}{dt} = syn_{PepX}[mRNAX] - K_{mature}[PepX]$$

$$\frac{d[PepX_m]}{dt} = K_{mature}[PepX] - deg_{Pep}[PepX_m]$$

$$for X = 1, 2, ... 6$$

Table 3: Mathematical Formulations for Logic Gates System (NOT, AND, and OR gates)

Model = 'NOTgate'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2} \left(1 - K_{maxrep} \left(\frac{[Pep1]}{Pep_{max}}\right)\right) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \end{split}$$

Model = 'NOTgateKMat'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2} \left(1 - K_{maxrep} \left(\frac{[Pep1]}{Pep_{max}}\right)\right) - deg_{mRNA}[mRNA2] \\ \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - K_{mature}[Pep2] \\ \frac{d[Pep2_m]}{dt} &= K_{mature}[Pep2] - deg_{Pep}[Pep2_m] \end{split}$$

Model = 'NOTgateSingle'

$$\frac{d[mRNA1]}{dt} = syn_{mRNA}(1 - K_{maxrep}(state)) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

Model = 'NOTgateSingleKMat'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA}(1 - K_{maxrep}(state)) - deg_{mRNA}[mRNA1] \\ &\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - K_{mature}[Pep1] \\ &\frac{d[Pep1_m]}{dt} = K_{mature}[Pep1] - deg_{Pep}[Pep1_m] \end{split}$$

Model = 'ANDgate'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ANDgateBLeak1'

$$\begin{split} \frac{d[mRNA1]}{dt} &= K_{Leak} + syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ &\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ &\frac{d[mRNA2]}{dt} = syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ &\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ &\frac{d[mRNA3]}{dt} = syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3] \\ &\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ANDgateBLeak2'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= K_{Leak} + syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ANDgateBLeak3'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= K_{Leak} + syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ANDgateBLeak13'

$$\begin{split} \frac{d[mRNA1]}{dt} &= K_{Leak1} + syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ &\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ &\frac{d[mRNA2]}{dt} = syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ &\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ &\frac{d[mRNA3]}{dt} = K_{Leak} + syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3] \\ &\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ANDgateBLeak13KMat'

$$\frac{d[mRNA1]}{dt} = K_{Leak1} + syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = K_{Leak} + syn_{mRNA3} \left(\frac{[Pep1]}{Pep1_{max}}\right) \left(\frac{[Pep2]}{Pep2_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - K_{mature}[Pep3]$$

$$\frac{d[Pep3_m]}{dt} = K_{mature}[mRNA3] - deg_{Pep}[Pep3_m]$$

Model = 'ORgate'

$$\begin{split} \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \end{split}$$

$$\begin{split} \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}} \right) - deg_{mRNA}[mRNA3] \\ &\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ORgateDelay'

$$\begin{split} \frac{d[Ind_e]}{dt} &= -\left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e] \\ \frac{d[Ind_i]}{dt} &= \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e] \\ \frac{d[mRNA1]}{dt} &= syn_{mRNA1}[Ind_i](state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ORgate_Delay'

$$\begin{split} \frac{d[Ind_e]}{dt} &= - \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right) [Ind_e] \\ \frac{d[Ind_i]}{dt} &= \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right) [Ind_e] \\ \frac{d[mRNA1]}{dt} &= syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}[Ind_i](state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ORgateDegradation'

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[mRNA1]}{dt} = syn_{mRNA1}[Ind](state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}(state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3]$$

Model = 'ORgate_Degradation'

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[mRNA1]}{dt} = syn_{mRNA1}(state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}[Ind](state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3]$$

Model = 'ORgateDelayDegradation'

$$\begin{split} \frac{d[Ind_e]}{dt} &= - \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right) [Ind_e] \\ \frac{d[Ind_i]}{dt} &= \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right) [Ind_e] \\ \frac{d[Ind]}{dt} &= -deg_{Ind}[Ind] \\ \frac{d[mRNA1]}{dt} &= syn_{mRNA1}[Ind_i](state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{Pep}[mRNA1] - deg_{Pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}[Ind](state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{Pep}[mRNA2] - deg_{Pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{Pep}[mRNA3] - deg_{Pep}[Pep3] \end{split}$$

Model = 'ORgateDegradationDelay'

$$\frac{d[Ind_e]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[Ind_e]}{dt} = -\left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[Ind_i]}{dt} = \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[mRNA1]}{dt} = syn_{mRNA1}[Ind](state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}[Ind_i](state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3}\left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep}[mRNA3] - deg_{Pep}[Pep3]$$

Model = 'ORgateDelayDelay'

$$\begin{split} \frac{d[Ind_{e1}]}{dt} &= -\left(\frac{[Ind_{e1}]}{[Ind_{e1}] + K_{m1}}\right)[Ind_{e1}] \\ \frac{d[Ind_{i1}]}{dt} &= \left(\frac{[Ind_{e1}]}{[Ind_{e1}] + K_{m1}}\right)[Ind_{e1}] \\ \frac{d[Ind_{e2}]}{dt} &= -\left(\frac{[Ind_{e2}]}{[Ind_{e2}] + K_{m2}}\right)[Ind_{e2}] \\ \frac{d[Ind_{i2}]}{dt} &= \left(\frac{[Ind_{e2}]}{[Ind_{e2}] + K_{m2}}\right)[Ind_{e2}] \\ \frac{d[mRNA1]}{dt} &= syn_{mRNA1}[Ind_{i1}](state1) - deg_{mRNA}[mRNA1] \\ \frac{d[Pep1]}{dt} &= syn_{pep}[mRNA1] - deg_{pep}[Pep1] \\ \frac{d[mRNA2]}{dt} &= syn_{mRNA2}[Ind_{i2}](state2) - deg_{mRNA}[mRNA2] \\ \frac{d[Pep2]}{dt} &= syn_{pep}[mRNA2] - deg_{pep}[Pep2] \\ \frac{d[mRNA3]}{dt} &= syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3] \\ \frac{d[Pep3]}{dt} &= syn_{pep}[mRNA3] - deg_{pep}[Pep3] \end{split}$$

Model = 'ORgateDelayDegradeResCompete'

$$\frac{d[Ind_e]}{dt} = -\left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[Ind_i]}{dt} = \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[mRNA1]}{dt} = syn_{mRNA1}[Ind_i](state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}[Ind](state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3}\left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep3}[mRNA3] - deg_{Pep}[Pep3]$$

Model = 'ORgateDegradeDelayResCompete'

$$\frac{d[Ind]}{dt} = -deg_{Ind}[Ind]$$

$$\frac{d[Ind_e]}{dt} = -\left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[Ind_i]}{dt} = \left(\frac{[Ind_e]}{[Ind_e] + K_m}\right)[Ind_e]$$

$$\frac{d[mRNA1]}{dt} = syn_{mRNA1}[Ind](state1) - deg_{mRNA}[mRNA1]$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}[Ind_i](state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3}\left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep3}[mRNA3] - deg_{Pep}[Pep3]$$

Model = 'ORgateDelayDelayResCompete'

$$\begin{split} \frac{d[Ind_{e1}]}{dt} &= - \bigg(\frac{[Ind_{e1}]}{[Ind_{e1}] + K_{m1}} \bigg) [Ind_{e1}] \\ \frac{d[Ind_{i1}]}{dt} &= \bigg(\frac{[Ind_{e1}]}{[Ind_{e1}] + K_{m1}} \bigg) [Ind_{e1}] \\ \frac{d[Ind_{e2}]}{dt} &= - \bigg(\frac{[Ind_{e2}]}{[Ind_{e2}] + K_{m2}} \bigg) [Ind_{e2}] \\ \frac{d[Ind_{i2}]}{dt} &= \bigg(\frac{[Ind_{e2}]}{[Ind_{e2}] + K_{m2}} \bigg) [Ind_{e2}] \\ \frac{d[mRNA1]}{dt} &= syn_{mRNA1} [Ind_{i1}] (state1) - deg_{mRNA} [mRNA1] \end{split}$$

$$\frac{d[Pep1]}{dt} = syn_{Pep}[mRNA1] - deg_{Pep}[Pep1]$$

$$\frac{d[mRNA2]}{dt} = syn_{mRNA2}[Ind_{i2}](state2) - deg_{mRNA}[mRNA2]$$

$$\frac{d[Pep2]}{dt} = syn_{Pep}[mRNA2] - deg_{Pep}[Pep2]$$

$$\frac{d[mRNA3]}{dt} = syn_{mRNA3} \left(\frac{[Pep1] + [Pep2]}{Pep_{max}}\right) - deg_{mRNA}[mRNA3]$$

$$\frac{d[Pep3]}{dt} = syn_{Pep3}[mRNA3] - deg_{Pep}[Pep3]$$