Modeling: Modeling circuits with ODEs and experimental data

Section 1: Composing circuit models from Hill Functions

by Alejandro Vignoni (alvig2@upv.es)

An iGEM Measurement Committee Webinar
Week 3a, June 30th, 2020
Today Webinar’s Topics

△ Section 1: Composing circuit models from Hill functions (15 min)
△ Section 2: Relating parameters and data (15 min)
△ Section 3: Example: Incoherent feed-forward loop (model & data) (15 min)
△ Q&A – (at the end of each 15 minutes block, total 15 min)
Remember our journey: but now going directly to reduced models

Schematic → Biochemical Reactions → Reduced Mathematical Model

From Y. Boada (2018)
Modeling a genetic circuit: What do you want to do?

- **SENSE**
  - Biosensor
  - Promoter

- **COMPUTE**
  - Logic (Inverter)
  - Memory
  - Level detection

- **ACT**
  - Reporter
  - Enzyme
  - SM Signal
  - Therapeutic

Example: Detect Arabinose

Inverter (TetR)

Fluorescence Protein (RFP)
Modeling a genetic circuit

Example Sense-Compute-Act
Modeling a genetic circuit

Example Sense-Compute-Act

SENSE

Extracellular Arabinose

Arabinose
AraC

J23100 B0030

pBAD B0030

E.coli
Modeling a genetic circuit
Example Sense-Compute-Act
Modeling a genetic circuit
Example Sense-Compute-Act

Extracellular Arabinose

Arabinose
AraC

pBAD B0030
araC

TetR

pTet B0030
rfp

E.coli
Modeling a genetic circuit  Example Sense-Compute-Act

**SENSE**

\[
[\text{OUTPUT}] = \frac{\alpha_{pBAD}}{d_{OUT}} \left( \beta_{opBAD} + \frac{(1 - \beta_{opBAD}) [\text{Arab}]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [\text{Arab}]^{n_a}} \right)
\]
Modeling a genetic circuit

Example Sense-Compute-Act

**SENSE**

\[
[\text{OUTPUT}] = \frac{\alpha_{pBAD}}{d_{\text{OUT}}} \left( \beta_{opBAD} + \frac{(1 - \beta_{opBAD}) \text{[Arab]}^n_a}{(K_{d_{pBAD}})^n_a + \text{[Arab]}^n_a} \right)
\]

\[
\alpha_{pBAD} = \frac{k_{2\text{OUT}}}{d_{m_{\text{OUT}}}} k_{1_{pBAD}} C_N
\]

\[
K_{d_{pBAD}} = \frac{K_d K_{\text{dis}} C_N}{\text{[AraC]}^n_a}
\]

Modeling a genetic circuit

Example Sense-Compute-Act

**SENSE**

\[
[\text{OUTPUT}] = \frac{\alpha_{pBAD}}{d_{OUT}} \left( \beta_{opBAD} + \frac{\left(1 - \beta_{opBAD}\right) [\text{Arab}]^{n_a}}{\left(K_{d_{pBAD}}\right)^{n_a} + [\text{Arab}]^{n_a}} \right)
\]

\[
\alpha_{pBAD} = \frac{k_2\text{OUT}}{d_m\text{OUT}} \cdot \frac{k_1_{pBAD} C_N}{k_{1pBAD} C_N}
\]

\[
K_{d_{pBAD}} = \frac{K_d K_{dis} C_N}{[\text{AraC}]^{n_A}}
\]

Modeling a genetic circuit

Example Sense-Compute-Act

SENSE

\[
\alpha_{pBAD} = \frac{k_{2OUT}}{d_mOUT} \frac{K_{1pBAD} C_N}{k_{1pBAD} C_N}
\]

\[
K_{d_{pBAD}} = \frac{K_d K_{dis} C_N}{[AraC]^{n_A}}
\]

\[
\text{OUTPUT} = \alpha_{pBAD} \frac{d}{OUT} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}})}{(K_{d_{pBAD}})^{n_a}} [\text{Arab}]^{n_a} \right)
\]

Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

\[
\frac{\alpha_{\text{pBAD}}}{d_{\text{tetR}}} = 7.1 \times 10^4 \text{ molecules}
\]

\[
\beta_{o_{\text{pBAD}}} = 0.02
\]

\[
K_{d_{\text{pBAD}}} = 400 \ \mu\text{M}
\]

\[
[T\text{etR}] = \frac{\alpha_{\text{pBAD}}}{d_{\text{tetR}}} \left( \beta_{o_{\text{pBAD}}} + \frac{1 - \beta_{o_{\text{pBAD}}}}{K_{d_{\text{pBAD}}}} \right)^n_{\text{Arab}} + [\text{Arab}]^n_{\text{Arab}}
\]
Modeling a genetic circuit Example Sense-Compute-Act

SENSE

Let us try with different RBS

B0030  B0034  B0032

What effect does it have in the hill function?

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{\text{TetR}}} \left( \beta_{o_{pBAD}} + \frac{1 - \beta_{o_{pBAD}}}{K_{d_{pBAD}}} [\text{Arab}]^{n_a} + [\text{Arab}]^{n_a} \right)
\]

\[
\alpha_{pBAD} = k_{2_{\text{TetR}}} \frac{k_{1_{m\text{TetR}}}}{d_{m_{\text{TetR}}} C_N}
\]
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

Let us try with different RBS

\[ [\text{TetR}] = \frac{\alpha_{p\text{BAD}}}{d_{\text{TetR}}} d^{TetR} \left( \beta_{o_{p\text{BAD}}} \left( \frac{1 - \beta_{o_{p\text{BAD}}}}{K_{d_{p\text{BAD}}}} \right)^{n_a} + [\text{Arab}]^{n_a} \right) \]

\[ \alpha_{p\text{BAD}} = k_{2_{\text{TetR}}} \frac{k_{1_{mTetR}}}{d_{m_{\text{TetR}}} C_N} \]
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{opBAD} + \frac{(1 - \beta_{opBAD})[Arab]^{n_a}}{(K_d_{pBAD})^{n_a} + [Arab]^{n_a}} \right)
\]

\[
\alpha_{pBAD} = k_{2_TetR} \frac{k_{1mTetR}}{d_{mTetR}} C_N
\]

B0030: \( \alpha_{pBAD} \approx 7.1 \times 10^4 \) molecules

B0034: \( \alpha_{pBAD} \approx 2.5 \times 10^4 \) molecules

B0032: \( \alpha_{pBAD} \approx 3.3 \times 10^3 \) molecules
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}}) [Arab]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [Arab]^{n_a}} \right)
\]

\[
\alpha_{pBAD} = k_{2_{TetR}} \frac{k_{1m_{TetR}} C_N}{d_{m_{TetR}}}
\]

Now let us try with different Plasmid Copy Number (High/Medium)
Modeling a genetic circuit

**Example Sense-Compute-Act**

**SENSE**

\[
\alpha_{pBAD} = k_{2_{TetR}} \frac{k_{1_{mTetR}}}{d_{mTetR}} C_N, \quad K_{d_{pBAD}} = \frac{K_d K_{dis} C_N}{[AraC]^{n_A}}
\]

Changing from a High Copy (300) to a Medium Copy (50) not only moves the curve down (\(\alpha\)), but also to the left (Kd).
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

<table>
<thead>
<tr>
<th></th>
<th>High Copy</th>
<th>Medium Copy</th>
</tr>
</thead>
<tbody>
<tr>
<td>α_{pBAD}</td>
<td>7.1 × 10^4 molecules</td>
<td>1.2 × 10^4 molecules</td>
</tr>
<tr>
<td>B0030</td>
<td>3300 molecules</td>
<td>560 molecules</td>
</tr>
<tr>
<td>K_{d_{pBAD}}</td>
<td>440 μM</td>
<td>14 μM</td>
</tr>
</tbody>
</table>

Changing from a High Copy (300) to a Medium Copy (50) not only moves the curve down (α), but also to the left (K_d).
Modeling a genetic circuit: Example Sense-Compute-Act

**COMPUTE - ACT**

\[
[RFP] = \frac{\alpha_{pTet}}{d_{RFP}} \left( \beta_{o_{pTet}} + \frac{(1 - \beta_{o_{pTet}})(K_{d_{pTet}})^{n_t}}{(K_{d_{pTet}})^{n_t} + [TetR]^{n_t}} \right)
\]

\[
\alpha_{pTet} = k_{2_{RFP}} \frac{k_{1m_{RFP}}}{d_{m_{RFP}}} C_N
\]

\[
K_{d_{pTet}} = K_d C_N
\]
Modeling a genetic circuit Example Sense-Compute-Act

COMPUTE - ACT

Let us try with different RBS and Plasmid Copy Numbers
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE - ACT**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}}) [Arab]^n_a}{(K_{d_{pBAD}})^n_a + [Arab]^n_a} \right)
\]

\[
[RFP] = \frac{\alpha_{pTet}}{d_{RFP}} \left( \beta_{o_{pTet}} + \frac{(1 - \beta_{o_{pTet}}) [TetR]^n_t}{(K_{d_{pTet}})^n_t + [TetR]^n_t} \right)
\]
Modeling a genetic circuit Example Sense-Compute-Act

SENSE - COMPUTE

![Graph showing TetR (molecules) versus [Arabinose] (uM)](image-url)
Modeling a genetic circuit Example Sense-Compute-Act

SENSE - COMPUTE
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE**
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE**
Modeling a genetic circuit

Example Sense-Compute-Act

SENSE - COMPUTE - ACT
Modeling a genetic circuit

Example Sense-Compute-Act

**SENSE - COMPUTE - ACT**
Modeling a genetic circuit Example Sense-Compute-Act

SENSE - COMPUTE - ACT

![Graph showing experimental results for SENSE, COMPUTE, and ACT models.](image)
Questions?
Ask writing in the chat or contact me by email (alvig2 [at] upv [dot] es)

Stay tuned, next Section 2:
Relating parameters and data
Modeling a genetic circuit Example Sense-Compute-Act

Basal Expression

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}}) [Arab]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [Arab]^{n_a}} \right)
\]

\[
[TetR] = \beta_{o_{pBAD}} \frac{\alpha_{pBAD}}{d_{TetR}} + (1 - \beta_{o_{pBAD}}) \frac{\alpha_{pBAD}}{d_{TetR}} \frac{[Arab]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [Arab]^{n_a}}
\]

\[
[TetR] = \beta^*_{o_{pBAD}} + \frac{\alpha^*_{pBAD}}{d_{TetR}} \frac{[Arab]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [Arab]^{n_a}}
\]

\[
\beta^*_{o_{pBAD}} = \beta_{o_{pBAD}} \frac{\alpha_{pBAD}}{d_{TetR}} \quad \frac{\alpha^*_{pBAD}}{d_{TetR}} = \left(1 - \beta_{o_{pBAD}}\right) \frac{\alpha_{pBAD}}{d_{TetR}}
\]
Modeling: Modeling circuits with ODEs and experimental data

Section 2: Relating parameters and data

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- Q&A – (at the end of each 15 minutes block, total 15 min)
Relating model parameters and data
Example Sense-Compute-Act

E.coli
But first we need to get experimental data:
Measurement -> Calibrated measurement

Plate Reader

Fluorescein

Texas Red

https://2020.igem.org/Measurement/Protocols#validation
Stay in tune for Measurement Committee Webinars about Calibration:

Week 5 - Tuesday July 14th - 7am EDT - Quantifying fluorescence and cell count with plate readers
Week 6 - Tuesday July 23rd - 7am EDT - Quantifying fluorescence and cell phenotypes with flow cytometry

(Robinson et al, 2020, DOI: 10.1101/2020.06.01.127084)
Why? Because it is exactly what we get from the model

\[ \frac{d[R]}{dt} = \frac{p_{R} C_{N} k_{R}}{d_{R} + \mu} - (d_{R} + \mu) [R] \]

\[ \frac{d[cI]}{dt} = \frac{p_{cI} C_{N} k_{cI}}{d_{cI} + \mu} \left( \alpha + (1 - \alpha) \frac{1}{k_{\text{max}}} \frac{[R][A]}{k_{cI}C_{N}} \right)^2 - (d_{cI} + \mu) [cI] \]

\[ \frac{d[GFP]}{dt} = \frac{p_{GFP} C_{N} k_{GFP}}{d_{GFP} + \mu} \left( \alpha + (1 - \alpha) \frac{1}{k_{\text{max}}} \frac{[R][A]}{k_{cGFP}C_{N}} \right)^2 - (d_{GFP} + \mu) [G] \]

\[ \frac{dN}{dt} = \mu N \left( 1 - \frac{N}{N_{\text{max}}} \right) \]

MEFL/Particle unit is equivalent to number of molecules/cell from the mathematical model.
Measuring a genetic circuit  

**Example Sense-Compute-Act**

**SENSE - COMPUTE - ACT**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \left( \frac{1 - \beta_{o_{pBAD}}}{K_{d_{pBAD}}} \right)^n[Arab]^n_a \right)
\]

\[
[RFP] = \frac{\alpha_{pTet}}{d_{RFP}} \left( \beta_{o_{pTet}} + \left( \frac{1 - \beta_{o_{pTet}}}{K_{d_{pTet}}} \right)^n[TetR]^n_t \right)
\]
Measuring a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE - ACT**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{1 - \beta_{o_{pBAD}}}{K_{d_{pBAD}}} [\text{Arab}]^n_a \right) + [\text{Arab}]^n_a
\]

\[
[RFP] = \frac{\alpha_{pTet}}{d_{RFP}} \left( \beta_{o_{pTet}} + \frac{1 - \beta_{o_{pTet}}}{K_{d_{pTet}}} [\text{TetR}]^n_t \right) + [\text{TetR}]^n_t
\]

We can measure only RFP.
Measuring a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE - ACT**

\[
[TetR] = \frac{a_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}}) [Arab]^n_a}{K_{d_{pBAD}}^n_a + [Arab]^n_a} \right)
\]

\[
[RFP] = \frac{a_{pTet}}{d_{RFP}} \left( \beta_{o_{pTet}} + \frac{(1 - \beta_{o_{pTet}}) [TetR]^n_t}{K_{d_{pTet}}^n_t + [TetR]^n_t} \right)
\]

We can only change the amount of Arabinose

We can measure only RFP

E.coli
Measuring a genetic circuit Example Sense-Compute-Act

SENSE - COMPUTE - ACT

We can only change the amount of Arabinose

We can measure only RFP

We need more!!

What can we do?

\[ [\text{TetR}] = \frac{\alpha_{pBAD}}{d_{\text{TetR}}} \left( \beta_{opBAD} + \frac{(1 - \beta_{opBAD}) [\text{Arab}]^n}{(K_{d_{pBAD}})^n + [\text{Arab}]^n} \right) \]

\[ [\text{RFP}] = \frac{\alpha_{pTet}}{d_{\text{RFP}}} \left( \beta_{opTet} + \frac{(1 - \beta_{opTet}) [\text{TetR}]^n}{(K_{d_{pTet}})^n + [\text{TetR}]^n} \right) \]
Measuring a genetic circuit Example Sense-Compute-Act

**SENSE**

We can make another construct, with GFP as OUTPUT.
Measuring a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE - ACT** for measurement

[Diagram of a genetic circuit with labels for Arabinose, AraC, TetR, pBAD, B0030, rfp, GFP, and E.coli.]
Measuring a genetic circuit Example Sense-Compute-Act

**SENSE - COMPUTE - ACT** for measurement

We can use GFP as a proxy for TetR
(As they respond in the same way to the changes in Arabinose)
We make experiments with 8 different levels of Arabinose induction, measure GFP (TetR) in a flowcytometer and calibrate the measurement.
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{opBAD} \left( 1 - \beta_{opBAD} \right) [Arab]^n_a \right) + \frac{\beta_{opBAD}}{(K_{d_{pBAD}})^n_a + [Arab]^n_a}
\]

Error = \( \frac{1}{m} \sum^n_m ([TetR]_{model, i} - [TetR]_{measured, i})^2 \)

For the m different concentrations of Arabinose.

Then we minimize the error...
Modeling a genetic circuit Example Sense-Compute-Act

**SENSE**

\[
[TetR] = \frac{\alpha_{pBAD}}{d_{TetR}} \left( \beta_{o_{pBAD}} + \frac{(1 - \beta_{o_{pBAD}})[Arab]^{n_a}}{(K_{d_{pBAD}})^{n_a} + [Arab]^{n_a}} \right)
\]

\[
\frac{\alpha_{pBAD}}{d_{TetR}} = 7.056 \times 10^4 \text{molecules}
\]

\[
K_{d_{pBAD}} = 444.5 \mu M \quad \beta_{o_{pBAD}} = 0.02 \quad n_a = 1
\]
Modeling a genetic circuit Example Sense-Compute-Act

**COMPUTE - ACT**

\[ [\text{RFP}] = \frac{\alpha_{pTet}}{d_{\text{RFP}}} \left( \beta_{pTet} + \frac{(1 - \beta_{pTet}) [\text{TetR}]^{n_t}}{(K_{d_{pTet}})^{n_t} + [\text{TetR}]^{n_t}} \right) \]

- \( \alpha_{pTet} = 1039 \) molecules
- \( \beta_{opBAD} = 0.08 \)
- \( K_{d_{pTet}} = 2668 \) molecules
- \( n_t = 2 \)
Questions?
Ask writing in the chat or contact me by email (alvig2 [at] upv [dot] es)

Stay tuned, next Section 3:
Example: Incoherent feed-forward loop (model & data)
Modeling: Modeling circuits with ODEs and experimental data

Section 3 Example: Incoherent feed-forward loop (model & data)

by Alejandro Vignoni (alvig2@upv.es)

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- Q&A – (at the end of each 15 minutes block, total 15 min)
Incoherent type1 feedforward circuit (I1-FFL)

Change-fold detector

Responds to a change in its input and returns to the value it had prior to the stimulus.

In biology, this behavior is called adaptation.
Input $\text{AHL}_{\text{ext}}$ diffuses across the cell membrane. AHL together with LuxR protein activates the output protein GFP.
Structure of the I1-FFL gene circuit

Direct path
Input $\text{AHL}_{\text{ext}}$ diffuses across the cell membrane. AHL together with LuxR protein activates the output protein GFP.

Indirect path
AHL together with LuxR proteins also activate $\text{cl}$ protein. After some time, $\text{cl}$ represses the output protein GFP.
Model of the I1-FFL gene circuit

\[
\frac{d[R]}{dt} = \frac{p_R C_N k_R}{d m_R + \mu} - (d_R + \mu) [R]
\]

\[
\frac{d[cI]}{dt} = \frac{p_{cI} C_N k_{cI}}{d m_{cI} + \mu} \left( \alpha + (1 - \alpha) \frac{1}{k_{dlux}} \left( \frac{[R][A]}{k_{d2} C_N} \right)^2 \right) - (d_{cI} + \mu) [cI]
\]

\[
\frac{d[GFP]}{dt} = \frac{p_G C_N k_G}{d m_G + \mu} \left( \alpha + (1 - \alpha) \frac{1}{k_{dlux}} \left( \frac{[R][A]}{k_{d2} C_N} \right)^2 \right) - (d_G + \mu) [G]
\]

\[
\frac{dN}{dt} = \mu N \left(1 - \frac{N}{N_{\text{max}}} \right)
\]

Model of the I1-FFL gene circuit

Simulation of a construct

Different induction levels

But only one peak!

The system responds, but is insensitive to the different levels of AHL.
Model of the I1-FFL gene circuit

Simulation of another construct

Increasing the $C_N$ of the Hybrid promoter (to increase the Kd)

Different induction levels

Different peaks maxima!

Now the system responds and changes the peak maximum with different levels of AHL.
**In vivo** implementation of one version of I1-FFL circuit

*E. coli* bacteria

GFP protein after $\text{AHL}_{ext}$ induction.

I1-FFL circuit with its biochemical reactions.

DNA sequences of the three gene circuits $\text{cl}$, $\text{luxR}$ and $\text{gfp}$.

Source: Image x20, SB2CL Lab UPV 2019.
Model parameter estimation of the I1-FFL circuit

AHL$_{ext}$ input

Growth rate ($\mu$)

Calibrated Fluorescence MEFL/Particle

GFP molecules/cell

GFP output
Cost function of the I1-FFL circuit

\[
J_{[i=1,\ldots,5]}(\theta) = \frac{1}{n} \sum_{q=1}^{n} \frac{1}{m} \sum_{k=1}^{m} \left( \frac{x_{10_iq}(k) - x_{10_iq}(kT)}{2} \right)^2
\]

\[
\min_{\theta \in \mathbb{R}^{17}} J(\theta) = [J_1(\theta), \ldots, J_5(\theta)] \in \mathbb{R}^5
\]

subject to:
I1-FFL model (5.1)

5 experimental scenarios
Mean squared error (MSE)

17 decision variables \( \theta \in \mathbb{R}^{17} \)

<table>
<thead>
<tr>
<th>Unknown Parameter</th>
<th>Description</th>
<th>Range of values</th>
</tr>
</thead>
<tbody>
<tr>
<td>( d_{GFP} )</td>
<td>cl. GFP degradation rate</td>
<td>0.01-0.3 ( \text{min}^{-1} )</td>
</tr>
<tr>
<td>( \gamma_1 )</td>
<td>pLux Promoter Hill constant</td>
<td>50-100 ( \text{nM} )</td>
</tr>
<tr>
<td>( \gamma_3 )</td>
<td>Hybrid pLuxR/cl promoter coefficient</td>
<td>0.0001-0.5</td>
</tr>
<tr>
<td>( \gamma_4 )</td>
<td>Hybrid pLuxR/cl promoter coefficient</td>
<td>0.0005-5</td>
</tr>
<tr>
<td>( \gamma_5 )</td>
<td>Hybrid pLuxR/cl promoter coefficient</td>
<td>1-100</td>
</tr>
<tr>
<td>( k_{p_{cl}}, k_{p_{gfp}} )</td>
<td>cl. GFP translation rate</td>
<td>1 [0.60, 1 [100]] ( \text{min}^{-1} )</td>
</tr>
<tr>
<td>( \beta_1 )</td>
<td>Hybrid promoter basal expression</td>
<td>0.01</td>
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<tr>
<td>( \beta_2 )</td>
<td>Hybrid promoter leakiness</td>
<td>0.01</td>
</tr>
<tr>
<td>( k_{m_{cl}}, k_{m_{gfp}} )</td>
<td>cl. GFP transcription rate</td>
<td>1 [0.75, 0 [0.25]] ( \text{min}^{-1} )</td>
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<tr>
<td>( k_{2, k_3} )</td>
<td>Monomer and dimer dissociation rate</td>
<td>0.05-0.3 [0.1] ( \text{min}^{-1} )</td>
</tr>
<tr>
<td>( k_{2}, k_{3} )</td>
<td>Monomer and dimer association rate</td>
<td>0.0006-0.06 ( \text{min}^{-1} )</td>
</tr>
<tr>
<td>( k_{mat} )</td>
<td>GFP maturation time</td>
<td>20-120 ( \text{min} )</td>
</tr>
</tbody>
</table>

Parameter estimation based on MOOD
spMODE algorithm (http://matlabcentral/fileexchange/39215)
Comparison between model and data for the I1-FFL circuit
Parameter estimation

AHL Induction

Simulation

Experimental data
Questions?
Ask writing in the chat or contact me by email (alvig2 [at] upv [dot] es)

Scripts and files in the Git Repository