# User guide



## Model description

We have

- $S$ chemical species on the state vector $x_S$.
- $N$ reactions, each one with a reaction vector such that $x_S + R_S$ is the new each vector after the reaction, collected as rows in a matrix $R_{NS}$.
  - A full linear dependence term of the propensities on the state vector:

$$A_{NS}x_S + b_N$$

- The Hill rate function

$$\mathrm{Hill}(x, v, \alpha, n) = v\frac{x^n}{x^n + \alpha^n}$$

  where $n$ is called the hill factor; positive for activation, negative for repression.
  - This Hill-type interactions are expressed in matrix notation as

$$\mathrm{Hill}(T_{NS}x_S, v_S, \alpha_S, n_S)$$

    and the operations are elementwise.

So the propensities are calculated as

$$P(R_{NS}) = A_{NS}x_S + b_N + \mathrm{Hill}(T_{NS}x_S, v_N, \alpha_N, n_N)$$

(or if you don't like my matrix notation:)

$$P(R) = A\vec{x} + \vec{b} + \mathrm{Hill}(T\vec{x}, \vec{v}, \vec{\alpha}, \vec{n})$$

# Model Examples

## Housekeeping gene

The equations

$$\frac{\mathrm{d}m\left(t\right)}{\mathrm{d}t} = \gamma_m - k_m m\left(t\right)$$
$$\frac{\mathrm{d}p\left(t\right)}{\mathrm{d}t} = \gamma_p m\left(t\right) - k_p p\left(t\right)$$

correspond to the reactions

$$\mathrm{m} \xrightleftharpoons[\mathrm{k}_m]{\gamma_m} \emptyset \qquad \mathrm{m} \xrightarrow{\mathrm{k}_p} \mathrm{m} + \mathrm{p} \qquad \mathrm{p} \xrightarrow{\gamma_p} \emptyset$$

Which in matrix notation is:

$$P\left[\overbrace{\begin{pmatrix} +1 & 0 \\ -1 & 0 \\ 0 & +1 \\ 0 & -1 \end{pmatrix}}^{R_{MN}}\right] = \overbrace{\begin{pmatrix} 0 & 0 \\ \gamma_m & 0 \\ k_m & 0 \\ 0 & \gamma_p \end{pmatrix}}^{A_{NS}} \underbrace{\begin{pmatrix} m \\ p \end{pmatrix}}_{X_S} + \overbrace{\begin{pmatrix} k_m \\ 0 \\ 0 \\ 0 \end{pmatrix}}^{b_N} + \mathrm{Hill}\left[\overbrace{\begin{pmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}}^{T_{NS}} \underbrace{\begin{pmatrix} m \\ p \end{pmatrix}}_{X_S}, \overbrace{\begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{v_N}, \overbrace{\begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{\alpha_N}, \overbrace{\begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{n_N}\right]$$

We can recover the differential equations by operating

$$\frac{\mathrm{d}X}{\mathrm{d}t} = R_{MN}{}^{T} P(R_{MN}) = \begin{pmatrix} +1 & -1 & 0 & 0 \\ 0 & 0 & +1 & -1 \end{pmatrix} P(R_{MN})$$

where $^T$ is the transpose matrix.

## Self repressor

$$\frac{\mathrm{d}m\left(t\right)}{\mathrm{d}t} = \gamma_m - k_m m\left(t\right) + v\frac{p^{-n}}{p^{-n} + \alpha^{-n}}$$
$$\frac{\mathrm{d}p\left(t\right)}{\mathrm{d}t} = \gamma_p m\left(t\right) - k_p p\left(t\right)$$

$$\emptyset \xrightarrow{\mathrm{Hillr\,(p)}} \mathrm{m} \qquad \mathrm{m} \xrightleftharpoons[\mathrm{k}_m]{\gamma_m} \emptyset \qquad \mathrm{m} \xrightarrow{\mathrm{k}_p} \mathrm{m} + \mathrm{p} \qquad \mathrm{p} \xrightarrow{\gamma_p} \emptyset$$

$$P\left[\overbrace{\begin{pmatrix} +1 & 0 \\ -1 & 0 \\ 0 & +1 \\ 0 & -1 \end{pmatrix}}^{R_{MN}}\right] = \overbrace{\begin{pmatrix} 0 & 0 \\ \gamma_m & 0 \\ k_m & 0 \\ 0 & \gamma_p \end{pmatrix}}^{A_{NS}} \underbrace{\begin{pmatrix} m \\ p \end{pmatrix}}_{X_S} + \overbrace{\begin{pmatrix} k_m \\ 0 \\ 0 \\ 0 \end{pmatrix}}^{b_N} + \mathrm{Hill}\left[\overbrace{\begin{pmatrix} 0 & 1 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}}^{T_{NS}} \underbrace{\begin{pmatrix} m \\ p \end{pmatrix}}_{X_S}, \overbrace{\begin{pmatrix} v \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{v_N}, \overbrace{\begin{pmatrix} \alpha \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{\alpha_N}, \overbrace{\begin{pmatrix} -n \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{n_N}\right]$$

## Block matrix notation and generalizable examples

using the language of block matrices and vectors, we adopt the notation

$$\alpha_{33} = I_3 \alpha = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix} \alpha \qquad \alpha_3 = \begin{pmatrix} 1 \\ 1 \\ 1 \end{pmatrix} \alpha$$

with $I_3 = 1_{33}$ being the 3x3 identity matrix, and

$$\begin{pmatrix} a & b \\ c & d \end{pmatrix}_{33} = \begin{pmatrix} a_{33} & b_{33} \\ c_{33} & d_{33} \end{pmatrix} = \left(\begin{array}{ccc|ccc} a & 0 & 0 & b & 0 & 0 \\ 0 & a & 0 & 0 & b & 0 \\ 0 & 0 & a & 0 & 0 & b \\ \hline c & 0 & 0 & d & 0 & 0 \\ 0 & c & 0 & 0 & d & 0 \\ 0 & 0 & c & 0 & 0 & d \end{array}\right) \qquad \begin{pmatrix} a \\ b \end{pmatrix}_3 = \begin{pmatrix} a_3 \\ b_3 \end{pmatrix} = \begin{pmatrix} a \\ a \\ a \\ b \\ b \\ b \end{pmatrix}$$

It is to note that if, for instance $b$ where to be a matrix itself, $b_{33}$ is defined as $b$, and the same for $b_3 \equiv b$ if $b$ is a vector.

### Repressilator

With this language, the repressilator can be expressed as

$$P \left[ \overbrace{\begin{pmatrix} +1 & 0 \\ -1 & 0 \\ 0 & +1 \\ 0 & -1 \end{pmatrix}_{33}}^{R_{MN}} \right] = \overbrace{\begin{pmatrix} 0 & 0 \\ \gamma_m & 0 \\ k_m & 0 \\ 0 & \gamma_p \end{pmatrix}_{33}}^{A_{NS}} X + \overbrace{\begin{pmatrix} k_m \\ 0 \\ 0 \\ 0 \end{pmatrix}_3}^{b_N} + \mathrm{Hill} \left[ \overbrace{\begin{pmatrix} 0 & P_{312} \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}_{33}}^{T_{NS}} X, \overbrace{\begin{pmatrix} v \\ 1 \\ 1 \\ 1 \end{pmatrix}_3}^{v_N}, \overbrace{\begin{pmatrix} \alpha \\ 1 \\ 1 \\ 1 \end{pmatrix}_3}^{\alpha_N}, \overbrace{\begin{pmatrix} -n \\ 1 \\ 1 \\ 1 \end{pmatrix}}^{n_N}$$

where $X = \{m_1, m_2, m_3, p_1, p_2, p_3\}$. The only qualitative difference with the self-repressor is the row-permutation matrix

$$P_{312} = \begin{pmatrix} 0 & 0 & 1 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}$$

The expression

$$\frac{\mathrm{d}X}{\mathrm{d}t} = \begin{pmatrix} +1 & -1 & 0 & 0 \\ 0 & 0 & +1 & -1 \end{pmatrix}_{33} P(R_{MN})$$

gives the equations

$$
\begin{array}{rcccccl}
{m_1}' & = & k_m & - & m_1\ \gamma_m & + & \mathrm{Hill}\left(p_3, v, \alpha, -n\right) \\
{m_2}' & = & k_m & - & m_2\ \gamma_m & + & \mathrm{Hill}\left(p_1, v, \alpha, -n\right) \\
{m_3}' & = & k_m & - & m_3\ \gamma_m & + & \mathrm{Hill}\left(p_2, v, \alpha, -n\right) \\
{p_1}' & = & m_1\ k_p & - & p_1\ \gamma_p & & \\
{p_2}' & = & m_2\ k_p & - & p_2\ \gamma_p & & \\
{p_3}' & = & m_3\ k_p & - & p_3\ \gamma_p & &
\end{array}
$$

Notice that each of the the $\gamma_{m,p}, k_{m,p}$ could have been a 3-vector, so this is could have easily been the general repressilator.

## Loop chains

We can generalize this to a $\ell$-th order cyclic repressilator by replacing all the 3s by $\ell$ and the permutation matrix by

$$
P_{\mathrm{RotateRight}(\mathrm{Range}(\ell))} = \begin{pmatrix}
0 & 0 & 0 & 0 & \cdots & 1 \\
1 & 0 & 0 & 0 & \cdots & 0 \\
0 & 1 & 0 & 0 & \cdots & 0 \\
0 & 0 & 1 & 0 & \cdots & 0 \\
\vdots & \ddots & \ddots & \ddots & \ddots & 0 \\
0 & 0 & 0 & 0 & 1 & 0
\end{pmatrix}
$$

## Free chains

If we replace the permutation matrix $P_{312}$ with a -1 diagonal matrix

$$
P_{s-1} = \begin{pmatrix}
0 & 0 & 0 & 0 & \cdots & 0 \\
1 & 0 & 0 & 0 & \cdots & 0 \\
0 & 1 & 0 & 0 & \cdots & 0 \\
0 & 0 & 1 & 0 & \cdots & 0 \\
\vdots & \ddots & \ddots & \ddots & \ddots & 0 \\
0 & 0 & 0 & 0 & 1 & 0
\end{pmatrix}
$$

one obtains a free chain, that does not loop onto itself like the $\ell$-th order chain from before.

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# Usage examples

(Work in progress here, but head to the repressilator example or the benchmark)