

# Parameters and tools

Exhaustive table of each model's parameters are listed below.

## Recombinase section

| Name       | Description  | Value                                     | Reference                |
|------------|--|---|--------------------------|
| k_attBP    | Binding rate of integrase Bxb1 and attB/P sites      | 1.0 nM <sup>-1</sup> min <sup>-1</sup>    | Fitted                   |
| k_DattBP   | Dissociation rate of integrase Bxb1 and attB/P sites | 1.0E-6 nM <sup>-1</sup> min <sup>-1</sup> | Fitted                   |
| Gamma_Int  | Integrase Bxb1 degradation rate                      | 0.01 min <sup>-1</sup>                    | Assumed                  |
| Gamma_Int2 | Integrase Bxb1 dimer degradation rate                | 0.02 min <sup>-1</sup>                    | Assumed                  |
| k_Int2     | Integrase Bxb1 dimerization rate                     | 1.0 nM <sup>-1</sup> min <sup>-1</sup>    | Fitted                   |
| k_Dint2    | Dissociation rate of Bxb1 dimer                      | 1.0E-6 min <sup>-1</sup>                  | Fitted                   |
| Alpha_Int  | Integrase Bxb1 production rate                       | 0.1 min <sup>-1</sup>                     | Assumed                  |
| k_flip     | Bxb1 flipping Forward reaction rate                  | 0.04                                      | Fitted                   |
| k_flipr    | Bxb1 flipping Reverse reaction                       | 7.7E-4                                    | Fitted                   |
| k_basal    | pBAD basal (leaky) transcription rate                | 0.015 min <sup>-1</sup>                   | Fitted                   |
| k_max      | pBAD maximum transcription rate                      | 5.0 min <sup>-1</sup>                     | Estimated                |
| k_half     | pBAD half-maximum transcription rate                 | 1.6E5 nM                                  | Literature <sup>i</sup>  |
| n          | Hill coefficient                                     | 2.65                                      | Literature <sup>ii</sup> |

## Control unit section

| Name              | Description                       | Value                              | Reference                 |
|-------------------|-----------------------------------|------------------------------------|---------------------------|
| k_prodA (k_prodB) | Production rate of Integrase A/B  | $50(\mu\text{m}^3 \text{hr})^{-1}$ | Estimated                 |
| k_deg             | Degradation rate of Integrase A/B | $0.3(\text{hr})^{-1}$              | Estimated                 |
| k_flipA           | Flipping rate of integrase A      | $0.4(\text{hr})^{-1}$              | Literature <sup>iii</sup> |
| k_flipB           | Flipping rate of integrase B      | $0.4(\text{hr})^{-1}$              | Literature                |
| k_leakA           | Leaky expression of integrase A   | $0(\mu\text{m}^3 \text{hr})^{-1}$  | Estimated                 |
| k_leakA           | Leaky expression of integrase A   | $0(\mu\text{m}^3 \text{hr})^{-1}$  | Estimated                 |
| K_dA              | Binding constant                  | 10 Molecules                       | Estimated                 |
| K_dB              | Binding constant                  | 10 Molecules                       | Estimated                 |

Assumptions for parameters:

1. We assume the plasmid copy number is proportional to the volume of a cell.
2. We use  $1 \mu\text{m}^3$  (1 femtoliter) as the estimated volume of a single *E. coli* cell.

## Clock section

| Name   | Description   | Value   | Reference       |
|--------|---|---------|-----------------|
| Beta   | Ratio of protein to mRNA decay rates                                      | 0.2     | BIOMD0000000012 |
| Alpha0 | Leakiness in protein copies per promoter and cell                         | 0.2164  | BIOMD0000000012 |
| Alpha  | Protein copies per promoter and cell                                      | 216.404 | BIOMD0000000012 |
| Eff    | Translation efficiency: Average number of proteins per transcript         | 20.0    | BIOMD0000000012 |
| N      | Hill Coefficient of repressor repressing transcription                    | 2.0     | BIOMD0000000012 |
| KM     | Number of repressor molecules per cell giving half maximal repression, in | 40.0    | BIOMD0000000012 |

|            |  |        |                 |
|------------|--|--------|-----------------|
|            | monomers per cell  |        |                 |
| Tps_active | Transcription from free promotor in transcripts per second and promotor            | 0.5    | BIOMD0000000012 |
| Tps_repr   | Transcription from fully repressed promotor in transcripts per second and promotor | 0.0005 | BIOMD0000000012 |

Units:

|                   |              |
|-------------------|--------------|
| Physical quantity | Unit         |
| Time              | Minute       |
| Volume            | Cubic micron |
| Substance         | molecules    |

## Tools

We used following tools for modelling and simulation:

- MATLAB 2017a. Natick, Massachusetts: The MathWorks Inc., 2017. MATLAB Simbiology for recombinase mechanism deterministic model. Fimcon function for parameter estimation. Gillespie simulation of control unit is implemented in MATLAB code.
- Tellurium, a Python package for systems biology simulation. For clock module simulation.

<sup>i</sup> Sourjik V, Berg HC. Functional interactions between receptors in bacterial chemotaxis. *Nature*. 2004 Mar 25 428(6981):437-41.

<sup>ii</sup> Salto R, Delgado A, Michán C, Marqués S, Ramos JL. Modulation of the function of the signal receptor domain of XylR, a member of a family of prokaryotic enhancer-like positive regulators. *J Bacteriol*. 1998 Feb 180(3):600-4.

<sup>iii</sup> Singh S, Ghosh P, Hatfull GF (2013) Attachment site selection and identity in bxb1 serine integrase-mediated site-specific recombination. *PLoS Genet* 9: e1003490