Appendix 2 - BDSF

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1 Introduction

In order to help analyse, construct and optimise the biochemical pathways in the Lung Ranger, we used a variety of mathematical tools to create algorithms and simulations. The derivation of the BDSF model can be found in this appendix.

2 Chemical Reactions

$$\begin{aligned}
\mathrm{BDSF} + \mathrm{BCAM0227} &\underset{k2}{\overset{k1}{\rightleftharpoons}} \mathrm{BDSF} \cdot \mathrm{BCAM0227} \\
\mathrm{BDSF} \cdot \mathrm{BCAM0227} &\xrightarrow{k3} \mathrm{BDSF} \cdot \mathrm{BCAM0227_P} \\
\mathrm{BDSF} \cdot \mathrm{BCAM0227_P} + \mathrm{BCAM0228} &\xrightarrow{k4} \mathrm{BDSF} \cdot \mathrm{BCAM0227} + \mathrm{BCAM0228_P} \\
\mathrm{BCAM0228_P} + \mathrm{Pcbld} &\underset{k6}{\overset{k5}{\rightleftharpoons}} \mathrm{BCAM0228_P} \cdot \mathrm{Pcbld} \\
&\xrightarrow{K.BCAM0228_P.Pcbld} \mathrm{GFP}
\end{aligned}$$

3 Differential Equations

BDSF, S, binds to the cell receptor BCAM0227, R, at rate k_1 to form a complex, C. The complex degrades as S and R dissociate at rate k_2 and autophosphorylates at rate k_3 to form BCAM0227[P], C_P. There is then a phosphorelay between BCAM0227[P] and BCAM0228, B, to produce BCAM0228[P], B_P.

$$\begin{aligned}
\frac{dC}{dt} &= k_1 SR - k_2 C - k_3 C + k_4 R_P B \\
\frac{dR_P}{dt} &= k_3 C - k_4 R_P B
\end{aligned}$$

BCAM0228[P] binds to the promoter to form the activated-promoter complex, A, at rate k_5.

The complex degrades as B_P and P dissociate at rate k_6.

$$\begin{aligned} \frac{dB_P}{dt} &= k_4 R_P B - k_5 B_P P + k_6 A \\ \frac{dA}{dt} &= k_5 B_P P - k_6 A \end{aligned}$$

Finally, the expression of GFP, G, is proportional to the concentration of A.

$$\frac{dG}{dt} = KA$$

4 Default Parameters

We used the following parameters:

Default Parameters	Value	Reference
BDSF and BCAM0227 association rate $(k_1)[M^{-1}s^{-1}]$	0.005	Set here
BDSF and BCAM0227 dissociation rate $(k_2)[s^{-1}]$	$8.3 * 10^{-4}$	Set here
Autophosphorylation rate $(k_3)[s^{-1}]$	$1.6 * 10^{-4}$	Set here
Phosphorelay rate $(k_4)[s^{-1}]$	$1.6 * 10^{-4}$	Set here
BCAM0228[P] and P$cblD$ association rate $(k_5)[M^{-1}s^{-1}]$	0.0033	Set here
BCAM0228[P] and P$cblD$ dissociation rate $(k_6)[s^{-1}]$	$3.3 * 10^{-4}$	Set here
Maximal rate of GFP expression per promoter $(K)[s^{-1}]$	0.016	Set here
Concentration of promoters in the cell $(P)[\mu M]$	0.083	[1, 2]
Concentration of BCAM0227 in the cell $(R)[\mu M]$	4.98	[1, 2]
Concentration of BCAM0228 in the cell $(B)[\mu M]$	4.98	[1, 2]

References

[1] Leake, M.C. et al. *Variable stoichiometry of the TatA component of the twin-arginine protein transport system observed by in vivo single-molecule imaging*, Proc Natl Acad Sci USA, 40, 15376-15381 (2008).

[2] Twigg, A. et al. *Trans-complementable copy-number mutants of plasmid ColE1*, Nature, 283, 216-218 (1980).