Supplementary Material

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Understanding Bistability
in
Complex Enzyme-Driven Reaction Networks

Parameter Specifications for Several Examples

In several instances assertions were made that certain reaction networks (in particular, entries 4, 6 and 8 in Table 1) have the capacity to admit bistability in the open homogeneous cell context described in Section 2. Here we provide parameter values (mass action rate constants, mass transfer coefficients, and substrate or inhibitor supply rates) for which bistability will obtain. In each instance we provide two stable steady states compatible with the appropriate differential equations (formed as in Section 2). First order rate constants and mass transfer coefficients have units of $(\text{time})^{-1}$, and second order rate constants have units of $(\text{concentration}*\text{time})^{-1}$. Substrate or inhibitor supply rates have units of concentration/time. The parameter values were generated by *The Chemical Reaction Network Toolbox* [1], Version 1.1, a computer program written by Martin Feinberg and Phillipp Ellison to implement theory described in References 15 and 16 of the main article. See also [2]-[4] below. The same program also serves to preclude, independently, the possibility of two distinct stoichiometrically compatible steady states for the remaining entries of Table 1. (An enhanced version was required, however, for the largest entry, 9.)

Parameter specification for Figure 1 (and for Table 1, Entry 6)

$$
\begin{aligned}
S1 + E &\xrightarrow{93.428629} ES1 \\
ES1 &\xrightarrow{2538.9705} S1 + E \\
S2 + E &\xrightarrow{481.59316} ES2 \\
ES2 &\xrightarrow{1182.6181} S2 + E \\
S1 + ES2 &\xrightarrow{2.2130\ E-2} ES1S2 \\
ES1S2 &\xrightarrow{1688.6765} S1 + ES2 \\
ES1S2 &\xrightarrow{121192.44} S2 + ES1 \\
ES1S2 &\xrightarrow{85842.253} P + E \\
S2 + ES1 &\xrightarrow{1556.411} ES1S2
\end{aligned}
$$

Mass transfer coefficients: $\xi_{S1} = \xi_{S2} = \xi_P = 1$
Substrate supply rates: $F_{S1} = 2500$ $F_{S1} = 1500$
Total concentration of enzyme = 1

The (stable) steady state concentrations shown below are both consistent with the parameters indicated:

Steady State No. 1	Species	Steady State No. 2
1002.67	S1	2000
2.6711	S2	1000
4.0008 E-2	E	2.5039 E-3
0.87538	ES1	7.5293 E-4
6.7164 E-2	ES2	0.99092
1.7442 E-2	ES1S2	5.8246 E-3
1497.33	P	500

Parameter specification for Table 1, Entry 4

E + S ——25979.537——> ES
ES ——3.3722455——> E + S
ES ——5844.999——> E + P
E + I ——5.3341555——> EI
EI ——16623.325——> E + I
ES + I ——12200.836——> ESI
ESI ——1472.3849——> ES + I
ESI ——15145.809——> EI + S
EI + S ——9647.324——> ESI

Mass transfer coefficients: $\xi_S = \xi_I = \xi_P = 1$
Substrate and inhibitor supply rates: $F_S = 1734.2661$ $F_I = 1$
Total concentration of enzyme = 1

The (stable) steady state concentrations shown below are both consistent with the parameters indicated:

Steady State No. 1	Species	Steady State No. 2
0.18747109	E	2.3135 E-5
1	S	1096.6331
0.29653831	ES	0.10909034
1	I	1
0.18871954	EI	1.2715 E-3
0.32727104	ESI	0.88961493
1733.2661	P	637.63297

Parameter specification for Table 1, Entry 8

S1 + E1 ---3364.1546-> E1S1
E1S1 ---2294.1904-> S1 + E1
S2 + E1S1 ---1269.402--> E1S1S2
E1S1S2 --0.74734189-> S2 + E1S1
E1S1S2 ---1334.1143-> P1 + E1
S2 + E2 ---74.022639-> E2S2
E2S2 ---2979.9579-> S2 + E2
E2S2 + S3 ---970.04443-> E2S2S3
E2S2S3 ---6.389056--> E2S2 + S3
E2S2S3 ---1489.9546-> P2 + E2
S3 + E3 ---1.2718418-> E3S3
E3S3 --0.67944409-> S3 + E3
E3S3 ---528.27187-> 2S1 + E3

Mass transfer coefficients: $\xi_{S1} = \xi_{S2} = \xi_{S3} = \xi_{P1} = \xi_{P2} = 1$
Substrate supply rates: $F_{S1} = 231.13396$, $F_{S2} = 2019.3501$, $F_{S3} = 1730.1809$
Total concentrations of enzymes: E1: 4.2353475, E2: 3.3208065, E3: 2.3225683

The (stable) steady state concentrations shown below are both consistent with the parameters indicated:

Steady State No. 1	Species	Steady State No. 2
1	S1	1.8315 E-2
1.4901953	E1	4.050771
1.4070766	E1S1	3.4877 E-3
1785.146	P1	241.59324
1	S2	54.59815
3.1639534	E2	1.1639534
3.355 E-4	E2S2	1.0003355
719.47077	S3	1.7833897
233.20418	P2	1723.1587
0.8507769	E3	2.3126515
1.4717914	E3S3	9.9168 E-3
1.3380756	E1S1S2	0.1810888
0.1565176	E2S2S3	1.1565176

REFERENCES

[1] Feinberg, M. and P. Ellison, The Chemical Reaction Network Toolbox, available at http://www.chbmeng.ohio-state.edu/~feinberg/crnt.

[2] Feinberg, M. (2005) Arch. Rational Mech. Anal. **132**, 311-370.

[3] Feinberg, M. (2005) Arch. Rational Mech. Anal. **132**, 371-406.

[4] Feinberg, M. (1979) Lectures on Chemical Reaction Networks, University of Wisconsin, available at

http://www.chbmeng.ohio-state.edu/~feinberg/LecturesOnReactionNetworks