Energy-based Analysis of Biomolecular Pathways
Supplementary Material

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1 Introduction

The system equations for the three examples of the paper are given in § 2, § 3 and § 4. These were automatically derived from the bond graphs of the three systems given in Figures 1b, 3b and 7b respectively using the approach outlined in the paper pAppendix and other publications [1–4].

§ 5 gives the simulation parameters for the SGLT example of § 6 of the paper. The parameters are derived as discussed in § 6 of the paper.

Section 6 derives a formula for the steady-state flow for a special case of the Hill model.

2 Glycolysis example (§ 2 of paper)

2.1 Chemical Equations

$$ATP \overset{r1}{\rightleftharpoons} ADP$$

$$ATP + F6P \overset{r2}{\rightleftharpoons} ADP + F2P$$

$$F2P \overset{r3}{\rightleftharpoons} F6P$$

$$GLC + ATP \overset{r4}{\rightleftharpoons} ADP + G6P$$

$$G6P \overset{r5}{\rightleftharpoons} F6P$$

$$ATP + F6P \overset{r6}{\rightleftharpoons} ADP + 2TP$$

$$2ADP + TP \overset{r7}{\rightleftharpoons} Pyr + 2ATP$$

$$ATP + AMP \overset{r8}{\rightleftharpoons} 2ADP$$

$$G6P \overset{r9}{\rightleftharpoons} G1P$$

2.2 Stoichiometric Matrices

$$X = \begin{pmatrix} x_{GLC} \\ x_{Pyr} \\ x_{ATP} \\ x_{ADP} \\ x_{G1P} \\ x_{G6P} \\ x_{F6P} \\ x_{TP} \\ x_{F2P} \\ x_{AMP} \end{pmatrix} \quad N = \begin{pmatrix} 0 & 0 & 0 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ -1 & -1 & 0 & -1 & 0 & -1 & 2 & -1 & 0 \\ 1 & 1 & 0 & 1 & 0 & 1 & -2 & 2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & -1 & 0 & 0 & 0 & -1 \\ 0 & -1 & 1 & 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 2 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 \end{pmatrix} \quad V = \begin{pmatrix} v_{r1} \\ v_{r2} \\ v_{r3} \\ v_{r4} \\ v_{r5} \\ v_{r6} \\ v_{r7} \\ v_{r8} \\ v_{r9} \end{pmatrix}$$

$$N^f = \begin{pmatrix} 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{pmatrix} \quad N^r = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 2 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 1 & 0 & 2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 2 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$N^{cd} = \begin{pmatrix} 0 & 0 & 0 & -0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -0 & -0 & 0 & -0 & 0 & -0 & 0 & -0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & -1 & 0 & 0 & 0 & -1 \\ 0 & -1 & 1 & 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 2 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 \end{pmatrix} \quad K_p = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \\ 0 & 0 & 2 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

2.3 Differential equations

$$
\begin{aligned}
\dot{x}_{GLC} &= -v_{r4} \\
\dot{x}_{Pyr} &= +v_{r7} \\
\dot{x}_{ATP} &= -v_{r1} - v_{r2} - v_{r4} - v_{r6} + 2v_{r7} - v_{r8} \\
\dot{x}_{ADP} &= +v_{r1} + v_{r2} + v_{r4} + v_{r6} - 2v_{r7} + 2v_{r8} \\
\dot{x}_{G1P} &= +v_{r9} \\
\dot{x}_{G6P} &= +v_{r4} - v_{r5} - v_{r9} \\
\dot{x}_{F6P} &= -v_{r2} + v_{r3} + v_{r5} - v_{r6} \\
\dot{x}_{TP} &= +2v_{r6} - v_{r7} \\
\dot{x}_{F2P} &= +v_{r2} - v_{r3} \\
\dot{x}_{AMP} &= -v_{r8}
\end{aligned}
$$

2.4 Flows

$$
\begin{aligned}
v_{r1} &= \kappa_{r1}(K_{ATP}x_{ATP} - K_{ADP}x_{ADP}) \\
v_{r2} &= \kappa_{r2}(K_{ATP}x_{ATP}K_{F6P}x_{F6P} - K_{ADP}x_{ADP}K_{F2P}x_{F2P}) \\
v_{r3} &= \kappa_{r3}(K_{F2P}x_{F2P} - K_{F6P}x_{F6P}) \\
v_{r4} &= \kappa_{r4}(K_{GLC}x_{GLC}K_{ATP}x_{ATP} - K_{ADP}x_{ADP}K_{G6P}x_{G6P}) \\
v_{r5} &= \kappa_{r5}(K_{G6P}x_{G6P} - K_{F6P}x_{F6P}) \\
v_{r6} &= \kappa_{r6}(K_{ATP}x_{ATP}K_{F6P}x_{F6P} - K_{ADP}x_{ADP}K_{TP}^2x_{TP}^2) \\
v_{r7} &= \kappa_{r7}(K_{ADP}^2x_{ADP}^2K_{TP}x_{TP} - K_{Pyr}x_{Pyr}K_{ATP}^2x_{ATP}^2) \\
v_{r8} &= \kappa_{r8}(K_{ATP}x_{ATP}K_{AMP}x_{AMP} - K_{ADP}^2x_{ADP}^2) \\
v_{r9} &= \kappa_{r9}(K_{G6P}x_{G6P} - K_{G1P}x_{G1P})
\end{aligned}
$$

3 Biomolecular Cycle example (§ 5 of paper)

3.1 Chemical Equations

$$Mi + E \overset{em}{\rightleftharpoons} EM$$

$$Li + EM \overset{lem}{\rightleftharpoons} LEM$$

$$LEM \overset{lesm}{\rightleftharpoons} LEsM$$

$$LEsM \overset{esm}{\rightleftharpoons} Lo + EsM$$

$$EsM \overset{es}{\rightleftharpoons} Mo + Es$$

$$Es \overset{e}{\rightleftharpoons} E$$

$$EM \overset{slip}{\rightleftharpoons} EsM$$

3.2 Stoichiometric Matrices

$$X = \begin{pmatrix} x_{Li} \\ x_{Lo} \\ x_{Mi} \\ x_{Mo} \\ x_{E} \\ x_{EM} \\ x_{LEM} \\ x_{Es} \\ x_{EsM} \\ x_{LEsM} \end{pmatrix} \qquad N = \begin{pmatrix} 0 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 & 1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 \end{pmatrix} \qquad V = \begin{pmatrix} v_{em} \\ v_{lem} \\ v_{lesm} \\ v_{esm} \\ v_{es} \\ v_{e} \\ v_{slip} \end{pmatrix}$$

$$N^f = \begin{pmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \end{pmatrix} \qquad N^r = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$N^{cd} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 & 1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 \end{pmatrix} \qquad K_p = \begin{pmatrix} 1 & 1 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 1 \\ 1 & 1 \\ 0 & 1 \end{pmatrix}$$

3.3 Differential equations

$$\begin{aligned} \dot{x}_{Li} &= -v_{lem} \\ \dot{x}_{Lo} &= +v_{esm} \\ \dot{x}_{Mi} &= -v_{em} \\ \dot{x}_{Mo} &= +v_{es} \\ \dot{x}_{E} &= -v_{em} + v_{e} \\ \dot{x}_{EM} &= +v_{em} - v_{lem} - v_{slip} \\ \dot{x}_{LEM} &= +v_{lem} - v_{lesm} \\ \dot{x}_{Es} &= +v_{es} - v_{e} \\ \dot{x}_{EsM} &= +v_{esm} - v_{es} + v_{slip} \\ \dot{x}_{LEsM} &= +v_{lesm} - v_{esm} \end{aligned}$$

3.4 Flows

$$
\begin{aligned}
v_{em} &= \kappa_{em}(K_{Mi}x_{Mi}K_E x_E - K_{EM}x_{EM}) \\
v_{lem} &= \kappa_{lem}(K_{Li}x_{Li}K_{EM}x_{EM} - K_{LEM}x_{LEM}) \\
v_{lesm} &= \kappa_{lesm}(K_{LEM}x_{LEM} - K_{LEsM}x_{LEsM}) \\
v_{esm} &= \kappa_{esm}(K_{LEsM}x_{LEsM} - K_{Lo}x_{Lo}K_{EsM}x_{EsM}) \\
v_{es} &= \kappa_{es}(K_{EsM}x_{EsM} - K_{Mo}x_{Mo}K_{Es}x_{Es}) \\
v_e &= \kappa_e(K_{Es}x_{Es} - K_E x_E) \\
v_{slip} &= \kappa_{slip}(K_{EM}x_{EM} - K_{EsM}x_{EsM})
\end{aligned}
$$

4 SGLT example (§ 6 of paper)

4.1 Chemical Equations

$$
\begin{aligned}
2Mi + E &\overset{em}{\rightleftharpoons} EM \\
Li + EM &\overset{lem}{\rightleftharpoons} LEM \\
LEM &\overset{lesm}{\rightleftharpoons} LEsM \\
LEsM &\overset{esm}{\rightleftharpoons} Lo + EsM \\
EsM &\overset{es}{\rightleftharpoons} 2Mo + Es \\
Es &\overset{e}{\rightleftharpoons} E \\
EM &\overset{slip}{\rightleftharpoons} EsM
\end{aligned}
$$

4.2 Stoichiometric Matrices

$$
X = \begin{pmatrix} x_{Li} \\ x_{Lo} \\ x_{Mi} \\ x_{Mo} \\ x_E \\ x_{EM} \\ x_{LEM} \\ x_{Es} \\ x_{EsM} \\ x_{LEsM} \end{pmatrix}
\qquad
N = \begin{pmatrix} 0 & -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ -2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 2 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 & 1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 \end{pmatrix}
\qquad
V = \begin{pmatrix} v_{em} \\ v_{lem} \\ v_{lesm} \\ v_{esm} \\ v_{es} \\ v_e \\ v_{slip} \end{pmatrix}
$$

$$N^f = \begin{pmatrix} 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 2 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \end{pmatrix} \qquad N^r = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$N^{cd} = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 1 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & -1 & 0 \\ 0 & 0 & 0 & 1 & -1 & 0 & 1 \\ 0 & 0 & 1 & -1 & 0 & 0 & 0 \end{pmatrix} \qquad K_p = \begin{pmatrix} 1 & 1 \\ 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 1 \\ 1 & 1 \\ 0 & 1 \end{pmatrix}$$

4.3 Differential equations

$$\begin{aligned} \dot{x}_{Li} &= -v_{lem} \\ \dot{x}_{Lo} &= +v_{esm} \\ \dot{x}_{Mi} &= -2v_{em} \\ \dot{x}_{Mo} &= +2v_{es} \\ \dot{x}_{E} &= -v_{em} + v_{e} \\ \dot{x}_{EM} &= +v_{em} - v_{lem} - v_{slip} \\ \dot{x}_{LEM} &= +v_{lem} - v_{lesm} \\ \dot{x}_{Es} &= +v_{es} - v_{e} \\ \dot{x}_{EsM} &= +v_{esm} - v_{es} + v_{slip} \\ \dot{x}_{LEsM} &= +v_{lesm} - v_{esm} \end{aligned}$$

4.4 Flows

$$
\begin{aligned}
v_{em} &= \kappa_{em}(K_{Mi}^2 x_{Mi}^2 K_E x_E - K_{EM} x_{EM}) \\
v_{lem} &= \kappa_{lem}(K_{Li} x_{Li} K_{EM} x_{EM} - K_{LEM} x_{LEM}) \\
v_{lesm} &= \kappa_{lesm}(K_{LEM} x_{LEM} - K_{LEsM} x_{LEsM}) \\
v_{esm} &= \kappa_{esm}(K_{LEsM} x_{LEsM} - K_{Lo} x_{Lo} K_{EsM} x_{EsM}) \\
v_{es} &= \kappa_{es}(K_{EsM} x_{EsM} - K_{Mo}^2 x_{Mo}^2 K_{Es} x_{Es}) \\
v_{e} &= \kappa_{e}(K_{Es} x_{Es} - K_E x_E) \\
v_{slip} &= \kappa_{slip}(K_{EM} x_{EM} - K_{EsM} x_{EsM})
\end{aligned}
$$

5 SGLT example: simulation parameters

Reaction	k_f	k_r	$K_{eq} = \frac{k_f}{k_r}$	$\kappa \,\mathrm{mol\,s^{-1}}$
r12	80000	500	160	10.1796
r23	100000	20	5000	202.023
r34	50	50	1	505.058
r45	800	12190	0.0656276	8080.93
r56	10	4500	0.00222222	67.1184
r61	3	350	0.00857143	8.67804
r25	0.3	0.00091	329.67	0.00610777

Table 1: Reaction Parameters for the SGLT example. As discussed in Appendix A, the formulation used here has dimensionless k_f, k_r and K_{eq}. However the constants given by Eskandari et al. [5, Figure 6] have units of either mol^{-1} or mol^{-2} according to the reaction. In this paper, the reference quantity is taken as $1\,\mathrm{mol}$ and thus the numerical values of the dimensionless k_f, k_r and K_{eq} are the same as the numerical values of the quantities given by Eskandari et al. [5, Figure 6]. See Keener and Sneyd [6, § 1.1] for a discussion of this point.

6 Biomolecular Cycle: steady-state analysis

Consider a special case of the Hill model of Figure 3 of the paper where all of the thermodynamic constants $K_{ci} = 1$, all of the rate constants $\kappa_i = \kappa_0$, the slippage (via **Re**:**slip**) is zero, and the chemostats are defined by:

$$
x_{Mi} = x_M \qquad x_{Mo} = 1 \qquad x_{Li} = 1 \qquad x_{Lo} = x_L \tag{6.1}
$$

Species	K
So	10.0777
Si	10.1247
Nao	13.9591
Nai	13.9263
Co	40.3317
CNao	49.1178
SCNao	0.0989984
Ci	0.3457
CNai	0.148991
SCNai	0.0989984

Table 2: Species Parameters for the SGLT example

It is convenient to index the free species and the reactions numerically (as in Figure 7 of the paper) so that:

$$X = \begin{pmatrix} x_{Li} \\ x_{Lo} \\ x_{Mi} \\ x_{Mo} \\ x_E \\ x_{EM} \\ x_{LEM} \\ x_{Es} \\ x_{EsM} \\ x_{LEsM} \end{pmatrix} = \begin{pmatrix} 1 \\ x_L \\ x_M \\ 1 \\ x_1 \\ x_2 \\ x_3 \\ x_6 \\ x_5 \\ x_4 \end{pmatrix} \qquad V = \begin{pmatrix} v_{em} \\ v_{lem} \\ v_{lesm} \\ v_{esm} \\ v_{es} \\ v_e \\ v_{slip} \end{pmatrix} = \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \end{pmatrix} \tag{6.2}$$

In this case, the equations given in § 6 of this document become

$$v_1 = \kappa_0(x_M x_1 - x_2) \tag{6.3}$$
$$v_2 = \kappa_0(x_2 - x_3) \tag{6.4}$$
$$v_3 = \kappa_0(x_3 - x_4) \tag{6.5}$$
$$v_4 = \kappa_0(x_4 - x_L x_5) \tag{6.6}$$
$$v_5 = \kappa_0(x_5 - x_6) \tag{6.7}$$
$$v_6 = \kappa_0(x_6 - x_1) \tag{6.8}$$
$$v_7 = 0 \tag{6.9}$$

Assuming steady-state conditions, $v_1 = v_2 = v_3 = v_4 = v_5 = v_6 = v$ and defining $\bar{v} = \dfrac{v}{\kappa_0}$,

the reactions defined by the six equations (6.3) - (6.8) imply that:

$$x_m x_1 = x_2 + \bar{v} \tag{6.10}$$
$$x_2 = x_3 + \bar{v} \tag{6.11}$$
$$x_3 = x_4 + \bar{v} \tag{6.12}$$
$$x_4 = x_L x_5 + \bar{v} \tag{6.13}$$
$$x_5 = x_6 + \bar{v} \tag{6.14}$$
$$x_6 = x_1 + \bar{v} \tag{6.15}$$

Consider the limiting case when $x_M \to \infty$. From equation (6.10), it follows that $x_1 \to 0$. Hence, working backwards through the six equations (6.10) - (6.15), gives

$$x_6 = \bar{v} \qquad x_5 = 2\bar{v} \qquad x_4 = 2x_L\bar{v} + \bar{v} \qquad x_3 = 2x_L\bar{v} + 2\bar{v} \qquad x_2 = 2x_L\bar{v} + 3\bar{v} \tag{6.16}$$

Now the six states x_1–x_6 form a conserved moiety hence:

$$\sum_{i=1}^{6} x_i = x_{tot} \tag{6.17}$$

Combining Equations (6.16) and (6.17) it follows that, in the steady-state, v saturates as $x_M \to \infty$ at a value given by

$$v_{max} = \frac{\kappa_0 x_{tot}}{9 + 6x_L} \tag{6.18}$$

References

[1] Peter J. Gawthrop and Edmund J. Crampin. Energy-based analysis of biochemical cycles using bond graphs. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Science*, 470(2171):1–25, 2014. doi: 10.1098/rspa.2014.0459. Available at arXiv:1406.2447. 3

[2] Peter J. Gawthrop, Joseph Cursons, and Edmund J. Crampin. Hierarchical bond graph modelling of biochemical networks. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 471(2184):1–23, 2015. ISSN 1364-5021. doi: 10.1098/rspa.2015.0642. Available at arXiv:1503.01814.

[3] P. J. Gawthrop and E. J. Crampin. Modular bond-graph modelling and analysis of biomolecular systems. *IET Systems Biology*, 10(5):187–201, October 2016. ISSN 1751-8849. doi: 10.1049/iet-syb.2015.0083. Available at arXiv:1511.06482.

[4] Peter J. Gawthrop. Bond-graph modelling and causal analysis of biomolecular systems. In Wolfgang Borutzky, editor, *Bond Graphs for Modelling, Control and Fault Diagnosis of Engineering Systems*, pages 587–623. Springer International Publishing, Berlin, 2017. ISBN 978-3-319-47434-2. doi: 10.1007/978-3-319-47434-2_16. 3

[5] S. Eskandari, E. M. Wright, and D. D. F. Loo. Kinetics of the Reverse Mode of the Na+/Glucose Cotransporter. *J Membr Biol*, 204(1):23–32, Mar 2005. ISSN 0022-2631. doi: 10.1007/s00232-005-0743-x. 16007500[pmid]. 2, 10

[6] James P Keener and James Sneyd. *Mathematical Physiology: I: Cellular Physiology*, volume 1. Springer, 2nd edition, 2009. 2, 10