Note on perturbation responses for open equilibrium systems

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A. Perturbing chemostats vs perturbing conservation laws

Let us start with a closed CRN with $\ell_\circ$ conservation laws. We now open the CRN through $s^Y < \ell_\circ$ chemostats, such that no new cycles emerge ($a = 0$). Then there are $b = s^Y$ broken conservation laws corresponding to chemostats. We let $\ell = \ell_\circ - b$ denote the conserved quantities that are left. Just as for the closed system, the equilibrium abundance of each species can be expressed in terms $\ell_\circ = s^Y + \ell$ concentrations: ℓ internal ones $\mathrm{X}_1, .., \mathrm{X}_\ell$ and s^Y chemostats $\mathrm{Y}_1, .., \mathrm{Y}_{s^Y}$. The abundance of a given species $[\mathrm{Z}_j]$ is now given by the equilibrium expression

$$[\mathrm{Z}_j] = K_j \prod_{k=1}^{s^Y} [\mathrm{Y}_k]^{n_k^{(j)}} \prod_{q=1}^{\ell} [\mathrm{X}_q]^{m_q^{(j)}} \tag{1}$$

Where we recall that the stoichiometric coefficients $n_k^{(j)}, m_q^{(j)}$ directly follow from an underlying choice of basis of conservation laws in the closed system.

Ipso facto, shifting the (concentration) value of a chemostat ([1]) can equivalently be viewed as shifting conservation laws in the associated closed system. These chemostat are independent, and if we replace all conservation laws with them $b = \ell = s^Y$ then we have

$$\begin{aligned} \left(\partial_{Y_k}[\mathrm{Y}_j]\right)_{Y_q, q\neq k} &= \delta_i^j & (2)\\ \left(\partial_{Y_k}[\mathrm{Z}_j]\right)_{Y_q, q\neq k} &= \frac{n_k^{(j)}}{[\mathrm{Y}_k]}[\mathrm{Z}_j] & (3)\\ \left(\partial_{\log(Y_k)}\log[\mathrm{Z}_j]\right)_{Y_q, q\neq k} &= n_k & (4) \end{aligned}$$

More generally, letting $s^Y > 0, \ell > 0$, we fix a mixture of conservation laws and chemostats, and then perturb one. By construction, the remaining conservation laws do not depend on chemostat species

$$\begin{aligned} \left(\partial_{Y_k}[\mathrm{Y}_j]\right)_{Y_q, q\neq k, L_m} &= \delta_k^j, & (5)\\ \left(\partial_{Y_k}L_j\right)_{Y_q, q\neq k, L_m} &= 0, & (6)\\ \left(\partial_{L_k}[\mathrm{Y}_j]\right)_{Y_q, L_m, m\neq k} &= 0, & (7)\\ \left(\partial_{L_k}L_j\right)_{Y_q, L_m, m\neq k} &= \delta_k^j. & (8) \end{aligned}$$

then

$$\partial_{Y_k}[Z_j] = \frac{n_k^{(j)}[Z_j]}{[\mathrm{Y}_k]} + \sum_{q=1}^{\ell} \frac{m_q^{(j)}[\mathrm{Z}_j]}{[\mathrm{X}_q]}\partial_{Y_k}[\mathrm{X}_q] \tag{9}$$

The ℓ partial derivatives $\partial_{Y_k}[\mathrm{X}_1], ..\partial_{Y_k}[\mathrm{X}_\ell]$ can be solved for by using ℓ conservation laws, using the system $\partial_{Y_k}L_j = 0$

$$\begin{aligned} \begin{pmatrix} \partial_{Y_k}L_1 \\ \partial_{Y_k}L_2 \\ \vdots \\ \partial_{Y_k}L_\ell \end{pmatrix} = \mathbf{0} &= \begin{pmatrix} W_{11} & W_{12} & \dots & W_{1\ell} \\ W_{21} & W_{22} & \dots & W_{2\ell} \\ \vdots & \vdots & \ddots & \vdots \\ W_{\ell 1} & W_{\ell 2} & \dots & W_{\ell\ell} \end{pmatrix} \begin{pmatrix} [\mathrm{X}_1]^{-1}\partial_{Y_k}[\mathrm{X}_1] \\ [\mathrm{X}_2]^{-1}\partial_{Y_k}[\mathrm{X}_2] \\ \vdots \\ [\mathrm{X}_\ell]^{-1}\partial_{Y_k}[\mathrm{X}_\ell] \end{pmatrix} + [\mathrm{Y}_k]^{-1} \begin{pmatrix} W_{1Y_k} \\ W_{2Y_k} \\ \vdots \\ W_{\ell Y_k} \end{pmatrix} & (10)\\ \mathbb{W}\partial_{Y_k}\log[\boldsymbol{X}] &= -[\mathrm{Y}_k]^{-1}\boldsymbol{W}^{(k)} & (11) \end{aligned}$$

where $\mathbb{W}$ is a Gram matrix

$$
\begin{aligned}
W_{ij} &= \sum_{k=1}^{s} m_k^{(i)} m_k^{(j)} [\mathrm{Z}_k] = \sum_{k=1}^{s} \ell_k^{(i)} \ell_k^{(j)} [\mathrm{Z}_k] = W_{ji} && (12) \\
\boldsymbol{w}_i &= (\ell_1^{(i)} [\mathrm{Z}_1]^{1/2}, \ell_2^{(i)} [\mathrm{Z}_2]^{1/2}, ..., \ell_s^{(i)} [\mathrm{Z}_s]^{1/2})^T && (13) \\
W_{ij} &= \boldsymbol{w}_i^T \boldsymbol{w}_j = \boldsymbol{w}_j^T \boldsymbol{w}_i && (14)
\end{aligned}
$$

i.e. W_{ij} can be interpreted as an inner product. From the Cauchy-Schwarz inequality we then immediately see that

$$
W_{ij}^2 \leq W_{ii} W_{jj} \qquad (15)
$$

A Gram matrix is positive semidefinite, and postive definite if the underlying $\boldsymbol{w}_i$ are linearly independent (for our CRNs this is usually the case). In the latter case, all eigenvalues are positive and - ipso facto - the determinant is positive $|\mathbb{W}| > 0$. The inverse $\mathbb{W}^{-1}$ is also a Gram matrix.

Our system of equations can be written more compactly as

$$
\begin{aligned}
\boldsymbol{\Phi}^{(k)} &= \partial_{\log Y_k} \log[\boldsymbol{X}] = -\mathbb{W}^{-1} \boldsymbol{W}^{(k)} && (16) \\
\Phi_i^{(k)} &= \partial_{\log Y_k} \log[\mathrm{X}_i] = -\hat{e}_i \mathbb{W}^{-1} \boldsymbol{W}^{(k)} && (17)
\end{aligned}
$$

Hence

$$
\begin{aligned}
\partial_{\mathrm{Y}_k} [Z_j] &= \frac{[Z_j]}{[\mathrm{Y}_k]} \left(n_k^{(j)} - \boldsymbol{m}^{(j)} \mathbb{W}^{-1} \boldsymbol{W}^{(k)} \right) && (18) \\
\Gamma_j^{(k)} &= \partial_{\log Y_k} \log[Z_j] = \left(n_k^{(j)} - \boldsymbol{m}^{(j)} \mathbb{W}^{-1} \boldsymbol{W}^{(k)} \right) && (19) \\
&= n_k^{(j)} - \boldsymbol{m}^{(j)} \boldsymbol{\Phi}^{(k)} && (20)
\end{aligned}
$$

where $\boldsymbol{m} = (m_1^{(j)}, m_2^{(j)}, .., m_\ell^{(j)}) = (\ell_j^{(1)}, \ell_j^{(2)}, .., \ell_j^{(\ell)})$. Under conditions where $\boldsymbol{m} \mathbb{W}^{-1} \boldsymbol{W}^{(k)} \geq 0$ the logarithmic derivative is bounded from above by the stoichiometric bound $n_k^{(j)}$. CRNs satisfying $\boldsymbol{m} \mathbb{W}^{-1} \boldsymbol{W}^{(k)} \geq 0$ can readily be realized, but it is certainly not universal and several subtleties and couplings arise with increasing ℓ.

Note that in particular when $\ell = 0$ conservation laws remain, then the logarithmic derivative becomes exactly $n_k^{(j)}$,

$$
\ell = 0 \rightarrow \Gamma_j^{(k)} = n_k^{(j)} \quad \text{(at equilibrium)} \qquad (21)
$$

i.e. the bound then becomes tight and is both an upper and lower bound. We will refer to $n_k^{(j)}$ as the 'chemostat bound'.

After shortly considering the interpretation of $\mathbb{W}$, we will inspect the behavior of the logarithmic behavior in several contexts through examples.

1. Interpretation of $\mathbb{W}$

A fruitful physical interpretation to point out is that W_{ij} behaves similar to (mixed) 'moments' of distributions. In 1d, a related object is found in polymer chemistry, where one is interested in several moments of mass distribution, e.g. number-averaged molar mass, mass-average molar mass, Z-average molar mass. For ℓ conservation laws (most readily appreciated when they have positive coefficients), W_{ij} captures the (stoichiometric) extent of combined incorporation of moieties.

For instance, consider

$$
\begin{aligned}
\mathrm{X}_1 &+ \mathrm{X}_2 \leftrightarrows \mathrm{Z}_4, \quad \mathrm{X}_2 + \mathrm{X}_3 \leftrightarrows \mathrm{Z}_5, && (22) \\
L_1 &= [\mathrm{X}_1] + [\mathrm{Z}_4] \quad L_2 = [\mathrm{Z}_4] + [\mathrm{X}_2] + [\mathrm{Z}_2] \quad L_3 = [\mathrm{X}_2] + [\mathrm{Z}_5] && (23) \\
[\mathrm{Z}_4] &= K_1 [\mathrm{X}_1][\mathrm{X}_2], \quad [\mathrm{Z}_5] = K_2 [\mathrm{X}_2][\mathrm{X}_3]. && (24)
\end{aligned}
$$

We now find

$$W_{11} = [\mathrm{X}_1] + [\mathrm{Z}_4], \quad W_{12} = [\mathrm{Z}_4], \quad W_{13} = 0, \tag{25}$$
$$W_{22} = [\mathrm{Z}_4] + [\mathrm{X}_2] + [\mathrm{Z}_5], \quad W_{23} = [\mathrm{Z}_5], \quad W_{33} = [\mathrm{X}_3] \tag{26}$$

As $[\mathrm{X}_1], [\mathrm{X}_3]$ do not simultaneously participate in a single species, $\ell_j^{(1)}\ell_j^{(3)} = 0$ hence $W_{13} = 0$.

Let us now consider some examples.

B. Example 1: A simple CRN

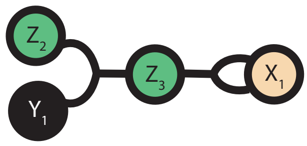

Figure 1: Hypergraph representation for $2\mathrm{X}_1 \leftrightarrows \mathrm{Z}_2, \quad \mathrm{Z}_2 + \mathrm{Y}_1 \leftrightarrows \mathrm{Z}_3$

Consider

$$2\mathrm{X}_1 \overset{1}{\leftrightarrows} \mathrm{Z}_2, \quad \mathrm{Z}_2 + \mathrm{Y}_1 \overset{2}{\leftrightarrows} \mathrm{Z}_3 \tag{27}$$
$$L_1 = [\mathrm{X}_1] + 2[\mathrm{Z}_2] + 2[\mathrm{Z}_3] \tag{28}$$

Then

$$[\mathrm{Z}_3] = K_2[\mathrm{Y}_1][\mathrm{X}_1]^2 \tag{29}$$
$$(\partial_{Y_1}[\mathrm{Z}_3])_{L_1} = \frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]} + \frac{2[\mathrm{Z}_3]}{[\mathrm{X}_1]}(\partial_{Y_1}[\mathrm{X}_1])_{L_1} \tag{30}$$

We have

$$W_{11} = [\mathrm{X}_1] + 4[\mathrm{Z}_2] + 4[\mathrm{Z}_3], \quad W_{1Y_1} = 2[\mathrm{Z}_3], \tag{31}$$
$$\partial_{Y_1} L_1 = 0 = \partial_{Y_1}[\mathrm{X}_1]\frac{W_{11}}{[\mathrm{X}_1]} + \frac{W_{1Y_1}}{[\mathrm{Y}_1]} \tag{32}$$
$$\partial_{Y_1}[\mathrm{X}_1] = -\frac{[\mathrm{X}_1]}{[\mathrm{Y}_1]}\frac{2[\mathrm{Z}_3]}{[\mathrm{X}_1] + 4[\mathrm{Z}_2] + 4[\mathrm{Z}_3]} \tag{33}$$

and then

$$(\partial_{Y_1}[\mathrm{Z}_3])_{L_1} = \frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]} - \frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]}\frac{4[\mathrm{Z}_3]}{[\mathrm{X}_1] + 4[\mathrm{Z}_2] + 4[\mathrm{Z}_3]} \tag{34}$$
$$= \left(\frac{[\mathrm{X}_1] + 4[\mathrm{Z}_2]}{[\mathrm{X}_1] + 4[\mathrm{Z}_2] + 4[\mathrm{Z}_3]}\right)\frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]} \tag{35}$$
$$\Gamma_3^{(1)} = \left(1 - 2\frac{W_{1Y_1}}{W_{11}}\right) = \left(1 - \frac{4[\mathrm{Z}_3]}{[\mathrm{X}_1] + 4[\mathrm{Z}_2] + 4[\mathrm{Z}_3]}\right) \tag{36}$$

i.e. the logarithmic derivative of $[\mathrm{Z}_3]$ wrt Y_1 is contained between 0 and 1.

Conversely, if we would chemostat X_1, so that $\ell = 0, s^Y = 2$, i.e.

$$2\mathrm{Y}_2 \overset{1}{\leftrightarrows} \mathrm{Z}_2, \quad \mathrm{Z}_2 + \mathrm{Y}_1 \overset{2}{\leftrightarrows} \mathrm{Z}_3, \tag{37}$$
$$[\mathrm{Z}_3] = K_2[\mathrm{Y}_1][\mathrm{Y}_2]^2. \tag{38}$$

then the logarithmic derivative is simply 1

$$(\partial_{Y_1}[\mathrm{Z}_3])_{Y_2} = 1\frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]}. \tag{39}$$

Mechanistically, increasing $[\mathrm{Y}_1]$ while maintaining $[\mathrm{Y}_2]$ fixed would here require some influx of mass from $[\mathrm{Y}_2]$. Our prior situation involving a conservation law does not allow for this influx, and can be interpreted as a counterbalancing effect that decreases the logarithmic response. From this example, one might come to expect that conservation weaken a perturbation response, but in Example 3 an example of coupled conservation laws will show that they can also do the opposite.

C. Example 2: negative coefficients ($s^Y = 2, \ell = 1$)

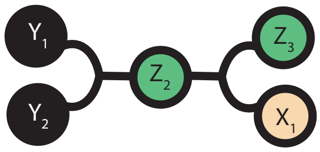

Figure 2: Hypergraph representation for $\mathrm{Y}_1 + \mathrm{Y}_2 \leftrightarrows \mathrm{Z}_2 \leftrightarrows \mathrm{Z}_3 + \mathrm{X}_1$

It is important to stress that (stoichiometric) conservation laws in open systems cannot always have purely positive coefficients. In closed systems one can choose a positive basis for the conservation laws, but upon opening the system up only certain linear combinations may still be conserved (i.e. a moiety interpretation remains possible when shifting to linear combinations of them).

As an example, let us consider an open system with $s^Y = 2$ chemostats, and $\ell = 1$ conservation law (which is hence unique) with coefficients of mixed sign

$$\mathrm{Y}_1 + \mathrm{Y}_2 \overset{1}{\leftrightarrows} \mathrm{Z}_2 \overset{2}{\leftrightarrows} \mathrm{Z}_3 + \mathrm{X}_1 \tag{40}$$

then

$$L_1 = [\mathrm{X}_1] - [\mathrm{Z}_3] \tag{41}$$

$$[\mathrm{Z}_3] = K_3\frac{[\mathrm{Y}_1][\mathrm{Y}_2]}{[\mathrm{X}_1]}, \quad m_1^{(3)} = -1 \tag{42}$$

and now

$$\partial_{Y_1}[\mathrm{Z}_3] = \frac{[\mathrm{Z}_3]}{[\mathrm{Y}_1]} - 1\frac{[\mathrm{Z}_3]}{[\mathrm{X}_1]}\partial_{Y_1}[\mathrm{X}_1] \tag{43}$$

$$W_{11} = [\mathrm{X}_1] + [\mathrm{Z}_3], \quad W_{1Y_1} = -[\mathrm{Z}_3] \tag{44}$$

$$\partial_{Y_1}L_1 = 0 = \partial_{Y_1}[\mathrm{X}_1]\frac{W_{11}}{[\mathrm{X}_1]} + \frac{W_{1Y_1}}{[\mathrm{Y}_1]} \tag{45}$$

$$\partial_{Y_1}[\mathrm{X}_1] = \frac{[\mathrm{X}_1][\mathrm{Z}_3]}{[\mathrm{Y}_1]\left([\mathrm{X}_1] + [\mathrm{Z}_3]\right)} \tag{46}$$

so

$$\Gamma_3^{(1)} = \left(1 - m_1^{(3)}\frac{W_{1Y_1}}{W_{11}}\right) = \left(1 - \frac{[\mathrm{Z}_3]}{[\mathrm{X}_1] + [\mathrm{Z}_3]}\right) \tag{47}$$

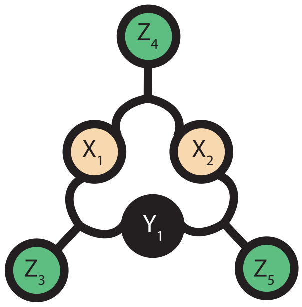

Figure 3: Hypergraph representation for $\mathrm{Y}_1 + \mathrm{X}_1 \leftrightharpoons \mathrm{Z}_3$, $\mathrm{X}_1 + \mathrm{X}_2 \leftrightharpoons \mathrm{Z}_4$, $\mathrm{X}_2 + \mathrm{Y}_1 \leftrightharpoons \mathrm{Z}_5$

D. Example 3, coupled conservation laws can exceed the chemostat bound ($s^Y = 1, \ell = 2$)

We now consider

$$\begin{aligned}
\mathrm{Y}_1 &+ \mathrm{X}_1 \overset{1}{\leftrightharpoons} \mathrm{Z}_3, \quad \mathrm{X}_1 + \mathrm{X}_2 \overset{2}{\leftrightharpoons} \mathrm{Z}_4, \quad \mathrm{X}_2 + \mathrm{Y}_1 \overset{3}{\leftrightharpoons} \mathrm{Z}_5, && (48)\\
L_1 &= [\mathrm{X}_1] + [\mathrm{Z}_3] + [\mathrm{Z}_4] && (49)\\
L_2 &= [\mathrm{X}_2] + [\mathrm{Z}_4] + [\mathrm{Z}_5] && (50)
\end{aligned}$$

so that

$$\begin{aligned}
[\mathrm{Z}_3] &= K_1[\mathrm{Y}_1][\mathrm{X}_1] && (51)\\
[\mathrm{Z}_4] &= K_2[\mathrm{X}_1][\mathrm{X}_2] && (52)\\
[\mathrm{Z}_5] &= K_3[\mathrm{Y}_1][\mathrm{X}_2] && (53)\\
\partial_{Y_1}[\mathrm{Z}_5] &= \frac{[\mathrm{Z}_5]}{[\mathrm{Y}]_1} + \frac{[\mathrm{Z}_5]}{[\mathrm{X}]_2}\,\partial_{Y_1}[\mathrm{X}_2] && (54)
\end{aligned}$$

and now

$$\begin{pmatrix}\partial_{Y_1}L_1\\ \partial_{Y_1}L_2\end{pmatrix} = \mathbf{0} = \begin{pmatrix}L_1 & Z_4\\ Z_4 & L_2\end{pmatrix}\begin{pmatrix}[\mathrm{X}_1]^{-1}\partial_{Y_1}[\mathrm{X}_1]\\ [\mathrm{X}_2]^{-1}\partial_{Y_1}[\mathrm{X}_2]\end{pmatrix} + [\mathrm{Y}_1]^{-1}\begin{pmatrix}Z_3\\ Z_5\end{pmatrix} \tag{55}$$

Which is readily inverted to obtain

$$[\mathrm{Y}_1]\begin{pmatrix}[\mathrm{X}_1]^{-1}\partial_{Y_1}[\mathrm{X}_1]\\ [\mathrm{X}_2]^{-1}\partial_{Y_1}[\mathrm{X}_2]\end{pmatrix} = -\frac{1}{L_1L_2 - Z_4^2}\begin{pmatrix}L_2 & -Z_4\\ -Z_4 & L_1\end{pmatrix}\begin{pmatrix}Z_3\\ Z_5\end{pmatrix} \tag{56}$$

and then

$$\begin{aligned}
\partial_{Y_1}[\mathrm{Z}_5] &= \frac{[\mathrm{Z}_5]}{[\mathrm{Y}_1]} + \frac{[\mathrm{Z}_5]}{[\mathrm{Y}_1]}\,\frac{L_1Z_5 - Z_3Z_4}{L_1L_2 - Z_4^2} && (57)\\
\Gamma_5^{(1)} &= \left(1 + \frac{K_3[\mathrm{X}_1][\mathrm{X}_2][\mathrm{Y}_1] + K_1K_3[\mathrm{X}_1][\mathrm{X}_2][\mathrm{Y}_1]^2 + K_2K_3[\mathrm{X}_1][\mathrm{X}_2]^2[\mathrm{Y}_1] - K_1K_2[\mathrm{X}_1]^2[\mathrm{X}_2][\mathrm{Y}_1]}{L_1L_2 - Z_4^2}\right)\\
\Gamma_3^{(1)} &= \left(1 + \frac{L_2Z_3 - Z_4Z_5}{L_1L_2 - Z_4^2}\right) && (58)
\end{aligned}$$

the term $\frac{L_1Z_3 - Z_1Z_2}{L_1L_2 - Z_2^2}$ takes values between -1 and 1, and thus the upper bound in the response is 2, the lower 0. Despite the symmetry, the variables $[\mathrm{Z}_1], [\mathrm{Z}_3]$, do not respond equivalently, i.e. $\Gamma_3^{(1)} \neq \Gamma_5^{(1)}$. Let us consider a combined response

$$\begin{aligned}
\partial_{Y_1}([\mathrm{Z}_3][\mathrm{Z}_1]) &= \frac{[\mathrm{Z}_1][\mathrm{Z}_3]}{[\mathrm{Y}_1]}\left(2 + \frac{L_1Z_3 + L_2Z_1 - Z_1Z_2 - Z_3Z_2}{L_1L_2 - Z_2^2}\right) && (59)\\
\Gamma_{3,5}^{(1)} &= \frac{[\mathrm{Y}_1]}{[\mathrm{Z}_1][\mathrm{Z}_3]}\partial_{Y_1}([\mathrm{Z}_3][\mathrm{Z}_1]) = \left(2 + \frac{(X_1 + Z_1)Z_3 + (X_2 + Z_3)Z_1}{L_1L_2 - Z_2^2}\right) && (60)\\
&= \Gamma_3^{(1)} + \Gamma_5^{(1)}. && (61)
\end{aligned}$$

Note that $\Gamma^{(1)}_{3,5} \in (2,3)$. Based on Y_1 alone, one would expect an upper bound of 2 (and lower bound of 0). Here, a synergystic coupling of conservation laws enables the response to have an upper bound of 3. It should be stressed that this would not happen in the absence of reaction r_2. In its absence case the conservation laws would become uncoupled, and a logarithmic response in between 0 and 2 would be obtained instead, which is seen upon inspection of

$$X_1 + Y_1 \leftrightarrows Z_3, \tag{62}$$

E. Example 4, a symmetric example ($\ell = 1$)

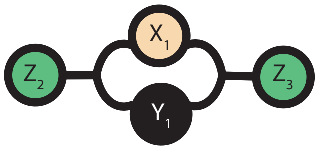

Figure 4: Hypergraph representation for $Z_2 \leftrightarrows Y_1 + X_1 \leftrightarrows Z_3$

We now consider

$$\begin{aligned} Y_1 \ &+\ X_1 \overset{1}{\leftrightarrows} Z_2, \quad X_1 + Y_1 \overset{2}{\leftrightarrows} Z_3, && (63)\\ L_1 \ &=\ [X_1] + [Z_2] + [Z_3] && (64)\end{aligned}$$

so that

$$\begin{aligned} [Z_2] &= K_1[Y_1][X_1] && (65)\\ [Z_3] &= K_2[Y_1][X_1] && (66)\\ \partial_{Y_1}[Z_2] &= \frac{[Z_2]}{[Y]_1} + \frac{[Z_2]}{[X]_1}\,\partial_{Y_1}[X_1] && (67)\\ \partial_{Y_1}[Z_3] &= \frac{[Z_3]}{[Y]_1} + \frac{[Z_3]}{[X]_1}\,\partial_{Y_1}[X_1] && (68)\\ & && (69)\end{aligned}$$

and now

$$\partial_{Y_1} L_1 = 0 = \frac{L_1}{[X_1]}\partial_{Y_1}[X_1] + \frac{L_1 - [X_1]}{[Y_1]} \tag{70}$$

so that

$$\begin{aligned} \partial_{Y_1}[Z_j] &= \frac{[Z_j]}{[Y]_1} - \frac{[Z_j]}{[Y]_1}\,\frac{L_1 - [X_1]}{L_1} && (71)\\ \Gamma^{(1)}_2 &= \frac{[Y_1]}{[Z_1]}\partial_{Y_1}[Z_j] = \left(1 - m_1^{(2)}\frac{W_{1Y_1}}{W_{11}}\right) = \left(1 - \frac{L_1 - [X_1]}{L_1}\right) && (72)\\ \Gamma^{(1)}_3 &= \left(1 - m_1^{(3)}\frac{W_{1Y_1}}{W_{11}}\right) = \Gamma^{(1)}_2 && (73)\end{aligned}$$

Up to equilibrium constant, Z_2, Z_3 are identical. In particular, the equivalence of their coefficients ($n_2^{(1)} = n_3^{(1)}$, $m_2^{(1)} = m_3^{(1)}$) means that their logarithmic derivatives must become equivalent, resulting in an identical logarithmic response to perturbation $\Gamma^{(1)}_j \in (0,1)$. The combined response $\Gamma^{(1)}_{1,2}$ is thus twice either response

$$\begin{aligned} \Gamma^{(1)}_{1,2} &= \frac{[Y_1]}{[Z_1][Z_2]}\partial_{Y_1}[Z_1][Z_2] = \left(2 - 2\frac{L_1 - [X_1]}{L_1}\right) && (74)\\ \Gamma^{(1)}_{1,2} &= \Gamma^{(1)}_1 + \Gamma^{(1)}_2 = 2\Gamma^{(1)}_1 = 2\Gamma^{(1)}_2 && (75)\end{aligned}$$

REFERENCES

[1] Or more precisely, chemical potential.