Supplementary material

Introduction

We consider a simple dynamical system model based on Michaelis-Menten reaction kinetics [1] which seeks to explain a subset of the single-cell RNA-sequencing data from experiments of embryonic stem cell development reported by [2]. We show the nondimensionalization in considerable detail since we arrive at a slightly different result from [1].

Mathematical model

Let C = [CDH1], Z = [ZEB1] and K = [KLF8] represent the time-dependent concentrations of these three genes and let

$$\frac{dC}{dt} = \frac{k_1}{k_2 + Z^2} + \frac{k_3}{k_4 + K^2} - d_1 C \quad (1)$$

$$\frac{dZ}{dt} = \frac{a k_5 K^2}{k_6 + K^2} - d_2 Z \quad (2)$$

$$\frac{dK}{dt} = \frac{r k_7}{k_8 + C^2} - d_3 K \quad (3)$$

subject to initial conditions

$$C(0) = C_0, \quad Z(0) = Z_0, \quad K(0) = K_0, \quad (4)$$

where k_1, k_3, k_5, k_7 are rates of reaction, k_2, k_4, k_6, k_8 are Michaelis parameters, d_1, d_2, d_3 are decay rates and a and r are dimensionless constants.

Nondimensionalization

In order to dimensionalize equations (1)–(3) we introduce dimensionless variables and parameters.

Units of dimensional parameters

We first need to determine the dimensions of parameters in equations (1)–(3). C, K and Z are concentrations with units L^{-3} and therefore all the LHS terms e.g., $\frac{dC}{d\tau}$ have units $L^{-3}T^{-1}$. To be consistent,

- d_1, d_2, d_3 have units T^{-1},
- k_2, k_4, k_6, k_8 have units of L^{-6},
- k_1, k_3 have units $L^{-9}T^{-1}$,
- k_7 has units $L^{-9}T^{-1}$ since r is dimensionless,
- k_5 has units $L^{-3}T^{-1}$ since a is dimensionless.

Nondimensional variables

The nondimensional variables are

$$y_1 = \left(\frac{k_2 d_1}{k_1}\right) C, \qquad y_2 = \left(\frac{k_6 d_1}{k_4 k_5}\right) Z, \qquad y_3 = \left(\frac{1}{\sqrt{k_4}}\right) K. \quad (5)$$

We note that

- $\dfrac{k_2 d_1}{k_1}$ has units L^3 therefore y_1 is dimensionless,
- $\dfrac{k_6 d_1}{k_4 k_5}$ has units L^3 therefore y_2 is dimensionless,
- $\dfrac{1}{\sqrt{k_4}}$ has units L^3 therefore y_3 is dimensionless.

The time scale is $\dfrac{1}{d_1}$, hence

$$\tau = d_1 t. \tag{6}$$

Nondimensional groups (parameters)

The nondimensional groups (parameters) are

$$\left.\begin{array}{ll} p_1 = \dfrac{k_4^2 k_5^2}{k_2 k_6^2 d_1^2}, & p_2 = \dfrac{k_2 k_3}{k_1 k_4}, \\ p_3 = \dfrac{k_4}{k_6}, & p_4 = \dfrac{d_2}{d_1}, \\ p_5 = \dfrac{k_2^2 k_7 d_1}{k_1^2 \sqrt{k_4}}, & p_6 = \dfrac{k_2^2 k_8 d_1^2}{k_1^2}, \\ p_7 = \dfrac{d_3}{d_1}. & \end{array}\right\} \tag{7}$$

Parameters p_3, p_4 and p_7 are trivially dimensionless since they are ratios of dimensional parameter with equal units. The remaining parameters are not so obviously dimensionless. However,

- p_1 has units $\dfrac{L^{-12} \cdot L^{-6} T^{-2}}{L^{-6} \cdot L^{-12} \cdot T^{-2}} = 1$,
- p_2 has units $\dfrac{L^{-6} \cdot L^{-9} T^{-1}}{L^{-9} T^{-1} \cdot L^{-6}} = 1$,
- p_5 has units $\dfrac{L^{-12} \cdot L^{-9} T^{-1} \cdot T^{-1}}{L^{-18} T^{-2} \cdot L^{-3}} = 1$,
- p_6 has units $\dfrac{L^{-12} \cdot L^{-6} \cdot T^{-2}}{L^{-18} \cdot T^{-2}} = 1$.

The nondimensional equations

The terms by which to multiply the LHS and RHS of equations 1, 2 and 3 are most easily determined by considering the decay term (LHS).

Equation (1) Multiply by $\dfrac{k_2}{k_1}$.

$$\begin{aligned} \text{LHS} &= \frac{1}{d_1}\frac{k_2 d_1}{k_1}\frac{dC}{dt} = \frac{1}{d_1}\frac{dy_1}{dt} = \frac{dy_1}{d\tau} \\ \text{RHS(1)} &= \frac{1}{1 + Z^2/k_2} = \frac{1}{1 + (k_4 k_5 y_2/k_6 d_1)^2/k_2} = \frac{1}{1 + p_1 y_2^2} \\ \text{RHS(2)} &= \frac{k_2 k_3}{k_1 k_4}\left(\frac{1}{1 + k_4 y_3^2/k_4}\right) = \frac{p_2}{1 + y_3^2} \\ \text{RHS(3)} &= \frac{k_2 d_1}{k_1} C = y_1 \end{aligned}$$

Equation (2) Multiply by $\dfrac{k_6}{k_4 k_5}$.

$$
\begin{aligned}
\text{LHS} &= \frac{1}{d_1}\frac{k_6 d_1}{k_4 k_5}\frac{dZ}{dt} = \frac{1}{d_1}\frac{dy_2}{dt} = \frac{dy_2}{d\tau} \\
\text{RHS(1)} &= \frac{k_6}{k_4}\left(\frac{K^2}{k_6(1+K^2/k_6)}\right) = \frac{K^2/k_4}{(1+(k_4/k_6)(K^2/k_4))} = \frac{y_3^2}{1+p_3 y_3^2} \\
\text{RHS(2)} &= \frac{d_2}{d_1}\left(\frac{k_6 d_1}{k_4 k_5}\right) Z = p_4 y_2
\end{aligned}
$$

Equation (3) Multiply multiply by $\dfrac{1}{d_1\sqrt{k_4}}$.

$$
\begin{aligned}
\text{LHS} &= \frac{1}{d_1\sqrt{k_4}}\frac{dK}{dt} = \frac{1}{d_1}\frac{dy_3}{dt} = \frac{dy_3}{d\tau} \\
\text{RHS(1)} &= \left(\frac{k_2^2 k_7 d_1}{d_1^2\sqrt{k_4}}\right)\left(\frac{k_1^2}{k_2^2 d_1^2}\frac{1}{k_8+C^2}\right) = p_5\left(\frac{1}{k_2^2 d_1^2/k_1^2(k_8+C^2)}\right) = \frac{p_5}{p_6+y_1^2} \\
\text{RHS(2)} &= \left(\frac{d_3}{d_1\sqrt{k_4}}\right) K = \frac{d_3}{d_1} y_3 = p_7 y_2
\end{aligned}
$$

The resulting non-dimensional system of equations is

$$
\frac{dy_1}{d\tau} = \frac{1}{1+p_1 y_2^2} + \frac{p_2}{1+y_3^2} - y_1 \tag{8}
$$

$$
\frac{dy_2}{d\tau} = \frac{a y_3^2}{1+p_3 y_3^2} - p_4 y_2 \tag{9}
$$

$$
\frac{dy_3}{d\tau} = \frac{r p_5}{p_6 + y_1^2} - p_7 y_3 \tag{10}
$$

subject to initial conditions

$$
y_1(0) = y_{1,0}, \quad y_2(0) = y_{2,0}, \quad y_3(0) = y_{3,0}. \tag{11}
$$

References

[1] Xiao Tu, Qinran Zhang, Wei Zhang, and Xiufen Zou. Single-cell data-driven mathematical model reveals possible molecular mechanisms of embryonic stem-cell differentiation. *Mathematical biosciences and engineering: MBE*, 16(5):5877–5896, 2019.

[2] Li-Fang Chu, Ning Leng, Jue Zhang, Zhonggang Hou, Daniel Mamott, David T Vereide, Jeea Choi, Christina Kendziorski, Ron Stewart, and James A Thomson. Single-cell rna-seq reveals novel regulators of human embryonic stem cell differentiation to definitive endoderm. *Genome biology*, 17(1):173, 2016.