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1 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-sequence data of embryonic stem cell development reported by [2].

2 Mathematical model

Let $C = [\text{CDH1}]$, $Z = [\text{ZEB1}]$ and $K = [\text{KLF8}]$ represent the time-dependent concentrations of three genes that have been recognized as key actors in embryonic stem cell development. Let

$$\frac{dC}{d\tau} = \frac{k_1}{k_2 + Z^2} + \frac{k_3}{k_4 + K^2} - d_1 C \tag{1}$$

$$\frac{dZ}{d\tau} = \frac{a k_5 K^2}{k_6 + K^2} - d_2 Z \tag{2}$$

$$\frac{dK}{d\tau} = \frac{r k_7}{k_8 + C^2} - d_3 K \tag{3}$$

subject to initial conditions

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

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.

In order to dimensionalize this system of equations we introduce dimensionless variables and parameters.

3 Nondimensionalization

3.1 Units of dimensional parameters

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, therefore

- 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

3.2 Nondimensional variables

The nondimensional variables are

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

We note that

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

3.3 Nondimensional groups (parameters)

The nondimensional groups (parameters) are ...

$$\left.\begin{array}{ll} p_1 = \dfrac{k_4^2 k_5^2}{k_2 k_6^2 d_1^2}, & p_2 = \dfrac{k_2 k_3}{k_1 k_4}, \\ p_3 = \dfrac{k_4}{k_6}, & p_4 = \dfrac{d_2}{d_1}, \\ p_5 = \dfrac{k_2^2 k_7 d_1}{k_1^2 \sqrt{k_4}}, & p_6 = \dfrac{k_2^2 k_8 d_1^2}{k_1^2}, \\ p_7 = \dfrac{d_3}{d_1}. & \end{array}\right\} \tag{6}$$

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

3.4 Nondimensionalizing governing 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. The time scale is $\frac{1}{d_1}$.

3.4.1 **Equation** (1)

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

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

3.4.2 **Equation** (2)

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

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

3.4.3 **Equation** (3)

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

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

4 Nondimensional model

The resulting non-dimensional system of equations is

$$
\begin{aligned}
\frac{dy_1}{dt} &= \frac{1}{1+p_1 y^2} + \frac{p_2}{1+y_3^2} - y_1 && (7) \\
\frac{dy_2}{dt} &= \frac{a y_3^2}{1+p_3 y^2} - p_4 y_2 && (8) \\
\frac{dy_3}{dt} &= \frac{r p_5}{p_6+y_1^2} - p_7 y_3 && (9)
\end{aligned}
$$

subject to initial conditions

$$
y_1(0) = y_{1,0}, \quad y_2(0) = y_{2,0}, \quad y_3(0) = y_{3,0}. \tag{10}
$$

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.