

Progress report

Mingdong He

15 Feb 2022

Contents

1	What I have done	1
1.1	Literature Survey	2
1.2	Mathematical Analysis	2
1.3	Computational Simulations	3
2	Current Problems	3
3	What I plan to do	3

1 What I have done

Repressilator is an artificial gene network structure. The aim of my project is to study the conditions that makes the repressilators oscillate. Through the first weekly meeting with my supervisor, I got to know the biological background of the gene network and I also got some essential papers from him. Mathematically speaking, oscillations mean the biological system is unstable thus finding the mathematical conditions requires us to use theoretical tools and computational simulations are also helpful. Thus, what I have done includes: **literature study** about repressilator, **mathematical analysis** for current proposed models, and **computational simulations** for oscillations.

1.1 Literature Surrey

[J. Tyson, 1975][1]: This paper summerised the problems met in the studies of the proper Hill coefficient in computational simulations and it also prove the existence of a periodic solution for equations (J. S, Griffith, 1968)[2].

[L. Galss, J.S. Pasternack, 1978][3]: This paper presented the topological properties of Piecewise Linear Equations and the proof of the derivation of Poincare Map.

[M.B.Elowitz, S.L Leibler, 2000][4]: This paper described the artificial process of design and construction of a genetic network and its dynamical behaviors. It is the first synthetic genetic oscillator to be successfully applied to biological experiment. (O. Purcell, *et al.*, 2010).[5]

[R. Edwards, L. Glass, 2014][6]: This paper provides a precise illustration of how protein was produced in cell level. It presented the biological switch model and how piecewise linear equations are being used in modeling.

1.2 Mathematical Analysis

I mainly focused on three genes network structure thus the model I have got is a 6 dimensional nonlinear ODE systems, which means that I cannot solve them analytically. Instead, I conducted qualitative analysis for this model, which includes:

- Rescaling parameters
- Finding the fixed points
- Linear stability analysis
- Bifurcation analysis

After lots of algebraic work, I figured out the characteristic equation for corresponding 6 by 6 Jacobian.

1.3 Computational Simulations

This parameters of this model are:

- 1) α_0 : production rate of protein.
- 2) α : transcription rate.
- 3) β : protein decay rate divided by mRNA decay rate.
- 4) n : hill coefficient.

In order to better understand my exploratory analysis of the occurring of oscillations, I developed an interactive program by Python, where I could adjust the value of parameters by simply moving the buttons. I finally could see the oscillations after the typo of my code was corrected by my supervisor in our second meeting. The simulations results were consistent with the description of the biological experiment, however, I cannot conclude a generalized range of instability thus bifurcation analysis was really needed.

2 Current Problems

- I haven't solve the characteristic equation completely.
- I have no idea how to conduct the bifurcation analysis.
- Computational simulation result has not been matched with my theoretical analysis.

3 What I plan to do

- Read papers more deeply, especially the papers about the piecewise linear equations.
- Study the dynamical system theory (Bifurcation theory) deeply, the model requires advanced knowledge to be studied.
- Learn how to plot bifurcation diagram by Python, this is needed latter.

References

- [1] John J Tyson. On the existence of oscillatory solutions in negative feedback cellular control processes. *Journal of Mathematical Biology*, 1(4):311–315, 1975.
- [2] John S Griffith. Mathematics of cellular control processes i. negative feedback to one gene. *Journal of theoretical biology*, 20(2):202–208, 1968.
- [3] Leon Glass and Joel S Pasternack. Stable oscillations in mathematical models of biological control systems. *Journal of Mathematical Biology*, 6(3):207–223, 1978.
- [4] Michael B Elowitz and Stanislas Leibler. A synthetic oscillatory network of transcriptional regulators. *Nature*, 403(6767):335–338, 2000.
- [5] Oliver Purcell, Nigel J Savery, Claire S Grierson, and Mario Di Bernardo. A comparative analysis of synthetic genetic oscillators. *Journal of The Royal Society Interface*, 7(52):1503–1524, 2010.
- [6] Roderick Edwards and Leon Glass. Dynamics in genetic networks. *The American Mathematical Monthly*, 121(9):793–809, 2014.