February 27, 2020

Tanaka model analysis

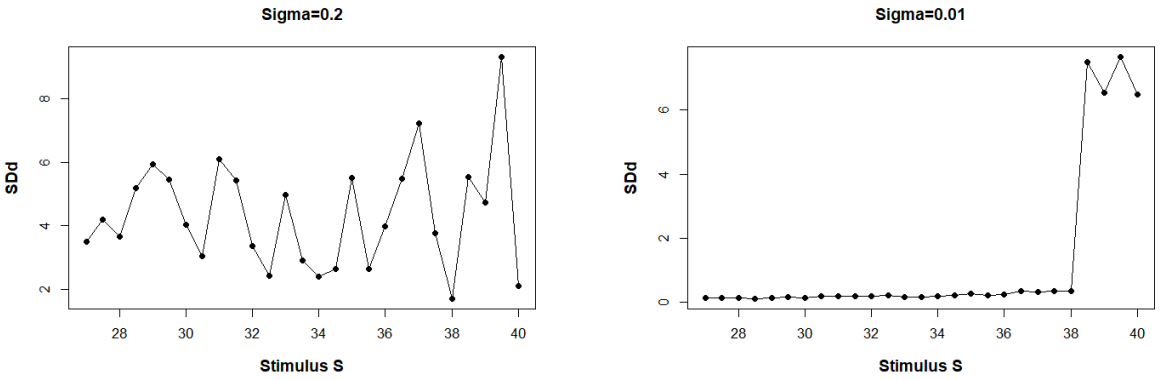
Tanaka, R. J., Ono, M., & Harrington, H. A. (2011). Skin barrier homeostasis in atopic dermatitis: feedback regulation of kallikrein activity. PloS one, 6(5).

As in the Chen model, I made the analysis using Grindr. Firstly, I transformed the deterministic model to a stochastic one by adding additive noise. The functions `run` and the option `after`, allowed me to do this easily.

Observations

Flickering

To analyse this model, I chose the noise magnitude as $\sigma = 0.2$, set the integration time at the Mean First Passage Time $t = 192$, and the initial conditions at the corresponding steady-state. This election of σ caused flickering on the standard deviation behaviour (see Figure 1) which could be attributed to a jump between vaccines of attraction.



(a) (b)

Figure 1: **Standard deviation with different noise magnitudes.** Figures show the curves of SDs for the variables against the stimulus S. (a) Setting the noise magnitude as $\sigma = 0.2$ the systems shows flickering in a width region of parameters. (b) When the noise magnitude is smaller, the flickering region became narrower.

How to solve the flickering problem

There are two options to solve this problem: (1) cut the trajectories to be sure that they are not converging to the other steady-state (2) reduce the noise intensity.

1. Calculating the passage time

   The main idea, in this case, is to obtain a time t^* where the system is near the second steady-state, collect this times for one simulation for each parameter

value, and store the t^*'s to calculate the standard deviations over the truncated trajectories. To do this, we need to do the following:

(a) Create a 1xn vector (lets called it PT_{vec}), where n = length of P.

(b) Create six (one for each variable) nxm matrices, where n = length of P, $m = \Delta t * t_{int}$ and t_{int} is the integration time (it must be a long time).

(c) Simulate one trajectory T_i for each value of the stimulus and store the corresponding output in the six matrices. For each T_i:

i. Collect the time t^* in which the output is at ϵ distance from the second steady state.

ii. Locate t^* in the matrices (it must be at one column).

iii. Store the value of t^* in PT_{vec}

(d) One we have filled PT_{vec}, we use this information to truncate all the T_1's to guarantee that T_i is not converging to the second steady state.

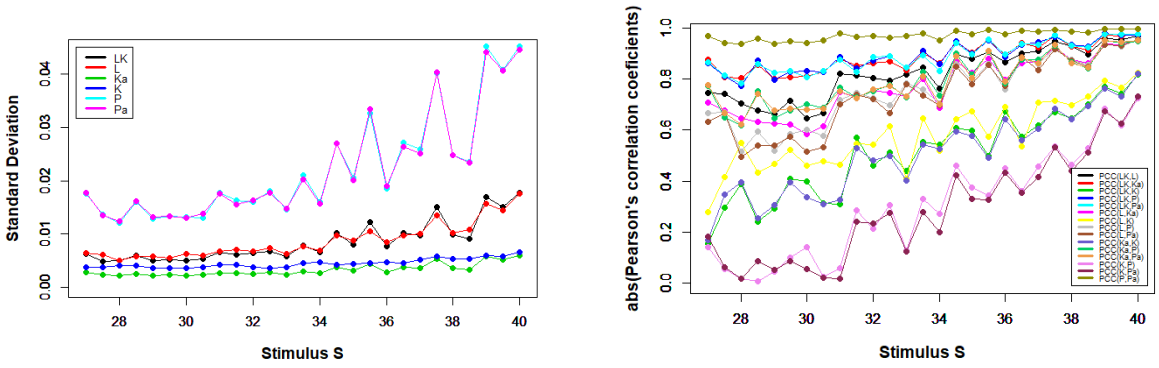
(e) Finally, calculate the standard deviation over the truncated trajectories.

2. Reduce the noise intensity

This option is easier. Here we just had to decrease the noise intensity to narrow the region in which the flickering appeared.

Complete analysis

General observations



(a) (b)

Figure 2: **Standard deviation and Pearson's Correlation Coefficient.** (a) Shows the curves of SDs for the variables against the stimulus S, which indicate that the tendency of P and P^*. (b) Shows the PCC between every two pair of variables.

To find the dominant group, I calculated the standard deviation of each variable simulating one trajectory for each parameter value. I saw that the SD of P and P^* are the ones who increase the more near the bifurcation (see Figure 2(a)). For

this reason, I made the hypothesis that these two variables comprise the Dynamical Network Biomarker. Next, I computed the PCC for ever pair of variables. In this analysis, I found that the PCC(P, P^*) is very strong (see Figure 2(b)).

[**DOP:** Aquí me sigue haciendo mucho ruido que el sistema no se comporte como dice en el artículo, es decir, que para las variables dentro de la DNB el promedio de los PCC debe crecer en valor absoluto y los otros decrecer, pero yo no veo que vaya a pasar eso.]

P^* & P analysis

Supposing that P and P^* are the variables in the DNB, I continued with the computation of the composite index. One important observation is that the average Pearson's Correlation Coefficient of molecules between this group and any others, does no decreases in absolute value. For this reason, I calculated the normalized composite index, *i.e*, $I = SD_d * PCC_d$, where SD_d is the average SD of the dominant group and PCC_d is the average PCC of the dominant group in absolute value. In Figure 3, we can see that the composite index drastically increases near the bifurcation.

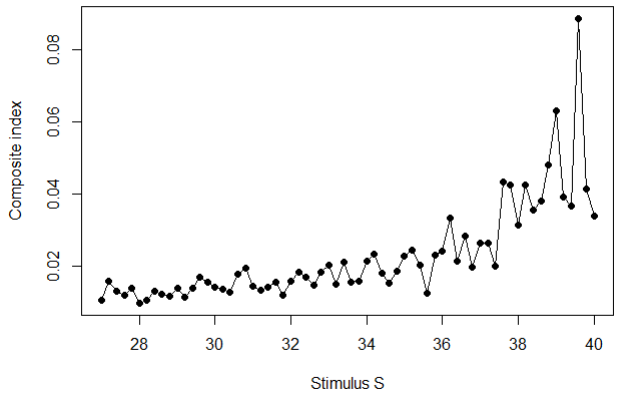


Figure 3: **Composite index for P and P^*.**

P^* & K^* analysis

In the previous section, I supposed that the DNB was comprised of P and P^*. In this section, I will assume that P^* and K^* are the two variables in the dominant group. This is because these variables are the ones that can be measured in the laboratory or by a doctor. In Figure 4 we can see that the composite index also increases near the bifurcation.

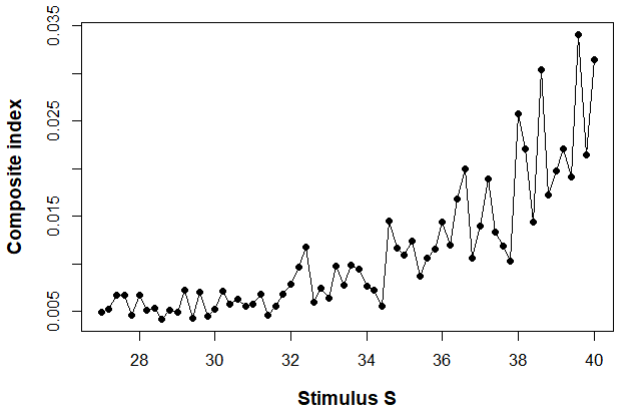


Figure 4: **Composite index for K^* and P^*.**