A possible network for T cell activation

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T cells are activated by antigen concentrations and undergo a stage of proliferation until a moment where their concentration peaks and then immediately decays (in a linear fashion). This resembles an excitable system. Anton and co. have been thinking of different models that express this behaviour and would like to test this model under different conditions to find if it exhibits similar dynamics as what is observed expereimentally. Let's try things...

Right now there is a model of coupled differential equations that explain the basic interactions. I should look at the how the starting concentration of antigen changes the dynamics of the T cell proliferation. What is the limit of the antigen on the explosion of T cell? In the same line of thought, how does the initial population of potentially activated T cells affect the number of proliferated T cells? Since activated T cells are a function of antigen and affinity, what are different limits?

There should be some 'gobbling' up of the cytokine by the proliferating T cells. This is not in the model.

Further down the line... **We should look into the internal accumulation of Myk by T cells. When T cells divide there is a decrease in concentration fo Myk (which helps them divide). At some point the concentration is too low so there are no more divisions.**

Need to read some papers by Gregoire... Additionally are there other mechanisms that stop antigen presentation?

I. T CELL ACTIVATION: THE BIOLOGY

At the moment antigen appears in the system, they get detected by T cells who become activated. These T cells start producing cytokine IL-2 which itself starts recruiting other agents of the immune system. This IL-2 is picked up by T cells who start to actively proliferate. It's also picked up by T reg T cells (who deplete the quantity of cytokine). The proliferating T cells decrease the concentration of antigen until there is no more.

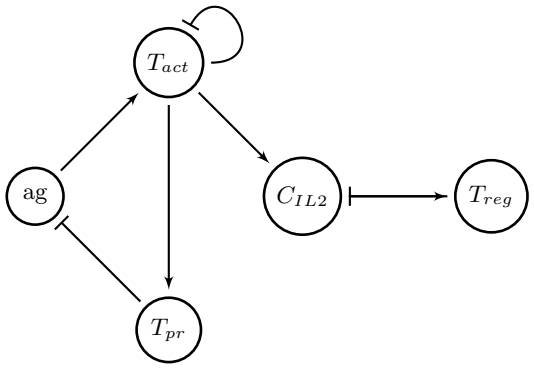
Experimentally, observations show that after 24 hours of certain antigen levels being present, there is a linear increase of proliferating T cells until a couple days in. After this time, the concentration of proliferating T cells starts to suddenly decrease linearly until there are no more. It is unclear how this all works out.

II. THE MODEL

We will describe the using a network and define their differential equations. Some activation functions might not be quite right yet, however this hopefully captures the basic dynamics of this system.

A. Network 1

We will focus first on a simple network which looks something like this [STILL NEEDS TO BE FINISHED]

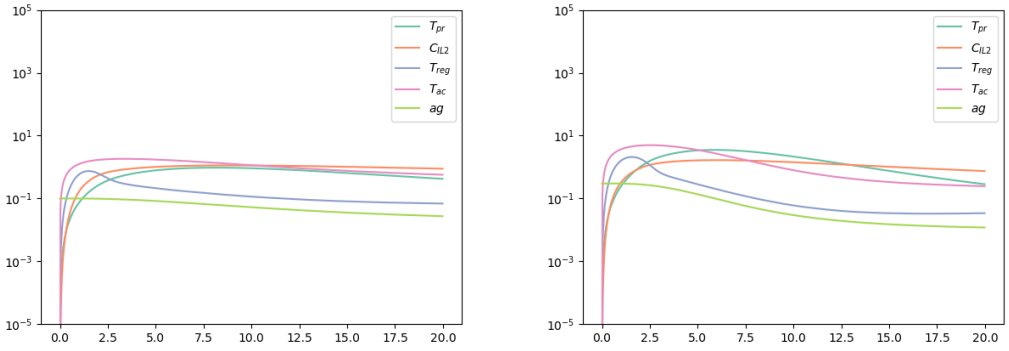


1. The differential equations

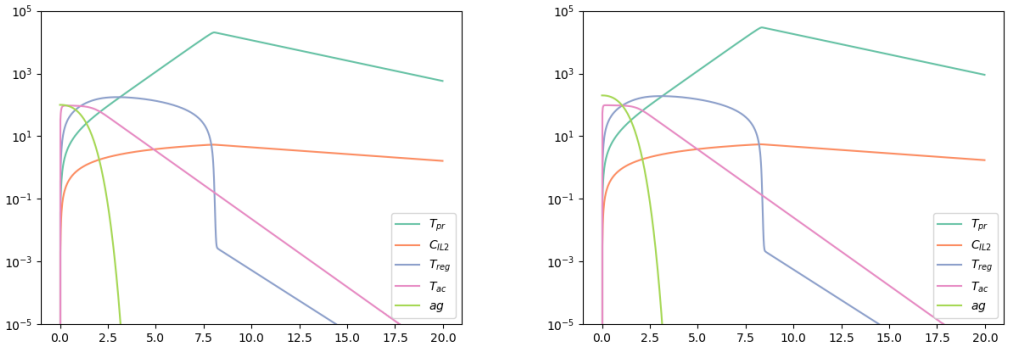
$$\begin{aligned}
\frac{dag}{dt} &= -0.1ag(t)T_{pr}(t) \\
\frac{dTac}{dt} &= 0.2ag(t)(100 - T_{ac}(t)) - T_{ac}(t) \\
\frac{dC_{IL2}}{dt} &= T_{ac} - 10\frac{C_{IL2}(t)T_{reg}(t)}{1 + C_{IL2}(t)} \\
\frac{dT_{reg}}{dt} &= \frac{C_{IL2}(t)}{1 + C_{IL2}(t)} - 0.1T_{reg}(t) \\
\frac{dT_{pr}}{dt} &= T_{pr}(1 - \frac{1.3}{1 + C_{IL2}(t)}) + 0.1T_{ac}
\end{aligned} \tag{1}$$

2. Results

First, I investigated what the solution of these equations would look like for different initial concentrations of antigen.



(a) $ag(0) = 0.1$ (b) $ag(0) = 0.3$



(c) $ag(0) = 100$ (d) $ag(0) = 200$

FIG. 1: Plots of solutions to network 1 with $ag(0)$ varied and all other initial concentrations set to 0.

According to these plots, there is always a slight activation of proliferating T cells (in blue). Is this biological? Are proliferating T cells always somewhat activated or is there a threshold below which no activation happens? If there is a strict threshold, there needs to be a harder cut-off in equations 1, such as a hill function $\frac{x^n}{c^n+x^n}$ with n large (≈ 10).

In Figure 2, we clearly see that the maximum concentration of T cell is attainedat later times when the initial concentration of antigen is increased.

However we do not see that the increase in time is significant over a large range of initial concentrations of antigen.

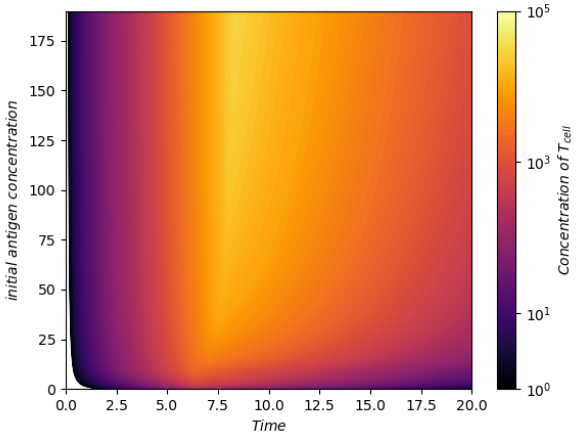


FIG. 2: Change in proliferating T cell concentration