A possible network for T cell activation

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I. RECEPTOR CROSSTALK AND SPECIFICITY: THE BIOLOGY

II. MASTERS EQUATION

We will describe the using a network and define their masters equations. For now there are 2 different modes which are described below.

A. Mode 1

We start with the process that creates a product n with rate k_p when a ligand is bound to the receptor. It binds with rate $k_{on}c$ and unbinds with rate k_off to the receptor.

(Need to make the figure for this)

The master equations are

$$\begin{aligned} \dot{P_0^n} &= k_{on}cP_1^n - k_{off}P_0^n \\ \dot{P_0^n} &= k_{off}P_1^n - k_{on}cP_1^n + k_pP_1^{n-1} - k_pP_1^n \end{aligned}. \tag{1}$$

What we are interested in this equation is the average and variance of the prouct n within the cell as we can find what the best estimate the cell can make of the ligand concentration outside. Anton also argues that a second quantity is important, the cell needs to also estimate k_{off} to know what is the identity of this ligand. There are a couple ways to solve this system: generating functions is one venue but is difficult to solve analytically. Using this method, Anton gets a certain average and standard deviation

Instead, we will try another method using the master equation. Note that we will use the solution for the probability of being bound as a function of time (derived by Anton and confirmed by us, type it out)

$$\begin{aligned} P_1(t) &= P_1^{ss}(1 - \frac{k_{on}c}{r}e^{-rt}) + P_1(0)e^{-rt} \\ &= \frac{x}{1+x} + \Delta e^{-rt} \end{aligned} \tag{2}$$

where

$$\begin{aligned} P^{ss} &= \frac{x}{1+x} \\ r &= k_{on}c + k_{off} \\ \Delta &= P_1(0) - P_1^{ss}. \end{aligned}$$

We write down the time derivative of average n and replace terms by the master equations to solve the equation

$$\begin{aligned} \dot{\langle n \rangle} &= \sum_{n=0} n(\dot{P_0^n} + \dot{P_1^n}) \\ &= k_p \sum_{n=0} n(P_1^{n-1} - \dot{P_1^n}) \\ &= k_p \sum_{n=0} (P_1^n \\ &= k_pP_1(t). \end{aligned}$$

Replacing our expression in equation 2 in this formula, we integrate to get the solution

$$\langle n \rangle = k_p\frac{x}{1+x}t + n_0 + \frac{k_p\Delta}{r}(1 - e^{-rt}). \tag{3}$$

Assuming that the initial product number $n_0 = 0$ and that the initial probability of being bound is the same as steady state $\Delta = P_1(0) - P_1^{ss} = 0$ we find

$$\langle n \rangle = k_p\frac{x}{1+x}t.$$

For the variance, as similar approach can be taken

$$\begin{aligned} \dot{\langle n^2 \rangle} &= \sum_{n=0} n^2(\dot{P_0^n} + \dot{P_1^n}) \\ &= k_p \sum_{n=0} n^2(P_1^{n-1} - P_1^n) \\ &= k_p \sum_{n=0} (n+1)^2(P_1^n - n^2P_1^n) \\ &= k_p \sum_{n=0} (2n+1)P_1^n \\ &= k_p(2\sum_{n=0} nP_1^n + \sum_{n=0} P_1^n) \\ &= k_p(2\langle n \rangle) + P_1(t)) \end{aligned}$$

By using the expression for $\langle n \rangle$ in equation 3 we can integrate this obtain $\langle n^2 \rangle$

$$\langle n^2 \rangle = k_p\frac{x}{1+x}t^2 + n_0t + \frac{k_p\Delta}{r^2}(rt + e^{-rt}) + \langle n \rangle. \tag{4}$$

It is straightforward at this point to combine equations 3 and 4 to obtain the variance

$$\begin{aligned} Var(n) &= \langle n^2 \rangle - \langle n \rangle^2 \\ &= k_p\frac{x}{1+x}t^2 + n_0t + \frac{k_p\Delta}{r^2}(rt + e^{-rt}) + \langle n \rangle - \langle n \rangle^2 \end{aligned} \tag{5}$$