

# 1 Assumptions and Questions

1. A: All cells initially express RFP
2. A: Oxygen below 10 mmHg turns off expression of RFP, turns on expression of GFP
3. Q: What's a time scale for protein synthesis? (Early on, it's time to transcribe RNA, then synthesize protein. Later, it's time to just synthesize protein from already existent RNA.)
4. Q: What's the time scale for protein degradation?
5. Q: In 10 mmHg, does RFP gene get snipped out immediately and GFP gene enabled, or is there a mean time delay?

## 2 Model

### 2.1 Gene - Protein network

We will model a set of genes  $\mathbf{G}$  that encode proteins  $\mathbf{P}$  with the following model:

$$\frac{dP_i}{dt} = \alpha_i G_i - \beta_i P_i, \quad i = 1, 2, \dots \quad (1)$$

where  $\alpha_i$  is a protein creation rate, and  $\beta_i$  is a protein degradation rate. (Notice that this skips modeling RNA transcription.) Here, we will model the following genes:

index	protein	notes
0	RFP	default fluorescence
1	GFP	activated at $pO_2 = 10$ mmHg

Gene expression can be modeled in any way. Here, we set  $G_1 = 1$  if  $pO_2 < 10$  mmHg.

#### 2.1.1 Nondimensionalization

Let  $\bar{P}$  be the maximum protein level with  $G = 1$ . Then by equilibrium analysis,  $\bar{P} = \frac{\alpha}{\beta}$ . If we nondimensionalize the main ODE form, we get

$$\frac{dP_i}{dt} = \beta_i (G_i - P_i). \quad (2)$$

This functional form sucks, because it doesn't let us set the rate of reaching near  $P_i \sim 1$  independently of the decay rate. Blech!

#### 2.1.2 Better model and nondimensionalization

Now, suppose that  $P^*$  is a protein value where negative feedback reduces either transcription or synthesis. Then

$$\frac{dP_i}{dt} = \alpha_i G_i (P_i^* - P_i) - \beta_i P_i. \quad (3)$$

By equilibrium analysis, the maximum protein value is

$$\bar{P}_i = \frac{\alpha_i P_i^*}{\alpha_i + \beta_i} \quad (4)$$

If we nondimensionalize by this, we get:

$$\begin{aligned}\frac{dP_i}{dt} &= G_i(\alpha_i + \beta_i) - (\alpha_i G_i + \beta_i) P_i \\ &= G_i \alpha_i (1 - P_i) + \beta_i (G_i - P_i).\end{aligned}\tag{5}$$

Notice that in this form,  $\alpha_i$  sets the rate of approaching the maximum protein expression (1) when the gene is expressed, and  $\beta_i$  sets the rate of decay.

### 2.1.3 Parameter estimates

Let's suppose for now that it takes about 10 minutes to ramp up a protein level to 90% of its maximum value. Then in the absence of degradation, we have

$$\frac{dP_i}{dt} \approx G_i \alpha_i (1 - P_i).\tag{6}$$

So, if we want to reach  $P_i = 0.9$  after  $T_{S,i} = 10$  min time, then

$$\alpha_i = -\frac{\ln 10}{T_{S,i}} \approx 0.23 \text{ min}^{-1}.\tag{7}$$

Similarly, if  $G_i = 0$ , we can easily fit  $\beta_i$  by a decay time scale  $T_{D,i}$ , defined for us to be the time to degrade 90% of the protein. Let's suppose for now  $T_{D,i} = 120$  min. Then

$$\frac{dP_i}{dt} \approx -\beta_i P_i\tag{8}$$

and so

$$\beta_i = -\frac{\ln 10}{T_{D,i}} \approx 0.019? \text{ min}^{-1}.\tag{9}$$

### 2.1.4 Simple implicit numerical scheme

Suppose that  $P_i^n = P_i(t_n) = P_i(t_0 + n\Delta t)$ . Then

$$P_i^{n+1} = \frac{P_i^n + \Delta t G_i^n (\alpha_i + \beta_i)}{1 + \Delta t (\alpha_i G_i^n + \beta_i)}\tag{10}$$