# 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:

$$\frac{dP_i}{dt} = \alpha_i G_i - \beta_i P_i, \qquad i = 1, 2, \ldots \tag{1}$$

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 $\mathrm{pO}_2 = 10\,\mathrm{mmHg}$ |

Gene expression can be modeled in any way. Here, we set $G_1 = 1$ if $\mathrm{pO}_2 < 10\,\mathrm{mmHg}$.

### 2.1.1 Nondimensionalization

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

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

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

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

By equilibrium analysis, the maximum protein value is

$$\overline{P}_i = \frac{\alpha_i P_i^*}{\alpha_i + \beta_i} \tag{4}$$

If we nondimensionalize by this, we get:

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

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

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

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

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