1. Introduction

2. Method

The following model is a genetic circuit that functions as a bistable switch [3]. It is a system with two stable equilibrium point where each equilibrium point can represents a binary state: "on" or "off", "0" or "1" or "high" or "low". To facilitate this, the system allows for the supression of one protein by an inducer, enabling the an external input to force the system to switch states. The concentration of the two proteins are $p_A \geq 0$, $p_B \geq 0$, given some input I, the production rate parameter $\alpha > 0$ is how fast the proteins increases, and a cooperativity parameter $n > 1$ which represents how many proteins need to work together (i.e. cooperate) to turn off gene expresion.

$$\dot{p}_A = \frac{\alpha}{1 + (Ip_B)^n} - p_A$$
$$\dot{p}_B = \frac{\alpha}{1 + p_A^n} - p_B$$

Our goal is to solve the stabilization problem of getting the concentration of the different protiens, A and B to approach desired levels that might not necessarily be naturally possible. We will consider a MIMO sliding control for a modified version of the system above with noise, n_A, n_B, and added input, u_A, u_B.

$$\dot{p}_A = \frac{\alpha}{1 + p_B^n} - p_A + n_A + u_A$$
$$\dot{p}_B = \frac{\alpha}{1 + p_A^n} - p_B + n_B + u_B$$

The construction of the sliding controller comes from [1]. We will assume f is known and that the $|n_i| \leq n_{max}$

First we choose $s = [s_A \ s_B]^T = \vec{e}$, where $\vec{e} = \begin{bmatrix} p_A - p_A^d \\ p_B - p_B^d \end{bmatrix}$. Next we construct the following Lyapunov function $V = \frac{1}{2} s^T s$. Also let $\dot{p}_A = f_1(p_A, p_B) + n_A + u_A$, $\dot{p}_B = f_2(p_A, p_B) + n_B + u_B$, $f = \begin{bmatrix} f_1 \\ f_2 \end{bmatrix}$, $n = \begin{bmatrix} n_A \\ n_B \end{bmatrix}$. and $u = \begin{bmatrix} u_A \\ u_B \end{bmatrix}$. By differentiating V we get

$$\dot{V} = s^T \dot{s}$$

$$\dot{V} = s^T (f + n + u)$$

then choose $u = -f - \begin{bmatrix} n_{max}/s_A \\ n_{max}/s_B \end{bmatrix} - \begin{bmatrix} k_A \text{sat}_\phi(s_A) \\ k_B \text{sat}_\phi(s_B) \end{bmatrix}$

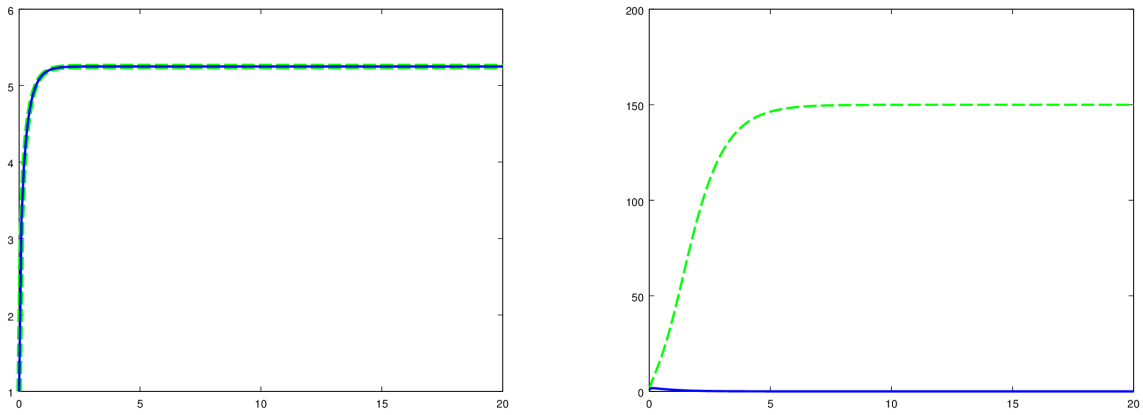
$$\dot{V} = s^T \left(- \begin{bmatrix} n_{max}/s_A \\ n_{max}/s_B \end{bmatrix} - \begin{bmatrix} k_A \text{sat}_\phi(s_A) \\ k_B \text{sat}_\phi(s_B) \end{bmatrix} \right)$$

$$\dot{V} = -2n_{max} - k_A \text{sat}_\phi(s_A) s_A - k_B \text{sat}_\phi(s_B) s_B \leq 0$$

Since V is positive definite and $\dot{V}$ is negative definite this is sufficient to say this system with this control law converges asymptotically. Last we sasitfy the condition $\frac{1}{2} \frac{d}{dt}[s] = (\dot{\phi} - \eta)|s|$ gives us $k = \eta - \dot{\phi}$.

3. Results

Given these $\alpha = 150$ and $n = 2$ parameters we expect to see both protein concentration reaching the same equilibruim point or one going to zero and the other to α as in Figure 1.



(A) p_A and p_B versus time, when $I = 1$

(B) p_A and p_B versus time when $I > 1$

Figure 1. Graphs of the original system without control

4. Discussion

5. Further Work

Since we only considered this control problem from a mathematical perspective we didn't consider implementation issues. How could we relate these theoretical control laws to our systems using the many built-in control systems biology. Another subject of interest would be extending this simple two part system and testing it on a variety of theoretical control laws.

References

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