Exercise 1.

1. A change in production rate. A gene Y with simple regulation is produced at a constant rate $\beta_1$. The production rate suddenly shifts to a different rate $\beta_2$.
   a. Calculate and plot the gene product concentration $Y(t)$.
   b. What is the response time (time to reach halfway between the steady states)?

2. Cascades. Consider a cascade of three activators, $X \rightarrow Y \rightarrow Z$. Protein $X$ is initially present in the cell in its inactive from. The input signal of $X$, $S_X$, appears at time $t = 0$. As a result, $X$ rapidly becomes active and binds the promoter of gene $Y$, so that protein $Y$ starts to be produced at rate $\beta$. When $Y$ levels exceed a threshold $K_Y$, gene $Z$ begins to be transcribed. All proteins have the same degradation/dilution rate $\alpha$. What is the concentration of protein $Z$ as a function of time? What is its response time with respect to the time of addition of $S_X$? What about a cascade of three repressors? Compare your solution to the experiments shown in the figure.

3. Fan-out. Transcription factor $X$ regulates two genes, $Y_1$ and $Y_2$. Draw the resulting network, termed a fan-out with two target genes. The activation thresholds for these genes are $K_1$ and $K_2$. The activator $X$ begins to be produced at time $t = 0$ at rate $\beta$. Its signal is degraded/diluted at rate $\alpha$, and its signal $S_X$ is present throughout. What are the times at which the gene products, the stable proteins $Y_1$ and $Y_2$, reach halfway to their maximal expression? Design a fan-out with three genes in which the genes are activated with equal temporal spacing, that is where they activated at times $t_1$, $t_2$, and $t_3$ such that $t_3 - t_2 = t_2 - t_1$.

4. Positive feedback. What is the effect of positive autoregulation on the response time? Use as a model the following linear equation:
   \[ \frac{dX}{dt} = \beta + \beta_1 X - \alpha X \]

   Explain each term and solve for the response time. When might such a design be biologically useful? What happens when $\beta_1 > \alpha$?