BE 150 Spring 2018
Homework #2
Due at the start of lecture, April 18, 2018.

Problem 2.1 (Design principles for toggles, 30 pts)**.**
Consider two components, A and B, which regulate each other. A may activate or repress B, and B may activate or repress A. There are three architectures, two with positive feedback and one with negative feedback, shown in Fig. 1.

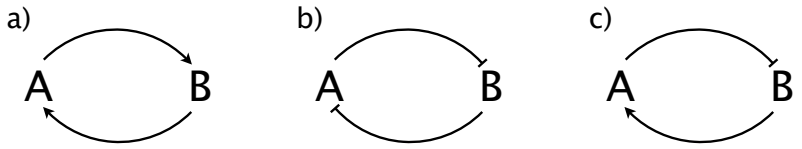

Figure 1: Three toggle-like architectures.

a) A circuit can behave like a toggle if it has two stable steady states, one with A high and B low and another with B high and A low. Only one of the architectures in Figure 1 can function as a toggle. Which one? Explain in words and sketches why *only* the one you chose can be a toggle.

b) A and/or B may show ultrasensitivity regulation, which we describe with a Hill coefficient, n, greater than one. Show that without ultrasensitive regulation, even the architecture you chose cannot have toggle behavior.

Problem 2.2 (Comparison of incoherent feedforward loops, 30 pts)**.**
In Fig. 2, we show two types of incoherent feedforward loops, type 1 (I1-FFL) and type 4 (I4-FFL). Interestingly, the I1-FFL is found much more often in naturally occurring gene regulation networks than the I4-FFL. Some speculate that this is because expression level of Z is sensitive both to changes in X and Y in the I1-FFL, while the level of Z is sensitive only to changes in X in the I4-FFL (thus making Y dispensable). In this problem, you will investigate this claim.

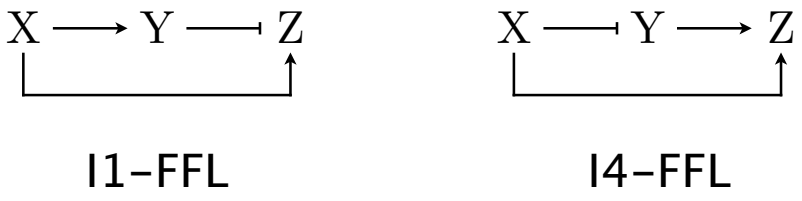

Figure 2: Two of the four types of incoherent feedforward loops.

a) Assume the I1-FFL circuit is at some nonzero steady state. Suddenly, the amount of X goes to zero. Sketch the response of Z, assuming AND logic for

the regulation of Z expression. Do this again again assuming OR logic. Comment on any features of the plot you think are noteworthy. *Hint*: AND logic in the case where X is an activator and Y is a repressor means "X AND (NOT Y)" and OR logic means "X OR (NOT Y)."

b) Repeat (a) except for the I4-FFL circuit.

c) Repeat (a) and (b) except with the amount of Y suddenly going to zero.

d) Are the discrepancies between the I1-FFL and the I4-FFL more pronounced when they have AND logic or OR logic? Explain.

Problem 2.3 (Autoregulation in a C1-FFL, 40 points)**.**
This problem is based off of problem 4.3 from Alon's book. The type 1 coherent feed-forward loop (C1-FFL) is another motif that is found in large numbers in naturally occurring networks. In Fig. 3, we show two C1-FFL networks in which the regulator Y is autoregulated. In the C1-FFL with AND logic, Y shows autorepression, and in the C1-FFL with OR logic, it shows autoactivation. These "decorations" on C1-FFLs often occur in nature.

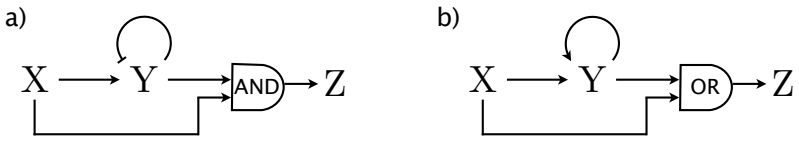

Figure 3: Decorated C1-FFLs. (a) Y is autorepressed and Z is dictated by AND logic. (b) Y is autoactivated and Z is dictated by OR logic.

a) As we learned in lecture, the C1-FFL with AND logic shows sign-sensitive delay. Specifically, if X is suddenly turned on, the response of Z is delayed, but if X is suddenly turned off, the response of Z is instantaneous. Analyze the circuit in Fig. 3a, and compare its dynamics to the canonical C1-FFL circuit with AND logic. Specifically address how the delay time changes. Assume that the regulation of Y follows AND logic.

b) The C1-FFL with OR logic also shows sign-sensitive delay. With OR logic, though, there is no delay when X is suddenly turned on, but rather delay when X is suddenly turned off. Analyze the circuit in Fig. 3b, and compare its dynamics to the canonical C1-FFL circuit with OR logic. Again, address how the delay time changes, this time assuming that the regulation of Y follows OR logic.