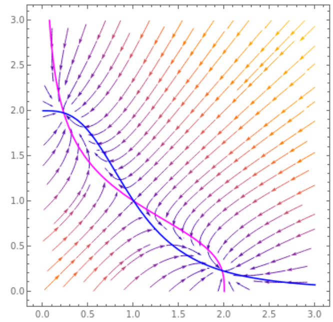
Assignment 4

Question 1: Toggle Switch

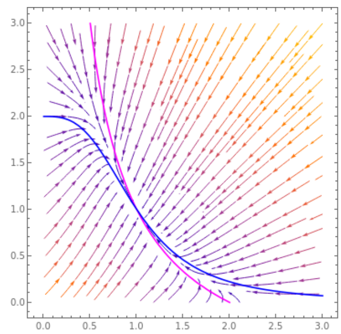
a) The system has three fixed points.



Phase portrait for a toggle switch circuit

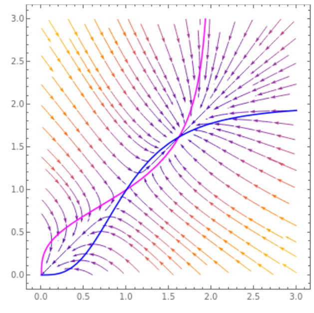
b) Two fixed points are stable ({X low, Y high} , {X high, Y low}).

c) No, we do not get a toggle switch if the hill coefficient for one repressive function equals 1. Both the nullclines should be sigmoidal in shape and must intersect in at least three points. In the case of hill coefficient = 1, the non-sigmoidal shape of nullcline prevents it from intersecting more than once, hence a monostable solution. This can be seen in the figure below.



Phase portrait for toggle switch circuit with non-sigmoidal repressor function

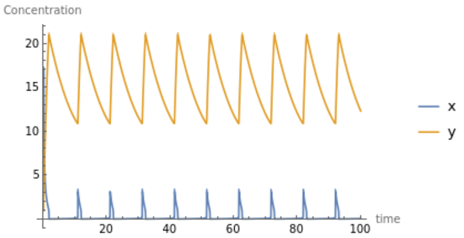
d) No, we do not get a toggle switch. The double-positive feedback loop has two stable, steady-state. In one stable steady-state, X and Y are both high, while X and Y are low in other stable steady-state.
The steady-state depends on the history of activation. If a signal in the past has produced protein X and Y, then the system can lock into the ON state (X high and Y high) else it will stay in the OFF state (X low, Y low).
The double-negative feedback loop can also produce two stable steady-states. However, the steady-states are different compared to the double-positive feedback loop. The stable, steady states in the double-negative feedback loop are X high, Y low and X low, Y high.



Phase portrait for the double-positive feedback circuit

Question 2: Oscillations

a) The circuit is oscillating, and oscillations can be seen in the plot below.



The concentration of protein x and y as a function of time

The oscillating period can be divided into two time domains.

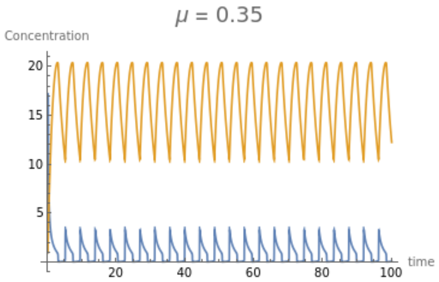
Time domain-1: x is high and y increases.

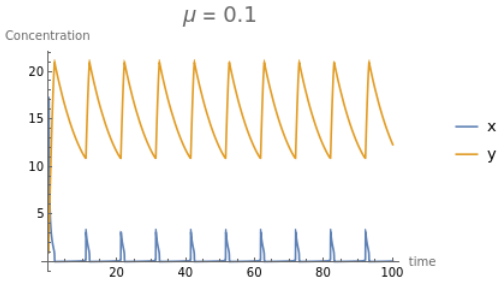
Time domain-2: x is low and y decreases.

b)

(i) Defining ratio, $r = \frac{duration\ of\ time\ domain-1}{duration\ of\ time\ domain-2}$

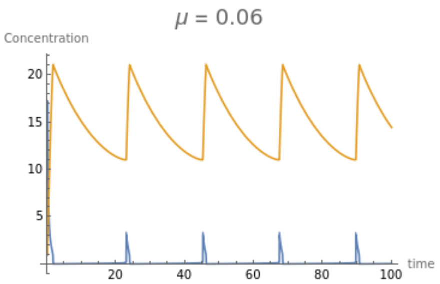
Case – 1: On increasing μ

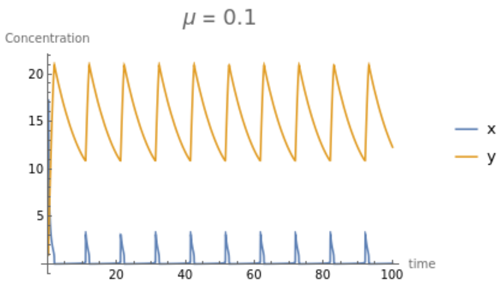




From the above plot, we can see, on increasing μ, the duration of time domain-1 increases and the duration of time domain-2 decreases. This means that the ratio r increases on increasing μ.

Case – 2: On decreasing μ.





From the above plot, we can see, on decreasing μ, the duration of time domain-1 decreases and the duration of time domain-2 increases. This means that the ratio r decreases on increasing μ.

(ii) The duration time domain-2 is inversely proportional to μ because response time for degradation of $y = \ln 2/\mu$. Hence when μ is high, protein y will be degraded quickly, thus, decreasing the duration of time domain-2.

(iii) The time period of oscillation of both protein x and y decreases with an increase in μ. The duration of time domain-2 is much larger than the duration of time domain-1. Moreover, the duration of time domain-2 is inversely proportional to μ. Hence time period of oscillation decreases with an increase in μ.

c) On increasing μ to 0.4, we can get our first bifurcation point. At this point, the concentration of protein y is high, and x is medium to low. This happens because y-nullcline ($y' = 0$) intersects the x-nullcline at local maxima.

On decreasing μ to 0.05, we can get our second bifurcation point. At this point, the concentration of protein y is relatively low, and x is low. This happens because y-nullcline ($y' = 0$) intersects the x-nullcline at local minima.