AMATH 423 HW #5 | Julien Goldstick | March 3, 2025

1. Consider a system of nonlinear biochemical reactions, known as reversible Schnakenberg model, which consists of four species and three reactions:

$$A \underset{k_{-1}}{\overset{k_{+1}}{\rightleftharpoons}} C, B \underset{k_{-2}}{\overset{k_{+2}}{\rightleftharpoons}} D, 2C + D \underset{k_{-3}}{\overset{k_{+3}}{\rightleftharpoons}} 3C \tag{1}$$

Denote the concentrations of $A, B, C,$ and D at time t as $c_A(t)$,$c_B(t)$, $c_C(t)$, and $c_D(t)$.

(a) Write down the system of nonlinear differential equations for the chemical kinetics according to the *law of mass action*.

$$\frac{dc_A}{dt} = -k_{+1}c_A + k_{-1}c_C$$
$$\frac{dc_B}{dt} = -k_{+2}c_B + k_{-2}c_D$$
$$\frac{dc_C}{dt} = k_{+1}c_A - k_{-1}c_C + k_{+3}c_C^2c_D - k_{-3}c_C^3$$
$$\frac{dc_D}{dt} = k_{+2}c_B - k_{-2}c_D - k_{+3}c_C^2c_D + k_{-3}c_C^3$$

(b) Assuming the total initial concentration, at $t = 0$, for A, B, C and D all together is c_0. Find the steady state concentrations for all four chemical species (c_A^*, c_B^*, c_C^*, c_D^*)

$$\frac{dc_A}{dt} = -k_{+1}c_A + k_{-1}c_C = 0 \rightarrow k_{-1}c_C = k_{+1}c_A \rightarrow c_A^* = \frac{k_{-1}}{k_{+1}}c_C^*$$

$$\frac{dc_B}{dt} = -k_{+2}c_B + k_{-2}c_D = 0 \rightarrow k_{-2}c_D = k_{+2}c_B \rightarrow c_Bz^* = \frac{k_{-2}}{k_{+2}}c_D^*$$

$$\frac{dc_C}{dt} = k_{+1}c_A - k_{-1}c_C + k_{+3}c_C^2c_D - k_{-3}c_C^3 = 0 \text{ cancel out } k_{-1}c_C = k_{+1}c_A$$
$$k_{+3}c_C^2c_D - k_{-3}c_C^3 = 0 \rightarrow k_{+3}c_C^2c_D = k_{-3}c_C^3 \rightarrow k_{+3}c_D = k_{-3}c_C \rightarrow c_C^* = \frac{k_{+3}}{k_{-3}}c_D^*$$

$$\frac{dc_D}{dt} = k_{+2}c_B - k_{-2}c_D - k_{+3}c_C^2c_D + k_{-3}c_C^3 = 0 \text{ cancel out } k_{+2}c_B = k_{-2}c_D$$
$$-k_{+3}c_C^2c_D + k_{-3}c_C^3 = 0 \rightarrow k_{-3}c_C^3 = k_{+3}c_C^2c_D \rightarrow k_{+3}c_D = k_{-3}c_C \rightarrow c_C^* = \frac{k_{+3}}{k_{-3}}c_D^*$$

$$c_A^* = \frac{k_{-1}}{k_{+1}}c_C^* \rightarrow c_A^* = \frac{k_{-1}}{k_{+1}}\left(\frac{k_{+3}}{k_{-3}}c_D^*\right) \rightarrow c_A^* = \frac{k_{-1}k_{+3}}{k_{+1}k_{-3}}c_D^*$$
$$c_0 = c_A + c_B + c_C + c_D \rightarrow c_0 = c_A^* + c_B^* + c_C^* + c_D^* \rightarrow c_0 = \frac{k_{-1}k_{+3}}{k_{+1}k_{-3}}c_D^* + \frac{k_{-2}}{k_{+2}}c_D^* + \frac{k_{+3}}{k_{-3}}c_D^* + c_D^* \rightarrow$$
$$c_0 = c_D^*\left(\frac{k_{-1}k_{+3}}{k_{+1}k_{-3}} + \frac{k_{-2}}{k_{+2}} + \frac{k_{+3}}{k_{-3}} + 1\right) \rightarrow c_D^* = \frac{c_0}{\frac{k_{-1}k_{+3}}{k_{+1}k_{-3}} + \frac{k_{-2}}{k_{+2}} + \frac{k_{+3}}{k_{-3}} + 1}$$

Steady state at:

$$\boxed{c_A^* = \frac{k_{-1}k_{+3}}{k_{+1}k_{-3}}c_D^*, \quad c_B^* = \frac{k_{-2}}{k_{+2}}c_D^*, \quad c_C^* = \frac{k_{+3}}{k_{-3}}c_D^*, \quad c_D^* = \frac{c_0}{\frac{k_{-1}k_{+3}}{k_{+1}k_{-3}} + \frac{k_{-2}}{k_{+2}} + \frac{k_{+3}}{k_{-3}} + 1}}$$

(c) Show that the following function of the c's:

$$L(\vec{c}) = \sum_{X=A,B,C,D} c_X \ln\left(\frac{c_X}{c_X^*}\right), \text{ where } \vec{c} = (c_A, c_B, c_c, c_d) \tag{2}$$

is a Lyapunov function of the dynamical system. That is:

i. $L(\vec{c}) \geq 0$? and $L(\vec{c}) = 0$? if and only if $\vec{c} = \vec{c}^*$

$f(x) = c_X \ln(\frac{c_X}{c_X^*}) = 0$ only when the natural log part equals zero or the variable in front c_X equals zero. So either when $\frac{c_X}{c_X^*} = 1 \rightarrow c_X = c_X^*$ or $c_X = 0$. Considering $c_A + c_B + c_c + c_d = c_0$ for $c_0 > 0$ there will always be a positive concentration of protein so there will be a c_X that will not equal zero. Then for function will only equal zero if $c_X = c_X^*$ as that will make the natural log function zero.
Function is negative for $c_X < c_X^*$ However, $L(\vec{c}) = c_X \ln(\frac{c_X}{c_X^*}) \geq c_X - c_X^*$ for $c_x^* \geq 0$ which it is as these are for positive concentration.
which means $L(\vec{c}) \geq c_X - c_X^*$ At steady state $c_X - c_X^* = 0$ so then $L(\vec{c}) \geq c_X - c_X^* = 0 \rightarrow L(\vec{c}) \geq 0$
If $c_X = c_X^*$ then $L(\vec{c}) = c_X^* \ln(\frac{c_X^*}{c_X^*}) \rightarrow L(\vec{c}) = c_X^* \ln(1) \rightarrow L(\vec{c}) = c_X^*(0) = 0$

ii. $L(\vec{c})$ is convex

$\frac{d^2}{dc_X^2}\left(c_X \ln(\frac{c_X}{c_X^*})\right) = \frac{d}{dc_X}\left(\ln(\frac{c_X}{c_X^*}) + 1\right) = \frac{1}{c_X}$. The function $\frac{1}{c_X}$ is positive for $c_X > 0$. A positive second derivative means the function is convex. This means that $L(\vec{c})$ is convex.

iii.

$$\frac{d}{dt}L[\vec{c}(t)] \leq 0 \tag{3}$$

$\frac{d}{dt}L[\vec{c}(t)] = \frac{d}{dt}\left(\sum_{X=A,B,C,D} c_X \ln(\frac{c_X}{c_X^*})\right) \leq 0 \rightarrow \sum_{X=A,B,C,D} \frac{dc_X}{dt} \ln(\frac{c_X}{c_X^*}) \leq 0$
At steady state $\frac{dc_X}{dt} = 0$ for all $X = A, B, C, D$ so therefore. $\sum_{X=A,B,C,D} \frac{dc_X}{dt} \ln(\frac{c_X}{c_X^*}) = 0 \leq 0$
For $c_X \neq c_X^*$, then $L[\vec{c}(t)] > c_X^*$. The Lyapunov functions goes towards equilibrium of c_X^* meaning the derivative is always negative.

(d) Is the fixed point c^* stable? Is it unique?

The fixed point is stable because the function $L(c)$ acts as a Lyapunov function, which means that it decreases along the trajectories of the system and is minimized at the fixed point c_X^*. This is from this hw parts $i.$, $ii.$, and $iii.$
The fixed point is unique because the fixed point is dependent on c_D^*. from part a. where $c_A^* = \frac{k_{-1}k_{+3}}{k_{+1}k_{-3}}c_D^*$, $c_B^* = \frac{k_{-2}}{k_{+2}}c_D^*$, T$c_C^* = \frac{k_{+3}}{k_{-3}}c_D^*$, $c_D^* = \frac{c_0}{\frac{k_{-1}k_{+3}}{k_{+1}k_{-3}} + \frac{k_{-2}}{k_{+2}} + \frac{k_{+3}}{k_{-3}} + 1}$
Since, $c_0 \geq 0$ and all the k's are positive which means c_D^* is always going to be a unique positive number based on c_0 and k's.

2. Consider the FitzHugh-Nagumo equation

$$\frac{dv}{dt} = f(v) - w + I_a \tag{4}$$

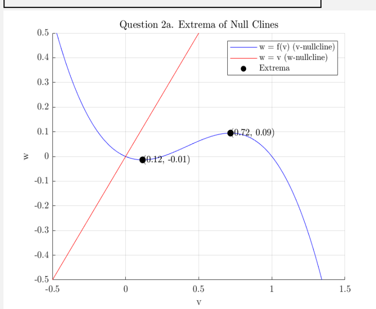
$$\frac{dw}{dt} = bv - \gamma w\text{‘} \tag{5}$$

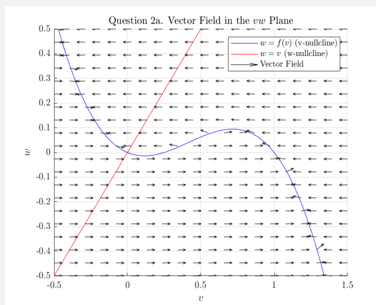
$$f(v) = v(a - v)(v - 1) \tag{6}$$

where $I_a = 0, a = 0.25, b = \gamma = 2 \times 10^{-3}$.

(a) Draw the nullclines in the vw plane. Draw the directions of the vector field in different regions. One of the null clines has a minimum and a maximum. Analytically determine the coordinates (v, w) for the minimum and the maximum

$\frac{dw}{dt} = bv - \gamma w \longrightarrow \frac{dw}{dt} = 2 \times 10^{-3}(v - w) = 0 \longrightarrow v - w = 0 \longrightarrow \boxed{w = v}$
$\frac{dv}{dt} = f(v) - w + I_a \longrightarrow v(a-v)(v-1) - w + I_a = 0 \longrightarrow v((0.25) - v)(v-1) - (w) + (0) = 0 \longrightarrow$
$\boxed{w = v(0.25 - v)(v - 1)}$





The coordinates for the minimum and maximum are
Local minimum: $(v_1, w_{localmin}) = \boxed{(0.1162, -0.0137)}$
Local maximum: $(v_2, w_{localmax}) = \boxed{(0.7171, 0.0948)}$

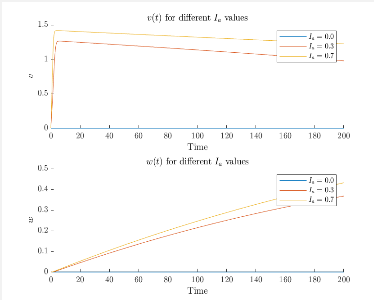
(b) With increasing $I_a > 0$, the fixed point (i.e., steady state) changes its stability at I_1 and I_2. What are the values for I_1 and I_2 with the above given values for a, b and γ?

The values for I_1 and I_2 with the above given values for a, b and γ are given by setting both derivatives equal to zero and solving for v or w.
$\frac{dw}{dt} = bv - \gamma w = 0 \longrightarrow bv = \gamma w \longrightarrow w = \frac{b}{\gamma} v = \longrightarrow w = v$
$\frac{dv}{dt} = f(v) - w + I_a = 0 \longrightarrow v(a - v)(v - 1) - w = -I_a \longrightarrow I_a = -v(a - v)(v - 1) + w$

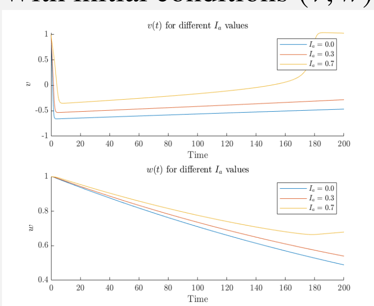
Plug in $v_1 = 0.1162, w = v$
$I_1 = -(0.1162)(0.25 - (0.1162))((0.1162) - 1) + 0.1162 \longrightarrow \boxed{I_1 = 0.1299}$
Plug in $v_2 = 0.7171, w = v$
$I_2 = -(0.7171)(0.25 - (0.7171))((0.7171) - 1) + 0.7171 \longrightarrow \boxed{I_2 = 0.6223}$

(c) Plot a solution to the FitzHugh-Nagumo equation with some I_a, inside and outside the interval $[I_1, I_2]$. Describe your finding. You need use MATLAB. If do not know how to use MATLAB, then try to find online resources such as the useful ODE solver that gives 2-dimensional phase plane at https://aeb019.hosted.uark.edu/pplane.html

$[I_1, I_2] = [0.1299, 0.6223]$
$I_a = 0.0, I_b = 0.3, I_c = 0.7$
With initial conditions $(v_0, w_0) = (0, 0)$

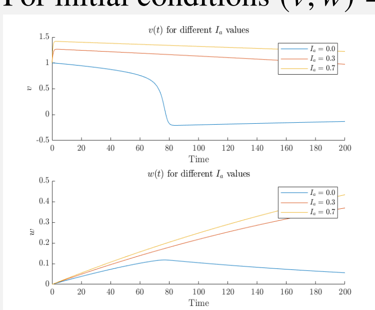


For $I_a > v_0$ an action potential is fired. The recovery function slowly increases to lower the voltage potential back. If $I_a = v_0$ the no action potential happens and it stays at equilibrium.
With initial conditions $(v, w) = (1, 1)$



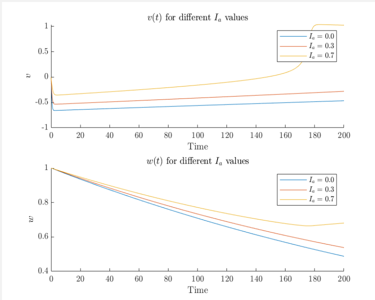
No action potential is fired for a while till $I_a = 0.7$ reaches the threshold. The recovery function $w(t)$ slowly increases to lower the voltage potential back. Otherwise $v(t)$ slowly increases and $w(t)$ slowly decreases.

For initial conditions $(v, w) = (1, 0)$



None of the values for I_a all three function are like on the tail end of the action potential firing. Meaning the recovery function will slowly increase till it reaches another possible action potential. For $I_a = 0$ there is an equilibrium at $v = 0$

With initial conditions $(v, w) = (0, 1)$



None of the I_a functions reach the action potential spike for a while. For $I_a = 0.0, v(t)$ increases slowly. but for $w(t)$ it decreases. $I_a = 0.3$ decreases for $v(t)$. and increases for $w(t)$ $I_a = 0.7$ decreases for $v(t)$. and increases for $w(t)$

3. Consider a stochastic population model for SIR epidemic

$$S + I \xrightarrow{r} 2I, I \xrightarrow{a} R \tag{7}$$

In the very early time of the epidemic, the population of the infectious individuals $I(t) \ll S(t)$, the population of the susceptible individuals. So it is reasonable to assume that $S(t) \equiv S_0$ is a constant.

(a) Denote the probability of having k number of infectious individuals at time t as $PrI(t) = k = p_k(t)$. Show that

$$\frac{dp_k(t)}{dt} = r(k-1)S_0 p_{k-1} - rkS_0 p_k. \tag{8}$$

To go from p_{k-1} to p_k the rate is $r(k-1)S_0p_{k-1}$ To go from p_k to p_{k-1} the rate is rkS_0p_k. So simply adding those to obtain $\frac{dp_k(t)}{dt} = r(k-1)S_0p_{k-1} - rkS_0p_k$.

(b) Assuming that $I(0) = n$, show that the solution to the system of ODEs in (a) is

$$p_k(t) = \binom{k-1}{k-n} e^{-rS_0nt}\left(1 - e^{-rS_0t}\right)^{k-n} \tag{9}$$

where $k \geq n$. This is known as a negative binomial distribution. Furthermore

$$p_k(t) = \left[\binom{k-1}{k-n} e^{-rS_0nt}\left(1 - e^{-rS_0t}\right)^{k-n}\right]_{t=0} = \begin{cases} 0 & k \neq n \\ 1 & k = n \end{cases} \tag{10}$$

$\frac{dp_k(t)}{dt} = r(k-1)S_0p_{k-1} - rkS_0p_k$.
Initial conditions given as.
$p_k(0) = \begin{cases} 1, & k = n \\ 0, & k \neq n \end{cases}$
Using $X(t) = I(t) - n$
then $p_k(t) = Pr\{I(t) = k\} =$
$Pr\{I(t) = k\} = Pr\{X(t) = k - n\}$
This is textboook negative binomial distribution
$p_k(t) = \left[\binom{k-1}{k-n} e^{-\text{rate}(t)}\left(1 - e^{\text{rate}(t)}\right)^{k-n}\right]$
$e^{\text{rate}(t)} = e^{-rS_0t}$
To get the equation:
$p_k(t) = \binom{k-1}{k-n} e^{-rS_0t}\left(1 - e^{-rS_0t}\right)^{k-n}$

Does this satisfy initial conditions $t = 0, p_k(0) = 1$?
$p_k(0) = \binom{k-1}{k-n} e^{-0}(1-e^{-0})^{k-n} \to p_k(0) = \binom{k-1}{k-n}(1)(1-1)^{k-n}$
If $k = n$ then:
$p_k(0) = \binom{n-1}{0}(1)(1-1)^{n-n} \to p_k(0) = \binom{n-1}{0}(1)(0)^0 \to p_k(0) = \binom{n-1}{0}(1)(1) \to$
$p_k(0) = 1$
If $k \neq n$ then:
$p_k(0) = \binom{k-1}{k-n}(1)(1-1)^{k-n} \to p_k(0) = \binom{k-1}{k-n}(1)(0)^{k-n} \to p_k(0) = 0$

(c) Show that the expected value $\mathbb{E}[I(t)]$ satisfies the ordinary differential equation $\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\mathbb{E}[I(t)]$.

$\mathbb{E}[I(t)] = \sum_{k=n}^{\infty}(k)p_k(t)$
$\frac{d}{dt}\mathbb{E}[I(t)] = \sum_{k=n}^{\infty}(k)\frac{dp_k(t)}{dt}$
$\frac{dp_k(t)}{dt} = r(k-1)S_0p_{k-1} - rkS_0p_k.$
$\frac{d}{dt}\mathbb{E}[I(t)] = \sum_{k=n}^{\infty}(k)\frac{dp_k(t)}{dt} = \sum_{k=n}^{\infty}(k)r(k-1)S_0p_{k-1} - \sum_{k=n}^{\infty}(k)rkS_0p_k$
Factor out rS_0
$\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\left(\sum_{k=n}^{\infty}(k)(k-1)p_{k-1} - \sum_{k=n}^{\infty}k^2p_k.\right)$
Index shift $m = k-1, m+1 = k$
$\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\left(\sum_{m=n-1}^{\infty}(m+1)(m)p_m - \sum_{k=n}^{\infty}k^2p_k.\right)$
Separate terms
$\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\left(\sum_{m=n-1}^{\infty}m^2p_m + \sum_{m=n-1}^{\infty}mp_m - \sum_{k=n}^{\infty}k^2p_k.\right)$
Identities:
$\sum_{m=n-1}^{\infty}m^2p_m = \mathbb{E}[I^2(t)]$
$\sum_{m=n-1}^{\infty}mp_m = \mathbb{E}[I(t)]$
$\sum_{k=n}^{\infty}k^2p = \mathbb{E}[I^2(t)]$
$\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\left(\mathbb{E}[I^2(t)] + \mathbb{E}[I(t)] - \mathbb{E}[I^2(t)]\right)$

Cancel out like terms to get.
$\frac{d}{dt}\mathbb{E}[I(t)] = rS_0\mathbb{E}[I(t)]$