APPM2360
Project 3:
Mathematical Investigation of Cardiac Dynamics

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I. Introduction

Cardiac Arrhythmia(irregular heart beat) is a family name of cardiac abnormalities from electrical behavior of the heart. In this report, we will the set of nonlinear ordinary differential equations (ODEs) systems to display the cardiac dynamics model. So, in the following part, this report will use 2 variables system of voltage and cardiac cell membranes to describe the behavior of heart beat. And then, the FitzHugh-Nagumo model of neural excitation and propagation from ion-flow can be our study model to get more information of arrhythmias form. The characteristic roots with eigenvalues and eigenvectors and the variation parameters solutions will be the main solved method help us to find the final results.

II. Background

These impulses spread to nearby cardiac cells and signal the cells to contract in a coordinated manner, producing a natural and regular heartbeat. The electrical impulse generated by the pacemaker cells is the cardiac action potentials. It is a kind of brief change in electric charge across the cell membrane. So, people always use the "excitation/recovery" model to describe the basic concept: $\frac{dv}{dt} = -kv(v-a)(v-1) - vh + S(t)$ and $\frac{dh}{dt} = (\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v-a-1))$. The v represents the voltage across the cell membrane, and h represents non-negative gating values. The $S(t)$ is the stimulus parameter function that can maintain a regular heartbeat with parameter T, where the periodically T values come from the number of time units that pass between each stimulation. And the Action Potential Duration(APD) is the duration from the cell stimulated time as the time difference: $APD_{beat} = t_{down} - t_{up}$.

III. Problem Statements

3.1.1.a)

The problem related model is a type of "excitation/recovery" model as the following part: $\frac{dv}{dt} = -kv(v-a)(v-1) - vh + S(t)$ and $\frac{dh}{dt} = (\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v-a-1))$. In this problem, the initial condition condition is the function $S(t) = 0$ and the other parameters: $a,\ k,\ \varepsilon_0,\ \mu_1,\ \mu_2$ are positive, unitless constants. So, for the nullclines of v, we set $\frac{dv}{dt}$ = 0, and get the nullclines of v equals to $\frac{k(a+1)\pm\sqrt{k^2(a+1)^2-4k(ka+h)}}{2k}$ and 0. To solve the nullclines of h, we set $\frac{dh}{dt} = 0$ and we get the nullclines of h are $h = -kv(v-a-1)$ and $h = \frac{\varepsilon_{0(v+\mu_2)}}{\mu_1}$.

3.1.1.b)

The only one non-negative equilibrium solution is the specific condition at $(v_0,\ h_0)$. The function $f(v,h) = h(v) = -kv(v-a)(v-1)$ will help us to discuss the equilibrium solution. And we will set $\frac{dv}{dt} = 0$ and $\frac{dh}{dt} = 0$ to discuss the condition: the nullclines of $v = 0$ and the nullclines of $h = 0$ can result in the non-negative solution. So, the only non-negative solution condition is at $(0,0)$.

3.1.1.c)

The eigenvalues of the Jacobian matrix are solutions of the equation $det(J(v_0,h_0)) = f_{v0}g_{h0} - f_{h0}g_{v0} = 0$, by solving the ordinary differential equations we get $f_v(0,0) = -ka$, $f_h(0,0) = 0$, $g_v(0,0) = \varepsilon_0 k(a+1)$ and $g_h(0,0) = -\varepsilon_0$. Plugging those values into the first equation, then we get two eigenvalues are $-\varepsilon_0$ and $-ka$.

3.1.1.d)

The two eigenvalues of $J(v_{0\,,}\ h_0) = J(0\ ,\ 0) =$ are $-\varepsilon_0$ and $-ka$. Both of them are negative, so, the non-negative equilibrium solution point will be sinked. So, this solution is stable.

3.1.2.a)

Put the variables $a = 0.15,\ k = 8, \varepsilon_0 = 0.002,\ \mu_1 = 0.2,\ \mu_2 = 0.3$ into the function part. So, we'll get $\frac{dh}{dt} = (0.002 + \frac{0.2h}{v+0.3})(-h - 8v(v - 0.15 - 1))$ as the nullclines function. The blue lines show the voltage nullclines and the red lines are the gating nullclines. And the equilibrium solution will be the black line which is passed by $(0,\ 0)$. The relationship between voltage and gating will be shown as the figure 1.

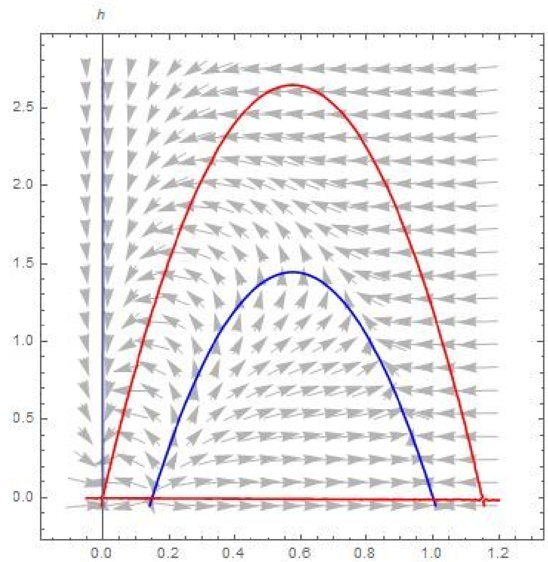

Figure 1. Voltage nullclines and Gating nullclines

3.1.2.b)

When dx/dt is positive, arrows point right, and when dx/dt is negative, arrows point left.

When dy/dt is positive, arrows point up, and when dy/dt is negative, arrows point down.

So, the movement directions are shown as grey arrows form the figure 1.

3.1.3.a)

The following graph figure 2 can show the solution curve in the vector field. The arrows can show the direction of solution curve in the vector field.

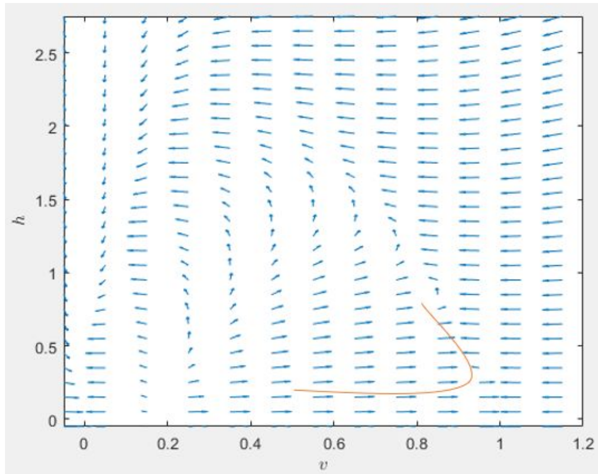

Figure 2: (starting from (v0, h0) = (0.5, 0.2)

3.1.3.b)

The following graph figure 3 can show the solution curve in the vector field. The arrows can show the direction of solution curve in the vector field.

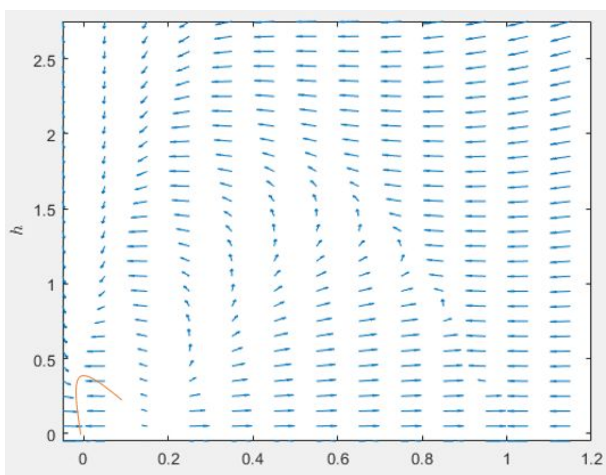

Figure 3: (starting from (v0, h0) = (0.1, 0.2)

3.1.3.c)

By comparing two solution's trajectory, we can see the initial condition do have influence on the solution curves. Although the two initial condition are close, the vector field go to the opposite direction. Therefore, the two curves are pretty different. The solutions behave as what we expected, both solution curves move close to the nullclines we found in part 2(a).

3.2 Model Improvement: Periodic stimulation

3.2.1.

Based on the previous solution, if we add a large, positive stimulus β on the voltage, the trajectory direction will move upward and span towards outside.

From the Figure 3, we can figure out that maximum of v exists when h = 0. Several values of v exist, the biggest value will be the maximum. Use both v and h expression from 3.1.1.a which have found. $v = \frac{k(a+1) \pm \sqrt{k^2(a+1)^2 - 4k(ka+h)}}{2k}$, $h = -kv(v-a-1)$ and $h = \frac{\varepsilon_{0(v+\mu_2)}}{\mu_1}$. Let h = 0, we can get the maximum of v is equal to 1.15.

3.2.2.

The flow is counter-clockwise. If no more stimuli are given after the initial "push", the system will go infinite from the condition when the v is at the maximum point. So, the answer agrees with the question 1 above.

IV. Conclusion

We can use the mathematical model to describe the behaviors of cardiac dynamics. In this report, the nonlinear ordinary differential equations(ODEs) help us to discuss the actual heartbeat system behaviors. So, the voltage flux across cardiac cell membranes will build the model based on FitzHugh-Nagumo model. And the cardiac cell is at rest, the outside charge is more than inside of cell. Then, the electrical impulse will be produced by cells in the cardiac action potentials. The characteristic roots method with eigenvalues can help us to discuss the typical solution of this model and other specific solution condition. And these solutions will give us the periodic stimulation of T, which is the number of time units that pass between each stimulation.

References

[1] Farlow, Jerry. *Differential Equations & Linear Algebra.* Prentice Hall, Harlow, England;Upper Saddle River, NJ;, 2007.

Appendix

Calculations:

III. Problem Statements

<u>3.1.1.a).</u>

$\frac{dv}{dt} =- kv(v-a)(v-1) - vh + S(t)$

$\frac{dh}{dt} = (\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v-a-1))$

$S(t) = 0$, $\frac{dv}{dt} = 0$, $\frac{dh}{dt} = 0$

$v_1 = \frac{k(a+1) \pm \sqrt{k^2(a+1)^2 - 4k(ka+h)}}{2k}$ or $v_2 = 0$

$h_1 =- kv(v-a-1)$ or $h_2 = \frac{\varepsilon_{0(v+\mu_2)}}{\mu_1}$

<u>3.1.1.b)</u>

$f(v,h) = h(v) =- kv(v-a)(v-1)$

$\frac{dv}{dt} = 0$, $\frac{dh}{dt} = 0$

$(\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v-a-1)) = 0$

$h = 0 \; or \; h = \frac{\varepsilon_0 \mu_2}{\mu_1}$

So, $v = 0, \; h = 0$ $\Rightarrow$ $(0, 0)$ is the equilibrium solution point

<u>3.1.1.c)</u>

$f(v,h) =- kv(v-a)(v-1) - vh$

$g(v, h) = (\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v - a - 1))$

$det(J(v_0, h_0)) = f_{v0}g_{h0} - f_{h0}g_{v0} = 0$

$f_v =- k(3v^2 - 2(1 + a)v + a) - h)\ and\ f_h =- v$

$g_{v} = (-\varepsilon_0 k(zv - a - 1) + \frac{\mu_1 h^2}{(v+\mu_2)^2}) - k\mu_1 h(\frac{(v+\mu_2)(2v-a-1)-(v^2-va-v)}{(v+\mu_2)^2})$

$g_h =- \varepsilon_0 - \frac{2\mu_1 h}{v+\mu_2} - k\mu_1(\frac{v^2-va-v}{v+\mu_2})$

$g_v(0, 0) = \varepsilon_0 k(a + 1)$

$g_h(0, 0) =- \varepsilon_0$

$f_v(0, 0) =- ka$

$f_h(0, 0) = 0$

3.2.1

$\frac{dv}{dt} =- kv(v - a)(v - 1) - vh + S(t)$, set $\frac{dv}{dt} = 0$

$0 =- 8v(v - 0.15)(v - 1) - vh$, let $h = 0$

We get $v = 0$, $0.15\ or\ 1$

$\frac{dh}{dt} = (\varepsilon_0 + \frac{\mu_1 h}{v+\mu_2})(-h - kv(v - a - 1))$, set $\frac{dh}{dt} = 0$

$0 = (-h - 8v(v - 0.15 - 1))$, let $h = 0$

We get $v = 1.15\ or\ -0.3$

The max of v is 1.15.