Exitable Media & FitzHugh-Nagumo Model

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Abstract

Contents

1 Introduction

In this section, firstly, we introduce *Excitable Media* and *FitzHugh-Nagumo Model* and then state the objective of this paper and how the chapters are organised.

1.1 Excitable Media

Excitable media, which are spatially distributed "dynamical systems", can be characterised by their "threshold of excitability" and their ability to generate and support "propagation of undamped solitary excitation waves or wave trains".Threshold of excitability means; for a system, there is certain level excitation which needs to be applied or attained for the system to get excited and when it's in its excited state it generates undamped propagating waves. Undamped propagating waves imply; waves keep their shape and speed while moving through a medium.They are also called "Travelling waves" For example, a forest fire can be considered as an excitation wave, which starts at its initiation point at a certain extreme temperature and regenerates by igniting its adjacent trees. This kind of wave propagation is called active wave propagation unlike the passive wave propagation like passing of sound through air, where signal damping happens due to friction.

Generally, excitability is refereed to as a property of living organisms where they as a whole or their constituent cells respond strongly to the action of a relatively weak stimulus. An Ideal example is the generation of a spike of transmembrane action potential by a nerve or cardiac cell. In such cases, the shape of the generated action potential does not depend on the stimulus strength, strong response is generated, as long as stimulus exceeds some threshold level. After the generation of this excitation, the system returns to its initial resting state and subsequent excitation can only be generated after a certain length of time, which is called the "refractory period".

Other notable examples of excitable media are:

1. concentration waves in the bromate-malonic acid reagent (The Belousov-Zhabotinsky reaction).
2. propagating waves(called CMAP) during the aggregation of social amoeba (Dictyostelium discoideum).
3. calcium waves within frog eggs.

1.2 FitzHugh-Nagumo Model

The FitzHugh-Nagumo model was put forward by Dr. Richard FitzHugh in 1961 [1], as a simplification of the Noble prize winning Hodgkin-Huxley model [2], which very successfully modelled the initiation and propagation of neural action potential using a squid axon. The Hodgkin-Huxley model is a four variable model with four ordinary differential equations(ODEs) and it's phase space can only viewed as a projection to two dimensional space, hence, FitzHugh devised a simplified two variable model with two ODE by modifying The Van der Pol "relaxation oscillator" [1], which itself is a modification of a damped linear oscillator, and called it Bonhoeffer-van der Pol model or BVP model for short.Although, being a simplified version, the BVP model captured all the key features of the Hodgkin-Huxley model(H-H model) [1]. In 1962, a Japanese engineer named Jin-Ichi Nagumo, Inspired by FitzHugh published a paper [3] where used

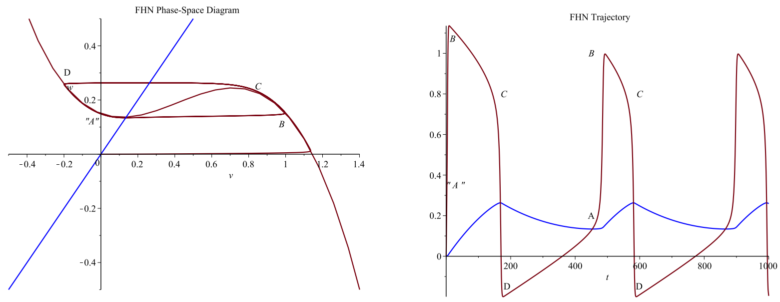

Figure 1: Dynamics of the FHN model.

electrical circuits to simulate BVP model and since then the BVP model has been renowned as FitzHugh-Nagumo model (FHN model).

The FHN can be written in a general form as;

$$V' = f(V) - W + I + V_{xx} \; W' = a(bV - hW) \tag{1}$$

Here, V is the excitation variable and V' represent first derivative, an example of V would be; membrane potential in a living cell, W is the recovery variable, and I is the magnitude of stimulus. Also, V_{xx} is the diffusion term, which is a second partial derivative with respect to spatial variable x, this term is required for the propagation of excitation waves. Without the diffusion term, the model is called "space-clamped" i.e. homogeneous or "no diffusion" model, and this model doesn't involve partial differential equations (PDEs) and has only two ODEs. This space clamped model was used by FitzHugh(1961) [1] for his analysis of nonlinear dynamics of the model and Nagumo(1962) [3] used the reaction diffusion model to simulate the Travelling waves.There are mainly two formulations of $f(V)$, one is where $f(V) = V^3 - \frac{V}{3}$ and $c(f((V) - W))$, as in FitzHugh(1961) [1] and other is $f(V) = V(a - V)(V - 1)$ and $a = 1$, as in Rinzel(1981) [4]. a, b and c are constants, and either a or b is normally taken to equal 1.

The dynamics of FHN model at its excited state can be by the following diagram; In Figure 1, left, we see a phase portrait where a stimulus above threshold is applied and a "limit cycle oscillation" $ABCD$ is circling around the fixed point. In Figure 1, right, we see the corresponding trajectory plotted against time. The trajectory starts from A and very quickly moves to B, for this reason there is almost vertical movement from A to B at Figure 1(b), then, it moves slowly from B to C, hence we see bendy curve from B to C in Figure 1(b), afterwards, it again moves very quickly from C to D and then slowly goes to A from D and completes a cycle, these fast and slow movements are again reflected in Figure 1(b) and thus a "spike" or excitation wave is formed and repeating cycles generate repeating spikes.

Here are some area of research where FHN model is used;

1. Pattern formation in Reaction diffusion systems [5].
2. Modelling of Dictyostelium discoideum slug formation, morphogenesis and migration [6] [7] [8].
3. Research on the cause of Cardiac arrhythmia [9].

1.3 Objective & Flow of the paper

OBJECTIVE OF THIS PAPER FitzHugh and Nagumo papers
FLOW OF THIS PAPER

2 Derivation & Dynamics of FitzHugh-Nagumo Model

2.1 Derivation of FitzHugh Nagumo Model

As mentioned earlier, FHN model was derived modifying Van der Pol oscillator, and Van der Pol oscillator was derived from a damped linear oscillator. A damped linear oscillator can be written as:

$$V'' + kV' + V = 0$$

Van der Pol(1926) [10] replaced the damping constant by a damping coefficient which depends quadratically on x:

$$V'' + c(x^2 - 1)V' + V = 0$$

Where c is a positive constant.Then by using Lienard's transformation(Minorsky,1947 []):

$$W = \frac{V'}{c} + \frac{V^3}{3} - V$$

The two ODEs of Van der Pol oscillator are obtained as:

$$V' = c(W + V - \frac{V^3}{3}) \tag{2}$$

$$W' = -\frac{V}{C} \tag{3}$$

The W nullcline of this oscillator a vertical line and there is only one intersection with cubic nullcline V, and it is alway unstable. In order to resemble a real excitable medium, which has a stable rest point and display threshold phenomenon, FitzHugh introduced a rotated W nullcline and ensured there's only one intersection of nullclines by adding $\frac{b}{c}W$ and $\frac{a}{c}$ term to the second ODE, and thus derived the FHN model as:

$$V' = c(W + V - \frac{V^3}{3}) + I \tag{4}$$

$$W' = -\frac{-(V - a + bW)}{c} \tag{5}$$

where:

$$1 - 2b/3 < a < 1, 0 < b < 1 \text{ and } b < c^2$$

a, b, c, are constants and I is the stimulus. This is the FHN model and introduced as BVP model by FitzHugh. As we shall see later, when the phase portrait are plotted with this model, two nullclines intersect below x axis, i.e. fixed points are negative. John Rinzel (1981) [4] modified this model slightly to move the fixed point onto origin, so that at rest point, fixed point is $(0, 0)$, this model is written as:

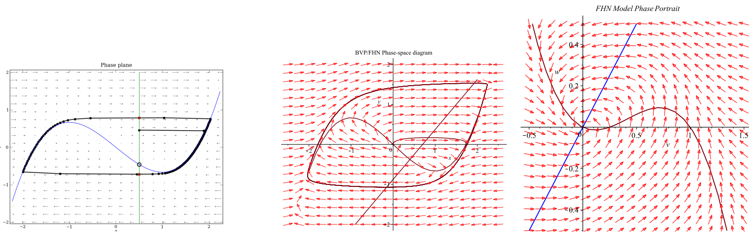

Figure 2: The Dynamics of FHN mode
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$$V' = V(a - V)(V - 1) - W + I \tag{6}$$
$$W' = bV - cW \tag{7}$$

Again, a,b and c are constants, where: $0 < a < 1$, b and c are positive constants. The diagram below shows the phase portraits of Van der Pol oscillator, BVP/FHN model and modified FHN model:

From now onwards, we would use the modified version of FHN model for our analysis of its nonlinear dynamics.

2.2 Dynamics of FitzHugh-Nagumo Model

FHN model is an *Autonomous Dynamical System* i.e. it has no explicit time dependency and it is *Nonlinear* which implies that *Superposition principle* does not apply here, and it can not be solved analytically like *Linear Systems*. Therefore, we use computer algebra software **Maple** to perform *Numerical Integration* and solve the sytem of ODE numerically, which also enabled us to plot, the phase portrait of the system and the time evolution of its trajectories. We also make linear approximation of the nonlinear system near the *Equilibrium point* or *Fixed point*, so that we can determine the *stability* property of the system and classify its phase paths according to the nature of *eigenvalues* of the *Jacobian Matrix*. At the rest position, our model has coordinate $(0, 0)$ as fixed point, which is easy to use for calculations, but for the calculations of the nonzero cases which involved solving a cubic polynomial and finding eigenvalues of a complicated matrix, we formulate few **Maple** *procedures* which automated the whole process. Thus, we analyse the excitability of the system in response to various amounts of stimulus and strive to determine the "threshold of excitability".

2.2.1 Linearistation

We know that by, Hartman-Grobman theorem[11], a nonlinear system is "topological conjugate" i.e. geometrically similar to a linear system, sufficiently close to its equilibrium point. FHN model at rest state is written as:

$$V' = V(a - V)(V - 1) - W \tag{8}$$
$$W' = bV - cW \tag{9}$$

Now they can be reorganised and named as:

$$F(V,W) = V' = V^3 - V^2(1-a) - Va - W$$
$$G(V,W) = W' = bV - cW$$

Now, fixed points (V_0, W_0) of the system are found by solving $F(V,W) = 0$ and $G(V,W) = 0$ simultaneously.

Now, lets take a point $V = V_0 + h$, where h is a very small number and equals; $h = V - V_0$. By differentiating, $V = V_0 + h$ we get; $V' = h'$

Similarly, from $W = W_0 + k$ we get; $k = W - W_0$ and $W' = k'$

Now, by *Taylor expansion* for two variables we can write:

$$V' = F(V,W) \rightarrow h' = h\frac{\partial F(V_0,W_0)}{\partial V} + k\frac{\partial F(V_0,W_0)}{\partial W}$$
$$W' = G(V,W) \rightarrow k' = h\frac{\partial G(V_0,W_0)}{\partial V} + k\frac{\partial G(V_0,W_0)}{\partial W}$$

We can neglect the higher order terms $O(h^2, k^2, hk)$ as long as h and k are taken to be very small.

These can be written in matrix form as:

$$\mathbf{V'} = \mathbf{A}\ \mathbf{V}$$

Where, $\mathbf{V} = (\mathbf{h}, \mathbf{k})^{\mathbf{T}}$, and the matrix $A = \begin{pmatrix} \frac{\partial F(V_0,W_0)}{\partial V} & \frac{\partial F(V_0,W_0)}{\partial W} \\ \frac{\partial G(V_0,W_0)}{\partial V} & \frac{\partial G(V_0,W_0)}{\partial W} \end{pmatrix}$.

$$\implies A = \begin{pmatrix} -3V_0^2 - 2V_0(1-a) - a & -1 \\ b & -c \end{pmatrix}.$$

As, $V_0 = 0$:

$$A = \begin{pmatrix} -a & -1 \\ b & -c \end{pmatrix}.$$

This is the *Jacobian Matrix* and we would need to find its *Trace*, *Determinant* and *Eigenvalues* to determine stability and phase paths orientation of our system.

2.2.2 Stability Criteria

Now, From matrix A of previous subsection, we can find the *characteristic equation* by writing:

$$det(A - \lambda I) = 0$$

Here, λ is the eigenvalue of the matrix, which we find by solving the characteristic equation, and I is an identity matrix.

$$\implies det \begin{pmatrix} -a-\lambda & -1 \\ b & -c-\lambda \end{pmatrix} = 0$$

$$\implies -(a+\lambda) - (c+\lambda) + b = 0$$

$$\implies \lambda^2 + (a+c)\lambda + (ac+b) = 0$$

$$\implies \lambda = \frac{-(a+c) \pm \sqrt[2]{(a+c)^2 - 4(ac+b)}}{2}$$

We know, "Trace" of a matrix is defined as the sum of the elements of the main diagonal(upper left to lower right), so for our matrix A it is $-(a+c)$. Also, determinant of matrix A is $(ac+b)$.

So, for determining the stability of a system we use the *Routh-Hurwitz criteria* [12], accordingly, the necessary and sufficient condition for a quadratic characteristic polynomial is to have nonzero determinant and negative trace of its Jacobian matrix, i.e. $trace < 0$ and $determinant > 0$. Therefore, at rest state with $V_0 = 0$, our system is stable, but to determine stability of other nonzero fixed points we implement a Maple procedure to produce the Jacobian matrix of system, get the trace and determinant of the matrix and determine stability with an *if/else* conditional.

2.2.3 Phase Path Classification

We use the trace, determinant and eigenvalues of previous subsection to classify the phase paths of our system at different states of evolution.

By calling, trace $-(a+c) = p$ and determinant $(ac+b) = q$ we can write the eigenvalue solution as:

$$\lambda = \frac{p \pm \sqrt[2]{(p^2 - 4q)}}{2}$$

We know there are two eigenvalues, so, calling them λ_1 and λ_2 and calling $(p^2 - 4q) = \triangle$ we can write the previous equation as:

$$\lambda_1, \lambda_2 = \frac{1}{2}(p \pm \sqrt[2]{\triangle})$$

Now, we can classify the phase paths according to the nature of the eigenvalues with the precondition of having non zero determinant. There are three distinct classes of scenario that can happen, they are:

1. λ_1 ,λ_2 real, distinct and having the same sign.
2. λ_1 ,λ_2 real, distinct and having opposite sign.
3. λ_1 ,λ_2 are complex conjugates.

For case 1, there are two possibilities, λ_1 ,λ_2 can be both positive or both negative. When both negative, the system is stable, and phase paths approach origin as $t \to \infty$. And this type of phase path is called *Stable Node*, in terms of p, q and $\triangle$, it can be written as:

$$\textbf{Stable Node} : \triangle > \mathbf{0}, \mathbf{q} > \mathbf{0}, \mathbf{p} < \mathbf{0};$$

When, $\lambda_1\lambda_2$ both positive, the system is unstable and phase paths approach infinity as $t \to \infty$. This type of phase path is called *Unstable Node*,and in terms of p, q and $\triangle$, it can be written as:

$$\textbf{Unstable Node} : \triangle > \mathbf{0}, \mathbf{q} > \mathbf{0}, \mathbf{p} > \mathbf{0};$$

For case 2, λ_1 ,λ_2 have opposite sign, i.e. if one is negative than other is positive and determinant of matrix A is negative, in this case only two phase paths that approach the origin and they are straight lines. There are two other straight line paths which moves out of origin to infinity as $t \to \infty$. These four lines are called *Asymptotes* and all other paths starts moving toward origin but bends outward to infinity coming near the asymptotes, this creates a pattern which is like a family of hyperbolas together with its asymptotes. This kind of equilibrium point at origin is called a *Saddle* and they are always unstable.

$$\textbf{Saddle Point} : \triangle > \mathbf{0}, \mathbf{q} < \mathbf{0};$$

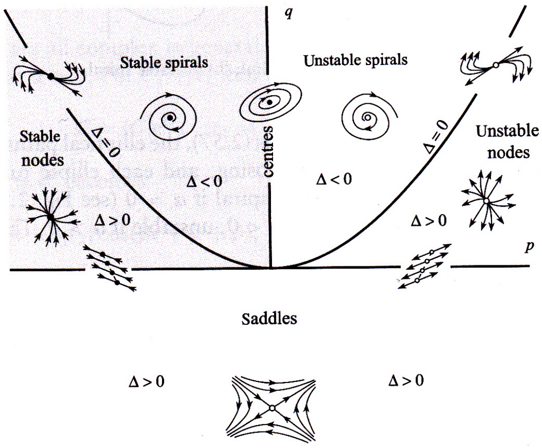

Figure 3: The Phase Classification Diagram
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For case 3, λ_1 ,λ_2 are complex numbers and always appear as complex conjugate pairs and they are written as:

$$\lambda_1 = \alpha + i\beta, \lambda_2 = \alpha - i\beta$$

Where α and β are real numbers, and α is called the real part of the eigenvalue. Now, there can be three scenarios depending on the real part α, they are: $\alpha = 0$, $\alpha > 0$ and $\alpha < 0$. When, $\alpha = 0$ the equilibrium point is a *Centre* and in this case phase paths form a family of geometrically similar ellipses which circle around the centre with a constant angle to the axes.

$$\textbf{Centre} : \mathbf{q > 0, p = 0};$$

When $\alpha \neq 0$, the ellipses turn into spirals, and the equilibrium points are called a *Focus* or *Spiral.* When $\alpha > 0$ it is an expanding spiral, i.e. phase paths spiral outward from origin and the system is unstable. When $\alpha < 0$ it is a contracting spiral, where phase paths approach the equilibrium point and the system is stable. In both cases direction can be clockwise or counterclockwise.

$$\textbf{Unstable Spiral} : \triangle < \mathbf{0, q > 0, p > 0};$$

$$\textbf{Stable Spiral} : \triangle < \mathbf{0, q > 0, p < 0};$$

In order to classify the phase paths along with their stability property, we integrate an *if/elif/else* conditional to our Maple program. This enabled us to determine the change in phase path orientation and stability, corresponding to various changes of parameters of the system. The diagram below would give a graphical representation plotted in a (p, q) coordinate system.

2.2.4 Simulations

Using our Maple procedure **FHN EXCITATION(a,b,h,i)**, we applied different amounts of stimulus i and observed at which levels the system produces a excitation wave or periodic excitation waves. We also varied the parameter a but parameter b and h are kept fixed only for this simulations, at .02.

Firstly, we run the program with $a = .2$, $b = .02$, $h = .02$ and $i = 0$, to observe the rest state of the system, which is stable with fixed point at $(0, 0)$, we also see no activity on our "FHN Trajectory" graph, which is a plot of V and W against time t.This scenario is reflected in Figure 4.

Then, we input a very little amount of stimulus and run the program with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0.05$. In this case, we observe one circular movement on phase space diagram and one excitation wave each for V and W. We also see that the cubic V nullcline has moved slightly upward and new fixed point is now at $(.043, .043)$ and this where the phase path converges to after one circular motion. This is depicted in Figure 5.

The most interesting scenario starts to occurs when we simulate with $a = .2$, $b = .02$, $h = .02$ and $i = .21$, at this stage the cubic nullcline moves further upward and the linear W nullcline intersects it at its middle section where the qubic nullcline has a positive gradient. In the phase space diagram we see a *limit cycle* oscillation appear, where all phase paths circle around the fixed point at a set distance, and this reflects on the trajectory graph, as appearance of seemingly infinite spiking waves. FitzHugh in his 1961 paper [1] wrote;"When x is plotted against t, an infinite train of spikes appears. It has not been possible to get a finite train of spikes from BVP model". Then we tried to investigate if the spikes were really infinite, thanks to the power of our computers we found that the spikes are finite and they end at around 3000 time interval. This is reflected on Figure 6. We carried on increasing the stimulus slightly and kept seeing spikes for longer time frame up to $i = .589$ where the spiking ended at around 9000 t , which is seen on Figure 7. Then at $i = .59$ the system becomes stable, when the linear nullcline approaches the flat right knee of cubic nullcline and super fast spiking becomes damped oscillations and eventually converges to its fixed point. Which can be seen of Figure 8.

Afterwards, we tried changing a and observe the consequence. We found out that a represent the "threshold of excitation", so when we increased a, we needed to put the stimulus very near or above new a, to get limit cycle oscillations, and any stimulus significantly below the threshold results in just one spiking and return to rest state. This is reflected on Figure 9.

We can summarise our findings from the simulations as: The FHN model successfully models an excitable media, as it has a threshold of excitability parameter a, a stable rest state, it is unresponsive to super threshold stimulus, produces one spike at sub threshold stimulus and undamped spiking only occurs at certain levels of stimuli.

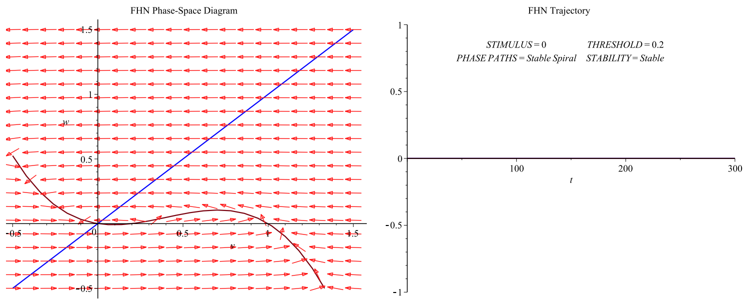

Figure 4: FHN Phase diagram and Trajectory. System at a stable resting state with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0$.

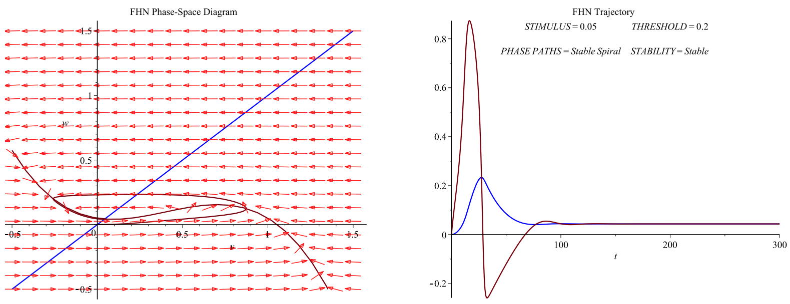

Figure 5: FHN Phase diagram and Trajectory. System at a stable state after emitting an excitation spike, due to stimulus below threshold, with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0.05$.

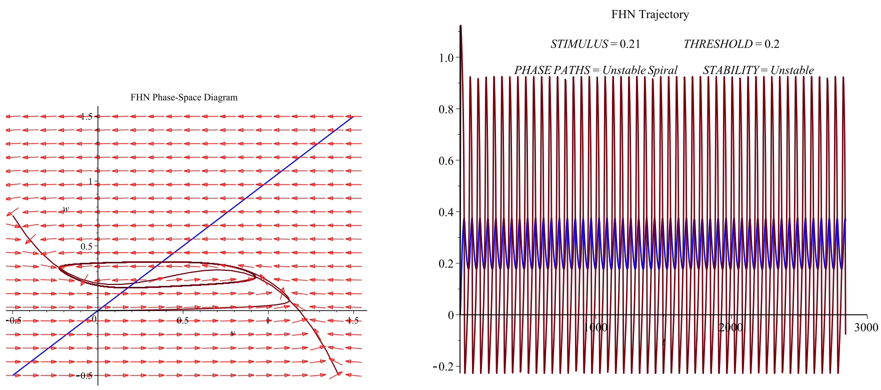

Figure 6: FHN Phase diagram and Trajectory. System at an unstable state after a stimulus above the threshold, with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0.21$.

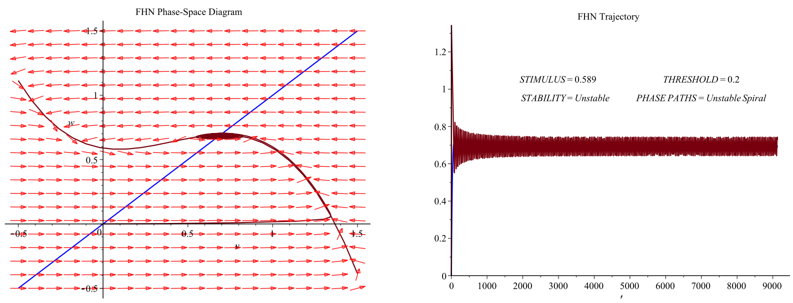

Figure 7: FHN Phase diagram and Trajectory. System at an unstable state after a stimulus above the threshold, with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0.589$

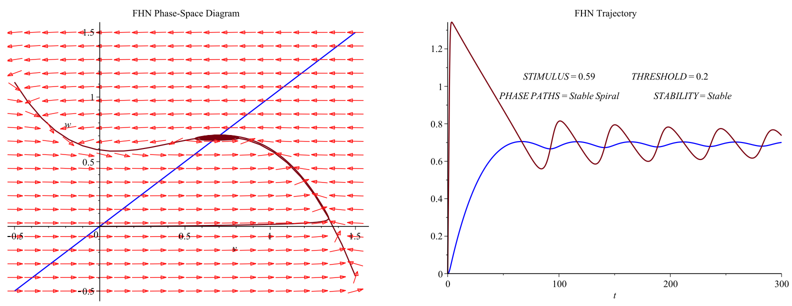

Figure 8: FHN Phase diagram and Trajectory. System at a stable state after emitting few excitation spikes, due to super threshold stimulus, with parameters $a = .2$, $b = .02$, $h = .02$ and $i = 0.59$

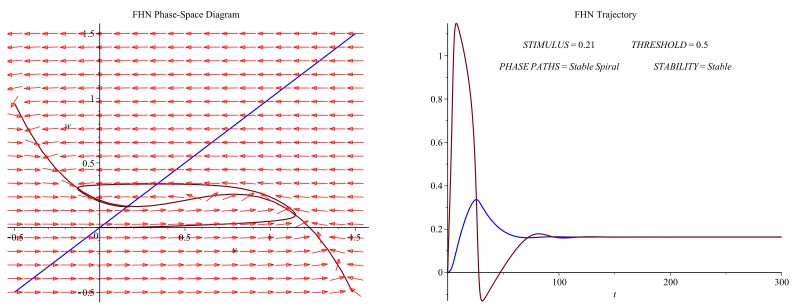

Figure 9: FHN Phase diagram and Trajectory. System at a stable state after emitting an excitation spike, due to increased threshold and stimulus below threshold, with parameters $a = .5$, $b = .02$, $h = .02$ and $i = 0.21$

3 Travelling Waves in FitzHugh Nagumo Model

3.1 The FHN model & It's Travelling Wavefront Solution

As we have seen, an excitable media generates excitation waves at its excited state, which is also called Travelling wave, and afterwards it travels through with a constant shape and speed. FHN equations can be used to model these travelling waves as FHN equations do produce travelling wave solutions at certain values of its parameters. For example, when modelling neural communication by nerve cells via electrical signalling, where travelling waves travel through great lengths of nerve axons without distorting the message, we use the FHN model instead of using space clamped model we use FHN model with spatial diffusion and it is written as:

$$\frac{\partial V}{\partial t} = V(V-1)(a-V) - W + D\frac{\partial^2 V}{\partial x^2} \tag{10}$$

$$\frac{\partial W}{\partial t} = a(bV - hW) \tag{11}$$

Here, $\frac{\partial V}{\partial t}$ and $\frac{\partial W}{\partial t}$ are the partial derivatives with respect to time, $\frac{\partial^2 V}{\partial x^2}$ is the second partial derivative with respect to space and D is the diffusion coefficient.

In order to study analytically we can consider b and h to be very small and write:

$$b = \epsilon L, h = \epsilon M, 0 < \epsilon << 1$$

Thus, FHN equations become:

$$\frac{\partial V}{\partial t} = V(V-1)(a-V) - W + D\frac{\partial^2 V}{\partial x^2} \tag{12}$$

$$\frac{\partial W}{\partial t} = \epsilon(LV - MW) \tag{13}$$

Now if we consider only the wavefront of the travelling wave, then in the limiting situation $\epsilon \to 0$ W tuns out to be constant as its derivative becomes zero. For the leading wavefront W is completely negligible, and the FHN model can be written as:

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + V(V-1)(a-V) \tag{14}$$

Which is also know as Reduced *Nagumo Equation*. The phase portrait of this equation is displayed in Firgure 10. We can see three fixed points $V1 = 0$, $V2 = .2$ which is a i.e.the threshold of the system and "V3=1". $V1$ and $V3$ are stable, but $V2$ is unstable as it is on the middle part of cubic nullcline and travelling waves will initiate due to this instability.

By assuming this equation to have travelling wave solution, we can further simplify it by turning the PDE into a second order ODE, which is solvable analytically. First we rewrite the equation in terms of its fixed points as:

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + V(V-V_1)(V_2-V) \tag{15}$$

We let,

$$V(x,t) = v(z), z = x - ct, v(-\infty) = V_3, v(\infty) = V_1.$$

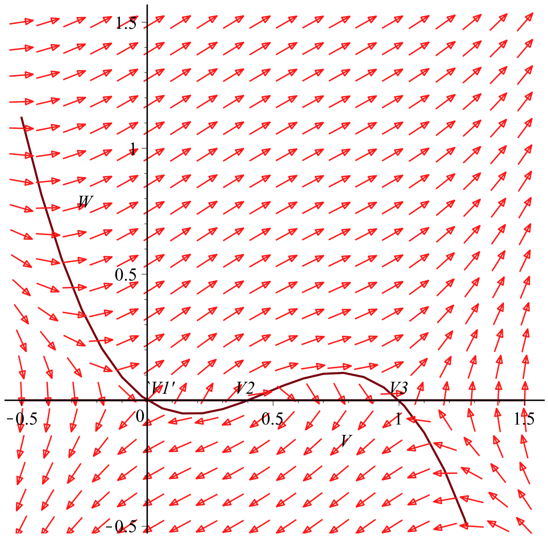

Figure 10: The Phase diagram of Reduced Nagumo Equation. Showing three fixed points V1, V2 and V3. V1 and V3 stable, V3 Unstable.

Where c is the constant wave speed of the travelling wavefront.

Now,

$$\frac{\partial V}{\partial t} = -c\frac{dv}{dz} \text{ and } \frac{\partial^2 V}{\partial x^2} = \frac{d^2 v}{dz^2}$$

Inserting back to PDE,

$$-c\frac{dv}{dz} = v(v - V_3)(V_2 - v) + D\frac{d^2 v}{dz^2}$$

This ODE can also be written as:

$$Dv'' + cv' + v(v - V_3)(V_2 - v) = 0 \tag{16}$$

Now assume that,

$$v' = av(v - V_3)$$

Inserting this into the ODE:

$$v(v - V_3)Da^2(2v - V_3) + ca - (v - V_2) = 0$$

or,

$$v(v - V_3)(2Da^2 - 1)v - (Da^2 V_3 - ca - V_2) = 0$$

Now,

$$2Da^2 - 1 = 0 \text{ and } Da^2 V_3 - ca - V_2 = 0$$

$$\implies a = \sqrt{\frac{1}{2D}}$$

$$\implies c = \sqrt{\frac{D}{2}}(1 - 2V_2) \text{ or } c = \sqrt{\frac{D}{2}}(1 - 2a)$$

3.2 The Numerical Scheme implementation in Maple

3.3 Simulations

4 Conclusion

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5 Appendix 1: Maple Codes

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