Exciability in FitzHugh-Nagumo model and a brief look into its dynamics

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Abstract

In this paper, I will talk about the basic features of the FitzHugh-Nagumo model before going into its dynamics and application in cardiac model.

1 Introduction

During the 1950s, Alan Hodgkin and Andrew Huxley developed the first quantitative model of the propagation of an action potential along a squid giant axon. In essence, a neuron doesn't fire until a threshold input stimulus is reached and, after firing, neurons exhibit a relaxation time, which prevents them from firing again for a short time.

Even though the Hodgkin-Huxley model is more realistic and without a doubt captures every details of manner activation and deactivation dynamics of a spiking neuron, the complexity and behavior of a four-dimensional system is difficult to visualize and even more difficult to analyze. However, two-dimensional differential equations can be studied in a clear manner by means of a phase plane analysis and its properties can therefore be visualized on a phase plane. Thus, a reduction of the four-dimensional equation of Hodgkin and Huxley to a two-variable neuron FitzHugh-Nagumo model is highly desirable. The simplicity of the FitzHugh-Nagumo model permits the entire solution to be viewed at once. This allows a geometrical explanation of important biological phenomena related to neuronal excitability and spike-generating mechanism.

2 FitzHugh-Nagumo model

2.1 Exciability

The FitzHugh-Nagumo model is a two-dimensional simplification of the Hodgkin-Huxley model of spike generation in squid giant axons:

$$\dot{V} = V - \frac{V^3}{3} - W + I_{app}$$

$$\dot{W} = \varepsilon(V + \beta - \gamma W)$$

where

- V is the membrane potential excitation variable, having cubic nonlinearity that allows regenerative self-excitation via a fast positive feedback.
- W is the recovery variable, having a linear dynamics that provides a slow negative feedback.
- I_{app} is the external applied current used to stimulate the model.
- $\varepsilon, \beta, \gamma$ are constants such that $\varepsilon = 0.08$, $\beta = 0.7$, $\gamma = 0.8$.
- Here, the variables are dimensionless quantity.

Below is the phase portrait that captures the trajectories and elements of the FitzHugh-Nagumo model. Depends on the initial condition and the intensity of the current I, if they are in the area of self-excitatory then the neuron fires, which they go through the regenerative region and as they pass the cubic nullcline $\dot{V} = 0$, they reach the active part of trajectory; immediately followed by a part in which it cannot be stimulated, no matter how great a stimulus is applied, which is the absolute refractory area, followed by a 'relative refractory' part (in which a second firing is possible - but only given enough stimulus or the current is strong enough) and then followed by the resting phase, or the stable steady state. The "no man's land" region of the phase space is highly unstable, containing trajectories starting very close to the quasi-threshold.

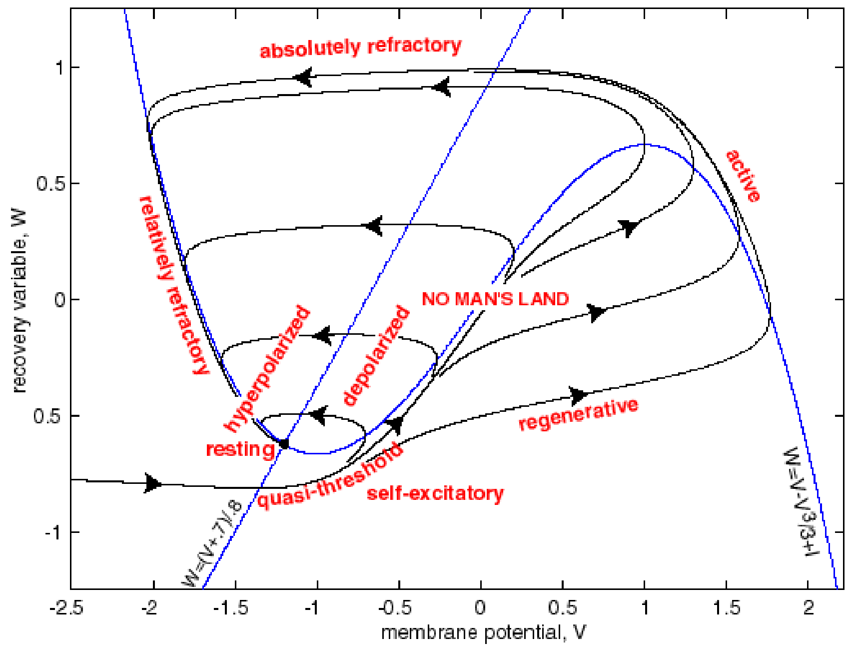

Figure 1: Phase portrait and physiological state diagram of FitzHugh-Nagumo model [6]

2.2 Absence of all-or-none spikes or firing threshold

The FitzHugh-Nagumo model explained the absence of all-or-none spikes in the HH model in response to the external applied current I. Weak stimuli (low intensity of I) result in small-amplitude trajectories that correspond to subthreshold responses (Figure 2 and Figure 3). Medium stimuli result in intermediate-amplitude trajectories that correspond to medium-amplitude spikes (Figure 4) while strong stimuli result in large-amplitude trajectories that correspond to suprathreshold response, leading to firing a spike (Figure 5). As a consequence of this, the model does not have a well-defined firing threshold. Thus, the concept of the "quasi-threshold" is born which is an unstable trajectory where nearby trajectories diverge sharply away from it to the left or right, producing an apparently threshold-like behavior.

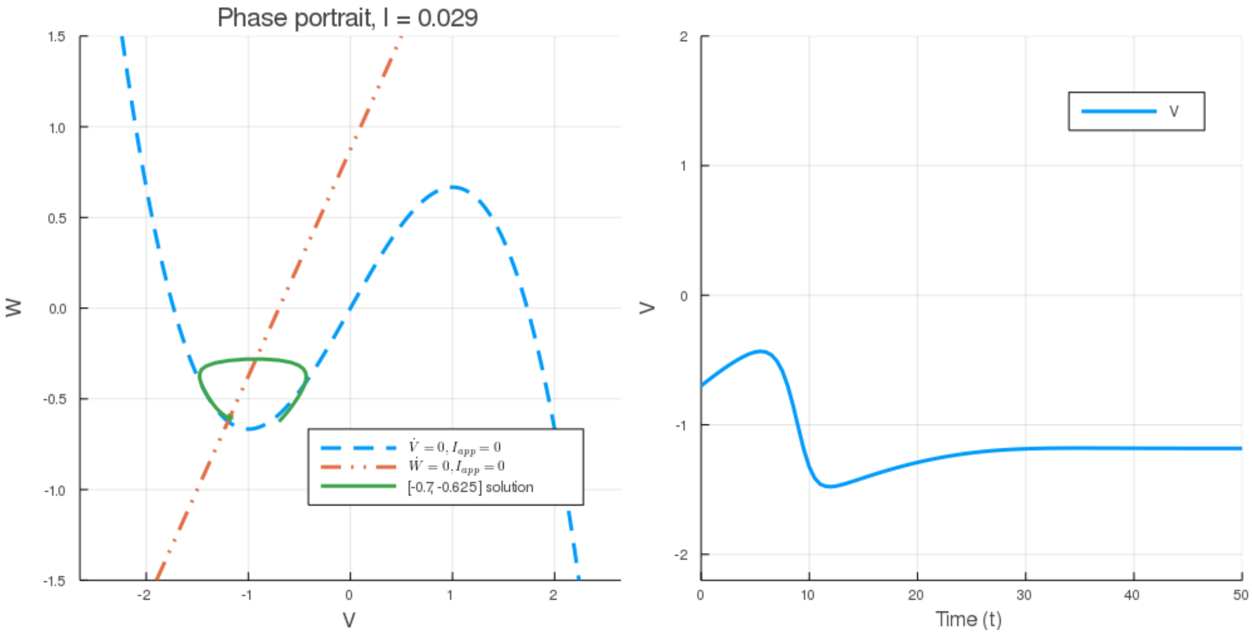

Figure 2: Phase portrait of weak current I = 0.029 (left) and action potential (right)

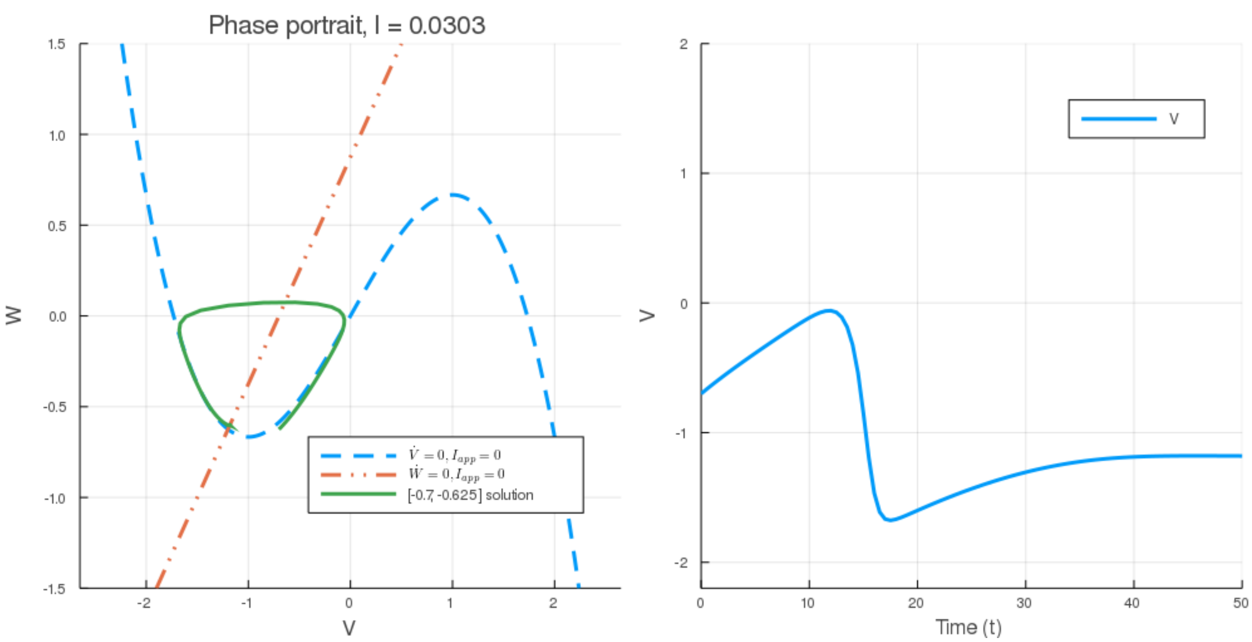

Figure 3: Phase portrait of slightly current I = 0.0303 (left) and action potential (right)

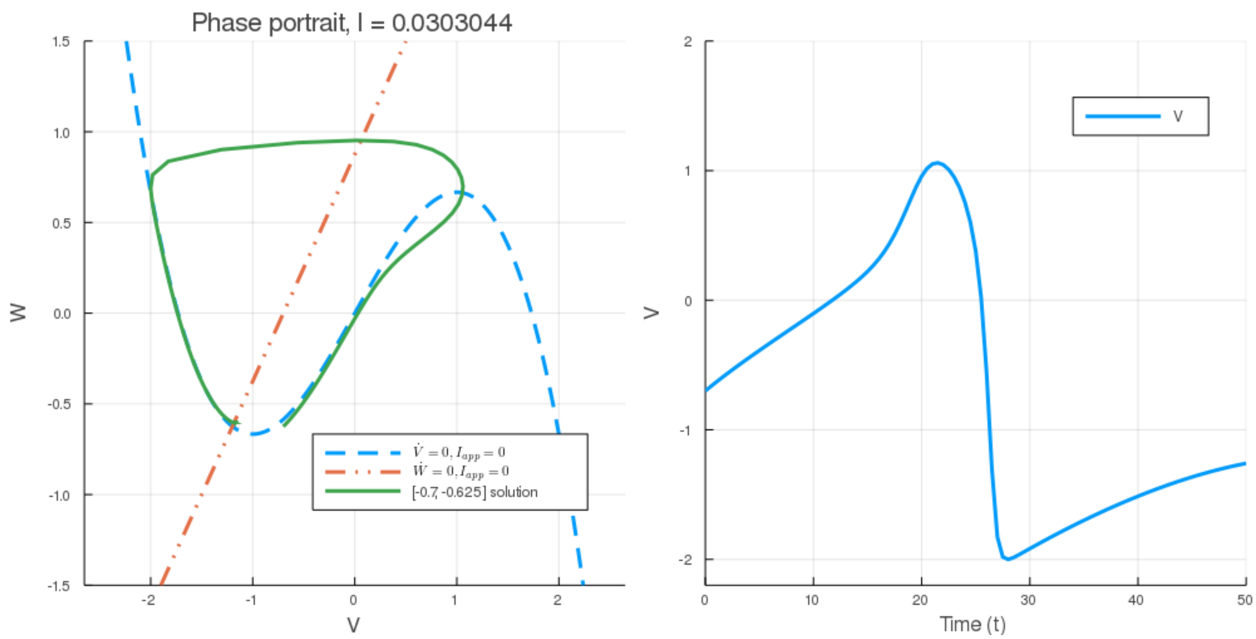

Figure 4: Phase portrait of medium current I = 0.0303044 (left) and action potential (right)

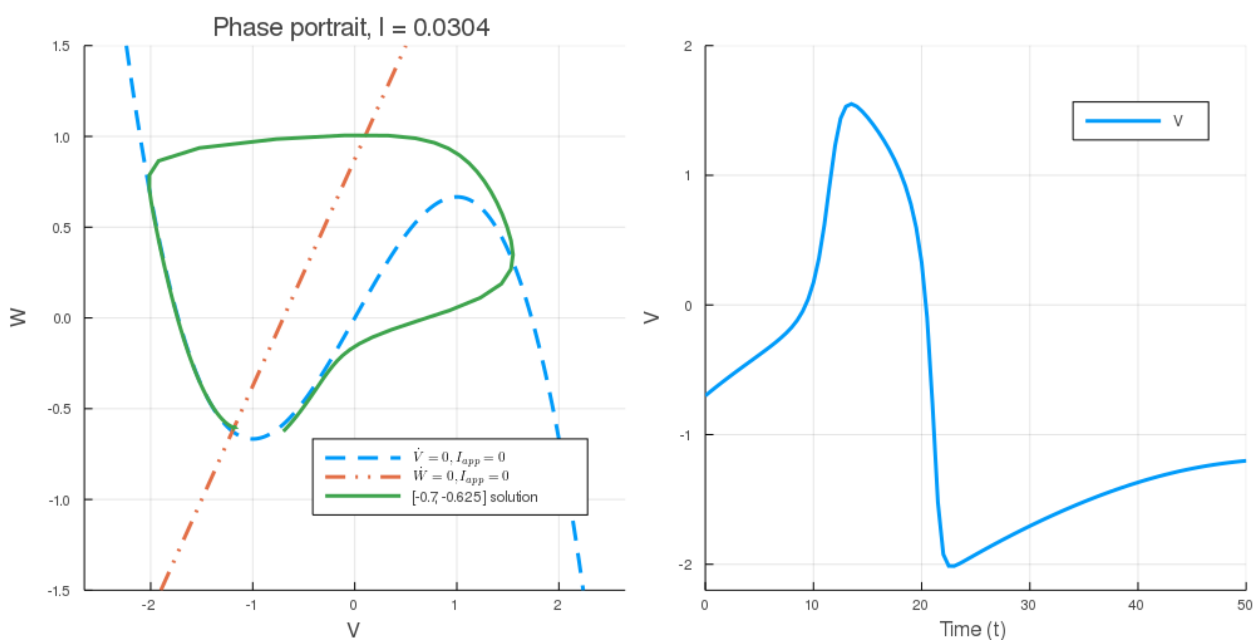

Figure 5: Phase portrait of "strong" current I = 0.0304 (left) and action potential (right)

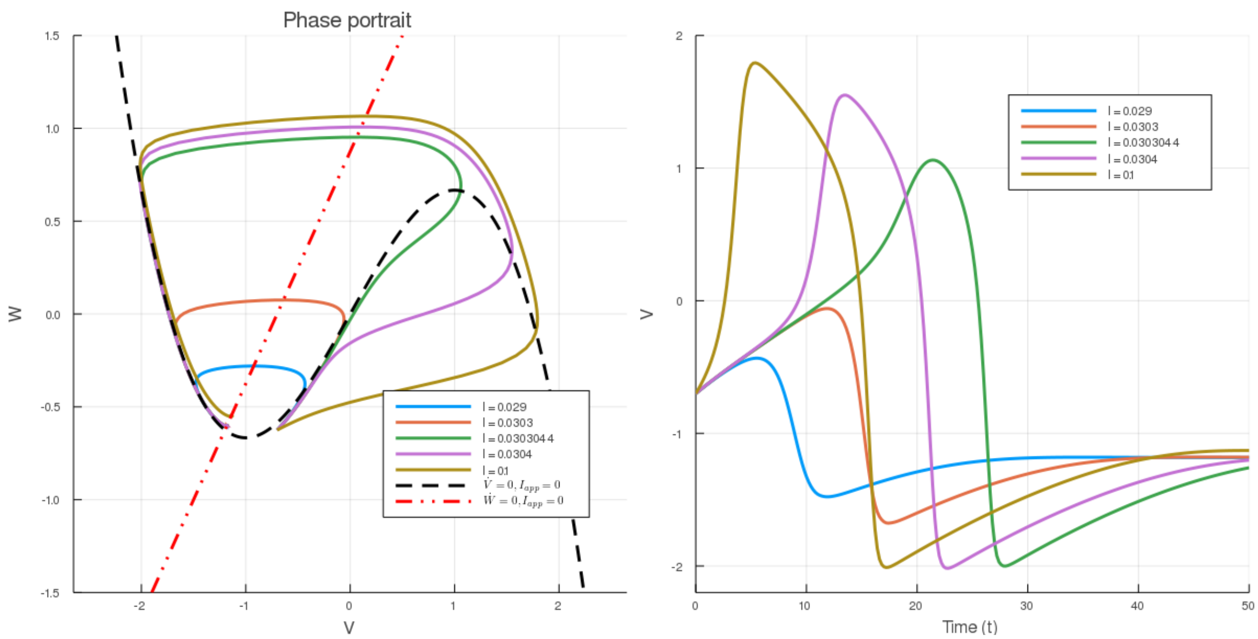

Figure 6: Phase portrait (left) and action potential (right)

To conclude this subsection, we can see that for the multiple action potential with graded amplitudes, there is no certain value that leads to a all-or-none response as it depends on the stimulus and the initial condition. Stronger stimulus invokes stronger action potential but eventually as t $\longrightarrow \infty$, they all go towards their corresponding steady state.

2.3 Repetitive firing

The FitzHugh-Nagumo model explains the excitation block phenomenon. Electrophysiology show that imposing a moderate current to the membrane result in a periodic spiking. When I is weak or zero (Figure 2), the steady state is on the left branch of the V-nullcline and the model is resting. Increasing I shifts the V-nullcline upward and the steady state slides on the W-nullcline. Before the model exhibits periodic spiking activity, the trajectories go into a stable focus, and the action potential spikes once then displays oscillations which get smaller as time goes on (Figure 7). When the model exhibits periodic spiking activity, the trajectories of the phase portrait form a stable limit cycle (Figure 8). We can take a quick notice is that the spike is quick and thin. Increasing the stimulus further shifts the equilibrium to the right (stable) branch of the V-nullcline, the action potentials here are long and thick while and the frequency between the spikes are short (Figure 9). It's really interesting to see how the trajectories unfold as we increases the intensity of the current, the spikes are reduced to smaller oscillations and the limit cycles in the phase portrait are reduced to stable focus (Figure 10 and Figure 11). When the applied current is too high then the oscillations are blocked by excitation (Figure 12). The precise mathematical mechanism involves appearance and disappearance of a limit cycle attractor, which is necessary if we want to dive deep in how the phenomenon unravels.

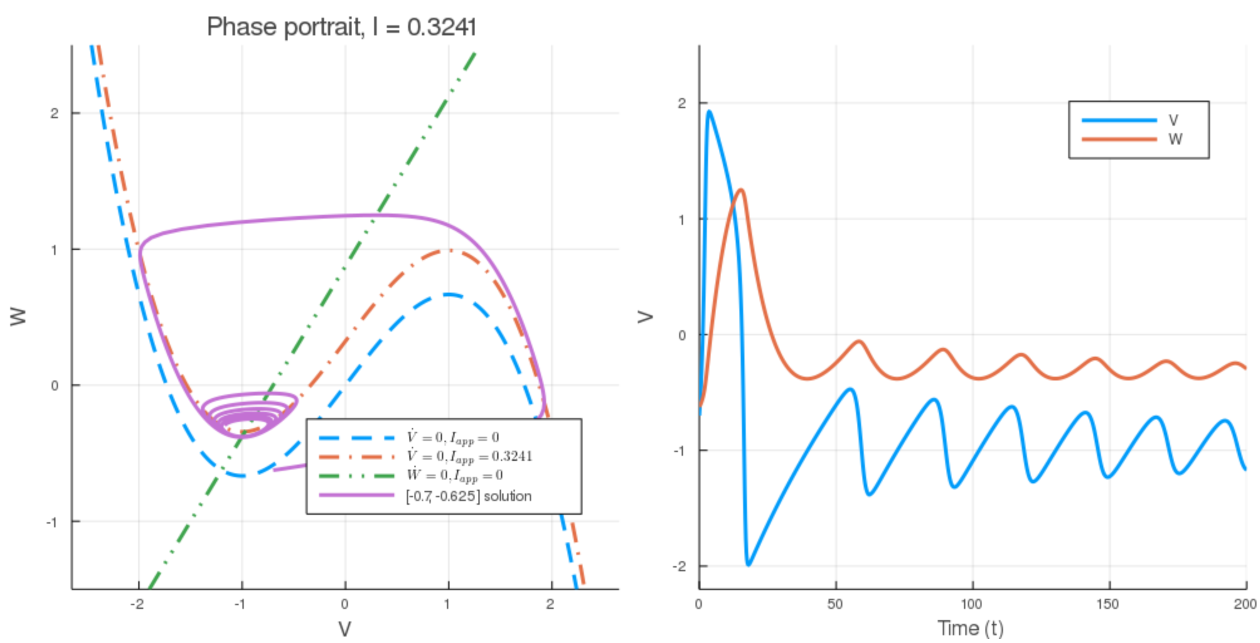

Figure 7: Phase portrait of current I = 0.3241 (left) and action potential (right)

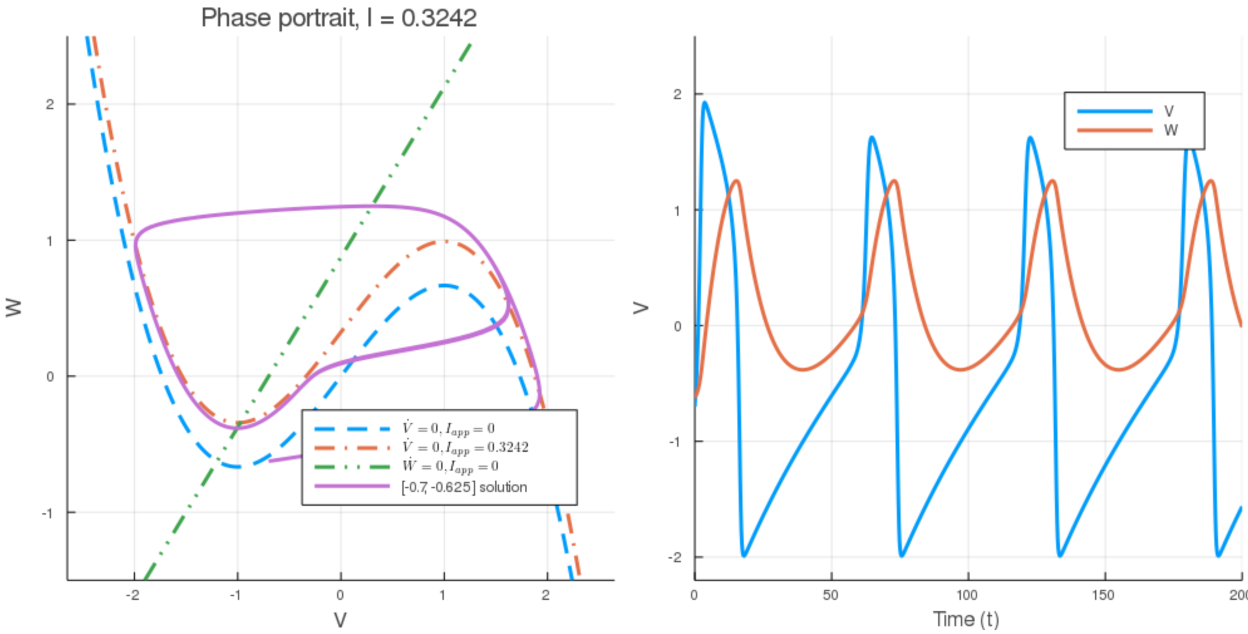

Figure 8: Phase portrait of current I = 0.3242 (left) and action potential (right)

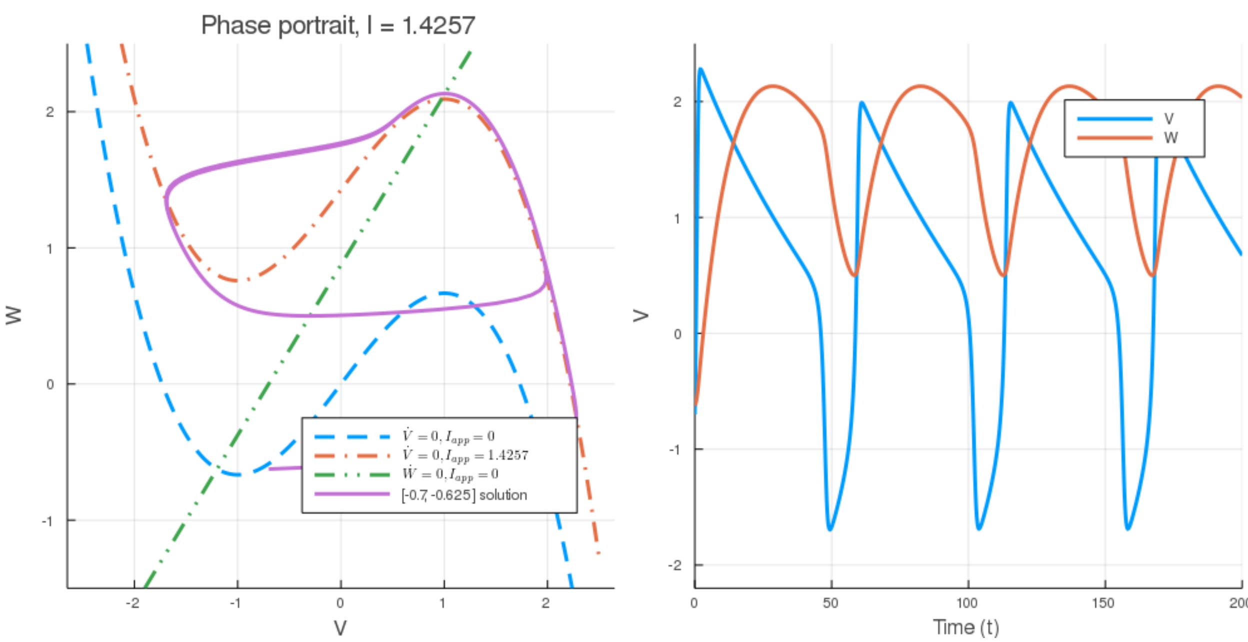

Figure 9: Phase portrait of current I = 1.4257 (left) and action potential (right)

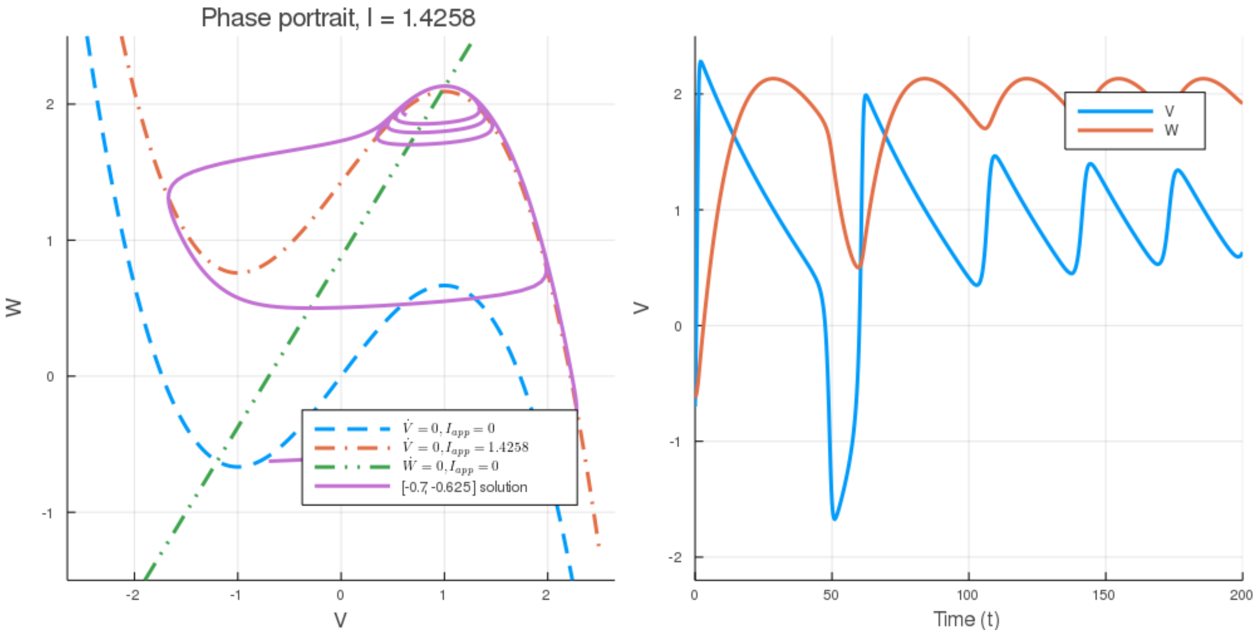

Figure 10: Phase portrait of current I = 1.4258 (left) and action potential (right)

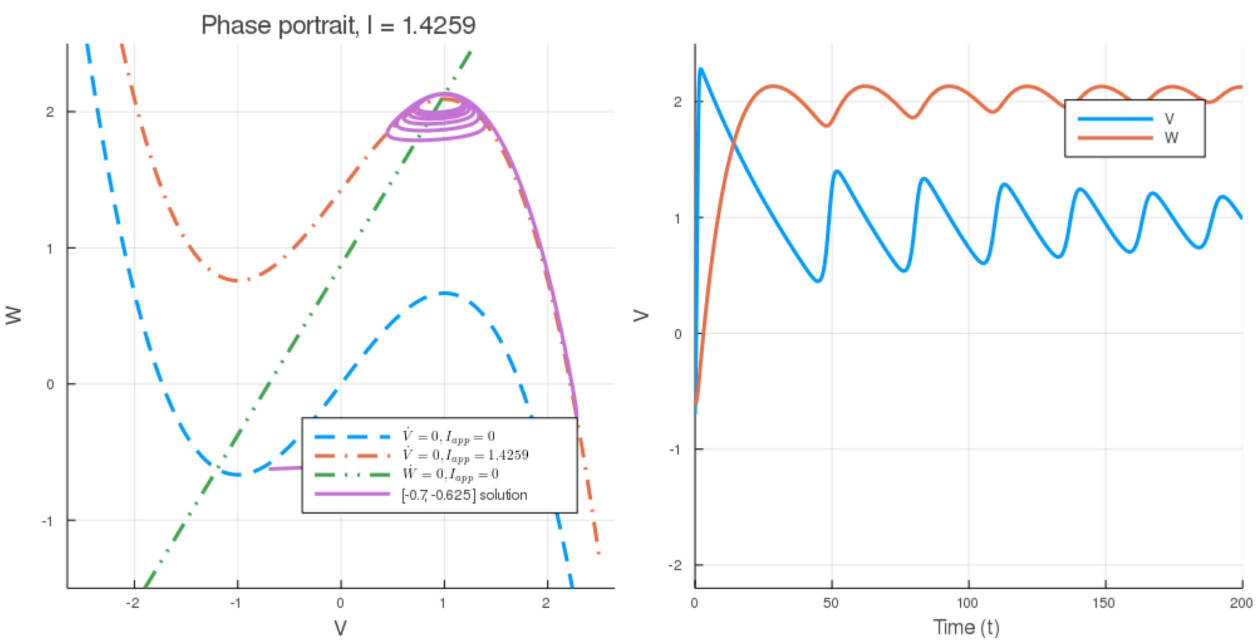

Figure 11: Phase portrait of current I = 1.4259 (left) and action potential (right)

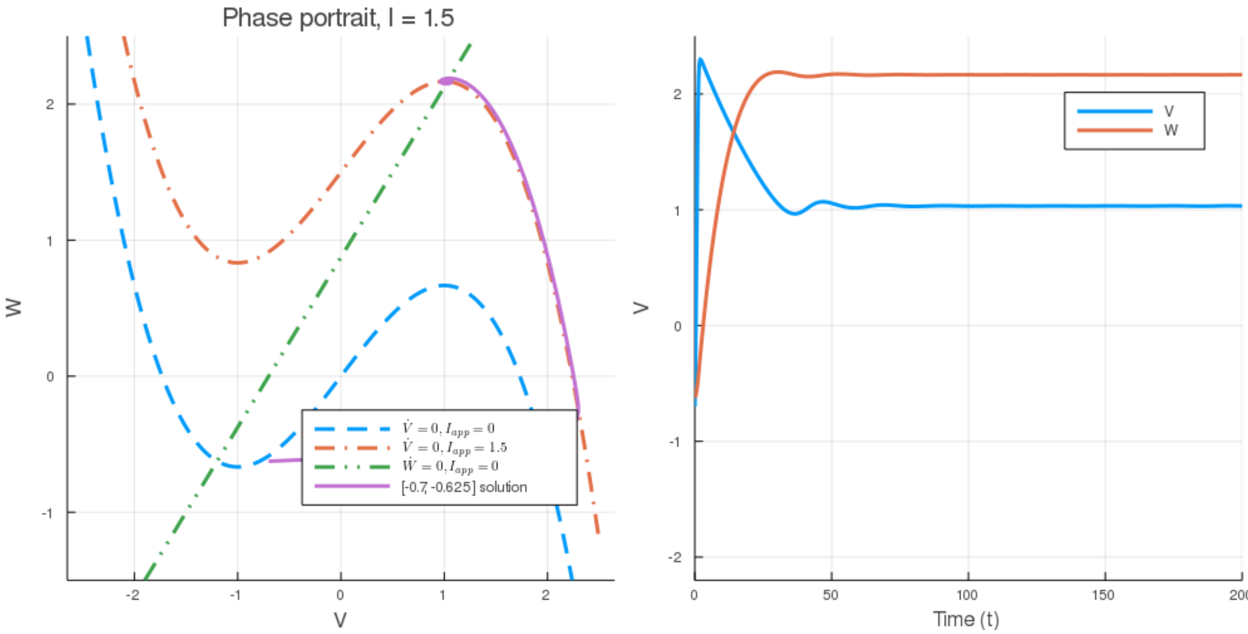

Figure 12: Phase portrait of current I = 1.5 (left) and action potential (right)

2.4 Anodal Break Excitation and Spike Accomodation

The FitzHugh-Nagumo model explained the phenomenon of post-inhibitory (rebound) spikes and dynamical mechanism of spike accommodation. As the stimulus I becomes negative (hyperpolarization), the resting state shifts to the left and then is released from it, the trajectory starts from a point far below the resting state that is outside of quasi-threshold area then fires a transient spike, and then returns to the resting state (Figure 13). As for spike accomodation, when the current I increases slowly, the neuron remains quiescent. The resting equilibrium of the FitzHugh-Nagumo model shifts slowly to the right, and the state of the system follows it smoothly then it fires a weak or no spikes at all (Figure 14)

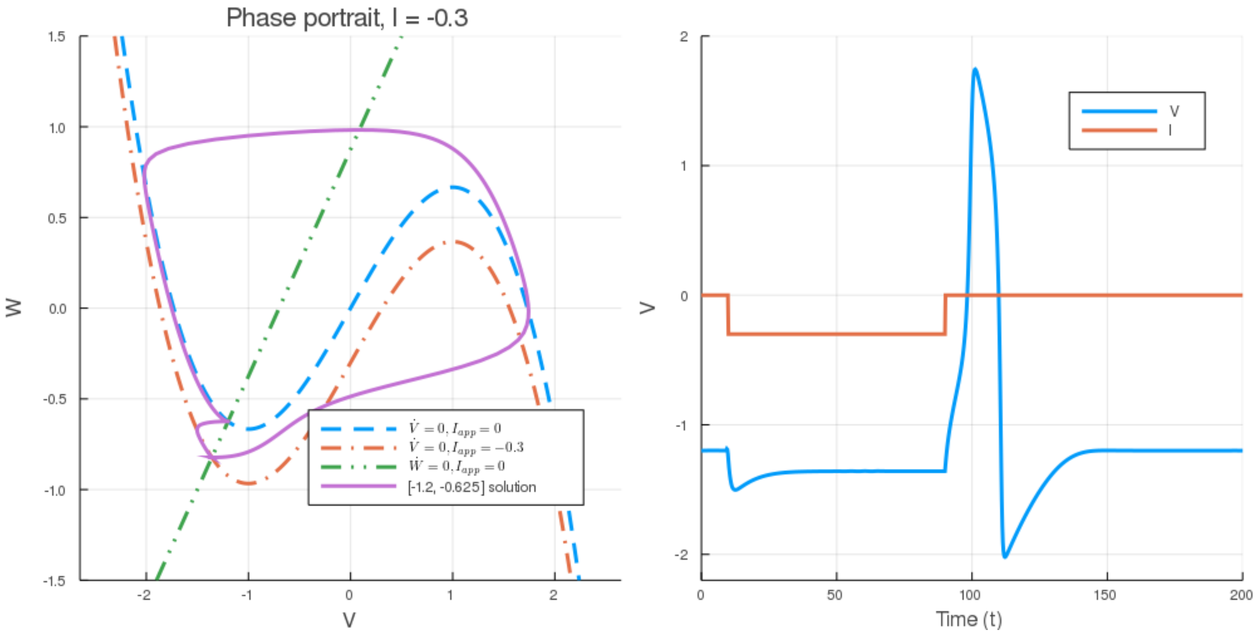

Figure 13: Phase portrait of break current I = -0.3 (left) and action potential (right)

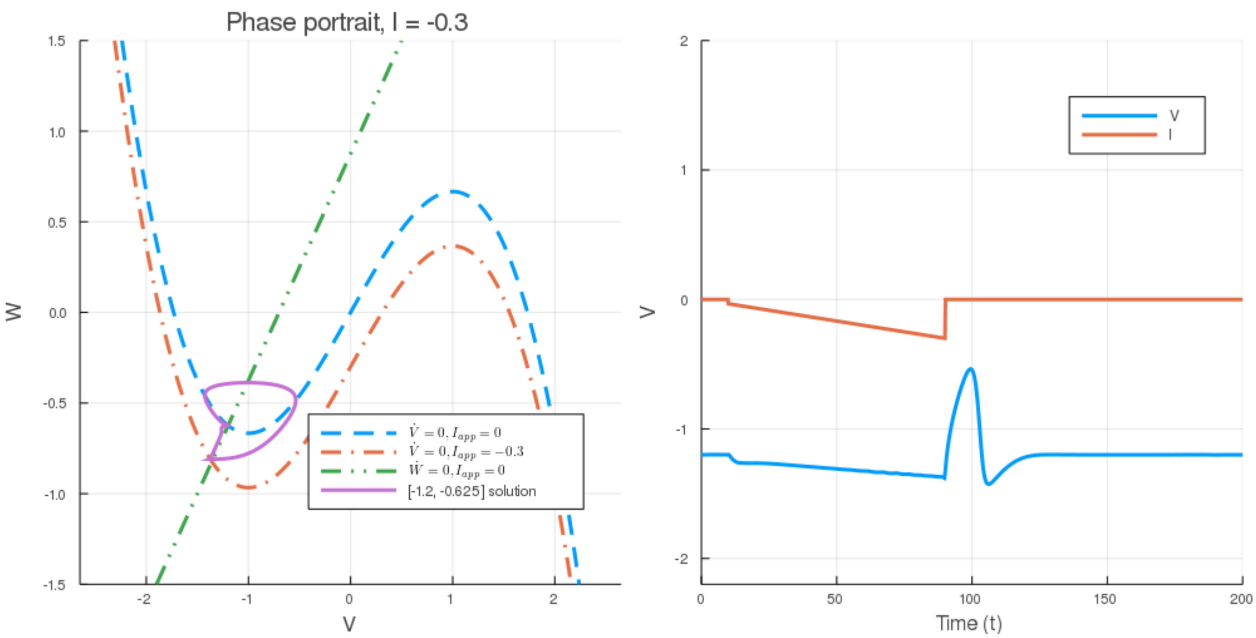

Figure 14: Phase portrait of accommodate current I = -0.3 (left) and action potential (right)

3 Application: Simplified cardiac models

Here, the FitzHugh-Nagumo model is a generic model for excitable media and can be applied to a variety of systems. Since neural and cardiac cells have many similarities, much of the mathematics and behavior of FitzHugh-Nagumo model can also be applied for cardiac models. The model is then be rewritten as

$$\dot{V} = (x - V)(V - 1)V - W + I_{app}$$

$$\dot{W} = \varepsilon(\alpha V - \beta - \gamma W)$$

where

- x is the threshold for excitation
- ε represents the excitability
- α, β, γ are parameters that can change the rest state and dynamics.

For application to cardiac dynamics, it can be modified to prevent the hyperpolarization phase at the end of repolarization and thus can represent a cardiac action potential by changing the first ODE to

$$\dot{V} = (a - V)(V - 1)V - \omega V W + I_{app}$$

where ω is a constant.

4 Conclusion

The Hodgkin-Huxley system represents a landmark achievement in the field of biomathematics, however it is difficult to analyze and largely inaccessible due to the fact that it is a four-dimensional system of equations. Richard FitzHugh and Nagumo successfully captured the important qualities of the H-H equations, in a system with only two dimensions.

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