DOING PHYSICS WITH PYTHON

COMPUTATIONAL NEUROSCIENCE

FITZHUGH-NAGUMO MODEL FOR SPIKING NEURONS

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DOWNLOAD DIRECTORIES FOR PYTHON CODE

Google drive **GitHub**

mnsFH01.py

The technique of phase plane analysis is used to model the action potentials generated by neurons with the Fitzhugh-Nagumo model where the dynamics is described by a two- state variable system: the membrane potential v and the recovery variable u. The Runge -Kuta method is used to solve the pair of coupled differential equations. For different models it may be necessary to make some changes to the Code. By changing the parameters, you can investigate in detail the dynamics of the Fitzhugh-Nagumo model of a spiking neuron and explore all the essential aspects of the model. The results are displayed as a phase space plot and a time evolution plot.

DYNAMICS OF THE FITZHUGH-NAGUMO MODEL

Nerve cells are separated from the extracellular region by a lipid bilayer membrane. When the cells aren't conducting a signal, there is a potential difference of about -70 mV across the membrane (outside of the membrane the potential is taken as zero). This potential difference is known as the cell's **resting potential**. On both sides of the nerve cell membrane, the concentrations of positive ions such as sodium, potassium and calcium and negatively chlorine ions and protein ions maintain the resting potential. When the cell receives an external stimulus, an **action potential** maybe evoked where the membrane potential **spikes** toward a positive value, in a process called **depolarization**, after which, **repolarization** (**hyperpolarization**) occurs where the membrane potential resets back to the resting potential.

The concentration of the sodium ions is much higher in the extracellular region than it is within the cell. The membrane contains gated channels that selectively allow the passage of ions though them. When the cell is stimulated, the sodium channels open and there is a rush of sodium ions into the cell. This sodium current raises the potential of the cell, resulting in depolarization. However, since the channel gates are voltage driven, the sodium gates close after a while. The potassium channels then open and

results in an outbound potassium current leading to the repolarization (hyperpolarization) of the cell.

In 1952, Hodgkin and Huxley explained this mechanism of generating action potential through their mathematical model. While this was a great success in the mathematical modeling of biological phenomena, the Hodgkin-Huxley model is complicated.

However, in 1961, R. Fitzhugh and J. Nagumo proposed a mathematical neuroscience model referred to as **Fitzhugh-Nagumo** model. This model is a simpler version of the Hodgkin-Huxley model which demonstrates the spiking potentials in neurons and emulates the potential signals observed in a living organism's excitable nerve cells. The Fitzhugh-Nagumo model has only a few parameters and two coupled differential equations for the **membrane potential** v, and the **recovery variable** u, which modulates v.

The pair of coupled first order equations defining the Fitzhugh-Nagumo Model are

(1A) $$\frac{dv}{dt} = v - v^3/3 - u + I_{ext}$$

(1B) $$\frac{du}{dt} = \frac{1}{c}(v + a - bu)$$

The variable v is a voltage-like **membrane potential** having cubic nonlinearity that allows regenerative self-excitation via a positive feedback and u is called the **recovery variable** having linear dynamics that provides slower negative feedback. The parameter I_{ext} corresponds to a stimulus current. A positive current, $I_{ext} > 0$ corresponds to a current directed from outside the cell membrane to inside. The parameters a and b are controlling parameters of the system. The parameter c (time constant for u) is responsible for the evolution of u being slower than the evolution of v.

fast sodium dynamics → v membrane potential

slow sodium / potassium dynamics → u current variable

$\dot{v} / \dot{u} \sim 10$

The two nullclines in the v-u plane are given by

***v*-nullcline** $\frac{dv}{dt} = 0 \Rightarrow v - v^3/3 - u + I_{ext} = 0$ **cubic polynomial**

***w*-nullcline** $\frac{du}{dt} = 0 \Rightarrow v + a - bu = 0$ **straight line**

The intersection of the two nullclines gives the **critical points** (**fixed points or equilibrium points**) of the model.

The parameter I_{ext} simply shifts v-nullcline up or down, but does not have any effect on the u-nullcline. Changing I_{ext} modulates the position of the critical point. The position of the critical point determines the dynamics of the membrane potential v. A phase portrait plot shows the v-u vector field by arrows pointing in the direction of increasing time. The vector field is normalized so that each arrow has unit length. The v-u trajectory is always tangential to the vector field described by the arrows. The vector field (direction of the arrows) indicates the sign of dv/dt and the sign of du/dt. The trajectories cannot cross (uniqueness of solutions).

Fitzhugh-Nagumo model describes an excitable system and the model is a two-dimensional simplification of the Hodgkin-Huxley. The action of an excitable neuron has the following characteristics that we know from experiments:

- The neuron cell is initially at a resting potential value.
- If we experimentally displace the potential a little bit, it returns to the resting value.
- If the perturbation is higher than a threshold value, the potential will shoot up to a very high value. In other words, a spike will occur. After the spike the membrane potential will return to its resting value.

We model the fact that the neuron as a resting potential. Since it is a stable equilibrium, small perturbation always leads to trajectory that converge on it, whereas a big perturbation will start the spiking. This equilibrium cannot be unique and the self-excitation occurs by a positive feedback loop. It is the recovery variable u that has a slower dynamic (time scale parameter c) that brings back the system toward the resting potential.

SIMULATIONS

All quantities in the model are expressed in arbitrary units and not in S.I. units. The external current is taken as a constant

$$I_{ext} = constant.$$

For all simulations: a = 0.70, b = 0.80, and c = 12.50.

We can estimate the coordinates of fixed points (v_E, u_E) in v-u phase space by finding the roots of a cubic polynomial.

$$\frac{dv}{dt} = 0 \Rightarrow v_E - {v_E}^3/3 - u_E + I_{ext} = 0$$

$$\frac{dw}{dt} = 0 \Rightarrow v_E + a - b u_E = 0 \quad u_E = (v_E + a)/b$$

$$(-b/3){v_E}^3 + (b-1)v_E - (a + B I_{ext}) = 0$$

Simulation 1 $I_{\text{ext}} = 0$

When the external current stimulus is zero, $I_{\text{ext}} = 0$, the membrane potential v and the recovery variable u are at the resting values for the system which is the stable fixed point $v_E = -1.20$, $u_E = -0.62$. If the system is briefly disturbed from its equilibrium, then the system will evolve back to its stable fixed point. This response of the system is clearly shown by examination of the vector field displayed as a quiver plot and a streamplot (figure 1).

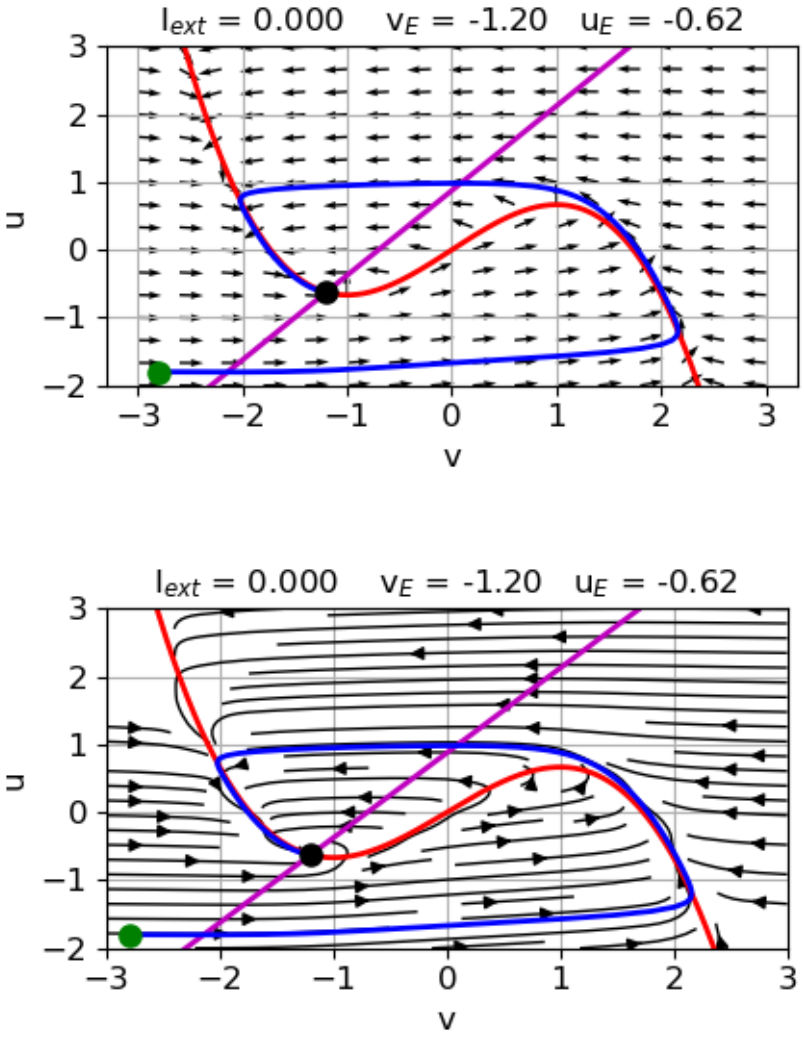


Fig. 1.1. The vector field shown as a quiver plot and as a streamplot. The red cubic curve is are the v-nullcline and the magenta straight line is the u-nullcline. The intersection of the v-nullcline and the u-nullcline gives the single stable fixed point (v_E, u_E) of the system. $v_E = -1.20$, $u_E = -0.62$. The green dot gives shows the initial condition $v(0)$ and $u(0)$ and the blue curve is the trajectory.

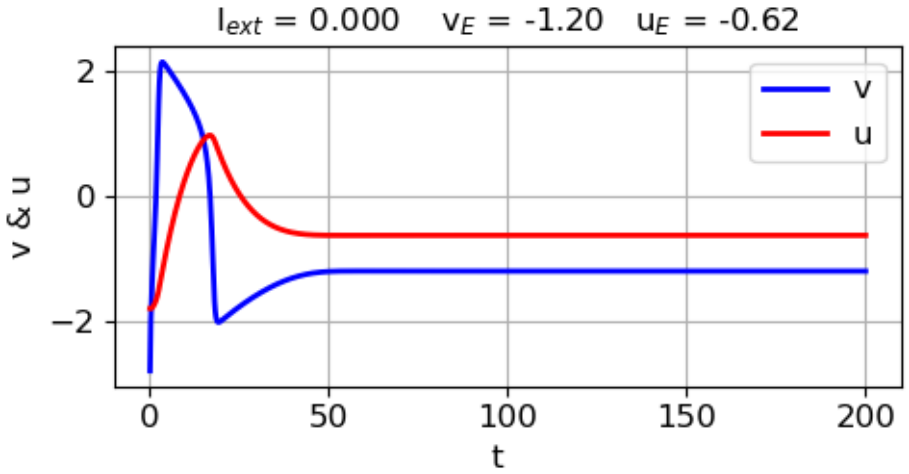


Fig. 1.2, All trajectories with different initial conditions will converge to the stable fixed point $v_E = -1.20$, $u_E = -0.62$. For the initial condition $v(0) = -2.8$ and $u(0) = -1.8$ a single spike is fired and there is no spike train.

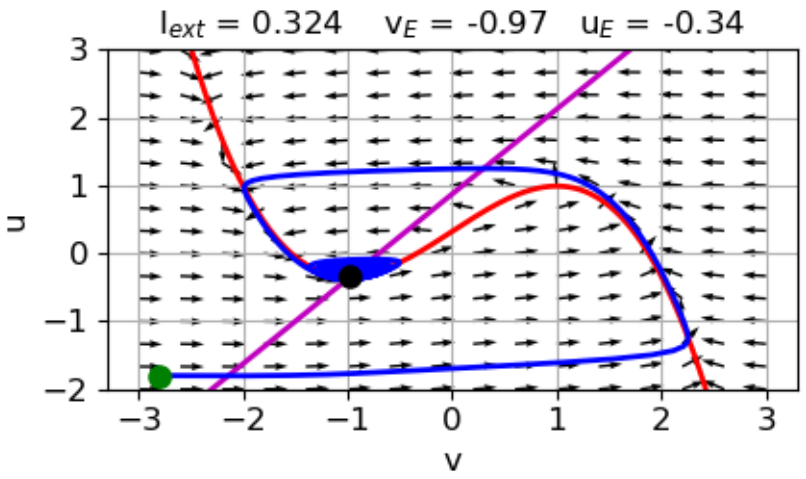
Simulation 2 I_{ext} = 0.324 and I_{ext} = 0.325

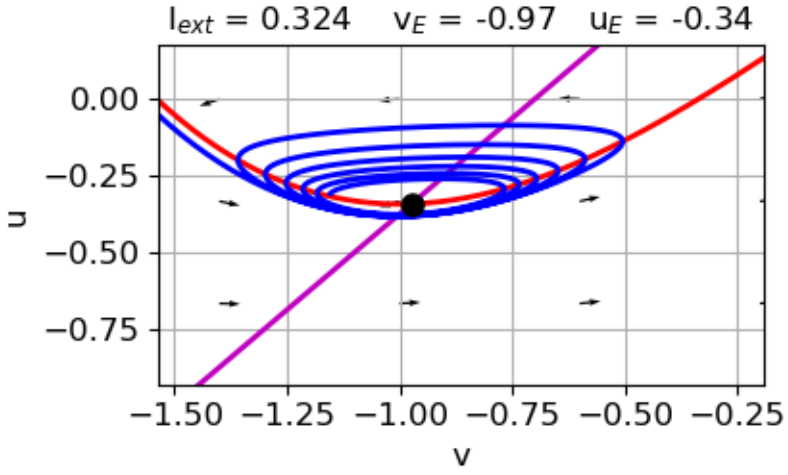
The external current stimulus is a bifurcation parameter. A slight change in the bifurcation parameters can lead to a dramatic change in the response of the system.

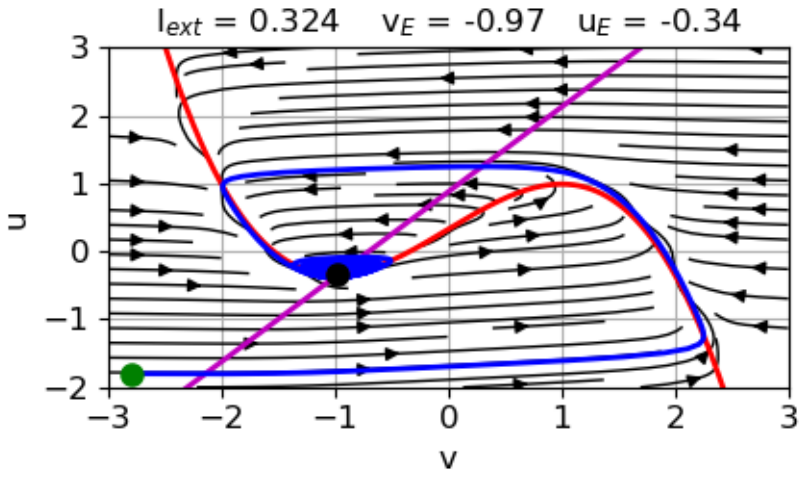
$I_{ext} = 0.324$ Subthreshold current

Fixed point remains stable ⇒ small damped oscillations

After an initial spike, there are small oscillations around the stable fixed point which become quickly damped without an action potential being initiated. The phase space trajectory is attracted to the fixed point. For this weak current stimulus, there is a single **stable** fixed point ($v_E = -0.97$, $u_E = -0.34$).




I_{ext} = 0.324 v_E = -0.97 u_E = -0.34
0.00
−0.25
−0.50
−0.75
u
−1.50 −1.25 −1.00 −0.75 −0.50 −0.25
v


I_{ext} = 0.324 v_E = -0.97 u_E = -0.34
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1
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−3 −2 −1 0 1 2 3
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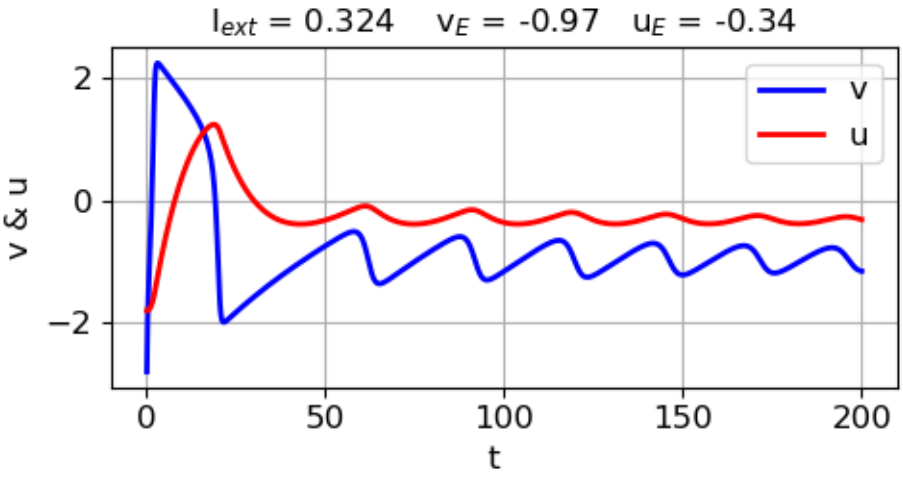
I_{ext} = 0.324 v_E = -0.97 u_E = -0.34
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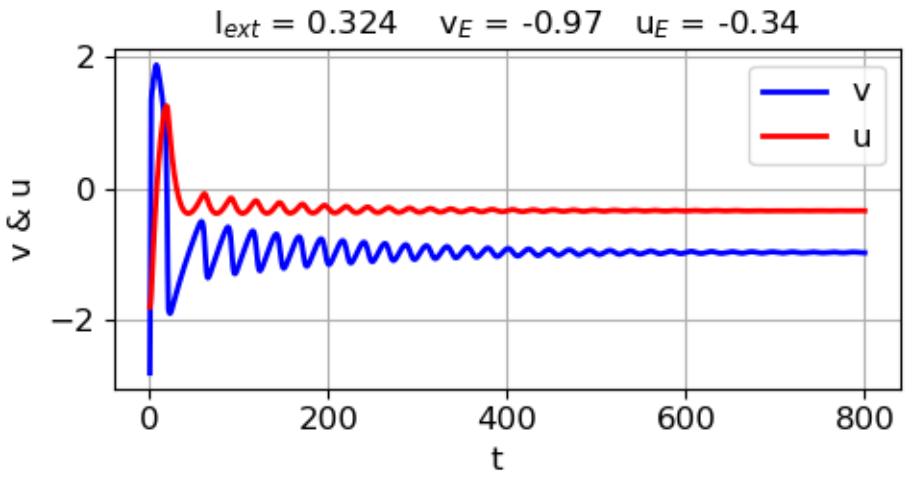


Fig. 2.1. Fixed point v_E = -0.97 and u_E = -0.34.

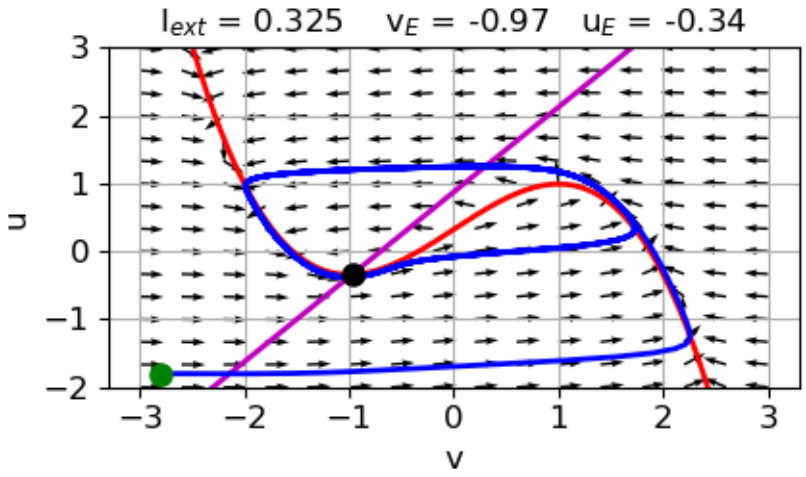
$I_{ext} = 0.325$ Super-threshold current

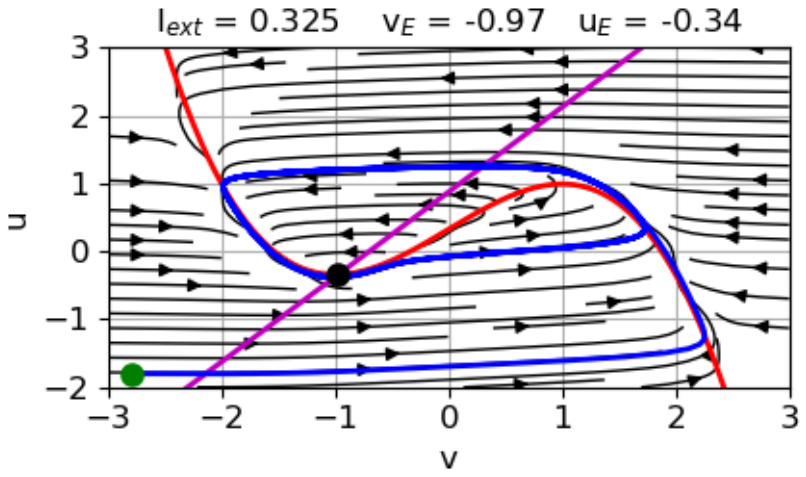
The fixed point becomes unstable

Onset of sustained oscillations (Hopf-bifurcation)

The fixed point is an unstable equilibrium point. A series of action potentials are generated. The neuron spikes repetitively, that is, the model exhibits periodic (**tonic spiking**) activity. The fixed-point acts as a centre. The trajectory forms closed loops around the fixed point which results in the repetitive spiking of the neuron. At the start, v increases and u remains nearly unchanged. When the trajectory approaches the v-nullcline, $dv/dt \rightarrow 0$ and the trajectory follows the v-nullcline as u rapidly increases until the u-nullcline is reached where and the evolution of v dominates and the curve becomes horizontal

once again. This continues until the trajectory hits the left part of the v-nullcline. The trajectory begins to hug the v-nullcline and starts a slow downward ward journey. Thus, the trajectory sweeps out a closed orbit and never hits the critical point and therefore keeps repeating itself.





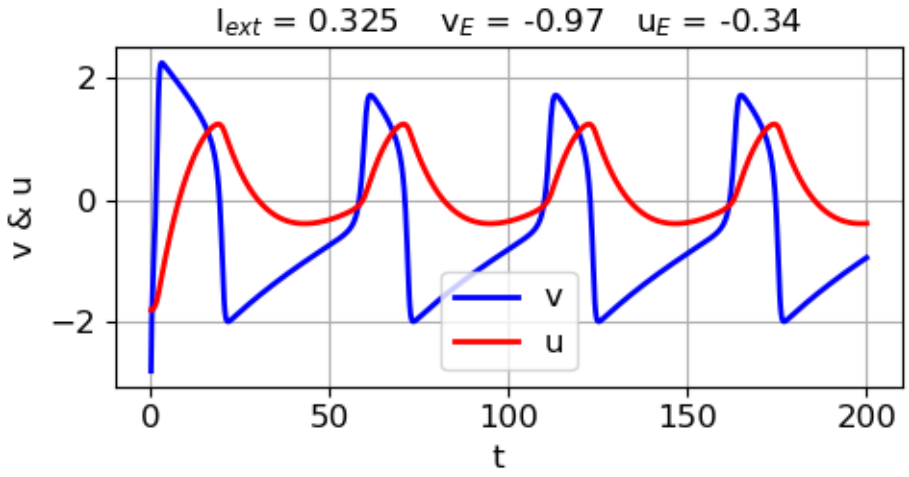


Fig. 2.2. A series of action potentials are produced. The fixed equilibrium point is **unstable** and leads to tonic firing of the neuron. After a spike, the neuron returns to its resting state and during the following refractory period, the system is indifferent to any external stimulus.

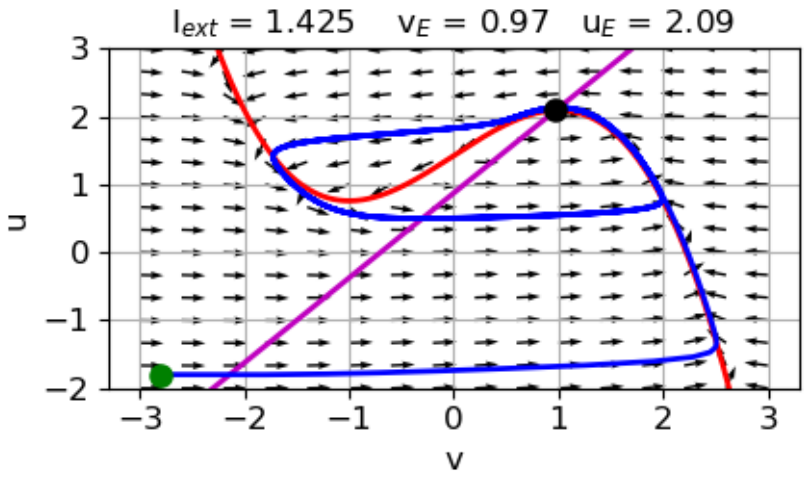
As I_{ext} increases through I_{ext} ~ 0.325, a **Hopf bifurcation** occurs where the stable fixed point loses its stability and becomes unstable. The phase space trajectory changes from being attracted to the stable fixed point to a trajectory attracted to a limit cycle and a periodic spiking of the neuron occurs.

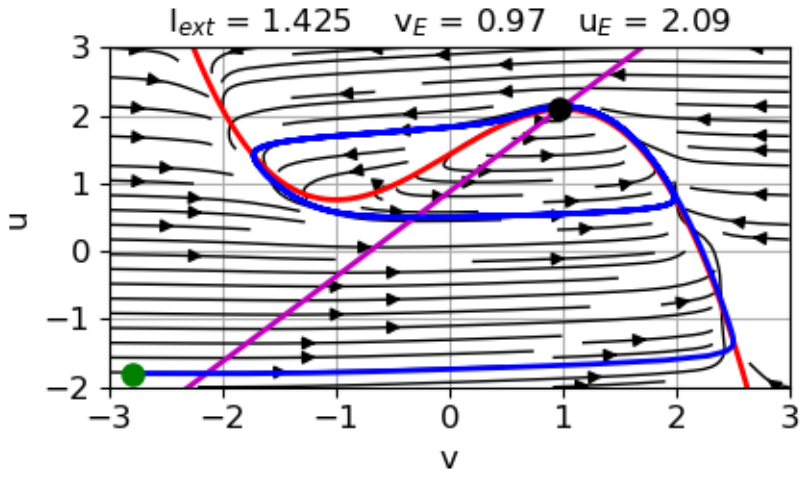
Simulation 3 I_{ext} = 1.425 and I_{ext} = 1.426

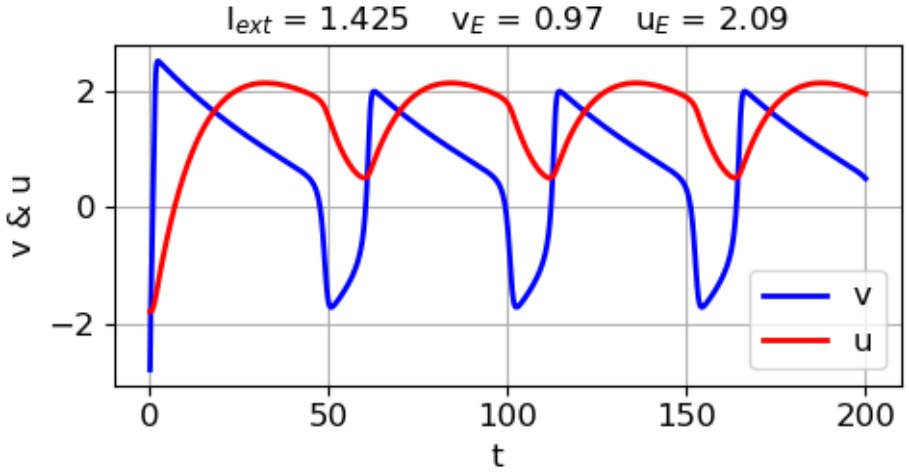
I_{ext} = 1.425 Fixed point unstable ⇒ Hopf-bifurcation to sustained oscillations on limit cycle

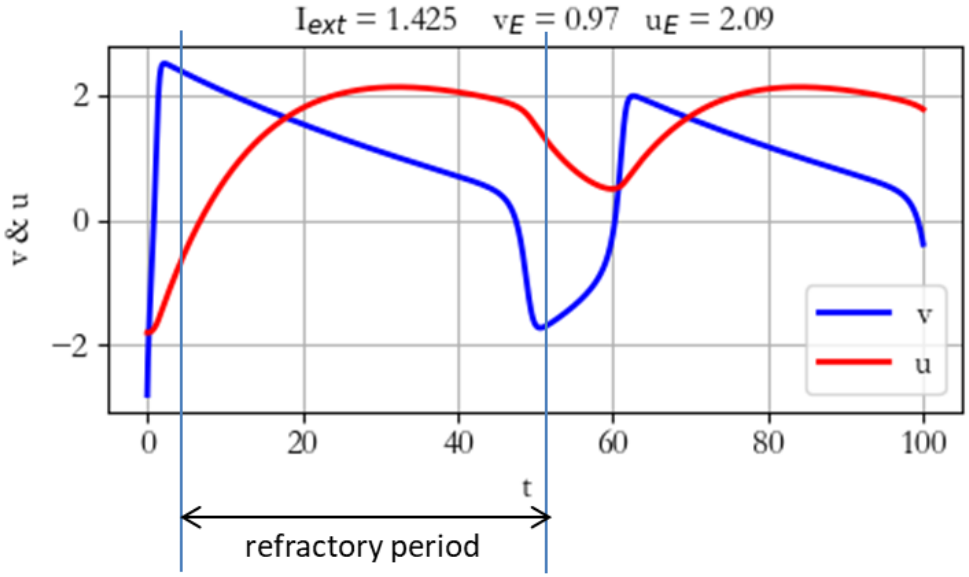
I_{ext} = 1.426 Fixed point stable ⇒ Hopf-bifurcation to damped oscillations

For I_{ext} **= 1.425** the fixed-point acts as a center and the trajectories form closed loops around the fixed point which results in the repetitive spiking of the neuron. However, when I_{ext} **> 1.425** the trajectory is attracted to the fixed point and no action potentials are generated.









Immediately after spike the neuron is indifferent to further input

Fig. 3.1.

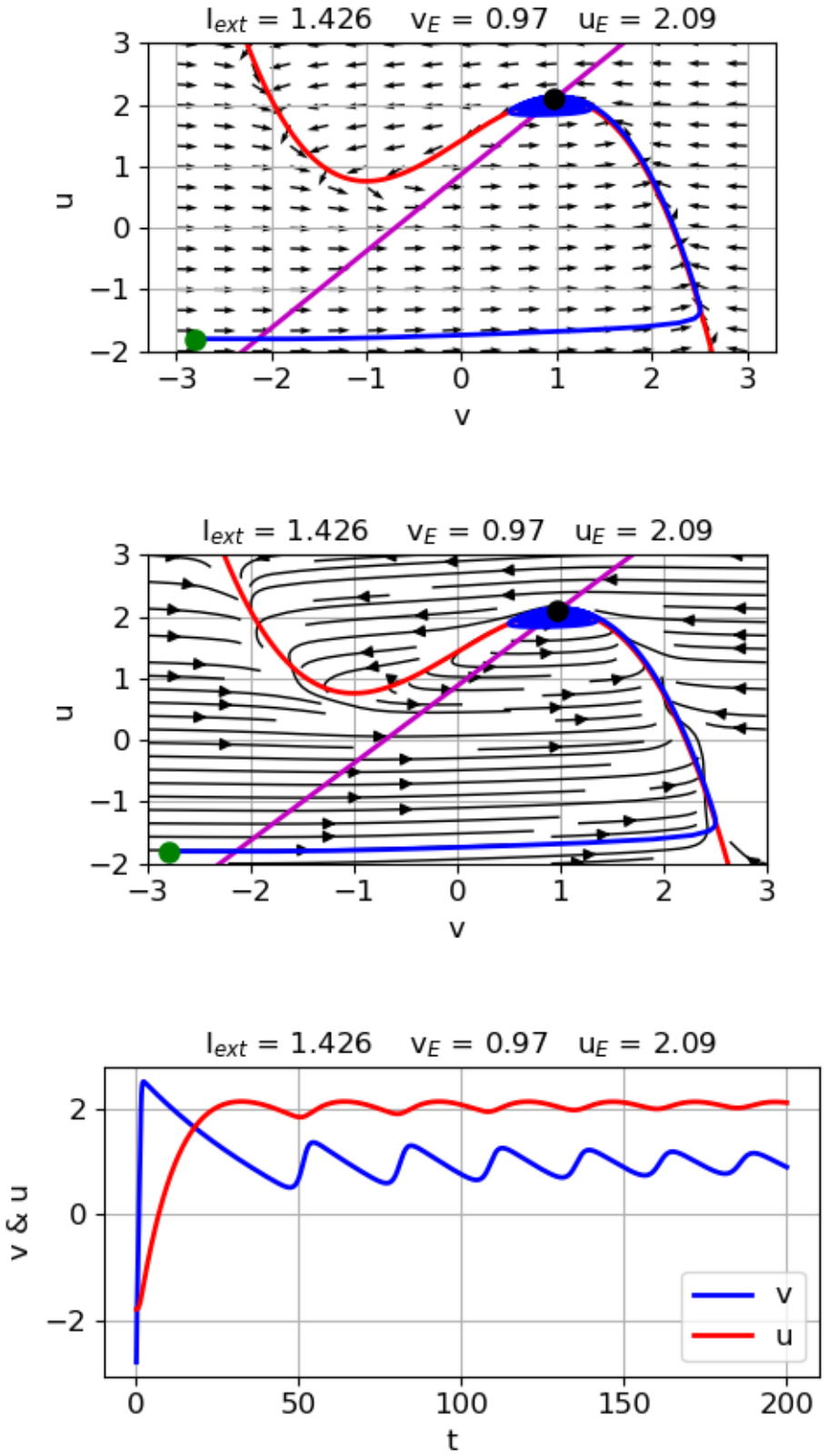
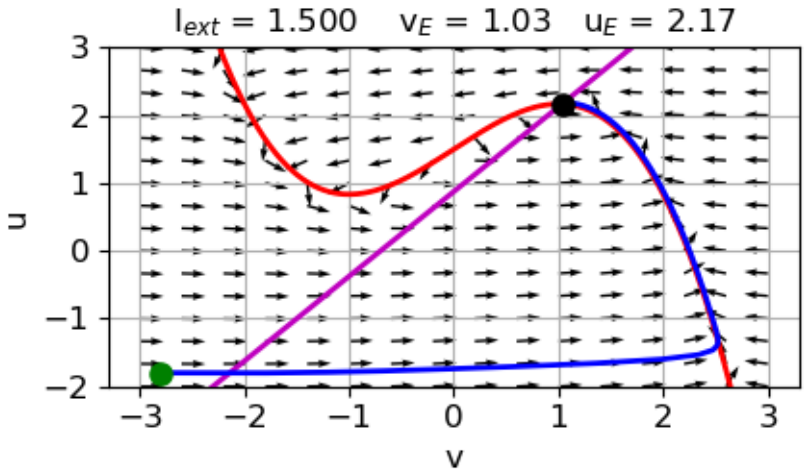
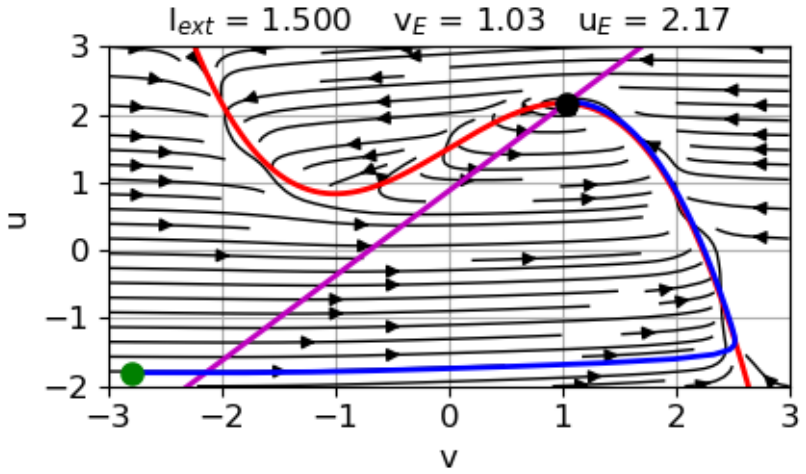


Fig. 3.2. At the start $\left(dv/dt > 0 \quad dw/dt > 0\right)$, v evolves faster than u, that is, v increases rapidly while u remains virtually unchanged

(near-horizontal part of the v-u trajectory). As the trajectory approaches the v-nullcline, the rate of change of v slows down and u becomes more prominent. Since du/dt is still positive, u must increase, and the trajectory moves upwards. The fixed-point then attracts this curve and the evolution ends at the fixed-point.





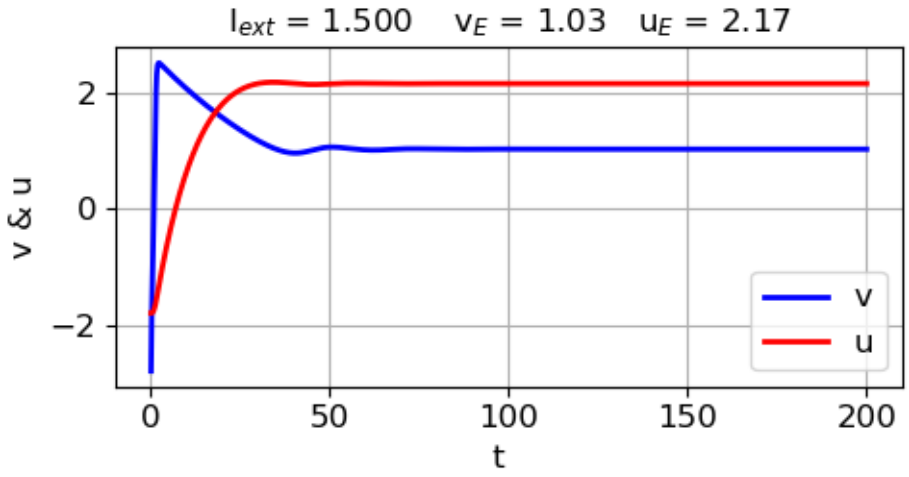


Fig. 3.3.

SUMMARY

The motivation for the Fitzhugh-Nagumo model was to isolate conceptually the essentially mathematical properties of excitation and propagation from the electrochemical properties of sodium and potassium ion flow. The model consists of a voltage-like variable having cubic nonlinearity that allows regenerative self-excitation via positive feedback, and a recovery variable having a linear dynamics that provides slower negative feedback. The model gives only a single fixed point. The external current stimulus is a bifurcation parameter where slight changes at the bifurcation points result in very different system responses.

I_{ext}	v_E	u_E	Description
0	-1.20	-0.62	single stable fixed point
0.324	-0.97	-0.34	decaying orbits to single stable fixed point
0.325	-0.97	-0.34	spike train: limit cycles around fixed point
1.425	0.97	2.09	spike train: limit cycles around fixed point
1.426	0.97	2.07	trajectory decays to stable fixed point
1.500	1.03	2.17	trajectory decays rapidly to stable fixed point

LINKS

Scholarpedia: Fitzhugh-Nagumo Model
http://www.scholarpedia.org/article/FitzHugh-Nagumo_model

https://www.normalesup.org/~doulcier/teaching/modeling/excitable_systems.html

https://perso.u-cergy.fr/~atorcini/ARTICOLI/lezione4-zillmer.pdf

pbs006.htm cnsFNA.m