COMPUTATIONAL NEUROSCIENCE REPORT

Biophysical Basis for Three Distinct Dynamical Mechanisms of Action Potential Initiation

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INTRODUCTION

Hodgkin, in 1948, based on excitability, classified neurons into three classes Type I, Type II, and Type III neurons. The authors have derived a single two-dimensional and a three-dimensional model to explain the biophysical basis of excitability for all three classes of neurons. They took recordings from the spinal sensory neurons representing each neuron class and reproduced their transduction properties. The neuronal model is a modification of the famous Morris- Lecar neuronal model (1981).

THE THREE CLASSES OF NEURONS AND THEIR SPIKING PATTERNS:

Class I or the Type I neurons show a tonic spiking pattern to give a continuous f-I curve.

Class II neurons show a phasic spiking pattern to give a discontinuous f-I curve.

Class III neurons fail to spike repeatedly: typically, they spike only once at the onset of stimulation.

THE 2-D NEURONAL MODEL

$$C\,dV/dt = I_{stim} - \bar{g}_{fast}\, m_{\infty}(V)(V - E_{Na}) - \bar{g}_{slow} w (V - E_K) - g_{leak}(V - E_{leak})$$

V = fast acting variable, the membrane potential; it controls instantaneous activation of fast inward current

w = slow recovery variable; it is a function of voltage that controls the activation of slow outward current

$$dw/dt = \phi_w \frac{w_{\infty}(V) - w}{\tau_w(V)}$$

dw/dt corresponds to the relaxation process by which the ion channel opens or closes.

$$m_{\infty}(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_m}{\gamma_m}\right)\right]$$

$$w_{\infty}(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_w}{\gamma_w}\right)\right]$$

m_{∞}, w_{∞} = open state probability functions.

m, w = instantaneous open state probability

$$\tau_w(V) = 1/\cosh\left(\frac{V-\beta_w}{2\cdot\gamma_w}\right)$$

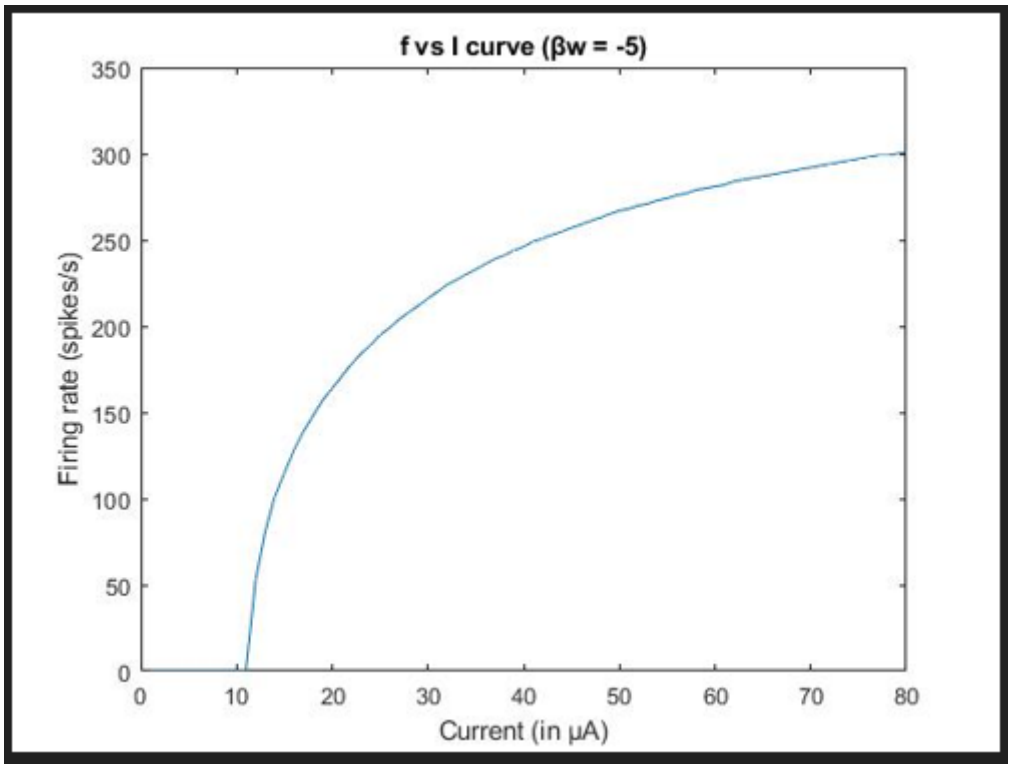
τ_w = time scale for the recovery process; it is the time constant for K^+ channels relaxation in response to the change in voltage

β = an independent variable that converts the model between all three classes of excitability, it corresponds to the voltage dependency of slow outward current; the value of β defines the neuronal class, $\beta > -10$ corresponds to Class I whereas $\beta < -10$ corresponds to other Classes.

Spiking pattern for different classes of neurons

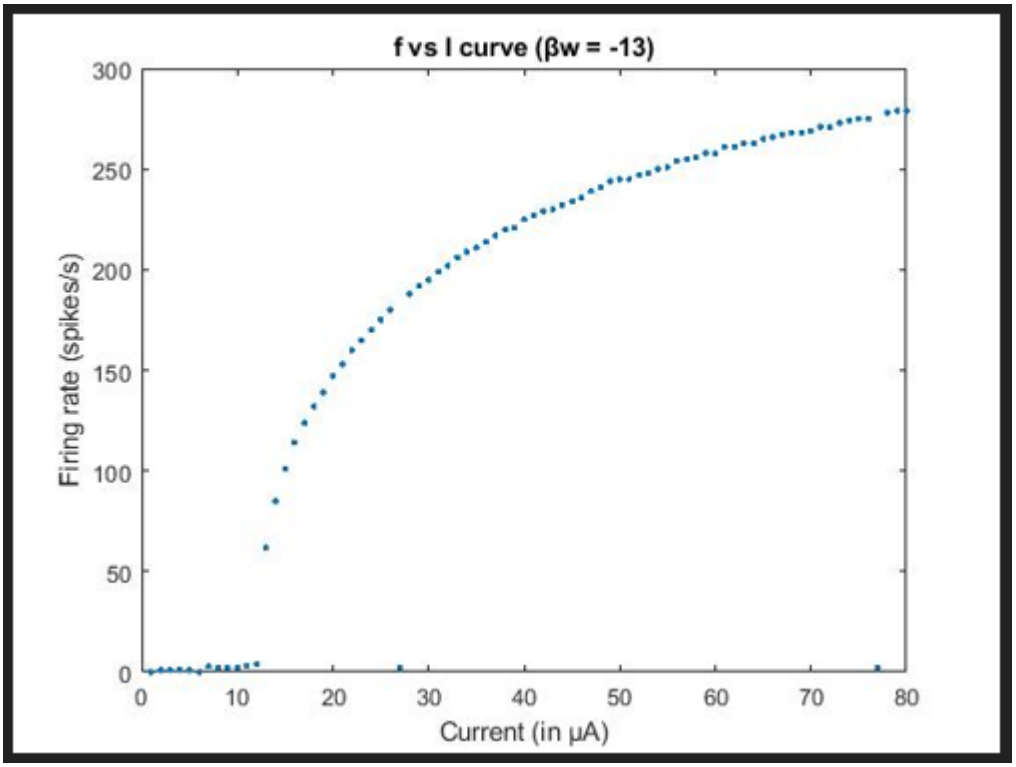
Freuency-current curve

Class I neurons



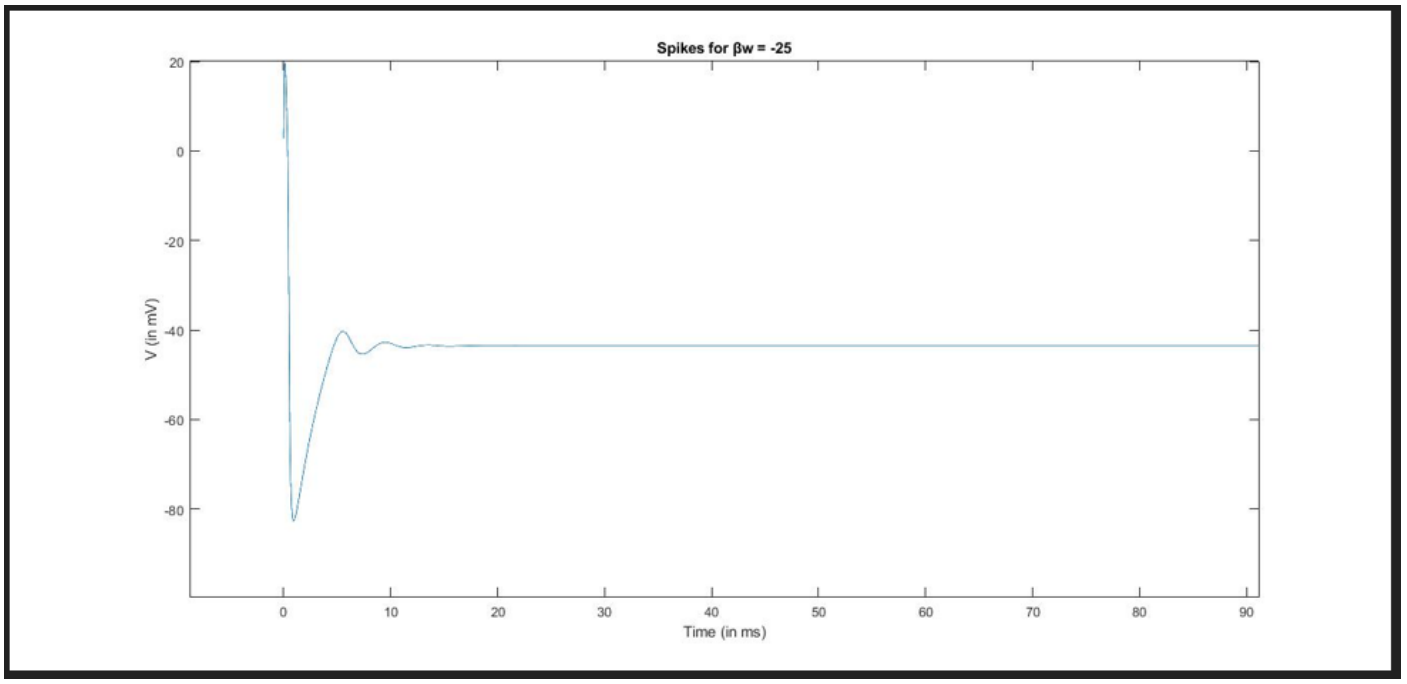
Class I neurons show a continuous f-I curve because of their ability to fire even at weak stimulation. In addition, these neurons can spike till the stimulation lasts.

Class II neurons



Class II neurons show a discontinuous f-I curve because these neurons only at a critical range of frequency.

CLASS III NEURONS

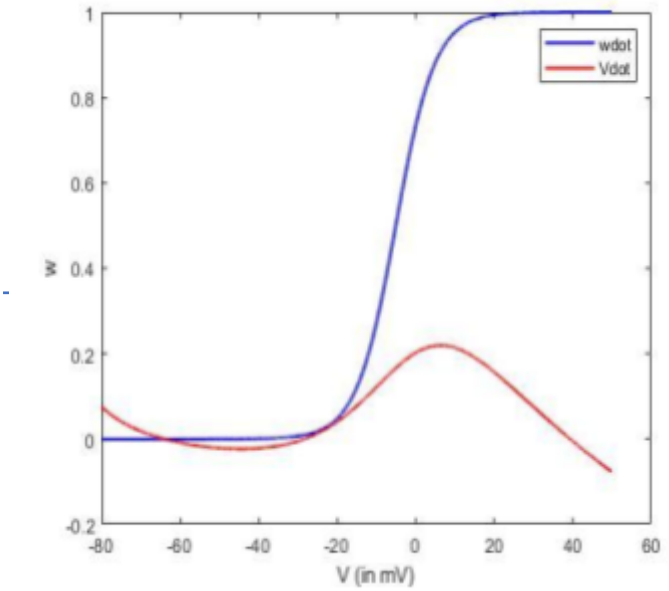


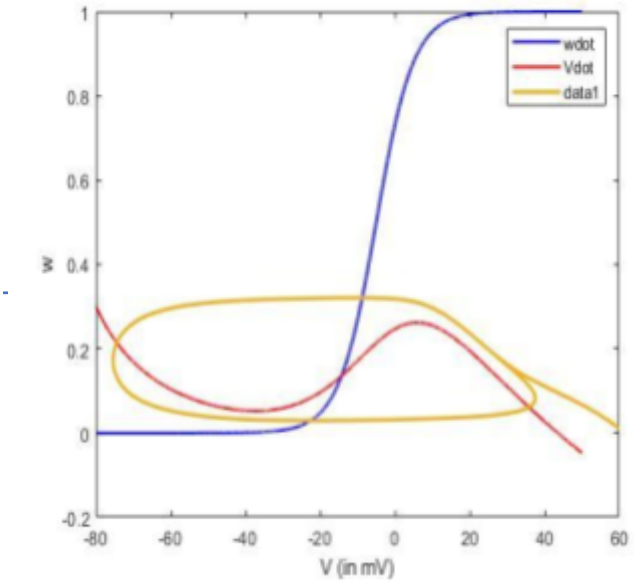
Class III neurons spike only once and fail to spike repeatedly leading to a complicated f vs I curve.

DYNAMICAL BASIS OF DIFFERENT CLASSES OF EXCITABILITY

The interaction between the fast activation variable V and the slower recovery variable w explains the dynamics of this neuronal model. The phase portraits explain the behavior of the model.

PHASE PORTRAIT OF CLASS I NEURONS





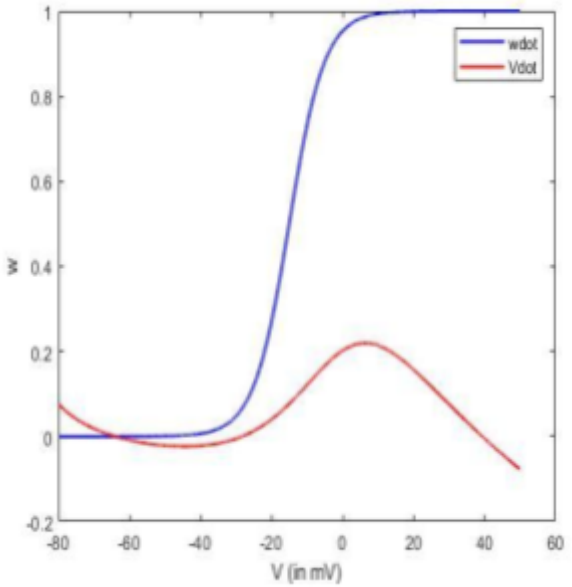
$I = 10\mu A/cm^2$ (before stimulation)

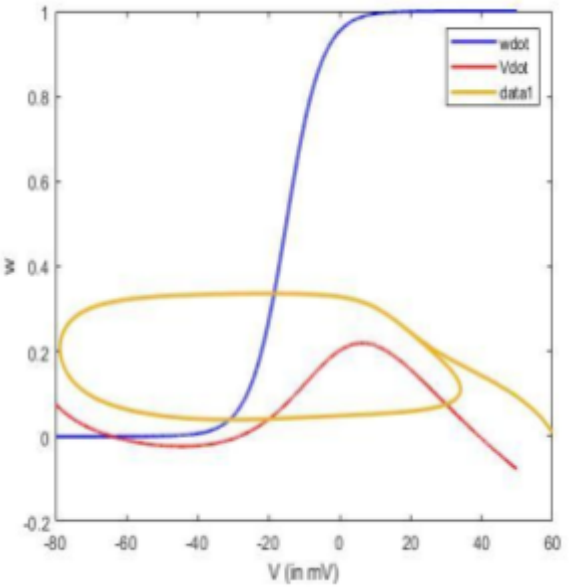
$I = 10\mu A/cm^2$ (after stimulation)

$\beta = -5$

Before stimulation, V-nullclines intersect the w-nullclines at three points. The leftmost intersection constitutes a stable fixed point that controls membrane potential. Stimulation shifts the V-nullclines upwards; when the stimulation is above rheobase, two of the intersection points are destroyed, and the Class-I model begins to spike repeatedly. This disappearance is the consequence of saddle-node on invariant circle (SNIC) bifurcation.

PHASE PORTRAITS OF CLASS II NEURONS





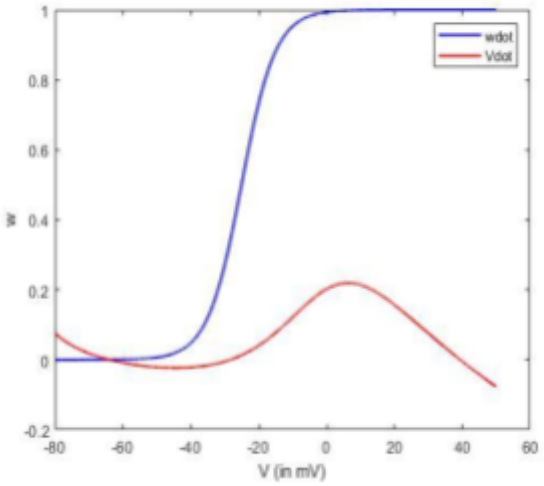
$I = 10\mu A/cm^2$ (before stimulation)

$I = 100\mu A/cm^2$ (after stimulation)

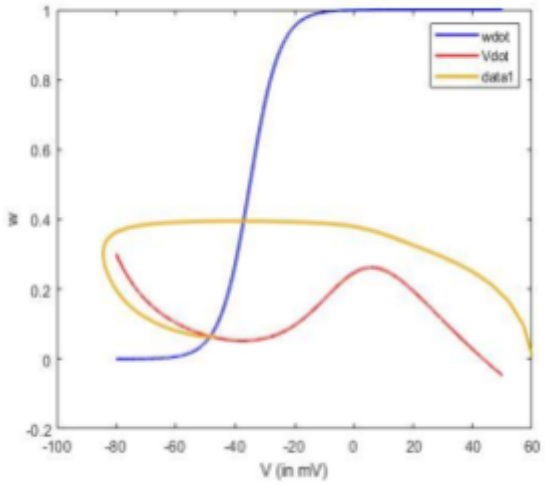
$\beta = -15$

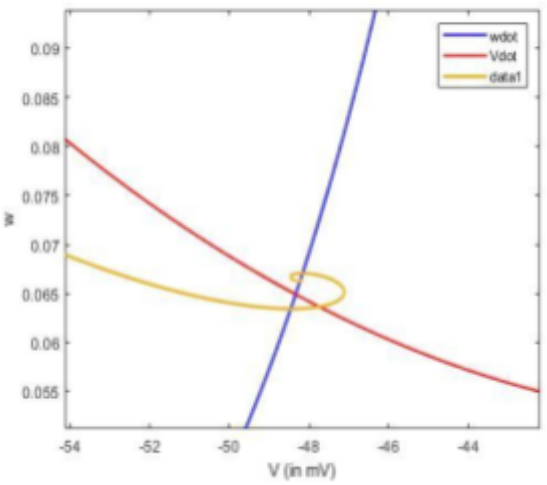
Before stimulation V-nullclines and w-nullclines intersect at a single, stable point, the stimulation caused destabilization of that point by a Hopf-bifurcation. This destabilization causes the creation of a stable limit cycle, and thus, the neuron spikes repeatedly.

PHASE PORTRAITS OF CLASS III NEURONS



$I = 10\mu A/cm^2$ (before stimulation)





$I = 100\mu A/cm^2$ (after stimulation)

In this, the V-nullclines and w-nullclines intersected at a single, stable fixed point that remained stable even after stimulation, i.e., spike initiation occurred without a bifurcation. There is no creation of a limit cycle; instead, the system moves to a newly positioned stable fixed point. Also, it could do so via different paths: trajectories starting below the quasi-separatrix made a long excursion around the elbow of the V-nullclines, resulting in a single spike; trajectories starting above the quasi-separatrix follows a more direct, subthreshold route.