Biophysical Basis for Three Distinct Dynamical Mechanisms of Action Potential Initiation

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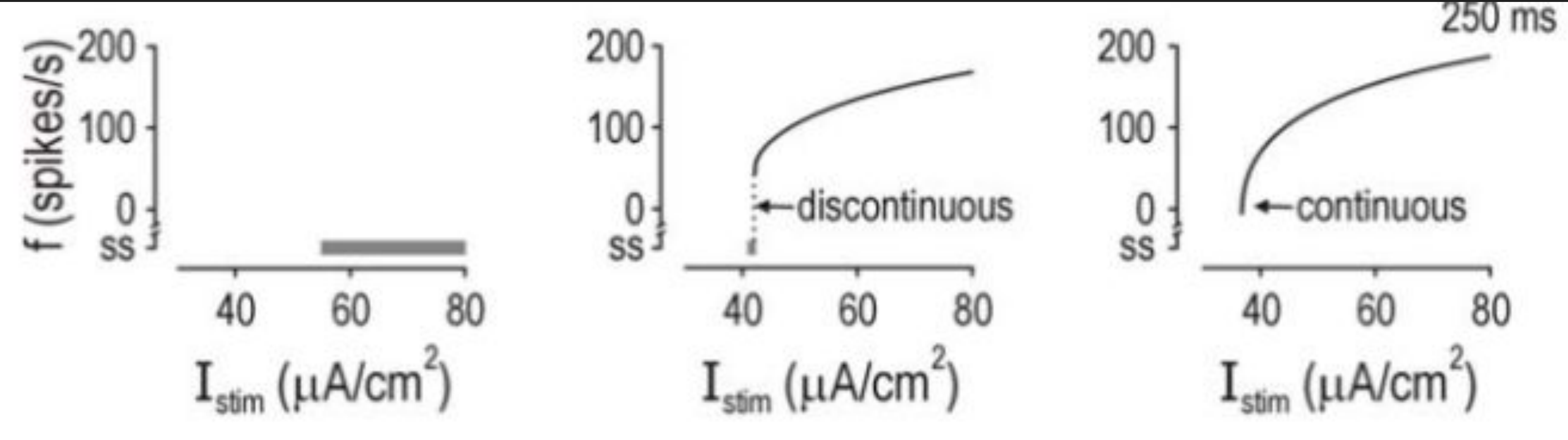
Rajat Joshi

Introduction

- Hodgkin classes of excitability (1948), based on the f-I curves of different neurons.

CLASS III CLASS II CLASS I



- Morris-Lecar model (1981).

Morris Lecar Model

$$CV' = -g_{\mathrm{Ca}} M_{\mathrm{ss}}(V)(V - V_{\mathrm{Ca}}) - g_{\mathrm{K}} W(V - V_{\mathrm{K}}) - g_{\mathrm{L}}(V - V_{\mathrm{L}}) + I_{\mathrm{app}}$$

$$W' = (W_{\mathrm{ss}}(V) - W)/T_{\mathrm{W}}(V)\,.$$

V’ = fast acting variable

W’ = slow recovery variable

V= membrane potential

Mss, Wss = open state probability functions

M, W = instantaneous open state probability

Tw = time scale for the recovery process

$$M_{\mathrm{ss}}(V) = (1 + \tanh[(V - V_1)/V_2])/2\,,$$

$$W_{\mathrm{ss}}(V) = (1 + \tanh[(V - V_3)/V_4])/2\,.$$

$$T_W(V) = T_0 \operatorname{sech}[(V - V_3)/2V_4]$$

The β_w Parameter

$$C\, dV/dt = I_{stim} - \bar{g}_{fast}\, m_\infty(V)(V - E_{Na}) - \bar{g}_{slow} w(V - E_K) - g_{leak}(V - E_{leak}) \tag{2}$$

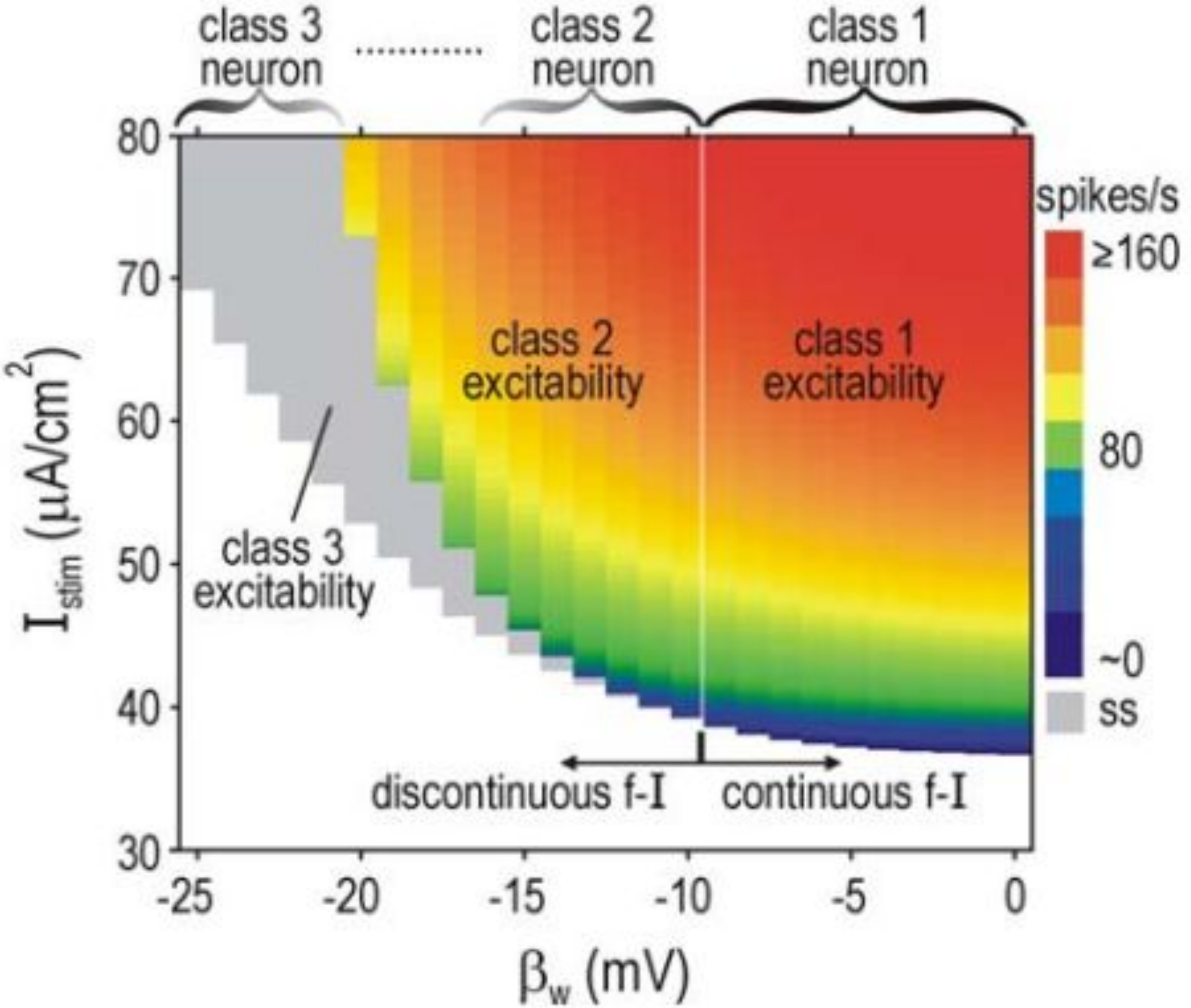
$$dw/dt = \phi_w \frac{w_\infty(V) - w}{\tau_w(V)} \tag{3}$$

$$m_\infty(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_m}{\gamma_m}\right)\right] \tag{4}$$

$$w_\infty(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_w}{\gamma_w}\right)\right] \tag{5}$$

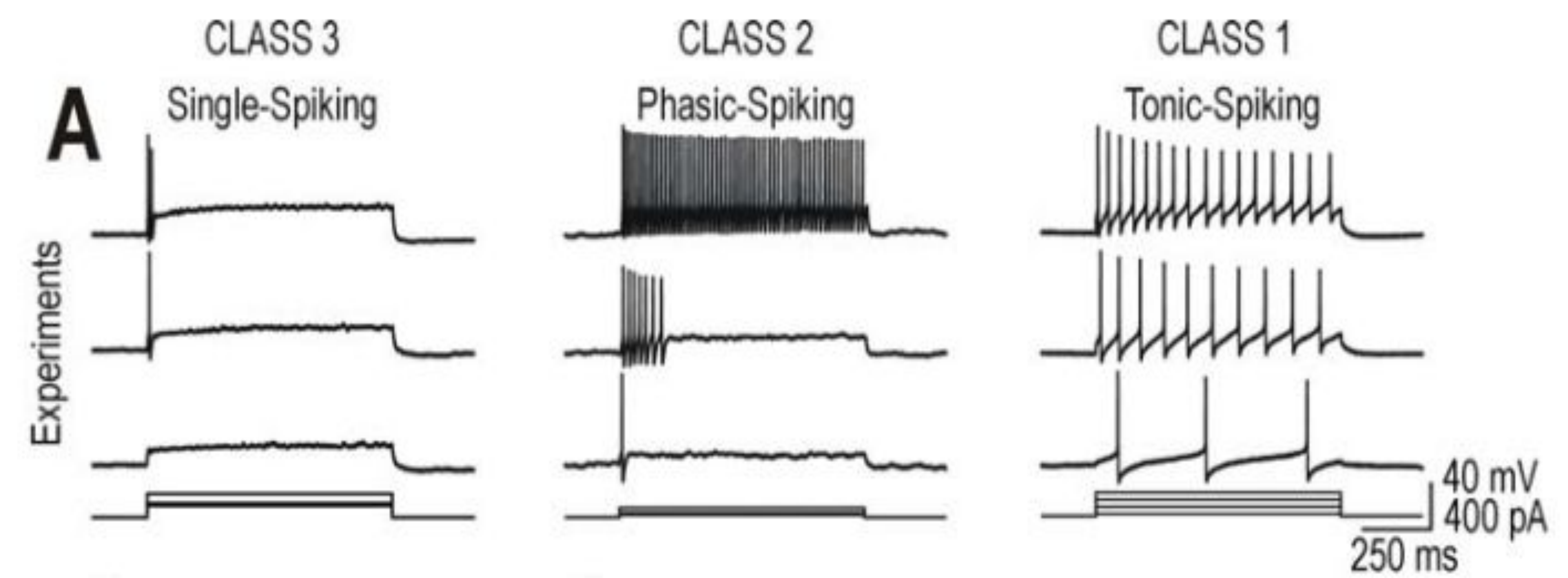
$$\tau_w(V) = 1/\cosh\left(\frac{V - \beta_w}{2 \cdot \gamma_w}\right) \tag{6}$$

Excitability

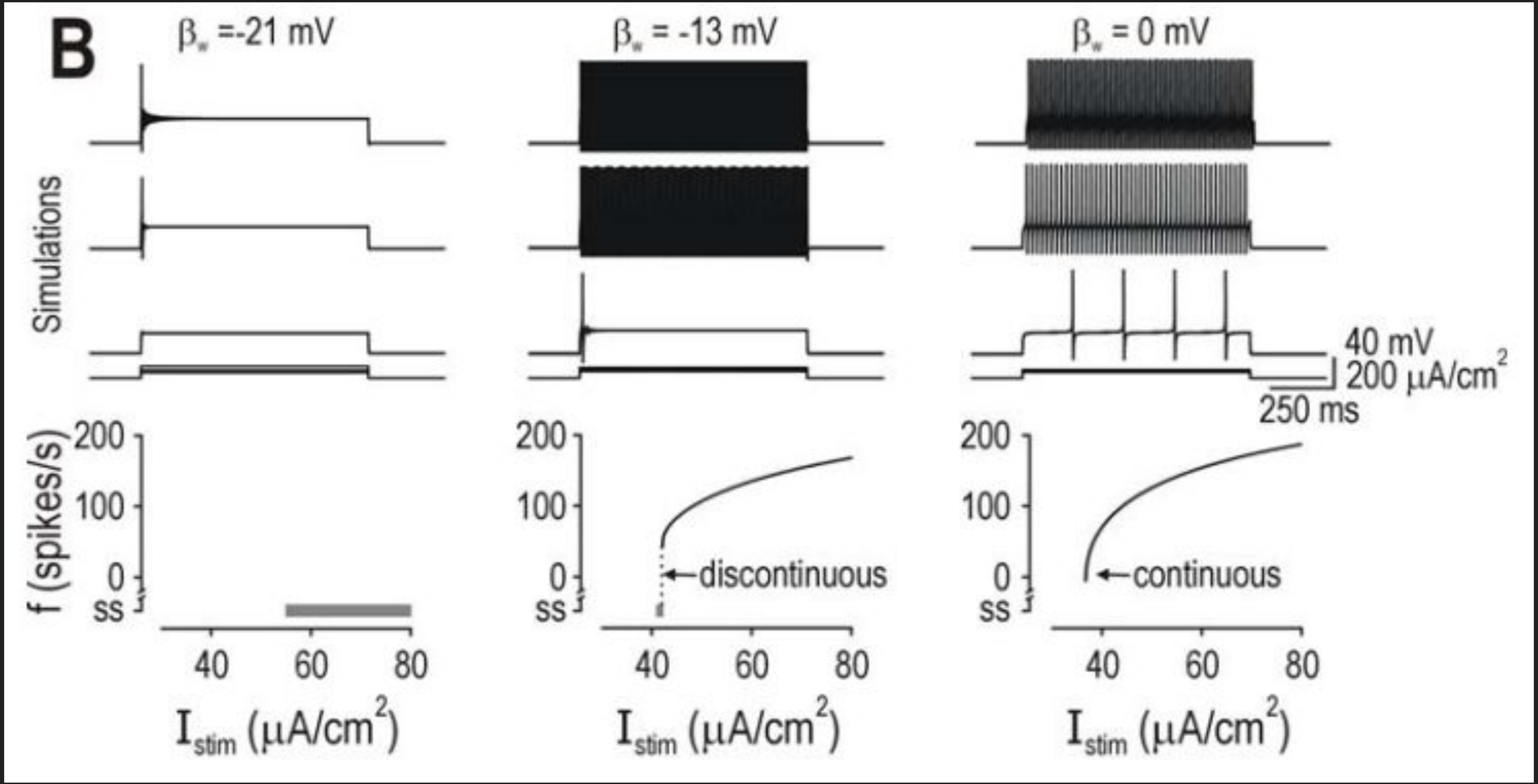


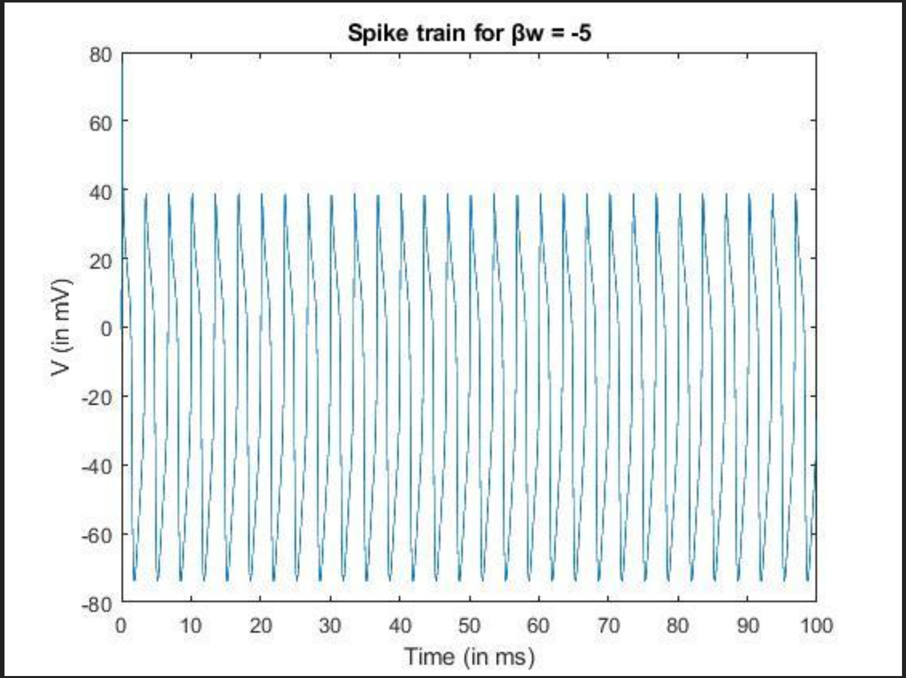
Biophysical Recordings

- Lamina I spinal neurons.

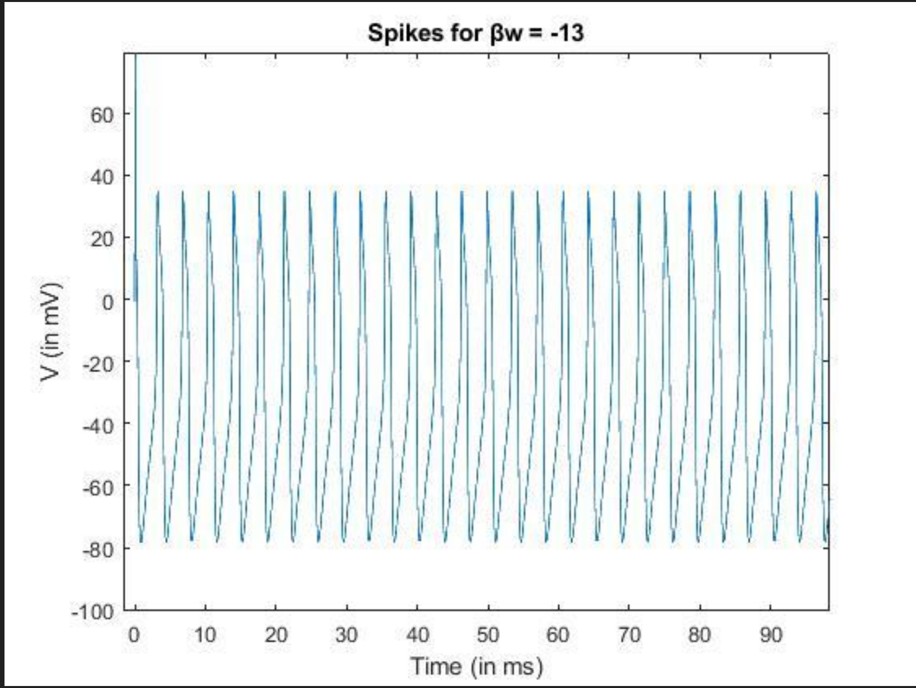


Data from the computational model

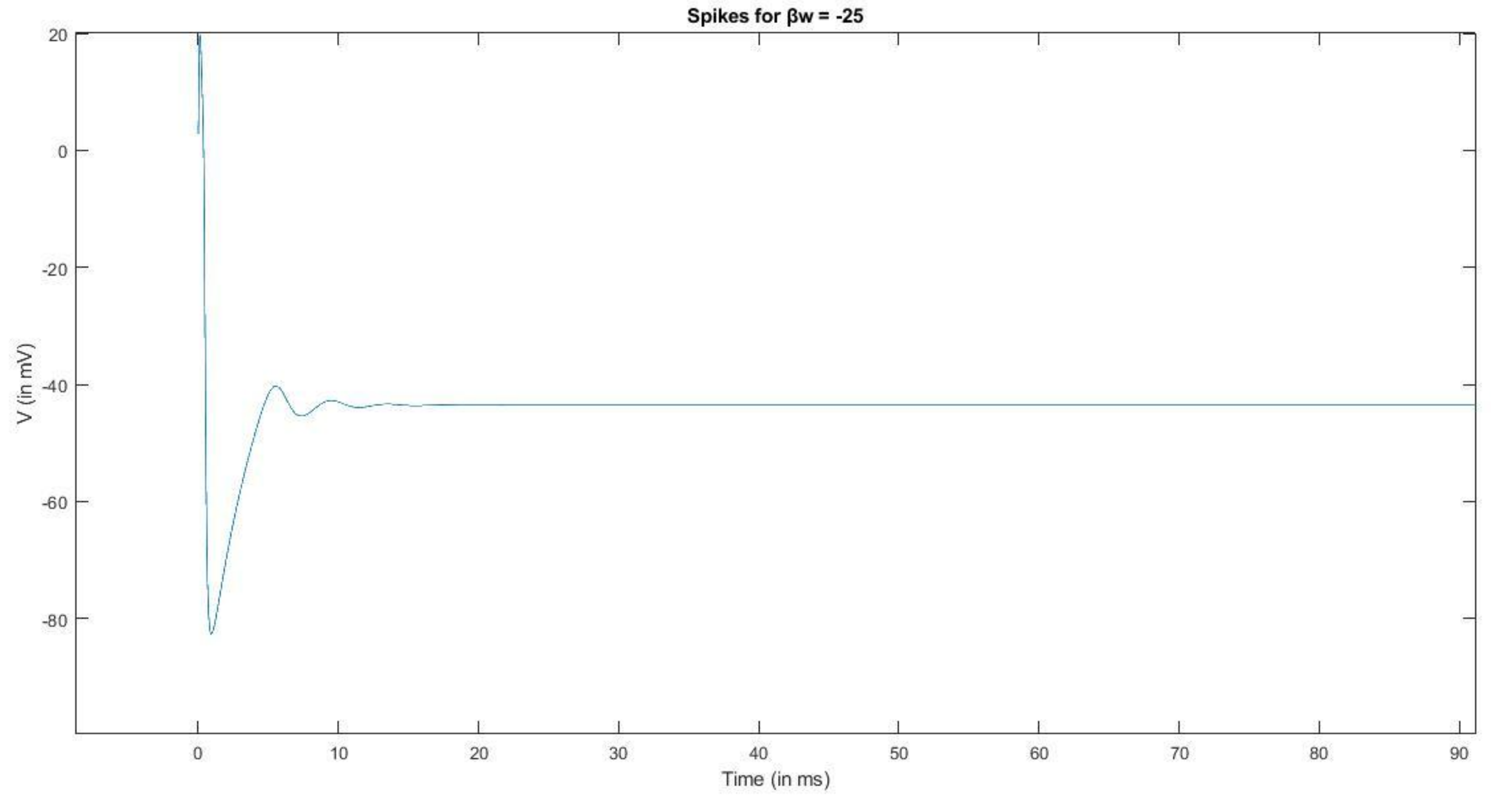




Class I excitability

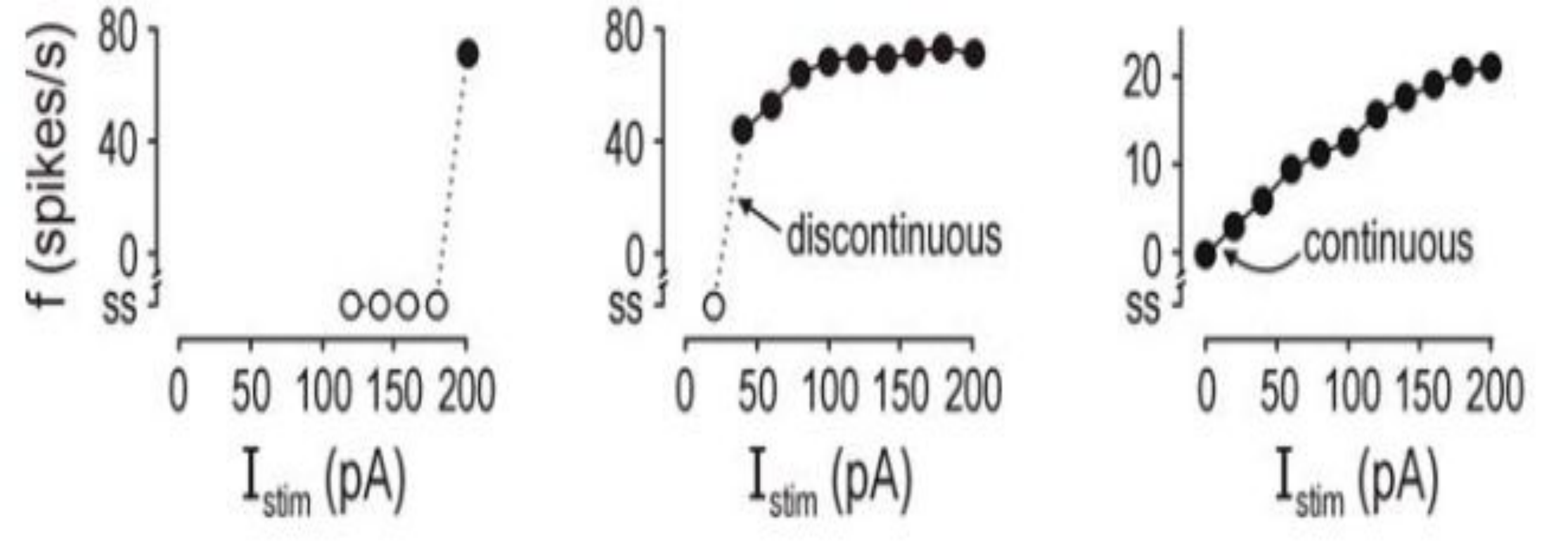


Class II excitability

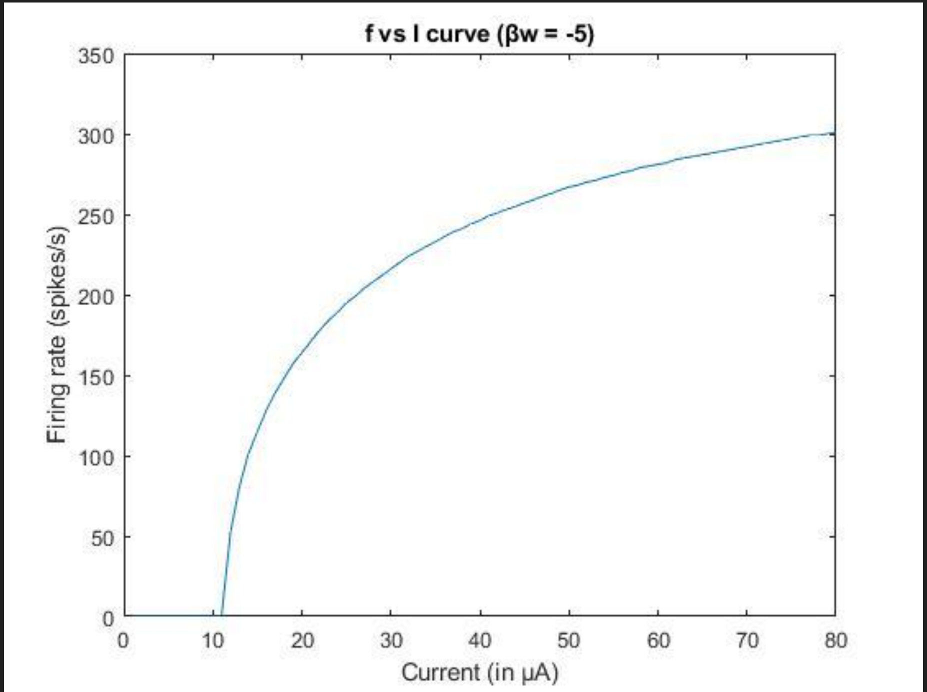


Class III excitability

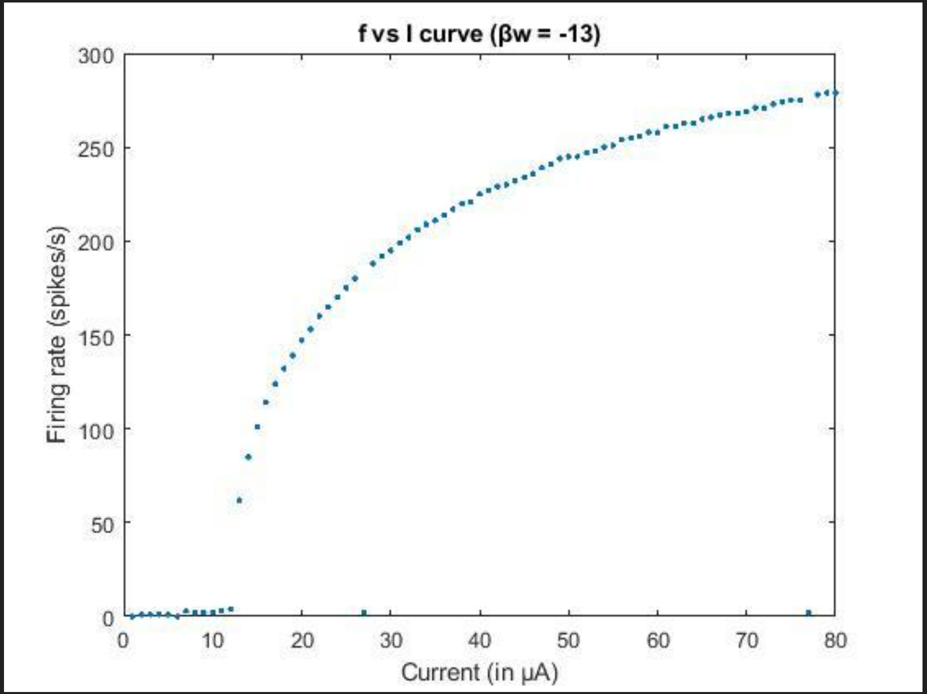
f vs I characteristics of the different classes of excitability



f-I Curves

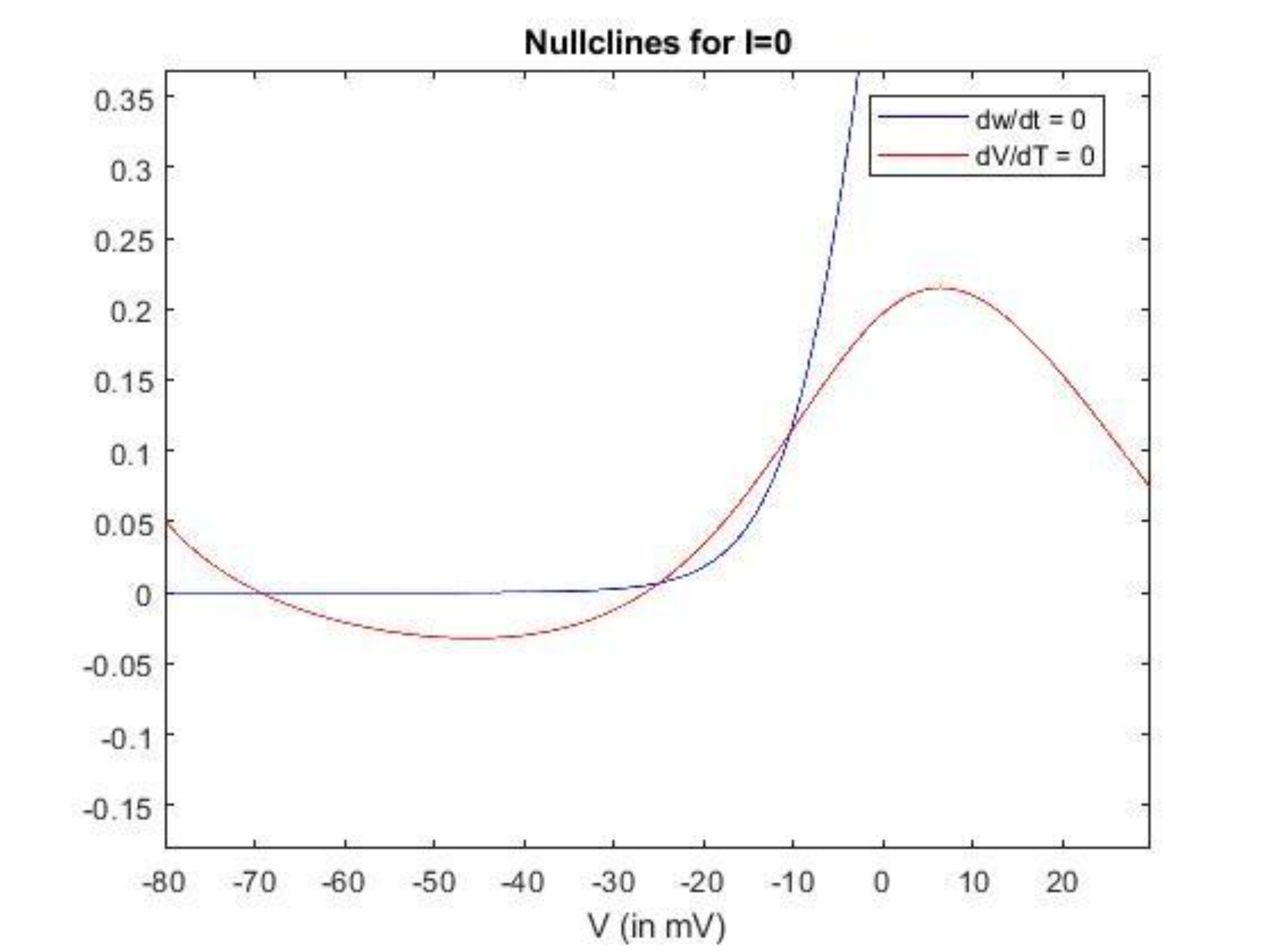


Class I



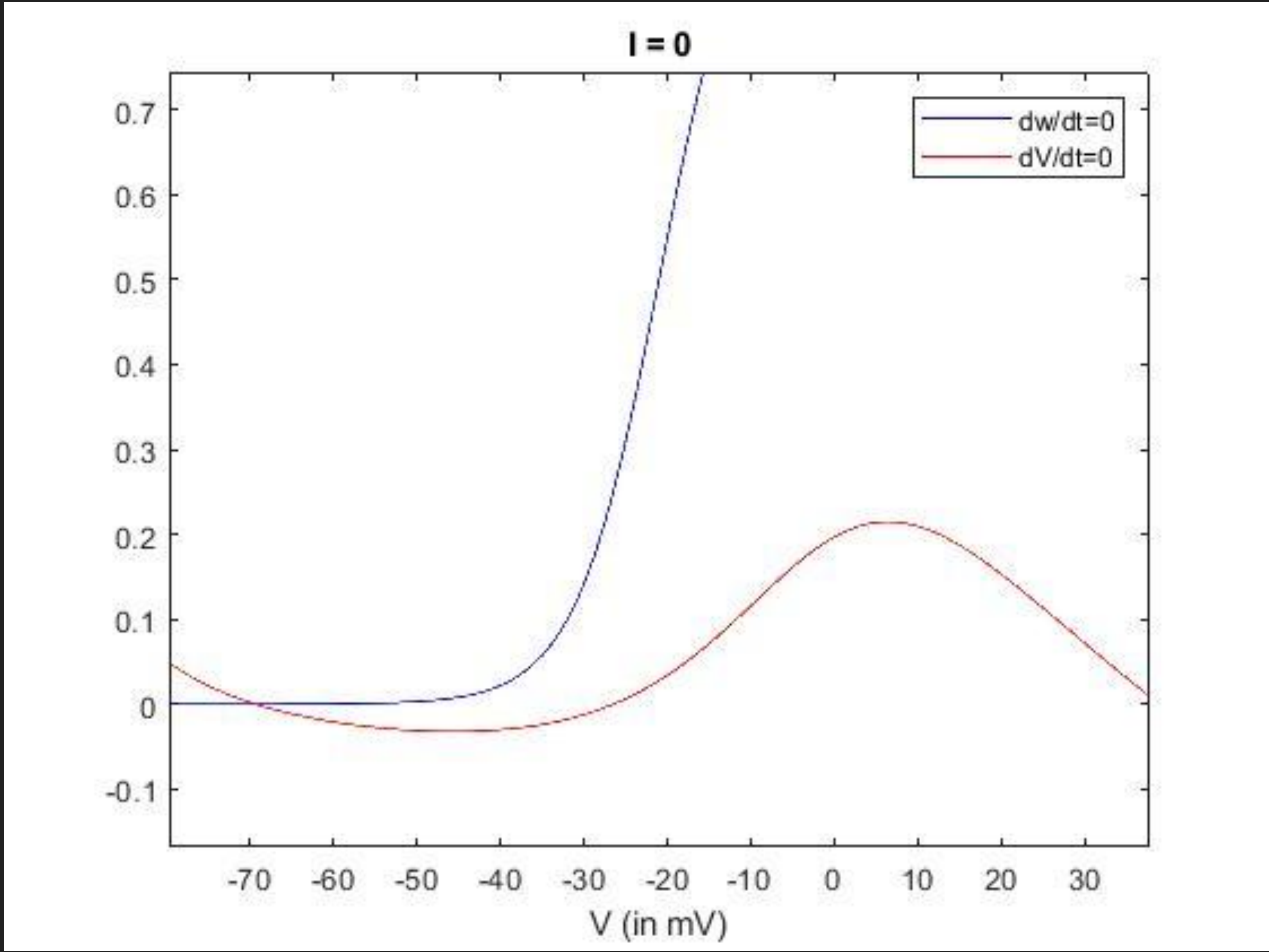
Class II

Class I

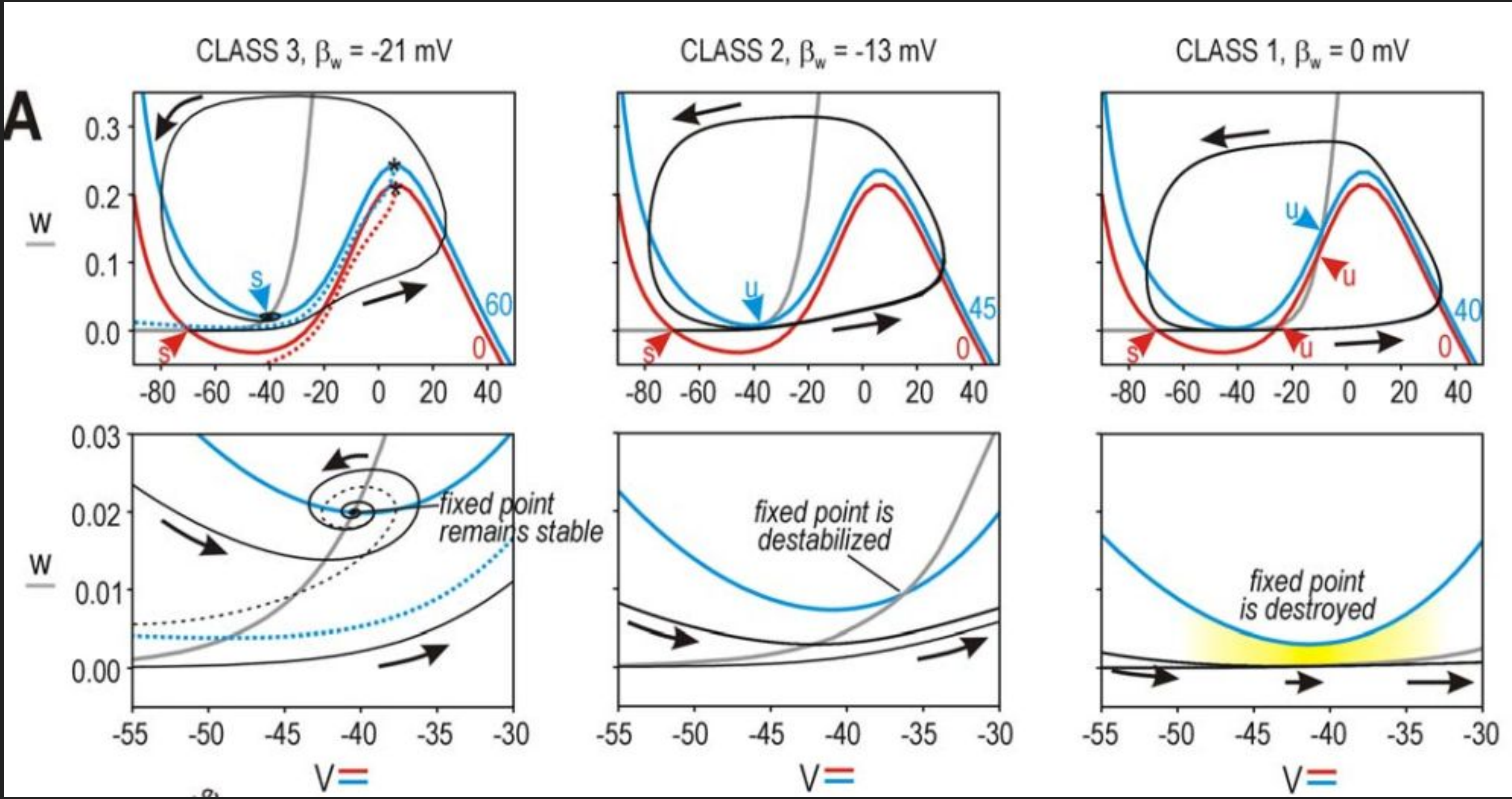


Nullclines for I=0
dw/dt = 0
dV/dT = 0
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-80
-70
-60
-50
-40
-30
-20
-10
0
10
20
V (in mV)

Class II and Class III

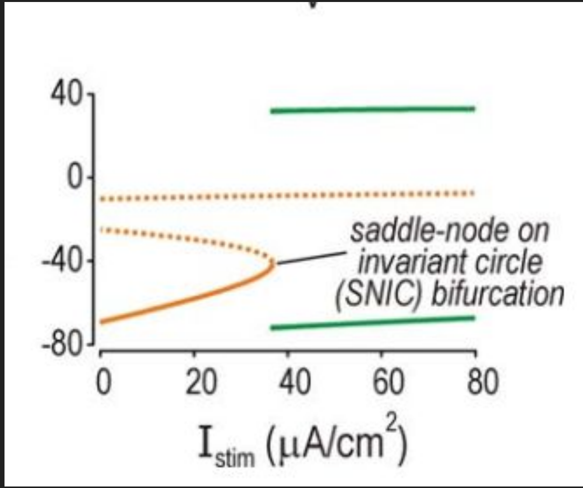


Phase plane analysis

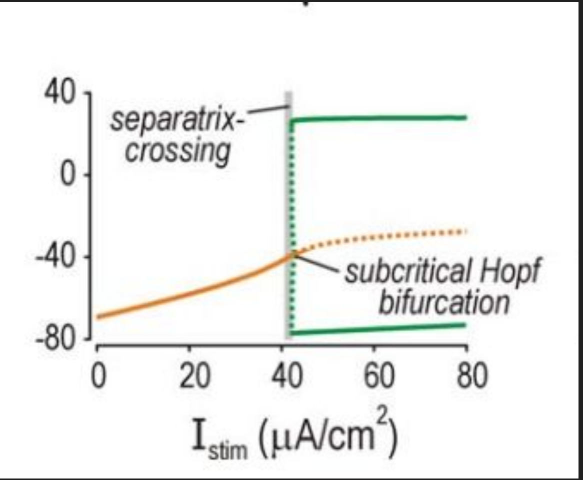


Bifurcations caused due to parameter β_w

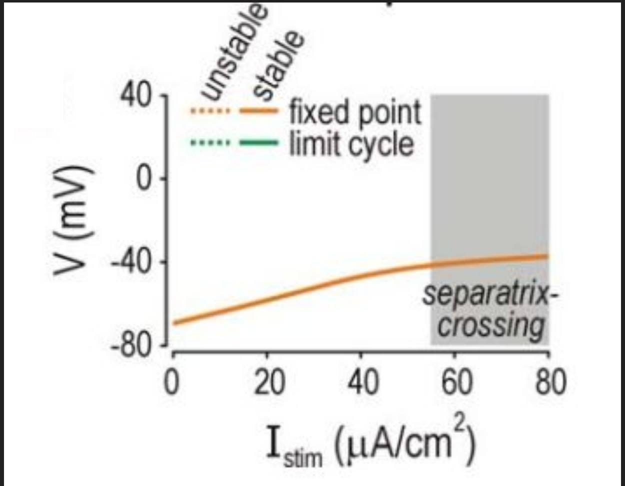
Class I excitability



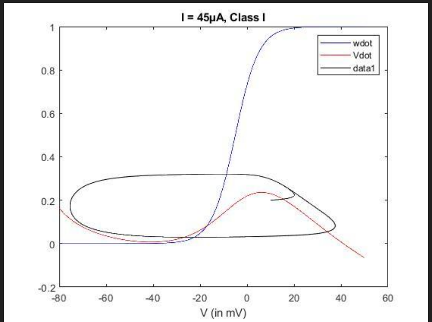
Class II excitability

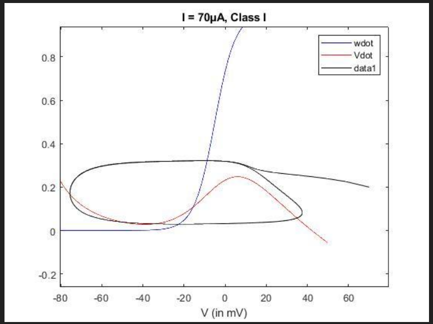


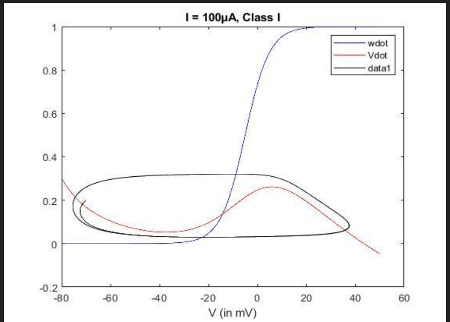
Class III excitability

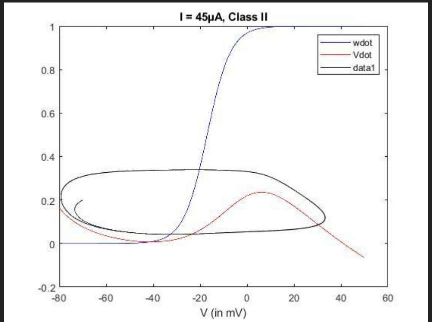


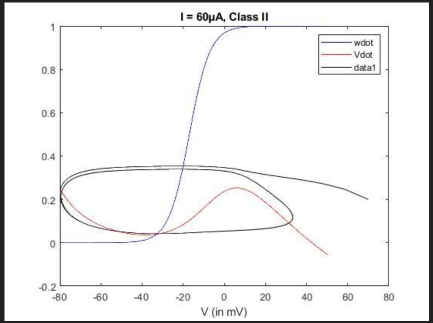
Phase portraits

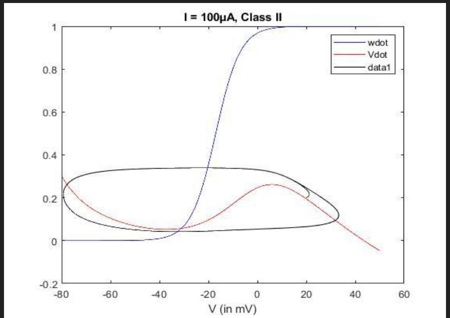


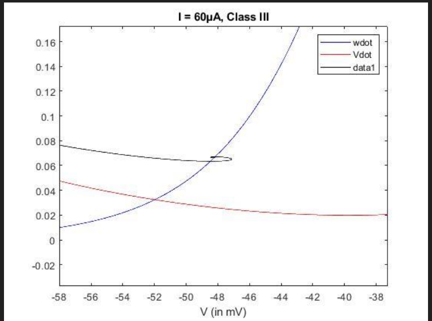


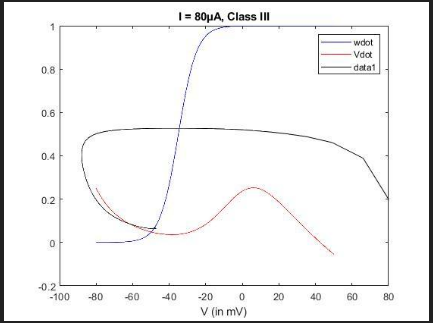


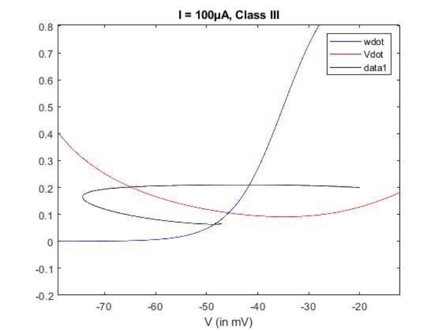












3D model

$$C\, dV/dt = I_{stim} - \bar{g}_{fast}\, m_\infty(V)(V - E_{Na}) - \bar{g}_{K,dr}\, y(V - E_K) - \bar{g}_{sub}\, z(V - E_{sub}) - g_{leak}(V - E_{leak}) \quad (7)$$

$$dy/dt = \phi_y \frac{y_\infty(V) - y}{\tau_y(V)} \quad (8)$$

V’ = fast acting variable

y’ z’ = slow acting variable

V= membrane potential

yinf, zinf = open state probability functions

y, z = instantaneous open state probability

Tau = time scale for the recovery process

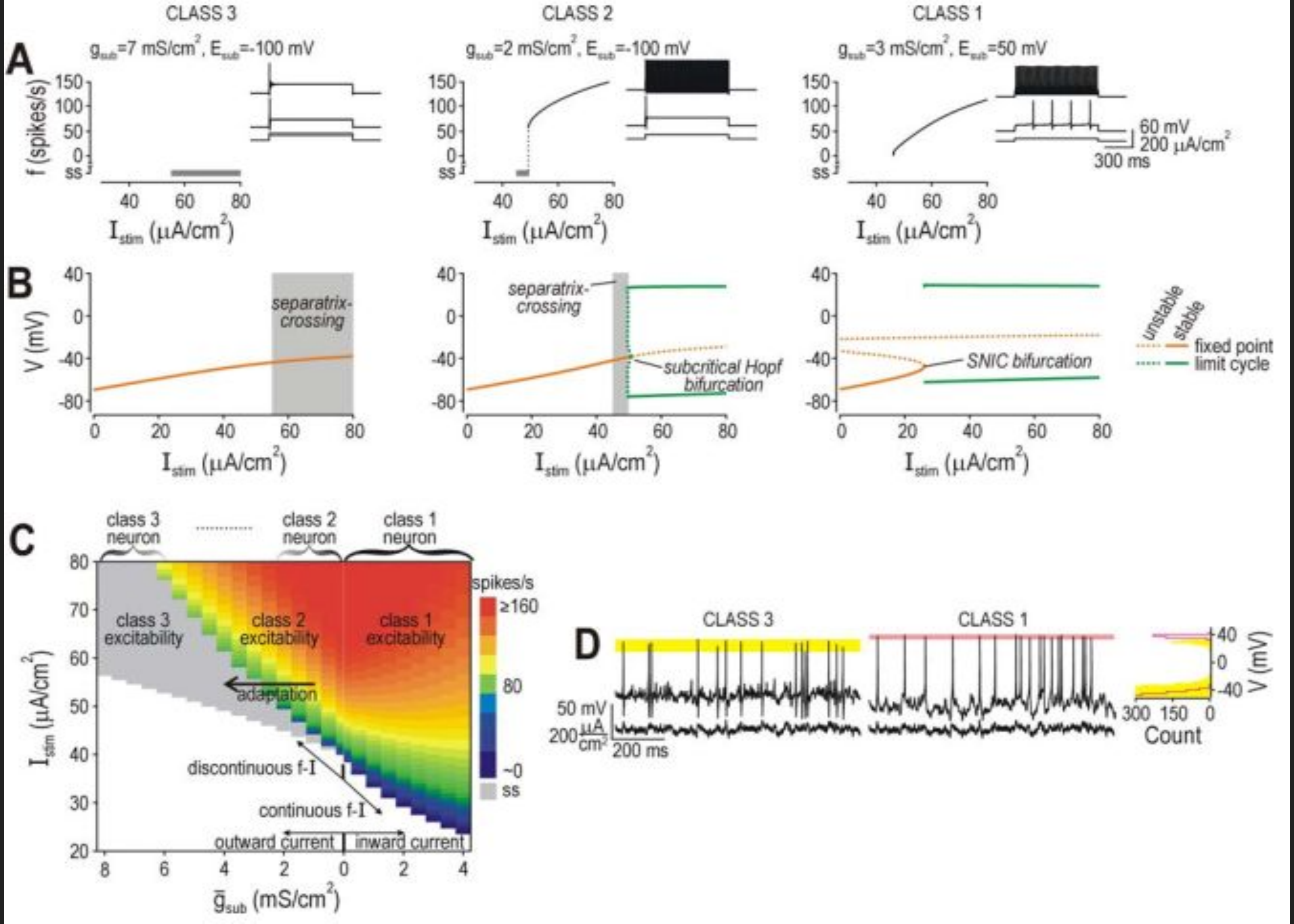
$$y_\infty(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_y}{\gamma_y}\right)\right] \quad (9)$$

$$\tau_y(V) = 1/\cosh\left(\frac{V - \beta_y}{2 \cdot \gamma_y}\right) \quad (10)$$

$$dz/dt = \phi_z \frac{z_\infty(V) - z}{\tau_z(V)} \quad (11)$$

$$z_\infty(V) = 0.5\left[1 + \tanh\left(\frac{V - \beta_z}{\gamma_z}\right)\right] \quad (12)$$

$$\tau_z(V) = 1/\cosh\left(\frac{V - \beta_z}{2 \cdot \gamma_z}\right) \quad (13)$$



CLASS 3
CLASS 2
CLASS 1
A
g_sub=7 mS/cm², E_sub=-100 mV
g_sub=2 mS/cm², E_sub=-100 mV
g_sub=3 mS/cm², E_sub=50 mV
f (spikes/s)
I_stim (μA/cm²)
60 mV
200 μA/cm²
300 ms
B
V (mV)
separatrix-crossing
subcritical Hopf bifurcation
SNIC bifurcation
unstable
stable
fixed point
limit cycle
C
class 3 neuron
class 2 neuron
class 1 neuron
class 3 excitability
class 2 excitability
class 1 excitability
adaptation
discontinuous f-I
continuous f-I
outward current
inward current
spikes/s
≥160
80
~0
ss
I_stim (μA/cm²)
g̅_sub (mS/cm²)
D
CLASS 3
CLASS 1
50 mV
200 μA/cm²
200 ms
Count
V (mV)

Thank you!

Special thanks : **Anagh Pathak**