Exploring Dynamics of Neurons
(Hodgkin-Huxley Model)

Arnav Jain, Kanishk Modi & Thivyanth M V

OVERVIEW

- Hopf Bifurcation
- Introduction to Neurons and Action Potentials
- Electric Circuit Analogy
- Mathematical Modeling
- Simulations and Graphs
- Biophysical Analysis
- Bifurcation with 'g_l' Parameter
- Bifurcation with 'V_{Na}' Parameter

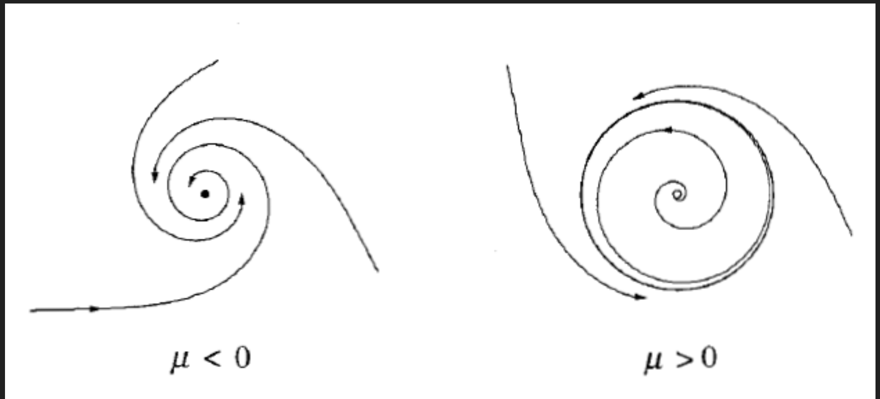
HOPF BIFURCATION

Shifting of Complex Eigenvalues from Negative Real Part to Positive Real Part

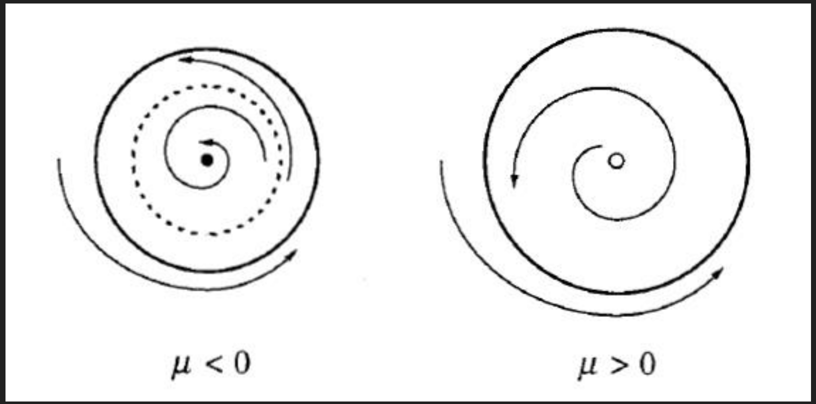
OR

Changing of a Stable Focus to an Unstable Focus

Supercritical Hopf Bifurcation

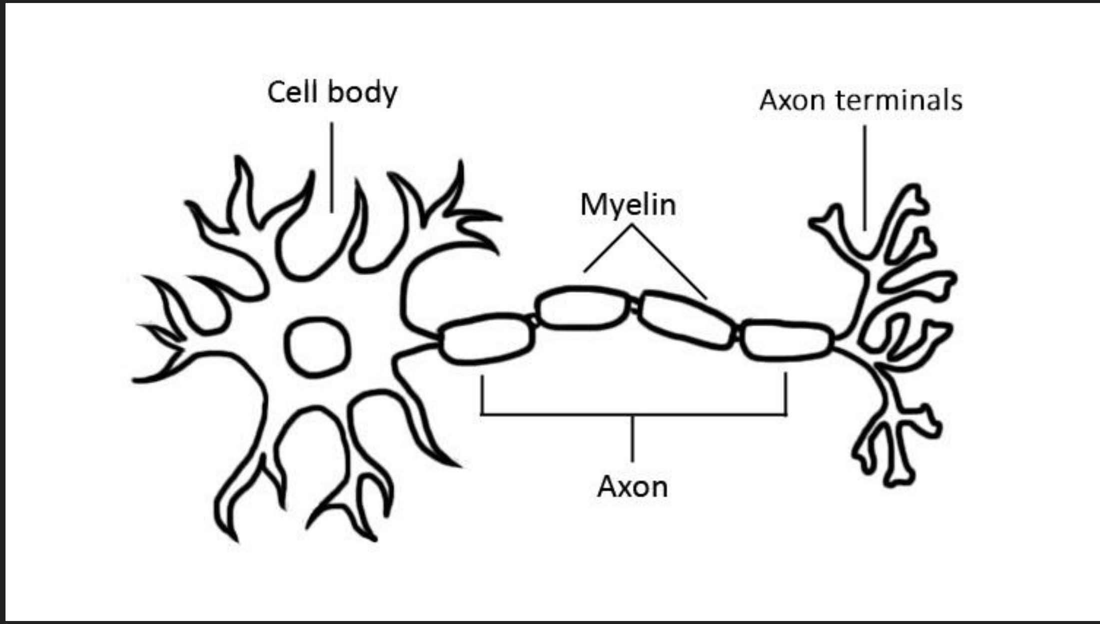


Subcritical Hopf Bifurcation



Steven H. Strogatz - Nonlinear Dynamics and Chaos_ With Applications to Physics, Biology, Chemistry, and Engineering

NEURON & ION CHANNELS



https://www.humanbiomedia.org/action-potential-lesson/

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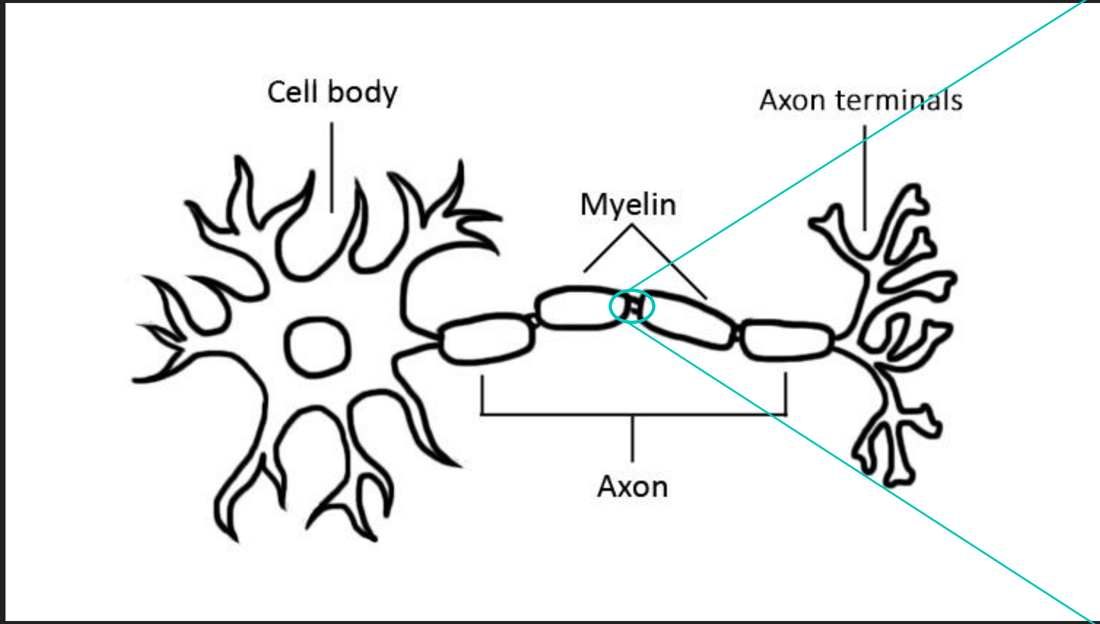

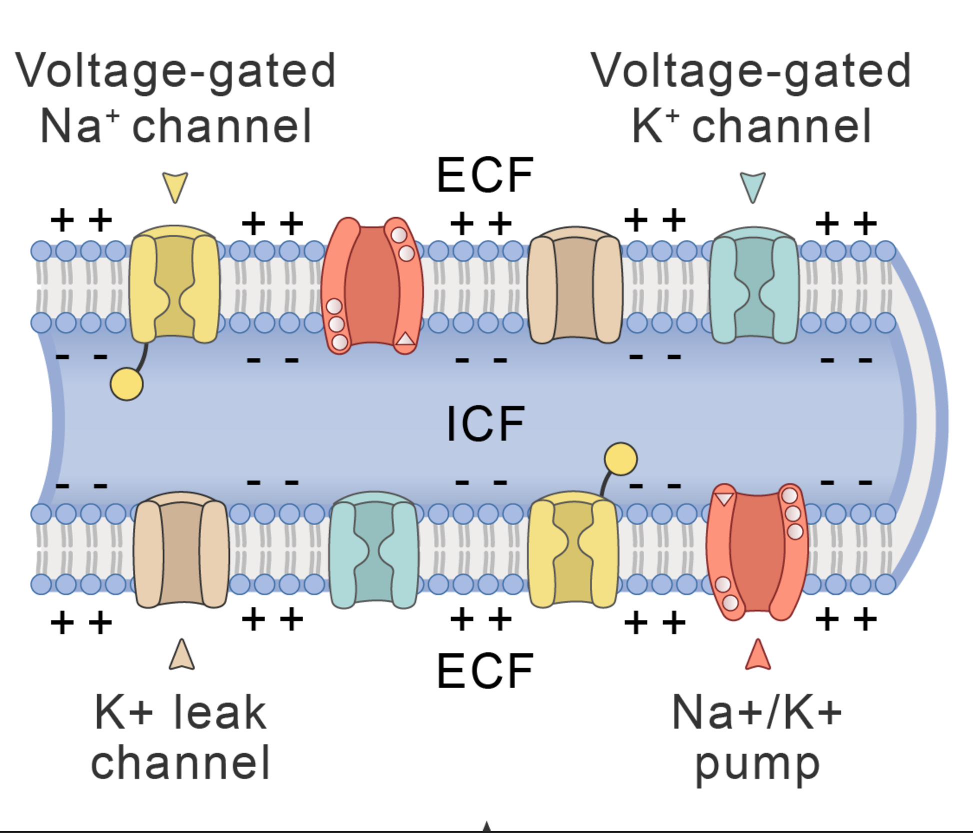

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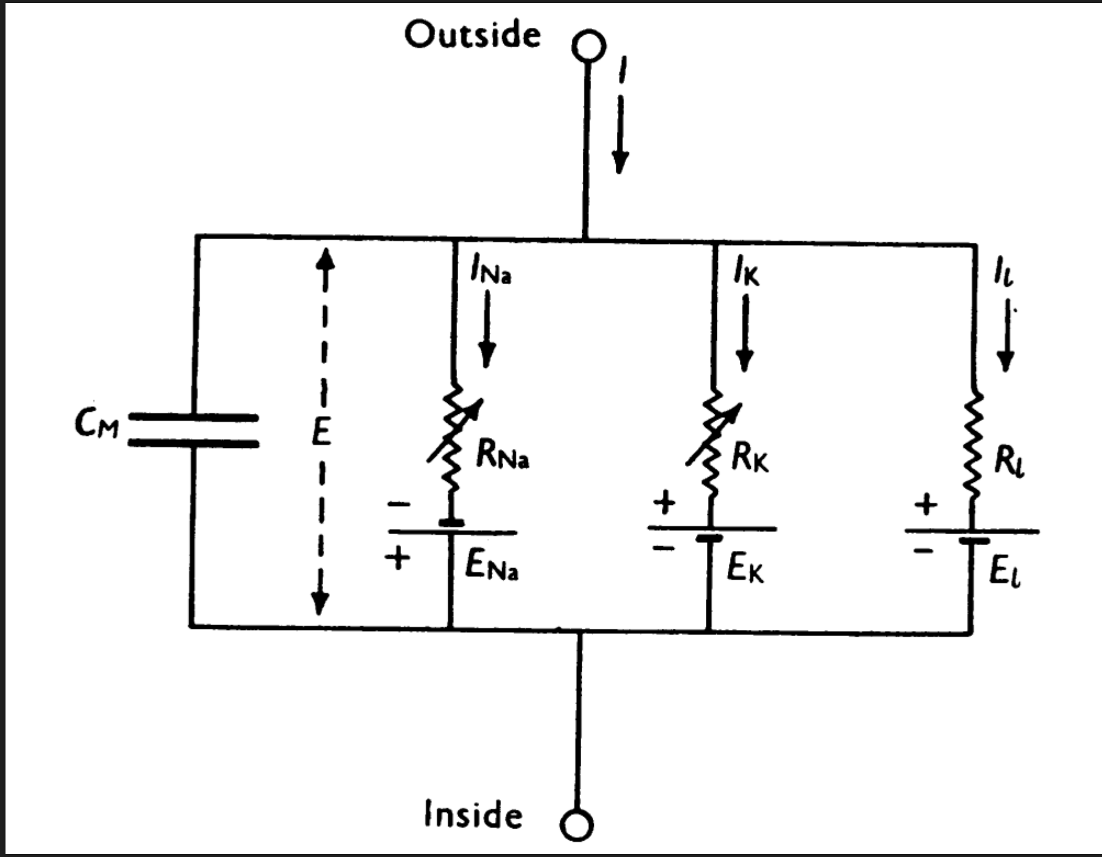
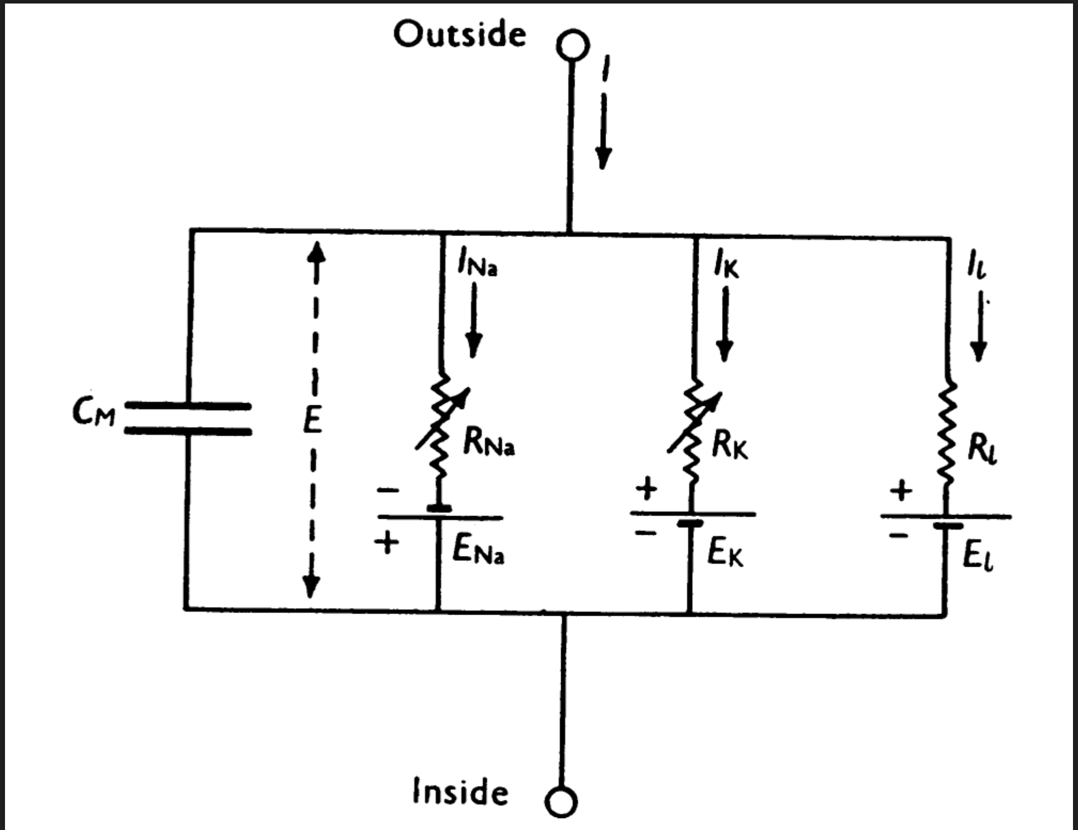
ELECTRIC CIRCUIT ANALOGOUS TO MEMBRANE



A Quantitative Description Of Membrane Current And Its Application To Conduction And Excitation In Nerve -BY A. L. HODGKIN AND A. F. HUXLEY

ELECTRIC CIRCUIT ANALOGOUS TO MEMBRANE



$$C_m \frac{dV}{dt} = I_{\text{inj}} - I_{Na} - I_K - I_L$$
$$I_{Na} = g_{Na} m^3 h (V - E_{Na})$$
$$I_K = g_K n^4 (V - E_K)$$
$$I_L = g_L (V - E_L)$$
$$\frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m$$
$$\frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h$$
$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n$$

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GATES CLOSING & OPENING

Gating variable (n): probability that one subunit is open

$$\text{Closed} \; (1 - n) \underset{\beta_n}{\overset{\alpha_n}{\rightleftharpoons}} \text{Open} \; (n)$$

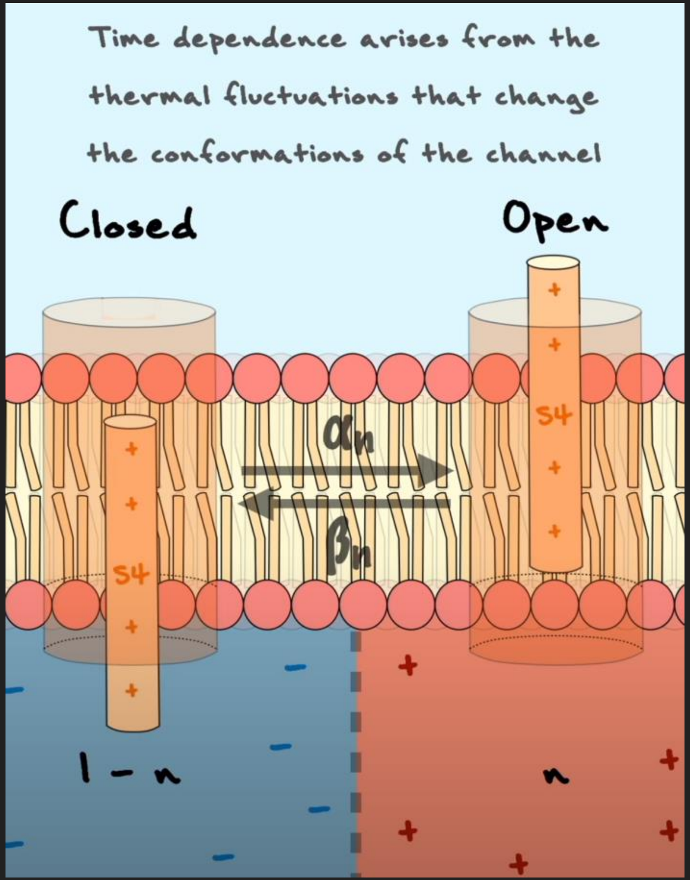
α_n: transition rate from closed to open (s^{-1})

β_n: transition rate from open to closed (s^{-1})

dn: change in the gating variable

$$dn = \left(\text{Number of closed subunits that open}\right) - \left(\text{Number of open subunits that close}\right)$$

$$\frac{dn}{dt} = \left(\text{Rate at which closed gates open}\right)\left(\text{Proportion of closed subunits}\right) - \left(\text{Rate at which open gates close}\right)\left(\text{Proportion of open subunits}\right)$$



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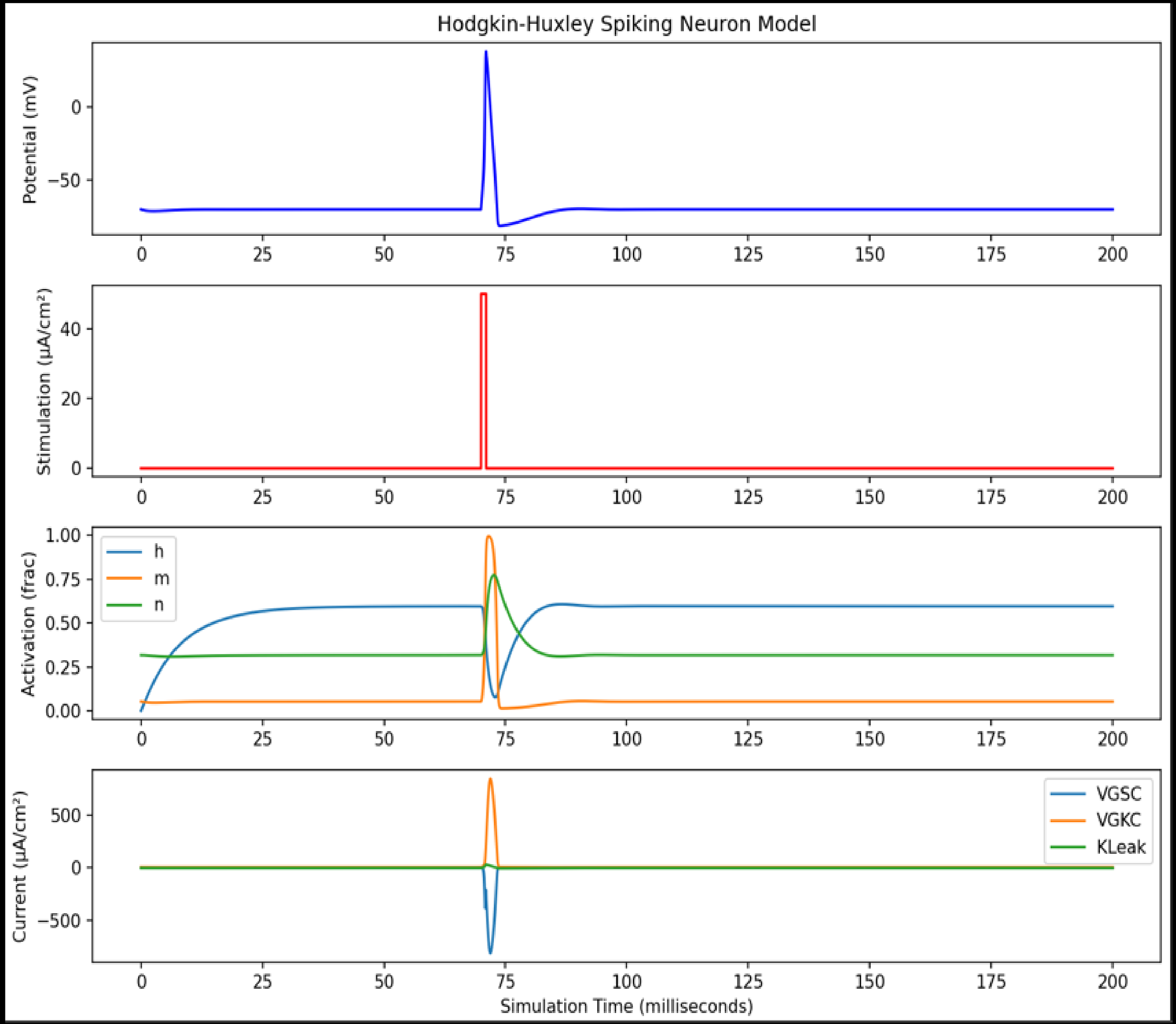
$$\frac{dn}{dt} = \alpha_n (1 - n) - \beta_n n$$

Hodgkin-Huxley Model of Voltage-Gated Channels Explained (Gating Variables n, m, h) | Clip

MODEL SIMULATION

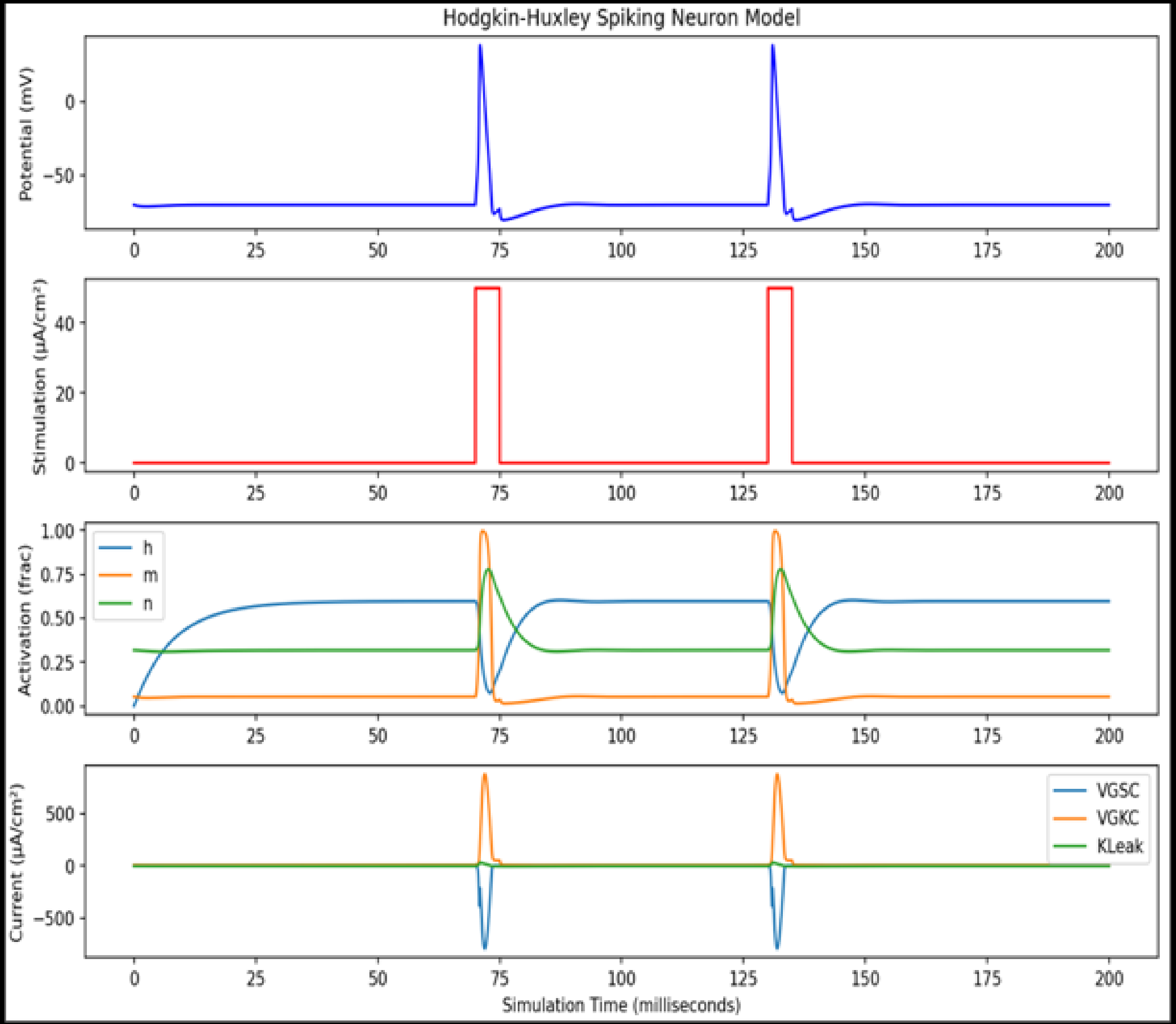
- Basic Numerical Integration (constant time-steps)
- Current(across the membrane) input is fed into the model as a waveform
- Some waveforms simulated:
  - Single spike
  - Double spike
  - …

ACTION POTENTIAL
(SINGLE SPIKE)

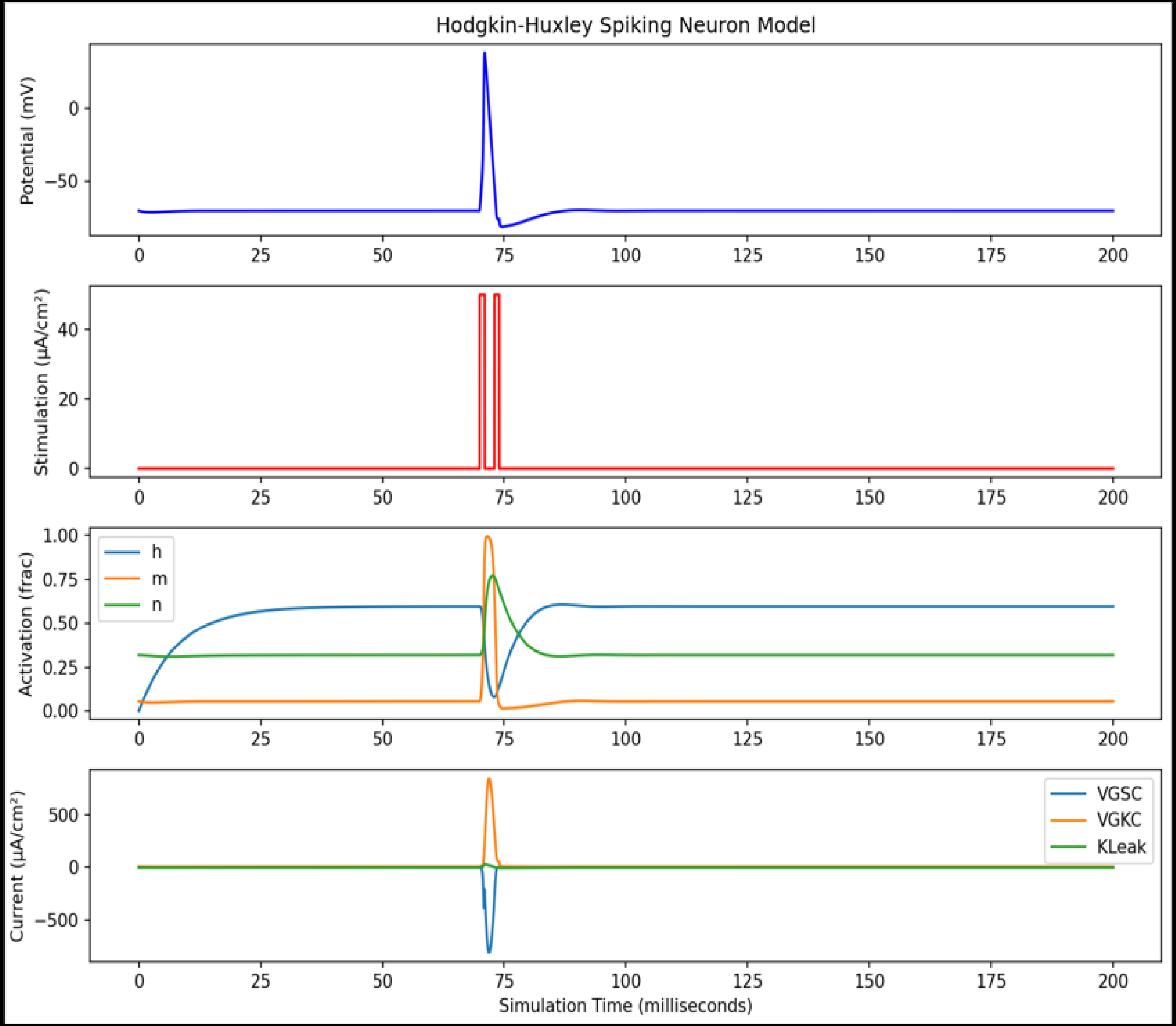


ACTION POTENTIAL

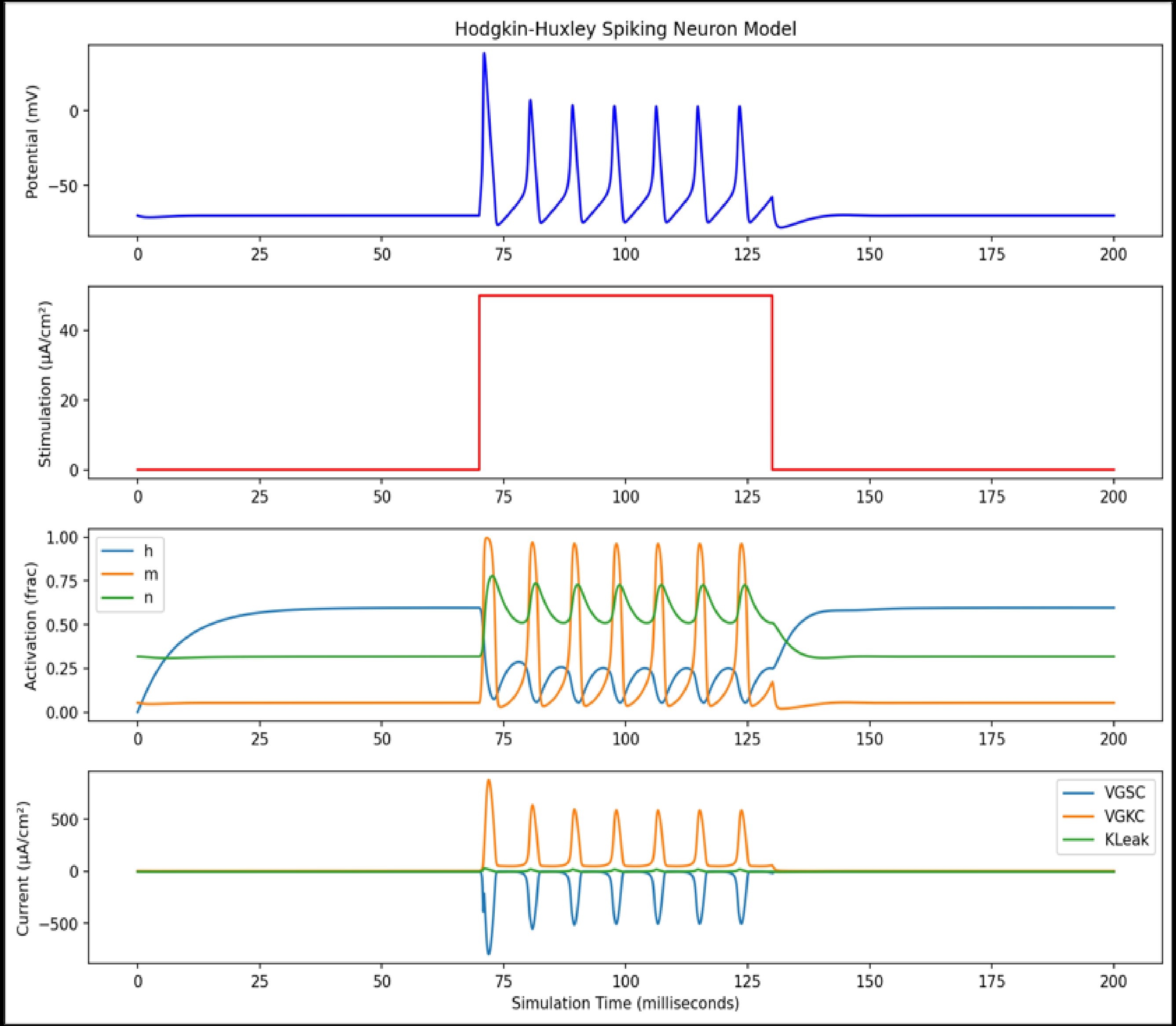
(TWO DISTANT SPIKES)



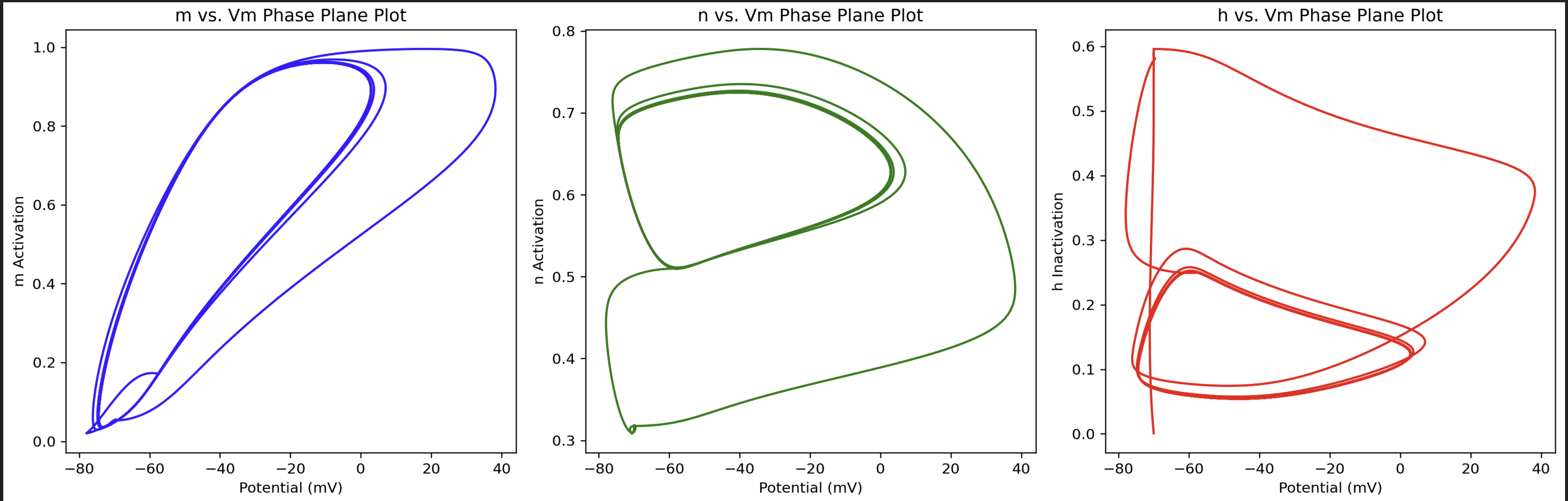
ACTION POTENTIAL
(TWO CONSECUTIVE SPIKES)



CURRENT INPUT FOR LARGE TIME INTERVALS



MEMBRANE POTENTIAL vs GATING VARIABLES



Bifurcation of HH model

- 'V_{Na}' and 'g_l' are some parameters that can be related to ion channel diseases. The 'g_l' is mainly chloride conductance, which is known to decrease in myotonia congenita. Sodium permeability increases in paramyotonia and hyperkalemic periodic paralysis.
- We first look at the single bifurcation, which is of 'g_l' and then of both.

Wang et al, Chaos, Solitons and Fractals, Vol 23 Issue 3, Feb 2005, pg 973-980

EQUILIBRIUM POINTS OF HH MODEL

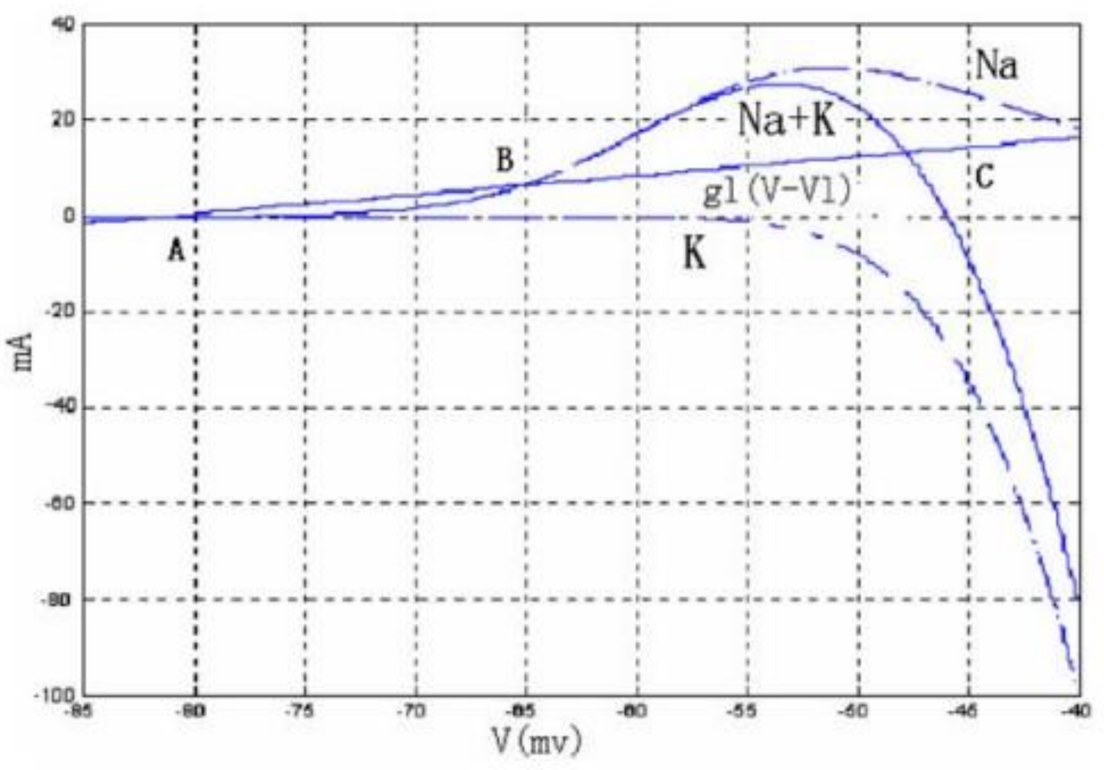


Fig. 2. Equilibrium point of HHM.

Equilibrium points	V_e (mV)	m_e	h_e	n_e
A	−81.0000	0.01351471113	0.9315694776	0.009933359801
B	−65.1530	0.1433815730	0.3736828476	0.08276135123
C	−47.8901	0.6193937147	0.02499417132	0.4247083348

$$\lambda_A = -3.442240423, -0.2063113255, -0.09797633682, -0.104564318$$

$$\lambda_B = -2.536149441, 0.6240905424, -0.05260197690, -0.07567909$$

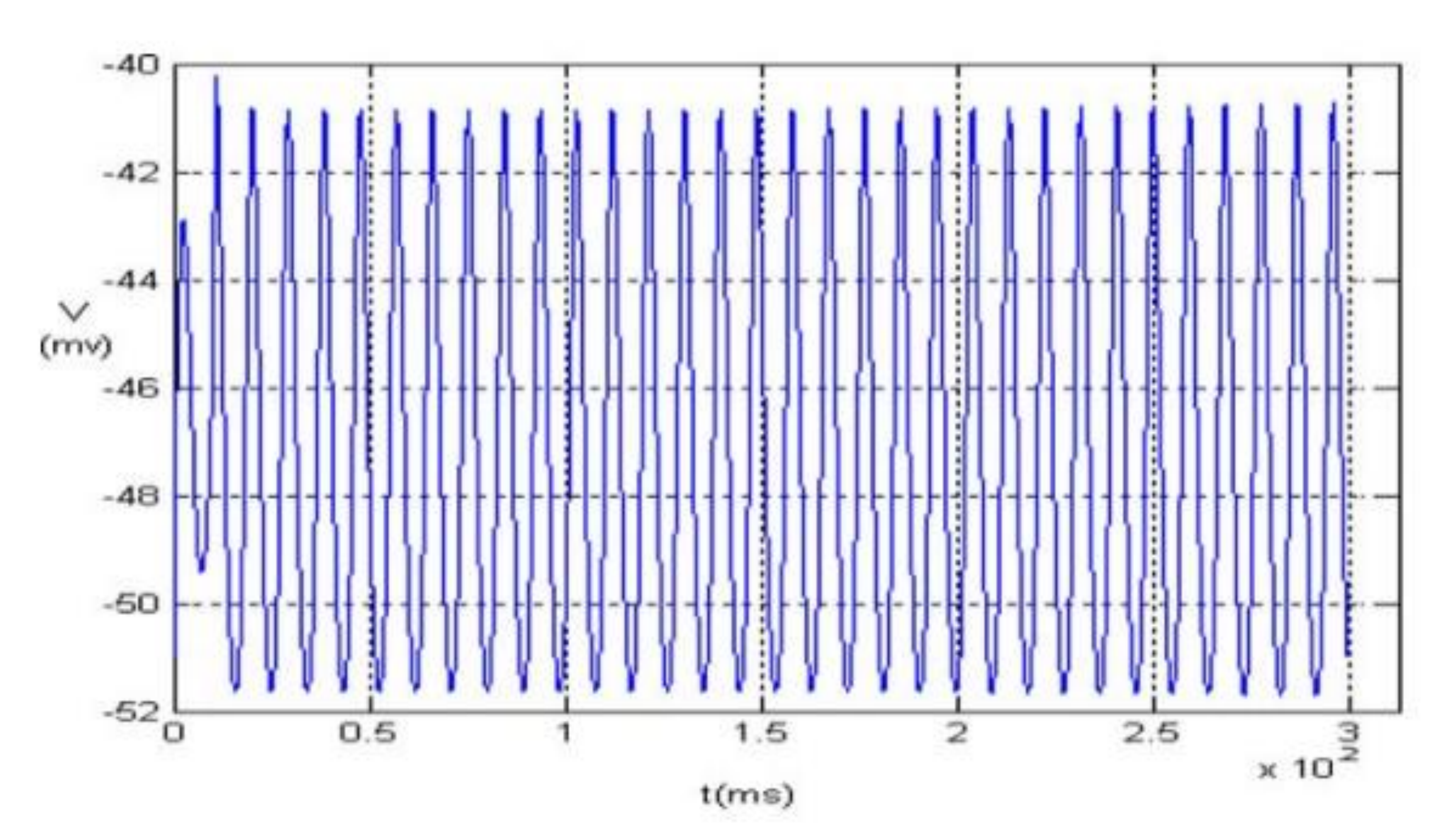
$$\lambda_C = -2.634015036, 0.08142848470 + 0.5826683466i, 0.08142848470 - 0.5826683466i, -0.1503550285$$

COMPUTING 'g_l' AT BIFURCATION

- Assign all variables values given in Wang et (Sept 2005), except 'g_l' and then compute the Jacobian.

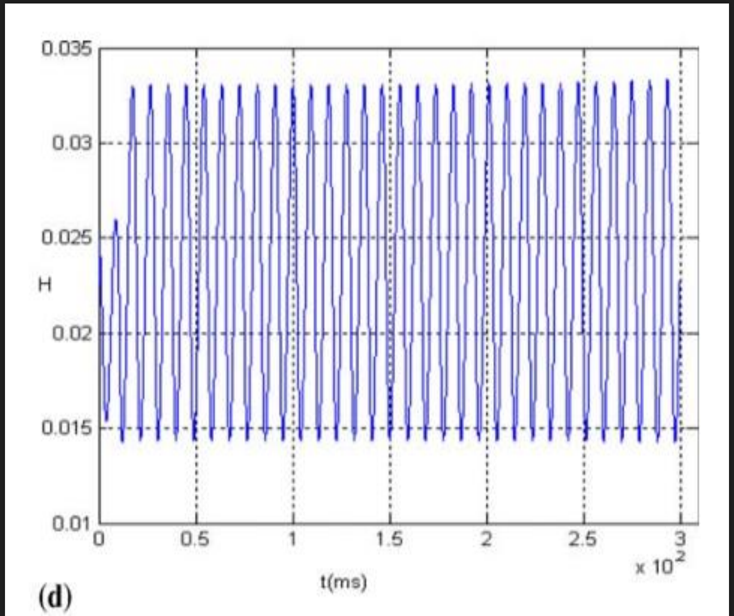
$$J(g_l) = \begin{bmatrix} \frac{\partial f_V}{\partial V} & \frac{\partial f_V}{\partial m} & \frac{\partial f_V}{\partial h} & \frac{\partial f_V}{\partial n} \\ \frac{\partial f_m}{\partial V} & \frac{\partial f_m}{\partial m} & 0 & 0 \\ \frac{\partial f_h}{\partial V} & 0 & \frac{\partial f_h}{\partial h} & 0 \\ \frac{\partial f_n}{\partial V} & 0 & 0 & \frac{\partial f_n}{\partial n} \end{bmatrix} = \begin{bmatrix} -0.533030502 - 0.526315789 g_l & 74.10521313 & 612.1467637 & -78.44914264 \\ 0.03888978155 & -1.416022399 & 0 & 0 \\ -0.001512049448 & 0 & -0.3835946452 & 0 \\ 0.002097273245 & 0 & 0 & -0.07833923285 \end{bmatrix}$$

BIFURCATION CONDITION (V_m)

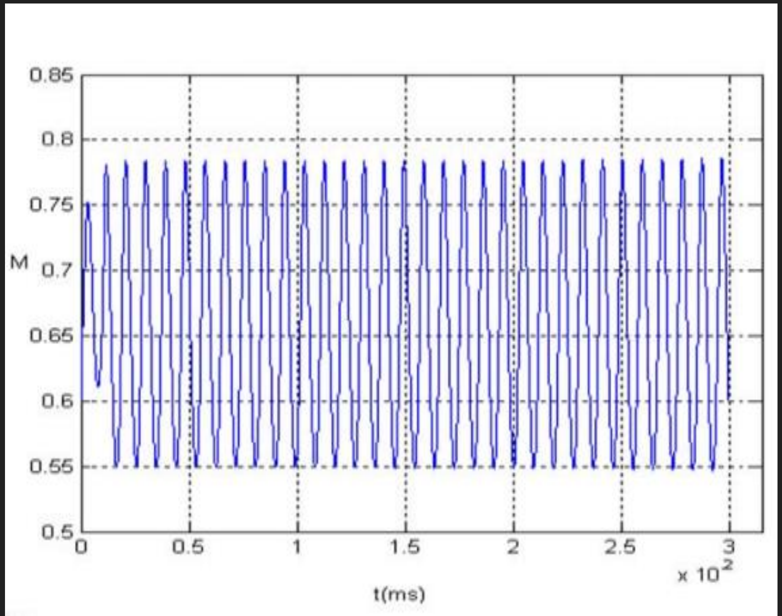


BIFURCATION CONDITION (h, m, n)

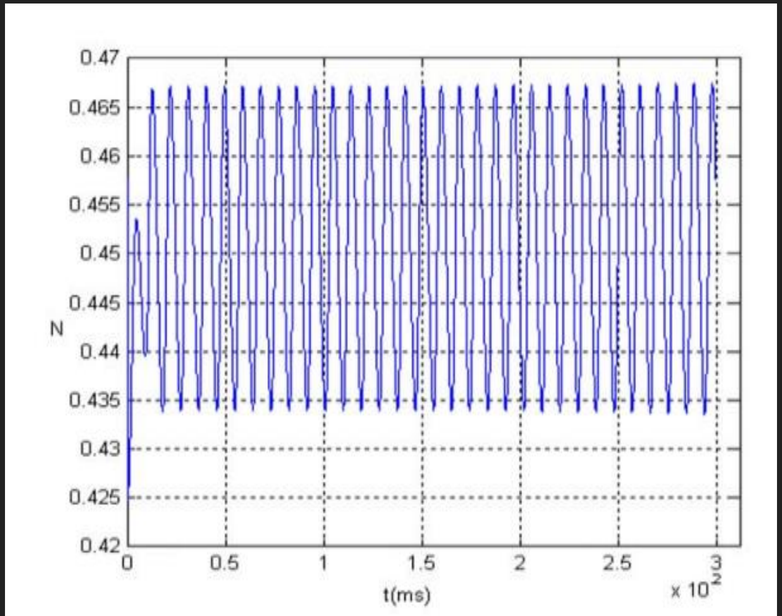
Time Series of ‘h’



Time Series of ‘m’

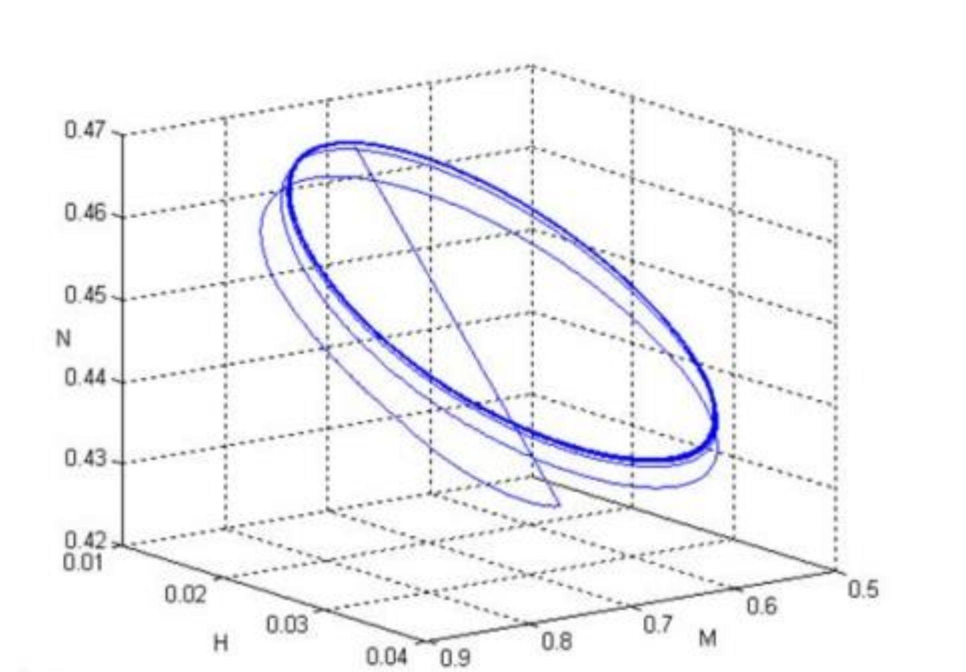


Time Series of ‘n’

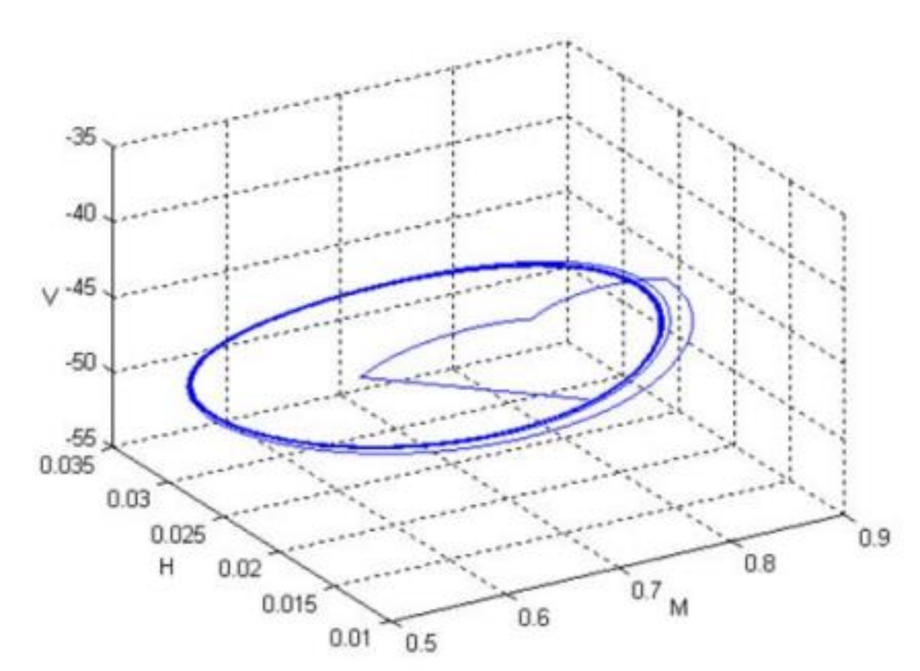


LIMIT CYCLES

n vs h vs m



v vs h vs m



HOPF BIFURCATION IN HH

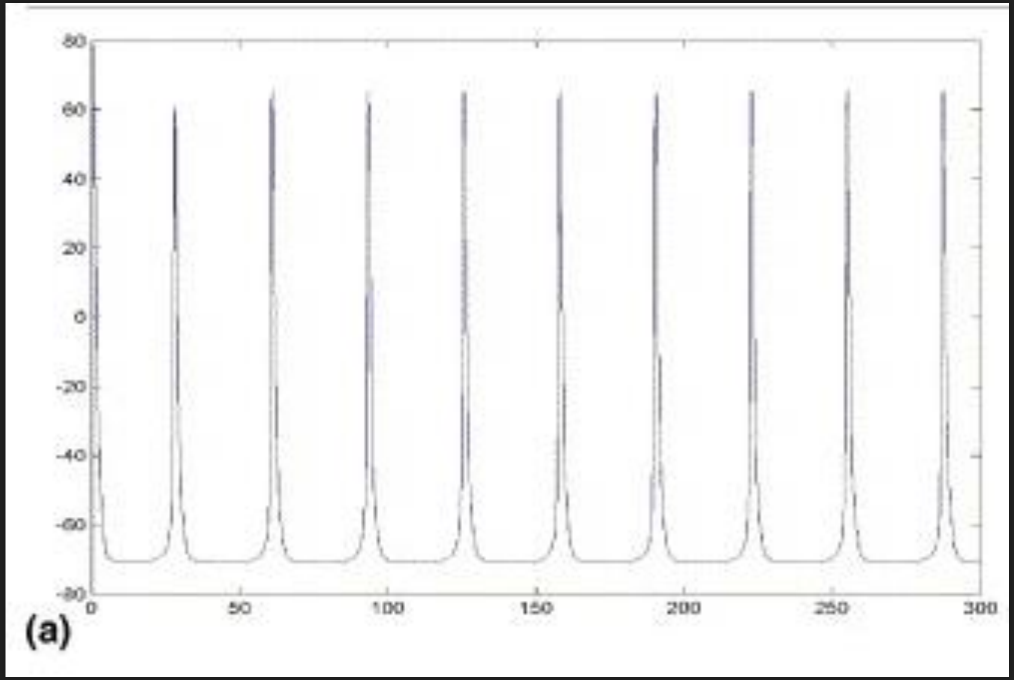
- The system has a sub-critical Hopf bifurcation at:

  'g_l' = 0.299406 mS/cm^2

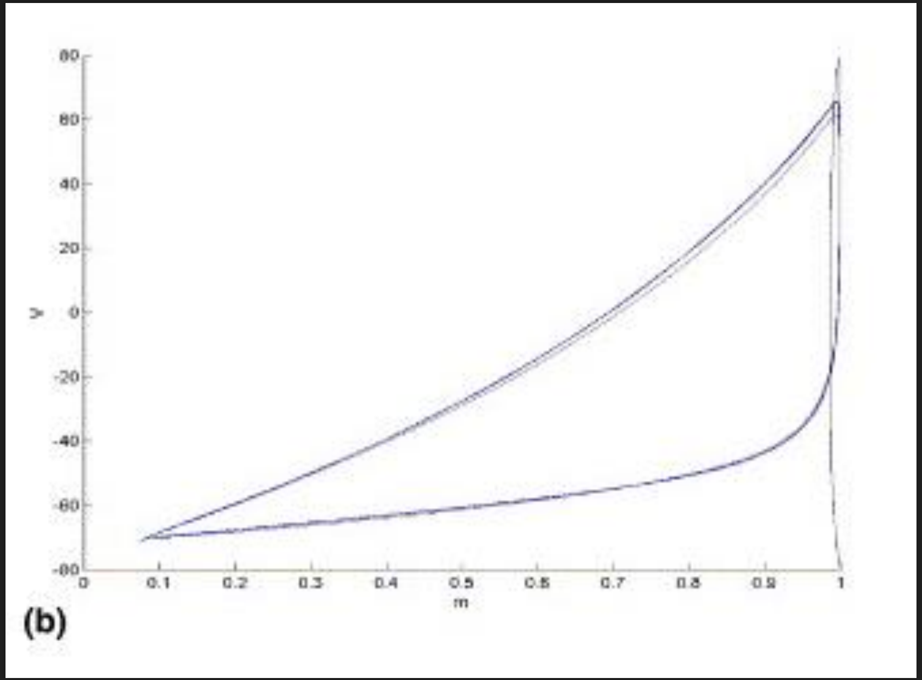
- It means after this limit cycle appears and bifurcation happens.
- Generally, for 'g_l' greater than the above value, the cell will send a single action potential and come to rest. However at smaller values the cell gets stuck in a limit cycle and keeps firing.

BIFURCATION WITH ‘V_{Na}’ & ‘g_l’

Time Series of V_m



V_m vs M



Mercé
Xièxie
Sagolun
Obrigado
ありがとう
Takk
Tak
Hvala
Grazie
Sagolun
Mahalo
Mauruuru
Matondo
Obrigado
Efharisto
Kiitos
Dankjewel
Köszönöm
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Спасибо

Appendix: Detailed Biophysics of HH

- https://www.youtube.com/watch?v=88tKZLGOr3M&pp=ygUVbWl0b2N3IGhvZGdraW4gaHV4bGV5

- https://www.youtube.com/watch?v=K1pxJVdqlxw