# Mathematical Modelling of a single Neuron

## An internship project

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# WORKFLOW

Hodgkin Huxley Model

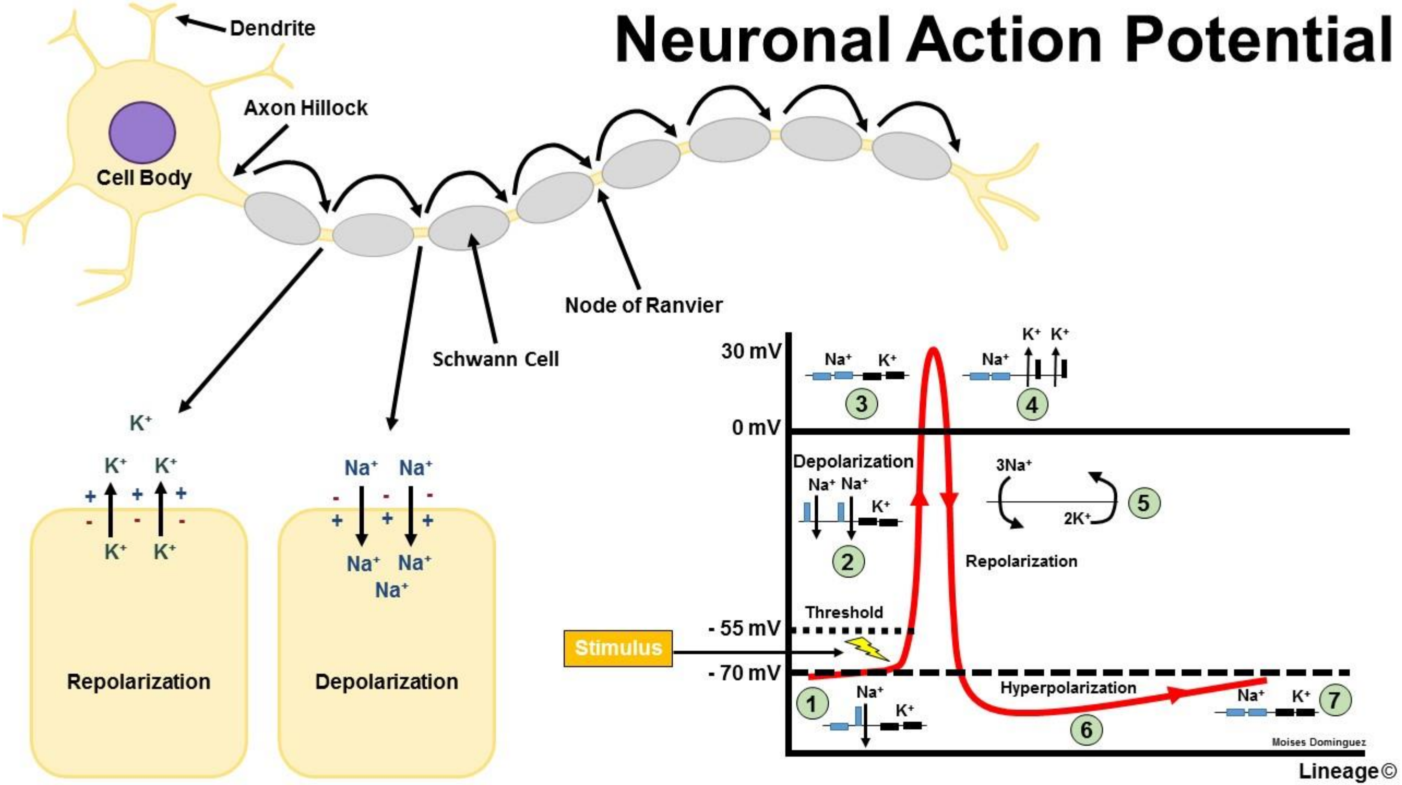
Voltage clamp experiments

Numerical methods used to solve the model:

- Euler's method
- Runge_Kutta method
- Predictor- Corrector method
- ODE45
- Comparison of models

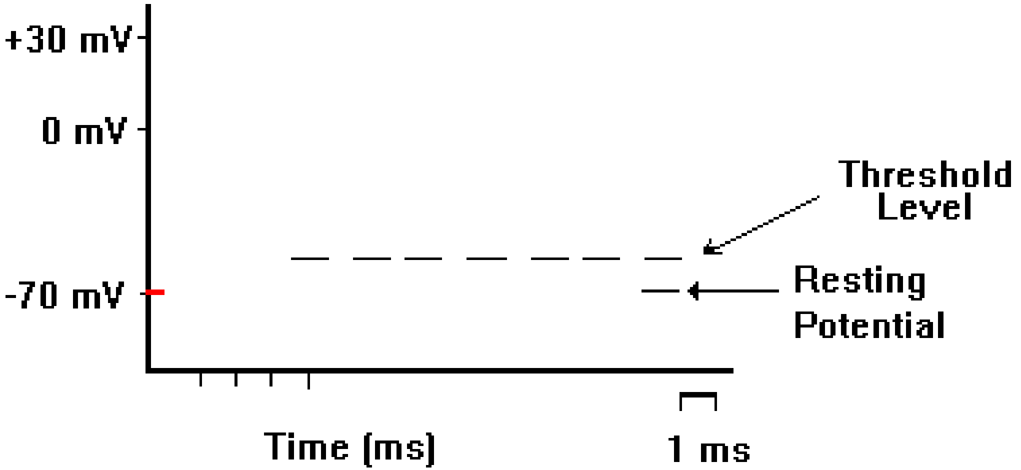
Results obtained using MATLAB

# Introduction

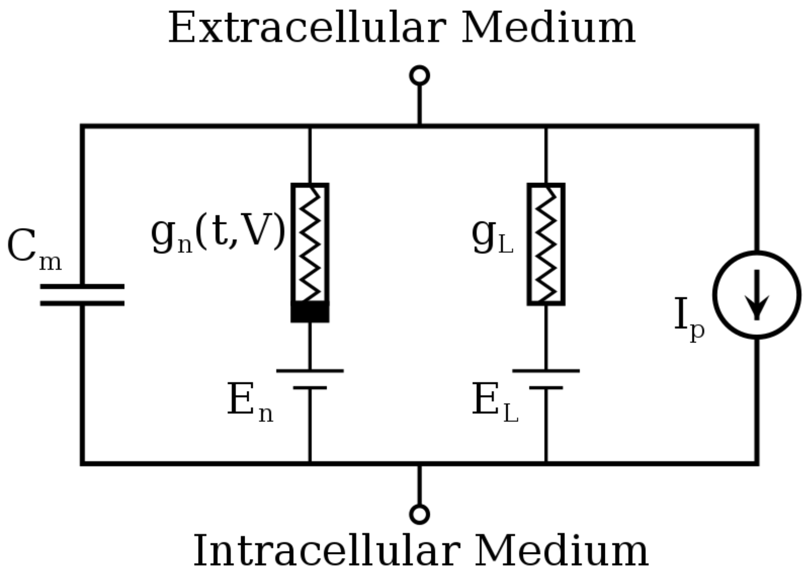


This model is a simulation of single neuron's action potential using Matlab

This model is developed using Hudkin-Huxley model.

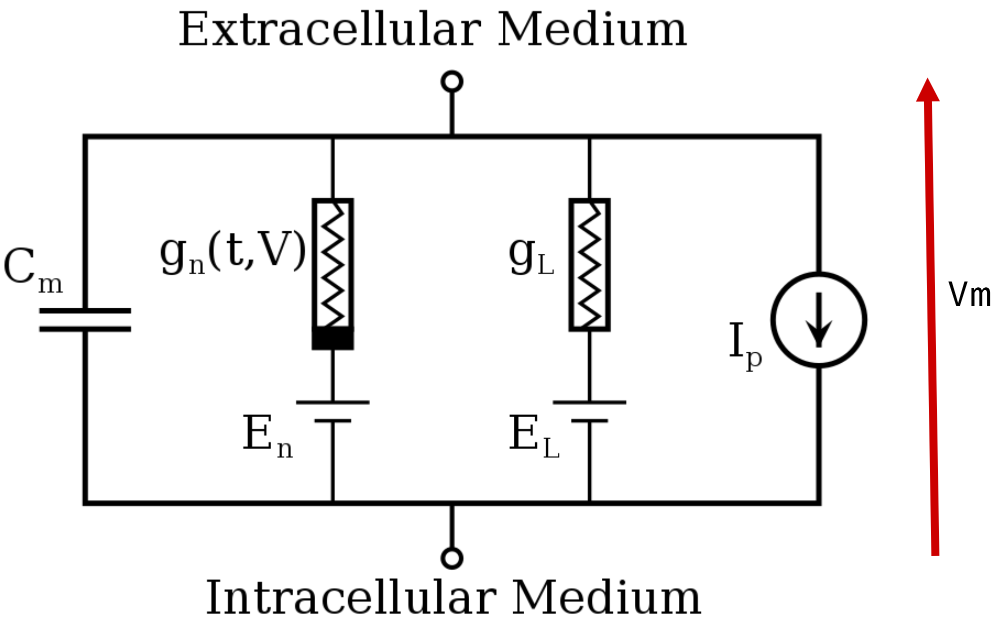


# Hodgkin-Huxley model



- The **Hodgkin–Huxley model**, or **conductance-based model**, is a mathematical model that describes how action potentials in neurons are initiated and propagated.
- It is a set of nonlinear differential equations that approximates the electrical characteristics of excitable cells such as neurons and cardiac myocytes.
- It is a continuous-time dynamical system.
- Alan Hodgkin and Andrew Huxley described the model in 1952 to explain the ionic mechanisms underlying the initiation and propagation of action potentials in the squid giant axon.

- Conductivity is equivalent to permeability and also it is variable with channel opening and closing.
- En is equivalent to the electrostatic potential that drives during natural diffusion.
- El is equivalent to the leakage of unspecific channels.
- Ip represents the pumping of Na ions into the membrane during excitation.
- Cm is the membrane capacitance



# PARAMETERS

- m,n,h - gates
- Cm- membrane capacitance
- I- external current stimulus
- gNa,gK,gl- conductances of sodium,potassium and leak channels
- ENa,EK- equilibrium potentials of sodium and potassium ions
- Alpha,beta-rate constants

# The voltage clamp experiment

- As they kept the voltage constant, the conductance of the channel increased to a steady value dependant on the initial voltage .
- Their most significant finding was that the rate at which the conductance reached its maximum depended greatly on the clamped voltage.

- Initially, the resting value of n is

$$n_\infty(0) = \frac{\alpha_n(0)}{\alpha_n(0) + \beta_n(0)}.$$

- But as the voltage is clamped to a different voltage, Vc, the steady state becomes

$$n_\infty(V_c) = \frac{\alpha_n(V_c)}{\alpha_n(V_c) + \beta_n(V_c)}.$$

A solution can then be found mathematically to solve

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

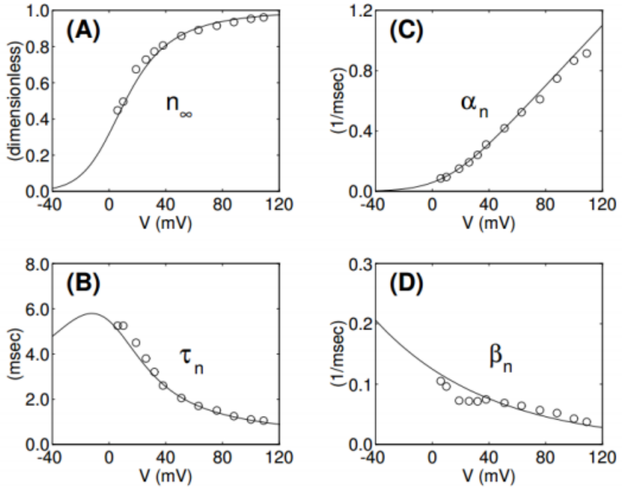
with the above restraints. This simple solution is an exponential of the form

$$n(t) = n_\infty(V_c) - \left(n_\infty(V_c) - n_\infty(0)\right)e^{-\frac{t}{\tau_n}},$$

Where

$$\tau_n(V_c) = \frac{1}{\alpha_n(V_c) + \beta_n(V_c)}.$$

- Trial-and-error method to find the proper order of the gates sigmoidal conductance found from previous results.




$$\alpha_n = \frac{0.01(v+50)}{1-\exp\left(\frac{-(v+50)}{10}\right)}$$

$$\beta_n = 0.125\exp\left(\frac{-(v+60)}{80}\right)$$

$$\alpha_m = \frac{0.1(v+35)}{1-\exp\left(\frac{-(v+35)}{10}\right)}$$

$$\beta_m = 4.0\exp\big(-0.0556(v+60)\big)$$

$$\alpha_h = 0.07\exp\left(-0.05(v+60)\right)$$

$$\beta_h = \frac{1}{1+\exp\big(-0.1(v+30)\big)}$$

# Equations used

$$\frac{dv}{dt} = \frac{1}{C_m} \cdot [I - g_{Na} m^3 h(v - E_{Na}) - g_K n^4 (v - E_K) - g_l (v - E_l)]$$

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

$$\frac{dm}{dt} = \alpha_m(v)(1 - m) - \beta_m(v) m$$

$$\frac{dh}{dt} = \alpha_h(v)(1 - h) - \beta_h(v) h$$

$$\alpha_n = \frac{0.01(v+50)}{1-\exp\left(\frac{-(v+50)}{10}\right)}$$

$$\beta_n = 0.125\exp\left(\frac{-(v+60)}{80}\right)$$

$$\alpha_m = \frac{0.1(v+35)}{1-\exp\left(\frac{-(v+35)}{10}\right)}$$

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$$\alpha_h = 0.07\exp\left(-0.05(v+60)\right)$$

$$\beta_h = \frac{1}{1+\exp\big(-0.1(v+30)\big)}$$

# Parameters

$C_m = 0.01 \mu F/cm^2$ Found experimentally

$E_{Na} = 55.17 mV$

$E_K = -72.14 mV$

$E_l = -49.42 mV$

$G_{Na}(max) = 1.2 mS/cm^2$

$G_K(max) = 0.36 mS/cm^2$

$G_l(max) = 0.003 mS/cm^2$

# Algorithm for different numerical approaches

EULER METHOD

Define $f(t, y)$
Define $t_o, y_o$
Define step size $h$ and number of steps $n$
**for** $i = 1 : n$ **do**
    $m = f(to, yo)$
    y1=yo+h.m
    t1=t$_o + h$
    t$_o = t1$
    y$_o = y1$
**end**
Ouput $y$

# RUNGE-KUTTA METHOD

Define $f(t, y)$
Define $t_o, y_o$
Define step size $h$ and number of steps $n$
**for** $i = 1 : n$ **do**
    $k1 = h.f(t_o, y_o)$
    k2=h.f($\mathrm{t}_o + h/2, y_o + k1/2$)
    k3=h.f($\mathrm{t}_o + h/2, y_o + k2/2$)
    k4=h.f($\mathrm{t}_o + h, y_o + k3$)
    y1=$\mathrm{y}_o + k1/6 + k2/3 + k3/3 + k4/6$
    t1=to+h
    $\mathrm{t}_o = t1$
    $\mathrm{y}_o = y1$
    **end**
    Ouput $y$

# PREDICTOR_CORRECTOR METHOD

Define $f(t, y)$
Define $t_o, y_o$
Define step size $h$ and number of steps $n$
**for** $i = 1 : n$ **do**
    $y1 = y_o + h.f(t_o, y_o)$
    t1=$\mathrm{t}_o + h$
    y1c=$\mathrm{y}_o + h/2f(t_o, y_o) + f(t1, y1)$
    $\mathrm{t}_o = t1$
    $\mathrm{y}_o = y1c$
**end**
Ouput $y$

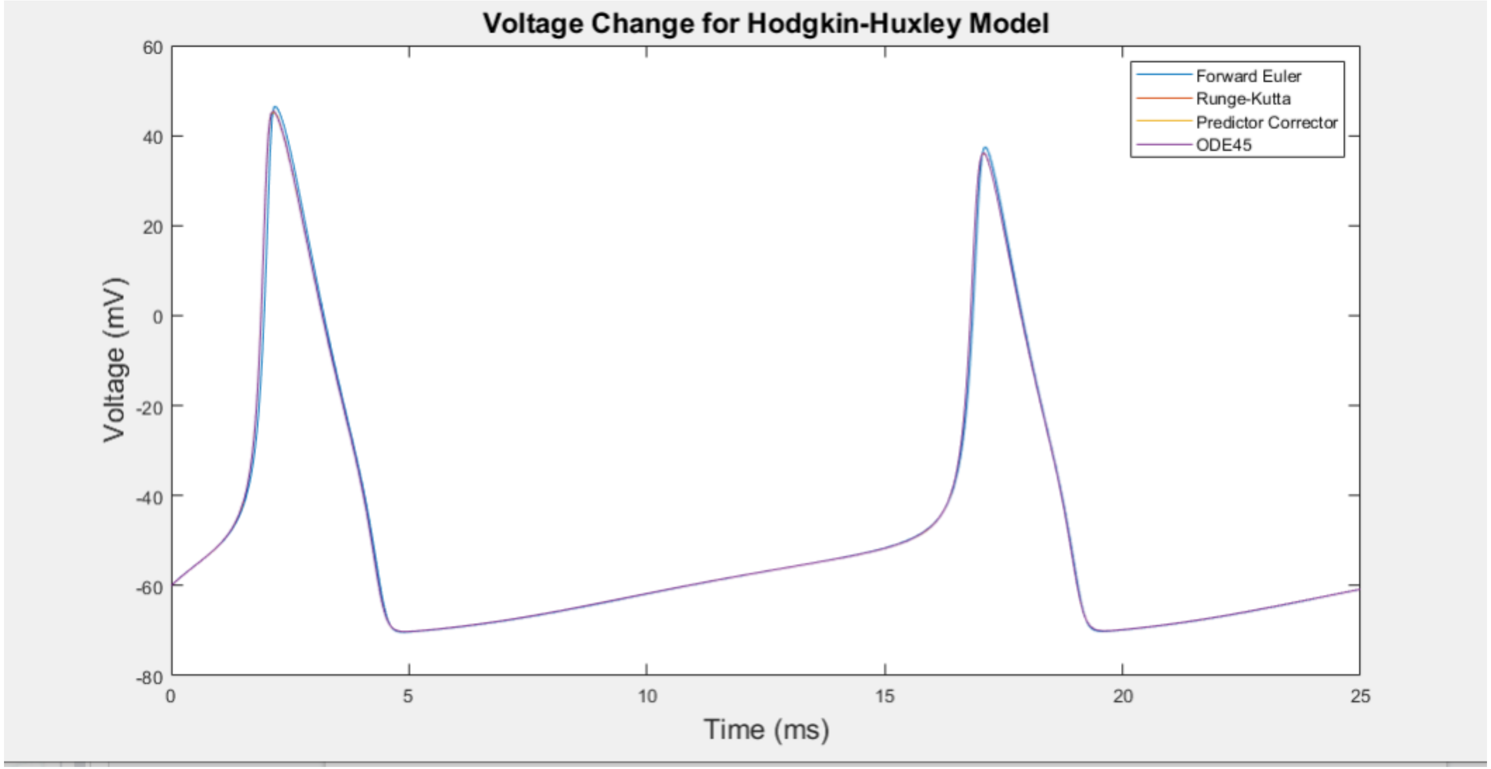
# Algorithm for solving HH model

Define parameters
Apply external current
Define time step and time array
Initialize$V(1), m(1), h(1), n(1), gNa(1), gK(1), gl(1), INa(1), IK(1), Il(1), alpha(1), beta(1)$
Define HH function
**for** $i = 1 : size(timearray)$ **do**
    Any of the above methods to solve $v(t)$
**end**
Ouput $v(t)$

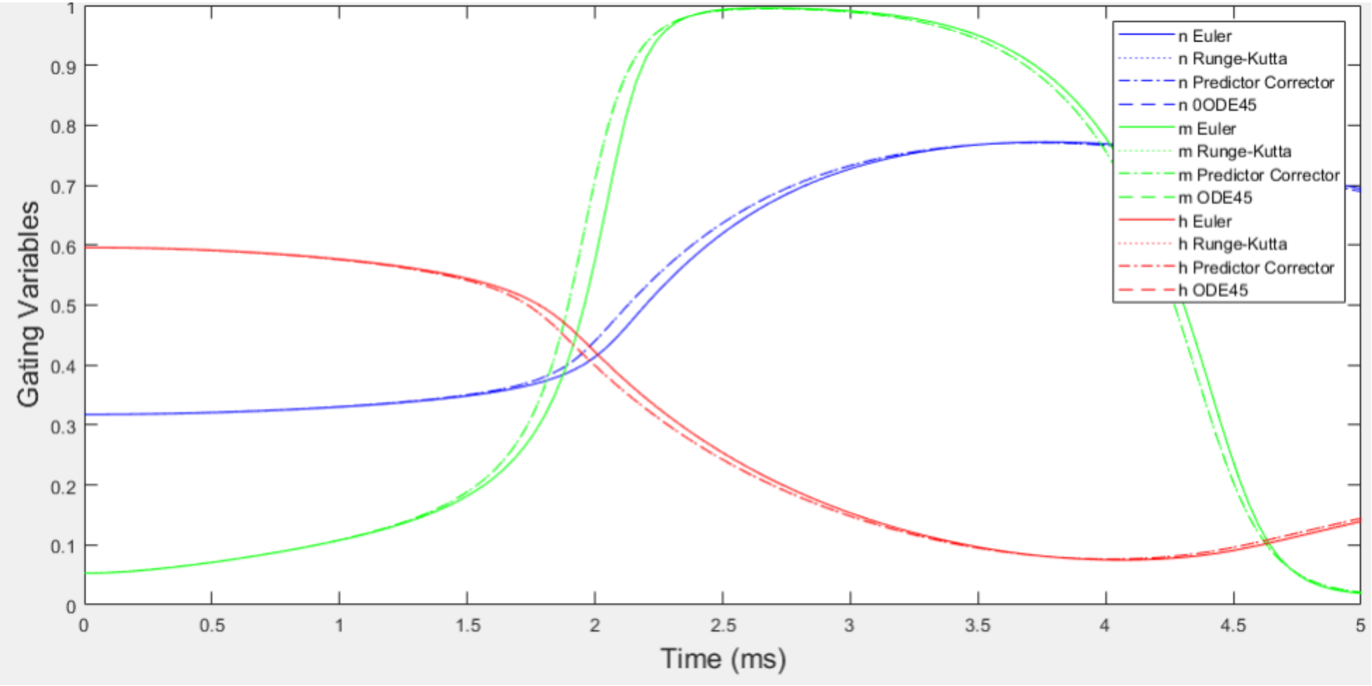
For the ODE45,

Define HH, alpha and beta functions

# Results



Voltage Change for Hodgkin-Huxley Model
Voltage (mV)
Time (ms)
60
40
20
0
-20
-40
-60
-80
0
5
10
15
20
25
Forward Euler
Runge-Kutta
Predictor Corrector
ODE45

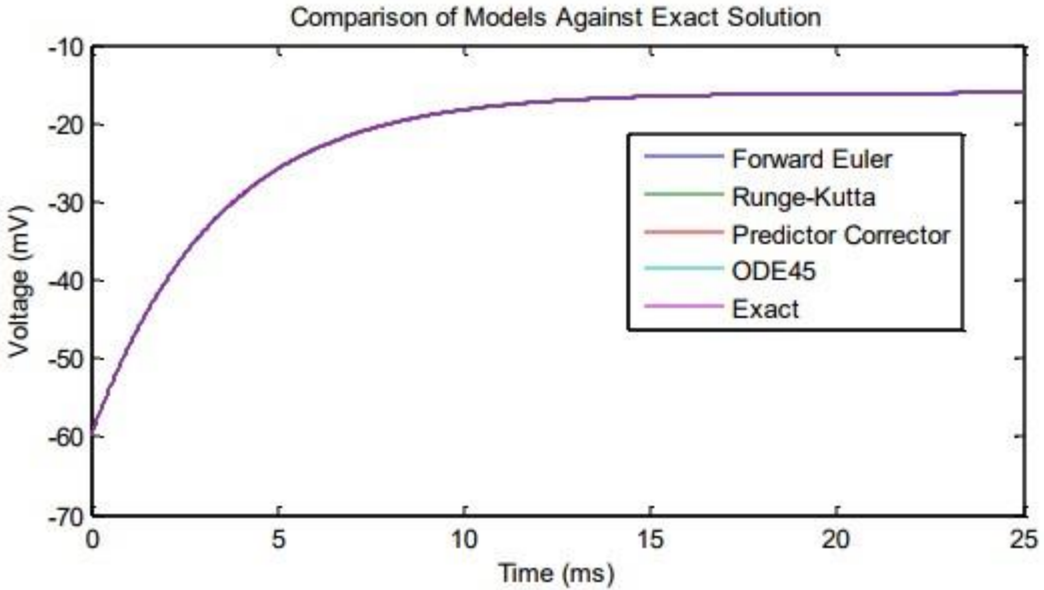


Gating Variables
Time (ms)
n Euler
n Runge-Kutta
n Predictor Corrector
n 0ODE45
m Euler
m Runge-Kutta
m Predictor Corrector
m ODE45
h Euler
h Runge-Kutta
h Predictor Corrector
h ODE45

By setting conductances to zero

$$\frac{dv}{dt} = \frac{1}{C_m}[I - g_l(v - E_l)]$$

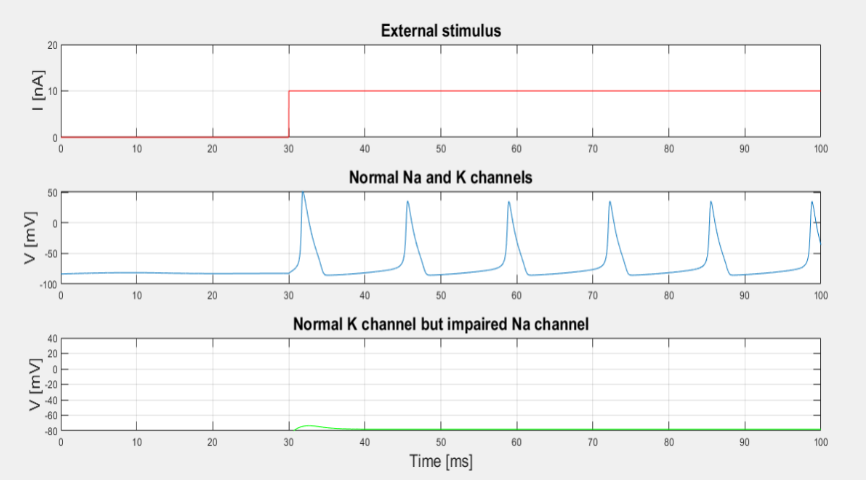
$$v = \frac{1}{g_l}[-\exp\left(-\frac{g_l}{C_m}t\right)(I + 60g_l + g_lE_l) + I + g_lE_l]$$

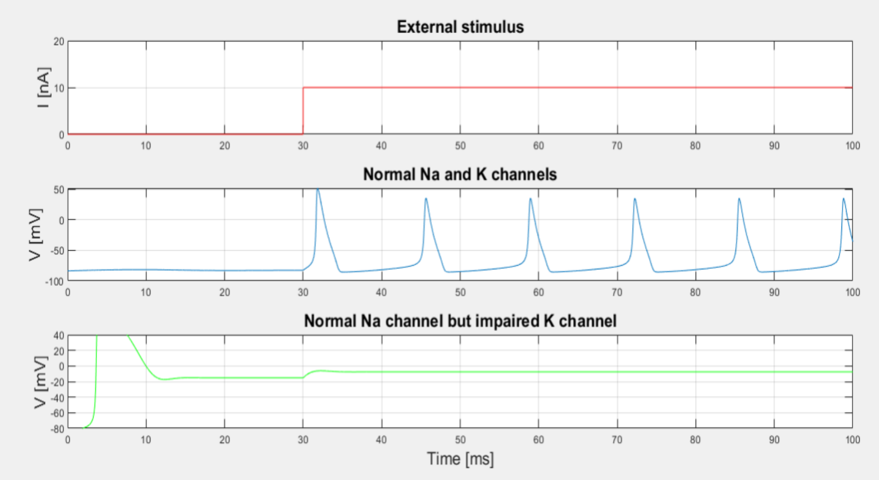



| Method | Average Error |
|---|---|
| Forward Euler | 0.034984 |
| Runge-Kutta | 0.00000010155 |
| Predictor Corrector | 0.000000012004 |
| ODE45 | 0.00030036 |

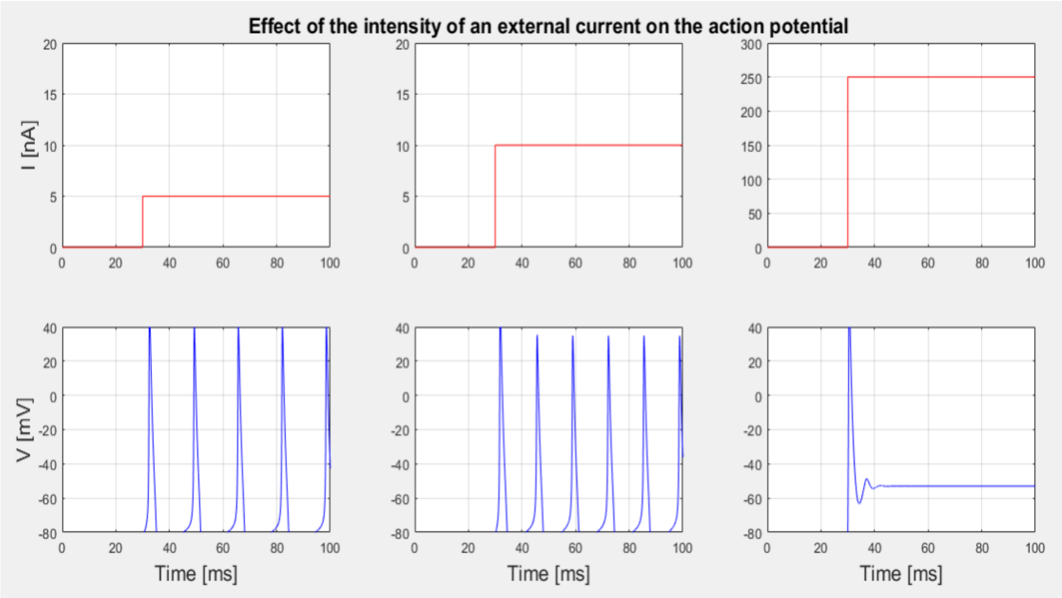
# Further analysis

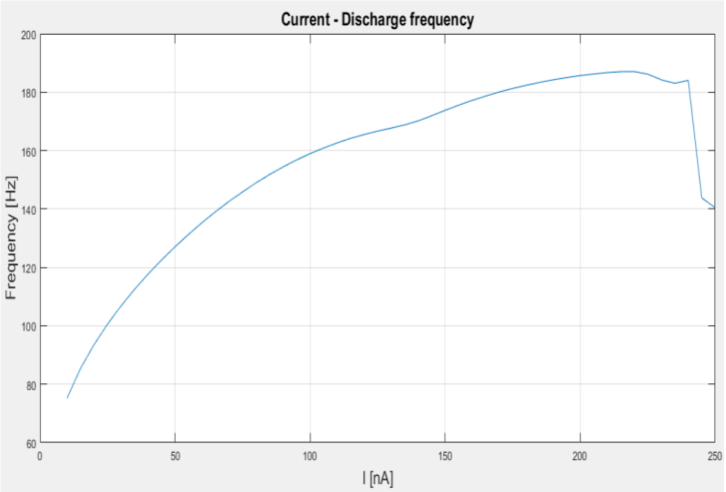
Channel impairment



# Effect of current intensity



# Conclusions and future work

- Information about neural signaling-all or none
- The Runge-Kutta and predictor-corrector methods gave the most accurate results
- Relation between frequency and current intensity
- Response to time varying stimuli
- Learning algorithm
- Neural networking and energy efficiency

# References and citations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