DOING PHYSICS WITH PYTHON

GEOMETRICAL OF ANALYSIS OF [1D] DYNAMICAL SYSTEMS

LEAK / FAST Na^+ CHANNELS

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mns007.py Lleaky ion channel and Na+ channel with constant conductance. Solve ODE using **odeint**. Calculate steady-state values

$t \; vs \; V_M$, $t \; vs \; I$, $V_M \; vs \; dV_M / dt$, $I \; vs \; V_M$

mns007A.py Leaky and Na^+ ion channels, Na^+ conductance as a function of V_M, fixed points $dV_M(t)/dt = 0$. Find zeros.

$V_M \; vs \; dV_M / dt$, $I \; vs \; V_M$, $V_M \; vs \; G_{\mathrm{Na}}$

mns007B.py Leaky ion current and Na^+ ion channel with variable Na^+ conductance. Solve ODE using odeint →

$t \; vs \; V_M$, $t \; vs \; I$

mns007AA.py Bifurcation diagram where I_{ext} is the bifurcation parameter. Find zeros.

INTRODUCTION

This article considers geometrical methods of analysis of the [1D] dynamical system for a segment of a neuron modelled as an *RC* circuit where the membrane potential $V_M(t)$ is a scalar time-dependent variable which represents the state of the system and is known as a **state variable.** The membrane has capacitance C, a leak ion channel with constant resistance R_L (constant conductance G_L), and a fast Na^+ channel with resistance R_{Na} (conductance G_{Na}). The system is stimulated by a constant external current I_{ext} where $I_{ext} \leq 0$. The negative sign indicates a net flow of positive charge into the neuron from the extracellular region.

In general, [1D] dynamical systems are described by ordinary differential equations of the form

$$dV(t)/dt = f(V(t))$$

The direction of movement of the state variable $V(t)$, and hence the evolution of the dynamical system is determined by the sign of the function $f\left(V(t)\right)$.

$$f\left(V(t_0)\right) < 0 \Rightarrow \left.\frac{dV(t)}{dt}\right|_{t_0} < 0 \Rightarrow V(t_0) \text{ is decreasing at time } t_0$$

$$f\left(V(t_0)\right) > 0 \Rightarrow \left.\frac{dV(t)}{dt}\right|_{t_0} > 0 \Rightarrow V(t_0) \text{ is increasing at time } t_0$$

$$f\left(V(t_0)\right) = 0 \Rightarrow \left.\frac{dV(t)}{dt}\right|_{t_0} = 0 \Rightarrow V(t_0) \text{ is a fixed point}$$

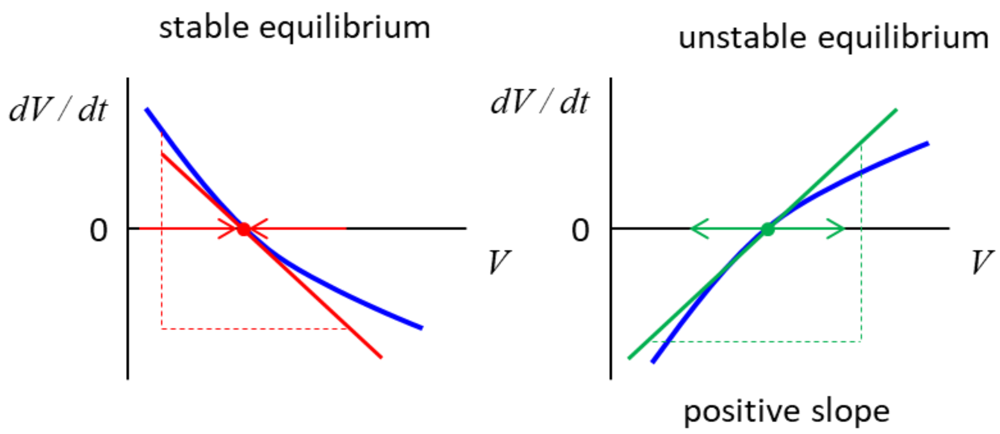


Fig. 1. The sign of the slope of the curve dV_M / dt vs V_M at an equilibrium point determines the stability of the fixed point

slope > 0 → unstable fixed point

slope < 0 → stable fixed point

The phase portraits for the dynamics of a neuron are plots of $V_M(t)$ vs $dV_M(t) / dt$ and are important in the analysis of any dynamical system. It depicts all **stable** and **unstable** equilibria, trajectories and corresponding attraction domains in the system. It shows all possible evolutions of the state variable and how they depend upon the initial state. Looking at the phase portrait, one immediately gets all the important qualitative information about the behaviour of the system without even knowing the solution. If the initial value of the membrane potential variable is exactly at a fixed point, then $dV_M / dt = 0$ and the membrane potential will stay there forever. For an initial value is near equilibrium, then the membrane potential may approach or diverge from it.

At an equilibrium point, when the slope of the curve $dV_M / dt \;\; vs \;\; V_M$ is **negative**, then the **equilibrium is stable.** We say that an equilibrium is **asymptotically stable** if all solutions starting sufficiently near the equilibrium will approach it as $t \to \infty$. Hence, a stable equilibrium point attracts all nearby solutions, and is called an **attractor**. In a [1D] system, an attractor is the only type of stable equilibrium.

At an equilibrium point, when the slope of the curve $dV_M / dt \;\; vs \;\; V_M$ is **positive**, then the **equilibrium is unstable**. All solutions starting sufficiently near the equilibrium will diverge from it as $t \to \infty$. Hence, an unstable equilibrium point repels all nearby solutions, and is called a **repeller**.

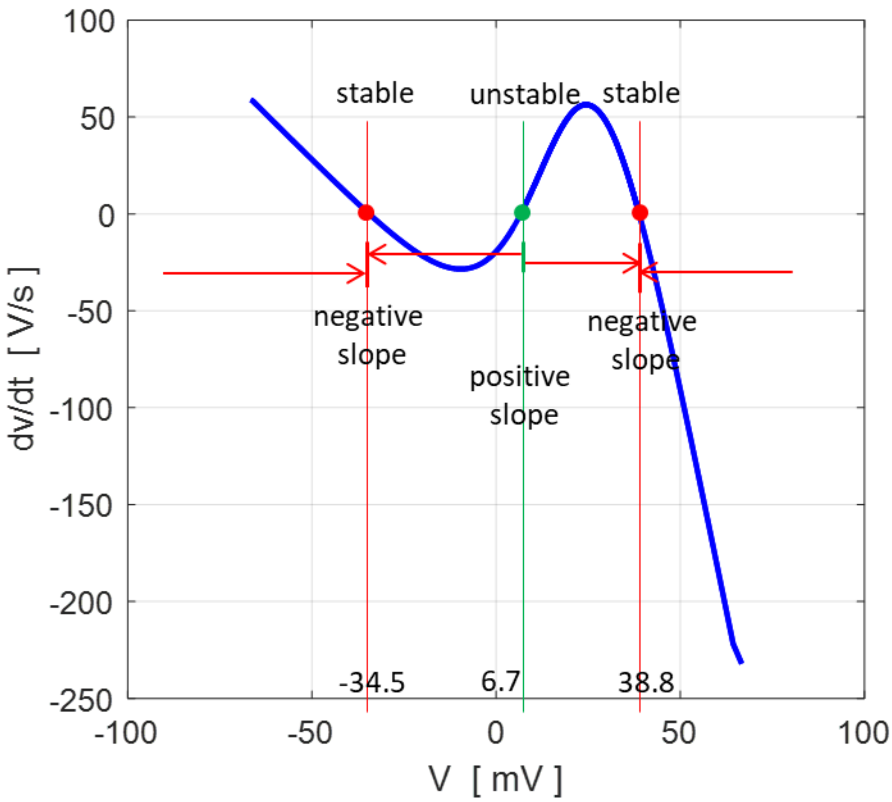


Fig. 2. I_{ext} = -0.60 mA. There are two attraction domains which are separated by the unstable equilibrium point at +6.7 mV. For any initial membrane potential, the membrane potential will converge to one of the two stable equilibrium points: - 34.5 mV (rest state) or + 38.9 mV (excited state). The red arrows show the attraction domains. An attraction domain of an attractor is the set of all initial conditions that lead to the attractor. **mns007A.py**

If a [1D] system has two stable equilibrium points (figure 2), then they must be separated by at least one unstable point since the slope of a stable equilibrium point is negative. At membrane potentials near an unstable point, the membrane potential can diverge either to the rest state or excited state depending on whether the membrane potential is slightly lower or greater than the unstable value. Unstable equilibria play the role of **thresholds** in [1D] bistable systems (systems having two attractors). Suppose the membrane potential is just below the unstable value when a perturbation increases the membrane potential. If the perturbation is small and **sub-threshold**, the membrane potential will be attracted to the resting state. However, a larger perturbation may increase the membrane potential about the unstable value and the membrane potential will be attracted to the excited state. This perturbation is called **super-threshold** or **supra-threshold**. Thus, the unstable equilibrium acts as a threshold that separates two states.

[DYNAMICAL SYSTEMS [1D]: FIXED POINTS AND STABILITY]

MATHEMATICAL MODEL: LEAK / FAST Na^+ CHANNELS

A simplified version of the Hodgkin-Huxley model of a neuron is considered where the membrane's electrical properties are described by a combination of fast sodium Na^+ channels (responsible for action potential generation) and leak channels (responsible for establishing the resting potential). The leak channels are non-gated and stay open, setting the resting membrane potential. Na^+ channels open rapidly, then close quickly via an inactivation gate. The circuit diagram for the model is shown in figure 3.

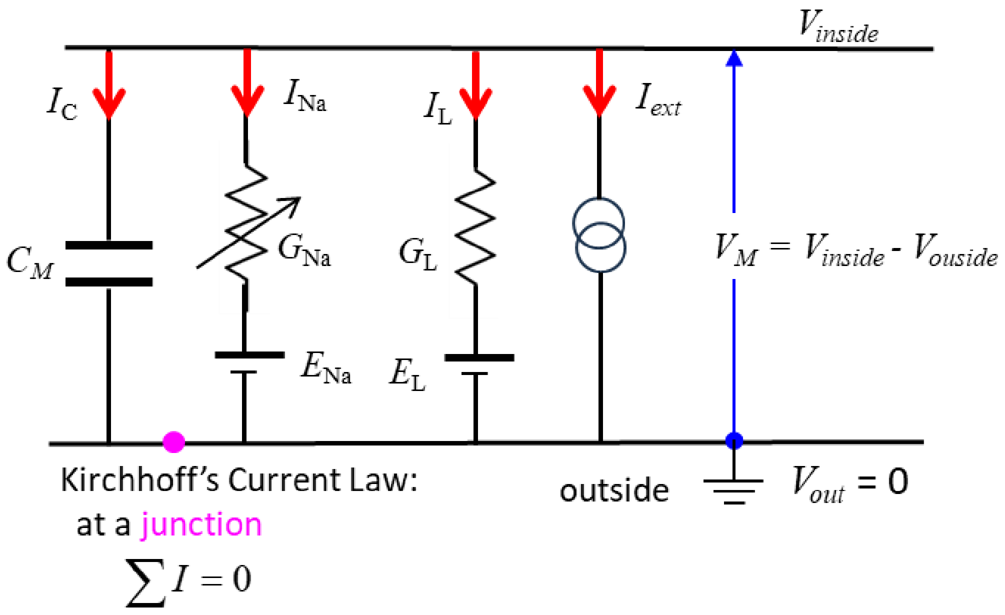


Fig. 3. Circuit diagram for the leak / fast Na^+ channels

Table 1 gives a summary of the model parameters, values and units.

Figure 4 shows the convention for the sign of the current.

Table 1. Model parameters,

symbol	**Parameter**	**Value & unit**
C_M	membrane capacitance	$10x10^{-6}$ F
G_{Na}	sodium conductance	S
G_{Na_max}	max sodium conductance	$74x10^{-3}$ S
G_L	leak conductance	$19x10^{-3}$ S
E_{Na}	sodium reversible potential	$+60x10^{-3}$ V
E_L	leak reversible potential	$-67x10^{-3}$ V
I_C	capacitor current	A
I_{Na}	Na^+ current	A
I_L	leak current	A
I_{ext}	external current stimulus	A
I_M	membrane current $I_M = I_{Na} + I_L$	A
V_M	membrane potential	V
V_{SS}	steady-state potential	V
t	time	s

Model equations

$$I_C + I_{Na} + I_L + I_{ext} = 0 \qquad I = V / R = GV$$

$$I_C = -\left(I_{Na} + I_L + I_{ext}\right)$$

$$I_C = C_M \, dV_M / dt \quad I_{Na} = G_{Na}\left(V_M - E_{Na}\right) \quad I_L = G_L\left(V_M - E_L\right)$$

$$dV_m / dt = -\left(I_{Na} + I_L + I_{ext}\right) / C_M$$

$$dV_m / dt = -\left(G_{Na}\left(V_M - E_{Na}\right) + G_L\left(V_M - E_L\right) + I_{ext}\right) / C_M$$

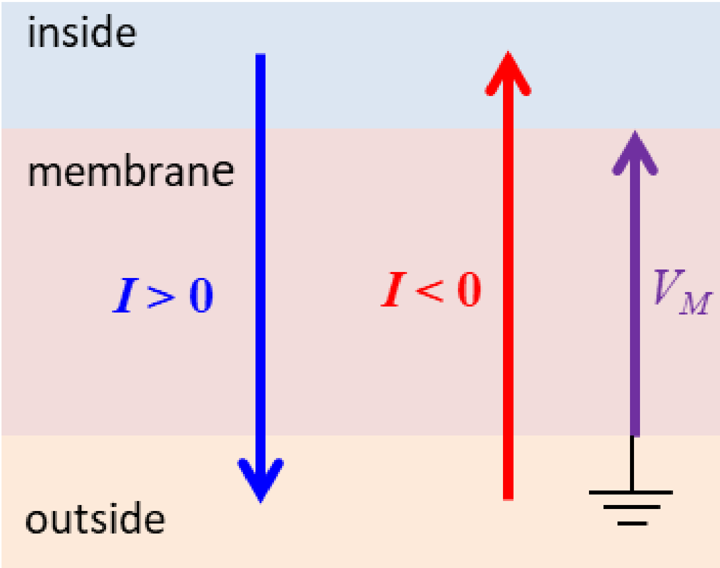


Fig. 4. The sign convention for the currents. The positive direction for the current is from the inside of the neuron to the outside and negative for currents directed from outside to inside. A positive current transfers positive charges from the inside to the outside, thus hyperpolarizing the neuron by reducing the membrane potential (becomes less positive). A negative current transfers positive charges from the outside to the inside, thus depolarizing the neuron by increasing the membrane potential (becomes more positive).

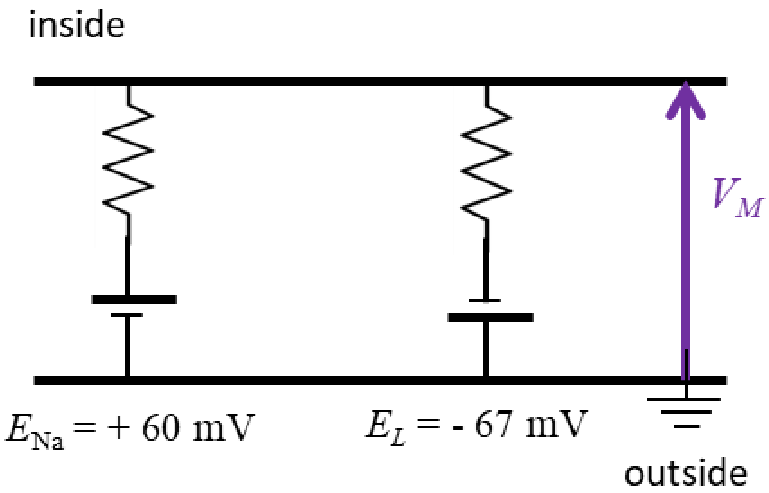


Fig. 5. Reversal potentials.

SIMULATION 1

Leak channels and Na$^+$ channels with constant conductances

In this model it is assumed that the conductances for both the leak and Na$^+$ channels are constants

$$G_L = 19\text{x}10^{-3}\ \text{S} \qquad G_{\text{Na}} = G_{\text{Na\_max}} = 74\text{x}10^{-3}\ \text{S}$$

The system ODE that needs to be solved is

$$dV_m / dt = -\left(G_{Na}\left(V_M - E_{Na}\right) + G_L\left(V_M - E_L\right) + I_{\text{ext}}\right) / C_M$$

The fixed point for the steady state solution V_{SS} is

$$dV_m / dt = 0 \;\Rightarrow\; V_{SS} = \frac{I_{ext} + G_{\text{Na}}\, E_{\text{Na}} + G_L\, E_L}{G_{\text{Na}}\, E_{\text{Na}} + G_{Na}\, E_{Na}}$$

and the steady-state currents are

$$I_C = 0 \quad I_{Na} = G_{Na}\left(V_{SS} - E_{Na}\right) \quad I_L = G_L\left(V_{SS} - E_L\right)$$

$$I_M = I_{Na} + I_L = -I_{ext} \qquad I_{net} = I_{ext} + I_C + I_{Na} + I_L = 0$$

If the membrane potential is disturbed from its rest potential V_{SS} then it will exponentially decay back to its resting level V_{SS} and the currents go to their steady-state values (figures 6 and 7). The external current is negative, thus positive charges are transferred from outside the cell to inside the cell $\left(I_{ext} = -0.60 \text{ mA} < 0\right)$.

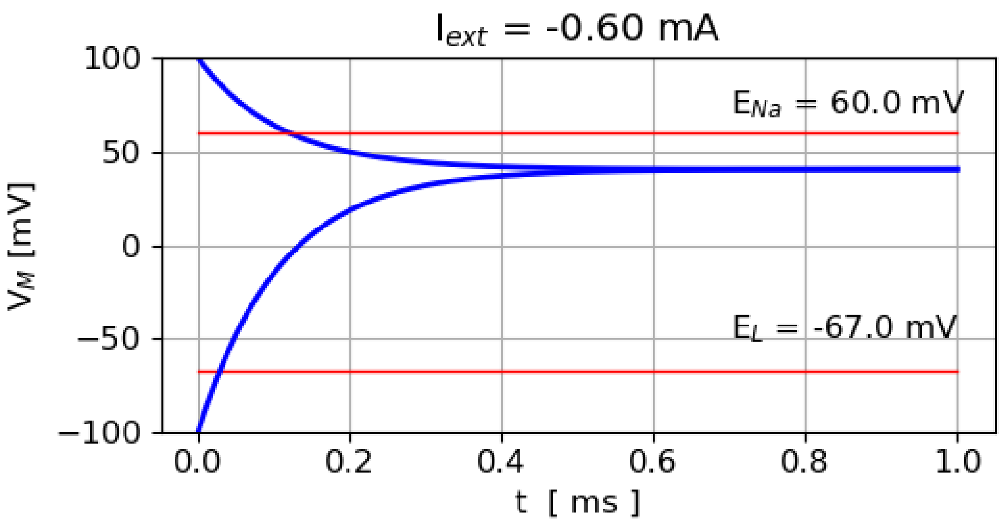
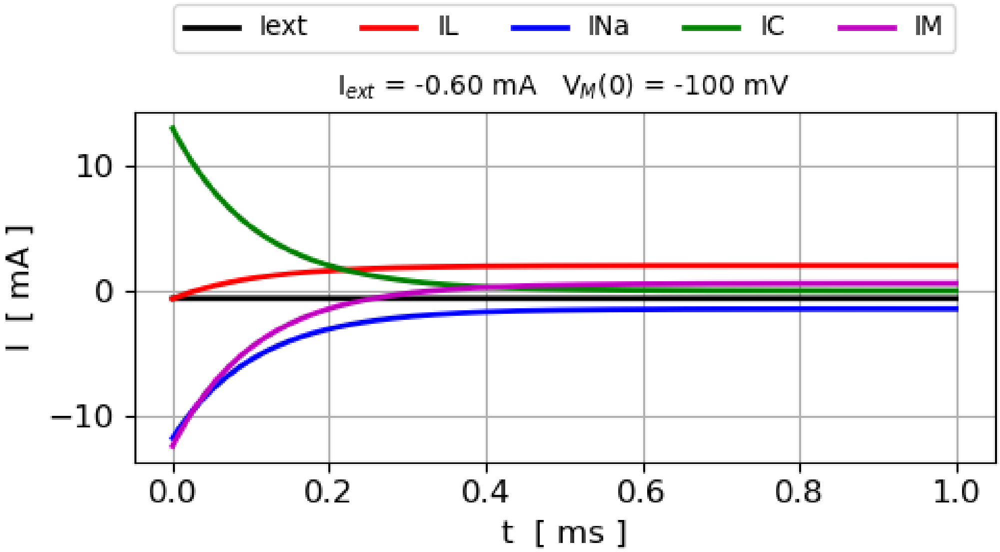


Fig. 6. I_{ext} = -0.60 mA, $V_M(0)$ = + 100 mV, and $V_M(0)$ = - 100 mV. The membrane potential V_M relaxes exponentially back to the resting potential V_{SS} = 40.5 mV $\left(E_L < V_{SS} < E_{Na}\right)$. **mns007.py**



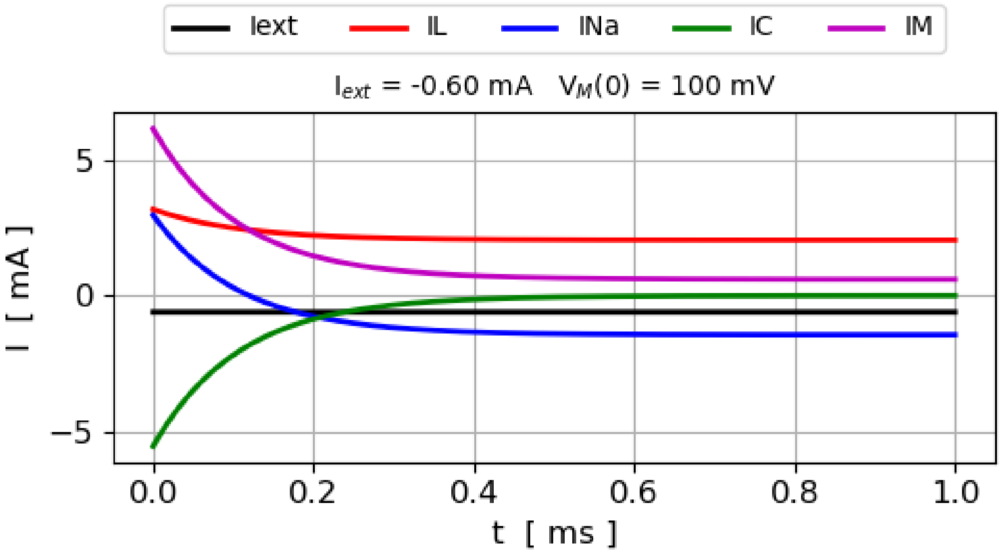


Fig. 7. The evolution of the circuit currents.

I_{C_ss} = 0.0 mA $I_{\mathrm{Na\_ss}}$ = -1.4 mA I_{L_ss} = 2.0 mA IM_ss = 0.6 mA

When $V_M(0)$ = -100 mV, the initial Na^+ current is negative and the Na^+ flow from the outside of the membrane to the inside which increases the membrane potential V_M.

When $V_M(0)$ = +100 mV, the initial Na^+ current is positive and the Na^+ flow from the inside of the membrane to the outside which decreases the membrane potential V_M. **mns007.py**

A **phase portrait** is a geometric representation of the trajectories of a dynamical system in the phase plane. Each set of initial conditions is represented by a different curve or point. Phase portraits are an invaluable tool in studying dynamical systems. The phase portrait is a straight line (figure 8) for our neuron model of the plot of the time derivative of the potential against the potential. For all initial conditions, the membrane potential will be pulled (attracted) to the steady-state potential $V_{SS} = 40.5$ mV.

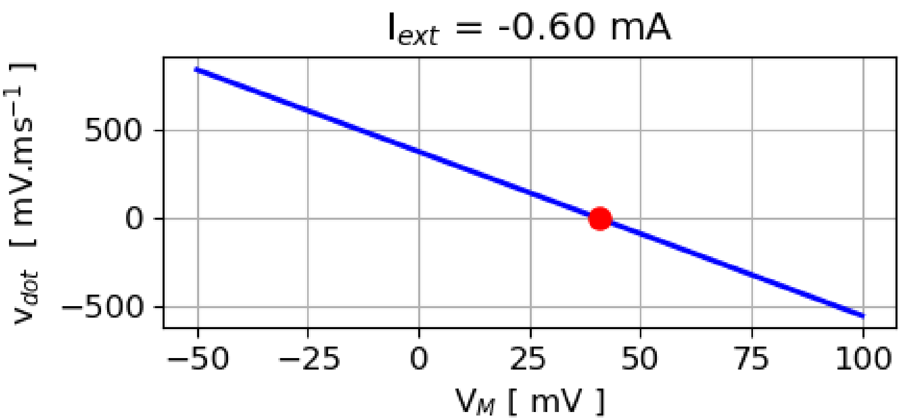


Fig. 8. The straight line corresponds to the phase portrait plot for the ohmic elements. The red dot shows the fixed point for the membrane potential when the time derivative of the potential becomes zero. All initial conditions for the membrane potential V_M will be attracted to the fixed point $V_{SS} = 40.5$ mV. There is only one fixed point for the system and the system is said to be monostable. **mns007.py**

A useful plot is the *I-V* characteristic curve as shown in figure 9.

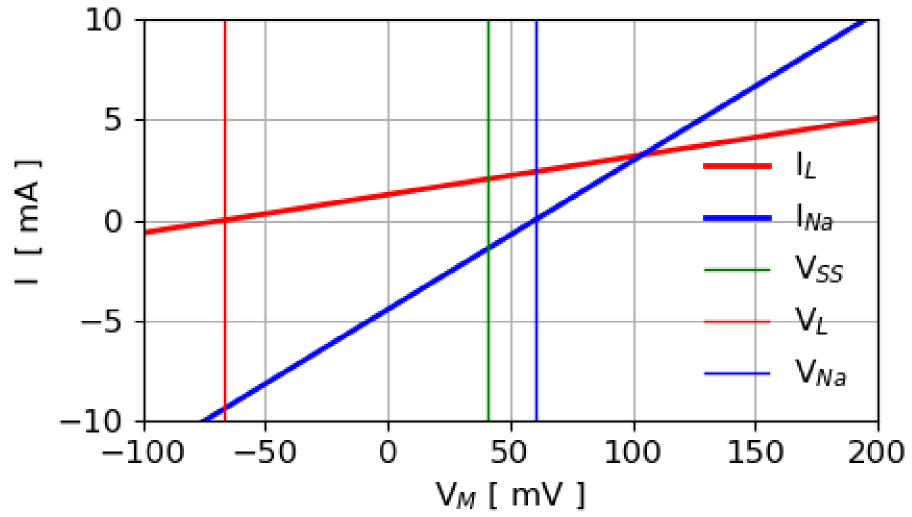


Fig. 9. *I-V* characteristic. A positive value of the current indicates an outward current (inside → outside) to decrease the membrane potential, while a negative current is an inward current (outside → inside) which increases the membrane potential. The straight lines means that the conductance G is constant and the slope of the line gives the numerical value of the conductance

$$G_L = 19 \text{ mS} \qquad G_{\text{Na}} = 74 \text{ mS}$$

$$I_L = 0 \Rightarrow V_M = E_L \qquad I_{\text{Na}} = 0 \Rightarrow V_M = E_{\text{Na}}$$ **mns007.py**

SIMULATION 2

Leak current / fast Na^+ ion channel model

In the model where the conductances G_L and G_{Na} are constant and independent of the membrane potential, it is impossible for an action potential to be generated. The only consequence of the membrane potential being briefly disturbed from its steady-state value is that the membrane potential will relax back to its steady-state value. So, we need a more complex model in which the conductance of the Na^+ channel is voltage dependent.

A comprehensive model of neuronal membrane dynamics, such as the Hodgkin–Huxley (HH) model, incorporates both fast, voltage-gated sodium Na^+ channels (responsible for action potentials) and independent, passive leak currents that help set the resting membrane potential. These two components work together to control neuronal excitability, with leak channels ensuring the cell does not remain hyperpolarized, while fast Na^+ channels allow for rapid depolarization phase of the action potential.

The conductance of the Na^+ channel is time-voltage-dependent, opening quickly in response to membrane depolarization, and inactivating shortly thereafter.

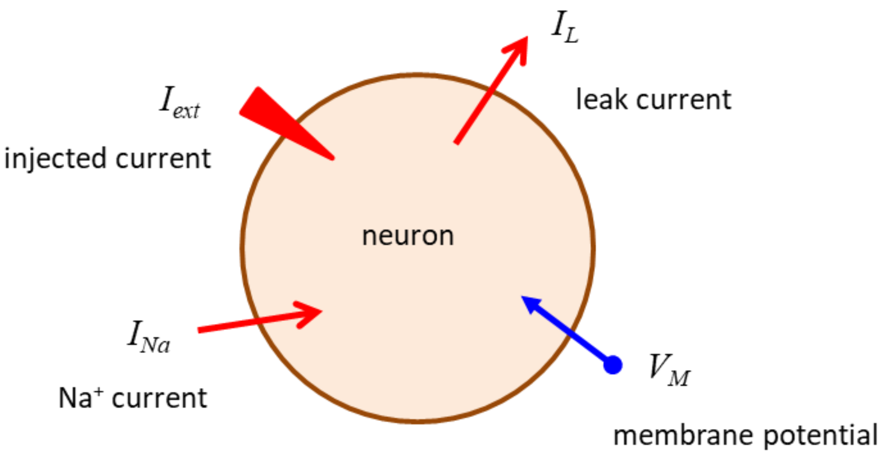


Fig. 8. Leak / Na$^+$ ion channels model.

Consider a space-clamped membrane having a leak current and a fast voltage-gated sodium ion current having only one gate variable m. The gating process is assumed to be instantaneous such that the variable m is equal to its asymptotic value m_{inf} where

$$(3) \qquad m \to \mathrm{m}_{\mathrm{inf}} = \frac{1}{1+\exp\left(\left(V_{1/2}-V_M\right)/k\right)}$$

$$V_{1/2} = 19 \text{ mV and } k = 9.0 \text{ mV}$$

The activation function $\mathrm{m}_{\mathrm{inf}}$ for a voltage-gated Na$^+$ channel describes the opening of the Na$^+$ ion channels such that the Na$^+$ conductance G_{Na} of membrane increases with increasing membrane potential V_M

$$(4) \qquad G_{Na} = G_{Na\_\max}\, m_{\mathrm{inf}}$$

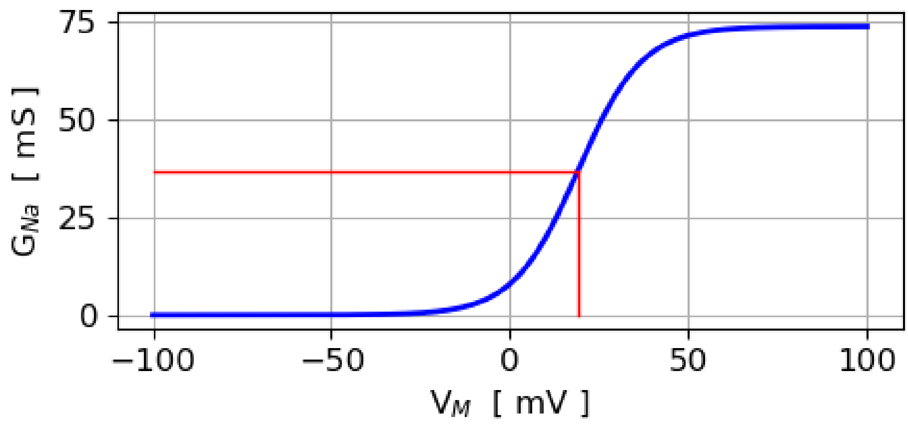


Fig. 9. Voltage dependent conductance G_{Na} for the Na^+ ion channel (equation 4). $V_{1/2} = 19$ mV, $k = 9$ mV , $G_{Na\_max} = 74$ mS. The shape of the curve is a sigmoid function where the Na^+ conductance rises to half its maximum value at $V_M = V_{1/2} = 19$ mV. **mns007A.py**

The dynamics of the system is described by the equation

$$(5) \qquad dV_m / dt = -\left(I_{ext} + G_L\left(V_M - E_L\right) + G_{Na}\, \mathrm{m}_{\mathrm{inf}}\left(V_M - E_{Na}\right)\right) / C_M$$

Typical model parameters in S.I. units are:

```
CM = 10e-6      # Membrane capacitance [F]
GL = 19e-3      # leak conductance [S]
GNa_max = 74e-3   # max Na+ conductance  [S]
EL  = -67e-3     # Leak reversal potential / Nernst potential  [V]
ENa = 60e-3      # Na+ reversal potential
Vh = 19e-3       # m_inf
k  = 9e-3        # m_inf
```

A system is said to undergo a **bifurcation** when its qualitative behaviour changes. We can investigate this bifurcation behaviour by considering the external current injected into a neuron as the bifurcation parameter.

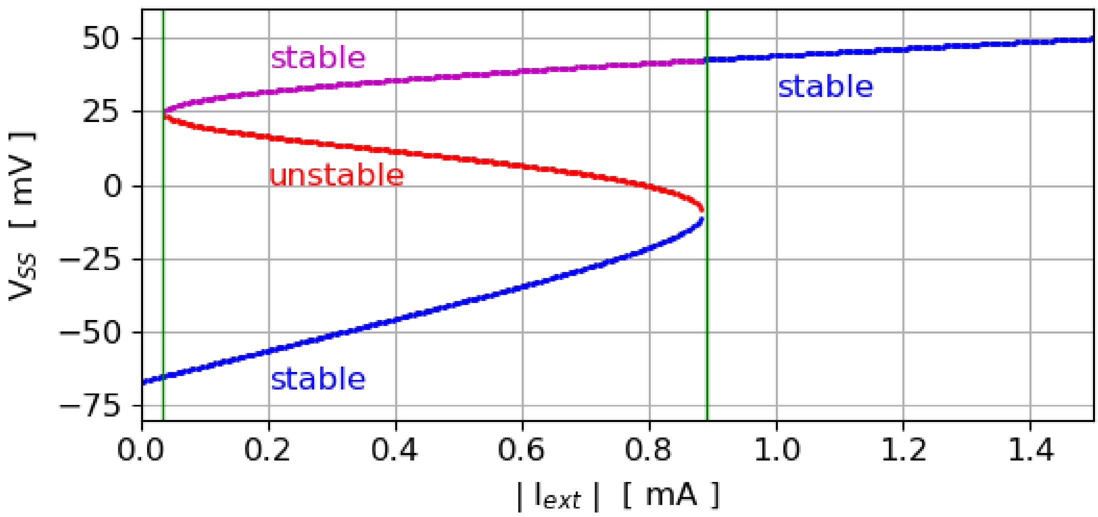


Fig. 10. Bifurcation diagram (I_{ext} bifurcation parameter). Bifurcations occur at I_{ext} = -0.035 mA and I_{ext} = -0.89 mA.

mns007AA.py

Pitchfork bifurcations

Monostable system

The system is **monostable** when

$$0 \leq |I_{ext}| < 0.035 \text{ mA} \qquad |I_{ext}| > 0.89 \text{ mA}$$

All trajectories are attracted to a stable single steady-state potential V_{SS}.

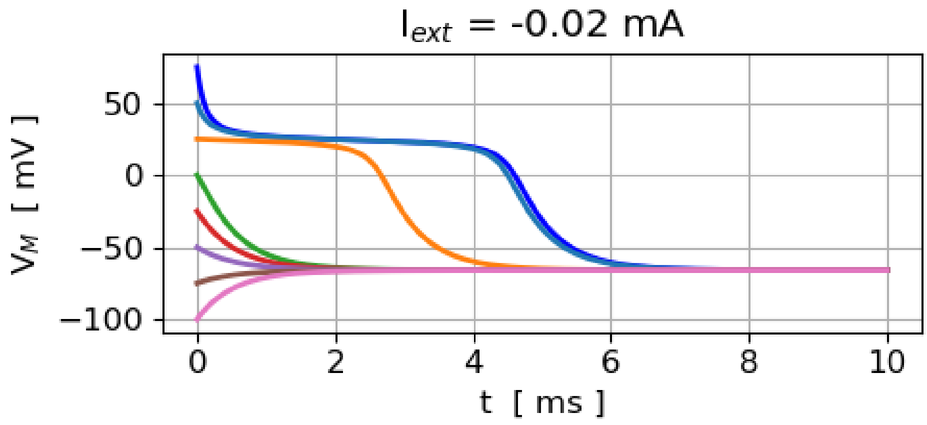


Fig. 11. I_{ext} = -0.02 mA. All trajectories of the membrane potential are pulled to the single stable fixed point at the resting state V_{ss} = -65.9 mV. **mns007B.py**

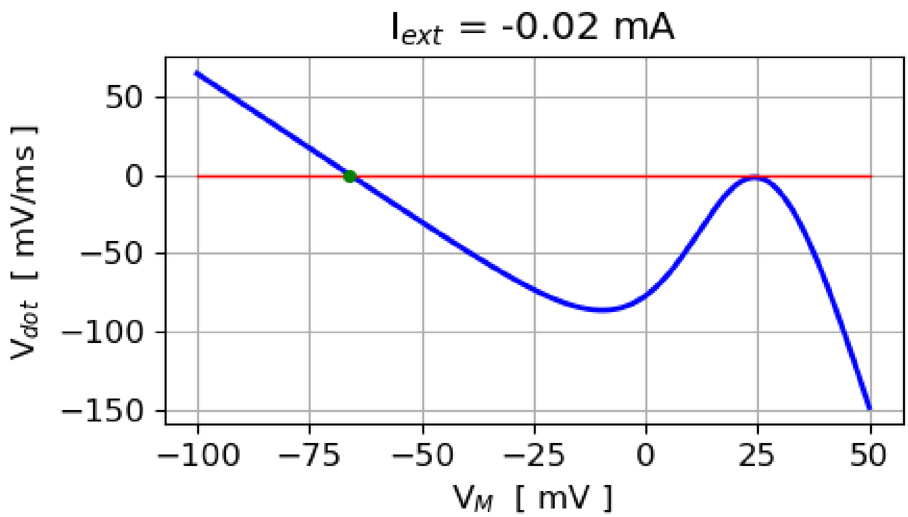


Fig. 12. I_{ext} = -0.02 mA. There is a single stable fixed point V_{SS} = -65.9 mV. **mns007A.py**

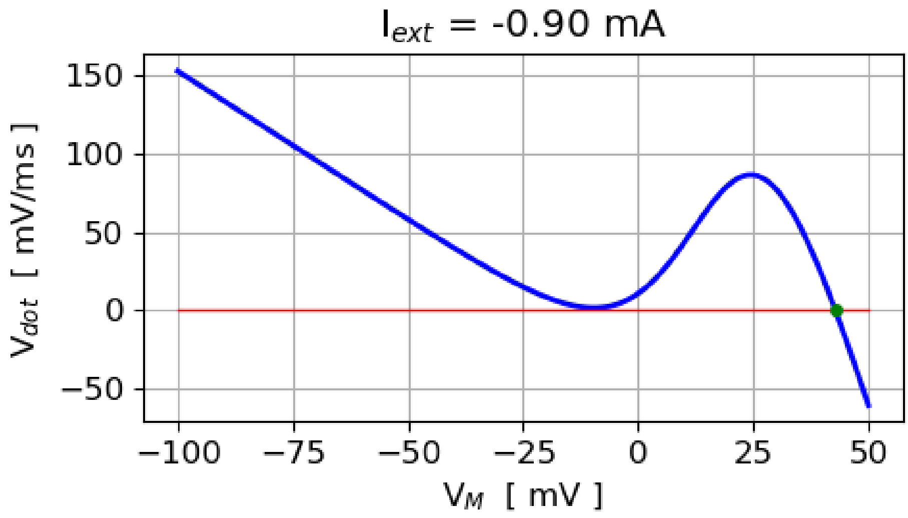


Fig. 13. $I_{ext} = 0.90$ mA Monostable fixed point

$V_{SS} = 42.8$ mV. **mns007A.py**

When $I_{ext} \sim 0.9$ mA a subcritical imperfect pitchfork exists since slight variations in I_{ex} results in the system evolving to a bistable or monostable state. As I_{ext} is increased, the $dV_M \,/\, dt \;\; vs \;\; V_M$ plot is lifted up, and the stable and unstable equilibrium approach each other. At the saddle point, they coalesce when the slope of the tangent to the curve becomes zero, and then disappear.

Bistable system

The system that has two stable fixed points (rest and excited states) is **bistable**. The two stable fixed points are separated by an unstable fixed point for the external current range

$$0.035 \text{ mA} < \left| I_{ext} \right| < 0.89 \text{ mA}$$

When $|I_{ext}|$ passes through 0.035 mA, the single fixed point losses stability and a new pair of stable branches bifurcate, that is, the stable branch divides (bifurcates) into two stable branches and one unstable branch. This is a supercritical imperfect pitchfork bifurcation.

When $|I_{ext}|$ passes through 0.89 mA, the three fixed points coalesce to form a new stable excited fixed point (figure 10). This is a subcritical imperfect pitchfork bifurcation

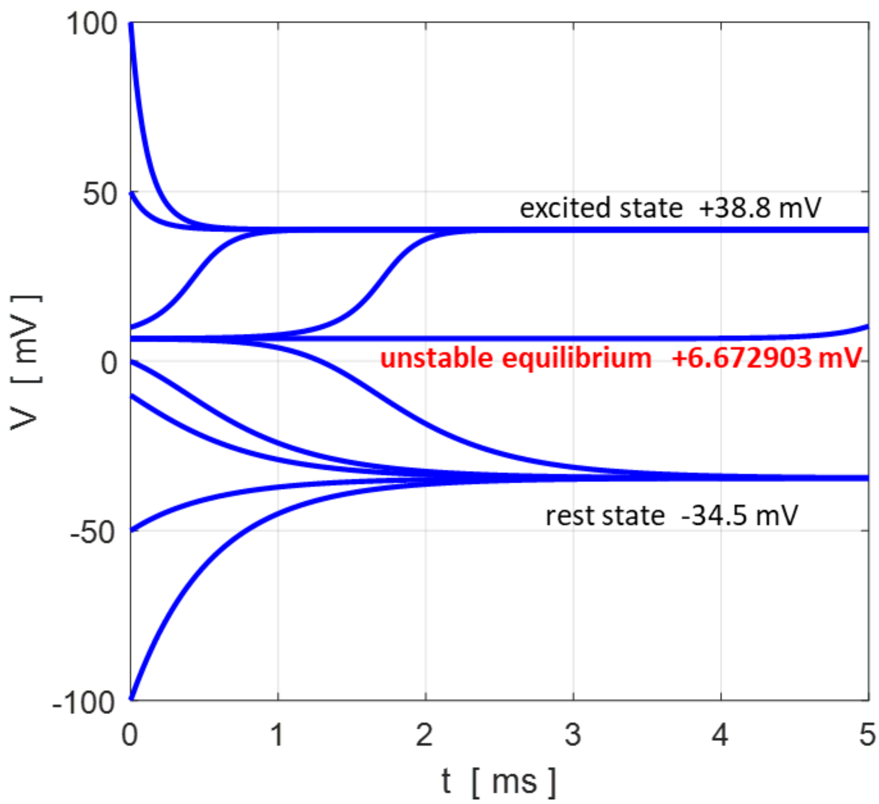


Fig. 14. I_{ext} = -0.60 mA Voltage trajectories for the leak / fast sodium ion model for different initial conditions. **nms007B.py**

In figure 14, for all initial values of the membrane potential greater than the unstable membrane potential, the membrane potential is attracted to the excited state and for initial values less than the unstable equilibrium potential, the membrane potential is drawn to the resting state (**bistability**). The attraction to a stable equilibrium point can take a relative long time when an initial membrane potential is close to the unstable equilibrium potential.

We can now compute the membrane currents from the membrane potential (figure 15).

$$I_{ext} = \text{constant} = -0.60 \text{ mA}$$

$$I_L = G_L\,(V_M - E_L) \qquad I_{Na} = G_{Na_m\text{ax}}\, \mathrm{m}_{\inf}(V_M - E_{Na})$$

$$I_C = -\left(I_{ext} + I_L + I_{Na}\right) \quad I_{net} = I_{ext} + I_L + I_{Na} + I_C$$

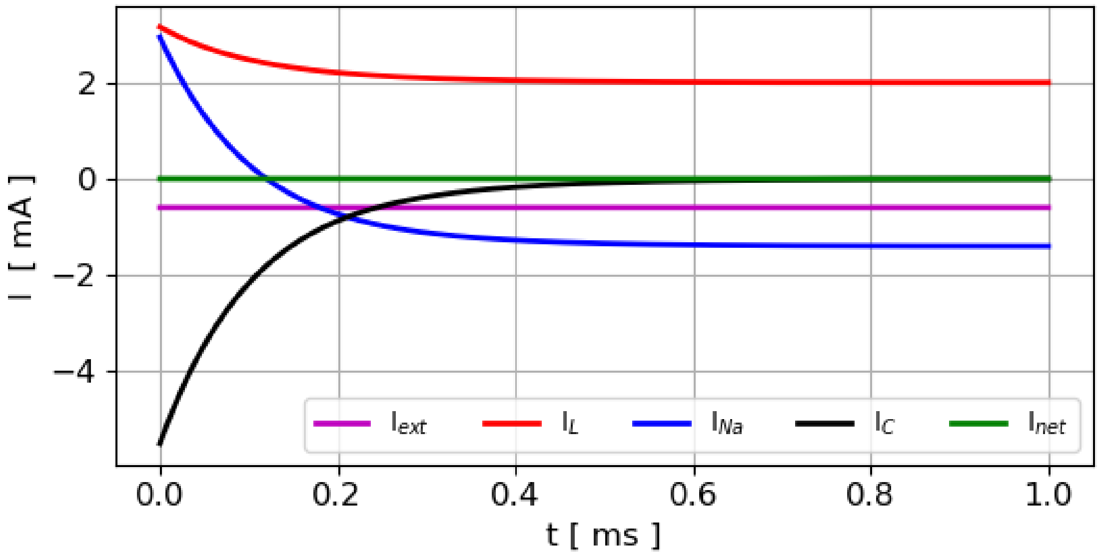


Fig. 15. Membrane currents for I_{ext} = -0.60 mA and V_0 = +100 mA.

$$t \to \infty \;\Rightarrow\; V_M \to V_{SS} = +38.9 \text{ mV}$$

$$I_C = 0 \text{ mA} \;\; I_L = 2.01\text{mA} \;\; I_{Na} = -1.41\text{mA}$$

$$I_{net} = I_{ext} + I_L + I_{Na} = 0$$

mns007B.py

The initial membrane potential is V_0 = +100 mV and the membrane potential decreases to the excited fixed point +38.9 mV. Initially both the leakage current and the Na^+ current flow from the inside of the membrane to the outside which results in the decrease in the membrane potential. When an equilibrium is reached the external current is balanced by the sum of the leak and sodium currents where the leak current transfers positive charge from inside to the outside (leak current is positive) and there is a net flow of Na^+ into the cell (Na^+ current is negative).

Figure 16 shows the *I-V* characteristic plot

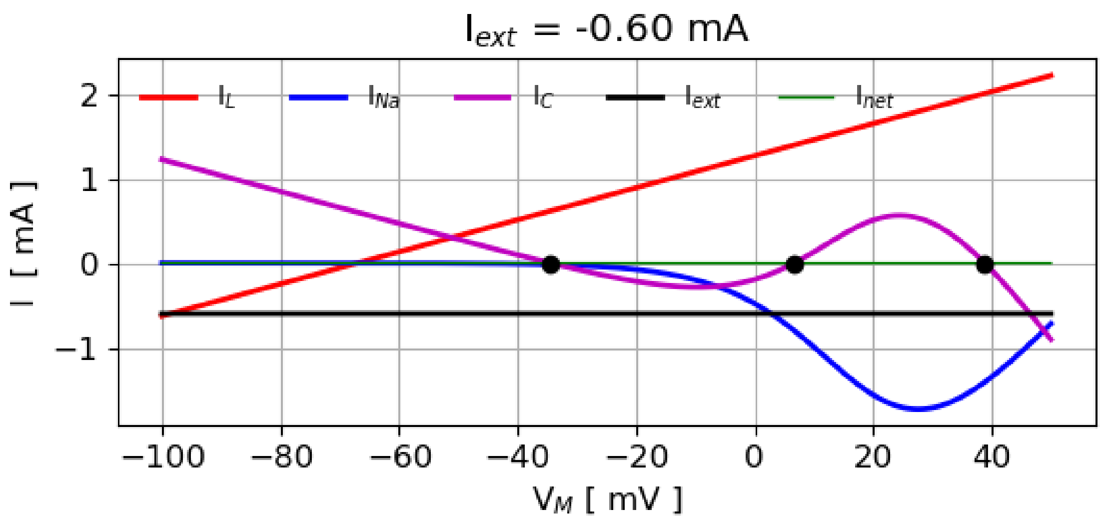


Fig. 16. *I-V* characteristics curves for I_{ext} = -0.60 mA. **mns007A.py**

The capacitor current is zero at the fixed points $I_C = dV_M \,/\, dt = 0$.

The zero crossing for the capacitor current I_C gives the fixed points V_{SS} = [-34.47   6.67   38.82].

The I-V curve is a straight line for the leakage current I_L which means that the leakage conductance is constant.

The I-V curve for the sodium ions I_{Na} shows a region of negative conductance (negative slope).

The transition between two stable states separated by a threshold is relevant to the mechanism of excitability and generation of action potentials of many neurones. In our Leak / fast Na^+ model, the existence of the rest state is largely due to the leak current I_L, while the existence of the excited state is largely due to the persistent inward Na^+ current I_{Na}. Small (sub-threshold) perturbations leave the state variable in the attraction domain of the rest state, while large (super-threshold) perturbations initiate the regenerative process where the upstroke of an action potential, and the voltage variable becomes attracted to the excited state. Generation of the action potential must be completed via repolarization that moves V_M back to the rest state. Typically, repolarization occurs because of a relatively slow inactivation of Na^+ current and/or slow activation of an outward K^+ current, which are not taken into account our model.

Negative conductance

The conductance of the Na^+ channel can be negative (figure 16) and this negative conductance is responsible for the rapid influx of Na^+ ions into the neuron causing the membrane potential to rise and this may result in the firing of an action potential. Figure 12 shows a very interesting aspect of the dynamics of the membrane potential. The slope of a *I-V* plot gives the conductance. In the range from about ~ -20 mV to ~ +20 mV the conductance of the sodium channel is negative.

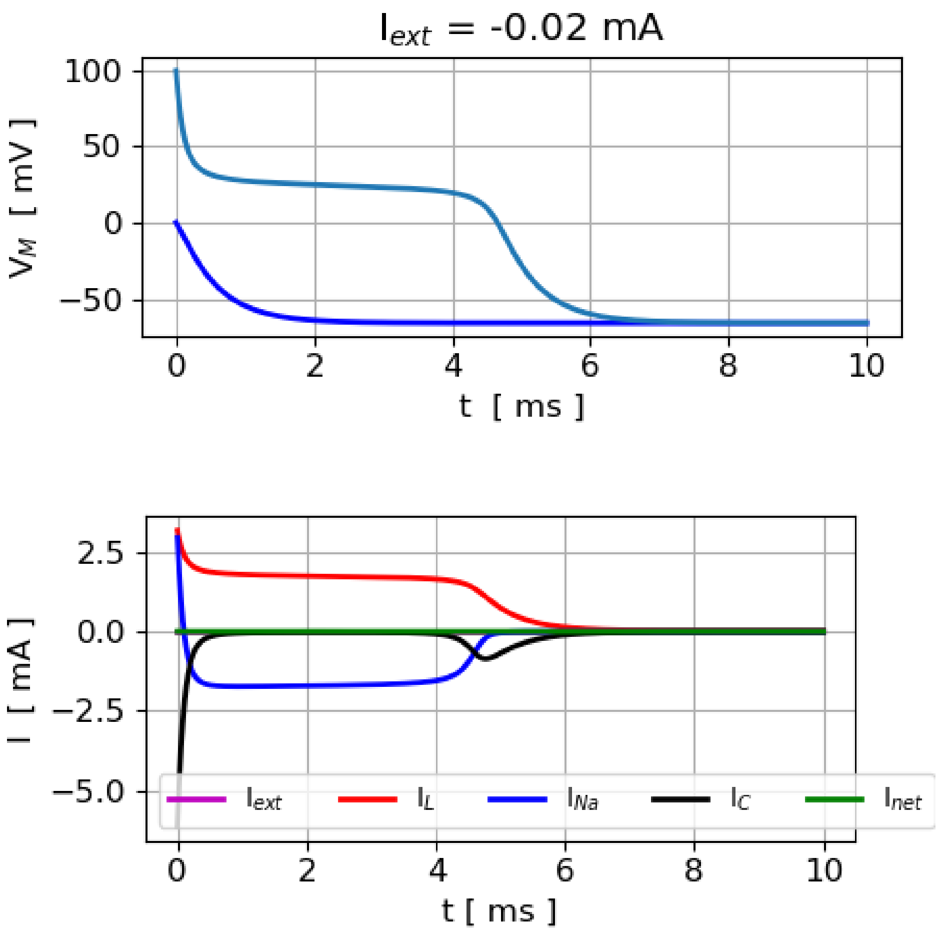
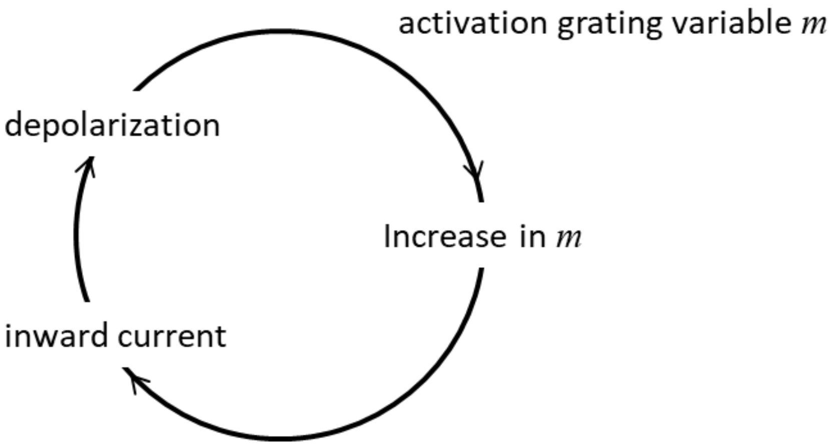


Fig. 17. I_{ext} = -0.02 mA (monostable system V_{SS} = -65.9 mV). Time evolution plots. Bottom graph V_0 = +100 mV. **mns007B.py**

Figure 17 shows that for $V_0 = 0$ mV the membrane potential falls exponentially to the steady-state membrane potential $V_{SS} = -65.9$ mV. However, if the initial membrane potential $V_M(0) > \sim 20$ mV, the membrane potential will not fall exponentially to the resting potential since the negative conductance leads to an excessive influx of Na^+ ions into the cell reducing the rate of the fall in the membrane potential. For $V_0 = +100$ mV, initially there is a rapid flux of Na^+ ions out of the cell ($I_{Na} > 0$) causing the membrane potential to fall. However, as the membrane potential falls, the sodium conductance changes from being positive to negative and the flow of Na^+ reverses and Na^+ enter into the cell ($I_{Na} < 0$). This negative conductance causes an influx of sodium ions into the cell reducing the rate at which the membrane potential falls to the resting potential. The system is monostable, since trajectories with different initial membrane potentials are all attracted to the single stable equilibrium point, $V_M = -65.9$ mV.

This negative conductance creates positive feedback between the voltage V_M and the gating variable m_{inf} and it plays an amplifying role in neurone dynamics. Such currents are referred to as amplifying currents.



Negative slope conductance region: positive feedback loop

Neuron negative conductance refers to specific voltage ranges where an inward current increases as the cell depolarizes (becomes more positive), creating a paradoxical effect where increased inward flow raises the membrane's resistance, amplifying and prolonging synaptic signals (like EPSPs) and shaping intrinsic neuronal activity, unlike normal positive conductance that decreases resistance with depolarization. This "negative slope" arises from voltage-gated currents, such as persistent sodium I_{NaP} and certain calcium I_{Ca} or hyperpolarization-activated I_{H} currents, which activate rapidly but inactivate slowly or partially, leading to regenerative inward currents crucial for neural oscillations and synaptic integration. Usually, as a neuron depolarizes, more channels open e.g., Na^+, increasing current flow and decreasing membrane resistance (positive slope). However, in specific voltage ranges, certain inward currents like I_{NaP} activate with depolarization but don't fully inactivate, causing a region where $\mathrm{d}I_{\mathrm{inward}}$ / $\mathrm{d}V_M$ is negative. Paradoxically, this negative conductance region actually increases the neuron's input resistance R_{in} and time constant τ_M, making subthreshold potentials (like synaptic potentials) larger and longer-lasting. Negative conductances are essential for generating slow waves and rhythmic activity in networks. and modulates how easily a neuron fires, helping control firing patterns and bursts.

https://www.kenhub.com/en/library/physiology/leak-channels

https://people.engr.tamu.edu/choe/choe/courses/12fall/644/lectures/slide04.pdf