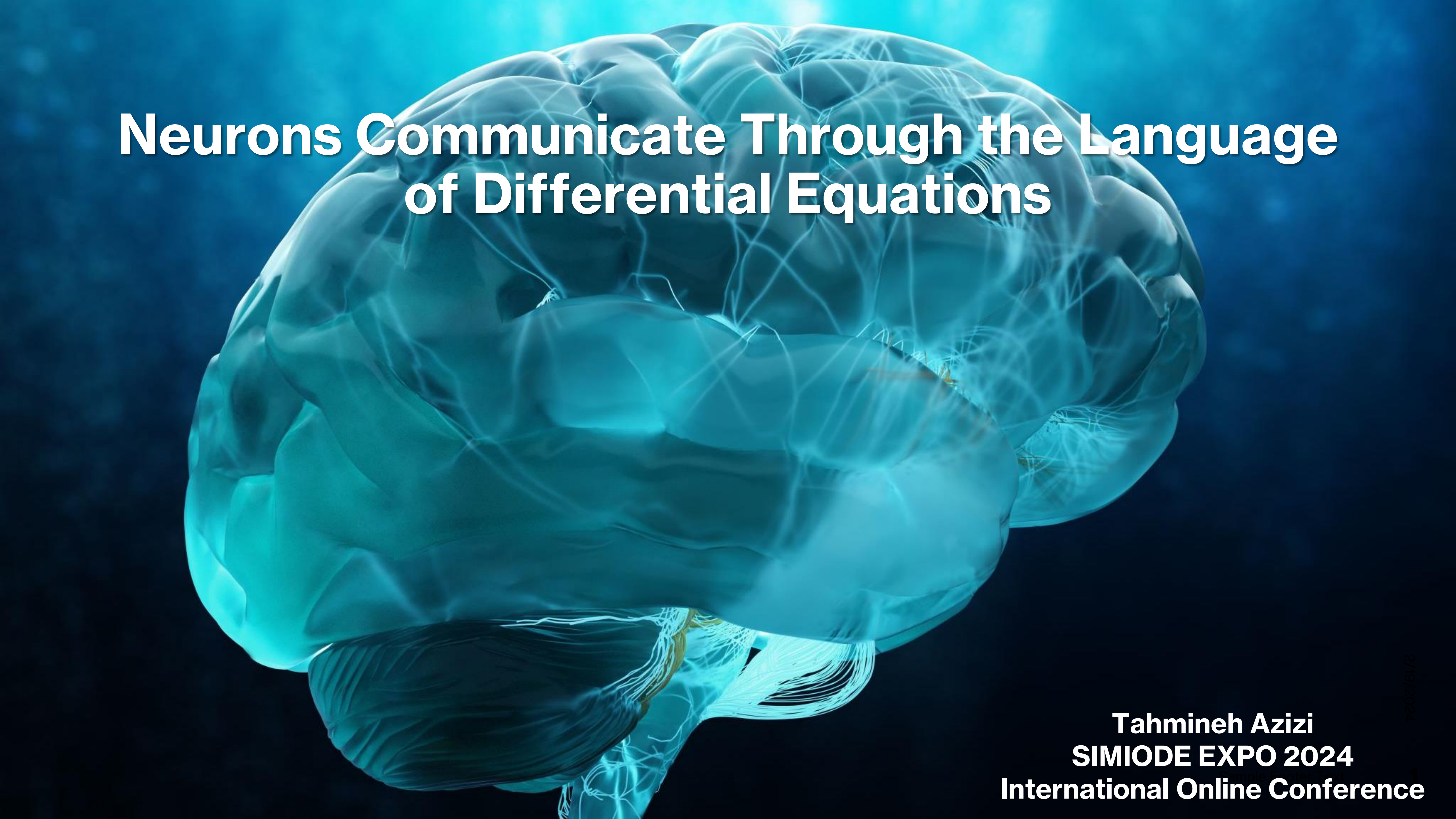

Neurons Communicate Through the Language of Differential Equations

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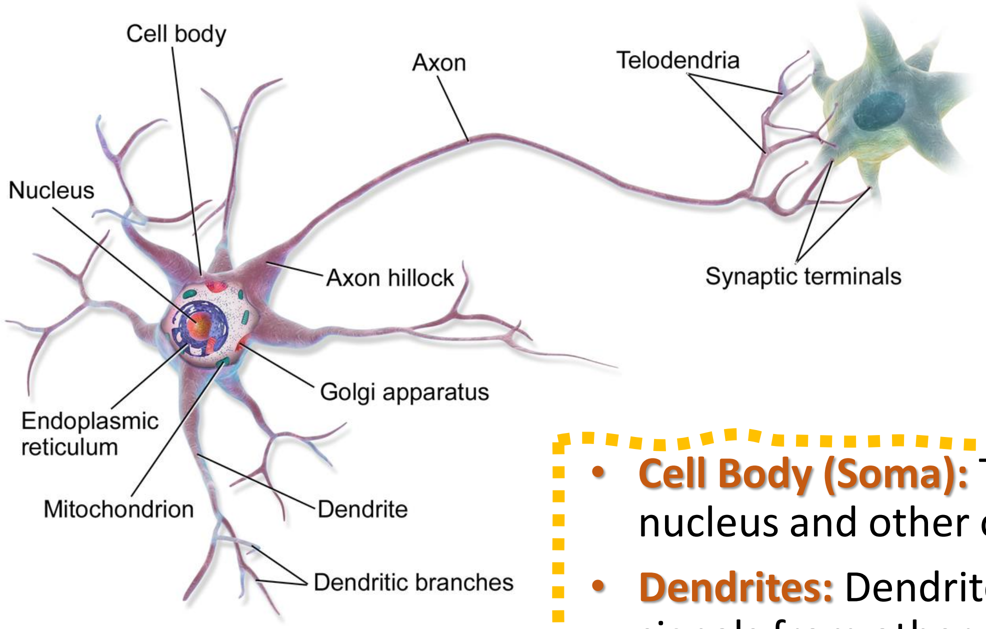
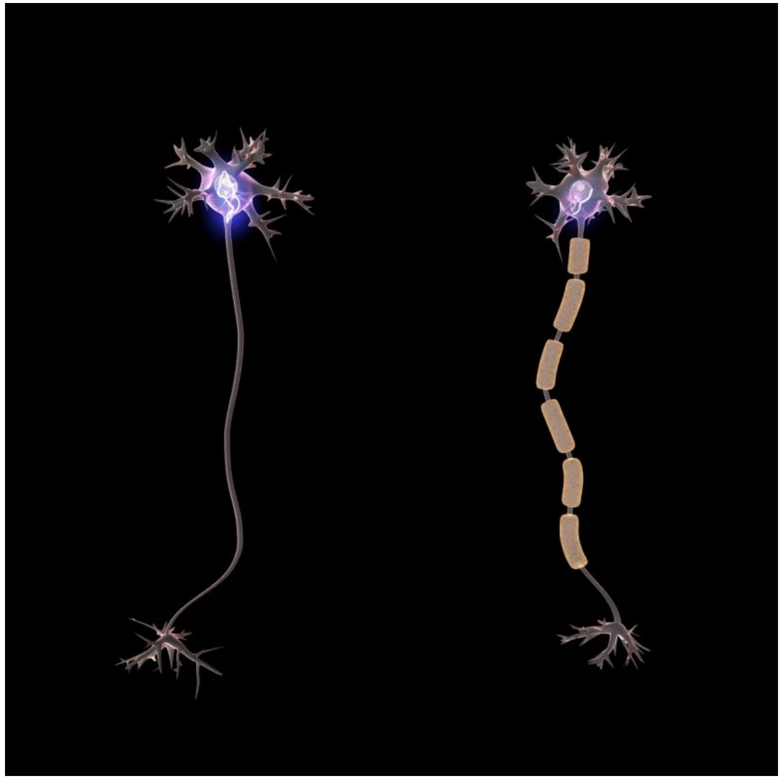
SIMIODE EXPO 2024
International Online Conference



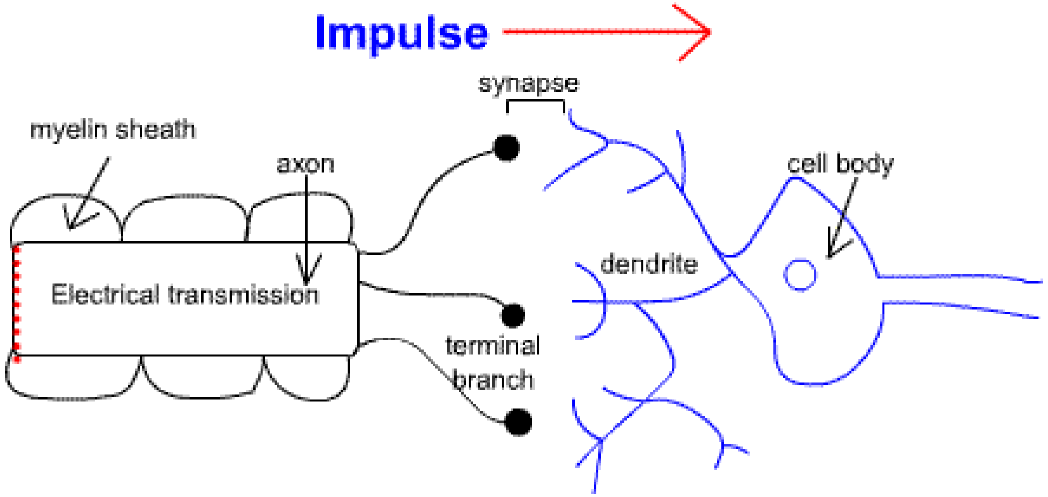
Anatomy of a Neuron

- **Cell Body (Soma):** The cell body, or soma, is the central part of the neuron that contains the nucleus and other organelles. It is responsible for the basic life processes of the cell.
- **Dendrites:** Dendrites are branched extensions protruding from the cell body. They receive signals from other neurons or sensory receptors and transmit these signals toward the cell body.
- **Axon:** The axon is a long, slender projection that extends from the cell body. It conducts electrical impulses away from the cell body toward other neurons, muscles, or glands.
- **Axon Terminals (Axon Endings):** The axon terminals are small branches at the end of the axon that form synapses with other neurons, muscles, or glands. They release neurotransmitters to transmit signals to the next cell.
- **Synapse:** A synapse is a junction or connection between the axon terminals of one neuron and the dendrites or cell body of another neuron. It is the site where information is transferred from one neuron to another.
- **Neurotransmitters:** Neurotransmitters are chemical messengers that transmit signals across the synapse. They are released from vesicles in the axon terminals and bind to receptors on the receiving neuron, initiating a response.

Electrical and Chemical Transmission



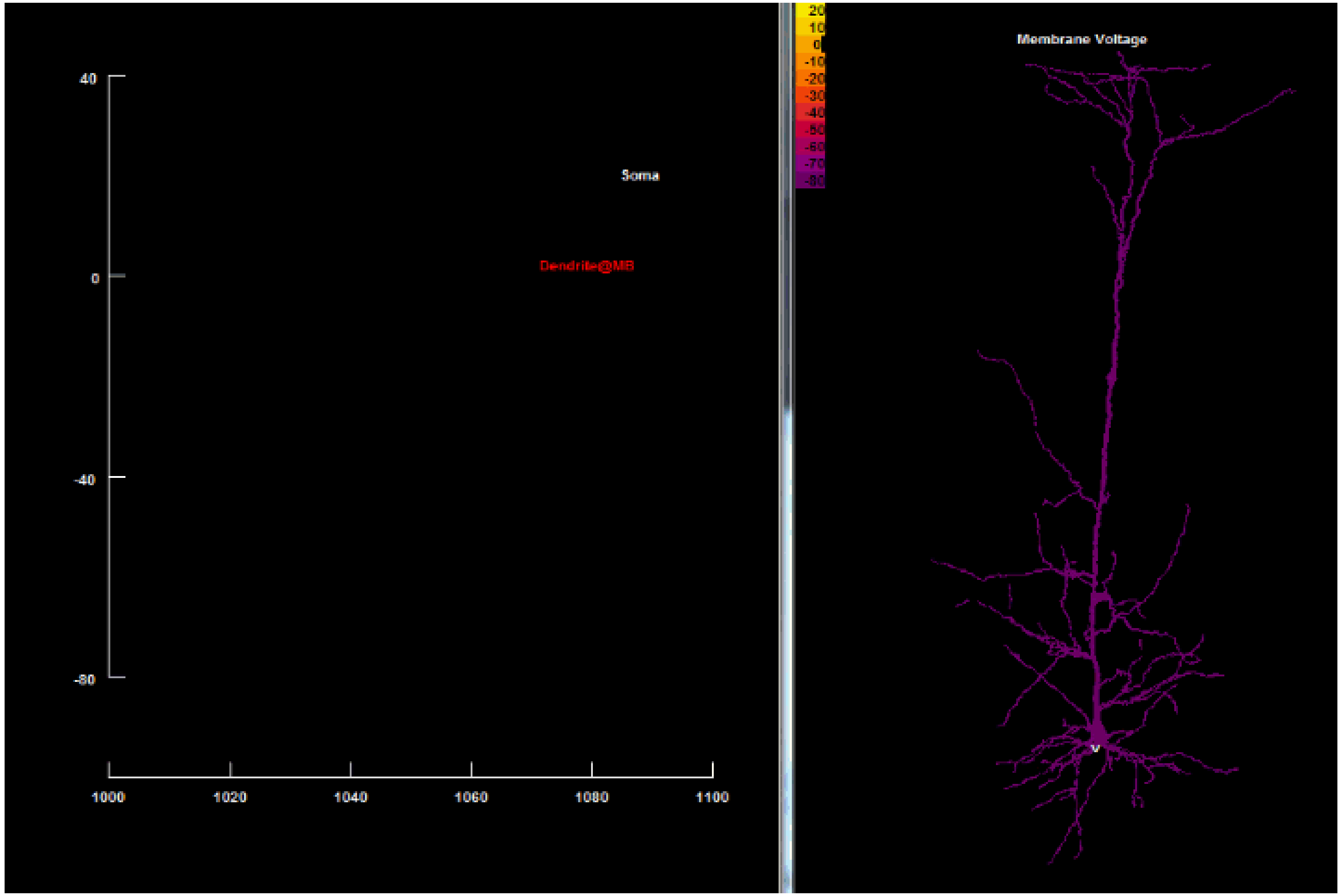
- Neurons communicate with each other through a combination of electrical and chemical signals.
- The transmission of signals within neurons is primarily electrical, while the communication between neurons occurs through chemical transmission at synapses.



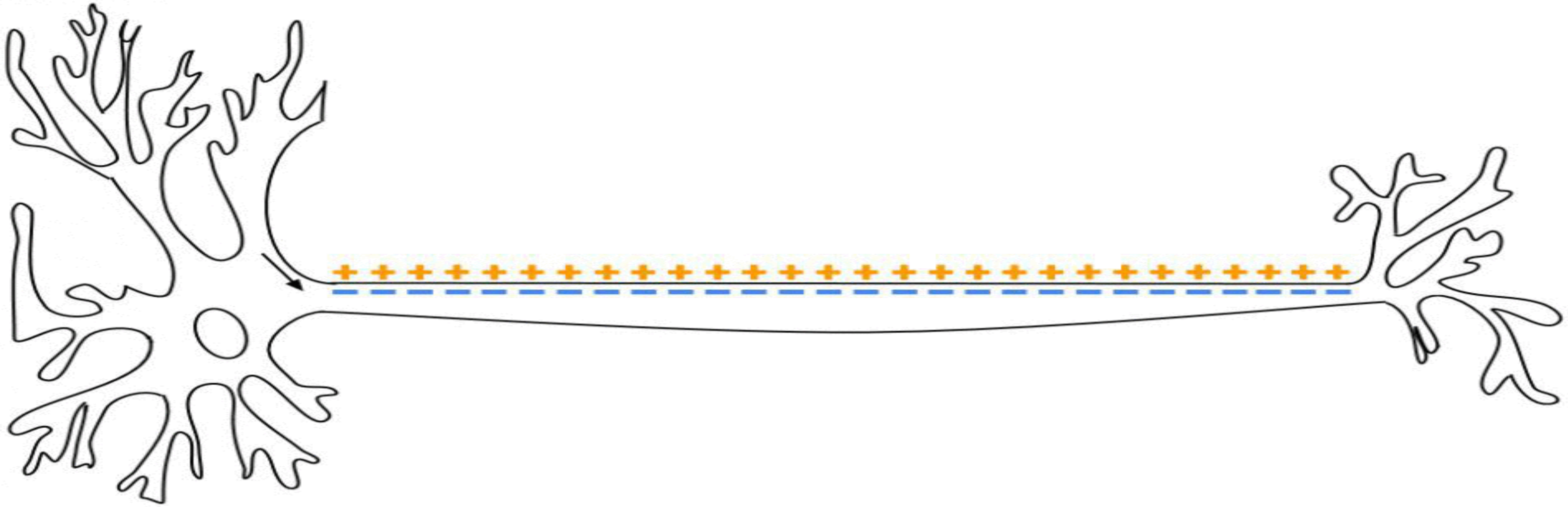
The combination of electrical and chemical signals allows for the transmission of information within neurons and between neurons in complex neural networks, enabling various functions of the nervous system, including sensory processing, motor control, and cognitive processes.

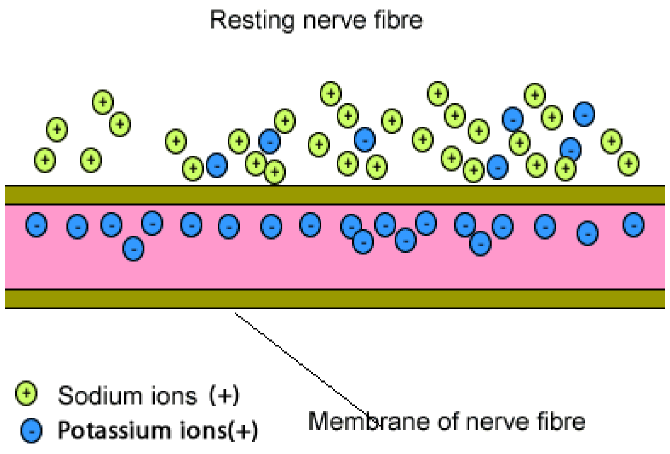
The Action Potential, a Rapid Change in Membrane Potential

- The action potential is a rapid and transient change in the membrane potential of a neuron, essential for the transmission of electrical signals along the length of the neuron.
- It is a key mechanism in the communication within the nervous system.



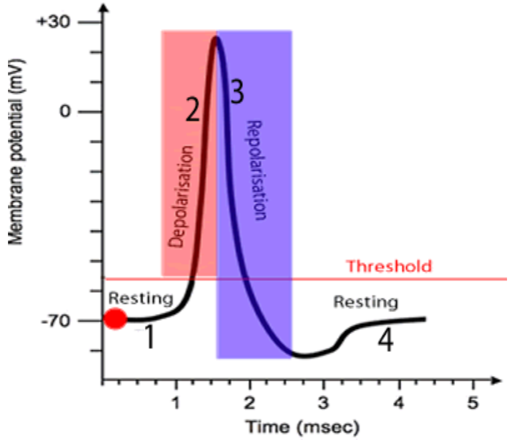
- As an action potential travels down the axon, there is a change in polarity across the membrane.
- The Na+ and K+ gated ion channels open and close as the membrane reaches the threshold potential, in response to a signal from another neuron.
- This creates a change in polarity between the outside of the cell and the inside.
- The impulse travels down the axon in one direction only, to the axon terminal where it signals other neurons.



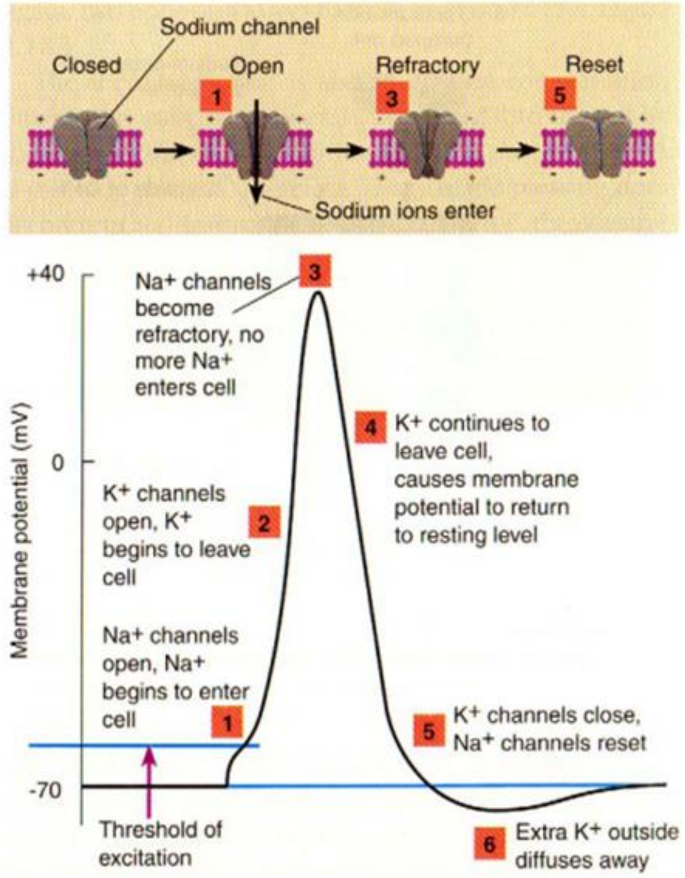


Transforming Neural impulse from one neuron to another one

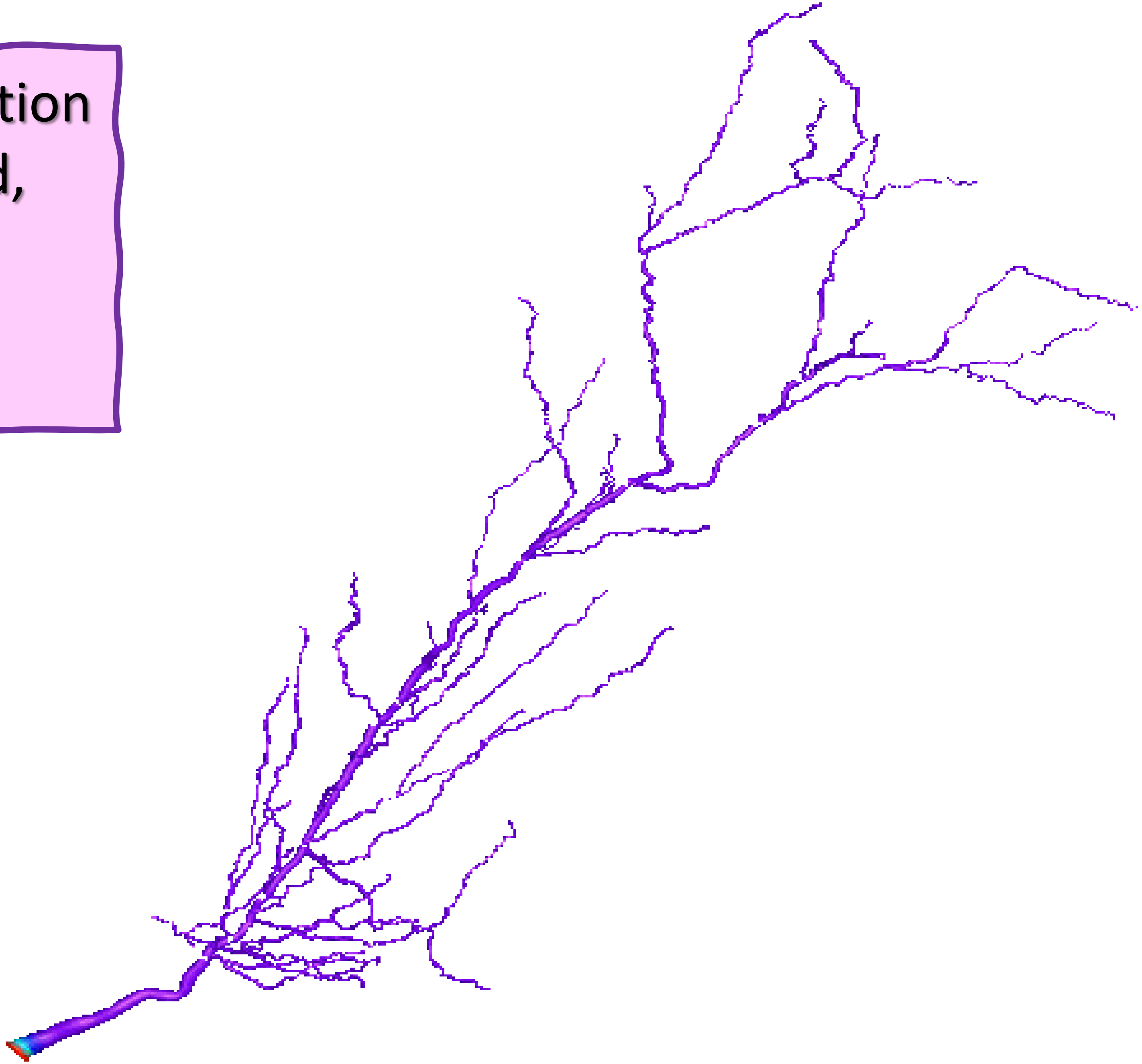
At the beginning of the action potential, the Na+ channels open and Na+ moves into the axon, causing depolarization.

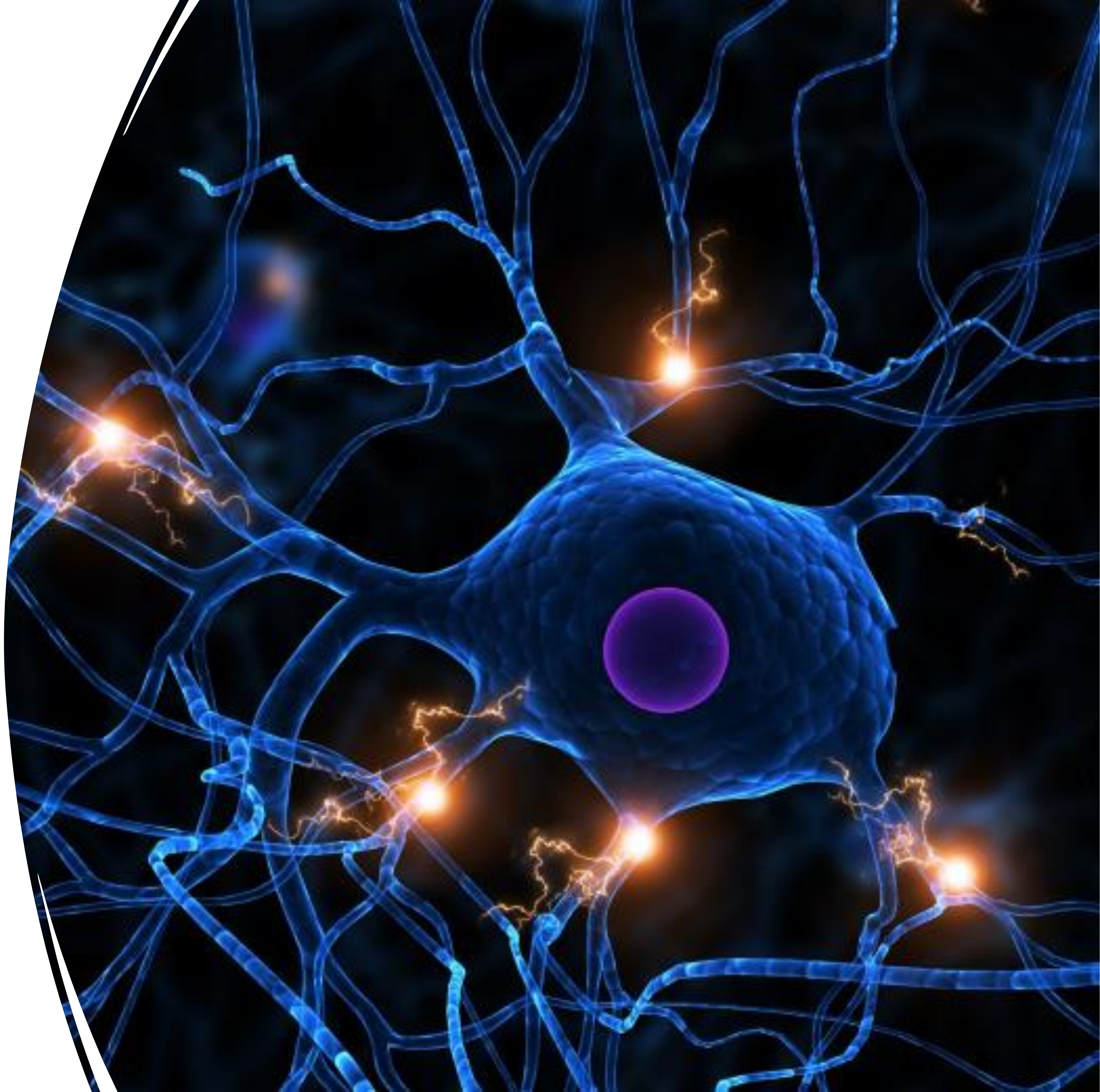


Repolarization occurs when the K+ channels open and K+ moves out of the axon.

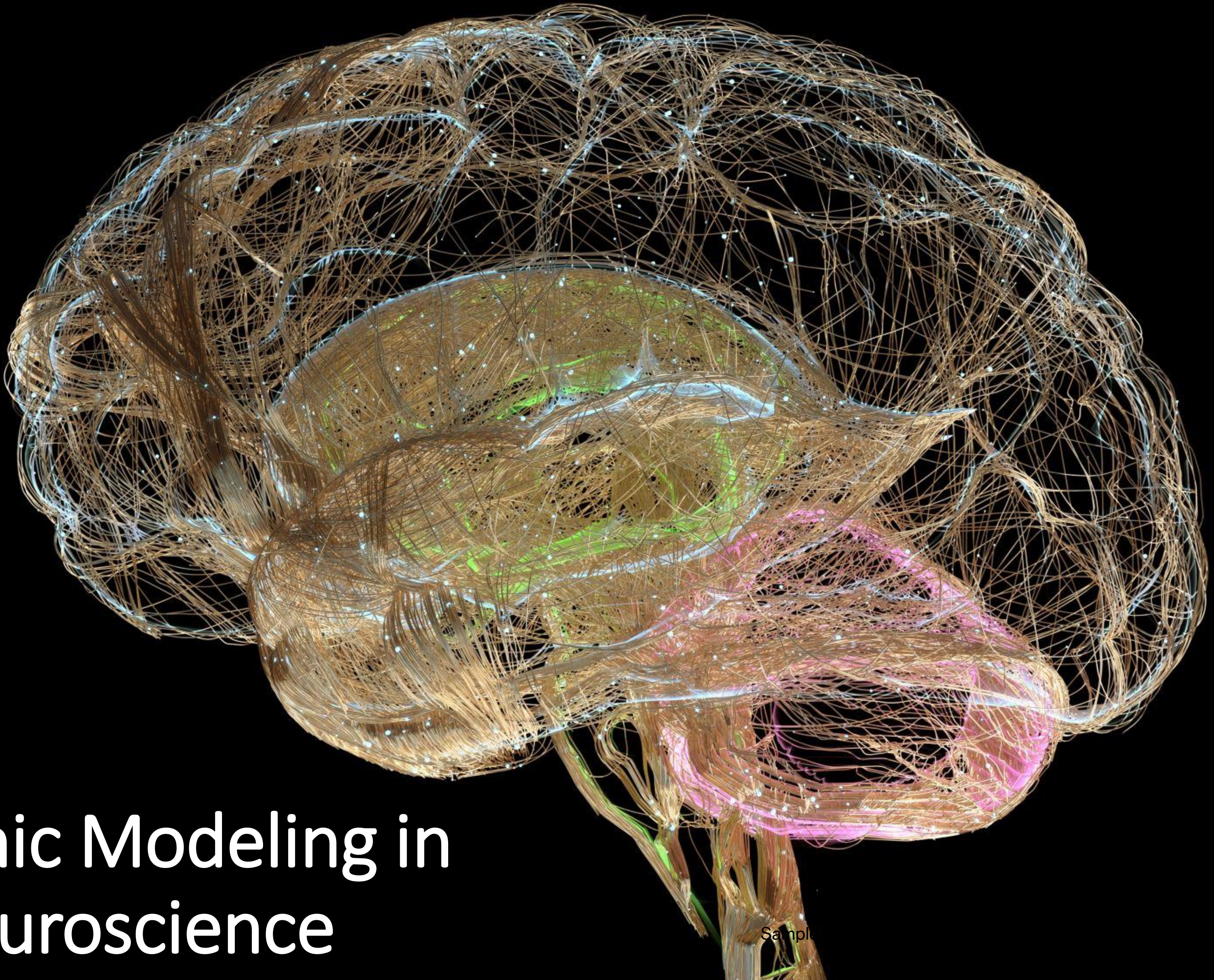


Example of a propagating action potential (high voltage in red, low voltage in blue) in the dendritic.





- Neurons communicate by generating action potentials (potential difference through their cell membranes), which propagate along the axon towards the synapses of other cells.
- There exist various models, based on systems of ordinary differential equations, describing the dynamics of action-potential generation: The Hodgkin-Huxley equations, the FitzHugh-Nagumo equations, the Morris-Lecar equations, etc.

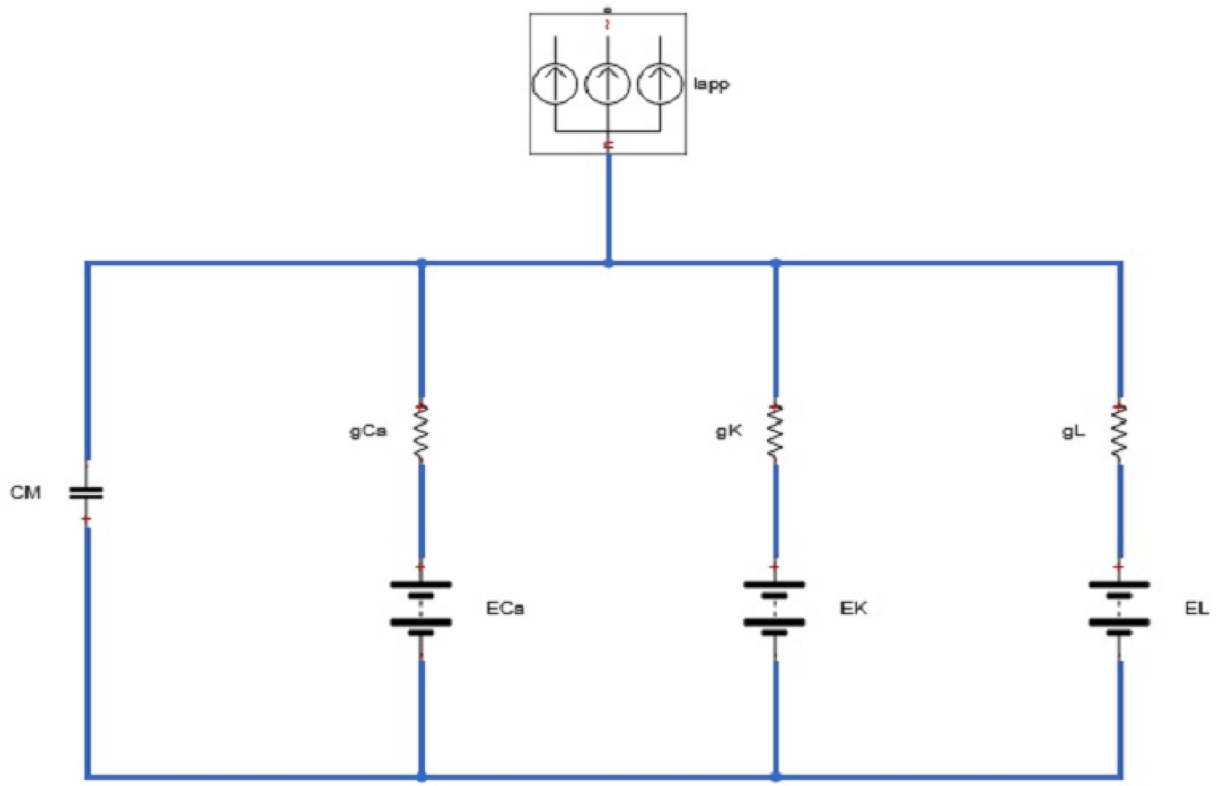


Dynamic Modeling in Neuroscience

The Morris-Lecar Model

- The Morris-Lecar model combines the relative simplicity of the FitzHugh-Nagumo Model with the biological detail of the Hodgkin-Huxley model.

- The Morris-Lecar model describes neurons as circuits with Ca and K voltage gated ion channels and a leak.
- Calcium and potassium channels were used because Morris and Lecar found that the barnacle muscle fiber's production of oscillatory behavior depended on external calcium concentration and potassium conductance.
- In our body, neurons are in a salt solution, so there are charged ions, in particular K and Ca ions, that generate electrical potentials and move in response to potentials.
- When ions move through cell membranes, currents are produced as a result. Thus, we can think of neurons as circuits.



- One of the simplest models for the production of action potentials is a model proposed by Kathleen Morris and Harold Lecar.
- The model has three channels: a potassium channel, a leak, and a calcium channel.

$$\begin{cases} C_M \frac{dV}{dt} = I_{app} - g_L(V - E_L) - g_K n(V - E_K) - g_{Ca} m_\infty(V)(V - E_{Ca}) = I_{app} - I_{ion}(V, n), \\ \frac{dn}{dt} = \Phi(n_\infty(V) - n)/\tau_n(V), \end{cases}$$

$$\begin{aligned} m_\infty(V) &= \frac{1}{2}[1 + \tanh((V - V_1)/V_2)], \\ \tau_n(V) &= 1/\cosh((V - V_3)/(2V_4)), \\ n_\infty(V) &= \frac{1}{2}[1 + \tanh((V - V_3)/V_4)]. \end{aligned}$$

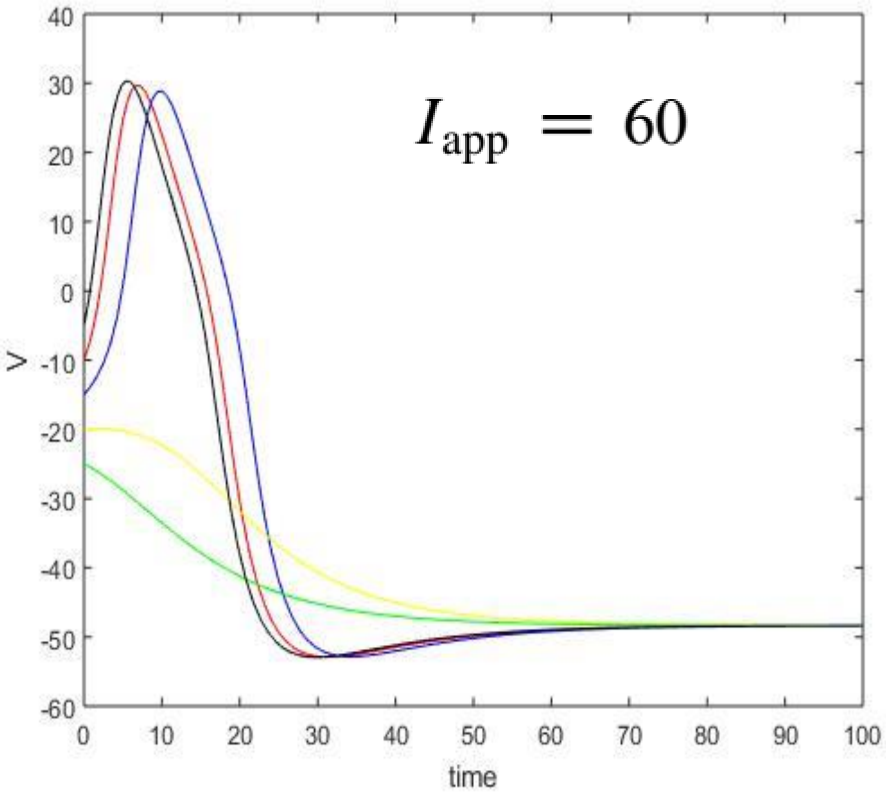
Biological Parameters of the M-L Model

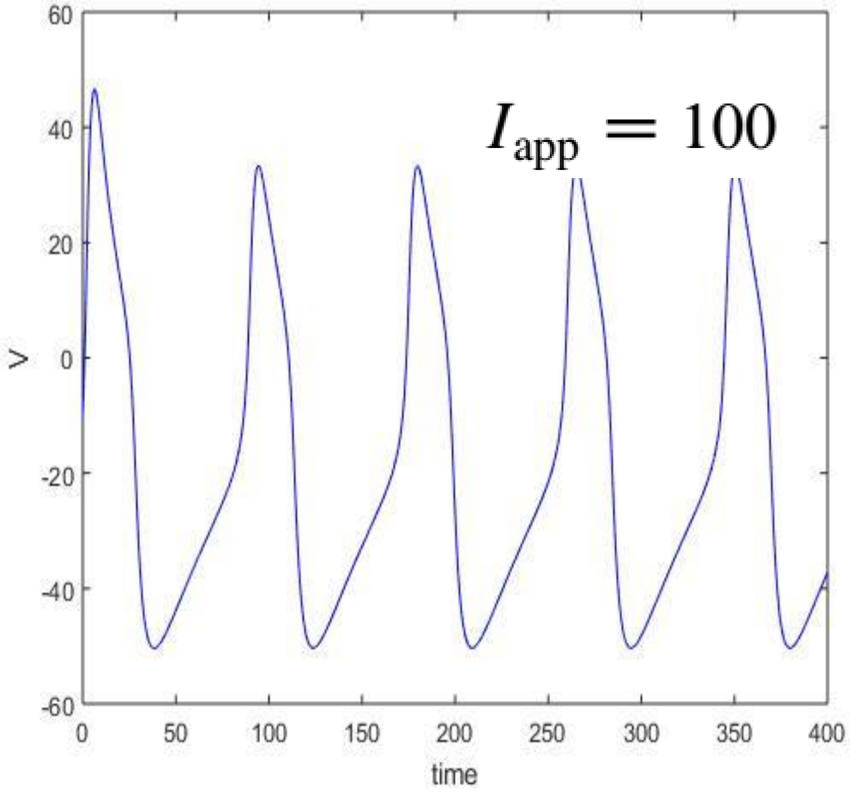
Parameter	Definition
C_M	membrane capacitance
I_{app}	external current applied to the neuron circuit
g_{Ca}	conductance of the calcium channel
E_{Ca}	potential generated by the calcium channel battery
E_K	potential generated by the potassium channel battery
E_L	potential generated by the leak battery
g_K	conductance of the potassium channel
g_L	conductance of the leak
ϕ	temperature factor

- ✓As parameters are varied, there may be qualitative changes in the dynamics of a model.
- ✓Fixed points can appear, disappear, or change their stability as we change the parameter values.
- ✓We call such qualitative changes in a model's dynamics bifurcations.
- ✓ The special parameter values at which bifurcations occur are called bifurcation points.
- ✓Saddle-node and Hopf bifurcations are very common and can describe the single-spike properties of the spike-generating mechanisms of most neurons.

- ✓ There are many ionic mechanisms of spike generation, but only four generic bifurcations of equilibria.
- ✓ This transition from a stable steady state to a stable limit cycle through variation of a parameter is called a Hopf bifurcation.
- ✓ It is one way in which periodic motion can arise from a previously stationary system, or vice versa.
- ✓ Here for the Hopf case, the equilibrium point is a stable focus that has a pair of complex conjugate eigenvalues with negative real part.
- ✓ With increasing the injected current, the real part of the eigenvalues changes from negative to zero and with further increasing, to positive.
- ✓ It means that the stable focus loses its stability and a limit cycle appears.
- ✓ With increasing the injected current, the amplitude of the limit cycle also increases.

At the MorrisLecar model is excitable because at large enough perturbations in voltage, an action potential is generated, while at small perturbations from rest, the voltage quickly decays back to the resting state.



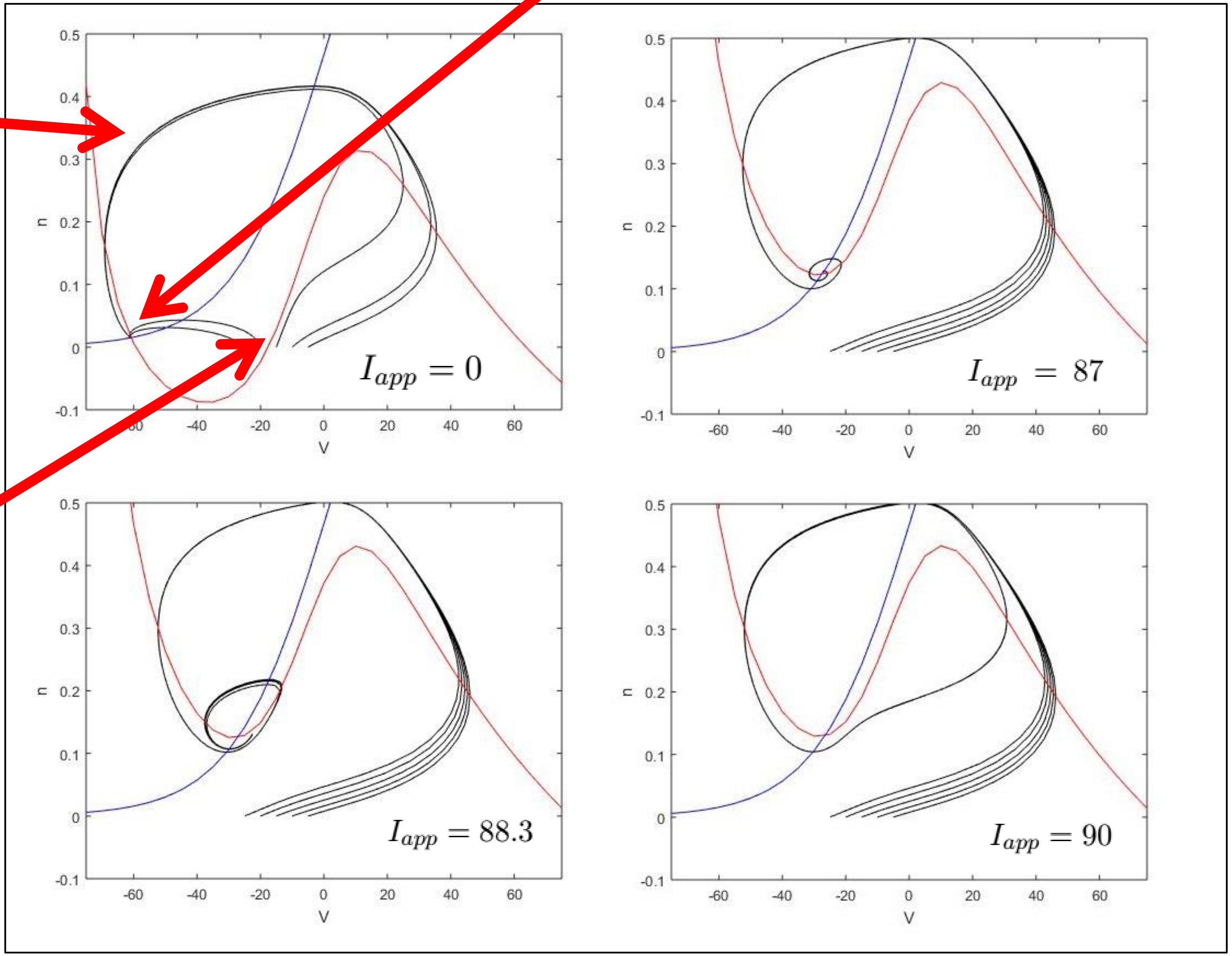


We can see different behaviors of the neuron from resting to spiking (the stable constant solutions are corresponding to the resting state and spiking state shows the existence of periodic solutions.)

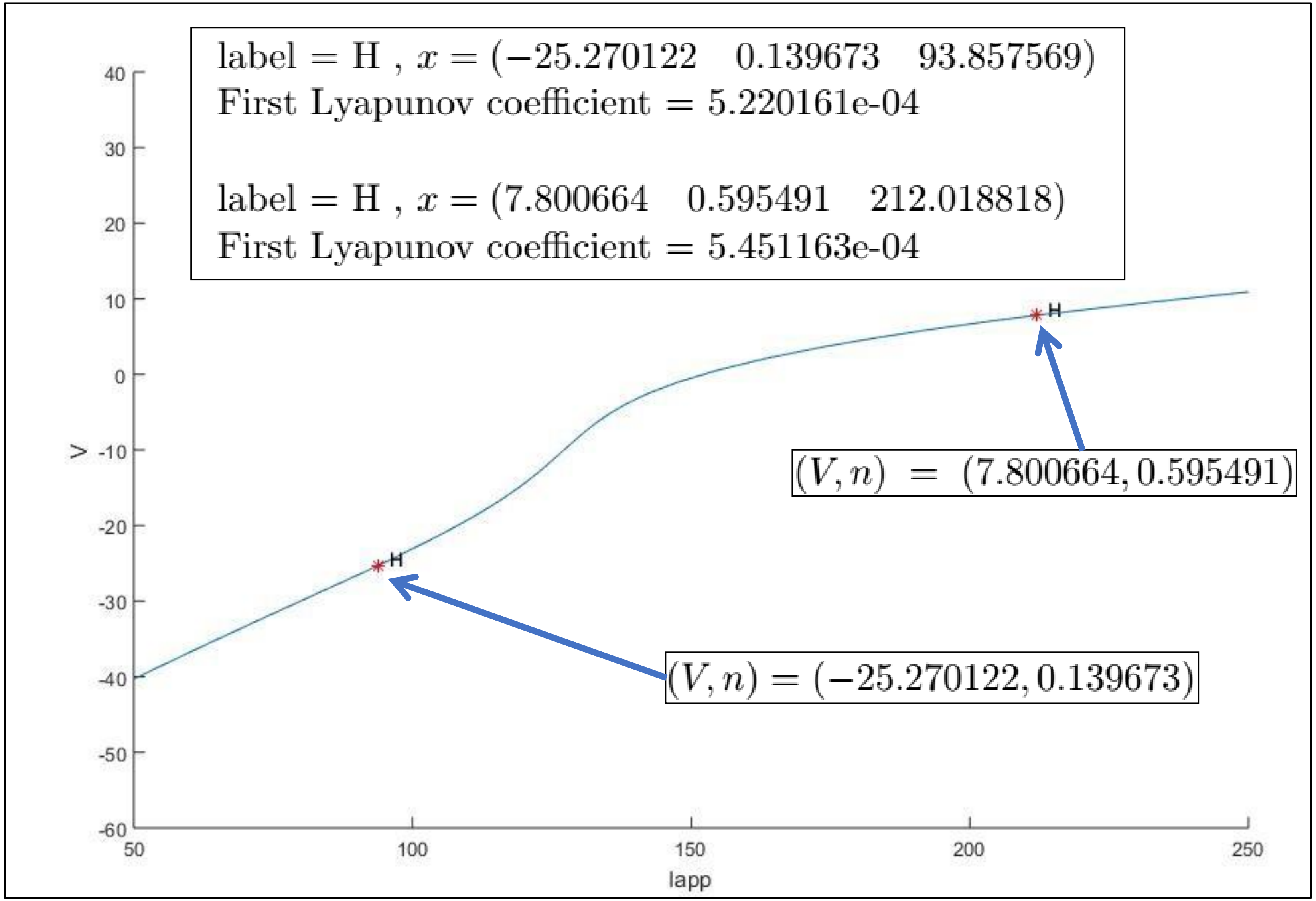
We have a continual series of action potentials. Thus, we have a periodic solution to the Morris-Lecar equations at $I_{app} = 100$.

a small perturbations in voltage, which is represented by the perturbation that lies to the `left' of the middle branch of the V -nullcline, will return to rest

while a big enough perturbation will generate an action potential

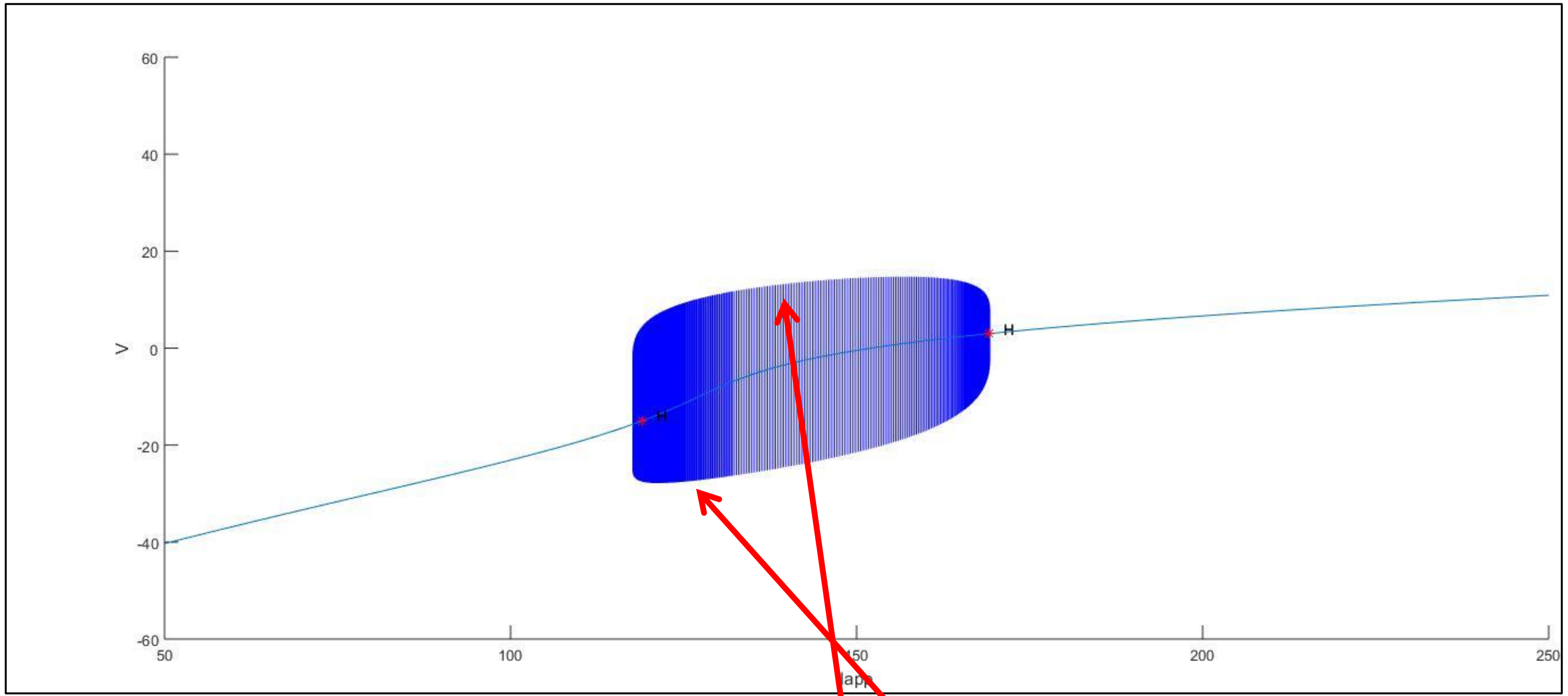


an excitable system with threshold at about -20 mV

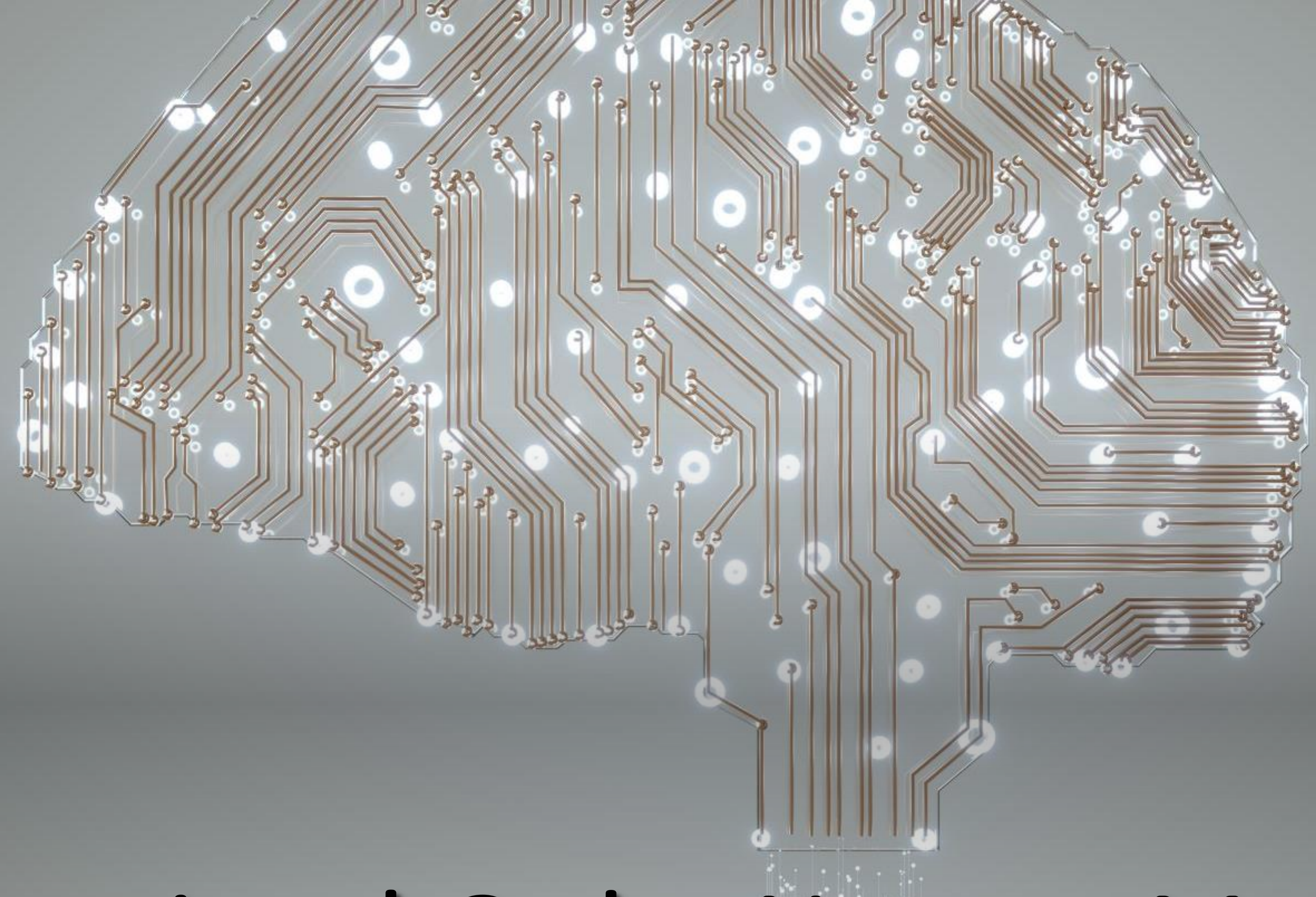


- The first Lyapunov coefficients for two Hopf points are positive. Thus, there should exist an unstable limit cycle, bifurcating from the equilibrium and it indicates the appearance of SubCritical Hopf Bifurcation.

Continuation of Equilibrium points



The curve above the fixed-point curve represents the maximum voltages on the periodic orbits and the curve below the fixed-point curve represents the minimum voltages.



Fractional-Order Neuron Model explore different dynamical classes of the model

Fractional-Order Neuron Model
explore different dynamical classes of the model

To find the fractional order Morris-Lecar model, we define the fractional differential operator as the form

$$\begin{cases} D^{\gamma}V(t) = f(t, V(t)), \quad V(t_0) = V_0, \\ D^{\gamma}n(t) = g(t, n(t)), \quad n(t_0) = n_0 \end{cases} \qquad \gamma \in (k-1, k]$$

where $\gamma > 0$ is the order of derivative and D^{γ} denotes the fractional derivative and can be obtained using:

$$\begin{cases} D^{\gamma}V(t) = J^{k-\gamma}D^{k}V(t), \\ D^{\gamma}n(t) = J^{k-\gamma}D^{k}n(t) \end{cases} \qquad \gamma \in (k-1, k]$$

J^k is an integral operator which is called the Riemann-Liouville operator of order k and has the following form

$$J^{k}Y(t) = \frac{1}{\Gamma(k)} \int_0^t (t-\tau)^{(k-1)} Y(\tau)\, d\tau, \quad t > 0$$

Fractional-Order Neuron Model
explore different dynamical classes of the model

To descretize the model, we apply Grünwald-Letinkov approximation on our model equations based on nonstandard finite difference method (NSFDM) or Micken's scheme. Therefore, we have

$$\begin{cases} D_\gamma V(t) = \lim_{h\to 0} h^{-\gamma} \sum_{i=0}^{T} (-1)^i \binom{\gamma}{i} V(t-ih), \\ D_\gamma n(t) = \lim_{h\to 0} h^{-\gamma} \sum_{i=0}^{T} (-1)^i \binom{\gamma}{i} n(t-ih) \end{cases}$$

$$T = [t]/h$$

C_i^γ are the Grünwald-Letinkov coefficients

Next, we discretize the equation

$$\begin{cases} \sum_{i=0}^{T} C_i^\gamma V(t_{k-i}) = f(t_k, V(t_k)), \\ \sum_{i=0}^{T} C_i^\gamma n(t_{k-i}) = g(t_k, n(t_k)), \end{cases}$$

C_i^γ are the Grünwald-Letinkov coefficients

$$C_i^\gamma = \left[\frac{i-1-\gamma}{i}\right] C_{i-1}^\gamma, \quad C_0^\gamma = H^{-\gamma} \quad i = 1, 2, \ldots$$

Fractional-Order Neuron Model
explore different dynamical classes of the model

Fractional calculus as a new approach for modeling has been used widely to study the non-linear behavior of physical and biological systems with some degrees of fractionality or fractality using differential and integral operators with non-integer orders.

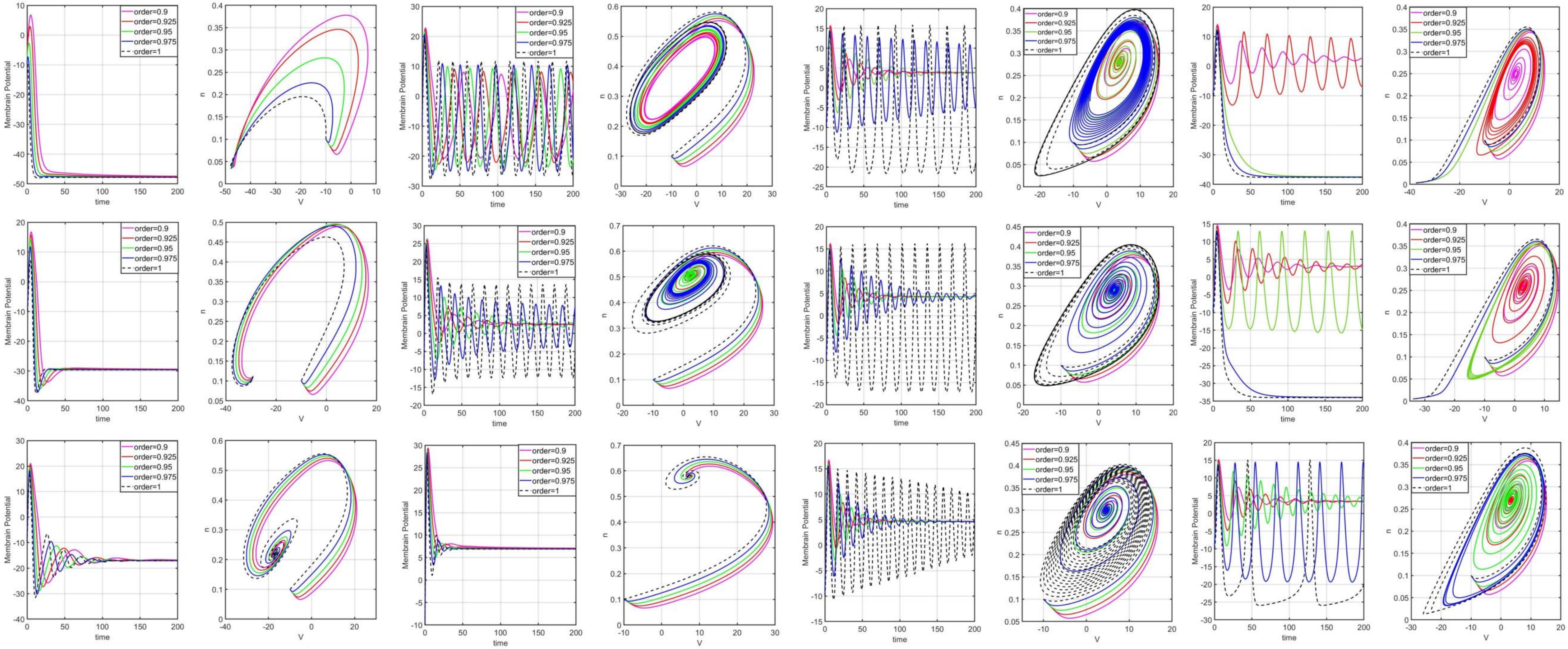
$$\begin{cases} C_M \sum_{i=0}^{k+1} C_i^{\gamma} V_{k+1-i} = I_{app} - I_{ion}(V_k, n_k), \\ \sum_{i=0}^{k+1} C_i^{\gamma} n_{k+1-i} = \Phi(n_\infty(V_k) - n_k)/\tau_{n_k}(V_k), \end{cases}$$

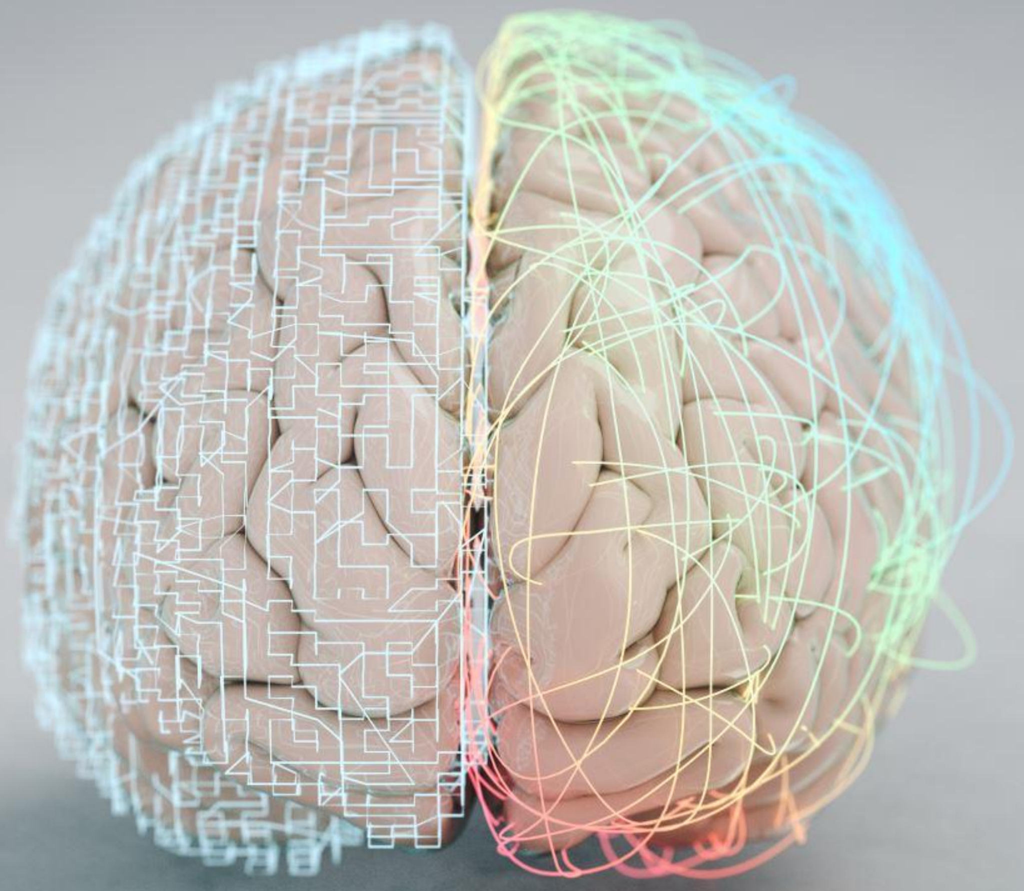
C_i^{γ} are the Grünwald-Letinkov coefficients

$$I_{app} = I_{ion} + I_{C_M} = I_L + I_K + I_{Na} + I_{Cl} + C_M D_{\gamma} V$$

$$D^{\gamma} V(t) = J^{k-\gamma} D^k V(t)$$

Fractional-Order Neuron Model Trajectories





Current Study in multiscale modeling of brain dynamics

Multiscale modeling of brain dynamics

Novel advances in mathematical approaches and rigorous theories, such as topological and computational methods for describing and extracting macroscopic activity states of neural populations and deriving principles of their emergence from underlying synaptic, cellular and network dynamics.

There is also considerable promise in analyses and applications of learning algorithms as multiscale dynamical systems.

There are two main approaches to analyze and modeling of networks of neurons:

The details of action potentials or spikes are important and does matter.

We need to pay attention to the firing rates of populations not the timing of individual neurons when we model and analyze the neural activities.

Current Study in multiscale modeling of brain dynamics

Basically, we have three main categories for components of a network:

1. The intrinsic properties of the cells within the neuronal networks.
2. The synaptic properties of the neuronal connections.
3. The topological properties of the network connections.

The first and the second components of the network contain multi time scales and depend on the parameters, however, the third component does not include multiple time scales and depends on the parameters of network.

1. The intrinsic properties of the cells within the neuronal networks.

- When we talk about the intrinsic properties of the neuronal cells, their channel gating variables are crucial in determining the neuronal cells dynamics.
- These channels may be activate or inactivate on disparate time scales.
- We assume a general two dimensional neuronal model:

$$\frac{dv}{dt} = f(v,w),$$
$$\frac{dw}{dt} = \epsilon g(v,w).$$

including ***v*** as the membrane potential of the cell, ***w*** the channel gating variable which displays a channel state variable that either activates or inactivates on a slower time scale compare to other processes, and a small positive parameter ϵ .

2. The synaptic properties of the neuronal connections.

We follow the following three dimensional differential equations to model a pair of mutually coupled neurons:

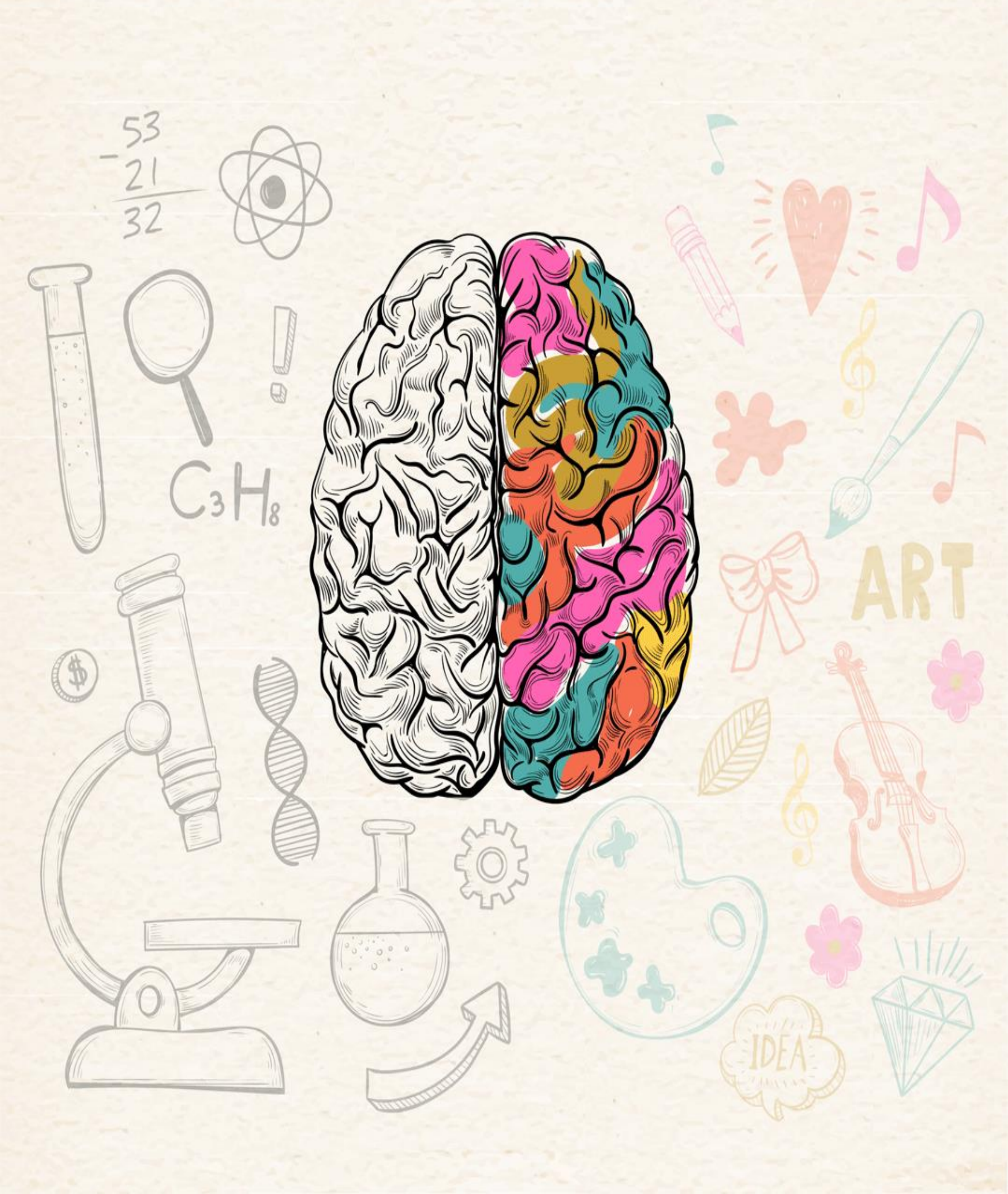
$$\frac{dv_i}{dt} = f(v_i, w_i) - g_{syn} s_j (V_i - v_{syn}),$$
$$\frac{dw_i}{dt} = \epsilon g(v_i, w_i),$$
$$\frac{ds_i}{dt} = \alpha (1 - s_i) H_\infty (V_i - V_T) - \beta s_i, \quad i,j = 1,2; \quad i \neq j$$

3. The topological properties of the network connections.

Finally, for studying the third components of the network, network architecture, we may assume that the network has sparse or dense connectivity.

In this case, we assume that cells communicate with a small or large number of cells. There are other types of network architecture such as local or global, random or structured.

$$\begin{cases} \dfrac{dv_i}{dt} &= f_i(v_i, w_i) - g^i_{syn}\left(\sum_j W_{ij} s_j\right)(v_i - v^i_{syn}), \\[2ex] \dfrac{dw_i}{dt} &= \epsilon\, g_i(v_i, w_i), \\[2ex] \dfrac{ds_i}{dt} &= \alpha_i (1 - s_i) H_\infty (v_i - V_T) - \beta_i s_i, \end{cases}$$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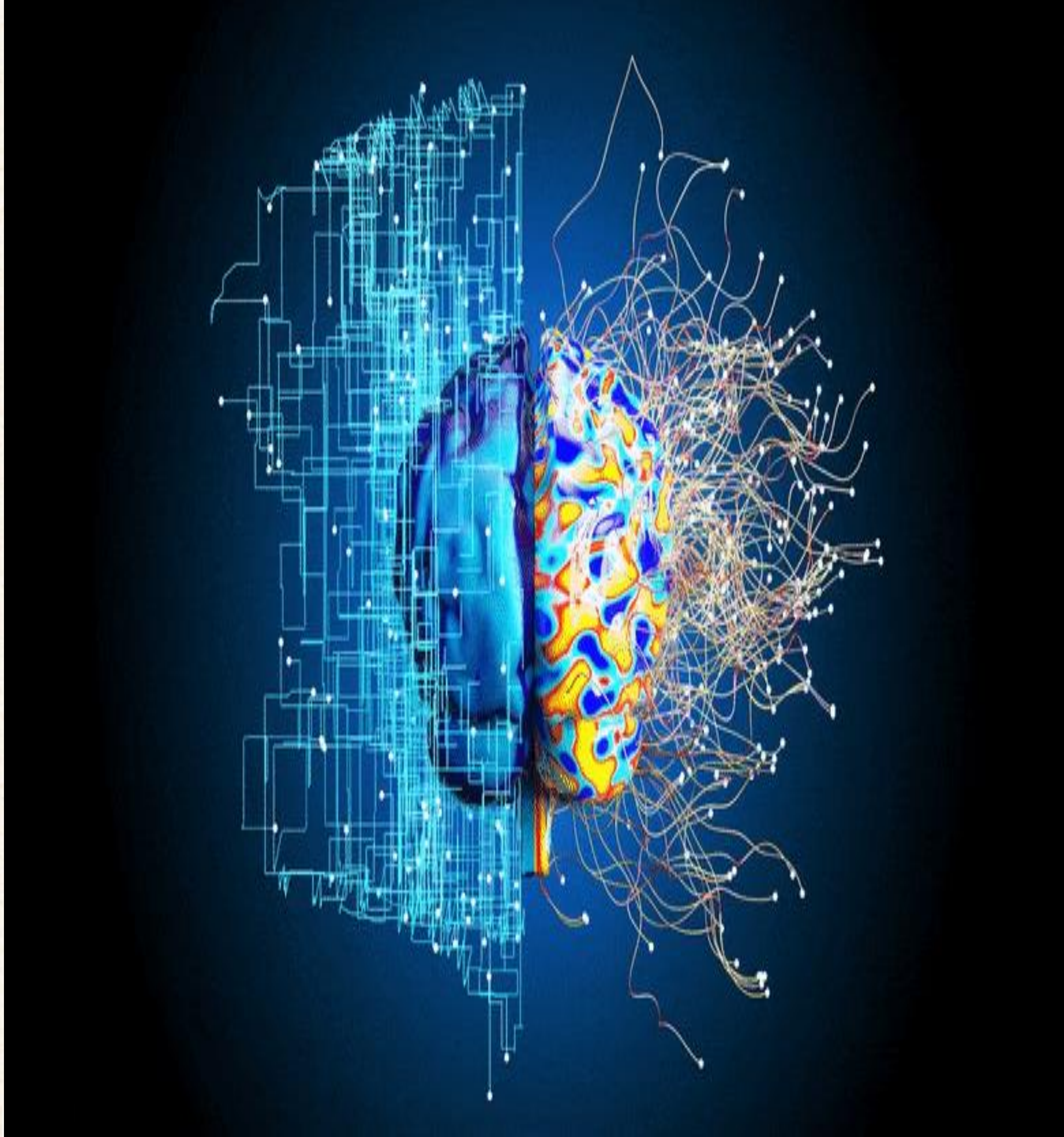

Thank you for your attention.