Computational Neuroscience

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Lecture - 14

Lecture 14 : Reducing the HHE and Moris-Lecar Equations (MLE)

Welcome. We have discussed the Hodgkin-Huxley equations and briefly explained, at least qualitatively, how the action potential occurs. To actually observe the phenomena, we need to simulate the system of Hodgkin-Huxley equations to fully understand it. Therefore, reading material and codes will be provided regarding the Hodgkin-Huxley equations, which you can use to explore their behavior using current injections and observe various threshold phenomena. The Hodgkin-Huxley equations explain a number of phenomena, and to analyze the system so that we can understand what the Hodgkin-Huxley equations can explain, we need to be able to reduce the system to fewer dimensions. The system of equations is essentially represented by this vector, let us say \(ԁb{X}), which is the set of four state variables (V), (m), (n), and (h).

The system of differential equations is described by the derivative of (**X**),which are $(\dot{V}), (\dot{m}), (\dot{n}), and(\dot{h})$,and can be expressed as a sum function of this vector (**X**). In this case, what we have is $(f_1(V,m,n,h)), (f_2(V,m,n,h)), (f_3(V,m,n,h)), and(f_4(V,m,n,h))$, or we can refer to them as $(f_V), (f_m), (f_n), and(f_h)$. Visualizing and applying techniques to understand the behavior of such systems of equations is challenging. Often, if we can reduce the system to two dimensions by making some assumptions, we can understand a lot about phenomena related to action potentials and generally the Hodgkin-Huxley type equations.

What we mean by reducing it to two dimensions involves making certain assumptions, which must be meaningful for a range of parameter values or a region of the phenomena we are trying to understand, not necessarily throughout the entire period of the phenomena, but maybe a part of it. Given that (m) is very fast, \(n\) is intermediate, and \(h\) is very slow, we can assume, in one case, that (m) is so fast that its dynamics are not required and (m) instantaneously changes to $(m_\infty(V))$. Therefore, $the(\frac{dm}{dt})$ equation is not needed anymore, and (m) in the Hodgkin-Huxley system of equations can simply be replaced by $(m_\infty(V))$.

Now, we can set (h) to its initial value. Since (h) is very slow, we can also remove the $(\frac{dh}{dt})$ equation and replace (h) in the Hodgkin-Huxley equations by $(h_\infty(V_0))$, where (V_0) is the initial voltage when the system simulation begins. We can assume that (h) is so slow that it does not change at all; it stays at its original value from the very beginning. Thus, we eliminate two variables here, $(m)\ and\ (h)$, and we are left with essentially a system of two equations: $(V)\ and\ (n)$. Obviously, as we mentioned, these assumptions need to be meaningful.

This means that the reduced system of equations has to work within a small range of values or a small region of parameter space. We cannot explain behavior here that depends strongly on (m), such as the very fast change in the kinetics of (m), which means we will not be able to explain the threshold phenomena. Remember, we require the voltage to gradually increase until the threshold is reached and then it escalates even faster to produce the action potential. If the dynamics of (m) are removed from this set of equations, then we will see that the true threshold nature of neurons cannot be explained without (m). Similarly, since the time scales at which (h) starts to change, we would not be able to accurately show the behavior of the system with the $(V)\ and\ (n)$ system.

What we have is something called the $(V)-(N)$ reduced system where (m) is fixed to $(m_\infty(V))and(h)$ is fixed to $(h_\infty(V_0))$, where (V_0) is the initial voltage. Now that we have only $(\frac{dN}{dt})and(\frac{dV}{dt})$ to govern the system, this will be meaningful only at intermediate time scales, not the very early time for the current injection period if we are trying to explain the action potential. Obviously, it is also not very useful to explain inactivation behavior or after the action potential is trying to bring the voltage down to complete the action potential, the behavior after that would not be accurate in this case because the dynamics of (h) are gone. However, it will allow us to understand the behavior at the intermediate time scales.

Now, we can extend this whole idea going forward where we set $(n)\ and\ (h)$ to their initial values and include the dynamics of (m), $since\ (n)\ and\ (h)$ are both extremely slow compared $to\ (m)$. We can have a $(V)-(M)$ reduced system such that (n) and (h) are not changing and are set to their initial values. This kind of system will allow us to observe the behavior at the very beginning of the action potential to understand the threshold phenomena. In this case, as you can see, if we have a $(V)-(M)$ reduced system, we would not even be able to model the action potential because potassium currents are gone and (h) is not there. So, once the voltage increases and (m) reaches (1), we cannot bring it back down, or rather, whatever the potassium channels did, that phenomena is gone.

So, since $(M = 1)$, the voltage will not change and it will stay there; hence, we cannot model the entire action potential, but we can model the very beginning part of the action potential and explain threshold behavior with the $(V) - (M)$ reduced system. We will delve into these types of analyses when we discuss more about the Hodgkin-Huxley equations. To develop the tools that are required to understand these two-dimensional reduced systems, we will study a set of equations called the Morris-Lecar equations. These equations are very similar to the Hodgkin-Huxley equations. They were developed to explain the behavior of a particular ganglion cell in a particular species and do not have the exact same kind of channels that the Hodgkin-Huxley equations show, but they possess similar properties to the Hodgkin-Huxley type of ion channels.

The Morris-Lecar equations tell us that the dynamics of a certain ganglion cell involve the following equations:

$$\frac{dV}{dt} = I_{\text{external}} - G_{\text{calcium}} \cdot (V - E_{\text{calcium}}) - G_{\text{K}} \cdot W \cdot (V - E_{\text{K}}) - G_{\text{leak}} \cdot (V - E_{\text{leak}})$$

$$\frac{dW}{dt} = \phi \cdot \frac{W_{\infty}(V) - W}{\tau_W(V)}$$

Here, (ϕ) is a temperature factor which we will not concern ourselves with at the moment. It simply scales the $(\frac{dW}{dt})$. We now need to understand $(W_{\infty}(V)), (\tau_W(V)), and (M_{\infty}(V))$ as functions of voltage to describe this entire system.

These neurons have a calcium channel that can be described by one activation gate, denoted as (M) and it is extremely fast like the sodium channels. This is set $to (M_{\infty}(V))$ as we discussed earlier for the $(V) - (N)$ reduced system. They also have a potassium channel to explain their behavior, described by the gating variable (W), which exhibits first-order kinetics similar to what we see in the Hodgkin-Huxley equations. The $parameters(C), (I_{\text{external}}), (G_{\text{calcium}}), (G_{\text{potassium}}), (G_{\text{leak}}), (E_{\text{leak}}), (E_{\text{K}}), and (E_{\text{Ca}})$ are all experimentally obtained and are provided for anyone who simulates this system of equations. Additionally, the equations for $(W_{\infty}(V)) and (\tau_W(V)) and (M_{\infty}(V))$ are described. For $(M_{\infty}(V))$, we have:

$$M_{\infty}(V) = \frac{1}{2}\left(1 + \tanh\left(\frac{V - V_1}{V_2}\right)\right)$$

$where(V_2)$ is another parameter added to the list.

So, the parameters $(V_1), (V_2), (V_3), and(V_4)$ are experimentally and empirically determined, and this functional form is the best that the developers of the Morris-Lecar model came up with to explain the data. Similarly, $(w_{\infty}(V))$ has the same form:

[

$$w_{\infty}(V) = \frac{1}{2}\left(1 + \tanh\left(\frac{V - V_3}{V_4}\right)\right)$$

]

Here, $(V_3)and(V_4)$ are the new parameters that describe $(w_{\infty}(V))$. If plotted, these functions resemble activation plots similar to $(m_{\infty}(V))$ and $(n_{\infty}(V))$, resembling a sigmoid curve. The function for $(\tau_w(V))$ is best explained by:

[

$$\tau_w(V) = 2\cosh\left(\frac{V - V_3}{V_4}\right)$$

]

Given these parameters, we have all the information needed to simulate or numerically solve the equations, including the first equation $(\frac{dV}{dt})$ and the second equation $(\frac{dw}{dt})$.

This system of equations is known as the Morris-Lecar equations, which can reveal a lot about action potential behavior among other phenomena. Considering numerical solutions, let's say:

[

$$C\frac{dV}{dt} = I_{\text{external}} - I_{\text{Calcium}} - I_{\text{Potassium}} - I_{\text{Leak}}$$

]

we replace those terms with conductance terms (G_{Calcium}) and gating variables, and have:

[

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

]

For any system of differential equations, we need a starting point or initial condition.

Often, the starting point is the resting state or (V_{rest}), determined numerically from these equations as the value where the total current is zero with no current injection. The solution shows how (V) changes over time starting at (V_{rest})$with$(w) starting at ($w_{\infty}(V_{\text{rest}})$). If we consider perturbing the system from (V_{rest}) with current injection or a voltage clamp, we can solve these equations and understand what happens, and how (w) changes with time.

Thinking of (V) and (w) as a pair of state variables, we can plot them on a plane, with (V) on one axis and (w) on the other. Starting at a particular point (V_0)and(W_1), the solution to these equations is simply a trajectory in this plane, showing how (V) and (w) $change$ together over time. This plane is called the phase plane where (V) and (w) are the state variables. At any point in this plane, the system's equations provide (dV/dt) and (dw/dt), telling us how (V) and (w) will change at that location.

With small time steps, we can predict the system's behavior quite well, creating a grid of points in this plane, and plotting tiny arrows (a quiver plot) that show the direction of system movement at each point. This helps us predict whether the system will reach a particular state or follow a specific path. Ideal numerical simulation with small time steps is managed by solvers that allow us to simulate the system efficiently without extremely small steps, which are time-consuming.

We will continue with the Morris-Lecar equations to understand more about the Hodgkin-Huxley set of equations and how to understand their behavior. Thank you.