Lab Report 2 - The Na^+ Action Potential Tutorial Ali El Ali

1. Question:

“What underlies the depolarizing ramp at the beginning of the action potential?”

Answer:

Leveraging the NEURON library to capture the action potential that marks the kickoff of the stimulus. The bottom graph shows the depolarisation of the current when more and more Na^+ ions rush into the channels. The stimulus current depolarises the membrane to threshold (shifting from -75mV to -55mV), triggering the first few voltage-gated sodium channels to open. This kicks off a self-reinforcing cycle that begins with just a trickle of **Na^+** entering the neuron membrane, but rapidly picks up pace. Na^+ opens additional Na^+ channels, creating a cascading effect. This flood of Na^+ drives the membrane potential towards the sodium equilibrium potential. The image shows a Plain Bilayer Membrane model with **Na/K** pump, displaying both the Membrane Voltage (blue line) and Stimulus current (green line) over time, demonstrating this process in a simplified way.

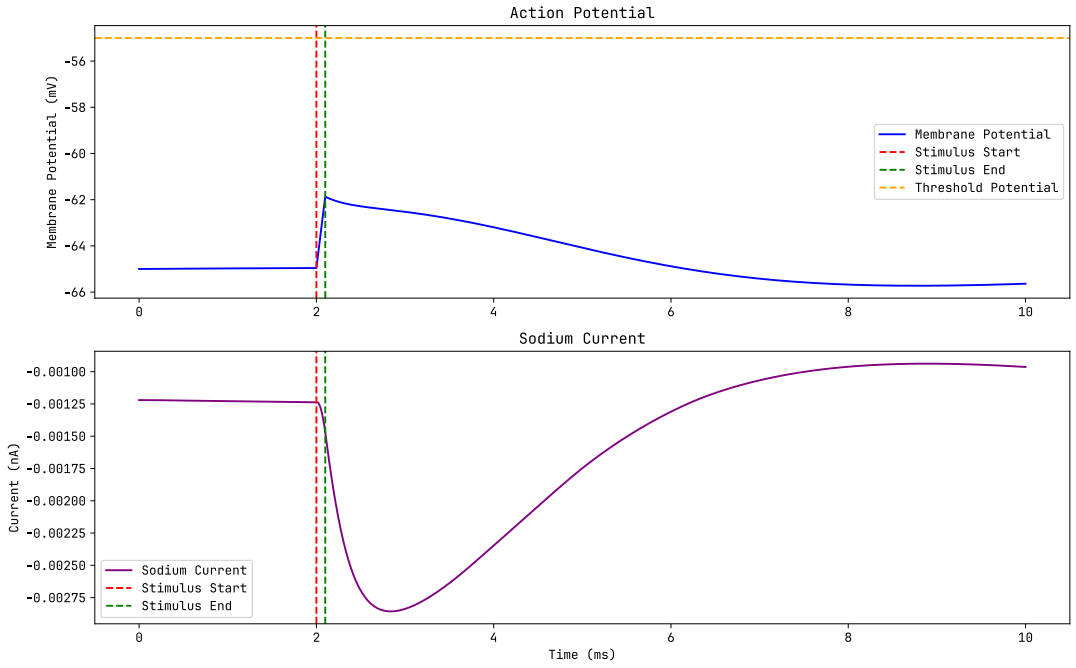


Figure 1: Membrane action potential of items

2. Question:

Why is I_{Na} so kinky with two phases?

Answer:

I^{Na} is described as kinky because of the non-linear behaviour. The pattern of staying active during sustained deplolarisation isn't simple. It shows a rapid rise followed by an abrupt fall despite the continued depolarising stimulus. If you look at the current trace, it forms a 'kinked' shape rather than a flat or gradually changing response.

The properties of the voltage-gated **Na** channels give it the unique characteristic, which simulataneously contain the activation and inactiviation gates. These operate at different time scaled. You can see the reference via the Hodgkin-Huxley model where:

> $V \rightarrow$ m increases $\rightarrow g_{\mathrm{Na}}$ increases $\rightarrow$ more Na current flows in $\rightarrow$ more depolarisation $\rightarrow$ V rises rapidly toward reversal potential of $V_{\mathrm{Na}} \rightarrow$ h starts to decrease $\rightarrow g_{\mathrm{Na}}$ shrinks $\rightarrow$ V falls

The automatic inactivation immediately after automatic inactivation creates that kinky two-phased pattern that makes the sodium current distinctive and crucial for action potential generation in neurons.

To finish, the two-phased nature of the **Na** current, being rapid activation followed by inactivation, is vital for action potential generation and the refractory period. Kinky behaviour ensures that action potentials are brief, unidirectional events that propagate along neurons.

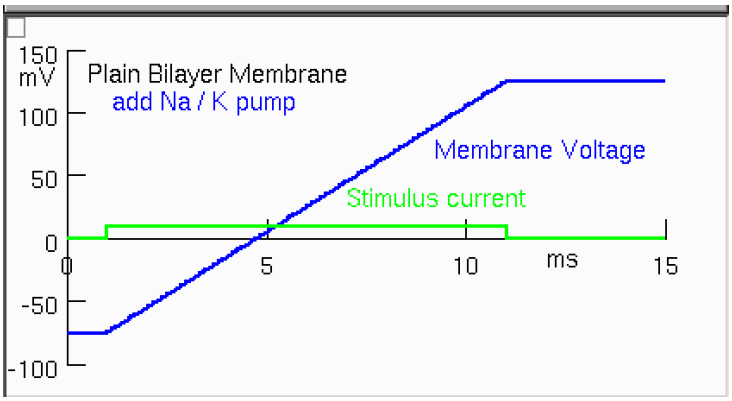


Figure 2: Membrane action potential of items

3. Question:

Does changing either the length or diameter of the patch alter the action potential in any respect? Should it?

Answer:

Based on what's been discussed in our materials, the changing of these dimensions(length, diameter, etc.) doesn't change the form necessarily, but it does affect the propagation based on said dimensions. This is shown in a experiments and theories.

Deriving from the Hodgkin-Huxley model, action potential is based on Voltage-dependent activation and inactivation of sodium channels, delayed activation of potassium channels, relative conductivity of said channels and the concentration gradient of ions. This more concretely describes its importance in terms of membrane and the channels rather than dimensions.

Cable theory examines that while dimensions affect signal propagation, they don't change the fundamental action potential mechanism. That is:

The length constant $\lambda = \sqrt{\frac{\mathrm{rm}}{\mathrm{ri}}}$ determines the potential passive spread, but doesn't affect the action potential generation. And the time constant $\tau_m = \mathrm{r}_m * \mathrm{c}_m$ is independent of shape, length or width. For example:

Diameter changes: increases along the length constant $\lambda \infty \sqrt{d}$ which allow signals to spread farther before regeneration is required.

Axon thickness: faster conduction velocities because of how length constants increases diameter

Cable Theory: shows that propagation velocity is dependent on both the time and length constants

One final mention is the patch clamp experiment. Where changing the patch size could affect the magnitude of the recorded currents. Where in this case the larger patches would - by its nature - have more channels and so larger currents. The capacitance of the membrane, which scales the surface area. And finally the input resistance. Which decreases with increasing membrane area.

In this case the shape, threshold, and timing characteristics of the action potential still remain unchanged(in no absolutes) because of these properties are determined by individual channels and ion concentrations.

So while dimensions affect how signals propagate, they don't fundamentally alter the action potential waveform or generation mechanism, which is described in the Hodkin-Huxley model. With further evidence on the theories and experiments mentioned above.

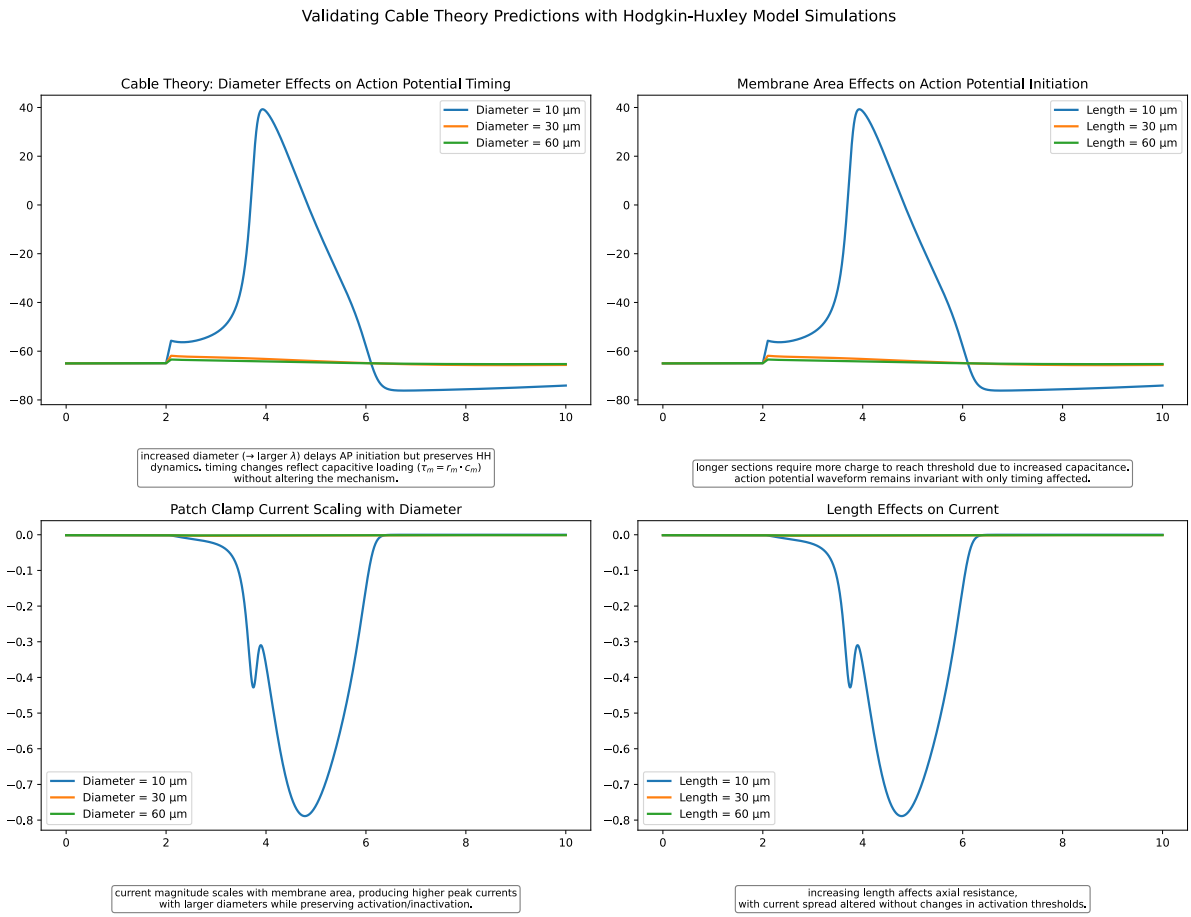


Figure 3: Runs of experiments and theories to test how signals propagate and how dimensions affect action potentials

4. Question:

What happens to the duration of the action potential if you change the temperature? Why?

Answer:

Temperature affects the kinetics of the channels that allow the movements of ions during action potentials. Below is an explainer on what happens based on the temperature:

Low temp.:

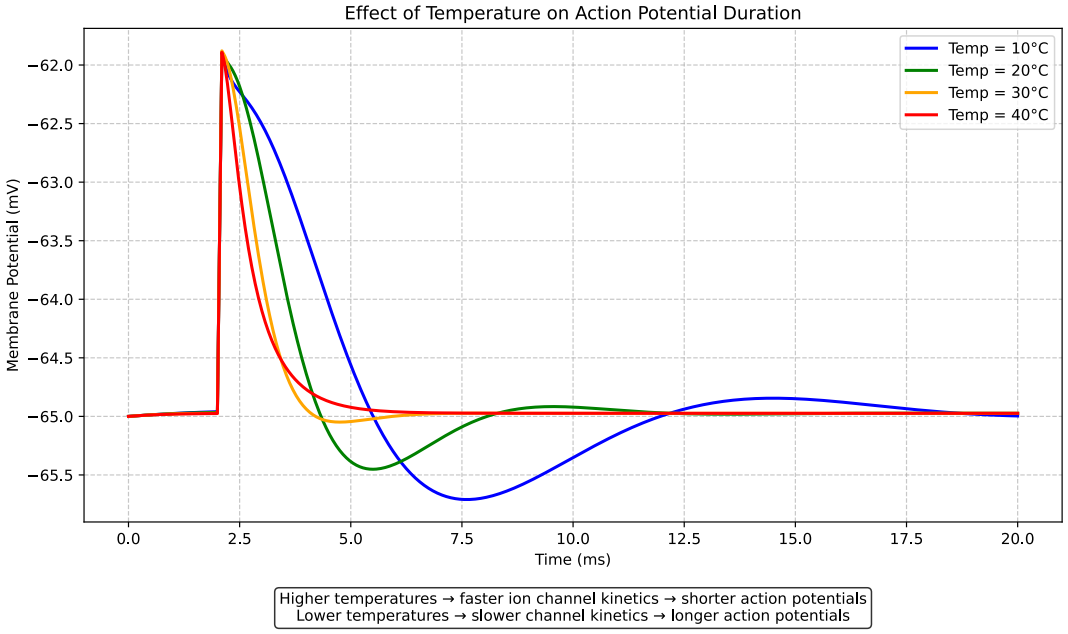
- Ion channel kinetics slow down
- open/close channels take longer
- action potential is prolonged

High temp.:

- ion channels become faster
- activation/inactivations accelerate
- the action channel is shorter due to rapid channel state transitions

Temperature affects the time constants of the membrane and rate constants when basing it off the Hodgkin-Huxley model equations that dictate the channel state transitions. Membrane-time constant being mentioned as the equation: $\tau_m = \mathrm{r}_m * \mathrm{c}_m$

The magnitude of difference between high and low temperature is quite large. The reduction in action potential duration can be up to 20 times when making calculations at 30°C or 10°C.



5. Question:

Which is more effective at blocking action potentials, a toxin that selectively blocks Na+ channels or the anesthetics (investigated above) that block both Na+ and K+ channels?

Answer:

TTX is mentioned as a 'highly specific blocker of many(but not all) of the voltage-gated Na^+ channel subtypes, including the HH Na^+ channel.' This is a reference to the fugu puffer fish. I'll discuss the mechanism and then follow through on the efficacy of blocking action potentials. Abbreviating tetrodotoxin as **TTX**.

Generally speaking, the **HH** model states that much of the change in membrane potential during an action potential can be explained by the Na^+ current.

So to look into the effectiveness of when *a)* Na^+ *channels are blocked by TTX* and *b) the* Na^+ *and* K^+ *channels are blocked by aesthetics*

a. initial depolarisation is unable to occur and so without depolarisation, no action potential can be generated. No matter how

much stimulation is received, the membrane will remain at resting potential.

b. The depolarisation phase is prevented in much the same way as **TTX**. With the repolarisation *also* being compromised. Na^{+} and K^{+} channels being blocked also affected the membranes' ability to restore its equilibrium.