Axon Diameter Change
Computer Modeling of Neuronal Systems
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Introduction

This tutorial explores the transmission of impulses through a region of a neuron where there is an abrupt change in diameter (in the default example, a 10-fold change). These simulations will represent what happens to the action potential when it encounters a branch point or when it tries to invade a cell body.

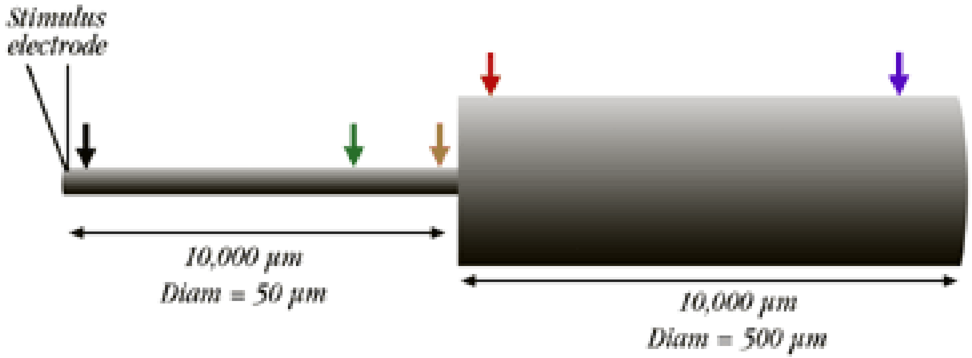
Goals/Experiments

In order to fully comprehend how an action potential travel in a neuron with complicated geometry, such as between a neuronal process and a soma, we must investigate an action potential traveling from an axon of smaller diameter to that of a larger diameter and visa versa, how the behavior of the axon potential is related to the ratio's of the diameters, and how temperature affects an action potential traveling through a region of a neuron where there is an abrupt change in diameter. The 'experiments' prepared by NIA to conceptualize the underlying principles of this tutorial are:

1) Propagation from a Smaller Diameter Process into a Larger Diameter Region
2) How does propagation from the smaller into the larger axon depend on the ratio of the diameters?
3) How does invasion depend on temperature?
4) What happens if we reverse the direction of propagation?

Parameters

We will experiment with an unmyelinated axon's diameter change. The smaller-diameter (50 µm) segment on the left may be thought of as a branch of the larger-diameter (500 µm) axon on the right. These parameters represent the 500 µm-diameter squid giant axon that often has 50 µm-diameter branches. Furthermore, the inhomogeneous axon in this tutorial may also be thought of as a neuronal process (e.g. dendrite and axon) and a soma. There will be five locations of recording from the cell: three locations in the smaller axon and two locations in the larger axon.



NIA also provides three graphs with this tutorial: The Voltage-vs-Time, Na Current-vs-Time, Voltage-vs-Space graphs.

1) Propagation from a Smaller Diameter Process into a Larger Diameter Region

In order to understand how an action potential propagates from a smaller diameter process into a larger diameter region, we first begin by listing observations of voltage and current profiles unique to this set up, such that they differ from propagation down a homogeneous unmyelinated axon. These unique voltage and current profiles are: (1) The change in shape of the rising phase of the advancing impulse when it encounters the junction between the two segments, (2) The voltage profile in the large axon as the voltage hesitates at threshold, (3) The voltage profile as it finally gives an action potential in the large axon, and (4) The changing amplitude of the action potential at the junction as it re-establishes itself in the small-diameter axon.

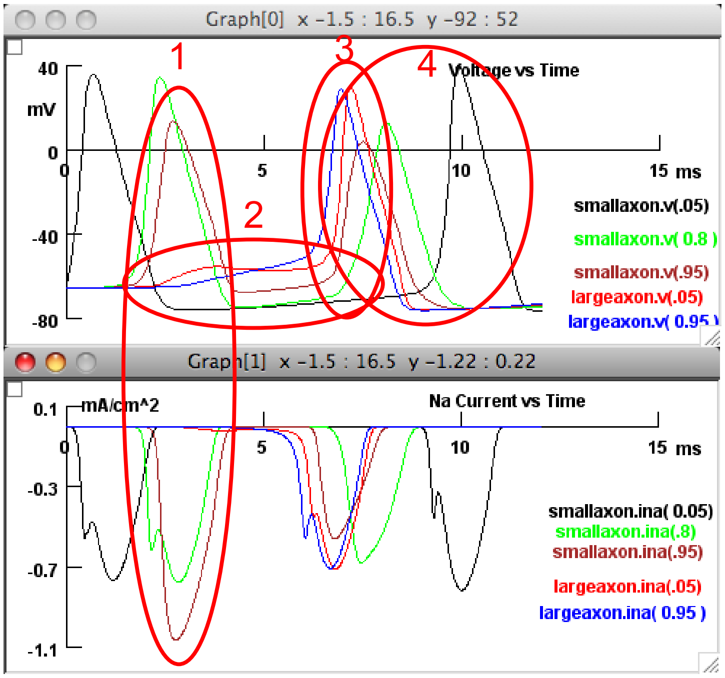


Fig. 1: Propagation of an action potential from a small-diameter axon to a large-diameter axon

First, as longitudinal current in front of the propagating action potential spreads from the smaller axon into the larger axon, it encounters the much larger membrane area, and thus capacitance, of the larger axon. Now this longitudinal current, which is normally a small fraction of the total current of the action potential, has the difficult assignment of depolarizing all of this membrane. Since the required longitudinal current must come from somewhere, the radial Na current through the small axon's membrane must supply it, and this is why we see the voltage profile in the large axon hesitate. At the location just before the junction with the large axon, the amplitude of the action potential is smaller than usual, pulled down by the low voltage in the big axon. Consequently there is a greater driving force on Na (the amplitude of the action potential is farther from ENa) and the Na current is greater than usual, explaining the change in shape of the rising phase of the advancing impulse when it encounters the junction between the two segments.

Once the AP passes completely through the axon of smaller diameter and the voltage profile in the large axon initially hesitates to rise as the longitudinal current supplied by the small axon struggles to charge the membrane of the larger axon, it can be seen that a back-propagating action potential begins at the far end of the large axon and back-propagates. The time course is faster for the action potential due to the faster conduction velocity in the larger axon.

Finally, once the back-propagating action potential meets the junction, the peak amplitude of the action potential recorded at the first electrode (smallaxon[.95]) is low and the amplitude of action potential grows as it re-establishes itself in the small-diameter axon such that it reaches a value comparable to when stimulated directly. This is most likely due to re-activation of Na channels due to the repolarization of the membrane in the time course following the previous action potential.

2) How does propagation from the smaller into the larger axon depend on the ratio of the diameters?

Recall that the resting membrane has a fixed capacitance and conductance per unit area. When the axon's diameter is changed, its area per unit length is changed. This results in two electrical changes: (1) its capacitance per unit length is changed proportionally, and (2) its conductance per unit length is changed proportionally (its resistance is increased). Therefore, as the difference in the diameters increases, the difference in capacitance between the two axons increases such that when the smaller axon is stimulated,more current is required to depolarize the large axon and initiate a spike, and as the difference in the diameters decreases, the difference in capacitance between the two axons decreases such that less current is required to depolarize the larger axon and initiate a spike.

3) <u>How does invasion depend on temperature?</u>

Temperature changes affect longitudinal current flow. The longitudinal current is determined by the difference in potential between the region where the impulse is at its peak and the region ahead (normally resting).

Cooling increases the probability of impulse propagation by enabling the impulse to supply more charge to the region ahead. Furthermore, if the axon is cooled and action potential dwells for a longer time at its peak, more longitudinal current will flow.

Warming decreases the probability of impulse propagation due to the inability to supply enough charge to the region ahead. If the axon is warmed and the action potential shortens at its peak, less longitudinal current will flow. Furthermore, as the safety margin for propagation narrows, it becomes more and more likely that propagation will fail at a danger zone--any discontinuity where there is an increase of capacitance ahead (an increase in the amount of membrane that needs to be charged).

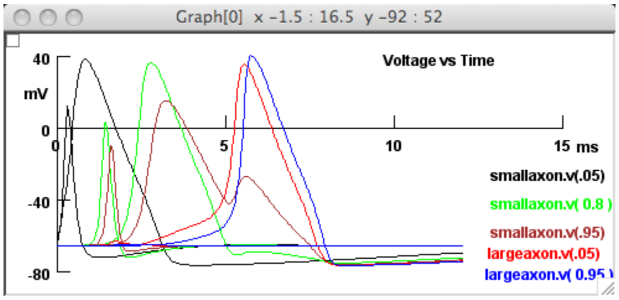


Fig. 2 The effects of warming and cooling on the action potential encountering an abrupt axonal diameter change. The figure shows two stimulations, one at 26.3ºC and one at 6.3ºC, distinguished by the inability to strike an action potential in the large diameter axon due to the increased kinetics at 26.3ºC and the slowed yet long and complete action potential at 6.3ºC.

4) <u>What happens if we reverse the direction of propagation?</u>

When the location of stimulation is moved to the end of the large-diameter axon, stimulation with default parameters fails to change the voltage profile in the large-diameter axon and, thus, the small-diameter axon. Since the larger axon has more surface area, it requires more current to charge its membrane and depolarize it to threshold. The amplitude of the current pulse must be increased to evoke an action potential in this axon.

When we raise the amplitude of the stimulus enough to see an action potential and the current pass into the second axon, the first thing to note is that compared to the when we stimulate the small-diameter axon the velocity of the action potential is much faster in that of the large-diameter axon. This is due to the fact that the capacitance per area load and current required to depolarize the membrane increases proportionally with axonal diameter.

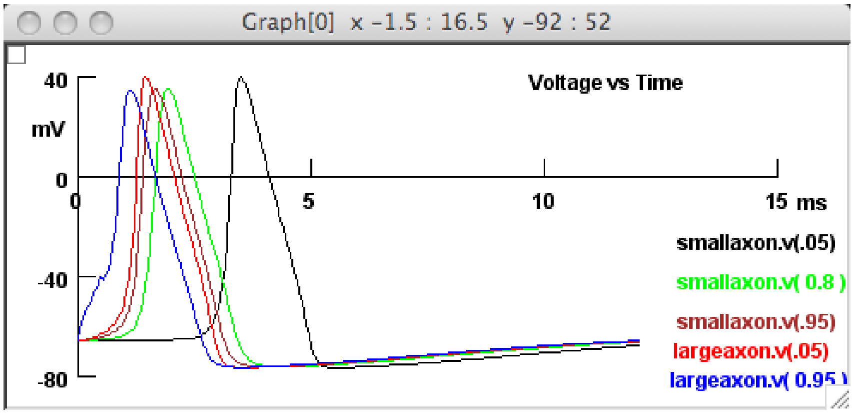


Fig 3. Propagation of an action potential from a large-diameter axon to a small-diameter axon

The next observation is the of the changing voltage profile of the action potential in the small-axon diameter such that the velocity of the action potential slows down and it's peak amplitude increases. The latter is due to the decreased capacitance per unit load in the small-axon diameter after the junction and the greater lamda of the large-diameter axon, which has depolarized some of the membrane in the small-diameter axon before the action potential arrives causing a decrease in the driving force for Na and, ultimately, an action potential of weaker amplitude. The action potential slows down because the velocity of the action potential is proportional to axonal diameter because of the capacitance per unit load.

Lastly, there no back-propagating action potential. The velocity of propagation must be faster than the time course of inactivation, such that the channels are still inactivated upon seeing a depolarization which results in the inability of these channels to become reactivated. Note that the velocity of an impulse increases with the diameter of the axon. As the impulse moves faster in the larger axon, it is more spread out.

Conclusion

This tutorial has examined how an action potential propagates through an abrupt change in axonal diameter, how it depends on the ratio of the diameters, and how temperature affects propagation. This concludes the summary for the tutorial on 'Axonal Diameter Change.'