

ILLUMINATIONS

Visualizing fundamental neuronal computation for life science students

 Alon Korngreen^{1,2}

¹The Mina and Everard Goodman Faculty of Life Sciences, Bar Ilan University, Ramat Gan, Israel; and ²The Leslie and Susan Gonda Interdisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel

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PASSIVE CABLE THEORY is the foundation for formulating and explaining the computational properties of single neurons. It can be described by Eq. 1, first written by Lord Kelvin to explain the propagation of electricity in an underwater telegraph cable (13). In practice, this is a propagating wave equation.

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V \quad (1)$$

where τ is the membrane time constant, λ is the membrane space constant, and V is the membrane potential. This equation describes the propagation of electricity along a core conductor, as some of the current escapes through a nonperfect insulator to an infinite external conductor. This cable equation was successfully adapted from the underwater telegraph to axons (4) and later to dendrites (9–12) and forms the basis for modern modeling of biophysically detailed neurons (1).

This equation is simply not self-explanatory, and, in my experience, the difficulty in explaining passive cable theory to life science undergraduates is far from trivial. This difficulty is evident when browsing textbooks of neurophysiology, which offer various explanations of passive cable theory. Some provide a mathematical tracking of the subject (6), while others offer a more descriptive view (7). Over the years, I have tried these and other textbooks with equally dismal results: the students did not grasp the basics of passive cable theory. Since this subject is fundamental to the understanding of neurophysiology and appears early in the course material, the students' failure to understand it leaves them with a knowledge gap and leaves me exasperated.

In another part of the neurophysiology course, I describe the classical experiment of Hodgkin and Keynes (3), who built a physical model for ion permeation through membranes using steel balls, two connected chambers, and an electrical motor. This wonderful physical model has been able to predict that ions traverse the membrane in single file and that several of them should be found in the membrane. This led me to search for an everyday physical system that may help to better visualize the passive propagation of the electrical wave in axons and dendrites. I found my solution in drip irrigation. Unlike Hodgkin and Keynes, I did not build the actual physical system, but developed a series of thought experiments for use in the classroom while teaching passive cable theory.

Drip irrigation as a model system for cable theory. Drip irrigation involves dripping water onto the soil directly on or close to the roots of a plant. The water is dripped at very low rates from plastic pipes fitted with outlets called water emitters. For readers not familiar with drip irrigation, Fig. 1 shows drip irrigation in action in my backyard as a visual introduction to the physical system. The advantage of drip irrigation over surface or sprinkler irrigation, which involves wetting entire fields homogeneously, is the application of water directly to the plant, which saves precious water.

Drip irrigation has clear similarities with the passive propagation of electricity in axons and dendrites. First, it is a system with a core conductor with small resistance to the passage of the propagating wave (friction of the water with the tube walls). Second, along the wall of the tube, there are high-resistance shunting points (water emitters), causing small water currents to flow through the tube wall. Clearly, drip irrigation is not a true facsimile of axons and dendrites. Principle differences are the lack of inward water current through the water emitters to the core conductor, and that water does not obey the Nernst equation. The flow of water in a system of pipes may be better described as analogous to an electrical capacitor (2). Thus the two systems are not physically and mathematically similar. However, the relative similarity can be used to generate several thought experiments, detailed below, demonstrating the basic principles of passive cable theory.

Visualizing an infinite cable. Having developed Eq. 1 from basic electric circuit components (I find the steps described in Ref. 8 to be clearer for this part of the lesson), I review several solutions of the theory. The first is the case of the infinite cable under steady-state conditions. The solution of Eq. 1 in this case is:

$$V(x) = V_0 e^{-x/\lambda} \quad (2)$$

where V_0 is the membrane potential at the site of current injection. This exponential decay of the membrane potential from the point of injection can be easily visualized using drip irrigation. The intracellular electrode is replaced by a water tap and the axon with an infinite tube with many, evenly distributed, water emitters. Turning on the water tap, which is equivalent to injecting current via the electrode, generates a wave of water flowing along the tube. This is quite analogous to the flow of ions along the cytoplasm in an infinite axon. When the wave of water passes over a water emitter, a small amount of water is extruded from the tube to the outside world. This process is cumulative, leading to distance-dependent decreases in water pressure along the tube. Again, the analogy with the exponential decay of the membrane potential (Eq. 2)

Address for reprint requests and other correspondence: A. Korngreen, Bar Ilan University, The Leslie and Susan Gonda Interdisciplinary Brain Research Center, The Mina and Everard Goodman Faculty of Life Sciences, Ramat Gan 52900, Israel (e-mail: alon.korngreen@biu.ac.il).



Fig. 1. Image of a water drop falling from a water emitter in a drip irrigation tube. [Photographed by the author in his backyard and freely available for download and reuse under the creative commons license.]

along infinite axons and dendrites is straightforward. When we consider an infinite drip irrigation tube, it is simple to deduce that, regardless of the tap's water pressure, there will be a distal location along the tube that no water will reach. In my experience the students reach this conclusion very easily in class. From this point, it is simple to direct them to understanding the core conductor wrapped by a leaky membrane. It is important to note that it is simple, and rather accurate, to demonstrate the steady-state solution of the infinite cable using drip irrigation. However, time-dependent solutions are not similar in both systems and thus do not present a good visualization.

Visualizing a semi-infinite cable with a sealed end. Real neurons have short axons and dendrites, not infinite ones. The course material is amiss if this issue is neglected. There are several solutions of cable theory for short neurites (5, 6, 8). However, the most relevant for living neurons is the sealed-end boundary condition. Under steady-state conditions, the decay of the membrane potential along a finite cable having an electronic length $L = l/\lambda$ and defining X to be x/λ is expressed as:

$$V(X) = V_0 \frac{\cosh(L - X)}{\cosh(L)} \quad (3)$$

As X approaches L , closer to the sealed end, the curve of Eq. 3 flattens out. Thus the voltage decay in a sealed-end cable is slower than in an infinite cable with the same passive parameters. This is due to rebound of the axial current from the sealed end of the cable. Whereas understanding this from the mathematics is not trivial, it is simple to visualize using drip irrigation. When the students are asked to imagine a relatively short drip irrigation tube with a sealed end (also much more realistic than an infinite drip irrigation tube), they immediately come up with the conclusion that the water wave will rebound from the sealed end, leading to an apparently shallower decay along the tube.

Visualizing current sources, sinks, and synapses. There are several further examples beyond the two detailed above. Here I present just one example that is less tractable analytically but greatly contributes to the discussion in the class. The drip irrigation system (even without the drip) is a good example for the general phenomenon of current sources and sinks and, derived from this, the attenuation and summation of synaptic input. I start with a simple system of a large water container (soma) connected to one thin long drip tube (dendrite). Adding

water to the container (injecting current to the soma) increases the level of water in the container, while some of the water escapes to the drip tube. The tube (dendrite) thus acts as a current sink. Now I, mentally, add another long thin tube to the main container. Adding water to the main container in this system will result in more water escaping to the tubes. The conclusion is the more dendrites there are, the more the current sinks. The same thought experiment is repeated and the diameter of the tube is increased. This leads to the conclusion that a larger diameter gives a larger current sink. When we move the water tap to a location on the thin drip tube and open it for a short time, there is a local increase in water pressure that decays along the tube due to water loss via the emitters. If the initial current was large enough, some water will arrive at the main container, slightly increasing its water level. In one blow, we have simulated a synapse, explained the function of the neurites as a current sink, and demonstrated the impact of an excitatory synapse on the somatic membrane potential. Now we can add many more water taps to the drip tube and inject pulses of water through all of them. The more water taps, the higher the level of water in the main tank. We have used irrigation to explain synaptic integration! To keep the discussion realistic, we may add several water emitters to the main container so that the water level will slowly decrease back to zero. Unfortunately, the drip irrigation system cannot explain inhibitory synaptic integration.

Conclusions. Teaching a course with a substantial computational component to life science students is a precarious endeavor. We who lecture are well versed in the analytic aspects of the subjects, while those who listen struggle to follow mathematical scripts. The case of the passive cable theory presented here is representative but far from unique. Several contemporary textbooks shy away from the analytic, satisfying themselves with a soft descriptive approach. This approach widens the rift between life science students and neural computation. Over the years, I have presented the equations in class, while developing a set of mundane examples conveying the essence of the theory. Providing the students with a recognizable mental image to associate with the subject helps them understand and remember the computational principles being discussed.

DISCLOSURES

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AUTHOR CONTRIBUTIONS

A.K. conceived and designed research; prepared figures; drafted manuscript; edited and revised manuscript; approved final version of manuscript.

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