

## ARTICLE

# MetaNeuron: A Free Neuron Simulation Program for Teaching Cellular Neurophysiology

**Mark H. Newman and Eric A. Newman**

*Department of Neuroscience, University of Minnesota, Minneapolis, MN 55455.*

MetaNeuron, a neuron simulation program, is an effective interactive tool for teaching cellular neurophysiology. The computer program simulates a wide range of neuronal behavior in its six lessons: i) Resting Membrane Potential, ii) Membrane Time Constant, iii) Membrane Length Constant, iv) Axon Action Potential, v) Axon Voltage Clamp, and vi) Synaptic Potential. The program is designed foremost as a platform for conducting neurophysiology experiments *in silico*. Neuronal parameters are easily modified and a virtual stimulator injects single or double current pulses into the neuron. Phenomena such as temporal summation of synaptic potentials, passive spread of a synaptic potential from the dendrite to the soma, the refractory period, families of

voltage-clamp traces, and the reversal potential of synaptic responses, are easily illustrated in MetaNeuron. Responses are displayed graphically and can be measured with a cursor. Families of traces can be generated and viewed in rotatable 3D plots. Mac and Windows versions of the program can be downloaded, free of charge, onto individual student computers from the website [www.MetaNeuron.org](http://www.MetaNeuron.org). A manual containing operating instructions, a description of the lessons, and exercises conducted on MetaNeuron, can also be downloaded for free.

*Key words: Neurophysiology; neuron; simulation; action potential; voltage-clamp; teaching neuroscience*

The principles of cellular neurophysiology are generally taught didactically in neuroscience courses. Recent studies have established, however, that active learning, where students conduct experiments on computer models of neurons, is an effective method for teaching core neurophysiology principles (Stuart, 2009; Grisham et al., 2008; de Jong et al., 2013). Numerous computer simulations of neurons are currently available on the internet. Some of these illustrate specific neurophysiology principles, such as the generation of the resting membrane potential (Branch and Wright, 2013) or action potential (Bezanilla, 2012). These programs are useful but are not designed to illustrate a wide range of neuronal behavior. One program, "Neurons in Action" (Moore and Stuart, 2013; Stuart, 2009), is a comprehensive model of the neuron. This is an excellent program but is not easily accessible to the beginning neuroscience student as it has a complex interface, must be installed on students' computers via a DVD, and must be purchased for a significant fee.

We have developed a computer model of the neuron that circumvents these limitations (Leslie, 2004). The program, MetaNeuron, simulates a wide range of neuronal behavior and can be downloaded free of charge from the MetaNeuron website, [www.MetaNeuron.org](http://www.MetaNeuron.org). MetaNeuron is designed to be used by students who have no prior experience with computer simulations. The program is designed foremost as a platform for conducting neurophysiology experiments *in silico*. Neuronal parameters such as  $\text{Na}^+$  and  $\text{K}^+$  concentrations, equilibrium potentials and conductances are logically laid out and easily modified. A virtual stimulator injects single or double current pulses into the neuron. Responses are displayed graphically and can be measured with a cursor. Families of traces can be easily generated and viewed in rotatable 3D plots.

MetaNeuron is used in many college and university

courses in the United States and elsewhere. At the University of Minnesota, we utilize MetaNeuron in undergraduate, graduate and medical school courses. Typically, MetaNeuron is used after students have been introduced to the core principles of neurophysiology in didactic lectures. We use MetaNeuron in interactive classes where the instructor conducts experiments on the model neuron and asks students to interpret the results. These exercises invariably lead to additional questions about the behavior of neurons. Students often suggest additional experiments to conduct on the model, leading to further insights. We supplement these interactive classes with homework assignments where students conduct experiments on MetaNeuron on their own. MetaNeuron is also used in a laboratory setting where individual students or groups conduct experiments, collect data, and analyze and interpret the results.

MetaNeuron runs as a stand-alone program on individual computers. It is downloaded as a single executable file from the MetaNeuron website. Mac and Windows versions of the program are available. The MetaNeuron manual, containing a description of the program and student exercises, can also be downloaded from the website. MetaNeuron is free and can be used without restriction.

MetaNeuron consists of six lessons illustrating different aspects of neuronal behavior. We will first describe these six lessons and detail the underlying properties of the neuron represented in each lesson. We will then describe experiments that can be conducted on MetaNeuron which can be used in the classroom, in labs, or for homework assignments. Finally, we will evaluate MetaNeuron as an educational resource.

## DESCRIPTION OF METANEURON

Controls for changing the values of parameters appear in the top portion of the MetaNeuron screen and a graph of

select parameters appears on the bottom (Figure 1). MetaNeuron lessons are selected from the “Lesson” pull-down menu or from function keys. The six lessons run independently of each other. If the parameters in one lesson are changed, the changes will not affect the operation of the other lessons.

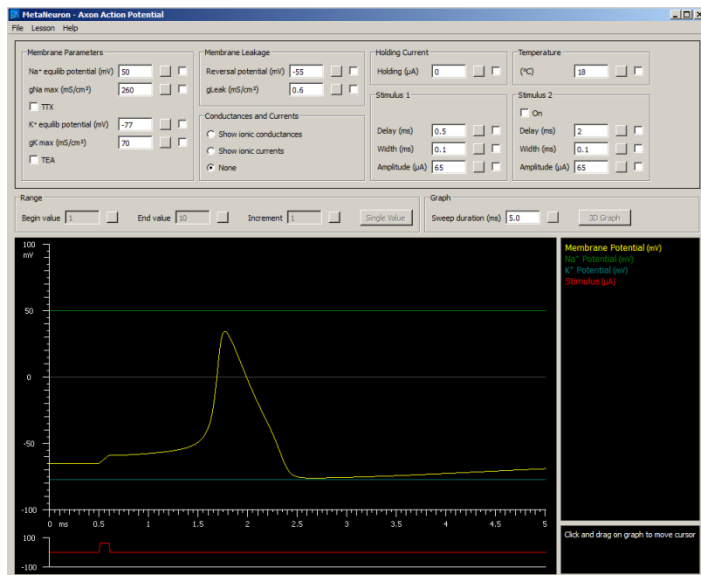


Figure 1. The MetaNeuron screen, open to Lesson 4. Injected current (red trace) depolarizes the neuron membrane potential (yellow trace), triggering an action potential. The blue and green traces show the  $K^+$  and  $Na^+$  equilibrium potentials, respectively.

There is no “Start” button to begin an experiment in MetaNeuron. Rather, stimuli are continuously applied to the model neuron and neuronal responses are continuously displayed and updated on the graph. Experiments are run by changing neuronal parameters. Parameter values are changed by clicking on a parameter and typing a new value or by clicking on the button to the right of a parameter value and dragging the mouse (Fig. 2).

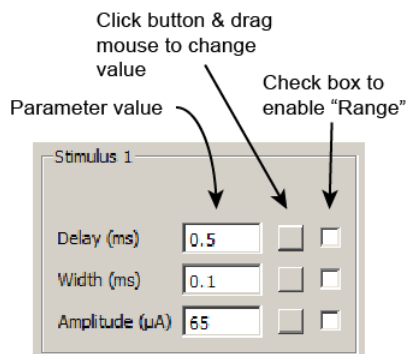


Figure 2. Controlling parameter values. A parameter value can be changed by typing in a new value in the parameter value box or by clicking on the button to the right of the parameter value box and dragging the mouse. Moving the mouse up or to the right increases the value in increments of 1. Moving the mouse down or to the left decreases the value by 1. If the “Shift” or “Ctrl” keys are depressed while moving the mouse, the parameter values change in increments of 10 or 0.1, respectively. All parameters can be reset to their default values by selecting “Restore All to Default” (Ctrl+D) in the “File” pull-down menu.

A family of traces can be generated in a graph by selecting the check box to the right of a parameter value box, enabling the “Range” function (Figure 2). A family of traces can be displayed in three dimensions by clicking the “3D Graph” button above the graph. The 3D display can be rotated by clicking on the window and dragging the mouse. The X and Y values of any point on a graph can be determined by moving the mouse over the graph and clicking. Cursor values are displayed to the right of the graph. Complete operating instructions are opened from the “Help” pull-down menu.

## METANEURON LESSONS

Different aspects of neuronal behavior are highlighted in the six lessons presented in MetaNeuron. The lessons do not attempt to model the full complexity of neuronal behavior. The simulations simplify neuronal properties, highlighting the basic principles of neuronal function.

**Lesson 1 - Resting Membrane Potential.** Lesson 1 illustrates how  $K^+$  and  $Na^+$  channels contribute to the generation of the resting membrane potential. The neuron in this lesson is modeled by passive conductances to  $K^+$  and  $Na^+$ . These conductances are voltage-independent and the neuron does not generate action potentials. The intracellular and extracellular concentrations of  $K^+$  and  $Na^+$  can be varied. The program calculates the electrochemical equilibrium potential for each ion from the Nernst equation. The resting membrane potential of the neuron is determined by the membrane permeability to  $K^+$  and  $Na^+$ , calculated from the Goldman-Hodgkin-Katz equation.

**Lesson 2 - Membrane Time Constant.** Lesson 2 illustrates the effect of the membrane time constant,  $\tau$ , on the time course of electrical responses in neurons. The neuron in this lesson is modeled by a passive membrane resistance,  $R_m$ , a membrane capacitance,  $C_m$ , and a current source. The membrane capacitance equals  $1 \mu F/cm^2$ , or simply  $1 \mu F$ , since MetaNeuron represents  $1 cm^2$  of membrane. The value of the membrane resistance as well as the time course and amplitude of the current source can be varied. The membrane resistance and capacitance together determine the time constant of the membrane, as described by the equation  $\tau = R_m C_m$ . The neuron in this lesson does not generate action potentials.

**Lesson 3 - Membrane Length Constant.** Lesson 3 illustrates the effect of the length constant,  $\lambda$ , on the passive spread of voltage down a neuronal process. For simplicity, the process is assumed to be a dendrite, although the lesson can also represent an axon. The lesson models the dendrite as a cylindrical process of uniform diameter and infinite length having a passive leak conductance. The dendrite has a membrane capacitance of  $1 \mu F/cm^2$ . Values of the membrane resistance ( $R_m$ ), the internal (cytoplasmic) resistivity ( $R_i$ ), and the diameter ( $d$ ) of the dendrite can be varied. Stimuli are applied to the dendrite at  $X = 0$ . Responses are calculated from the cable equations. The stimulus is scaled to  $R_m$ ,  $R_i$ , and  $d$ , such that the steady-state depolarization at  $X = 0$  produced by a stimulus does not change when these parameters are varied. Responses can be displayed in two modes: “Potential vs. Distance” and “Potential vs. Time.” Potential

vs. Distance vs. Time relations can be viewed in 3D plots.

**Lesson 4 - Axon Action Potential.** Lesson 4 illustrates how voltage- and time-dependent  $\text{Na}^+$  and  $\text{K}^+$  conductances generate the action potential. The MetaNeuron model in this lesson is based on the Hodgkin-Huxley equations. The  $\text{Na}^+$  conductance in the model represents fast, tetrodotoxin-sensitive  $\text{Na}^+$  channels. The  $\text{K}^+$  conductance represents delayed rectifier  $\text{K}^+$  channels.

Several parameters controlling  $\text{Na}^+$ ,  $\text{K}^+$ , and leak conductances can be adjusted:

- The  $\text{Na}^+$ ,  $\text{K}^+$ , and leak equilibrium potentials. Modifying these values change the driving force for ion flux through the  $\text{Na}^+$ ,  $\text{K}^+$ , and leak channels.
- The  $\text{Na}^+$ ,  $\text{K}^+$ , and leak maximal conductances. These parameters represent the number of  $\text{Na}^+$ ,  $\text{K}^+$ , and leak channels in the membrane.
- The presence of TTX (tetrodotoxin) and TEA (tetraethylammonium). Selecting TTX blocks the  $\text{Na}^+$  conductance. Selecting TEA blocks the  $\text{K}^+$  conductance but not the leak conductance.
- Temperature. Raising the temperature reduces the time constants controlling  $\text{Na}^+$  conductance activation and inactivation and  $\text{K}^+$  conductance activation, resulting in faster action potentials.

Activation of the neuron is controlled by several stimuli:

- Stimulus 1. The delay, width and amplitude of this current pulse can be adjusted.
- Stimulus 2. A second current pulse is added when the "Stimulus 2 On" box is selected.
- Holding Current. This continuous current source can be used alone or together with the current pulses.

$\text{Na}^+$  and  $\text{K}^+$  conductances or currents are displayed along with the membrane potential when the appropriate boxes are selected in the "Conductances and Currents" window.

**Lesson 5 - Axon Voltage Clamp.** Lesson 5 uses the voltage-clamp technique to illustrate the voltage- and time-dependent properties of the  $\text{Na}^+$  channels and delayed rectifier  $\text{K}^+$  channels that generate the action potential. Lesson 5 uses the same Hodgkin-Huxley model of the axon that is used to generate action potentials in Lesson 4. The only differences in Lesson 5 are that the axon is now voltage-clamped and the stimuli used are command voltages rather than currents. The "Holding Potential" parameter determines the voltage of the axon at the beginning of the trial. The "Stimulus 1" and "Stimulus 2" amplitudes determine the voltage to which the membrane is stepped during the two pulses. Note that these stimulus amplitudes represent absolute voltages, not relative voltages added onto the Holding Potential.

**Lesson 6 - Synaptic Potential and Current.** Lesson 6 illustrates the synaptic voltages and currents generated by fast ionotropic synapses. The neuron in Lesson 6 is modeled by a leak conductance and by the opening of an ionotropic receptor conductance, simulating a synaptic response. A fast excitatory synapse is modeled by a receptor that is permeable to both  $\text{Na}^+$  and  $\text{K}^+$ . The relative permeabilities of the two ions determine the reversal potential of the synapse. A fast inhibitory synapse is modeled by a  $\text{Cl}^-$ -permeable receptor. The neuron in

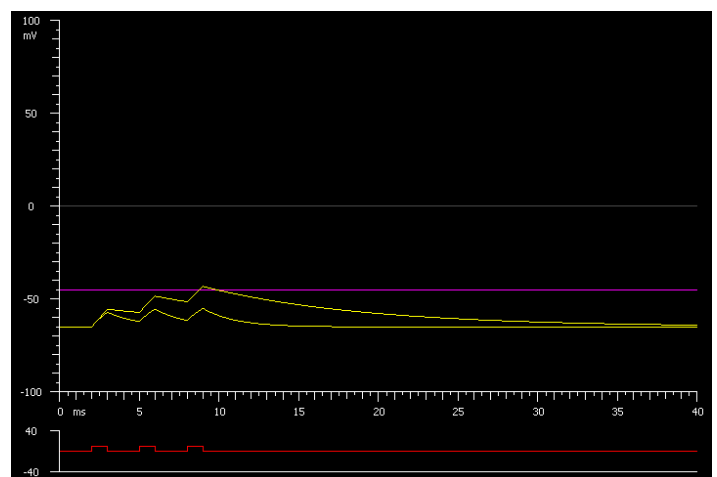
lesson 6 does not generate action potentials. The synaptic conductance is modeled with rising and falling time constants of 0.1 and 1.0 ms.

## STUDENT EXERCISES

Fundamental principles of cellular neurophysiology can be taught through experiments performed on MetaNeuron. The MetaNeuron manual describes many of these experiments. Some of them are discussed here.

**Lesson 1.** The generation of the resting membrane potential depends on the  $\text{K}^+$  and  $\text{Na}^+$  gradients across the neuron membrane and the permeability of the membrane to these ions. (MetaNeuron ignores the contribution of other ions to the resting membrane potential.) Lesson 1 illustrates the effect of ion concentrations and membrane permeabilities on the membrane potential. By varying the parameters of the virtual neuron, students learn how the intracellular and extracellular  $\text{K}^+$  and  $\text{Na}^+$  concentrations determine the  $\text{K}^+$  and  $\text{Na}^+$  electrochemical equilibrium potentials (calculated from the Nernst equation) and how the  $\text{K}^+$  and  $\text{Na}^+$  membrane permeabilities affect the membrane potential (calculated from the Goldman-Hodgkin-Katz equation).

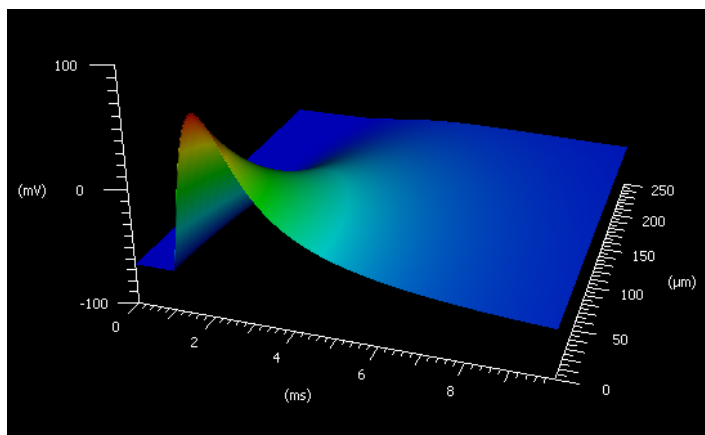
**Lesson 2.** The membrane time constant is an important neurophysiology concept. The time constant affects many neuron phenomena, including the time course of neuron responses, the summation of synaptic potentials, and the propagation of action potentials in axons. In Lesson 2, students learn how the membrane resistance,  $R_m$ , affects the time constant by varying  $R_m$  and noting changes in the rise and fall of neuronal responses evoked by injection of a square wave of current. Using the cursor function of MetaNeuron to measure the membrane potential at different times during the rising and falling phases of the response, students can empirically determine the time constant and compare it to the theoretical value,  $R_m C_m$ .



**Figure 3.** Temporal summation of synaptic potentials. The three current pulses (red trace) simulate three synaptic inputs. With a long  $\tau$  (10  $\text{k}\Omega$  membrane resistance), the synaptic potentials summate and reach the threshold for firing an action potential (purple line). With a short  $\tau$  (2  $\text{k}\Omega$  membrane resistance), the synaptic potentials do not summate and do not reach threshold.

MetaNeuron can be used to illustrate the effect of the time constant,  $\tau$ , on temporal summation of excitatory postsynaptic potentials (EPSPs). EPSPs are simulated in Lesson 2 by trains of 1 ms current pulses injected into the virtual cell. A single current pulse produces a rapid depolarization followed by a decay back to the resting membrane potential with a time constant determined by the membrane resistance,  $R_m$ . Temporal summation is simulated by stimulating the neuron with a sequence of current pulses at 2 ms intervals (Figure 3). The latter EPSPs add on top of earlier ones. The degree to which the EPSPs summate is determined by  $\tau$ . When  $\tau$  is short, little summation occurs and the combined EPSP does not reach threshold (indicated by the purple line in Figure 3). When  $\tau$  is longer, temporal summation is greater and threshold is exceeded.

**Lesson 3.** Passive conduction of responses through dendrites and axons is an important principle of cellular neurophysiology. Conduction is dependent on the membrane length constant and time constant. MetaNeuron simulates passive conduction by solving the cable equations. The familiar steady-state exponential decay of potential with distance along a process can be illustrated in the "Potential vs Distance" mode of Lesson 3 when a long lasting current pulse (eg 50 ms) is applied to the virtual neuron at  $X=0$ .

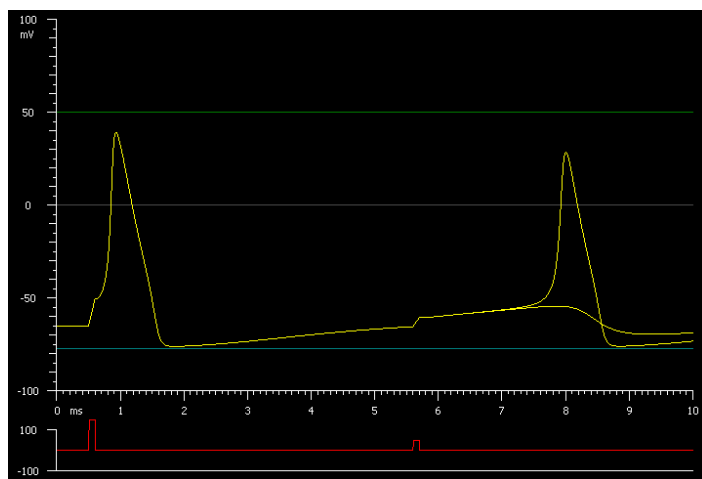


*Figure 4.* 3D plot of passive conduction of a synaptic potential. The amplitude of an EPSP (mV axis) is plotted as a function of time (ms axis) and distance from the site of generation ( $\mu\text{m}$  axis). Note that the synaptic potential is attenuated and slowed as it is conducted down the dendrite. The amplitude of the synaptic potential has been increased for illustrative purposes. This and other 3D MetaNeuron plots can be rotated by clicking on the graph and dragging the mouse.

The passive conduction of a synaptic potential down the length of a dendrite is a more difficult concept for students to grasp as it is influenced by both the membrane length constant and time constant. Passive conduction of synaptic potentials can also be simulated in Lesson 3. An EPSP is generated with a current pulse having a 0.1 ms rise time and a 1 ms decay. The passive spread of the resulting depolarization is viewed in the "Potential vs Time" mode. The third dimension, distance along the dendrite, is viewed when the 3D Graph option of MetaNeuron is selected. A range of distances is displayed by selecting

the "Range" function for "Position." The resulting 3D graph (Figure 4) illustrates that the amplitude of the EPSP is attenuated and the time course is slowed as the synaptic potential is conducted down the dendrite towards the soma.

**Lesson 4.** The action potential threshold is one of the more difficult concepts for students to grasp. Threshold is not a fixed membrane potential value but rather is influenced by many parameters, including the number of  $\text{Na}^+$  and  $\text{K}^+$  channels in the membrane, the previous history of the neuron, and temperature. Many experiments can be performed on the virtual neuron in Lesson 4 of MetaNeuron to help students gain an intuitive understanding of threshold. In one exercise, students vary the number of  $\text{Na}^+$  and  $\text{K}^+$  channels ( $g_{\text{Na}_{\text{max}}}$  and  $g_{\text{K}_{\text{max}}}$ ) and note its effect on threshold. This helps students to understand that threshold is determined by the balance between  $\text{Na}^+$  influx and  $\text{K}^+$  efflux. In a second exercise, students ponder the seemingly paradoxical phenomenon of anodal break excitation. When a neuron is hyperpolarized by a negative current pulse, an action potential is evoked when the current is turned off. Students simulate the phenomenon in Lesson 4 and are asked why a hyperpolarizing pulse can evoke an action potential. Students are divided into small groups to talk this over and at least one group usually comes up with the correct answer: hyperpolarization removes inactivation from the small number of  $\text{Na}^+$  channels that remain inactivated at the resting membrane potential and hyperpolarization closes the few delayed rectifier  $\text{K}^+$  channels that are open at rest. This lowers threshold to below the normal resting membrane potential.



*Figure 5.* The refractory period. The time course of the refractory period following an action potential can be determined using a two-stimulus protocol. The first stimulus is well above threshold and reliably evokes an action potential. The second stimulus, at a delay following the first, is adjusted so that it just triggers an action potential. The amplitude of the second stimulus is a measure of the threshold at that delay.

A classic experiment which illustrates that threshold depends on the previous history of a neuron is to measure the change in threshold during the refractory period which follows an action potential. This is easily accomplished in



Lesson 4, which contains a virtual stimulator that delivers pairs of current pulses. The amplitude of the first stimulus is set to be well above threshold to ensure reliable activation of an action potential (Figure 5). The amplitude of the second stimulus is adjusted so that it is at threshold (a slightly larger stimulus will reliably evoke an action potential while a slightly smaller stimulus will fail to evoke an action potential; Figure 5). The student systematically varies the delay between the first and second stimuli and determines the threshold stimulus amplitude at each delay. A graph of the refractory period is obtained by plotting the threshold amplitude of the second stimulus as a function of the delay.

There are many Lesson 4 exercises that illustrate the effect of pathology on neuronal behavior. These are particularly engaging to students, who appreciate the clinical relevance of the experiments. One exercise addresses the effect of temperature on multiple sclerosis patients. In MS, demyelination leads to block of action potential conduction in axons. Conduction block is alleviated in MS patients by the lowering of core body temperature (Guthrie and Nelson, 1995). Students observe that lowering temperature in MetaNeuron results in a decrease in action potential threshold, thus explaining the temperature effect in MS (Schauf and Davis, 1974).

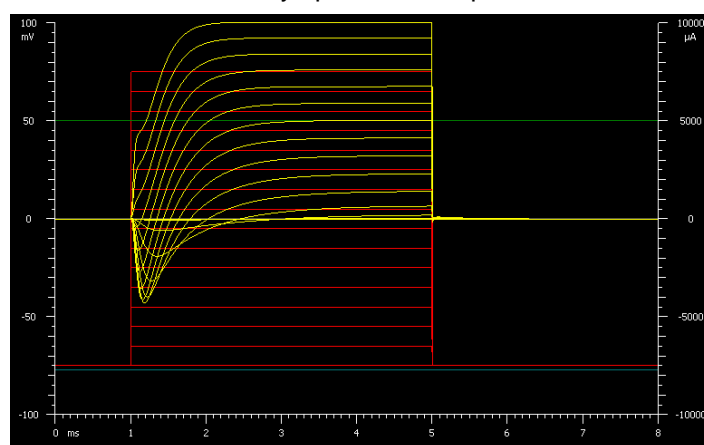
A second pathology exercise illustrates the phenomenon of spreading depression, which is responsible for generating the visual auras and scotomas that are often associated with migraine headaches (Lauritzen, 1994; Hadjikhani et al., 2001). In classes of 50 or more, there is a good chance that at least one student will have experienced migraines with auras. It is instructive to have the student describe his or her symptoms before beginning the exercise. The migraine aura arises from spontaneous activity in the visual cortex due to neuronal depolarization generated by increases in extracellular  $K^+$  (among other factors). The scotoma is caused by even larger extracellular  $K^+$  increases, leading to depolarization block and the silencing of neurons. These phenomena can be reproduced in Lesson 4 by raising  $E_K$ , which mimics an increase in extracellular  $K^+$ . As  $E_K$  is raised and the resting membrane potential is depolarized, the following sequence of events is observed: i) spontaneous spikes are generated, ii) the spike frequency increases and spike amplitude declines, iii) spiking is abolished. Students are asked to explain this sequence of neuronal events.

**Lesson 5.** The voltage-clamp experiments of Hodgkin and Huxley (Hodgkin and Huxley, 1952) were crucial in elucidating how action potentials are generated. These experiments are often taught in introductory neuroscience courses with mixed success. We have found that conducting voltage-clamp experiments on the virtual neuron in Lesson 5 helps students understand the rationale of the voltage-clamp technique as well as appreciate the voltage- and time-dependent properties of  $Na^+$  and  $K^+$  channels.

In Lesson 5, stimuli control the voltage at which the axon membrane potential is held. The resulting membrane currents are plotted on the MetaNeuron graph. Students measure  $Na^+$  and  $K^+$  channel ionic currents, graph current

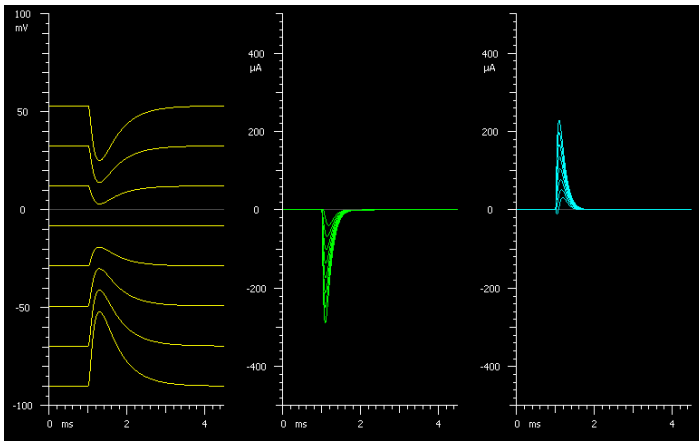
vs. voltage relations, and calculate conductance vs. voltage relations from the cord conductance equation. Students can also plot the time course of recovery of  $Na^+$  channels from inactivation using a two-pulse stimulus protocol.

A family of voltage-clamp traces is easily created in Lesson 5 by selecting the "Range" function for "Stimulus 1 Amplitude." The resulting graph (Figure 6) shows the transient inward (negative)  $Na^+$  current and the sustained outward (positive)  $K^+$  current at different holding potentials. The voltage-dependence of  $Na^+$  and  $K^+$  channel kinetics is clearly illustrated in this family of traces. The temperature-dependence of channel kinetics can be illustrated as well. The slowing of  $K^+$  channel activation and  $Na^+$  channel inactivation with cooling results in a reduced action potential threshold. These factors account for the cooling-induced alleviation of symptoms in MS patients.



**Figure 6.** Family of voltage-clamp traces showing inward (negative)  $Na^+$  currents and outward (positive)  $K^+$  currents. The membrane potential was raised from a holding potential of -75 mV to more positive potentials (-65 mV to +75 mV in 10 mV increments). Membrane currents are shown in the yellow traces and the command voltages in the red traces.

**Lesson 6.** The reversal potential of synaptic responses is a particularly difficult concept for students to understand. Lesson 6 illustrates the reversal potential of excitatory and inhibitory synaptic potentials and displays the currents that generate the potentials. In experiments on real neurons, the reversal potential can be measured under current-clamp conditions, where neuron voltages are measured, or under voltage-clamp, where currents are measured. MetaNeuron illustrates the reversal potential under current-clamp conditions, as this is conceptually simpler for students to understand. For an excitatory synapse, the membrane potential and  $Na^+$  and  $K^+$  currents that generate the potential are displayed in separate panels (Figure 7). The stimulus is a current that generates an EPSP. A family of EPSPs generated at different membrane potentials is created by selecting the "Range" function for "Holding current." The resulting graph (Figure 7) shows how the EPSP changes amplitude and polarity as the membrane potential is varied. The reversal potential of the EPSP is evident. The dependence of the reversal potential on receptor permeability to  $Na^+$  and  $K^+$  is illustrated by changing the permeabilities.



**Figure 7.** Reversal potential of an excitatory synaptic response. A family of membrane potential traces (yellow) is shown as the membrane potential is varied by injecting a holding current into the cell. The synaptic potential changes from a depolarizing to a hyperpolarizing response as the membrane potential is raised. The membrane potential at which the synaptic response reverses polarity is known as the reversal potential and is determined by the relative permeability of the synaptic receptor to  $\text{Na}^+$  and  $\text{K}^+$ . The  $\text{Na}^+$  and  $\text{K}^+$  currents flowing through the receptor are shown in the green and blue traces, respectively.

## FEEDBACK ON METANEURON

A formal assessment of the effectiveness of the MetaNeuron program as a teaching tool has yet to be conducted. However, anecdotal evidence suggests that the program aids students in understanding neuroscience concepts. Students in a medical school neuroscience course that one of us (EAN) teaches (INMD 6813, University of Minnesota Medical School) were asked to rank the usefulness of the MetaNeuron exercises they were assigned for homework as a tool for learning neurophysiology concepts. Student responses to this question (Table 1) demonstrate that most students rated the MetaNeuron exercises as exceptional, very useful, or satisfactory.

Response	2011	2012
Exceptional	11%	8%
Very useful	47%	53%
Satisfactory	38%	33%
Substandard	4%	3%
Very poor	0%	1%

**Table 1.** Responses of students in a 2011 and 2012 medical school neuroscience course to the question, "Please rank the usefulness of this [MetaNeuron] exercise." There were 214 responses for both years.

We have also received comments from instructors who have used MetaNeuron in their neuroscience courses. Dr. Claude Rouillard of the Faculty of Medicine, Laval University, Quebec City, Canada, writes:

The MetaNeuron program has been very useful for teaching neuroscience fundamentals to undergraduate students enrolled in biomedical sciences. We used this interactive simulation program for classroom demonstrations and modified student exercises. The software is easy to install

and use and well adapted for beginning neuroscience students.

Dr. John Williams of the Oregon Health & Science University writes:

I organize the core course in Cellular Neurophysiology for the Neuroscience Graduate Program and have used MetaNeuron for the past 5 years. This program has become a key component of the early part of the course. It gives the students a chance to examine firsthand how the Hodgkin-Huxley model of neuronal function actually works. It is the best way for the students to apply what they hear in lecture to a realistic model of function. The program is completely intuitive so that little or no introduction is required for students to get started.

The way that I have used the program is by preparing a list of stepwise problems, asking for explanations for the results that follow and then posing questions that can be approached through manipulation of various aspects of the program such as voltage step protocols, ion concentrations, and the role of leak conductance. Finally, I write a series of questions and have the students present the answers in class using the program. I have gotten very good feedback using this approach.

We plan to conduct a formal assessment of MetaNeuron as a teaching tool in the future. We encourage instructors to conduct their own assessments of MetaNeuron and to communicate their results to us.

## DISCUSSION

We believe MetaNeuron to be an effective tool for teaching basic neurophysiology principles. Certain principles are difficult for students to understand when explained in a lecture, but become intuitive when students conduct their own experiments on MetaNeuron. Students can learn such concepts as temporal summation of synaptic potentials, action potential threshold, the voltage-clamp technique, and the reversal potential by conducting experiments on the MetaNeuron virtual neuron. We typically have students work in groups of four to six when performing experiments in class or for homework. We find that this enhances student understanding, as students are accomplished at explaining experimental protocols and analysis procedures and discussing experimental conclusions with each other.

In our experience, students retain knowledge they have gained from MetaNeuron because they have actively participated in instructional exercises. One of us (EAN) recently had the sobering experience of learning that students who took a course he taught many years ago did not remember his name but instantly remembered his classes when told that the classes were the ones that used MetaNeuron. They had remembered him as the MetaNeuron man!

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Address correspondence to: Eric A. Newman, Ph.D., Department of Neuroscience, University of Minnesota, 321 Church St SE, Minneapolis, MN 55455. Email: [ean@umn.edu](mailto:ean@umn.edu)