ARTICLE

NeuroLab: A Set of Graphical Computer Simulations to Support Neuroscience Instruction at the High School and Undergraduate Level

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Young students struggle with concepts that involve the parallel activity of large numbers of similar entities, precisely the kind of concepts that abound in neuroscience. While a direct experience to laboratory work cannot be replaced, such activities include a steep learning curve and may be impractical in certain course settings. This article describes a set of computer simulations of a number of neural processes using NetLogo (Wilensky, 1999), a software environment for the design and implementation of multi-agent simulations that has an intuitive graphical interface and minimal learning curve. *NeuroLab* is a group of graphical simulations that portray ions, molecules, synapses or cells as individual recognizable agents with particular behaviors, depending on the level at which the particular process is simulated. On a typical assignment, students run the simulation a few times manipulating specific variables by means of buttons, switches and sliders and observe the results of their manipulations on the main window. Many simulations include one or more plots that help visualize statistical data in real time and allow for the testing of experimental hypotheses. Students may repeat the simulation as many times as they wish and collect data or answer questions based on their observations. Assignments may take just a few minutes to perform, but could conceivably be part of more involved activities as designed by the instructor.

Key words: graphical computer simulations; virtual experiments; neuroscience; freeware

INTRODUCTION

It is not uncommon to find that young students struggle with concepts involving the parallel activity of large numbers of similar entities that exhibit self-organization and dynamic behavior based on local rules. The tendency to seek central control mechanisms to explain these behaviors, aptly called the Centralized Mindset, may underlie some of the reticence to the consideration of non-centralized scientific explanations by people who intuitively expect complexity to be the result of purposeful design (Resnick, 1994, 1996).

Complexity and self-organization concepts abound in scientific explanations in the expanding biological and social fields. Examples from neuroscience include concepts that are critical for the comprehension of processes such as development, neural communication, perception and motor control, in which large numbers of relatively simple agents (cells, channels, synapses) self-organize to build a brain, allow an organism to learn through association, provide a unified perception of the world and coordinate motor output.

As neuroscience topics find their way into undergraduate and high school curricula, it becomes critical to provide instructors with the necessary tools to convey some of the complexity of neural processes without the risk of alienating the students through explanations at levels of abstraction for which they are not yet prepared.

Common solutions to this problem include the use of digital media that allow the demonstration of dynamic events through videotaped or animated visuals that can be commented on by the instructor as they unfold (Korey, 2009).

While such resources can be helpful in the classroom, they are limited by the inability to provide the students with a realistic view of the variability of biological processes.

Though a direct experience with physiological preparations through laboratory exercises would be the ideal solution to this problem, such activities are rarely feasible at small educational institutions during the allotted lecture time.

Moreover, laboratory work requires the development of advanced skills on the part of the experimenters, not only in the sense of technical abilities, but also conceptually. Most current neuroscientific research is carried out through the manipulation of a small number of structures (channels, cells, nuclei) leaving the brunt of the conceptualization to a process of inference, which requires a level of scientific sophistication unavailable to young students.

Digital Visualization
Present day neuroscience employs computer simulations of population and network processes both as a means to test theoretical postulates and as a source for experimental hypotheses (De Schutter, 2003).

Computer simulations have also been used successfully in undergraduate settings as teaching tools (Av-Ron et al., 2006; Molitor et al., 2006, Stuart, 2009; Lott et al., 2009). A number of these (e.g., *Neuron* at neuron.yale.edu) simulate electrophysiological recordings, allowing for the manipulation of both stimulation parameters and cellular characteristics and for the visualization of results as two-dimensional graphs. While such software packages are very flexible and favor student experimentation in lab settings, their use requires a certain level of mathematical sophistication and presents

a steep learning curve.

On the opposite side of the spectrum are the common textbook animations, which are basically animated movies with a set timeline and which provide little opportunity for interaction. In terms of experimentation, such media are generally unable to present interesting questions or allow for hypothesis testing.

The simulations in **NeuroLab** offer students an intermediate experience by bringing together the visual interface typical of animations as well as some of the interactivity and plotting options of math-based simulations.

While graphical simulations at a similar level to those of NeuroLab are available (viz. *PhET* at phet.colorado.edu), the limitations of the programming language constrain the number of independent elements that can be controlled in tandem as can be readily observed in the *Neuron* simulation. On the other hand, NetLogo was designed from the bottom-up to allow for multi-agent programming (see Box 1).

When working with the simulations, students can put forward one or more hypotheses for the phenomena they observe and then proceed to test them by means of user-friendly controls. Moreover, students can repeat the process any number of times, always obtaining slightly different results due to the randomization of variables by the program.

Box 1

NetLogo (Wilensky, 1999) is a software environment for the design and implementation of multi-agent simulations that has an intuitive graphical interface and a minimal learning curve. A NetLogo installer can be freely downloaded and can be made available to students (http://ccl.northwestern.edu/netlogo/).

NetLogo is a powerful multi-agent simulation package that has a number of in-built primitives that permit the interaction between the agents as well as with their background. Good examples of this are the developmental simulations (Axon Guidance and Cortical Development) in which agents (growth cones and neuroblasts, respectively) track gradients of specific substances present in the substrate and released by other elements of the simulation. Currently, NetLogo is in version 5.0.

Neurolab
This article describes a set of graphical computer simulations of a number of neural processes developed by the author in NetLogo (Box 1). The simulations in NeuroLab portray ions, molecules, synapses or cells as individually recognizable agents with particular behaviors based on local rules, depending on the level at which the particular process is simulated. For example, agents representing developing cortical cells respond to the levels of chemical factors present in the substrate, which are, in turn, released by other agents and diffused through the substrate as a function of time.

The article also describes the use of the simulations as part of an undergraduate level introductory course in neuroscience and provides examples of the assignments the students were asked to complete to reinforce the topics studied in class.

The typical timeline
The author has used NeuroLab as part of his 200-level *Introduction to Neuroscience* course for a number of years. Since most of the simulations involve basic neuronal processes, they are typically assigned during the first third of the course. The assignments are given as 'extra-credit' and optional.

On a typical assignment, students run the simulation a few times, manipulating specific variables by means of buttons, switches and sliders, and observe the results of their manipulations on the main window (or "World"). Each assignment takes about 20 minutes to conduct guided by a set of questions provided by the instructor.

Many simulations include one or more plots that help visualize the data in real time. Students may repeat the simulation as many times as they wish and collect data or answer questions based on their observations. Assignments may take just a few minutes to perform, but could conceivably be part of more involved activities as designed by the instructor.

A short 'Working with NetLogo' document is provided to the students early in the course to let them know how they should prepare and turn in their work for grading. Briefly, as the students solve their assignments using NeuroLab, they collect image snippets of their work using the **Print Screen** option on their computers. These images are then pasted onto a PowerPoint presentation and cropped and annotated using text boxes and arrows.

Examples
Though the best way to observe what each one of the simulations in NeuroLab does is to work with them (see below for links to my website where you can test the simulations), the following two examples provide some information regarding their usefulness as educational tools (see supplemental materials for full descriptions of the assignments).

Temporal Integration
The Temporal Integration assignment (see Figure 1) is designed to facilitate the understanding of input integration by neurons. The typical undergraduate student has had little experience with dynamic signals and is ill at ease with new vocabulary such as postsynaptic potentials, excitatory/inhibitory, tonic/phasic, etc. This simulation helps them create their own circuit, choosing number of inputs, whether they are excitatory or inhibitory and their relative strength. It also allows them to add one or two tonic inputs at different cycles. Once they have selected their parameters, pressing the 'Go' button will start the simulation and produce a baseline signal for the target (cyan) neuron. Pressing the corresponding 'fire' buttons for each input neuron will cause an easily recognizable deflection on the target neuron's potential. The appropriate
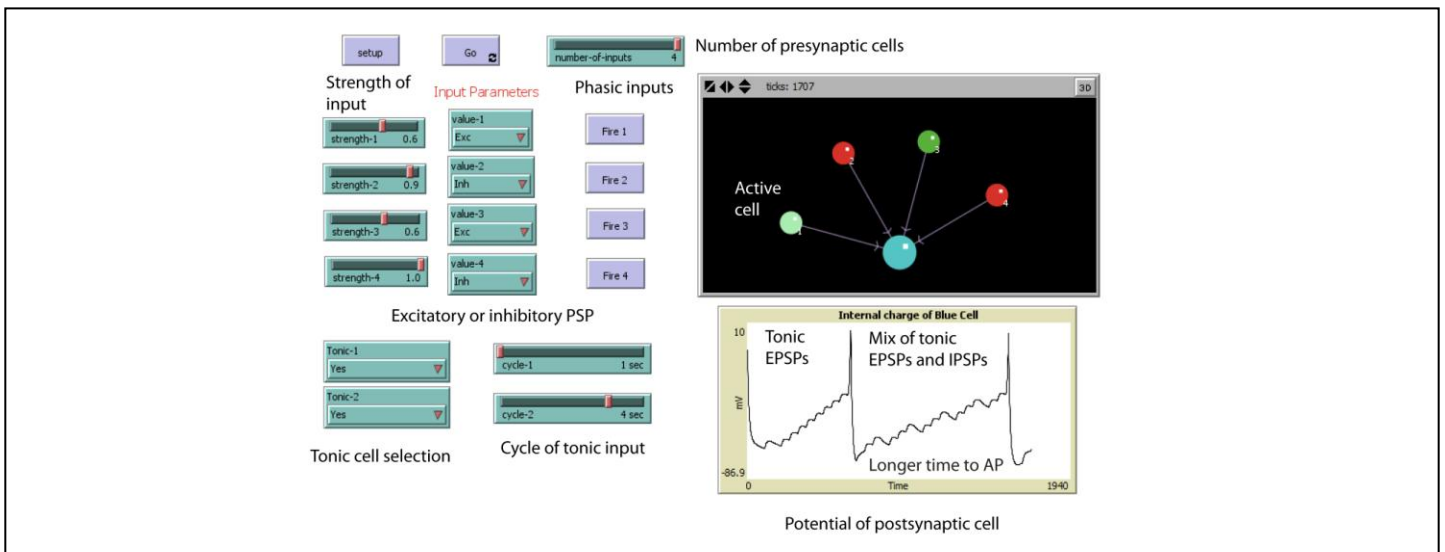
Figure 1. The Temporal Integration simulation showing its elements and output (with added descriptions).

combination of PSPs will result in the production of an action potential.   The integration assignment asks the student to first read the Information Tab in the simulation in order to understand what the simulation capabilities are and to refresh the student on the vocabulary they have learned in class.   The information tab also asks students to try a few things to familiarize themselves with the meaning of the graph they are observing and the functionality of the different control buttons and sliders.

Once they have done that, the students are asked to conduct three short experiments and to explain their results.   Figure 2 shows an example of the work by a student who produced a clean, well thought-out report.

Neural Development
As mentioned earlier, it is sometimes difficult for people to recognize the possibility that order may be the result of a large number of local decisions made by agents with partial information. One of the most interesting examples of this centralized point of view took place a few years
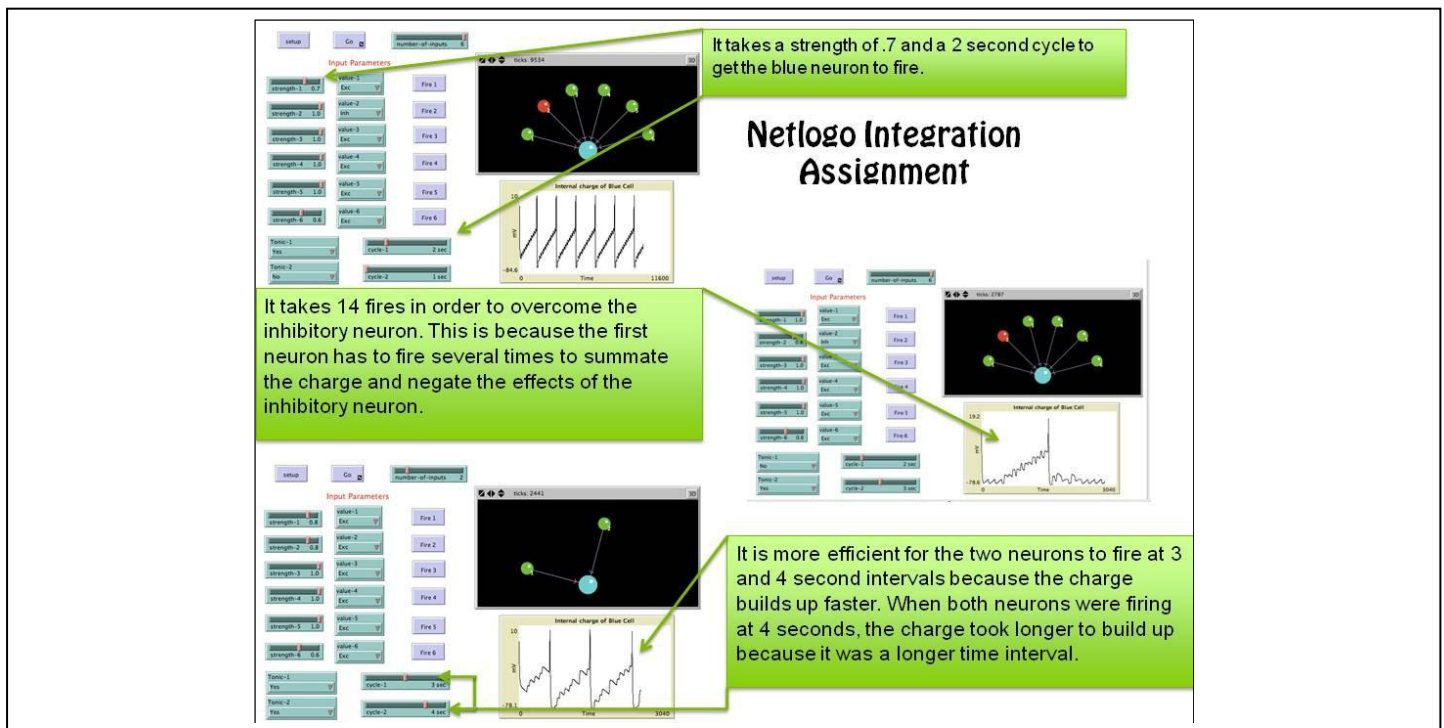

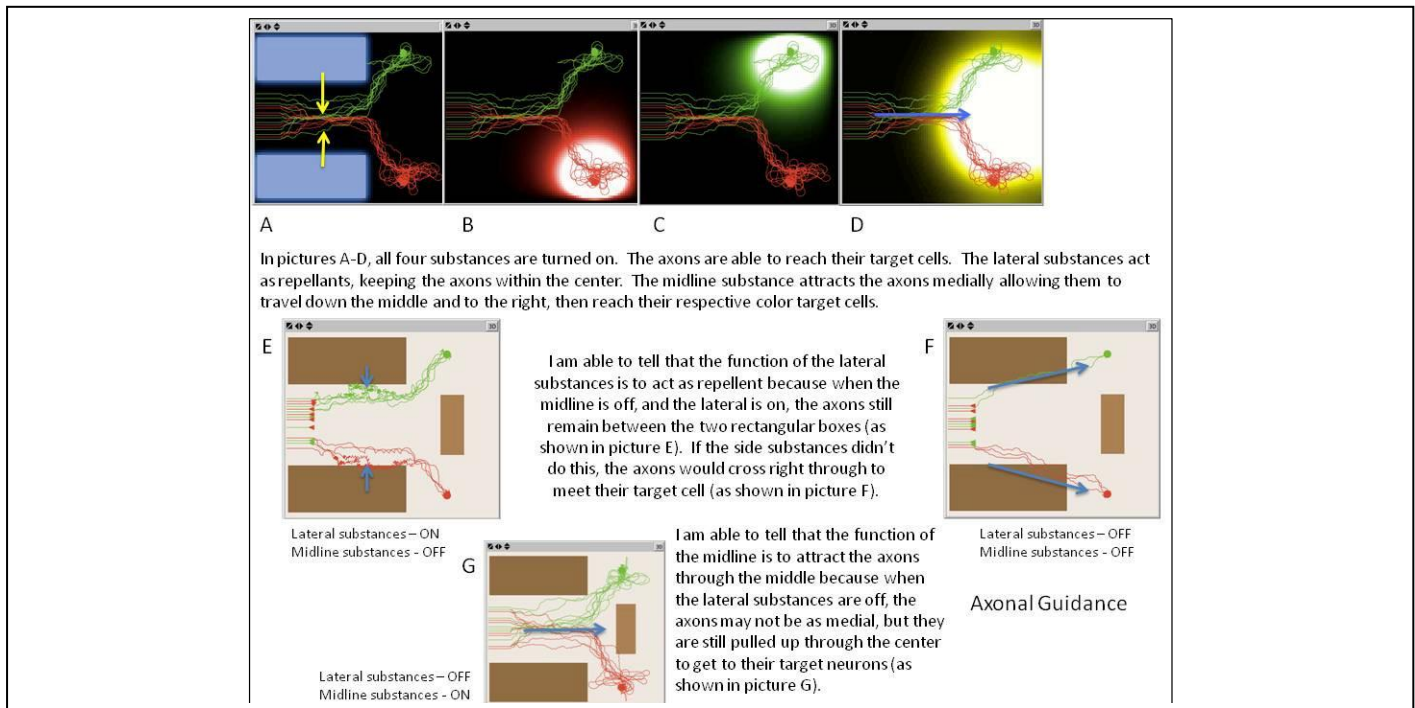*Figure 2.* A student's report for the temporal integration assignment.

In pictures A-D, all four substances are turned on. The axons are able to reach their target cells. The lateral substances act as repellants, keeping the axons within the center. The midline substance attracts the axons medially allowing them to travel down the middle and to the right, then reach their respective color target cells.

I am able to tell that the function of the lateral substances is to act as repellent because when the midline is off, and the lateral is on, the axons still remain between the two rectangular boxes (as shown in picture E). If the side substances didn't do this, the axons would cross right through to meet their target cell (as shown in picture F).

Lateral substances – ON
Midline substances - OFF

Lateral substances – OFF
Midline substances - OFF

Axonal Guidance

I am able to tell that the function of the midline is to attract the axons through the middle because when the lateral substances are off, the axons may not be as medial, but they are still pulled up through the center to get to their target neurons (as shown in picture G).

Lateral substances – OFF
Midline substances - ON

Figure 3. A student's report for the axonal guidance assignment.

back when it was finally revealed that the human genome contains "only" around 20,000 genes (as compared to corn, which has about 30,000). This was a shock to many who felt that humans should be the product of a very large set of coding instructions, particularly when our brains are touted in the popular press as 'the most complex objects in the known universe.'

For our students, who are just beginning to learn the amazing processes that result in the anatomical organization of brains, the idea that groups of cells self-organize to select the neurons that will remain in the adult individual and to guide axonal terminals to their targets tens of centimeters away, proves sometimes difficult.

NeuroLab includes two neural development simulations, Cortical Development and Axonal Guidance. In the latter (see Figure 3), a set of axonal terminals reach their targets (color-coded red and green) using chemical cues present in their environment.

The assignment asks students to turn on and off the release of each one of four distinct factors and to run the simulation a number of times to determine the function of each one of them (whether they are attractants or repellants).   The students can observe the extent of diffusion of each factor with the press of a button and must reach logical conclusions for each result. The challenge is not easy and most students can support their conclusions for only three of the four answers, which gives the instructor an opportunity to model critical thinking. The student whose work is presented in Figure 3 was able to solve all four problems.

Assessment
You do not need to subscribe to the idea that the new

generations of students are 'Digital Natives' who learn in different ways from their predecessors (Prensky, 2001) to notice that their familiarity with video games presents educators with an opportunity to transmit information in novel, more efficient ways.

Computer simulations are not meant to take the place of textbooks and assigned readings, but to complement them by presenting information in a way that more closely resembles the dynamic nature of the processes studied. A particular advantage of simulations relative to text is that users can experiment with different conditions.   Another advantage is that the inherent variability of biological systems is clear in the simulations as each trial produces slightly different results that are best interpreted through some (basic) statistical analysis. Furthermore, the exposure to population processes through visual means may favor the comprehension of decentralized phenomena, resulting in readiness for more advanced concepts.

The simulations in NeuroLab can be also used as educational tools in class through a data projector, permitting the instructor to comment on the results of a number of trials with the relevant parameter manipulations.

Grading
The author gives extra credit for NeuroLab assignments completed during the course. Assignments typically include three activities and each one is worth a point, with excellent work (such as those in Figures 2 and 3) receiving an extra point.

Grading single pages with short, precise text accompanied by graphics is one of the advantages of the simulations in NeuroLab. It is usually very easy to detect

Simulation	Brief Description
Potentials. A simulation of a neuronal membrane containing voltage-gated channels that open to produce an action potential. The sodium-potassium pump can be turned off and ionic in- or efflux can be blocked to observe the effects on the cellular potential.	Students are asked to turn on the simulation and observe the potential reach resting state as potassium ions leave the cell. Subsequently, students cause an action potential (AP) by pressing a button and are asked to observe the opening and closing of channels as the AP develops. They are asked to describe what they see on the plot that is created concurrently. Lastly, students are asked to do the same with the Na\K pump switch turned off and to describe their observations.
Propagation of Action Potential. An action potential travels left to right, opening channels all throughout the axon or at nodes of Ranvier in myelinated axons. The speed of conduction can be compared across different myelination levels.	Employed in class to show the effects of myelinization on the speed of conduction and the effects of de-myelinization.
Synapse. Depicts the release of neurotransmitters by the presynaptic terminal and their effects on the postsynaptic membrane. It shows the function of reuptake receptors and calcium channels and their antagonists.	Employed in class to show the function of reuptake receptors and blockers on the number of PSPs. The number of molecules of SRIs can be controlled to show the effects of dose.
Antagonism. Depicts a postsynaptic membrane with ionotropic receptors. The effects of antagonists (selective and non-), agonists and enzyme antagonists can be compared as the number of total PSPs produced.	In this assignment, students are asked to run an experiment to test the effects of different types of agonists and antagonists, including competitive versus non-competitive antagonists and antagonists. The students run three trials of each condition and calculate the average number of PSPs observed for each. They turn in the bar plots produced by the simulation together with their observations and interpretation.
Temporal Integration. Shows the effects of phasic and tonic PSPs of either excitatory or inhibitory nature to the potential of a downstream neuron. The relative strength of each connection to the neuron can be controlled.	Described in main text.
Cortical development. Simulates the development of layers III –V of the cortex as neuronal precursors migrate following radial glia and chemical cues. Labeled cells can be 'implanted' to observe their cortical targets and to test hypotheses regarding neuronal fate.	Students are asked to run a number of trials and observe the fate of 'labeled' precursors as the cortical tissue develops. They are asked to turn in a small table that describes their observations and interpret the data.
Axonal Guidance Simulates the path-finding behavior of growth cones as they locate their cellular targets through gradients of different factors.	Described in main text.
Tactile Lateral Inhibition Shows the effects on cellular activity of tactile stimuli with and without lateral inhibition.	Students are asked to observe the effects of lateral inhibition on the experience of feeling one versus two tactile stimuli. They are asked to run the simulation and turn on and off inhibitory cells activated by the tactile receptors with the highest activity levels. The 'experience' of the organism is represented by squares of different colors. A plot is produced in parallel that shows the typical 'Mexican hat' distribution of activation.

Table 1.   NeuroLab simulations used in the author's *Introduction to Neuroscience* course Full descriptions are available as a PDF file (NeuroLab_doc.pdf) available at the author's website.

Simulation	Brief Description
Visual Lateral Inhibition. Shows the calculations carried out by a simplified lateral inhibition algorithm on simple visual stimuli as a means to detect edges. It includes explanations for a couple of visual illusions.	Students are asked to draw a simple image in different values of grey. Then they are asked to process the image using a simple algorithm that favors the detection of dark pixels (a very basic Gaussian kernel). The students can see the amount of activity created in each pixel by their process by pressing a button and thereby realize how the process works. Finally, the students are asked to run the same processing on two well known visual illusions (Vassarely and simultaneous contrast) and asked to explain why they cause the effects we experience from them.
Other simulations. These and other simulations can be used in class or given out as assignments to facilitate student understanding of particular concepts.	**Back-propagation network:** a small BP network that learns to recognize four different drawings (typically letters or numbers) created by the user. The change in communication strength between nodes is graphically shown by thinner or thicker links.
	Musical Network: an interactive simulation that allows the user to create a neural network that plays simple melodies by activating a graphical piano keyboard. Networks can be saved and loaded. It demonstrates the complexity that networks may reach and the difficulty in understanding the behavior of non-linear systems.
	Kitaoka Sakura: this simulation shows the well-known visual illusion by Kitaoka and demonstrates that its effects depend on an interplay of dark and light elements. The effects size and shape of the elements can also be observed.

Table 1. NeuroLab simulations (continued)

whether the student interpreted his/her results correctly. Another advantage is that each run with NeuroLab is different and easily distinguishable from others. Therefore, it is very easy to tell whether students are turning in original work. This is something that I mention to my students prior to their first assignment so that they are aware that they must produce their own work.

Student Response
Student response to NeuroLab assignments has been for the most part very positive. Students in general are engaged by electronic media and are happy to interact with their homework assignments and figure out what the results will be. Most students download NetLogo to their personal computers or run it on library computers and turn in reasonably good work. In some cases (perhaps 10 percent of students), as in those shown in figures 2 and 3, the students take the extra time to produce visually attractive work.

The following are some (unsolicited) comments obtained from the Course Evaluation forms that our students fill out at the end of each course: "NetLogo assignments were very helpful in clarifying concepts (do more of these!)." "The projects and NetLogo assignments helped me to focus on important material." "NetLogo projects were relevant and not overly demanding." "I liked using NetLogo in this course… [the simulations] were very interesting and made learning the material easier."

Analysis of student performance
In order to test the idea that working with the NeuroLab assignments favors conceptual understanding, a correlation analysis was conducted to find out if a higher number of NeuroLab assignment extra-credit points results in higher number of correct responses in multiple-choice questions directly related to the topics covered by the simulations.

The fact that the assignments are given as optional work for extra credit must be taken into account, as many students end up doing just a portion of the assignments and therefore, accrue just a portion of the possible extra points.

For this analysis, I looked at the last two iterations of my Introduction to Neuroscience course (spring 2010 and spring 2012), identified the questions in the first partial exam related to the concepts covered in the NeuroLab assignments, and tabulated the total points for correct answers on seven multiple-choice questions per student (n=101). A Pearson's correlation between the total number of correct answers and the total number of extra-credit points obtained from the assignments produced a significant correlation ($r_{(101)} = 0.34$, $p < 0.01$), suggesting that there was a relationship between carrying out the assignments and higher test grades.

While it could be argued that the correlation value is, at best, moderate, a closer look at the data offers some interesting patterns. The student population can be broken

down into four different groups: a) those who did not do most of the assignments yet did well in the course (above the mean grade of B, n=29), b) those who did most of the assignments and did well in the course (n=27), c) those who did not do most of the assignments and did badly (at the mean or below, n=36) and d) those who did most of the assignments yet did badly (n=9). For this analysis, I defined 'most of the assignments' as having received more than half of the possible extra-credit points.

In order to test if the fact of having done the assignments made a difference in the expected distribution of students' grades, a chi-square for independence was conducted on the observed distributions. A significant result ($X^2_{(1)}$ = 10.74, p< 0.005) was obtained, suggesting that the population of students who did the assignments had higher course grades more often than expected.

Clearly, a number of caveats are in order. To begin with, the data do not tell us why it is that those students who did the assignment received higher grades. A relevant reason is that those students did receive extra credit, thereby increasing their grades. While the extra credit was only applied to their first partial grades, it is an important point to take into account. Another reason may be that those students who do the assignments are, in general, more conscientious and therefore, would have obtained a high grade even in the absence of the assignments.

While the above analysis and results should be taken as a preliminary assessment of the beneficial effects of engaging in the NeuroLab simulations, nonetheless the data compellingly suggest that the students in group (c) could have raised their conceptual learning and thereby their final class scores by working with the NeuroLab assignments.

To try out:

The simulations described in this article and other ancillary simulations are available for free download at (http://sites.lafayette.edu/schettil/neurolab/). The file NeuroLab_doc.pdf contains brief descriptions and screenshots of the simulations as well as the assignments used in my *Introduction to Neuroscience* course.

The website also allows visitors to run the simulations directly on their web browser (note: the latest Java updates include stringent security settings that may interfere with the applets. Please see the supplemental materials file for a work around that allows Java to create exceptions).

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