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ARTICLE
The Use of Modular, Electronic Neuron Simulators for Neural Circuit Construction Produces Learning Gains in an Undergraduate Anatomy and Physiology Course

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During the spring of 2016 at the University of Wisconsin-Milwaukee, we implemented a novel educational technology designed to teach undergraduates about the nervous system while allowing them to physically construct their own neural circuits. Modular, electronic neuron simulators called NeuroBytes were used by the students in BIOSCI202 Anatomy and Physiology I, a four-credit course consisting of three hours per week each of lecture and laboratory time. 162 students participated in the laboratory sessions that covered reflexes; 83 in the experimental sections used the NeuroBytes to build a model of the patellar tendon reflex, while 79 in the control sections participated in alternate reflex curricula.

To address the question of whether or not the NeuroBytes-based patellar tendon reflex simulation brought about learning gains, the control and experimental group students underwent pre/post testing before and after their laboratory sections. We found that for several of the neuroscience and physiology concepts assessed on the test, the experimental group students had significantly greater declarative learning gains between the pre- and post-test as compared to the control group students. While there are numerous virtual neuroscience education tools available to undergraduate educators, there are relatively few designed to engage students in the basics of electrophysiology and neural circuitry using physical manipulatives, and none to our knowledge that allow them to build circuits from functioning hand-held "neurons."

Key words: Neuron, Simulation, Hands-On, Electrophysiology, Anatomy and Physiology, Neural Circuits

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Science, technology, engineering and math (STEM) education is an identified priority for our nation. Careers in STEM will grow almost twice as fast as those in non-STEM fields, and STEM workers experience roughly half the unemployment rate of non-STEM workers (Langdon et al., 2011). In 2012, the President's Council of Advisors on Science and Technology authored a report endorsed by the president that called for 1 million additional college STEM graduates by 2022 to fill STEM career roles (President's Council of Advisors on Science and Technology, 2012). However, the problem is that many young students who have an interest in science and technology lose that passion during their college experience. Among college students who initially declare as a STEM major, only 35% go on to complete a STEM degree (Department of Education, 2012). In addition, STEM degrees as a percentage of all degrees conferred has declined since 2001 at the college level. This lack of interest and perseverance in the STEM fields disproportionately affects underrepresented minorities. When asked, underrepresented minorities profess the same intention to major in STEM fields as non-minorities, although substantially fewer of them actually do, and those who do major in STEM fields are more likely to drop out (Astin 1994; Morning and Fleming 1994).

Students often decide whether or not they will major in STEM fields on the basis of their experiences in introductory courses, and many of these students report leaving STEM fields due to the lack of an engaging experience (reviewed in Seymour and Hewitt, 1997). Engaging early undergraduates in concepts that highlight the interdisciplinary nature of science has been emphasized by both governmental and private institutions as having the potential to attract and retain undergraduate STEM majors (National Research Council, 2004; Kezar and Elrod, 2012). This interdisciplinary experience is also critical for advanced undergraduates. The BIO2010 report authored by the National Research Committees Council stated that engineering concepts should be included in organismal physiology courses (National Research Council, 2003). A recent NSF strategic plan specifically called for "investigations that cross disciplinary boundaries and require a systems approach to address complex problems (e.g., the neural basis of behavior…)" at the frontiers of discovery (National Science Foundation, 2006), and the current strategic plan lists interdisciplinary STEM education as a strategic goal (National Science Foundation, 2014).

Virtual simulations in the STEM fields can allow for rapid and continuous alterations and improvements to curriculum, access to systems and technologies that may not otherwise be feasible in educational settings, and lower cost. Examples in the field of neuroscience education include SWIMMY (Grisham et al., 2012) and Neurons in Action (Stuart, 2009). These simulations can provide benefits such as increased student conceptual understanding and factual knowledge of STEM concepts (Finklestein, 2005; Dobson, 2009) that are equal to or greater than students working with physical, hands-on experiments. However, other studies in these disciplines have shown that hands-on experiences have a positive impact on declarative knowledge in anatomy (Franklin, 2002) and student attitude, including a more realistic view of the testing and data analysis process that challenges experimentalists (Bourque, 1987). As evidence of the potential benefits of both virtual and hands-on experimentation, students prefer that both should be used in parallel to maximize their engagement (Dewhurst et al., 1994; Macaulay et al., 2009).

During the 2016 spring semester at the University of Wisconsin-Milwaukee, we tested hands-on, electronic neuron simulator prototypes called NeuroBytes (http://www.neurotinker.com/neurobytes) that allow students to learn about the nervous system while physically building their own neural circuits, synapse by synapse. NeuroBytes are programmable simulations of individual neurons that exist on small circuit boards that students can physically manipulate and connect into functional neural circuits using “neurotransmitter” cables (Figure 1). Red cables simulate excitatory neurotransmitters, and depolarize postsynaptic cell “membrane potential,” while blue cables model inhibitory neurotransmitters and hyperpolarize postsynaptic cell membrane potential. An LED integrated into the circuit board provides feedback about this virtual membrane potential. Sensory input to the NeuroBytes can be provided via sensors that detect touch, light, temperature, or sound. If this input depolarizes the membrane potential to a preset threshold level via temporal or spatial summation, an action potential fires in the NeuroBytes unit. The LED flashes bright white, and a signal is propagated from pre- to post-synaptic NeuroBytes via the neurotransmitter cables. These action potentials can also produce virtual muscle contractions by stimulating servo motors to control physical objects. Thus, we believe that this technology is best described as a “microworld” (Papert, 1980): a playground of the mind where students can explore neural circuits in a way that is open-ended, fun, and intuitive.

We have developed a comprehensive set of explanatory and inquiry based curricula suitable for undergraduate education to accompany the NeuroBytes neuron simulators. Reflexes are typically one of the types of circuits with which students experiment and learn about. The patellar tendon reflex in particular is one that is well known to most introductory undergraduate students through personal experience at the physician’s office, as well as through high school and introductory undergraduate biology courses. We chose this circuit (Figure 2, bit.ly/patellartendonreflex) for student construction during the course due to its relative simplicity, ability to be implemented into the existing curricula within one lab period, and relatively quick learning curve by the teaching assistants.

Our aim for this course integration was to analyze the effectiveness of the neuron simulators in engaging students and producing learning gains in neuroscience and physiology.

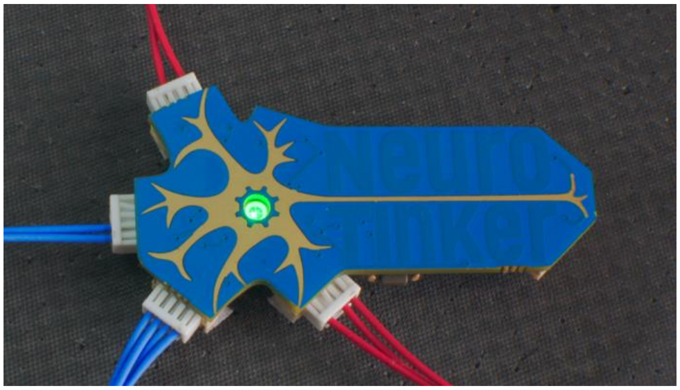

Figure 1. The NeuroBytes Neuron Simulator. The LED in the cell body region indicates the virtual membrane potential level, with shorter wavelengths (blue to violet) indicating hyperpolarization, and longer wavelengths (yellow to red) indicating depolarization. Cables are used to connect the NeuroBytes together and model excitatory (red) and inhibitory (blue) neurotransmitters, respectively.

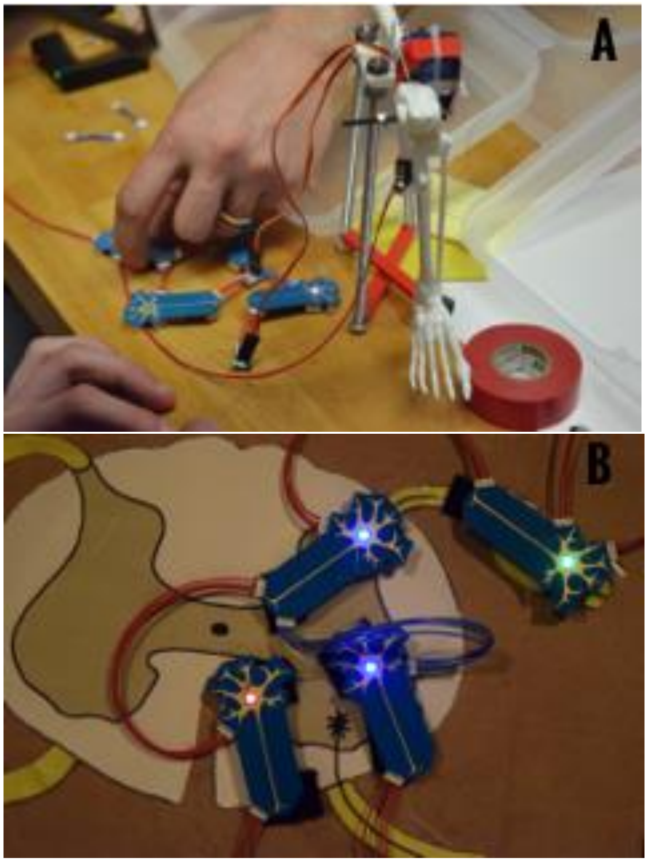

Figure 2. *(A)* Students in the process of constructing the patellar tendon reflex simulation using NeuroBytes, a mechanical switch for the patellar tendon stretch receptor, 3D printed leg bones, and servo motors for the quadriceps and hamstrings muscles. *(B)* Final result of the student reflex pathway construction.

COURSE IMPLEMENTATION

The study was carried out under guidelines of the UW-Milwaukee Institutional Review Board under protocol 16-085 as “exempt” under CFR 46.101.b.1 (https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.101): “Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.”

During the Spring 2016 semester at UW-M, one of us (A.P.) taught BIOSCI202 Anatomy and Physiology I, a four-credit course consisting of three hours per week each of lecture and laboratory time. This course is required of nursing, biomedical engineering, computer-science, and many public-health students, as well as all the majors in the College of Health Sciences. The patellar tendon reflex is featured prominently in both the lecture and laboratory components of this course through the text, lab manual, on-line learning simulation, and on-line student assessment programs. All students in the course first encountered this reflex in the lecture portion of the course before experimenting with it in the lab, as discussed below.

There was a total of 162 students who participated in the reflex laboratory sections: 79 in the control sections, and 83 in the experimental sections. Each teaching assistant who participated in this study was assigned to one control and one experimental section. In the experimental section of the lab, the students worked in groups of 3-4 to build the NeuroBytes based patellar tendon reflex, with the end goal being proper NeuroBytes signal processing and a successful leg kick when the “patellar tendon” switch was tapped. The control sections of the course participated in lab manual-based learning activities historically used in this course, consisting of completing a demonstration on each other with reflex hammers as well as studying diagrams of reflex arcs and the roles of interneurons.

To address the question of whether or not the NeuroBytes patellar tendon reflex simulation brings about learning gains, the control and experimental group students underwent pre/post testing before and after their laboratory sections took place. These tests consisted of 32 questions covering the anatomy and physiology of the spinal cord, as well as associated peripheral nerve and skeletal muscle structures. Twelve of these questions (See Supplementary Material) specifically addressed reflex physiology and neuron function. The same questions were asked during both testing sessions.

The pre/post tests were delivered in lab using the McGraw-Hill Connect platform and consisted of questions that were not otherwise used in the course. Upon completion of the reflex lab, student performance on both the pre- and post-tests was calculated, and the data were de-identified before being exported to Microsoft Excel spreadsheets.

To assess for efficacy, the student performance data were analyzed as percent change in score between the pre- and post-tests, and compared between control and experimental groups (two group between-subjects comparison) by means of T-tests using Microsoft Excel. 95% confidence intervals (CI) were also calculated from the student performance data using Microsoft Excel.

RESULTS AND DISCUSSION

We found that for four of the twelve neuroscience and physiology concepts assessed for on the test (See Supplementary Material), the experimental group students had significantly greater declarative learning gains between the pre- and post-test compared to the control group students (Figure 3). For question #2, “Applying the Functions of the Components of the Tendon Reflex,” students in the experimental group showed a 7.7% (95% CI [5.1,10.3]) better improvement than those in the control condition. For question #8, “The Components of Spinal Reflex Arcs,” students in the experimental group showed a 7.0% (95% CI [0.8,14.6]) better improvement than those in the control condition. For question #11, “Depol Chemistry,” students in the experimental group showed a 7.0% (95% CI [2.4,11.6]) better improvement than those in the control condition. For question #12, “Hyperpol Chemistry,” students in the experimental group showed a 8.2% (95% CI [4.6,11.8]) better improvement than those in the control condition. The effect size for all four of these questions is nearly a full grade level improvement for the group exposed to NeuroBytes compared to the control group who did not use NeuroBytes in their lab sections.

These four questions with significant differences in student performance relate to structure/function relationships of the patellar tendon reflex, the anatomy of reflex arcs in general, and interestingly, to the electrochemistry of membrane depolarizations and hyperpolarizations. This improvement in electrochemistry knowledge is unexpected. Prior to the week in which NeuroBytes was introduced into the labs, all students in the course (i.e., both control and experimental groups) spent one week in lecture on combined "systems integration" lessons that explored in particular the exchange of ions among the skeletal, muscular, and nervous system. These lessons emphasized the roles of calcium, sodium, and potassium ions in these three systems. In the reflex lab session, the teaching assistants (TA) provided learning support, but not direct instruction, on neurophysiological concepts. Hence, we do not believe that the TAs were drawn to teach ion flux to the experimental group students in particular, but that possibility cannot be completely ruled out.

We believe that the latter improvements in student performance may have been brought about in part through the unique mode of membrane potential indication in the NeuroBytes. The changing color of the LED (Figure 1) is a constant reminder to students of the excitable nature of neurons, and how that visual feedback changes based upon student construction of particular neural connections may make it easier to draw analogies to particular ion flux across the neuron membrane that leads to changes in membrane potential level.

During the post-test, the students were asked to provide their thoughts about the enjoyment and utility of using NeuroBytes to model the nervous system. A sampling of their comments:

> *“I learned a lot through this simulator!”*
> *“Doing the activity with the reflex and the leg was helpful because it was hands on.”*
> *“I believe that NeuroBytes had some great information that helped me learn very well.“*
> *“It was helpful to learn how the sensory and motor neurons are connected.”*
> *“They helped show us the exact track that the transmitions (sic) go through to make a reflex happen. I liked the hands on experience.”*

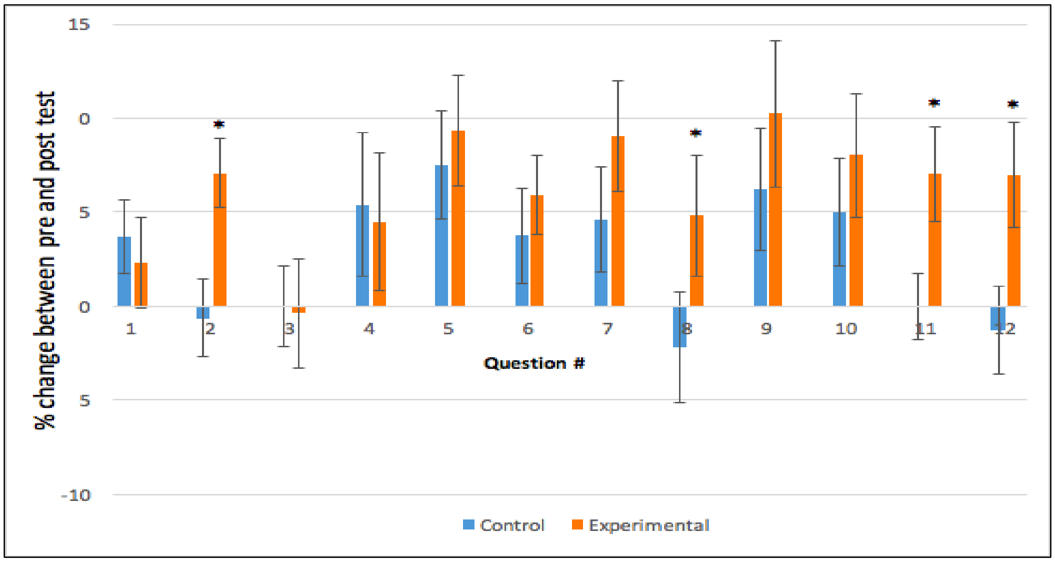

Figure 3. Changes in Neuroscience and Physiology Declarative Learning Between Pre- and Post-Tests. * indicates a significant difference in the experimental group compared to the control group on that particular question. Experimental = NeuroBytes based lab sections (n=83), Control = Standard curriculum sections (n=79). The error bars indicate standard error of the mean.

UTILITY FOR UNDERGRADUATE NEUROSCIENCE EDUCATION

Despite the fact that hands-on experimentation is of substantial benefit to student learning, it can be difficult to find or develop suitable experiences that involve basic neuron function, emergent properties of circuits, electrophysiology, and sensory and motor processing. There are several experiences that do involve one of more of these topics, including Backyard Brains Spiker Box and optogenetics experiments (Marzullo and Gage, 2012), and the Crawdad neurophysiology labs (Wyttenbach et al., 2014), but these both involve experimentation with live animal preparations. NeuroBytes allows students to build a synthetic nervous system while examining and experimenting with neuron and circuit properties that otherwise may be difficult to grasp at a basic level. The simulators make the invisible, visible.

While the course implementation described above utilized NeuroBytes in the prototype stage, they are under active development for commercial release in the near future with the help of an NSF Small Business Innovation Research (SBIR) grant. The exact kit contents have not been determined as of this writing, but our goal is to include sufficient environmental detection sensors (light, sound, and touch), motor and sound output devices, and physical substrates such as 3D printed or plastic injection molded models, along with instructions and curricula to involve groups of 3-4 students in experiments that can span anywhere from several class sessions up to a substantial portion of a semester. Pricing will be in line with other hardware-based neuroscience education offerings from Backyard Brains (www.backyardbrains.com) and Open BCI (www.openbci.com), for instance. We believe in the importance of an open source model for education, therefore all of our firmware encoding the neuron behavior, the PCB and 3D model design files, and the curricula will be made available for no extra cost under open source licenses.

To support students performing more in-depth experimentation, we are developing an Android / iOS app that displays graphical changes in NeuroBytes membrane potential in a traditional oscilloscope-like manner (Figure 4). This will allow students to visualize changes in membrane potential and action potential generation over time based upon their particular circuit construction and inputs to the system. Quantitative data export will allow for statistical modeling and experimentation using student constructed networks.

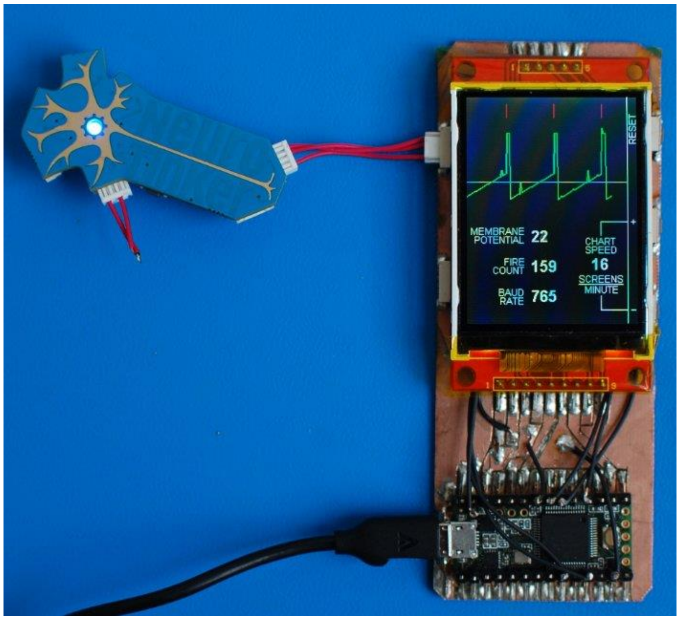

Figure 4. Prototype oscilloscope used to display the NeuroBytes action potential waveform. The finalized version will be implemented in an Android / iOS app.

Connections between neurons within circuits are not static, but change over time and space based on patterns of activity. This synaptic potentiation is thought to be one of the main mechanisms for the encoding of memories (reviewed in Cooke and Bliss, 2006), and NeuroBytes-based simulations of this phenomenon are one of the unique strengths of this platform. NeuroBytes will possess a memory mode which will allow the synaptic weighting to dynamically change (both increase and decrease) based upon the activity of particular synapses. In this way, memory of the previous activity patterns is stored in the connections between NeuroBytes. The synaptic weighting can be visualized using the oscilloscope app so the user can quantitatively and qualitatively track how circuit activity leads to changes in synaptic plasticity over time.

Another circuit type amenable to NeuroBytes based modeling is the central pattern generator (CPG). An excellent virtual program (SWIMMY) exists that challenges students to decipher the anatomy and physiology of an existing CPG network in a virtual fish, and this simulation has been shown to produce student learning gains as measured by pre-post testing (Grisham et al., 2012). However, SWIMMY does not allow students to build a CPG of their own design, with the accordant false starts, confusion, occasional frustration, but ultimately satisfaction and a deep understanding that comes from hands-on tinkering and experimentation. We have developed prototype hardware and curriculum around a CPG-controlled insect (Figure 5) that utilizes a 3D printed body, servo motors that drive leg movement, and a student designed and constructed a “brain” to control the motors. While this simulation has not yet been implemented in the classroom, anecdotal evidence from beta testers indicates that experimenting with different CPG organizations and the resulting insect behavior has the ability to engage students in the learning process.

Figure 5. Central Pattern Generator based NeuroBytes circuit driving walking behavior in a model insect.

In conclusion, we have found that student use of hands-on, electronic neuron simulators produces learning gains for concepts commonly taught in neuroscience and anatomy and physiology courses, and appears to engage students in enjoyable, constructivist learning experiences that might entice them to continue their STEM education. As the use of NeuroBytes spreads to additional courses and classrooms, we will investigate the utility of additional NeuroBytes based simulations to increase STEM learning and interest.

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