ARTICLE

Engaging Undergraduates in a Unique Neuroscience Research Opportunity: A Collaborative Research Experience Between a Primarily Undergraduate Institution (PUI) and a Major Research Institution

Matthew A. Kreitzer¹ & Robert P. Malchow²

¹Department of Biology, Indiana Wesleyan University, Marion, IN 46953; ²Departments of Biological Sciences and Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL 60607.

This report describes a unique undergraduate research and teaching collaboration between investigators at two institutions, one a relatively small, primarily undergraduate institution and the other a large, urban research-intensive university. The program incorporates three major facets. First, undergraduates participate in a weekly collaborative lab meeting involving instructors from both institutions and held via remote video. Student-led discussions and presentations dominate these meetings, and the unique format promotes novel interactions between students and instructors. Second, students carry out investigative studies centered on understanding the role extracellular pH dynamics play in regulating neuronal processing. Students carry out studies on isolated neurons and glia throughout the fall and spring semesters, and primarily use a noninvasive electrophysiological technique, termed selfreferencing, for extracellular pH measurements. technique is relatively simple and readily learned and employed by undergraduates, while still being powerful enough to provide novel and meaningful research results. The research component is expanded for several students each summer who are selected to participate in summer research with both PIs and graduate students at the major research institution. Finally results gathered during the year and over the summer are disseminated at institutional symposia, undergraduate neuroscience symposia, national society meetings, and in submitted journal manuscripts. Preliminary observations and findings over three years support the aim of this research experience; to create a productive environment that facilitates deep-level understanding of neurophysiological concepts at the undergraduate level and promotes intellectual development while cultivating an excitement for scientific inquiry in the present and future.

Key words: undergraduate research; collaborative research; primarily undergraduate institution (PUI); retina; electrophysiology; self-referencing

Stimulating interest and engaging undergraduates in the exciting possibilities of science should be of foremost importance to educators as they contribute to the development of future scientists. There is a growing body of evidence to suggest that more extensive interweaving of undergraduate research can be pivotal in catalyzing interest and engagement by students in the sciences, while at the same time being a useful tool to enhance educational curriculum and student learning in the academy (Lopatto, 2004; Healey and Jenkins, 2009). Numerous reports have suggested that undergraduate research programs serve to improve student retention, strengthen their connection to their major, help clarify the future directions of students, and increase the likelihood of students pursuing graduate school (Chaplin et al., 1998; Nagda et al., 1998; Bauer and Bennett, 2003; Russell et al., 2007). In addition, creating student-engaged research opportunities positively correlates with teaching that promotes active learning and results in "deep-level processing" by students (Brew and Boud, 1995; Baxter Magolda, 1999; Prosser and Trigwell, 1999; Blackmore and Cousin, 2003: Healey, 2005: Kuh et al., 2007).

Carefully developed undergraduate neuroscience research programs should also improve students' ability to think critically and to apply complex core neuroscience principles in a meaningful research context. A significant

challenge is enabling students to understand and apply critical principles such as Nernst equilibria, relative permeabilities, and the functioning of voltage-gated conductances, amongst others, to neuronal function. Although a number of fine simulation programs exist to help develop and extend such concepts, hands-on work with these principles within the context of a meaningful scientific research question is likely to more fully engage students. Here, we describe a unique research experience for undergraduates utilizing a novel electrophysiological methodology that facilitates greater understanding of key concepts such as Nernst equilibria.

In this new program, undergraduates are integrated into an ongoing neuroscience research collaboration between a PI from an primarily undergraduate institution, Indiana Wesleyan University (IWU), and a PI and graduate students from a research-intensive institution, the University of Illinois at Chicago (UIC). The program has three major facets. First, undergraduates participate in a weekly collaborative lab meeting involving PIs from both the PUI and the major research institution. Second, students carry out investigative studies throughout the fall and spring semesters, examining the role that changes in pH regulation may play in neuronal processing in the retina. The research component is expanded for selected students who participate in summer research with both PIs

and graduate students at the major research institution. Finally, students present results gathered during the year and over the summer at institutional symposia, undergraduate neuroscience symposia, and national society meetings. The aim of this collective experience is to facilitate deep-level understanding of neuroscience and promote intellectual development while cultivating an excitement for scientific inquiry in the present and future. Preliminary observations from student self-reporting surveys after the first three years of this unique collaborative experience suggest research that undergraduates perceive the experience to have a positive impact. Additionally, research outcomes have included numerous student presentations at institutional and local symposia, five abstracts coauthored by undergraduates and presented at the Society for Neuroscience meetings, and two research manuscripts with undergraduate authors.

MATERIALS AND METHODS

Undergraduate students taking part in this research experience typically register for one credit hour as a research course. Students are expected to spend at least four hours a week working on research-related activities (1 hour in a lab meeting and 3 hours working in lab). Ideally, students enter this program in their sophomore or junior years and continue for the duration of their undergraduate education. New students enter this experience each year creating a diverse experiential dynamic; new students are generally paired with students already having prior experience with the course. The curriculum of the undergraduate research endeavor includes a collaborative lab meeting, a laboratory component, a summer research opportunity, and an emphasis on dissemination.

Collaborative Lab Meeting

The collaborative lab meeting is designed to create a unique venue that immerses students into a collaborative research environment centered around the scientific understanding of the nature of extracellular pH dynamics in regulating neuronal processing. This allows students to participate in developing scientific questions, crafting experimental designs, and working through challenges in The PI from the research-intensive technical issues. institution is brought into the classroom with ~8-12 students and the PI at the PUI utilizing Skype (freeware from or Google Hangout (freeware skvpe.com) plus.google.com) for videoconferencing. This requires a computer connected to the internet and to a projector. To enhance the audiovisual communication from the PUI a Logitech USB driven stem microphone is used to acquire group conversation. Video of the group from the PUI is acquired with a Logitech USB-driven webcam positioned at a distant point creating a holistic view for the remote PI. Audio is projected into the class through an external speaker connected to the computer. This relatively small number of accessories creates a setup allowing the remote PI to be integrated into the PUI classroom using primarily the same equipment found in traditional classrooms (see Fig. 1). The remote PI requires a standard computer with audiovisual capabilities (microphone, stereo, and webcam). A secondary monitor allows for simultaneous observation of the PUI group and any document being observed on the projector in the PUI classroom. The program Scriblink (available on the web at scriblink.com) facilitates the drawing and sharing of explanatory diagrams on the fly. In addition to enabling the live video link that permits instructors and students to interact in real time. Skype/Google Hangout also permits each instructor to share other materials derived on the web by sharing their computer screen with the remote audience, again facilitating the presentation of web-based material that the instructor deems beneficial at a moment's notice.



Figure 1. Picture taken during Skype-mediated lab meeting illustrating PIs view from a remote location.

Laboratory Experience

The weekly collaborative lab meeting is coupled to a technical laboratory experience. This experience focuses on the retina as a model system for addressing fundamental questions about neuronal function and modulation in the nervous system. The specific aims of the research have been focused on the role that alterations in extracellular pH may play in shaping visual signals, and on the specific roles that different cells play in regulating extracellular pH in the retina. Students employ an ultrasensitive, non-invasive extracellular recording technique called self-referencing to measure changes of extracellular pH adjacent to single cells isolated from the retina. In addition to being essential for increasing the sensitivity of pH electrodes and thus enabling many of the measurements, the self-referencing technique has the great additional benefit of being highly amenable to use by Students first create pH-selective undergraduates. microelectrodes, a technically simple process that is complete in two-three minutes. While observing via television monitor, the electrode is lowered into a cell culture dish and moved by a computer-controlled manipulator to a position about 1 µm from the membrane of a cell. This process most closely resembles a video game and is easily accomplished (and enjoyed) by undergraduates. Since the recordings are extracellular, the measurements are surprisingly easy to make and robust in nature. Self-referencing also provides an excellent opportunity for introducing students to the underpinnings of basic electrophysiological methods and techniques (see Kreitzer et al., 2007 for a more technical description of the cell-culture and self-referencing methodology used in these experiments).

Primary cell culture

Undergraduate students are guided through the process of primary cell culture by isolating retinal cells from fish or

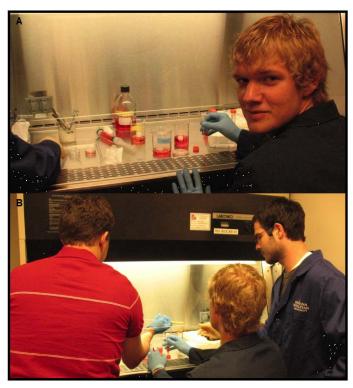


Figure 2. A and B picture of undergraduates from PUI being guided through primary cell culture of retinal neurons.

salamander retina (protocols approved by the Indiana Wesleyan University and University of Illinois Institutional Animal Care and Use Committees). This process introduces undergraduates to solution preparation, microdissection, chemical and mechanical dissociation, and general aseptic cell culture techniques (Fig. 2). There are several advantages of the fish retina as a model for study, including ready availability, a relatively simple protocol for isolating cells and the ease with which cells can be maintained. Additionally, the somas of the neurons and glia can be quite large (30-150 µm), making for easy targets for the students. The 1-2 day lifespan in culture gives sufficient time for students to record responses from cells, but does require repeated dissociations which can be time consuming in an undergraduate research context.

pH-selective electrode fabrication

Small bore pH-selective microelectrodes are used to make measurements of extracellular pH. Students pull capillary tubes to tip diameters of 2-4 μm (essentially identical to typical patch pipettes) using a Sutter Instruments P-97 puller. The glass pipettes are then coated with silane to make the surface hydrophobic (see Smith, 2007 for details); these silane-coated pipettes can be maintained for several months. Electrodes are then back-filled with a solution containing 100 mM KCl and 10 mM HEPES adjusted to a pH of 7.0 with KOH and are made pH-selective by front-filling the capillaries (Fig. 3) with a highly H⁺-selective ionophore (Sigma-Aldrich; again, see Smith 2007 for details).

Self-referencina

The pH-selective microelectrode is connected to the head-



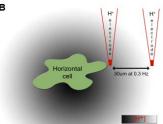


Figure 3. A. Undergraduate research student making an H⁺-selective probe. B. Schematic of self-referencing technique making a differential measurement with a probe to measure extracellular pH around an isolated retinal horizontal cell.



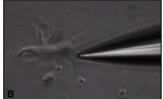


Figure 4. Self-referencing setup at the PUI. A. Undergraduate student working with system. B. Representative microscopic view of isolated retinal neuron with H⁺-selective electrode.

stage of an IonView voltametric amplifier (BioCurrents Research Center, Marine Biological Laboratory, Woods Hole, MA) via a silver-silver chlorided wire and holder. The head-stage is connected to a specially micromanipulator with a resolution of 0.25 µm that is secured to a platform attached to a Zeiss Axiovert 13CFL inverted light microscope. The microscope is placed on an air-isolation table to reduce mechanical vibration and surrounded by a Faraday cage to reduce electrical noise (Fig. 4A). Micromanipulation of the electrode is operated through a computer keyboard control module similar to that of a video game providing an easy introduction into micromanipulation. A video camera is used to display a larger image of the cell on a monitor for precise placement of the electrode. The electrode is manipulated so that it is about 1-2 µm away from an isolated cell (Fig. 4B). IonView software is then used to move the electrode between two locations – first, the point close to the cell, and then a point 30 µm distant, at a rate of 0.3 Hz. The software takes the pH-dependent voltage measurement from the distant point and subtracts it from the reading taken at the point near the cell to obtain the small cell-dependent H⁺ flux. The system allows very small H⁺ fluxes to be measured; the simple subtraction protocol increases the useful sensitivity of ionselective electrodes by about 1000x more than the sensitivity of a stationary pH-selective electrode. setup allows for meaningful extracellular pH measurements to be made from individual neurons and examination of the potential role of pH in neuronal processing. Data are exported to either Microsoft Excel or Prism (GraphPad software) where it can be further analyzed.

Additional methodologies such as calcium imaging (see Kreitzer et al., 2012) or intracellular recordings in whole retina are incorporated when scientific questions not easily addressed with self-referencing alone are raised by students in collaborative lab discussions. Most commonly

these experiments are designed and carried out during intensified summer research.

Summer research

During the academic year undergraduates in the program are given the opportunity to apply to participate in an intensified summer research experience. Two or three students are selected based preferentially on statements of student's interest in the experience and GPA. Strong preference is given to students expressing a potential future interest in graduate school in biology, or a more specific interest in neuroscience.

The PI along with the selected students from the PUI go for four weeks to the major research institution (UIC). At UIC the undergraduates work closely with graduate students from UIC and both Pls. In addition to the intensified hands-on laboratory component they are exposed to the broader research atmosphere of UIC. Students are given an opportunity to see the research facilities present, are introduced to other graduate students and investigators and are given the opportunity to listen to research seminars. Following the time at UIC, the students and PI return to the PUI for an additional intensive 4 to 6week period. This time is important in allowing the undergraduate researchers to expand in their leadership in the lab as they become more deeply and independently engaged in the research.

Dissemination

This undergraduate research experience places emphasis on dissemination of research findings. students participating in the experience present at an institutional symposium each year. Many of the students submit posters to present at the symposium while those who participate in the summer research component as well as those who make more substantial contributions during the year give oral presentations. Students are also strongly encouraged to participate in regional or national undergraduate neuroscience symposia. Students at each level of dissemination are involved in a rich learning experience by gathering and analyzing data, putting data into a presentable format, and interpreting the data. In addition, students help to craft manuscripts for submission to research journals and thus become involved in learning how to prepare their work for publication. Thus far, two articles have been published in peer reviewed scientific journals, with 6 undergraduates as co-authors (Jacoby et al., 2012; Kreitzer et al., 2012).

RESULTS/DISCUSSION

A significant component of our undergraduate program is the weekly collaborative laboratory discussions run through video-conferencing with Skype or Google Hangout. The classroom discussions cover a wide variety of topics. The lab meeting exposes undergraduates to broad facets of scientific investigation that can be missed in abbreviated or more technique-focused research programs. discussions are led by students with PIs interjecting comments as needed. Representative topics include:

✓ PIs lead a general introduction to the scope and

- background of the research.
- ✓ Students guide introductions to primary laboratory techniques utilized in the lab.
- ✓ Students conduct literature searches on specific topics and discuss findings as a group.
- ✓ Students lead discussions of key scientific articles recognized by the lab.
- ✓ Students propose scientific experiments and designs to test specific research questions
- ✓ Undergraduate and graduate students report new data acquired from laboratory investigation and discuss interpretations and suggested next steps.
- ✓ PIs introduce students to possible summer research opportunities as well as future opportunities that exist in science including graduate school.
- ✓ PIs discuss the nature of scientific funding that supports the scientific enterprise
- ✓ PIs discuss the details of the review process for grants submitted to funding agencies and manuscripts submitted to scientific journals

The discussions developed in this environment actively bring students into the middle of conversations evaluating results, developing measurable questions, experimental design, and data analysis associated with the research endeavors the students are pursuing. The presence of a second investigator from a major research university brought virtually into the classroom immediately exposes students to the learning benefits of inter-laboratory scientific discussion and enlivens the dynamics of the discussions in sometimes unexpected ways. For example, numerous times, unanticipated questions from students are best dealt with on the fly by drawing on the resources of the Internet to quickly share results from journal articles the Pls are aware of. This enhanced flexibility, enabling the introduction of materials that otherwise would not make it into the classroom, is facilitated by having one of the instructors effectively on their computer at all times of the conversation, and is something that would be much more daunting for the instructor to perform in the classroom. This unique learning experience cannot easily be replicated through typical classroom settings or classroom laboratory exercises.

In the process of shaping these laboratory discussions, the PIs use methods that have previously been found to be effective in cultivating better learning environments and outcomes. As much as possible, discussions are led by students themselves, with instructors guiding the flow of discussion. The student-led format encourages students to engage the topics sufficiently to be able to present in front of peers, always a highly motivating factor. assignments and relevant literature searches discussed at these sessions also appear to be effective in bringing students quickly to levels of understanding that enable experimental design and analysis. The student interest and excitement that we have observed during these discussions between faculty, graduate students and undergraduate students supports numerous studies correlating the interaction between PIs and undergraduates in a "learning community" with meaningful undergraduate research (Foertsch et al., 2000; Shellito et al., 2001; Prince

et al., 2007).

In the laboratory, undergraduates are quickly able to develop the technical skills needed to conduct meaningful research. They are quite adept at manufacturing ionselective electrodes and in positioning pH-selective electrodes next to cells, enabling a rapid ability to make extracellular measurements. All students begin by learning how to manufacture their own pH-selective microelectrodes

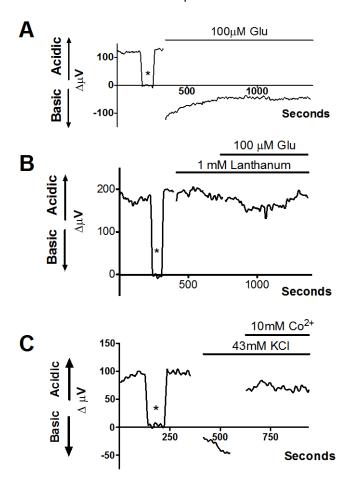


Figure 5. Data acquired by undergraduates using the selfreferencing system. A. A representative recording from an isolated retinal horizontal cell using a self-referencing pH-The initial positive voltage differential selective electrode. suggests a standing proton efflux with the proton concentration being greater adjacent to the cell than 30 µm away. The asterisk here and in subsequent traces denotes a background control in which the microelectrode was moved 200 µm above the cell. The differential voltage measurement reads 0 because there is no difference in proton concentration between the two electrode Glutamate induces an extracellular alkalinization immediately around the horizontal cell indicated by a negative change in the differential voltage measurement due to less protons present adjacent to the cell than 30 µm away. B. A representative trace showing that lanthanum abolishes the glutamate-induced extracellular alkalinization. These results suggest the effect is dependent on activation of a plasma membrane calcium ATPase. C. A representative trace in which depolarization of an isolated horizontal cell with 43mM KCI mimics the glutamate-induced extracellular alkalinization. This change in H+ flux is reversed with cobalt, an antagonist of voltage-gated calcium channels.

and then completing a simple calibration assignment, requiring them to fabricate five pH-selective electrodes and measure their pH sensitivity by immersing them in three saline solutions of different and defined pH (8, 7, and 6). This initial process affords the instructors the important opportunity to discuss the physical principles underlying measurements obtained with ion-selective electrodes and what role the Nernst potential plays in this process. The concept of Nernst equilibria can be dauntingly difficult for students to become comfortable with, and the opportunity to discuss it in such practical detail offers students an unusual opportunity to master this notoriously challenging concept. In this context, we now have an undergraduate experienced with the technique give a presentation on the underpinnings of ion-selective membranes to the other students (a mix of novice and experienced students) during one of our weekly collaborative gatherings, with instructors interjecting comments to emphasize key points and concepts. These presentations have proven very useful for orientation of new students as they join the research

This is also the opportunity to explain the concept of self-referencing, the relatively simple technique that significantly enhances the useful sensitivity of these electrodes by removing the slow electrical drift that is common to all membrane-based ion-selective electrodes. The schematic diagram shown in Figure 3B illustrates the method. A single electrode is placed next to a cell, shown with a diffusional field of protons being emitted that declines in concentration with distance away from the cell. A measurement is first taken at a location next to the cell, then the electrode is moved to a known distance away and a second reading taken. The system then subtracts the second reading from the first, essentially eliminating the slow electrical drift that is common to the two points. At this stage, we typically ask students to consider whether they would see any advantage to having two stationary electrodes in place of the single one moving to make such measurements (the answer is no- the electrical drift, which is random, is different in the two electrodes and so cannot be subtracted out). Students also are asked to consider the speed of movement of the electrode and how its alteration could affect the recordings. Here, students learn that an important consideration for the technique to work is that the rate of movement of the electrode is fast relative to the electrical drift, but not so fast as to stir the solution and reduce or abolish the diffusional gradient of protons. It is also worth mentioning that this simple technique works not only with pH-selective electrodes, but with any membranebased ion-selective electrode (e.g., Na⁺, Ca²⁺, K⁺, Cl⁻), greatly expanding the potential series of experiments that can be undertaken by undergraduates.

Students then begin using the self-referencing system to make extracellular pH measurements from isolated retinal cells. Figure 4A shows one student making recordings in the Faraday cage that houses the microscope, manipulator and head stage of the amplifier, with all the equipment sitting on an air isolation table to remove mechanical vibration. We typically begin by having students conduct a positive control experiment by

recording the responses of an isolated retinal horizontal cell to application of glutamate, the neurotransmitter believed to be released from photoreceptors onto horizontal cells. Cells typically have an initial standing acidic flux, which we have ascribed to Na⁺/H⁺ exchange. The application of glutamate leads to an increase in intracellular calcium, which activates a plasmalemma calcium / H+ ATPase that removes intracellular calcium ions in exchange for H⁺ from the extracellular space, resulting in the observed extracellular alkalinization (Molina et al., 2004; Kreitzer et al., 2007; Jacoby et al., 2012). A representative trace generated by one of undergraduates in the lab is illustrated in Figure 5A. Figures 5B & C show recent supportive data collected by undergraduates at Indiana Wesleyan University in support of this hypothesis. For these experiments, students designed and carried out trials testing the hypothesis that activation of calcium channels and plasmalemma calcium / H⁺ ATPases are necessary to induce the extracellular alkalinization. Figure 5B shows that lanthanum, an agent known to block both voltage-gated calcium channels and plasmalemma calcium pumps, abolishes the ability of glutamate to induce an extracellular alkalinization. Figure 5C shows that depolarization of retinal horizontal cells with high extracellular potassium also causes an extracellular alkalinization, likely by activating calcium influx through voltage-gated calcium channels, and that cobalt, a blocker of voltage-gated calcium channels, eliminates potassium-induced extracellular alkalinization.

Undergraduates flourish technically throughout this experience and also become much more adept at In addition, the experimental experimental design. approach also introduces and emphasizes a number of foundational cellular neuroscience principles. In design of experiments undergraduates engage concepts neuron/glial signaling, synaptic transmission, excitability, signal transduction, and membrane transport, to name a few. In the experimental setup they engage comparative gross anatomy, microdissection, cell culture principles, and osmotic balance of solutions. While acquiring data with the electrophysiological setup students are continually immersed with concepts including electrochemical gradients, pH measurement, and variables addressed in Ohm's law. Such experiential coverage of foundational neuroscience principles cannot be easily recreated in a traditional classroom. The students' foundation in making physiological measurements with the self-referencing methodology also has a positive impact on their ability to understand additional neuroscience-related techniques such as intracellular recordings, voltage-clamping, and fluorescence imaging.

The summer research component of our program plays an important role in enabling the further development of selective students within the lab. This intensive 8-10 week experience is designed according to principles of many Research Experience for Undergraduates programs such as the Biological Discovery in Woods Hole program run at the Marine Biological Laboratory (and for which one of the co-authors serves as a Co-Director), in which students are expected to live, breathe and work as researchers. The undergraduates involved in the program described here have reported that the experience has a strong impact on their technical understanding in addition to a more broad appreciation for scientific inquiry. In subsequent academic semesters students quickly take on leadership roles within the lab, leading discussions in meetings and mentoring other undergraduates. Although this intensified summer experience has great impact on the students who participate, it is limited to a small subset of the undergraduates in the lab. Thus far, 20 students have worked in the lab during the regular semesters, and seven have participated in summer research. This ratio emphasizes the importance of continuing to find ways to translate more of the positive impact of students' development into the experience during the academic year.

student survevs from Outcome araduatina undergraduates and the dissemination of research results acquired by undergraduates lend further support to the positive impact of this experience. The results reemphasize that this is a unique, beneficial learning experience that cultivates excitement for scientific inquiry and is capable of producing scientific results worthy of dissemination. Fourteen graduating seniors participated in this undergraduate research program were asked to complete an evaluation aimed at gaining insight into the unique educational value this experience had, the impact the experience had on development of their critical thinking particularly as it relates to scientific inquiry, and the impact the experience had on development of technical lab competencies. They were asked to record their level of agreement with the statements (using a Likert scale) from 1-5 with 5 being the strongest level of agreement. A few questions were also asked to gather feedback about the motivational impact for scientific research this experience had, and to assess the impact the student's time commitment had on the experience.

Statements comprising the survey are displayed in Table 1. Most of the statements are categorized by their relationship to one of three groups: 1. Student perception of the unique educational value of the experience. 2. Student perception of the impact this experience had on their critical thinking development. 3. Student perception of the experiences impact on development of their technical lab competency. The second column of the table reports average levels of agreement from the 14 reporting students + the standard error of the mean (SEM). The rightmost column reflects the category the statements were grouped into.

Grouped results reveal that students had a high level of agreement with statements suggesting this was a unique, beneficial educational experience. It is worth noting the response to statement 9 of the survey (Table 1); the response of the students suggests that the experience we designed was perceived as being significantly different from other courses and academic activities the students had experienced (2.54 \pm 0.31). The mean level of agreement of students to statements suggesting this experience led to significant gains in their critical thinking development, particularly in scientific inquiry, was 4.60 + The mean level of agreement of students to

statements suggesting this experience led to significant gains in development of their technical wet lab competency was 4.41 + 0.17. Collectively, the quantitative results suggest students perceived the program as a unique undergraduate research opportunity with significant educational impact and leads to both critical thinking development and development of students' wet lab competencies.

The benefit this collaborative research environment has in generating undergraduate excitement, discussion, and learning is in agreement with previously documented benefits of collaboration in research as a whole (Loan-Clarke and Preston, 2002). Further, it is supported by another study investigating the benefit of collaboration in an undergraduate research project in nutrition. This latter

Student Exit Assessment Survey		
Statement	Agreement (1-5)	Category (1-3)
 This collaborative research course significantly enhanced my preparation for my next level of education/career. 	4.57 <u>+</u> .14	1,2
I would strongly recommend this course to other biology undergraduates.	4.71 <u>+</u> .16	1
This course significantly enhanced my understanding of the nature of scientific inquiry.	4.93 <u>+</u> .07	2
 I heavily invested myself in this research experience. 	4.04 <u>+</u> .28	NA
The collaboration with investigators at the University of Illinois at Chicago was an important piece of this collaboration.		1
The weekly lab meeting that included collaborators via Skype contributed positively to my learning in this course.	4.50 <u>+</u> .25	1
 Reading and presenting scientific literature was an important and meaningful piece of my learning outcomes. 	4.57 <u>+</u> .14	2
 I feel that I have good grasp of primary cell culture as a result of my research experience. 	3.93 <u>+</u> .37	3
 The collaboration in this class is similar to other collaborative environments I have experienced during my time as an undergraduate. 	2.54 <u>+</u> .31	NA
 The competency I developed in scientific techniques in this research lab was much greater than competencies I developed in traditional lab science courses. 	4.71 <u>+</u> .16	3
11. My ability to critically evaluate scientific literature and results has improved significantly as a result of my research experience in this lab.	4.79 <u>+</u> .11	2
 I feel that I have good understanding of self-referencing methodology. 	4.50 <u>+</u> .20	3
13. My ability to analyze scientific data has greatly improved as a result of this research experience.	4.50 <u>+</u> .25	3
14. My experience in this lab has changed my opinion of scientific research.	4.34 <u>+</u> .20	NA
15. Completing at least 3 semesters of research is essential to the outcomes I gained from this experience.	3.93 <u>+</u> .27	NA
16. Investing more time (within semesters) in this experience would have further increased what I learned from this experience.		NA
17. My ability to do literature research has improved significantly as a result of this course.	4.14 <u>+</u> .21	2
18.1 feel that a summer research experience would be an important additional improvement to an undergraduate research experience.	4.14 <u>+</u> .25	NA
 Having multiple primary investigators (professors) improved the discussion and quality of laboratory seminar meetings. 	4.36 <u>+</u> .20	1
20. The presence of a research investigator from a major research institution in this laboratory experience creates an improved learning environment unique to my other undergraduate courses/experiences.	170 ± 15	1

Table 1. Student response survey given to graduating seniors where students were asked to rate their level of agreement with the following statements in relationship to the undergraduate research experience. Column 1 lists the statements. Column 2 reflects mean level of agreement + SEM for each statement. Column 3 reflects whether the statements were grouped into the unique educational impact of the experience (1), critical thinking development (2), or lab competency development (3) for further analysis.

study assessed the benefit that collaboration between an undergraduate and graduate student had on research outcomes. The undergraduate report on the experience revealed similar positive learning outcomes in their development of the ability to work in a team, develop their understanding of the process of research, and successfully complete assigned collaborative projects (Dooley et al., 2004).

Undergraduates disseminating their results obtained in research is important for developing the student's ability to analyze and critically evaluate data, organize work, and communicate in both a written and oral manner. Looking at the scholarly production is also a method to assess the ability of an undergraduate research endeavor to make a contribution to a scientific field. The first year of this undergraduate-driven research experience resulted in scholarship at many levels. In this first year, five posters presented at Indiana Wesleyan University's institutional scholarship symposium (2010). Posters from the lab were generated and presented by undergraduates at all levels of experience (first semester through graduating seniors). In addition two students presented a poster at a regional undergraduate neuroscience research symposium (mGluR 2010). A comprehensive study from all of the work from the first year of this experience was presented at the 2010 Society for Neuroscience Conference in San Diego. At the end of the second year six posters were presented at Indiana Wesleyan University's institutional scholarship symposium (2011). In addition one student was a presenting author of a poster at the 2011 Society for Neuroscience Conference. This past fall an additional four undergraduates were authors of an abstract presented at the 2012 Society for Neuroscience Conference. To date data acquired from this experience has contributed to two research manuscripts, one published in the Journal of Neurophysiology (Jacoby et al., 2012;), and a second published in the European Journal of Neuroscience (Kreitzer et al., 2012). Both of these manuscripts have undergraduates as authors. This level of dissemination indicates that this experience is not only of unique educational benefit to undergraduates but also may serve as an effective mechanism for developing undergraduate-driven scholarly production.

As this experience continues to develop it will be informative to continue analyzing student-perceived outcomes from this experience. Comparing perceptions of critical thinking development and technical development between groups who have spent more semesters taking part in research or those who have participated in intensified summer research may shed light to the importance of duration or intensified engagement in different learning outcomes. Analysis of a control group to compare student outcomes with would be impactful in assessing this experience. Participants could be compared with students who do not participate in undergraduate research, with students who participate in a research without the inter-institutional collaboration, or with those students who only participate in summer research.

The qualitative findings from preliminary assessments of this experience suggest that the collaborative

undergraduate research venture described here is a successful mechanism to enhance the "community" between undergraduates and mentors in the lab. The collaborative discussion leads to deeper level processing of the methods and content of scientific inquiry. This experience is also effective in establishing a program that results in undergraduate-driven scholarly production. Collectively this suggests that this novel collaborative research experience may be an effective model to be more broadly utilized at institutions, like primarily undergraduate where research is carried institutions. undergraduates and the aim is to develop and excite undergraduates about the possibilities of scientific research.

REFERENCES

- Bauer KW, Bennett JS (2003) Alumni perceptions used to assess undergraduate research experience. J Higher Educ 74:210-
- Baxter Magolda MB (1999) Creating contexts for learning and self-authorship: constructive-developmental Nashville, TN: Vanderbilt University Press.
- Blackmore P, Cousin G (2003) Linking teaching and research through research-based learning. Educational Developments 4:24-27.
- Brew A, Boud D (1995) Teaching and research: establishing a virtual link with learning. Higher Education 29:261-273.
- Chaplin S, Manske JM, Cruise JL (1998) Introducing freshmen to investigative research: a course for biology majors at Minnesota's University of St. Thomas. J Coll Sci Teach 27:347-350.
- Dooley DA, Mahon RM, Oshiro EA (2004) An undergraduate research opportunity: collaboration between undergraduate and graduate students. J Food Sci Educ 3:8-13.
- Foertsch J, Alexander B, Penberthy D (2000) Summer research opportunity programs (SROPs) for minority undergraduates: a longitudinal study of program outcomes. Counc Undergrad Res Q 20:114-119.
- Healey M (2005) Linking research and teaching: exploring disciplinary spaces and the role of inquiry-based learning. (Barnett R, ed) pp 67-78. McGraw Hill / Open University Press.
- Healey M, Jenkins A (2009) Developing undergraduate research and inquiry. York, UK: The Higher Education Academy.
- Jacoby J. Kreitzer MA, Alford S. Qian H. Tchernookova BK, Naylor ER, Malchow RP (2012) Extracellular pH dynamics of retinal horizontal cells examined using electrochemical and fluorometric methods. J Neurophysiol 107:868-879.
- Kreitzer MA, Collis LP, Molina AJ, Smith PJ, Malchow RP (2007) Modulation of extracellular proton fluxes from retinal horizontal cells of the catfish by depolarization and glutamate. J Gen Physiol 130:169-182.
- Kreitzer MA, Jacoby J, Naylor ER, Baker A, Grable T, Tran E, Booth SE, Qian H, Malchow RP (2012) Distinctive patterns of alterations in proton efflux from goldfish retinal horizontal cells monitored with self-referencing H+-selective electrodes. Eur J Neurosci 36:3040-3050.
- Kuh KD, Chen D, Laird TFN (2007) Why teacher-scholars matter: some insights from FSSE and NSSE. Liberal Education 93:40-
- Loan-Clarke J, Preston D (2002) Tensions and benefits in collaborative research involving a university andanother organization. Studies in Higher Education 27:169-185.
- Lopatto D (2004) Survey of undergraduate research experiences (SURE): First findings. Cell Biol Educ 3:270-277.
- Nagda B, Gregerman S, Jonides J, von Hippel W, Lerner JS

- (1998) Undergraduate student-faculty research partnerships affect student retention. Review of Higher Education 22:55-72.
- Molina AJA, Verzi MP, Birnbaum AD, Yamoah EN, Hammar K, Smith PJS, Malchow RP (2004) Neurotransmitter modulation of extracellular H+ fluxes from isolated retinal horizontal cells of the skate. J Physiol 560:639-657.
- Prince MJ, Felder RM, Brent R (2007) Does faculty research improve undergraduate teaching? An analysis of existing and potential synergies. J Engineering Education 96:283-294.
- Prosser M, Trigwell K (1999) Understanding learning and teaching: the experience of higher education. Buckingham: SRHE and Open University Press.
- Russell SH, Hancock MP, McCullough J (2007) The pipeline. Benefits of undergraduate research experiences. Science 316:548-549.
- Shellito C, Shea K, Weissman G, Mueller-Solger A, Davis W (2001) Successful mentoring of undergraduate researchers: Tips for creating positive student research experiences. J Coll Sci Teach 30:460-464.
- Smith PJS, Sanger RS, Messerli MA (2007) Principles, development applications of self-referencing and electrochemical microelectrodes to the determination of fluxes at cell membranes. In: Methods and new frontiers in neuroscience (Michael AC, ed) pp 373-405. CRC Press.

Received June 18, 2013; revised August 22, 2013; accepted September 05, 2013.

This work was supported by two grants from the National Science Foundation, 0924383 and 0924372, as well as Indiana Wesleyan University's Hodson Summer Research Institute for funding summer undergraduate research studies. The authors thank Jason Jacoby, a graduate student in the Malchow lab, for his willingness to mentor undergraduates in research. We also thank Dr. Mark Messerli of the Marine Biological Laboratory for continued assistance with the selfreferencing systems used in these studies.

Address correspondence to: Matthew A. Kreitzer Ph.D., Dept. of Biology, Indiana Wesleyan University, 4201 S. Washington Street, Marion, IN 46953. Email: matthew.kreitzer@indwes.edu