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NeuroLab Research Experiences: Extending the CURE Design Framework into an Informal Science Setting Dedicated to Pre-College STEM Instruction

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ABSTRACT: Course-based undergraduate research experiences (CUREs) represent distinctive learning environments that are organized around a well-articulated design framework aimed at broadening student participation in scientific research. Among the published descriptions of CURE models that are currently available in the education research literature, the vast majority have been implemented in four-year institutions of higher learning with undergraduate students. In this programmatic article, we utilize the CURE design framework to characterize a highly structured instructional intervention that engages upper-level high school students in basic research that bridges comparative functional genomics and developmental neuroscience. Our goal is to demonstrate the feasibility of using the CURE framework as a uniform reference point for other informal science programs aimed at making life science research accessible to younger learners. We conclude by discussing preliminary data on the program's effects on students' self-efficacy for conducting scientific research, collaborative abilities, and understanding of how scientific knowledge is constructed.

INTRODUCTION

Course-based undergraduate research experiences or CUREs have emerged as a promising strategy to involve all biology learners in conducting scientific research. Although published descriptions of CURE models assume a diversity of forms and target different cognitive, affective, psychosocial, and behavioral outcomes (Dolan, 2016), they are distinguished from more familiar instructional approaches by their ability to engage entire classes of students in generating research findings that accommodate the interests of the scientific community and expand the scientific knowledge base. In this respect, CUREs resemble an integration of independent university internships, which are typically offered by research groups to small numbers of select students who have already developed an interest in science, and more structured university courses that engage significantly larger numbers of students in either prescriptive or inquiry-centered laboratory instruction.

Beyond this basic conceptualization, CUREs are operationally defined by their integration of specific activity-based dimensions that engage students in: 1) science practices; 2) the process of scientific discovery with uncertain outcomes; 3) broadly relevant research that links to a larger body of knowledge (and that is important to stakeholders outside of the classroom); 4) group collaboration; and 5) iterative work that demonstrates how scientific knowledge is built over time across research groups or projects (Auchincloss et al., 2014; Dolan, 2016). Although the frequency and intensity of the activities encompassed by each dimension exhibit considerable variability across courses, this basic framework establishes uniform standards for CURE development and lays the groundwork for studies aimed at identifying robust linkages between specific design elements and desired learning outcomes (a community-level goal that is currently in its infancy; Auchincloss et al., 2014; Linn et al., 2015).

Our interest in CUREs emerged from a 12-year institutional mission to develop model programs that provide upper-level high school students with early exposure to the daily practice of scientific research and early membership into the scientific community as real data contributors (Santschi et al., 2013, Henter et al., 2016). While elaboration of the CURE framework was intended to guide the design and assessment of CUREs for undergraduate students, we recognized its alignment with our ongoing efforts to make scientific research accessible to precollege students. This

goal is especially relevant for groups that are actively assisting high school teachers in developing three-dimensional instructional approaches and classroom learning opportunities that tightly align with the research-based performance expectations encompassed by the Next Generation Science Standards (NGSS Lead States, 2013; NASEM, 2019).

In this report, we use the CURE design framework to characterize the most salient components of an instructional intervention developed in connection with NeuroLab, an education research project funded by the NIH Science Education Partnership Award (SEPA) program. Launched in 2014, NeuroLab is a multifaceted effort that provides novel opportunities for students to adapt research products generated by the Lawrence Berkeley National Laboratory to aid future studies of nervous system development and function in model vertebrate systems. To this end, we recruited the participation of rising 11th and 12th grade high school students in a series of immersive residential summer research institutes that organize mentoring activities, instructional resource design, and active learning strategies around a coherent laboratory workflow that culminates in the identification of new molecular genetic tools to study neuronal connectivity in the developing spinal cord. These interdisciplinary experiences unfold under the direct guidance of scientist instructor-mentors within a specialized biosciences laboratory that maintains the physical resources and collaborative networks necessary to support a wide-range of student-centered research activities.

We anticipate that this program description will help address an important knowledge gap with respect to the processes underlying CURE adaptation (Dolan, 2016), and provide novel insights into how the development of CUREs in an as yet unexplored institutional setting can be further modified to establish connectivity with formal high school instruction and emerging P-16 STEM pipelines. Scientific datasets generated by students through this effort will be presented in a separate manuscript along with a complete description of an open-access informatics platform that we developed for students and mentors to organize, annotate, attribute, validate, and share their data with relevant segments of the scientific community.

PRE-INSTITUTE ACTIVITIES

Student Recruitment. Small cohorts of 10 students are selected to participate in summer research institutes hosted in connection with the NeuroLab program (10 students/institute). A professionally illustrated request for applications containing a brief program description, institute dates, and hyperlinks to the NeuroLab website (www.NeuroLabSEPA.org) is shared directly with teacher partners (many of whom serve a high proportion of underrepresented students). This information is also disseminated via e-newsletters, event calendars, and online directories maintained by the California Science Teachers Association, the Bay Area Biotechnology Education Consortium, the Los Angeles/Orange County Economic Workforce Development (EWD) Biotechnology Center, the San Diego County EWD Biotechnology Center, the San Diego STEM Ecosystem (formerly the San Diego Science Alliance), and the Orange County STEM Initiative. Over the last two project years, residential research experiences were also posted in a searchable database maintained by the Institute for Broadening Participation (www.pathwaystoscience.org), which has developed a suite of online resources specifically aimed at connecting underrepresented students to STEM research opportunities (see Table 1 for student demographics arranged according to gender and ethnic group). At present, our annual recruitment strategy has attracted the participation of students representing 13 states (CA, AZ, HI, LA, IL, IA, MI, FL, NJ, CT, RI, MA, and NH). The vast majority of student applicants indicated that they learned about the NeuroLab program through online web searches or direct referrals from teacher partners who participated in professional development programming hosted by our organization.

Table 1. *Gender and ethnic composition of NeuroLab participants (Cohorts 1-8).*

Student Demographics		
Female	60	(76%)
Male	19	(24%)
African American	4	(5%)
Asian | Pacific Islander	20	(25%)
Caucasian	32	(40%)
Hispanic or Latino	11	(14%)
Mixed Race	1	(1%)
Native American	1	(1%)
Other	6	(8%)
Prefer not to respond	4	(5%)

Recruitment of Teaching Assistants. As discussed in greater detail below, undergraduate and postgraduate teaching assistants (TAs) play central support roles during each NeuroLab institute (1 TA/institute). Referrals for qualified TA candidates are solicited through direct communications with university faculty and department chairs within our partnership network. During the recruitment process, candidates participate in one or more phone interviews with project staff to learn more about the NeuroLab experience and the specific roles that they are expected to assume during each institute. TAs who are selected to participate in the NeuroLab project receive continual guidance on their mentoring strategies during one-on-one discussions with

instructor-mentors. Mentoring guidance is frequently linked to daily briefings with TAs, who provide various forms of information on students' social, interpersonal, and intellectual progress.

Enrollment Process. Admissions guidelines and a password-protected enrollment application are accessible to students through the NeuroLab website. Online guidelines indicate that special emphasis will be placed on selecting students from groups that are historically underrepresented in STEM fields. Applications are maintained on a secure server and capture personal information, academic history and performance (via official transcripts), and short essays (500 words or more) that relate students' academic interests and career aspirations to their expectations for the NeuroLab research experience. During the application submission process, students also provide the name and email address of one or more referees, who automatically receive an online recommendation form that must be submitted to complete a student's application. The form contains a series of response items that enable referees to rate a student's leadership qualities, self-motivation, maturity, and academic abilities (using a 10-point Likert scale), and an open text field for referees to provide specific comments on an applicant's suitability for the program. The enrollment system was configured to provide each applicant with real-time feedback on the completion status of his/her application. It also contains onboard administrative tools that permit our team to track a student's progress in completing his/her application, update the status of each active account and application, and monitor the submission of required documentation.

During the initial phase of the selection process, our admissions committee places considerable emphasis on referee evaluations and prior life science coursework (especially in chemistry and biology). The final selection process is guided, in large part, by the level of passion, intellectual curiosity, and motivation that students convey in their essay responses.

Students who are selected to participate in the program are required to complete three online laboratory safety courses prior to the institute start date. Students also receive login credentials to access learning resources (e.g., virtual seminars, video protocols, review articles) and challenging study questions that reside on a content management system linked to the NeuroLab website. Study questions (S1) are intended to focus independent learning on some of the dominant themes, issues, and concepts that are covered/deconstructed during program lectures and collaborative discussions. As discussed in greater detail below, these questions also form an extremely important focal point for peer-centered learning during each institute. Given the advanced nature of the pre-institute study materials, students are also provided with a guidance document containing practical tips for effective study practices (e.g., time management, organization, reading for comprehension, etc.).

STUDENT RESEARCH BACKGROUND (TECHNICAL DESCRIPTION)

The biological mechanisms by which spinal cord neurons form interconnected networks is a fundamental question in neurobiology that has important implications for the treatment of trauma and degenerative diseases that impair spinal cord function and movement. Efforts to understand this process have benefitted significantly from the targeted delivery of transgenes to specific populations of spinal cord neurons (Bonanomi and Pfaff, 2010). Transgenic technology enables researchers to visualize and manipulate specific populations of neurons to better understand the cellular and molecular factors that govern their development and function. For instance, transgenes can code for fluorescent proteins that illuminate neurons and their processes from the inside when they are exposed to certain wavelengths of light, specially modified proteins that impair the function of cell surface receptors implicated in a particular biological process (e.g., cell fate specification or the guidance of axons to their target cells), and calcium-responsive sensors that emit light when a particular group of neurons is activated.

The targeted expression of transgenes is controlled by regulatory elements (e.g., promoter and enhancer sequences) that are bound and activated by transcription factors present in specific subsets of cells. The rather limited numbers of regulatory elements that are currently available to drive transgene expression in select vertebrate neurons represents a fundamental barrier to future studies aimed at examining nervous system development and function. To overcome this obstacle and expand the repertoire of regulatory sequences available to control the location and timing of transgene expression in embryonic neurons, several approaches have been employed.

One approach exploits the prior identification of evolutionarily conserved regulatory sequences (ECRs) within non-coding genomic regions of phylogenetically divergent organisms. Ranging in length from 200 – 2000 base pairs, these conserved sequences represent candidate enhancer elements that can be experimentally validated for cellular activity by examining their ability to drive reporter gene expression in transgenic mouse embryos (Fig. 1A, inset). Along with related strategies (Visel et al., 2007, 2009), this experimental approach has led to the creation of a comprehensive online library of tissue-specific enhancers that are accessible through the VISTA Enhancer Browser (Visel et al., 2007). Developed and maintained by the Lawrence Berkeley National Laboratory (Berkeley Lab) and the U.S. Department of Energy Joint Genome Institute, the VISTA Enhancer Browser is a public access database that currently contains 2893 in vivo-tested regulatory elements that are organized into searchable data records (https://enhancer.lbl.gov). Each data record aggregates: 1) DNA sequence information (e.g., sequence coordinates, neighboring gene names,

comparative information regarding conservation depth of an element, and the PCR primers used to amplify the fragment); 2) high-resolution digital images of whole-mount transgenic mouse embryos (embryonic day 11.5) showing tissue-specific expression of a lacZ reporter gene; and 3) an anatomic description of the reporter gene expression pattern.

It is important to emphasize here that the majority of validated elements cataloged in the VISTA Enhancer Browser were examined for their ability to drive reporter gene expression in embryonic tissue regions vs. individual cell types (see Fig. 1A, inset). Determining the identity of the specific neuronal cell types in which the elements are active (and the pathways their axons follow) represents an extremely valuable research iteration (see Hadas et al., 2014) that forms the focus of student work during each NeuroLab institute (Fig. 1).

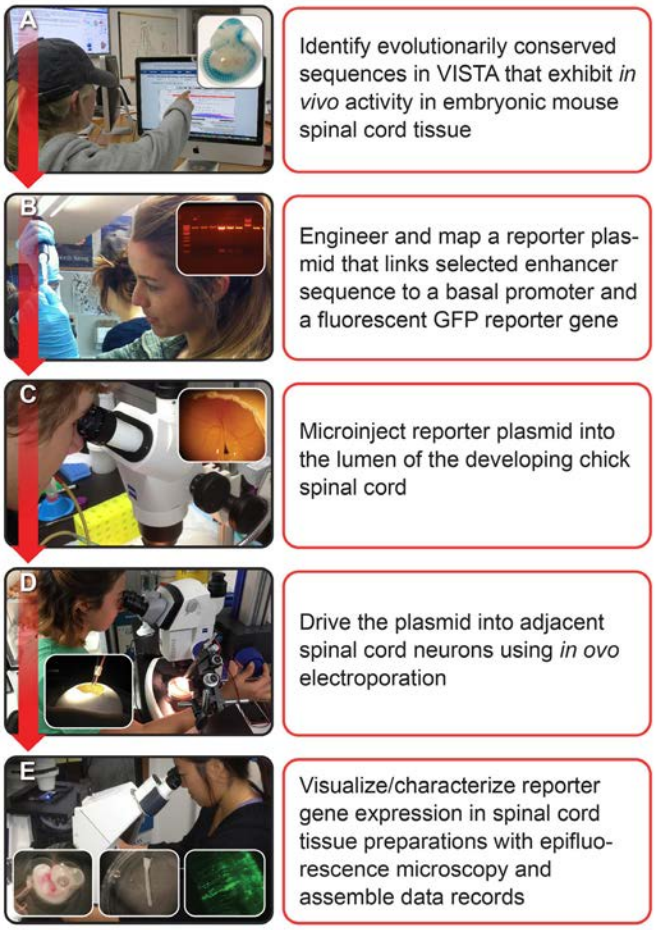

Figure 1. The research pipeline executed by students during NeuroLab research institutes. During more recent institutes, students subclone ECRs with modified ends into an intermediate TA cloning vector. The insert is then shuttled to a destination vector (containing a GFP reporter) by local high school interns and later provided to an upcoming cohort of NeuroLab students for microinjection/electroporation and expression analysis.

PROGRAM DESCRIPTION

General Characteristics and Roles of Instructor-Mentors. Two Ph.D.-level faculty members with strong research backgrounds in neurophysiology and developmental neurobiology play central roles in program design and implementation, both of which are aimed at creating an environment that emulates, inasmuch as possible, a graduate-level learning milieu. During program implementation, their shared scope of influence as instructor-mentors not only converges on knowledge building/knowledge integration and the development of technical proficiency required for students to successfully complete a particular laboratory task or workflow segment, but also on professional socialization and early enculturation into the scientific research enterprise. These mentorship functions emerge within an intimate learning setting where faculty and students (at a 2:10 ratio) participate in every facet of the NeuroLab experience as members of a unified research team. This aspect of program enactment results in an exceptionally high level of mentorship contact that readily lends itself to a group mentorship model (i.e., instrumental and psychosocial support is provided through group discourse rather than isolated interchanges between individual students and an assigned mentor). It also aligns with the highly collaborative nature of the NeuroLab experience as emphasized elsewhere in this report.

Logistics. Each NeuroLab institute is implemented over 10 consecutive days to maintain strict continuity and coherency among different research components and learning activities, which are tailored to challenge students at different levels. A provisional daily schedule is provided to students during the enrollment process to help prepare them for several unavoidably long workdays. Upon their arrival, students are advised that the schedule is subject to revision given the unpredictable nature of scientific inquiry. As shown in Figure 2, the total amount of time that students devote to lec-

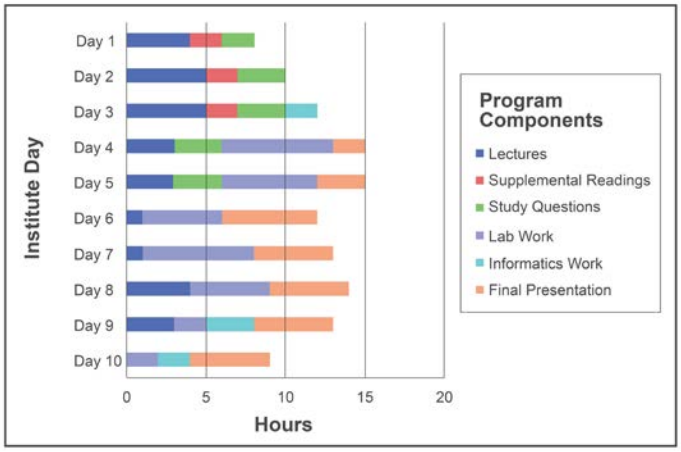

Figure 2. The number of hours invested by students in various program components during each day of the NeuroLab research experience. The values estimated for supplemental readings, study questions, and the final presentation reflect time invested both in and out of the laboratory.

tures, collaborative activities, lab and informatics work, and research communication exceeds the workload of a typical 3-credit, 15-16 week university course.

Students and TAs are housed offsite within a short walking distance from our lab. TAs supervise students during evening breaks and provide various forms of social and mentoring support aimed at promoting group cohesiveness and productive collaborative discourse (see sections below for specific examples).

Instructional Resource Design. Instructional resources primarily consist of mixed-media presentations that blend high quality scientific images and illustrations, molecular simulations and animations, video clips, and other dynamic representations of biological phenomena into a series of learning units (Fig. 3). The development of each unit was tightly anchored to the research logic model presented in Figure 4, which outlines several overlapping knowledge strands that link the project's broader biomedical relevance to research design and expected outputs.

Lectures centered on biomedical relevance begin by highlighting the following overarching program topics: 1) the relationship between mature central nervous system (CNS) function and the formation of neural circuitry during embryogenesis; 2) the role of organizing centers, morphogenic gradients, and intracellular signaling cascades in dictating the fate of developing spinal cord neurons (and the forms and functions that they will ultimately assume in the mature CNS); and 3) the importance of navigational cues and their cognate receptors in altering growth cone architecture and the directionality of axon growth during neuronal circuit formation.

To link this knowledge strand with research design and expected outputs/products, the logic model contains several intervening components that are aimed at helping students recognize deficits in our current understanding of nervous system assembly, the consequent need for new molecular genetic tools to help fill these knowledge voids, and the potential value of newly acquired knowledge for the future treatment of spinal cord trauma or neurodegenerative disease. From our perspective, exposure to the scientific model building enterprise – a prominent feature of our educational approach – is essential for students to sort out and contextualize these important interrelationships. To this end, instructional resources use visual representations of conceptual models to introduce the key biomolecular programs that unfold during neuronal fate specification and axon pathfinding, and their ties to nervous system structure and function. As select components of each model are presented in stepwise fashion by instructor-mentors, students are challenged to make interpretations, propose future studies, and formulate testable predictions based on findings obtained from a diversity of model organisms and scientific approaches (e.g.,

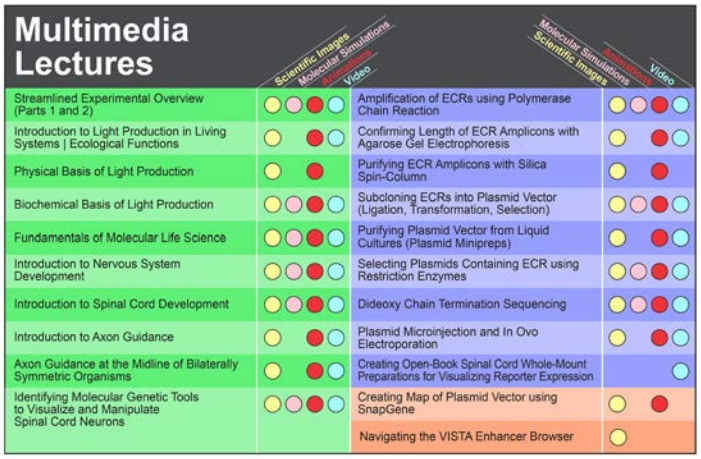

Figure 3. Multimedia lecture units and the types of content introduced to represent scientific processes. Green shading indicates lectures focused on foundational knowledge and the exploration of conceptual/predictive models of relevant biological phenomena. Blue shading denotes lectures focused on the science underlying lab methods and procedures. Orange shading corresponds to activities rooted in bioinformatics (e.g., data retrieval, restriction and plasmid mapping, sequence alignment and analysis, data record assembly, etc.).

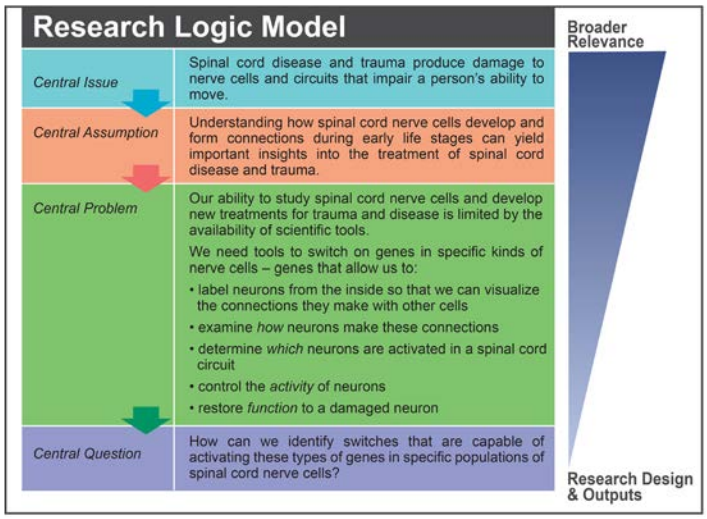

Figure 4. Logic model connecting the project's underlying rationale to research design and anticipated outputs. The overlapping knowledge strands encompassed by this model formed the basis of instructional resource design (see text for details).

detailed anatomical studies, in vitro assay systems, mutagenesis screens, gene knockouts, etc.).

The logic model eventually converges on a central question that forms the basis of students' hands-on laboratory work, which represents an adaptation of a comparative genomics approach utilized by scientists at the Berkeley Lab to identify and experimentally validate the activity of conserved regulatory sequences (see section above for additional details). A series of instructional materials were assembled to facilitate student understanding of the evolutionary assumptions underlying this approach, deconstruct the scientific underpinnings of its component laboratory proce-

dures, and highlight the methodological variations required to iterate this work in an embryonic chick model and thereby generate potentially valuable new information for future studies of spinal cord development.

Implementation of this adapted research strategy ultimately involves the execution of multiple laboratory procedures/protocols that are sequentially linked together in discrete workflow segments with specific intermediate objectives (e.g., the creation of an expression plasmid containing a fluorescent reporter gene downstream of an enhancer sequence, the delivery of the expression plasmid into spinal cord neurons, the characterization of neurons in which the enhancer activity is detected, etc.). Methods-focused instructional resources (Fig. 3, blue shading) were not only designed to help students understand and visualize the physical, chemical, or biological processes that unfold during each protocol, but also to assist them in understanding how the outputs generated from successive protocols relate to one another and the intermediate objective of a given workflow segment. These materials also place significant emphasis on the natural origins of methodological tools that students use to implement their protocols (e.g., marine-derived fluorescent proteins, restriction endonucleases, antibiotics, heat-stable DNA polymerases, etc.), and the biological/biochemical contexts within which they function in the natural world.

Promoting Knowledge Development and Synthesis through Collaborative Group Learning. Given the advanced and varied nature of the material presented to students across lectures and project elements, we adopted a pedagogical approach that conforms to the scaffolded knowledge integration framework (SKIF), which is organized around the following metaprinciples: 1) making science accessible and building upon students' prior knowledge; 2) making thinking visible so that students understand the process underlying knowledge integration; 3) helping students learn from each other; and 4) promoting autonomous life-long science learning (Linn et al., 2014).

In pursuance of these goals, instructor-mentors make extensive use of active learning strategies throughout each institute. In addition to our pervasive use of Socratic questioning (see Paul and Elder, 2008 and references therein) and think-pair-share activities, strategic pauses are often made for breakout discussions and brainstorming sessions that enable students to connect their views to alternative perspectives and build upon each other's understanding of project-related concepts and methods.

The study questions (S1) that students independently complete before their arrival represent another important focal point for peer-centered collaboration and knowledge synthesis. At the end of each day, students are instructed to discuss a particular study question and reach consensus on a detailed response that consolidates the perspectives of everyone in the group. TAs play an extremely important role outside of the lab in moderating discussions so that they unfold with objectivity and inclusiveness, and in accordance with professional standards of courtesy. The following day, one or more students are randomly selected to orally present and defend the consensus response in the presence of instructor-mentors, who provide constructive feedback and guidance on revisions, wherever necessary.

In addition to these group-based learning activities, students are required to develop a 60-90 minute synthesis of their research experience, which they present on the final night of their NeuroLab institute in a format that resembles a public oral thesis defense (i.e., in addition to presenting material, students are challenged with extemporaneous questions from instructor-mentors; S2-S7). Preparation for this high-stakes program component begins with a presentation outline that students submit for review and comment by instructor-mentors before initiating work on talking points and slides. TAs play an instrumental role in the collaborative development process by: 1) referring students to resources that provide general tips on giving scientific presentations; 2) moderating group discussions centered on presentation storyline, structure and content; 3) addressing gaps in students' knowledge; 4) ensuring an equitable division of labor; 5) providing technical assistance on the creation of slide graphics, embedded video, etc.; 6) offering objective feedback on the clarity of talking points and their relevance to a particular presentation segment; 7) guiding students in the selection/creation of graphics that support their talking points; and 8) assisting students in establishing continuity between and among slides.

Instructor-mentors monitor student progress toward a draft presentation through daily briefings with TAs, direct observations of student interactions in the lab, and periodic reviews of slide content. Students receive extensive critical feedback on their draft presentation during each of two practice talks that are scheduled near the endpoint of the NeuroLab experience. During these sessions, instructor-mentors offer suggestions on organization and slide transitions that will improve coherency and bring the presentation into closer alignment with the logic model presented in Figure 4. Students are also encouraged to discard superfluous methodological/technical details that may divert attention away from the more salient features of their overall research approach during the final talk, which is presented in a forum consisting of family members, local educators and school administrators, and area scientists. Apart from its value in facilitating student collaboration and promoting research communication skills, the concluding presentation presents a final opportunity for instructor-mentors to help students demonstrate their depth of knowledge and understanding through rigorous question-and-answer dialog, which is vid-

eo recorded for future analysis of specific learning outcomes (S2-S7). For parents and other audience members, these scientific interchanges also provide a glimpse into the academic rigors of the NeuroLab experience and the intensity of scientific discourse that occurs among students and faculty during each institute.

Student Research Progression. Students are assigned to one of five pairs during the plasmid construction phase of the workflow to assist each other in the proper execution of laboratory protocols. For this initial segment of the lab workflow, students who report a higher level of relevant lab experience (or a greater degree of confidence in their basic laboratory skills) are paired with students who rate themselves as having less experience or lower confidence. For subsequent workflow segments involving the application of highly specialized laboratory skills, participants are randomly assigned to small teams of three-five students to increase the faculty-student ratio and thereby allow a greater degree of individualized supervision. Irrespective of these logistical considerations, NeuroLab currently adopts a conjunctive research approach in which every student performs every component of the lab workflow (i.e., students are not assigned to groups with specialized roles in the completion of any particular laboratory task or protocol).

Consistent with our goal to help students sort out the various forms of scientific information encompassed by the research experience, laboratory work does not commence until Day 4 of each NeuroLab institute, after students have demonstrated an understanding of research design and its connection to the project's broader biomedical relevance and anticipated outputs/research products. At that time, the focus of lectures shifts from foundational concepts and predictive models of relevant developmental processes (e.g., neuronal cell fate specification and axon guidance) to the science underlying various lab procedures (i.e., detailed explanations of how various lab procedures exploit our prior knowledge of physical, chemical, and biological processes to achieve a particular experimental or practical objective).

As indicated above, the plasmid construction segment of the workflow encompasses multiple laboratory procedures/protocols that are linked together in a cumulative sequence (Figure 1, panel B). Several strategies are employed by project staff to increase the probability of student success during this progressive work sequence. In addition to validating/optimizing lab protocols prior to each institute, instructor-mentors ensure that each step of a given procedure is performed synchronously by all student pairs to maintain focus, minimize the occurrence of procedural errors, and simplify corrective interventions by project staff if a deviation is observed or reported. Reagents and consumables required for a given step are distributed to students on an as needed basis to prevent sample mix-ups and other potential pitfalls. Prior to executing a given protocol step, students are also asked to verbalize its associated action (load the supernatant from Step 5 onto a spin column), methodological purpose (to separate plasmid DNA from other biological materials present in the supernatant), and underlying scientific process(es) (specific ions present in the solution enable negatively charged plasmids to form a reversible electrostatic interaction with the silica matrix inside the spin column). This approach is intended to reinforce ideas introduced during methods-focused lectures and further minimize the occurrence of technical errors.

The ensuing segment of the research workflow unfolds in our transgenics lab, which is organized into specialized workstations that enable larger groups of students (5 students/group) to work cooperatively on the delivery of expression plasmids into embryonic chick spinal cord neurons (Figure 1, panels C, D). Every student rotates through each workstation over three consecutive days (~ 4 hours/day) to develop the technical proficiency required to perform each component work task with minimal faculty assistance [e.g., correct embryo staging and handling, egg windowing (to expose embryos), microinjections (to introduce expression plasmids into the fluid-filled lumen of the developing spinal cord), electroporation (to drive plasmid into adjacent spinal cord neurons), and egg sealing (to prevent desiccation of embryos during an additional incubation period)]. Instructor-mentors make extensive use of video protocols and physical demonstrations to assist students in their research goals. Demonstrations are aided by video camera-mounted stereomicroscopes and high-resolution monitors, which enable project staff to model the execution of more difficult techniques, especially those that require the identification of important anatomic landmarks that cannot be visualized with the naked eye. These tools also permit project staff to offer specific forms of real-time guidance to students while they perform various types of work under the microscope (e.g., microinjections, electroporation, and spinal cord microdissections).

The concluding segment of the wet lab workflow engages students in the identification and characterization of neuronal cell types in which a particular ECR is activated (as assessed by expression of a GFP reporter in cell bodies, axons, and growth cones; Fig. 1, panel E). This exciting phase of the project unfolds in our imaging lab, where students work in small groups (3-4 students) to assign provisional identities to labeled spinal cord neurons based on the position of their cell bodies along the dorsal-ventral axis and the trajectory of their axons. Instructor-mentors provide practical guidance in the use of our fluorescence microscope and image analysis software, assist students in relating their observations to the most recently published spatial maps of embryonic neuronal sub-types, and make recommendations on the selection of images that best represent their collective findings.

A publicly accessible workbench and data repository

was developed de novo for students to organize, analyze, annotate, attribute, validate, and disseminate their primary expression data (and corresponding metadata) to the broader scientific community. This resource, which is intended to promote data literacy and foster student ownership of their work, will be described in a separate publication along with datasets generated by students during their research experience.

Building Awareness of the Research Career Pathway and Culture. In addition to guiding knowledge development and student research activities, our scientists discuss a diversity of issues aimed at helping students understand disciplinary norms and other important facets of the graduate and postdoctoral research experience that converge on professional socialization and enculturation into the scientific research community (Table 2). During these largely impromptu discussions, instructor-mentors share information, personal reflections, and anecdotes that highlight many of the interpersonal, financial, and practical aspects of the research career pathway, which is presented to students as a life-long learning process characterized by specific professional and intellectual milestones and achievements. TAs also offer their own personal insights and perspectives on the undergraduate science learning experience during intensive out-of-lab interactions with students.

Guest Speakers. In keeping with our goal to frame NeuroLab in the context of a graduate-level learning experience, researchers from UCSD, USC, or the Salk Institute for Biological Studies are invited to present research in areas that highlight the different scales and dimensions of neuroscience inquiry (e.g., neuroinformatics, the use of MRI and other emerging imaging technologies to reconstruct brain connections, etc.). These experiences introduce students to other societally relevant research questions and the diversity of experimental tools and approaches that research teams adopt to explore them. As guest speakers discuss their data, interpret findings, and present working models, they also demonstrate the iterative nature of the scientific discovery process and its significance in identifying new avenues of inquiry and experimentation.

Guest presentations are developed in consultation with project staff, who provide speakers with specific forms of guidance aimed at making their research accessible to younger students. Instructor-mentors also provide scaffolding during each guest presentation to facilitate understanding of unfamiliar concepts, engage students in scientific reasoning practices, and assist them in recognizing important connections between their NeuroLab work and the research endeavors described by outside speakers. Guest talks are followed by lunch meetings, which provide an unstructured forum for students and guest scientists to interact and discuss a range of career-centered issues.

Exit Interviews. Following the Q&A segment of their presentation, students participate in independent, semi-structured exit interviews with instructor-mentors. These brief (10-15 min.) interactions enable students to reflect on their experience, evaluate their own performance and growth, and discuss program elements that they found to be especially challenging and/or rewarding. They also present an oppor-

Table 2. *Science career topics discussed by instructor-mentors during each institute to promote early professional socialization and enculturation into the scientific research enterprise.*

Research Career Topics
Research opportunities available to undergraduate students
Major milestones along the research scientist career pathway
Common graduate school admission requirements
Stipend and tuition support, subsidized housing, and other financial considerations
Graduate school coursework, lab rotations, comprehensive exams, Ph.D. candidacy, and dissertations
Grade-independent performance expectations
Issues to consider when declaring a thesis/dissertation lab
Factors that research groups evaluate before inviting a graduate student or prospective postdoctoral fellow to join their team
The role of a thesis advisor in shaping a student's research focus and experimental approach
The role of a thesis committee in monitoring the scientific development and professional maturity of students
Sources of intellectual support from thesis advisors, faculty, other graduate students, and postdoctoral fellows
Opportunities to improve oral and written science communication skills
Social and interpersonal issues that influence collaboration and productivity within and across labs
The importance of persistence when confronted with inevitable experimental failures and setbacks
The peer review process as it relates to research articles and grant applications
The need for objectivity when evaluating and responding to critical feedback
The various dimensions and scales of research collaboration

tunity for instructor-mentors to acknowledge each student's contributions to the research effort, and help students relate their experience to the expectations and learning goals that they articulated in their application essays.

ALIGNMENT TO THE CURE FRAMEWORK

As noted above, CUREs are distinguished from traditional and inquiry-based lab courses by the opportunities they provide for students to produce novel findings that are linked to a larger body of knowledge and important to constituencies outside of the classroom. Engagement in collaboration and science practices are also defining features of CUREs, although research aimed at documenting the extent to which students engage in the latter is currently limited (Dolan et al., 2016). In Table 3, we organize specific program elements and student-centered research activities around these defining CURE constructs. In the following section, we present preliminary evaluation data, including student responses to select survey items, that establish congruency between students' perceptions of the NeuroLab experience and our intentions for course design and learning outcomes.

PRELIMINARY FINDINGS

Overview. The NeuroLab project's external evaluation is being conducted by Rockman et al, an independent educational evaluation firm. Students participating in the project complete surveys on the first and last days of each residential research institute, and later at one and six months post-institute. The surveys contain fixed-choice and open-ended questions that are collectively aimed at soliciting students' general reactions to the NeuroLab experience and measuring program effects on students':

- science content and process knowledge spanning the following topic areas: light production in biological systems, basic molecular genetics, model organisms and systems, conceptual models, and developmental neurobiology;
- self-efficacy for conducting research;
- perceived collaboration skills (examined post-institute only); and
- attitudes towards the nature and purpose of scientific research.

Table 3. *Mapping of program elements and research activities to the five CURE dimensions.*

Characteristics of the NeuroLab Experience

CURE Dimensions	
Broader Relevance	• The relevance of student research to future studies of spinal cord development is a prominent and consistent focus of mentor-led instruction, collaborative group discussions, and the final student presentation • Students recognize that the research presents an opportunity for them to receive authorship on digital data records that are ultimately assembled, validated, and published in an open-access informatics platform (and shared with other community-specific databases) • Students are informed that they may be acknowledged in a data release paper describing experimental strategy and collective research findings
Discovery	• Students lack sufficient familiarity with the current body of knowledge to independently define the research purpose of NeuroLab, but they are able to articulate the purpose by the end of the experience, after significant knowledge-building, mentor guidance, and peer-peer collaboration • Students understand that they may produce novel research products (plasmids and corresponding expression data) for others to generate or test new hypotheses related to spinal cord development and/or function • Students recognize that prior findings in an embryonic mouse model limit the number of outcomes that they can expect in a comparably staged chick model (e.g. enhancer activity is expected in embryonic chick spinal cord neurons based on data presented in VISTA, but their anatomical identity is unknown) • Students understand that the workflow is a cumulative process and that a procedural error in one workflow segment can hinder progress in upstream segments
Iteration	• Mentors carefully deconstruct prior research by the Berkeley Lab that establishes the groundwork for students' research efforts • Students identify knowledge gaps inherent to prior work and the value of their work in addressing these deficits • Students recognize that variation in the number of labeled neurons (a likely form of *messy data*) is tied to technical limitations that can be mitigated through additional work by their successors • Students propose additional work that will enhance the value of their initial findings (e.g. the use of antibodies and other probes to determine the molecular identity of spinal cord neurons in which a given enhancer is shown to be active, the detection of enhancer activity in neurons examined at different developmental stages and/or in different spinal cord tissue preparations, etc.).
Science Practices	• Although the research design is pre-established by mentors, students use the strategy employed by Berkeley Lab scientists as a model to delineate the key segments of their own research workflow and its component procedures and objectives • During the knowledge-building phase of the experience (which promotes conceptual understanding of biological phenomena and the science underlying lab methodologies) students engage in multiple science practices that include: asking questions, evaluating models of nervous system development and related processes, and developing/critiquing interpretations of key research assumptions • During the research and research communication phases of the experience, students engage in additional science practices that include: evaluating underlying assumptions of the comparative genomics approach used by Berkeley Lab scientists to identify ECRs, using multiple tools of science, generating/analyzing various forms of nucleotide sequence and neuronal expression data, and communicating their most salient findings
Collaboration	• NeuroLab employs multiple collaborative strategies for students to expose their collective thinking, communicate ideas about their research and its broader societal relevance, and recognize shortcomings in their knowledge and reasoning skills • Mentors present student research as an extension of a highly collaborative effort that involved the participation of scientists with expertise in computational biology, informatics, molecular and developmental biology, and other domains • Students understand that the information shared on VISTA and other open-access informatics platforms is intended to promote additional scientific communication, participation, and collaboration • Students recognize that their online data sharing can facilitate additional collaboration and research extensions

We briefly present preliminary data on the latter three outcomes given their relevance to research on CURE assessment (Auchincloss et al., 2015; Dolan et al., 2016). A more comprehensive description of program outcomes and corresponding assessment scales will be presented in a separate publication, after the current phase of the NeuroLab project concludes.

Science Practices. Recognizing that persistence is one of the *human qualities* associated with scientific practice (NGSS Lead States, 2013), NeuroLab developers composed a series of items to gauge students' ability to persevere in challenging situations. Before and after the NeuroLab experience, students used a seven-point scale to rate their self-efficacy for 15 elements of scientific research (e.g., *I can accurately link different laboratory procedures/protocols in a sequence or workflow that achieves a scientific goal, I can successfully use my scientific knowledge to formulate a question that can be tested through experimentation*, etc.; see Table 4 for selected response items and response scales). Although students reported statistically significant improvements in efficacy on all survey items, they experienced the largest gains in their perceived ability to interpret scientific models, select analytic tools appropriate for a given research aim, and delineate a research workflow/pathway.

Collaboration. On the last day of the NeuroLab research experience, students rated the extent to which they learned 20 skills necessary for interacting productively with members of the scientific community, a major outcome sought by the program's developers (e.g., *learned that the current body of scientific knowledge resides within a community rather than with individual experts/scientists, learned how to productively interact with individual team members who possess varying knowledge*, etc.). Students (*N*= 58) reported moderate to large gains in collaborative skills and their understanding of the dimensions and scales through which scientific collaboration unfolds (refer to Table 5 for selected response items and response scales).

Discovery, Broader Relevance, and Iteration. Students also expressed their perceptions of neurobiology research in a series of open-ended questions that they answered six months post-institute. One item asked students to describe the most valuable thing that they learned from NeuroLab regarding the kinds of issues and problems that neurobiologists explore. Across project years and student cohorts, between 30-40% of participants commented specifically on

Table 4. *Students' shifts in self-efficacy for conducting scientific research, selected items*

Shifts in Self-Efficacy for Conducting Research

Item	*n*	Pre		Post		*Paired samples t*	*p*	Effect Size (Cohen's *d*)
		M	SD	M	SD			
I can successfully select a model organism or model system that is suitable for the experiment I wish to conduct.	49	3.41	1.24	6.06	0.90	13.48	.000	1.93
I can effectively select the appropriate computational or laboratory tool to analyze my results.	54	3.57	1.46	5.87	1.05	10.72	.000	1.46
I can accurately use my scientific knowledge to interpret a scientific model.	58	4.64	1.36	6.31	0.84	10.97	.000	1.44
I can accurately link different laboratory procedures/protocols in a sequence or workflow that achieves a scientific goal.	58	4.22	1.61	6.33	0.89	9.70	.000	1.27
I can successfully use my scientific knowledge to formulate a question that can be tested through experimentation.	58	4.90	1.25	6.17	0.88	9.06	.000	1.19

(N = 6 cohorts, 58 students | Max value = 7). Scale: (1) Cannot do at all; (4) Moderately confident I can do; (7) Highly certain I can do. For unfamiliar activities, students could also select I've never heard of this/ I've never done this.

Table 5. *Students' gains in selected collaboration skills*

Gains in Collaborative Skills

Item	Mean	SD
Learned that the current body of scientific knowledge resides within a community rather than with individual experts/scientists	3.76	0.51
Learned that scientific knowledge is shared with a global community of scientists	3.69	0.54
Learned that ideas introduced at the start of a collaborative effort may assume a very different form than in the end of a collaborative effort	3.67	0.54
Learned how to productively interact with individual team members who possess varying knowledge	3.59	0.62
Learned how to assume an active role in the work being conducted by the group/team as a whole	3.55	0.51

(N = 6 cohorts, 58 students). Scale: (1) no gain, (2) small gain, (3) moderate gain, and (4) large gain. Ratings were obtained at a single time point post-institute.

current knowledge gaps and/or the numerous opportunities available for research discovery:

> *The most valuable thing that I learned about issues that neurobiologists have is that society assumes that neurobiologists know more than we actually do. There is still so much to learn and understand; we are barely scratching the surface. This is why we need students to be exposed to these opportunities to see all that they can do.*

> *Because neurobiology is so complicated and hard to study, one of the biggest issues of neuroscience is simply lack of data. It takes a lot of work to make any small amount [of] progress in the field, especially since it's so new. We don't even have a complete map of the connectome for all but the simplest organisms.*

Students from Cohorts 3-6 responded to another series of questions about NeuroLab approximately one month following each institute. One item asked students if they thought they were generating professional quality data to the scientific community. All students responded in the affirmative, with some students noting the novelty of their results and the importance of data sharing:

> *I did feel like I was generating profession[al] quality data. We learned that a database was being created that allowed for a pathway for student data like ours to enter the scientific world (such as the cell image library). That legitimized a lot of our hard work.*

> *I did, as I saw our research building off of other data and going directly into a public database for other scientists to use. Furthermore, our specific data demonstrated a neuronal pattern never witnessed before, and we felt like excited and like our work had true value.*

In their responses to the same question, other students commented on the biomedical relevance of their work and/or the role that iteration plays in the scientific enterprise:

> *I did feel like I was producing professional quality data. We learned how our research relates to certain spinal [cord] diseases, and because these diseases are very relevant today, our data was valuable.*

> *I did feel like I was generating professional quality data to the scientific community because although we based our research off someone else's research we had a different end product which people in the scientific community can use.*

Summary. Across three years and six cohorts of NeuroLab participants, preliminary evaluation data consistently demonstrate that exposure to an immersive, research-based exploration of developmental neuroscience increased students' collaborative abilities, self-efficacy for conducting scientific research, persistence on challenging tasks, and attitudes towards science (Annual Evaluation Report, Patel and Bass, 2018, p. 19). When mapped onto the CURE dimensions, these results suggest that NeuroLab students not only gain experience in a diversity of hard and soft skills required for success in professional research settings, but they also develop a more realistic and nuanced understanding of how scientific knowledge is constructed.

DISCUSSION

The development of authentic science experiences that better reflect what scientists do and how they think is a widely recognized goal of science education reform directives (AAAS, 2011; NGSS Lead States, 2013). In our experience, however, conceptions about the authenticity of research experiences – particularly those involving high school students – vary considerably among relevant stakeholder groups (e.g., students, teachers, and members of the broader scientific community), an observation supported by prior research (see Spell et al., 2014 and references therein). In light of these inconsistencies, we utilized the five dimensions of a widely accepted design framework to characterize the most conspicuous elements of the NeuroLab model.

As noted in a recent review of published CURE models, the information and ideas that students learn in undergraduate research experiences are often fragmentary, which may reinforce inaccurate perceptions of the nature of science (Linn et al., 2015). To provide NeuroLab participants with a more coherent picture of the scientific inquiry process, we exploited insights gained from the learning sciences on how to promote integrated learning. To this end, the SKIF (Linn et al., 2004) was superimposed on the CURE framework during program design and enactment to help younger students with limited science backgrounds: 1) connect knowledge acquired through high school coursework to new and sometimes complex information that is rooted in a variety of knowledge strands and science domains (e.g., molecular genetics, comparative genomics, developmental neurobiology, informatics, etc.); 2) understand the dynamic interplay of experimental design/tool selection, data analysis and interpretation, model-building and revision, and research communication; 3) engage in a spectrum of science reasoning practices, particularly those centered on the evaluation of conceptual models; and 4) envision their future roles and responsibilities as members of a scientific social network. Given the complex interrelationships that exist among these learning objectives, the importance of intensive mentorship for knowledge integration and positive learning outcomes cannot be overstated.

Among the positive learning outcomes observed in our preliminary analyses, self-reported gains in collaborative abilities warrant special emphasis given the prominence of collaboration not only in our CURE model (Table 3), but also in the larger social context of science. Based on open-ended response data, we attribute these gains to complementary

program components requiring intensive peer-reliance, most notably the development, oral defense, and revision of consensus-level study question responses, and the cooperative design/delivery of a culminating oral presentation that integrates different knowledge strands of our research logic model (Fig. 4). Interestingly, when commenting on these components of the NeuroLab experience in post-surveys, students reported some of the same challenges that early career investigators encounter in their own efforts to establish and maintain productive collaborations with faculty peers (see Mediati, 2017 for examples). These include contribution pressure (*there were times that I felt like I wasn't contributing enough to group*), personality clashes (*I remember having some problems with group work … there were times when people including myself didn't listen to the opinions of others*), and maintenance of group focus (*during the group presentation, we had many conflicting opinions and ideas*). At the same time, students collectively acknowledged the rewards of overcoming these challenges, which included intellectual support (*solving a problem by yourself is a difficult task but it is eased by having a community of passionate individuals who can help you)*, self-motivation (*group work challenged me to work harder)*, personal knowledge development (*I never realized that one could learn so much from explaining concepts to others, or having others explain concepts to you*), and the perpetuation of scientific discovery at large (*from our own experiences in the lab and the guests that spoke about their research, I was able to see that discoveries are most often made while utilizing the knowledge and expertise of others*). The extent to which these pedagogical program elements contributed to observed gains in content knowledge and other positive outcomes will be examined in our final program analyses.

As noted in a recent meeting report on CURE design and assessment (see Auchincloss et al., 2014), scientific research is characterized by a diversity of practices, many of which form – to varying degrees – an important focal point of NeuroLab's discovery science-based research model (Table 3). These include formulating questions, constructing and evaluating models, proposing hypotheses, designing research plans, selecting appropriate methodologies and protocols, utilizing scientific tools, collecting and analyzing data, identifying meaningful data variability, developing and critiquing interpretations and arguments, and communicating research findings.

Evidence of student gains in their development and/or execution of science practices is currently inferred from preliminary self-efficacy data. It is interesting to note that students reported some of the highest gains in areas relevant to research design. Because the development of NeuroLab's multifaceted research plan is critically reliant on expert-level scientific and technical knowledge, the involvement of precollege students in the de novo design of their research plan (and in the selection of tools necessary to implement the plan and its component methods/protocols) was an unrealistic goal for program enactment. However, as indicated in Table 3 and elsewhere in this report, students were challenged to accurately articulate the purpose of the tools/methods that were pre-selected by instructor-mentors to pursue the program's predefined research plan, the rationale underlying tool/method placement in a given workflow segment/sequence, and the function of a workflow segment in achieving a particular outcome. During lectures centered specifically on research design, they were also challenged to propose adaptations to the Berkeley Lab research plan that would enable them to extend its findings in an embryonic chick model system.

NeuroLab's reliance on a pre-determined, discovery science-based research plan also fosters significant gains in scientific reasoning practices that are typically associated with more open-ended, hypothesis-based research (e.g., formulating testable questions, interpreting scientific models, etc.; see Table 4). We ascribe shifts on these measures to our deconstruction of scientific models relevant to students' research progression, and the scaffolding provided to help students recognize how their research products can be utilized in future studies to deepen our understanding of spinal cord assembly.

We acknowledge that in its current form, our early-stage CURE model engages a limited number of academically advanced and highly motivated students who have already developed a broad interest in science or medicine (a limitation that we seek to overcome through program iteration in broader educational contexts as discussed below). Extending residential experiences to students with more mixed interests and academic performance histories would undoubtedly require additional instructional time and scaffolding, which would in turn increase the duration of each institute and the costs associated with student housing, meals, and other factors. Restructuring NeuroLab so that it unfolds in our facility over a full semester or academic school year (as a non-residential experience) is a program iteration that we considered to mitigate these financial considerations and provide ample instructional time to effectively engage more mixed cohorts of students. This strategy would also enable our team to examine the extent to which key learning outcomes are affected by program intensity and the conceptual continuity afforded by a short duration format. On the other hand, insurmountable constraints imposed by laboratory space restrictions and commuting distance would still limit the total number of students that our group could realistically accommodate in a given calendar year.

In considering other nonresidential strategies for scaling, we favor a more holistic iteration that not only broadens student access to the NeuroLab experience (in terms of numbers and inclusivity), but that also improves the instruc-

tional practices of teachers who are seeking clear models to confront difficult educational challenges imposed by NGSS adoption. To this end, we will leverage prior work on a related biodiversity genomics project (Santschi et al., 2013; Henter et al., 2016) to design a professional development and curriculum extension aimed at adapting and integrating didactic and experimental elements of the NeuroLab research experience into life science coursework offered at partner high schools throughout the region. This new effort will be aided by the teaching and learning resources already developed in connection with the current project, and the inherently modular nature of the program's laboratory workflow, which readily divides into discrete segments (Fig. 1) that can be completed through the collective and coordinated contributions of student groups operating within a distributed regional network (e.g., students enrolled in high school coursework at partner schools and local student interns operating under the supervision of scientists in our own lab). We are also developing more introductory and standalone lab workflows to help lower the technical barrier of entry into the NeuroLab extension and promote early successes that teachers and students can build upon through their continued participation in the project. We anticipate that this approach will provide valuable insights for practitioners seeking innovative strategies to expand P-16 STEM pipelines by connecting formal and informal science instruction.

ASSOCIATED CONTENT

There are seven supplemental documents uploaded with this manuscript, including a set of study questions and 6 videos excerpts obtained from student culminating presentations.

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ABBREVIATIONS

CNS: Central Nervous System; CURE: Course-based Undergraduate Research Experiences; EWD: Economic Workforce Development; SEPA: Science Education Partnership Award; SKIF: Scaffolded Knowledge Integration Framework; TA: Teaching Assistant

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