

MINIREVIEW – Professional Development

Course-based undergraduate research experiences in molecular biosciences—patterns, trends, and faculty support

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One sentence summary: Engage your students in science through course-based undergraduate research experiences—an overview of the laboratory techniques and inquiry-design elements of peer-reviewed laboratory activities in life sciences.

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ABSTRACT

Inquiry-driven learning, research internships and course-based undergraduate research experiences all represent mechanisms through which educators can engage undergraduate students in scientific research. In life sciences education, the benefits of undergraduate research have been thoroughly evaluated, but limitations in infrastructure and training can prevent widespread uptake of these practices. It is not clear how faculty members can integrate complex laboratory techniques and equipment into their unique context, while finding the time and resources to implement undergraduate research according to best practice guidelines. This review will go through the trends and patterns in inquiry-based undergraduate life science projects with particular emphasis on molecular biosciences—the research-aligned disciplines of biochemistry, molecular cell biology, microbiology, and genomics and bioinformatics. This will provide instructors with an overview of the model organisms, laboratory techniques and research questions that are adaptable for semester-long projects, and serve as starting guidelines for course-based undergraduate research.

Keywords: course-based undergraduate research experiences; molecular biosciences; biochemistry and molecular biology; molecular cell biology; microbiome; genomics and bioinformatics

INTRODUCTION

The ‘-omics’ era within life sciences research has resulted in an explosion of molecular data, transforming the complexity of analyses required to interrogate the underlying trends. To make sense of this vast network of knowledge, students need more than just a good memory—training in critical reasoning, problem solving and analytical skillsets are crucial for identifying patterns and extracting meaningful findings amongst this sea of information. The Boyer commission report established the importance of making research-based learning the standard experience

in higher education (The Boyer Commission 1998), which has since been echoed by BIO 2010 (National Research Council [NRC] 2003), and more recently the Vision and Change report (AAAS 2011). To put these recommendations into action, ongoing meetings between faculty members and pedagogical experts have resulted in the development of shared learning resources, and the dissemination of effective models of implementation and best practice guidelines (Wood 2003; Woodin, Carter and Fletcher 2010; Auchincloss et al. 2014). Instructors have collectively moved away from didactic models of transmission towards active student-centered approaches in the form of

group problem solving, case studies, inquiry-based laboratory classes and interactive computer exercises (Handelsman et al. 2004; Wood 2009). Amongst these initiatives, particular emphasis has been placed on the value of engaging students in the scientific process through inquiry-based learning and undergraduate research experiences (URE).

Inquiry-based learning can take place across a continuum of student responsibility, ranging from simple verification exercises via cookbook-style laboratory classes to an immersive apprenticeship-style URE (Weaver, Russell and Wink 2008). Students are challenged with inquiry-driven questions in laboratory classes, the answers to which are unknown to them. These questions may not be innovative or of interest to a broader audience, but the inherent value of this teaching approach lies within the students' integration of cognitive problem-solving skills used by scientists into their learning (Auchincloss et al. 2014). Inquiry-based learning has been shown to improve student performance, processing skills and attitudes towards science as compared to didactic instruction (Lord and Orkwiszewski 2006). When comparing the impact of research-based experiences to traditional cook-book laboratory classes, students who complete research experiences demonstrated higher confidence and enthusiasm towards research (Brownell et al. 2012) with significantly higher learning gains in analytical skills, experimental planning and result validation than their cook-book laboratory classmates (Rowland et al. 2012).

The majority of published examples of inquiry-based learning in biology (as reviewed by Adams 2009; Healey and Jenkins 2009; Beck, Butler and da Silva 2014) revolve around guided and open models of inquiry, where instructors limit the number of variables students can control in their investigations. As of 2014, only 25% of published inquiry-based learning exercises in biology involved authentic open-ended research in the form of URE (Beck, Butler and da Silva 2014), where the inquiry-based learning revolves around research questions that are of interest to the broader scientific community. A survey of 1135 students across 41 universities and colleges revealed that URE participation led to increased learning gains in understanding the processes of research and problem solving, working independently, interpreting and analyzing data, integrating theory and practice, as well as laboratory and communication skills (Lopatto 2004). URE engagement has been correlated with an increase in GPA (Fechheimer, Webber and Kleiber 2011), and connected with graduate school enrollment (Lopatto 2007; Russell, Hancock and McCullough 2007), retention (Hathaway, Nagda and Gregerman 2002) and overall success (Nnadozie et al. 2001).

UREs are commonly offered using the apprenticeship-style model, where individual students join a laboratory to work on an ongoing research project under the close one-on-one guidance of their faculty supervisor. Despite the clear benefits, this model of undergraduate research is not designed to accommodate large class sizes (Wei and Woodin 2011), and alternative modes of research engagement involving collaborative group work (Carson 2007) and peer-mentoring (Borgon, Verity and Teter 2013) have emerged to fill the void. Course-based undergraduate research experiences (CUREs) represent the most scalable version of undergraduate research currently documented in the literature, which are defined as modules where students address research questions, the answers to which are unknown to both students and instructors and of interest to the broader community (Auchincloss et al. 2014). CUREs are built into the core learning activities of undergraduate coursework, thereby allowing students with personal or financial burdens to access research opportunities during the semester rather than through unpaid sum-

mer internships (Bangera and Brownell 2014). CUREs commonly feature simple protocols for students to collect data, a central dataset to which all students can contribute their findings, hypothesis-driven exercises in data analysis and validation, and authentic assessment tasks focusing on scientific communication of novel findings (Kloser et al. 2011). CURE participation can promote learning gains in analytical research skills (Brownell et al. 2015), collaboration and networking (Hanauer and Hatfull 2015), improved attitudes towards scientific careers (Harrison et al. 2011), and is positively correlated with higher education graduation rates (Rodenbusch et al. 2016). Moreover, a 4-year longitudinal study of more than 1000 undergraduate students revealed similar self-reported learning gains across both apprenticeship-style UREs and CUREs (Shapiro et al. 2015).

CUREs are designed to accommodate large classes through systematic integration throughout the undergraduate curriculum; therefore, CURE implementation is inherently resource intensive and involves many stakeholders. Instructors must source the infrastructure and equipment necessary to run research-based laboratory sessions (Wood 2003; Desai et al. 2008), address the diversity in technical expertise for students entering lower-level CUREs (Butler et al. 2008) and deliver training in research mentoring for inexperienced teaching assistants (Dolan and Johnson 2010), all while delicately balancing instructor workload allocations (D'Avanzo 2013; Moore and Teter 2014). In a study surveying 279 instructors across 534 biology courses spread across liberal arts, comprehensive and research universities: the long lead time necessary for faculty to develop novel ideas for authentic research experiences acts as the main disincentive to CURE implementation (Spell et al. 2014). Similar themes emerged through interviews with experienced CURE implementers in life science courses, where logistics, time and financial constraints, and the uncertainty in adapting research into the CURE format were identified as the main barriers (Shortlidge and Brownell 2016).

This minireview will examine CUREs through the lens of time-poor faculty members looking for ideas to develop new research experiences for their students, and provide an overview of inquiry-based laboratory exercises for introductory biology courses. These laboratory activities span across the research-aligned disciplines of biochemistry, molecular cell biology, microbiology and bioinformatics, collectively under the umbrella of molecular biosciences, and focus on peer-reviewed exercises published in bioscience education journals with sections dedicated to novel curricular resources. Patterns and trends in these laboratory-based learning activities will be highlighted, and the adaptability of the exercises towards research questions in novel CUREs will also be considered.

RECOMBINANT DNA TECHNOLOGY

Recombinant DNA technology represents a common point of entry into inquiry-based laboratory classes. Students design PCR primers targeting a gene of interest, prepare reactions for PCR amplification, set up restriction digest and ligation experiments for the amplified DNA fragments, and verify the cloning of recombinant plasmids through gel electrophoresis and DNA sequence analysis. The sequential nature of these experiments highlights the importance of controls at each step, providing students with a system where troubleshooting and incremental optimization are vital for success. Students have applied molecular cloning techniques towards many diverse research questions, including genes implicated in antimicrobial resistance

(Robertson and Phillips 2008), tissue proliferation in Burmese pythons (Harvey et al. 2014), immunosuppression in melanoma cells (Hargadon 2016), blood clotting and wound repair in vertebrates (Bornhorst, Deibel and Mulnix 2004), and novel vaccine targets against bacterial urinary tract infections (Wang et al. 2012). To facilitate the detection of gene products, the genes are cloned into plasmids that co-express a variety of reporter genes and epitopes, including lacZ, antibiotic resistance cassettes, luciferase, 6xHis, GFP and GST tags. Students apply these skills towards authentic research questions from an ongoing research project, and the student-generated recombinant plasmids are of immediate value to the affiliated researchers. Moreover, the modest cost of reagents and wide availability of PCR machines and agarose gel equipment in teaching laboratories improves the accessibility of inquiry-based molecular cloning techniques.

PROTEIN EXPRESSION AND PURIFICATION

Following on from cloning novel plasmids that encode genes of interest, students can characterize plasmid libraries generated by research laboratories to express and purify novel proteins of interest. The experimental workflow involves transformation of plasmids into cells (most commonly bacterial expression systems), induction of protein overexpression, detection of protein levels through SDS-PAGE and western blotting, protein purification via gel filtration, ion-exchange and/or affinity chromatography, and functional assays to measure protein activity. Each protocol within protein chemistry has many variables that can be optimized, including incubation times, reagent concentrations and choice of buffer solutions, and students can be given a high degree of autonomy to survey the literature in search of optimal experimental conditions for their protein of interest (Gray et al. 2015).

Students can be allocated a protein of interest to work on, or choose from a subset of closely related novel proteins, focusing on targets with enzyme activity that can be easily measured. Published examples of inquiry-driven protein chemistry activities include Taq polymerase (Bellin, Bruno and Farrow 2010), malate dehydrogenase (Knutson et al. 2010), *Escherichia coli* CMP kinase (Garrett et al. 2015), *Helicobacter pylori* urease (Farnham and Dube 2015), protein tyrosine phosphatase 1B (Lipchock et al. 2017) and inosine triphosphate pyrophosphatase (Kreiling et al. 2011), all of which have enzyme kinetics that can be measured through PCR and spectrophotometric assays.

This mode of inquiry neatly couples with site-directed mutagenesis experiments, where students generate mutant plasmid libraries useful to research laboratories by systematically mutating individual protein residues (Bellin, Bruno and Farrow 2010)—each mutant protein is then expressed, purified and characterized to determine the amino acid residues involved in the enzyme activity of the wild-type protein (Rasche 2004). Given the iterative nature of the protocols involved, CUREs involving site-directed mutagenesis are scalable in the total number of mutants generated per semester (Lefurgy and Mundorff 2017), and therefore have great potential for contributions to authentic research. Students have been able to participate in the novel study of proteins implicated in diabetes and obesity (Lipchock et al. 2017), neurodegenerative disorders (Brame, Pruitt and Robinson 2008), transcriptional regulation linked with cervical and endometrial cancer (Shanle, Tsun and Strahl 2016), inherited colorectal cancer (Gammie and Erdeniz 2004) and naturally occurring mutations in the human tumor suppressor protein p53 (Hekmat-Scafe et al. 2017). Instructors have also adapted pro-

tein biochemistry learning activities for the analysis of biological networks—two-hybrid protein interaction systems in both yeast (Gammie and Erdeniz 2004) and bacteria (Cardinale 2011) have been described for undergraduate laboratories, and recently a systems biology CURE conducting proteomic analyses of bacteria with unknown metabolic potential using multidimensional liquid chromatography coupled with tandem mass spectroscopy (LC-MS/MS) was published (Kappler, Rowland and Pedwell 2017).

MOLECULAR CELL BIOLOGY

Laboratory activities in cell biology can highlight the phenotypic impact of molecular events across different cell systems and model organisms, demonstrating key threshold concepts in introductory courses. Students can select techniques from a diverse toolkit to initiate changes at the cellular level, including the addition of growth factors (Bugarcic et al. 2012) and pathogen-associated molecular patterns (Gunn et al. 2013) to stimulate cell signaling, and incubation with pharmacological agents to regulate the activity of the actin cytoskeleton (Howard and Miskowski 2005), endocytic uptake (Ledbetter and Lippert 2002; Bugarcic et al. 2012) and apoptosis (DiBartolomeis and Moné 2003; Srougi and Carson 2013; Byrd 2016). Coordinated control of gene expression can also be conducted by students using homologous recombination for bacterial cells (Li et al. 2017), short-interfering RNA (siRNA) for *Caenorhabditis elegans* (Cox-Paulson et al. 2012; Kowalski, Hoops and Johnson 2016) and mammalian cells (Birnbaum et al. 2010), and single-guide RNAs via the CRISPR/Cas9 pathway to delete *Drosophila* genes in the undergraduate laboratory (Adame et al. 2016).

Membrane transport in fibroblast and epithelial cells have been demonstrated to be sensitive to drug inhibitors and growth factor stimulation, the impact of which can easily be measured through the uptake of fluorescent markers (Ledbetter and Lippert 2002; Bugarcic et al. 2012). The effects of antitumor drugs on cell division and motility can be assayed using immunofluorescent labeling of the cytoskeleton, coupled with cell-counting via hemocytometers, and Bradford assays to quantify total protein levels for each experimental condition (Howard and Miskowski 2005). Other complex cellular processes such as inflammation (Gunn et al. 2013), cell differentiation (Birnbaum et al. 2010) and apoptosis (DiBartolomeis and Moné 2003; Srougi and Carson 2013; Byrd 2016) can all be investigated in CUREs by choosing end-point assays that examine the presence or absence of biomarkers using a combination of microscopy, real-time PCR, SDS-PAGE and western blotting. Cell-based assays have consistently been used for high-throughput testing of novel drugs (Shoemaker 2006) and genome-scale knockout screening (Erfle et al. 2007; Shalem et al. 2014); their scalability is therefore ideal for CURE implementation, especially if instructors can collaborate with researchers to gain access to novel drug compounds and siRNA libraries.

GENOMICS AND BIOINFORMATICS

The introduction of genomics and bioinformatics research into life sciences curricula has been the result of many meetings and cross-institutional collaborations over the past two decades (Dyer and LeBlanc 2002; Lopatto et al. 2008; Smith et al. 2015). Much of the work involved the vertical and horizontal integration of genomics and bioinformatics learning activities across introductory, intermediary and advanced level courses (Furge et al. 2009), and defining distinct skill-based learning objectives

for both biology and computer science students (Dyer and LeBlanc 2002). Technology and open-source bioinformatics databases are continually being revised and updated, so educators largely rely on the stable suite of tools provided by the National Centre for Biotechnology Information (NCBI), Swiss Institute of Bioinformatics and the European Bioinformatics Institute created by the European Molecular Biology Laboratory. Within a research context, students should be able to utilize Basic Local Alignment Search Tool (BLAST) algorithms (e.g. BLASTp, tBLASTx); annotate DNA and protein sequences (Furge et al. 2009); identify genetic elements such as promoters, open reading frames, phosphorylation sites and signal peptide cleavage sites (Brown 2016); perform multiple sequence alignments to generate phylogenetic trees (Campo and Garcia-Vazquez 2008); and corroborate gene expression profiles and protein structural data across different databases (Makarevitch, Frechette and Wiatros 2015; Melloy 2015; Brown 2016). Equipped with these core competencies, undergraduate students have been able to actively contribute to genomics research. Through CURE participation, students have curated gene entries for novel plants that were published in NCBI Genbank (Lau and Robinson 2009), developed novel genetic maps for maize gene mutations isolated across different phenotypes (Makarevitch and Kralich 2011), participated in novel phage genome annotation and discovery from soil and mycobacterial infections (Hanauer et al. 2006; Pope et al. 2011; Staub et al. 2016), produced hundreds of manually curated gene models from *Drosophila* dot chromosomes (Leung et al. 2010; Shaffer et al. 2010) and characterized novel micro RNA sequences which led to 45 undergraduate authorships across three peer-reviewed articles (Smith et al. 2015).

The availability of genomic data has exponentially increased along with the advances in massively parallel next generation DNA sequencing techniques, and the Genomics Education Partnership (Lopatto et al. 2008; Boyle 2010) along with the Integrated genome and metagenome comparative data analysis system (IMG/M) (Chen et al. 2016) have provided novel genomic sequences for use in undergraduate research. Students conducted open reading frame analyses and BLAST searches to map the expression of hypothetical proteins in Archaeal genomes (Beagley 2013), as well as metabolic reconstructions for unknown bacterial species (Reed and Richardson 2013). Molecular phylogeny techniques can be applied towards comparative genomics by constructing sequence alignments, distance matrices, evolution models and phylogenetic trees optimized for maximum-likelihood, neighbor-joining and maximum parsimony functions (Campo and Garcia-Vazquez 2008); students have compared different *E. coli* O157:H7 strains following an outbreak, and determined the validity of new molecular diagnostic tests based on evidence of horizontal gene transfer (Baumler et al. 2012; Klein and Gulsvig 2012). The value of integrating whole genome analyses into learning activities greatly expands the possibilities for instructors to explore novel research questions in CURE development.

CITIZEN SCIENCE AND MICROBIOMES

Citizen science projects—where members of the general public are recruited as coinvestigators in research—have risen in popularity as scientists turn to crowdfunding efforts to support novel projects. There are many parallels between citizen science and CUREs—both are designed to accommodate large numbers of participants, all of whom use simple methods for data collection with low technical expertise requirements to contribute to

authentic research (Kloser et al. 2011; Council and Horvath 2016). Studies into the microbiome—all of the microorganisms that can be found within a specific environment—integrate molecular biology, microbiology and phylogeny techniques, relying upon large sample sizes to obtain an accurate representation of bacterial diversity. Microbiome studies are therefore optimal projects to adapt for novel CUREs involving many students, and will become increasingly common place as personal microbiomes become linked with individualized medicine and sequencing costs come down (Hartman et al. 2016).

The workflow for microbiome projects involves student isolation of bacterial genomic DNA from chosen body sites or environmental locations, PCR amplification of the 16S rRNA gene for sequencing using the Illumina Miseq platform, identification of relative abundance of bacterial taxa identified through operational taxonomic units (OTU) tables, and bioinformatics analyses to compare the bacterial diversity across different sites or locations. The human microbiome has been characterized for student and general public volunteers in projects mapping the gut, belly button and oral microbiomes (Wang et al. 2015; Debelius et al. 2016; Garbarino and Mason 2016). Similar approaches have been used to study the microbiomes of aquatic ecosystems (Boomer, Lodge and Dutton 2002; Gibbens et al. 2015; Agate et al. 2016), soil (Martinez-Vaz et al. 2015; Finer, Fox and Finer 2016; Rahman, Charles and Kaur 2016), air in specific environments (Weber and Werth 2015) and different public locations across New York city (Muth and McEntee 2014). Given the broad applicability and robustness of the methodology in microbiome experiments, students can be given autonomy to design novel research questions without the need to optimize experimental techniques; the site and size of the sample population are the key variables that can be modified in these inquiry-based learning activities. The main impediment to implementation is cost, and instructors should aim for an upper limit of 96 samples (consistent with the 96-well plate processing workflow) and budget up to \$4000 for sequencing expenditure (Hartman et al. 2016).

Analogous experimental approaches can also be taken to characterize biodiversity in different organisms as part of large-scale CUREs. Environmental maps of yeast diversity can be identified by extracting DNA from leaves collected in different areas and sequencing the D1/D2 region of Yeast 26S ribosomal DNA (Safranek 2014); sequencing of the CO1 barcoding gene in field specimens can generate geo-tagged analyses of insect biodiversity and align with entomology and ecology curricula (Russell et al. 2015). Human genetic diversity can also be determined through sequencing and restriction fragment length polymorphism detection of single nucleotide polymorphisms (SNP), and students can correlate lactose tolerance phenotypes with lactase sequence genotypes by amplifying DNA isolated from their own buccal cells (Weinlander, Hall and De Stasio 2010). In each case (especially projects involving human participants), ethics approval from institutional review boards should be obtained prior to the commencement of the project.

OUTLOOK

As we approach the 20-year anniversary of the publication of the Boyer commission report, much progress has been made in undergraduate life sciences education to better equip our students with problem-solving and analytical skills. The proportion of NSF biology-related proposals citing Vision and Change priorities increased from 0.93% in 2009 to 59.4% in 2013, and the value of inquiry-driven learning continues to be cited amongst

Table 1. Summary of key techniques, inquiry elements and references for inquiry-based laboratory exercises in the life sciences.

Key techniques	Inquiry elements and references
Recombinant DNA technology: PCR primer design, retrieve and interpret DNA, protein sequences, PCR amplification, restriction digests, DNA ligation, colony-screening, molecular cloning, gel electrophoresis	• Can we design PCR primers against a gene of interest and verify their quality using multiple methods? (Robertson and Phillips 2008) • Can we fuse epitope tags to our gene product of interest without affecting its function? (Bornhorst, Deibel and Mulnix 2004; Wang et al. 2012) • Is our gene of interest expressed in other organisms, whose genomes have not been sequenced? (Harvey et al. 2014) • Is our gene of interest expressed at different levels in different cell types, and what impact does this have on their phenotypes? (Hargadon 2016)
Protein expression and purification: Plasmid transformation, SDS-PAGE, western blotting, gel filtration, ion-exchange chromatography, affinity chromatography, spectrophotometry, site-directed mutagenesis, protein crystallography, 2-hybrid protein interaction systems, LC-MS/MS	• Can we express and purify a recombinant protein, and measure its activity relative to the wild-type protein? (Bellin, Bruno and Farrow 2010; Knutson et al. 2010; Farnham and Dube 2015; Garrett et al. 2015; Gray et al. 2015) • Can we systematically mutate our protein of interest to test which residues affect protein function? (Rasche 2004; Shanle, Tsun and Strahl et al. 2016; Hekmat-Safe et al. 2017; Lefurgy and Mundorff 2017; Lipchick et al. 2017) • What are the optimal conditions for using our purified protein to grow crystals and determine its structure and function? (Kreiling et al. 2011) • Can we determine if our protein of interest interacts with subunits in specific protein complexes? (Gammie and Erdeniz 2004; Cardinale 2011) • Can we utilize proteomics to determine different metabolic pathways used by novel bacteria? (Kappler, Rowland and Pedwell 2017)
Molecular cell biology: Tissue culture, treatment with growth factors and/or pharmacological agents, gene deletion via homologous recombination, siRNA, CRISPR/Cas9, endocytosis assays, fluorescence microscopy, real-time PCR, SDS-PAGE, western blotting	• Which pharmacological agents interfere with endocytosis across different cell types? (Ledbetter and Lippert 2002; Bugarcic et al. 2012) • Which cellular signals induce apoptosis and what impact do they have on cells? (DiBartolomeis and Moné 2003; Srougi and Carson 2013; Byrd 2016) • Which stimuli induce inflammation in macrophages, and how can we measure this? (Gunn et al. 2013) • Which genes are involved in osteoclast differentiation and how can we test this? (Birnbaum et al. 2010) • Which gene deletions lead to disease phenotypes in different model organisms? (Cox-Paulson et al. 2012; Adame et al. 2016; Kowalski, Hoops and Johnson 2016; Li et al. 2017)
Genomics and bioinformatics: BLAST, BLASTp, tBLASTx, DNA and protein sequence annotation, identify genetic elements such as open reading frames, intron/exons, phosphorylation sites, signal sequence splice sites, SNPs, multiple sequence alignments, phylogenetic analysis	• Using bioinformatics databases, can we predict the function and expression profile of our novel protein of interest? (Beagley 2013; Makarevitch, Frechette and Wiatros 2015; Melloy 2015; Brown 2016) • Which model of phylogeny best matches molecular and morphological data collected from different species? (Campo and Garcia-Vazquez 2008) • Which genes are unique to a novel <i>E. coli</i> strain, and which have undergone horizontal gene transfer? (Baumler et al. 2012; Klein and Gulsvig 2012) • Can we annotate novel genomes and genetic elements using a format that is ready for submission to bioinformatics databases? (Hanauer et al. 2006; Leung et al. 2010; Shaffer et al. 2010; Pope et al. 2011; Smith et al. 2015; Staub et al. 2016)
Citizen science and microbiomes: Extraction of genomic DNA, PCR amplification of barcode genes, indexing PCR (adapters for sequencing), DNA cleanup and quantification, DNA sequencing, OTU table analysis, relative abundance measures of taxa, diversity index measures	• Can different microbiome profiles be detected in different human body sites from student volunteers? (Wang et al. 2015; Debelius et al. 2016; Garbarino and Mason 2016) • How different are the microbial populations across closely connected aquatic ecosystems? (Boomer, Lodge and Dutton 2002; Gibbens et al. 2015; Agate et al. 2016) • Can microorganisms be cultured from air, and correlated to differences in air quality? (Weber and Werth 2015) • Do different urban locations in New York City have distinct microbial signatures? (Muth and McEntee 2014)

meetings at professional societies, universities and in peer-reviewed journal articles (Vasaly et al. 2014).

Despite these promising trends, obstacles for CURE implementation still exist for faculty members, especially those who work within primarily undergraduate institutions with limited access to research personnel and federally funded facilities (Seeling and Choudhary 2016). These issues span across biology education in general, but are exacerbated for instructors in molecular biosciences, which rely on complex research methods that require persistent optimization to bolster the low success rate of any individual experiment.

This minireview outlined key experimental techniques and inquiry elements utilized in CUREs across these disciplines (summarized in Table 1), with the aim of lowering the perceived risk and uncertainty experienced by instructors looking to implement research and inquiry-based learning into their courses. These CURE examples have been peer reviewed and designed with scalability in mind, focusing on techniques in recombinant DNA technology, protein expression and purification, molecular cell biology, genomics and bioinformatics, and citizen science and microbiome studies. The research methodology is deconstructed and streamlined in these exercises, so that students

can apply a core set of standard operating protocols iteratively to address many discrete but interrelated components of the central research question.

Even with these logistical guidelines in place, time investment and financial constraints are still common barriers to CURE implementation (Shortlidge, Bangera and Brownell 2015; Shortlidge and Brownell 2016). To overcome these issues, new instructors can develop a pilot inquiry-based learning program, and conduct rigorous assessment of its impact using standardized evaluation instruments (Weston and Laursen 2015; Shortlidge and Brownell 2016). Inquiry-based learning laboratory classes can be implemented in a cost-effective manner, and any resulting student learning gains can be used as leverage for further expansion of the learning activities into CUREs. Faculty members can seek small pockets of seed funding to support future CURE initiatives, build consensus through stakeholder engagement and communities of practice, and continuously engage in multiple development cycles for novel research-based learning activities (Bell et al. 2017). Support can also come in the form of faculty mentorship programs (Goedhart and McLaughlin 2015; Prunuske, Wick and Wolyniak 2015), and participation in collaborative initiatives such as CUREnet and the Genomics Education Partnership (Lopatto et al. 2008; Boyle 2010; Auchincloss et al. 2014). Collaborations through existing large-scale CUREs with detailed resources and funding models in place is yet another mechanism available to new instructors, as exemplified by the Small World Initiative (<http://www.smallworldinitiative.org>) and the Science Education Alliance-Phage Hunters Advancing Genomics and Evolutionary Science (SEA-PHAGES) program (<https://seaphages.org>).

As science continues to innovate and push against boundaries of knowledge and understanding, our graduates more than ever need the cognitive skills and scientific training to embrace all of the multidisciplinary challenges the future will bring. There is clear momentum towards the widespread integration of authentic research into undergraduate curricula, and all instructors should be encouraged by the increasing number of high-impact collaborative CUREs (Kowalski, Hoops and Johnson 2016). Looking forward to the next 20 years in the post-Boyer commission report landscape, widening instructor participation in research-based learning across all institutes should be at the forefront of the global scientific agenda.

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