Journal of Hazard Literacy
eISSN 3091-6402

Review
J. Hazard Lit. 2025;1(1)e4
https://doi.org/10.63737/jhl.25.0016

Integrating mammalian cell culture into undergraduate biology education: benefits, challenges, and innovative strategies

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Received: Mar 22, 2025
Revised: Apr 13, 2025
Accepted: Apr 14, 2025

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Funding sources
Not applicable.

Acknowledgements
Not applicable.

Availability of data and material
The authors confirm that data supporting the findings of this study are available within the article.

Authors' contributions
The article is prepared by a single author.

Ethics approval
Not applicable.

Abstract

Mammalian cell culture has become fundamental in biological and biomedical research, enabling discoveries in virology, cancer biology, pharmacology, and biotechnology. Despite its importance, undergraduate biology curricula often lack practical mammalian cell culture experiences due to logistical, financial, and safety constraints. Early exposure to cell culture fosters students' problem-solving capabilities, critical thinking, and science identity, making them better prepared for future careers or advanced research training. This review identifies educational benefits gained from integrating mammalian cell culture into undergraduate curricula. The significant barriers to implementation, such as sterile environment requirements, high costs, time constraints, contamination risks, and ethical considerations, are acknowledged. Various effective strategies to overcome these challenges are explored, including short inquiry-based laboratory modules and course-based undergraduate research experiences. Special attention is given to innovative approaches like blended learning modules, primary cell culture experiments, gene expression analyses, and virtual laboratory simulations, which have proven effective even under challenging conditions such as the COVID-19 pandemic. This review also provides a comprehensive overview of how mammalian cell culture can be feasibly and effectively incorporated into undergraduate education. It aims to bridge the gap between theoretical instruction and practical application in biological education, preparing a generation of students who are proficient experimentalists capable of advancing scientific discovery and innovation.

Keywords: cell culture, undergraduate education, laboratory curriculum, inquiry-based learning, course-based undergraduate research experiences

Introduction

Mammalian cell culture has become a cornerstone of modern biological and biomedical research, underpinning breakthroughs in fields ranging from virology and cancer biology to pharmacology and biotechnology [1,2]. The ability to grow and maintain animal cells *in vitro* has revolutionized how scientists study cellular processes and disease, enabling experiments that would be impossible in whole organisms. The major advantage of cultured cell models is the consistency and reproducibility of results obtained from clonal cell populations, making cell culture an indispensable tool in both academic research and industrial biotechnology [3]. On the academic side, it allows students to directly apply and reinforce concepts from cell biology, biochemistry, and molecular biology in a hands-on setting [4]. Engaging in cell culture experiments helps concretize abstract concepts such as cell growth, metabolism, or signaling by letting students observe and manipulate living cells outside the organism [5]. Students learn essential techniques which not only enhance their laboratory competencies but also teach them how to design experiments, troubleshoot protocols, and analyze data [6].

Despite these clear benefits and the pervasive use of cell culture in research, many undergraduate biology programs have historically offered limited opportunities for hands-on mammalian cell culture experience [7]. Students are often introduced to experimental biology through microbial models like *Escherichia coli* or yeast rather than animal cells, largely because bacteria and yeast are easier to grow with basic lab equipment and carry fewer safety requirements. However, as the life sciences advance, there is growing recognition that even at the undergraduate level, students should engage with authentic cell culture techniques to better prepare them for the realities of modern research. The challenge lies in how to effectively incorporate cell culture training in undergraduate education in a feasible, safe, and pedagogically sound manner.

This review addresses that challenge by analyzing best practices for integrating mammalian cell culture into undergraduate curricula. Through examples from the literature, we highlight strategies that range from simple exercises in introductory courses to advanced multi-week research projects, noting their objectives, requirements, and impact on student learning. Our goal is to provide a comprehensive overview of how mammalian cell culture can be woven into the fabric of undergraduate biology education, so that future graduates enter research or industry with both the theoretical knowledge and the hands-on skills to culture living cells effectively.

Educational Benefits of Mammalian Cell Culture Training for Undergraduates

Introducing mammalian cell culture into undergraduate programs yields multifaceted educational benefits. Students gain practical skills and techniques that are directly applicable to research. Mastery of cell culture protocols (e.g., passaging cells, counting cells with a hemocytometer, performing viability assays) gives students a toolkit of hard lab skills that are often prerequisites in biomedical research labs [1,6,8]. Early training in these skills means students require less on-the-job training later and can contribute to research projects more quickly [9].

Working with living cells allows students to directly observe biological phenomena and link them to concepts learned in lectures. Rather than memorizing facts, students actively experience concepts like cell growth curves, contact inhibition, or the effects of gene overexpression/knockdown in real time [10]. Cell culture projects often involve formulating a hypothesis and designing experiments to test it. By learning to plan experiments with proper controls and troubleshooting issues like contamination or unexpected results, students cultivate critical thinking and problem-solving abilities [11]. This process demystifies research and can spark students' curiosity, motivating them to pursue further scientific investigations.

Furthermore, there is evidence that students find working with mammalian cells exciting and engaging, likely because it feels closer to real research than cookbook-style labs [12]. The novelty and responsibility of maintaining live cells can increase a student's sense of ownership of their lab work. As students successfully carry out complex protocols, their confidence grows. They begin to see themselves as capable scientists, which can enhance science identity and self-efficacy [13].

In summary, embedding cell culture experiences in the curriculum enriches undergraduate education by bridging theory and practice. It transforms passive learners into active experimenters, reinforces classroom learning with hands-on application, and cultivates a skill set and mindset that benefit students academically.

Challenges in Incorporating Mammalian Cell Culture into Undergraduate Labs

Implementing mammalian cell culture training for undergraduates can be challenging due to several practical and pedagogical considerations [1,14]. Recognizing these challenges is important when designing curricula so that appropriate solutions can be devised.

Mammalian cells must be handled in near-sterile conditions. Ideally, this means having access to a biosafety cabinet for aseptic manipulations, as well as CO_2-regulated incubators to maintain proper temperature and pH for cell growth [15]. Many teaching laboratories are not equipped with these specialized facilities, which are expensive to acquire and maintain. Unlike microbial culture, which can be done on a benchtop or simple incubator, cell culture demands a dedicated, clean space meeting. Setting up such a lab for a large undergraduate class can strain departmental resources. In addition, beginners often find it difficult to master sterile technique on the first try. Even a momentary lapse can introduce fungi or bacteria that quickly overgrow and destroy mammalian cultures [16]. In a class setting, one student's mistake can contaminate shared reagents or incubators, jeopardizing the experiments of others. Managing contamination risks requires vigilant supervision and sometimes extra repetitions of the lab, which can be time-consuming. Instructors must be prepared to teach proper aseptic methods and possibly have backup cultures available in case of contamination.

Meaningful cell culture work often spans multiple days or weeks, as cells need time to grow [17]. Coordinating such multi-session experiments with academic schedules is tricky. This can necessitate instructor or teaching assistant (TA) involvement outside of normal class times to tend the cultures, or creative scheduling. Compressed academic terms make it hard to fit in all steps of an experiment (seeding cells, treating them, assaying outcomes) unless carefully planned. Fast-growing cell lines or pre-prepared cultures can mitigate this issue but add complexity to the prep work.

Moreover, working with human or animal cell lines introduces discussions about biohazards and ethics [18]. Students must be trained in handling potentially biohazardous materials especially if cell lines carry viruses or are derived from human tumors. While most cell culture in teaching uses well-established cell lines, institutions still must enforce safety protocols (lab coats, gloves, possibly vaccinations or health monitoring for certain cell types). Additionally, the use of certain cell lines may prompt ethical considerations, which instructors should be ready to address educationally. These considerations, while valuable as learning opportunities, add another layer of complexity to implementing cell culture labs.

Additionally, limited lab capacity and resources might restrict mammalian cell culture experiences to smaller groups of students, potentially raising concerns regarding educational equity. Institutions can mitigate this by adopting creative strategies such as rotating students through lab modules over several semesters, leveraging blended learning to broaden participation, or incorporating virtual simulations to complement limited physical lab time. Clearly communicating the criteria for student selection and striving to provide equitable access

https://doi.org/10.63737/jhl.25.0016

to all interested students over time are critical considerations for instructors.

Because of challenges like these, it's understandable that some undergraduate programs have been slow to adopt mammalian cell culture in their lab courses. However, numerous educators have reported creative strategies to overcome these hurdles and successfully bring cell culture into undergraduate classrooms. By examining those approaches, we can identify best practices that make cell culture education more accessible and effective.

Strategies for Integrating Cell Culture into the Curriculum

Despite the obstacles, there are effective strategies to incorporate mammalian cell culture training into undergraduate education. Educators have developed innovative approaches that balance resource limitations with learning goals, ensuring students can experience cell culture first-hand. Below are several best practices, along with examples from the literature, for teaching cell culture to undergraduates in a feasible and impactful way.

Instead of immediately launching a full-blown tissue culture course, instructors can introduce cell culture through a short module or lab exercise within an existing course. For instance, an introductory biology or cell biology class might include a one- or two-week lab where students culture a robust cell line and perform a basic experiment such as a cell viability assay. Bowey-Dellinger and colleagues devised a straightforward inquiry-based lab using HeLa cells that fit into a general biology course without requiring a dedicated sterile facility [5]. They accomplished this by performing critical sterile manipulations in advance and having students work with plates that were pre-seeded with cells. In the module, students learned to trypsinize adherent cells, count them with a hemocytometer, and assess viability with trypan blue. Such a module gives a taste of cell culture within the time frame of a normal lab period.

Another valuable model system for integrating cell culture into the undergraduate laboratory involves the exploration of gene expression using murine melanoma cell lines [10]. In a student-centered laboratory module, undergraduates utilized traditional reverse-transcription polymerase chain reaction (RT-PCR), quantitative real-time PCR, and flow cytometry-based *in situ* hybridization methods, thereby gaining practical experience in both qualitative and quantitative analysis at population and single-cell levels. Another example of a short, yet impactful laboratory module is described by McIlrath et al., who developed a lab activity using mouse mammary tumor cells as a model to teach core biology concepts, such as the cell cycle, cellular signaling, and cancer biology [4]. This module allows undergraduate students to grow, characterize, and treat these cells with antiproliferative agents while learning to determine optimal cell concentrations, drug dosages, and treatment durations. Students employ both hemocytometer-based and software-based microscopy methods to measure cell viability, thus gaining hands-on proficiency with fundamental laboratory skills and techniques not commonly taught at the undergraduate level.

A particularly innovative approach introduced medical undergraduate students to bone marrow mesenchymal stem cells, emphasizing the importance of aseptic technique, primary cell isolation, cell culture, and directional differentiation [19]. Students isolated rat BMSCs, cultured them, and induced their differentiation into adipocytes, which were subsequently identified through oil-red-O staining. Despite the challenges, more than 90% of the participating students found the exercise engaging, useful, and educationally valuable. Building on this, Xu et al. further developed a comprehensive stem cell laboratory module employing a blended learning approach [20]. The blended learning structure effectively promoted self-paced learning and hands-on laboratory proficiency, demonstrating the effectiveness of combining digital resources with traditional laboratory practice in modern biomedical education.

Moreover, Phelan and Szabo developed an cell biology laboratory series centered around the K562 human leukemia cell line [11]. Students progressed to independent research projects investigating chemically induced differentiation of K562 cells into specific hematopoietic lineages such as erythroid or megakaryocytic. Through this structured yet open-ended laboratory experience, students practiced core techniques like cell counting, viability assays, and microscopy, while also applying advanced methods such as western blotting and benzidine staining. Assessments demonstrated that students gained substantial conceptual knowledge, technical proficiency, and appreciation for the complexity and challenges inherent in biomedical research. Furthermore, Robinson et al. introduced the clonogenic assay using HeLa cells into an undergraduate laboratory to teach concepts of mammalian cell colony formation and cancer biology. Students learned to fix and stain cell colonies and analyze the results microscopically. This module provided a robust, yet accessible approach to engaging students in practical laboratory skills, while reinforcing core biological concepts related to cell survival, proliferation, and the impact of environmental changes on cellular behavior [21]. Marion et al. describe a multiweek project in an upper-level physiology lab course where students cultured mammalian cells and conducted experiments over several weeks, culminating in analysis of cell proliferation under different conditions [6]. Students in that course gained substantial hands-on practice and independence in working with cell cultures, as well as experience troubleshooting long-term experiments. While these courses require significant faculty expertise and lab resources, they produce graduates with a strong competency in cell culture, which can be a standout feature of a biology program.

Embedding cell culture in a course-based undergraduate research experience (CURE) can provide students with a more immersive, research-like exposure [22,23]. In this approach, an entire lab course is structured around an open-ended investigation using cell culture. For example, Guttilla Reed implemented a semester-long CURE in a molecular biology course where students cultured cancer cells to explore gene regulation in cancer [24]. This model allowed many students to participate in research who otherwise might not have had the opportunity under the traditional apprenticeship model. Similarly, McLaughlin et al. created a multi-week cell culture project in a cell biology class where students tested anti-inflammatory drug effects on cultured cells as a novel investigation [8]. In such projects, students formulate hypotheses, carry out experiments over multiple weeks, and finally present their findings. The CURE approach not only teaches technical skills but also engages students in the full research process, from experimental design to data analysis and scientific communication. Research has shown that participating in CUREs can increase students' science identity and their persistence in STEM, making it a powerful pedagogical strategy when resources allow [25,26]. With careful planning, CUREs using cell culture can simulate a professional lab environment and yield publishable or at least presentation-worthy student results, greatly enriching the undergraduate experience. Designed for sophomore-level cell biology students, CURE centered around culturing PtK2 mammalian epithelial cells and using fluorescence microscopy to investigate student-chosen experimental factors affecting cell viability [27]. The semester-long duration allowed students multiple experimental trials, promoting mastery of techniques and deeper engagement with research. The overall educational outcomes of this CURE indicate its effectiveness in enhancing both skill acquisition and conceptual understanding.

Assessing student learning outcomes following cell culture educational interventions is crucial for measuring their effectiveness. Evaluations can include practical assessments of laboratory techniques, written lab reports, presentations, and reflective surveys. For instance, pre- and post-module quizzes or surveys can quantify gains in conceptual understanding, practical skills, and student confidence. Direct observational assessments during lab sessions provide immediate feedback on practical skills. Combining these methods allows comprehensive evaluation of both technical competencies and conceptual knowledge, guiding continuous improvement of laboratory modules.

The transition to online education during the COVID-19 pandemic highlighted novel strategies for conducting cell culture-based CUREs remotely. To accommodate remote learning, instructors used previously collected data sets, virtual demonstrations, recorded method videos, and bioinformatics-based activities to maintain authentic research experiences [28]. Remote labs emphasized skills such as microscopy techniques, tissue culture calculations, flow cytometry, DNA sequencing analysis, and image forensic analysis [29]. Students positively responded to the realistic scenarios, the ability to repeatedly practice laboratory techniques, and embedded quizzes reinforcing theoretical understanding, suggesting that virtual simulations are valuable tools in supporting practical bioscience education under challenging circumstances [30]. David et al. described the implementation of a virtual cell culture lab practical for an introductory biomedical engineering course, using recorded videos, MATLAB(MathWorks, Natick, MA, USA)-generated hemocytometer simulations, and online quizzes to assess student understanding of cell culture protocols [31]. These resources were subsequently identified as beneficial supplements for future in-person teaching, emphasizing the potential long-term value of virtual assessments in laboratory education. Despite the challenges of moving hands-on cell culture experiences online, many students maintained strong engagement, successfully achieving key learning outcomes such as experimental design, data analysis, and critical thinking.

A best practice that accompanies all the above strategies is ensuring that both students and instructors are adequately prepared for the challenges of cell culture. This can involve providing pre-lab training. For example, instructional videos or simulations on sterile technique, or small-group practice sessions with dummy samples before handling real cells. Additionally, TAs and lab instructors should be well-trained in cell culture methods so they can confidently mentor the students [32,33]. If TAs are inexperienced, investing time in their training is crucial. Institutions may address this by providing dedicated training sessions for TAs, hiring additional personnel when feasible, or integrating peer mentoring models where advanced students assist novice learners. During the labs, maintaining a low student-to-instructor ratio can prevent mistakes. One instructor or TA per a small group of students allows close supervision when students are at the biosafety cabinet, for instance [34]. Finally, setting appropriate learning goals and expectations is important. Students should understand that cell culture requires patience and precision. Instructors should be prepared with backup plans (extra cells, alternative data sets) in case of failures. By cultivating a supportive learning environment, educators can help students gain the full benefit of cell culture training without becoming discouraged by its challenges [35].

By implementing these best practices, undergraduate programs have demonstrated that mammalian cell culture can be taught effectively, even outside of a specialized research setting. The key is thoughtful curriculum design that aligns the level of complexity with available resources and student preparedness. Whether through a brief module or a semester-long research course, students can be given the opportunity to work with living cells in a meaningful way. The cumulative result of these efforts is a generation of biology undergraduates who are not only well-versed in theory but also capable in practice.

https://doi.org/10.63737/jhl.25.0016

Conclusion

Incorporating mammalian cell culture into undergraduate education is both a challenge and an opportunity. It is challenging because of the resources, training, and care required, but it is a tremendous opportunity to elevate the quality of biology education and better prepare students for the demands of modern science. This review has highlighted why cell culture skills are increasingly essential, detailed the benefits to student learning, and presented a range of successful strategies for bringing cell culture into the undergraduate curriculum. As technology evolves, we may also see the introduction of new tools like automation or 3D cell culture and organoids into teaching labs, further enriching the student experience. Ultimately, the goal is to ensure that all biology undergraduates have the chance to grow cells in a dish and witness biology unfolding before their eyes. Achieving this will produce graduates who are not only knowledgeable about life at the cellular level but also skilled experimentalists ready to contribute to scientific discovery and innovation. By embracing mammalian cell culture education, universities will continue to bridge the gap between classroom learning and real-world research, cultivating the next generation of scientists and professionals with the expertise to push the frontiers of biology.

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