Cutting-Edge Microscopy Systems as Remote Teaching and Research Tools for Undergraduate Students

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Whether due to illness, weather, safety, or other concerns, it is very difficult for biology students to gather meaningful and timely data without access to campus. This has been especially evident during the COVID-19 pandemic, in which most laboratory exercises have been conducted as a simulation. Simulated experiments provide a stopgap for certain courses, but for upper-level and research courses, they are often insufficient. Many new microscopy tools now on the market can be adapted to allow students to generate and analyze novel data with little aid of instructors. Remote brightfield-based systems like the CytoSMART Lux2 can be used to gather real-time insight into the progression of cell growth, cell migration, and cell viability over time. The data from these systems can be viewed via the Internet or downloaded for later analysis. Confocal microscopy also offers unique remote learning opportunities. Because these fluorescence-based microscopes are controlled almost exclusively by a computer, free “remote desktop” software can allow students to learn how to use this cutting-edge technology and can also allow for the generation and analysis of novel data. While these systems can be expensive, they offer a variety of benefits for undergraduate students and researchers whether they are in the laboratory or working remotely.

INTRODUCTION

Teaching laboratory experiences to undergraduate biology students is inherently challenging; many times, it requires specialized equipment and workspaces, living specimens, and the intentional building of community. Previously, faculty have done their best to adapt to short-term closures due to weather, illness, or other issues with great success through rescheduling labs, through eliminating some material, or through other creative approaches. Due to the COVID-19 pandemic, we were faced with the unintended and rapid pivot from traditional and comfortable methods of instruction—often refined over years or decades—to virtual teaching with the need for highly impactful solutions that would work for long-term closures. Across the world, we saw faculty (and students) rise to the challenge, keeping classes moving smoothly, ensuring quality education, and finding novel ways to deliver complex lecture topics. Achieving the educational goals traditionally addressed in the laboratory is significantly more difficult. While faculty have found ways to develop laboratory skills for students working remotely by sending laboratory kits, performing and creating simulations, etc., students involved in courses requiring novel microbiology or cell biology research have not been able to continue their work. This represents a significant gap in our current abilities and compromises some of the highest impact practices undergraduate faculty have at their disposal. Here, a novel mechanism for using cutting-edge microscopy to facilitate teaching, data generation, and data analysis for undergraduate researchers is described. While some related methods have been previously described for telepathology (1–3) and scanning electron microscopy (4, 5), these do not target undergraduate research and do not address the need created by the COVID-19 pandemic.

PROCEDURE

Video monitoring of cell cultures can be a highly effective way to showcase and assess the health of cell cultures, migration of cells within a sample, and responses to various stimuli. Internet-connected, remote, brightfield microscopy, such as that found in the CytoSMART Lux2 system, can allow students to generate real-time data, view time-lapse videos of the data, and analyze the data on different platforms. There are many ways to achieve this. For instance, a faculty member could seed cells or bacteria in a tissue culture plate, place the cells and the microscopy system into an incubator (with or without CO₂, depending on the assay), and begin imaging at recurring intervals for hours or weeks. At any time during the experiment, students can view or download the video of growth or other changes and compare between different treatments. This sort of imaging system is especially useful for wound

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healing assays in which epithelia or immune cells can migrate into the “wound.” This same protocol could easily be adapted to assess the growth of biofilms, the movement of unicellular microorganisms, etc. By comparing the time-lapse videos of multiple treatment conditions, students can both envision the processes occurring at the cellular level and can research ways to analyze and quantify the changes in growth, migration, etc. Image analysis can be performed using a variety of free resources including ImageJ by the National Institutes of Health. While systems like the CytoSMART are somewhat expensive, the functionalities they offer for both “normal” and remote learning and research may be worth the initial investment. If not, it is possible that instructors could collaborate with an institution that has this sort of device already on-site.

In addition to brightfield microscopy–based technologies, confocal microscopy offers another novel area for remote teaching and research. Confocal microscopes are powerful devices capable of imaging fluorescence in living or fixed cells, determining colocalization of intracellular molecules or structures, and creating three-dimensional reconstructions of cells and tissues after optical sectioning. Samples are generated through fluorescently tagging structures, cells, or molecules in cells on a coverslip or slide. The slide is then placed on the microscope for imaging. After that point, everything can be controlled via the associated computer. Using free software like AnyDesk, TeamViewer, Chrome Remote Desktop, etc., students can be allowed to remotely control the confocal’s computer. This allows students to move the stage, focus, and take images without the aid of the instructor. Using either proprietary software from the confocal’s manufacturer or free software like ImageJ, students can quantify intensity, colocalization, size, etc. An example protocol is provided in Appendix 1. Again, while the acquisition of a confocal microscope is a huge investment, institutions that have one can utilize it for teaching and for research in both in-person and remote capacities or instructors could collaborate with an institution that has one on-site.

Safety issues

For remote experiments, there are no safety issues for students. (See the supplemental example protocol.)

The safety issues for using these techniques relate solely to in-person usage and will largely depend on the samples, treatments, and chemicals being used in each class. For example, imaging living cells may require common proper personal protective equipment (gloves, lab coat, eye protection, etc.) and larger equipment (e.g., biological safety cabinets). While most procedures will require BSL-1 or -2 practices, precautions, training and documentation, and a risk analysis will need to be performed by each user.

Working with high-intensity lasers required for confocal microscopy is associated with two concerns: exposure to the laser beam and exposure to the high voltages within the laser and its power supply. Most of these have been well-addressed through the incorporation of safety features by the manufacturer (e.g., beam shutters and key-controlled interlocks). As with other laboratory dangers, warning signs should be properly posted, and all users should be properly trained.

CONCLUSION

Six students in my research laboratory have successfully been trained to remotely generate data using the CytoSMART system and a Nikon A1 confocal microscope. As examples, Fig. 1 shows how students utilized confocal microscopy to determine whether various treatments affect neutrophil differentiation as measured by phagocytic ability and the supplementary video shows cell division over many days. All the students have been incredibly excited to learn this cutting-edge (and visually beautiful) technique. In contrast to the typical laboratory experience, each of these students has continued to request the chance to continue doing this research and working with the confocal microscope. Some of our data has been presented at regional, virtual meetings, where our ability to do such novel work remotely has been consistently praised.

While acquisition of these devices can be an expensive undertaking and require significant effort by the faculty members, there are clear benefits, especially for students conducting research. The ability for undergraduate students to work remotely for research or microbiology-based laboratory courses is incredibly important for academic continuity and for student affect. Students clearly recognize that they are doing “real” research or experiments, and the ability to generate actionable data excites them, helping both students and faculty to overcome some of the issues encountered during remote learning throughout the pandemic.

FIG 1. DMSO and DMF-treated HL-60 cells differentiate into neutrophils. After being exposed to GFP-expressing Staphylococcus aureus for 45 min, HL-60 cells were stained (Texas Red-phalloidin and DAPI) and analyzed via confocal microscopy. The control, undifferentiated cells have minimal actin staining while the DMSO- and DMF-treated cells have strong actin staining and significant phagocytosis (yellow staining indicating colocalization of bacteria and F-actin). DMSO, dimethyl sulfoxide; DMF, dimethylformamide; GFP, green fluorescent protein; DAPI, 4′,6-diamidino-2-phenylindole.

6-diamidino-2-phenylindole.
SUPPLEMENTAL MATERIALS

Appendix 1: An example protocol for remote generation of confocal data.

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