The Biophysicist

Remote Exploration of Experimental Biophysical Instrumentation in Core Facilities

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ABSTRACT Biophysics is defined by the experimental data that are collected on an extensive array of powerful and elegant tools. To solve important problems in biophysics, an understanding of the capabilities and limitations of the current instrumental methods is needed. Although lecture-based courses can instruct students on the physical principles of biophysical instrumentation, the actual practical use of instrumentation can seem far from the concepts taught through presentations or books. Traditionally, laboratory courses can expose students to hands-on use and understanding of experimental methods. During the COVID-19 pandemic, laboratory-based courses were challenging or, at times, prohibited. The educational aim of this article is to connect the instrumental concepts learned in lecture to the use of instruments for experiments when students are unable to go into laboratory environments. I present a low-stakes assignment for students to explore the biophysical instrumentation at core facilities. Prompts were provided to guide students through methods and challenges when using an instrument in a laboratory. These were then shared in a group environment so students could learn about multiple instruments in a single class and further benefit from social interactions with their peers, combating isolation during remote courses. Beyond remote instruction during COVID-19, this assignment can be applicable to future courses where laboratory work is cost-, time-, or location-prohibitive. Adaptations for in-person instruction are also discussed.

KEY WORDS remote instruction; core facilities; instrumentation; experimental methods; undergraduate biophysics; graduate biophysics

I. INTRODUCTION

Biophysics is driven by the experimental data acquired on instrumentation. An extensive array of experimental methods are used to obtain quantitative and qualitative information about the physics of biology. Students are typically introduced to biophysics through 2 primary types of courses: through a model-based approach presenting the molecular-level statistical physics and thermodynamics that underlie the dynamics of proteins, cells, and other biological systems, or through an experimental-based approach covering the instrumentation used to obtain said molecular and higher level information. The latter addresses a critical aspect in the education of biophysics students: experimentalists and theorists alike must understand the physical principles of biophysical instrumentation, how experiments are performed, and the limitations of methods. This

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understanding allows appropriate choices to be made, measurement tools to be used efficiently, and accurate data to be obtained.

Student use of instrumentation is key to their ability to understand the physical concepts behind instruments and to perform experiments properly. First, understanding the individual components within an instrument is important to go beyond treating them as simple "black boxes" (1). Seeing instruments in person allows students to observe their inner workings (2) and visualize how source, sample, and detector components are assembled (e.g., the 90° arrangement of light source and detector within a fluorometer compared with the 180° alignment in an ultraviolet-visible spectrophotometer). Additionally, a hands-on effort for developing the skills to work with experimental methods is needed. Recent pedagogical reports have generated laboratory modules for developing biophysics student skills in home-built microscopy and optics (3–5), along with labs with commercial instrumentation that study recent, cutting-edge areas of biophysics research, such as phase separation in the cell (6, 7).

The COVID-19 pandemic has limited students' ability to use and therefore learn the practical steps and problem solving required to perform experiments on commercial instrumentation. In the initial uncertainty of the pandemic, much instruction went fully remote, preventing any in-person experiments. As campuses reopened, many students were still limited to remote instruction because of travel restrictions, limited campus housing availability, or personal health concerns. Therefore, innovative and alternative teaching approaches were and continue to be explored to achieve the same learning objectives in remote and hybrid lectures or virtual labs (8–11). Many of the remote laboratory approaches that were developed before and in response to the pandemic used equipment that students purchased to carry out experiments at home (8, 9) or provided data (10) or simulations and video tutorials to replace hands-on experiments (12, 13); however, how can experiments that require expensive commercial equipment or biosafety regulations that are oftentimes used in biophysics research be conveyed in a remote environment?

Here, I present a class exercise to explore biophysics instrumentation through a student-led presentation of core facilities. This low-stakes assessment focuses on exploration of instrumentation from core facilities to achieve the main learning goal of linking physical concepts introduced in lectures to "real" experimental use of an instrument. I used the material of this article in the course PHYS 330/PHYS 430 Experimental Methods in Biophysics, a cross-listed, interdisciplinary physics course for upper-level undergraduate students and graduate students, respectively. First, I describe the nature of the pedagogical issue I encountered while teaching this course remotely during COVID-19. I then frame the assignment and provide a demonstrative example of a student's answer to the assignment. I present the results of a qualitative assessment of the assignment from anonymous students course evaluations and mid-course surveys. Overall, students had a favorable response to the assignments, both to achieve learning objectives about the practical use of instruments and to build community in the classroom. Finally, I discuss my impression of the students' performance on the assignment and achievement of the learning goals, along with potential future adaptions for both in-person and remote instruction. Post–COVID-19, this assignment will still be applicable to lecture-based courses and courses where the development of an experimental lab is challenging because of access to instrumentation.

II. SCIENTIFIC AND PEDAGOGICAL BACKGROUND

Traditional instrumentation-based courses are typically divided into lecture and laboratory portions (Fig 1) (14). The lecture portion of the class provides the theoretical background of the physical phenomenon that underlies the instrument function (Fig 1A). Details of how a physical force (e.g., electronic, magnetic, mechanical) interacts with the sample and results

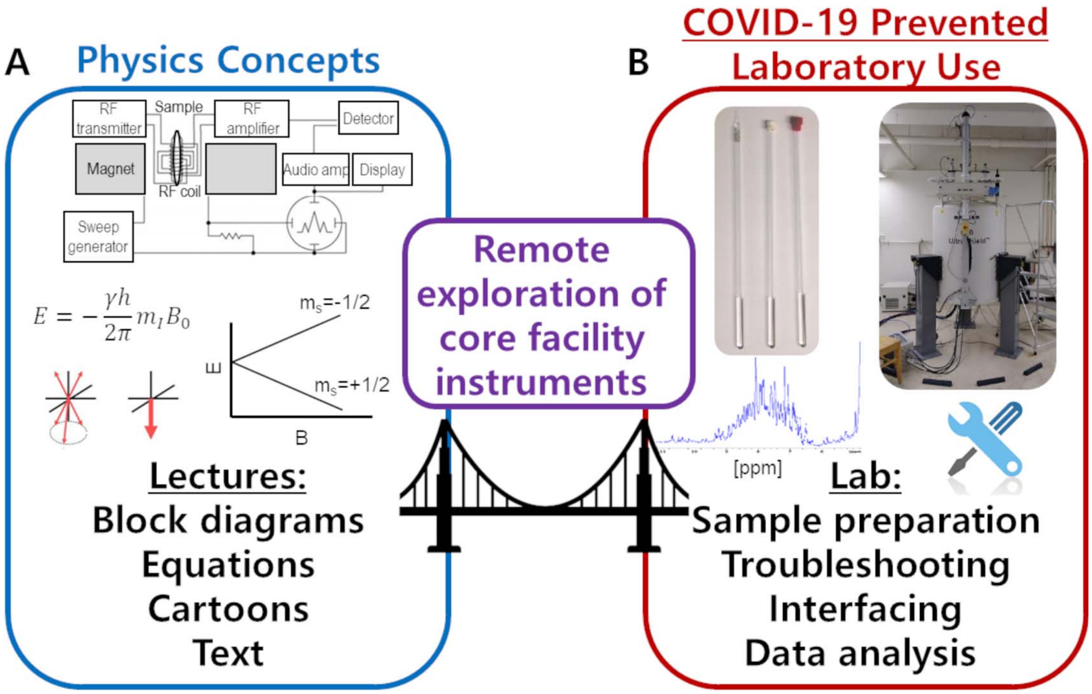

Fig 1. Remote exploration of instrumentation bridges the theoretical concepts of instrumentation presented in lectures and the laboratory use of an instrument. Nuclear magnetic resonance (NMR) is used as an illustrative example where (A) the lecture includes block diagrams, equations, and illustrations of the quantum and classical concepts that form the basis of the instrument. This approach can be quite different from (B) the experimental use of NMR, which includes sample preparation, step-by-step instrument protocols, spectral analysis, and troubleshooting. The proposed assignment bridges these 2 areas.

in a measurement are described in a classical or quantum mechanical fashion, or in both ways. The components of the instrument are broken down into the source, sample, and detector. Their geometric arrangements are sketched in block diagrams. Equations are derived to explain the quantitative measurements and analysis of signals.

The laboratory portion of the course can include sample preparation, with special consideration of the state of matter and concentration of the sample and care of the sample cuvette or holder (Fig 1B). A commercial instrument is used to take the measurement, and steps in a protocol are followed. Students must consider controls, replicates, and variables within the experiment. Problems can often arise with the inability to get the measurement to function properly because of common errors, such as missing a step in the protocol, irreproducible measurements, computer communication errors, or data formatting.

Courses typically taught in this format that have a relation to biophysics can include analytical and advanced instrumentation courses in chemistry, electronics-based labs in physics, molecular biophysics and spectroscopy courses in biophysics and physiology departments, and dedicated experimental biophysics courses, among others.

Figure 1 provides a demonstrative example of physics concepts compared with the laboratory use of nuclear magnetic resonance (NMR) that may be taught in a biophysics instrumentation course. The lecture may cover the quantum and classical treatments of spin and introduce the radio frequency source, magnets, and pulse-sequenced locked-in detection of radio frequency to produce a Fourier-transformed spectrum. Derivations of the Larmor frequency and signature peaks for specific chemical bonds that are present in small molecules, proteins, lipids, and so on are introduced. Yet, this is quite different from the practical use of an NMR apparatus with considerations of deuterated solvents, concentrations, loading and spinning samples, and setting the correct computer communication to take and extract measurements. Therefore, both lecture and laboratory use are required for students to have a holistic understanding of instrumentation used in biophysics research.

COVID-19 prevented or made laboratory portions of courses challenging. In the PHYS 330/PHYS 430 Experimental Methods in Biophysics course that is the focus of this article, the original plan during a regular, nonpandemic semester was for the entire class to visit the core facilities physically for a guided tour with the facility manager and to observe an example measurement on one of the instruments during a course period. The course is lecture-based and scheduled over a 1h15min period, so in-depth student-led experiments would be time prohibitive. However, COVID-19 prevented in-person visits, and there was a pedagogical need to link the physical concepts introduced in the lecture to practical use of instruments without performing extensive experiments or being physically present in laboratory facilities.

III. METHODS

Three core facilities on the Case Western Reserve University campus were selected to be discussed in 3 lectures dispersed throughout the semester. These included the following:

(a) bio[box], a collaborative learning and research space in the Department of Biology developed in the spirit of makerspaces (https://biology.case.edu/biobox/). It houses DNA and RNA processing equipment, such as that used for polymerase chain reaction methods, and a microscopy facility for biological research.
(b) The Light Microscopy Imaging Core Facilities housed in the School of Medicine include standard light, live-cell, and super-resolution fluorescence microscopes (https://case.edu/medicine/research/som-core-facilities/light-microscopy-and-imaging).
(c) The Department of Chemistry Instrumentation Facility includes NMR, mass spectrometry, spectroscopy, and chromatography instrumentation (https://chemistry.case.edu/research/instrumentation/).

A list of the instruments in each core is provided in the Supplemental Material and on the referenced core websites. The remote discussion of a core facility assignment days were scheduled after the instrumentation in the cores were presented in lecture (e.g., optical microscopy and super-resolution imaging were discussed in the 2 lectures before the Light Microscopy Imaging Core Facilities discussion).

Students were provided a sign-up sheet a week before the scheduled class discussion to self-select and break into groups of ∼6–8 students. Students within groups each had to present on a unique instrument. All of the instruments in each core facility were available on which students were to present (see Supplemental Material). The sign-up sheet included a list of possible instruments, a link to the core facility home page, and the following prompted questions to prepare for the discussion:

(a) What do you use it for?
(b) What is the source, sample holder, detector?
(c) How big is it?
(d) How much does it cost? (Investigate vendor websites, used equipment websites, and so on.)
(e) Look at the manual—anything interesting stand out?
(f) Look at ResearchGate questions or other shared facilities at other universities—are there any common troubleshooting tips?
(g) What is an example experiment or application from a manuscript?

The learning goals these questions were intended to address included the following:

(a) Link physical concepts in the lecture to the real use of the instrument on campus.
(b) Know what and where the key components of the instrument are (i.e., not a black box).

Table 1. Example student responses for remote discussion of biophysical instrumentation (nuclear magnetic resonance, NMR) in the Department of Chemistry Instrumentation Facilities, Case Western Reserve University (CWRU).

Question	Answer
Instrument	400-MHz Varian Inova NMR
What do you use it for?	1D and 2D NMR experiments on $^{1}H/^{19}F/^{13}C/^{31}P/^{29}Si$
	Quantitative NMR
	(Bio)pharmaceutical development
What is the source, sample holder, detector?	Details of the superconducting magnet, tube/probe, coils
How big is it?	Large; takes a full room space in a laboratory (magnet, console, etc.)
	Provided example photo available from other cores online
How much does it cost?	Several $100K estimate; quotes not easily obtainable for large instrumentation; no used sales available online
	Large pricing difference between internal CWRU users and external users for hourly use
Interesting information in manual?	Variable-temperature experiments with −100 °C to 100 °C range
	Extensive safety information on the magnet
	Detailed the space requirements for the NMR to be installed properly and used in a lab space
	Probe can be converted to observe any broadband nucleus falling in the frequency range between ^{31}P and ^{15}N
Any common troubleshooting?	Customer support has changed hands since Varian was acquired by Agilent in 2009 and NMR branch was shut down in 2014
	Restart experiment is the best approach if gradient shimming fails
Give an example experiment/application	Focus on analysis: diffusion-ordered spectroscopy (DOSY) measurements with local covariance analysis to identify species in a mixture
	Focus on application: ^{1}H NMR identification of metabolites in rat brain tissue

(c) Understand common errors that can occur in an experiment and how to troubleshoot them.
(d) Know the type of experiments for which the instrument would be appropriate.
(e) Know which core facility to use, whom to contact, and the type of samples to prepare if they need to do measurements themselves.

On the day of the scheduled class, the students were separated into their groups in the Breakout Room feature in Zoom. Students decided themselves either to provide the answers orally or to prepare a PowerPoint presentation to share with the group through the Share Screen function of Zoom. Table 1 presents the assignment questions and demonstrative answers for NMR. After each student presented, the other students were allowed to ask questions or share if they had experience using the instrumentation. Question periods were handled by students orally asking questions and self-managing the discussion as a group because group size was kept relatively small (6–8 people per group). The instructor would rotate among Zoom breakout rooms to listen to the presentations and answer any questions that could not be directly addressed by the presenting student. Typical group discussion sessions took ∼30–45 min, or about 5–10 min per student.

IV. RESULTS

The effectiveness of the assignment was assessed through anonymous student comments provided in 2 surveys during the semester and the final course evaluation. Twenty total comments were received specifically about the 3 core discussions. Comments were categorized as positive (55%), wishing that in-person instruction was possible (35%), negative (5%), or miscellaneous (5%). Figure 2 provides a visual representation of the percentage breakdown. The full results of the survey are provided in the Supplemental Material, with some general observations detailed here. On average, participating students enjoyed the assignment because it allowed them to go into more detail about a specific instrument (e.g., "Lab visit days have been good for reading up

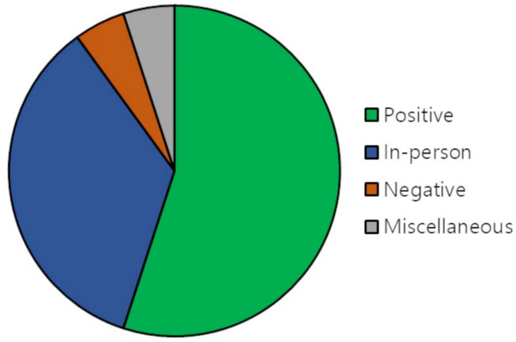

Fig 2. Graphical representation of student comments from course evaluation and surveys throughout the semester. See Supplemental Material for a full list of comments.

on a particular instrument that I might be interested in"; "gave a really good idea of how the instrument is REALLY used, not just its theory or instrumentation"), and they could learn what instrumentation is available on campus (e.g. "exposed us to the great resources we have at CWRU").

The wish for in-person instruction and ability to go to the cores or perform experiments was common (e.g. "would have been great if done in person") and will be taken into account when the assignment can be implemented in person. The negative comment highlighted the limitations of the assignment, "since the course was online and best possible was to google information about the equipment."

The student-led arrangement and low-stakes nature of the assignment were designed to promote student interaction and classroom community in a remote environment. The days that group discussions were held had near 100% attendance, despite not having a graded component. Additionally, 2 scheduled discussions had an option for students to sign up for a group that would meet in person, socially distanced with masks, outdoors (the third and final discussion was not able to host an in-person option because of weather). About 50% of students elected to meet in person. These were the only days the students had in-person interaction that enriched the learning experience of seeing faces instead of names or images on Zoom screens. Students commented on how the assignment helped build community in the surveys: "It was cool to meet in person."

V. DISCUSSION

A. Instructor assessment of the assignment

As a qualitative assessment based on the personal perception of the instructor, the assignment did lead to students achieving the learning goals in variable degrees of depth. Identification of the key components (i.e., source, sample holder, detector) was done well. This was a major focus of the lecture portion of the course, so students were used to the format of identifying the components behind the "black box" view of instruments, but a description of components in the lecture were kept broad (e.g., a radiofrequency coil). Students often found more detailed, specific instrument components (e.g., a 400-MHz, 5-mm, pulsed field gradient, auto-switchable probe that is configured for 4-nucleus detection [1H, 19F, 13C, 31P]) on the core website or in user manuals that were accessible on vendor websites. If the instrument were out of date, they would use a more recent model as an example. This led to some interesting identification of company history when instrumentation companies would be acquired by a competitor. The exploration of the Light Microscopy Imaging Core Facility with setups that have customizable excitation lasers, filter cubes, and detectors for different spectral ranges and geometries for different samples was a markedly useful exercise for students to identify why a core facility requires a range of similar instruments with different components.

Students topically covered common errors from information available online, but a brief discussion cannot replace the persistence and troubleshooting skills that are developed with hands-on laboratory work. The academic social networking site ResearchGate.net, which provides a forum for questions and answers (15), was used almost exclusively by students to find common problems that arise during use of specific instruments unless students had personally used an instrument themselves. Forum questions could briefly identify some common errors through questions, with answers ranging from detailed changes in sample preparation to simple and trivial “try turning it on and off” solutions. Crowdsourced information has limitations, with studies showing more responses to shorter, and possibly easier questions (15), in contrast to the in-depth time required for real laboratory problem solving. Therefore, the assignment was not able replicate the detail that in-lab experiences of students finding solutions themselves provides.

The most engaging presentations were those in which students related the selected instrumentation to their own research interests. First, if students had used an instrument themselves, they often provided much more detail on the motivation on why a selected instrument would be used and on sample preparation details, and even hints on the use and access on campus (e.g., “this core is on the seventh floor of the medical school and you need a scheduled meeting with the core manager for security to let you into the building”). Second, by identifying examples from literature in which the selected instrumentation had been used, students tailored the use to their specific research interests. The students came from a range of majors (physics, chemistry, macromolecular science and engineering, nutrition, materials science, biomedical engineering), so examples were broad: from instrumental and data analysis development to applications with samples ranging from molecular to medical (Table 1).

B. Alternative arrangements for in-person instruction and grading

The assignment can be modified for postpandemic, in-person instruction. Fall 2020 was the first time the PHYS 330/430 course was offered, so there were no prior experiences or assignments with which to compare the pandemic-obtained results. Instead, future offerings of the course postpandemic will be used to compare the remote assignment to assignments in which students are able to visit the core facilities in person. Although the original plan as discussed in section II was a simple tour of the core facilities, the remote assignment discussed here has shown students' ability to access and convey information accurately about instrumentation to their peers.

This assignment could be modified to provide more depth by directly engaging with the core facilities. Given the size of the student discussion groups and 30–45-min length of discussion as described in section III, there would be adequate time within the course period to add a general introduction to the core facility by the core manager. The manager could provide insight into the history of the core, the most frequently used instrumentation, aspects of registering for use, and future plans for new instrumentation. This tour could be done either in a remote assignment over Zoom with the core facility manager leading a discussion for the entire class before the breakout sessions or at the start of in an in-person visit. Students would also be able to put a face to a name listed on a website for any needs they may have outside of the course for their research if their core is at their university. At universities that do not have extensive shared instrumentation, video meetings with a facility manager at a nearby or relevant core could expose students to the concept of core facilities overall in addition to the instrumentation.

I therefore plan to adjust the assignment for in-person instruction in future offerings of the course. I anticipate having students lead the in-person discussion. Students will answer the same prompts before the visit. The class will meet at the core, and the core facility manager will provide a brief overview of the core mission and access in general. Then, going instrument-to-instrument within the facility, each student will present orally in a similar fashion to the remote Zoom discussions. The in-person component will enhance the student understanding of the geometry of the instrumentation and components, where to find the instrument on campus, and which core facility manager to contact for more details or access. Future follow-up work comparing the remote with in-person formats is planned.

The assignment could be made to have higher stakes by incorporating a graded component. I chose not to include grades to lower obligations on students during a stressful semester of taking multiple courses during a pandemic. "Quarantining" higher stakes assessments was an approach also taken by physics course instructors at other universities (16) and universities overall (17). As previously noted, not having a graded component did not have any effect on participation, which may have been because of the small course size and seniority of the students (juniors, seniors, and graduate students). Grades could be included when attendance and participation is an issue through multiple formats dependent on class size. For a smaller class where the entire class can present in one class period, the instructor can observe all of the student presentations and assign a grade based on the quality of their answers to each of the prompts in Table 1. For a larger course with breakout sessions, students can turn in an additional PowerPoint or written document with their answers to the Table 1 questions for the instructor to grade. In both of these formats a rubric could be provided to the students for clarity on how grades are assigned.

VI. CONCLUSION

Overall, I have described a course assignment for students to explore and consider aspects of the hands-on use of instrumentation available in core facilities when in-person experiments are not possible. The course module presented here is easy to implement and received generally positive responses from students. The group aspect built comradery between students that was particularly pertinent in an isolating semester of remote instruction. The assignment is beneficial to expose students to instrumentation available on their own campus at doctoral universities with research activity, or at nearby universities or facilities when implemented in courses taught at primarily undergraduate institutions that do not have on-campus access to specialized instrumentation. Furthermore, outside of the pandemic, this assignment could be applicable to many courses that may not have dedicated laboratory time, space, or funds for experiments. The assignment also highlights the interdisciplinary nature of biophysics. Core facilities can be used in the classroom to expand students' knowledge of instrumentation that they may otherwise be unaware of if they stayed in their home department. Future work will pursue comparing this assignment to on-campus, in-person exploration of core facilities when the pandemic is over.

SUPPLEMENTAL MATERIAL

Supplemental material is available at https://doi.org/10.35459/tbp.2021.000189.s1.

AUTHOR CONTRIBUTIONS

LK designed and implemented the lesson plan and wrote the manuscript.

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