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OPINION
Lessons Learned in Developing Virtual Neuroscience Labs

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The global COVID-19 pandemic has had a major impact on teaching approaches across higher education institutions. In this article, we reflect on the lessons learned designing and developing two virtual neuroscience labs and how they can positively contribute to Neuroscience teaching beyond this pandemic.

Key words: virtual labs, online practical teaching, neuroscience undergraduate education

A virtual laboratory is one where the student interacts with an experiment or activity which is remote or which has no immediate physical reality (Hatherly et al., 2009). Virtual labs can adopt different forms and approaches. For example, students can access lab equipment remotely, they can be asked to watch live or pre-recorded experiments, conduct experiments at home, perform computer simulations of experiments, or analyze freely available experimental data sets. Before the Covid-19 pandemic, only a handful of Higher Education Institutions around the world had adopted online virtual labs into their courses, alongside their face-to-face offerings. Generally, virtual labs have been successfully incorporated into practical-based courses in instances when, due to capacity (i.e., large student cohorts), time (e.g., experiments lasting several days) or safety (e.g., use of toxic, explosive or radioactive chemicals), for example, they would not be possible in a usual lab setting (Coleman and Smith, 2019). In recent years, there has been a major increase in the development of sophisticated computer lab simulations by both for-profit companies and non-profit institutions. Flashy virtual labs with fancy graphics, however, can be both expensive for the institution and distracting for students. On the other hand, virtual labs may look cheap compared to video games, so fee-paying students may feel short-changed. In addition, many will argue that nothing teaches science better than a hands-on experiment in a real lab. Ultimately, and according to experts, the key factor determining whether a virtual lab simulation will improve understanding or just entertain students, critically depends on the fine details of how it was designed (Jones, 2018).

At the School of Biological Sciences at the University of Manchester (UK), we have successfully developed two Neuroscience-based virtual lab practicals aimed at second- and third-year Bioscience undergraduate students. We share below our experience, lessons learned, and we end with future perspectives for virtual labs.

DEVELOPING AN ONLINE VIRTUAL SCIENCE LAB PRACTICAL: TWO EXAMPLES

First Example: Neurophysiology Simulations Lab

The first virtual lab we developed was a Neurophysiology practical, which is taken by approximately 110 second-year Neuroscience and Cognitive Neuroscience and Psychology undergraduate students in our School each year and is one of eight labs included in a mandatory second year Research Skills Module (RSM). In this lab, students learn about the specific changes in neuronal membrane currents during an action potential and the underlying changes in ion flow, by using computer simulations of current-clamp and voltage-clamp electrophysiology experiments. Specifically, the Intended Learning Outcomes (ILOs) of this lab are as follows: By the end of this course the student will be able to:

1. Explain the ionic conductances underlying action potentials and investigate the effects of channel blockers on neuronal electrical activity.
2. Explore the concepts of reversal potential and postsynaptic potentials, together with their relevance.
3. Formulate and test hypotheses using interactive simulations of current-clamp and voltage-clamp electrophysiological experiments.
4. Interpret and evaluate electrophysiological data.
5. Carry out independent research and summarize and present the findings in a scientific output.

Proficiently running electrophysiology-based experiments in a lab is something that takes years of experience and cannot be provided easily to a large cohort of students. Fortunately, since neuronal ionic mechanisms have been mathematically modelled since the initial experiments by Hodgkin and Huxley (Schwiening, 2012), computer simulations of these phenomena are readily available. We opted for the free educational software MetaNeuron, developed by Eric A. Newman and Marc H. Newman, University of Minnesota (Newman and Newman, 2013). MetaNeuron was our preferred choice because this program is simple and easy to use, yet it allows the user to simulate a wide range of experiments. Specifically, this educational computer program models the basic electrical properties of neurons and it is organized into six lessons, ranging from membrane potential to action and synaptic potentials. For each lesson, a few student exercises are proposed. In addition, this program is intended for the starting neuroscience student and requires no prior experience with computer simulations or computer programming; it is therefore ideal for the teaching of a large cohort of second year undergraduate students.

First, we developed a pilot version of the online lab, which consisted of three parts: pre-lab activity, practical simulations and post-lab assessment (Figure 1A). The pre-lab activity was a series of lessons created using Softchalk©. These lessons aimed to introduce basic concepts (e.g., action potential) and included a combination of text, images, videos, quizzes and interactive activities (e.g., drag and drop). After completion of the pre-lab activity, students were given access to MetaNeuron and provided with a lab handbook with instructions, exercises and questions to answer. Finally, students completed a summative post-lab assessment, consisting on a total of 30 questions, combining multiple choice, short answer, calculations and creating four graphs. All components of the lab were fully online and were taken by each student asynchronously, in their own time, over a period of two weeks in September 2020. A total of 17 students tested the pilot version of this online lab and completed pre- and post-lab surveys. When analyzing the survey feedback, we found an overwhelming positive response, with 86% of students rating their experience of taking the online lab as either good or excellent, and 92% students also reporting that they felt they had been challenged and that the lab enhanced their understanding of action potential mechanisms. In terms of what could be improved, 77% students raised the issue of lack of immediate assistance and feedback from instructors, and the lack of live discussion with peers and demonstrators. In addition, we noticed that several students struggled with plotting and submitting their results graphs. We also realized that grading four graphs and 10 short-answer questions was doable with a small group of 17 students, but this would be an exceedingly time-consuming task for staff with the full cohort of 106 students. Therefore, before the launch of the final version of the lab to the full group of students in March 2021, we revised the virtual lab to address the issues above. Our aims for the revised lab were to: 1) Provide opportunities for student-staff interactions to enhance support of students and provide formative feedback; 2) provide opportunities for student-student interactions and collaboration; 3) help students with data collection and graph plotting, and 4) devise assessments that would allow us to check attainment of the ILOs in a large student cohort in a sustainable and time-effective manner. In order to address the aims above, we introduced a group exercise before the practical simulations, and changed the summative assessment to include MCQ tests and a group poster (Figure 1B). The final version of the lab took place over two weeks in semester 4. The group exercise, individual practical simulations and MCQ tests took place in week 1 and students were given week 2 to work on the group poster assessment in their own time (Figure 1B). Students were divided into 28 groups of four, which worked together in both the group exercise activity and the group poster assessment. The final (revised)

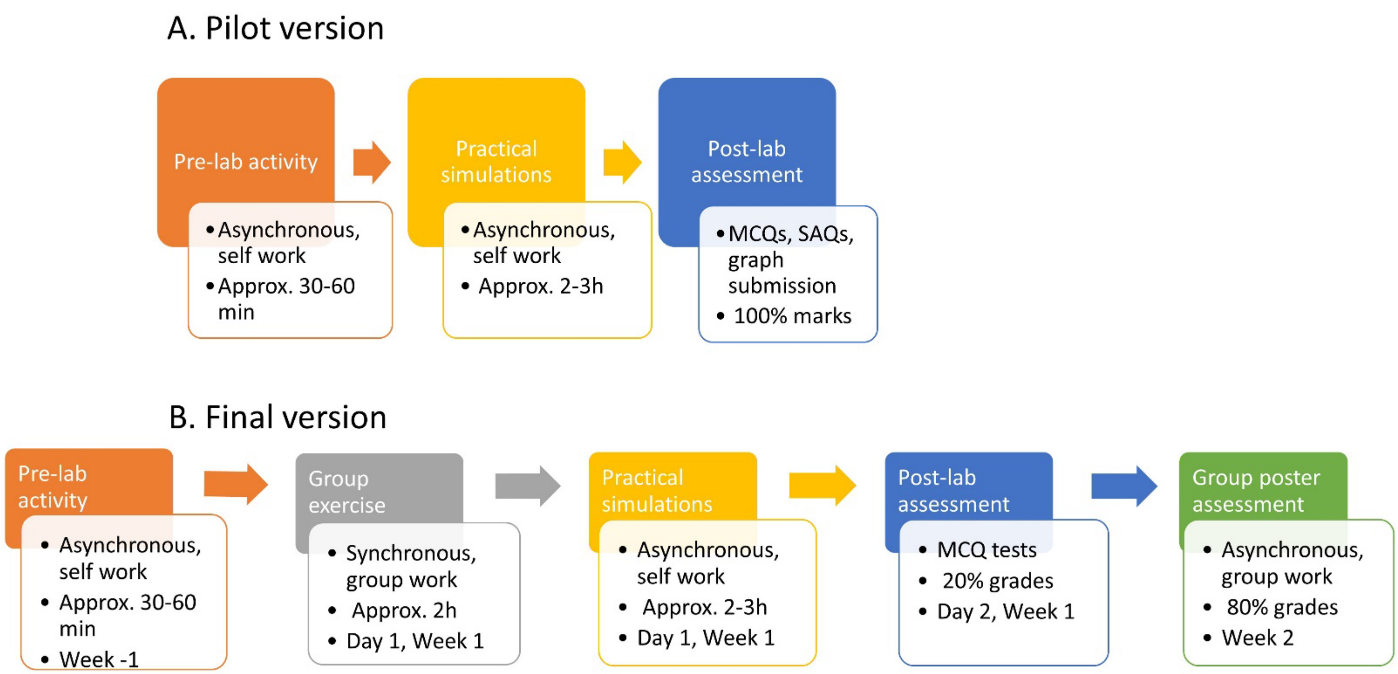

Figure 1. Neurophysiology lab structure. *A)* Pilot version. The pilot version of the lab consisted of three parts: a pre-lab activity, the practical simulations and a post-lab assessment. All three parts were fully online and taken by students individually, on their own time. *B)* Final version, which incorporated revisions following student feedback. The final version of the lab consisted of a pre-lab activity, which students had to complete on their own time ahead of the practical session (week -1). On the day of the practical (day 1, week 1), a live group exercise via Zoom took place in the morning and the individual practical simulations took place in the afternoon. On that day, teaching staff were available on Zoom to answer questions, resolve technical issues and provide formative feedback. The final version of the lab incorporated two different types of summative assessments, Multiple Choice Questions (MCQ) tests, taken the day after the practical (day 2, week 1) and a group poster, submitted a week later (week 2).

1. What effect does an increase in the outer concentration of K+ ([K+]o) have on the K+ equilibrium potential and on the membrane potential? Select one answer. (1 point)
   a. As the outer concentration of K+ increases, both its equilibrium potential and the membrane potential become less negative (more positive).
   b. As the outer concentration of K+ increases, both its equilibrium potential and the membrane potential become less positive (more negative).
   c. As the outer concentration of K+ increases, the equilibrium potential will become more negative, while the membrane potential will become more positive.
   d. As the outer concentration of K+ increases, the equilibrium potential will become more positive, while the membrane potential will become more negative.

2. Using the Na+ current-voltage plot that you obtained in class, what is the reversal potential for Na+? Select one answer. (2 points)
   a. The reversal potential for Na+ is approx. -60 mV.
   b. The reversal potential for Na+ is approx. -50 mV.
   c. The reversal potential for Na+ is approx. 0 mV.
   d. The reversal potential for Na+ is approx. +45 mV.

3. MetaNeuron Lesson 5. Starting with the default parameter values, select the TEA box to view the Na+ current in isolation, turn on “Stimulus 2”, set “Sweep Duration” to 14 msec, “Stimulus 1” and “Stimulus 2 Amplitude” to +5 mV, “Stimulus 1” and “Stimulus 2 Width” to 2 msec and “Stimulus 2 Delay” to 2 msec. Note that the amplitude of the peak Na+ current evoked by the second stimulus is smaller than that evoked by the first stimulus.

   Why is this? Select one answer. (1 point)
   a. Because Stimulus 2 amplitude is not big enough.
   b. Because Stimulus 2 duration is not long enough.
   c. Because TEA is interfering with the Na+ channels.
   d. Because Na+ channels have not yet recovered from inactivation.

4. Using the settings specified in the question above, what is the minimum “Stimulus 2 Delay” that you have to set in order to obtain a Na+ current with an amplitude similar to that obtained after “Stimulus 1”? Select one answer. (2 points)
   a. The delay should be set at a minimum of 4 ms.
   b. The delay should be set at a minimum of 5 ms.
   c. The delay should be set at a minimum of 6 ms.
   d. The delay should be set at a minimum of 7 ms.

Figure 2. Examples of assessment multiple-choice questions included in the final version of the lab. The wide range of questions served to test attainment of the lab’s ILOs (question 1 – ILOs 1, 2; question 2 – ILOs 2, 3; questions 3 and 4 – ILOs 1-4).

version of the lab included multiple opportunities for personal interactions, such as synchronous live sessions, where students would work in teams in order to run a simulation experiment, collect data, produce graphs and discuss the results obtained, under the guidance of a member of the teaching staff. These sessions, therefore, also served as an opportunity for staff to provide formative feedback to students, which was something missing in the pilot version (Aims 1 and 2). These group sessions also served the purpose to help students with data collection and graph plotting (Aim 3). In addition, we introduced drop-in online live sessions to allow students to easily contact a member of the teaching staff if experiencing technical or data collection issues (Aim 1). Students were also offered the option of directly emailing staff with their questions, or to post their questions on a discussion board on Blackboard®, which is the web-based virtual learning environment used at The University of Manchester (Aim 1).

The assessments in the final version of the lab were changed compared to the pilot version, to make for a more streamlined and less time-consuming process (Aim 4). In the final version of the lab the summative assessment consisted of a total of 25 questions, worth 20% of the final lab grade (4% of the RSM) combining multiple choice questions and calculations. These questions were set up on Blackboard® and automatically graded. The questions served to assess attainment of ILOs 1-4 (see example questions in figure 2). Furthermore, we introduced a group poster assessment, worth 80% of the final lab grade (16% of the RSM), which assessed attainment of ILOs 3-5. The group poster provided yet another opportunity for personal interactions and collaboration between students (Aim 2) and critically, it enabled student-driven development of experiments and subsequent communication in a scientific poster format. For the group poster activity, students had to apply the knowledge and skills learned in week 1, to the particular clinical setting of multiple sclerosis. Specifically, students were asked to use MetaNeuron simulations to investigate the effect of temperature on action potential generation and sodium channel currents and then present their results and conclusions in a scientific poster. Posters were submitted as PDF files and teaching staff marked them according to both content (e.g., concise aims, critical evaluation of results and their significance) and format (e.g., overall design, quality of figures).

When surveyed, the majority of students who took the revised (final version) lab found that the group exercises were useful and engaging and overall enjoyed the interactive aspects of the lab (Table 1). Despite this overwhelmingly positive feedback, 10% of the students were unhappy with the interactive aspects of the lab and cited other team members not contributing actively or equally in discussions and group poster work as the main reason. We should, therefore, address the issue of individual contribution in group work in future versions of the lab, for example, by incorporating group work strategies in the course (Holmes and Treibergs, 2022).

Furthermore, we compared the grades of 14 assessment MCQ questions which overlapped between the pilot and the revised labs, and found a significant 23% increase in the average grades for the revised lab (mean grade ± standard error: pilot version, 55.6 ± 4.3%; final version, 78.9 ± 5.1%; $p<0.001$, t-test). Therefore, these results suggest that providing sufficient opportunities for personal interactions and formal feedback within an online course can lead to a substantial improvement in students' academic performance. This is in line with findings that group work stimulates learning and supports acquisition of knowledge in higher education environments (Chiriac, 2014).

Second example: Allen Brain virtual lab

The second virtual lab we developed is taken by around 8-10 third-year Biosciences (Neuroscience, Pharmacology, Biochemistry, Biomedical Sciences) undergraduate students in our School each year and is one of twelve labs included in a mandatory third year Experimental Skills Module (ESM). This module runs over 12 weeks in semester 6 and is lab-based. Because of last-minute changes to local Covid-related regulations, however, online alternatives to several of the labs had to be developed at short notice. Armed with our experience developing the first virtual lab, we developed a second virtual lab, which was launched in February 2021, and used publicly available data from The Allen Institute (https://alleninstitute.org/). Because of the short time frame, we were unable to test the lab before it was launched to the whole student cohort.

The Allen Brain Atlas is increasingly used as an effective resource to teach neuroscience to undergraduate students (Chu et al. 2015; Gilbert, 2018; Grisham et al., 2017; Ho et al. 2021; Jenks, 2009; Juavinett, 2020; Ramos et al., 2007; Ryan and Casimo, 2021), and several educational resources have been developed by The Allen Institute as part of their outreach strategy (Allen 2021b).

The main objective of this second lab was to advance students' understanding of neuroanatomy and genetics in the brain. The specific ILOs for this lab were: By the end of this course, the student will be able to:

1. Analyze and interpret brain gene expression data.
2. Design experiments using the same type of data.
3. Work in teams in a research environment.
4. Carry out independent research, and then evaluate and summarize the results in written and oral scientific formats.

The lab consisted of a pre-lab, virtual experiment and post-lab assessment. The pre-lab (weeks 1-5) consisted of three one-hour tutorials to discuss the ESM general module approach and assessments (tutorial 1, week 1): experimental problem, approaches to be used, and experimental design (tutorials 2 and 3). Tutorials were run as synchronous, live sessions via Zoom and used adaptations of some of the materials included in the "The Building Blocks of the Brain" education resource developed by the Allen Institute (2021a).

For the pre-lab, students were given three assignments to complete around the tutorial sessions, to familiarize themselves with The Allen Brain datasets and with the scientific literature around the topic of genetics underlying dementia. For the first assignment (week 1), students read two general papers about neuroscience research and watched two videos about the purpose and work of the Allen Institute. Discussion of these assignments then took place in tutorial 2 (week 2), which also served to introduce students to the design of virtual experiments using Allen Brain Atlas data. For the second assignment (week 3), students were asked to familiarize themselves with the microarray data available in the Allen Brain databases and start thinking about data collection and design of their own experiments. Staff discussed these designs and provided formative feedback in tutorial 3 (week 4). In this tutorial session, students were also given a small exercise, where they practiced collection, sorting and analysis of gene expression data from the "Ageing, Dementia and TBI" database (https://aging.brain-map.org/). For the third assignment (week 5), students were provided with three recent scientific papers on the topic of "genes underlying dementia". Students were then asked to individually think of a research question on the given topic, and design an experiment to address this question, based on the information covered in the tutorials and assignments. Students were given free rein to design their own experiments, and were allowed to use data from the "Ageing, Dementia and TBI," "Human Brain," "Developing Human Brain," "Mouse Brain," and "Developing Mouse Brain" atlases. Students were asked to investigate the expression of genes involved in any aspect of brain physiology of their choosing (e.g., metabolism, cell function, circadian function), and to design an experiment with at least 3 independent variables (e.g., dementia vs. non-dementia, brain region, age, male vs. female, human vs. mouse). Students then submitted (week 6) a 2-page experimental background, which contributed 15% to the final module grade.

For the virtual lab, students were divided into groups of 2-3 and were expected to complete approximately 36 hours of independent project work over a period of two weeks (weeks 7-8). Each team had to agree on one experimental design, based on the individual experimental designs that each student had submitted in week 6. Students then worked collaboratively in their own teams, carrying out virtual experiments investigating the role of genetic factors in dementia. During these two weeks, we organized several online, live, synchronous sessions via Zoom, covering aspects of data collection, data analysis and report writing tips, together with drop-in clinics to resolve any kind of technical or experimental problems that students faced. The post-lab assessments consisted of submission of an individual 5-page lab report (week 10, 45% final grade),

QUESTION	RESULTS
Was all the necessary information provided?	97% yes
Was there anything you missed in the practical delivery?	83% no
Did you feel that the aims of the lab were met?	85% yes
Which aspect of the lab did you enjoy the most?	50% group work/activities 50% MetaNeuron simulations
Has technology been used effectively to facilitate learning?	72% yes
What did you think of the interactive aspects of the lab?	90% positive
Did you interact with an instructor?	87% yes
If yes to the above question, was the interaction useful?	88% yes

Table 1. Summary of the results of the student feedback survey for the first virtual lab. The survey was completed by 39 students (37% cohort), after they had completed the full version of the lab.

submission of a group poster (week 11, 20% final grade) and individual oral presentation of the group poster (week 12, 10% final grade). The individual presentations of the group poster took place in an online session via Zoom, with approximately 10 minutes presentation by the student, plus 5 minutes questions by the teaching staff. Students' overall performance throughout the duration of the module was also assessed (10% final grade).

With regards to personal interactions, students worked within a team for all stages of the project, except report writing. Therefore, this lab benefited from an interdisciplinary, communities of learning- and problem-based learning approach, where students from different degree backgrounds interacted and worked together in groups in order to learn about brain function and disease and apply this knowledge to real clinical data. The multiple benefits of this form of educational approach are well-described (Davies et al., 2019; Weller and Appleby, 2021). This second lab was well received by the students and, in addition to achieving its Intended Learning Outcomes (ILOs), it was successful in providing a flexible, creative, accessible, interactive and risk-free learning environment for students.

SUMMARY OF LESSONS LEARNED

Practical work is an essential element in the teaching of science-based courses and presents a particular challenge in the context of distance learning. For our first virtual lab, given the technical complexity of setting up and the training required to run electrophysiology experiments, we believe that the use of computer simulations is the best option available for the teaching of large cohorts of undergraduate students. For smaller cohorts of more advanced students, like those that took part in our second virtual lab, the use of open source databases (e.g., brain data from the Allen Brain Institute) represents an invaluable opportunity for students to be exposed to unique, real, clinical data, which would otherwise take an average lab years to obtain.

Based on our experience developing and running these two online virtual Neuroscience labs, we have learned the following lessons:

1. Feedback is key: For our first lab, being able to run a pilot study with a few students was critical in the success of the final version. Although running a pilot takes additional time and effort (e.g., recruiting volunteer students, obtaining ethics approval), the student feedback and the lessons learned by the staff are invaluable, as they help correct any technical or pedagogical issues beforehand and thus improve the overall student experience later. Continued student feedback after the final version of the lab was launched a year ago, is helping us now to refine and develop our labs further.
2. Student interactions need careful planning: Our experience has demonstrated that incorporating student collaborative work and providing multiple opportunities for student-staff interactions will not only provide a chance to resolve technical issues, foster scientific discussions and offer formative feedback, but will also enhance the learning experience and improve the academic performance of students. Consequently, communication within a course should be carefully planned and facilitated.
3. Student co-creation has many benefits: for the development of our first lab, we enrolled two undergraduate students as partners, who were involved in the project creation process from the start. This collaboration between students and staff has many advantages, including the balancing of student lived experience and academic scholarship/research.
4. Consider the workload: Both for students (e.g., time it would take a student to complete all of the lab activities and assessments), and for teaching staff (e.g., time it takes to grade all of the assessments and for in-person/online support and supervision).
5. Working backwards is best: When designing new virtual labs, there is sometimes a tendency to try to achieve the same goals as in in-person labs. We found, however, that a backwards design is best: define your goals and ILOs first and then design and plan the practical activities around them.

6. Use freely-available online educational resources if you can: We found that this has many advantages. On the one hand, it can save a considerable amount of time. In addition, these resources do not require institutional IT support or maintenance, they are easy to embed in any virtual learning environment, and they are cost-effective.
7. Mix and match: We incorporated different educational resources for different parts of our labs (e.g., tutorials, videos, quizzes, computer simulations), to provide a diverse, interactive and fun learning environment for students.

CONCLUSIONS AND FUTURE PERSPECTIVES

The use of electrophysiology simulations to teach students about action potentials is not new, whether it takes place in the classroom or online. The novelty of our approach is that, in the two virtual labs that we developed, we effectively used online tools to teach students not only about how the brain works, but importantly, we also taught them about the research process: from reviewing the literature and experimental design, to running experiments, collecting data, analyzing and interpreting data, and communicating results. We believe that this is a more holistic approach that actually benefits from the combination of in-person and online activities. Here, students can take ownership of the scientific process from start (as they plan and design their own experiments) to finish (as they write a lab report and/or produce a scientific poster). During this process, students also learn about scientific collaboration as they work in teams. The beauty of virtual labs is that students can be creative in their approach; they can try different experimental parameters and approaches as many times as they want to, and they are allowed to make mistakes and rectify. Furthermore, in this day and age students are comfortable and used to communicating via electronic means and virtual labs can exploit this to provide an interactive interface for learning and collaborating online.

The development of online virtual labs is rapidly becoming more widespread across Higher Education Institutions. We believe that virtual labs have many advantages and benefits, and can be much more than a replacement for lengthy or risky experiments. As we return to the classrooms after the global pandemic, we believe that keeping a number of online learning elements into our courses has many benefits. For example, there are numerous goals in our practical modules that do not require hands-on lab experience, such as learning about the research process and science communication. Creating online learning resources that effectively address these goals can significantly decrease lab space usage, and ultimately save staff time and costs. Furthermore, integrating virtual labs in a course is a way to develop more flexible, interactive and personalized learning environments, eliminate barriers to learning, and improve accessibility for all students, thereby opening new opportunities for both the learner and the educator (Diwakar et al., 2016).

On the other hand, we believe that virtual lab learning activities such as running computer simulations or utilizing publicly available datasets need not be restricted to practical-based modules only. Carefully-chosen examples and short exercises can be incorporated into lecture-based modules as a form of "active learning", which has repeatedly been shown to promote equity and inclusivity in higher education, engage students, improve learning outcomes and experience, and foster community (Sandrone et al., 2021).

Although virtual labs can never replace the skills learnt by performing real experiments, considerable evidence demonstrates that embedding virtual labs in a course, when done carefully and thoughtfully, can actually improve the students learning experience and grades. Beyond the Covid-19 global pandemic and looking to the future, there are many excellent reasons why higher education courses should develop and include virtual labs into their curricula.

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