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TEACHING INNOVATIONS

Using a physiology virtual laboratory to explore vascular reactivity: feedback from undergraduate biology students in France

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Abstract

The evolution of European and French regulations regarding animal experimentation in higher education has prompted universities to develop alternative methods to animal testing. The University of Angers (France) has created a web-based virtual lab (VL) called *ExAVir* (https://labua.univ-angers.fr/Projets/exavir/) designed to simulate practical lab work in animal physiology and pharmacology. In this study, we evaluated the perception of *ExAVir* among third-year undergraduate physiology students at the University of Lyon, France, as a tool for studying vascular physiology. Students completed the VL activity independently and were then asked to fill out a postcourse survey. Of the 268 students enrolled in the course, 197 completed the questionnaire (73.5%). Most students appreciated the VL (65%) and valued the fact that it avoided the use of laboratory animals (90%). A majority (69%) believed that the VL could effectively replace one session of lab work, although 88% stated that it should not replace all hands-on lab activities, as it does not engage the same practical skills. Nevertheless, 71% of students reported a significant improvement in their perceived level of vascular physiology through the use of the VL. We believe that the targeted use of VLs such as *ExAVir* can be a powerful educational tool, particularly when integrated with traditional wet lab practicals.

NEW & NOTEWORTHY Facing evolving European regulations on animal experimentation, universities are turning to innovative teaching tools. Our study explores *ExAVir*, a virtual lab developed by the University of Angers, used by physiology students at the University of Lyon to learn vascular physiology without animal testing. Most students found the virtual lab engaging, effective, and ethically valuable, highlighting its potential to complement, but not replace, traditional hands-on lab work.

3Rs; vascular physiology; virtual laboratory

INTRODUCTION

Teaching cardiovascular physiology is essential for understanding the functioning of the cardiovascular system in both health and disease. Traditionally, this subject relies in part on hands-on laboratory experiments. Many of these experiments involve studying the effects of bioactive compounds (e.g., neurotransmitters, hormones, drugs) on the cardiovascular system of laboratory animals, either in vivo (e.g., blood pressure or electrocardiogram measurements) or ex vivo (e.g., isolated organs such as perfused beating hearts or aortic rings). These disciplines are fundamental in numerous educational programs, including general biology, medicine, and pharmacy. However, the widespread use of laboratory animals raises ethical concerns (1), along with various practical and economic challenges (2). Over the past two decades, significant efforts have been made to align with international regulations regarding the scientific use of animals. These efforts have been largely driven by increasing awareness of animal welfare and the need to reduce the number of animals used in experiments, in accordance with the "three Rs" (3Rs) principle (1, 3, 4). First introduced by Russell and Burch in 1959, the 3Rs framework serves as the ethical foundation for the use of animals in research (5, 6). The three principles are Replace: developing alternative methods to avoid animal use whenever possible; Reduce: minimizing the number of animals needed through improved experimental design; and Refine: implementing techniques that prevent or minimize pain, suffering, or distress, thereby improving animal welfare. Through Directive 2010/63/EU on the protection of animals used for scientific purposes (7) and in accordance with *The Principles of Humane Experimental Technique* (8), the European Union has reinforced the application of the 3Rs in research and education. Recently, the French National Committee on Ethics in Animal Experiments [*Commission Nationale de Réflexion Ethique sur l'Expérimentation Animale* (CNREEA)] has recommended reducing or even replacing the use of live animals in higher education with simulated experiments, to comply with evolving ethical standards and legal requirements (9). Beyond ethical considerations, the high costs of acquiring

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and maintaining laboratory animals (2), along with the need for skilled personnel, have led many academic institutions to seek alternatives to live animal experiments in teaching (10, 11).

Although considerable progress has been made in reducing and refining the use of animals in education, the goal of replacing them with alternative methods has gained increasing traction. One promising solution is the virtual laboratory (VL), a digital platform that simulates real-world experimental scenarios and provides interactive, immersive learning environments (12).

VLs offer several advantages over traditional laboratories: they eliminate the need for physical laboratory space or materials, are more cost-effective, and allow students to repeat experiments without resource constraints (2), thus deepening their understanding through practice (13–17). Integrating virtual laboratories into educational curricula aligns with modern pedagogical trends toward digital and self-paced learning (18–20). These platforms often feature realistic simulations, real-time data analysis, and interactive modules that enhance student engagement. Serious games are games primarily designed for purposes beyond entertainment, such as education, training, or professional development. This term was introduced by Abt (21), who defined them as "structured experiences created with an explicit educational purpose." Serious games combine game mechanics with pedagogical objectives to achieve measurable learning outcomes (22). In university, they can be used to create immersive and interactive learning environments that promote active engagement, problem-solving, and experiential learning. Systematic reviews further demonstrated that simulation-based games can improve declarative and procedural knowledge compared to traditional instructional methods (23). Within VL models, serious games allow students to experiment, test hypotheses, and observe consequences in realistic but risk-free settings, thereby bridging the gap between theoretical knowledge and practical application.

In France, the University of Angers has recently developed a virtual animal experimentation web platform called *ExAVir* (short for *Experimentation animale Virtuelle*, i.e., Virtual Animal Experimentation; https://labua.univ-angers.fr/Projets/exavir/). Designed to simulate laboratory work in animal physiology, pharmacology, and toxicology, *ExAVir* can be used to recreate a variety of experiments for educational purposes (24). Through an innovative approach that combines serious games with diverse simulations, *ExAVir* encourages students to take a more active role in their learning and fosters greater autonomy.

The present study examined how the use of a virtual laboratory for teaching vascular physiology was perceived by undergraduate biology students in Lyon, France.

MATERIALS AND METHODS

Participants

This study was conducted in the Department of Biosciences (https://ufr-biosciences.univ-lyon1.fr/) at Claude Bernard University Lyon 1 (Lyon, France) between March 2023 and March 2025. Third-year undergraduate students enrolled in the Cardiovascular and Respiratory Physiology course (UE-BIO3036L) participated in the study. All participants were officially registered in the Life Sciences–Animal and Human Physiology specialization of the License 3 program. A total of 197 students completed the evaluation across three academic years: 75 in March 2023, 50 in March 2024, and 72 in March 2025. We chose to aggregate the data from the 2023, 2024, and 2025 cohorts to improve the robustness and representativeness of the dataset and ensure a more robust representation of the student population. To ensure the validity of this merger, we maintained strict longitudinal consistency across all three years. Specifically, the course delivery, curriculum content, and assessment criteria (including the laboratory report) remained identical. Furthermore, a preliminary analysis of the mean scores across cohorts showed no statistically significant differences, justifying the consolidation of the datasets. As the project involves solely the secondary use of anonymized data and offers no possibility of participant reidentification, it is exempt from ethics committee review (CER, *Comité Ethique de la Recherche*). Students were given the questionnaires but were under no obligation to complete them, as demonstrated by the response rate of 75% of all course participants.

The *ExAVir* Platform

The *ExAVir* web application comprises five modules that provide access to different experimental setups and tools (24): the Isolated Organ setup, the Chemistry Lab, the Animal Facility, the Experimental Results, and a Dashboard for management of experiments (Fig. 1). In the Setup module, students can select the required instruments for their experiment (e.g., an isolated organ bath and a force transducer). The Chemistry Lab module enables them to prepare all the necessary solutions and adjust parameters such as pH, e.g., for physiological buffered solutions. In the Animal Facility, students choose the appropriate species for the experiment from a list including mouse, rat, pig, dog, monkey, and frog. Although the experimental protocol specified the use of rats, students were permitted to select the specific strain (e.g., Black-hooded, Lewis, Long-Evans, or Dark Agouti), sex, and age of the subjects, provided the rats were adults. Once the equipment is selected, the solutions prepared, and the animal chosen, students move to the Dashboard, where they select a method for animal euthanasia, perform dissection, and mount the organ onto the equipment. To guide students through the protocol, "blocking steps" can be activated. These prevent access to the next stage if previous selections are inconsistent with the experimental requirements. The protocol itself is available via a toggle button, allowing students to view or hide it as needed. The Results module displays data generated by each experiment. These data are precoded with a four-parameter logistic equation [the 4 parameters being Baseline, Maximum effect (i.e., plateau), Sensitivity (i.e., EC_{50}), and Slope]. This equation generates experimental outcomes (e.g., the tension developed by an aortic ring) based on the concentration of the tested compound.

Course Design and Implementation

The course focused on understanding the role of the vascular endothelium and endothelium-derived vasorelaxing factors in acetylcholine-induced vasodilation. Students were

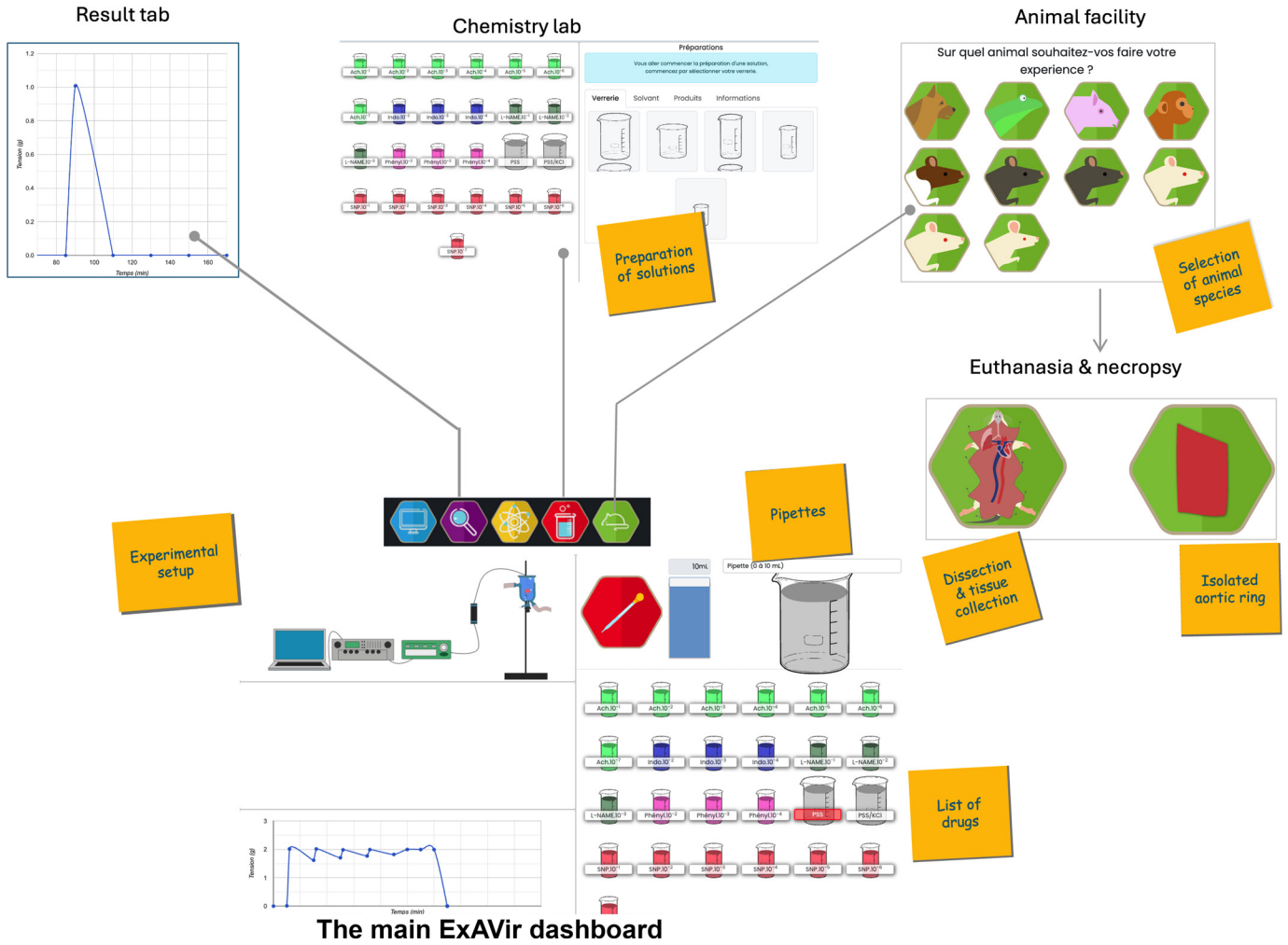


Figure 1. Overview of the *ExAVir* interface. The *ExAVir* web application is composed of 4 modules providing access to various setups and equipment: *1*) the Dashboard for conducting experiments showing the isolated organ setup, *2*) the Chemistry Lab to prepare buffer and solutions, *3*) the Animal Facility, *4*) the Results tab to display the results of virtual experiments.

tasked with conducting dose-response experiments using isolated aortic rings. The rings were precontracted with the α_1-adrenergic agonist phenylephrine, after which cumulative dose-response curves were generated with acetylcholine (ACh) at concentrations ranging from 10^{-10} to 10^{-4} mol/L. These experiments were then repeated in the presence of *1*) a nitric oxide synthase inhibitor [N^G-nitro-L-arginine methyl ester (L-NAME), 10^{-4} mol/L], *2*) a cyclooxygenase inhibitor (indomethacin, 10^{-4} mol/L), and *3*) both inhibitors simultaneously. Further experiments using ACh were conducted on deendothelialized aortic rings. Additionally, dose-response curves were generated with the nitric oxide (NO) donor sodium nitroprusside (SNP, 10^{-10} to 10^{-4} mol/L) on both intact and deendothelialized aortic rings. Before the experiments, the students were responsible for calculating the pipetting volumes required for the dose-response curves and determining the final drug concentrations in the organ bath. To prepare their concentration ranges, they could choose from stock solutions ranging from 10^{-2} to 10^{-6} mol/L for each compound. Aortic contraction and relaxation tension is calculated by *ExAVir* and displayed in a table, which students can use directly to construct their concentration-response curves.

Figure 2 provides an overview of the course structure. Before the course, the students were asked to evaluate their knowledge of vascular physiology using the following 5-point Likert scale: 1 = Very poor, 2 = Poor, 3 = Fair, 4 = Good, 5 = Very good). The course was divided into three phases: *1*) An introductory session (90 min) where students were introduced to the fundamental concepts of vasomotor regulation, with a particular focus on the role of the vascular endothelium and endothelium-derived factors. They were also taught how to construct dose-response curves and calculate pharmacodynamic parameters such as half maximal effective concentration (EC_{50}). This session included hands-on training on how to use the *ExAVir* platform. *2*) A sequence of autonomous work (3–4 wk): Students independently conducted the experiments using *ExAVir*, generating their own datasets. Students were tasked with producing a 3- to 5-page laboratory report discussing the acetylcholine (ACh) signaling pathway, specifically focusing on the roles of nitric oxide (NO) and the vascular endothelium in mediating ACh effects. Additionally, they were required to generate a schematic diagram illustrating the intracellular signaling pathways that underlie the vascular actions of ACh. *3*) A final

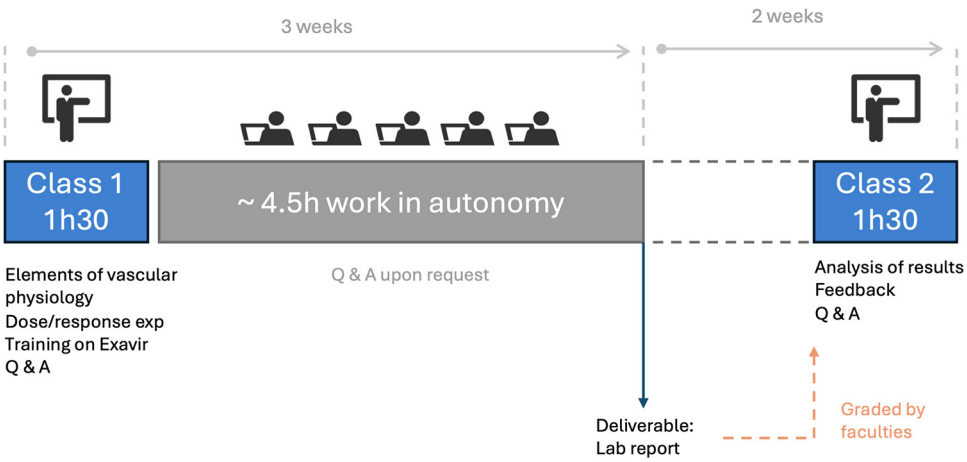


Figure 2. Design of the learning sequence using the *ExAVir* virtual laboratory (VL). Students participated in a 90-min class introducing the main concepts underlying the regulation of vasomotor tone, along with hands-on training in using *ExAVir* and performing the required experiments. They were then given 3–4 wk to independently complete the experiments and prepare a laboratory report. A final 90-min session provided feedback on their work and discussed the results of the different experiments performed.

session (90 min): Faculty returned the graded laboratory reports and held a feedback session to discuss the students' results and interpretations. At this time, students were asked to complete an anonymous 16-item questionnaire assessing their learning experience.

Student Perception and Perceived Level of Knowledge

At the conclusion of the course, students completed a questionnaire designed to evaluate their experience with the VL platform. The survey was completed in class on a voluntary basis and was totally anonymous. Three criteria were evaluated: *1*) Perception and usability: 15 items assessed students' perceptions using a 5-point Likert scale (1 = Strongly disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, 5 = Fully agree); *2*) Satisfaction: students rated their satisfaction using a 5-point scale (1 = Very unsatisfied, 2 = Unsatisfied, 3 = Neutral, 4 = Satisfied, 5 = Very satisfied); and *3*) Student-perceived level of knowledge: students evaluated their perceived level of knowledge of vascular physiology before and after the course, using a 5-point Likert scale. The two statements used in the survey were "Prior to this course, my understanding of vasomotor control is: Very Good/Good/Average/Poor/Very Poor" and "After completing this course, my understanding of vasomotor control is: Very Good/Good/Average/Poor/Very Poor." Finally, their final course grade was collected for performance analysis.

Qualitative Data Analysis: Thematic Analysis

Qualitative data from open-ended comments were analyzed via AI-assisted thematic analysis according to the method described by Braun and Clarke (25). We employed ChatGPT (based on version GPT-5.3) to perform initial coding and identify recurring patterns through a recursive prompting process. To ensure interpretive validity, the AI-generated themes were manually audited and refined by the research team, ensuring that all findings remained strictly grounded in the original student responses. The prompts used for AI-assisted thematic analysis are provided in Supplemental Materials.

Data Analysis

Statistical analyses were performed with GraphPad Prism 6 software (Prism 6.0; GraphPad Software, San Diego, CA) and R software (https://www.r-project.org/). Categorical data were compared by chi-square or Fisher's exact test. Ordinal data were compared by Wilcoxon signed-rank test and Friedman test. A P value < 0.05 was regarded as significant.

RESULTS

Demographics

Student characteristics are summarized in Table 1. Of the 268 students enrolled in the course, 197 completed the questionnaire, representing a response rate of 73.5%. The student response rate varied significantly over the 3-yr period: 60% (75/124) in 2023, 77% (50/65) in 2024, and 91% (72/79) in 2025 (chi-square test, $P < 0.001$). The majority of participants were women (76%), and the sex ratio remained consistent across academic years (Fisher's exact test, $P = 0.269$). Most students (78%) used a computer to perform their virtual laboratory experiments, whereas a small proportion (7%) used a tablet.

Table 1. *Characteristics of the students involved in the study*

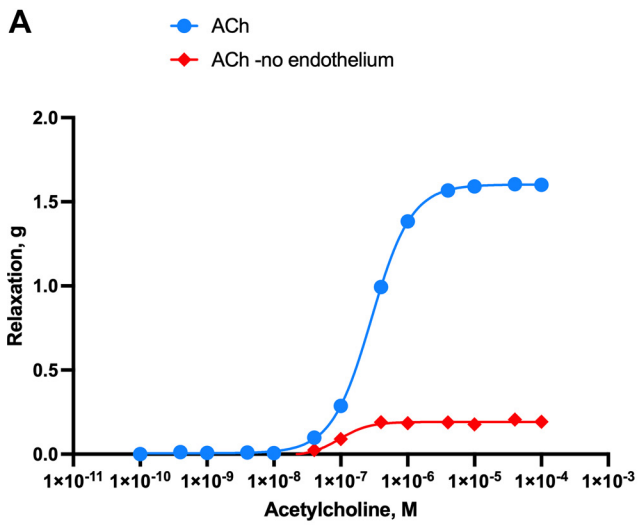
	2023	2024	2025	Overall
N	75	50	72	197
Sex M/F (%F)	11/64 (85%)	9/41 (82%)	18/53 (74%)*	38/158 (76%)
Devices used				
Computer	65 (87%)	43 (86%)	66 (92%)	174 (88%)
Tablet (e.g., iPad)	6 (8%)	2 (4%)	5 (7%)	13 (7%)
Smartphone	0	0	0 (0%)	0 (0%)
Two of these devices	4 (5%)	4 (8%)	0 (0%)	8 (4%)
Three of these devices	0	1 (2%)	0 (0%)	1 (0.5%)
Device(s) owned by the student	74 (99%)	50 (100%)	69 (96%)$	193 (98%)

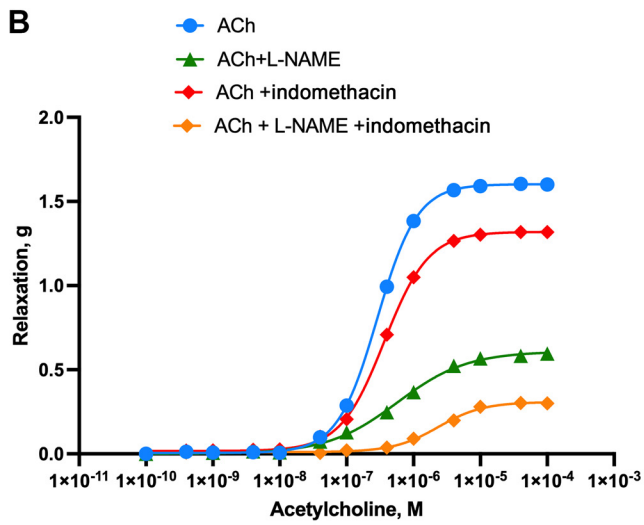
*One student did not wish to declare his/her gender (0.5%). $Two students did not answer the question (2%).

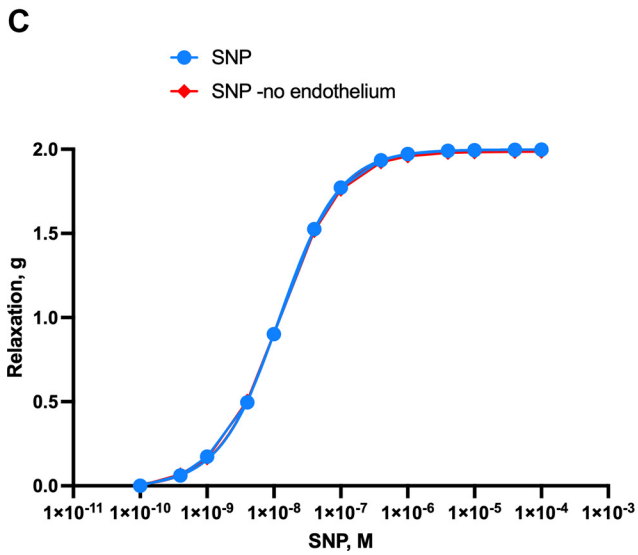
Notably, the *ExAVir* platform was designed specifically for desktop use, and instructors recommended using a computer. Nearly all students (98%) used their own device, with < 2% using equipment provided by the university.

ExAVir Outputs

Representative results from the virtual experiments are shown in Fig. 3. Incubation of phenylephrine-precontracted aortic rings with acetylcholine (ACh) induced a dose-dependent decrease in vascular tone, with a calculated EC_{50} in the submicromolar range (<0.5 μmol/L) and a maximum relaxation of 1.6 g. Example tracings are shown in Supplemental Fig. S1. Endothelial denudation nearly abolished the response to ACh (−88%), demonstrating that ACh-induced vasodilation was predominantly endothelium dependent. Pretreatment with pharmacological inhibitors further reduced ACh-induced vasorelaxation. L-NAME (nitric oxide synthase inhibitor) and indomethacin (cyclooxygenase inhibitor) decreased the vascular relaxation by 63% and 27%. The combination of L-NAME and indomethacin further decreased the vasorelaxation by 81%. These results suggest that nitric oxide (NO) is the main signaling mediator of ACh-induced vasodilation in this model, with a possible additive contribution from prostanoids. In contrast, sodium nitroprusside (SNP), a potent NO donor, induced stronger and more potent vasorelaxation than ACh, with an EC_{50} of 1.1×10^{-8} mol/L and a maximum effect close to 2 g, independent of endothelial integrity. The EC_{50} values calculated by students based on the *ExAVir* outputs are shown in Fig. 4. Median EC_{50}s computed by the students were 4.00 [interquartile range (IQR): 2.98–5.00] $\times 10^{-7}$ mol/L for ACh and 1.15 (IQR: 1.00, 2.00) $\times 10^{-8}$ mol/L for SNP. *ExAVir* incorporates a "noise effect" into the simulation to mimic biological







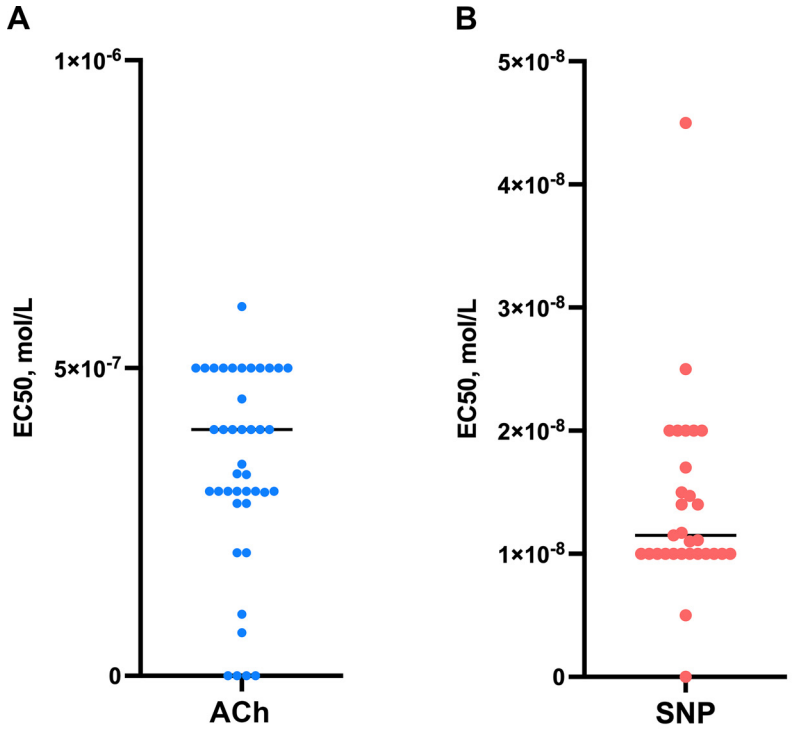
D

Pharmacodynamic indexes for acetylcholine (ACh) and Sodium nitroprusside (SNP)

	ACh	SNP
E_{max}, g	1.60 (1.59, 1.61)	2.00 (1.99, 2.01)
EC_{50}, M	2.86 (2.80, 2.93) x10 $^{-7}$	1.21 (1.17, 1.24) x10 $^{-8}$
pD_2	-6.54 (-6.55, -6.53)	-7.92 (-7.93, -7.90)

E_{max}, maximal effect, EC_{50}, Half maximal effective concentration, pD2 was calculated as –log (EC_{50}).

Figure 3. Representative dose-response curves generated from *ExAVir* virtual laboratory (VL) outputs. Aortic rings were precontracted with phenylephrine (10^{-6} M). *A*: role of the vascular endothelium in the vasodilatory effect of acetylcholine (ACh; 10^{-10} to 10^{-4} M). Aortic rings were mechanically denuded of endothelium. *B*: effects of pharmacological inhibitors of nitric oxide (NO) synthase [N^G-nitro-L-arginine methyl ester (L-NAME), 10^{-4} M] and cyclooxygenases (indomethacin, 10^{-4} M) on ACh-induced vasodilation. C: effects of the NO donor sodium nitroprusside (SNP; 10^{-10} to 10^{-4} M) on vasodilation. *D*: main pharmacodynamic parameters calculated from the dose-response curves: EC_{50} (half-maximal effective concentration) and E_{max} (maximal effect).



C

Pharmacodynamic indexes calculated by students for Acetylcholine (ACh) and Sodium nitroprusside (SNP)

	ACh	SNP
N	43	33
EC_{50}, mol/L	4.00 (2.98-5.00) $\times 10^{-7}$	1.15 (1.00-2.00) $\times 10^{-8}$
pD_2	6.40 (6.30-6.53)	7.94 (7.70-8.00)

EC_{50}, half-maximum effective concentration, pD_2 was calculated as -log(EC_{50})

Figure 4. Pharmacodynamic parameters calculated by students from *ExAVir* virtual laboratory (VL) outputs. *A*: half-maximal effective concentration (EC_{50}) of acetylcholine (ACh). *B*: EC_{50} of sodium nitroprusside (SNP). *C*: summary statistics.

and experimental variability. To assess this, we repeatedly stimulated the aortic ring with mol/L of phenylephrine, which produced a potent contraction. The resulting mean tension was 2.01 g (range: 1.98–2.02 g; coefficient of variation: 0.71%). Subsequent experiments using vasodilatory stimuli (ACh and SNP, both at 10^{-6} mol/L) yielded similar results, with a coefficient of variation of 0.68% for both (see Supplemental Fig. S2).

Students' Perception of the VL

Approximately two-thirds of the students (65%) expressed a positive opinion of the virtual laboratory as an alternative teaching method. Moreover, 78% believed that this approach could be extended to other subjects or disciplines (Fig. 5). A majority (69%) agreed that the VL could substitute for one practical laboratory session, but 88% opposed replacing all hands-on laboratory sessions, emphasizing the importance of developing practical skills; From an ethical standpoint, 90% of students appreciated that the VL avoided the need to euthanize laboratory animals. Despite these advantages, only 21% of students felt capable of performing real pharmacological experiments independently at the end of the course, whereas 59% reported lacking confidence in doing so. Sixty-five percent of students found the VL easy to use, and 74% felt that the VL protocol was clear and detailed enough (Fig. 6). Eighty-four percent of students considered they had sufficient physiological knowledge to use the platform autonomously, and 55% believed the VL helped them become more autonomous. Seventy-eight percent of students found the experience interesting, and nearly all students (95%) reported completing the requested experiments conscientiously. When asked about their overall level of satisfaction, 80% of students reported being satisfied or very satisfied whereas 8% were dissatisfied (only 1 student reported being very dissatisfied) (Fig. 7*A*). When asked whether they would recommend the use of a VL, 65% recommended it whereas 9% would not recommend it (26% neutral) (Fig. 7*B*).

Student-Perceived Level of Knowledge on Vascular Physiology

Students self-reported their perceived level of knowledge of vascular physiology using a Likert scale (1 = Very poor, 5 = Very good) before and after the course (Fig. 8, *A* and *B*). Before the course, 30% ($n = 59$) rated their knowledge as good

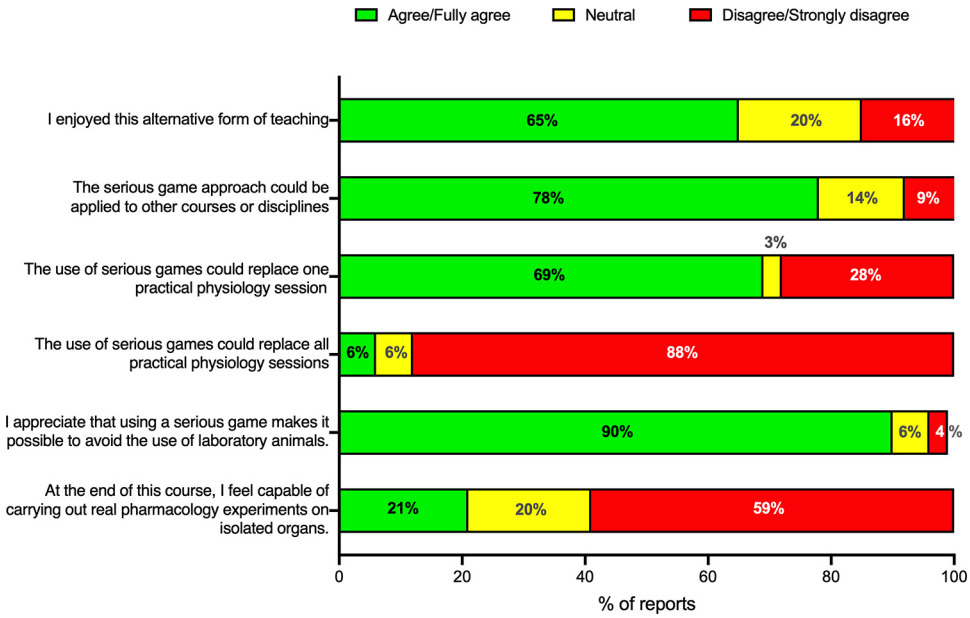


Figure 5. Student evaluations of the *ExAVir* online physiology learning platform. Values represent percentages for the 197 students who completed the questionnaire (76.5% response rate). Responses were scored with a 5-point Likert scale: 1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, and 5 = fully agree. For readability, categories were grouped into 3 classes: Strongly agree/Agree (green), Neutral (yellow), and Disagree/Strongly disagree (red). Detailed results for all 5 categories are provided in Supplemental Table S1.

or very good, 56% ($n = 111$) rated it as fair, and 14% ($n = 27$) rated it as poor or very poor. After using the VL, the mean score increased from 3.19 (SD = 0.78) to 4.12 (SD = 0.61), indicating that most students gained at least 1 level of knowledge (Wilcoxon signed-rank test, $W = 9907$, $P < 0.0001$). Fifty-six students (28%) reported no improvement (however, 73% of these had already reported a good or very good knowledge before using the VL). Among these students, 9 students (24%) had rated themselves at 5/5, 18 (49%) at 4/5, and 10 (27%) at 3/5. Most students improved by 1 level (52%, $n = 102$), whereas fewer progressed by 2 levels (17%, $n = 33$) and even 3 (2%, $n = 4$) or 4 (0.5%, $n = 1$) levels. The mean grade obtained by the students for their laboratory reports is shown in Fig. 9. The mean grade for the laboratory report was 71 ± 8%, reflecting a generally good understanding of the role of endothelium in the control of vascular tone by the end of the course.

Thematic Analysis of Students' Free Comments

Thematic analysis of students' comments reveals four major clusters that describe how learners experienced the VL (see Table 2 and Fig. 10). These clusters highlight both the pedagogical value of VLs and their limitations in preparing students for real laboratory work. The first cluster is related to the pedagogical potentialities of VL, such as its flexibility and the large autonomy of students. Students consistently emphasized the flexibility afforded by the VL, particularly the ability to complete the session from home, at one's own pace and with limited time pressure. This format enabled a sense of autonomy, which several students explicitly valued. The VL experience also benefited from preparatory sessions, which students described as really crucial for understanding the objectives and navigating the activity effectively. When well

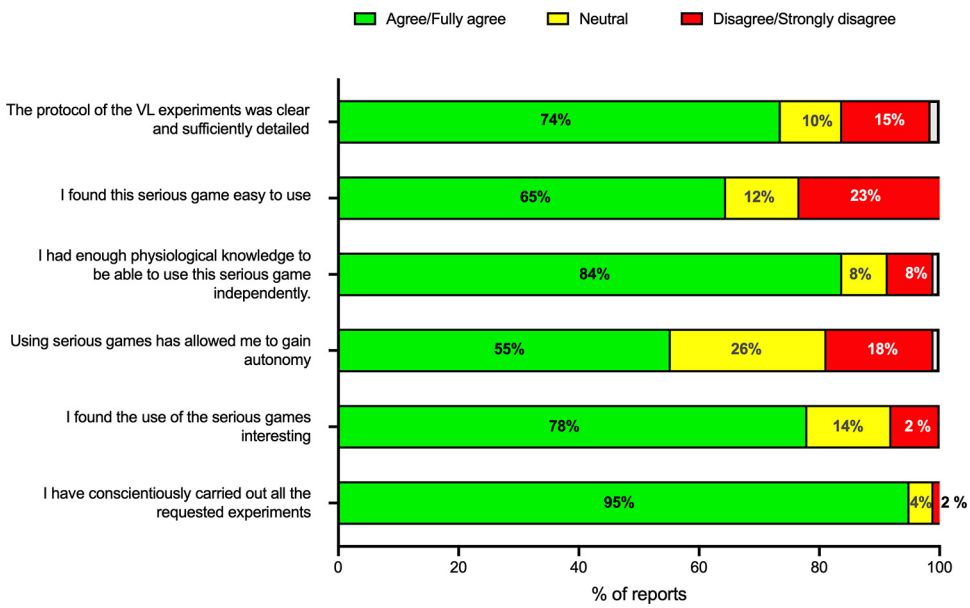


Figure 6. Student evaluations of the *ExAVir* online physiology learning platform. Values represent percentages for the 197 students who completed the questionnaire (76.5% response rate). Responses were scored with a 5-point Likert scale (1 = strongly disagree to 5 = fully agree). For readability, categories were merged into 3 classes: Fully agree/Agree (green), Neutral (yellow), and Disagree/Strongly disagree (red). Detailed results for all 5 categories are provided in Supplemental Table S1.

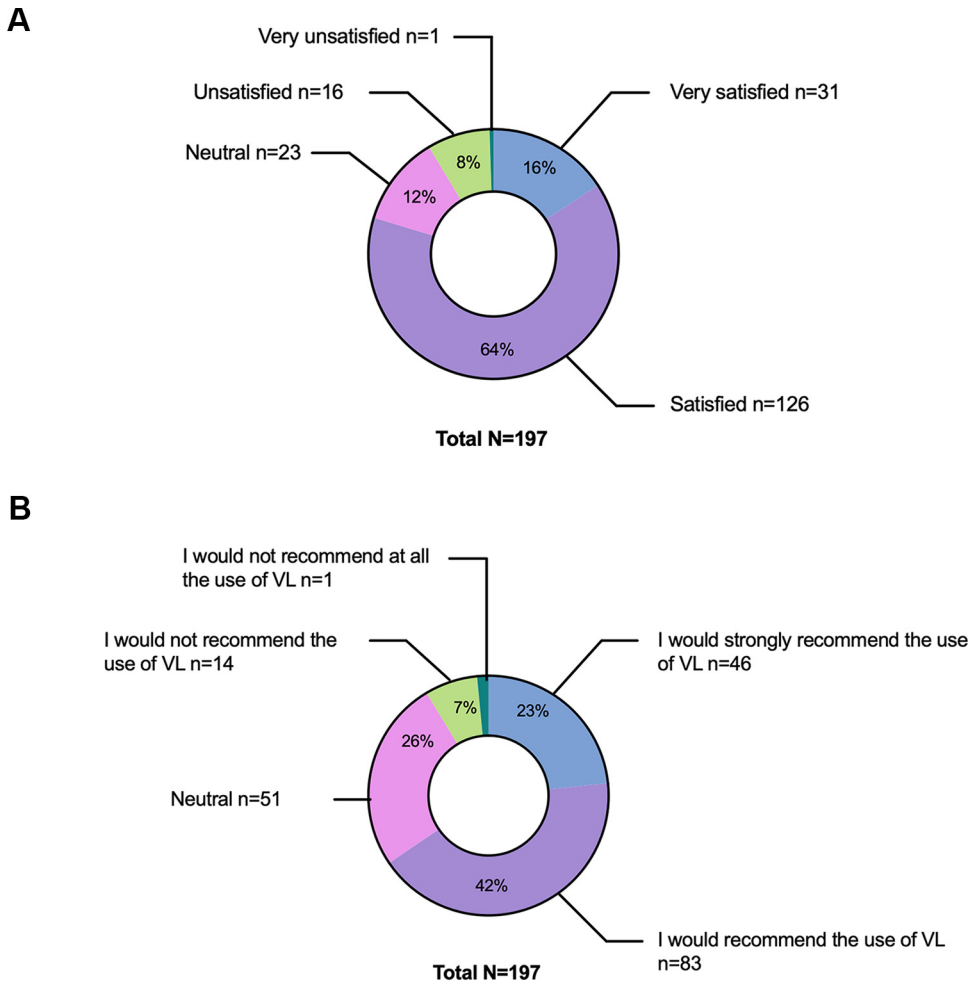


Figure 7. Student satisfaction indices for the *ExAVir* online physiology learning platform. Values represent percentages for the 197 students who completed the questionnaire (76.5% response rate). *A*: overall level of satisfaction. *B*: recommendation of virtual laboratory. Responses were scored with a 5-point Likert scale. Detailed results including all 5 categories are presented in Supplemental Table S1.

supported, the platform was perceived as rather pleasant, engaging, and cognitively clear, sometimes even preferable to passive learning formats such as data analysis or theoretical lectures. The second cluster deals with ethical concerns, as VLs allow reduction of animal use without eliminating practical learning. Students generally appreciated the VL as an ethically responsible alternative to animal experimentation. Many expressed alignment with the principle of reducing animal use and viewed the VL as a meaningful contribution to this goal. However, students simultaneously expressed concerns that this ethical benefit may come at the cost of experiential richness and real acquisition of practical skills. The third cluster deals with technical and instructional drawbacks of the VL, as sometimes platform design hinders learning. A substantial cluster of comments highlights difficulties arising from the design and functioning of the VL platform. Students reported numerous problems: confusing instructions, insufficient detail, unintuitive interfaces, software bugs, and time-consuming procedures (e.g., having to restart the whole experiments after an error). These issues contributed to frustration and, in some cases, hindered understanding of the scientific protocol. Some students felt they improved more in "IT skills" than in experimental technique, indicating that interface complexity shifted cognitive load away from learning physiology. The fourth cluster aggregates insufficiencies of VL for skill acquisition and the irreplaceability of hands-on laboratory experience. The largest and most emphatic cluster concerns students' belief that the VL cannot substitute for real laboratory practice. Students reported feeling unprepared to perform actual manipulations, lacking confidence with real biological materials, and experiencing anxiety about transitioning from virtual to real settings. Many lacked the absence of tactile, embodied, and sensory cues that characterize laboratory work. In their view, VL remains a theoretical environment that does not actually develop procedural competence or motor skills. Students also stressed that direct interaction with instructors, particularly in moments of error or uncertainty, remains essential for learning and managing the emotional component of laboratory work.

DISCUSSION

Virtual laboratories have gained substantial attention as effective tools for teaching physiology, especially in response to the limitations imposed by the COVID-19 pandemic and the need for scalable, ethical learning solutions (18). This study was conducted to evaluate the student perception of using a virtual laboratory (VL) to teach vascular physiology to undergraduate students. The VL, named *ExAVir*, was developed by the University of Angers (24) with four main objectives: *1*) to provide an alternative to animal experimentation

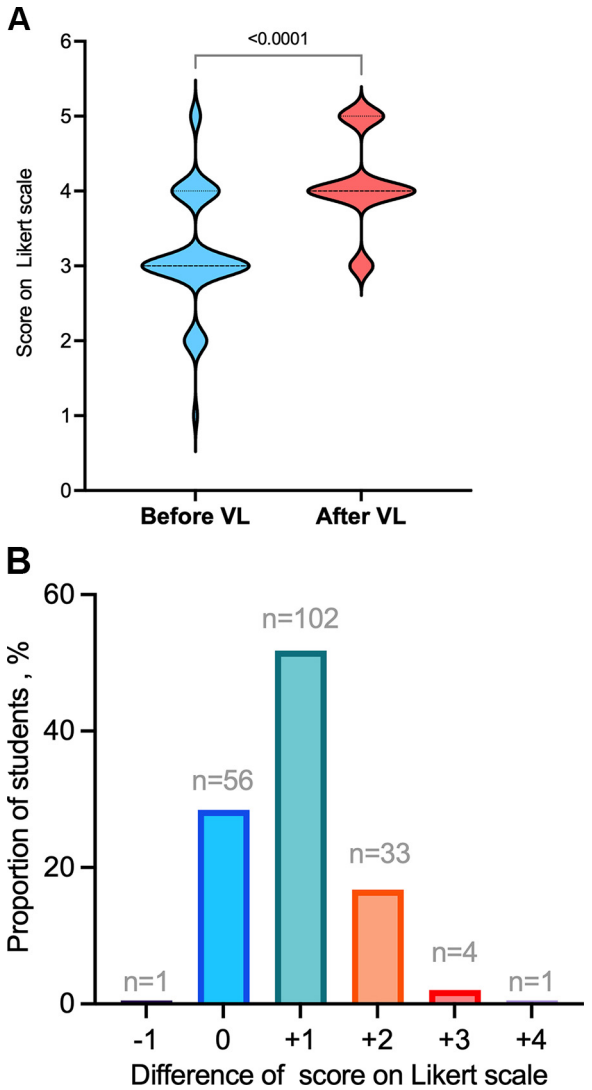


Figure 8. Student-perceived level of knowledge in vascular physiology before and after training with the ExAVir platform. *A*: knowledge scores before and after the training course. *B*: individual progression following completion of the training. Values represent scores for the 197 students who completed the questionnaire before and after the use of the virtual laboratory (VL) (76.5% response rate). The two statements used in the survey were "Prior to this course, my understanding of vasomotor control is: Very Good/Good/Average/Poor/Very Poor" and "After completing this course, my understanding of vasomotor control is: Very Good/Good/Average/Poor/Very Poor." Scores before and after the training were compared using Wilcoxon signed rank test. A $P < 0.05$ was considered significant.

and reduce the number of animals used in laboratory teaching; *2*) to offer an innovative and engaging learning method for students; *3*) to encourage students to become more active and autonomous in conducting experiments; and *4*) to reduce the overall cost of practical teaching in a context of tightening educational budgets. Our results show that the majority of students appreciated using the VL and recognized its role in reducing animal use. This platform integrates serious games and interactive scenarios, offering a viable replacement for certain animal-based practical sessions. In this study, we specifically chose to use the *ExAVir* VL to explore the role of the vascular endothelium in ACh-induced vasodilation.

VL as a Tool to Replace Animal Experiments

Virtual laboratories provide an interactive and dynamic environment for studying animal physiology without involving live animals (11, 12). Replacing animal models with computer-based simulations directly supports the *Replacement* principle of the 3Rs. These platforms also allow unlimited repetition of experiments without additional animal use, contributing to the *Reduction* principle. Furthermore, VLs often offer more precise protocols and feedback, improving the learning experience and reducing errors, thus aligning with the *Refinement* principle. The integration of VLs into university curricula offers a comprehensive and ethical approach to teaching animal physiology. By supporting the 3Rs, VLs not only enhance scientific understanding but also promote humane and responsible educational practices (11, 12). In our course, we estimate that using the VL avoided the use of ~30–45 rats over 3 yr for this teaching unit. Although this number may seem modest, it is worth noting that isolated organ experiments are already optimized to use a single animal per 10–16 students. Importantly, nearly 90% of students valued the fact that the VL replaced the use of laboratory animals.

Other Benefits of Using VL in Physiology

VLs also save time, resources, and money. Students can conduct multiple pharmacological experiments in a short time frame, generating high-throughput data that would be time-consuming and labor-intensive in a traditional wet laboratory (see for instance Fig. 3). For example, building a single dose-response curve in a wet laboratory typically takes 1–2 h because of tissue dissection, equilibration, washing, and drug incubation steps. By contrast, the VL provides high-quality and reproducible datasets efficiently. The EC_{50} values calculated by students using *ExAVir* were highly consistent with published literature (Fig. 4). For instance, the median EC_{50}

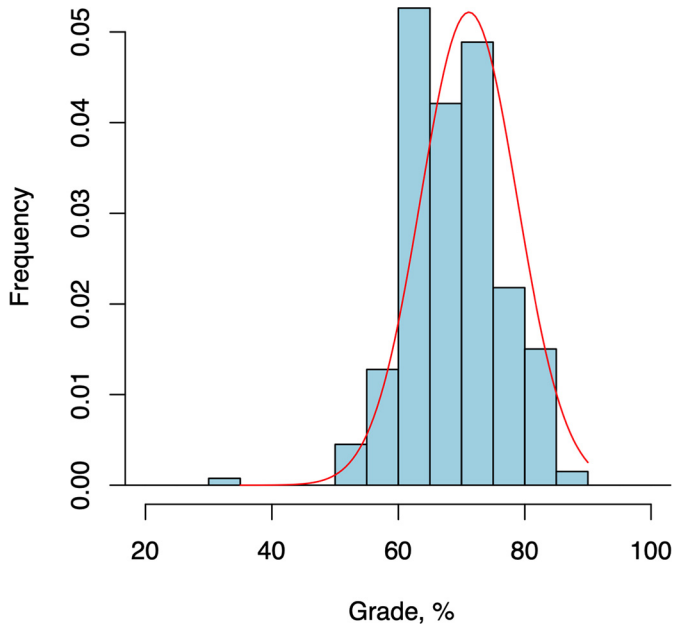


Figure 9. Distribution of student grades for laboratory reports based on *ExAVir* vascular physiology simulations. Grades are expressed as a percentage of the maximal possible score (0–100%).

Table 2. *Thematic analysis of the qualitative feedback provided by the students*

Theme Name	Codes	Occurrences	Interpretation
Pedagogical benefits of VL	Appreciation of remote work/flexibility	2	Students appreciate VL for autonomy, flexibility, novelty, and reduced stress, especially when preparation is strong.
	Value of working independently	2	
	Preparation session helpful	5	
	VL reduces stress entering real lab	3	
	VL is interesting/enjoyable	6	
	Preference for VL over passive learning	2	
Ethical value of reducing animal use	VL as a good alternative to real organs		Students support reduction of animal use.
	Concern about reducing animal use but risking educational quality	4	
Technical issues with the VL platform	Instructions sometimes unclear/insufficient	10	Some technical barriers can hinder learning flow.
	Software issues/bugs	7	
	Tedious/too long	7	
	Disconnection from reality	6	
	VL blocking/unclear error mechanisms	7	
Insufficiency of VL for skill acquisition	Lack of hands-on experience	12	VL alone does not provide tactile, procedural, or motor skills. Students fear inadequate skill acquisition.
	VL insufficient for real lab preparation	13	
	Fear/stress about real labs	3	
	No confidence in handling real materials	13	
	Need for visualization of materials	5	
	Need for professor interaction	6	
Preference for real labs	Preference for real lab sessions	11	Real laboratories are perceived as essential and irreplaceable for deep understanding.
	VL should not replace practical sessions	12	
	Desire for in-class format		
Suggested improvements	Provide more detailed instructions	10	Students suggest structural changes to make VL more intuitive and supportive.
	Provide paper protocol (rather than electronic)	10	
	Real-time feedback	6	
	Presentation of real equipment	5	
	More interaction with professor	6	

The AI-assisted thematic analysis of free comments was performed according to Braun and Clarke (25). The number of occurrences of each in students' free comment is indicated. Note that these counts refer to the number of quotes coded, not the number of students. A total of 59 students' free comments were collected. VL, virtual laboratory.

computed by the students for ACh was 4.0×10^{-7} mol/L [vs. 1.1×10^{-7} to 7.5×10^{-8} mol/L in various animal models (26–29)]. The median EC_{50} computed by the students for SNP was 1.2×10^{-8} mol/L [vs. 5.2×10^{-9} to 1.7×10^{-8} mol/L (30, 31)]. On the basis of their data, most students were able to draw key conclusions regarding ACh-induced vasodilation, including that *1*) ACh effects on vascular smooth muscle are endothelium dependent (32); *2*) nitric oxide (NO) is the primary mediator, with prostacyclin (PGI_2) playing a secondary role; and *3*) NO donors like sodium nitroprusside (SNP) act independently of the endothelium and are potent vasodilators with clinical relevance. Some students' schematic summaries of these mechanisms are included in Supplemental Fig. S3.

Effects of VL on Student Perception and Students' Perceived Level of Knowledge

In the cardio-respiratory physiology course, several laboratory sessions are conducted using the students themselves as subjects. These include, for instance, the exploration of respiratory function via pneumotachography and the analysis of electrocardiograms (ECGs). Students are tasked with producing a formal laboratory report based on these experiments. To reduce the use of animal models, no "wet laboratories" are, however, performed in this course; these are reserved for implementation at the Master's level. VLs offer a complementary pedagogical approach to traditional laboratory work, supporting the development of digital literacy, autonomy, and conceptual understanding (13–17). However, they cannot fully replicate hands-on experiences that require physical manipulation, such as pipetting, dilutions, or dissection (24). Our students recognized this distinction: whereas 69% agreed that VL could replace one laboratory session, 88% believed it should not replace all practical work. Many students reported gaining autonomy and found the experience educational, but only 21% felt capable of performing real experiments afterward. Student comments reflected this mixed perception (see verbatim in Supplemental Table S2), including: "*A VL session is great, but it absolutely should not replace all practical sessions*", "*VL is convenient, but real practical sessions are essential for understanding*", "*I don't currently feel capable of doing the same experiments on a real organ, even though it was an interesting session*", and "*It's great to avoid using animals but it is definitely less educational than a real laboratory session*". The thematic analysis (based on students' free comments) reveals that students perceive the virtual lab (VL) as a valuable pedagogical resource, particularly for enhancing conceptual understanding, reducing stress, and supporting autonomous and flexible learning. These benefits are amplified when preparatory sessions provide clear conceptual grounding, suggesting that VLs function most effectively as cognitive scaffolds. At the same time, students strongly appreciated the reduction in animal use afforded by the VL, aligning with broader ethical imperatives in physiology education. However, they also expressed concern that these ethical gains may come at the cost of meaningful hands-on experience, underscoring a persistent tension between reductionist and experiential learning goals. Technical limitations, such as unclear instructions, interface difficulties, and software bugs, further constrained the educational potential of the platform by diverting cognitive effort away from physiological reasoning

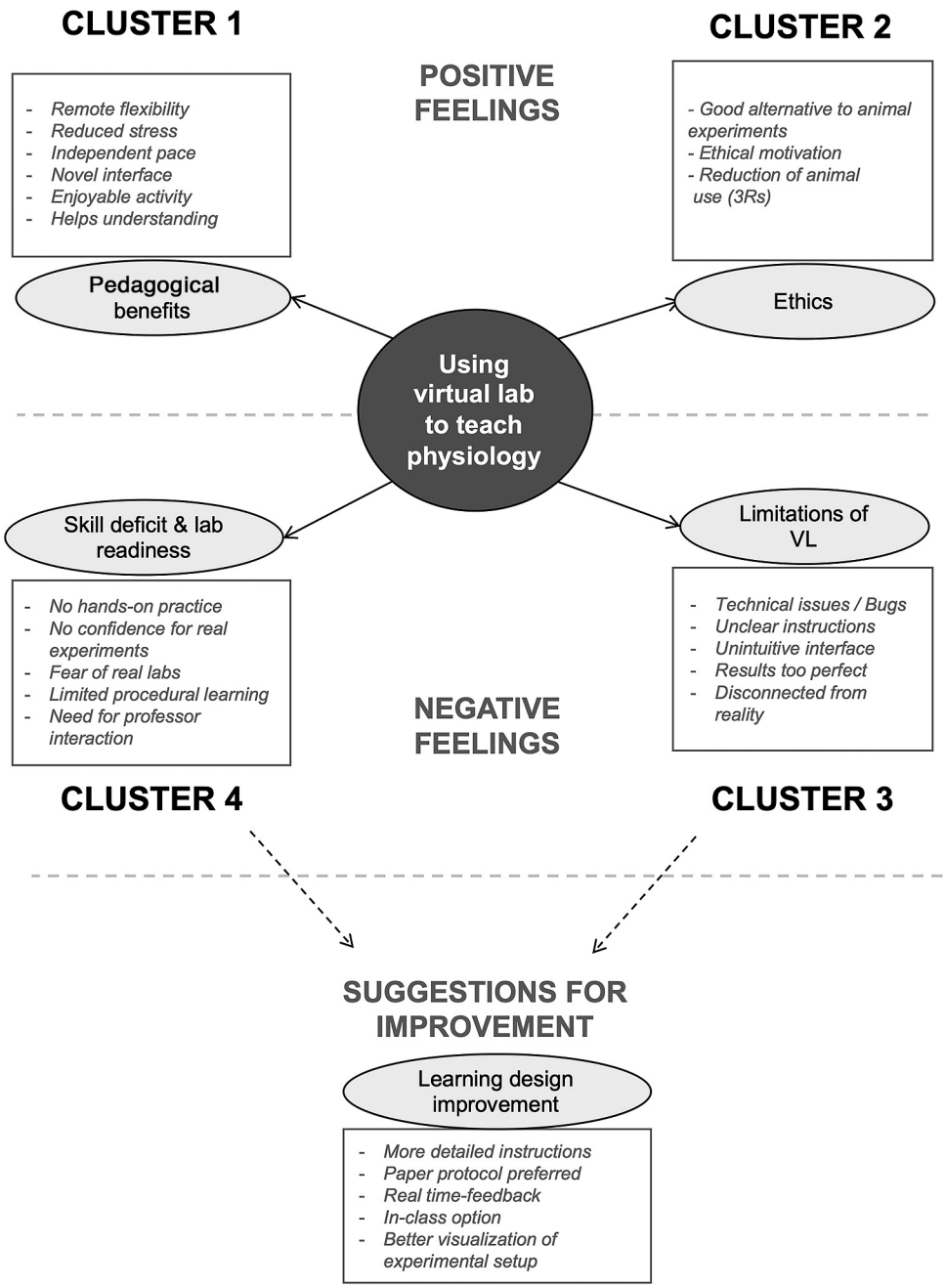


Figure 10. Visualization of the results of the thematic analysis performed on students' free comments as a text-based cluster map. Listed items are open codes grouped under axial themes. VL, virtual laboratory.

and toward troubleshooting the system itself. Most importantly, students consistently emphasized that VLs cannot replace the procedural, tactile, and affective dimensions of real laboratory practice. Many reported feeling unprepared or anxious about performing real manipulations after completing the VL, highlighting the irreplaceability of direct instructor interaction and embodied engagement with biological materials. Collectively, these findings position VLs as effective complementary tools rather than substitutes for hands-on laboratory sessions. A hybrid pedagogical model, combining VLs for conceptual preparation and real laboratory practice for skill acquisition, appears most responsive to student needs and learning outcomes.

The student perception reported in the present study fully supported data from the literature. Several studies support the blended learning approach. A study in China (33) compared three groups (VL only, wet laboratory only, and blended learning) in a neurophysiology course. Students in the VL-only condition scored significantly lower on the posttest, suggesting that virtual laboratories are most effective when used to complement, rather than replace, traditional wet laboratory sessions. Many free comments from students supported this latter view (see verbatim in Supplemental Table S2). Similarly, Griffin et al. (34) assessed VL use across >600 life science students in Ireland and found that although VLs increased confidence and engagement, students strongly preferred them as supplements rather than replacements for in-person laboratories. In a German study, students who attended traditional face-to-face physiology practical courses achieved slightly higher

exam scores than those taught online (although the effect size was small), suggesting that both teaching formats can be effective but may benefit from a hybrid approach (35). Other research warns that replacing all practical laboratories with VLs could result in a loss of essential technical skills (e.g., solution preparation, tissue handling) and awareness of biological sample limitations (e.g., tissue viability, storage conditions). According to their comments, these limitations were perceived by the students. In contrast, the blended model has been shown to enhance learning and improve technical skills beyond what is achievable in wet laboratories alone (19, 36–38). A systematic review reported that VL are effective for teaching physiological concepts (20). Unfortunately, the effectiveness of VL in improving students' motivation to learn and their technical skills remains inconclusive. It was found that blended models of virtual laboratories are at least as effective as in-person laboratories for conceptual learning. At the University of Angers, *ExAVir* is currently used in blended mode, supplementing wet laboratory sessions. Students first perform real pharmacological experiments and later run additional simulations with the VL to confirm or expand their findings. In a study involving 22 pharmacy students, the blended model led to better acquisition of pharmacological skills compared to traditional wet laboratory work alone (24). The rise of Generative AI tools necessitates a careful reevaluation of how laboratory reports are used as assessment metrics. Because AI can proficiently describe physiological pathways like those of acetylcholine, there is a risk that student reports may no longer accurately represent individual mastery. Consequently, we are considering a shift toward assessment models that require more personalized data interpretation and critical analysis to ensure academic rigor is preserved.

Limitations

This study has, however, several limitations. First, it was conducted in a single department at a single institution, limiting generalizability. Second, the study was purely observational, without a control group for direct comparison between VL, wet laboratory, and blended learning methods (as in Ref. 33). Third, the study was completed over 3 yr/three different cohorts. Fourth, the learning outcomes were assessed with self-reported questionnaires (applied before and after the intervention), which may introduce bias. Although most students reported statistically significant improvements, these were not measured with standardized tests. Future studies should include objective assessments and interventional designs to better evaluate the impact of VLs on learning outcomes. It should be emphasized that the study was not designed to monitor the impact of using a VL on learning outcomes but rather to evaluate students' perceptions.

Conclusions

This study assessed the perception of *ExAVir*, a virtual physiology laboratory, as an innovative pedagogical tool for undergraduate students at Claude Bernard Lyon 1 University, France. Students appreciated the VL and recognized its contribution to reducing animal use in education. However, they also acknowledged that VLs could not fully substitute for hands-on laboratory sessions, as they involve a different set of skills and learning objectives. We conclude that virtual laboratories could be used in conjunction with, not as a replacement for, wet laboratory sessions, to optimize both conceptual understanding and practical skill development in physiology education.

DATA AVAILABILITY

Data will be made available upon reasonable request.

SUPPLEMENTAL MATERIAL

Supplemental Tables S1–S3, Supplemental Figs. S1–S3, and prompts for thematic analysis: https://doi.org/10.6084/m9.figshare.29621438.

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During the preparation of this manuscript, the authors used ChatGPT (version GPT-4o mini) for the purposes of English polishing. The authors have reviewed and edited the output and take full responsibility for the content of this publication. The AI tool was used in a manner that does not conflict with APS ethical policies.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

C.O.S. conceived and designed research; C.O.S. performed experiments; C.O.S. analyzed data; C.O.S. interpreted results of experiments; C.O.S. prepared figures; C.O.S. drafted manuscript; C.O.S., S.L., T.C., and D.B. edited and revised manuscript; C.O.S., S.L., T.C., and D.B. approved final version of manuscript.

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