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Research article

Gamifying cell culture training: The 'Seru-Otchi' experience for undergraduates

Victoria T. Ly [a,d,1,*], Drew Ehrlich [b,d,1], Jess Sevetson [c,d,1], Ryan N. Hoffman [c,d], Sofie R. Salama [c,d], Sri Kurniawan [b,d], Mircea Teodorescu [a,d]

[a] Electrical and Computer Engineering Department, University of California, Santa Cruz, CA, 95060, USA
[b] Computational Media Department, University of California, Santa Cruz, CA, 95060, USA
[c] Department of Cellular, Molecular, and Developmental Biology, University of California, Santa Cruz, CA, 95060, USA
[d] University of California, Santa Cruz Genomics Institute, Santa Cruz, CA, 95060, USA

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ABSTRACT

Working in a stem cell laboratory necessitates a thorough understanding of complex cell culture protocols, the operation of sensitive scientific equipment, adherence to safety standards, and general laboratory etiquette. For novice student researchers, acquiring the necessary specialized knowledge before their initial laboratory experience can be a formidable task. Similarly, for experienced laboratory personnel, efficiently and uniformly training new trainees to a rigorous standard presents a significant challenge. In response to these issues, we have developed an educational and interactive virtual cell culture environment. This interactive virtual lab aims to equip students with foundational knowledge in maintaining cortical brain organoids and to instill an understanding of pertinent safety procedures and laboratory etiquette. The gamification of this training process seeks to provide laboratory supervisors in highly specialized fields with an effective tool to integrate students into their work environments more rapidly and safely.

1. Introduction

Culturing human stem cells requires comprehensive training in procedural techniques and safety protocols. This training is crucial to ensure proper maintenance of cell sterility and viability for biological experiments, as well as to safeguard the researchers themselves [1]. However, the complex and highly technical nature of this process often presents a significant barrier to entry for undergraduate students interested in research in this area [2]. Training in laboratories that culture these types of cells can vary widely between groups, typically involving the study of relevant journal articles [3]. However, these articles are often written in dense, specialized jargon, intended for peer review by experts in the field [4], and do not necessarily impart practical knowledge on laboratory safety, lab citizenship skills that are essential for developing competent laboratory scientists, or even procedural knowledge about experimental design. This steep learning curve, coupled with the challenges in interpreting academic papers, disproportionately impacts students from marginalized or disadvantaged backgrounds, who might have had limited exposure to research opportunities before college. Therefore, it is crucial to develop a tool that offers a low-stakes learning environment, supplementing traditional educational pathways, and is adaptable across different languages to promote inclusivity among non-native English-speaking aspiring

* Corresponding author. Electrical and Computer Engineering Department, University of California, Santa Cruz, CA, 95060, USA.
E-mail address: vily@ucsc.edu (V. T. Ly).
[1] These authors contributed equally to this work.

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scientists [5].

Each laboratory group has its unique onboarding procedures and specialized etiquette, making the task of bringing new trainees up to speed often time-intensive. Senior personnel need to cover all the necessary protocols, policies, and best practices of their specific laboratory group. This can result in inconsistencies in training due to differences in instructors' approaches or can place an undue time burden on certain senior lab members, either of which can negatively impact the research productivity of a group. Furthermore, in labs at primarily undergraduate or teaching institutions, the frequent turnover of lab personnel necessitates efficient training methods that do not rely heavily on any single individual [6].

To address these challenges, we have created an interactive virtual cell culture training environment focused on the basics of cortical organoid cell culture in vitro. Human cortical organoids are a type of brain organoid, a term for self-organizing three dimensional aggregates of cell types found in the brain, typically derived from stem cells. This virtual lab, complemented with information on protocol-specific safety measures and general laboratory conduct, is designed for a group specializing in the growth and study of human brain organoids. The virtual lab specifically models the cell growth protocols and organizational techniques used in this lab's research. Its underlying code, being open-source and written in JavaScript, allows for easy modification to suit the needs of other research groups.

While there have been efforts to educate undergraduates about the science of organoids through publications [7] and online courses like Harvard University's LabXchange [8], these programs are not designed to be specialized at the research laboratory level, and therefore may not cover the specific protocol materials that mentors seek to impart.

After reviewing the current gaps in laboratory training for undergraduates, this study aims to.

1. Develop and assess a virtual training activity, 'Seru-Otchi', designed to supplement traditional educational resources for learning cell culture protocols and laboratory safety by simulating long term experimental procedures.
2. Evaluate the effectiveness of 'Seru-Otchi' in enhancing undergraduates' understanding and confidence in cell culture techniques when compared to lecture and literature review alone.
3. Investigate Seru-Otchi's potential in making scientific education more accessible and inclusive, particularly for students with limited prior exposure to laboratory settings.

1.1. Laboratory safety and cell culture care

Laboratory safety protocols and cell culture care are critical components of research environments for several reasons. Laboratories often function as shared spaces where respect for ongoing experiments is paramount. Strict adherence to containment and waste protocols is essential to ensure the safety of personnel. Additionally, laboratory equipment, often costly and sensitive, requires meticulous handling to prevent damage. Regular maintenance and prompt repairs, as necessary, are vital for the optimal functioning of these devices. A comprehensive understanding of personal protective equipment, safety protocols and correct equipment usage is crucial to mitigate risks [9].

Safety training procedures differ across institutions. For example, within the University of California system, foundational safety training is typically conducted through online courses, followed by more specific lab-oriented training, which can vary greatly between labs. Some individual laboratories have explored alternate approaches including gamification [10], digital laboratory safety platforms [11,12] or human biology interaction educational modalities [13]. Early and thorough safety training, starting at the undergraduate level, is pivotal in fostering a culture of safety in both educational and research laboratories, as well as in classroom settings [14–16].

Cell culture protocols demand high precision and can differ substantially among various models. This hands-on process requires close attention to detail to maximize cell viability and repeatability, while minimizing the risk of contamination by extraneous microorganisms [17]. Contamination poses a significant threat to cell cultures, potentially ruining weeks or months of meticulous work and creating health and safety hazards in the lab [18]. Additionally, given the biological materials involved, there are inherent risks associated with bloodborne pathogens, necessitating further specialized knowledge for safe operations.

Incorporating comprehensive training on laboratory safety and cell culture care, 'Seru-Otchi' aims to.

1. Enhance students' comprehension of essential safety protocols and proper cell culture techniques.
2. Foster a culture of safety and responsibility among undergraduate students embarking on laboratory research.

1.2. Games & interactive educational activities in biology

The integration of gaming into scientific education has garnered significant attention in recent years. A notable example is the creation of 'Foldit' by Khatib et al., a puzzle game that transforms the complex challenge of protein folding into an interactive problem-solving activity [19]. This innovative approach has allowed individuals from diverse backgrounds to contribute to significant scientific advancements. Educational games, when aligned with classroom learning, have demonstrated both efficacy and limitations, as evidenced by various studies [20–23].

These investigations underscore the critical role of educators in both the design and implementation of educational games. Key considerations include the mechanism of providing feedback to students within the game environment and strategies to leverage student motivation to enhance engagement and learning outcomes. In disciplines such as mathematics and the sciences, educational games have been shown to not only boost student motivation but also to enhance retention of the presented material [24]. In the field of biology, games like 'Discovering the Cell' [25] and the biology vocabulary card game by Gutierrez et al. [26] serve as exemplars of effective tools for reinforcing disciplinary knowledge. Research by Sadler et al. highlights the positive impact of such games in science education [27,28].

In an effort to augment traditional educational resources, some educational institutions have adopted virtual reality (VR) technologies, exemplified by companies like Labster, to simulate basic biological laboratory experiments [29]. VR training offers the advantages of eliminating the costs associated with running a physical laboratory and reducing safety risks. Jones et al. have emphasized these benefits in their work on virtual laboratories, presenting them as safer and more accessible alternatives, particularly beneficial for those unable to access physical lab spaces [30]. However, it is noteworthy that while VR is a potent educational tool for undergraduates, platforms like Labster may pose financial constraints. Additionally, as of the current time, these mass-produced VR labs primarily offer general laboratory procedure education, lacking customization to specific research protocols.

Through the deployment of 'Seru-Otchi', this study seeks to.

1. Explore the potential of educational games to improve retention and application of complex biological concepts and terminology, with a focus on cell culture.
2. Assess the impact of interactive learning tools on student engagement and motivation in the field of biology.

2. Research approach: design of organoid culturing interactive virtual lab

The virtual experimentation environment, we have developed is tailored to replicate the cortical human brain organoid growth protocols employed in the Salama laboratory [31]. Traditionally, new members joining the laboratory are oriented with scientific literature covering protocols, organoid generation, and tissue analysis techniques like immunofluorescence or RNA sequencing. This literature review is complemented by hands-on training sessions focused on specific equipment, procedures, and protocols pertinent to brain organoid maintenance. However, the reliance on academic journal articles as a primary tool in introductory training can present challenges to novice researchers. The skill of interpreting scientific literature is not universally taught at the undergraduate level, leading to a disparity in preparedness. Consequently, students unfamiliar with scientific reading may require additional time to grasp fundamental concepts before progressing to more advanced techniques.

To address this educational gap, the interactive virtual lab was developed using p5.js, a JavaScript library derived from the Processing programming language, renowned for its capabilities in creating digital, visual, and interactive content. The design philosophy of p5.js emphasizes remixing and open-source collaboration, making it an ideal platform for this educational tool. The web-based interactive lab includes adjustable modules for protocols and safety questions, allowing for easy customization to accommodate different cell culture protocols used in various research settings.

2.1. Design principles

In the development of our educational interactive virtual lab, we adhered to four primary design principles.

1. *Clear Communication of Scientific Concepts*: The virtual lab is designed to convey the information from scientific papers in an accessible manner. This is achieved by supplementing the content with technical definitions, visual aids, and an easy-to-understand presentation of complex concepts.
2. *Illustration of the Cell Culturing Process*: The interactive virtual lab provides a comprehensive view of the cell culturing process, guiding players through the steps of following specific protocols in a practical, interactive setting.
3. *Incorporation of Laboratory Safety and Etiquette*: Alongside technical skills, the virtual lab emphasizes the importance of laboratory safety and good lab citizenship, providing essential information in these areas.
4. *Open-Source Adaptability*: The open-source nature of the web-based interactive lab ensures its adaptability for various scientific topics, facilitating customization for different research contexts.

The conceptual framework of the interactive virtual lab draws inspiration from 'Tamagotchi,' a game centered around nurturing and caring for a living entity. This model is also seen in educational games like 'Magic Flowerpot' [32], 'StudyGotchi' [33], and 'Tamagotchi++' [34], where nurturing and learning about specific subjects are intertwined. Analogous to the nurturing aspect in 'Tamagotchi,' meticulous care and intervention are crucial in the culturing of biological samples, including stem cells.

Effective cell culturing demands consistent maintenance, such as regular feeding and waste management. Neglecting even simple tasks like ensuring adequate humidity can lead to abnormal growth or cell death. Given the repetitive nature of these tasks, our interactive virtual lab employs spaced-repetition learning to reinforce key concepts [35]. This method has been proven effective in educational settings, particularly when combined with quiz and test components to enhance engagement and knowledge retention [36].

2.2. Interactive virtual lab mechanics

The primary goal of the interative virtual lab is to instruct players in an experimental procedure, emphasizing the importance of meticulous actions in research. The success criterias is based on sustaining the organoid's life for 77 days, paralleling the time required for organoids, cultured using this protocol, to reach readiness for electrophysiological recording and experimentation. Users commence with a 2-day post-aggregation organoid and are provided with a detailed schedule. This schedule, reflecting the procedure practiced by one of the authors at the time of writing, lists the necessary components for the cell culture media, varying with the organoid's age. Furthermore, the web-based interactive lab enables users to delve into the functions and impacts of different media ingredients by interacting with their names, as depicted in Fig. 1B. This feature serves to centralize information, allowing students to familiarize themselves with reagents without the pressure of direct interaction with senior lab personnel.

The virtual lab's primary interactive mechanism involves the addition of specified chemicals or reagents to a mixture column, which visually alters to represent the added components. Correctly feeding the organoid advances its age according to the protocol's feeding schedule. If a player makes a mistake and catches it before feeding the organoid, they can empty the mixture they have created to try again. This was done to mirror the careful preparation and distribution of media in actual lab settings and encourage thoroughness.

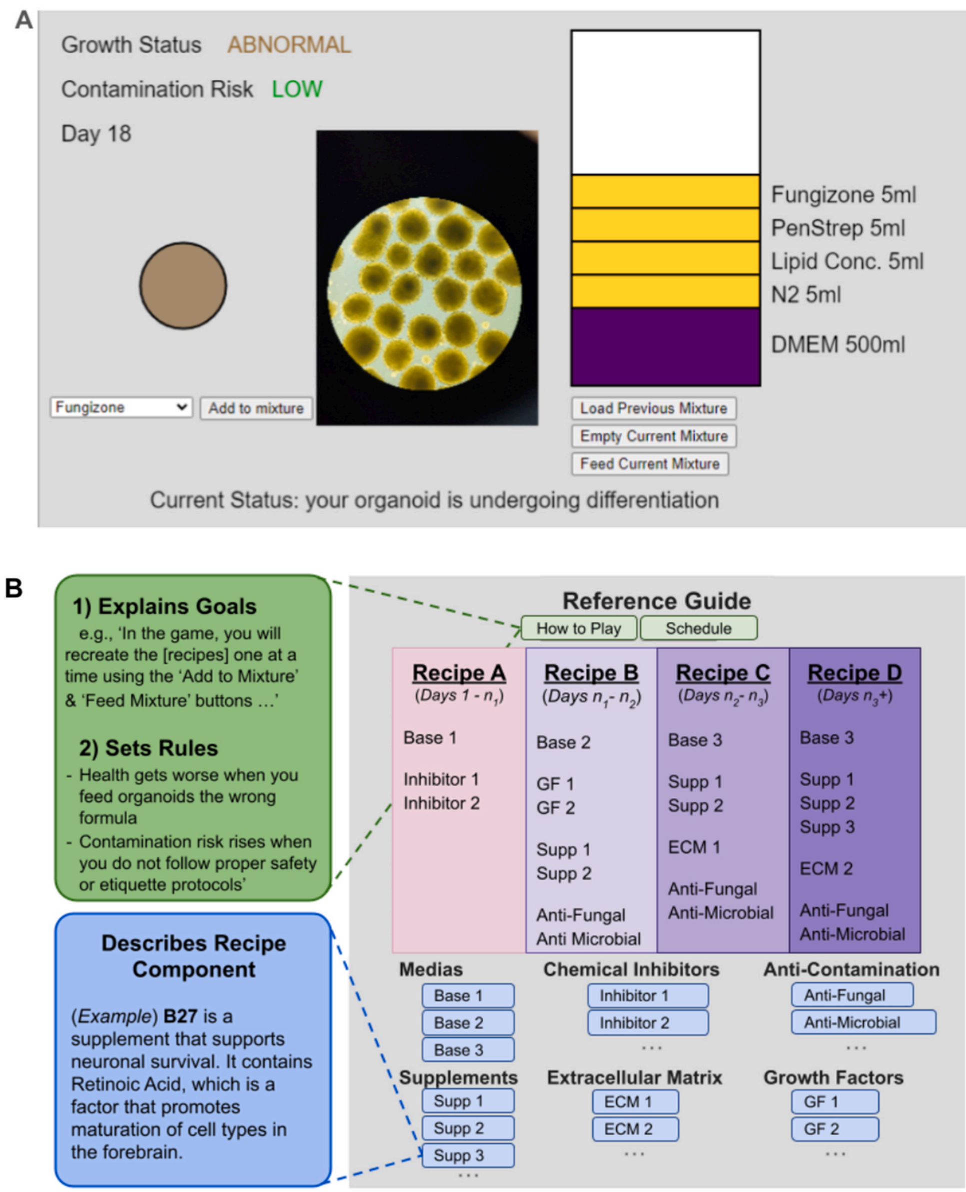

Fig. 1. ***Interface and Customizable Features of the 'Seru-otchi' Game.*** *This figure provides a visual overview of the information* encountered *by players during the gameplay of 'Seru-otchi'.* (A) Displays the organoid management interface, capturing a moment 18 days into the game, where an organoid is being managed. (*B) An overview of the 'Schedule' tab for players. This tab provides a fully customizable timeline for the feeding of specific recipes to organoids at certain timepoints. The 'How to Play' tab explains the game's goals and sets rules (top popout). Media components are split into several sections — 'Media', 'Supplements', 'Extracellular Matrix', 'Growth Factors', and 'Anti-Contamination' measures. Players can click on each component to learn about their roles in organoid culturing (bottom popout - supplement B27 used as an example).*

The interactive element is displayed on the left side of the screen, as shown in Fig. 1A. It features a single modeled organoid that exhibits growth in alignment with the player's progression through the experimental procedure. This growth is based on data from prior experiments, with the organoid's image and a status message updating players on its developmental stage. Players can choose to prepare a new mixture or use the previous feeding's mixture, reflecting typical laboratory practices of advance media preparation and allocation.

As illustrated in Fig. 1A, two metrics evaluate user's performance: 'Growth Status' and 'Contamination Risk'. 'Growth Status', displayed in the top left corner, indicates the organoid's health, ranging from healthy to dying. Deviations from the prescribed media recipe affect the organoid's health status. A critical error at the 'Dying' stage results in the organoid's death, necessitating a restart. The 'Contamination Risk' metric assesses the sterility of the organoid's environment, with levels from low to extreme. A popup quiz on laboratory safety or etiquette appears randomly post-feeding, derived from the expertise of our co-author's group. Correct answers maintain sterility levels, whereas incorrect responses increase the contamination risk, symbolizing the hazards of non-compliance with safety protocols.

2.3. Organoid growth model

The growth pattern of organoids in the game is based on empirical data collected from our extensive image database, comprising experiments with cortical organoids analyzed using the Picroscope [37,38]. The Picroscope, an open-source remote imaging device capable of imaging 24 wells simultaneously, facilitates periodic image capture. These images are subsequently uploaded to a cloud database for web-based access. A custom Matlab script was developed to enhance the images, which involves brightening and sharpening the original image, followed by splitting it into RGB color channels, as depicted in Fig. 2. Through bilateral filtering, the script isolates the organoid, rendering it white against a black background. The size of the organoid is approximated by counting the white pixels in the image.

This image processing technique was applied to multiple batches of organoids aged between 1 and 70 days. By analyzing a substantial number of organoids at identical timepoints (Fig. 3a), we were able to calculate both the standard deviation among different organoids at the same developmental stage (illustrated in Fig. 3b). The data derived from these images have enabled us to establish a realistic model of organoid growth rates for incorporation into the interative virtual lab.

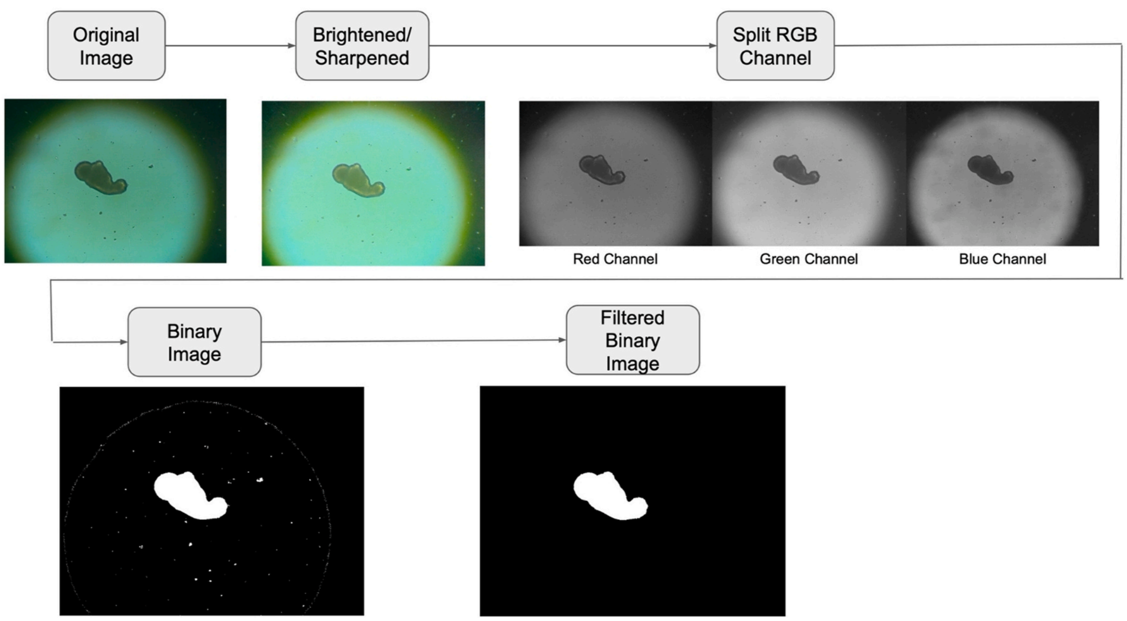

Fig. 2. Image Processing Workflow for Organoid Growth Analysis. This figure details the sequential steps involved in processing images of Cortical Human Brain Organoids to model their growth. The process begins with a representative image of an organoid, specifically selected to highlight the variability in shape, exemplifying the non-spherical nature of the organoids. The image undergoes a series of processing steps: it is first sharpened, then decomposed into its red, blue, and green components. These components are transformed into a binary mask, which subsequently undergoes size-based filtering. The resulting filtered binary image is integrated with images from other timepoints to calculate the organoid's growth rate over a specified period. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

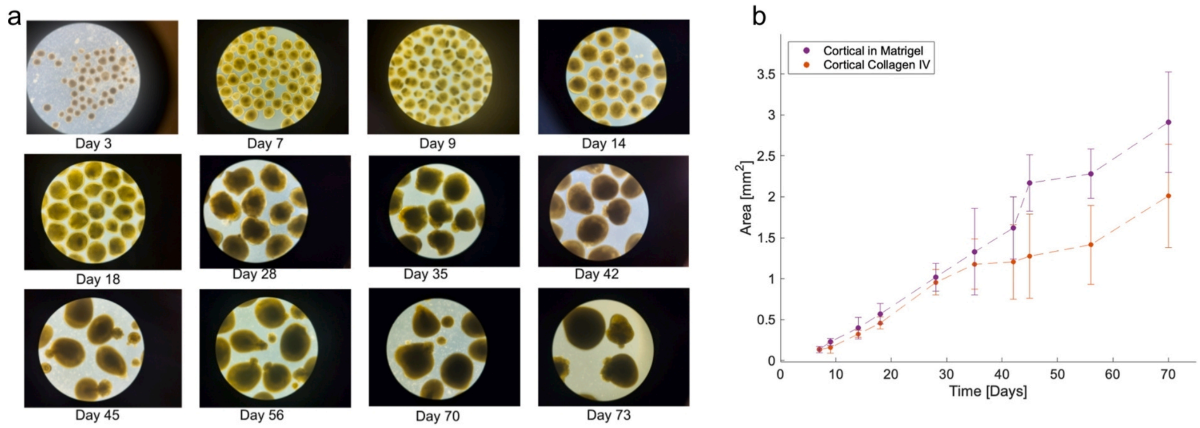

Fig. 3. Visual Representation and Quantification of Cortical Human Brain Organoid Growth. This figure showcases a series of images depicting Cortical Human Brain Organoids at various stages, ranging from day 3 to day 73. These images were utilized as visual references in the game 'Seru-otchi'. The progression of organoid growth was meticulously documented using multiple protocols, allowing for the calculation of an average growth rate based on observations at 12 distinct timepoints.

3. User study

3.1. Institutional approval

In preparation for performing user studies, we submitted documentation to the Institutional Review Board (IRB) at the University of California, Santa Cruz Office for Research Compliance Administration and our protocol was deemed as exempt from further review due to the low risk involved.

User Study Design: The primary hypothesis of our study was that the introduction of our interactive virtual lab would enhance students' confidence and understanding in the process of growing organoids, thereby reducing the learning curve for those aspiring to work in a laboratory setting. To test this hypothesis, we engaged participants who had a keen interest in biology but possessed minimal prior experience in cell culture laboratory settings. Our study design included two initial pilot studies followed by a more extensive user study, aimed at both validating our protocol and assessing our hypothesis.

Selected Population and Sample: The two pilot studies were conducted with distinct student groups from the University of California, Santa Cruz, and California State University, Monterey Bay. These preliminary studies were instrumental in refining the protocol for the subsequent user study and in fine-tuning the confidence and comprehension survey questions to yield meaningful data. The first pilot study encompassed a group of five engineering and science undergraduates from the University of California, Santa Cruz, all of whom expressed a strong interest in science. The second pilot study involved 11 participants from an undergraduate neuroscience psychology course, instructed by one of the authors at California State University, Monterey Bay. The main user study was conducted with 28 students from a different section of the same undergraduate neuroscience course, albeit taught by a different instructor.

3.2. Data collection method: pilot study 1 - evaluation and methodological adjustments

In the initial phase of Pilot Study 1, participants were provided with a scholarly article on organoids for review. Subsequently, their comprehension of the material was assessed through an interview designed to evaluate their understanding of the concepts discussed in the paper. This interview was followed by a short survey aimed at measuring their confidence in discussing the paper's contents with an expert. The participants were then introduced to the virtual cell culture training environment, which they played to completion. Post-activity, a second interview and another confidence survey were conducted to gauge any shifts in their understanding and confidence.

The interviews were conducted virtually via Zoom. To maintain participant anonymity, their voices were altered using Voicemod software, and their video feeds were disabled. Conversely, the interviewer (one of the authors) kept their video visible and audio unmodified, simulating a realistic interaction akin to an initial meeting in a laboratory setting. The interviews were scheduled at different times for each participant, with the interviewer blinded to the participants' treatment conditions prior to the interview. The interviewer operated under the assumption that each participant was involved in only one study condition, unaware of the study's true design until its conclusion. This approach aimed to simulate the interviewer's experience of interacting with a larger participant pool. The participants in this pilot study were five undergraduates from the University of California, Santa Cruz, all interested in biology but lacking cell culture laboratory experience.

The findings from this pilot study indicated that the blind interview protocol was overly complex, and conducting two in-depth, one-on-one interviews was time-consuming for both participants and facilitators. To address these issues, subsequent studies replaced in-person interviews with surveys. This modification aimed to streamline the process for facilitators, accommodate larger sample sizes more feasibly, and ensure consistent coverage of key topics with all participants.

3.3. Data collection method: pilot study 2 - refinement of study approach with psychology undergraduates

In this phase of our study, we tailored the research approach to suit a new demographic: psychology undergraduates enrolled in a neuroscience course. Our participant group comprised 11 students, none of whom had formal training in a biology laboratory setting. Initially, these students were provided with a carefully selected academic paper relevant to their course. Following their review of the paper, they completed a survey designed to assess their understanding of its content. This survey had 16 sixteen questions, which included information about demographics, Likert scale evaluations, and short answers. Not all questions yielded meaningful data-points. While the validity of the questions used for this survey have not been tested outside of our studies, the questions were developed in concert with the instructors of the courses we surveyed to line up with or mirror questions used in these courses to assess pedagogical outcomes.

Subsequently, the students engaged with the organoid training in the virtual lab. After completing the activity, they took a second survey. This survey not only reiterated questions from the first to gauge changes in understanding but also included queries regarding their confidence in their comprehension of the material. The aim was to evaluate how their perceptions of the paper's content might have evolved post-interactive virtual lab. A subset of these survey questions is presented in supplementary material 1 and supplementary material 2. This second survey had 19 questions, which added questions asking about the experience of participating in both stages of the user study.

Although the use of surveys provided a more consistent dataset and valuable quantitative insights, we noted a lack of qualitative data elucidating the reasons behind the respondents' evaluations of the virtual lab and its perceived effects. To address this, the subsequent user study incorporated additional questions into the survey. These questions were specifically designed to elicit detailed explanations from participants about their responses to certain critical queries, thereby enhancing our understanding of their perspectives.

3.4. User study 1 - implementation and enhanced feedback mechanisms

Building upon the insights garnered from the two preceding pilot studies, we initiated a more extensive user study. This study involved 28 students from a different section of the same neuroscience course utilized for participant recruitment in the second pilot study. In response to the feedback received, a new academic paper was selected to better align with the students' academic background and interests.

For this user study, we refined our survey methodology to more effectively capture qualitative feedback. The revised surveys were

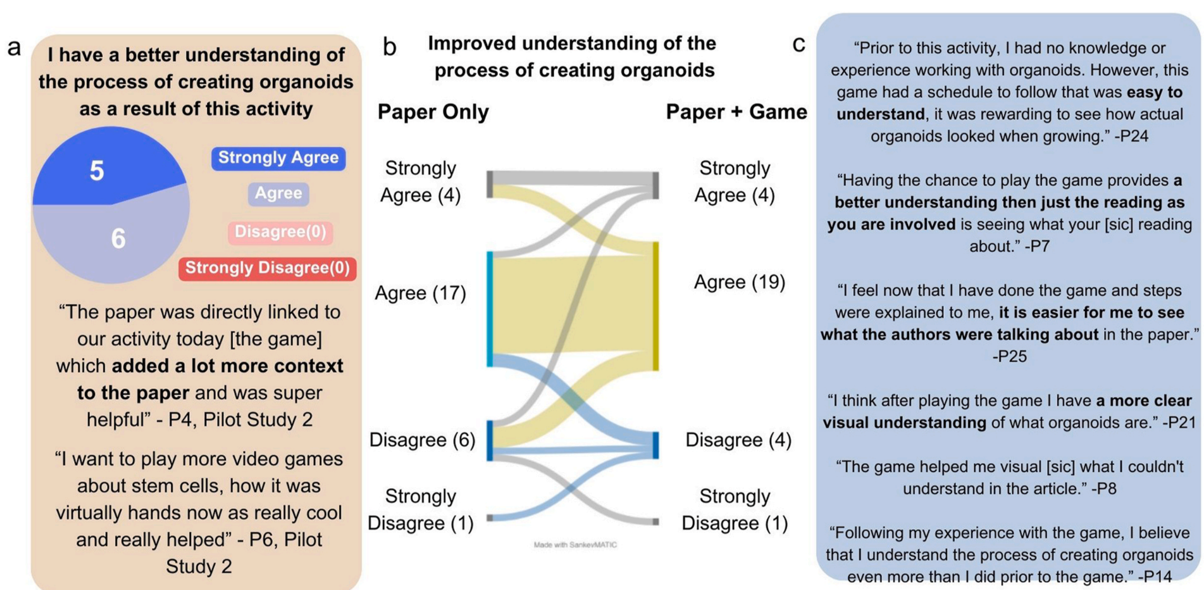

Fig. 4. Finding 1: Facilitating Low-Stakes Practice and Learning through Playing 'Seru-otchi.' This figure demonstrates the role of 'Seru-otchi' as a risk-free environment for skill development and comprehension enhancement. (a) Results and excerpts from participant feedback in the second pilot study (n = 11), conducted after participants had interacted with both the paper and the game 'Seru-otchi'. This study was separate from the main user study. (b) Sankey diagram illustrating changes in participant self-assessments from the user study (n = 28) regarding their confidence levels before and after engaging with 'Seru-otchi'. (c) Representative comments from user study participants (n = 28) highlighting the perceived benefits of 'Seru-otchi' in learning [emphasis added]. (d) Sankey diagram revealing shifts in comfort levels of participants from the user study (n = 28) about the prospect of joining a cell culture laboratory, before and after their experience with 'Seru-otchi'.

designed to provide participants with increased opportunities to articulate their experiences and perceptions of the interactive virtual lab. This adjustment aimed to gather more in-depth qualitative data, complementing the quantitative analysis and offering a richer understanding of the participants' engagement with the virtual lab and its impact on their learning process.

4. Results

In the conducted studies, the primary quantitative data were derived from surveys assessing each participant's confidence in understanding the presented material. These surveys, utilizing a Google Form, were administered at two distinct junctures: initially after the participants read the selected paper, and subsequently after they had completed both the reading and the interactive virtual lab. The surveys employed a Likert Scale for participants to express their level of agreement with various statements regarding their confidence in understanding the material. Key findings from these surveys are visually represented in Fig. 4a. The results tracked over two time points shown in Figs. 4 and 5 were found to not be correlated with each other. The data shown in Fig. 4b has a correlation of 0.46, the data shown in Fig. 5b has a correlation of 0.47, and the data shown in Fig. 5c has a correlation of 0.61.

A significant observation from the survey results was a discernible increase in participant confidence between the two surveys (Fig. 4a and 5a). This was particularly evident in aspects such as their self-assessed understanding of the paper's topics, their perceived ability to respond to interview questions, and their confidence in joining a laboratory engaged in related research (Fig. 5d). An interesting aspect was the heightened confidence observed during the second survey, likely influenced by the experiential learning through thegamified cell culture training, though it must be noted that repeated exposure to the material may have also contributed to this outcome.

While our quantitative findings resonate with the established benefits of interactive experiences in educational settings, as observed by Felszeghy et al. [39] and Jones et al. [40], our study extends these insights to the nuanced domain of cell culture training. Unlike previous studies that primarily focused on general scientific education or the use of gamification in large classroom settings, 'Seru-Otchi' specifically addresses the gap in interactive learning tools for laboratory protocols and safety. This not only corroborates the utility of interactive virtual experiences in enhancing learning outcomes but also introduces a novel application of interactive learning tools in the specialized context of cell culture training, an area less explored in existing literature.

In summary, the results suggest that our initial hypothesis has merit. While the sample size of our study was not large enough to yield statistically significant conclusions, the trend observed in the participants' responses indicates a positive impact of the experimental intervention. Detailed qualitative feedback from the participants, which we discuss in the following section, further elucidates the perceived value of our intervention in enhancing their understanding and confidence.

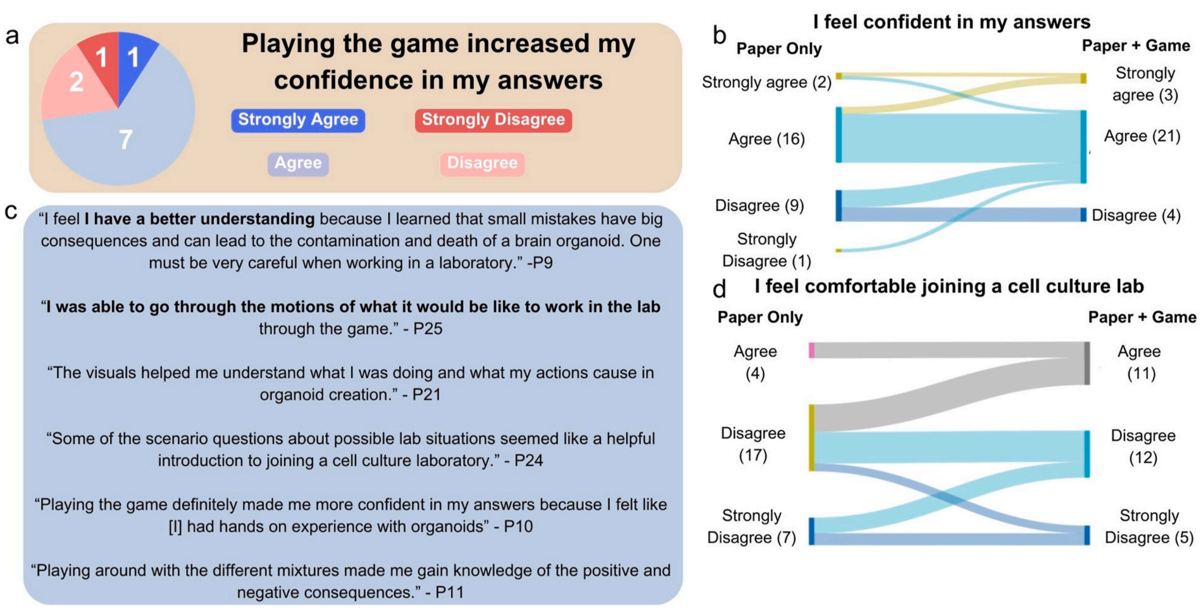

Fig. 5. Finding 2: Enhanced Understanding through Game-Based Learning. This figure illustrates the impact of the training game 'Seru-otchi' on the comprehension of concepts and methods presented in the paper. (a) Results and representative excerpts from participant feedback in the second pilot study (n = 11) conducted after participants engaged with both the paper and the game 'Seru-otchi' [emphasis added]. (b) Sankey diagram depicting the evolution of participant understanding about the process of creating organoids, based on responses from the user study (n = 28), before and after interaction with 'Seru-otchi'. (c) Representative comments from participants in the user study (n = 28) reflecting their perceptions of 'Seru-otchi's influence on their knowledge regarding organoid creation. (d) Sankey diagram demonstrating shifts in participants' self-rated understanding of the organoid growth process, as gathered from the user study (n = 28).

5. Qualitative data analysis method

The qualitative data collected from user feedback primarily highlighted how the training in the virtual cell culture environment rendered the material in the paper more comprehensible and helped demystify the associated laboratory methods. This feedback underwent thematic analysis by two co-authors and was subsequently verified by a third, focusing predominantly on two aspects.

1. *The Interactive Virtual Lab as a Low-Stakes Learning Environment:* Participants described the game as a 'low-stakes arena for practice', free from the usual apprehensions associated with making mistakes, especially in the presence of others. This environment facilitated exploration and learning without the typical fears linked to querying authority figures. The web-based interactive lab successfully simulated the challenges of cell culturing found in real laboratories, specifically the difficulty in maintaining cell viability, yet allowed for procedural errors without real-life consequences. Selected student quotes, as shown in Fig. 5, illustrate how novices in cell culturing could learn about potential lab mistakes indirectly. Notably, 30 % of respondents in our largest sample, despite being psychology undergraduates, expressed interest in joining a laboratory to learn cell culturing after engaging with both the paper and the interactive virtual lab.
2 Enhanced Comprehension through Virtual Lab-Paper Integration: Feedback suggested that combining the interactive virtual lab with the paper facilitated a deeper engagement with the material, encouraging the use of scientific terminology. The dense, domain-specific language in the papers often poses a barrier to those outside the field. However, a significant majority of students in our largest study (more than two-thirds) reported increased confidence or improved understanding of the material after interacting with the virtual lab. This was particularly evident when participants were asked to elaborate on their confidence ratings post-virtual lab. Initially, only 5 out of 28 participants expressed full confidence in their understanding of the material. Post-virtual lab, this trend reversed, with only 3 out of 28 participants continuing to express a lack of confidence. Extracts from the post-virtual lab survey, detailing student perceptions of how the virtual lab aided their understanding, are presented in Fig. 5.

Our thematic analysis of qualitative feedback aligns with insights from Felszeghy et al. [39], and Adkins-Jablonsky et al. [41], both of whom utilized Kahoot to gamify classroom settings, leading to decreases in anxiety and increases in engagement. Jones et al. [40], and Chans et al. [42] also used gamified classroom settings to improve student motivation and engagement. The feedback from 'Seru-Otchi' users not only supports the effectiveness of gamification in science education, but also illuminates how such strategies can make highly specialized laboratory practices more accessible and less intimidating for novices. This specificity provides valuable insights for mentors in life sciences seeking innovative approaches to laboratory training.

6. Discussion: enhancing accessibility in scientific education

Mastering the skill of engaging with domain-specific literature is crucial for undergraduate researchers. However, the inherently complex nature of these texts, tailored for a scholarly audience within specific fields, often leads to reduced accessibility for broader or novice readers. This can render scientific articles seemingly dense and challenging, even for early-career scholars. Consequently, while the ability to comprehend intricate academic texts is vital, it is equally important to provide aspiring researchers with accessible learning tools to grasp the concepts foundational to their research interests. In this context, we advocate that interactive virtual labs and educational games like the one presented in this study can play a pivotal role in democratizing scientific research. By circumventing the sole reliance on technical texts, such games can render the initiation into biological research more approachable, thereby broadening participation.

Furthermore, these games and interactive activies offer a more holistic view of working in a laboratory, incorporating elements like lab safety and ethical practices. By integrating these aspects into an interactive virtual lab experience, we aim to better equip students for their initial forays into research laboratories, facilitating smoother integration into research groups and enhancing their overall preparedness.

7. Future work: expanding the scope and impact

Future developments based on this study could proceed in three directions.

1. *Wider Population Study for Statistical Validation:* Conducting the study with a significantly larger sample size would enable the application of statistical tests with confidence measures. The limited sample size from our studies limits our ability to make claims regarding the interactive virtual lab's impact and a larger participant population would help identify which groups benefit most from serious games in STEM education. One intriguing avenue, suggested by a participant with ADHD, is to investigate the effectiveness of this approach for neurodivergent students.
2. *Assessment by Senior Laboratory Personnel:* Exploring how educational games & interactive activies impact students' readiness for laboratory work from the perspective of experienced laboratory personnel could provide valuable insights into the practical utility of such tools in real-world settings.
3. *Web-based Interactive Lab Enhancement and Expansion:* Continuous development of the interactive virtual cell culture training environment, including improvements to visuals and interface, as well as broadening the content to cover areas such as neural development and metabolism, would enhance its educational value. The interactive virtual lab's adaptable design lends itself to

customization for various cell culturing protocols, presenting an opportunity to evaluate its applicability and efficacy in diverse scientific disciplines.

8. Conclusion: the impact of interactive learning on scientific education

Our study introduces a novel educational tool in the form of a cell culture training in our virtual labenvironment, designed to enhance the learning experience in the maintenance of in vitro brain organoids. This virtual lab effectively translates the complex concepts and protocols from scientific literature and laboratory safety guidelines into a more accessible, interactive format. A key feature of the virtual lab is its use of authentic images of cortical organoids, which vividly illustrate the impact of inadequate care and subpar safety practices on cell culture quality—a nuance often not captured in traditional scientific papers that typically highlight optimal results.

The findings from our study suggest that even games or interactive activites with relatively simple visuals can significantly enhance the comprehension of scientific content and boost confidence in understanding these complex topics. This approach not only facilitates a deeper understanding of the material but also potentially democratizes access to scientific knowledge, making the initial steps into scientific research more approachable for a broader range of students. In conclusion, our cell culture training within a virtual lab environment exemplifies the potential of interactive learning tools in augmenting traditional methods of scientific education, underscoring their value in fostering a more inclusive and effective learning environment.

Data availability

The source code for the interactive virtual lab "game" is available at https://github.com/braingeneers/seruotchi-supplement.

CRediT authorship contribution statement

Victoria T. Ly: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Formal analysis, Data curation, Conceptualization. **Drew Ehrlich:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jess Sevetson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ryan N. Hoffman:** Writing – review & editing, Visualization, Validation, Resources, Methodology. **Sofie R. Salama:** Supervision. **Sri Kurniawan:** Supervision. **Mircea Teodorescu:** Supervision, Investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix B. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.heliyon.2024.e30469.

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