Biodetect: development of a serious game to train Zika Virus detection using biosensors

Biodetect: desenvolvimento de um jogo sério para treinar a detecção do Vírus Zika usando biosensores

Biodetect: desarrollo de un juego serio para entrenar la detección del Virus Zika utilizando biosensores

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ABSTRACT
The use and handling of biological laboratory components are activities that require great care and attention from professionals, as incorrect handling of any component in this environment can cause numerous harms to health and ongoing research. In this sense, this article proposes the development of an educational game aimed at teaching and training professionals and students who deal with biological laboratory protocols. The game simulates the construction of a Biosensor to identify the Zika virus, from collecting biological material to analyzing the results. The plot unfolds in two main phases: in the forest, where the main character, the Little Scientist, seeks to capture the Zika virus, and in the laboratory, facing challenges such as eliminating contaminating viruses and manipulating DNA. Specific missions are assigned to each phase, ranging from eliminating mosquitoes to washing your hands correctly. The game incorporates historical elements about the emergence of the Zika virus and seeks to teach laboratory protocols through interaction and entertainment.

Keywords: Educational Game, Zika Virus Biosensor, Biological Laboratories, Pixel Art RPG, Manipulation Protocols.
RESUMO

A utilização e manuseio de componentes biológicos de laboratório são atividades que exigem muito cuidado e atenção dos profissionais, pois o manuseio incorreto de qualquer componente neste ambiente pode causar inúmeros danos à saúde e às pesquisas em andamento. Nesse sentido, este artigo propõe o desenvolvimento de um jogo educativo voltado ao ensino e capacitação de profissionais e estudantes que lidam com protocolos laboratoriais biológicos. O jogo simula a construção de um Biosensor para identificação do Zika vírus, desde a coleta de material biológico até a análise dos resultados. A trama se desenrola em duas fases principais: na floresta, onde o personagem principal, o Pequeno Cientista, busca capturar o vírus Zika, e no laboratório, enfrentando desafios como eliminar vírus contaminantes e manipular o DNA. Para cada fase são atribuídas missões específicas, que vão desde eliminar os mosquitos até lavar as mãos corretamente. O jogo incorpora elementos históricos sobre o surgimento do vírus Zika e busca ensinar protocolos laboratoriais por meio de interação e entretenimento.

Palavras-chave: Jogo Educativo, Biosensor do Vírus Zika, Laboratórios Biológicos, RPG Pixel Art, Protocolos de Manipulação.

RESUMEN

El uso y manipulación de componentes de laboratorio biológico son actividades que requieren gran cuidado y atención por parte de los profesionales, ya que una manipulación incorrecta de cualquier componente en este entorno puede provocar numerosos daños a la salud y a las investigaciones en curso. En este sentido, este artículo propone el desarrollo de un juego educativo dirigido a la enseñanza y formación de profesionales y estudiantes que se ocupan de protocolos de laboratorio biológico. El juego simula la construcción de un Biosensor para identificar el virus Zika, desde la recolección de material biológico hasta el análisis de los resultados. La trama se desarrolla en dos fases principales: en el bosque, donde el personaje principal, el Pequeño Científico, busca capturar el virus Zika, y en el laboratorio, afrontando retos como eliminar virus contaminantes y manipular el ADN. A cada fase se asignan misiones específicas que van desde eliminar mosquitos hasta lavarse las manos correctamente. El juego incorpora elementos históricos sobre el surgimiento del virus Zika y busca enseñar protocolos de laboratorio a través de la interacción y el entretenimiento.

Palabras clave: Juego Educativo, Biosensor del Virus Zika, Laboratorios Biológicos, Pixel Art RPG, Protocolos de Manipulación.

1 INTRODUCTION

The construction of biosensors has emerged as a crucial tool in the early and effective detection of arboviruses, such as those transmitted by Aedes aegypti, including
dengue, Zika virus and chikungunya (Shahrtash et al., 2014). These diseases pose a significant challenge to global public health, with recurrent outbreaks impacting communities around the world, as they are treated as neglected diseases throughout the world (Campos et al., 2020). The complex and dynamic nature of these diseases requires innovative and sensitive approaches to diagnosis and monitoring, which makes the construction of biosensors a vital area of research and development. However, the development of biosensors faces a series of challenges and difficulties. Firstly, the genetic and phenotypic diversity of arboviruses presents a substantial obstacle, requiring the design of biosensors capable of detecting multiple pathogens in a specific and sensitive manner (Charrel, 2016; Shahrtash et al., 2024). Furthermore, the need for high sensitivity and selectivity, coupled with the demand for affordable and user-friendly devices in areas affected by limited resources, adds additional complexity to the construction process. Among the arboviruses transmitted by *Aedes aegypti*, the Zika virus is of particular concern due to its devastating consequences, such as microcephaly in fetuses and other neurological complications (Eivazzadeh-Keihan et al., 2019). Early detection and monitoring of the spread of Zika is crucial to implementing effective public health measures and protecting vulnerable populations.

A promising approach that can contribute to these challenges is the integration of serious games into the biosensor construction process. One of the attributes of serious games is that they can offer an iterative and educational environment for training professionals, simulating scenarios and optimizing detection algorithms. By enabling collaboration between experts from diverse fields, including biology, engineering and computer science, serious games can catalyze innovation and advance knowledge about developing biosensors in a more efficient and accessible way (Antoniou et al., 2020).

In this context, we will explore the challenges faced in building biosensors for detecting arboviruses, with a special focus on the Zika virus, discussing the potential of serious games as a tool to overcome these obstacles and advance the fight against these debilitating diseases. Thus, the main objective of this article is to create a serious game that reproduces the process of detecting arboviruses, especially the Zika virus, adopting an innovative approach that integrates the construction of biosensors as a diagnostic tool.
Furthermore, the game will also have the role of transmitting information in a contextualized way about manipulation protocols and interaction with a biological laboratory.

2 THEORETICAL FRAMEWORK

Arboviruses are viral diseases transmitted by arthropods, such as mosquitoes, and represent a significant public health challenge worldwide (Madewell, 2020). These diseases are caused by a variety of viruses, including the Zika virus, dengue virus, yellow fever virus, chikungunya virus, among others. The impact of arboviruses on public health is substantial, given their global prevalence and their potential for rapid dissemination. These diseases affect millions of people every year, especially in tropical and subtropical regions, where climatic conditions favor the reproduction of transmitting vectors, such as *Aedes aegypti* and *Aedes albopictus* mosquitoes. The need for early and effective detection of arboviruses is crucial for controlling and preventing outbreaks. The rapid identification of suspected cases allows the implementation of control measures, such as the elimination of mosquito breeding sites, the treatment of infected patients and the implementation of prevention strategies, such as vaccination (in the case of yellow fever) and the use of repellents (Madewell, 2020; Labib and Chigbu, 2022).

In this sense, serious games emerge as a valuable tool in training for the early detection and adequate treatment of arboviruses. They offer a practical, interactive and standardized approach that allows healthcare professionals and disease control teams to acquire essential skills in an effective and engaging way. Furthermore, serious games provide a safe environment for practicing diagnoses and decision-making, without the risk associated with real clinical practice. By providing immediate, personalized feedback, these games allow participants to identify areas for improvement and continually hone their skills. Therefore, serious games play a crucial role in strengthening the capacity of health professionals and disease control teams to confront arboviruses, contributing to a more effective and coordinated response to these threats to public health (De Lima, *et al.*, 2021; Hungaro, *et al.*, 2021).
2.1 ZIKA VÍRUS

The Zika Virus was discovered in April 1947 in Rhesus monkeys in the Zika forest in Uganda, Africa, and only in 1954 was it associated with a human disease in Nigeria, Africa (Dick et al., 1952). Belonging to the Flavivirus genus, its envelope contains proteins whose binding to the surface of host cells facilitates the process of attachment, fusion and entry into host cells. Other viruses that are pathogenic to humans have these same characteristics, such as Dengue, Hepatitis C, Yellow Fever, Japanese Encephalitis, and West Nile viruses (Liu et al., 2019; Labib and Chigbu, 2022). Its first case was reported in 1966 in Asia, spreading throughout the Pacific region and America between 2007 and 2015. Between 2015 and 2016, outbreaks of microcephaly predominantly affected the Brazilian Northeast, representing an international health problem. This occurs because ZIKV can cross the placenta and cause serious congenital and neurological defects in fetuses, such as microcephaly (Mlakar et al., 2016; Hoen et al., 2018). Still in 2016, the Zika virus was declared a “Global and Public Health Problem” by the WHO (WHO, 2022).

Among the two modes of transmission, the vectorial one occurs through the female A. aegypti mosquito, which can be found in almost all countries in the hemisphere, apart from Canada and mainland Chile (Nelson et al., 2019; Haddow et al., 2020; WHO, 2022). There are reports that in addition to A. aegypti, infection can occur with A. albopictus, A. africanus, A. luteocephalus, A. vittatus, A. furcifer, A. hensili and A. apicoargenteus (Younger, 2016). As they are predominantly domestic mosquitoes, they can easily reproduce in any environment or reservoir that holds stagnant water. As a mosquito-borne arbovirus, it enters the bloodstream and replicates in various organs. This is because the female A. aegypti needs human blood for the development of her eggs and for her metabolism. Non-vector transmission occurs vertically, from mother to child via the placenta or breastfeeding, horizontally through sexual and ocular transmission, blood transfusion, organ transplantation and laboratory exposure (Haddow et al., 2020; Major et al., 2021; Ali et al., 2022; Labib and Chigbu, 2022).
2.2 BIOSENSOR

Biosensors are essential devices that help detect specific substances in samples, such as blood or water. They are classified into different types, varying according to their functionality and what they are looking for. The use of these devices is closely linked to the purpose of the analysis, requiring characteristics such as high sensitivity, selectivity, linearity, reproducibility and low response time (Dincer et al., 2019; Naresh and Lee, 2021). These devices are composed of a detection system, comprising a receiver, a transducer and a reading system, capable of directly measuring a target analyte present in the sample. After detecting the signal, it is recorded and transmitted to a display (Naresh and Lee, 2021).

The bioreceptors in biosensors are the elements responsible for specifically recognizing what they are looking for. These can be enzymes (proteins), antibodies (components of the immune system) or nucleic acids (such as DNA), acting as keys that fit only into a specific "lock". As far as electrochemical detection methods are concerned, they use electricity to observe the changes that occur in the sample. For example, amperometry measures the electricity generated when the target reacts with something in the sample, while potentiometry measures changes in electricity related to pH or the amount of ions present. Electrochemical impedance evaluates how electricity is affected by the presence of the target (Li et al., 2021).

These biosensors function as additional eyes, helping to find important substances such as viruses in blood samples. This is especially useful in areas such as medicine, the environment and food. The variety of available biosensors results from the continuous innovation of specific diagnostic tools, integrating biological detection elements with the main objective of identifying specific targets quickly and cost-effectively (Presutti et al., 2022). The precise interaction of the biological element with the target results in the modification of physicochemical properties, generating signals proportional to the concentration of the analyte. This final response is then measured qualitatively and/or quantitatively, allowing specific target detection based on specific bioreceptor (Li et al., 2021).
2.3 SERIOUS GAMES AS AN EDUCATIONAL TOOL

Serious games, designed with educational goals in mind, are emerging as effective learning tools. In contrast to entertainment games, these games have a clear mission to impart knowledge while engaging players in competitive narratives with tangible rewards. They have become valuable tools in both formal teaching and corporate training, offering an interactive space for communicating concepts and an environment conducive to instant (Delela and Barbosa, 2023).

The benefits of these games are diverse and wide-ranging, catering to all age groups and educational contexts. They promote essential skills such as teamwork, concentration, communication and problem solving, as well as providing opportunities to improve communication and conflict management skills. An emerging trend is the integration of biosensors into serious games, especially corporate training. While this presents technical and design challenges, this innovative approach promises to simulate diagnostic and therapeutic processes, providing a more authentic and immersive learning experience (De Lima et al., 2021; Hungaro, et al., 2021; Souza, 2021).

Furthermore, the development of serious games for the detection of arboviruses, such as the Zika virus, is gaining prominence in the healthcare community. These games can play a crucial role in training healthcare professionals, improving effectiveness in early detection and appropriate treatment of these diseases. They also have the potential to contribute to continuing education by keeping professionals up to date on best practices and guidelines (Souza, 2021).

3 METHODOLOGY

The methodology of an article outlines the procedures employed to conduct the research, including the type of study, sample selection, data collection and analysis methods, ethical considerations, and limitations of the study. Its detailed and transparent description is essential to guarantee the replicability and reliability of the results, in addition to providing a solid basis for the interpretation and generalization of the findings.
The development of this project followed a flow based on the Kanban development methodology, from the planning stage to the application testing stage. The development team was made up of two professionals, a software developer and architect and a Pixel art designer, who was also responsible for Game Design and management of matters related to the application domain. The main tools used were: the Unity 3D development engine, using C# as a base language and some external libraries to improve the functioning of some of the application's features, the Piskel pixel art creation platform, for building the entire graphical part of the application and, the Trello platform for managing activities, deadlines and resources arranged on the Kanban board. The sound design used was obtained through free sources, such as the website www.incompetech.com, which has a wide range of free resources available to the community. The game's code is available on GitHub and its initial version for Android will soon be released on the Google Play Store.

The process of carrying out the activities was based on the methodology used by (Blind Review), being adapted to the development context of the project in question. The first stage was the ideation and construction of the Game Design, followed by the creation of Storyboards and definition of the primary and secondary persona. After this stage, the implementation of the game began and, in parallel, the creation of pixel art elements and application animations. Finally, exploratory tests were carried out seeking to refine the application by finding and solving development errors. All these activities followed an iterative and incremental flow, where new ideas, features and elements were adjusted and added according to the development status. Figure 1 demonstrates this process in greater detail.
The first stage of the development process, called Ideation, is based on the CBL methodology (Challenge Based Learning), which seeks to identify and solve real-world problems (Johnson and Brown, 2011). The approach focuses first on the problem and then technologies and possible solutions are imagined based on the challenges listed.

In this sense, based on personal experiences of one of the authors, and supported by studies that widely discuss the subject, the intention arose to seek to address problems related to difficulties in learning the process of handling equipment and biological material in the laboratory (Souza and Santos, 2019; Silva and Alves, 2023; Souza, 2023). For many, whether they are new students or not, in the field of biology and the like, understanding the protocols for disinfection, handling and treatments of microorganisms is a task that can be stressful and traumatic, in some cases. Since small errors can trigger serious health problems or harm the progress of ongoing research.

As a result of the ideation, in addition to the problem, we have the definition of a possible solution based on two personas, which corresponds to step two of the process. In short, the base personas of this research were a postgraduate student who has just started his research and a student in his final years of high school, who has doubts about which course he will take the entrance exam. These personas are representative profiles of possible users of the solution presented, where each of them has characteristics of people who could experience the problems defined in the ideation stage, therefore, the final
solution was built based on the needs of the chosen personas. All of this culminated in a Minimum Viable Product (MVP), used as a basis to define the scope of development of the solution.

With the first steps completed, the development stage began, grouping the activities of Game Design, Pixel Art Creation, Implementation and Exploratory Testing. In the construction of the Game Design, the StoryBoard construction technique was used as a basis, which are drawings representing what the possible flows of the game's phases will be like, which elements should be included in each phase, victory and defeat conditions, bonus elements for the player, known as Power-Ups and, which would be the enemies to be faced by the main character. At this stage, the plot came to life, and it was defined who the main character would be, the mechanics, what challenges would be necessary for each stage of the game and, most importantly, how to balance information and entertainment, leaving the game as faithful as possible to the challenges real-life challenges faced by professionals working in laboratories. From this point on, there is a junction between two activities, the implementation and creation of pixel art, which were carried out in parallel. The creation of pixel art elements used the book “Make Your Own Pixel Art” by authors Dawe and Humphries as a knowledge base (Dawe and Humphries, 2019). In the book, the authors report good creation tips, such as building elements based on shapes and shadows, silhouettes, color palettes and several other important concepts. In the implementation stage, as previously mentioned, Unity was carried out, and within this stage a series of other activities are included, such as character animation, inclusion of the soundtrack, interface development and implementation of design patterns such as Singleton and State-Machine to facilitate the organization and structure of certain points in the game.

The entire application was built in a modular way, so that it can be easily expanded in the future, with new phases and challenges. Finally, a series of exploratory tests were carried out, seeking to find possible problems in programming, mechanics or interface. In Figure 1, all this information is encapsulated, highlighted by arrows that indicate the bidirectionality of the process. This visual representation reflects the dynamic nature of the process, where adjustments to the code or images may be required in response to issues identified during testing. Just as the emergence of new ideas brings the need for a
new development activity and/or creation of new images, this causes the need for a new round of exploratory tests on the application. In addition to exploratory tests, unit and integration tests were also performed throughout the development phase.

4 RESULTS AND DISCUSSIONS

BioDetec is a serious game, in third person, top down in the pixel art style, aimed at teaching and training professionals and students who deal with the protocols of biological laboratories in the process of manipulation and interaction with the components existing in this environment. The game seeks, through challenges, to simulate the construction of a Biosensor to identify the Zika virus, inspired by the work of (Blind Review), the idea is that the player can simulate everything from collecting the biological material, going into the field to do mosquito capture, until the DNA manipulation phase in the laboratory, construction of biosensors and analysis of results (Blind review). For the player to do this, he will have to solve a series of problems, such as eliminating mosquitoes, viruses, rats that escaped from the laboratory, and much more. Furthermore, to be able to move from one level to another, the player must complete Missions. They include hygiene protocols, appropriate sequences for the manipulation and construction of biosensors, the elimination and capture of animals, mosquitoes and viruses and the implementation of certain essential protocols that must be adopted in the laboratory.

The game begins in the Forest phase, where the main character, who is called Little Scientist, will seek to capture the Zika virus, aiming to collect its genetic material for her research. The choice of the forest and the monkey as one of the characters in this phase was due to the story of the emergence of the Zika Virus in the world. As already briefly mentioned, the Zika Virus was discovered in April 1947 in Rhesus monkeys in the Zika forest in Uganda, Africa. In this sense, we sought to indirectly insert this fact into the game, making the character go after the mosquito in a forest with some monkeys as his enemies. In this phase of the forest, there are also other mosquitoes as enemies, some venomous snakes, carnivorous fish and frogs, which can also hinder the Little
Scientist on her scientific journey. Figure 2 demonstrates the StoryBoard created for the general map of the Forest phase, and Figure 3 is the final version implemented in the game.

Figure 2: Storyboard of the forest phase map, used as a sketch for creating and finalizing the positioning and iteration of the phase elements.

Source: Authors

Figure 3: General map of the Forest phase, inspired by the story of the emergence of the Zika virus, in the Zika forest, Uganda, in 1947.

Source: Authors
In this phase, the main missions are limited to eliminating mosquitoes, collecting a specific number of coins or diamonds, taking the monkey to its food, collecting the Zika mosquito and distributing awareness pamphlets to the local population. These last two missions are only on the final island, which will give the passport to the laboratory phase. Figure 4 gives more details about some of the scenes in the forest phase. In the laboratory, new challenges await the Little Scientist. First, she must eliminate all the viruses that are spread in Laboratory 1, as it was contaminated due to the wrong handling of some microorganisms. After eliminating all these viruses, the new challenge is in the Big Labyrinth, which is infested with rats and mosquitoes that were accidentally released by employees who did not have the necessary knowledge to correctly handle the animals. They ended up spreading some viruses across the surfaces of various furniture, which must also be eliminated by the Scientist. The next mission is to go through the Central Laboratory, which is guarded by some small stalking viruses, they are attracted by fear. The next laboratory is the decontamination laboratory, where the Scientist must wash her hands, eliminate all mosquitoes, put on her lab coat and finally carry out her experiments. But she can't forget to wash her hands when she leaves the room, or her mission won't be completed. Already wearing her lab coat, the young researcher must go to the Main Laboratory, and her mission will be to eliminate the mosquitoes again, extract the DNA from the Zika mosquito, cultivate it in culture medium and wait for the microorganisms to grow in the greenhouse.
Figure 4. Forest phase in more detail. (a) The path of the piranhas, (b) The well of hope (c) The snake forest (d) The monkey forest.

For each step to be carried out, some items must be collected throughout the laboratories, such as the culture medium itself, Petri dishes, pipettes, biosensors, and the items resulting from each step, which are generated after the correct completion of each one of them. To collect some of these items, the Scientist must complete another mission in the next room, the equipment laboratory. After that, we will have 3 more missions. The creation of the biosensor, in the manipulation laboratory, the reading of the results, in the reading laboratory and, finally, the washing of all dirty glassware, which must be collected throughout the entire scenario. Upon completing all the missions, the Little Scientist will receive a certificate of completion from BioDetect, congratulating her on successfully completing all the challenges, and for having learned a little more about the protocols of a laboratory and the process of building a biosensor. Figure 5 represents the final version of the laboratory map after implementation.
To illustrate this phase in greater detail, Figure 6 provides some more detailed views of some of the laboratories and challenges that the little Scientist will have to face. In addition, the game also has an inventory system, which is used so that the characters can store all the items necessary to complete their missions during their journey. The inventory system is represented in Figure 6 (c). Distributed throughout these two initial phases are several enemies, each with their own behavior, applying a specific amount of damage to the character. Some of these enemies only patrol specific points in the scenario, and others have Artificial Intelligence-driven pursuit behavior, made using Unity’s NavMashAgent library. This chase is initiated depending on the player's distance from the enemy, which also varies from character to character. In addition to enemies, there are items, which are used to complete missions, enemy equipment, used to eliminate some of these threats, and some power-ups, such as coins, diamonds and survival hearts, used to complete missions and, in future versions, some of them can be used as currency within the game. Figure 7 demonstrates a sprite sheet with most of the game's elements.
Figure 6. Forest phase in more detail. (a) External side of the laboratories, (b) Main laboratory (c) Inventory system with items collected by the player (d) Certificate of completion of all missions in the game.

Figure 7. *SpriteSheet* with the representation of game elements and characters.

In this way, the entire narrative of the game, as well as its characters, seeks to convey historical information and about the protocols for using the laboratories, using as
a basis the flow of building a biosensor for detecting the Zika Virus. All of this, diluted within the plot of a pixel art RPG game, aimed at learning and memorization through interaction, association and entertainment that the game can bring to the user.

5 CONCLUSION

The use of games in different contexts and areas has been a common practice today. The so-called Serious Games have sought to prove that it is possible to combine the useful with the pleasant, turning tedious and boring processes into something subtle and pleasant, using the sensations of pleasure and satisfaction that games bring when receiving a reward or completing a specific challenge. This work, through the BioDetect game, had as its main target, building a simple solution through a digital game, to represent everything from the history of the Zika virus, to the step-by-step process for building a biosensor that could carry out its identification. To achieve this, the player needs to go through a series of missions, which represent, among other things, the protocols and steps that must be carried out within a biological laboratory, triggering learning in a way that parallels the evolution of the game.

However, for us to further evolve the application, an on-site testing stage is necessary, with potential users of the game. This should give us feedback on improvements to the gameplay and the game’s plot itself. This test must be carried out with students in the first periods of biological sciences, biomedicine and similar courses, as well as students in their final years of high school, to awaken interest and curiosity about science and the world of research. Furthermore, other phases with the creation of biosensors for other diseases are in planning and may enter the future application backlog after their first validation.
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