# From Pages to Play

A Comparative Study Evaluationg Immunoloogy Learning through Games and Textbooks

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**Abstract:**

This study investigates the effectiveness of an immunology-themed learning game, *Kampen om Kroppen*, compared to traditional learning resources in enhancing high school students' understanding of immunological concepts. The work evaluates student engagement, comprehension, and retention. Using a quantitative-measures approach, we collected quantitative data from a survey measuring engagement and knowledge gain. Results indicate that while the game elicited significantly higher engagement scores in areas such as Focused Attention and Aesthetic Appeal than the control condition, the overall engagement level remained moderate. These findings suggest that although learning games can enhance student interest, the design must be refined to improve engagement and learning outcomes. The possibility of replacing cells and pathogens in pixel-style representations with metaphors or anthropomorphized characters emerges as a potential strategy to deepen understanding and retention. This research contributes to the discourse on learning game design, highlighting the need for innovative approaches to teaching challenging subjects like immunology.

# Contents

# 1 Introduction

The field of immunology plays a critical role in understanding the body's defence mechanisms against pathogens, making it a cornerstone of modern biology and medicine. Despite its importance, immunology is considered a challenging subject to teach effectively, particularly at the high school level. This complexity arises from the abstract nature of many immunological concepts, such as cellular communication, antigen recognition, and immune memory, which can be difficult for students to visualize and comprehend [1].

Traditional educational methods, primarily based on textbooks and lectures, often fall short of engaging students or helping them retain these complex ideas [2]. As global health concerns such as pandemics and antibiotic resistance continue to emerge, the need for an informed and scientifically literate population has never been more crucial. Immunology, in particular, is at the forefront of these challenges, as it underpins our understanding of how to combat diseases and maintain public health [3].

In recent years, learning games have shown promise as an innovative way to enhance learning and increase engagement in various subjects [2]. However, the potential of game-based learning in the context of immunology remains largely unexplored. While some studies have investigated the benefits of digital tools in teaching complex biological concepts, there is a noticeable gap in the literature when it comes to interactive media specifically designed to teach immunology at the high school level [4].

## 1.1 Motivation

The motivation for this study arises from the ongoing challenges educators face in making complex subjects like immunology accessible and engaging for students. With the rise of digital media in education, it is important to explore how these tools can be used to overcome traditional barriers to learning [2]. The potential of learning games to make abstract concepts more tangible and engaging provides a unique opportunity to improve both the quality and accessibility of science education. By investigating the impact of a game-based learning approach, this study seeks to contribute to the growing body of research on educational innovation and student engagement.

## 1.2 Initial problem statement (IPS)

*How can a roguelike learning game improve the understanding of complex biological concepts, such as immunology, for high school students?*

# 2 Theoretical Framework

In this section, we have explored existing research on learning games, and the design and potential advantages of roguelite games in the context of learning games. We also investigated two learning games and a roguelite tower defence game, to inform the design of our prototype.

## 2.1 Learning Games

Learning games, also known as educational games or serious games, are designed with the primary purpose of facilitating learning in an interactive and engaging way. These games integrate educational content and objectives into gameplay mechanics, providing players with opportunities to acquire knowledge, skills, and concepts while immersed in a gaming environment.

One of the key advantages of learning games is their ability to enhance engagement and motivation among learners. By leveraging the inherent enjoyment and challenge of gameplay, these games can captivate players' interest and sustain their attention throughout the learning process. This increased engagement can lead to improved learning outcomes, as learners are more likely to actively participate and invest effort in mastering the content presented within the game [5], [6].

Learning games cover a wide range of subjects and educational domains, including mathematics, science, language arts, history, and more. They can be tailored to different age groups, educational levels, and learning objectives, making them versatile tools for educators and learners alike. Additionally, learning games often incorporate elements of feedback, progression, and adaptation, allowing for personalized learning experiences that cater to individual learner needs and preferences [7].

The design of effective learning games requires careful consideration of both educational principles and game design principles. Developers must strike a balance between pedagogical effectiveness and gameplay enjoyment, ensuring that the game mechanics align with the learning objectives while remaining engaging and enjoyable for players. Iterative design processes, user testing, and feedback collection are essential components of creating high-quality learning games that effectively facilitate learning while maintaining player engagement [8].

In recent years, advances in technology have expanded the possibilities for learning game development, with the emergence of virtual reality, augmented reality, mobile gaming, and other innovative platforms. These technologies offer new opportunities for immersive and interactive learning experiences, further enhancing the potential impact of learning games on education and training [5].

The interactive nature of video games allows players to learn in a more experiential context compared to non-interactive media. Through the mechanics of a video game, players can gain an understanding of complex real-world systems. This is the concept of procedural rhetorics, a term coined by Ian Bogost and defined as:

> *"The art of persuasion through rule-based representations and interactions rather than the spoken word, writing, images, or moving pictures."* [9]

Bogost proposes that designers of learning games should aim to integrate learning content through the mechanics and the systems of the game rather than just through some type of audio/visual presentation [9].

Many learning games aim to teach players factual information and descriptions about a specific topic. This type of knowledge is known as declarative knowledge and it has been suggested by Lemoine et al. [10] that the roguelite genre is particularly adept at teaching this type of knowledge. The specifics of roguelites and the often conflated roguelikes will be explored further in the Section 2.3, but in summary: they propose that since declarative knowledge is gained through repetition, and since the roguelite genre promotes replayability, using roguelites to teach declarative knowledge could prove advantageous over other game genres.

## 2.2 Engagement in games

Engagement in games is a multifaceted concept that encompasses the player's involvement, immersion, and enjoyment throughout the gaming experience. It goes beyond mere participation, as it reflects the depth of connection and interaction between the player and the game environment [11].

One of the key concepts related to engagement in games is "flow," a term coined by psychologist Mihaly Csikszentmihalyi [12]. Flow refers to a state of intense focus and immersion in an activity, where the individual experiences a sense of enjoyment and loses track of time. In the context of gaming, achieving flow indicates that the game's challenges are well-matched to the player's skills, leading to a highly rewarding and engaging experience.

Engagement in games can significantly enhance learning outcomes. When players are deeply engaged in a game, they are more likely to be receptive to new information and concepts presented within the game environment. This phenomenon has led to the emergence of educational games that utilise the engaging nature of the game to facilitate learning in various domains, including science, mathematics and language arts [11]. By integrating educational content seamlessly into gameplay mechanics, these games can promote active learning and skill development while keeping players motivated and entertained.

Game Designer Raph Koster [13] proposes that video games are systems for learning and that the experience of 'fun' when playing video games, comparable to high engagement, is caused by the reward system of the brain releasing endorphins whenever we learn something. According to Koster, games consist of patterns that need to be analysed, learnt, and eventually 'grokked'. 'Grokking' is used as a term for complete mastery of a pattern. Once a player has grokked a pattern and there is nothing new for them to learn, they will lose interest in that pattern. If the game does not provide a player with new patterns to recognize and grok, or if a game introduces new patterns too slowly as the player progresses, they will eventually become bored and stop playing. However, if a game unfolds too many or too complex patterns at once, a player might perceive the patterns as non-sensical noise which leads to frustration and boredom. Boredom in video games, in the sense described by Koster, also occurs when the player has grokked all patterns in the game or if the player fails to see any patterns whatsoever as this will be interpreted as nothing but noise. To maintain a consistent enjoyment of the game throughout, an increased level of challenge should be introduced gradually, and new patterns should be introduced continuously. Koster argues that the way to achieve this is through "emergent behaviour", which Koster defines as "patterns that emerge spontaneously out of the rules, allowing the player to do things that the designer did not foresee."(2005, p. 128) The procedural nature of roguelites provides a strong basis for emergent gameplay to occur [14].

## 2.3 Roguelikes & Roguelites

The term roguelike refers to a genre of videogames that includes a specific set of game mechanics originating from the 1980 video game Rogue [15]. In 2008 a proposal for a definition of the roguelike genre was put forth at the International Roguelike Development Conference in Berlin, Germany [16]. This definition became known as the Berlin Interpretation and it defined 9 so-called high-value factors; essential features that a roguelike should include:

- Random environment generation
- Permadeath
- Turn-based
- Grid-based
- Non-modal
- Complexity
- Resource management
- Hack'n'slash
- Exploration and discovery

Games that include permadeath and procedural generation but disregard some of the other factors of the Berlin Interpretation are commonly referred to as roguelites to distinguish themselves from true roguelikes. However, the terms roguelikes and roguelites are often used interchangeably today as even developers describe their games as roguelikes despite them lacking most factors mentioned in the Berlin Interpretation [17]. Though roguelites are varied and include several sub-genres such as action-roguelites (*Hades*, *Binding of Isaac* [18]) and Deck-bulding-roguelites (*Slay the Spire* [19]), common denominators in these types of games can be identified as procedurality, permadeath, progression, resource management and replayability.

### 2.3.1 Procedurality

Roguelites feature different degrees of procedural generation. A typical structure of roguelite such as the structure found in *Hades*[17], Slay the Spire[19] and Binding of Isaac[18] would be a progression through different biomes/rooms of lesser enemies and events before facing a boss. The biomes/rooms a player encounter is determined by a seed, which is a short string of text or a number used to procedurally generate the map layout and enemy composition. Within these rooms, the environment itself may also be procedurally generated. This ensures that no run is the same as both the environment, the enemies and the order in which the player will face them vary from run to run.

### 2.3.2 Permadeath

Permadeath means that once the player dies they will have to start the game over again. There are no checkpoints and the only way to complete a playthrough is to reach the end without dying. In roguelites, a playthrough is also referred to as a "run". The length of a successful roguelite run varies between games, but for some of the more popular games within the genre, a successful run takes anywhere from minutes to hours.

### 2.3.3 Progression

There are typically two types of progression in roguelites. In-run progression and meta-progression. The in-run progression refers to any progress made while playing a single run. This progression includes abilities, upgrades and items that make a character more powerful for the remainder of the run but will be lost upon death. The item/upgrade pool may be randomly determined and in many roguelites, there are potentials for powerful synergies between items making the player almost invincible. Losing all in-run progression upon death or completion of a run ensures that the next run will be a fresh challenge. To compensate for the increased power of the player, roguelites will also get progressively harder during a run.

The meta-progression refers to any type of permanent progression that is kept between runs and will usually yield an advantage for the player in their following runs. This can occur in the of unlocking items and abilities that will appear in the following runs or as in *Hades*, where the player collects several resources which persist between runs and can be used to upgrade health, damage, weapons and abilities. In some cases such as *Hades* [17] and Returnal [20], the narrative is also part of the meta-progression as each may unlock new dialogue and cutscenes that progress the story. The meta-progression systems in roguelites are often mentioned as the defining feature that distinguishes this genre from roguelikes.

### 2.3.4 Resource Management

Resource management is a crucial part of completing a roguelite run. Both *Hades* [17] and *Binding of Isaac*[18] feature a limited health pool, that does not automatically regenerate. Health regeneration is tied to specific events and rooms, and is usually a reward in itself, meaning players will often find themselves in a position, where they have to carefully make a choice between a reward that improves their combat abilities for the rest of the run, or a reward that provides some sort of health regeneration. Many roguelites also feature shops where resources acquired during the run can be spent on rewards that will empower the player for the rest of the run. In Slay the Spire [19], players encounter shops where they may use gold acquired from clearing rooms to purchase one-time-use potions, new cards, and powerful relics that provide a buff for the remainder of the run or remove existing cards at a cost. As gold is limited and the offer of items sold in the shop is randomized, players will have to make several important strategic decisions that may make or break their run. Games such as Rogue Legacy, and Hades [17] also feature resources that persist between runs, meaning that the strategic decision and resource management extend beyond a single run in these games.

### 2.3.5 Replayability

Roguelites are games that heavily encourage replaying. The genre is known for its challenging difficulty meaning players usually make several unsuccessful attempts before successfully finishing a run without dying. The meta-progression allows the player to keep progressing and build a stronger character even if their run is unsuccessful. For some games, such as *Hades*[17], *Binding of Isaac*[18] and *Returnal*[20] both dying and completing several runs are required to experience the full narrative of the game. The procedural nature of roguelites makes each run unique and the relatively short length of a run ensures that a player will not lose hours of progress upon death.

### 2.3.6 Framework for roguelite learning games

Lemoine et al. [10] propose a framework for analysing roguelite games that train declarative knowledge. The framework consists of five criteria: Generation, Death/Hurt, Variety, Progress and Difficulty. Within each criterion, several questions can be asked from both an educational and game perspective.

| Criteria | | Educational perspective | Game Perspective |
|---|---|---|---|
| Generation | Which elements are generated? | | |
| | When are they generated? | | |
| | On what basis are they generated? | | |
| Death/Hurt | When can the avatar get injured or die? | | |
| | What are the consequences of being injured? Being killed? | | |
| | Where can the avatar be injured or killed? | | |
| Variety | Which elements vary? | | |
| | How do elements vary? | | |
| Progress | What is retained in-between each death?' | | |
| Difficulty | What are the elements that increase or decrease the difficulty? | | |
| | How is the difficulty progression designed? | | |

Figure 1: Analysis Framework for Designing Declarative Knowledge Training Games Using Roguelite Genre [10]

The criteria in the framework match the aforementioned characteristics of roguelites and the main point of this framework is to ensure that the educational content and gameplay and the dynamic between them is taken into consideration during development by asking a series of questions depicted in Figure 1.

## 2.4 A roguelite immunology learning game

Immunology is a branch of medicine and biology that concerns itself with the study of the ever-ongoing interactions between pathogens and the immune system. It is considered a particularly challenging subject for students to understand as it includes many complex systems, is interdisciplinary, and rapidly evolving [21].

It is also a topic that lends itself particularly well to a learning game with roguelite elements, as there are several overlapping characteristics between the gameplay loop found in roguelites and how the immune system fights off pathogens.

### 2.4.1 Procedurality

There are more than 1200 pathogens known to cause disease in humans[22], meaning a roguelite learning game could feature a wide variety of enemies with vastly different characteristics. To simulate the unpredictable nature of infections within humans, enemy stats, composition and rate of mutations could be determined procedurally. The concept of rooms or biomes in roguelites also ties in nicely with the human anatomy, as these could consist of different types of tissue, body parts or organs with certain types of pathogens more likely to appear in certain parts of the body.

### 2.4.2 Progression

**The human immune response** is inherently progressive as it continuously learns and adapts to new pathogens. On a cellular level, the immune system can be divided into the innate and adaptive immune systems; the innate immune system being a more generalized response and the adaptive immune system being a more specific response.

When a pathogen is first encountered, the innate immune system ensures a generalized response by activating the white blood cells of the innate immune system: Neutrophils, basophils, eosinophils, mast cells, macrophages, dendritic cells, and natural killer cells (NK cells).

The primary functions of these cells are:

- **Neutrophils** and **macrophages** will engulf and digest pathogens through a process known as phagocytosis. Macrophages also contribute to activating the adaptive immune system through antigen presentation, but are less effective than dendritic cells at this.
- **Mast cells** and **basophils** will release histamine and other mediators to promote inflammation in an area, creating an inhospitable environment for pathogens while increasing blood flow and signalling for other immune cells to engage pathogens in the area.
- **Eosinophils** will fight parasitic infections and play a crucial role in allergic responses.
- **NK cells** will recognize and kill cancerous or infected cells by inducing apoptosis (programmed cell death).
- **Dendritic cells** will recognize and present antigens to T cells, thereby activating the adaptive immune system.

The adaptive immune system consists of **T cells** and **B cells** that primarily attack pathogens based on their antigens. Antigens are identifiers that pathogens display on their surface. Cells like dendritic cells and to a lesser extent macrophages will capture and recognize specific antigens, which they will present to T cells, activating the adaptive immune system.

After an antigen has been presented to a naive T cell, the T cell proliferates and differentiates into:

- **Cytotoxic T cells**, which kill infected cells carrying the antigen presented to them.
- **Helper T cells**, which aid other immune cells and activate B cells.
- **Memory T cells**, which live in the body for years, remember previous pathogens and reactivate the adaptive immune system if said pathogen appears again.

When a Helper T cell activates a B cell, the B cell proliferates and differentiates into:

- **Plasma cells**, which produce antibodies aimed at specific antigens. The antibodies will attach themselves to the surface of pathogens carrying said antigen, neutralizing or weakening the pathogen and signaling other immune cells to attack it.
- **Memory B Cells**, which remembers a specific antigen, ready to differentiate into antibody-producing plasma cells if they re-encounter pathogens carrying this antigen.

As such, there is a natural progression in the manner in which the body responds to threats from pathogens, going from activating cells that are part of the innate immune system to activating T cells and finally activating B cells and antibody production. [23] [24] [25]

**Abstracting into roguelite mechanics**

There are several possibilities to abstract this progression into a roguelite gameplay loop both in terms of in-run progression and meta-progression. During a run, the player could gradually increase their power, as they start with only the cells included in the innate immune system, but gradually unlock T and B cells by defeating pathogens and presenting their antigens to T cells. Memory T and B cells could also serve as meta-progression in that once they are created, they will persist through runs. There is also a wide variety of real-life factors that may increase the efficiency of the immune system, such as proper diet, sleep, exercise, and medicine, meaning the pool of upgrades the player gets to choose from during a run, has the potential to be very large and mirror how the body works.

### 2.4.3 Perma-death

If the immune system persistently fails to fight off pathogens infecting the body, it will result in a weakened body succumbing to disease and eventually death. In that sense implementing perma-death in a game about protecting the body from pathogens seems like an obvious choice; however, if memory B and T cells are used to represent metaprogression, perma-death may be harder to implement in a factually meaningful way, given that the memory cells would die along with the rest of the body.

## 2.5 State of the art

This section presents an analysis of an influential title in the tower defense genre and two learning games, FLERP, CellCraft, and the Blood Typing Game. Each game contributes with unique mechanics and design principles that inform our development process. By examining these titles, we aim to identify best practices and innovative strategies that can enhance player engagement and educational efficacy in our learning game prototype.

### 2.5.1 FLERP

FLERP[26] offers a unique twist on the tower defense genre by incorporating roguelite and autobattler elements. Developed and published by Foolsroom[26], FLERP challenges players to fend off waves of enemies using units that can be bought and upgraded through a strategic resource management system [26].

**Dynamic Gameplay Mechanics:**

FLERP[26] differentiates itself from traditional tower defense games by allowing players to recruit units from a shop rather than placing towers. These units automatically engage enemies, adding a layer of strategic depth, as players must choose the right units and upgrades to optimize their defenses. The game emphasizes resource management, with players earning gold and interest after each level, which can be reinvested into more powerful units and upgrades.

**Strategic Decision-Making:**

Players face numerous strategic choices throughout each game. With a variety of units and items available, each run is unique, requiring players to adapt their strategies based on the resources they acquire. This variability ensures that no two playthroughs are the same, maintaining a high level of engagement and replayability.

**Adaptive Challenges and Replayability:**
FLERP[26] features a roguelite progression system where each run offers different challenges and opportunities. The procedural generation of the game and the variety of available units and items keep players constantly adapting and refining their strategies to overcome increasingly difficult enemy waves.

**Unique Selling Points:**
FLERP[26] combines arcade-style tower defense mechanics with roguelite progression, providing a fresh take on both genres. The automatic combat system and strategic depth in unit recruitment and synergy formation set FLERP[26] apart, making it appealing to fans of strategy and roguelite games alike.

### 2.5.2 CellCraft

CellCraft[27] was funded by the Digital Media & Learning Competition in 2009 and made it to full release in 2010 [28] [29]. The game's objective is to develop a cell from a membrane into a fully realized cell with all its organs and the challenges it faces from foreign objects like viruses and changing temperatures. The stated design philosophy behind the game was "a truly educational game that was also genuinely fun to play." [27], i.e., a distinction was drawn between learning games that are fun to play and those that are not.

The designers emphasized the necessity of the game being fun to play because many learning games are made to convey information first and be games second. By prioritizing fun gameplay, the hope was that students playing the game would feel enticed to learn more about the subject, or at least play the game from start to finish, retaining more information along the way than they might have by reading relevant educational material.

Cellcraft[27] also provides players with an encyclopedia, accessible at any point in the game, where relevant information about anything to do with the relevant cellular element can be found. However, the game also provides this information in a much more organic way by depicting its real-world subject matter realistically. All the gameplay presented in the game is grounded in the real-world behaviour of cellular organisms. By closely simulating the behavior of a cell, if players recall how a mitochondrion works in the game, they will know how the real thing functions. This aspect is what sets apart learning games from traditional teaching methods.

The game earned multiple awards and was played by 2.5 million players within 3 months of its free-to-play online release, which does imply a certain level of gameplay quality [29].

### 2.5.3 The Blood Typing Game

The Blood Typing Game is a notable educational tool that won the 'Best Game' category at the Swedish Learning Awards in 2012. Its minimalistic yet captivating graphic design effectively engages users while teaching them about blood types and their compatibility for transfusions. This game utilizes a playful teaching method that enhances the learning experience by fostering curiosity about the subject matter [30].

**Engaging Design:**
The game's design stands out through its simplicity, allowing players to focus on the learning objectives without unnecessary distractions. By presenting blood typing in an interactive format, the game encourages users to actively participate in their learning process, which can lead to a deeper understanding of the concepts involved.

**Educational Impact:**
The Blood Typing Game addresses a crucial area in biology education — understanding blood types and their compatibility. The game effectively conveys this information through gameplay mechanics that challenge players to identify blood types and make decisions based on compatibility. This approach not only reinforces theoretical knowledge but also emphasizes the practical implications of blood typing in real-world medical situations [31].

**Playful Learning:**
By integrating playful elements into its design, the Blood Typing Game reduces the anxiety often associated with learning complex biological concepts. This enjoyable experience promotes sustained engagement, encouraging players to explore and learn more about the topic. The success of the game in capturing user interest demonstrates the potential of using interactive gaming as a complementary educational tool.

**Significance:**

The Blood Typing Game exemplifies how educational games can effectively teach foundational biological principles in a manner that is both engaging and memorable. Its innovative design principles serve as a valuable reference for developing learning games that aim to enhance player engagement and learning outcomes in subjects such as immunology.

## 2.6 Research Question

At the start of the project, the **Initial Problem Statement** was formulated as follows:

*How can a roguelike learning game improve the understanding of complex biological concepts, such as immunology, for high school students?*

Taking into account all the information gathered from the Theoretical framework, we arrived at the following **Final Problem Statement** which poses the following question:

*Does the use of an immunology learning game with roguelite game elements, result in a better understanding of immunological concepts among high school students compared to reading material?*

### 2.6.1 Null Hypothesis (H0):

The use of an immunology learning game with roguelite game elements does not result in a significantly better understanding of immunological concepts among high school students compared to reading material.

### 2.6.2 Alternative Hypothesis (H1):

The use of an immunology learning game results in a significantly better understanding of immunological concepts among high school students compared to reading material.

# 3 Design requirements

Based on our examination of the available literature, the following design requirements apply:

**Functional:**

- The game should include roguelite mechanics and systems meaning it should feature procedurality, progression, permadeath and resource management
- Pathogens should be the main enemy and the game should feature different types of pathogens with different characteristics.
- The game should feature behaviour for all essential immune cells
- The game should include an encyclopedia of subjects in the game 2.5.2

**Non-Functional:**

- The game should teach the player the essential functions of the innate and adaptive immune systems
- The game should encourage replayability through a varied pool of enemies and upgrades
- The game should primarily teach the learning content through mechanics and systems rather than text
- The difficulty of the game should match the skill level of the target group to create engagement and flow

# 4 Design

Before and during the pre-design, design and development of our prototype, we involved biology teachers in the process. Three teachers from three different high schools were interviewed before the development had even begun, to get their input regarding what, if any, learning games they already use in their teaching, and what immunological concepts they felt were most important to include. We involved a fourth biology teacher in the final design of our prototype, making adjustments based on their feedback regarding the gameplay and educational content. Our design incorporated insights from sections 2.1 and 2.3, detailing the gameplay loop and the functions of various in-game elements.

## 4.1 Learning content

Before commencing development on the prototype, we conducted interviews with 3 different high-school teachers to inform our design, these interviews can be found in the appendix D. Interview 1-3 were conducted before development, while Interview 4 was conducted during the final stages of development of the prototype. We asked them which topics they would like to see covered by the game based on the biology curriculum at Danish gymnasiums and if they had any previous experience using digital games as part of their teaching material. All teachers included games as part of their teaching; however, they struggled to find games on immunology that showcased how the immune system works on a cellular level. Two of the teachers mentioned using The Blood Typing Game[30] in their classes, however, as this game only provides information on antigens and antibodies in relation to blood transfusion, its use case for teaching immunology is limited. None of the teachers had been able to find games that focused on how the human immune system works on a cellular level. One of the teachers provided a chronological walkthrough of how they taught immunology, starting with a pathogen infecting the body followed by the activation of the immune system, first the innate system followed by the adaptive immune system. This was in line with how the other teachers described the content in which they covered during immunology lectures and could be condensed into the following topics:

- Innate immune system
- Adaptive immune system
- White blood cells and their functions
- Vira and bacteria
- Antigens and antibodies

Furthermore, taking inspiration from the learning game Cellcraft [27] this game will feature an encyclopaedia, which we dubbed "Leksikon" in which players can get more information on the content presented during gameplay.

## 4.2 Initial design and ideas

During our initial design discussions, we arrived at 3 game genres that aligned with our design requirements of teaching immunological concepts through gameplay and roguelite elements:

- Tower defence
- Auto-battler
- Deck-builder

To settle on the genre that resonated with our target group the most, we asked the target group to fill out a questionnaire on which genre they preferred to play. The questionnaire had 62 respondents, all of which were high-school students, and the results were as follows:

- 17,7% preferred the deck-builder genre
- 24,2 % preferred the tower defence genre
- 19,4 % preferred the auto-battler genre
- 29 % did not know of any of the above genres
- 9,7 % had no preferred genre

Based on the results of the questionnaire we decided to develop a tower defense game. We applied the roguelite learning game framework[10] and arrived at table 1:

| Criteria | | Educational Perspective | Game Perspective |
|---|---|---|---|
| **Generation** | Which elements are generated? | Different types of pathogens and buffs to the immune system | Enemies and buffs |
| | When are they generated? | Buffs: Between every round. Pathogens: Between every round and after a certain time that the pathogen is left alive | |
| | On what basis are they generated? | Pathogens are based on pathogens commonly infecting the human body. Buffs are presented as life choices that may increase the effectiveness of the immune system | |
| **Death/Hurt** | When can the avatar get injured or die? | Whenever a healthy cell is attacked by a bacteria or infected by a virus, the cell will take damage and eventually die | Whenever a healthy cell dies, the body health percentage will go down |
| | What are the consequences of being injured? Being killed? | Being injured will reduce the number of healthy cells. If there are no healthy cells left, the body has been overrun with pathogens, leading to irreparable damage, immune failure, and death | If the body health reaches 0, the player will die, forcing them to start over |
| | Where can the avatar be injured or killed? | The cells of the body can be injured or killed every time a pathogen attacks it | |
| **Variety** | Which elements vary? | Pathogens and buffs | |
| | How do elements vary? | Various pathogens with various characteristics. Pathogens may mutate into different strains with different characteristics. Buffs are presented as options to lead a healthier lifestyle, taking antibiotics or getting vaccinated, and will be presented to the player between rounds | |
| **Progress** | What is retained in-between each death? | N/A | Permanent upgrades to immune cells and resource generation |
| **Difficulty** | What are the elements that increase or decrease the difficulty? | Increasing difficulty: Pathogens reproducing. New pathogens are being introduced. An increasing number of total pathogens. Decreasing difficulty: Buffs, more resources, more white blood cells, presenting antigens. | |
| | How is the difficulty progression designed? | Gradual increase in the number of pathogens. More dangerous pathogens are introduced the longer the game goes on. | |

Table 1: Comparison of Educational and Game Perspectives

Whenever a design element remains the same between the educational and game perspective, the cell is merged. This table is what helped us ensure that the roguelite framework was adhered to during development.
Before the prototype development process began, a number of digital mock-up prototypes were designed, resulting in a final design which was largely adhered to throughout development.

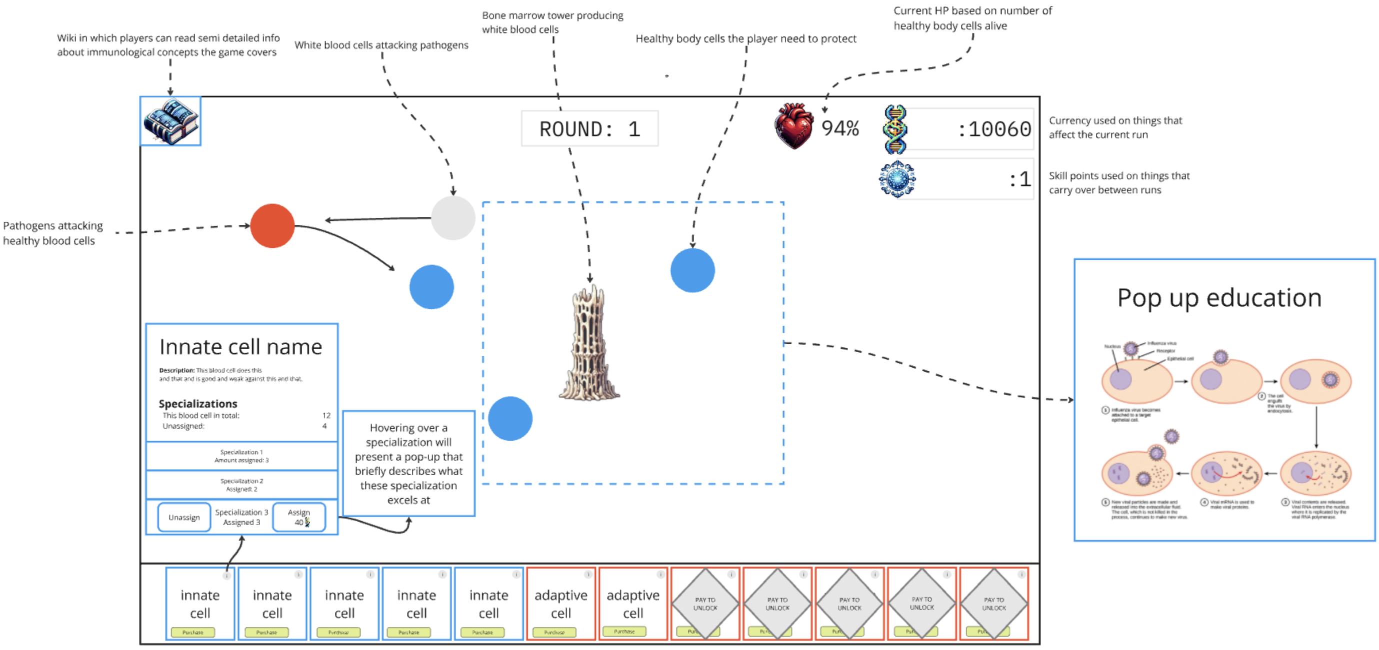



Figure 2: Early design prototype

The mock-up seen in figure 2 served as a guideline for the implementation of both the user interface and the core gameplay loop. The final iteration maintains the overall UI design, in a more refined manner.

## 4.3 Gameplay loop

When the game begins, the player starts with 200 healthy body cells, henceforth referred to as "neutral cells", that are under constant attack from pathogens. The neutral cells are spread evenly across the screen, and whenever pathogens attack them, they will take damage. If all neutral cells die, the player will lose the game. As in most tower defense games, players accumulate resources over time which are used to purchase units. In our game, these units are white blood cells, that will automatically seek out and attack pathogens. The game consists of 12 rounds, and pathogens spawn at the beginning of each round. Whenever a player survives a round, they will get the choice between 2 different buffs that increase their power for the rest of the game. The buffs are taken from a randomized pool, and are based on actual scenarios that would strengthen the immune system such as better sleep, diet, antibiotics and vaccinations. The number of pathogens spawned will increase for each round, and the pathogens that spawn will do more damage, have a higher movement speed and health. Pathogens will also have a chance of mutating into a different strain with different characteristics, making it harder for the player to combat them.

### 4.3.1 White Blood Cells

Initially, the idea was for white blood cells to be able to differentiate into specialized immune cells. This was to simulate how cells such T-cells and B-cells differentiate, and to demonstrate the various different roles the same type of cell could fill. Given the limited development time, this type of simulation proved too ambitious and given that this feature would also drastically increase the complexity of the game, making it less accessible to our target group, we opted to cut it out. We also chose not to include a type of white blood cell called Eosinophil, as these were not mentioned in any of the literature typically given to high school students in Denmark. The fact that eosinophils primary role is to fight off parasitic infections and we had no parasites in our game also helped inform the decision not to include them in the design. The white blood cells actually included in the game and their roles are as following:

- **Neutrophils:** To simulate the fact that neutrophils are short-lived and abundant in numbers, they are produced by the bone marrow at short intervals, which can be reduced by buying more. They follow the nearest pathogen and attack them once they reach it, simulating how phagocytosis works. After an attack, the neutrophil will disappear simulating their short lifespan.
- **Macrophages:** A big white blood cell, that both chases after pathogens and performs phagocytosis like

the neutrophils. Macrophages also contributes slightly to antigen presentation, which activates the adaptive immune system. Unlike Neutrophils, they will not disappear after performing an attack.

- **NK cells:** Finds the nearest cell that has been infected by a virus and kills the cell, ensuring the virus can not spread.
- **Mast cell:** Finds the nearest dead cell and revives it. This simulates mast cells' role in tissue repair.
- **Basophils:** Creates an area of inflammation in which everything inside it takes damage until the inflammation disappears. The player chooses where and when to create these inflammation areas based on a cooldown that is reduced by buying more basophils.
- **Dendritic cells:** Performs phagocytosis although less effective than Neutrophils and Macrophages. Boosts antigen representation at a much greater rate than macrophages.
- **T cells:** Targets cells that have been infected by pathogens with antigens that have been presented. Much more effective than NK cells. Can only be purchased after antigen presentation has taken place.
- **B cells:** Produces antibodies that attach to pathogens with an antigen that has been presented. When an antibody attaches to a pathogen their maximum health and movement speed is reduced. Can only be purchased after purchasing a T cell.

### 4.3.2 Pathogens

Because the reading material found in Yubio[23], an interactive learning platform used by some of the teachers who participated in the study, mostly focused on the traits and peculiarities of virus and bacteria, it was decided to focus on just those two as potential enemy types for the player to defend against.

- **Virus:** As it would have been impractical to simulate the actual size difference between a virus and human cells, the size of these game objects were scaled to be significantly smaller than all others to represent the size difference. Its attack action was designed such that when it approaches a cell, instead of doing damage to it, it will simply disappear into the cell, thus simulating a viral infection. The more viruses that infect the same cell, the quicker the "lytic release" will happen, which is when an infected cell bursts open, releasing a flood of virus clones it had been incubating. Virus generally have smaller health pools than bacteria, partly because they usually are smaller and more fragile organisms, but also because they give other parts of the immune system a chance to kill it before it infects a cell and has to be killed by NK-cells, or T-cells.
- **Bacteria:** The size of the bacteria game objects falls somewhere between a human cells and a virus. Although not all bacteria simply attack individual cells, as some instead release toxins that damage the body in a wider area around it, for the scope of this project, it made more sense to design the bacteria as a more traditional video game enemy that attacks individually. After the bacteria has attacked neutral cells enough times, it will begin to clone itself, and depending on the danger individual strains of bacteria pose, this cloning process will be shorter or longer. Bacteria generally have larger health pools than virus, because the player can constantly attack them and because they are visually bigger, so to the player's eye it would seem odd that bulky enemies died faster. They also heal themselves whenever they attack, so that they cannot be safely ignored but have to be dealt with.

## 4.4 Designing the tutorial

To avoid information overload for a first-time player, a tutorial was designed to gradually introduce the mechanics of the game to the player. The tutorial uses a yellow highlight color on buttons and arrows to draw the attention to points of interest in the UI, while a text panel on the left side of the screen features a short description of the rules and mechanics. The player progresses through the tutorial by purchasing white blood cells one by one. Whenever the highlighted blood cell is purchased, the player gets to see how this blood cell interacts with pathogens on screen, while the text describes what is happening and why it is happening. The player can only interact with the highlighted buttons and cannot progress until they have performed the task, the text box prompts them to. This ensures all players follow the same progression through the tutorial. The cells are introduced in the order of left to right, and the text box descriptions provide relevant information on how to most effectively use the cells when the game starts. When the player has completed the tutorial, the main menu will load.

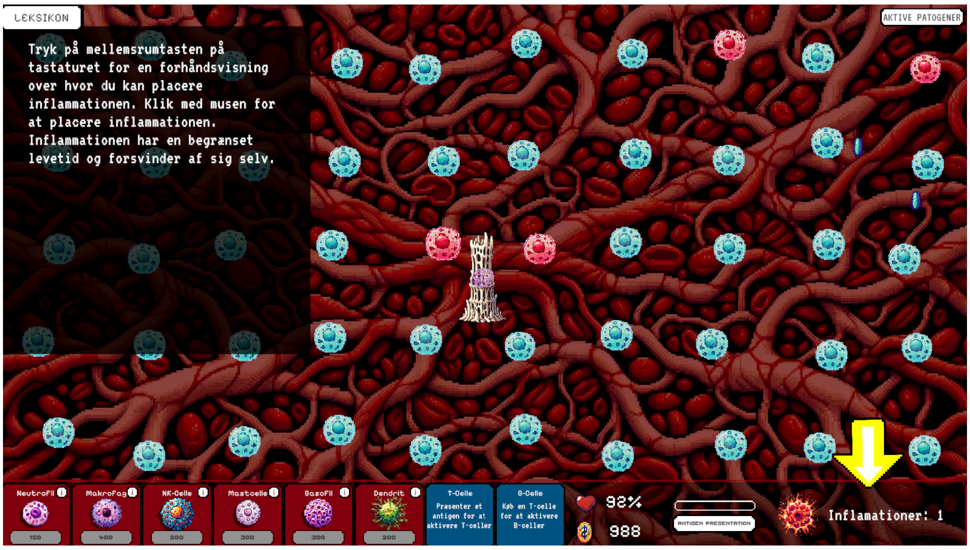



Figure 3: In-game screenshot of the tutorial

## 4.5 Adjusting the design based on feedback

The initial prototype was adjusted based on feedback received from one of the high-school teachers during Interview 4 D. The two main concerns raised were:

- **Gameplay screen too busy** The teacher was a bit overwhelmed by how much was going on the screen at the same time. It was hard to see which cells did what and what difference it made when buying new cells.
- **Text descriptions were overwhelming** The encyclopaedia, describing what every cell does in the game and how that relates to their real-life counterpart, seemed overwhelming for the teacher. The teacher suggested summarizing the essentials of any given article in a couple of paragraphs at the top of the text, leaving the rest of the text as-is for students to dive further into content, should they choose to.

Concerns about the gameplay screen being too busy were alleviated by reducing the number of neutral cells from 200 to 50. The size of the neutral cells was also increased. The rate of resource generation was decreased and movement speed, attack speed and spawn rate of pathogens was also decreased. These changes resulted in game that was slower paced with less interactions happening on the screen at the same time.

The overwhelming text descriptions were solved through the advice of the teacher, summarizing the essentials of each entry in the encyclopaedia in the first couple of paragraphs.

# 5 Implementation

In this section, we detail how some of the most important features of the prototype were implemented, either because they make up fundamental parts of the prototype or because they illustrate how certain biological realities were simulated.

## 5.1 Game world

The game world is made up of a background image that functions as an abstraction of the human body, and then a semi-regular distribution of "neutral cells", which is another abstraction that symbolises all kinds of vital cells in human body tissue.

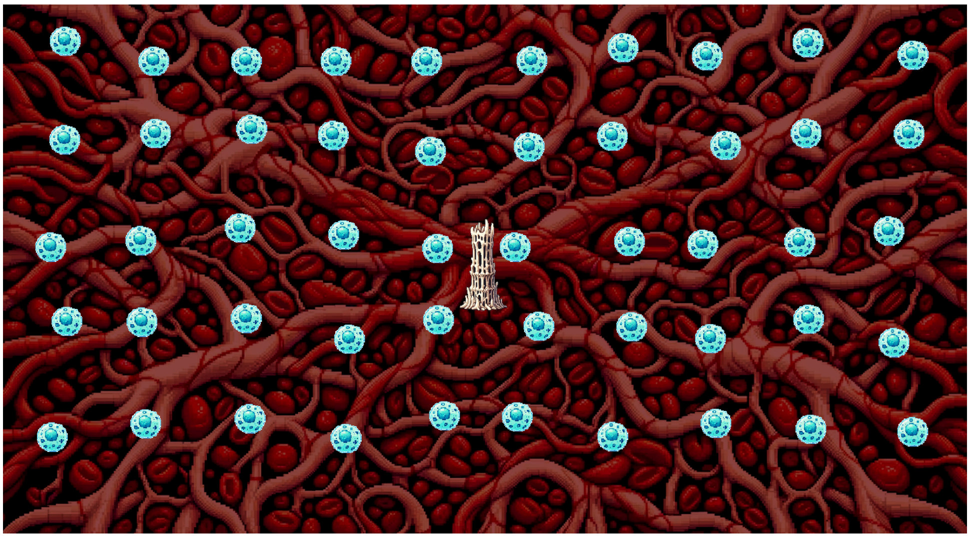


Figure 4: Game World without any UI elements, functions as abstraction of the inside of the human body

### 5.1.1 Player Health

To simulate the health of the human body, several so-called "neutral cells" were created. If all of them are alive, the player's health is at 100%, if half of them are dead, the player's health will be at 50%, etc.

## 5.2 Roguelite game elements

Here we lay out how some of the roguelite elements that make up our prototype, were implemented. The examples shown here are non exhaustive, but shows the most interesting solutions we used to fulfill our design requirements.

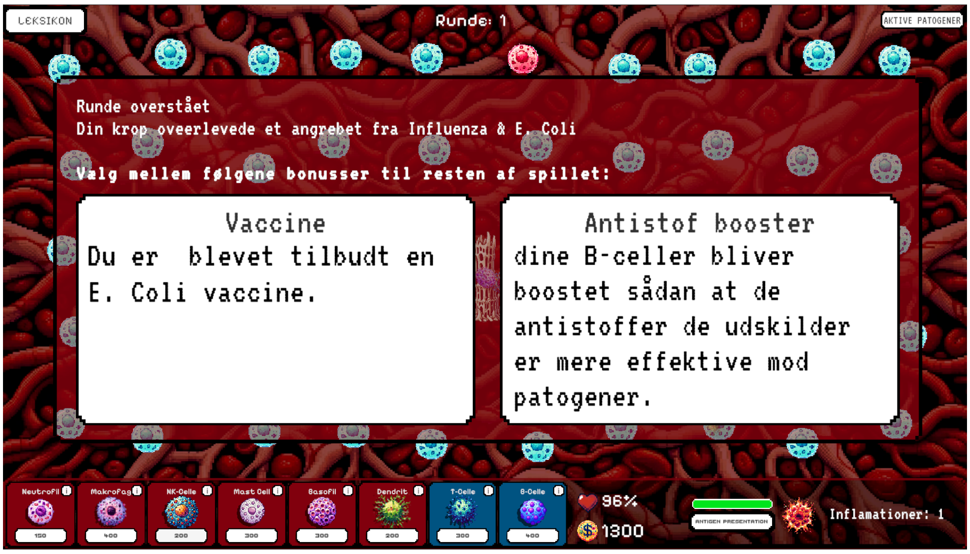



Figure 5: Example of how players are presented with different enhancement choices at the end of a game round.

If a player survives a round, they will be presented with a quick summary of the pathogens they managed to survive, and be presented with the choice between two gameplay enhancements, as seen in figure 5. These enhancements are randomly selected so players are unlikely to see the same enhancements throughout multiple playthroughs, hopefully enticing them to play again to discover the many different enhancements.

### 5.2.1 Buffs

To facilitate an evolving game experience, every aspect the player interacts with can be "buffed" in some way, that is, certain values that have to do with the balance of the game can be changed over the course of a playthrough should the player pick a specific "buff".

```
using UnityEngine;

namespace ScriptableObjects
{
    public class BaseBuff : ScriptableObject
    {
        public string buffName;
        public string buffDescription;
        public bool beneficialBuff;
    }
}
```

Figure 6: BaseBuff script - BaseBuff class definition

In figure 6 is how the base class on which all buffs in the game are based. All buffs have a "buffName", "buffDescription", and a boolean that denotes whether a buff is beneficial or not.

```
1 namespace ScriptableObjects
2 {
3     [CreateAssetMenu(fileName = "Pathogen Buff", menuName = "Pathogens/Pathogen")]
4     public class PathogenBuff : BaseBuff
5     {
6         [Header("assign affected pathogentype")]
7         public PathogenBehavior pathogenType;
8 
9         [Header("Vaccinate specific pathogen")]
10        public string pathogenName;
11
12        [Header("higher = better")]
13        public float maxHPIncrease;
14        [Header("higher = better")]
15        public float speedIncrease;
16        [Header("higher = better")]
17        public float attackSpeedIncrease;
```

Figure 7: PathogenBuff script - Constructor for the PathogenBuff scriptable object

Figure 7 shows a snippet of the pathogenBuff class. On line 3 it is defined how a buff can be created in the Unity IDE menu so that it is easier to make them for any member of the development team. From line 6 onwards are some of how a pathogen buff can be adjusted. All child classes of the BaseBuff are similarly structured. The buff will have a pathogen type or white blood cell type, so a developer can define which type of gameObject is being affected by the buff, and then values specific to that gameObject that can be adjusted, which will then alter how it functions in the game from now on.

### 5.2.2 Distributing Buffs

At the end of each round, when the round timer has elapsed or there are no more pathogens to spawn, the game will pause and a window will open telling the player what pathogens just attacked them and prompting them to pick one of two buff options.

```
1     public void AddBuffs(PathogenBuff buff)
2     {
3         this.buffs.Add(buff);
4         Debug.Log(this);
5         Debug.Log(buffs.Count);
6     }
7 
8     public void ApplyBuffs()
9     {
10        foreach (PathogenBuff buff in buffs)
11        {
12            this.maxHP *= buff.maxHPIncrease;
13            this.attackDMG *= buff.attackDamageIncrease;
14            this.attackSpeed *= buff.attackSpeedIncrease;
15            this.forceMagnitude *= buff.speedIncrease;
16            this.growthTimer *= buff.fissionTimeIncrease;
17            this.numOfAtksBeforeFission *= buff.numOfAtksBeforeFission;
18            this.viralInfectionTimer *= buff.viralInfectionTimer;
```

Figure 8: PathogenBehavior script - ApplyBuffs function governing how variables in buffable game object

Figure 8 is an example of how buffs are applied to pathogens. The function on line 1 to 6 is what the PathogenSpawner uses to add a buff to the list of buffs that a pathogen carries. Every part of the game that has a list of buffs has a similar function that is used to apply the changes that an incoming buff can make. On line 8 and onwards the values from every buff in the "buffs" list, is multiplied with their corresponding values in the pathogen. Every buffable game object applies buffs in a similar fashion.

### 5.2.3 Pathogen Spawner

To regulate the frequency with which the player is attacked, a script called PathogenSpawner was created. It contains a list of all pathogens in the game, as well as a list of all the pathogenBuffs that have so far been chosen by the player.

```
1     public void StartPathogenRound(Round round)
2     {
3         this.groupSize = round.diffPathogenTypes;
4         this.pathogensWaveSize = round.waveSize;
5         this.totalNumberOfPathogensToSpawn = round.maxActivePathogens;
6         this.currentNumberOfPathogensToSpawn = this.totalNumberOfPathogensToSpawn;
7         this.maxNumActivePathogens = round.numberPathogensRound;
8         this.spawnInterval = round.spawnTimer;
9
10        foreach (PathogenBehavior pathogen in activePathogens)
11        {
12            if (pathogen.isAlive)
13            {
14                pathogen.TakeDamage(100);
15            }
16
17        }
18        ChoosePathogensThisRound(groupSize, round.maxDifficulty);
19
20        if(circleRadius == 0)
21        {
22            this.circleRadius = world.GetComponent<SpriteRenderer>().bounds.max.x;
23        }
24
25
26        StartCoroutine(SpawnAtRandomPoints());
27    }
```

Figure 9: PathogenSpawner script - StartPathogenRound function governing how pathogens are spawned

In figure 9 is the function that governs the beginning of a new round. The GameManager script calls this function and supplies it with a "round" class, which contains information about how the new round is supposed to run. From lines 3 to 8 are where the public variables from the "round" are used to update variables to concern the distinct qualities of the current game round in PathogenSpawner.
After the variables have been updated, all still living pathogens that haven't infected a neutral cell is killed.
Next, the ChoosePathogensThisRound function is called, taking the updated groupSize and "round's" maxDifficulty as arguments. This function populates a list called "roundPathogens" with as many randomly selected pathogen types as the groupSize calls for and of a difficulty equal to or lower than the maxDifficulty.
With the "roundPathogens" list populated, the coroutine "SpawnAtRandomPoints" is called, which will run until there are no more pathogens to spawn, or the player loses the game.

## 5.3 Pathogens

The PathogenBehavior script inherits from the MovingAgent base class, which controls how pathogens move around and find suitable targets to attack. The PathogenBehavior script deals with making sure the virus or bacteria is animating correctly, that it "checks in" to the list of active pathogens that the pathogen spawner maintains, and basic functionality such as dying and attacking.

```
    public void Mutate()
    {
        string mutation = this.mutator.GetRandomMutation(this.mutationChance);
        if (mutation != null)
        {
            this.pathogenName = originalName + mutation;
        }
    }
    // Public function to return a random Greek letter based on a percentile chance
    public string GetRandomMutation(float percentileChance)
    {
        // Generate a random number between 0 and 100
        float randomValue = Random.Range(0f, 100f);

        // Check if the random value is less than or equal to the given percentile chance
        if (randomValue <= percentileChance)
        {
            // Generate a random index and return the corresponding Greek letter
            int randomIndex = Random.Range(0, greekLetters.Length);
            return " " + greekLetters[randomIndex];
        }

        return null;
    }
}
```

Figure 10: PathogenBehavior script - Mutate function dealing with how pathogens mutate over time.

In figure 10 is a snippet of PathogenBehavior which governs how pathogens mutate. Whenever the Mutate function is called, it takes the mutation chance of the pathogen to which the script is attached and calls the GetRandomMutation function. Either GetRandomMutation will return the name of the pathogen in question appended with a Greek symbol, or it will return null. This simple method simulates real pathogen mutation quite well, as the white blood cells that generate antibodies rely on the name of the pathogen to know what pathogen they can or cannot attack, so if a pathogen's name appears different, it will no longer be on the list of known antigens. The mutate function is called every time a bacteria attacks, and every time an infected neutral cell performs the LyticRelease function (when it dies and spawns new viruses).

```
1    private void LyticRelease()
2    {
3        int numVirusSpawn;
4        if (this.virusPS.activePathogens.Count > this.virusPS.maxNumActivePathogens)
5        {
6            numVirusSpawn = 1;
7        }
8        else
9        {
10           numVirusSpawn = infection.GetComponent<Virus>().virusSpreadFactor;
11       }
12       for (int i = 0; i <  numVirusSpawn; i++)
13       {
14           GameObject newGameObject = Instantiate(infection, this.transform.position,
     Quaternion.identity);
15           newGameObject.transform.GetChild(0).gameObject.SetActive(true);
16
17           // Get the component script attached to the instantiated GameObject
18           Virus script = newGameObject.GetComponent<Virus>();
19           // Check if the component script is attached to avoid null reference exceptions
20           if (script != null)
21           {
22               // Call the CustomFunction on the instantiated GameObject
23               script.canMove = true;
24               script.SetWorld(world);
25               script.ChooseNewPatrolTarget();
26               script.PS = virusPS;
27               script.PSCheckIn();
28               script.WhiteBloodCellsTargetingThis.Clear();
29               script.antigenCounter = this.antigenCounter;
30           }
31       }
32       KillInfection(true);
33       objectRenderer.material.color = Color.white;
34       FirstTImePathogenAppearance.Instance.ShowVirus();
35   }
```

Figure 11: NeutralCellBehavior script - LyticRelease function, which is called if a neutral cell is infected

Once a neutral cell has been infected, it will initiate a countdown timer until it dies and releases a burst of viruses. On line 10 it is determined how many viruses will spawn depending on how large it's "virusSpreadFactor"; an integer that simulates how proficiently a type of virus replicates itself. After the virus has been instantiated we use lines 23 to 29 to reset the new virus so that it won't try to attack the neutral cell that just instantiated it, as well as allowing it to move again, which its progenitor no longer could. Lastly, on lines 32 a 33, we clear the neutral cell from viruses so that, when it is eventually revived, it won't immediately be infected again resetting the colour of the neutral cell from green to white.

```
1     private void BinaryFission()
2     {
3         currentNumOfAtk = 0;
4         var fissionLocation = new Vector2(this.transform.position.x + Random.Range(-1, +1),
5             this.transform.position.y + Random.Range(-1, +1));
6         SetNewGoal(fissionLocation);
7         StartCoroutine(FissionProcess(growthTimer));
8
9     }
10
11    private IEnumerator FissionProcess(float time)
12    {
13        yield return new WaitForSeconds(time);
14        this.EndCurrentGoal();
15        Mutate();
16        GameObject newBacteria = Instantiate(this.gameObject, this.transform.position,
      Quaternion.identity);
17
18        Bacteria script = newBacteria.GetComponent<Bacteria>();
19
20        if (script != null)
21        {
22            script.SetWorld(this.squareArea);
23            script.PS = this.PS;
24            script.PSCheckIn();
25            script.ChooseNewPatrolTarget();
26        }
27        ChooseNewPatrolTarget();
28        FirstTImePathogenAppearance.Instance.ShowBacteria();
29
30
31    }
```

Figure 12: Bacteria script - BinaryFission function, used to simulate how bacteria multiply

On figure 12 is how binary fission was implemented. Once the int "currentNumOfAtk" reaches "numOfAtksBeforeFission" the "BinaryFission function is called. This ensures that a bacteria has to do damage to the player before it can start multiplying, as well as making it possible to create particularly fecund bacteria by lowering "numOfAtksBeforeFission". On line 7 the coroutine FissionProcess is called using "growthTimer" as an argument, another variable that we adjust to make bacteria more or less capable of multiplying. After the "growthTimer" has elapsed, the bacteria will stop whatever is it's current goal, and try to mutate. On line 16 a clone of the bacteria is instatiated at it's current position and until line 26 the new bacteria clone is properly activated so that it can operate in the game world. Then the original bacteria restarts its patrol around the body on line 27.

## 5.4 White Blood Cells Targeting

The white blood cells in this game will find a target based on certain conditions. Once a target is acquired, the blood cell will move towards it and interact with it when the target and the blood cell are within a certain distance threshold of each other.

```
1     public void AssignTargetWhiteBloodCell(WhiteBloodCellStats whiteBloodCell)
2     {
3         PathogenBehavior nearestTarget = null;
4         float nearestDistance = Mathf.Infinity;
5         List<PathogenBehavior> pathogensInScene = new List<PathogenBehavior>();
6         if (!IsTutorial)
7         {
8              pathogensInScene = new List<PathogenBehavior>(pathogenSpawner.activePathogens);
9         }
10        if(IsTutorial)
11        {
12              pathogensInScene = new List<PathogenBehavior>(tutorialController.pathogenList);
13        }
14
15        // Filter out pathogens that already have a WhiteBloodCellStats with the same tag targeting them
16        var filteredPathogens = pathogensInScene.Where(pathogen => pathogen != null &&
17            !pathogen.WhiteBloodCellsTargetingThis.Any(wbc => wbc != null && wbc.CompareTag(whiteBloodCell.tag))).ToList();
18
19        // Find the nearest pathogen from the filtered list
20        foreach (var pathogen in filteredPathogens)
21        {
22            float distance = Vector3.Distance(whiteBloodCell.transform.position, pathogen.transform.position);
23            if (distance < nearestDistance)
24            {
25                nearestDistance = distance;
26                nearestTarget = pathogen;
27            }
28        }
29
30        // If no pathogen was found in the filtered list, find the nearest pathogen regardless
31
32        if (nearestTarget == null)
33        {
34            nearestDistance = Mathf.Infinity;
35            foreach (var pathogen in pathogensInScene)
36            {
37                if (pathogen == null) continue;
38                float distance = Vector3.Distance(whiteBloodCell.transform.position, pathogen.transform.position);
39                if (distance < nearestDistance)
40                {
41                    nearestDistance = distance;
42                    nearestTarget = pathogen;
43                }
44            }
45
46        }
47
48        if (nearestTarget != null)
49        {
50            whiteBloodCell.currentTarget = nearestTarget.transform;
51            whiteBloodCell.currentTarget.GetComponent<PathogenBehavior>().WhiteBloodCellsTargetingThis.Add(whiteBloodCell);
52        }
53    }
```

Figure 13: TargetingLists script - AssignTargetWhiteBloodCell(): A method used to assign the nearest target to any white blood cell calling it

Using a macrophage as an example, the code seen in figure 13 demonstrates how white blood cells find their target. First, as seen in line 1 to 13, a new list of the pathogens currently in the scene is created based on a list found on either the pathogenspawner sript or the tutorialController script depending on whether the IsTutorial bool is true or false. This list is called pathogensInScene. The creation of a new list avoids any error that may occur if the original list is modified during the runtime of this method. This list is then filtered to leave out any pathogens currently targeted by any white blood cells with the same tag as the white blood cell calling the method, in this case a macrophage. The filtered list is then put through a foreach loop, comparing distance between the macrophage and all the pathogens on the filtered list, until the pathogen closest to the macrophage is found. If no pathogens are found on the filtered list, the same foreach loop is then applied to the pathogensInScene list, ensuring that the macrophage will always have a target if there any pathogens in the scene, regardless of whether another macrophage is targeting the same pathogen. If any target is found, that target is then assigned to the white blood cell calling the script, and the white blood cell is then added to a list of white blood cells currently targeting the pathogen.

```
private void FixedUpdate()
{
    if (currentTarget != null)
    {
        Vector3 rbDirection = (currentTarget.position - transform.position).normalized;
        rb.AddForce(rbDirection * speed);

        if (damageTimer >= damageInterval && (currentTarget.transform.position - transform.position).magnitude < 0.1f)
        {
            Attack();
            ApplyDamage();
        }
    }
}
```

Figure 14: Macrophage script - FixedUpdate(): A method called at a fixed time interval. In this case used to calculate the movement of macrophages

Once a target has been assigned, the macrophage will then move towards its target through the code seen in figure 14. To avoid null reference errors, there is a check to see if the macrophage actually has a current target. If the macrophage does have a target, the direction to the target is obtained by subtracting the position of the macrophage from the position of the current target and normalizing the result. This direction is then multiplied by a float value called speed and that result is added as force to the rigidbody of the macrophage. Assuming the macrophage moves faster than the pathogen, the macrophage will then continually move closer to the pathogen, and once the magnitude of the distance is less than 0.1 units, the macrophage will play its attack animation and apply damage if its damage timer is higher than the declared damage interval.

## 5.5 Leksikon

. "Leksikon" is the name of the informative encyclopedia that we included in the prototype, which was also used as reading material for the control group. The "Leksikon" appears both in the game and in the reading application the control group was tasked with using. This ensured that no information would be missing from either experience except the information players of the game could gain by interacting directly with the concepts in question.

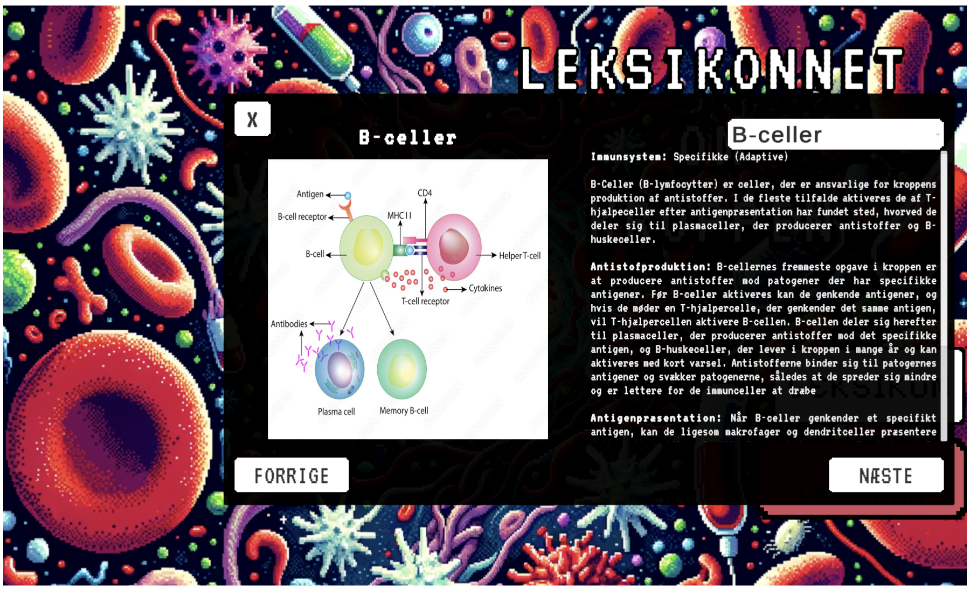



Figure 15: Leksikon interface as seen in the "leksikon" application

In the top right is a drop-down menu for quick access to specific articles, in the bottom corners users the "forrige/næste" buttons take users to the next page in the database. The main body of the UI element displays the contents of the current article and the one figure that accompanies it.
Using the Leksikon in both the game itself and the control group application, ensured that the same information was available to both groups and that only the qualitative experience of playing the game should affect the learning outcome of both groups.

```
[System.Serializable]
public class CellData
{
    public string name;
    public string description;
    public Sprite image;

    public CellData(string name, string description, Sprite image)
    {
        this.name = name;
        this.description = description;
        this.image = image;
    }
}
```

Figure 16: CellWiki script - CellData constructor, used to avoid having to hard code every article.

Figure 16 shows how we define individual articles in the "Leksikon", both in the application that the control group interacted with and the "Leksikon" to which participants in the control group had access. The "CellData" class contains the name of the article, the string that comprises the text in the article, and a single figure to go along with that article, as well as a constructor for the class itself, to facilitate creating articles within the Unity IDE as needed.

```
1
2       public void IdentifyIndex(string cellName)
3       {
4
5           for (var i = 0; i < cells.Count; i++)
6           {
7               var cell = cells[i];
8               if (cell.name == cellName)
9               {
10                  ShowCell(i);
11              }
12          }
13
14      }
```

Figure 17: CellWiki script - IdentifyIndex function, used to access specific articles in the Leksikon without knowing their specific position in the database.

Figure 17 shows an important function of the "Leksikon", namely how we access a specific article without knowing where it is in the list of articles (the "cells" list) by providing the function with the name of the desired article. When the function is called with the argument "cellName" on line 1, the for loop on line 6 is responsible for comparing the "cellName" to the name of every article in the "cells" list until it finds the correct article and then displays it.

## 5.6 Art & UI

This section presents the implementation of various sprites and the UI design of the prototype.

Since none of the team members have artistic experience or background in creating sprites and given the need for a variety of sprites to represent different pathogens and white blood cells, we decided to use ChatGPT's image generation function [32]. The AI was tasked with creating designs for pathogens based on images from biology textbooks. We aimed to ensure that the sprites closely resembled the visual representations high school biology students might encounter. However, not all generated models were suitable for use, and we also needed to consider how easy they would be to animate for future sprite sheets.

Once the group was satisfied with the designs, we used the website RemoveBG to remove the backgrounds from the sprites [33]. Afterwards, the sprites were imported into pixel art software for further refinement. We chose to use

Pixilart.com due to its accessibility and lower learning curve compared to other pixel art software [34]. The process of animating the sprites was the most time-consuming aspect of the UI and art design.

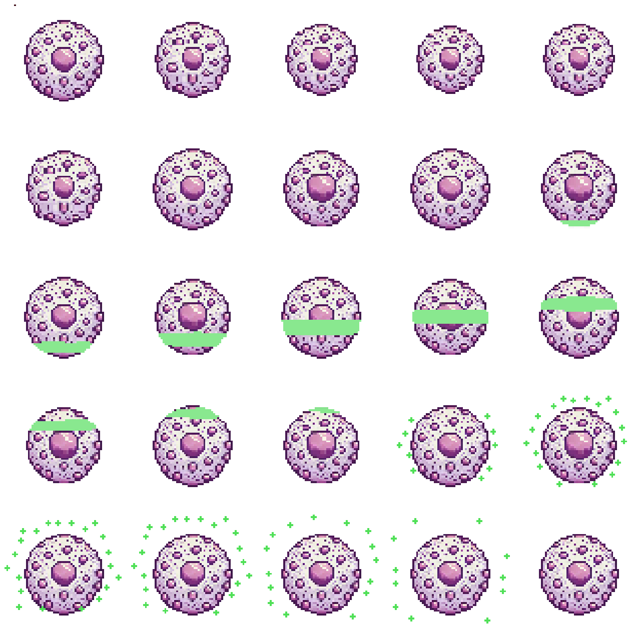


Figure 18: Mast cell spritesheet

For the sprite sheets, each different type of sprite would have a list of different required animations that they should have. An example of this is seen in figure 18. For this sprite only two different animations had to be created an Idle/Move animation for when the cell moves around, and a healing animation for when the cell heals the dead Neutral cells. Even though the sprites themselves were created with the assistance of AI, all of the animations are 100% original and had to be simple and convey the action that the cell had to do in each moment of gameplay. When creating the sprite sheets all of the different frames for the animations were also gathered into one single sprite sheet as Unity had easy ways to implement the right frames into each separate animation that would then later be put into animation controllers for each sprite to be easily applied in scripts to call the right animations.

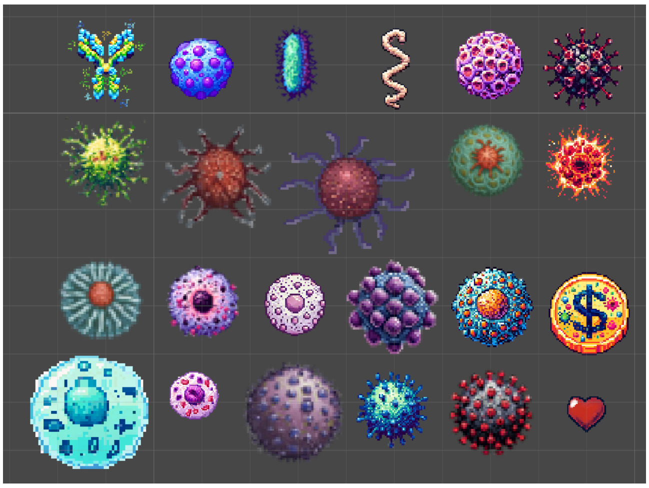


Figure 19: All cells listed

When implementing the various cells into Unity they all also had to be made into prefabs which can be seen in figure 19.

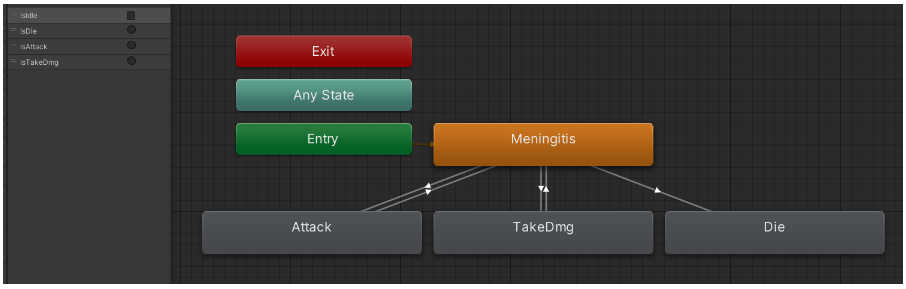



Figure 20: Animation Controller for various Pathogens.

Once the sprite sheets were complete, the next step involved separating them into individual sprite frames. These frames were then imported into the animation controller, where appropriate names were assigned to their respective animations. The animation controller was then configured with the correct parameters to ensure smooth transitions between animations. All transitions were triggered using specific parameters, except idle animation, which was governed by a boolean condition, as illustrated in Figure 20.

### 5.6.1 UI

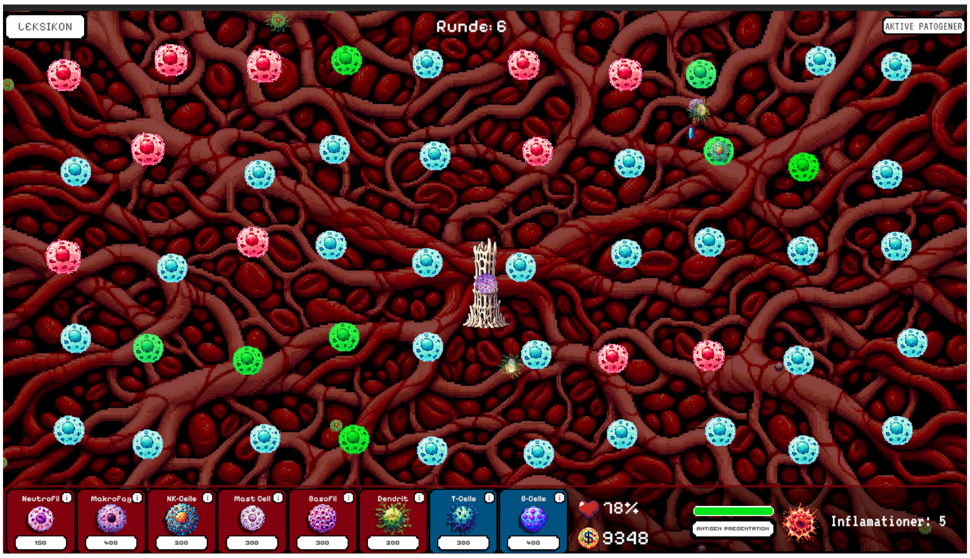



Figure 21: Example of the game in play

Figure 21 is depicted as a moment during a typical play. Along the bottom are the white blood cells that the player can buy to defend their body. The cells in the red boxes are part of the innate immune system, the ones in the blue are part of the adaptive immune system, and they only unlock once certain conditions have been met, simulating the slower activation of the adaptive immune system.
To the right of the white blood cells players can see how much health they have left, expressed as a percentage, and how many resources they currently have available to buy cells from.
Further to the right is the "Antigen Præsentation" button and its associated progress bar that fills over time if the right conditions are met.
Finally, rightmost is the "Inflammation" counter, which tells the player when inflammations are ready to be deployed in the game world.
The red cells in the game world denote dead cells, which will have to be healed by a Mast cell before contributing to the player's total health. The cells that are more or less intensely green are neutral cells that have been infected with a virus. As the infected cells get closer to dying from the viral infection, they turn more green, this lets the player know how dangerous individual infections are.
In the top left is the "Leksikon" button, which opens the information database, where detailed explanations of all concepts and cells in the game are presented.
In the top middle is a simple counter that tells players what number of rounds they have reached.

In the top right is the "Aktive patogener" button, which disappears when the mouse hovers over it, instead a box will appear which displays the model and name of each pathogen currently in the game world including mutations.

# 6 Methodology

In this section we outline the research design chosen for the prototype evaluation, how the participants were recruited, and the composition of the sample. Furthermore, the procedure of the experiment and how the data was collected and handled is also covered.

## 6.1 Research Design

This research design was experimental and between groups, in which subjects were randomly assigned to the control group or the experimental group. The independent variable of the experiment was *knowledge gain*, and the dependent was what mode of knowledge gain was used (*learning game or reading material*).

## 6.2 Goal of experiment

The goal of the experiment is to test the hypotheses presented in Section 2.6. To do this, we measured both engagement and knowledge gain. For engagement, we aimed to assess how effectively our prototype functioned as an engaging learning game. As discussed in Section 2.1, increased engagement is a key factor that can enhance learning outcomes. To measure knowledge gain, we used a multiple-choice test covering the topics presented in both the prototype and Leksikon to evaluate participants' understanding of the material.

## 6.3 Participants

The test subjects we acquired for our experiment were all students from Danish high schools in their last year of education, that is 3.G. Through negotiation with biology teachers at Sukkertoppen Gymnasium and Frederiksberg Gymnasium, we were allowed to run our experiment in their classrooms.

<table>
<tr><td colspan="4">Demographics</td></tr>
<tr><td colspan="4">Experiment Condition</td></tr>
<tr><td>Experiment</td><td>Control</td><td colspan="2">Total</td></tr>
<tr><td>27</td><td>21</td><td colspan="2">48</td></tr>
<tr><td colspan="4">Highschool</td></tr>
<tr><td colspan="2">HTX</td><td colspan="2">STX</td></tr>
<tr><td colspan="2">33</td><td colspan="2">15</td></tr>
<tr><td colspan="4">Gender</td></tr>
<tr><td>Female</td><td>Male</td><td>Non-binary</td><td>-</td></tr>
<tr><td>21</td><td>25</td><td>1</td><td>1</td></tr>
</table>

Table 2: Distribution of the participants across experiment condition, high school and gender.

No formal power analysis was conducted for this experiment. However, efforts were made to ensure that the sample size was large enough to provide meaningful results and reduce the impact of outliers, by having at least three different high school classes participate in the study.

## 6.4 Sample

Participants were required to be high-school students, currently studying biology at a level that included immunology in their curriculum, so that a baseline knowledge and interest in biology could be guaranteed and that immunology was a subject relevant to their education. Ideally, participants should have had minimal prior education or exposure to immunology so that our intervention could generate the maximum potential impact.

## 6.5 Apparatus

To participate in the experiment, all students were required to run either the game or the Leksikon application on their laptops. Almost all students fulfilled this requirement. Biology teachers distributed a link to the Itch.io address where both the game and Leksikon were located, as well as a link to the post-test survey. The engagement questionnaire used in this study was the short form User Engagement Scale[35](UES-SF). The UES-SF features 12 items in total, in four groups of three covering the topics of: Focused Attention, Perceived Usability, Aesthetic Appeal and Reward Factor. Answers range from 1 - 5, where 1 is strongly disagree, and 5 is strongly agree. A user's overall score is

the mean of all their answers, so it will be between 1 and 5, 1 being minimal to no engagement, and 5 being highly engaging.
The multiple-choice knowledge test was based on the learning content the game contained and was written to resemble multiple-choice tests typical for high-school biology classes. Both questionnaires are found in appendix [A].

## 6.6 Data Collection

All the data participants provided by completing the questionnaires were gathered using SurveyXact [36]. Observations made during the experiment were written by test invigilators in a way keep the identities of the participants private. No identifiable trait of the participant was recorded, only the statement made by the individual student.

## 6.7 Data Management

The data collected was stored in SurveyXact[36] or downloaded by the group member responsible for the data analysis. Upon completion of the data analysis, the local file containing the data was deleted.

## 6.8 Variable Operationalisation

The independent variable for this project was the form of the learning content; either more traditional homework readings or the gameplay content of the prototype. The dependent was the learning content itself, which was the same across both conditions.

## 6.9 Procedure

On the day of testing, we met up with the biology teacher responsible for the class that would participate in our experiment beforehand. The biology class would then start with the teacher introducing the two invigilators who would be responsible for running the test. Students in the class were divided into two groups giving every student a number (1 or 2). Subjects in group 1 were instructed to download the prototype from itch.io and run it on their laptops. Students in group 2 downloaded the control group reading material "Leksikon" also available from itch.io. Both groups read or played the game for 20 minutes. After 20 minutes had elapsed, both groups responded to an engagement questionnaire[A] and then a multiple choice immunology quiz[A], regarding the learning content they had consumed. Finally, the test invigilators spent 2-10 minutes posing open questions to the class about the experience they had had, answers to which were recorded by the invigilators. This was done at the request of the teachers responsible for the classes to make the overall experience more relatable to the typical format of lectures that high school students are used to. It also served to get some more personal feedback from the test subjects on the qualitative experience of engaging with the prototype.

## 6.10 GDPR

Both groups surveyed at Sukkertoppen Gymnasium did not include students under the age of 18 years due to the lack of consent of the principal at the school for students under the age of 18 to share personal data. However, the principal at Frederiksberg Gymnasium did provide their consent[B] for us to be allowed to test on all their students, which meant that the data collected from students under the age of 18 - at Frederiksberg Gymnasium - could be used in our data analysis.

To ensure compliance with GDPR guidelines and protect the personal data of all participants, including minors, the following measures were implemented:

- **Anonymisation**: All data collected was anonymised to prevent any direct identification of participants. No names or identifiable information were recorded.
- **Data Minimization**: Only data relevant to the study objectives was collected, minimizing the risk associated with handling personal information.
- **Secure Storage**: Data was stored securely in SurveyXact, with access restricted to authorized researchers only. After analysis, all local files containing data were deleted to prevent unauthorized access.
- **Informed Consent**: Prior to data collection, participants, principals, and teachers at the schools were informed about the purpose of the study and their rights concerning their data.

- **Confidentiality**: All observations and notes made during the experiment were recorded in a way that maintained the confidentiality of all participants.

These measures were put in place to safeguard the rights of all participants and to comply with GDPR requirements.

# 7 Results

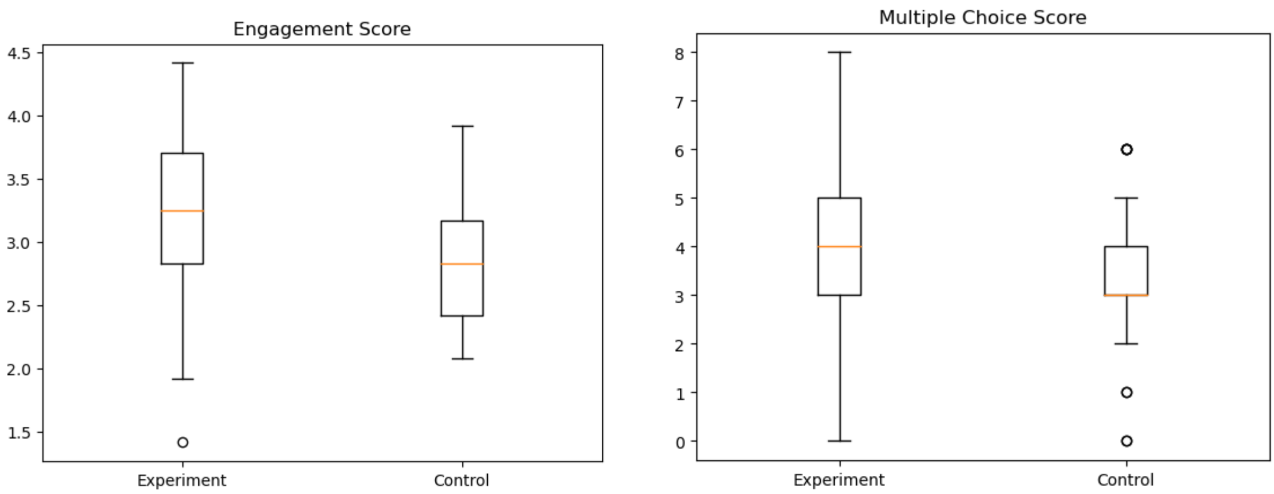
In this section, we present the results of three tests conducted on a sample of 48 participants, distributed among three different high school classes (as shown in figure 2). Various statistical analyses have been applied to test for statistical differences between the 2 groups: the group that played the prototype of our game (experimental) and the participants who read the "leksikon" (control).

## 7.1 Calculating scores

Before testing for normality and calculating the significance of the results, the overall scores from both questionnaires had to be calculated. The engagement items regarding "perceived usability" in the user engagement questionnaire [35] are all reverse-coded, before the individual engagement scores could be calculated, these items had to be inverted by multiplying them by -1 and adding 6 to the resulting score. The individual engagement score was calculated by taking the sum of all answers and dividing by 12 (the number of individual items). The multiple-choice score was found by awarding 1 point for each complete and correct answer and 0 for each incorrect or partially complete answer. Due to a mistake made in the first test, only 9 of the 10 multiple-choice questions could result in a point, because this question was not identical for both groups, so the highest potential multiple-choice score was 9.

## 7.2 Result analysis

With the engagement and multiple-choice scores calculated, the results were analysed and are presented in this section.




(a) How engagement score differed across experimental and control condition

(b) How multiple-choice score differed across experimental and control condition

Figure 22: Boxplots depicting the resulting mean scores of the engagement questionnaire and multiple-choice questionnaire

In figure 22 is an overview of the results from the test with the final scores calculated. Both in terms of engagement and multiple choice scoring, the control group showed smaller variance and a lower mean score.

| **Engagement** | | | | | |
|---|---|---|---|---|---|
| **Category** | **Mean** | | **Test** | **P-Value** | **Significance** |
| **Experiment v Control** | 3.24 | 2.88 | T-test | 0.044 | Yes |
| *Focused Attention* | 3.14 | 2.75 | Mann-Whitney U | 0.014 | Yes |
| *Perceived Usability* | 3.30 | 3.32 | Mann-Whitney U | 0.882 | No |
| *Aesthetic Appeal* | 3.15 | 2.55 | Mann-Whitney U | 0.005 | Yes |
| *Reward Factor* | 3.35 | 3.08 | Mann-Whitney U | 0.582 | No |

Table 3: Differences in engagement scores between test participants in the experimental group and the control group, alpha = 0.05

To analyse the data from the engagement questionnaire a Shapiro-Wilks analysis was performed showing that the data was normally distributed. A one-tailed student T-test was used to reveal whether there was a significant difference between the groups, as we were expecting the prototype to produce an improvement in engagement and learning. To explore the data more fully, the subcategories were also analysed for significance. Half of the engagement sub-categories were not normally distributed, so the Mann-Whitney U test was used on all of them so that statistical test results would be comparable to each other.
At a p-value of 0.044, we learned that the prototype was more engaging to interact with for the participants in the experimental group than participants in the control group. More specifically, we learned that the prototype was better at retaining the focused attention of test participants as well as being more aesthetically pleasing to them.
However, it is important to note that a mean engagement score of 3.20 still falls within a moderate range on the scale. While the prototype succeeded in producing higher engagement than the control, it did not elicit a generally high level of engagement.

| **Engagement** | | | | | |
|---|---|---|---|---|---|
| **Category** | **Mean** | | **Test** | **P-Value** | **Significance** |
| **Male v Female** | 3.12 | 2.92 | T-test | 0.150 | No |
| **HTX v STX** | 3.14 | 2.89 | T-test | 0.113 | No |

Table 4: Differences in engagement scores between male and female test participants and test participants from HTX or STX, alpha = 0.05

To further explore the data, mean score differences were also analysed in male vs. female test participants and HTX versus STX high school types. The Male versus Female and HTX versus STX data sets were all normally distributed, so the student's T-test was also used here. From these tests, we learnt that what high school a test subject attended and their gender did not play a significant role in how engaging their experience was.

| **Mutiple-Choice** | | | | | |
|---|---|---|---|---|---|
| **Category** | **Mean** | | **T-Test / Mann-Whitney U** | **P-Value** | **Significance** |
| Experiment v Control | 3.85 | 3.38 | T-test | 0.206 | No |
| Male v Female | 4.08 | 3.05 | Mann-Whitney U | 0.091 | No |
| HTX v STX | 3.82 | 3.27 | Mann-Whitney U | 0.287 | No |

Table 5: P-Values for multiple choice scores, alpha = 0.05

Similar to the engagement questionnaire, the results from the multiple-choice test were tested for normality using the Shapiro-Wilk test. After confirming normality, a one-tailed student's T-test was employed, indicating no statistically significant difference between the scores of participants in the experimental and control groups, at a p-value of 0.206.

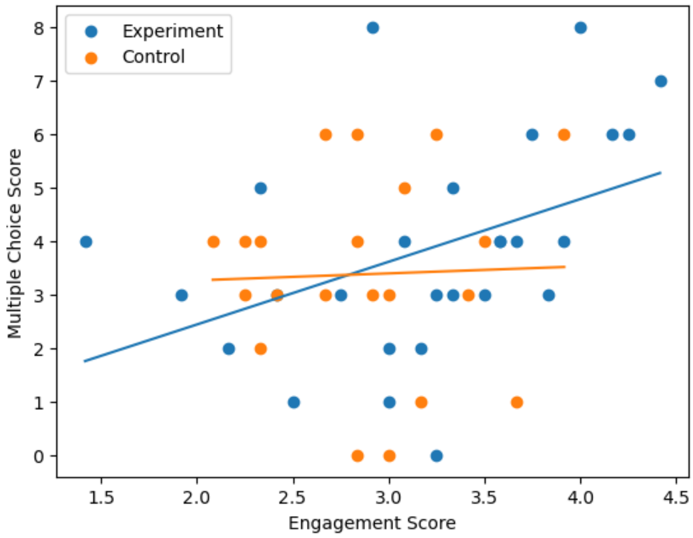



Figure 23: Relation between engagement score and multiple-choice score, alpha = 0.05

| Pearson correlation coefficient | | |
|---|---|---|
| **Group** | **P-value** | **Significance** |
| Experimental | 0.014 | Yes |
| Control | 0.440 | No |

Table 6: Table organizing results of Pearson correlation coefficient test, alpha = 0.05

Figure 23 shows the relationship between engagement scores and multiple-choice performance, with Table 6 summarizing the results of the Pearson correlation test. The results indicate a significant correlation for the experimental group (p = 0.014), suggesting that higher engagement may have contributed to higher multiple-choice scores. In contrast, the p-value for the control group was 0.440, indicating no significant evidence of correlation, meaning that whether or not a test subject was engaged in the act of reading, the resulting multiple-choice score would be unaffected.

## 7.3 Hypothesis testing

Since the results presented in figure 5 did not show a significant difference in scores between the experimental and control group, we could not reject our null hypothesis (see section 2.6). Since we could not reject the null hypothesis based on the multiple-choice results, we conclude that, while the game may have been more engaging, this did not translate into significantly better knowledge retention compared to the control group.

## 7.4 Summary of Findings

In summary, the experimental group demonstrated higher engagement scores compared to the control group, indicating the prototype was more engaging. However, the higher engagement did not translate into a significant improvement in multiple-choice scores, as indicated by a p-value of 0.206 5.

Moreover, while the analysis of demographic variables such as gender and high school type (HTX vs. STX) did not show significant differences in engagement, the significant correlation within the experimental group suggests that engagement may play a role in learning outcomes. This highlights the potential for game-based learning environments to enhance engagement, which could influence learning effectiveness in other contexts.

# 8 Discussion

In this section, we will explore the implications of the results, considering how various factors such as sample size, the quality of the testing environment, and individual differences among participants may have impacted the findings. Additionally, we will reflect on the relationship between engagement and learning retention, the implications for future game design, and potential directions for further research and development in this field.

## 8.1 Fulfilling Design Requirements

As part of our development process, we established a set of key design requirements to guide the development of our learning game prototype, as seen in Section 3. Looking at the final iteration of our learning game prototype and comparing it to the functional requirements, we confirm that they have all been met.

In terms of fulfilment of the non-functional requirements, the mean score achieved by participants in the experimental group on the multiple-choice test, as seen in table 5 in Section 7.2, was 3.85 out of a possible 9, meaning that the average score was lower than 50%. This low score could indicate that the prototype does not adequately teach its players the essential functions of the innate and adaptive immune system. However, the mean score in the control group was lower, at 3.38, a statistically insignificant difference, therefore the prototype taught subjects at least as well as well as reading material commonly used in high-school education. Because of the limited amount of time participants were allowed to interact with the prototype, it is difficult to say if the varied pool of enemies and upgrades did much to encourage participants to play the game again.

Since participants in the control group reported that the amount of time allotted to read the material was adequate but not by much. Participants in the experimental group would have difficulty attaining the same level of familiarity with the material as the control group, while also playing the game. We assert that it was mainly through their mechanical representation that the experimental group experienced the learning content.

While not a perfect analogy for difficulty, the "Perceived Usability" items in the User Engagement Scale(UES)[35] arguably concern similar feelings that a frustratingly high difficulty would elicit. As the experimental group's "Perceived Usability" score mean is 3.3, that signifies that the prototype was not frustrating to engage with, i.e. not too difficult. As discussed in Section 2.2, the flow state is attainable when the challenge of an activity is well balanced to the individual experiencing it, while we cannot say with certainty that the prototype was not too easy to elicit the flow state, it likely wasn't too hard.

## 8.2 Confounding Variables

The study relied on existing research, particularly in the design of learning games, as discussed in Section 2.1, to ensure both engagement and educational efficacy. Research emphasizes that successful video games inherently require players to learn and master complex systems, which can enhance motivation and engagement through immersive gameplay. This is particularly relevant for our learning game prototype "Kampen om Kroppen," where we aimed to integrate educational content effectively within its mechanics, consistent with the concept of procedural rhetoric outlined in Section 2.1 [9].

However, several external factors impacted the game's delivery and student engagement, ultimately affecting knowledge gain. Participants in the control group reported a lack of motivation, likely due to the awareness of missing out on the gaming experience. This diminished their engagement compared to those playing the game. As studies have indicated, motivational differences can significantly influence learning outcomes [11], it would have been preferable had they not known that there was a learning game alternative to reading the content in the "Leksikon" application.

Additionally, the unstructured and distracting environment, coupled with the absence of proper audio equipment, likely hindered deeper engagement for both groups. Koster's theory in Section 2.2 emphasizes the importance of clear, engaging patterns to maintain focus and interest in games [13].

## 8.3 Engagement scores: Interpretation and implications

While the experimental group demonstrated higher engagement than the control group, with an average score of 3.24, this still reflects a relatively modest level of engagement. Improving usability and incorporating better-designed reward systems could greatly enhance these engagement scores in future versions of the prototype. Additionally, the prototype's roguelite mechanics, while designed to promote progression, may not have been fully realised due to the short playtime, as previously noted. Allowing for longer play sessions might enable players to better appreciate the prototype's mechanics and their educational benefits, leading to more meaningful and sustained engagement.

Reversing the order of the post-survey—having participants complete the multiple-choice questionnaire after rating their engagement—could also be more effective. This change might help participants connect their learning experience with the knowledge they just acquired. However, this approach may introduce new challenges; for instance, participants might recall answers directly from their recent gameplay rather than retaining them through meaningful learning. Additionally, linking gameplay with testing could diminish the game's appeal for participants.

## 8.4 Interpretation of Non-Significant Findings

While the prototype increased student engagement, reflected in a significant p-value ($p = 0.044$) (as seen in figure 3), this higher level of engagement did not result in significantly better performance in the multiple-choice assessment compared to the control group ($p = 0.206$) (as seen in figure 5. This gap between engagement and learning retention aligns with existing literature discussed in Section 2.2, which cautions that engagement alone does not always equate to higher learning outcomes [9]. Although increased engagement often leads to better learning retention over time, as indicated in Csikszentmihalyi's flow theory in Section 2.2 [12], our immediate post-exposure testing may not have captured the long-term educational effects of the prototype. Lemoine et al. suggest that genres like roguelites can be particularly effective for teaching declarative knowledge through repetition, but the short playtime in our study may not have afforded participants enough interaction with the prototype's learning mechanics to facilitate significant knowledge retention [10]. While we cannot conclude that our intervention created a better understanding of immunological concepts compared with a text-based resource, we can conclude that it was at least as good a learning tool as the text-based default.

## 8.5 Sample Size Differences

The imbalance in sample sizes likely affected the robustness of the results. Unequal sample sizes between the control and experimental groups diminished statistical power, limiting our ability to draw definitive conclusions. This issue is well-documented in educational intervention studies and often complicates generalisation, suggesting that future research would benefit from strategies like stratified random sampling to ensure balanced comparisons, as discussed in Section 2.1 regarding effective game design principles [8].

## 8.6 Focused Attention and Aesthetic Appeal

The increased focused attention and aesthetic appeal observed in the experimental group ($p = 0.014$ and 0.005, respectively) supports the argument that well-designed learning games can captivate student interest and maintain focus, as outlined in Csikszentmihalyi's flow theory in Section 2.2 [12]. However, while focused attention improved, this did not directly translate to better learning outcomes. Koster's analysis of fun and learning in games further highlights that understanding patterns within the prototype is crucial for sustained engagement and, ultimately, learning [13]. The potential of roguelite mechanics to enhance procedural learning through repetition might not have been fully realized in this study due to the limited playtime. Allowing students to explore more emergent patterns in the prototype's design could yield deeper learning outcomes, particularly when aligned with the idea of "grokking" new patterns over time.

## 8.7 Validity & Reliability

The lack of audio during the play sessions is another factor that reduced the ecological validity of the study. Audio is often key in fostering immersion, a critical element in maintaining high levels of engagement, as discussed in Section 2.2 [11]. Future iterations of the study should ensure that audio components are included to better simulate a complete gaming experience.

While the study's overall reliability was strong, as it was conducted consistently across three sessions in two schools, the unequal sample sizes and short playtime are limitations that future research should address. As prior research suggests in Section 2.1, iterative playtesting and adjustments in in-game mechanics may improve both engagement and knowledge retention over time [9].

## 8.8 Limitations and Future Research

While the study showed that the game-based learning approach can enhance engagement, the unequal sample sizes, absence of audio, and short gameplay duration limit the conclusions we can draw. A conversation with a teacher revealed that she sometimes uses media or reading material that incorporates metaphors to help students understand complex concepts [D]. This sparked thoughts of whether the inclusion of similar metaphors would result in participants having an easier time recalling and understanding the functions of cells and pathogens as represented in the prototype.

For instance, if the prototype's design utilised anthropomorphized characters or other metaphorical representations of white blood cells and pathogens, it might facilitate a more intuitive grasp of their functions. Instead of the pixelated representations in the prototype currently, these characters could embody traits associated with their roles, making them easier to relate to and understand.

Additionally, following up with students to assess long-term retention could provide deeper insights into the educational potential of learning games, particularly when using genres like roguelites that emphasize replayability and gradual mastery of content.

# 9 Conclusion

This project has explored the potential of learning games, specifically incorporating roguelite game mechanics, as an educational tool for teaching immunology. We developed and tested a prototype with Danish high school students, comparing it to text-based learning. While the game was found to be significantly more engaging than the reading material, this did not result in superior knowledge retention, as measured by multiple-choice scores.

Nevertheless, our findings demonstrate that our learning game prototype is at least as effective as traditional methods while offering a more engaging experience. These findings highlight the need for future research to further explore the relationship between engagement and learning outcomes, particularly by enhancing the game's reward systems, usability, and balancing audiovisual elements. Furthermore, improving the study design, such as using a more controlled environment and balanced sample sizes, could yield stronger conclusions.

Ultimately, this research underscores the importance of game-based learning in education, with implications for the development of more immersive and adaptive learning tools. The integration of metaphors for cells and pathogens, or the use of anthropomorphized characters in place of the pixel art sprites representations implemented in the prototype, could hold the key to facilitating deeper understanding and long-term retention of complex subjects like immunology. Future work should build on these findings, seeking to refine the educational efficacy of such games through more intuitive and relatable representations.

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# A Appendix A (Survey)

**Velkommen til undersøgelsen!**

Før vi går i gang, vil vi bede dig om at indtaste oplysninger om din skole, alder og køn. Disse oplysninger hjælper os med at få et overblik over deltagergruppen og analysere resultaterne.

Vær opmærksom på, at alle dine svar vil forblive anonyme, og ingen personlige oplysninger vil blive delt eller brugt til andet formål.

### Jeg går på

(1) ❍ STX

(2) ❍ HTX

### Din alder

(1) ❍ 16

(2) ❍ 17

(3) ❍ 18

(4) ❍ 19

(5) ❍ 20

(6) ❍ 21

(7) ❍ 22

(8) ❍ 23

(9) ❍ 24

(10) ❍ 25

## Dit køn

(1) ❍ Mand

(2) ❍ Kvinde

(3) ❍ Non-binær

(4) ❍ Foretrækker ikke at besvare

## Spil eller tekst

(1) ❍ Jeg har læst teksten

(2) ❍ Jeg har spillet spillet

### Engagementsspørgsmål

I denne del vil vi gerne vide, hvordan du har oplevet materialet, du lige har arbejdet med **teksten**. Vi vil stille dig nogle spørgsmål om, hvor engagerende og interessant du fandt aktiviteten.

Dine svar vil hjælpe os med at forstå, hvordan forskellige måder at lære på kan påvirke din interesse og opmærksomhed.

## FA-S.1: Jeg mistede mig selv i denne oplevelse.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## FA-S.2: Tiden, jeg brugte på at bruge læse, fløj af sted.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## FA-S.3: Jeg var opslugt af denne oplevelse.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## PU-S.1: Jeg følte mig frustreret, mens jeg læste materialet.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## PU-S.2: Jeg fandt artiklerne forvirrende at læse.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**PU-S.3: Det var anstrengende at læse.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**AE-S.1: Artiklerne var attraktive.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**AE-S.2: Artiklerne var æstetisk tiltalende.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**AE-S.3: Artiklerne appellerede til mine sanser.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

### RW-S.1: At læse artiklerne var det værd.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(6) ❍ 4 Enig

(5) ❍ 5 Meget enig

### RW-S.2: Min oplevelse var givende.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

### RW-S.3: Jeg følte mig interesseret i denne oplevelse.

(1) ❍ 1 Meget Uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget Enig

**Engagementsspørgsmål**

I denne del vil vi gerne vide, hvordan du har oplevet materialet, du lige har arbejdet med **spillet**. Vi vil stille dig nogle spørgsmål om, hvor engagerende og interessant du fandt aktiviteten.

Dine svar vil hjælpe os med at forstå, hvordan forskellige måder at lære på kan påvirke din interesse og opmærksomhed.

## FA-S.1: Jeg mistede mig selv i denne oplevelse.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## FA-S.2: Tiden, jeg brugte på at spille, fløj af sted.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## FA-S.3: Jeg var opslugt af denne oplevelse.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**PU-S.1: Jeg følte mig frustreret, mens jeg spillede.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**PU-S.2: Jeg fandt spillet forvirrende at spille.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**PU-S.3: Det var anstrengende at spille spillet.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

**AE-S.1: Spillet var attraktivt.**

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## AE-S.2: Spillet var æstetisk tiltalende.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## AE-S.3: Spillet appellerede til mine sanser.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## RW-S.1: At spille spillet var det værd.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(6) ❍ 4 Enig

(5) ❍ 5 Meget enig

## RW-S.2: Min oplevelse var givende.

(1) ❍ 1 Meget uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget enig

## RW-S.3: Jeg følte mig interesseret i denne oplevelse.

(1) ❍ 1 Meget Uenig

(2) ❍ 2 Uenig

(3) ❍ 3 Neutral

(4) ❍ 4 Enig

(5) ❍ 5 Meget Enig

**Quiz: Hvor meget har du lært om immunologi?**

Nu hvor du har arbejdet med **teksten**, vil vi gerne teste din viden om immunsystemet. Du vil få en række spørgsmål, der dækker nogle af de vigtigste begreber inden for immunologi.

Tag dig god tid, og husk, at formålet med denne quiz er at vurdere, hvor meget du har lært – ikke at bedømme dine evner.

Held og lykke!

## Hvad er en antigenpræsenterende celle?

(1) ❍ En celle, der optager antigener og præsenterer dem på sin overflade for T-celler

(2) ❍ En celle, der producerer antistoffer mod antigener

(3) ❍ En celle, der dræber virusinficerede celler

(4) ❍ En celle, der udskiller histamin for at skabe inflammation

### Hvilken celle producerer antistoffer?

(1) ❍ T-lymfocytter

(2) ❍ B-lymfocytter

(3) ❍ Makrofager

(4) ❍ Dendritiske celler

### Hvilke celler dræber antigener gennem fagocytose?(Vælg flere)

(1) ❑ Makrofager

(2) ❑ Neutrofiler

(3) ❑ B-lymfocytter

(4) ❑ Naturlige dræberceller (NK-celler)

### Hvilke celler udskiller histamin for at skabe inflammation?(Vælg flere)

(1) ❑ Mastceller

(2) ❑ T-lymfocytter

(3) ❑ Basofiler

(4) ❑ Makrofager

### Hvad er et antigen?

(1) ❍ Et protein, der produceres af immunsystemet

(2) ❍ Identitetsmarkører på overfladen af patogener

(3) ❍ Et stof, der neutraliserer toksiner i kroppen

(4) ❍ En type antistof

## Hvad er et antistof?

(1) ❍ Et protein, der bekæmper fremmede stoffer i kroppen

(2) ❍ En celle, der præsenterer antigener

(3) ❍ Et molekyle, der forårsager sygdom

(4) ❍ Et enzym, der nedbryder bakterier

## Hvordan formerer virus sig?

(1) ❍ Ved celledeling

(2) ❍ Ved at kapre værtsceller og bruge deres maskineri til at reproducere sig

(3) ❍ Ved at danne sporer

(4) ❍ Ved at danne biofilm

## Hvordan formerer bakterier sig?

(1) ❍ Ved celledeling (binær fission)

(2) ❍ Ved at parre sig med et andet bakterie

(3) ❍ Ved at danne sporer

(4) ❍ Ved at udskille toksiner

## Hvad er cytokiner?

(1) ❍ Proteiner, der signalerer mellem celler i immunsystemet

(2) ❍ En type antistof

(3) ❍ En form for hormon

(4) ❍ Enzymer, der nedbryder fremmede stoffer

### Hvilke celler kan bekæmpe virus efter de har inficeret kroppens celler?(Vælg flere)

(1) ❑ T-dræberceller (cytotoksiske T-celler)

(2) ❑ B-lymfocytter

(3) ❑ Naturlige dræberceller (NK-celler)

(4) ❑ Neutrofiler

**Tak for din deltagelse!**

Vi vil gerne takke dig for at have taget dig tid til at deltage i denne undersøgelse. Dine svar er meget værdifulde for vores forskning, og de vil hjælpe os med at forstå, hvordan forskellige undervisningsmetoder kan forbedre læringen om immunologi.

Hvis du har nogen spørgsmål eller bekymringer omkring undersøgelsen, er du altid velkommen til at kontakte os.

Tak igen for din tid og indsats!

# B Appendix B (Consent Form)

## Consent Form

**Project title**

"From Pages to Play: A Comparative Study Evaluating Immunology Learning through Games and Textbooks"

**Project description**

This project is part of a master's thesis at Aalborg University (CPH) and aims to evaluate whether using an immunology learning game can lead to a better understanding of immunological concepts among high school students compared to traditional textbook learning. The research will involve testing students' comprehension of immunology after interacting with either a game or a textbook, followed by answering a series of questions designed to measure engagement and knowledge.

**Research group**

Lukas Harkamp, Mathias Adrian Wagner Kristiansen & Peter Matthiesen.
Master's students in Medialogy, specializing in Educational Game Design, Aalborg University, Copenhagen.

**Data processing and data sharing**

In compliance with the European General Data Protection Regulation (GDPR), this study will not collect any personal data from participants. The questionnaire will focus on the students' understanding of immunology and their engagement with the material. The data collected will be used solely for research purposes and will be kept anonymous. The findings of this research may be shared with university personnel, including the project supervisor, to ensure proper academic oversight and validation.

The data might be shared with other members of the university staff such as our supervisor. The data will be stored under password protected server at the ASURE servers at the University of Aalborg, ensuring GDPR compliance. Security issues might happen (e.g., the server at the university can be hacked), if this occurs, we will not take responsibility for the leak of data. We will keep the data for a maximum of six months after we have handed in our exams (October 2024); afterwards, we will dispose of all the data in a secure manner.

**Purpose of the project**

The purpose of this project is to create and evaluate a biology-themed game that teaches immunology. By comparing students' comprehension and engagement through the game and a traditional textbook, this study aims to contribute to educational research by exploring how interactive media can be used to enhance learning outcomes, specifically in the field of immunology.

**Confidentiality**

All data collected during the study will be treated with strict confidentiality. While no personal data will be gathered, the responses will remain anonymous. The data will be accessible only to the research group, the project supervisor, and, if required, to the thesis examiners. The results will be presented in aggregate form, ensuring that no individual responses are identifiable.

**Risks of the research**

This study poses minum risk to participants. The activities involved—playing an educational game or reading a textbook—are routine and pose no physical or psychological harm. However, participants are free to withdraw from the study at any point without any negative consequences. The game and textbook materials used in this study have been reviewed to ensure they are educational and age-appropriate for high school students.

**Age of requirements**

The EU GDPR 2016/679 regulations regarding data only allows us to gather and store information from people below the age of 18 years with the explicit consent of their parents or children representatives. Therefore, we are asking you in the role of parent or child representative to give us consent to conduct our study.

**Queries**

The project is conducted under the direction of Lukas Harkamp, Mathias Adrian Wagner Kristiansen & Peter Mathiesen. MSc. For any questions or concerns regarding the research, please contact us via email at Create-24-med-10-gruppe1@student.aau.dk

**Consent**

- I, as the principal, confirm that I have read and understood the information presented in this document.
- I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily.
- I understand that participation is voluntary for the students involved, and that they are free to withdraw at any time without compensation or the need to provide a reason.

**<u>I understand how the data will be:</u>**

Collected, Stored, Analyzed, Shared, and Disposed of securely after the research has concluded.

**<u>By accepting this consent form, I confirm that I have read and agreed to the terms and conditions of the current research and for the purposes of:</u>**

- Understanding the effectiveness of an immunology learning game in improving students' understanding of immunological concepts compared to textbook learning.

By accepting this consent form, I confirm that I have read and agreed to the terms and conditions for the current research and consent to the study being conducted with high school students under my authority.

*Your signature goes here:*

16/9'24

100%

## C Grammarly Usage

Grammarly, an AI-powered writing assistant, was used throughout the thesis to help improve the clarity, grammar, and overall readability of the text. While Grammarly provided helpful suggestions, all final editorial decisions were made by the authors to ensure the content remained true to the intended meaning and academic style required for this thesis.

## D Interview Transcriptions

These are edited transcriptions of the interviews with teachers at Frederiksberg Gymnasium, Ørestad Gymnasium, Vestskoven Gymnasium and Sukkertoppen Gymnasium.

**Interview 1**

**04:14: Researcher 1:** Bruger du nogle alternative læringsværktøjer i undervisningen?
**04:22: Teacher 1:** Ja, tit og ofte. Jeg har ikke fundet noget til immunologi endnu rigtig. Der er The Blood Typing Game. Den bruger jeg til blodtyper. Det her med, hvem kan give blod til hvem og hvorfor. Men jeg er endnu ikke stødt over nogle immunforsvarsspil.

**00:20:19: Teacher 1:** Så den progression jeg oftest selv tager mig, når jeg underviser. Det er jo det her med, at du har en virus for eksempel, ikke? Den kommer ind i en værtscelle. Nå, men så får du mere virus. Og det næste man så lærer noget om, det er immunforsvarets celler, kunne det være. Altså alle de her celletyper, der er. Lær dem at kende som spiller, ikke? Og så skal man finde ud af den enkelte kontaktsignalering mellem cellerne. Det plejer jeg så at gå ind i. Og forklare dem, der er vigtige, hvor overflademolekylerne bliver præsenteret for hinanden. Og det næste, jeg så går ind i, det er hele det her immunrespons, hvor man får dannet antistoffer og så derfra går jeg oftest ind i hvad for nogle typer af antistoffer og den variable del og den faste del af antistofferne i forhold til at binde sig til antigenerne og deres specificitet, og hvordan de bliver fagocyteret. Og derfra kan man så gå over i noget omkring? Vacciner, altså både passiv og aktiv. Det er sådan typisk, jeg laver kronologien.

**Interview 2**

**01:12: Researcher 1:** Så hvad med specifikt immunsystemet? Hvad? Hvad lærer elever om det? [. . . ]
**01:37:Teacher 2:** Vi har responset på virus og bakterier. Vi har forskellige celletyper. Vi har differentiering af T celler til huskeceller og hvad fanden de hedder alle sammen. [..] Produktion af antistoffer også.
**02:28 Researcher 1:** Så også sådan rent mekanisk hvordan virus og bakterier de angriber kroppen og formerer sig. Er det også noget I kigger på?
**02:35: Teacher 2:** Ja, det gør vi.

**10:10: Researcher 2:** Har I egentlig gjort brug af nogen spil? Brætspil eller digitale spil eller noget som helst i dens stil? [..]
**10:53: Teacher 2:** Hvis jeg støder på noget, så bruger jeg det. Jeg kan huske Nobelprisens hjemmeside havde et med blodtyper, fordi det åbenbart havde givet Nobelprisen engang. Så kommer der en eller anden patient, og så skal du lægge ham op på båren og så finder vi blodtypen, og hvad for en kan så være donor, og nå han døde, fordi du tog den forkerte.

**Interview 3**

**01:55: Researcher 1:** Så hvor langt ned i mikrobiologien kommer i? [. . . ]
**02:16: Teacher 3:** Vi dækker jo det der har med bakterier at gøre. De skal kunne noget om virus også. [...] Og så vil man typisk blande det sammen med viden om immunforsvaret også. Og der kommer de til at lære helt ned på cellulært niveau også, hvor de lærer om de enkelt celler i immunforsvaret og hvordan de spiller sammen. [. . . ]
**03:01: Researcher 1:** Så hele rækken af innate og adaptive immunsytem, og hvilke celler er involveret og hvad de gør?
**03:11: Teacher 3:** Ja, lige præcis

**03:24: Researcher 1:** Har du personligt brugt nogle alternative læringsredskaber, fundet spil og sådan noget?
**04:22: Teacher 3:** Specielt til immunforsvaret, der indleder jeg nogle gange med et spil. Hvad er det nu det hedder? Man kan bare have det på sin telefon. Det sådan noget, hvor man så vælger, om man vil være en virus eller en bakterie eller svamp eller, og så skal man overtage hele verden.

**Interview 4:**

**14:00: Researcher 1:** Det kan faktisk godt være, at vi ikke har skrevet særligt tilgængeligt sprog i vores forklaringer endnu. Måske skal vi bruge lidt mere metaforer?
**14:10: Teacher 4:** Altså det gør jeg ret meget, fordi så er det nemt for dem. Jeg vil varmt anbefale. Der er simpelthen den mest platte film fra DRs arkiver om immunforsvaret. De har simpelthen lavet den mest platte stop motion-ish film om immunforsvaret, hvor makrofagerne er politibetjente, og T dræber cellen er sådan sheriffen med pistoler, der kommer. Eleverne plejer, når vi skal introduceres til det, så jeg viser jeg den. Og så plejer det at sidde der lidt: "Nå, men det er sheriffen og det er politibetjenten og det er detektiven."

**17:49: Researcher 3:** Måske lige have en sektion i starten, der siger, det her er de vigtigste pointer og så gå videre i dybden?
**18:05:Teacher 4:** Og så kan den interesserede elev gå videre og sige nå okay, det er det her, som rent faktisk sker. Men den der egentlig talt bare gerne vil spille spillet. Der hvor det hele går lidt hurtigt. De vil læse de første linjer, og så går de videre.

**41:23: Researcher 3:** Vi har lidt et problem med at der sker lidt for meget på skærmen på én gang.
**41:28:Teacher 4:** Ja, der sker rigtigt meget. Jeg ved ikke altid hvor jeg skal kigge.