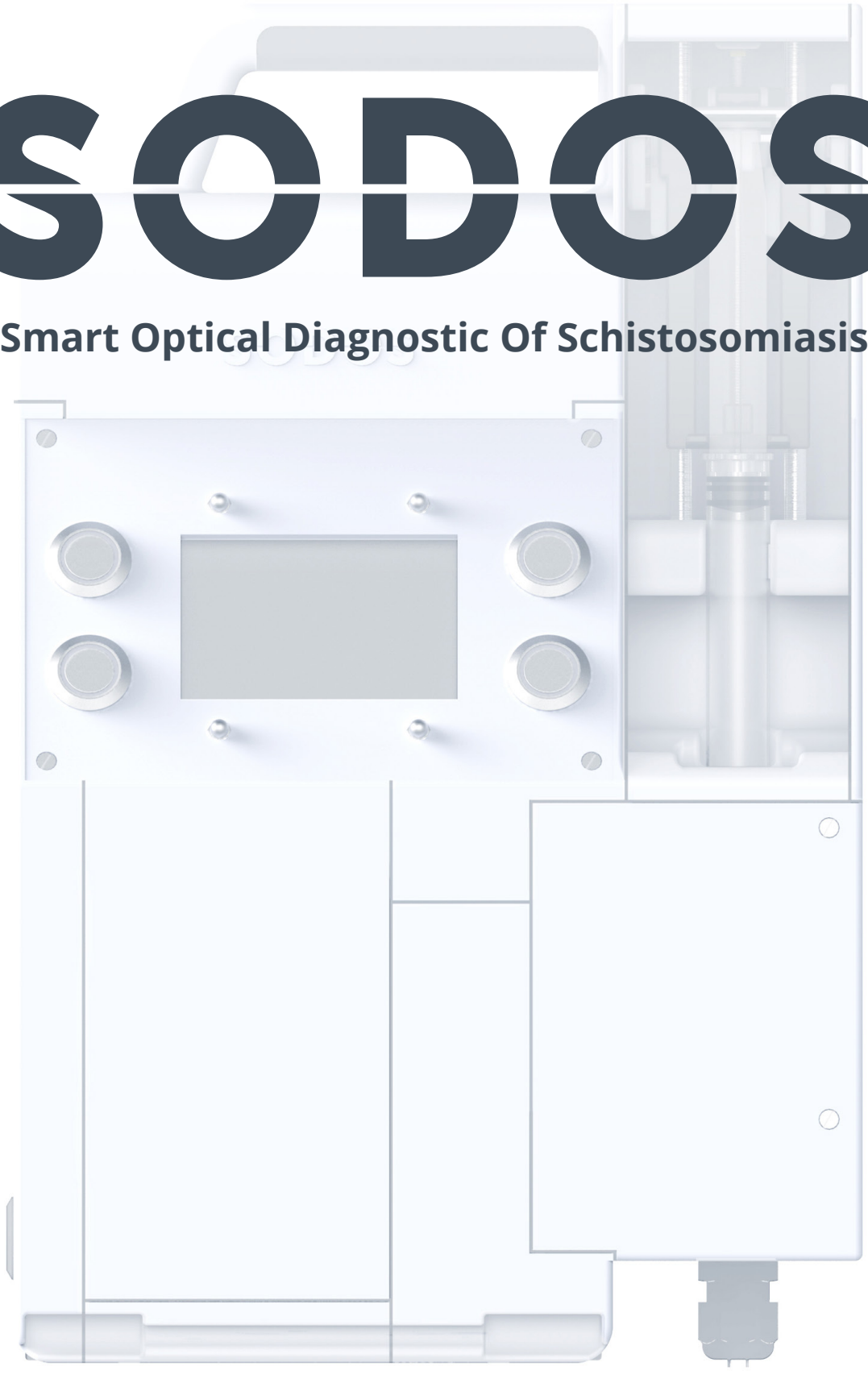
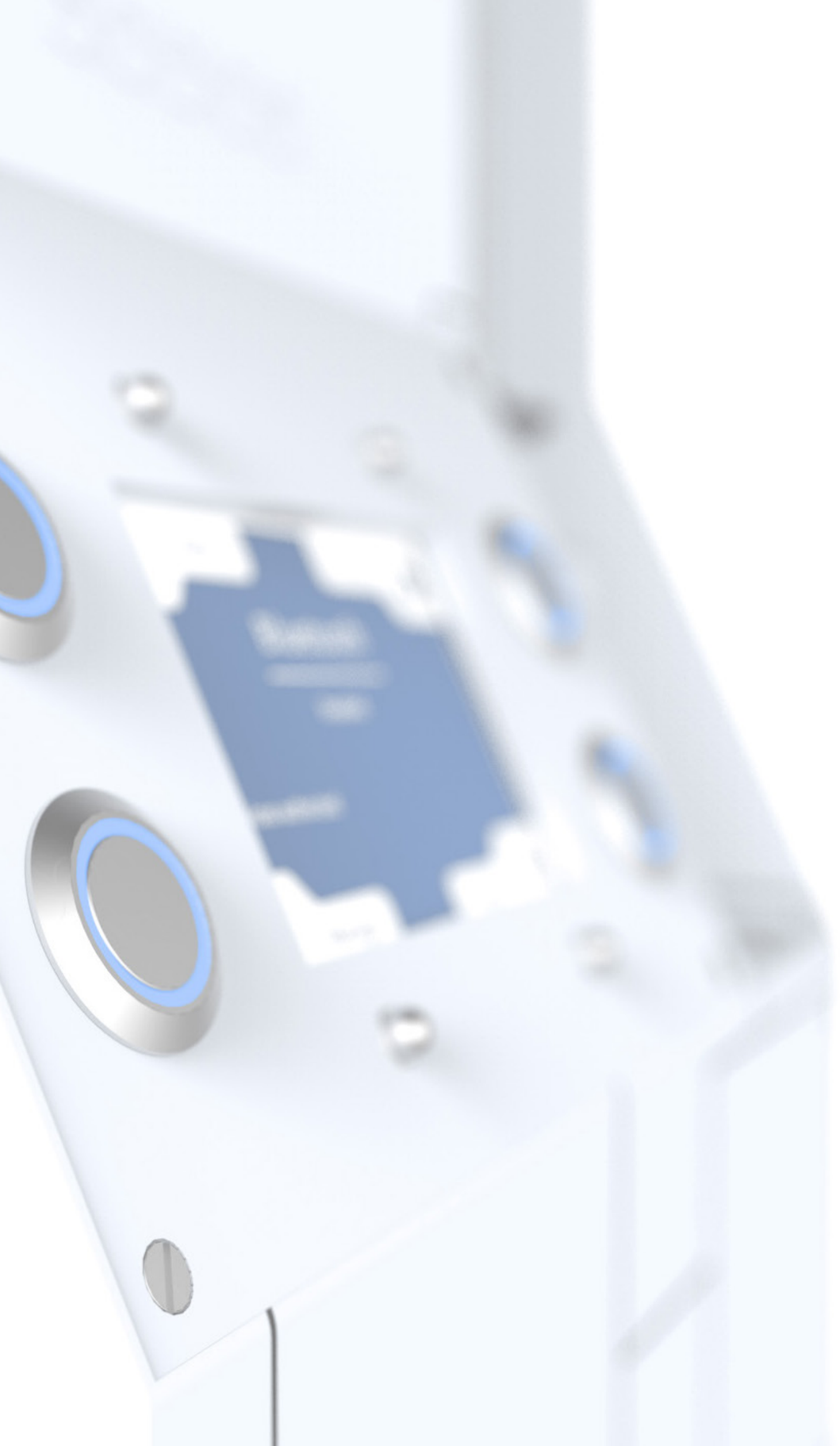
SODOS

- Smart Optical Diagnostic Of Schistosomiasis -



Master Thesis by Max Hoeboer
4207866 - September 2019



Master thesis in fulfillment of the requirements for
the degree of Master of Science in the fields of

Master Integrated Product Design
Medisign specialization
Faculty of Industrial Design Engineering
Delft University of Technology

Master BioMedical Engineering
Medical Instruments and Medical Safety
Faculty of Mechanical, Maritime and Materials Engineering
Delft University of Technology

Graduation committee

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Stefan van de Geer	*Mentor Industrial Design Engineering*
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Abstract

Urinary schistosomiasis is with over 110 million infected people one of the most common parasitic infections worldwide, most commonly found in Sub-Saharan Africa. Urinary schistosomiasis is caused by the Schistosoma Haematobium (SH) parasite. The most common diagnostic method is manual microscopy, in which urine is manually examined to see whether SH eggs are present. This method requires expensive materials and well-trained staff, and is therefore often not available in remote areas. Therefore, a more accessible and automated method is being developed at the Delft University of Technology, based on the automated flow-based holographic analysis of urine samples. As the technology and its algorithms have become well developed and a context analysis for a diagnostic device using this technology has been performed, a clear need presents itself for developing the experimental setup into a functional and interactive diagnostic device and prototype.

To do so, the different components within the development of the diagnostic technology and product interaction have been separately developed in parallel design processes. Once the components were deemed sufficiently developed to meet the lists of requirements set out, they were combined into a single product embodiment design and prototype. This integrated prototype was designed to be both functional interactive, and all software required for this purpose was created.

The resulting integrated prototype was validated and optimized at the facilities of the Delft University of Technology using SH eggs in saline solution provided by the Leiden University Medical Centre. After this, an extensive field research was performed in Ivory Coast. In this, high quality data of urine samples was obtained using the prototype, and diagnosis was performed via manual microscopy to determine the number of eggs that could be potentially observed by the prototype. Aside from this, the overall performance of the prototype and its interaction in the envisioned context were assessed. The data gathered can be used in the future to reassess the diagnostic potential of the holographic technology, and optimize the reconstruction and classification algorithms within the existing prototype to turn it into a fully functional diagnostic device, capable of providing reliable and accessible diagnoses to rural areas of Africa.

Preface

The master thesis before you forms the final step in my Individual Double Master's Degree of the masters BioMedical Engineering and Integrated Product Design at the Delft University of Technology. Looking back on this graduation project, it has been even more enjoyable than I anticipated, and has demonstrated to me that performing these kinds of diversified projects truly is my passion. I look forward to practicing this passion in the years to come.

I would like to sincerely thank those who helped me throughout this long project, and without whom this would not have been possible. First of all, my chair of Industrial Design Engineering, Jan-Carel Diehl, for enabling this unique project and for always being available to provide aid, guidance, inspiration, and a lot of enthusiasm.

Secondly, my chair of BioMedical Engineering, Jenny Dankelman, for the critical look on my work and the freedom given throughout this project. I would also like to thank my mentor of Industrial Design Engineering, Stefan van de Geer, for helping me maintain a wide view during the early stages and for having your support in this unusual project. And also my mentor of BioMedical Engineering, Roos Oosting, for aiding me in giving structure to my thesis, and for the nice collaboration we have had in our projects.

Special thanks to Patrick Nijman, for his previous and parallel work on the diagnostic technology, for the countless hours we have struggled together on developing software, for the many measurements we have performed together, and for a great team overall.

Similarly, I would like to thank Mirte Vendel for performing the essential research required for this project, and for taking the role of being my company mentor for the Medical Optics Fund.

I would also like to thank Temitope Agbana, for initiating the project, our work together, and your endless enthusiasm and ambition. I would also like to thank Gleb Vdovin for providing expert knowledge, and G-Young Van for aiding me throughout the process.

Throughout the graduation project, the suggestions and aid from employees at the PMB and Applied Labs in the faculty of Industrial Design Engineering have been invaluable. Especially during the first phases of development, the suggestions on prototype development and the use of existing components by Wiebe Draijer from the PMB have made the project a lot more manageable.

I wish to greatly thank local researchers Jean Coulibaly and Kigbafori Silue, without whose help in organizing the field trip to Ivory Coast it would have never been possible. Similarly, I wish to thank the local team, especially lab technician Touré, for the hard work during the intense field research. I also want to express my gratitude to the Centre Suisse de Recherches Scientifiques and the Centre de Santé Urbain d'Azaguié, for receiving me and aiding me throughout the field trip.

Besides this, I want to thank the Leiden University Medical Centre and Delft Global Initiative for supporting this project. Finally, I would like to thank my friends and family for supporting me throughout this long project, and for bearing with me continuously talking about it.

Max Hoeboer

Table of Content

Due this report serving as the thesis for two fields, it consists of sections with relevance to either or both fields, as indicated both in the Table of Content and on the bottom of each spread whenever applicable. This is indicated for both Integrated Product Design (IPD) and BioMedical Engineering (BME). Still, to obtain a complete overview of the graduation project, it is recommended to read the entire thesis.

Integrated Product Design (IPD)

BioMedical Engineering (BME)

List of Figures

Abbreviations

API	Application Programming Interface
CSRS	Centre Suisse de Recherches Scientifiques en Côte d'Ivoire
GPS	Global Positioning System
HAT	Hardware Attached on Top
LUMC	Leiden University Medical Center
PBS	Phosphate-buffered saline
S.	Schistosoma
SH	Schistosoma haematobium
Sodos	Smart Optical Diagnostic of Schistosomiasis
TU Delft	Delft University of Technology
UPS	Uninterruptable Power Supply
WHO	World Health Organization

Introduction

Schistosomiasis, also known as bilharzia, is a parasitic infection with an estimated 252 million people infected in 2015 1, making it one of the leading neglected tropics disease worldwide. It is caused by parasitic flatworms of the genus schistosoma (S.), which manifest themselves in the urinary tract or intestines and lay their eggs there [2]. As a result, some of the eggs are released from the body during defecation or urination.

If the eggs reach fresh water, they will hatch and release miracidia that will attempt to find a suitable snail to function as the intermediate host [3]. If a snail host is found, it is used by the miracidia to asexually multiply and develop into cercariae. When matured, the cercariae leave the intermediate host to find a definitive mammalian host [2]. If a definitive host is found, the cercariae penetrate the skin. Within the body of the host, the cercariae mature into schistosomula, find a mate, and move to the urinary tract or intestines to continue the cycle.

However, some of the schistosoma eggs may be retained in host tissues, where they induce inflammation and die [3]. This causes symptoms including chronic infections and can be fatal over time. As can be seen in Figure 1, schistosomiasis exists on a global scale, but is most prevalent in Sub-Saharan Africa. It can also be seen that there are different types of schistosomes causing schistosomiasis amongst humans, most common of which are the S. Mansoni, S. Japonicum, and S. Haematobium [2].

The Schistosoma Haematobium (SH) is with an estimated 110 million infected people the most common of the schistosomes [4], and is also the only one to manifest themselves in the urinary tract, lay their eggs there, and cause urinary schistosomiasis [3,4]. Urinary schistosomiasis can result in haematuria, anaemia, kidney failure and reduced female reproductive health, and is associated with increased risk of HIV transmission, bladder cancer and other carcinogenic effects [2,3,5]. In addition, it may result in impaired growth and cognitive development for children [6]. Schistosomiasis can be treated using Praziquantel. However, this drug is solely effective against mature schistosomes which have started egg production and does not prevent future contamination [2-4]. Additional information on Praziquantel can be found on page 69.

There are multiple existing methods for diagnosing urinary schistosomiasis. The current gold standard is based on the analysis of urine for the presence of SH eggs via manual microscopy [2]. In this, an urine sample is centrifuged or filtered, after which it is stained and manually examined using a microscope [7], as can be seen in Figure 2 and Figure 3. After this, SH eggs can be manually observed and counted using microscopy to determine the level of infection, as can

Figure 1. Global distribution of human schistosomiasis, obtained from Colley, Bustinduy [3].

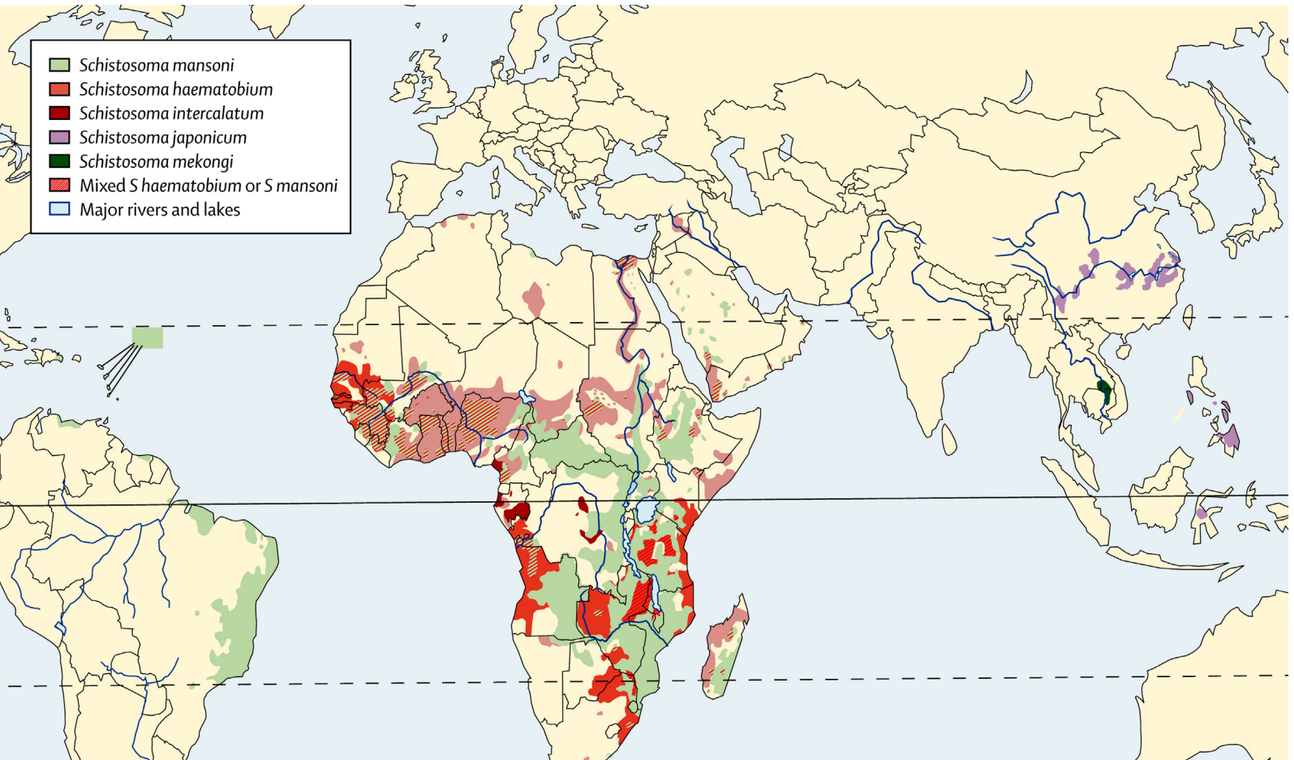


Figure 2. Filtration of urine for diagnosis of urinary schistosomiasis through microscopy in Ivory Coast.

Figure 3. Diagnosis of urinary schistosomiasis through microscopy in Ivory Coast. Front; a filter is being removed from the filter holder for examination. Back; a stained filter is being examined through manual microscopy.

be seen in Figure 4. For this, well-trained staff, an expensive microscope, disposables, and a minimum amount of 10ml of urine is required [7]. As these prerequisites are often unavailable, diagnoses can often not be performed. This is especially the case in rural conditions.

Existing alternative methods for diagnosis include haematuria questionnaires, dipsticks for microhaematuria, polymerase chain reactions, and antibody detection [2,3,8]. Still, these methods are considered inaccurate or are unavailable, and better diagnostic tests for schistosomiasis are deemed necessary [3,9].

Therefore, a new diagnostic method has been proposed by the TU Delft with the potential of automatically performing optical diagnosis of urine in SH endemic areas of Africa. The technology behind this method is the in-line digital holography of flowing urine. For the scope of this graduation project, this device was named the Smart Optical Diagnostics of Schistosomiasis, or Sodos in short.

Prior to this graduation project, the development of the diagnostic technology was mostly performed by fellow graduate Patrick Nijman of the master Systems & Control at the Delft Center for Systems and Control (DCSC) department. This development was commissioned and supported by PhD candidate Temitope Agbana from the DCSC department. At the onset of this graduation project, this development had resulted in an experimental setup, and provisional algorithms for reconstruction and classification. This experimental setup was only designed to enable a proof of principle for the technology, and could not be used to provide validation of the diagnostic technology in the envisioned context. Therefore, the next step in the development process would be to create a diagnostic embodiment design.

An embodiment design is defined as the part of the design process in which, starting from the concept of a technical product, the design is developed in accordance with technical and economic criteria to the point where subsequent detail design can lead directly to production [10].

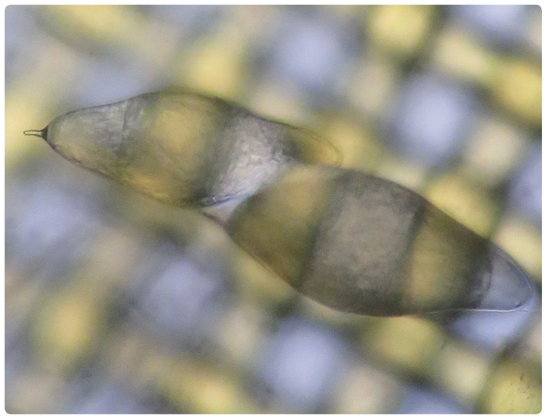


Figure 4. Schistosoma Haematobium eggs as seen through a microscopy with a 40x objective in Ivory Coast.

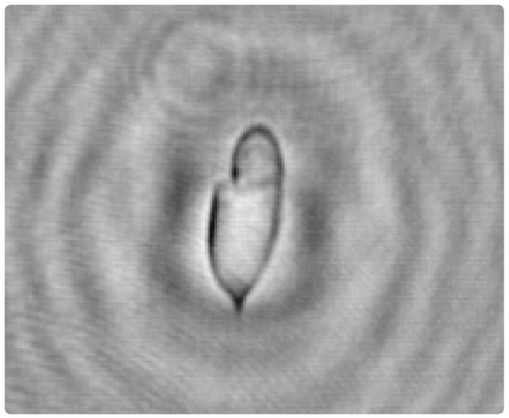


Figure 5. Schistosoma Haematobium egg as seen through the Sodos using reconstructive algorithms by Patrick Nijman.

Besides this, the development of reconstruction and classification algorithms required for the interpretation of the obtained footage was continued by Patrick throughout this graduation project. Therefore, the embodiment designs were developed in close collaboration, as a mismatch between the algorithms and the embodiment was not likely to result in a functional design. Using these algorithms, objects in the raw footage could be tracked, isolated, reconstructed, and classified to enable automatic diagnosis. An example of a reconstructed SH egg using the Sodos and the reconstructive algorithms can be seen in Figure 5.

For the diagnostic technology to be applicable in the envisioned context of SH endemic areas of Africa, a product embodiment design was to be made. This included the development of the physical embodiment, as well as the physical and digital interaction. Besides this, a business implementation plan was to be developed. Still, the latter was not considered to be within the scope of the project and may be further elaborated on by fellow graduate Justine Dai.

The combination of extreme environmental conditions and an unique socio-economic context introduced unique challenges for both the product and interaction design. Therefore, TU Delft alumna and Medical Optics fund employee Mirte Vendel did her graduation project on the conceptual development of the diagnostic device [9]. This resulted in both a context analysis and a conceptual interactive design.

The context analysis and exploratory field research performed in Ghana was used to map the specific context and explore potential user groups. From this, research institute employees and rural health facility employees were selected as the envisioned users for the continued product development. Based on this, requirements and wishes were set out for the diagnostic technology, product embodiment, and product interaction, which can be found in Appendix J of Vendel [9]. As these requirements are supported by the performed context analysis, they will form the basis for the lists of requirements and wishes throughout this graduation project.

Based on the requirements and wishes set out, a conceptual interactive design was created called the Egg Counter, as can be seen in Figure 6. In this, slightly different concepts were proposed for rural health facilities and research institutes to meet their requirements and wishes effectively. Namely, the design for research institutes included a wirelessly connected tablet for interaction and extended functionality. This tablet would enable more control over digital patient data and increase the computational power available. In addition, the interaction protocol was adapted to suit the available facilities and level of user expertise. As the diagnostic technology was still largely undefined at this stage, various assumptions were made and no diagnostic design was included. A complete report of the conceptual development can be found in Part 3 of Vendel [9].

The created prototype of this design was not validated, and it was recommended that further user research, technical development, materialization, and optimization were to be performed in future projects on the diagnostic method. The report created by Mirte formed the starting point for the product embodiment and product interaction, and will therefore often be referred to.

The context analysis performed and the recommendations made by Mirte Vendel, and the advancements made in the diagnostic technology development by Patrick Nijman and Temitope Agbana created the opportunity for performing a next step in the development process; the creation of a both functional and interactive prototype of the Sodos and gaining validation of this prototype in the envisioned context of SH endemic areas of Africa. Therefore, the following project goal was defined:

> *" To develop and design a both functional and interactive prototype of the Sodos, to obtain validation in the envisioned context, and to make a redesign based on the obtained feedback "*

In the next chapter, the overall method and process for meeting this project goal will be set out. After this, the results of the design process for the individual components and the integration of these components into a functional and interactive prototype will be discussed. This is followed by the validation of the prototype in the envisioned context. Lastly, an overall discussion will be held and recommendations will be proposed.

Figure 6. Conceptual interactive prototype of the Egg Counter developed by Mirte Vendel (right) and the integrated prototype of the Sodos developed during this graduation project (left).

Method

The project goal had multiple aspects that needed to be individually addressed. Therefore, the project was subdivided into two phases, each having their own goals and approaches. For the first phase, the major goal was to develop and design a both functional and interactive prototype of the Sodos. This design process was considered the first phase of the project, and required the development of multiple components in various areas of the envisioned Sodos. To maintain continuity within this report, the methods used for the individual design processes will not be centrally discussed, but only the general approach and methods used.

Based on previous development and recommendations, three main areas of development for the Sodos were identified, as can be seen in Figure 7. In this, the development of the diagnostic technology was considered leading in the development. As indicated, the diagnostic technology at this stage mainly required an embodiment design to be developed. Therefore, this was a major part of this graduation project and was performed in close collaboration with fellow graduate Patrick Nijman. Accompanying components that required development, such as a method for controlling the fluid insertion, were also developed to enable a completely functional design.

As the diagnostic embodiment and the accompanying components required both physical and digital interaction with the user, the process of developing the product interaction was performed parallel to the diagnostic technology development.

To ensure rapid development for the areas of product interaction and diagnostic technology development, parallel design cycles were performed for all components within each area. In each of these iterative design processes, designs were created, prototyped, and validated.

For the diagnostic technology development, validation was performed at the TU Delft using simulated diagnostic experiments. This was primarily performed using SH eggs in Phosphate-Buffered Saline (PBS) or urine solution, kindly provided by the Leiden University Medical Center (LUMC). For the physical and digital product interaction, validation was performed using user tests. If it was found during validation that not all requirements were met, or new requirements were identified, an additional design cycle was performed.

Once all requirements were sufficiently met and no new requirements could be identified, a product embodiment design and prototype was to be created. For this, general product requirements and wishes for the envisioned context of SH endemic areas of Africa were identified using literature and Vendel [9]. Based on this, the individual components of the diagnostic technology and interaction, and general elements of the product embodiment were developed for integration. This resulted in a single functional and interactive design and prototype, for which initial validation was performed at the TU Delft.

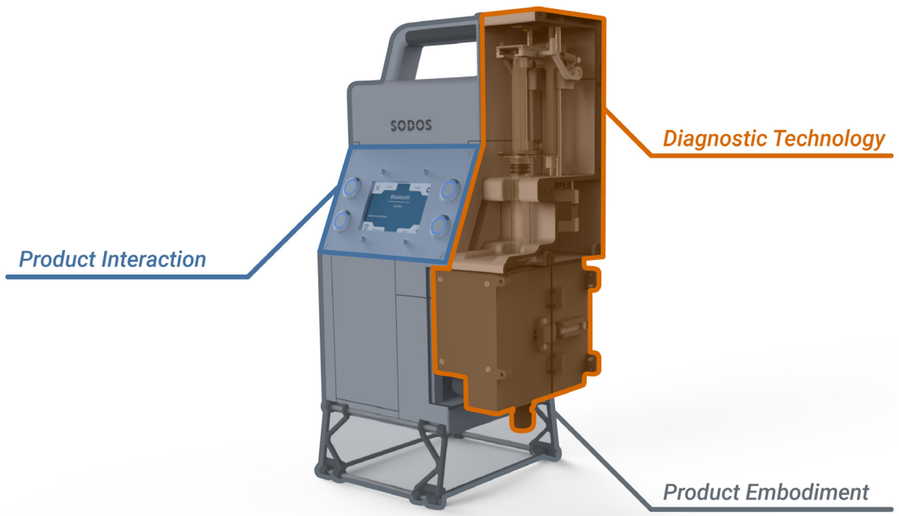


Figure 7. The three main areas of development for the proposed diagnostic solution, shown on the resulting functional and interactive design.

The second phase of the project had the main goals of validating the prototype in the envisioned context and making a redesign based on the obtained feedback. The method used for validation in the envisioned context are discussed where applicable to maintain continuity within this report. Besides this, if deemed necessary, a redesign was to be made based on the obtained feedback of the validation in the envisioned context.

The overall anticipated approach for the graduation project can be seen in Figure 8. In this, the summarized work partially or fully performed by Mirte Vendel and Patrick Nijman has been included.

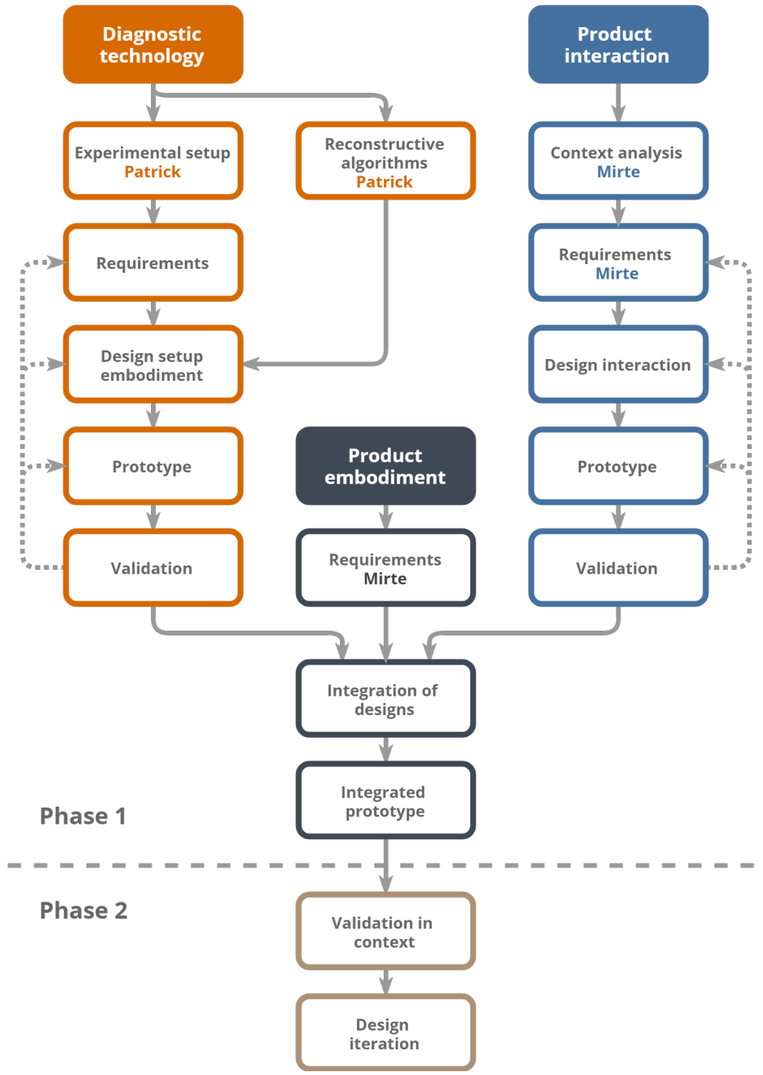


Figure 8. The phases and general anticipated approach for the graduation project.

Structure of the report

In Figure 9, the overall structure of parts A-D of the report can be seen. In this, introductory chapters and standard report elements have not been included. It can be seen that chapters of parts 1 and 2, and part 4 are performed in parallel. As a result, the chapters are frequently interdependent and cannot be discussed in complete chronological order.

To assist the reader with the relatively complex structure of this report, an abstracted version of Figure 9 will be frequently shown at the start of a chapter or part. In addition, the sections in parts A and B have been given a consistent structure.

In addition to this report, a summarizing research paper on the report and the official IDE graduation assignment form have been included as Appendixes A and B.

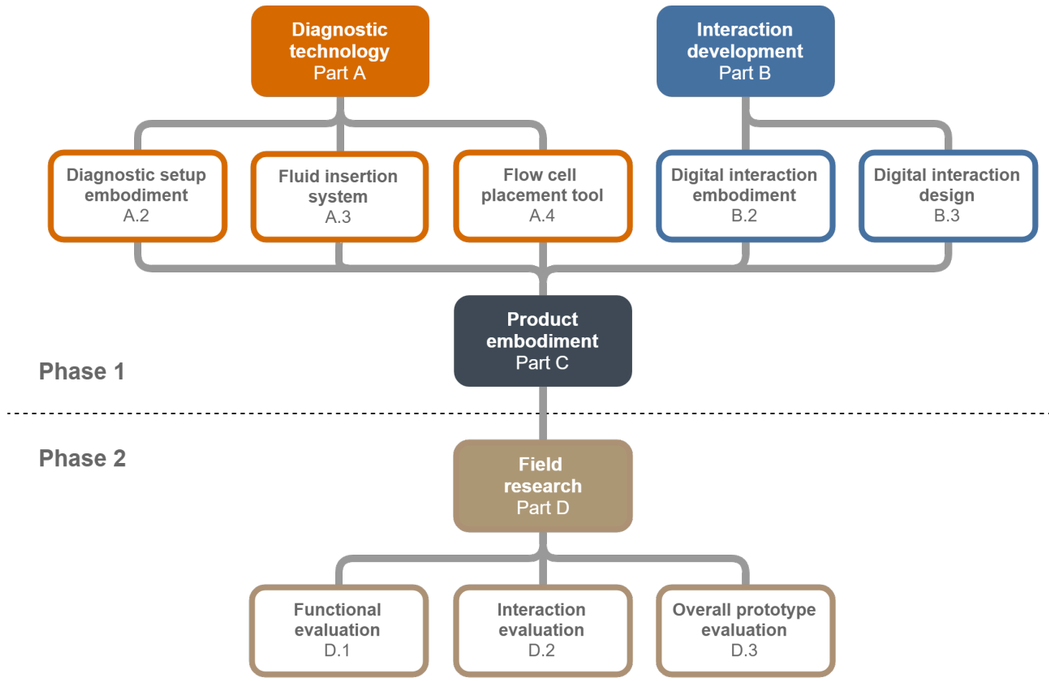


Figure 9. General structure of the report.

Part A

Diagnostic technology development

In this part of the first phase, the individually performed development of the diagnostic technology during the graduation project will be discussed. This will consist of a description of the diagnostic technology and experimental setup at the commencing of the project, followed by the individual development of the required components.

1. The experimental setup

The diagnostic technology used in the proposed diagnostic solution is based on digital holography, in which a hologram can be digitally recorded. A hologram is often defined as the photographic recording of a light field, rather than an image formed by a lens. This means that the optical sensor used in digital holography does not contain any lenses to change the directory of the light. Due to the lacking of a lens, the optical sensor may not be called a camera, as a camera contains a lens by definition. When holography is performed in combination with a single laser, the almost completely monochromatic light allows digital reconstruction of images [11]. This digital reconstruction can be performed for a variable depth of field, meaning that it can focus on multiple depths using a single recording. At the same time, the use of holography eliminates the need for expensive camera lenses, at the cost of having a higher computational demand.

The development of the diagnostic technology up to the onset of this graduation project had resulted in an experimental setup and provisional algorithms. This experimental setup, as seen in Figure 11, was designed to use in-line digital holography to capture SH eggs in saline solution and perform digital reconstruction. The experimental setup was designed by Patrick with the intend to provide a proof of principle for the technology. Therefore, it could not yet be used to provide validation of the diagnostic technology in the envisioned context, and a clear demand for an embodiment design for the experimental setup arose.

The experimental setup consisted of a diffused laser light source pointed at a lensless optical sensor with a flow cell in between. As the experimental setup uses in-line digital holography, these three parts were aligned parallel to each other [11]. The optical sensor used was of the type UI-1492LE-M by the company IDS and had 3840 x 2748 pixels with a sensor size of 6.413mm x 4.589mm. Optionally, the resolution of the optical sensor could be reduced to increase the frame rate and to reduce apparent distortions due to the rolling shutter. The optical sensor was connected to a computer to obtain the raw footage.

In front of the optical sensor was a flow cell of the type µ-Slide I Luer 0.8mm by the company Ibidi. As can be seen in Figure 10, this is a fully transparent slide with two cylindrical connections connected via an enclosed flow channel with a rectangular cross-section of 0.8 x 5.0mm. This flow cell was held as close as possible to the optical sensor, with the enclosed channel being completely in front of the sensor.

A syringe filled with urine could now be connected to the top connection of the flow cell using a silicone tube, allowing urine to be manually passed through the enclosed channel. The experimental setup was placed inside a completely darkened room to prevent light other than the laser light from reaching the optical sensor.

The algorithms that were being developed by Patrick to function alongside the experimental setup had multiple challenges that were to be addressed by Patrick. First of all, the algorithms needed to be able to track all objects of comparable size to SH eggs in the urine as they passed through the observable area of the setup. Once an object was fully tracked, a number of frames on which the object was clearly visible needed to be automatically selected and reconstructed to an observable image, an example of which can be seen in Figure 5 on page 11. This observable image could then be tested against a classifier to determine whether the object is a SH egg.

1.1. Components to be developed

Based on discussions with Patrick, it was decided to develop an embodiment design for the diagnostic setup to enable application of the technology in the envisioned context, as will be discussed in chapter 2.

Besides this, it was noted that controlling the flow rate of the system by hand reliably at a constant rate was a near impossible task. This was due to the low flow rates required by the system and the duration of a measurement. Therefore, it was also decided to develop a fluid insertion system that could be combined with the diagnostic setup embodiment to form a functional whole. This is discussed in chapter 3 on page 29.

In addition, it was found during the development of the diagnostic setup embodiment that the flow cells used in the setup were prone to breaking. This mostly occurred during the placement and removal of the flow cells from its connectors. Therefore, it was decided to develop a flow cell placement tool to be used alongside the diagnostic setup embodiment. The development of this tool is discussed in chapter 4 (p.34).

Figure 10. The flow cell µ-Slide I Luer 0.8 mm by the company Ibidi.

Figure 11. The experimental setup used by Patrick Nijman.

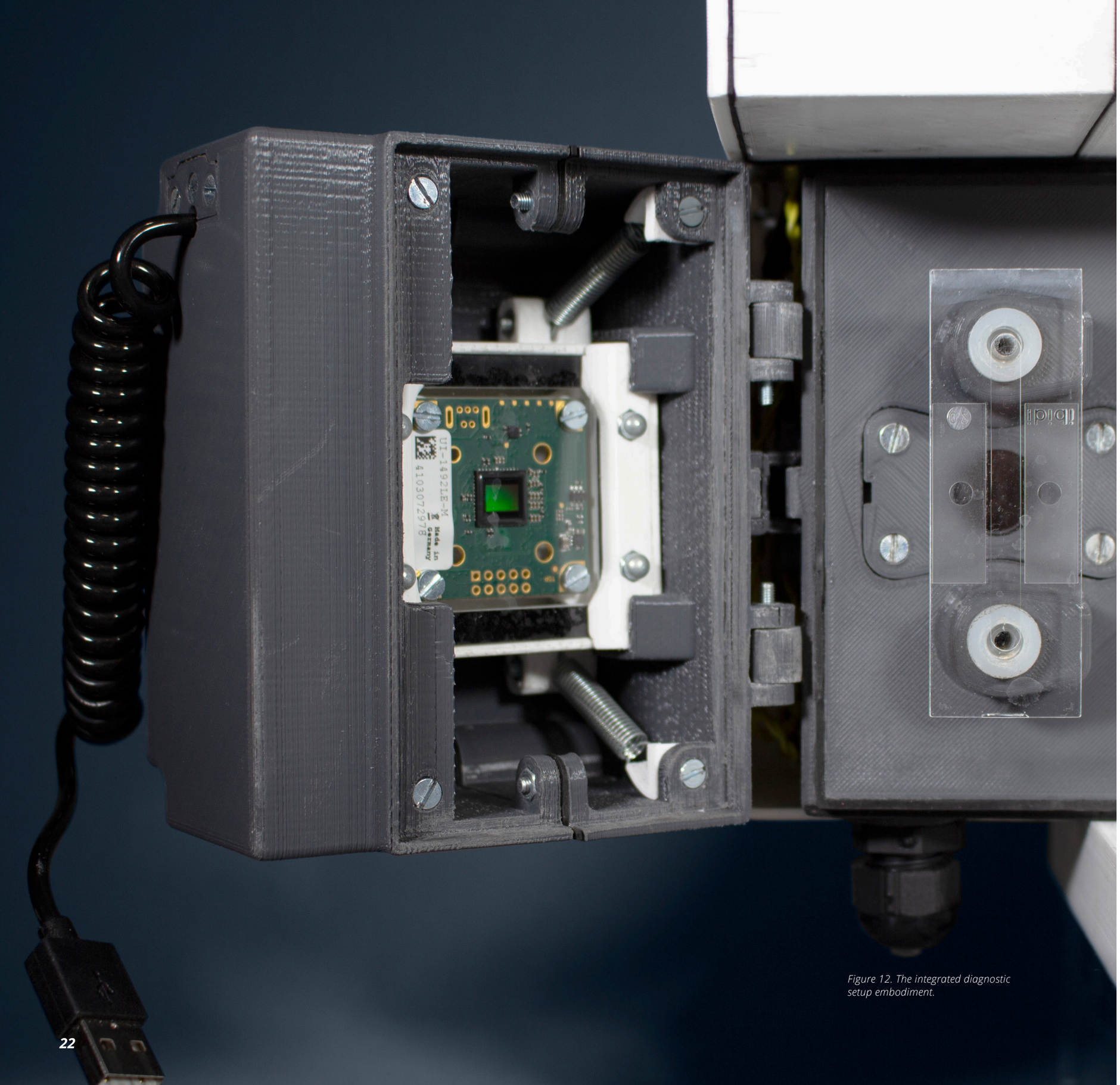
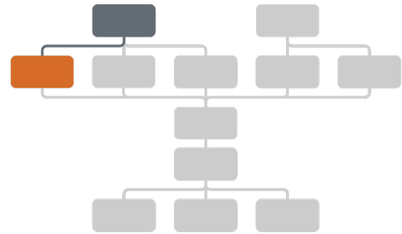


Figure 12. The integrated diagnostic setup embodiment.

2.
Diagnostic setup embodiment

The experimental setup was used as the starting point for developing the embodiment design for the diagnostic setup. The diagnostic setup embodiment had a main focus in the diagnostic technology development, yet the accompanying elements were also developed and will be discussed in the consecutive chapters of this part.

To support a well argued design process for the diagnostic setup embodiment, a list of requirements and list of wishes was first created. Based on this, an initial embodiment design and prototype was created. Based on the validation of the prototype, iterative design processes were performed until the requirements were met sufficiently. After this, an integrated design was created in which the diagnostic setup embodiment was combined with the other components developed in parallel.



As can be seen in Figure 9 on page 16 and the visual above, the chapter on the diagnostic setup embodiment is part of the diagnostic technology development.

2.1. Requirements and wishes

For designing the diagnostic setup embodiment, the non-prioritized lists of requirements and wishes were based on in-depth discussions with Patrick, observations of the experimental setup, and overall product requirements determined by Mirte.

Besides the requirements and wishes set out specifically for the diagnostic setup embodiment, general product requirements and wishes set out in part C, chapter 1 (p.54) were also applicable. Still, as it was not yet determined how the diagnostic setup embodiment would be incorporated in the product design, designs prior to the integrated design did not yet have to meet all relevant product requirements and wishes.

List of requirements

1. Urine must be able to flow through the system completely to allow full analysis and prevent cross contamination.
   - **a.** The urine pathway must not contain an area with an upward slope.
   - **b.** The urine pathway must not contain edges behind which particles can get stuck.
2. All parts of the urine pathway must be removable for maintenance.
3. Electronic components must be protected against dust, humidity, and high temperatures in accordance with their technical documentation (J.1) [12].
4. The setup embodiment must form a single unit to ease integration with other components.
5. The setup embodiment must fully prevent external light from reaching the optical sensor.
6. The setup embodiment must be able to hold the flow cell.
   - **a.** The flow cell must be removable for cleaning, replacement, and maintenance.
   - **b.** The flow cell connection must be reliable and reusable.
7. The setup embodiment must be able to hold the optical sensor UI-1492LE-M.
   - **a.** The optical sensor must be aligned with both the laser module and flow cell when in use.
   - **b.** The distance between the optical sensor and flow cell must be adjustable.
   - **c.** The distance between the optical sensor and flow cell must be less than 5.0 mm.
8. The setup embodiment must be able to hold a laser module.
   - **a.** The laser module must be able to provide a constant amount of monochromatic light over a long duration.
   - **b.** The laser module must be able to have an optical output of 5mW.
   - **c.** The setup embodiment must minimize the risk of users being exposed to laser light.
   - **d.** The laser module must have a wavelength approximating 635nm.
9. It must be possible to recollect and store urine samples after testing (J.3, J.6).

List of wishes

1. Urine should flow as easily as possible through the system.
   - **a.** The urine pathway should be as short as possible.
   - **b.** The urine pathway should have a downward slope as much as possible.
   - **c.** The urine pathway should be made of material that minimizes the attachment of particles and eggs.
   - **d.** The urine pathway should be made of a chemically resistant and durable material.
2. Electronic components should be shielded from potential urine leaks as much as possible.
   - **a.** The flow cell connection should be fully shielded from all electronic components.
   - **b.** Potential damage due to urine leakage should be minimized for all areas.
   - **c.** The setup embodiment should be able to detect potential leakages.
3. The setup embodiment should be able to self-diagnose its condition.
4. The setup embodiment should be as compact and durable as possible (J.1).
5. The setup embodiment should require as little maintenance as possible (J.1 *).
6. The setup embodiment should be easily cleanable on all areas potentially exposed to urine (J.1 *).
7. The risks of user error should be minimized by design (J.1, J.6 *).

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

2.2. Diagnostic setup embodiment design process

For developing and designing the diagnostic setup embodiment, a total of three design cycles were performed. In this section, each of the design cycles is shortly discussed. Besides this, the complete documentation of the three design cycles can be found in Appendixes C, D, and E.

For the design cycles, it should be noted that limited design requirements could be identified in literature for the current application of in-line flow-based digital holography. As a result, the effect of various design choices could only be validated through repetitive experimentation with prototypes and incremental improvements until the requirements were met.

Initial design

The starting point for the initial diagnostic setup embodiment was the existing experimental setup developed by Patrick. As the experimental setup was already relatively defined, the freedom of design was fairly limited. Therefore, it was deemed unnecessary to perform an overall conceptual exploration for the diagnostic setup embodiment. Instead, a single embodiment design was developed. Where applicable, different options for components within the design were considered and discussed before making a design choice.

Components that were to be addressed within the design included the electronic components, urine tubing, flow cell connectors, and laser module. After design choices were made for each of the components and the digital design was completed, a physical prototype was created, as can be seen in Figure 13.

During validation of the prototype, it became apparent that the flow cells were prone to breaking. As the flow cells could not be altered, it was decided to design a flow cell placement tool, as discussed in chapter 4 (p.34). Besides this, urine tubing and flow cell connectors functioned well, and correct alignment of the components could be achieved. Still, the laser module, laser module window, and 3D-printed housing required improvements. The complete documentation of this design cycle can be found in Appendix C.

Improved design

For the improved diagnostic setup embodiment, four major design changes were made. Firstly, the laser module window size was increased to ease cleaning and improve illumination. Secondly, a lens was added to the laser module to create a parallel laser beam. Thirdly, a less translucent filament was used for the 3D-printed housing to block out external light. Finally, the software control of the optical sensor was switched from the computer to the Raspberry Pi that the Sodos will be based on. The use of a Raspberry Pi will be elaborated upon in part C, section 2.1 (p.56) and Appendix P.

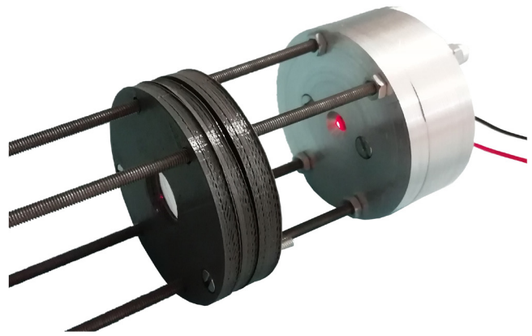


Figure 14. Adjustable laser module frame.

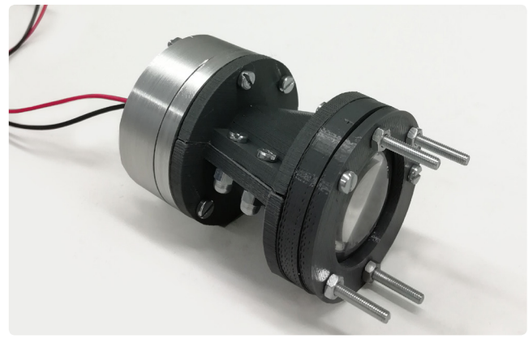


Figure 15. Improved laser module embodiment design.

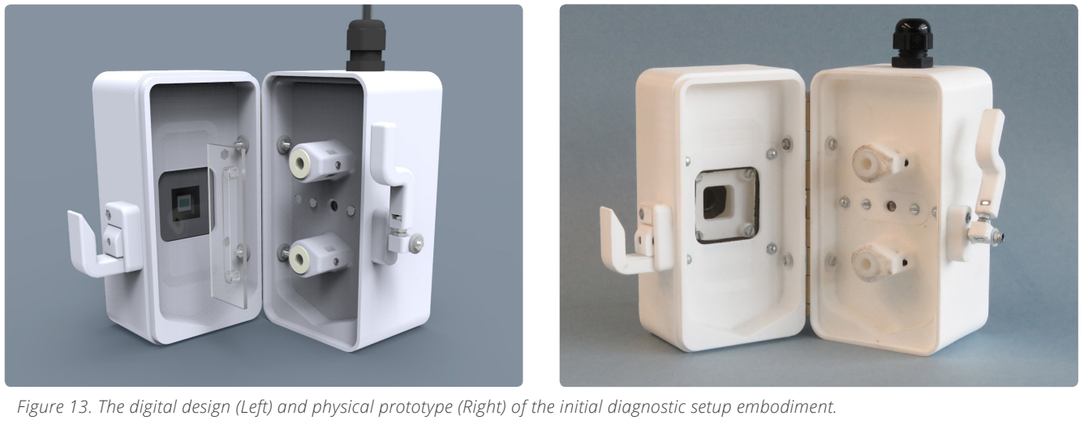


Figure 13. The digital design (Left) and physical prototype (Right) of the initial diagnostic setup embodiment.

For this design, a new prototype was created. In addition, an adjustable laser module frame was created to tune the distance between the new lens and the laser diode, as can be seen in Figure 14. The resulting laser module can be seen in Figure 15.

Validation of the prototype was performed together with the validation of the improved fluid insertion system, as seen in Figure 16. In this, it was clear that the prototype performed substantially better than the initial design. Still, there seemed to be variation in the exact position of the flow cell relative to the optical sensor, and the illumination seemed uneven at a low current. As the recommended changes were expected to ensure the diagnostic setup embodiment meeting its requirements, the next design iteration was to be an integrated design. The complete documentation of this design cycle can be found in Appendix D.

Integrated design

For the integrated diagnostic setup embodiment, a system was introduced for the automatic adjustment for variations in relative optical sensor and flow cell positioning. In addition, the hinge and hook design used to close the embodiment was simplified and the design was integrated with the components developed in parallel. Upon doing so, the software control for the optical sensor was changed from a continuous capture mode to a trigger based mode, to improve the timing and reliability of the sensor. The resulting design can be seen at the beginning of this chapter in Figure 12 on page 23.

During validation it was clear that the changes greatly improved performance. Still, the illumination was found to be insufficiently consistent. To improve this, changes were made to the materials used, and to the configuration of the laser module and optical sensor. This included the removal of the previously introduced lens. The improved configuration meets the requirements set out, and therefore did not require further development. The complete documentation of this design cycle can be found in Appendix E.

2.3. The resulting diagnostic setup embodiment

The integrated diagnostic setup embodiment shown in Figure 12 on page 23 is capable of performing reliable flow-based in-line digital holography measurements on fluids inserted into the flow cell. When opened, the setup allows the user to place a flow cell in the custom made watertight press fittings, after which the user can connect the USB cable of the optical sensor to the USB connector embedded in the integrated prototype, and close the diagnostic setup. By doing so, a spring-based system is automatically activated to adjust the system for any variation in the relative positioning of the optical sensor and the placed flow cell.

After closing the slide lock on the side of the setup, measurements can automatically be performed by the diagnostic setup. To do so, the laser diode is activated milliseconds before a measurement is to be taken. As the setup blocks out all external light, this is the only light illuminating the optical sensor through the flow cell. A command send by the Raspberry Pi causes the optical sensor to take a measurement, after which the laser diode is deactivated and the system is ready for the next measurement to be performed. If the setup is opened during a measurement, the opening of the slide lock is detected by the system and causes the laser diode to be immediately deactivated, reducing the chance of users exposing themselves to the laser light.

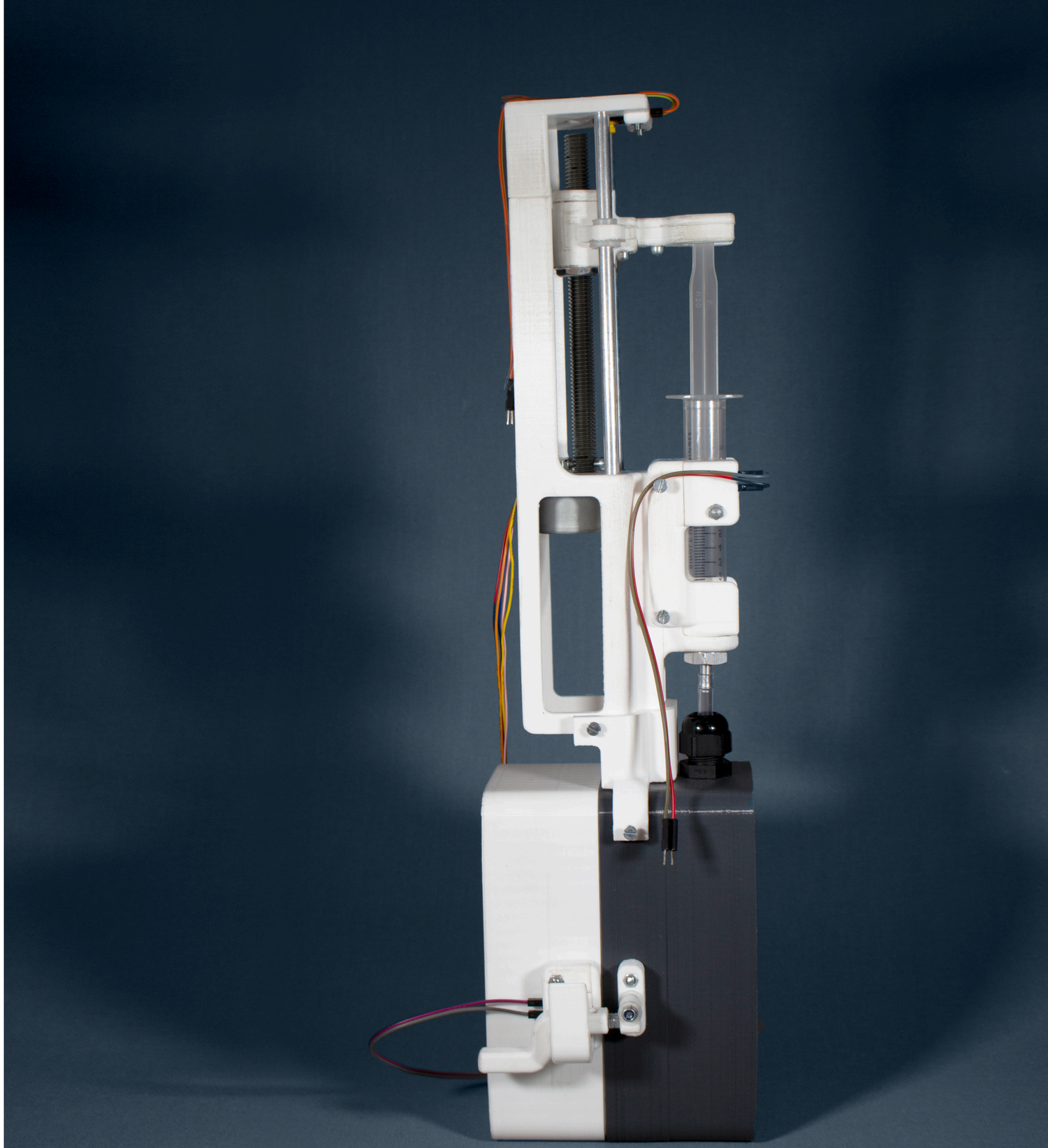


Figure 16. Combined improved diagnostic setup embodiment and improved fluid insertion system.

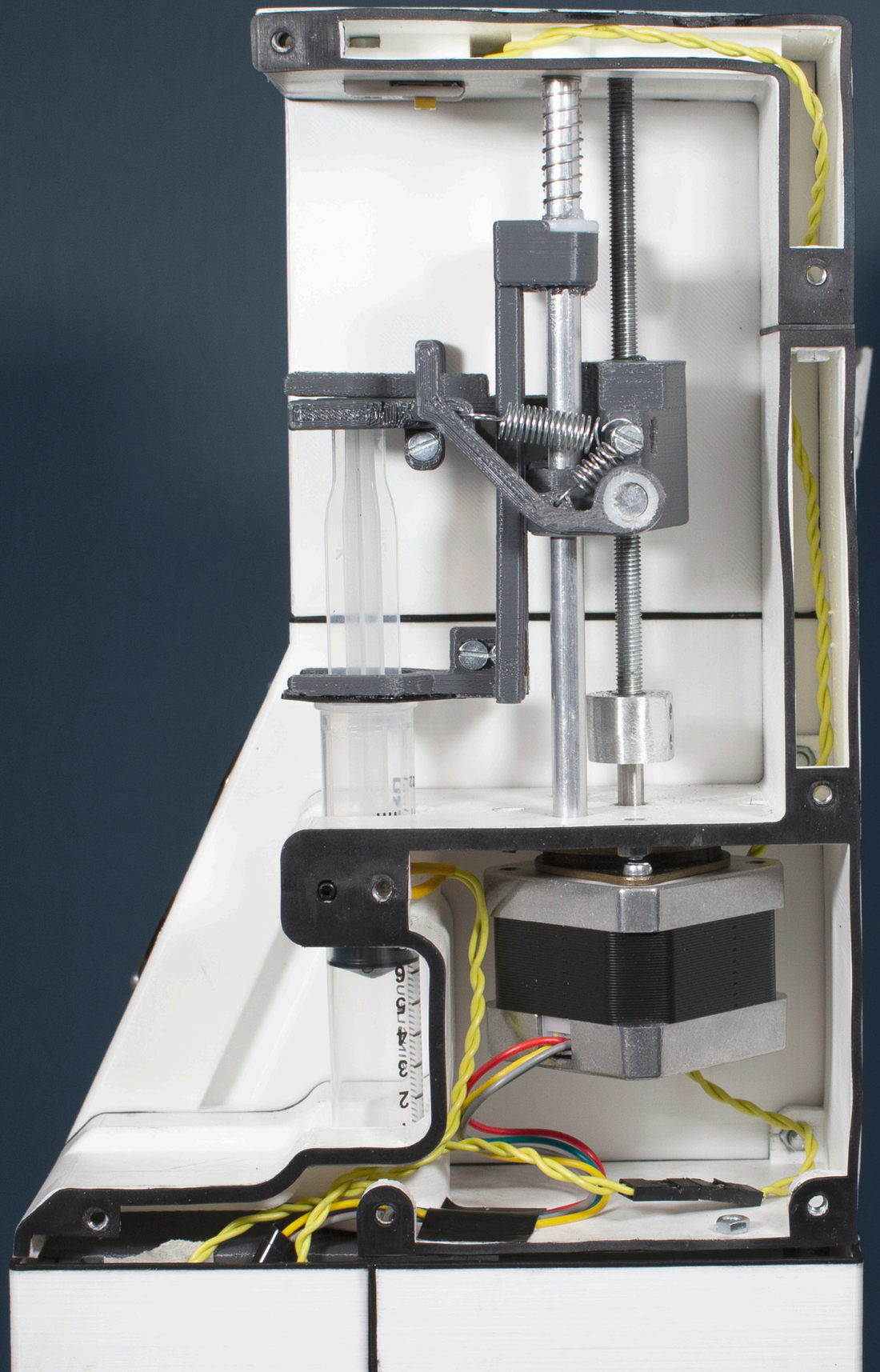


Figure 17. Side view of the improved integrated fluid insertion system.

3.
Fluid insertion system

In the conceptual design of the Sodos, it was mostly assumed that the use of gravity was sufficient for the urine to pass through the flow cell accordingly. However, during Patrick's development of the experimental setup it became apparent that a low and constant flow rate was required for the method to work accordingly. Therefore, it was decided to insert urine directly and controlled using a syringe.

Still, Patrick experienced great difficulty in manually achieving a sufficiently low and constant flow rate for a long duration. As this was already considered difficult in highly controlled conditions, the manual use of syringes was not considered feasible in the envisioned context. Therefore, it was decided to design a system for the automatic insertion of fluids.

To ensure a well argued design process for the fluid insertion system, a list of requirements and list of wishes was first created. Based on this, a conceptual exploration was performed, followed by the creation of an initial embodiment design and prototype. Based on the validation of the prototype, iterative design processes were performed until the requirements were met sufficiently. After this, an integrated design was created in which the fluid insertion system was combined with the other components developed in parallel.

As can be seen in Figure 9 on page 16 and the visual above, the chapter on the fluid insertion system is part of the diagnostic technology development.

3.1. Requirements and wishes

For designing the fluid insertion system, the non-prioritized list of requirements and list of wishes were again based on in-depth discussions with Patrick, requirements identified during the context analysis by Mirte, observations of the experimental setup, and logic reasoning. Besides the requirements and wishes set out specifically for the fluid insertion system, general product requirements set out in part C, chapter 1 (p.54) were also applicable. As it was not yet certain how the fluid insertion system would be positioned and designed for in the product embodiment design, this was not a major consideration in designs prior to the integrated design.

List of requirements

1. The fluid insertion system should not leak during insertion.
2. Spillage should not be able to reach internal compartments or electronics.
3. The flow rate must be easily and digitally controllable.
   - **a.** It must be possible to insert fluids at a variable rate.
   - **b.** The exact flow rate during insertion must be known.
4. The fluid insertion system must be easily and completely cleanable (J.1).
   - **a.** The components of the fluid insertion system exposed to fluids must not contain edges behind which particles can get stuck.
5. The fluid insertion system must not require disposable materials.
6. The fluid insertion system must be able to process 10ml of urine (J.3).

List of wishes

1. The risks of user error should be minimized by design (J.1, J.6 *).
2. The fluid insertion system should have minimal energy consumption.
3. Fluid insertion should require a minimal duration of user interaction.
4. The fluid insertion system should have a low cost and require little maintenance.
   - **a.** The fluid insertion system should be reachable for maintenance.
5. The fluid insertion system should be able to process more than 10ml of urine (J.3 *).
6. The fluid insertion system should be usable with syringes, as this is desirable in the envisioned context (J.3).
7. The fluid insertion system should be as cheap as possible.
8. The fluid insertion system should be directly combinable with the diagnostic setup embodiment.
9. The fluid insertion system should be position based (Appendix F.1).
10. The fluid insertion system should be able to self-diagnose its condition.

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

Figure 18. The digital design of the initial fluid insertion system.

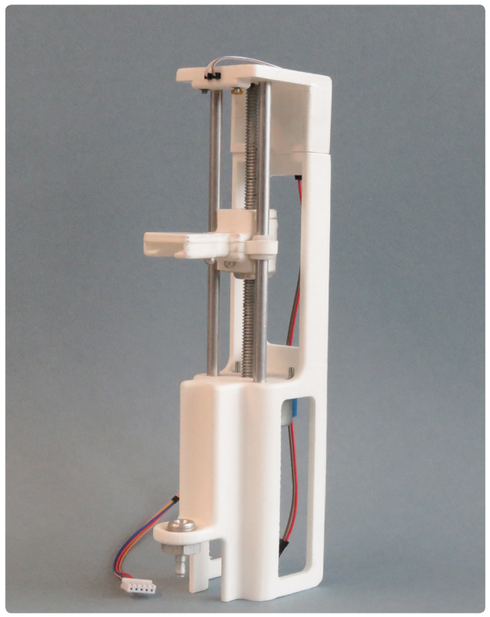


Figure 19. The physical prototype of the initial fluid insertion system.

3.2. Fluid insertion system design process

For developing and designing the fluid insertion system, a total of four design cycles were performed. In addition, small design improvements were often made within the cycles. In this section, each of the design cycles is shortly discussed. The complete documentation of the four design cycles can be found in Appendixes F, G, H, and I.

It should be noted that throughout the design process, various unknown parameters were present that could not be easily estimated, including fluid viscosity and internal resistances. To ensure a rapid design process, trial-and-error approaches were often implemented. In this, prototypes with single parameter changes were created and evaluated to determine the influence of specific design choices. This resulted in a large number of prototypes with incremental changes, as demonstrated in Figure 20.

Initial design

As no design choices were made for the fluid insertion system prior to the project, a conceptual exploration was first performed. In this, potential solutions were identified in literature. Using this and the lists of requirements and wishes set out, it was decided to develop a position based syringe control system suiting the specific needs of the diagnostic setup.

To do so, an initial design was created and prototyped, as can be seen in Figure 18 and Figure 19. This design used a standard stepper motor with an internal gearbox in combination with a motor driver to rotate a lead screw rod. Aside from this rod, there were two guiding optical axes. A syringe holder was designed to hold the top of the syringe and to slide over the optical axes, as seen in Figure 20. This syringe holder also contained a nut that was placed over the lead screw rod to enable precise linear movement of the syringe. On the top of the optical axes, a button was placed to enable calibration of the system. The prototype was controlled directly by a Raspberry Pi via Python algorithms to perform calibration and to move at predetermined speeds. The use of a Raspberry Pi will be elaborated upon in Part C, section 2.1 (p.56).

In addition, the prototype could be combined with the initial diagnostic setup embodiment to form a functional whole. When doing so, the urine pathway was kept vertical to allow the urine to flow through the system completely.

Initially, validation of this prototype was performed by directly connecting it to a flow cell via the flow cell connectors and testing its performance. Upon improving the algorithms, the prototype was also validated in combination with the experimental setup by Patrick, as seen in Figure 21. This, to observe the direct influence of the prototype on the quality of the measurements.

When testing with SH eggs in saline solution, the prototype

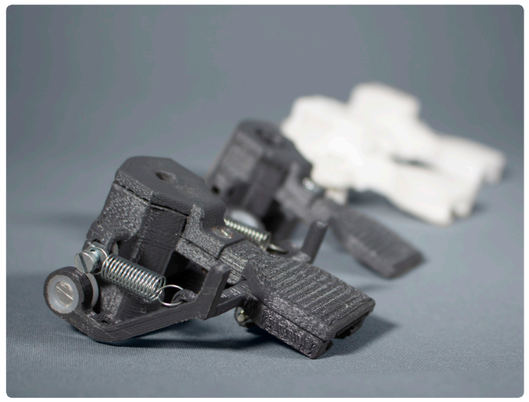


Figure 20. Four syringe holder prototypes out the six created.

worked completely as expected, and typical footage could be obtained. Still, when performing tests with SH eggs in urine solution, the system was unable to move near the fully extended and compressed syringe positions. It is therefore recommended to increase the exertable force of the system and to improve the support of the syringe to reduce undesirable deflection. The complete documentation of this design cycle has been included as Appendix F.

Improved design

For the improved fluid insertion system, two major improvements were to be made. The first was to improve the maximum force that can be exerted on the syringe. For this, the motor driver and pitch of the lead screw rod were

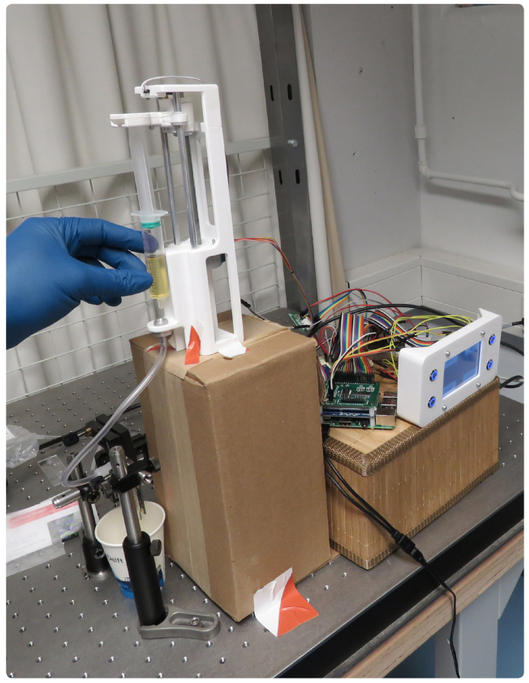


Figure 21. Setup for validating the initial fluid insertion system and experimental setup.

evaluated. In addition, attempts were made to reduce the resistance in the system. The second point was to improve the support and guidance provided to the syringe. For each of these points, prototypes were created and individually evaluated. The resulting changes formed the improved design and prototype.

The validation of the prototype was performed together with the validation of the improved diagnostic setup embodiment prototype, as can be seen in Figure 16 (p.27). It was found that the performance of the prototype had significantly improved and syringes could now be completely compressed. However, it was found that air bubbles often tended to remain within contaminated flow cells. These bubbles had a disruptive effect on the footage obtained, and prevented the desirable laminar flow. These bubbles were found to be removable by compressing the syringe shortly at a high rate. As the maximum speed of the current system was insufficient for this purpose, it was recommended to increase the maximum speed of the design. As only a single recommendation remained, the next design iteration was to be an integrated design. The complete documentation of this design cycle can be found in Appendix G.

Integrated design

For the integrated fluid insertion system design, quite a few changes were made to ensure compatibility with the other components developed in parallel. Most of these changes were based on general product requirements and therefore discussed in part C: Product embodiment. As a result, the main design change to be made was to increase the stepper motor's maximum speed.

The stepper motor used up to this point has a highly limited maximum speed. Therefore, a different stepper motor was to be selected to reach the estimated required speed of 960°/s or 4mm/s. Still, the exact required speed and torque were unknown, and the output torque of a stepper motor depends on its speed, motor design, motor driver, and provided voltage. Therefore, a standardized stepper motor size was chosen to enable experimentation with multiple stepper motors in a single prototype. This enabled the selection of a suitable stepper motor configuration, and resulted in the prototype seen in Figure 22.

During validation of the prototype with urine samples, the system seemed capable of pushing out air bubbles. Still, heavily contaminated flow cells could not always be cleared and air bubbles were also found to rise from the bottom of the flow cell during measurements. Removing these bubbles with this method would result in an excess of urine being disregarded. Therefore, experiments were performed to find alternative methods. During this, it was quickly noticed that the retraction of urine into the syringe allowed air bubbles to rise towards the syringe, whilst downwards motion had relatively little effect. Still, the current prototype is not designed for fluid retraction. Therefore, it is recommended to adjust the design to enable automatic fixation of the

Figure 22. Integrated fluid insertion system prototype Integrated fluid insertion system prototype

syringe barrel and to reduce vertical play within the syringe holder. The complete documentation of this design cycle has been included as Appendix H.

Improved integrated design

As recommended, the improved integrated fluid insertion system should be redesigned to fixate the barrel of the syringe and to reduce vertical play of the syringe holder.

Based on identified requirements and wishes for these functionalities and the existing design, a redesign was made. In this, a system was made that is only activated when the fluid insertion system is performing a cleaning or measuring procedure. Due to this, the user is only able to place and remove the syringe when this is required, reducing the chance of user errors and protecting the user against potential urine spillages. The introduced system consists of a redesigned syringe holder that eliminates vertical play during procedures and an addition part that keeps down the syringe barrel during procedures. Both make use of springs to achieve these effects. The resulting prototype can be seen at the beginning of this chapter in Figure 17 on page 29. In addition, a digital Anti-Bubble System (ABS) has been developed in collaboration with Patrick to detect and remove air bubbles prior and during measurements. For this, the maximum speed of 4mm/s was not required.

During validation, the prototype worked nearly perfect, and no further improvements could be identified. It was only after prolonged usage that the nylon plain bearings used by the syringe holder started to wear out. As a result, the accuracy of the system was reduced and increased friction caused severe malfunctioning. To permanently solve this problem, the syringe holder was redesigned to include linear ball bearings, and the aluminum optical axes were replaced with precise hardened steel rods, resulting in the final prototype seen in Figure 23. The complete documentation of this final design cycle has been included as Appendix I.

3.3. The resulting fluid insertion system design

The improved integrated fluid insertion system shown in Figure 23 is capable of reliably and precisely inserting and retracting fluids into the flow cell. The system automatically performs calibration when required, and can move at a maximum vertical speed of 2.5mm/s or 0.47mL/s at an accuracy of 4µm or 0.7µL, exerting a maximum pressure of 163kPa.

During procedures, the syringe is automatically fixated in the system to reduce play, user error, and the potential for urine spillage. The system is digitally and physically combined with the diagnostic setup embodiment to form a functional whole, enabling the automatic detection and removal of air bubbles, and synchronization between the movement of fluid and the capturing of data.

Figure 23. The improved integrated fluid insertion system with improved bearings and steel optical axes.

4.
Flow cell placement tool

As introduced in section 2.2 on page 25, it was quickly noticed that the flow cells were relatively easily contaminated at the area of interest, and vulnerable to mishandling in the surroundings of the flow channel. This was especially the case when the flow cells were frequently placed and removed from the flow cell connectors of the diagnostic setup embodiment. Therefore, the need was identified for creating a specially designed flow cell placement tool. As this is considered a relatively small part of the project with a temporary nature, the design process was intentionally kept short.

As with the other components, a list of requirements and list of wishes was first created. Based on this, an initial embodiment design and prototype was created and validated. After this, iterative design processes were performed until the requirements were met sufficiently.

The resulting flow cell placement tool is an addition to the product embodiment design rather than a part of it. This design is therefore not integrated during the product embodiment development.

As can be seen in Figure 9 on page 16 and the visual above, the chapter on the flow cell placement tool is part of the diagnostic technology development.

Figure 24. The improved flow cell placement tool.

4.1. Requirements and wishes

For designing the flow cell placement tool, the non-prioritized list of requirements and list of wishes were based on the geometry and physical properties of the flow cell, observations of the flow cell breaking during placement and removal from the flow cell connectors, and logic reasoning.

As the flow cell placement tool is not part of the product embodiment, but rather an addition, the general product embodiment requirements and wishes set out in part C, chapter 1 (p.54) will not be included in this design process.

List of requirements

1. The flow cell placement tool must be able to hold the flow cell without relying on external forces.
2. The flow cell placement tool must not contaminate the area of interest of the flow cell.
3. The flow cell placement tool must not require excessive space during usage, as this may complicate usage in the limited space available.
4. The flow cell placement tool must enable placement and removal of the flow cell in the flow cell connectors.
   - **a.** The positioning of the flow cell after placement must be constant.
   - **b.** The flow cell placement tool must not exert its forces on the vulnerable center of the flow cell during placement.
   - **c.** The flow cell placement tool must not exert its forces on the vulnerable center of the flow cell during removal.

List of wishes

1. The flow cell placement tool should not be prone to user errors.
   - **a.** The flow cell placement tool should be intuitive to use.
   - **b.** The flow cell placement tool should not allow unintended forces to be exerted on the flow cell due to mishandling.
   - **c.** Placement of the flow cell in the flow cell placement tool should be user friendly.
   - **d.** Removal of the flow cell from the flow cell placement tool should be user friendly.
   - **e.** It should be possible to operate the flow cell placement tool with a single hand.

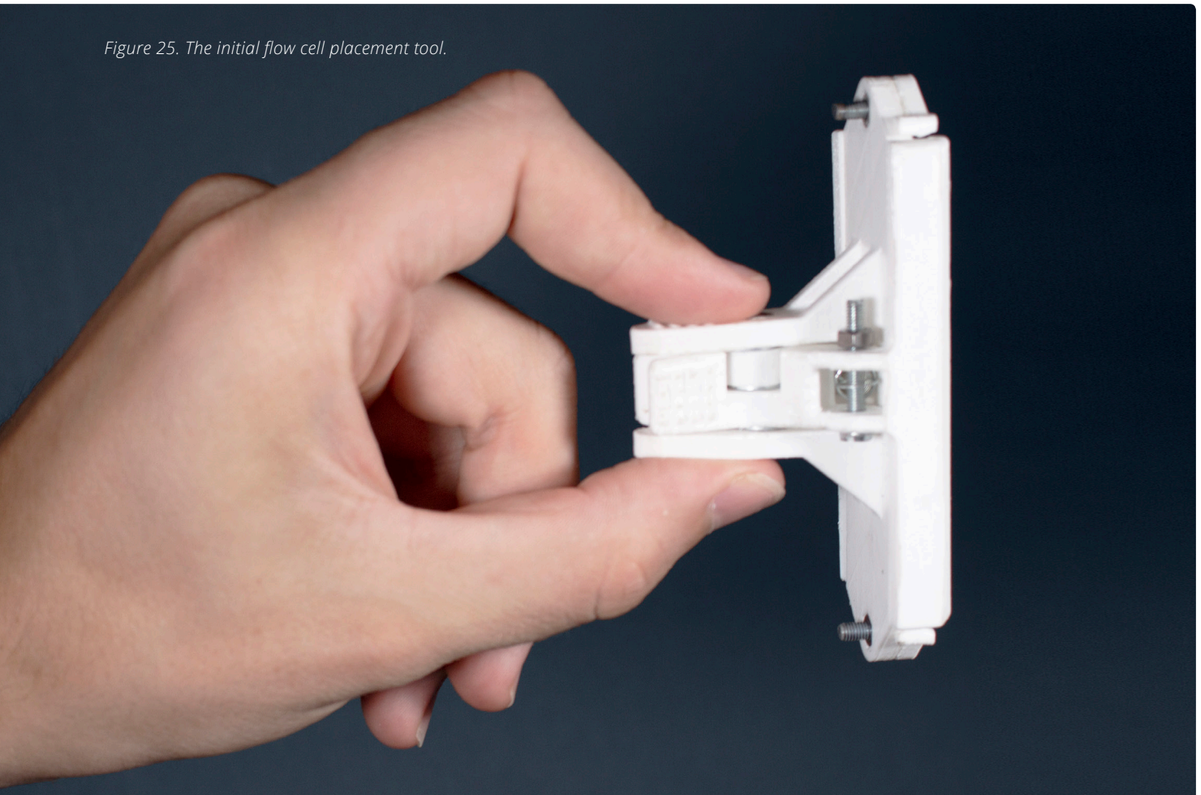


Figure 25. The initial flow cell placement tool.

4.2. Flow cell placement tool design process

For the development of the flow cell placement tool, two rapid design cycles were performed. In this section, both cycles are shortly discussed, whilst the complete documentation of the cycles is available in Appendixes J and K.

Initial design

As the flow cell placement tool is considered a smart part of the total project with a temporary nature, no conceptual exploration was performed. Instead, an embodiment design was quickly created using the lists of requirements and wishes set out. This resulted in the prototype seen in Figure 25.

This simple tool consists of three main parts; being a basis and two rotatable arms. Due to a spring between the arms, the tool can hold on to the long edges of the flow cell without relying on external forces. During placement, the stress is distributed by the basis of the tool. During removal, the stress is distributed over the long edges of the flow cell by the arms. The envisioned usage of the tool can be seen in Figure 26.

The functional validation of the flow cell was performed throughout experimentation with the diagnostic setup. In addition, interactive validation was performed with short user tests with fellow students. From this, it was found that even though the prototype was functional, it was not able to prevent some flow cells of being damaged. Aside from this, the arms were not always able to hold the flow cell without manual adjustments, and the intended usage was not always reproduced by the user. Therefore, it was recommended to improve the stress distribution and reliability of the design and to better guide the user towards the intended usage. The complete documentation of this design cycle can be found in Appendix J.

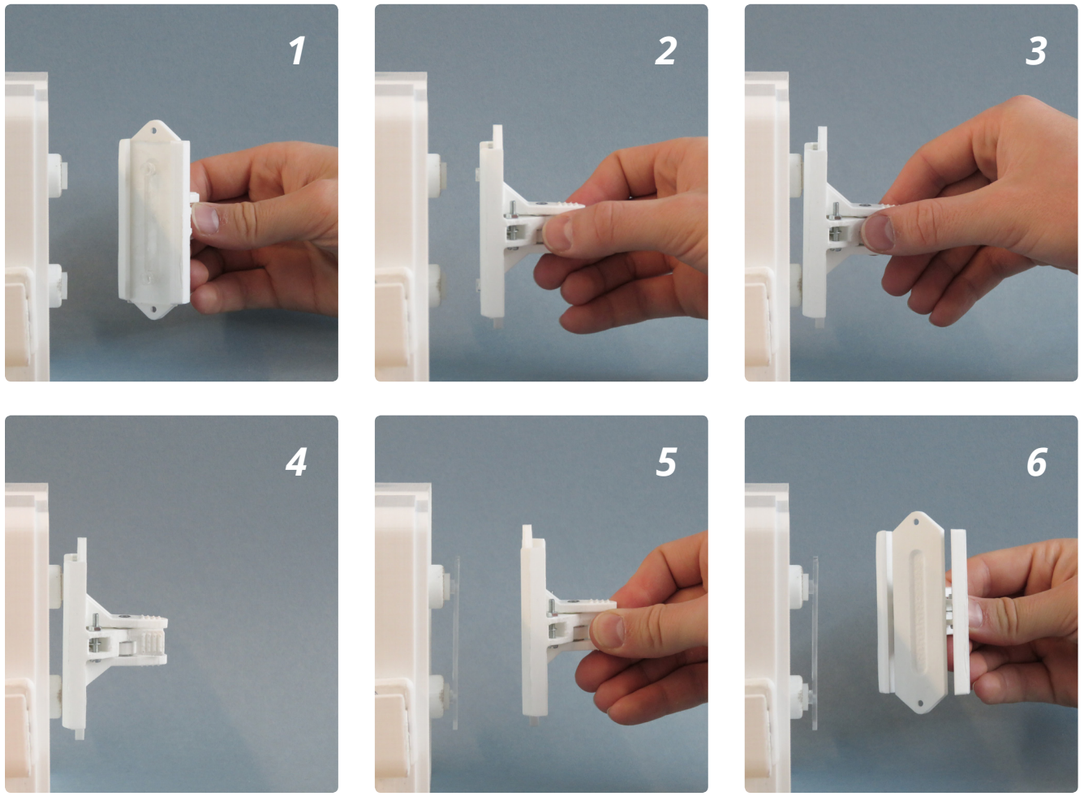


Figure 26. Envisioned usage of the initial flow cell placement tool on the initial diagnostic setup embodiment.

Improved design

As the arms of the initial design were not sufficiently distributing the stresses being exerted and often required manual adjustments, they were reconsidered as a whole. This resulted in a complete redesign using a different working method. In this, the contact area between the flow cell and tool is maximized on both sides to better distribute the stresses being exerted. To do so, a design was made in which the front and back of the tool can move relative to one another when desired, to hold or release the flow cell. By default, the flow cell is being held into place using a spring, which forces the front towards the back. When pushing the button on the back of the tool, the front is pushed away from the back, allowing the flow cell to be slided in and out to the side. In addition, all surfaces potentially in contact with the flow cell have been covered in rubber to prevent peak stresses.

To guide the user in using the tool, rubber has also been used to cover all intended interfaces on the back of the tool. During placement and removal of a flow cell, the back and front part should be respectively used to exert forces. This can be seen in the envisioned usage during placement, showed in Figure 27. To guide the user in exerting forces on the correct part, arrows have been laser cut into the rubber interfaces indicating the associated direction of movement for using each interface. Still, using the wrong interfaces would not result in damage to the flow cell. The resulting prototype can be seen in Figure 24 on page 34.

Validation again consisted of functional validation throughout experimentation with the diagnostic setup, and interactive validation using short user tests with fellow students. From this, it was found that the prototype was functional and able to prevent flow cells from being damaged. Besides this, the usage was still relatively unintuitive for fellow students, but could be well performed once the envisioned usage was explained to the user. Due to users being able to place the flow cell reliably without damaging the flow cell, and the limited importance of the tool, no further iterations were performed.

4.3. The resulting flow cell placement tool design

The improved flow cell placement tool as seen in Figure 24 on page 34 is capable of holding flow cells without relying on external forces. It can be safely used to place and remove flow cells from the flow cell connectors of the diagnostic setup without contaminating the area of interest or damaging the fragile flow channel.

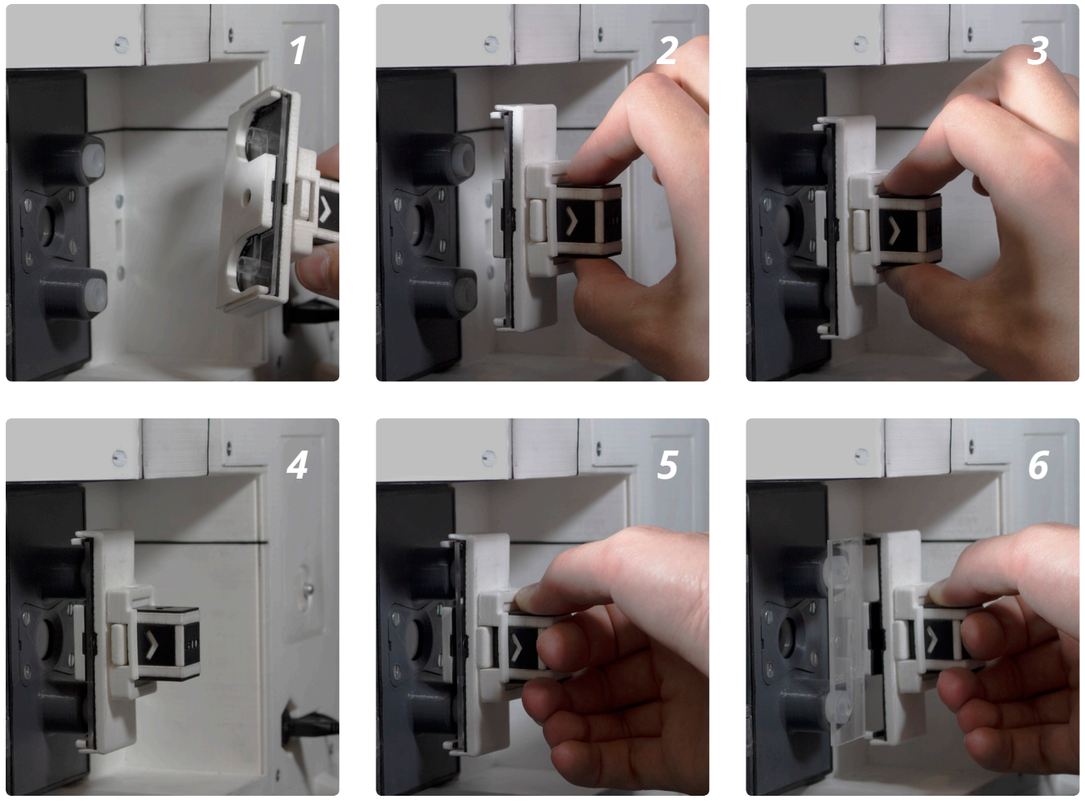


Figure 27. Envisioned usage of placement with the improved flow cell placement tool on the integrated diagnostic setup embodiment.

Part B
Product interaction

The development of the product interaction can be subdivided into two parts; the physical interaction development and the digital interaction development.

The physical interaction development consisted of both the physical interactions required for the handling of fluids and the physical embodiment design required to enable the digital interaction with the device. As the physical interaction of the fluid handling was mostly determined by the diagnostic technology, these interactions were partially given during the diagnostic technology development. Therefore, this part mostly consisted of combining the defined physical interactions and validating the physical interaction as a whole.

The digital interaction development consisted of the digital interaction directly on the physical interface of the Sodos. Optional interactions performed on secondary smart devices were not addressed or validated in this phase due to the scope of the project.

It should be noted for this part, that the resulting designs were made to be suitable for prototyping and validating purposes. Whether the designs were the only or best solution is arguable, as user experience (UX) design is generally considered subjective in nature [13].

Figure 28. The integrated digital interaction embodiment and improved digital interaction design.

1. The handling of fluids

As stated before, the handling of fluids was primarily determined by the diagnostic technology and that what was deemed necessary to ensure the functioning of the prototype. As a result, the general actions required were defined throughout the first part on diagnostic technology development. At an early stage of development, it was determined that these actions consisted of filling a syringe with urine, placing the syringe in the fluid insertion system, waiting for the urine to be analyzed, taking out the empty syringe, filling the syringe with clean water, placing the syringe in the fluid insertion system, waiting for the water to be used for cleaning, and finally taking out the empty syringe. As the urine ultimately does not have to be stored after a diagnosis has been performed by the Sodos, no cups would be placed underneath the device. Instead, it was suggested by Mirte Vendel that a tube could be used to connect the device to a large container. This container could contain chemicals to neutralize potentially present SH eggs.

Even though it had already been established that these actions were required, how they were to be executed and communicated to the user had not yet been elaborated on. To explore the actions, early tests were performed with fellow students to see how they interacted with syringes in combination with the initial digital interaction embodiment design and initial digital interaction design, as can be seen in Figure 29. At this stage there was not yet a representative prototype of the fluid insertion system, and therefore placing a syringe was simulated by laying them down in a paper box, and filling syringes was simulated using empty labeled cups.

As a result, these tests did not yet provide representative insights into the participants' usage of syringes. It was concluded that the representativeness of testing the handling of fluids would remain limited until the integrated prototype was ready for user testing.

1.1. The handling of fluids with the integrated prototype

With the integrated prototype, new tests were performed to assess both the handling of fluids, the integrated digital interaction embodiment, and the improved digital interaction. This was again tested with fellow students at the TU Delft. In this, the most complex interactions within the improved digital interaction design were tested with the participants being asked to think out loud. Thus, no additional focus was set on the handling of fluids. As these tests were only a simulation of the eventual usage no actual fluids were used, but labeled empty cups were used instead.

From these tests it became apparent that most participants were able to handle the syringes correctly without major problems. Still, it was found that placing the top of the syringe correctly in the syringe holder required multiple attempts for some participants. In addition, not all syringes were filled completely. This could cause problems, as it delays the moment at which the syringe gets a watertight connection with the funnel. As a result, the flow cell may not be completely filled with urine at the start of a measurement. Besides this, the current prototype still required a cup to be placed underneath the device to collect the urine for analysis. This had up to this point not been included in the tasks that were to be performed, and was therefore also not included in the improved digital interaction design.

To highlight that the syringe should be completely filled, and a cup should be placed underneath the device, the texts of the improved digital interaction design were adapted to improve the handling of fluids (Appendix O.1).

1.2. The handling of fluids in preparation for the field research

As part of the final preparations for the field research, the handling of fluids was further specified to ensure consistent quality in measurements. In this, the use of gloves, movement of syringes, and movement of cups were envisioned.

Ultimately, it was decided that for every measurement a clean syringe and cup should be used to prevent cross-contamination of the samples. Before the syringe was filled with urine, gloves must be put on and the urine sample must be mixed to distribute the sunken SH eggs across the sample.

After this, the clean syringe was completely filled with urine. If an excess of air was present in the syringe, the filling process must be repeated. After this, the syringe was held upside down up to the moment that it could be placed, and the measurement could be started immediately after. This, as SH eggs sink in urine, and the first 0.6-0.7 ml of urine could not be analyzed by the system. By holding the syringe upside down, the eggs were less likely to be present in the first 0.6-0.7 ml of urine, reducing the chance of missing light infections.

After each measurement, a cleaning procedure must always be performed. First, the cleaning procedure software was started. This caused the empty syringe of the measurement to be lifted, retracting the urine still present in the urine pathway. After the syringe was released, the cup could be removed without the potential dripping of urine, and the retracted urine in the contaminated syringe was added to the cup. A syringe only used for cleaning procedures was filled with clean water and placed. The cup filled with urine was again placed to collect the cleaning water, as this could still contain particles that remained present in the urine pathway.

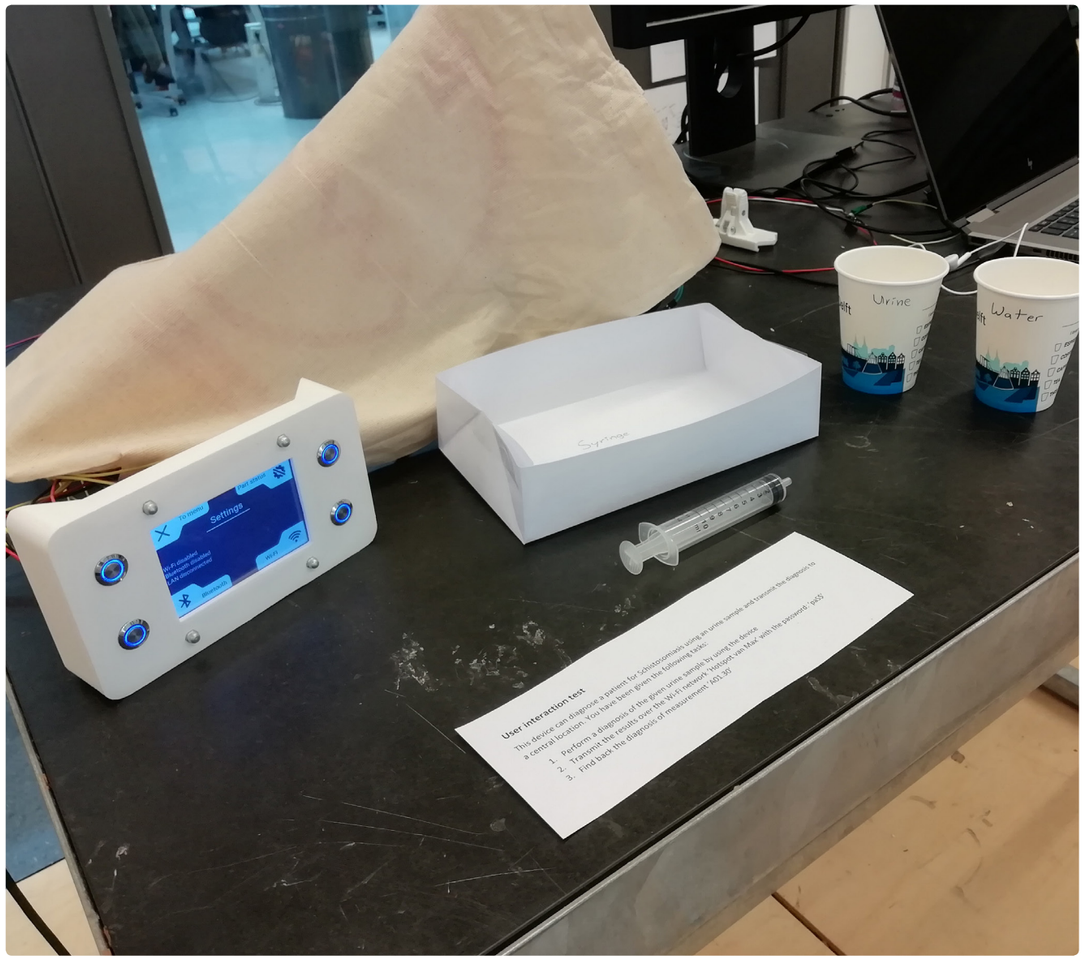


Figure 29. Validation of the fluid handling, initial digital interaction embodiment, and initial digital interaction design

After the cleaning procedure was completed, the empty syringe of the cleaning procedure was automatically lifted, retracting the water still present in the urine pathway. After the syringe was released, the cup was again removed and the retracted water in the syringe was added to the cup.

The contaminated syringe from the measurement could now be used with the collected urine sample and water to perform diagnosis via filtration and manual microscopy, and a new measurement could be started. Throughout this entire procedure, at least one glove must have been worn to handle all potentially contaminated surfaces.

2. Digital interaction embodiment

The physical embodiment design required for the digital interaction was to be directly applicable to the product embodiment design. This, as it could be determined from the start which parts of the digital interaction embodiment would be exposed in the product embodiment design, and a design not accounting for the eventual product design had limited value.

As can be seen in Figure 9 on page 16 and the visual above, the chapter on the digital interaction embodiment is part of the product interaction development.

2.1. Requirements and wishes

For designing the digital interaction embodiment, the non-prioritized lists of requirements and wishes were based on requirements identified during the context analysis by Mirte Vendel and logic reasoning. As the goal of the digital interaction embodiment was to be directly applicable to the product embodiment design, the design should strictly meet the relevant requirements and wishes set out in part C, chapter 1 (p.54). Therefore, these requirements and wishes were added to the lists of requirements and wishes for the digital embodiment design.

List of digital interaction requirements

1. The interaction embodiment must be clearly usable in both low and high illuminated conditions (J.1 *).
2. The interaction embodiment must be able to facilitate all potentially desirable interactions and interfaces.

List of product embodiment requirements

3. The product must be resistant to environmental conditions present in the envisioned context (J.1).
   - **a.** The product must be resistant to water and humidity (J.1 *) [12].
   - **b.** The product must be resistant to dust (J.1) [12].
   - **c.** The product must be able to withstand temperatures up to 60°C (J.8).
   - **d.** The product must resist chemicals potentially used for cleaning purposes (J.8 *) [12].
   - **e.** The product must be able to handle rough handling during transport (J.1).

List of digital interaction wishes

1. The risks of user error should be minimized by design (J.1, J.6 *).
   - **a.** Interactions should be quick whilst not being prone to user error.
2. The device should be able to draw attention when interaction is required (J.1 *).
3. The interface content should be adjustable to suit deviating scenarios and errors.
4. Instructions for correct usage of the device should be included, or should be self-explanatory (J.1 *).
5. Presented information should be easily and quickly understandable (J.7 *).
6. The interaction embodiment should not have an excessive amount of keys or buttons (J.7).
7. Contamination of interaction interfaces should be prevented (J.7).

List of product embodiment wishes

1. The device should be long lasting with minimal maintenance (J.1, J.6).
2. The device should be able to function for multiple hours with an insufficient power supply (J.1 *).
3. The product should be affordable for remote areas (J.2).
   - **a.** The product should be the most economically beneficial option (J.3).
4. The product should be resistant to environmental conditions potentially present in the envisioned context (J.1).
   - **a.** The product must have excellent durability for UV radiation exposure (J.8).
   - **b.** The product should be able to function in temperatures up to 45°C (J.1 *).
5. The device should be easy to use (J.7).
   - **a.** The device should be simple to use (J.7).
   - **b.** The device should be as small as possible (J.7).
6. The device should be easy to clean properly (J.1).
7. Correct usage of the device must require little training (J.7).

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

2.2. Digital interaction embodiment design process

For designing the digital interaction embodiment, two design cycles were performed. During this, the digital interaction embodiment was highly interdependent with the digital interaction design. In this section, both design cycles will be shortly discussed. The complete documentation of the cycles has been included in Appendixes L and M.

Initial design

For the digital interaction embodiment, an initial conceptual exploration was already performed by Mirte Vendel. Still, with the new insights on the diagnostic technology and previous personal experience, it was decided to reconsider this conceptual design.

Based on the requirements and wishes set out, a wide variety of concepts could be envisioned. To systemically process the various options, a morphological chart was created, as can be seen in Figure 30. As can be seen, four concepts were created using this chart. These concepts were further elaborated upon, and evaluated using a Harris profile, as can be seen in Figure 31. This resulted in the selection of the basic concept.

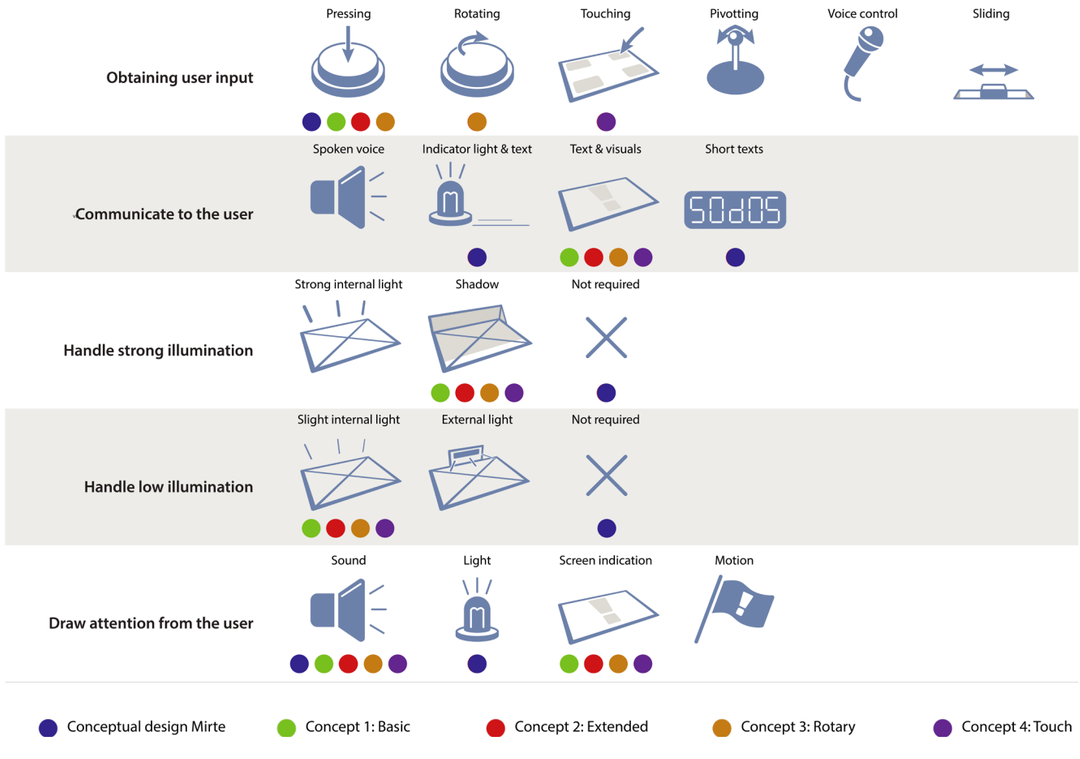
Based on the basic concept, an initial embodiment design and prototype were created, as can be seen in Figure 21 on page 31. In this, a TFT screen, a passive speaker, and four momentary switches were directly connected to a Raspberry Pi and held together using a 3D-printed part. The use of a Raspberry Pi will be elaborated upon in part C, section 2.1 (p.56) and Appendix P.

The initial prototype was validated with user tests together with the fluid handling and initial digital interaction, as seen in Figure 29 on page 43. During this, the participants considered themselves able to navigate through the interfaces. Still, the currently used momentary switches were often considered too small. In addition, it was recommended to place the screen at an angle and to maintain slots for the placement of fingers during usage. Besides this, it was noted that the current mechanism for holding the screen did not result in a watertight system. The complete documentation for this design cycle can be found in Appendix L.

Integrated digital interaction embodiment design

As the recommendations for this design cycle did not require fundamental changes to the design, it was decided that the design was sufficiently developed to perform this next design cycle as an integrated design. Thus, the previously made part for holding the functional components was now to be combined with the overall embodiment design.

Figure 30. Morphological chart for the digital interaction embodiment.



Due to this, the recommended finger slots were integrated with the panels to the sides of the digital interaction embodiment. In addition, an angled and watertight design was achieved by creating a special frame to fixate both the TFT screen and additional general electronics, as can be seen in Figure 28 on page 40 and Figure 36 on page 56. In this, larger momentary switches of the same type were obtained and implemented.

The resulting prototype was again validated together with the improved digital interaction and the fluid handling. From this, it became clear that the momentary switches can now be comfortably used, but not all users intuitively used the slots designed for placing the fingers. This is potentially undesirable, as it increases the chance of the prototype moving or falling over. For this purpose, design recommendations were formulated, as can be seen in the complete documentation of this design cycle in Appendix M.

2.3. The resulting digital interaction embodiment design

The integrated digital interaction design as seen in Figure 28 on page 40 can facilitate all potentially desirable interactions and interfaces of the digital interaction design. In this, it can guide the users towards the possible interactions using LED rings in the momentary switches, and draw the users' attention when deemed necessary using sound. In addition, slots have been designed for placement of the fingers during usage.

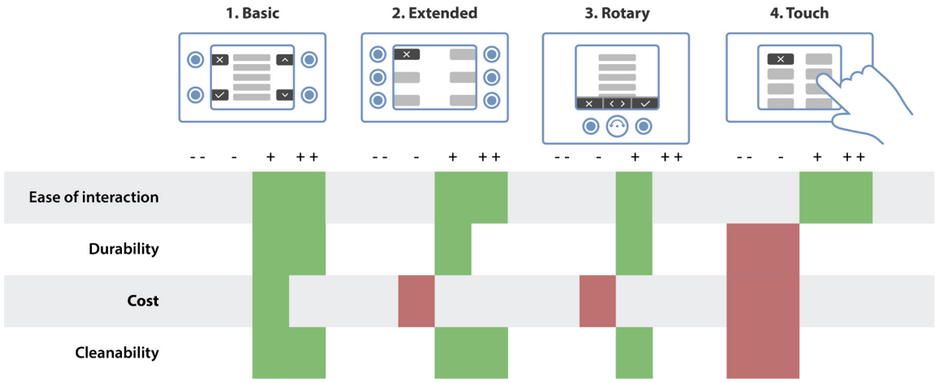
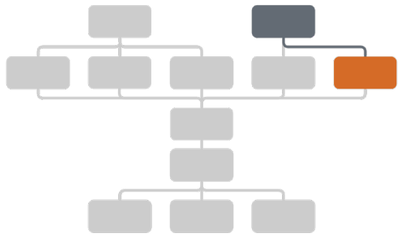


Figure 31. Harris profile for the digital interaction embodiment.

3. Digital interaction design

In the graduation project by Mirte Vendel, a conceptual interaction design was proposed, as shown in Part 3.10 of Vendel [9]. In this, different needs for the digital interaction were identified for the different potential user groups. Due to this, it was decided to have all essential interactions included in the Sodos itself, and to optionally extend on these interactions using a wirelessly connected smart device (Part 3.2, Vendel [9]).

This well-argued subdivision of digital interaction has been maintained within this project. The optional interactions that are to be made available using the connected smart device have not been designed for, as the scope is of the project has been limited to the direct design of the Sodos.



As can be seen in Figure 9 on page 16 and the visual above, the chapter on the digital interaction design is part of the product interaction development.

3.1. Requirements and wishes

For designing the digital interaction, the non-prioritized lists of requirements and wishes were based on requirements identified during the context analysis by Mirte Vendel, the general digital interaction embodiment concepts, and logic reasoning. During this logic reasoning, prolonged personal experience with the development of software applications and interface designs was applied.

List of requirements

1. The digital interaction design must be translatable to a custom segmented, passive matrix, monochrome LCD display.
   - **a.** The digital interaction design must only use two colors.
   - **b.** The digital interaction design must be translatable to a potentially low resolution display.
2. The diagnostic results must be communicable to users (J.1 *).
3. Correct usage of the device must require little training (J.7).
4. The digital interaction design must enable all essential digital interactions.
   - **a.** The digital interaction design must enable measurements to be performed.
   - **b.** The digital interaction design must enable the configuration of Bluetooth devices.
   - **c.** The digital interaction design must enable the configuration of Wi-Fi networks.
   - **d.** The digital interaction design must allow the user to revisit previous measurements.
   - **e.** The digital interaction design must enable the communication of system errors to the user.

List of wishes

1. The risks of user error should be minimized by design (J.1, J.6 *).
   - **a.** Interactions should be quick whilst not being prone to user error.
2. The device should be usable without the presence of a medical expert (J.1 *).
3. Presented information should be easily and quickly understandable (J.7 *).
   - **a.** Presented information should be interpretable for partially illiterate users (J.1. *).
   - **b.** Presented information should contain all necessary information (J.7).
4. Instructions for correct usage of the device should be included, or should be self-explanatory (J.1 *).
5. The interfaces should be adjustable to suit deviating scenarios and errors.

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

3.2. Digital interaction design process

For creating the digital interaction design, one complete design cycle and one partial design cycle were performed. In addition, small improvements and functional extensions were often made within the cycles. Throughout the process, the digital interaction design is highly interdependent with the earlier described digital interaction embodiment. In this section, both cycles will be shortly discussed. The complete documentation of the two cycles has been included in Appendixes N and O.

Initial design

To design the digital interaction the lists of requirements and wishes were used to create a flowchart of the essential digital interactions, as can be seen in Figure 32. Using this flowchart, concept selection could be performed for the digital interaction embodiment, as discussed in section 2.2 (p.46) and Appendix L.2. After this, the flowchart and the initial design and prototype of the digital interaction embodiment were used to create and validate the digital interaction design.

For this, various layouts potentially meeting the requirements and wishes were set out and evaluated with fellow students. Based on this, a layout was selected, tuned, and applied to the interfaces required to enable the flowchart of essential interactions. The resulting flowchart of interfaces can be seen in Figure 33. In this, the most complex interaction is establishing a connection to a Wi-Fi network, as this entails a virtual keyboard containing all 95 printable ASCII characters with a length of up to 63 characters [14]. The initial design for this can be seen in Figure 34.

To validate the digital interaction design, an individual Cognitive Walkthrough was first performed. After this, the slightly adapted designs were prototyped using Python and the Kivy library and integrated with the initial digital interaction embodiment.

The prototyped interaction design was validated together with the fluid handling and initial digital embodiment design, as seen in Figure 29 on page 43. During the validation, feedback obtained during each individual session was discussed with the participant after the session, and implemented in the digital interaction design before the

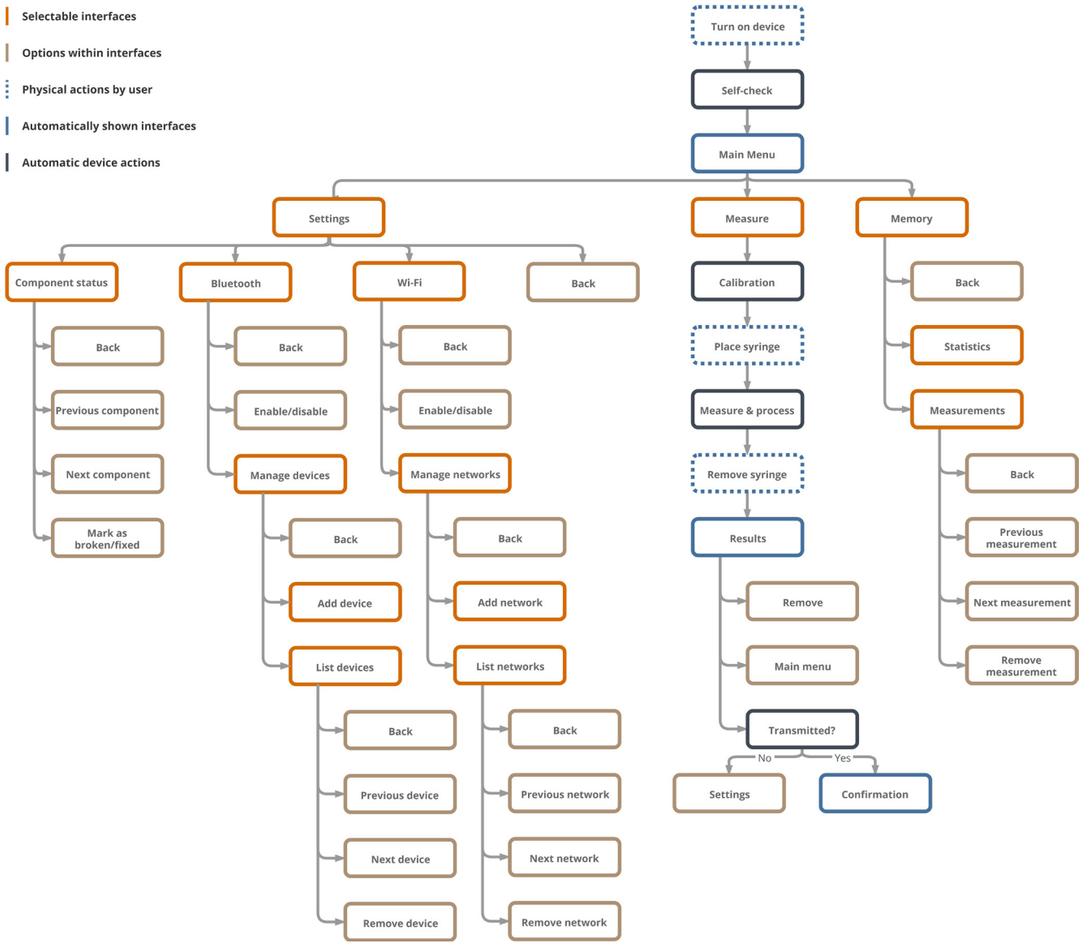


Figure 32. Flowchart of the essential interactions for the digital interaction.

next session was started. This was repeated until no more points for improvement were found, resulting in a total of eight participants and an adapted design that was further elaborated upon to form the improved digital interaction design. The complete documentation of this design cycle can be found in Appendix N.

Improved design

The iterative validation of the initial digital interaction design had resulted in consecutive changes that gradually transformed the initial design into an improved design. In addition to changes in the icons and words used, the virtual keyboard used for entering Wi-Fi passwords was changed various times. The result of this can be seen in Figure 35. After the iterative validation, the digital interaction prototype has been extended upon to include control of the fluid insertion system and to include a French version that can be selected during start-up.

To validate the accuracy of the translations, all interfaces were discussed with a native French speaking student. As the iterative validation already provided support for most changes and interaction evaluation was also to be performed in Ivory Coast, no overall validation was performed, making this only a partial design cycle. The complete documentation for this partial design cycle can be found in Appendix O.

3.3. The resulting digital interaction design

The improved digital interaction design and prototype as seen in Figure 28 on page 40 enables all interactions with the diagnostic device currently deemed desirable. The fully coded bilingual prototype entails all interactive functionalities, and simulates their intended functional behavior. The latter was preferred during development and validation due to the limited impact of user errors, and can easily be adapted to make the digital interaction prototype part of a fully functional and user friendly diagnostic device.

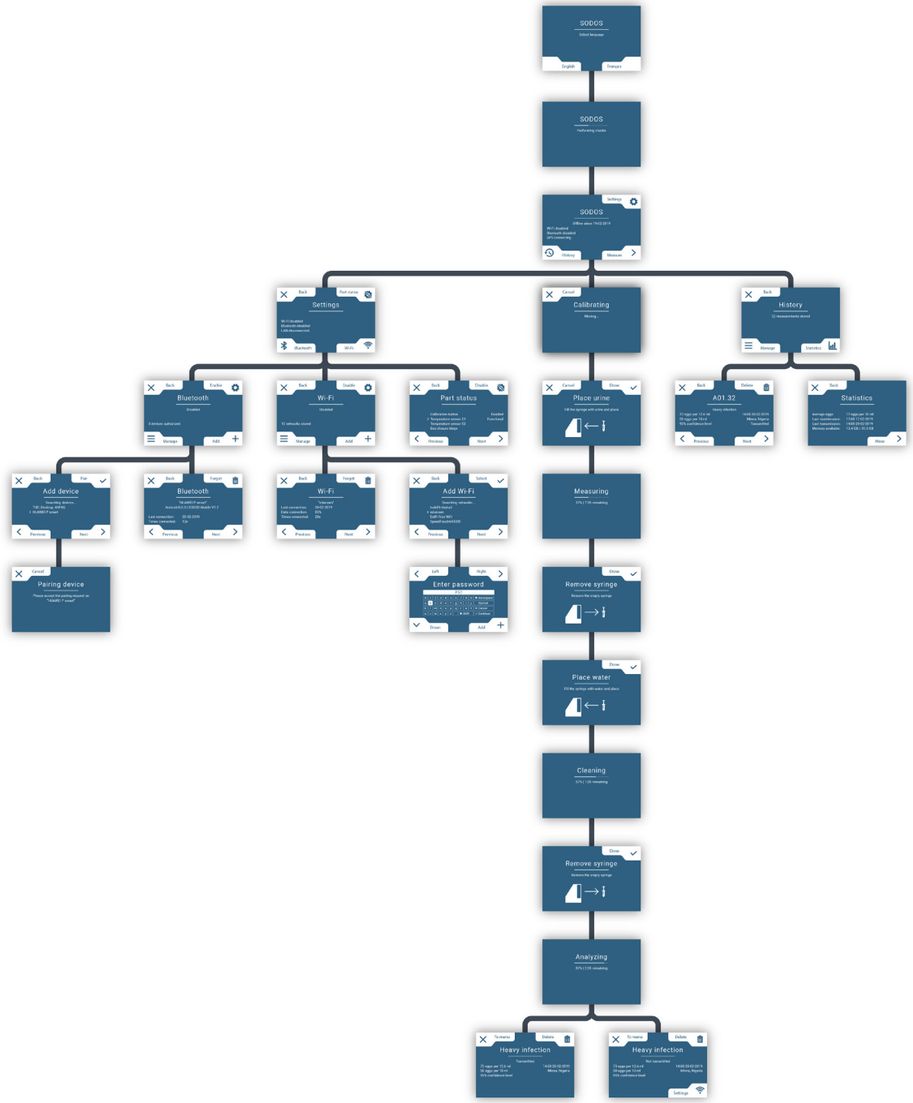


Figure 33. Interface flowchart for the digital interaction design

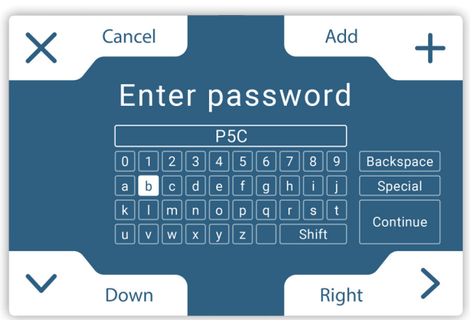


Figure 34. Initial interface with virtual keyboard for entering Wi-Fi passwords shown on scale 1:1.

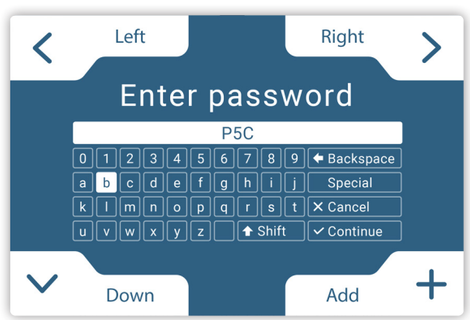
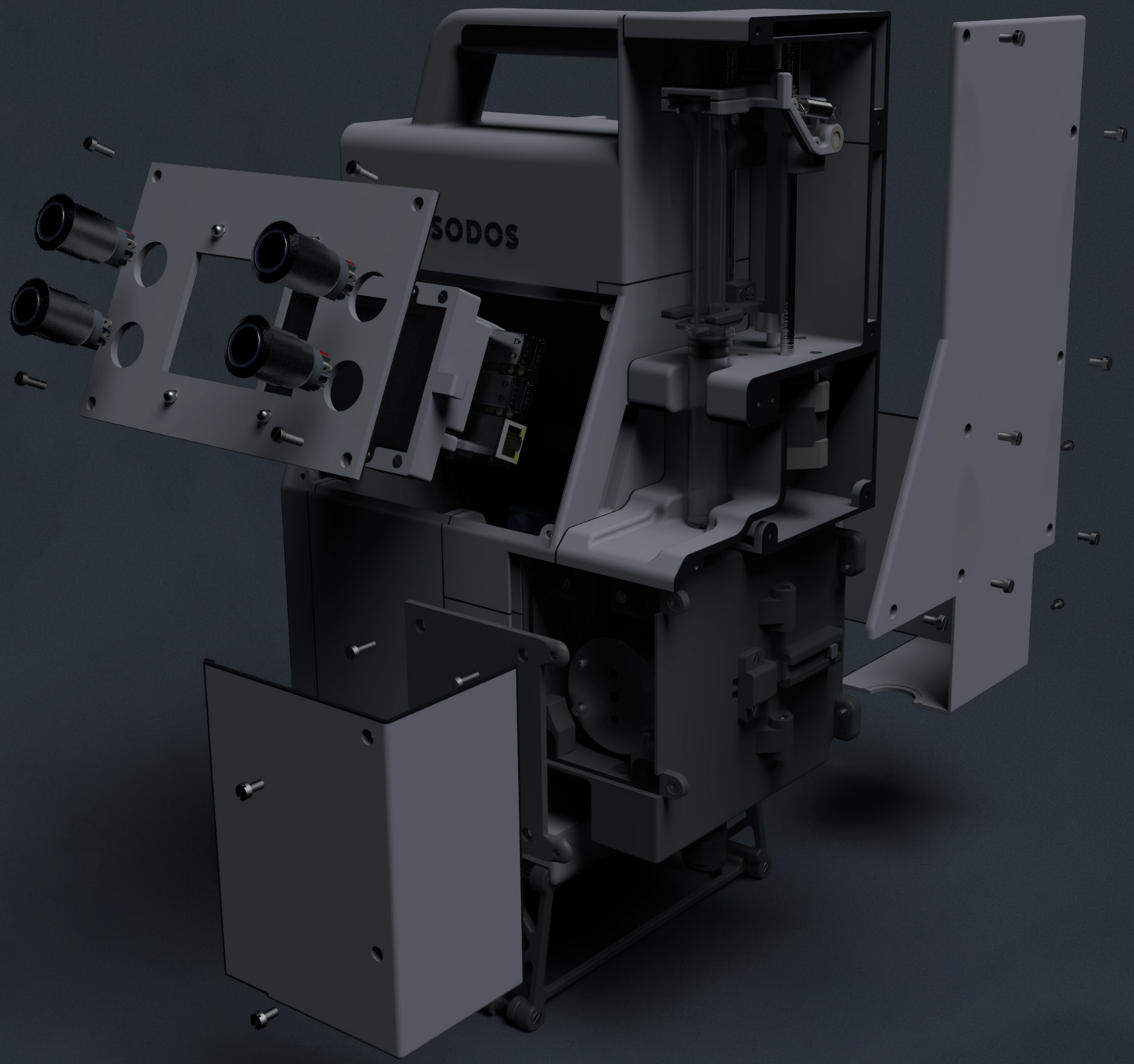


Figure 35. Improved interface with virtual keyboard for entering Wi-Fi passwords shown on scale 1:1.

Part C

Product embodiment



Once the individual components of the diagnostic technology and interaction required for the Sodos were sufficiently developed, a product embodiment design could be created to integrate the components and address overall design requirements.

The resulting integrated prototype was to be made both functional and interactive. In this part, general design considerations will be discussed, whilst considerations for individual components are discussed in Appendixes E, H, M, and O.

1. Product embodiment requirements and wishes

For the product embodiment, the non-prioritized lists of requirements and wishes were based on the requirements identified during the context analysis by Mirte Vendel, literature, and logic reasoning. These general requirements and wishes were often already applied or considered in the previously discussed design processes. This, to ensure compatibility during the product embodiment.

List of requirements

1. The device must be able to store at least four weeks of field research data locally (J.1).
2. The device must be portable for strong adults (J.1, J.3, J.7 *).
   - **a.** The device must be light enough to be lifted by strong adults (J.7 *).
3. The product must be resistant to environmental conditions present in the envisioned context (J.1).
   - **a.** The product must be able to handle an insufficient power supply (J.1 *).
   - **b.** The product must be able to withstand electrical disturbances potentially present in the electrical grid (J.1 *) [12].
   - **c.** The product must be resistant to water and humidity (J.1 *) [12].
   - **d.** The product must be resistant to dust (J.1) [12].
   - **e.** The product must be able to withstand temperatures up to 60°C (J.8).
   - **f.** The product must resist chemicals potentially used for cleaning purposes (J.8 *) [12].
   - **g.** The product must be able to handle rough handling during transport (J.1).
4. The user must be protected against potential urine spillages (Appendix F.5).
5. The device must be able to process at least 50 samples per day (J.1).
6. The device must be able to process 10ml of urine (J.3).
7. It must be possible to recollect and store samples after testing (J.3, J.6).
8. The device must be small enough and suitable for transportation as airplane hand luggage [15, 16].

List of wishes

1. The device must be long lasting with minimal maintenance (J.1, J.6).
2. The device should be able to function for multiple hours with an insufficient power supply (J.1 *).
3. The risk of the device moving on a surface should be minimized (J.1 *).
4. Using the device should safe time in comparison to the current protocol (J.3, J.7).
   - **a.** The device should be able to process up to 200 samples per day (J.2).
5. The product should be affordable for remote areas (J.2).
6. The product should be resistant to environmental conditions potentially present in the envisioned context (J.1).
   - **a.** The product should have excellent durability for UV radiation exposure (J.8).
   - **b.** The product should be able to function in temperatures up to 45°C (J.1 *).
7. The device should be able to process more than 10ml of urine and correct for the deviation in fluid amount (J.3 *).
8. The device should minimize the use of disposables (J.6 *).
9. The device should use syringes for the handling of fluids (J.3).
10. The device should be easy to use (J.7).
    - **a.** The device should be simple to use (J.7).
    - **b.** The device should be as small as possible (J.7).
11. Instructions for correct usage of the device should be included, or should be self-explanatory (J.1 *).
12. The device should be portable for all potential users (J.1, J.3, J.7 *).
    - **a.** The device must be light enough to be lifted by all potential users (J.7 *).
    - **b.** The device should be easy to hold on to by hand (J.7).
13. The device should not contain any loose wires (J.7).
14. The device must be easy to clean properly (J.1).
15. Correct usage of the device must require little training (J.7).

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

2. Product embodiment design

To create the complex product embodiment design, sketches, digital models, and prototypes were used to create a single suitable design. As there were many requirements and wishes for the design and various aspects were already determined during the development of the individual components, no overall conceptual exploration was performed.

First, the general composition of the internal components was to be determined. For this, several boundaries were present. This included the approximate dimensions of the digital interaction embodiment, diagnostic setup, and fluid insertion system. In addition, the requirements and wishes set out for the diagnostic setup embodiment forced the fluid insertion system to be vertically aligned above the diagnostic setup (req. 1, page 22). In addition, the current design must enable placement of a cup underneath the diagnostic setup to recollect the sample during validation. This forced the design to become very tall. Yet, the design needed to be small enough for transport as hand luggage (req. 8), and should be as small as possible in general (wish 10.b).

Due to this, it was decided to integrate a retractable stand into the design. This stand needed to create the elevation required for the placement of the collection cup and be reliably and quickly retractable during transport without increasing the height of the overall design. For this, different approaches were explored. Ultimately, a design was envisioned that could be quickly retracted to the back of the prototype to not further increase the height of the design. This stand consisted of three functional parts connected to each other and the main body of the design via aluminum rods that function as hinges. When retracted, the three parts were held in place by a small spring-based clip on the top back of the main body. When used, the stand was rotated towards the bottom of the main body where a slot was present to receive and clamp the far end of the stand. The angle between the three parts was limited by the geometry of the parts to create the exact angles required to form a stable stand. The stand could not be directly placed underneath the diagnostic setup, as this would complicate placement of the collection cup. Therefore, it was placed to the side of the diagnostic setup on other general components. To ensure a stable design, internal electronics were relocated to reposition the center of mass above the stand. This design was made to be feasible for prototyping purposes, and is not necessarily the most optimal solution for application during production.

Aside from the diagnostic setup and fluid insertion system, the digital interaction embodiment and general electronics also needed to be integrated into the design. As the digital interaction embodiment was to be usable parallel to the fluid insertion system and the design's height is not to be further increased, it was decided to place this component on the left side of the fluid insertion system from the user's perspective. This was decided, as it enables right-handed users to quickly alternate between using the digital interaction embodiment and the fluid insertion system, whilst keeping sight on both at all times.

Besides the digital interaction embodiment, the housing for general electronics was placed on this side of the design to keep the design as small as possible (wish 10.b). This housing and the housing of the individual components should integrate the components, whilst protecting the internal electronics against environmental conditions present in the envisioned context (req. 1.a and 3.a-g, wish 6.a-b). This should also eliminate any loose wires previously found in the prototypes (wish 13). In addition, the required external connections for power, Ethernet, and USB were integrated using off-the-shelf extension cables. To achieve this, a housing was designed to be made using regular 3D-printing of PLA. As 3D-printing is expected to contain imperfections, laser cut rubber was used on all interfaces between 3D-printed parts to ensure protection against environmental conditions.

This was also included in the designs of the previously discussed integrated designs of individual components. For the diagnostic setup embodiment, a removable outer layer was added to protect the internal components, hide the required wires, and improve the overall appearance of the design. For the fluid insertion system, the wires were also hidden and the required buttons were integrated into the design, as can be seen in Figure 17 on page 29. In addition, a large side panel was included to protect the user against potential spillage, to protect the relatively vulnerable syringe holder and to improve the rigidity of the overall design. Still, due to the required replacement of flow cells and the opening required for the stepper motor shaft, both components were still partially exposed to the environment. Thus, to provide more protection to the general electronics, protection has also been added between these two components and the housing for general electronics. This is not required between the digital interaction embodiment and general electronics, as this uses watertight momentary switches, and a specially designed housing for the screen, as can be seen in Figure 36 on page 56.

As the device was to be portable for all potential users, this was to be designed for (wish 12). To do so, different types of handles and straps were explored together with fellow students by looking at everyday products. This resulted in a handle design based on a vacuum cleaner. For the handle to function accordingly, it should be placed directly above the center of mass. For this, the center of mass was determined using the CAD model of the product embodiment. To indicate the intended usage, the bottom half of the handle has been fitted with laser cut rubber, as can be seen in Figure 36.

2.1. Electronics of the product embodiment design

The general electronics of the product embodiment design had a large range of functions. These included the control of the screen, buttons, speaker, laser diode, optical sensor, and stepper motor. In addition, various internal sensors were included to provide additional information on the performance of the design, including temperature, humidity, and GPS sensors.

All these components were to be controlled by a single Raspberry Pi. The use of a Raspberry Pi was a predetermined aspect of the project. I personally agree with this decision, as the Raspberry Pi is a broadly applicable, powerful, standardized, and well-documented prototyping computer with native support for Python 3. As the computational demands for the existing Python algorithms developed by Patrick were high, the most powerful Raspberry Pi at the time was obtained for this project, being the Raspberry Pi 3B+. Also, the selection of a suitable power supply for the envisioned context was evaluated. This resulted in an electronics package, as seen in Figure 36, and various circuit boards mounted on PET-G panels within the housing of the embodiment design. More information on the optimization process of the electronics within the product embodiment design can be found in Appendix P.

2.2. Software of the product embodiment design

So far, the development of the required software was mostly performed separately for the individual components, as discussed throughout parts A and B, and appendixes D.1, E.4, F.4, I.1, and N.4. Still, as the integration of these software components was anticipated from the start, all code was kept compatible with each other throughout the development process and could therefore be easily combined.

For the measurement procedure to become fully functional, the software developed for the diagnostic setup embodiment and fluid insertion system was integrated. In this, the software was made to enable switching between the automatic reconstruction and classification of footage, and the automatic storing of the footage at a high quality for later analysis. As this would introduce a high computational demand and a Python process can only use a single core, multithreading and multiprocessing was implemented using personally developed Python classes

Through this, all four cores of the Raspberry Pi could be used, and tasks distributed evenly amongst them. It was decided that core 1 should be used for controlling general tasks, including interface and procedure control (main thread), capturing and checking images (camera thread), and moving the syringe (prepare thread). The computationally demanding tasks of compressing and storing images or reconstructing and classifying images are distributed amongst cores 2-4.

In Figure 37, three representative simplified scenarios for the resulting software procedure can be seen. In this, scenario 01 represents the capturing and storing of an image without already fully active image storing threads. This occurs at the beginning of a measurement, or after the Anti-Bubble System (ABS) had previously detected a bubble.

Scenario 02 represents the capturing and storing of an image with already fully active image storing threads. As the image cannot be directly passed to the store threads of cores 2-4, the camera thread will pause until this is possible. The next image will not be captured until both the previous image has been passed on and the syringe has been moved. As the capturing of an image and moving of the syringe is currently faster than both the storing and analyzing of images, this scenario will often occur during measurements.

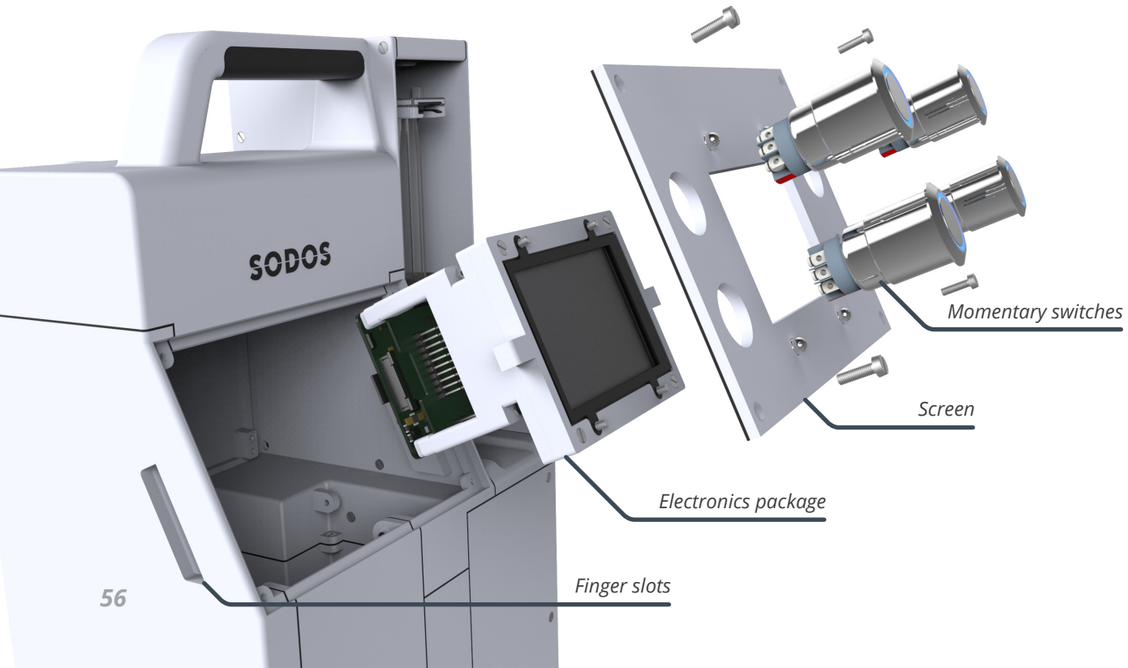
Finally, scenario 03 represents the procedure that is followed if an air bubble is detected by the ABS. If this occurs, the captured image and statistics of the bubble are stored to a database. As bubbles can have a disruptive effect on the analysis, the captured image is excluded from the dataset and an attempt is made to remove the bubble by moving the syringe up and down. After this, a new image is captured and checked again for the presence of air bubbles, resulting in either scenario 01 or scenario 03.

Besides performing measurements, there were also various interactive and general functionalities that required development. For each of these elements, individual Python classes were developed to ensure full control and potentially extend or reduce capabilities during development.

Ultimately, this resulted in the development of well-structured classes for managing processes, threads, local databases, speakers, cameras, sensors, buttons, motors, lights, interfaces, and Bluetooth and Wi-Fi connections. For the latter, an additional class was created to manage the transfer of data to an online server. In the end, over 6400 lines of personally written Python code was being used by the product embodiment design.

The resulting code can be used to either test the interaction or perform a measurement. This division was intentionally made, to limit the impact of user errors during user tests, and to have transparency of the internal systems during measurements via logging.

Figure 36. Simplified exploded view of the integrated digital interaction embodiment and electronics package



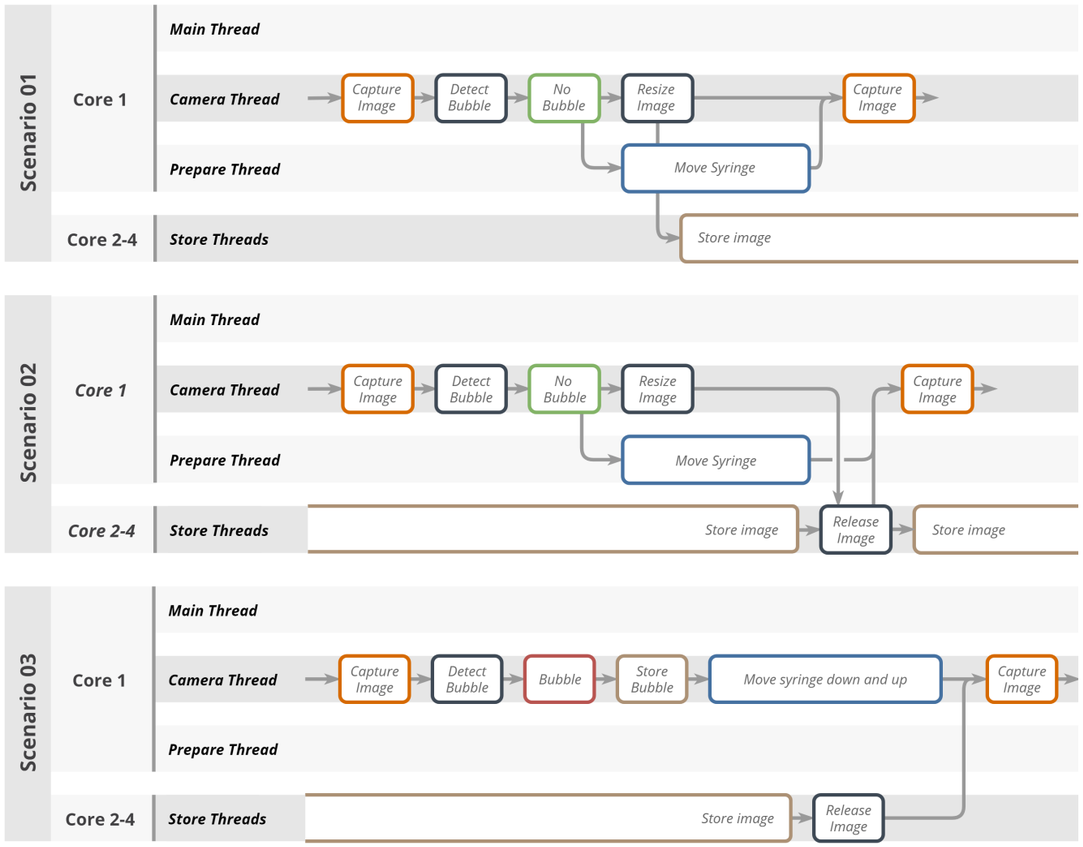


Figure 37. Three simplified scenarios for the software procedure during measurements. This includes the capturing of an image without fully active storing threads and preparing for the next recording (01), the capturing of an image with fully active storing threads and preparing for the next recording (02), and the capturing of an image with air bubbles and the preparing for recapturing the image after removing the bubble (03).

3. Data handling in the product embodiment design

Besides the overall development of the required software, it was decided to shortly look into the data handling protocols and methods that the product embodiment design could best incorporate. This is mainly outside of the original project scope, but was considered interesting to look into and incorporate. To do so, short lists of requirements and wishes were created, and based on this a realistic data handling protocol was envisioned. Due to the limited relevance of the data handling protocol within the project, only the most vital elements were elaborated into a functional prototype.

List of Requirements

1. The device must be able to store at least four weeks of field research data locally (J.1).
2. The device must be able to function independently of external connections (J.1 *).
3. The obtained results must be digitally collected (J.3).

List of wishes

1. The risks of user error should be minimized by design (J.1).
2. The device should enable frequent online data back-ups (J.7).
   - **a.** The device should be able to directly make back-ups to the internet.
   - **b.** If back-ups are performed, the connection must be safe.
3. It should be possible to make a paper back-ups of the digital data (J.3).
4. The digital data should be optionally expandable using smart devices.
5. The online data should be communicable to third parties if desirable.

Annotations in the form J.1-8 refer to the requirement's originating section in Appendix J of Vendel [9]. Annotations marked with an asterisk (*) have been adapted.

3.1. Requirements and wishes

For creating the data handling protocol for the product embodiment design, the non-prioritized lists of requirements and wishes were based on the requirements and wishes set out by Mirte, discussion with fellow researchers, logic reasoning, and personal experience as a web developer.

3.2. The envisioned data handling protocol

Based on the requirements and wishes set out and discussions with software developers, the core functionalities for each device within the data handling protocol were set out and related to each other, as can be seen in Figure 38. In this, there were three functional devices, being the Sodos, the central server, and optional smart devices. The devices could be directly or wirelessly connected to each other using their native functionalities.

3.3. The created data handling protocol

For creating the envisioned data handling protocol, the most vital functionalities were selected and prototyped. In Figure 38, it can be seen which functionalities and connectivity capabilities were made functional.

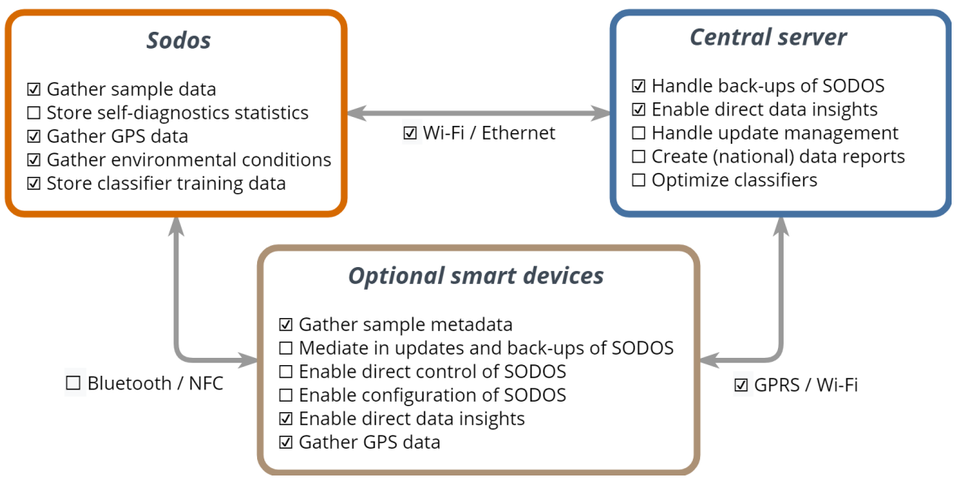


Figure 38. Envisioned devices and their functionalities related to the data handling protocol of the product embodiment design. Prototyped functionalities have been checked off.

For the Sodos, local database capabilities were enabled by creating extended classes based on the SQLite library for Python 3 [17]. This was extended by a self-made transfer procedure for sending sensor and measurement data to a central web server. For this, a configuration file was made in Python in which the tables and columns were listed that were to be transferred to the server. Each of the tables included a hidden column to track whether the latest version of each record has been received by the server. When inserting or updating data, this column was reset, causing the introduced data to be transferred. In addition, the prototype had credentials unique to the device that allowed it to send data to the server.

The transfer requests were handled by an Application Programming Interface (API) within a web application created using the Laravel framework for PHP. This website was hosted on my personal Ubuntu server running a Nginx web server. Here, the transfer request was validated and stored accordingly in a MySQL database. In this, the local identifier and the session number were stored for each row to allow rows to be updated following changes to the local database, functioning as an idempotency key. In addition, the local transfer protocol could transfer files of up to 60Mb in size. This allowed preview images and air bubbles to be uploaded automatically to the server. If the Sodos was to be offline for a long period of time and a large amount of data was to be transferred, multiple smaller transmissions would be performed to ensure correct handling by the server.

The created web application

To access the online data, a web application was created on the Laravel framework, as can be seen in Figure 39. For this, code was written in HTML, CSS, and JavaScript. It can be accessed via the public website on: https://sodos.maxhoeboer.nl/

At the time of this report, the data collected by the prototype in the field could be accessed with the username "public" and password "sodos". This account has no editor or administrator rights and does therefore not have access to all functionalities of the web application. If these credentials are no longer usable, please register an account and request permission for accessing the Sodos-A01.

As the web application can be opened on both smart devices and computers, it could facilitate the functionalities set out for the optional smart device in Figure 38. As this was not considered part of the scope of the project, some of these functionalities were not implemented until after feedback from the field research was obtained, and is therefore further discussed in part D, section 3.1 (p.76).

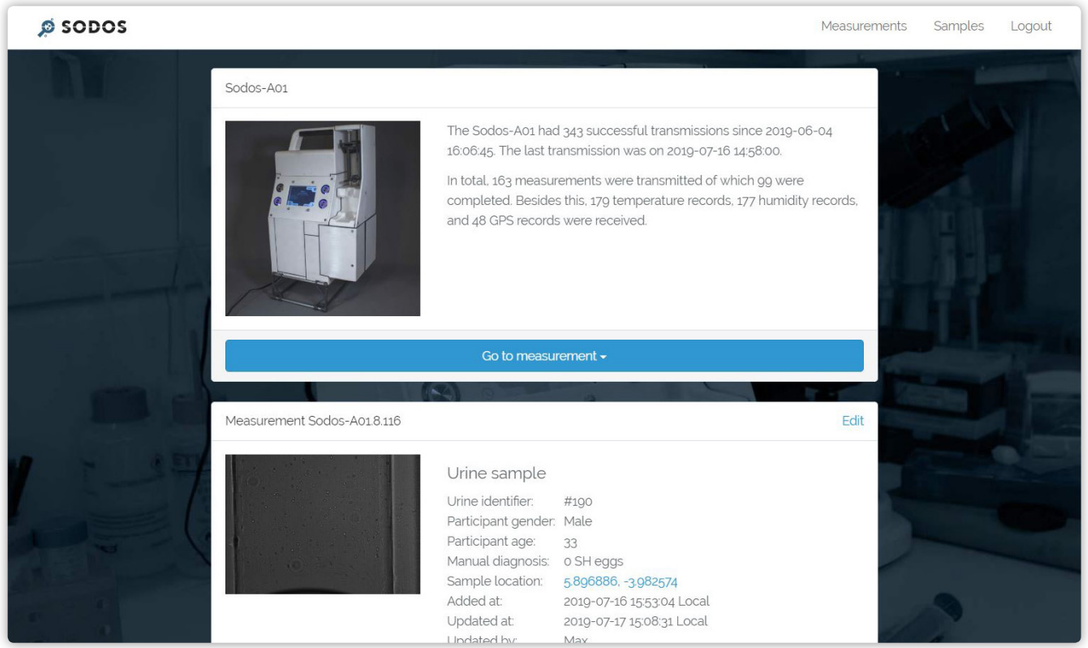


Figure 39. Web application created for accessing transferred data by Sodos prototypes

4. The integrated prototype

Now that the digital product embodiment design has been completed, it is time turn the design into a both functional and interactive prototype. As discussed, most of the product embodiment was designed for prototyping using the 3D-printing of PLA and the laser cutting of rubber and PET-G. In total, it took two 3D-printers of the type Ultimaker 2+ around two weeks to print the large number of parts required for the prototype, as can be seen in Figure 40. In addition, a large number of parts were laser cut from 1.0mm rubber sheets, as can be seen in Figure 41. Besides this, rubber foam was laser cut used to suspend the relatively vulnerable electronics in the design. For these electronics, multiple electronic boards were manually soldered and mounted on laser cut PET-G plates, as discussed in Appendix P.

Due to the extensive CAD model developed throughout the product embodiment design, no major design errors were found during the prototyping process. As a result, the product embodiment design highly resembled the integrated prototype, as can be seen in Figure 42. Still, the prototyping process was a time consuming process, due to the complexity and scale of the design.

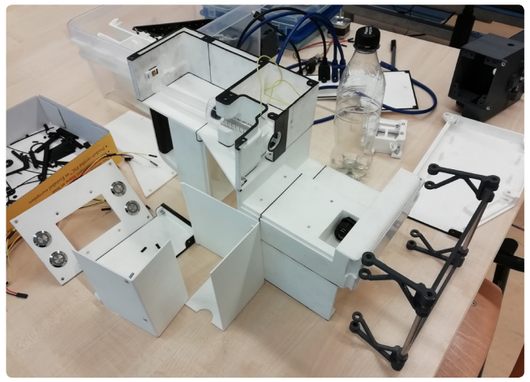


Figure 40. The partially assembled 3D-printed parts of the integrated prototype.

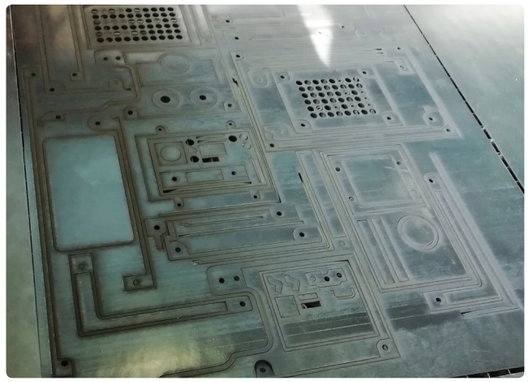


Figure 41. Freshly laser cut rubber sheets for the integrated prototype.

Figure 42. The high level of resemblance between the product embodiment design (left) and prototype (right).

5. Validation of the integrated prototype in the Netherlands

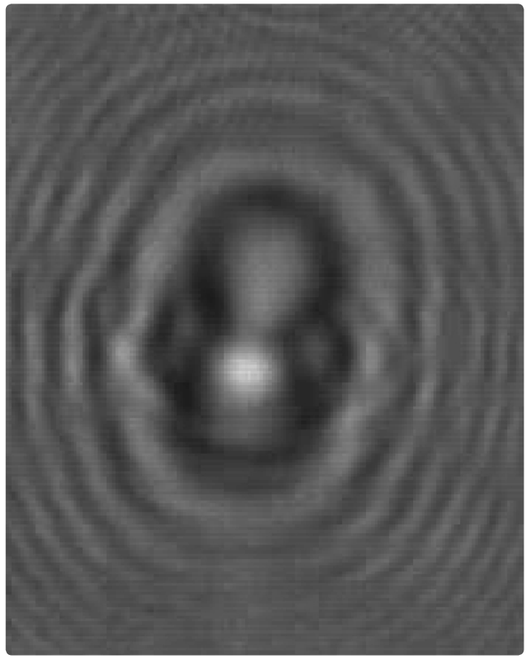
Initial validation of the integrated prototype was performed in the Netherlands and consisted of two parts. First, the integrated digital interaction embodiment, improved digital interaction and fluid handling were validated using user tests, as discussed in part B, section 1.1 (p.42) and Appendixes M.1 and O.1.

After this, functional validation of the integrated prototype with the improved integrated fluid insertion system was performed together with Patrick. Up to this point in the development process, validation was performed using old SH eggs in Phosphate-Buffered Saline (PBS) solution. For these final tests in the Netherlands, fresh SH eggs in saline solution were obtained from the Leiden University Medical Center (LUMC). This solution was further diluted using PBS and distributed to enable prolonged measurements.

Initial validation consisted of assessment of the functional components using SH eggs in PBS solution. In this, final optimization of the digital configurations was performed after which high quality footage was obtained using the integrated prototype. Of this footage, the quality was assessed by performing digital reconstruction with the algorithms developed by Patrick.

Once it was confirmed that the quality was sufficient to enable reconstruction, the SH eggs in PBS were mixed with urine and additional measurements were performed. When again performing digital reconstruction with the algorithms developed by Patrick, it could clearly be seen that the system was well capable of observing SH eggs, as can be seen in Figure 43.

In total, nine complete measurements were performed with high concentrations of SH eggs in urine. The obtained footage could form the basis for the training data required for the automatic classifiers being developed by Patrick. Still, as the analyzed fluids almost exclusively contained SH eggs, the classifier was expected to have a confirmation bias. To obtain more representative data and additional validation of the integrated prototype, a field research was to be performed.



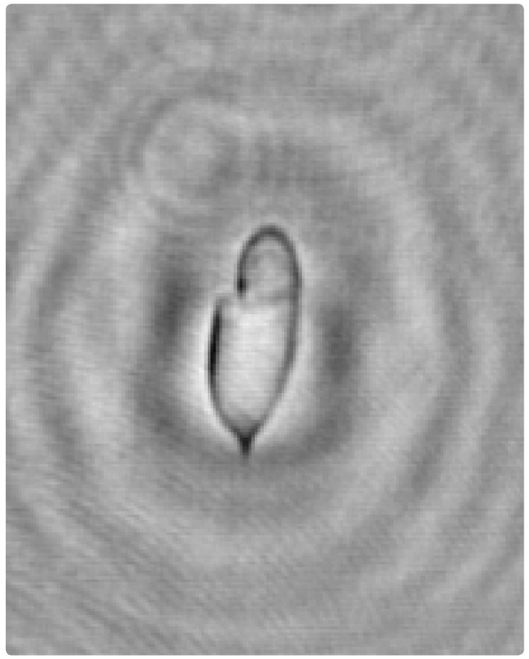


Figure 43. SH egg in urine solution observed by the integrated prototype before (left) and after (right) reconstruction by Patrick Nijman.

Part D

Field research

In order to validate the overall performance of the integrated prototype, field research was performed. In this field research, the primary goal was to evaluate the performance of the diagnostic embodiment and the technology in general. The secondary goals were to evaluate the interaction with the device and the overall performance of the prototype in the envisioned context.

The field research consisted of a two week field trip to Ivory Coast, performed in collaboration with the Centre Suisse de Recherches Scientifiques en Côte d'Ivoire (CSRS), located in Adiopodoumé. In this part, each of the three goals is individually discussed.

1.
Functional evaluation and data collection

The primary goal of the field trip was to collect high quality footage of actual urine samples using the integrated prototype. In addition, the urine samples were also to be examined using standard manual microscopy, as this allows us to determine the accuracy of the prototype and the reconstruction and classification algorithms following this graduation project.

Still, it was decided to not directly run the reconstruction and classification algorithms developed by Patrick in their current state, but instead only record the highest quality of footage available. This, as the algorithms were not yet optimized for the actual samples found in the field, as we do not yet have any footage of this. By recording the maximum quality of footage available and by determining the number of eggs that could be found in each sample via microscopy, it becomes possible to perform accurate optimization of the algorithms long after the field research.

As can be seen in Figure 9 on page 16 and the visual above, the functional evaluation and data collection is part of the field research, which continues on the product embodiment development.

This optimization can be performed by Patrick during the remainder of his graduation project, but also by future students or student groups for whom developing such algorithms might be relevant in their curriculum. Hopefully, this will result in the optimization of the current algorithms and make the fully automated Sodos a reality.

1.1. Method

To ensure sufficient footage is available for future development, a large amount of urine samples was to be examined. Together with the CSRS, it was decided to aim on examining between 100 and 120 urine samples from local villagers. This was considered the highest number of urine samples that could be examined with the resources available. The examination was to be performed over the course of six days in the village of Azaguié, approximately 30 km North of Abidjan. The urine collection itself was performed in the village of Mopé, which had 921 inhabitants at the time of the field research. These locations were selected by the researchers at the CSRS.

To examine the samples, a team of local people was required. This team consisted of a lab technician to perform analysis via microscopy, an assistant to help operate the prototype, two researchers, a driver, and two people to go by houses and collect urine.

The procedure for obtaining and processing urine samples was standardized to ease comparison. This was completely in accordance with WHO guidelines for urinary SH diagnosis [7]. Every evening the urine collectors in Mopé handed out cups to 20 to 25 participants with instructions to completely fill them with urine. In the early morning, the filled cups were collected and handed over to the team to be taken to the health center in Azaguié. Here, photos were taken of the individual urine samples in similar lighting conditions for future color comparison.

When analyzing an urine sample, the procedure described in part B, section 1.2 (p.42) was precisely followed. For this, the sample was first brought to the prototype where the sample was shaken and 12ml of urine was taken using a disposable sterile syringe. The syringe was placed in the prototype and a measurement was performed, collecting the analyzed urine in an empty cup. Upon starting the measurement code, a call was made to internal sensors to register the temperature, humidity, and GPS location of the measurement.

After the measurement was completed, the urine retracted into the syringe was inserted into the cup underneath the device. The same cup remained under the device whilst a standard cleaning procedure was performed using a clean syringe and clean drinking water. After this, the retracted cleaning water was also inserted into the cup, after which the cup and syringe used for the urine were taken to the lab technician. Here, filtration and staining was performed as normal, after which the number of eggs in a sample was manually determined via microscopy. During the manual counting of eggs, the lab technician was asked to time the procedure from the moment the syringe was filled till the moment the number of eggs was determined, to allow comparison with the prototype.

Besides this, after every 10 measurements, the flow cell was replaced with a new, sterile flow cell. In addition, every day was started with a new flow cell to reduce potential biases. Which flow cell was used for which measurement was recorded in logs to enable future analysis on the effects of specific conditions. The replacing of flow cells and cleaning of the prototype was also recorded here.

During validation of the integrated prototype in the Netherlands, the same logs were already maintained. For the field research, they had been expanded upon by including a patient register and a log for the results and durations of the manual diagnoses.

As the prototype was to perform a large number of measurements per day, the memory card would be quickly full. Therefore, a data transfer script was developed to transfer all memory intensive files to an external USB stick after a measurement was completed. Besides this, it also copied the files that were to be uploaded and exported the recorded data of a measurement, as it was unlikely for internet to be locally available. The script was made to be light and to be controlled in a terminal parallel to the one used to perform measurements and cleaning procedures.

Materials

The materials required for the field research were partially taken along from the Netherlands. This consisted of the syringes and flow cells required for the measurements, as well as the prototype and all electronics required for the prototype to operate. Besides this, local materials were gathered with the help from the local team. In total, the following materials were made available for the field research.

- The integrated prototype with accessories
- 100-120 urine samples
- 130 cups, to be used by urine collectors
- 25 cups, used and cleaned during analysis every day
- 150 syringes, disposed after analysis
- 15 flow cells (Ibidi µ-Slide I Luer 0.8 mm)
- 2 external hard drives (1TB)
- 2 external USB sticks (8GB)
- 2 external power banks (10400mAh)
- Disposable gloves in various sizes
- Cotton buds for cleaning the measurement box
- 90% ethanol for cleaning the measurement box
- 480 tablets of Praziquantel

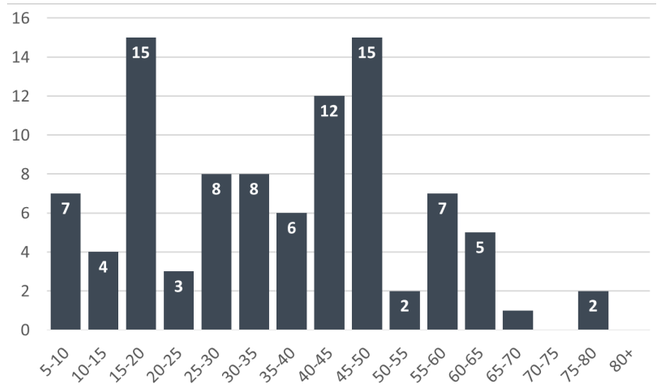


Figure 44. Age distribution of the participants grouped per five years in age.

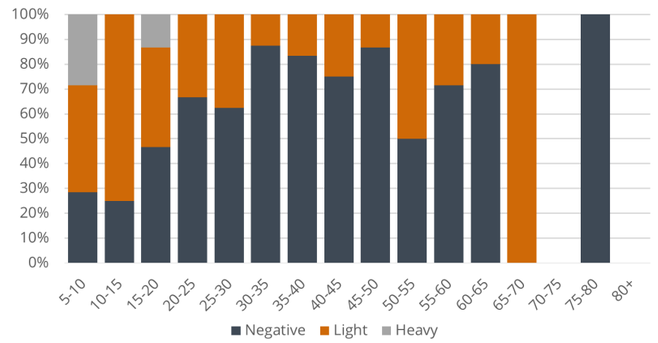


Figure 45. Level of infection over age of the participants grouped per five years in age; Light infections for <50 SH eggs per 10ml; Heavy infections for ≥50 SH eggs per 10ml.

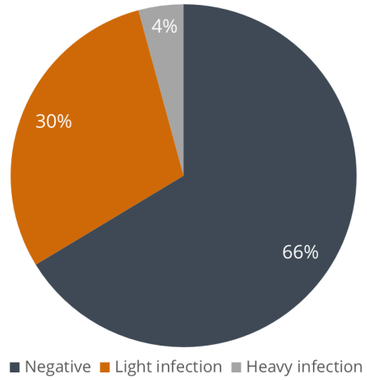


Figure 46. Diagnosis results via microscopy; Light infections for <50 SH eggs per 10ml; Heavy infections for ≥50 SH eggs per 10ml.

1.2. Results

During the field research, urine samples were obtained from the first 102 participants on a list of 200 voluntary participants from the village of Mopé, composed by the local urine collectors. Of the 102 obtained urine samples, 95 were analyzed in the health center of Azaguié using both the prototype and manual microscopy. The remaining 7 samples were only analyzed by manual microscopy due to unanticipated time restrictions. In total, 64425 holographic images were taken during the field research with a total size of 198.7Gb. To do so, the prototype had been actively running for over 53 hours in 5 days, with additional time required for transferring the data to external USB sticks.

A summarized and anonymized version of the urine sample data can be found in Appendix F. The summarized measurement data can be found in Appendix R and the summarized local maintenance data can be found in Appendix S.

The 95 participants included in the analyses were both male (52%) and female (48%). In the participant selection, no age restrictions were introduced, as this was not desirable for the representatives of the village of Mopé. The resulting age distribution can be seen in Figure 44. Using manual microscopy, diagnoses were performed for each of the 95 participants, the results of which can be seen in Figure 46.

Even though the number of participants was very limited for some of the age groups, it was possible to determine the level of infection for each of the groups, as can be seen in Figure 45. Due to this, the significance of some age groups is very limited (50-55, 65-70, 75-80 years). Still, it can clearly be observed that participants of younger age groups were more likely to be infected, and were the only ones diagnosed with heavy infections (≥50 SH eggs per 10ml of urine).

In terms of duration, it was clear that the prototype required a lot more time than the manual microscopy, as can be seen in Figure 47. This was anticipated, but the experienced lab technician was even faster than expected. In addition, high levels of contamination in some urine samples limited the prototype's ability to compress image files. This resulted in an increased file size of up to 3.0Gb per measurement, whilst previous measurements in the Netherlands were only 1.8Gb in size on average. As the writing speed to the internal micro SD card already was the limiting factor, the measurement duration with the prototype was significantly increased by up to eight minutes. Still, the automated

process of the prototype required little interaction with the user, and the duration of interaction seemed to be less than that of manual microscopy with room for further optimization.

Cleaning procedures were performed following every individual measurement and after every measurement failed due to excessive air bubble formation. This resulted in a total of 99 successful cleaning procedures during the field research.

In Figure 48, a selected and partially gray-scaled overview of the urine samples obtained during the field research can be seen. In this, it can clearly be seen that there are large differences in the transparency and color of the samples obtained. For taking the pictures, the same exact location in the building was used at the same time during the morning. For all pictures the urine sample number is clearly visible on the tape placed on the cups. The names of participants were digitally removed if visible to maintain anonymity.

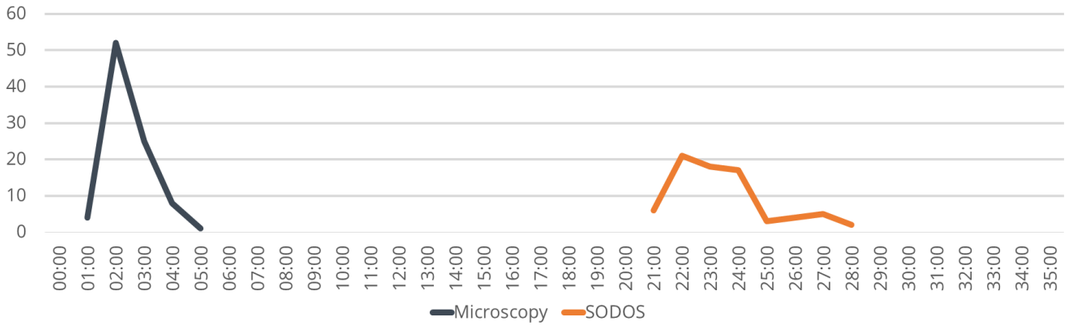


Figure 47. Total duration distribution of performing a measurement via manual microscopy and the Sodos grouped per minute of duration.

Figure 48. Selected and partially gray-scaled overview of the urine samples obtained in Ivory Coast for color comparison.

Providing Praziquantel to infected participants

As in accordance with the local ethical approval, treatment by Praziquantel was provided to all participants tested positive for schistosomiasis via microscopy, as can be seen in Figure 49. This was performed upon consultation with local medical professionals.

During the field research, Praziquantel was provided to 55 infected participants of the field research and a previous field research facilitated by the CSRS. Praziquantel should be well dosed to prevent potentially dangerous side effects. To do so, either the participants' weight or length can be used to determine the suitable dose. It was decided to use the participants' length, as the accuracy of the available scales was unknown.

Tasks were divided amongst the team to prevent errors. One person called out the name of the participant who was to receive treatment. After this, two team members measured the participant's length together to prevent errors, as can be seen in Figure 50 and Figure 52. The length was communicated to two other members of the team, including myself. They together translated the participant's length into a number of tablets, instructed the participant on how to consume the tablets, wrote the participant's name on an envelope, sealed the according number of tablets inside the envelope, and maintained a log of the tablets handed out, as can be seen in Figure 51. Besides this, female participants were asked about the possibility of pregnancy, as local doctors indicated it to be an important contraindication for the use of Praziquantel. The number of tablets provided was noted on the list of infected participants to ensure treatment was provided to all and to track the number of tablets being provided.

Figure 49. Praziquantel treatment made available for the participants of the field research.

Figure 50. Infected participant being measured in the village of Mopé whilst other participants await their results. Permission for taking and using picture was obtained from village elders.

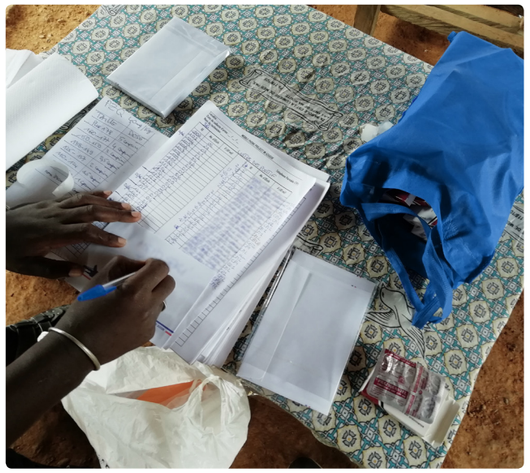


Figure 51. Handing out Praziquantel tablets to infected participants whilst maintaining a log of the tablets handed out.

Figure 52. Infected participants and their parents awaiting their results. Permission for taking and using picture was obtained from village elders.

In addition, treatment by Praziquantel has later been made available to all other participants of the field research. This, as they are still at risk of having light infections whilst being tested negative during the field research, and thus treatment should be provided according to the local ethical approval. Due to an internal communication error, this was not known by the team at the time of the field research.

For this, an additional 323 Praziquantel tablets were made available to be later provided to the participants who were tested negative during the field research. Based on the number of tablets handed out during the field research, this would provide treatment to an estimated 115 additional participants. This would bring the total number of treated participants to 170, treating all participants diagnosed during the field research, and almost the entire list of 200 voluntary participants.

1.3. Discussion

Initially, various problems occurred during measurements with the prototype; the Anti-Bubble System was overly sensitive, the Classifier class produced errors, and multiprocessing gave errors when a parallel terminal was used for transferring data to external USB devices. These problems were discovered during the first day of measurements and could be resolved by small changes to the algorithms and by no longer performing parallel transfer of data. The latter significantly increased the duration of the measurements as only 9 measurements could be stored internally in the prototype, requiring transfers to be performed throughout the day. To quickly solve problems throughout the measurements, additional notes were kept of all abnormalities observed during measurements, as can be seen in Appendix R. As a result, the sources of problems could be quickly identified.

After eliminating these initial problems, the efficiency of performing measurements was quickly increased. Already after the analysis of the fourth urine sample (urine sample 104, measurement #7), the local team was able to prepare syringes for measurements without supervision. The digital control of the device was not shared with the local team, as the system ran without the interfaces and was therefore very complex to operate. The interfaces were not activated to increase the transparency of the internal system during measurements and allow quick identification of potential problems.

Still, it was not possible to analyze 100 urine samples during the field research. This had two main causes. First, the field research was 5 days instead of the initially planned 6 days due to the high financial costs of Praziquantel reducing the budget available for the remaining field research. As the Praziquantel also needed to be handed out in the village of Mopé, only 4.5 days could be effectively used for performing measurements. Secondly, performing measurements took far longer than anticipated due to the high levels of contamination in some urine samples increasing the file sizes, and due to the data transfer not functioning in parallel to measurements. With these limitations, the team still attempted to perform measurements on 100 urine samples, but at some point continuing measurements was considered irresponsible for the completely exhausted team. It must therefore be concluded that with the current prototype, it is not possible to perform the minimum of 50 measurements per day. Thus, the prototype does not yet meet product embodiment design requirement 5.

It is then also not surprising that Figure 47 on page 68 clearly shows manual diagnosis taking significantly less time than the method used by the prototype. This difference was especially noticeable for samples where there was little contamination, as the lab technician could adopt a wider field of view with a 10x objective rather than a 40x objective. The duration of measurements with the prototype also reduced with less contaminated samples, but this was in a lesser degree. Yet, the duration of a measurement with the prototype requiring involvement of the user actually seemed to be less than that of the manual microscopy, as little interaction with the prototype was required. The only actions for which the user was to be present were for the preparation, placement, and removal of the syringes. As these were less actions than required for manual microscopy, less involvement of the user would be required.

In theory, this could mean that a single user would be capable of controlling multiple Sodos devices simultaneously. In this, a single smart device could potentially be used to control the devices over a Bluetooth connection, allowing a large number of measurements to be performed in a single day by a single operator.

Besides this, some physical problems were noticed with the prototype. For example, it was noticed that during some instances of the bubble removal procedure of the Anti-Bubble System, that the increased viscosity of the urine caused the tension springs of the syringe holder to be extended instead of retracting the urine. This prevented air bubbles from being removed without manual assistance. Therefore, the force exerted by the tension springs should be increased, or the opening of the syringe holder should be physically limited. As neither was possible during measurements, the prototype was physically aided if problems with the bubble removal procedure persisted.

Assessment of the footage obtained

When looking at the footage obtained by the prototype, it could clearly be seen that large differences were present in the levels of contamination, as illustrated by footage of two negatively tested samples in Figure 53. In this, the footage of urine sample 162 shown on the right contains high levels of contamination which were commonly found during the field research. As the algorithms developed by Patrick are designed to perform reconstruction and classification on every individual particle found, these countless unrelated particles would likely result in a large increase in the computational demand of the system.

Besides this, it could also clearly be observed that particles were present at different depths within the flow channel. As a result, the fringes and shadows of particles often seemed to be overlapping or intersecting. Even though comprehensive analysis of the footage is still to be performed, this intersection of fringes is expected to have a disrupting effect on the algorithms' capabilities to reconstruct the data. This important and potentially fundamental problem is to be further explored in order to assess the potential of flow-based in-line holography as a diagnostic method. If the intersection indeed has a disrupting effect on the algorithms' capabilities, adjustments could be made to the flow channel depth to reduce its occurrence.

On the other hand, seeing such a large number of particles would suggest that the device is potentially capable of observing additional indicators of the participants' overall health. This could potentially result in the application of digital holography for the diagnosis of medical conditions other than urinary schistosomiasis. Future analysis of the data obtained could hopefully determine up to which degree the computational demand is increased and up to which degree other medical conditions could potentially be identified. Besides this, the data obtained is to be used to both test and optimize the algorithms for the reconstruction and classification of particles. For this, previous data lacked unrelated particles, resulting in a confirmation bias within the algorithms. When using the data obtained during the field research, this is no longer expected to be a problem.

1.4. Limitations

Within the study, various limitations were present. Most obvious is the fact that only 95 urine samples were analyzed, being less than the minimum of 100 urine samples set out. As discussed before, this was due to unanticipated practical limitations to the study that could not be addressed in the field. However, the relevance of the study with 95 analyzed urine samples was still considered to be very high and not severely influenced by the lacking number of samples.

To reduce the time required to store a sample, slight JPEG compression was applied to the footage obtained. In the Netherlands, it was determined that maintaining 95% quality did not negatively influence the apparent quality of the footage obtained.

As introduced before, the prototype is capable of analyzing 12ml of the urine sample. As a result, if more urine was available this could not be included in the measurement. This may have caused light infections to remain unnoticed. To see whether this was the case, the remaining urine of 22 negatively tested urine samples was analyzed via microscopy. In this, four light infections were found that were not found in the 12ml sample. Still, the method used throughout the remainder of the field research was completely in accordance with the WHO guidelines, and the light infections would not be noticed if the minimum guidelines were followed [7]. However, these light infections remaining unnoticed during the field research did not have a negative effect on the outcome of the study. This, as the goal of the field research was not to perform completely reliable diagnoses, but to gather data on urine samples and the number of SH eggs that could have been observed by the prototype.

Besides this, the first 0.6ml and last 0.6ml of the urine sample were not analyzed by the prototype. This was due to the space between the syringe nozzle and the flow cell, and the fluid required to remove air bubbles from the flow cell. This did not necessarily affect the reliability of the measurement on itself, as the 10.7ml analyzed by the prototype still exceeds the 10ml amount required by WHO guidelines [7]. Still, it did mean that the number of eggs found via manual diagnosis may have deviated from the number observable to the prototype. To reduce the chance of the prototype missing eggs, the syringes with urine were held inverted prior to placement. This caused the eggs to sink to the top of the syringe. After placing the syringes in the prototype,

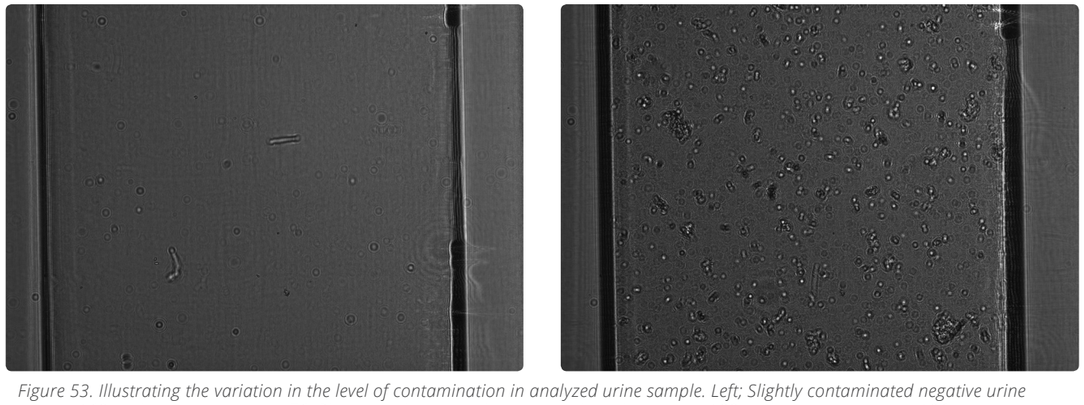


Figure 53. Illustrating the variation in the level of contamination in analyzed urine sample. Left; Slightly contaminated negative urine sample 162 during measurement #76. Right; Heavily contaminated negative urine sample 182 during measurement #106

the eggs were expected to slowly sink to the bottom. As a result, they were not in the bottom at the beginning of the measurements when urine was disregarded to remove bubbles, and not at the top of the sample at the end of the measurement, when urine could no longer reach the flow cell. The effectiveness of this method remains difficult to determine at this stage and can best be confirmed during future experiments with the prototype if deemed necessary.

In some measurements, bubbles were frequently detected due to the Anti-Bubble System being overly sensitive. As a small amount of urine was lost during the removal of the bubble, not all samples had 10.7ml of analyzed urine. Still, as can be seen in Appendix R, every completed measurement met the requirement of having 10.0ml of analyzed fluid or more [7]. However, in three cases the urine sample was less than the 12ml required to perform a measurement. To enable analysis of these samples, water was added until 12ml of fluid was present. This was done for urine samples 124 and 128, which therefore have less than 12ml of urine analyzed. Whether these samples should be included during analysis remains open for discussion. The third urine sample 191 only had 4ml of urine available. This was considered insufficient for analysis by the prototype. Still, manual microscopy was performed on this sample.

Besides this, part of the urine pathway within the prototype was not replaced during measurements. As a result, it could be that cross-contamination of samples occurred. Unfortunately, there was no reliable way to determine this without disrupting the measurement process, and this can best be confirmed during future experiments with the prototype if deemed necessary.

Finally, when taking photos of urine samples, the exact position of the camera varied. This resulted in varying background illumination levels, as can be seen in Figure 48 on page 68. This might influence the apparent color and transparency of the samples obtained, but can be easily taken into account by the interpreter.

1.5. Conclusion

During the field research, high quality footage was successfully obtained for 95 actual urine samples. Besides this, the actual number of SH eggs present within the analyzed part of the sample was determined for each urine sample. This was slightly less than the minimum set for 100 urine samples, but was not considered to have a major impact on the relevance of the study. Treatment for schistosomiasis has been provided to 55 infected participants, and was expected to be provided to an additional 115 participants.

The footage collected during the field research can be used to reassess the potential of flow-based in-line holography as a diagnostic method and to optimize the algorithms used for reconstruction and classification of objects.

Figure 54. Evaluation of the product interaction design during the field research.

2. Interaction evaluation

One of the secondary goals of the field research was to evaluate the interaction with the prototype in the envisioned context.

As can be seen in Figure 9 on page 16 and the visual below, the interaction evaluation is part of the field research, which continues on the product embodiment development.

The evaluation of the interaction with the prototype was expected to be performed in the form of informal user tests both in the field and at the CSRS. However, this proved to be more difficult than anticipated. This was primarily due to the unexpectedly large language barrier with the envisioned users. Besides this, few potential users were present at the CSRS. As a result, only limited user tests were performed during the field research.

In this, the interaction with the programmed interfaces discussed in part B, chapter 3 (p.48) was tested with the local team. As the local team was already familiar with the general functioning and goal of the prototype, no additional information was provided, and users were only instructed to perform a measurement using the available interfaces. To ease the user tests, no fluids were used.

During the user tests, as shown in Figure 54, it could be observed that interaction with the prototype was clear overall. The users were able to select the desired language and perform a measurement. Due to not using fluids during the user tests, interactions with the syringes were not always acted out. Besides this, most interfaces were correctly interpreted by the users on the first attempt. Still, it was not noticed by one user that the interface for placing the syringe filled with water was a different one than the previous one instructing him to remove the empty syringe after a measurement. To highlight this new interface, it is recommended for future iterations to create a noticeable transition between the two interfaces, or to make distinct changes in their appearance.

As was already noticed during the validation of the integrated digital interaction embodiment design, discussed on page 42, the slots for placement of the fingers were not always noticed or used. It was stated that this is potentially undesirable, as it increases the chance of the prototype moving or falling over. Ironically, the latter was exactly what occurred during a user test, as seen in Figure 56 on page 75. This highlighted the need for a redesign of the slots and stand, for which a design has been proposed in Appendix M.1. The redesign of the retractable stand is discussed in chapter 3 (p.74).

Aside from this, obtaining in-depth and critical feedback proved to be difficult due to the language barrier. Still, the lab technician indicated that he only used classification of light (<50 SH eggs) and heavy (≥50 SH eggs) infections. This was in contrast with the interfaces, which also included medium infections due to earlier assumptions. Still, it was also indicated that this classification was not often used by him in practice. In terms of physical interaction, the buttons required quite some force to press, which might have contributed in the prototype falling over.

The handling of urine seemed to be relatively intuitive and was often performed by the untrained lab assistant during measurements without supervision. Still, at one occurrence the urine sample was knocked over by the lab technician before the sample was analyzed. Luckily, sufficient urine remained to perform measurements. Other than this, urine spillage during handling was limited to a single drop hanging on the tip of the syringe, and no spillage occurred with syringes placed in the prototype.

Within the current prototype, the replacement of flow cells was considered the main difficulty in terms of interaction. Due to this and the potential complications of user errors for the functional evaluation, this was not tested during the field research. As of now, the replacement has many steps and points of failure for the user. It is therefore recommended for future design iterations that this is to be simplified or even eliminated.

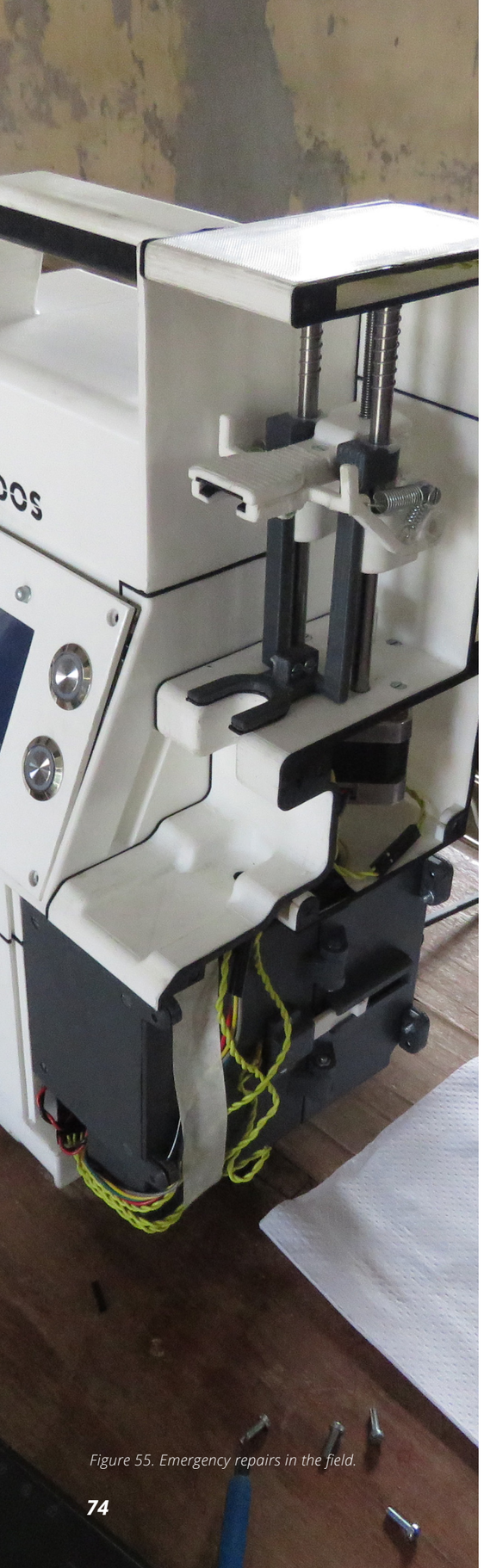


Figure 55. Emergency repairs in the field.

3.
Overall prototype evaluation

By performing both functional and interaction evaluation of the prototype, the overall performance could automatically be validated in the process.

As can be seen in Figure 9 on page 16 and the visual below, the overall prototype evaluation is part of the field research, which continues on the product embodiment development.

As discussed in section 1.3 on page 70, various problems occurred during the initial measurements with the prototype in the field. This included the Anti-Bubble System being oversensitive, the inactive Classifier class causing errors, and multiprocessing causing errors when a parallel terminal was used for transferring data to external USB devices. The first two problems could easily be resolved by small changes to the algorithms.

However, the third problem could only be reliably resolved by no longer performing parallel transfer of data. This was because the errors were the direct result of limitations introduced by the currently used Raspberry Pi 3B+. Namely, the high quality footage obtained by the prototype needed to be constantly moved from the working memory to a storage memory. For this, the Raspberry Pi 3B+ has an internal microSD card and four USB 2.0 ports which can be connected to external storage devices [18]. In this, the microSD writing speed is limited to around 20MB/s and the USB 2.0 writing speed to 34MB/s [19, 20]. Still, these writing speeds could not be obtained by the Python scripts, and there was a slight personal distrust towards the direct usage of removable USB devices during measurements. As a result, it was decided prior to the field research to store the footage to the internal microSD card and to transfer data of a measurement to an USB device during a consecutive measurement, as discussed in section 1.1 (p.66).

Still, it turned out that the simultaneous storing and transferring of data caused queues and conflicts to occur. This expressed itself in enormous delays in storing and transferring data, and a new type of camera error. In this, the delays caused by the limited writing speed could only be prevented by discontinuing the parallel transfer of data. Still, the camera error occurred randomly, even after discontinuing the parallel transfer of data. Overall, camera errors were no new occurrence. As introduced in Appendix E.4 on the trigger based software control, the camera was frequently not able to perform a measurement. This could be detected by the software, after which a new measurement command could quickly be send. However, this new type of camera error could not yet be automatically detected, and as a result the measurement stopped working and needed to be restarted. After a few failed measurements of the first day it was found that the problem was caused by a failed transfer of the trigger command to the optical sensor, and a timeout function could be introduced to handle this condition and allow the measurement to continue by repeating the trigger command.

Due to the low writing speeds obtained by the Python scripts, moving files to the storage memory became the determining factor in the duration of a measurement. In addition, as discussed in section 1.2 (p.67), the high levels of contamination in some urine samples limited the prototype's ability to compress image files. This increased the size of a measurement by up to 67%, from 1.8Gb to 3.0Gb. With the writing speed already being the limiting factor, this resulted in an increased duration of up to eight minutes. In hindsight, it would probably have been better to adapt the code to directly write the data to removable USB devices, as this had a higher maximum writing speed and eliminated the need for data transfers.

Besides these digital limitations, it was often found that the GPS module of the prototype was often not functional when performing analysis inside the hospital building, which had a metal roof. The digital GPS console in the prototype showed that no connections with GPS satellites could be established. Still, the GPS module worked as expected outdoors at the CSRS. If the GPS signal cannot be improved in a future design iteration, its value is to be reconsidered.

However, the value of the GPS location during analysis is to be reconsidered in general, as analysis was not performed at the location where the samples were obtained, but at a health center 45km away. If this turns out to be a common occurrence, the GPS location during analysis might have little contribution to the mapping of schistosomiasis. Instead, it might be more relevant to record the GPS location whilst obtaining the urine samples. In this, an (web) application on a smart device digitally linked to the Sodos could be used to collect data on urine samples and participants, and automatically record their geographical location whilst doing so. This optional extension to the Sodos would enable the accurate mapping of schistosomiasis prevalence.

Also, when evaluating the physical performance of the prototype, some points of improvement were identified. The most obvious one was to improve the reliability of the retractable stand. As discussed in chapter 2 (p.73), the slots for placement of the fingers were not always noticed or used, resulting in undesirable forces being exerted on the prototype. This was already noticed during validation of the integrated digital interaction embodiment design (Appendix M.1), where it was stated that this was potentially undesirable, as it increased the chance of the prototype moving or falling over. Ironically, the latter was exactly what occurred during a user test, as seen in Figure 56. Luckily, emergency repairs could be performed and measurements could be continued, as shown in Figure 55. This highlighted the need for both a redesign of the slots (Appendix M.1) and the stand. For the stand, it is important to create a design that remains stable when forces are exerted on it in perpendicular directions, whilst keeping in mind the considerations discussed during the original product embodiment design of the stand in part C, chapter 2 (p.55).

Figure 56. Integrated prototype as it is falling from its stand during a user test in Ivory Coast.

The falling of the prototype also highlighted the vulnerability of the electronics inside the prototype. Namely, it caused a wire essential to the functioning of the motor to disconnect. Due to the large amount of wires and internal connections, it took a long time before the cause of the motor's malfunctioning could be established. Reducing the number of wired connections as much as possible would therefore be recommended for a future design iteration. Where possible, wires could be replaced by integrating PCB designs and using Hardware Attached on Top (HAT) for the Raspberry Pi.

On a more positive note, the prototype was able to handle the rough conditions during transport. This can partially be contributed to the removable layer around the diagnostic setup embodiment. This layer was mainly intended to provide protection against dirt and to improve the appearance of the prototype, but has also prevented the setup embodiment from being damaged during transport.

Throughout the field research, the prototype was able to run complete days on two full power banks of 10400mAh. Still, the power bank not being used was charged throughout the day to reduce the chance of power problems. The current prototype was not able to read its power levels and cannot be charged during usage. For this, an integrated Uninterruptable Power Supply (UPS) supporting uninterrupted pass-through charging at a constant voltage would be required.

In general, the flow cells remained relatively expensive and difficult to clean after a procedure, as they were designed to be a disposable. In addition, the replacement of a flow cell was considered prone to user error. Due to the use of a removable flow cell, additional protective layers were required for the electrical components, introducing more potential locations for contamination. As a result, the potential of the Sodos as a whole was reduced. For the Sodos to meet its full potential, the flow cell is to be redesigned such that it can be accessed for quick cleaning between measurements. This redesigned flow cell could be combined with other components to remove the additional protective layers currently present in the design. The main challenges in this are that the redesigned flow cell must be reliably watertight, cleanable, and not cause optical interference during measurements.

3.1. Overall recommendations for future design iterations

If future design iterations of the Sodos are to be performed, it is primarily recommended to get rid of the disposable flow cell, and to redesign it into a reusable flow cell that can easily be accessed for cleaning. This is deemed necessary for the Sodos to meet its full potential and is likely to influence the overall design of the Sodos, and the diagnostic setup embodiment in particular. Besides this, the depth of the channel in the flow cell used by the Sodos might also need to be reconsidered. This, as the currently observed stacking of particles in urine might negatively influence the algorithms' abilities, and is likely to be reduced by reducing the channel's depth.

In general, it is recommended to highly simplify the design. Currently, there are a lot of optional electronics embedded in the design that may not be desirable for a product that is to be affordable within the envisioned context. This might include the temperature and humidity sensors, but potentially also the GPS module. Namely, it is recommended to reassess the relevance of the geographical location during analysis for mapping purposes. As discussed, this location can differ largely from the location where the sample was actually obtained.

Therefore, it is recommended to consider practical alternatives, such as the optional use of an (web) application on a smart device digitally linked to the Sodos, as proposed in Part C, section 3.2 (p.58). This could be used to both collect data on urine samples and participants, and automatically record their geographical location whilst doing so. This optional extension to the Sodos would enable the accurate mapping of schistosomiasis prevalence. To demonstrate the potential of this method, the functionalities described above have been prototyped into the Sodos web application discussed in part C, section 3.3 (p.58), as can be seen in Figure 57. These functionalities were based on the experiences with the urine collectors in the field, and can be demonstrated upon request as they are only available for accounts with editor rights.

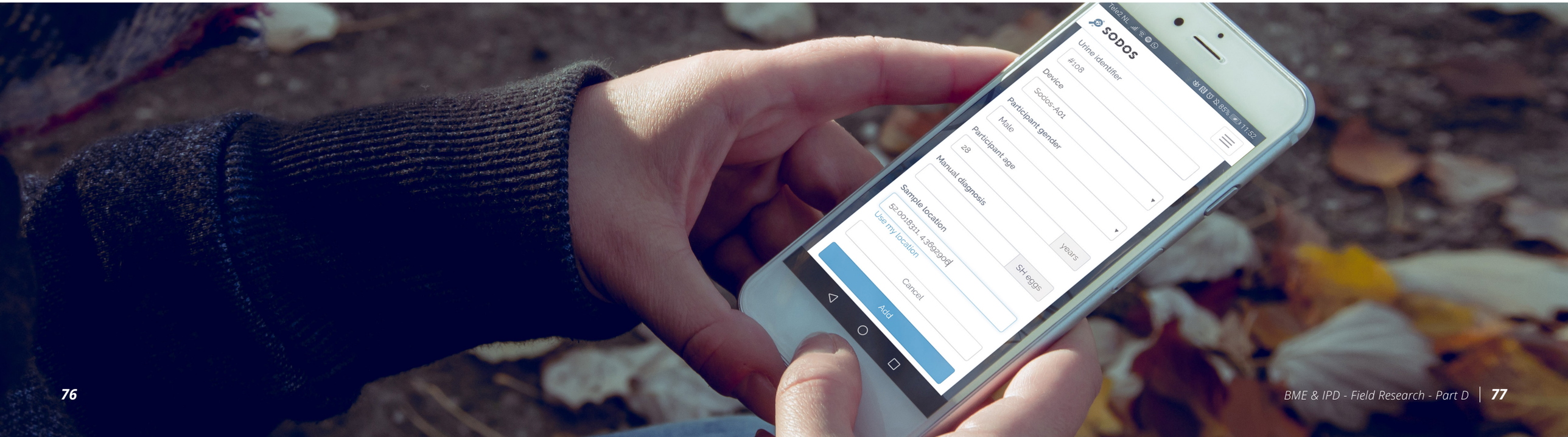
In addition, the electronics of the current design often have unnecessary wired connections, which are relatively vulnerable and complicate the overall design. Also, as discussed in Appendix L.2, it may be preferable to switch the currently used TFT LCD screen with a more affordable and durable custom segmented LCD display.

In terms of embodiment design, the number of parts should be reduced as much as possible. Besides this, parts that cannot be off-the-shelf components must be made suitable for mass production methods. In addition, the retractable stand and slots for finger placement are to be redesigned to meet their functional requirements, as discussed in chapters 1 and 2, and in Appendix M.1.

If the Sodos is still to be based on a Raspberry Pi in the future, it is recommended to replace the currently used Raspberry Pi 3B+ with the recently released Raspberry Pi 4B+ or other future models in combination with an external SSD. This, as the Raspberry Pi 3B+ has a relatively low writing speed to its storage memory and relatively little computational power [19, 20]. These are currently considered bottlenecks in the validation of the prototype and the potential of the diagnostic application. If this switch is to be made, it is also recommended to reconsider the currently used optical sensor of type UI-1492LE-M with USB 2.0 support. Namely, as the Raspberry Pi 4B+ supports the use of USB 3.0, the communication speed of the optical sensor might become a limiting factor within the Sodos.

On a longer term, it is also recommended to exchange the currently used external power banks for an internal Uninterruptable Power Supply (UPS). To do this, the exact power requirements for both capacity and output must be determined. Once these are known, an UPS should be selected or built that can be digitally read and controlled by the Sodos and that supports pass-through charging. For the latter, it is important to select an UPS that does not have an interruption or change of voltage when switching between discharging and pass-through charging. This was found to be a common property of power banks and integratable UPS systems, and can have a disrupting effect on the functioning of the Sodos.

Figure 57. Entering data on samples, participants, and the device's GPS location in the data integration web application of the Sodos.



Discussion

From early on, it became apparent that this was going to be an extensive graduation project. The starting conditions for the project were very good, and as a result the goals could be very ambitious. This was reinforced by the fact that this graduation project was for an Individual Double Master's Degree, meaning that more time could be spent on it.

At the start of the project, the project goal was set on developing and designing a both functional and interactive prototype of the Sodos, obtaining validation in the envisioned context, and making a redesign based on the obtained feedback.

As discussed in the method, the decision was made at an early stage to perform parallel design cycles for the different components that needed to be developed for the both functional and interactive prototype of the Sodos. Still, it was not yet realized at this stage that two additional components needed to be designed for the diagnostic technology; the fluid insertion system and the flow cell placement tool. As a result, five parallel design cycles were performed during the first stage of the project. This slightly complicated the design process. Still, the process was well manageable, as not all design cycles were actively designed for at the same time. Considering the outcome of the project, I am very satisfied with the approach used and consider the complexity of the design process to be acceptable.

However, it did complicate the documentation process, as many interrelated activities were being performed for different design cycles in different stages. Documenting on the development of the required software was especially difficult, as the software is related to each of the design cycles and changes were continuously made. Aside from this, activities not contributing towards the final result would not necessarily be worth including in the report. As a result, documenting was often deliberately delayed until it was sure which parts turned out to be a contribution. As this was an individual project, this could be reasonably well managed throughout the project.

Overall, most design cycles were performed within the expected time frame and without unexpected difficulties. This could not be said for the implementation of the required software. Aside from needing to learn new programming languages and to write tailored classes for specific functionalities (Python, Kivy, SQLite), documentation for the complex control of the optical sensor in combination with Python on Raspberry Pi was highly limited. As a result, a lot of time was spent on experimentally determining the correct control methods.

Besides this, the optimal configuration for most components were not yet determined in the experimental setup. Due to this and the lack of literature on the holographic analysis of SH eggs in flowing urine, the configurations of the optical sensor, laser diode, and stepper motor had to be mostly determined experimentally throughout the design process in collaboration with Patrick. Even though this was a time consuming process, it greatly improved my understanding of holography and its components, and in hindsight I would not have done it very differently.

During the project, a both functional and interactive prototype of the Sodos was successfully designed and developed. Still, the optimizations of the components within the Sodos were relatively time consuming and not anticipated in this degree at the start of the project. In addition, receiving SH eggs from the LUMC and making arrangements for the field trip to Ivory Coast took a lot longer than expected, resulting in the field trip being performed six weeks later than originally planned.

The field trip was considered a relatively ambitious undertaking from the start, and whether it could be realized as intended with the practical and financial means available remained uncertain for a very long time. In this end, it was decided to perform the field trip in collaboration with the CSRS in Ivory Coast. By coincidence, the activities planned for the field research were highly corresponding with the field research of another institute in the same period. As a result, it was possible to combine the request of the ethical approval, avoiding administrative problems and saving costs. In the end, it was possible to perform all desired functional evaluation and most of the secondary goals. Overall, it can be said that without the help of the CSRS in organizing the field research it would never have been possible.

During the functional evaluation in Ivory Coast, a total of 95 urine samples was analyzed using both the prototype of the Sodos and manual microscopy. This was slightly less than the goal of 100 urine samples, but is still considered more than sufficient to reassess the potential of the technology for diagnostic purposes and optimize the algorithms for automatic reconstruction and classification. For this purpose, it was decided to not directly perform analysis of the footage using the algorithms, but to capture it at a high quality instead. This, as the algorithms are not yet trained on actual footage. The footage collected now can be used in the future for the continued validation and optimization of the algorithms. This decision was made together with Patrick, and we are both still convinced of the appropriateness of the choices made. Besides this, the secondary goal of evaluating the interaction with the envisioned users was more difficult to perform. This was mostly contributed to the unexpectedly large language barrier.

In addition to the measurements, the remaining urine of 22 negatively tested urine samples was manually analyzed via microscopy. In this, four light infections were found that were not found in the 12ml sample. Still, the method used to analyze the 12ml samples was completely in accordance with WHO guidelines, and these light infections would not be noticed if the minimum guidelines were followed [7]. Therefore, it might be worth reconsidering the accuracy of the WHO method and whether the sensitivity of this method can be considered sufficient for future diagnostic solutions. If the accuracy is considered insufficient, increasing the volume that is to be analyzed would bear a large negative effect on the time efficiency of the Sodos in comparison to other methods, such as microscopy.

Using the data obtained during the field research, it has become possible to fully assess the potential of flow-based in-line holography as a diagnostic technology. As discussed in part D, section 1.3 and shown in Figure 53 on page 71, large differences are present in the levels of contamination. As the current algorithms perform reconstruction and classification on every individual particles found, the countless unrelated particles observable in some urine samples would likely result in a large increase in the computational demand on the system. Besides this, overlapping and intersection of the shadows and fringes of particles could potentially have a fundamentally disruptive effect on the algorithms' capabilities to reconstruct the data. On the other hand, seeing such a large number of unrelated particles would suggest that the device is potentially capable of observing additional indicators of the participants' overall health. This could potentially result in the application of flow-based in-line holography for the diagnosis of medical conditions other than urinary schistosomiasis. The degree to which computational demand is increased, disruptive effects are present, and other medical conditions can be identified is still to be determined during future analysis of the data obtained.

Overall, the prototype performed as expected and was able to reliably collect data in the field. Aside from this, the envisioned users were able to interact with the device accordingly and were enthusiastic about the potential of the Sodos. Therefore, it can be said that the prototype of the Sodos meets the expectations set out. The Sodos was also well received in the Netherlands, where the project was featured at the TEDx Delft talk by Temitope Agbana, as seen in Figure 58, and in a local newspaper. In addition, a publication discussing the design is currently in the process of being submitted, and the project has been submitted for the James Dyson Award.

Figure 58. Temitope Agbana presenting the Sodos on TEDx Delft

As the prototype of the Sodos meets the requirements set out and reassessment of flow-based in-line holography has not yet been performed, there is currently no clear need for redesigning the prototype towards a towards a producible product design. Due to this, the additional time required for optimization of the internal components, and the delaying of the field trip, it was decided together with the project supervisors to no longer perform this redesign. Still, some points for improvement remain for both the prototype and for developing the Sodos towards a producible design.

For the prototype, the stand of the prototype is to be redesigned, as it is relatively prone to failing. Also, the internal Raspberry Pi 3B+ has a relatively low writing speed to its storage and little computational power. To solve this, a switch can easily be made to the more powerful and recently released Raspberry Pi 4B+ in combination with an external SSD. In addition, the external power banks can be exchanged for an internal Uninterruptable Power Supply once the exact power requirements can be determined. For developing the Sodos towards a producible design, recommendations are given in part D, section 3.1 (p.76). Due to the discontinued redesign, the current Sodos prototype is the final deliverable of this graduation project.

Recommendations for future research

The main recommendation for future research is to perform analysis on the high quality data obtained in Ivory Coast to reassess the diagnostic potential of flow-based in-line digital holography. In this, it should be determined whether the method is computationally feasible, whether it remains sufficiently undisrupted by the overlap of shadows and fringes for reconstruction, and whether other medical conditions could potentially be identified. Only if the method shows sufficient potential after this analysis, the prototype should be further developed and simplified towards a producible product design.

If it is decided to improve the prototype, the main recommendations are to redesign the stand, to switch to the more powerful Raspberry Pi 4B+ with an external SSD, and to include an internal Uninterruptable Power Supply. If it is decided to develop the Sodos towards a producible design, additional recommendations are given in part D, section 3.1 (p.76).

Aside from this, it is recommended to reconsider the accuracy of the WHO guidelines set out for urine analysis. This, as various light infections were only found when analyzing more urine than the required 10ml. Therefore, it might be worth considering whether the sensitivity of this method is sufficient for future diagnostic solutions.

Finally, if future field trips are to be performed on parasitic infections, organizing this in collaboration with the CSRS is highly recommended and highly encouraged from their side. Still, the language barrier with the local population and employees at the CSRS is to be considered when doing so.

Conclusion

The project goal of this graduation project was set on developing and designing a both functional and interactive prototype of the Sodos, obtaining validation of this prototype in the envisioned context, and making a redesign based on the obtained feedback.

To do so, five iterative design cycles on individual components of the Sodos were performed in parallel, and the resulting designs were integrated to form a both functional and interactive prototype. This prototype was validated and optimized in the Netherlands, after which field research was performed in Ivory Coast. During the field research, the prototype was validated in terms of functionality and interaction, and data was gathered for future optimization.

As reassessment of flow-based in-line digital holography using the data obtained during the field research has not yet been performed, there is no clear need for a redesign towards a producible product design. Due to this and delays during the project, no redesign has been made.

The main recommendation for future research is to perform analysis on the data obtained before further developing the Sodos. This, as it would proof the potential of Sodos becoming the first fully automated diagnostic solution for urinary schistosomiasis. Enabling the reliable diagnoses deemed essential for mapping and combating one of the most common parasitic infections worldwide.

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