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FloWear Kit: Paper-Based Microfluidic Modules for Customized Wearable Sensing Device Using Colorimetric Analysis

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Abstract of Master's Thesis of Academic Year 2022

FloWear Kit: Paper-Based Microfluidic Modules for Customized Wearable Sensing Device Using Colorimetric Analysis

Category: Design

Summary

Recently, wearable devices received attention from many fields because of their potential in different applications. Wearable devices are widely used for health monitoring as they can be close to the body. However, most of the current wearable health monitoring devices use electric circuit which is expensive and not disposable. Using disposable wearable devices can be low-cost as it requires inexpensive materials such as paper. Paper-based microfluidics analytical technology is used as a disposable approach and has received extensive interest from many researchers in material science. This study aims to develop paper-based microfluidic modules to allow users to customize and use their own wearable sensing device to make a real-time screening health test. The device depends on detecting analytes in sweat on the skin's surface non-invasively. The wearable device will use paper and colorimetric indicators as the main materials. This approach is expected to provide a customized, real-time, low-cost, and disposable wearable device that monitors essential analytes non-invasively.

Keywords:

wearable, health monitoring, modules, paper-based microfluidics, sweat, coloromatric analysis

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Acknowledgements

بسم االله الرحمن الرحيم

In the name of God the most Merciful, the most Compassionate

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For my late mother and father who taught me the ethics and raised me to be a strong independent person. Their words will continue to be my guide and inspiration in this life. Tons of thanks goes to my dear sisters and brothers who encouraged me to persuade my dreams and goals.

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Chapter 1
Introduction

1.1. Background

Body fluid's analytes are anything that can be used as an indicator for a body health condition such as vitamins, electrolytes, and metabolites. Their alteration can be an indication of a critical health condition. Therefore, regular testing is essential. However, most of the analytes tests are done in a medical lab and based on blood samples, which is considered invasive, and can be expensive. Clinical laboratories tests remain to be a central component of people health care, but they are now complemented by tests performed outside of the clinical laboratory [11]. Screening tests can be done by users anywhere using point-of-care devices.

1.1.1 Wearable Medical Devices

Some point-of-care devices can be integrated into wearables. [12]. A wearable medical device can be defined as an independent, non-invasive system that performs a specific medical function such as monitoring or support. The term "wearable" implies that the device is either attached directly to the human body or a piece of clothing and has an appropriate design enabling its prolonged use as a wearable accessory [13]. Wearable medical devices have the advantage that they can be worn in comfort for a long time while making daily activities. However, most health monitoring wearable devices use digital sensors which are expensive and required power source and maintenance.

1.1.2 Microfluidics

Microfluidics are widely used in chemistry and biology specially for disease diagnosis. One of the main advantages of microfluidic devices is the ability to employ small sample volumes in analytical tests [14]. Using a non-electrical device can provide a low cost, real-time, customizable, lightweight, and more environment-friendly device. This can be done by implementing paper-based microfluidic technology that uses paper as the main material. Papers do not require pumps as the liquid will flow due to capillary action. In addition, paper microfluidic is flexible and can be folded to create different designs. The sensing function in paper-based microfluidics is implemented by taking the advantage of colorimetric indicators that initiates a reaction with a specific analyte resulting in a color change. Colorimetric indicators provide easy-to-understand results. The user only compares the color result with the indicator's color scale. In addition, paper-based microfluidic engaged for developing point-of-care devices [15].

1.1.3 Human Sweat

A sweat sample can be used as a non-invasive approach for medical tests as it can be collected on the skin's surface. Sweat samples are composed mostly of water in addition to different analytes such as sodium, potassium, and chloride electrolytes, inhibitors, anti-gens, antibodies, and different xenobiotics such as drugs, cosmetics, and ethanol (Figure 1.1). Diseases can change sweat composition either by altering the concentration of common components or reporting new components that, in any case, could act as biomarkers of the given disease [16]. Sweat is used to diagnose diseases such as cystic fibrosis (CF), where sodium and chloride can be easily measured in this body fluid [17].

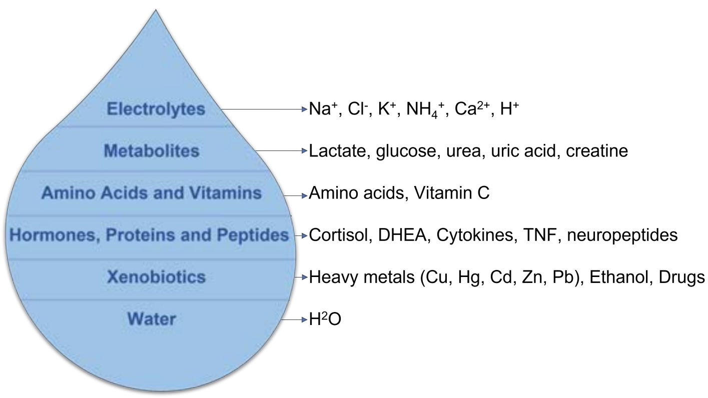

Figure 1.1 Composition of Sweat

Sweat glands are distributed all over the skin the largest organ in the human body. “The skin is the largest organ of the human body and provides a very large surface for the placement of and interface with a sensor.”

The sweat rate differs among body regions (Figure1.2) [1].

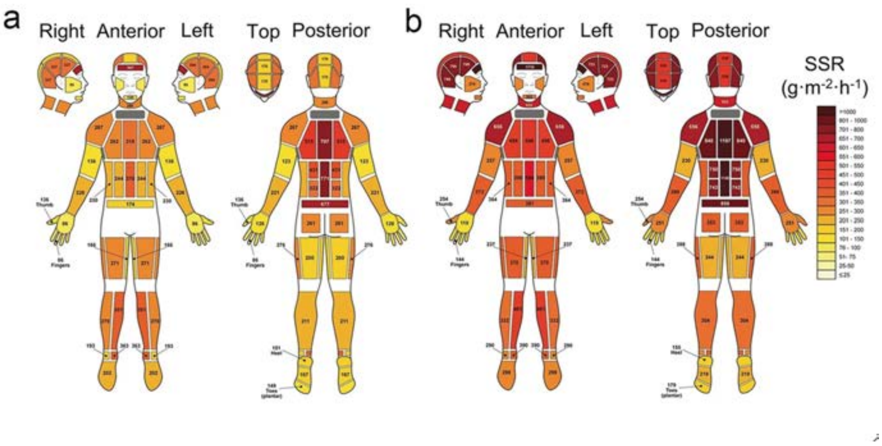

Figure 1.2 Mapping of Sweat in Human Body [1]

1.2. Motivation

In medieval Europe, they use to know that child who tastes salty from a kiss on the brow will die soon [18]. This is because salty sweat is an indicator of a high level of sodium chloride, which is a diagnosis of cystic fibrosis disease that damages the lungs, digestive tract, and other organs leading to death, if not treated. Many people do not know that the diagnosis of a deadly disease can be as simple as a kiss on a child’s brow. To this end, health monitoring can be delivered to people in a very simple and enjoyable way. If they enjoy the experience they will likely adopt it to their daily life and it will be part of their routine. This approach has the potential of preventing them from having serious health problems due to a late diagnosis and give them the chance to react before it is too late.

1.3. Objectives

This study aims to develop paper-based microfluidic modules that allow users to customize and use their own wearable sensing device to make a real-time screening health test. The device will use the sweat as a test sample to provide a non-invasive approach. Paper-based microfluidic modules will provide an enjoyable and fun user experience. In addition, to the visual feedback that will be provided by the colorimetric indicators. As the paper will be the main material of the device it will be low-cost, flexible, foldable and more environmentally friendly. The device will not appear as a medical tool but as a fashion component.

1.4. Thesis Outline

This thesis is organized into different chapters, and each is described as follows:

- Chapter 1 provides a general background, motivation and the objectives for this thesis.
- Chapter 2 presents some work related to this thesis with their limitations and is divided into four different categories.
- Chapter 3 gives a general overview of technologies and materials that were used to make the prototypes. It also introduces subsequently the methodology and implementation of different prototypes developed with their evaluations.
- Chapter 4 presents the final developed prototype. In addition, this chapter presents a user study implemented with the analyses of the results using charts and tables to provide detailed information. At the end of this chapter, a discussion is presented.
- Chapter 5 summarizes the thesis and also suggests how the thesis topic could be extended in the future.

Chapter 2
Literature Review

This study is related to research in wearable sensing devices, analytes sensing and customizable interfaces.

2.1. Digital Wearable Devices

Digital wearable devices widely used nowadays spatially for health monitoring.

In SkinKit research, a construction toolkit for on-skin interfaces was developed to be used for different applications, such as in health to monitor body temperature or detecting breaths, safety, social, notification, fashion, dance and sport [2].The kit contains flexible printed circuits board blocks with different types such as sensor, actuator, modifier and power module. The blocks can be connected in three different ways: PCB connection with flaps, PCB connection without flaps or wire connection (Figure 2.1).

Figure 2.1 SkinKit [2]

Rose et al. developed a radio-frequency identification (RFID) sensor bandage for sensing of electrolytes, such as magnesium, potassium and chloride in sweat, by integrating a commercial RFID sensor in a bandage. The study proposed two ways to collect and allow the sweat sample to reach the sensor using paper microfluidics wick to allow the flow of swear from the skin to the sensor, or placing the sensor directly on the skin [19].

A low-power, highly responsive and reusable sweat pH monitoring device was developed by Wang et al. [20]. The device contains a flexible and fast reactive pH sweat sensor that can be integrated into a pulse oximeter that was fabricated using polyaniline polymer. The pH sensor is made using a material that changes color when mixed with sweat. By integrating the customed pH sensor and the developed pH sensing algorithm into existing fitness devices such as smartwatches that already have a pulse oximeter, the watch can monitor the pH value of a user's sweat, heart rate, and blood oxygen levels all together in real-time, with accuracy, reaches 90 percent.

The main limitations for digital wearable devices are the expensive price and the need of maintenance and power supply.

2.2. Permanent Tattoo for Analytes Test

Permanent tattoo provides a better approach for health monitoring, as it does not require power supply or maintenance.

In Dermal Abyss project, researchers focused on human skin to be used as an "interactive display" by applying biosensors on the skin as ink for permanent tattoo patterns [21]. The research focused mainly on detecting sodium, glucose, and pH of the skin's interstitial fluid. The ink used for the tattoo was colorimetric and fluorescent biosensors. The research clarifies that using biosensors in wearable materials can be safer, comfortable to use, and easier to improve and maintain. On the other hand, it can be difficult to use since it will not be close to the body biomarkers. The research used diaza-15-crown-5 to detect sodium ions and it changes color from yellow to red when sodium ions are detected. In a research done by Viirj Kan et al. organic materials that are working as detectors by changing color, smell, and shape when mixed with acid or alkaline were introduced [22].

One of the applications for these materials is to sense lactic acid in sweat.

The challenges for permanent tattoo is the difficulty of maintaining the indicator accuracy after sometime. Also, the indicator is applied directly on the skin which may not be a safe approach. The permanent tattoo patter can be selected once and it will be difficult to change.

2.3. Design Tools

The design tools provide a customized method for making different design patterns.

Many methods for developing design tools were studied. Some of the studies focused on building a design tool for printing circuits directly on the skin while others focused on developing a design tool to customize patterns to make flexible devices.

Youngkyung Choi et al. developed a body printer to make conductive circuits on the skin [3]. The printer depends on a software to provide a graphical interface to make custom shapes, which can be directly printed on the skin (Figure 2.2). The software is programmed with Java and hardware, which are controlled with an Arduino microcontroller. In a research study done by Muling Huang et al. the tattoo customization design“ColorGuardian” system was developed to design and print a customized temporary tattoo for children with vitiligo [4]. The system is

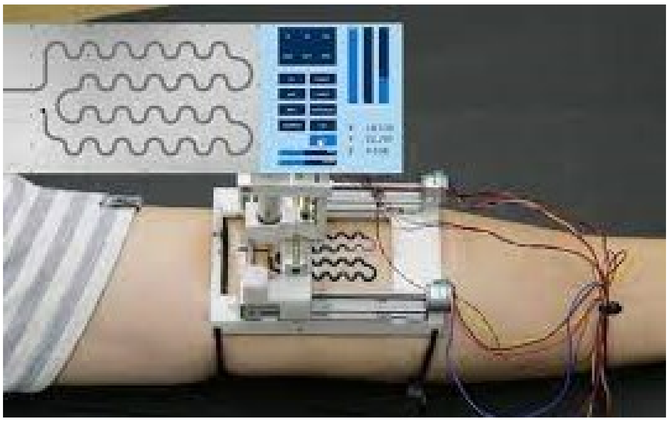

Figure 2.2 Design Tool and Printer for Tattoo Printing [3]

divided into two main parts (Figure 2.3). The first part is tattoo pattern design

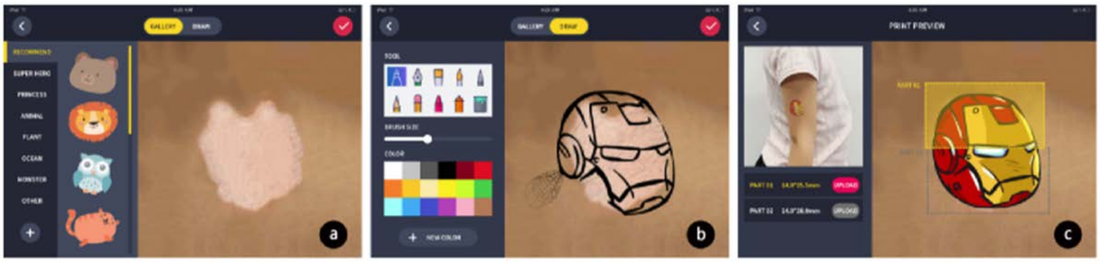

Figure 2.3 Design Tool and Printer for Children with Vitiligo [4]

or pattern selection customization, while the second part is pattern printing. The printer uses as a safe ink for children. In the FoldTronics project, new software was introduced to design 3D models [23]. Their approach starts with a 2D plastic sheet that should be folded to make a 3D shape. Daniel Groeger et al. introduced a LASEC design tool that enables users to customize the stretchability and stretch direction of a material [24]. Paredes et al. presented a system that enables the design and fabrication of customized functional hand electronic wearables [25]. It is designed to generate a printable pattern for fabrication which can be used to detect a hand's motion, orientation, or tracking vital signs. DeChiara et al. introduced an open software platform for the automated design of paper-based microfuidic devices called AutoPAD (Figure 2.4) [5]. AutoPAD is an open source

Figure 2.4 AutoPAD Software [5]

for researchers in laboratories and school students.

The disadvantages of using design tool as a customization approach are that it needs knowledge to use the software, equipment like laser cutter and materials for fabrication.

2.4. Microfluidic Interfaces

Microfluidic approach allows to make a non-digital device that can be used for different application such as analytes monitoring.

Many research focused on creating new methods to make microfluidics.

In the Flowcuits project, a DIY fabrication approach was presented to make physical, interactive, and functional electrical components using liquid metals [26]. Three D-printed stamps are used to make channels on moldable material such as 'Blu Tack'. Then a conductive liquid metal is applied to the channels to connect between electronic components placed at the start and endpoints of the channels. In another research by Jingyu Xiao et al. a wearable microfluidic chip for detecting glucose from sweat was developed as a noninvasive approach [27]. It was fabricated using polydimethysiloxane (PDMS) as the main material. The chip consists of four layers, sensing layer, balance tunnel layer, cavity layer, and adhesive layer. The research used sweat for testing glucose in the human body because it can be collected noninvasively from the surface of the skin.

Koh et al. focuseed on making a similar microfluidic chip with four outlets, to detect glucose, pH, chloride and lactate (Figure 2.5) [6]. Venous Materials

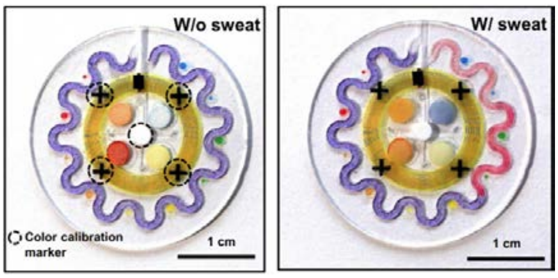

Figure 2.5 Microfluidic Chip [6]

project [7] introduced a design tool to allow users to easily design geometry for a variety of applications (Figure 2.6). The design tool was built in Rhinoceros 6 editor and Grasshopper environment. The user first selects a geometry pattern. Then, the user can configure the geometry by drawing the area in which the geometry will be generated. After that, the user defines the flow direction by setting a starting and ending points. Finally, the chosen pattern is automatically generated. Silicone Devices study presents a fabrication workflow for making

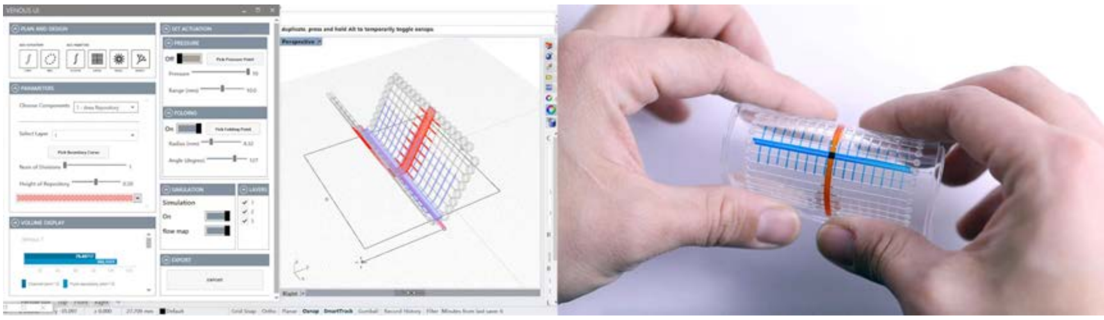

Figure 2.6 Venous Project [7]

stretchable silicon devices using a CO2 laser cutter [8]. The microfluidics circuits are created by designing silicone channels directly and filling them with conductive liquid metal (Figure 2.7).

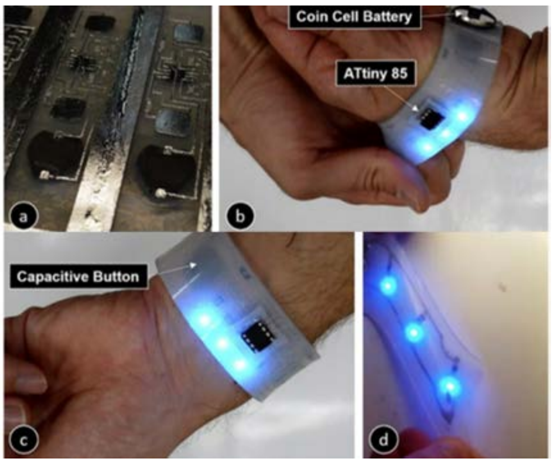

Figure 2.7 Flowcuits Project [8]

Microfluidic devices can be fabricated using different materials such as silicone and PDMS. However, the most cost-effective approach is paper.

2.4.1 Paper Based Microfluidics

Paper-based microfluidics provides a low-cost approach for making microfluidic devices. Paper-based microfluidic analytical devices are used to detect analytes (biomarkers, etc) in different body fluids such as saliva [28], tears [29], wound's interstitial fluid [30] and sweat [31–33].

There are many technologies that can be used to make a microfluidic patterns on paper such as photolithography, flexographic printing, wax printing [34], plotting, plasma etching, laser cutting [35, 36] and other technologies [37].

Gang Xiao et al. introduced, a wearable, cotton thread/paper-based microfluidic device that senses glucose in sweat [38]. The developed µTPAD contains three main parts which are the absorbent part, a hydrophilic cotton thread, and a functionalized filter paper. Chitosan, GOD, HRP, and TMB were used as glucose indicators. The absorbent cotton patch is attached to one side of waterproof fabric and directly close to the human skin as a store to collect sweat. The glucose indicator is dropped on the other side of the fabric to avoid any cross-contamination of the sweat sample. The hydrophilic thread is sewed on the fabric. A mobile application (Color Grab) is used to analyze the color change and gave a quantitative result of the glucose level in the sweat sample.

Abbasiasl et al. proposed a method to fabricate a wearable paper-integrated microfluidic device for sequential analysis of sweat based on capillary action to conduct colorimetric analysis for glucose and pH in sweat. The device consist of five layers: capping layer, filter paper, microfluidic layer, bottom layer and skin adhesive, which is sticked to epidermis [39].

2.4.2 Modular Based Microfluidics

Modular-based microfluidics continuously receive attention from researchersas it provides a customizable method to build microfluidic devices.

Microfluidics LEGO bricks were developed by MIT researchers (Figure 2.8) [9]. Jing Nie et al. introduced a method to make Lego blocks using 3D printer that were designed with CAD software [40]. The 3D printed Lego blocks has channels where the capillary materials is applied.

Yuen et al. made a reconfigurable stick-n-play modular microfluidic system

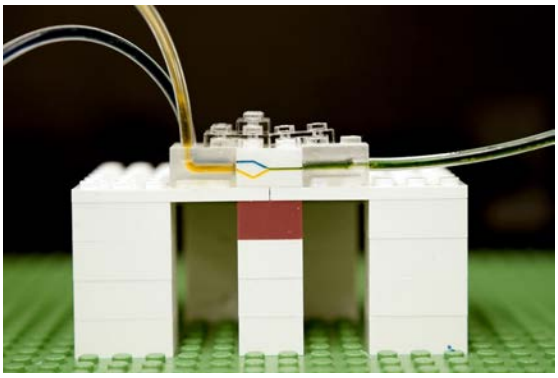

Figure 2.8 Lego Microfluidic bricks [9]

using magnetic interconnects [41].

Ampli project, introduced a modular paper-fluidics [10], which is similar to my modular approach. It is based on using different types of blocks, including connected together. There are six types of blocks sample, transport, conjugate, absorbent, protein carrier, and battery block (Figure 2.9).

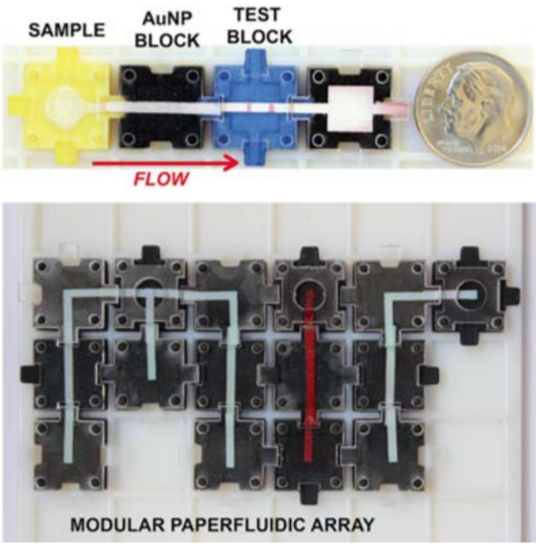

Figure 2.9 Ampli Reconfigurable Blocks [10]

2.5. Summary

Some of the highlighted studies focus on making digital wearable devices using electronic circuits, which is considered expensive, and required power source and maintenance.

The developed method in making a permanent tattoo for health monitoring is a good approach as the indicator will be directly on the skin and close to body analytes however, the disadvantages of this approach is that the efficiency of the indicator in the tattoo ink is reduced after some time. Also, the tattoo design will be fixed and cannot be changed easily and for some people, the tattoo ink may cause skin allergies.

The proposed approaches for making microfluidic interfaces are useful. However, it requires special materials, which are costly and require many steps. In addition, a small hole on the surface can cause liquid leaks.

Modular microfluidics blocks allow customization for building different microfluidic devices however, extra efforts must be made to overcome the weaknesses of leaking and aligning between individual modules [40]. Moreover, the blocks are not flexible and cannot be applied to make a wearable device.

In contrast, this study approach is to implement microfluidic technology using paper and colorimetric indicators which will be suitable for making a customizable and flexible wearable device at a low cost, and liquid is not leaked after soaking.

Chapter 3
Concept Design

In this chapter, the research materials and technologies are explained. Many prototypes were developed to overcome the weaknesses of the previous one and make an easy-to-make customizable paper-based microfluidic wearable device. The design and fabrication process for different prototype versions with their evaluations are presented.

3.1. Pre-User Study and Interview

3.1.1 Interview with clinical biochemistry specialist

To get an overview of the current situation for the analytes' tests, challenges, and opportunities, an interview with a clinical biochemistry specialist was conducted. The specialist explained that point-of-care testing is good for a screening test where users can have a general idea about their overall health condition and not for the diagnosis, as it is not accurate and precise. The specialist added that commonly used points of care teasing is for glucose and pregnancy hormone.

Currently, colorimetric strips are used for urine test samples for pregnancy or for babies that have some symptoms and are expected to have lactose intolerance.

3.1.2 Pre-User Study

An online user study was conducted to know if people are interested in making their own wearable sensing device. The user study was divided into three parts. In the first part, an introduction to the research was given. In the second part, participants were asked to make some patterns that they would like to have as wearable devices using pen and paper. Then, participants were asked to color their patterns, cut them, and stick them on their bodies using transparent tape. After that, the patterns were collected. In the last part of the user study, participants were asked to fill out a survey. The survey consists of three main sections demographic, health condition, and design section (Figure 3.1).

Demographic Section:
- Gender
- Age

Health status
- Health condition associated to altered analytes
- Importance of normal analytes level awareness
- Frequency of taking analytes level test
- Heavy exercises practice
- Frequency of participate in sport or physical activity
- Diet
- Awareness of analytes test
- Interest in checking the analytes level
- Interest in taking noninvasive analytes test

Design
- Device or sticker preference
- Pattern preference
- Interest in designing and manufacturing own wearable device
- Preference of indicator type
- Preference of indicators colors
- Wearable device size preference

Figure 3.1 Survey's Contents

The user study was conducted on three participants. In general, the pattern designed by participants can be divided into three main categories, which are geometric, natural, and emojis (Figure 3.2). The survey showed that all partici-

Figure 3.2 User Patterns

pants are interested in making their own wearable sensing device. Moreover, all participants would like to monitor analytes levels in their bodies noninvasively.

3.2. Technologies and Materials

In order to make a customizable wearable sensing device, different technologies were used (Figure 3.3). The device is based on microfluidic technology that allows

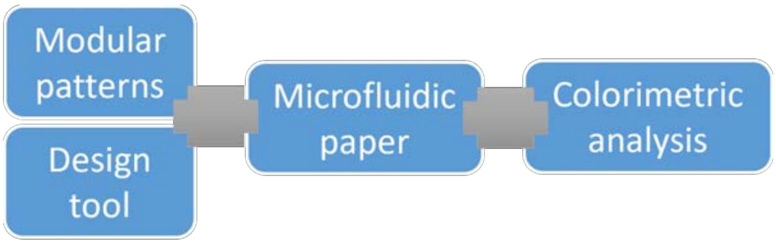

Figure 3.3 Technologies Implemented

the flow of small values of liquid from the start point of collecting the liquid to the endpoint of analyzing and sensing. Specifically, the paper-based microfluidic method was employed using hydrophilic paper to allow the flow of liquid with capillary action. The Modular patterns were used as a customizable approach. For the sensing functionality, colorimetric indicators were combined with the paper-based microfluidic modules.

3.2.1 Filter Paper

Advantec qualitative filter papers grade 1 was used in this research 3.4. It is made of cotton cellulose and has a fast flow rate and thickness of 0.20 (mm). Grade 1 Filter Paper was selected to be the main material because it is the most commonly used paper for the fabrication of analytical devices in laboratories such as Paper-based analytical devices (µPADs) [42].

Figure 3.4 Advantec Filter Paper

3.2.2 Colorimetric Indicators

Health Monitoring Indicator

pH indicator can be used for health monitoring. It measures how acidic or alkaline a sample is. Sweat pH gave information about if the body is dehydrated for example as the sodium will be highly concentrated and that will cause a high pH value. Moreover, sweat pH can help in the diagnosis of skin conditions, such as dermatitis, acne, and other skin conditions. In addition, for diabetic patients, sweat pH may provide a good indication of another life-threatening status, for example, a high sweat pH during extreme sweating at night may be caused by a long period of low blood glucose that required medical intervention [20].

To make the sensing modules, universal pH indicator strips were used. The universal indicator has four reaction zones. Only the third zone (4-9) was used as it reacts to a pH level around neutral pH 7, which is the case for the human sweat pH range (Figure 3.5). Human sweat's normal pH range is between 4.5 and 7.0, which is relatively acidic to neutral pH [43].

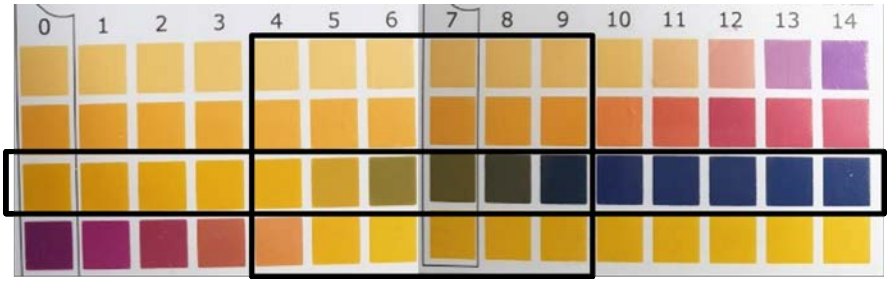

Figure 3.5 pH indicator

Glucose levels also can be monitored from sweat samples. Therefore, a glucose strip indicator was used to give the user the choice of making a multi-indicator device. The indicator range between 0 to 2000 mg/L 3.6. The normal range of glucose in human sweat is between 0.06 and 0.2 mM, which corresponds to 2.76 mg/L and 9.2 mg/L respectively [44].

Figure 3.6 Glucose Indicator Color Scale

Sample Flow Indicator

In order to show the flow of the sweat in the micro-channels potential of different colorimetric indicators was studied. A sweat colorimetric Ninhydrin-based reaction was found to be not suitable for a direct short-time reaction as it needs around one hour for the color change to be observed. Another potential indicator is the hydrochromic ink that changes color or becomes transparent when exposed to water. The hydrochromic paste ink was used by mixing it with water then the paper modules were inundation in the hydrochromic liquid after that it was dried. However, when the hydrochromic ink was applied to the pattern it makes a layer that reduces the liquid flow in the paper module (Figure 3.7). Finally, a water

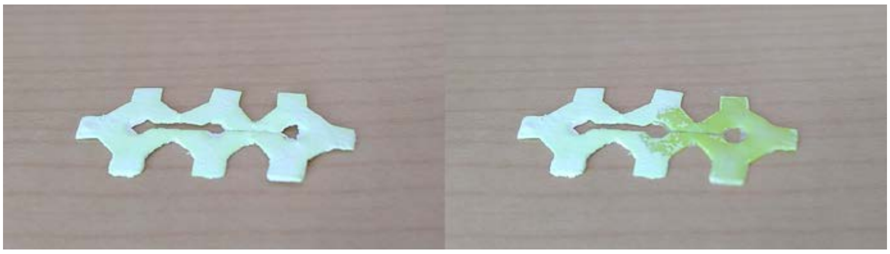

Figure 3.7 Liquid Flow When Hydrochromic Ink is Used

erasable ink was used to provide a direct reaction 3.8. The erasable ink will be

Figure 3.8 Erasable Ink

removed when the sweat sample flow in the micro-channels. The erasable ink was applied only to the transport modules so it does not affect the detection in the sensing module. Also, it was not used in the absorption module because it may color the skin or the wearable as it is not covered from one side for the absorption purpose and it will be hidden so it will not be observed anyway.

3.3. First Prototype

A design tool was developed to allow users to design wearable devices intuitively, using a 3D CAD software, Rhinoceros, and its add-on, Grasshopper. First, the user creates an arbitrary 3D model (figure 3.9 a). The finished object consists of a waterproof layer and a hydrophilic layer that can easily absorb liquids. The

Figure 3.9 Prototype 1

user sets the start and endpoints for the liquid diffusion. The starting point is where the liquid will be absorbed, and the endpoint is where the pH indicator will be applied. Two liquid pH indicators were used Anthocyanins and Bromothymol blue. Both points are generated by drawing a line through the center of each mesh using the Graph theory and then developing the shortest path using the Dijkstra method.

This approach may not be used by people who do not have an access to laser cutters. Therefore, developing a kit with modules can be used by everyone.

3.4. Second Prototype

In the second prototype, paper-based microfluidic modules were designed. Figure 3.10 shows the use case diagram for using a kit of paper-based microfluidic modules. Each user can customize their own wearable sensing device using the kit for paper-based microfluidic modules. The customized wearable sensing device can be attached to the wearable to make the daily wearable an interface for health or it can be an independent wearable. It can be placed on nearly any skin touching area on the human body: wrist, ankle, waist, chest, arm, legs, etc. After that, they should make any activity that makes them sweat such as exercising that will change the color of the indicator in the device based on the level of analyte detected. Then, the user should compare the color change with the indicator color scale. If the result color is within the normal range, it will be an indication of being healthy. Otherwise, the user should react depending on the analyte that was detected by taking supplements, drinking more water, or making an accurate test in a medical lab. The user may keep the device in their diary to track their health over time.

Figure 3.10 Use Case Diagram

The device has a start point, where the sweat is collected, and an end point where the analyte will be detected. The end-point act as the sensing point, where a liquid ink is applied (Figure 3.11). However, uncovered modules do not keep the

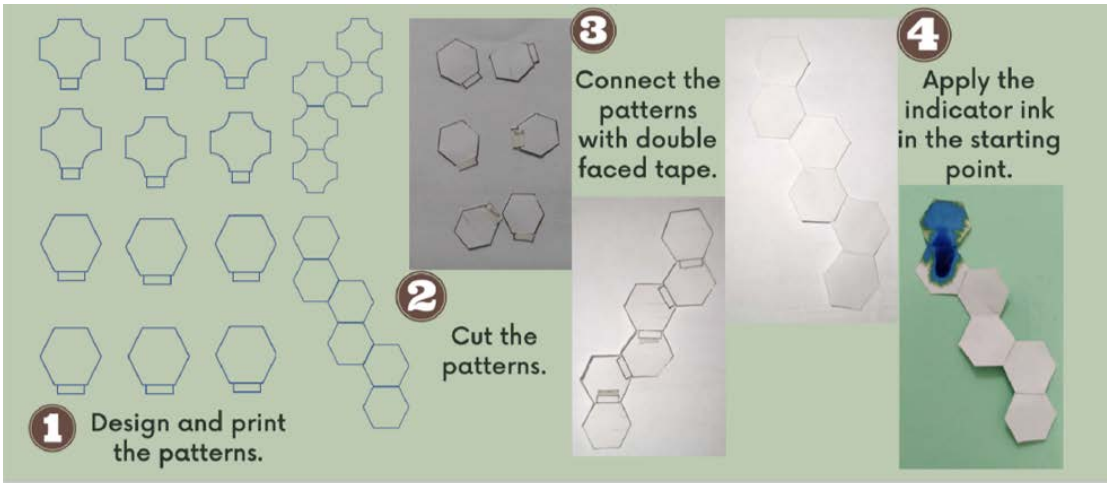

Figure 3.11 Prototype 2.1

sample for a long time, as it will be evaporated and become contaminated from the outside environment. Therefore, the prototype was fully covered except for the absorption module (Figure 3.12). First, the modules were connected together

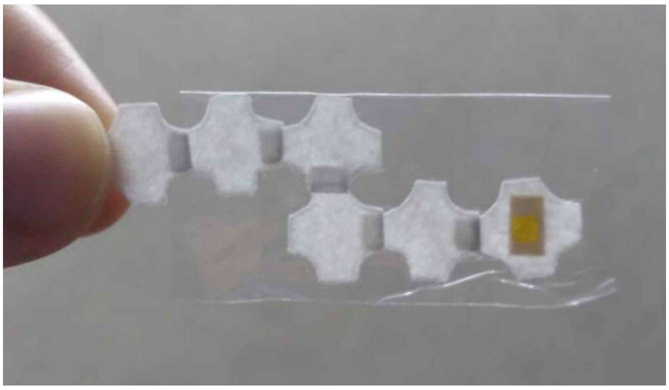

Figure 3.12 Prototype 2.2

with a double-sided tape. Then a cling wrap was used to cover the connected patterns by applying heat for the lamination. In addition, the liquid indicator was replaced with a strip indicator to insure accurate results. Covering the device fully with cling wrap after connecting the modules does not allow having independent modules. Therefore, this weakness was addressed in the next prototype.

3.5. Third Prototype

Many different modules shapes were designed 3.13. All the designed shapes were simple, as they will be used as a module for simple disposable devices. The shape

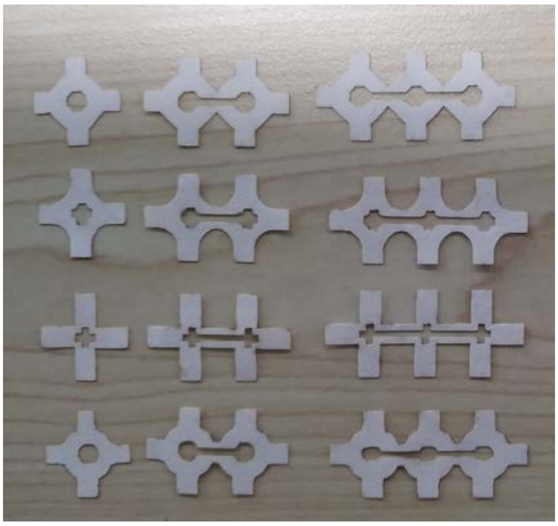

Figure 3.13 Other Module Shapes

of a regular octagon (regular polygon with eight sides) that has four wings was selected to be used as the main shape in this study (Figure 3.14). The four wings

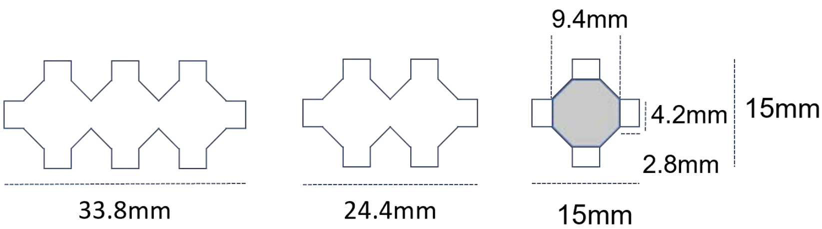

Figure 3.14 Modules Sizes

design provides four liquid flow directions. Three types of modules were fabricated to be used for different purposes including absorption, sensing, and transport module (Figure 3.15). The transparent tape is used to cover the modules [45–47].

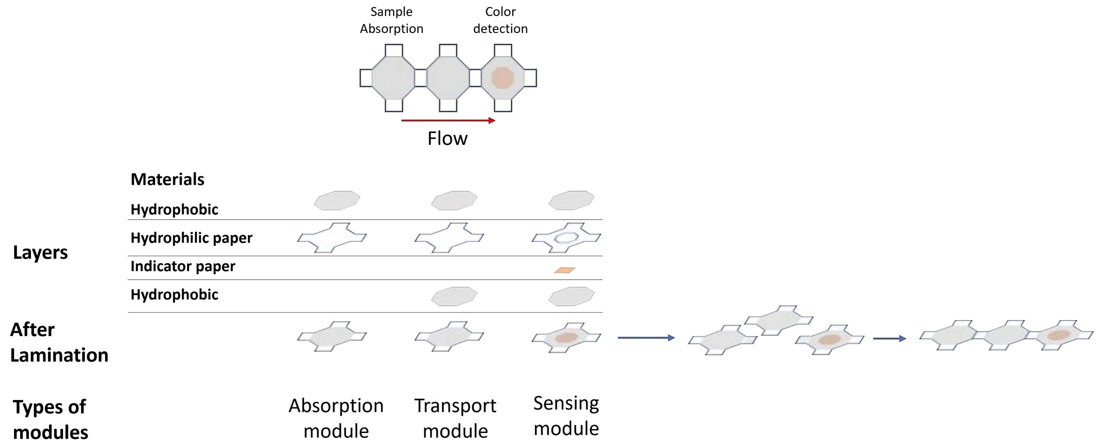

Figure 3.15 Modules Design Structure

It will provide a hydrophobic layer because it is transparent and flexible, which allows observing the sweat flow and color change and keeps the flexibility and foldability of paper while protecting it from being catted easily. The modules were designed in PowerPoint and saved in scalpel vector graphics format (svg). Then, the svg file was opened in Laserbox software and some modifications to the size were made. After that, the designs were catted using a laser cutter. Figure 3.16 shows the modules cutting process. The designs were catted on a qualitative

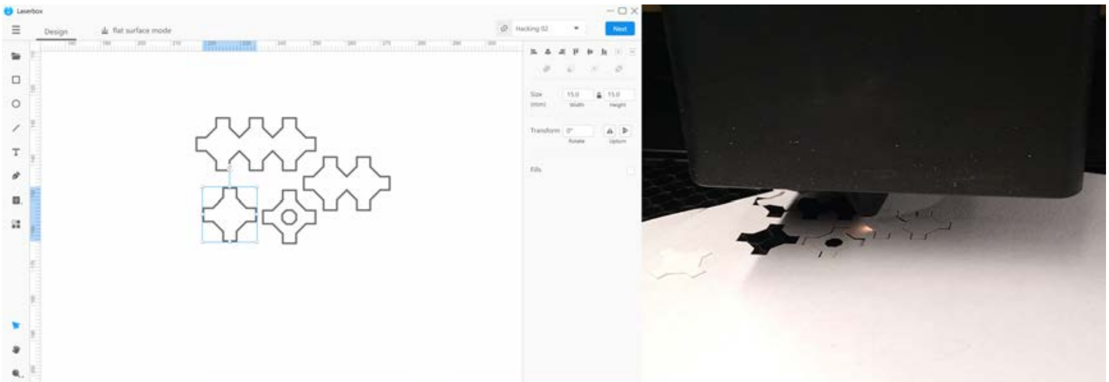

Figure 3.16 Cutting the Modules

Advantec filter paper grade 1 with a thickness of 0.20 (mm). A transparent tape was used to cover the modules to avoid contamination and evaporation of the collected sweat sample. For the sensing module, universal pH and Glucose indicator strips were used. In order to connect two modules, a tissue double-sided tape is used because the material of tissue tape will not block the flow of liquid between the two connected modules (Figure 3.17).

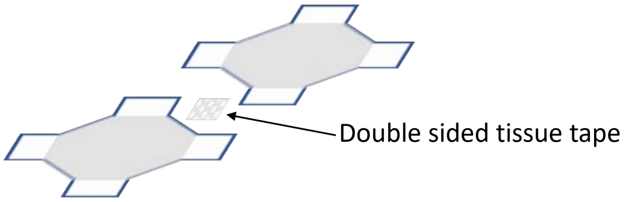

Figure 3.17 Connecting Two Modules

The absorption module is used to absorb sweat samples on the skin and is considered the start point for the flow. Therefore, it should be at a touch point with the skin surface. It is covered with transparent tape from the top side only to give the paper modules support and avoid sample evaporation and contamination. However, the wings are not covered to allow the liquid flow when connecting modules. The sensing module contains the colorimetric indicator and represents the endpoint for the sample flow. It is covered from both sides and has a small window (hole) for the indicator strip 3.18. The transport module is the module

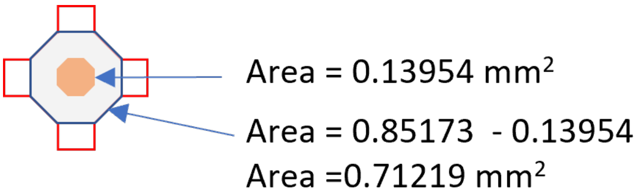

Figure 3.18 Area of Sensing Module

that can be used to connect between absorption and sensing modules. It is covered from both sides. There are three different shapes of the transport module: single, double, and tribal to allow customization for more patterns (Figure 3.19). Figure 3.20 shows examples of devices attached to a hand watch and collar.

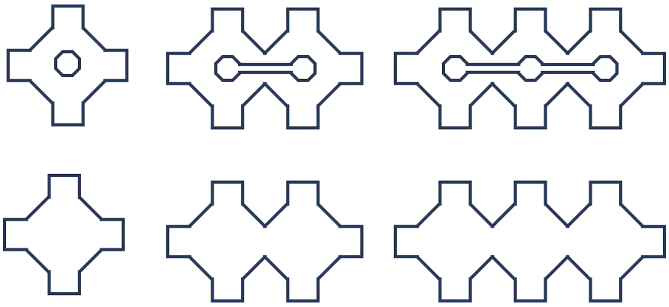

Figure 3.19 Transport Modules

Figure 3.20 Device Attached to Watch and Collar

3.5.1 Flow Experiment

There are many different ways to control the flow time for the paper-based microfluidic such as changing the paper thickness, or channel dimensions [48]. Usually, one of the main ways to control the flow time for the paper-based microfluidic is by changing the width of the microchannels. Wider microchannels mean less flow time and narrow microchannels mean more flow time [49].

In this research, different transport patterns with different channels width were fabricated. In order to get narrower channels and make a nice design, a hole was made in the middle of the modules. Figure 3.21 shows the area calculated for different transport modules.

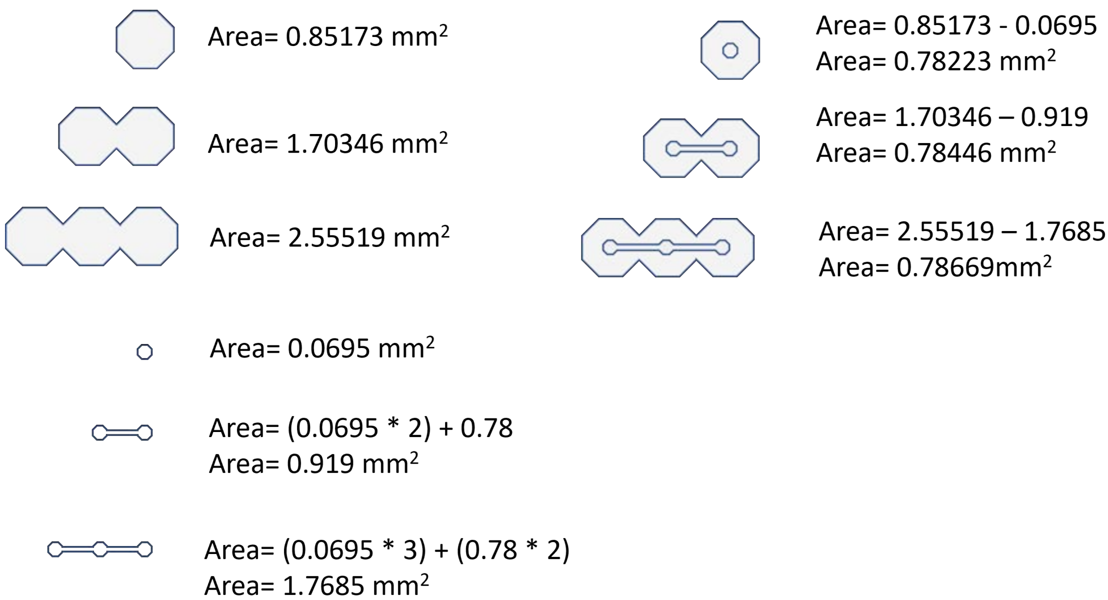

Figure 3.21 Modules Area

Regular polygon area formula was used to get the area for the regular octagon. Which state that for a regular n -gon whose side length is L, the area is

$$Area = \frac{nL^2}{4tan(\frac{180}{n})}$$

where tan is the tangent function calculated in degrees.

The time that the liquid took from the beginning of the module to the end was measured. The flow in the wider channels was faster and took less time compared with narrower channels. For the single and double modules, the difference was 16 and 17 seconds respectively whereas the difference for the triple module was 51 seconds. Figure 3.22 demonstrate the total flow time for each pattern. The user can use the patterns based on the activity they will make and the time. In order to get results faster, patterns with wide channels should be used. The flow will also be affected by other facts not addressed in detail in this thesis, for example, if the device is folded, then this will also affect the flow time.

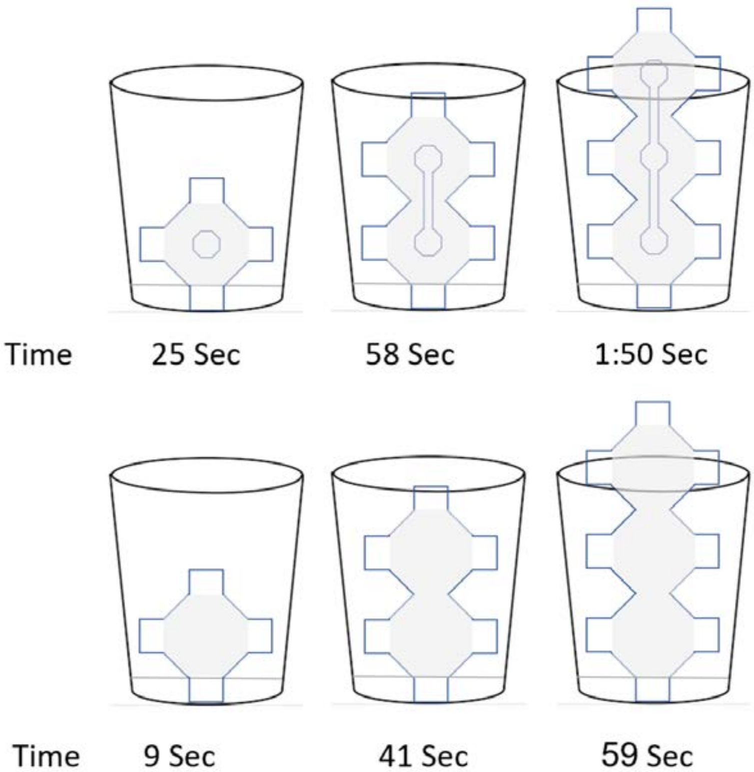

Figure 3.22 Comparison of Absorption Time for Different Modules

3.5.2 Third Prototype Evaluation

In this user study the device was evaluated from four different aspects: design customizability, enjoyability, usability and its effect on the lifestyle.

User Study Setup

Fifteen participants aged between 20-30 participated in the user study. The study was divided into three days. The first day is the workshop day, where the participants were introduced to the device and the materials were distributed (Figure 3.23). The materials are the three types of fabricated modules: absorption, transport, and sensing modules. For the sensing part, two types of indicators were used: pH and glucose indicators. Also, three types of transport modules were distributed: single, double, and triple. In addition, some waterproof modules were given, to help user make an independent device. Then, the participants were asked

Figure 3.23 Patterns

to make a sketch of the device they want to make and use to gave them chance for brainstorming(Figure 3.24). Before making their first device the participant filled

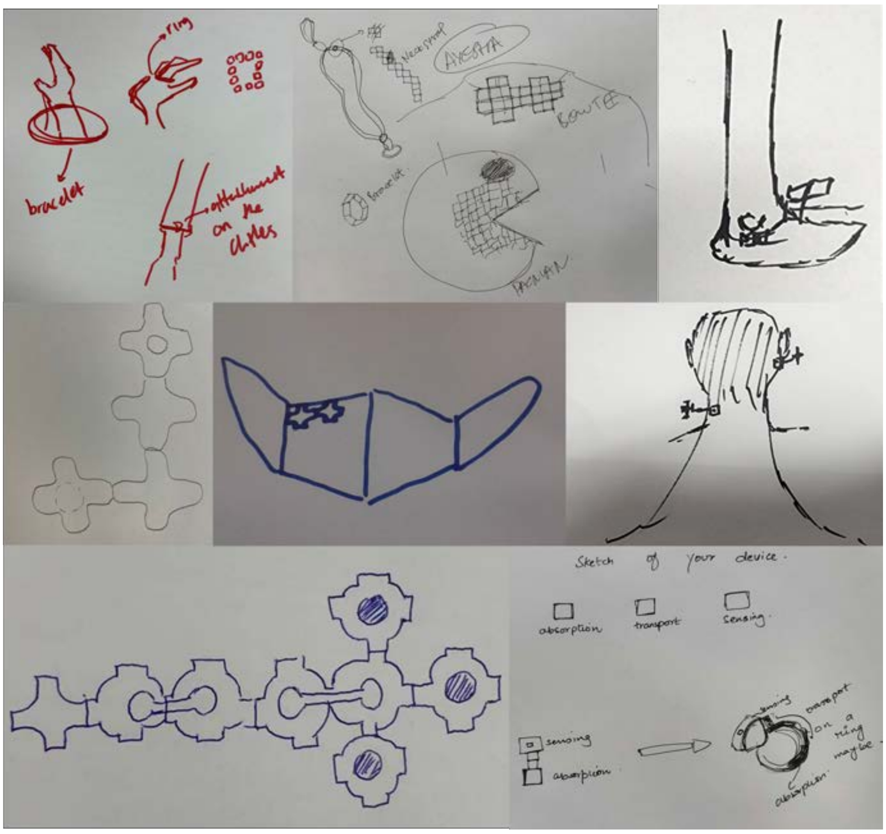

Figure 3.24 Some of Participants Sketches

out a before-use questionnaire in google forms that they had to fill based on their expectation of such a device. After that, the participants start with a hands-on activity where they made their first device (Figure 3.25). At the end of the first day, the participants took the materials and the device they made with them and were asked to use it and make two more devices for the next two days. On the third day, an after-use questionnaire was sent to the participants as a google forms link to fill out and upload pictures of their devices. Also, some participants were interviewed online with a zoom application.

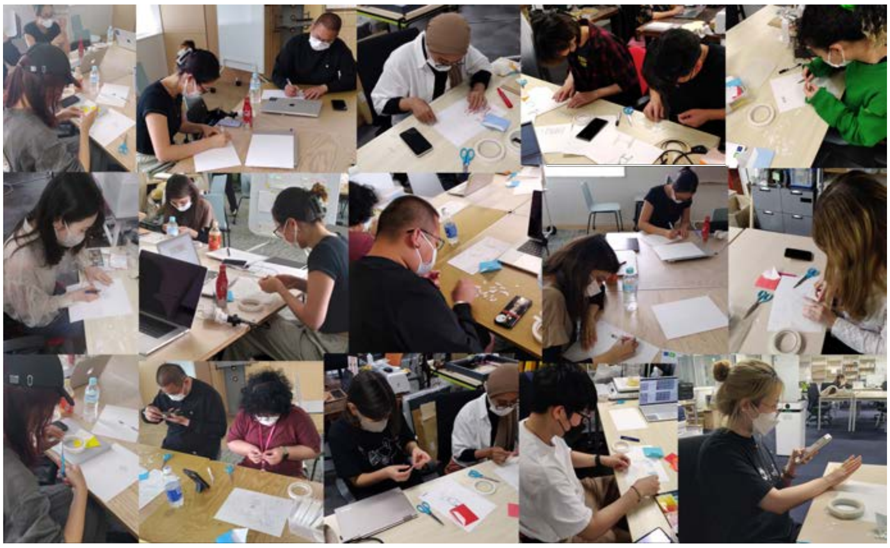

Figure 3.25 Workshop

Device Customizablility

The customizability of the device was evaluated based on the different devices produced using the papaer-based microfluidic modules. The devices that were made by participants can be divided into five different categories: on hand, on face and neck, on a shirt, on foot, and others. Based on the user study results, hand wearables were the most designed among users (Figure 3.26). Some users mentioned that because it is easy to make an independent device on hand like rings and hand bands. However, placing the device close to the hand's palm will

Figure 3.26 On hand Devices

increase the possibility of contamination of the sweat sample as people use the palm of the hand to touch and carry things. On the face and neck were the second most designed devices, where users attached the device to their masks, eyeglasses, headband, chain, and the neck (Figure 3.27). Some users attached their devices to

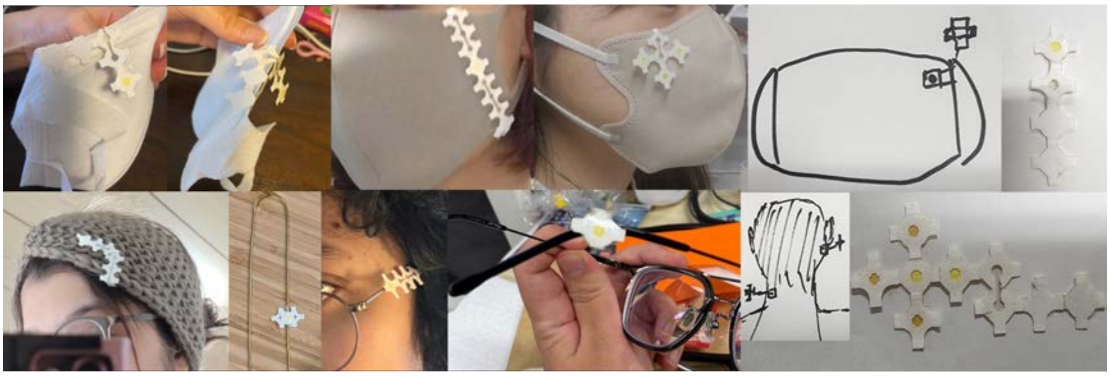

Figure 3.27 On Face and Neck Devices

their shirts (Figure 3.28). Three users attached the device to their socks (Figures

Figure 3.28 On shirt and belt Devices

3.29). In addition, a user thought about using the device, not as wearable but attaching it to attaching point to be on a mobile cover. Another user wants to use the device like a hair clip. The hair clip can not be a device to detect sweat as it is not with a teaching point with the skin. Different users want to make 3D shape devices without specifying where to be placed (Figure 3.30). Based on

Figure 3.29 On Foot Devices

the produced devices, the modules allowed users to make 2D and 3D shapes by folding the device on a wearable or connecting the device to be into 3D shape. Figure 3.31 demonstrates that most of the participants agreed that they can use

Figure 3.30 Other Devices

the paper-based modules to make any combination of patterns with 60 percent. 27 percent of participants strongly agreed. This result shows that the modules allow the customizability of the device.

Some of the produced devices may not be proper to be a sensing devices for analytes in sweat. Such as devices on the rings, mobile covers, and hair clips. However, the purpose of this part of this study is to test the customizability of the paper-based modules to get inspiration from participants' design creativity. Also, to know the preferred location on the human body for wearable devices.

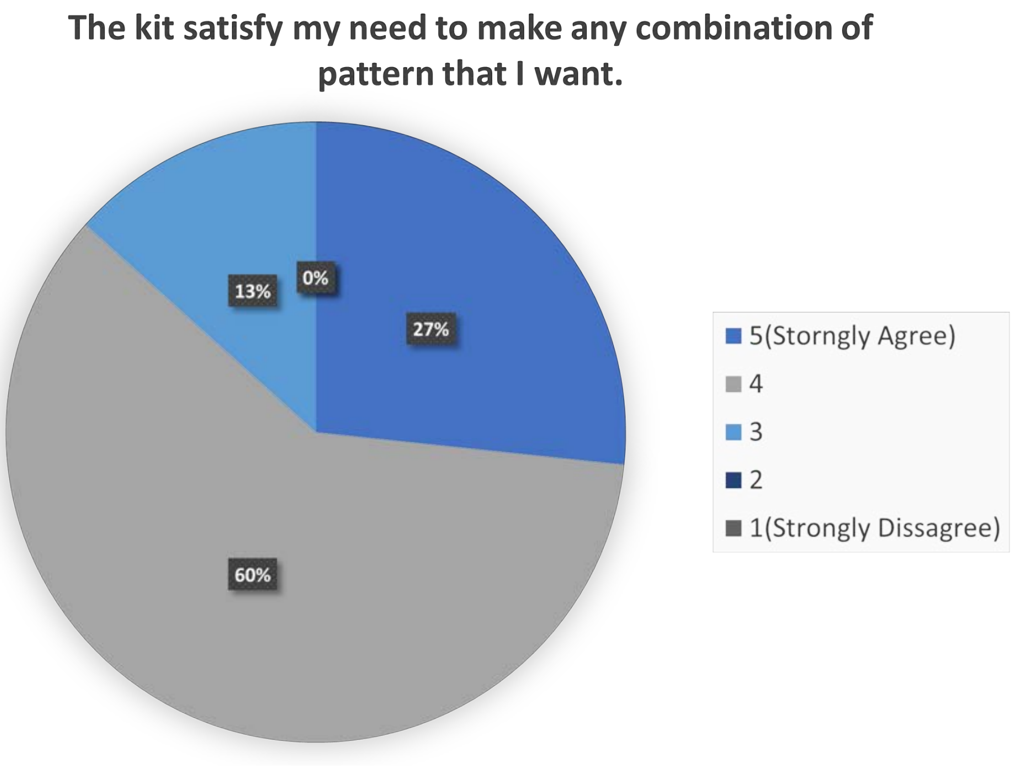

Figure 3.31 Customizability Results

Device Enjoyability

The participants were asked if they find the device enjoyable to make. Around 50 percent of participants agreed that they had an enjoyable experience making the device. In addition 14 percent strongly agreed (Figure 3.32).

User Impressions:

"I found the process of making the device very enjoyable because I'm into craft and art."

"I loved using this device."

"I liked using this device. Interesting."

"it's cool"

"It feels a little bit like a puzzle to me, so it's fun."

"I really like the idea."

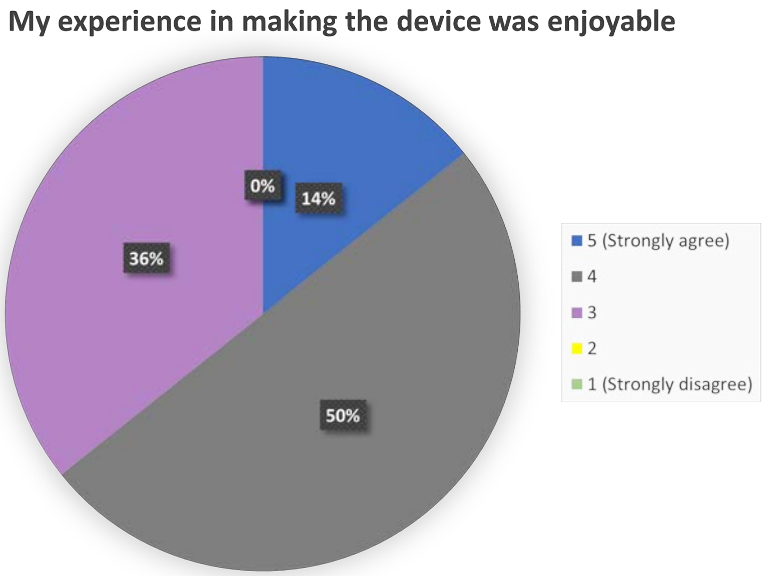

Figure 3.32 Enjoyability Results

Device Usability

System Usability Scale (SUS) of a 10-item questionnaire with five response options from "1" strongly disagree to "5" strongly agree was used to test the device's usability two times. The first time was before using the device based on their expectation after the introduction and explanation they got. The usability score was calculated by subtracting one from the odd number questions and subtracting the even number questions from the number five. Then, the results numbers were added to get the total for each user. Finally, the total for each user was multiplied by 2.5 to get the score for each user. To get the score for the usability test the average was calculated (Table 3.1). The score was 66.83333 which is corresponded to "Poor" usability. The second time was after the participants used the device the score was 64.16667 which corresponded also to "Poor" usability. As per participants' feedback, this is because they do not know if the sweat reaches the sensing module or not. Also, some of them said that they do not have an idea about the device they should make. In addition, some of the participants find it difficult to stick the double-sided tape on the modules as they are small. Another challenge they face is that the double-sided tape connecting the modules will not

Table 3.1 SUS for All Participants

No	1. Use frequently	2. Unnecessarily complex	3. Easy	4. Need support	5. Well integrated functions	6. Inconsistency	7. Learn quickly	8. Exhausting	9. Confident	10. Need to learn	Total	SUS	Grade
1	5	3	5	3	4	1	5	1	3	2	32	**80**	**B**
2	3	2	4	2	3	1	4	3	3	2	27	**67.5**	**D**
3	3	1	5	1	4	3	5	1	3	1	33	**82.5**	**A**
4	4	3	4	3	4	3	5	1	4	3	28	**70**	**B**
5	2	1	2	1	2	2	5	1	3	2	27	**67.5**	**D**
6	5	1	5	1	5	1	5	1	5	3	38	**95**	**A**
7	4	3	2	3	3	2	2	2	4	4	21	**52.5**	**D**
8	3	3	5	2	4	2	3	3	4	4	25	**62.5**	**D**
9	3	3	2	5	4	2	3	4	3	4	17	**42.5**	**F**
10	3	3	2	3	3	3	3	4	3	3	18	**45**	**F**
11	3	2	5	5	3	4	5	3	3	2	23	**57.5**	**D**
12	3	2	4	4	4	2	4	2	3	4	24	**60**	**D**
13	3	4	4	2	4	4	3	3	2	3	20	**50**	**F**
14	5	1	5	2	3	1	5	3	5	3	33	**82.5**	**A**
15	2	4	4	4	4	3	4	4	4	4	19	**47.5**	**F**
Average												**64.16667**	**D**

be strong to connect the modules when the patterns are wet.

Few number of participants with around 20 percent disagree that the device was comfortable to wear (Figure 3.33). Based on their feedback they were not sure where should they place it. Also, the weak connection between the modules when the device is wet did not make them feel comfortable while wearing the device.

User Impressions:

"*I think the device is a little bit small, so some people might feel hard when connect different parts together.*"

"*The devices were smaller than I thought.*"

"*The device is small and delicate, this could become troublesome for daily use.*"

"*The connection is kinda fragile, hope it can be connected more sturdy*"

"*Maybe different ways of connecting the parts of the device. This can make the experience more enjoyable.*"

Based on the user impressions during making the device, the small size of the paper-based modules can be a challenge for some people. In addition, the double sided tape was not stable after the modules are wet. These challenges affected the usability of the device.

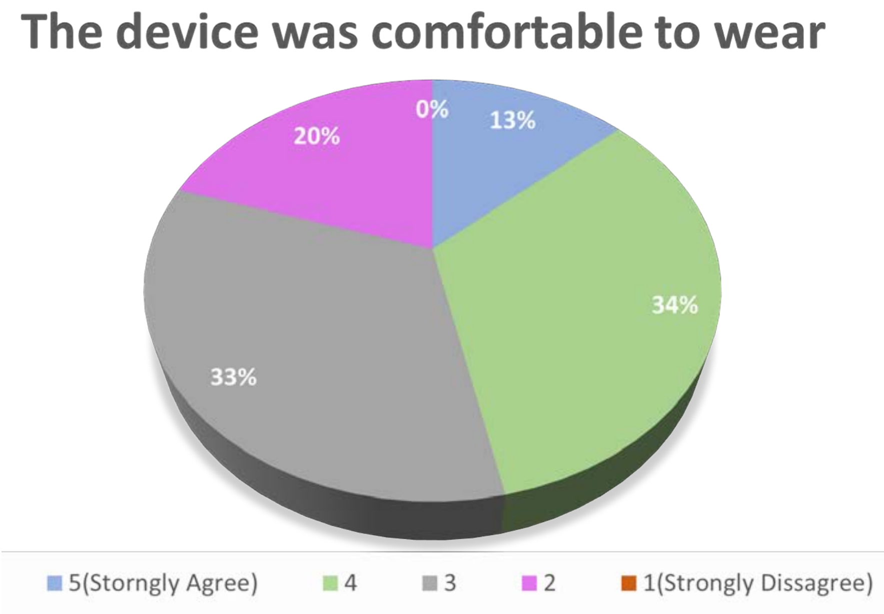

Figure 3.33 Comfortability of Wearing the Device

Improvement for better experience:

"*I am thinking if we use it every day, we can stick all the results on a dairy book! It will be so cute*"

"*The device making is really good. But maybe even customization can be done by the design tool.*"

"*maybe try different materials to increase the user experience because the wearing feelings are different if users wear it in different locations on their body*"

"*Maybe different sizes (and different shapes) for the module would be great besides the joint modules, also more color options (different indicators). If there is a possibility to make the module automatically attach (i.e. velcro) then all the better.*"

"*When my husband saw the device he was interested to see the color change but he was not interested in making the device*"

Participants gave some suggestions to improve the user experience when making the device. Some of the participants would like to have more shapes of modules and different colors. In addition, improving the connection method was suggested. Another participant would like to stick all the results on a dairy book to record their health condition in a fun way. Another user suggested having an option to design the device using design software. In addition, some people may be interested in using a ready customized device. In this case, some ready customized devices may be added into the kit in addition to a design tool option where the user can make their own design and cut it on filter paper and use colorimetric indicators in the kit.

Device Effect on the Lifestyle

Figure 3.34 shows that most participants were encouraged to monitor their health

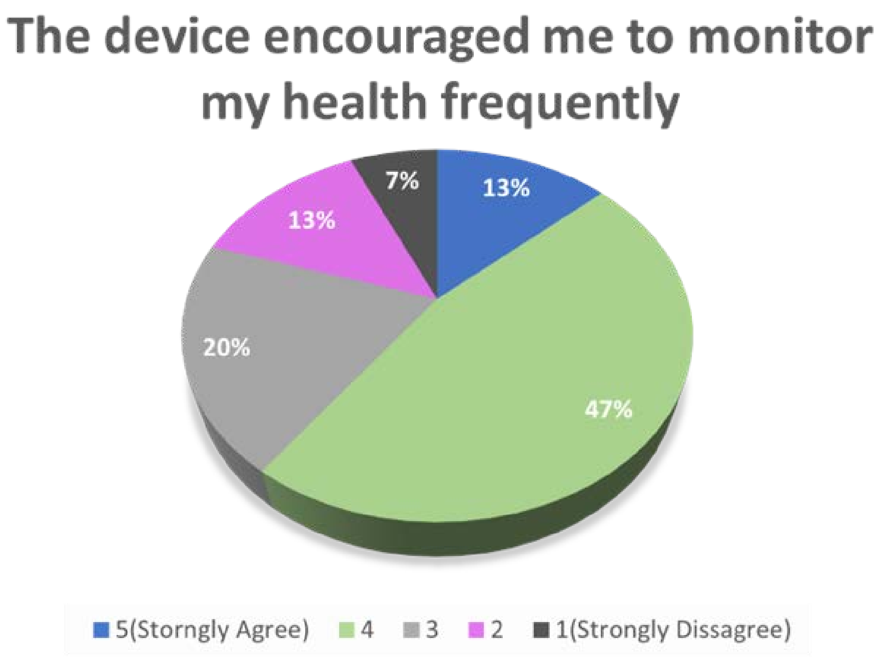

Figure 3.34 Encouragement for Health Monitoring

when using the device. However, one participant strongly disagree and said "*I think that constant monitoring of my health can cause me anxiety.*".

Chapter 4
Prove of Concept

In this chapter, the final prototype is presented, tested and evaluated from two different aspects:usability and enjoyability. It also contains the thesis discussion.

4.1. Final Prototype

The third prototype did not have any indication for the sweat flow in the device, making it difficult for the user to follow up with the device's functionality in absorbing and detecting analytes. Therefore, the prototype was improved by applying an erasable ink to show the liquid flow in the transport modules. In figure 4.1 a device consisting only of absorption and sensing modules was customized and then folded and attached to a hand watch to test the flow of sweat while using an erasable ink. It took 5 minutes and 55 seconds for the sweat to flow from the absorption point to the sensing point.

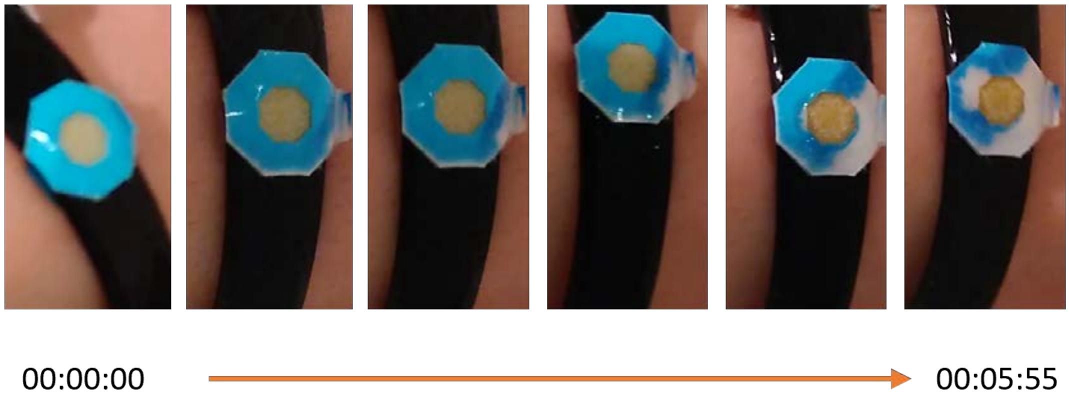

Figure 4.1 Sweat Flow in a Device

Figure 4.2 illustrates the fabrication process for the three types of modules: absorption, transport, and sensing from cutting the patterns to the final device is ready to be attached to a wearable. The designed modules will allow users to make

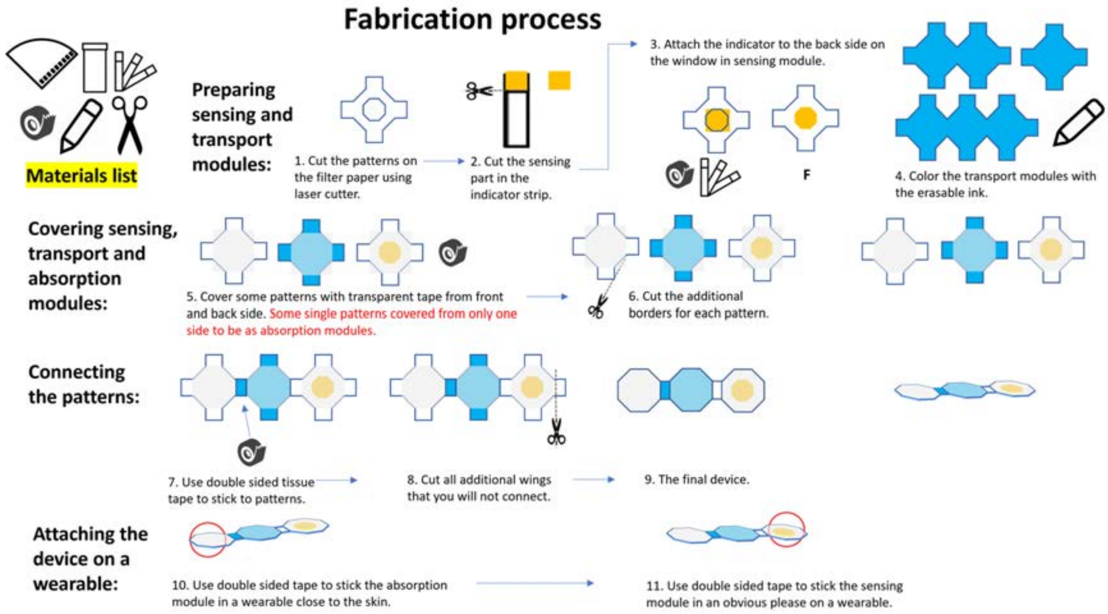

Figure 4.2 Fabrication Process

different customized devices. The device can contain multi-sensing modules to sense different analyses (Figure 4.3 a). It can also have multi-absorption modules to absorb sweat from different points to collect more amount of sweat samples (Figure 4.3 b). Two devices with the same number of modules were made to compare the flow of liquid with different channels width. The first device that has narrower channels took around 16 minutes and 6 seconds for the liquid to flow from the absorption module to the sensing module (Figure 4.4). While for the second device that has a wider channel it took around 12 minutes with around 4 minutes difference between the two devices (Figure 4.5).

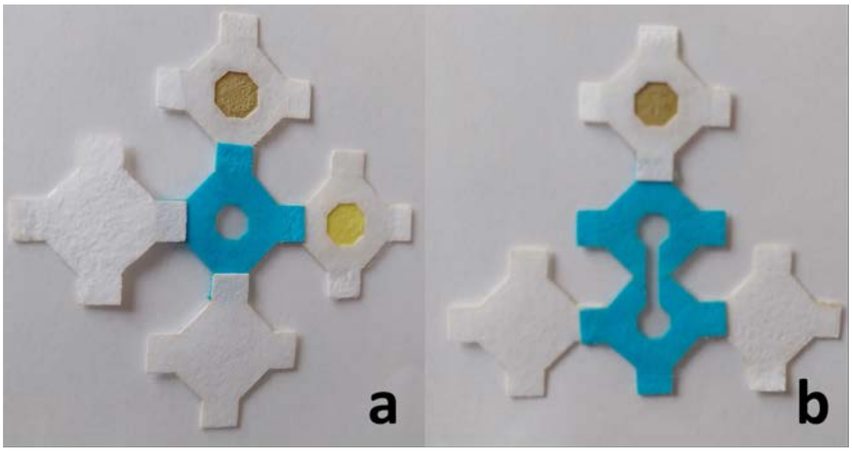

Figure 4.3 Modular Devices

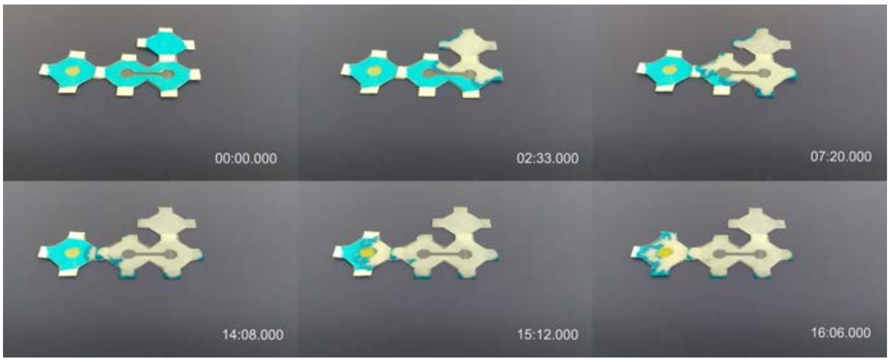

Figure 4.4 Liquid Flow in a Device with Time for Narrow Channels

Figure 4.5 Liquid Flow in a Device with Time for Wide Channel

4.1.1 Final Prototype Evaluation

In this user study, there were two groups of participants.

Group One

Group one had nine participants and they made the device and used it. The study setup was prepared considering the feedback of the previous study. Based on the previous study, users want more support and guidelines for making the device. This issue was addressed by developing an instruction website using Wix builder (Figure 4.6) . The website contains videos, pictures, and examples of how to make

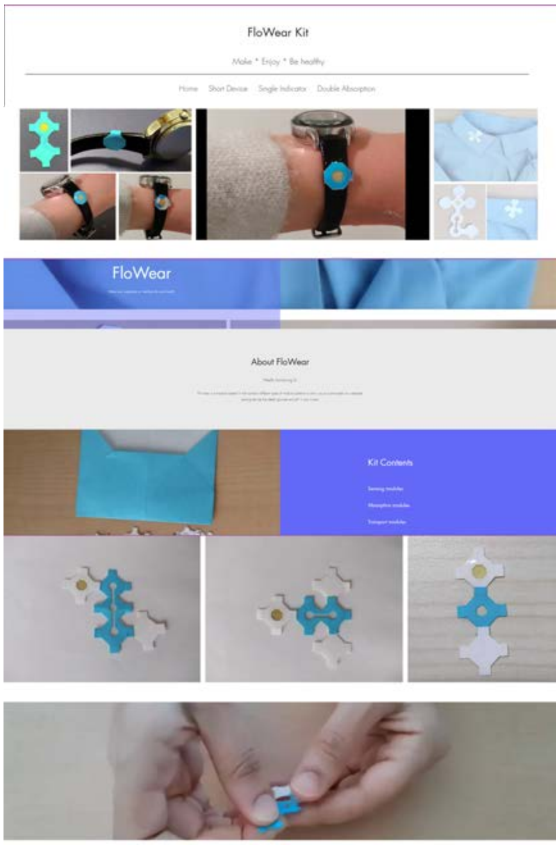

Figure 4.6 Website

some devices. It explains in detail all the processes from the required modules to the color change indication.

System Usability Scale (SUS)

The first group was asked to go through the website with all instructions and details about the paper-based microfluidic modules and the device. Then they were asked to make a device that they want to use (Figure 4.7) .After they make

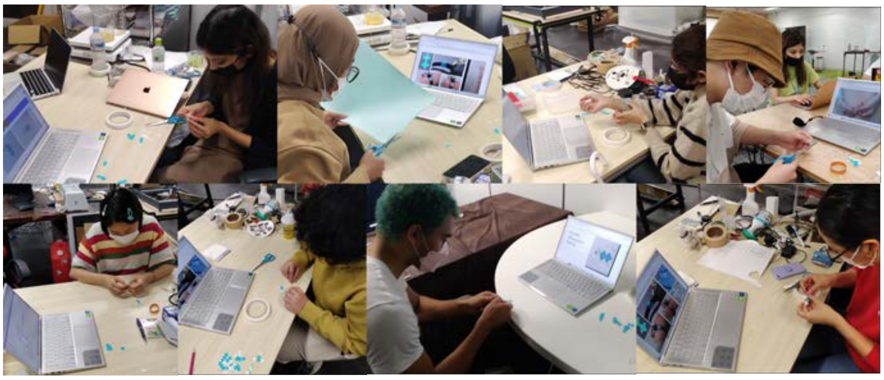

Figure 4.7 User Study Group 1

their device a questionnaire was sent to them using google forms link to be filled out after using the device. The system usability score was calculated using the same method in the previous user study by finding the SUS for each user and then getting the average as shown in table 4.1. The system usability score was improved compared with the usability study for the third prototype with score of 71.944444 which corresponds to "Good" usability.

Table 4.1 SUS for Group One Participants

No	1. Use frequently	2. Unnecessarily complex	3. Easy	4. Need support	5. Well integrated functions	6. Inconsistency	7. Learn quickly	8. Exhausting	9. Confident	10. Need to learn	Total	SUS	Grade
1	5	1	5	4	5	2	5	1	5	2	35	87.5	A
2	2	4	2	2	1	3	4	2	3	3	18	45	F
3	3	2	4	2	4	2	4	2	3	2	28	70	B
4	4	1	5	1	5	1	4	1	5	1	38	95	A
5	5	2	5	2	5	2	5	1	5	1	37	92.5	A
6	2	3	4	3	2	3	4	2	3	4	20	50	F
7	3	3	3	1	4	2	5	1	3	2	29	72.5	B
8	4	2	4	2	4	2	5	2	3	2	30	75	B
9	3	3	4	3	4	3	3	2	3	2	24	60	D
Average												71.94444	B

Group Two

Group number two contains four athlete participants were given ready customized devices attached to a hand band to use during a football match (Figure 4.8). Hand band was selected based on the results of the customizability part for the third prototype user study, where most participants preferred to make devices placed on hand wearables. A super glue was used to connect different modules from

Figure 4.8 Ready Customized Devices Attached to Hand Band

the two borders of wings to insure stable connection between the modules for the user devices (Figure 4.9).

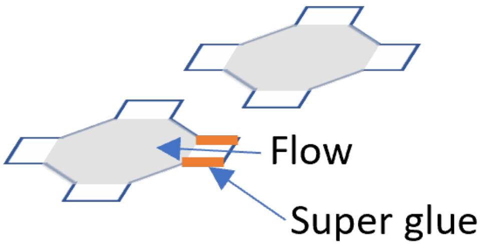

Figure 4.9 Connecting Modules Using Super Glue

System Usability Scale (SUS)

Table 4.2 represents the SUS score for each participant with the corresponding grade. The average system usability scale shows an "Excellent" score of 83.125.

Table 4.2 SUS for Group Two Participants

No	1. Use frequently	2. Unnecessarily complex	3. Easy	4. Need support	5. Well integrated functions	6. Inconsistency	7. Learn quickly	8. Exhausting	9. Confident	10. Need to learn	Total	SUS	Grade
1	3	1	5	1	3	2	4	1	3	1	32	**80**	B
2	3	1	4	2	4	1	4	1	3	1	32	**80**	B
3	4	1	5	2	4	1	3	1	5	2	34	**85**	A
4	4	1	5	2	4	3	5	1	5	1	35	**87.5**	A
Average												**83.125**	A

Enjoyability

Two of the user agreed that it was an enjoyable experience using the device. While one of the users strongly agreed (Figure 4.10).

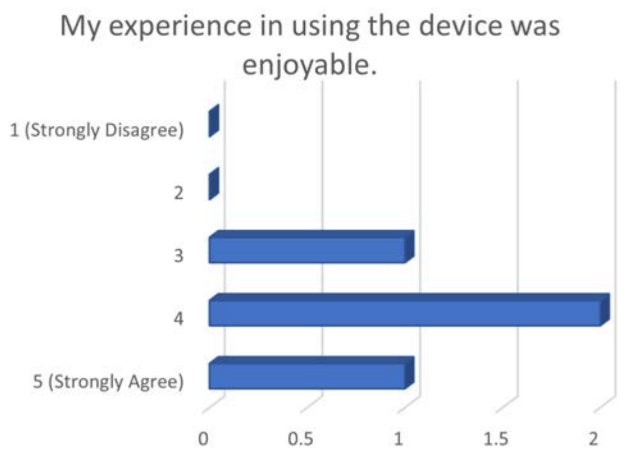

Figure 4.10 Device Enjoyability

Figure 4.11, shows the users devices after being used.

The participants express their excitement to observe the sample absorption and color change. After using the device in the match the devices gave inter-individual variation of colors which is an indication that the pH indicator react

Figure 4.11 Devices After Use

based on different levels of pH. Figure 4.12 shows two of the devices that changed color after use. For user A the device change color from light green to orange which indicate a sweat pH level between 4 and 4.5. While for user B the color changed to yellow which indicate a pH of 5. One of the users said that it was fun

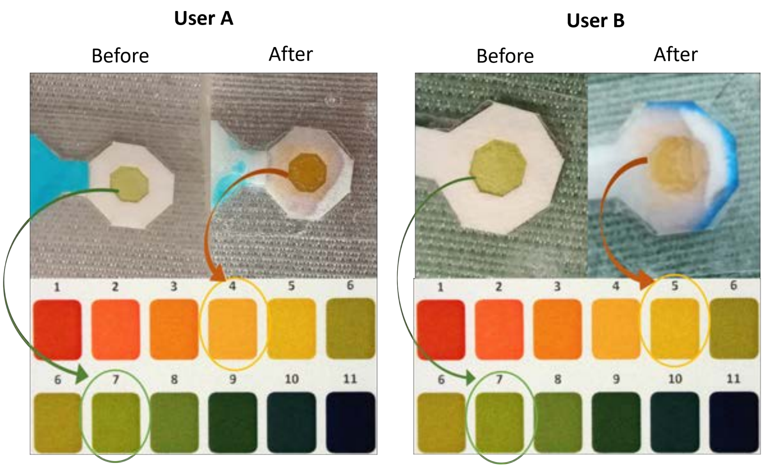

Figure 4.12 pH indicator Color Change

when the blue color (erasable ink) started to disappear. Another user added that he was glad to know that his sweat pH is within the normal range and his skin with good condition. Where other user expressed his interest in using other types of indicators.

4.2. Discussion

Based on the prototype testing and the evaluation, the fabricated modules successfully enabled developing a customized wearable device for monitoring pH in sweat, as a body analyte. The device was able to absorb the sweat from the skin surface. The capillary action in paper allowed the flow of sweat from the absorption to the sensing modules passing through different transport modules. The sensing module with a colorimetric indicator showed color change based on the analyte level detected.

The developed paper-based microfluidic modules overcome some limitation reported in previous approaches. The main advantage of a paper-based microfluidic modules kit is its low-cost making it affordable compared with other health monitoring digital-based devices. Compared with other module approaches, a paper-based approach overcome the leakage problem that appears in the module blokes, where the leakage can occur when connecting different blokes or when blokes are broken. The flexibility and foldability of the paper-based modules will make it possible to use them as wearable devices, which is not possible with plastic blocks. As it is disposable, users will be able to use a new device every day and the indicator functionality will not be reduced, which is the case in using permanent patterns. In addition, the indicator will be away from the skin, which will avoid any possibility of allergy. The ability to select the indicator will enable the user to test different analytes which is not possible with the microfluidic sticker approach with fixed indicators. The kit will be easy to use by all people from different ages and backgrounds as they will need only to connect different modules. This will overcome the limitation of using a design tool that may require some knowledge and equipment such as a laser cutter, which is not available for everyone.

Having such a device at a low cost can provide an enjoyable and fun experience for making a health monitoring device. Where the user can select the indicator, customize the shape and attach it to a wearable based on their preference. In addition, this device does not appear as a medical device, it will be seen as a fashion component. In the long-term, this device can provide a healthy lifestyle for users as they will be aware of the level of essential analyets. It will be an alarm to remind them to take supplements, drink more water or go to make a medical accurate test.

During testing and user study some hardware limitation were detected. The double sided tissue tape used to connect two modules was not strong enough to make the device connected after the modules become wet. Therefore, users in the second user study group two were given a device connected using super glue. This can be solved by testing different adhesive double-side tapes in the market to find a suitable tape that makes a strong connection while not blocking the flow between the modules. Regarding the indicators for analytes detection, there was a difficulty in finding existing indicators detecting analyses spatially in sweat.Therefore, only pH universal indicator was used as a functional indicator. In some cases, the results may make a confusion of distinguishing between some colors like yellow and light orange for instance. Thus, a mobile application can be used. The modules were fabricated to reduce the possibility of sample evaporation and contamination. However, evaporation and contamination will not be prevented as the absorption module is covered only from the top and the wings connecting modules are not covered. This device will be suitable for anyone except for people who have Anhidrosis, which is a medical term for the condition of not sweating. On the other hand people with Hyperhidrosis, excessive sweating that is not related to heat [50], may find it easy to use the device as they do not need to exercise to sweat.

In addition to detecting the levels of analytes in sweat, this device can be used to measure the amount of sweat loss. It also can be used for other body fluids like tears and saliva. The microfluidic paper-based modules can be used for educational purposes as well to encourage children from young age to monitor their health frequently in an enjoyable way. In addition to the main purpose of using the paper-based microfluidic modules to make a wearable sensing device, this device has also the potential to be used in a laboratory as a low-cost, customizable, and disposable analytical device.

Chapter 5
Conclusion and Future Work

This thesis focused on developing a kit for flexible, simple, low cost and disposable paper-based microfluidic modules. The modules can be connected to make a customizable health-monitoring wearable device and provide an enjoyable experience. Different modules were fabricated to allow the flow of sweat samples and prevent possible evaporation and contamination. The device monitors the analytes in sweat using colorimetric indicators. The modules prototypes were evaluated by conducting user studies as they were improved sequentially. In the user study customizability, usability, enjoyability, and effect on the lifestyle of the modules kit were evaluated. The usability of making and using the device using the modular kit improved from "Poor" to "Good". In addition, the usability of only using the device was "Excellent" for the last device prototype evaluation.

This research can be extended in the future by addressing how to prevent evaporation and contamination of the sweat sample. Adopting more types of indicators will highly affect the performance of the device and widen the scope of its applications and implementations. This requires developing more accurate, highly sensitive, and safe sweat colorimetric indicators. In addition, other types of visual indicators will be worth exploring such as fluorescence. The connection between different modules can be improved by comparing different types of double-sided tape in the market or proposing a different approach to connect the modules. The modules can also be used to make devices for different purposes such as monitoring other body fluids for instance tears and saliva spatially for babies. It can be an educational kit to encourage kids to monitor their health in an enjoyable context. Moreover, it can be used in laboratories and the field as a customizable, low cost paper-based analytical device (µPad).

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Appendices

A. Pre-Study Interview with clinical biochemistry specialist

1. What are the sample types used for testing minerals, vitamins and glucose levels)? Noninvasive: In criminal field, hear and body fluids like saliva are used to test levels of minerals and vitamins. In hospitals sweat is used to test for (NaCl) and urine for some elements and vitamins. Invasive: Blood is usually used as the main sample test type.

2. Are there any tests based on sweat, tears, saliva and exhaled breath are used in hospital labs?

   - Sweat for testing NaCl Cystic fibrosis
   - Tears for minerals and infections
   - Exhaled breath is used to test pH, Alcohol and diagnosis of Helicobacter pylori infection.
   - Saliva for minerals.

   In general they are many noninvasive tests using sweat, tears, saliva and exhaled breath as sample test but they are not used in the hospital lab because the hospital labs use only standard tests that are internationally approved to make sure the results are accurate and precise.

3. What are the methods used to make these tests do you use colorimetric methods or other please specify? Spectrophotometer similar to colorimetric Colorimetric strips using urine as sample (for pregnancy or for babies have some symptoms and expect to have Lactose Intolerance.) Stone Machine

4. Are the tests expensive in term of equipment and tools used? Some very expensive test they send it to be tested outside the country. Some other tests also are very expensive.

5. What are the limitations of the current test tools in term of shape, cost, and personalization? The Shape of the device used to collect the sweat samples for children are not comfortable. Some tests are very expensive in term of equipment used.

6. What are the diseases require frequent minerals, vitamins and glucose tests? And what are the most common one? Diabetes -¿ glucose. Problems in enzyme that works partially may make some problem like vitamin D deficiency and other.

7. How regular the tests are required? Depends on the each patient case it can be monthly or weekly or after 3 months and other.

8. What are the tests that can be conducted for patients on their own at home? Glucose and Pregnancy hormone.

9. Do you think that a wearable sensing device would be beneficial for monitoring the levels of analytes for patients? Why? It can be good for screening tests where the user can have a general idea about their overall health condition. But it is not effective to be used in hospital as in public hospital they focus on cost effectiveness when buying the equipment and tools. Also in hospital they are focusing on results to be accurate and precise.

10. Advantages and disadvantages of point of care testing? It is good for a screening test and not for diagnosis test because it is not accurate. If the test is not accurate it can make more people to go to hospital labs.

B. Prototype 2 User Guide

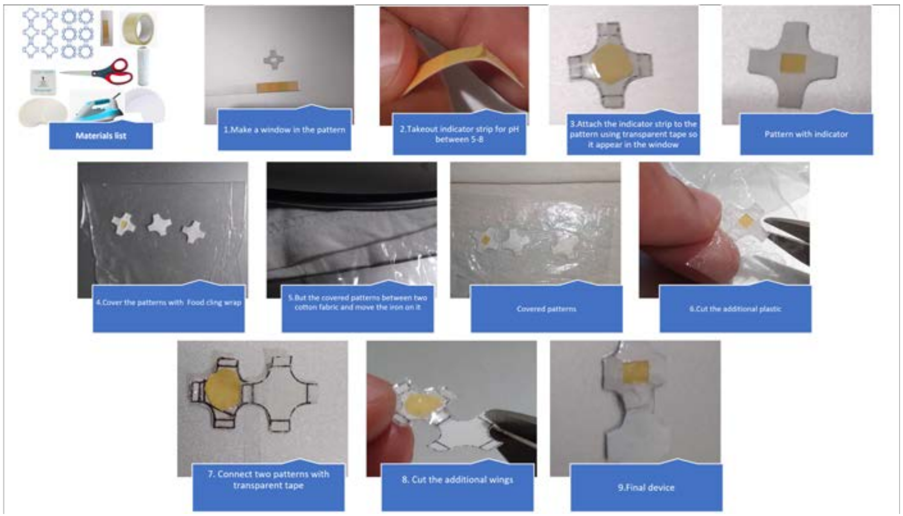

Figure B.1 Prototype 2 User Guide

C. Different Channels widths

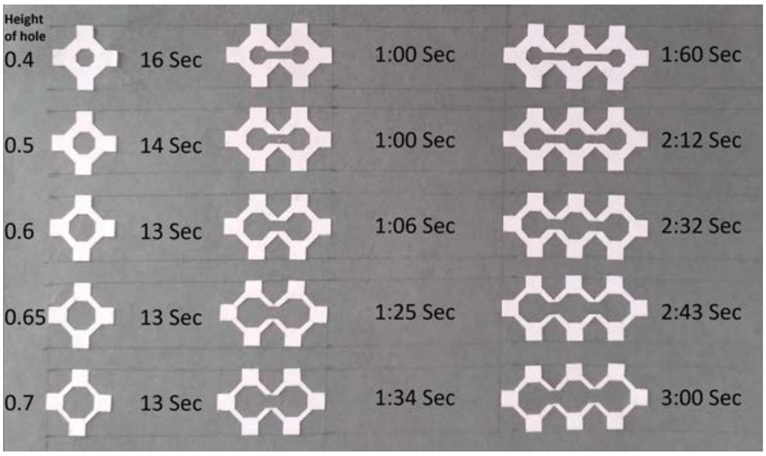

Figure C.1 Different Channels Widths and Totally Flow Time

D. Website

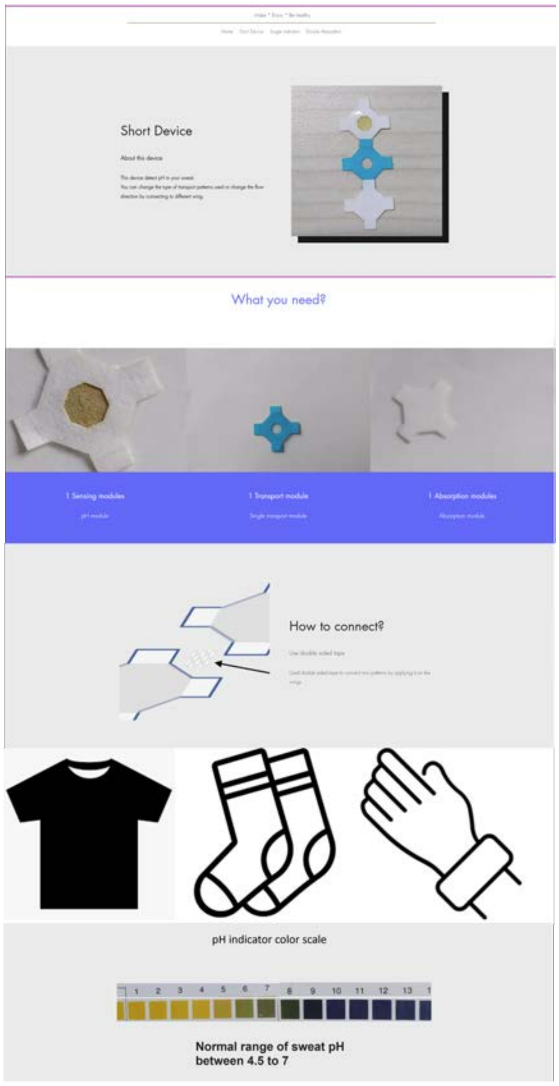

Figure D.1 Website