

ELEC-H424 : Active Medical Device

Smart Wound Care : Device Design

Project report

DE DEYN Thomas

DE MAREZ Hugo

ELAMRI Mohamed

TRAN NGOC Kiên

NONCLERCQ Antoine

AMMI Haroun

VERSTRAETEN Maxime

2023

Table des matières

1	Introduction	1
2	Selection of the bio-markers	2
2.1	Biochemical markers	3
2.1.1	pH	3
2.1.2	Nitric oxide	4
2.1.3	Uric acid	4
2.1.4	Proteases	5
2.1.5	New propositions	6
2.2	Physical markers	6
2.2.1	Temperature	6
2.2.2	Oxygen	6
2.2.3	Humidity	7
2.2.4	Pressure	8
2.2.5	New proposition	9
2.3	Images	9
2.4	Summary	10
3	Selection of the sensors	11
3.1	Control board	11
3.1.1	Final choice	11
3.2	Humidity and Temperature sensor	11
3.2.1	Final choice	12
3.3	Oxygen level sensor	13

3.3.1	Final choice	13
3.4	Pressure sensor	14
3.4.1	Final choice	15
4	PCB design	16
4.0.1	Wiring diagram	16
4.1	Components	18
4.2	Primary PCB	19
4.3	Practical issues	19
4.4	Current state	19
5	Prototype	20
5.1	Current state	20
5.1.1	Measuring the pressure :	20
5.1.2	Measuring the spO2 :	20
5.1.3	Measuring the Temperature through the MAXREFDES117#	21
5.1.4	Code and algorithm	21
5.2	Next steps	21
6	Ressources	23
6.1	Articles given as starting point :	23
6.2	Articles added :	27
6.3	Additional ressources :	28

Chronic wounds, which can result from a variety of medical conditions, represent a major healthcare challenge worldwide. The ability to monitor the progression of a wound and detect potential complications early on is crucial to prevent further damage and improve healing outcomes. Nowadays, the follow-up of a wound is mainly carried out by visual inspection of the skin and therefore involves a relatively subjective clinical decision by the treating person. Current methods do not offer the possibility to have a proactive response and prevent the infection.

In this context, the development of smart bandages that can provide continuous and non-invasive monitoring of wound parameters has emerged as a promising approach.

The original research project was initiated by a consortium of research groups including the BIOMED group (ULB), the ICTEAM (UCL) and the CMST (UGent) to propose an innovative solution in wound care.

The objective of this project is to provide a first prototype capable of monitoring several markers. This report will describe the different steps necessary to produce this prototype, starting from the selection of the bio-markers all the way to the description of the current prototype and a list of all the elements that should be made to transform this prototype in an actual smart bandage.

Selection of the bio-markers

According to their nature, the proposed markers have been classed in two categories : biochemical and physical markers. But according to the risk associated to the measure, all the sensors proposed could be classed in two different categories. The first one will be called the *healing* markers and are the parameters linked to a slow recovery of the wound. The second one will be called the *infection* markers. Important variations of those markers are often associated to an infection.

The markers given in the document at the beginning of the project will be presented in a determined importance order. The first one is the most important and the last one will be the least interesting. At the end of each section will be a note estimating the complexity of measuring this marker.

The analysis of each markers will be done using the following structure :

1. **Literature review** : The objective is to reference parts of different papers encouraging the use of the marker. Depending on the amount of information extracted from the literature, a **Summary of the litterature** might be added.
2. **Type of markers** : Infection VS Good healing monitoring
3. **Sensors review** : The objective is to verify that there are sensors available on the market to measure it. The required specifications and the chosen sensor will be depicted in the chapter 3.
4. **Advantages VS Disadvantages**

2.1 Biochemical markers

2.1.1 pH

Literature review

The pH of normal skin is alkaline, near from 7, thanks to bacterial colonisation. When there is a wound, the environment is acidic and pH is between 5.5 and 6.5. Above 6 human-pathogenic bacteria can appear, so a lower pH inhibits their growth. Wounds that deteriorate into a chronic condition are characterized by an alkaline pH. Knowing that, a wound pH increasing is a sign of infection, before clinical signs. Abnormalities in the enzymes and expression of the toxicity of bacterial secretions, caused by the alkaline by-product of bacterial proliferation, may break the healing process of a wound. Bacterial by-products have the potential to restrict oxygen supply to wound tissue, resulting in necrosis and creating an environment characterized by an elevated pH level within the wound. In alkaline environment, biofilm growth is increased for all strains of bacteria. Those biofilms are able to survive in pH ranges usually inhibiting growth of bacteria. Also, the effectiveness of antibiotics and antiseptics can be significantly impacted by pH of a wound. Indeed, a modulation of the performance can appear with a change in pH and cause bacteria growth and resistance development. However, the degree of bacterial contamination is not directly related to the measured pH.

The pH measurements alone is absolutely not insufficient for wound infection monitoring.

Wound pH measurement can be done by color indicator, colorimetric, fluorescence and spectroscopy.

Type of marker : Infection

Sensor Review

pH electrodes are already widely used in the labs. Unfortunately, these cannot be used in the smart bandages due to their sizes. Most of the time, the electrodes available on the market were quite long (more than 10cm) and costed a lot (about 100 euros). Yet, since this technology is well known, and micro pH electrodes already exists, it should be possible to design a new sensor.

One wearable pH sensor have been found, produced by ZimmerPeacock Tech. Since there is no documentation of project done with it and no documentation was available, it has not been considered. The link to this pH sensor is available in the GitHub (" Additional Documentation/1. Bio-markers/ELEC-H424-sensors.xlsx).

Advantages

- Good marker

Disadvantages

- Expensive
- Sensors exists, yet they are not adapted to this usage

2.1.2 Nitric oxide**Litterature review**

Nitric oxide (NO) plays an important role in wound healing by promoting cell growth, cell migration, new blood vessel formation, and stimulation of collagen production. The optimal level of nitric oxide for good wound healing varies depending on the size and depth of the wound, as well as the patient's health and other factors. However, many articles suggest that nitric oxide concentrations between 50 and 500 nM may be beneficial for wound healing.

Nitric oxide has been proven to play an important role in the healing of various types of wounds [Efron et al., 2000; Rizk et al., 2004].

It is produced as a defence mechanism against bacterial infection [Boykin, 2010]. Low concentrations of this biomarker have been associated with delayed wound healing and biofilm dispersal [Simoska et al., 2020].

Type of marker : Slow recovery monitoring

Sensors review

Several sensors are available to measure NO gas in air. Unfortunately, no sensor for NO in aqueous environments has been found as these data are usually obtained through blood tests. Due to the complexity of measuring this bio-marker, it will not be considered for the design of this prototype.

Advantages

- Indicates proper wound healing progression and absence of complications.

Disadvantages

- No suitable sensor capable of measuring this bio-marker was found to be suitable for this project.

2.1.3 Uric acid**Literature review**

Uric acid is a waste product created by the cells during the catabolic pathway of purine. The uric acid concentration in a wound is an indicator of oxidative stress and bacterial infection. Chro-

nic wounds are usually hypoxic which leads to an increase of purine metabolites concentration, such as uric acid [Fernandez et al., 2014; Pusta et al., 2022].

Type of marker : Good healing monitoring and infection detection

Sensors review

Many researches are currently carried out in order to develop all kinds of new wearable uric acid monitoring devices but only larger devices are currently available. It is thus impossible to implement in our device because of the size constraints. It is important to note that a tremendous amount of scientific articles presenting all kinds sensors capable of measuring Uric Acid in blood or sweat have been found. Such a sensor could be put on sale soon.

At the time of writing this report, the most interesting device is the UASure II meter.

Advantages

- Provides information on the healing process AND the infection state

Disadvantages

- nothing really usable for the project on the market yet

2.1.4 Proteases

Litterature review

Many different proteases play essential role in the healing process of a wound. They are thus very interesting indicators of how the wound is evolving. Indeed, it has been shown that proteases and their inhibitors are responsible for the balance between extracellular matrix (ECM) degradation and deposition. A disrupt in this balance such as an abundant level of proteases can lead the wound into a state of chronic inflammation [Eming et al., 2014].

Type of marker : Good healing monitoring

Sensors review

The methods currently used to measure protease levels rely on colorimetric or fluorescent study. That would require to add a reagent on the wound and be able to analyse the light emitted (assuming that the bandage will block any exterior light, only fluorescence can be used), using a camera or a photoresistor. It would also require to make sure that the reagent will not prevent wound healing nor having toxic side effects on the patient.

For these reasons, current technology cannot be used to implement protease measurement in the design of this smart bandage.

Advantages

- enables to determine the chronicity of the wound

Disadvantages

- Requires addition of a reagent which makes the device more complex

2.1.5 New propositions

Cytokines and interleukin are also biochemical markers associated to a bad wound healing (included in the first mechanisms of defence against the infection). Monitoring the activity of these substances could be used to evaluate the healing process. Yet, since no sensors have been found, they have not been investigated further.

2.2 Physical markers

2.2.1 Temperature

Literature review

A rise in temperature around a wound may be associated to the presence of an infection. [Sibbald et al., 2015]

Studies have shown that in patients with diabetes, regions of the foot with a higher skin temperature are more likely to develop ulcers. For example, it has been found that increased skin temperature is an indicator of increased risk for ulceration in the neuropathic foot in patients with diabetes [Avery, 2004].

Type of marker : Infection

Sensors review

Lots of sensors are available on the market with various specifications and prices. There is also lots of libraries for common boards such as Arduino.

2.2.2 Oxygen

The oxygen concentration in the area around a wound is an important factor for healing. Adequate oxygen supply is necessary for cell growth, new blood vessel production, and immune cell

Advantages

- Very easy to measure
- Associated to a defence mechanism
- Cheap

Disadvantages

- Depends on the environment's temperature
- Could vary a lot during the day (exercise, ...)

function to help eliminate bacteria and debris in the wound area.

Litterature review

An essential consideration in physiologic wound healing is oxygen in the wound bed. A wound requires at least a tissue oxygen tension of 20 mmHg to heal [Hunt & Hopf, 1997]. Poor vascularization at the site of chronic wounds deprives the wound of adequate oxygen supply [Castilla et al., 2012]. Thus, oxygen concentration becomes a potential bio-marker for monitoring wounds.

Type of marker : Slow recovery monitoring

Sensors review

Some sensors exist, coming with their own library. It is essential to keep in mind that the sensors are only capable of measuring the spO_2 (ration between the quantity of O_2 transported in the blood and the maximum quantity).

Even though the sensor costs much more than other sensors, the price remains affordable considering the objective of the project.

Advantages

- Constant value (do not vary depending on the environment)
- Small sensor

Disadvantages

- Does not directly measure oxygen level in tissues
- More expensive than other

2.2.3 Humidity**Literature review**

Wound moisture balance is critical in ensuring optimum wound care healing conditions [Schultz et al., 2005; Bishop et al., 2003].

A moist environment encourages the epithelialization of partial-thickness wounds, which can be achieved with semi occlusive [SCALES, 1963] or fully occlusive, impermeable dressings [Jonkman et al., 1989].

On the other hand, high humidity causes protein-degrading enzymes, neutrophils, and proinflammatory cytokines in wound exudate.

Type of marker : Slow recovery monitoring

Sensors review

Advantages

- Small sensor
- Easy to measure
- Cheap

Disadvantages

- Must be placed close to the wound (in contact with the skin for best accuracy)

Many sensors exist on the market and some come with their own library. Implementing this captor should be fairly easy.

2.2.4 Pressure

Literature review

Controlled mechanical pressures on a wound site can accelerate neovascularization and cellular proliferation for improved wound healing [Urschel et al., 1988; Agha et al., 2011]. The exerted pressure commonly ranges from 14 mmHg to 40 mmHg in the bandages used for pressure therapy, which improves the healing rates of some typical wounds, such as venous leg ulcers [Urschel et al., 1988; Agha et al., 2011; Mehmood et al., 2014].

Type of marker : Slow recovery monitoring

Sensors review

Different types of pressure sensors exist on the market. Some have a button and pressure depends on the pressing of it. Others are composed at the end of a round force sensitive resistor, the resistance of which depends on pressure applied to this resistor. The greater the pressure is, the smaller the resistance is. Those pressure sensors seem to be the best, especially because of the size of the device.

Advantages

- Easy to measure
- Improve healing speed

Disadvantages

- Must be placed close to the wound (in contact with the skin for best accuracy)

2.2.5 New proposition

The impedance has also been correlated to a good healing process. But it is difficult to know if the variation in the impedance is directly linked to the wound healing or is just due to a variation of humidity around the lesion.

2.3 Images

Image analysis has a potential in the evaluation of wound healing. Image processing and the use of Neural Networks could highlight some defects in the wound healing and helps a clinician assess the situation. Segmentation could be used to monitor the reduction in size of the wound.

Yet, there are some disadvantages to use such techniques. The lightning of the environment and the distance from the camera to the wound should be measured in order to have accurate measurements. A small pads of known dimensions could also be used as a reference for the measurement of wound size.

In the end, even if the solution has a high potential, it will not be investigated further since it is not possible to implement it in a smart bandage.

2.4 Summary

The objective of this section is to compare all the bio-markers in a single page, by using a grade-like system. Depending on the review, the characteristic's review will either be "Very positive " (The review encourages the use of this marker), "Positive", "Neutral", "Negative" (The review raises important issues) and "Very negative" (One point in the review prevents the use of this sensor).

Bio-marker	Type of marker	Litterature review	Sensor review	Price
pH	Infection	Very positive	Negative	Negative
Nitric oxide	Slow recovery	Positive	Negative	/
Uric acid	Slow recovery & infection	Positive	Negative	/
Proteases	Slow recovery	Positive	Very negative	/
Temperature	Infection	Very positive	Very positive	Very positive
Oxygen	Slow recovery	Very positive	Positive	Positive
Humidity	Slow recovery	Very positive	Positive	Very positive
Pressure	Slow recovery	Positive	Very positive	Positive

FIGURE 2.1: Comparison

Selection of the sensors

3.1 Control board

Since most of the groups members had already worked with Arduino boards, the choice was to pick one of their model.

3.1.1 Final choice

The Arduino Nano 33 BLE has been chosen to collect and communicates all the information from the sensors to a computer. This board offers several advantages such as :

- **Voltage output** : both 5V and 3.3V
- **Communication protocol** : I2C friendly, Bluetooth serial communication
- **Coding language** : C++ based
- **Accessibility** : fast delivery, relatively cheap
- **Improved performances^a** : enables to store all the data needed

a. compared to previous Arduino Nano

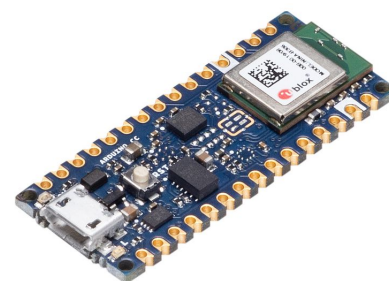


FIGURE 3.1: Arduino Nano 33 BLE

3.2 Humidity and Temperature sensor

Most of the humidity sensors already features a temperature sensor (used for the calibration and the measure of humidity). Since some sensors also communicate the temperature to the board, it will not be necessary to buy and implement a separate temperature sensor.

The following characteristics were identified as important :

The accuracy on the humidity : The first objective of this sensor is to measure the humidity level. The measure is defined as the percentage of relative humidity and ranges between 0 and 100. Most of the sensors offers accuracy of $\pm 3\%$ down to $\pm 1\%$

The accuracy on the temperature : Since the objective is also to measure the variation in temperature of the human body (specifically next to the wound), the sensor must be able to detect small variation around 37°C .

The power supply : The sensor should be powered directly by the board chosen. Most of the board (Arduino, Raspberry Pi) offers a 5V and a 3.3V power supply, the sensor should accept one of the 2 voltages. Furthermore, as the final objective is to make a wearable device, the power consumed should be as small as possible.

The accessibility : The objective is only to make a proof of concept. Therefore only one sensor is necessary.

The ease of use : Some sensors enable I2C communication or offer Arduino library. If two components are very similar and only one offers I2C communication and/or library, the one offering these functions will be preferred.

3.2.1 Final choice

Different types of temperature sensors have been compared. Some were only thermistors, or NTC, others were fully *ready to use* sensors.

The final choice is the **SHT40-AD1B-R2**

SENSIRION



- **Accuracy on the humidity :** $\pm 1\%$
- **Accuracy on the temperature :** $\pm 0.1^{\circ}\text{C}$ (@ 25°C)
- **Power supply :** 1.08V to 3.6V, *Ultra-Low-Power*
- **Accessibility :** available by 1
- **Ease of use :** Library available and I2C friendly

FIGURE 3.2: SHT40-AD1B-R2

Small note : This sensor offers great opportunities for the final product due to its size, price and accuracy. Yet, for the prototyping, this sensor is difficult to weld and couldn't be implemented before the due date.

3.3 Oxygen level sensor

Oxygen sensors generally enable measuring heart rate and blood oxygen saturation (spO_2). In the medical field, sensors generally use a red and an infrared LED to transmit light through the blood vessels, and a photodetector to capture the reflected light. The collected light signals are then processed and converted into digital signals to measure the heart rate and blood oxygen saturation.

The following characteristics were identified as important :

The power supply : The sensor needs to have the lowest possible energy consumption and to be compatible with the power supply of the selected board (3.3V or 5V).

The accuracy : The sensor must be accurate enough to be suitable for medical purposes.

The size : The final objective of this project is to develop a smart bandage. It is therefore important that the sensor fits in the bandage without disrupting the patient's movements.

The accessibility : The objective is only to make a proof of concept. Therefore only one sensor is necessary.

The ease of use : Some sensors enable I2C communication or offer Arduino library. If two components are very similar and only one offers I2C communication and/or library, the one offering these functions will be preferred.

3.3.1 Final choice

Following a thorough comparison of multiple sensors, the most cost-effective option with excellent capabilities.

The final choice is the **MAXREFDES117#**

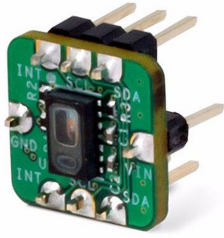


FIGURE 3.3: MAXREFDES117#

- **Accuracy** : $\pm 2\%$ (for saturation levels ranging from 70% to 100%)
- **Power supply** : 2 V to 5.5 V
- **Accessibility** : available by 1
- **Ease of use** : Open Source library ([spa22]) available and I2C friendly

3.4 Pressure sensor

Several architectures of pressure sensors are available for purchase. The first are using the excursion of a button-like component to evaluate the pressure. Others are using a variation in the resistance of a sheet component

The following characteristics were identified as important :

The power supply : The sensor needs to have the lowest possible energy consumption and to be compatible with the power supply of the selected board (3.3V or 5V).

The architecture of the sensor : The sensors using the excursion of a button to make a measurement will not be used since it will not provide a good evaluation of the pressure along the bandage. However, sheet-like sensors will provide this information and will perfectly fits in between the sheets of the bandage. Sheet-like sensors will therefore be preferred.

The accuracy : The sensor must be accurate enough to detect small variation of pressure. Since the pressure in the bandage will remain quite small (the wanted pressure is 14-40mmHg), lots of industrial sensors are ruled out.

The size : The final objective of this project is to develop a smart bandage. It is therefore important that the sensor fits in the bandage without disrupting the patient's movements.

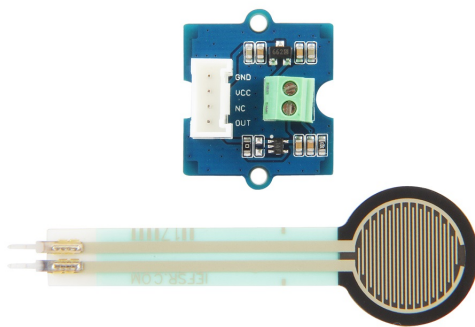
The accessibility : The objective is only to make a proof of concept. Therefore only one sensor is necessary.

The ease of use : Some sensors enable I2C communication or offer Arduino library. If two components are very similar and only one offers I2C communication and/or library, the one offering these functions will be preferred.

3.4.1 Final choice

After comparing the different types of sensors, the next one has been chosen :

The final choice is the **Round Force Sensor FSR402**



- **Accuracy :** Continuous (analog)
- **Power supply :** 3.3 V or 5 V
- **Accessibility :** available by 1
- **Ease of use :** Value directly read using the Micro controller (Analog input pin)

FIGURE 3.4: Round Force Sensor FSR402

This section of the report will describes the process leading to the production of the PCB.

The choice of using one has been made for several reasons :

- some of the sensors needed to be welded
- it enables a smaller circuit and thus more adapted for a smart bandage

4.0.1 Wiring diagram

The general schematic of the electronic circuit has been developed and subsequently implemented on EasyEDA.

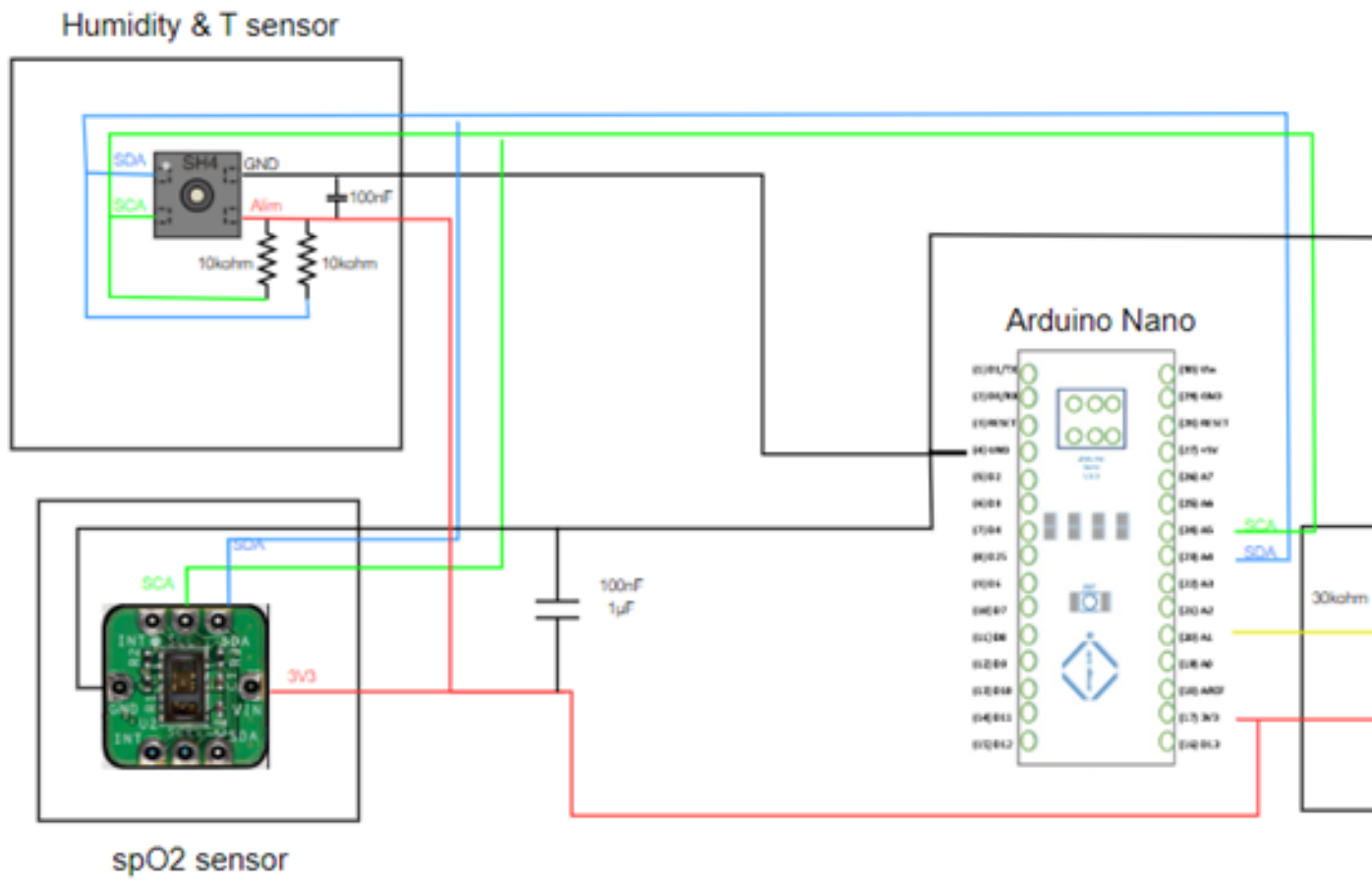


FIGURE 4.1: Global circuit (Draw.IO)

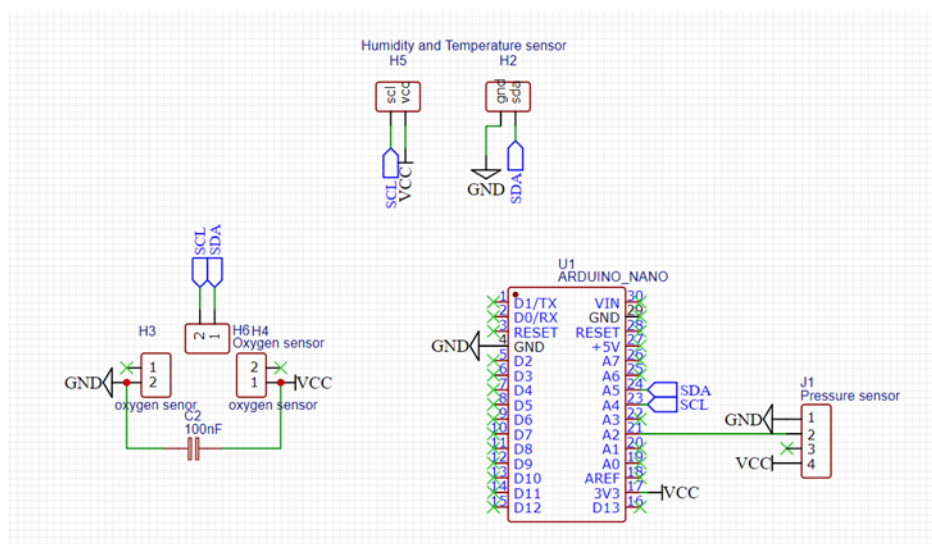


FIGURE 4.2: Schematic circuit (EasyEDA)

4.1 Components

Most of the components can easily be connected to the Arduino by welding pin headers. This solution will be preferred to enable recovery of the sensors for a new version of the PCB (or a new project). Male pins will be welded on the components and female pins will be welded on the primary PCB

The only components that cannot be used with header pins is the SHT-40. It will be necessary to weld it. The solution proposed is to develop a secondary printed circuits. The sensors, and the resistances and decoupling capacitor required will all be welded on it. This offers several advantages. The first one is that, since the sensor is very small, welding could be difficult and require several try. If an error is made, only the secondary PCB is ruined. Small traces are necessary around the sensor, and they are very sensible to error (short-circuit are more likely). If there is a problem in the engraving of the smaller traces, this will not affect the principal PCB.

Arduino Nano : The footprint is available on EasyEda

Oxygen sensor MAXREFDES117 : This sensor will be represented by headers (3x2 pins connector) on the PCB.

Pressure sensor Round Force Sensor FSR402 : represented by 4 pins on the PCB, matching the cables on the amount of cable in the sensor.

Temperature and humidity sensor SHT40-AD1B-R2 : Both PCB will be custom-made so that they can be connected using male and female headers.

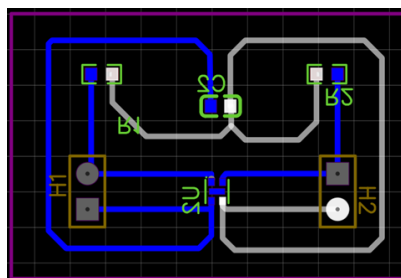


FIGURE 4.3: Secondary PCB for the Temperature and Humidity sensor

5.1 Current state

At the date of the end of the project (May 12, 2023), the prototype given is capable of :

5.1.1 Measuring the pressure :

The pressure applied on the sensor is measured and displayed on the Serial monitor in real time.

Validation step proposed :

1. Some weights are available in the UB.3, they could be used to make sure that the weight displayed on the Serial Monitor is close to the real weight placed on the sensor.

5.1.2 Measuring the spO_2 :

The saturation of the oxygen in the blood is measured and also displayed on the Serial monitor. The hearth rhythm (in BPM) is also calculated but is not shown in the monitor.

Validation step performed :

1. The algorithm computing the BPM has been validated by comparing the value shown on the serial monitor and the pulse measured.
2. The measure of the spO_2 has been read on the Serial monitor and compared with the value shown by an Oxymeter.

5.1.3 Measuring the Temperature through the MAXREFDES117#

The spO_2 sensor is also capable of measuring the temperature. This method is much less accurate and much slower than using the SHT40.

Using this sensor to monitor the temperature of the wound could be done as back up plan if the SHT40 fails. The measure is relatively stable and can be taken even if the sensor is not in contact with the skin. Also, the slow speed should not be a problem since the objective is to detect a raise in temperature caused by an infection.

Validation step performed :

1. When placing a finger on the sensor, the temperature measured increases
2. When placing a finger (previously cooled with an ice cube) on the sensor, the temperature decreases

Validation step proposed :

1. Comparing the measurement taken by this sensor and a second one.

5.1.4 Code and algorithm

The GitHub repository will includes all the codes used for the project.

https://github.com/ThDeDeyn/ELEC_424_Project

It is important to note that in order to start the device, the user must send a character (any) in the Serial monitor. The system will then start by sending a few red and infrared waves before displaying all the values. The code provided by the library uses 25 measurements to compute the spO_2 and the Heart Rhythm. More information are available in the code itself.

5.2 Next steps

The final objective of the project is to develop a smart bandage. The result described in this report is the first step towards this objective.

The next steps to do before implementing this solution are the following :

First of all, it would be necessary to use a smaller micro-controller that would fit in the bandage. It would also require to have another form of connection between the different sensors. Since most of them are very small, it would be possible to concentrate them on a much smaller PCB.

Secondly, some sensors and measures could be improved to better fit the constraints in the bandage. For example, the resistive surface sensible to the pressure could be changed in order to maximise the sensibility, and better represent the pressure in the whole sheet. Bigger sensors exist and could be used in the bandage. An example is the FSR406 (5.1)

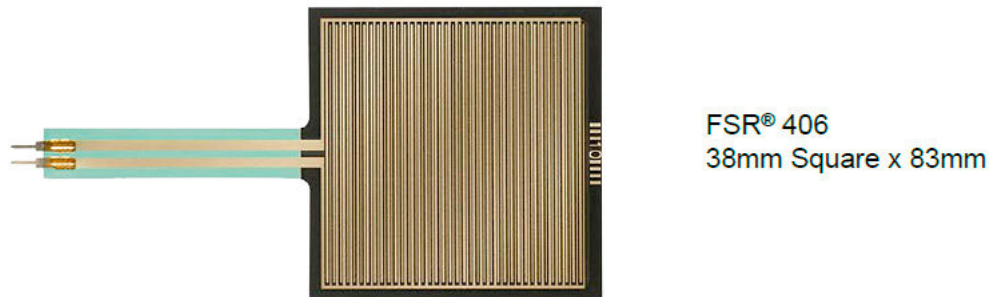


FIGURE 5.1: FSR 406, Interlink Electronics

For accurate measurement, the Oxygen sensor should remain close to the wound and a constant pressure should be applied. This could be monitored thanks to the pressure sensor. The method used to measure spO_2 in the prototype are highly sensitive to the movement of the skin. In order to have a good estimation of the oxygenation around the wound, the values measured should not be blindly accepted. A filter could be used to removed any abrupt variations of the measure since they are not linked to a variation of the spO_2 . A first filter is already provided by the library "SparkFun 3010x", calculating the average of the the 25 last data.

6.1 Articles given as starting point :

gha, R. et al., “A review of the role of mechanical forces in cutaneous wound healing.” *Journal of Surgical Research*, 171(2), pp.700–708. 2011.

Armstrong, D.G. et al., “Principles of best diagnostic practice in tissue repair and wound healing : An expert consensus.” *Diagnostics*, 11(1). 2021.

Avery, L.A.A.L., “Home Monitoring of Foot Skin.” , 27(11). 2004.

Bishop, S.M. et al., “Importance of moisture balance at the wound-dressing interface.” *Journal of wound care*, 12(4), pp.125–128. 2003.

Bjarnsholt, T. et al., “Why chronic wounds will not heal : A novel hypothesis.” *Wound Repair and Regeneration*, 16(1), pp.2–10. 2008.

Bowler, P.G., Duerden, B.I. & Armstrong, D.G., “Wound microbiology and associated approaches to wound management.” *Clinical Microbiology Reviews*, 14(2), pp.244–269. 2001.

Boykin, J. V., “Wound Nitric Oxide Bioactivity.” *Journal of Wound, Ostomy & Continence Nursing*, 37(1), pp.25–32. 2010.

Brem, H. et al., “Cholinergic Anti-Inflammatory Pathway Activity and High High Mobility Group Box-1 (HMGB1) Serum Levels in Patients with Rheumatoid Arthritis.” *Molecular Medicine*, 13(9), pp.30–39. 2007.

Caley, M.P., Martins, V.L.C. & O’Toole, E.A., “Metalloproteinases and Wound Healing.” *Advances in Wound Care*, 4(4), pp.225–234. 2015.

Castilla, D.M., Liu, Z. & Velazquez, O.C., "Oxygen : Implications for Wound Healing." *Advances in Wound Care*, 1(6), pp.225–230. 2012.

CK, S. et al., "Human Skin Wounds : A Major and Snowballing Threat to Public Health and the Economy." *Wound Repair Regen*, 17(6), pp.763–71. 2009.

Davis, S.C. et al., "Microscopic and physiologic evidence for biofilm-associated wound colonization in vivo." *Wound Repair and Regeneration*, 16(1), pp.23–29. 2008.

Efron, D.T., Most, D. & Barbul, A., "Role of nitric oxide in wound healing." *Current Opinion in Clinical Nutrition and Metabolic Care*, 3(3), pp.197–204. 2000.

Eming, S.A. et al., "Differential proteomic analysis distinguishes tissue repair biomarker signatures in wound exudates obtained from normal healing and chronic wounds." *Journal of Proteome Research*, 9(9), pp.4758–4766. 2010.

Eming, S.A., Martin, P. & Marjana, T.-C., "Wound repair and regeneration : mechanisms, signaling, and translation." *Sci Transl Med*, 6. 2014.

Fernandez, M.L. et al., "Elevated uric acid correlates with wound severity." *International Wound Journal*, 9(2), pp.139–149. 2012.

Fernandez, M.L., Upton, Z. & Shooter, G.K., "Uric acid and xanthine oxidoreductase in wound healing." *Current Rheumatology Reports*, 16(2), pp.1–7. 2014.

Gamerith, C. et al., "pH-responsive materials for optical monitoring of wound status." *Sensors and Actuators, B : Chemical*, 301(January), p.126966. 2019.

Greener, B. et al., "Proteases and pH in chronic wounds." *Journal of wound care*, 14(2), pp.59–61. 2005.

Han, G. & Ceilley, R., "Chronic Wound Healing : A Review of Current Management and Treatments." *Advances in Therapy*, 34(3), pp.599–610. 2017.

Harjai, K. et al., "Effect of pH on production of virulence factors by biofilm cells of *Pseudomonas aeruginosa*." *Folia Microbiologica*, 50(2), pp.99–102. 2005.

Hošťacká, A., Čížnár, I. & Štefkovičová, M., "Temperature and pH affect the production of bacterial biofilm." *Folia Microbiologica*, 55(1), pp.75–78. 2010.

Hunt, T.K. & Hopf, H.W., "Wound healing and wound infection : What surgeons and anesthesiologists can do." *Surgical Clinics of North America*, 77(3), pp.587–606. 1997.

Jonkman, M.F. et al., "Poly(ether urethane) wound covering with high water vapour permeability compared with conventional tulle gras on split-skin donor sites." *Burns*, 15(4), pp.211–216. 1989.

Kumaran, D. et al., "Structure of staphylococcal enterotoxin C2 at various pH levels." *Acta Crystallographica Section D : Biological Crystallography*, 57(9), pp.1270–1275. 2001.

Kurabayashi, H. et al., "Inhibiting bacteria and skin pH in hemiplegia : Effects of washing hands with acidic mineral water." *American Journal of Physical Medicine and Rehabilitation*, 81(1), pp.40–46. 2002.

Leal-Junior, A. et al., "Photonic smart bandage for wound healing assessment." *Photonics Research*, 9(3), p.272. 2021.

Maiuolo, J. et al., "Regulation of uric acid metabolism and excretion." *International Journal of Cardiology*, 213, pp.8–14. 2016.

McCarty, S.M. & Percival, S.L., "Proteases and Delayed Wound Healing." *Advances in Wound Care*, 2(8), pp.438–447. 2013.

Mehmood, N. et al., "Applications of modern sensors and wireless technology in effective wound management." *Journal of Biomedical Materials Research - Part B Applied Biomaterials*, 102(4), pp.885–895. 2014.

Metcalf, D.G. et al., "Elevated wound fluid pH correlates with increased risk of wound infection." *Wound Medicine*, 26(1), p.100166. 2019.

Mi, Q. et al., "Agent-based model of inflammation and wound healing : Insights into diabetic foot ulcer pathology and the role of transforming growth factor- β 1." *Wound Repair and Regeneration*, 15(5), pp.671–682. 2007.

Nagoba, B. et al., "Citric Acid Treatment of Surgical Site Infections : A Prospective Open Study." *Wound Practice & Research : Journal of the Australian Wound Management Association*, 19(2), pp.82–86. 2011.

Naomi J Trengove, Langton, S.R. & Stacey, M.C., "Biochemical analysis of wound fluid from

nonhealing and healing chronic leg ulcers.” *Wound Repair and Regeneration*, 4(2), pp.234–239. 1996.

O’Meara, S. et al., “Systematic reviews of wound care management.” *Health Technology Assessment*, 4(21). 2000.

Ono, S. et al., “Increased wound pH as an indicator of local wound infection in second degree burns.” *Burns*, 41(4), pp.820–824. 2015.

Panzarasa, G. et al., “The pyranine-benzalkonium ion pair : A promising fluorescent system for the ratiometric detection of wound pH.” *Sensors and Actuators, B : Chemical*, 249, pp.156–160. 2017.

Percival, S.L. et al., “Antiseptics for treating infected wounds : Efficacy on biofilms and effect of pH.” *Critical Reviews in Microbiology*, 42(2), pp.293–309. 2016.

Percival, S.L. et al., “The effects of pH on wound healing, biofilms, and antimicrobial efficacy.” *Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society*, 22(2), pp.174–186. 2014.

Power, G., Moore, Z. & O’Connor, T., “Measurement of pH, exudate composition and temperature in wound healing : A systematic review.” *Journal of Wound Care*, 26(7), pp.381–397. 2017.

Pusta, A. et al., “Wearable sensors for the detection of biomarkers for wound infection.” *Biosensors*, 12(1). 2022.

Rahimi, R. et al., “Highly Stretchable Potentiometric pH Sensor Fabricated via Laser Carbonization and Machining of Carbon-Polyaniline Composite.” *ACS Applied Materials and Interfaces*, 9(10), pp.9015–9023. 2017.

Rizk, M., Witte, M.B. & Barbul, A., “Nitric Oxide and Wound Healing.” *World Journal of Surgery*, 28(3), pp.301–306. 2004.

SCALES, J.T., “Wound healing and the dressing.” *British journal of industrial medicine*, 20, pp.82–94. 1963.

Schneider, L.A. et al., “Influence of pH on wound-healing : A new perspective for wound-therapy?” *Archives of Dermatological Research*, 298(9), pp.413–420. 2007.

Schultz, G. et al., “Wound healing and TIME; new concepts and scientific applications.” *Wound Repair and Regeneration*, 13(4 SUPPL.). 2005.

Serena, T.E. et al., “Defining a new diagnostic assessment parameter for wound care : Elevated protease activity, an indicator of nonhealing, for targeted protease-modulating treatment.” *Wound Repair and Regeneration*, 24(3), pp.589–595. 2016.

Sibbald, R.G., Mufti, A. & Armstrong, D., “Infrared Skin Thermometry : An Underutilized Cost-effective Tool for Routine Wound Care.” *Advances in skin & wound care*, 28(1), pp.37–44. 2015.

Simoska, O., Duay, J. & Stevenson, K.J., “Electrochemical Detection of Multianalyte Biomarkers in Wound Healing Efficacy.” *ACS Sensors*, 5(11), pp.3547–3557. 2020.

Singh, G. & Chanda, A., “Biomechanical modeling of progressive wound healing : A computational study.” *Biomedical Engineering Advances*, 4(June), p.100055. 2022.

Urschel, J.D., Scott, P.G. & Williams, H.T.G., “The effect of mechanical stress on soft and hard tissue repair; a review.” *British Journal of Plastic Surgery*, 41(2), pp.182–186. 1988.

Wlaschek, M. et al., “Protease inhibitors protect growth factor activity in chronic wounds.” *British Journal of Dermatology*, 137(4), p.646. 1997.

Yager, D.R. et al., “Wound fluids from human pressure ulcers contain elevated matrix metalloproteinase levels and activity compared to surgical wound fluids.” *Journal of Investigative Dermatology*, 107(5), pp.743–748. 1996.

Yang, P. et al., “Orange-Emissive Carbon Quantum Dots : Toward Application in Wound pH Monitoring Based on Colorimetric and Fluorescent Changing.” *Small*, 15(44), pp.1–11. 2019.

6.2 Articles added :

Malone-Povolny MJ, Maloney SE, Schoenfisch MH. Nitric Oxide Therapy for Diabetic Wound Healing. *Adv Healthc Mater*. 2019 Jun;8(12) :e1801210. doi : 10.1002/adhm.201801210. Epub 2019 Jan 15. PMID : 30645055; PMCID : PMC6774257.

Kobayashi Y. The regulatory role of nitric oxide in proinflammatory cytokine expression during the induction and resolution of inflammation. *J Leukoc Biol*. 2010 Dec;88(6) :1157-62. doi :

10.1189/jlb.0310149. Epub 2010 Aug 31. PMID : 20807706.

Agyare, Christian & Osafo, Newman & Boakye, Yaw. (2018). Biomarkers of Wound Healing. 10.5772/intechopen.80222.

Atte Kekonen, Mikael Bergelin, Jan-Erik Eriksson, Annikki Vaalasti, Heimo Ylänen, Sami Kie-
losto, Jari Viik, Bioimpedance method for monitoring venous ulcers : Clinical proof-of-concept
study, Biosensors and Bioelectronics, Volume 178, 2021, 112974, ISSN 0956-5663,
<https://doi.org/10.1016/j.bios.2021.112974>.

Sharifuzzaman M, Chhetry A, Zahed MA, Yoon SH, Park CI, Zhang S, Chandra Barman S, Sharma
S, Yoon H, Park JY. Smart bandage with integrated multifunctional sensors based on MXene-functionalized
porous graphene scaffold for chronic wound care management. Biosens Bioelectron. 2020 Dec
1;169:112637. doi : 10.1016/j.bios.2020.112637. Epub 2020 Sep 23. PMID : 33007617.

Jiang, Y., Trotsyuk, A.A., Niu, S. et al. Wireless, closed-loop, smart bandage with integrated sen-
sors and stimulators for advanced wound care and accelerated healing. Nat Biotechnol (2022).
<https://doi.org/10.1038/s41587-022-01528-3>

Pusta, A.; Tertiş, M.; Cristea, C.; Mirel, S. Wearable Sensors for the Detection of Biomarkers for
Wound Infection. Biosensors 2022, 12, 1. <https://doi.org/10.3390/bios12010001>

Petar Kassal, Jayoung Kim, Rajan Kumar, William R. de Araujo, Ivana Murković Steinberg, Mat-
thew D. Steinberg, Joseph Wang, Smart bandage with wireless connectivity for uric acid biosensing
as an indicator of wound status, Electrochemistry Communications, Volume 56, 2015, Pages 6-10,
ISSN 1388-2481, <https://doi.org/10.1016/j.elecom.2015.03.018>.

Hossein Derakhshandeh, Sara Saheb Kashaf, Fariba Aghabaglou, Ian O. Ghanavati, Ali Tamayol,
Smart Bandages : The Future of Wound Care, Trends in Biotechnology, Volume 36, Issue 12, 2018,
Pages 1259-1274, ISSN 0167-7799, <https://doi.org/10.1016/j.tibtech.2018.07.007>.

6.3 Additional ressources :

SPARKFUN (2022). « SparkFun MAX301x Particle Sensor Library ». In : GitHub. URL : https://github.com/sparkfun/SparkFun_MAX3010x_Sensor_Library.