UNIVERSITAT DE BARCELONA

Final Degree Project

Biomedical Engineering Degree

Study of a Self-Powered Lactate and Glucose Biosensor Platform

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I. Acknowledgements

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II. Abstract

Lactate and Glucose detection and monitoring have shown to have a significant impact on patients' wellbeing, for allowing the prognosis of worsening patient conditions in hospital settings and assisting on early diagnosis and detection of diabetes mellitus complications.

Biological Fuel Cell (BFC) technology allows the transformation from chemical to electrical energy and has recently emerged as a key lithium-ion battery competitor for its sustainability, miniaturization power, and high energy density. Their characteristics make them an interesting alternative to power electronic devices, and their possible application in the development of medical measurement platforms.

Point of Care (POC) Biosensor devices powered with BFC present a compelling perspective to medical monitoring and individualized proactive healthcare since these types of devices allow near-patient settings and encourage a more personalized medicine approach to improve quality of life in developed countries.

The two main objectives of this project are to develop a biosensing platform architecture for Glucose and Lactate Fuel Cells and the use of a commercially available DC-DC converter to apply said BFC to power the instrumentation and obtain a self-powered application. The proposed dual-layered platform attempts to provide a viable biosensor structure, based on the sensing of current proportional to sample concentration, a later amplification, and an event detection circuit to be used as a comparator. This study and proposal, if developed into reality, would comply with the "ASSURED" criteria for POC tests, which states they must be Affordable, Sensitive, Specific, User-friendly, Robust and rapid, Equipment-free, and Deliverable to those who need them.

III. Index

VI. Acronyms

- BFC: Biological Fuel Cell.
- EFC: Enzymatic Fuel Cell.
- FC: Fuel Cell.
- GFC: Glucose Fuel Cell.
- IVDs: In Vitro Diagnostic medical devices.
- LDO: Low Drop-out.
- LFC: Lactate Fuel Cell.
- MFC: Microbial Fuel Cell.
- Operational amplifier: OPAMP
- PMU: Power Management Unit.
- POC: Point of Care.
- UB: Universitat de Barcelona.
- VOC: Open Circuit Voltage.
- WHO: World Health Organization.

1. Introduction

The interest in this project started when trying to investigate sustainable alternatives to classical batteries and using Biological Fuel Cell (BFC) as an option was found.

Nowadays lithium batteries are the preferred choice for many of the medical devices on the market since they offer the highest energy per unit weight and energy density of any other battery type. It is not only in this field that this type of Fuel Cell (FC) is used, from battery-powered electric cars to computers and other types of electronics, a major part of the industry uses lithium as the main component to produce batteries. The impact these have on the environment when discarded is substantial, since they are a fire hazard, and may leak potentially dangerous chemical materials when improperly disposed of, or damaged [1].

Once brief research was done, an interesting approach of using BFC as both a power source and as a measuring element was found. In the medical field, continuous monitoring of vital signs by using wearable devices may allow for timely detection of deterioration in patients in comparison to detection by standard intermittent vital signs measurements [2]. This also presents a compelling reason as to why try to combine both applications to study the viability of such a device. Even though in this study, a continuous measuring approach has not been studied, developing a type of sensing more suitable for a Point-of-Care (POC) device, the study of self-powering devices and BFC characterization may be useful if that type of implementation electronics wants to be further studied.

Another motivation for the development of this project was the reality that as the quality of life improves, the population age, more people living with multiple chronic diseases rise [3]. Aging is a well-established risk factor for the development of multiple chronic diseases such as diabetes, further needing resources to avoid poorly controlled diabetes mellitus which will eventually lead to further complications [4]. A POC device is a good option to ensure that testing and measurement of glucose and lactate can be performed anywhere complying with the specific guidelines defined by the World Health Organization for medical devices: Affordable, Sensitive, Specific, User-friendly, rapid and robust, equipment-free, and deliverable to users [5].

Besides glucose, lactate brings very useful information in the medical field and is a very usual studied parameter in Intensive Care Unit settings to predict worsening patient conditions since there is a correlation between high lactate levels and increased mortality [6]. Moreover, it is also used to study athletic conditions as it is also an indicator of cellular stress, and it is a very convenient parameter to study effective training for professional athletes [7].

The importance in the medical field of both components, and the fact that information about these BFC and their characteristics are copious, have been motivators in choosing them both since a device capable of dual monitoring could be an interesting application. The information which has been found during the development of this project has reinforced my opinion that this field will be hugely influential in the future with regards to the implementation of biomedical devices' powering options and biomedical sensors.

1.1 Objectives

The aim of this project can be classified into two main objectives. Firstly, it consists of familiarizing with Lactate Fuel Cells (LFC) and Glucose Fuel Cells (GFC) to develop a biosensing platform architecture. The designed electronic unit detects the concentration of the sample, measuring the current provided by the BFC to give a valid reading of the measurement. The second goal is related to the use of a commercially available DC-DC converter to use said BFC to power the instrumentation to obtain a self-powered device [8].

The objectives are related to solving the issue of the use of conventional batteries, which are difficult to miniaturize and have a high long to mid-term impact on the planet's well-being. Another objective this project has is that of giving a valid biosensing option with high sensitivity and accuracy in signal detection for a portable medical device application. With the implementation of the presented platforms, it looks at more sustainable alternatives, more affordable solutions which may, in the future, be implemented to develop a continuous monitoring process.

To develop these analyses and simulations, various LFC and GFC characterization studies have taken place. A study of BFC, their voltage, current, and power have been generated to understand the limitations they have as well as to correctly choose appropriate low-voltage, low-current components for the biosensor platform. Multiple concentrations were analyzed to check if the created circuit could detect at multiple voltage and current ranges.

Therefore, this approach looks at the possibilities for POC devices to help follow the trend of a more personalized medicine approach with the help of portable devices. To be more precise, the optimal goal is to implement both platforms to create a self-powering lactate and glucose biosensor to be used as a portable device for medical applications.

To sum up, the following list exemplifies the main objectives and milestones of this project:

- A study of GFC and LFC characteristics and behaviors to understand the working ranges of the FC.
- A comparative analysis of multiple biological sensors and functionality to understand which application works better with the characteristics of the simulated FC.
- Design of the biosensor platform for the detection of two BFC: LFC and GFC.
- Design of circuit using a GFC with a DC/DC boost converter to be used in self-powering applications.
- Implementation of both platforms at the same time to create a self-powering device for biological sensing of BFC.

1.2 Methodology and location

Due to the Global pandemic created by the coronavirus SARS-CoV-2, the simulations have been generated remotely without physically going to the UB to make them. Regardless of this limitation, online sessions with the Director of the project, Dr. Miribel have taken place regularly to ensure doubts and simulation issues could be promptly resolved.

First, research has been done to fully understand what a FC is, how they are constructed, and their possible applications. When a basic understanding had been reached, a more specific analysis of GFC and LFC took place.

Different studies have been inspected to find an appropriate FC to be used later in the studies. Voltage and Power vs current graphs about the specific behavior of GFC and LFC have been extracted from different papers [9][10], different values have been defined to simulate both FC in an LTSpice environment. Using a look-up table of a voltage depending on voltage source, different resistor values have been calculated to mimic the real-life behavior of the FC, and switches have been employed to create a transient response graph.

With the simulations of the characterization of specific GFC and LFC, they have been repeated for multiple concentrations of the substrates to have multiple choices of detection, since both elements can change their concentration on the bloodstream depending on different circumstances.

A comparison of different types of biosensing platforms has been performed to find a viable way to create sensing instrumentation. Finally, based on the literature [8] an event-detection unit of the concentration of the sample provided by the BFC has been recreated, having this circuit three different modules: a current sensing module, a load resistance, and an event detector. It has been tested on LTSpice for multiple concentrations and both FC, having a good response.

Different DC/DC boost converters options have been examined to amplify the low-voltage of the GFC to a level that can supply the event-detection unit. The commercially available LTC3108 DC/DC converter has been chosen due to its ultra-low voltage step-up converter and power manager. Different simulations using both BFC at different concentrations have been used to see the response of the converter, and some issues have appeared which will be further explained in the limitations section.

The implementation of both platforms together could not be properly accomplished due to the limitations found with the amplification of the voltage of the BFC to be used as a supply for the sensor platform. This will be further explained in the next subsection.

1.3 Scope and span of the project

It is necessary to consider the most relevant limitations present in this project, which range from limited time, location, cost, computer power, and simulated electrical components characteristics.

Even though this project started in March 2020, due to the Covid-19 pandemic, some parts of the study, mainly the DC/DC boost converter to develop a self-powered application, suffered from lack of time. The study started with a study and development of the biosensor, therefore, when the commercially available component, LTC3108, failed to properly perform., there was insufficient time and experience to design one to match de characteristics of the BFC to make it work. Moreover, this is an expanding field, with limited information on BFC applications to power electronics. Research and some examples have been found, but well-defined schematics on other options for a DC/DC boost converter which could be implemented with limited time and resources, could not be applied. With more experience and time this, perhaps, could have been solved.

Another limitation that has been encountered has been limited computer power to simulate some scenarios, adding to the time limitation explained before. When trying different simulations using the LTC3108_TA02 component, due to the intricate nature of the circuit, and multiple switches used on the characterization of the BFC, some simulations took over 5 hours to complete, limiting the use of LTSpice meanwhile. Due to the low-voltage, low-current FCs that this work has investigated, multiple scenarios had to be analyzed, making the whole process take a frustratingly long time.

The FC characterization had to be scaled down to, at most, 10 switches to simulate the real behavior of the GFC and LFC, otherwise, as mentioned in the paragraph above, the simulation would take too long, making it not practical for further studies of stack BFC at multiple configurations. Therefore, the values and representation of their behavior have some margin of error due to the relatively low number of value points on the look-up table.

Since it has not been possible to develop a stable and reliable way to amplify the voltage of the BFC, it has not been possible to properly power the electronics of the biosensor with it. This has been solved by relying on external voltage supplies or connecting the DC/DC converter using ideal FC output values, which, while powering the event detection platform, does present some issues.

Therefore, only the characterization of the BFC and the sensorial part of the Final Degree Project has been able to completely and successfully be completed.

2. State of art

2.1 Biofuel Cell technology

In recent years BFC technology has been thoroughly researched, allowing for the possibility of transforming different types of organic components into electricity through multiple ways, such as microbial, enzymatic, or abiotic cathodic electrochemical reactions. This science manages to combine biological catalytic redox activity with classic abiotic electrochemical reactions and physics, giving the systems a level of complexity that is above classical systems such as batteries [11]. Their working principle is similar to classical FC, in which fuel is oxidized at the anode side, and the electrons released are driven through an outer electrical circuit generating electric current. The generated electrodes will reach the cathode, where they will combine with an oxidant and protons to produce water [12]. BFC is more sustainable than classical batteries and will continuously transform the stored chemical energy into electrical energy unless the fuel supply is exhausted, which means that they present as a very competitive alternative to batteries [8].

Performance tracking technologies have become extremely popular over the past several decades, which has increased the interest in BFC, in part thanks to their miniaturization potential and portability compared with classical power sources such as batteries. BFC technology presents great versatility, not only producing power from a wide range of organic substrates but also having the ability to work at room temperature [13][14].

Despite all these advantages, BFC suffers from severe kinetic limitations mainly due to inefficiency in electron transfer between the enzyme and the electrode surface, which elicits a low cell voltage, current density, and stability. This happens because redox proteins tend to exhibit their superior catalytic properties in their natural environment, meaning that there is a difficulty in establishing electrical communication between the protein and the electrode surface and, by the limited stability of the biocatalyst-electrode assembly, decreasing their activity with time. Another issue they have is a lower volumetric catalyst density than classical FC since the large size of BFC means a low number of active sites per volume compared with metal electrodes [12]. Overall, BFC presents a possibility for developing sustainable, low-priced, potentially self-powering, portable devices [15].

BFC can be classified into two primary types based on which biocatalyst is applied. There are enzyme fuel cells (EFC), which use enzyme catalysts at both anode and cathode such as glucose, lactose, ethanol, or lactate, and microbial fuel cells (MFC), which use living cells as a catalyst. EBC such as lactate or glucose, which will be the focus of this study, has been showing promise for the possibilities to use them in different types of biomedical electronic and wearable microelectronic devices [16]. Through multiple studies, EFC has shown promise in its possible applications as a sensor, integrated lab-on-chip power supplies, and advanced in vivo diagnostic medical devices that use reactants available at room temperature [13][17].

Lactate is an attractive BFC since it is present in several biological sources for instance blood or sweat. Its high energy density and elevated water solubility mean that it will be possible to extract a maximum theoretical energy density higher than other BFC with lower water solubility, making it a good material to study [18]. The downside it presents is its low voltage, low current, fuel incomplete oxidation, and lower lifetime stability, which can be solved using multiple enzymatic

cells arranged in series or in parallel configurations to generate enough energy to obtain the needed electrical parameters [13][10].

Moreover, the interest Lactate Fuel Cell (LFC) brings is in the sensing department, since it is an enzyme that brings valuable information on the medical field as well as the food industry. Lactic acid is a key biomarker of stress, and it is the main source of metabolically produced acid responsible for tissue acidosis. It can be found either as L- (+) and D- (-) enantiomers. While L- (+) is the one found in mammalian metabolism, lactic acid can also be found in the form of D- (-) enantiomer in microorganisms, algae, and plants. In the analysis of food, it can be used for the evaluation of the freshness and stability of milk, dairy products, fruits, vegetables, meats, and wines. Meanwhile, in medicine, the determination of L-Lactate is fundamental, since it is the major indicator of ischemic tissue, which is the deterioration of the tissue due to the diminishment of the flow of nutrients and oxygen to it. It can also be used to diagnose certain illnesses and has been linked as a prognosis for worsening patient condition, as well as to monitor the training status of an athlete and their fitness. This is the reason why the monitoring of L- and D-lactic acid can be interesting to study. Because methods such as the analytical, colorimetric tests, and chromatographic analysis are complex, require a pre-treatment of the sample, and, therefore, are time-consuming, a Point-of-Care (POC) approach can be interesting to study [19][10].

Glucose fuel cells (GFC) bring a very significant potential in the medical field for improving the management of blood glucose levels in individuals suffering from diabetes, therefore enabling a highly sensitive and real-time monitoring of blood glucose [9]. Long-term complications from increased blood sugar concentrations (hyperglycemia) result in huge costs and increased morbidity and mortality for people with diabetes. Nowadays, the most common way to analyze glucose concentrations is in the form of blood sampling with a POC device that requires a needle to be inserted to extract the blood from a finger. This can be cumbersome, painful, and can lead to poor patient compliance [20]. Moreover, these measurements are relatively infrequent, compared with the rate of blood glucose fluctuations, complicating the process to obtain regular blood glucose concentrations, risking complications. Bad control can lead to being more susceptible to other complications and diseases such as high blood pressure, blindness, nephropathies, and heart diseases. Therefore, the idea of continuous non-invasive blood glucose sensing can have huge improvements on the quality of life of diabetic patients [21] [22] [23]. Even though this approach has not been implemented in this project, opting for a design focused on a POC device, the structures, designs, and information found in the literature, have helped better understand the specific case scenario this Final Degree Project has presented.

GFC similarly to LFC presents limitations in the form of low voltage and low current extraction, but has a slight improvement on both counts, being a better option to use as fuel when trying to implement a self-powering device. Akin to LFC, these power shortages can be solved by adding GFC in different configurations to increase its voltage or current as needed or using operational amplifiers. [13]

2.2 Biofuel Cells application in self-powered devices

Another idea that, in recent years, has grown exponentially is that of creating self-powered biosensor devices. These types of devices vary in the way they are implemented. Some use the FC as both a power source and as the enzyme to sense simultaneously, creating a self-powered supply-sensing biosensor platform [8][24]. In some other cases, the development of the and the power management are two separate entities both using FC but not at the same time [20][25].

Regardless of the type of implementation, there has been a rise in the work and development of new technology regarding self-powering electrochemical lactate and glucose biosensors that can generate electrical power to drive its internal circuits using a capacitor circuit functioning as a transducer.

In reference [10] the authors propose a LFC of $6mm^2$ with lactate concentrations ranging from 1-25mM able to generate an open-circuit voltage (VOC) peak of 395.3mV, and a short circuit current density of 418.8μA/cm^2 when at 25mM concentration.

For the case of GFC, in reference [9] the authors propose a GFC of $4mm^2$ with concentrations of 3, 5, 7, 10, 15, and 20mM with a VOC peak of 550mV, and a short circuit current density of 1.285mA/cm^2.

Later a detailed explanation of the examples and types of implementations mentioned here will be analyzed and their instrumentation described.

2.3 Previous projects

The D2In (Discrete-to-Integrated Systems) research group at the Department of Electronics and Biomedical Engineering of Universitat de Barcelona (UB) has worked in the development of different types of POC devices that use multiple types of BFC. Their progress opens the approach of combining various types of technologies to create diagnostic tests that can be brought closer to the patient settings. This type of device must be smaller and low-cost, but it must remain, sensitive, robust, and fast. A key issue in POC is the way it is powered and its size. As explained previously, the need for miniaturization and portability of the machines is one of the reasons that has made it interesting for D2In to look at different BFC, since they are more sustainable, and they take a smaller space than other types of batteries [8]. Besides the portability potential, the research group has focused on designing devices that comply with the appropriate test attributes the World Health Organization (WHO) has referred to as the “ASSURED” criteria: Affordable, Sensitive, Specific, User-friendly, Robust, and rapid (less than 30 minutes), Equipment-free, and Deliverable to those who need them [5][14][20][24][26].

An example of what has the D2In studied and designed in the self-powering biosensor field is a three-module architecture defined as the sensor, the power source, and an e-reader. They have developed a circuit, which extracts the energy from the BFC to supply its electronic components concomitantly while performing the detection of the fuel concentration. The electronics rely on standards for low power consumption, not needing an external supply source to power the device. It can also process and display the data extracted from calculating the BFC concentration without requiring external instrumentation or equipment. They have achieved the feat of making it perform

with different emulated BFCs and sensors [14]. Their designed Power Management Unit (PMU) is comprised of a DC/DC boost converter in cascade with a low drop out (LDO) linear regulator. The DC/DC boost converter can step up the voltage provided by the FC to 3.0V to supply the sensor instrumentation. The circuit used can be seen in *Figure 1*.

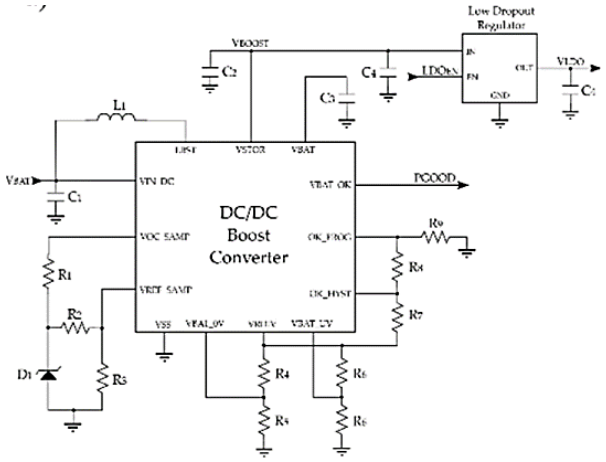

Figure 1. PMU circuit [14].

Another aspect D2In has studied, is the concept of Plug-and-Power in the POC field with CNM-CSIC. They have managed to design a device that allows the energy required to measure to be always available within the disposable test component, meaning that the e-reader contains all the required electronic modules to run the test, process the data, and display the result. In this case, though, they have not included the research on the power source, they have demonstrated the feasibility of a technology consisting of two parts, the power source in paper-based form, and the application-specific battery-less electronic reader designed to extract the energy from the test strip, process the signal provided and show it [20].

Studying power management, D2In has designed a BFC-based adaptable self-powered device that allows for the direct reading of the concentration of the BFC with the circuit shown in *Figure 2*. It is this model which has been used to create the GFC and LFC biosensor later in the project. It is comprised of two modules, the BFC and a self-powered event detection biosensing platform. The electronic unit detects the concentration of the sample provided by the BFC and a part of the energy is used to supply the low-power electronics unit. They have made it possible to be used for various types of BFC. The way they have designed the event-detection unit is such that it is conformed of four units: a current sensing module, a load resistance, an event detector, and a qualitative display [8].

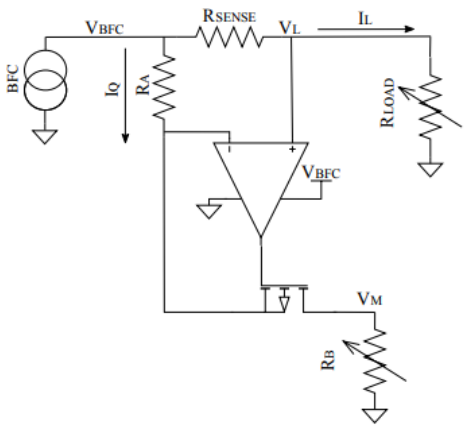

Figure 2. A high-side current sensing solution implemented to measure the current directly related to the concentration of the sample [8].

Other studies have investigated self-powered skin sensors since they are based on energy harvesters, that allow for the device to generate electrical signals triggered by the detected stimulus or analyte chemicals in sweat such as glucose or lactate. They have studied other means of extracting energy through different stimuli such as body motion, pressure, and acoustic sound, but they have found EBF to be the most reported because of their high catalytic activity and relatively low cost and biocompatibility [27].

3. Market analysis

3.1 Evolution of the concerning legislation

To understand the evolution of the market around this field, it needs to be considered that when commercializing a new medical device, restrictive legislation and numerous norms need to be followed. Taking as an example the United States of America (USA), these regulations were started by the Food and Drug Administration (FDA), which is responsible for protecting and promoting the development of human and veterinary drugs, biological products, medical devices, and radiation-emitting products, human and animal food, and cosmetics. In the 1960s, a public desire for more oversight over medical devices began to rise, creating one of the first medical device regulations in the world. In the 1970s a medical device classification was proposed, which classified based on a comparative study of the associated risk of each instrument, but it was not until 1976 that this regulation was implemented, and it was reflected in the amendments of 1976 (introduced by the 94th Congress of the United States of America). In the 1990s, extensive regulation began to pass on the USA Congress, which consolidated quality standards and safety precautions in all medical devices [28].

In addition, there is the European Union (EU) legislation that must be considered depending on where the object will be used or sold. There are over 500 000 types of medical devices and In Vitro Diagnostic medical devices (IVDs) on the EU market, since the EU has a competitive and innovative medical devices sector, so regulatory framework aims to ensure the safety and efficacy of the devices. Moreover, as the use of BFC in the medical field is still expanding and evolving, the legislation around it is dynamic to be suitable and coherent with the technological advances. The last update on regulatory action took place on 5 April 2017, when two new Regulations on medical devices and in IVDs established a modernized and more robust EU legislative framework to ensure better protection of public health and patient safety were adopted.

Due to the global pandemic due to Covid-19, on 23 April 2020, the Council and Parliament of the EU created a regulation which postponed the date of application for most Medical Devices Regulation provisions by one year – until 26 May 2021. This was made to lower the pressure for national authorities, notified bodies, manufacturers, and other actors so they could focus fully on urgent priorities related to the coronavirus crisis [29].

3.2 Evolution of healthcare needs

In many of the developed and developing countries in the world, as the quality of life improves, and mortality rates decline in most countries, population ages and people with chronic diseases rise. Life expectancy has almost doubled in the last 150 years, now being up to 80 years old. As natality rates decrease, the rate of populations 65 or older is increasing, therefore creating a burden for any health care system regardless of the country [3].

Aging is a well-established risk factor for the development of multiple chronic diseases, including cardiovascular disease, stroke, diabetes, and dementia. And as this trend continues, a higher

number of people with these diseases will appear, needing further devices and resources to have control of the advances of the diseases and possible complications [4].

3.3 Patents on the field of self-powered devices

Multiple companies are working in this field since the applications BFC has are many. This is an innovative idea, and a lot of the technology is under patent protection. There are a few regarding the invention of biosensors that allow for self-powering. One would be the patent "*Self-powered biosensor*" from the inventors Itamar Willner and Ecgeny Katz from the Yissum Research Development Company of the Hebrew University of Jerusalem. In which they provide a system for the determination of an analyte in a liquid medium. The system is comprised of a self-powered biosensor and a detector for measuring an electrical signal generated by said biosensor while the analyte is being oxidized or reduced [30].

Another existing patent is from the Regents of The University of California, "*Printed Biofuel Cells*". The invented technology includes a wearable epidermal BFC device that provides continuous power generation while being worn on a human or another user. It can be applied to the epidermis to scavenge a supply of L-lactic acid to generate power from the BFC. The electrodes of the wearable epidermal BFC can function with lactate oxidase and platinum black within the anode and cathode. The anode includes a catalyst to facilitate the conversion of fuel in a biological fluid in an oxidative process that releases electrons captured at the anode, this makes possible the extraction of energy from the fuel substance. The cathode is configured to be separated from the anode by a spacing region, and a load electrically coupled to the anode and cathode via electrical interconnects to obtain the extracted energy as electrical energy [31].

A related patent from Abbott Diabetes Care Inc, "*Self-Powered Analyte Sensor*", describes a self-powered analyte determining device for glucose and lactate in a body fluid. It includes a working electrode, a counter electrode, and an optimal resistance value. The working electrode includes analyte sensing components and the self-powered analyte determining device spontaneously passes a current directly proportional to the analyte concentration in the absence of an external power source. Also provided are systems and methods of using the, for example electrochemical, analyte sensors in analyte monitoring [32].

Siemens AG has presented a patent of a "*Pacemaker with biofuel cell*", that improves on the design of a heart pacemaker. It includes a stimulating electrode and counter electrode, a pulse generator, and an implantable glucose-oxygen BFC as the energy supply. The area of the glucose electrode of the BFC is made larger than of the stimulating electrode and the stimulating electrode is in electrically conductive connection with the glucose electrode to ensure the same potential. This patent shows that major companies are starting to develop technologies to improve already existing medical devices and implementing BFC to make them self-powered [33].

As can be seen in the patents, the sector in which this type of technology is directed is the medical field. Regardless, since the measurement of lactate can be used in the sports field and even the food industry, to detect food spoilage, the creation and fabrication of a self-powered lactate biosensor can be brought to multiple professional scenarios. And, for the case of glucose, the importance of its medical application has been thoroughly explained previously to early diagnose complications of hyperglycemia.

D2In has been working and has developed a patent for a “Self-powered system and method for power extraction and measurement of energy-generator units, in which a method for power extraction and measurement of energy-generator units has been created. The system comprises an energy generator unit providing an electrical current IFC and a voltage VFC; an instrumentation block to measure the electrical current 1FC, and a power management unit connected via a first input to collect the electrical current IFC, extracting an electrical power provided by the energy generator unit. The system also comprises a feedback element electrically connected, via a second input, to the PMU. It does so that it simultaneously extracts the electrical power and uses the PMU and the instrumentation block to set a given parameter of the energy generator unit to a controlled given value, by varying an equivalent input impedance of the power management unit [34].

3.3 Prospects on the field

As proven in the number of patents available, the prospects of the field of self-powered devices that use different types of BFC are a prosperous one. One of the reasons for it is that it gives an alternative to classical power cells that is more sustainable and safer to use in implantable devices. They have some problems that have yet to be overcome such as the low power density they have, but more and more companies and institutions are looking into it, so solutions are likely to be shortly introduced and devices made.

4. Concept engineering

As has been mentioned previously, this project began in March 2020 with an internship in the Electronics and Biomedical Engineering department at Universitat de Barcelona (UB). Even though it had an unusual development due to the Covid-19 pandemic and the lockdown on March 15th, 2020, it helped gather a wide range of opinions and information related to Biological Fuel Cells (BFC) and Self-Powered Devices. From the information gathered doing bibliographical research, the information Dr. Miribel provided, and LTSpice simulations, some conclusions were made. As explained previously, the usefulness of using BFC as a power source was made obvious, as well as the importance and practicality of developing a POC device to measure both Lactate and Glucose. These findings are the reason why this project is aimed at developing a biosensor platform that can function with simulated LFC and GFC for both sensing and powering the device.

4.1 Internship at the Electronics and Biomedical Engineering department at Universitat de Barcelona

During this internship, multiple studies have been evaluated to understand the behavior of LFC and BFC, the voltage, current, and power they were able to produce, and how the concentration in mM of this substrate, altered these values.

Another aspect that has been researched is the implementation of DC/DC Boost converters to power the instrumentation without needing external supply voltage.

Before starting the technical evaluation of each component, a brief explanation of the purpose of this project is needed to properly understand the proposed alternatives to each part of the project, and the criteria followed to select the more suitable option and discriminate the rest. As it has already been established, this project aims for the design of a Biosensor for Glucose and Lactate that does not require an external supply to power the electronics and uses the same BFC to power itself. This means that the project has been separated into two modules that will be further explained on the Detail Engineering.

4.2 LFC and GFC sensors and power management platforms

As mentioned in the State of the Art, there are multiple possible implementations when considering building a BFC.

Some case studies present the use of the FC as both a power source and as the element to sense simultaneously, creating a self-powered supply-sensing biosensor platform [8][24][26]. In some other cases, the development of the and the power management are two separate entities both using FC but not at the same time [20][25].

4.2.1 Self-Powered Point-of-Care Device for Galvanic Cell-Based Sample Concentration Measurement [24]

On one specific case study, a self-powered point-of-care low-power electronics approach for galvanic cell-based sample concentration measurement has been created. The designed electronic system harvests and senses at the same time using only one FC. This scenario has been interesting to study since it implements a solution to the issue of extreme low-power generation from FC.

The design does not require the implementation of a potentiostat amplifier to fix the operating voltage for the DC as a sensor, they have instead used a capacitive-based method, and the system generates such control that no timer or microprocessors are needed to define the time of measurement. This specific work tests the design on a NaCl solution but includes studies performed on GFC.

The way this work is distributed is in the form of a galvanic cell and an electronic reader consisting of a current-sensing, event-detector and analog-to-user-interface modules, and a capacitive load. The system activates when the sample is added. The FC starts to charge the capacitive load, therefore, the polarization voltage which will be applied to the cell corresponds to the charging voltage of the capacitor. The polarization curves created can be used to measure and identify different concentrations of the FC.

The current-sensing module continuously measures the cell output current providing a VSENSE indicator of the current of the FC. To read the results, the event detector module monitors the charging voltage of the capacitive load, and, when it reaches a pre-defined voltage, it sends a signal, VLATCH, to indicate to the analog-to-user-interface module that it can read the VSENSE value and convert it to a user-readable result.

The storage element allows for the self-powering aspect because of the implementation of a 4.7mF supercapacitor as capacitive load and storage element of the power extracted from the cell for its polarization. They have managed to exhibit a maximum coefficient variation of 6.1% which is an improvement compared with other studies, and develop a cost-effective, low complexity device without needing potentiostat amplifiers or external non-self-powered instrumentation. The drawback they have described is due to the 0.8V minimum voltage limitation due to the use of commercial-off-the-shelf components, and its incompatibility with continuous monitoring.

The way this device senses the concentration of the FC is very interesting, and the final option used does have some aspects in common with the chosen architecture, except for the capacitive load and the storage element. The reason as to has not been chosen as inspiration is due to the publish date being the 10th of April 2021. But regardless, it has helped me understand similar circuits and has presented as a very interesting state-of-art scenario.

4.2.2 'Plug-and-Power' Point-of-Care Diagnostics: A novel approach for self-powered electronic reader-based portable analytical devices [20]

In this specific case scenario, they have developed a self-powered plug-and-play glucometer with a disposable test strip acting as both the sensor and power source. In this case, the test strip is inserted into a specific battery-less electronic reader designed to extract the energy from the test strip, process the signal, and display the information.

Once the strip is inserted into the device and a sample put on the paper, the liquid bifurcates, and one-half reaches the power source so that the electronics can regulate the power and amplify it to 3V for the instrumentation. The chronoamperometric measurement is performed with the other half of the sample, and the FC responds to power output proportional to the glucose concentration in the sample. The power supplied by the test trip goes into the Power Management Unit (PMU) which will manage and generate the needed voltage supply.

It is in this paper that the use of DC/DC boost converter was first introduced to me as a solution to create a self-powered device. In this scenario, they use a boost DC/DC converter in a cascade with a Low-Dropout (LDO) linear regulator. It boosts the voltage to 3V to supply the screen and processing unit, and the LDO terminal provides a very stable 1.8V with high noise rejection to be used on the front-end module, which needs a very stable voltage supply. It must have these characteristics and high noise rejection to avoid switching noise and transient voltage variations at the power supply.

For the Control and Processing Unit, they have decided to choose an ultra-low-power microcontroller that needs only 1.8V to operate. This type of system architecture extends the autonomy of the system by increasing performance at lowered energy budgets, and ultra-low-power 16-bit control processing unit, and intelligent peripherals. Two ADC have been used, one to know if the sensor is ready to measure, and the other as a measurement signal related to the current across the FC, which is proportional to the glucose concentration.

In general, in this case, study, they have demonstrated the advantages and function of a POC self-powered device that can be extended to other BFC. The reason as to why this option has not been taken for this study has been due to the complexity of the system, the need for physical instrumentation, which it was not possible to acquire at the beginning of this Final Degree Project due to lockdown, and, finally, for the lack of expertise with microprocessors.

4.2.3 Autonomous self-powered potentiostat architecture for biomedical wearable applications [25]

The presented electronic in this study, consists of two modules, the electronic instrumentation, consisting of a potentiostat amplifier, that interacts with the sensor, and the energy harvesting module, to power the electronic device.

The potentiostat amplifier is designed to have a minimum power consumption while allowing the possibility of working with a wide range of electrochemical amperometric sensor characteristics. In addition to the harvesting power module and the potentiostat module, a control module consisting

of a microcontroller unit is also present. It allows for device management, data processing, and consists of a communication module for wireless interaction within an external device for the collection, visualization, and storage of data. To solve the issue of insufficient energy from the harvester block to perform wireless data transmission, the usage of a single super-capacitor has been followed.

When looking at the potentiostat module design, it is new to see that they have added a capacitor a first-order low pass filter in the architecture, which is based on a trans-impedance amplifier with a direct voltage bias application and a final non-inverting amplifier.

On the harvesting power module design, they present a self-powered continuous monitorization of lactic acid of multiple concentrations generating a VOC of 395mV at 25mM, meaning that they have used the same LFC in the literature as I. They have added a charge pump to set up the voltage to 1.8V. The harvester module is formed by BQ25504 (Texas Instruments; Dallas, TX, USA) boost converter and the voltage splitter, which is expected to have a power consumption of around 40μW.

One of the reasons as to why this approach has not been considered beyond state-of-art is due to the complexity, the impossibility to find the BQ25504 DC/DC boost converter to simulate on LTSpice and the inspiration on other papers. Regardless, it brings a new look at self-powered devices and has been very useful to understand electronic concepts and to give a good background of the state-of-art.

4.2.4 A Fuel Cell-based adaptable Self-Powered Event Detection platform enhanced for bio sampling applications [8]

This study has been the one followed to develop the BFC Biosensing platform, as it presents a self-powered event detection platform to sample biological agents, as well as uses the BFC to power the device while acting as a sensor. The entire approach to the biosensing platform will be explained in detail with examples and simulations later in this project, but the reason this has been the chosen article is due to the possibility to adapt it to any other BFC. Moreover, the study analyses GFC meaning that it has helped solve some of the issues this low-power, low-current BFC presents.

In summary, this project presents a self-powered event detection biosensing platform, which detects the current of the sample at the current sensing module, fixes the working point with a load resistor, and measures the current provided by the BFC in the event detector module. Simultaneously, a part of the energy is used to supply the low-power electronics unit.

In general, I found this study to be well explained, the circuit not unnecessarily complicated, precise and of use for medical applications if taken into development. The initial limitations of these implementations were acceptable, and the circuit and components available to simulate. This is the reason why I chose this as a guide to develop my circuit.

5. Detail engineering

This is the main section of this Final Degree Project. Here both the designing process of the biosensor platforms in terms of their modules will be explained in detail. The considerations that have been considered during the development of the circuits, the relative errors and the limitations will also be explained.

5.1 Schematic of the project

As it has been mentioned before, this project has two main objectives which are interconnected, a power management unit (PMU) and the biosensor. In *Figure 3,* a block diagram schematic can be seen, which explains how they are connected.

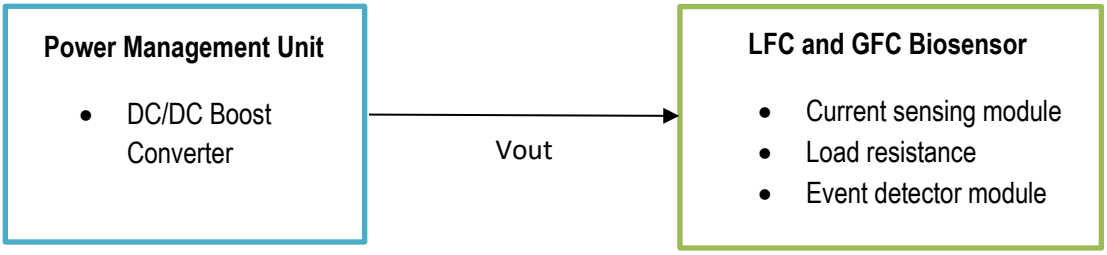

Figure 3. Diagram of the final project platform.

As can be observed in the previous figure, both modules are interconnected, but will be independently explained to deeper understand not only how the prototype has been designed, but also to state their functions and limitations.

The power supply for the PMU and the sensing sample for the sensor both come from simulated BFC, which has been reproduced from previous studies to understand the range of voltage and current these fuel cells can produce. The reason as to why two types of BFC have been used is due to the limitation LFC has regarding current, making GFC a better choice to use in the PMU, as well as an interesting EBC to study.

The potentiostat-based architecture for the Lactate and Glucose sensor can work without the designed PMU, which uses GFC, if an external power supply is connected instead, which is how the start of the research has been made, later connecting both modules. To more clearly understand how the sensor works, first, the simulations have been made applying an external +2V supply voltage.

5.2 LFC and BFC Biosensor

In this subsection, the structure of the biosensor circuit and the studies needed to develop it are explained in depth. A first study of the BFC has taken place, in which voltage, current, and power output signals have been analyzed to determine which components are best on the biosensor

circuit. First, a characterization approach has been implemented, later the current sensing module created, fixing the working point of the circuit with a Load Resistance, and finally, the detector module has been designed.

5.2.1 LFC and GFC characterization

To correctly choose the components to build this adaptable sensor, first, the ranges of current and voltage these FC can produce, either by themselves or stacked, needed to be clear. Using the architecture seen in *Figure 4 a) and b,* and changing the values for each specific FC, extracted from bibliographical research, the information obtained has been summarized in *Tables 1, 2, and 3.*

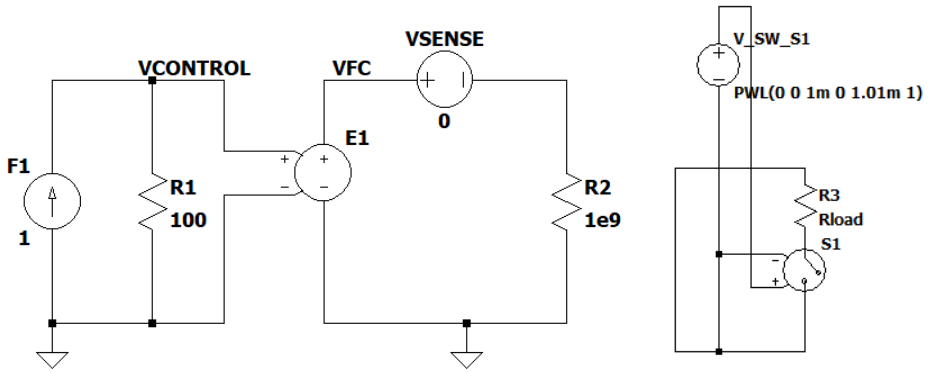

Figure 4. a) FC adaptable simulation structure. ***b)*** switch structure for a transient response.

This structure allows for the simulation of different FC only needing to vary the values of the look-up table of the *voltage depending on voltage source* (E1). A look-up table is used to specify the transfer function. The table is a list of pairs of numbers, which second value is the output voltage when the control voltage is equal to the first value of that pair, and the output is linearly interpolated when the control voltage is between specified points. If the control voltage (VCONTROL) is beyond the range of the look-up table, the output voltage is extrapolated as a constant voltage of the last point of the look-up table.

Once the data from the LCF and GFC was written on the look-up table, different resistor values have been calculated to mimic the real-life behavior of the FC. R2 has been set to the magnitude of Giga ohm to ensure that at time equal 0, the simulated FC would not deliver any current, therefore, VFC could be considered a VOC. The switches in *Figure 4 b)* were implemented to be controlled by voltage, and Rload being in parallel configuration with R2 means that for each switch connected at a parallel configuration, the R equivalent decreases, making the voltage drop and current increase, simulating an accurate transient response according to the literature. The working range of the FC has been studied through many simulations using different Rloads, which have been calculated to obtain the optimum working power. Current dependence on Rload has been observed using a. step *param* application with every FC characterized. In *Figure 5 a, b and c*, an example using a GFC of 20mM concentration can be seen, with the electrical circuit and the values obtained. The conclusions that have been extracted are that for an increase of Rload, the drawn current will decrease, and, for this specific GFC concentration, for a resistor value of 1Ω, the

maximum current will be of 1mA, meanwhile, with resistors smaller than 1kΩ, the current will only reach 50μA.

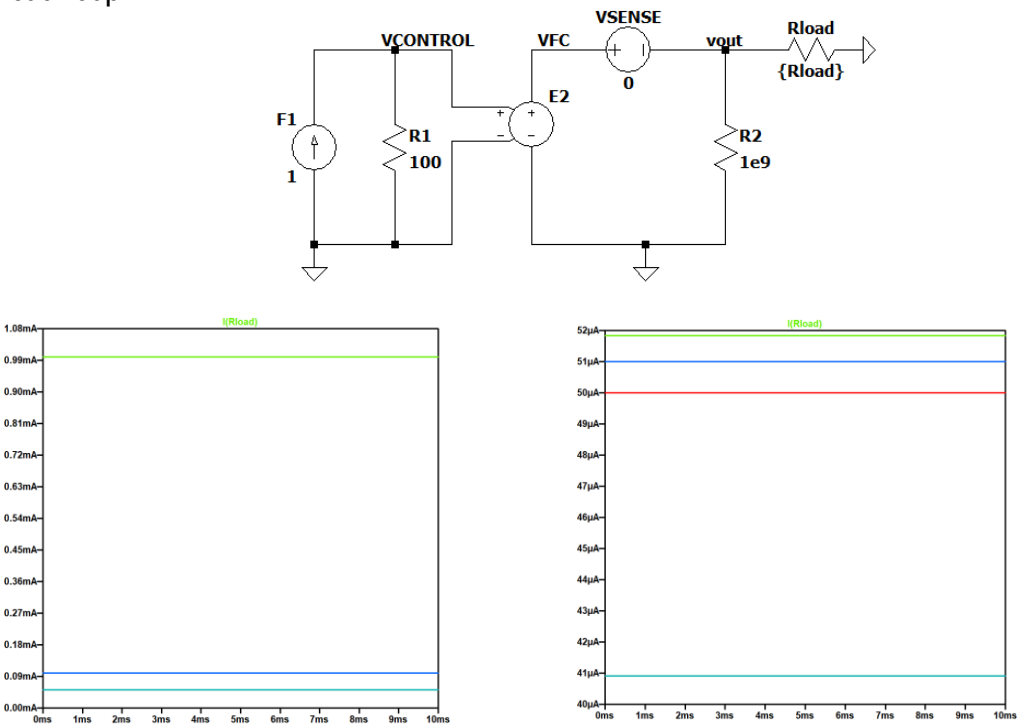

Figure 5. a) LTSpice circuit of current dependency on Rload. ***b)*** Current obtained at different Rload values (green 1Ω, blue 10 Ω, red 25 Ω, and turquoise 50 Ω). ***c)*** Current obtained at different Rload values (green 100 Ω, blue 500 Ω, red 1k Ω, and turquoise 5k Ω).

It needs to be considered that lactate and glucose concentration in blood can vary drastically depending on the time of measurement. Lactate levels at rest are typically around 1-2mM yet, during intense exercise, it can rise to 26mM. When considering glucose more variables need to be considered [35]. A non-diabetic person can have a concentration of glucose in blood between 3mM and 6mM depending on whether they are fasting or is a postprandial measurement. A diabetic person though, depending on their control can rise to higher than 10mM after eating [36].

When considering all these factors, different studies have been analyzed to obtain the data for multiple concentrations to ensure that the values used on the detection structure would be viable and useful in a clinical environment. In *Figure 6*, an example of the circuit of an LFC characterization of 7mM concentration using switches can be seen, as well as the graphs obtained. In *Figure 7 a)*, the graph from the extracted values from reference [10] can be seen to compare them to the generated simulations in *Figure 7 b)* to observe if the approximation is valid. Some margin of error is to be expected since only eight switches, with their respective resistor values, were employed.

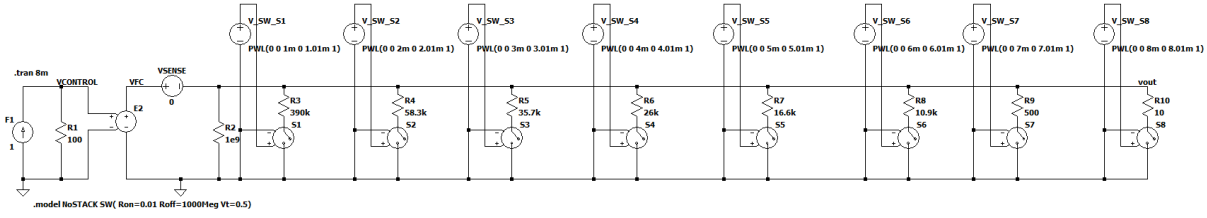

Figure 6. LFC of 7mM concentration simulation using LTSpice.

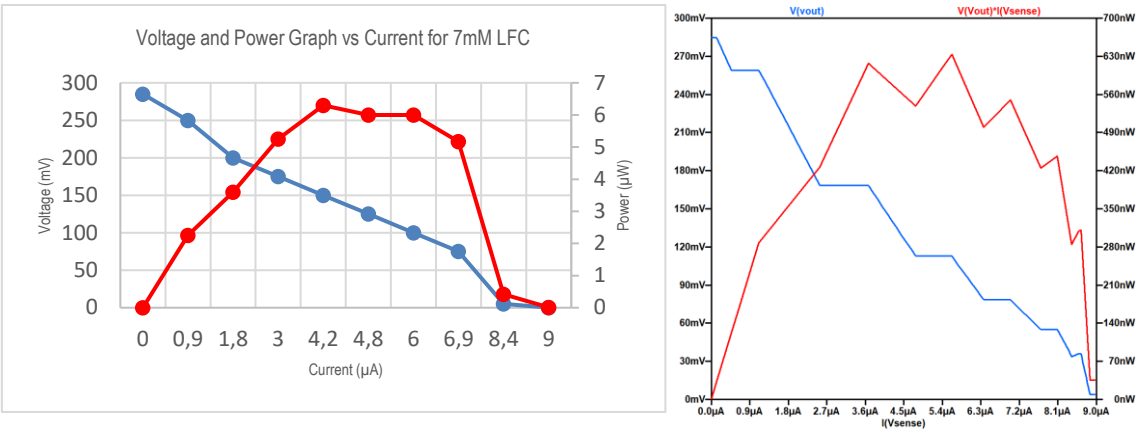

Figure 7. a) Voltage (blue) and power (red) vs current graph from extracted values in reference [10] for LFC of 7mM concentration. ***b)*** LTSpice simulation plot of circuit seen in *Figure 6* of voltage (blue) and power (red) vs current.

Another type of study that has been performed is stacking multiple FC to obtain a higher voltage or current, depending on the structure. This has been made to avoid issues with the components if the output values are too low. Multiple studies and configurations have been performed with the 25mM concentration for LFC and with 20mM concentration for GFC to see up how much voltage, current, and power the BFC could go. In *Figure 8*, an example of a circuit of a parallel configuration of two stacked GFC of 20mM concentration can be seen, and in *Figure 9*, the voltage and power vs current plot obtained are shown.

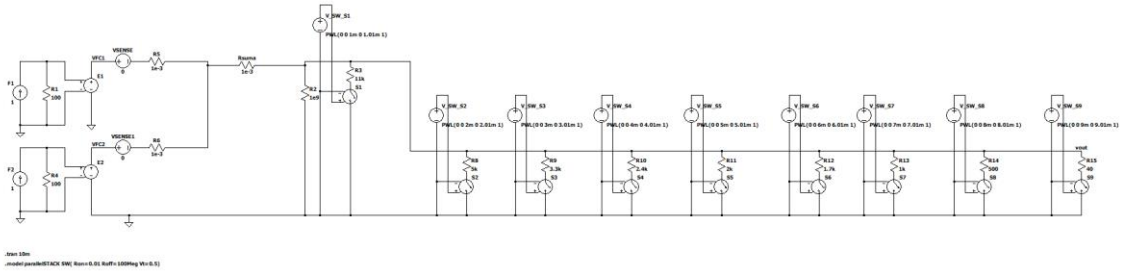

Figure 8. Two stacked in parallel configuration GFC of 20mM concentration simulation using LTSpice.

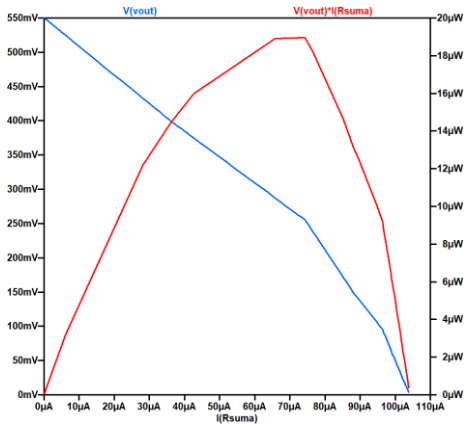

Figure 9. LTSpice simulation of voltage (blue) and power (red) vs current of two GFC in a parallel configuration having used the values from reference [9] of 20mM concentration.

In this example it can be seen how the current and power has doubled from the parallel configuration, meanwhile, the voltage has remained the same.

The results obtained from every simulation done in this project regarding LFC characterization have been summarized in *Tables 1 and 2.*

Lactate concentration (mM)	Current for Single LFC (µA)		Max Voltage (mV)		Max Power (µW)	
	Single LFC	Two LFC in parallel	Single LFC	Two LFC in series	Singe LFC	Two stacked LFC
1	5.1	10.2	225	450	0.25	0.50
7	9.0	18.0	285	570	0.63	1.26
15	20.1	40.2	368	736	1.63	3.26
25	25.1	50.2	395	790	2.16	4.32

Table 1. Current, voltage, and power provided by a Single LFC and Two stacked LFC for concentrations between 1mM and 25mM [10].

Lactate concentration of 25mM			
Configurations	**Current (µA)**	**Voltage (mV)**	**Power (µW)**
Single	25.1	395	2.16
Two FC in series	25.1	790	4.32
Two FC in parallel	50.3	395	4.32
Three FC in series	25.1	1,186	6.48
Three FC in parallel	75.4	395	6.48

Table 2. Current, voltage, and power provided by a Single, Two, and three stacked LFC for concentrations of 25mM [10].

The same study has been performed for the GFC, the only difference being that only two-stack configurations have been analyzed since the obtained values are significantly higher than those of LFC. The results can be seen summarized in *Table 3.*

Glucose concentration (mM)	Current for Single GFC (µA)		Max Voltage (mV)		Max Power (µW)	
	Single GFC	Two GLFC in parallel	Single GFC	Two GFC in series	Singe GFC	Two stacked GFC
3	15,2	30.4	350	700	2.24	5.48
5	24	48.0	400	800	3.20	6.40
7	36	72.0	450	900	5.20	10.40
15	44	88.0	510	1,020	8.16	16.32
20	52	104.0	550	1,100	9.50	19.00

Table 3. Current, voltage, and power provided by a Single, Two, and three stacked GFC for concentrations between 3 and 20mM [9].

Once these values were obtained, the current sensing module was developed.

5.2.2 Current sensing module

To monitor the current proportional to the sample concentration, a discrete high-side current sensing solution has been designed [8]. The first step is to select a BFC and a configuration that could work with the instrumentation of the sensor. As will be explained later in the Event detection module, this design operates with a minimum voltage of 0.58V, which is a restriction given by the design of the circuit, to correctly detect the sample, therefore, regardless of the BFC, a single BFC is not sufficient. There are two ways to solve this, one is to develop an amplification stage right before the event detection method, and another is to put stacked BFC until it reaches an appropriate voltage level. Both scenarios have been studied, using two stacked GFC of 3mM concentration in series for the case of Glucose, and two stacked LFC of 15mM concentration in series for the case of Lactate. In these scenarios, an external voltage supply of +2V has been used for the operational amplifiers (OPAMPS).

As mentioned previously, the current delivered by BFC's is proportional to the sample concentration and, generally, they present an exponential discharge when one load resistance is connected. To avoid this, this analysis has been performed in a non-dynamic environment.

The circuit, which can be seen in *Figure 10*, operates in a way that the current flowing through the sense resistor (Rsense) generates a voltage (VL). The voltage across Rsense is the same going through RA because of the feedback via the MOSFET, which maintains both high-impedance inputs of the OPAMP ADA4505 at the same voltage. The current flowing through RA is the same that flows through RB and, since the OPAMP and the PMOS act as a current source across RB, in the Vm terminal, a voltage proportional to the load current going through Rload will be generated. To relate the voltage in the Vm terminal to the voltage provided by the BFC (current going through RFC), the system consumption current going through RA needs to be subtracted. The relationship between the voltage of VM and the current going across Rload, IL, can be seen in *Equation 1.*

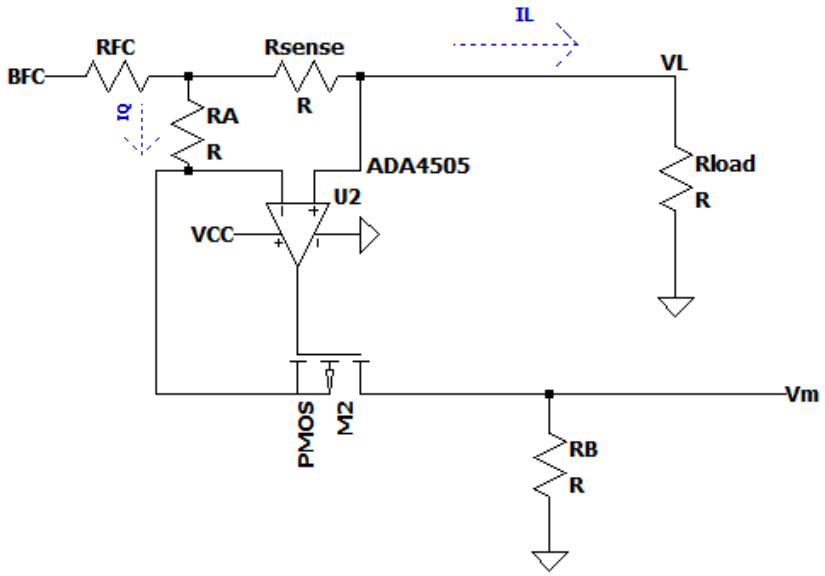

Figure 10. High-side current sensing instrumentation to measure the current directly related to the concentration of the sample.

$$V_m = I_L \cdot \frac{R_{SENSE} \cdot R_B}{R_A}$$

Equation 1. Relationship between the current of the circuit and the voltage in the VM terminal [8].

The main reason ADA4505 OPAMP has been chosen is due to its very low-current consumption, low leakage input currents, zero crossover distortion, and rail-to-rail input/output capability, which optimizes performance, and ensures maximum operation range and AOL gain. This OPAMP, coupled with a RA and RB of high value, reduces the power dissipation and allows for a good depiction of Vm proportional to the BFC current.

Regardless of the optimization of the components, one thing to consider is that it is an approximation due to resistors tolerance and unavoidable small current loss due to the components and supply.

With this circuit, it has been accomplished that for a current of the order of μA, a proportional voltage of the order of mV has been obtained.

The amplification method has been implemented into two different stages to simplify the calculations and make an easier adaptation to different BFC. A non-inverter amplification configuration has been used to obtain a higher voltage in the Va and Vamp terminals, the circuit can be seen in *Figure 11*. The relationship between them can be seen in *Equation 2*.

Since Vm is quite low in voltage, a first stage takes place to bring Va to a more suitable, though still too low value, to make the calculations to bring Vamp to a workable level easier to find out.

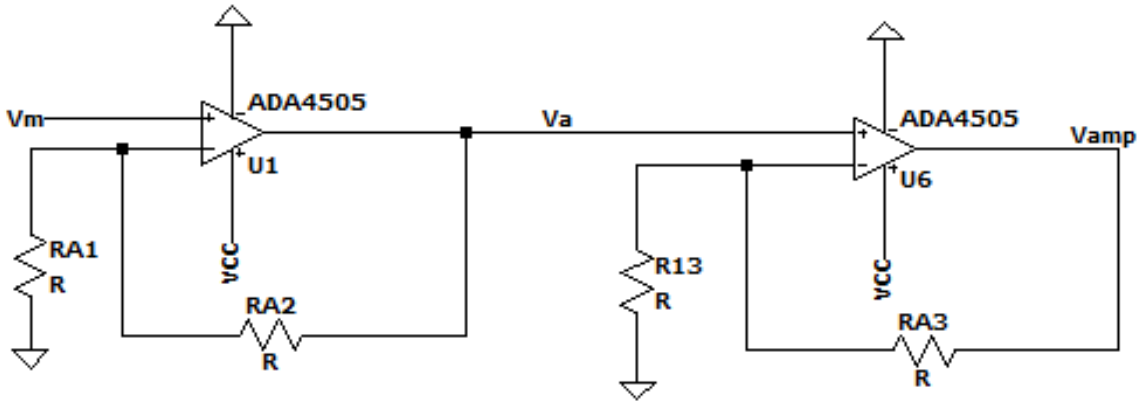

Figure 11. Amplification Stage pre detector stage

$$G = \frac{V_a}{V_m}\left(1 + \frac{R_{A2}}{R_{A1}}\right)$$

Equation 2. Relationship between Va, Vm, RA1, RA2 and Gain in the amplification stage

With the amplified proportional voltage, the detector stage can take place.

5.2.3 Event detector module and example of an entire circuit using independent current source

Once the voltage has surpassed the 0.58V needed to make the comparator work and detect the current depending on the concentration of the BFC, a voltage divider has been implemented. To understand how the entire circuit has worked so far, and how this event detector works, this part will be explained using some case study examples.

The first approximation has been performed without using a BFC, only applying an independent current source of 50µA with a PWL so that it would start supplying current al 10ms. This approximation has been done to make the circuit work with an ideal source, without considering the current variations of the GFC and LFC. The circuit can be seen in *Figure 12.*

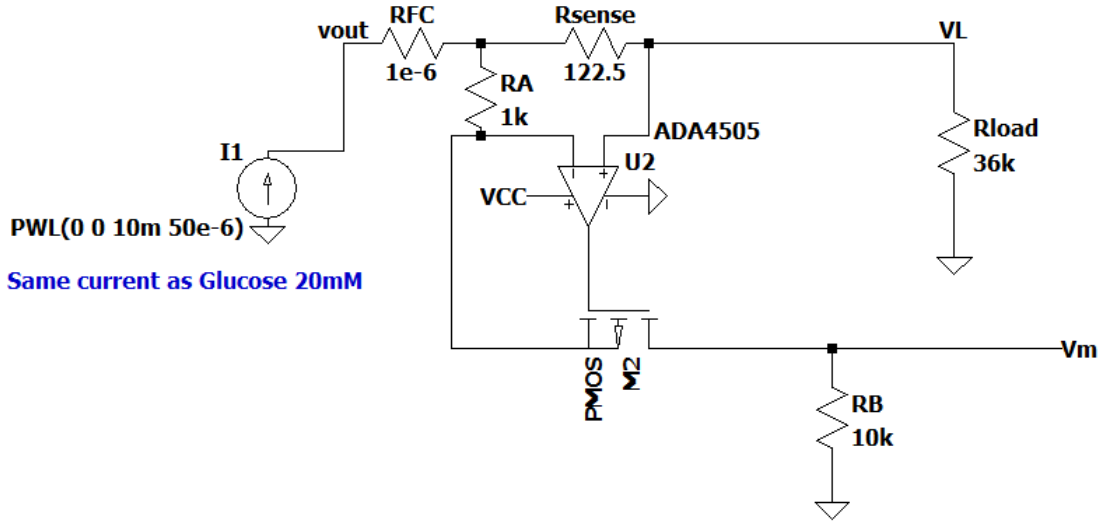

Figure 12. first approximation using an independent current source of 50µA.

The resistors' values can be found using *Equation 1*. The values have taken into consideration how the current IQ needs to be subtracted from the current IL to relate it to the current I1. In this case, IL is equal to 45µA, and IQ to 5µA.

$$V_m = 40\mu A \cdot \frac{122.5\Omega \cdot 10k\Omega}{1k\Omega} = 0.049V$$

Equation 3. Substituted values to find Vm.

The reason for that Rload value is related to the FC working point of operation and will be explained in the particular case study using GFC at a concentration of 20mM. In *Figure 13*, the transient analysis of this first stage can be seen, and how the current and the voltage in Vm are proportional at 50µA and 50mV, respectively.

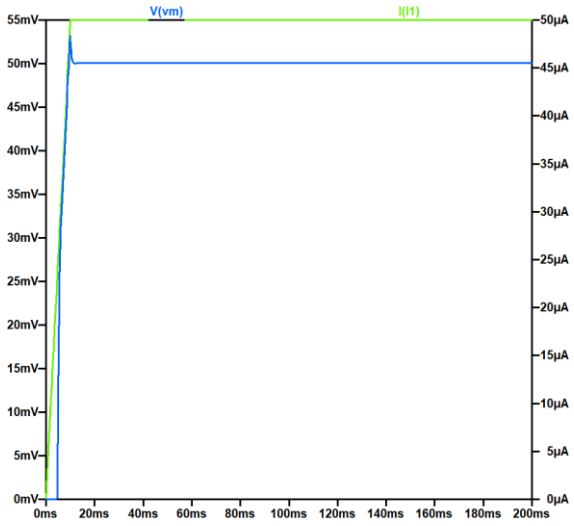

Figure 13. Independent current source at 50µA and Vm of the circuit at 50mV.

Then the signal is amplified, first with a Gain of 3 going from 50mV to 150mV at Va, and later, with an approximate Gain of 5, up to 760mV at Vamp. Even though resistors RA1 equal to 130kΩ and RA2 equal to 2MΩ, could have been used, to be versatile later with different values, these two stages have been used. The circuit and generated plot can be seen in *Figure 14 a) and b).*

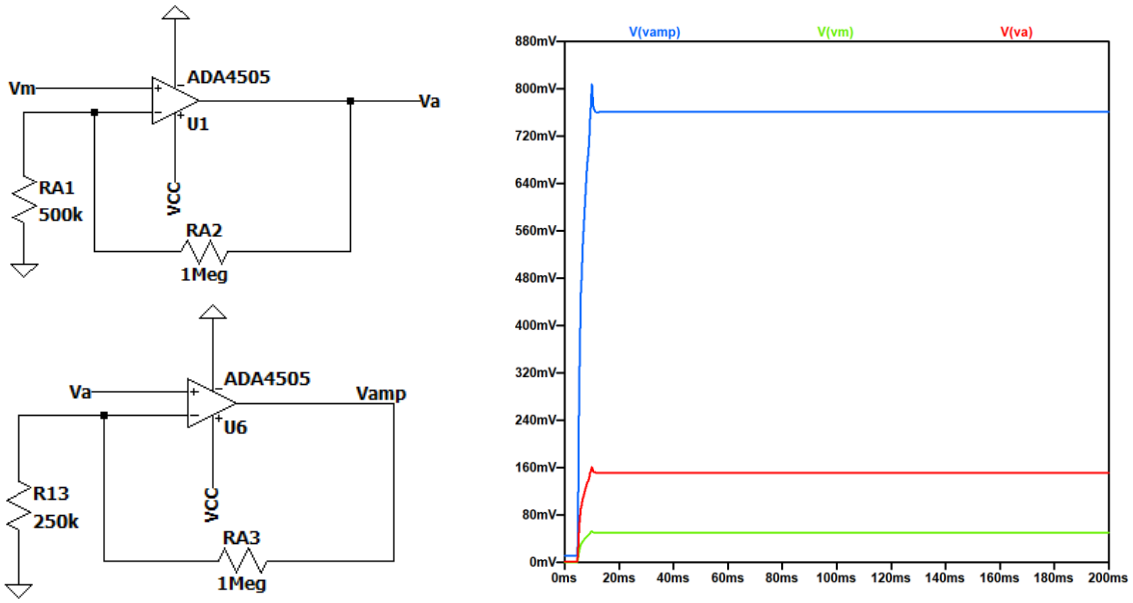

Figure 14. a) Amplification stage circuit. ***b)*** graph with Vm at 50mV and Vamp at 760mV.

After the amplification stage, Vamp is at 0.76V, high enough to work with the comparator. Since this instrumentation works like a switch, if the voltage does not reach 0.58V it will return 0V, once it has surpassed that value, it will go up to 2V. If an error margin of 0.005V is considered, some measures can be calculated, which can be seen in *Equation 4*.

$0.58V < 0.765V \cdot \text{n} \rightarrow$ “2” $\qquad\qquad$ $0.58V > 0.755V \cdot \text{n} \rightarrow$ “0”

Equation 4. Values in which the comparator will switch.

In *Figure 15,* the comparator circuit can be seen, and with it, the formulas for the voltage divider.

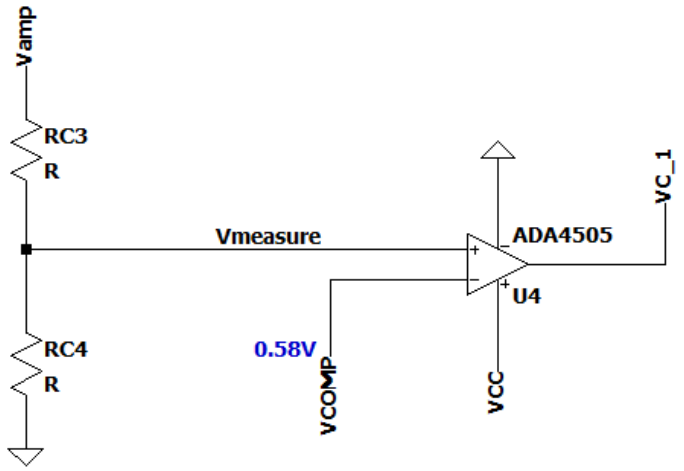

Figure 15. Voltage divider used as a comparator for the event detector module.

In *Equation 5*, the formula to find the n value in *Equation 3* is shown:

$$n = \frac{V_{amp}}{V_{measure}} = \frac{R_{C4}}{R_{C3}+R_{C4}} \rightarrow \frac{0.58V}{0.755V} > n > \frac{0.58V}{0.765V} \rightarrow 0.758 > n > 0.768$$

Equation 5. Calculations to obtain n value.

The mean value of the n range values is 0.763, and with it, the relationship between RC4 and RC3 can be calculated in *Equation 6*:

$$R_{C3} = R_{C4}\frac{1-n}{n} = R_{C4}\frac{1-0.763}{0.763} = R_{C4} * 0.311$$

Equation 6. Relationship between RC3 and RC4.

With these calculations, the values of the resistors for the voltage divider for a current of 50µA can be extracted. Taking into consideration the available resistor values on the market, the value for RC4 has been chosen to be 240kΩ, and RC3 would have a value of 74.64kΩ, which has been rounded up to 75kΩ. In the following figure, *Figure 16*, the comparator at work using the independent current source (I1) as a source for a dc sweep from 0 to 60µA in 10µA steps increment can be seen. In it, the comparator VC_1 can be seen in green, Vmeasure in pink, and Vcomp in blue. It can be appreciated how VC_1 starts to go up before the 50µA, and before Vmeasure has surpassed Vcomp. If looked closely though, it can be appreciated how it does not reach 2V until 50 µA, showing that the comparator works.

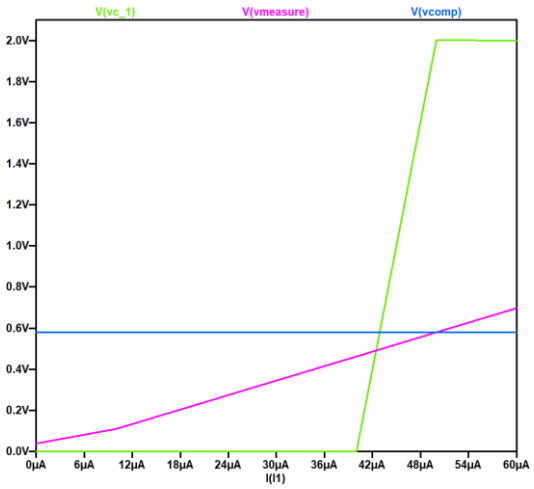

Figure 16. Comparator working with an independent current source of 50µA.

Once it was proven that the biosensor gave an accurate reading of the current, it was implemented with the LFC and GFC.

5.2.4 Entire Biosensor circuit with a single GFC

Some things need to be considered when connecting the Biosensor interface electronics platform to the simulated GFC. The first one is that due to the Rload of the circuit, the measurement of this specific GFC has been dimensionalized to adapt it to the FC limitations. In the characterization of the GFC at 20mM, it has been found how it should reach the 50µA current and 550mV voltage, but in this case, new calculations have been made to find the new Rload vale to discover the new working range considering the current that the FC faces with the sensing platform. In this case, when considering the circuit, a Glucose concentration of 20mM will have a current of approximately 13.45µA, and Vm will be 14.45mV. In *Figure 17* it can be seen how they are proportional.

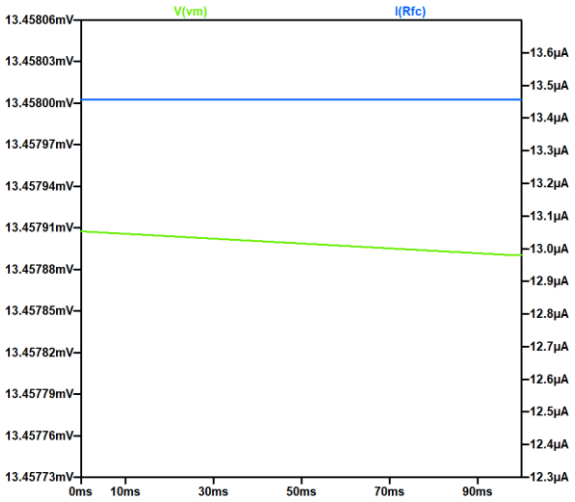

Figure 17. Vm and current of GFC proportionality.

When looking at the amplification stage, in this case, the gain must be bigger, a gain of 50 has been used (gain of 5 in the first amplification stage, gain of 10 on the second) to obtain a Vamp of 0.93V, high enough to be used in the detection module. In *Figure 18*, the voltage values of Vm, Va, and Vamp can be seen.

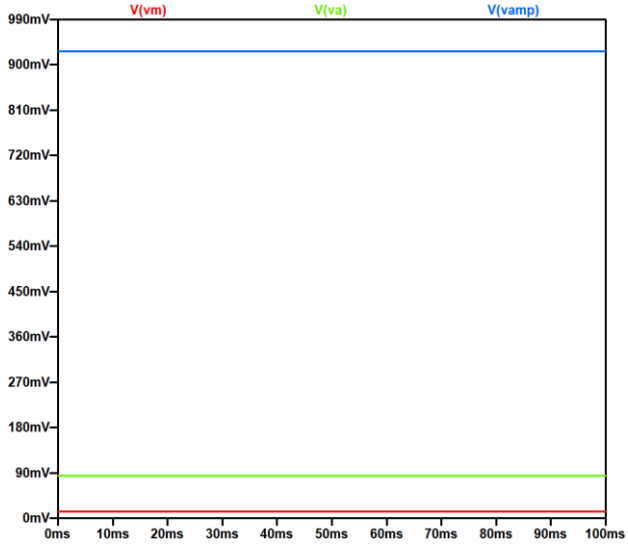

Figure 18. Vm, Va, and Vamp after amplification for a total Gain of 50.

Now, the values of the voltage divider for the event detector were calculated (*Equations 7 and 8*).

$$n = \frac{V_{amp}}{V_{measure}} = \frac{R_{C4}}{R_{C3}+R_{C4}} \rightarrow \frac{0.58V}{0.925V} > n > \frac{0.58V}{0.935V} \rightarrow 0.620 > n > 0.627$$

Equation 7. Calculations to obtain n value.

The mean value of the n range values is 0.623, and with it, the relationship between RC4 and RC3 can be calculated in *Equation 8*:

$$R_{C3} = R_{C4}\frac{1-n}{n} = R_{C4}\frac{1-0.623}{0.623} = R_{C4} * 0.604$$

Equation 8. Relationship between RC3 and RC4.

Looking at the resistors available on the market, RC4 has been chosen to be 270kΩ, and RC3, 160kΩ.

A transient simulation has been run, and a switch implemented so that the current starts after 10ms have passed. Its implementation can be appreciated in *Figure 19*, as well as the behavior of the comparator, and how it activates correctly. When looking closely, it can be seen how VC_1 reaches 2V at the time it reaches a stable current of 13.45μA, meaning that for a Glucose FC of 20mM concentration, this sensor activates at 13.45μA.

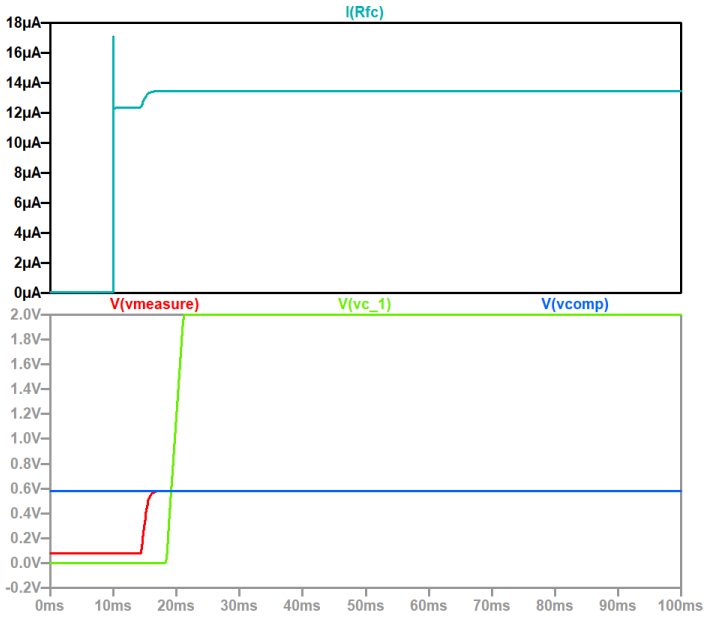

Figure 19. FC current and event detection module for a GFC of 20mM concentration.

5.2.5 Entire Biosensor circuit with a two stacked GFC

As mentioned before, the useful ranges of detection for Glucose are between 3 and 7mM, therefore, a simulation of two stacked GFC of 3mM concentration has been performed to study if the low voltage low current situation can be implemented.

In *Figure 20*, it can be seen how it again does not match the current and voltage that two stacked in series GFC of 3mM should produce due to the instrumentation of the sensor due to the current that the FC faces with the sensing platform. Therefore, a new working point has been calculated. In this case, the current is 11.57µA for stacked GFC of 3mM concentration. *Figure 20* also shows the proportionality between Vm and the current of the GFC.

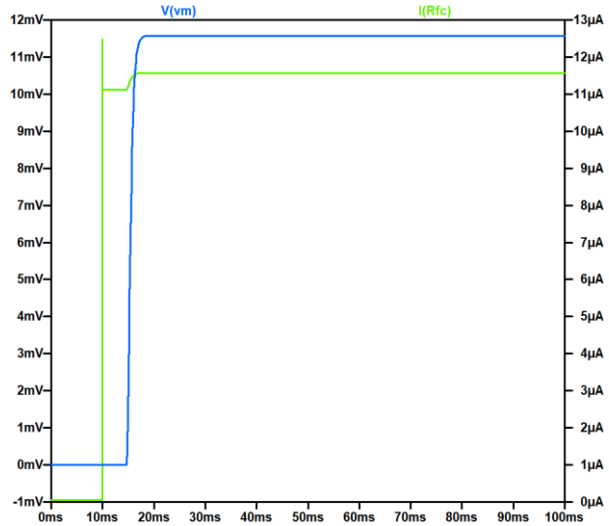

Figure 20. Vm and two stacked in series GFC of 3mM concentration proportionality at 11.57mV and 11.57µA, respectively.

In this case, a total amplification Gain of 50 has been to obtain a Vamp of 0.8V.

The calculations made to obtain the values for the detection module resistors can be seen in *Equations 9 and 10*.

$$n = \frac{V_{amp}}{V_{measure}} = \frac{R_{C4}}{R_{C3}+R_{C4}} \rightarrow \frac{0.58V}{0.795V} > n > \frac{0.58V}{0.805V} \rightarrow 0.720 > n > 0.729$$

Equation 9. Calculations to obtain n value.

The mean value of the n range values is 0.725, and with it, the relationship between RC4 and RC3 can be calculated in *Equation 10*:

$$R_{C3} = R_{C4}\frac{1-n}{n} = R_{C4}\frac{1-0.725}{0.725} = R_{C4} * 0.379$$

Equation 10. Relationship between RC3 and RC4.

The chosen resistor values have been RC4 equal to 240kΩ and RC3 equal to 91kΩ. In *Figure 21* the FC current and the response at the event detector module can be seen.

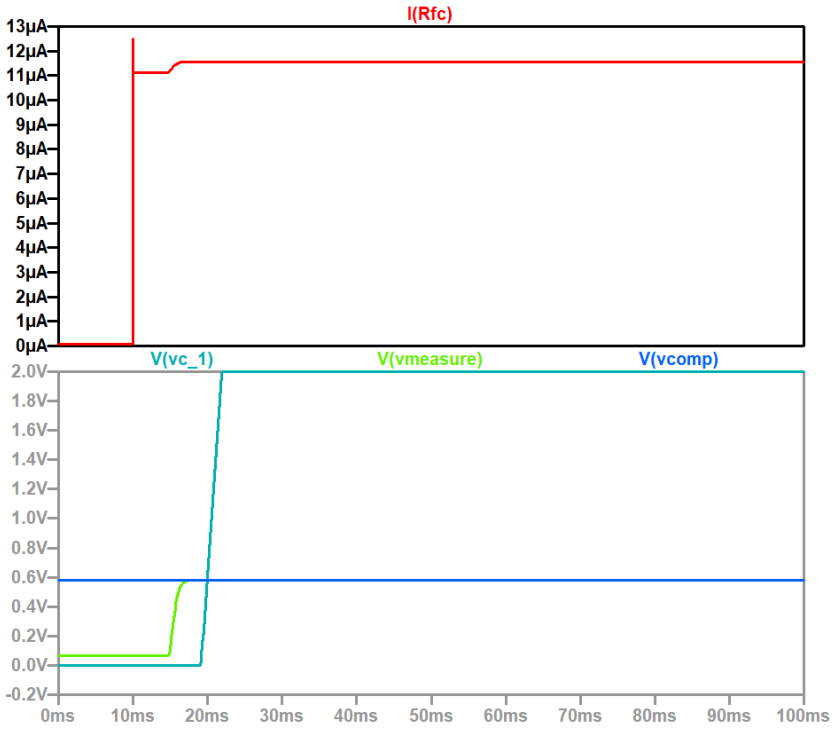

Figure 21. FC current and event detection module for two GFC of 3mM concentration in series.

5.2.6 Two LFC of 15mM concentration in series sensor

Once it had been proven that the low voltage and low current values that GFC can provide are not an issue with the architecture of this sensor, lactate studies, have been analyzed. The methodology behind these simulations is the same as explained previously. In *Figures 22 and 23*, the graphs of the study can be seen.

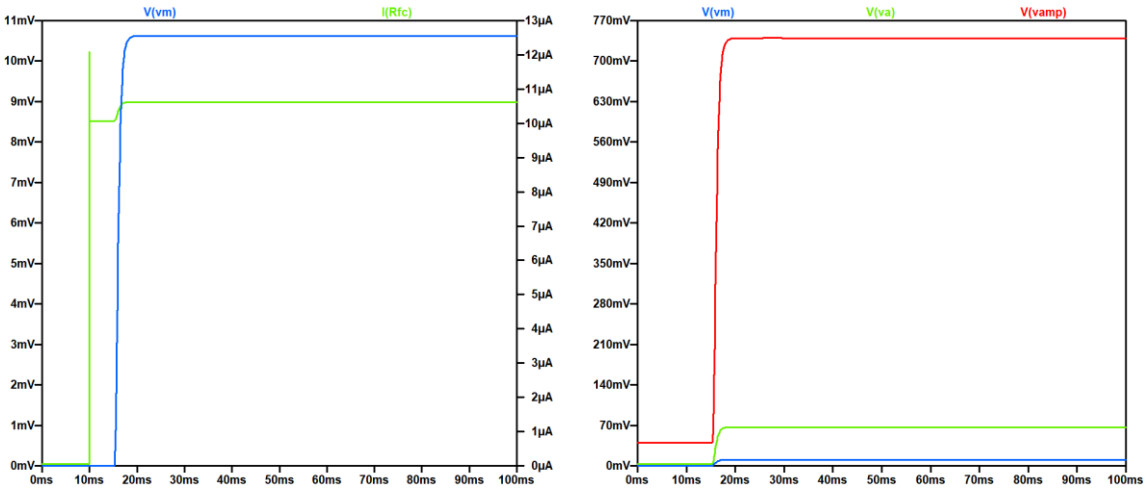

Figure 22. a) Proportionality of Vm and current provided by two stacked LFC in series of 15mM concentration. b) amplification stage with a Vamp of 0.74V.

The calculations were made to obtain the values for the detection module (*Equations 11 and 12*).

$$n = \frac{V_{amp}}{V_{measure}} = \frac{R_{C4}}{R_{C3}+R_{C4}} \rightarrow \frac{0.58V}{0.795V} > n > \frac{0.58V}{0.805V} \rightarrow 0.778 > n > 0.789$$

Equation 11. Calculations to obtain n value.

The mean value of the n range values is 0.784, and with it, the relationship between RC4 and RC3 can be calculated in *Equation 12*:

$$R_{C3} = R_{C4}\frac{1-n}{n} = R_{C4}\frac{1-0.784}{0.784} = R_{C4} * 0.275$$

Equation 12. Relationship between RC3 and RC4.

The chosen values were RC4 equal to 300kΩ, and RC3 equal to 82kΩ.

The final graph showing the correct sensing of two LFC can be seen in *Figure 23*.

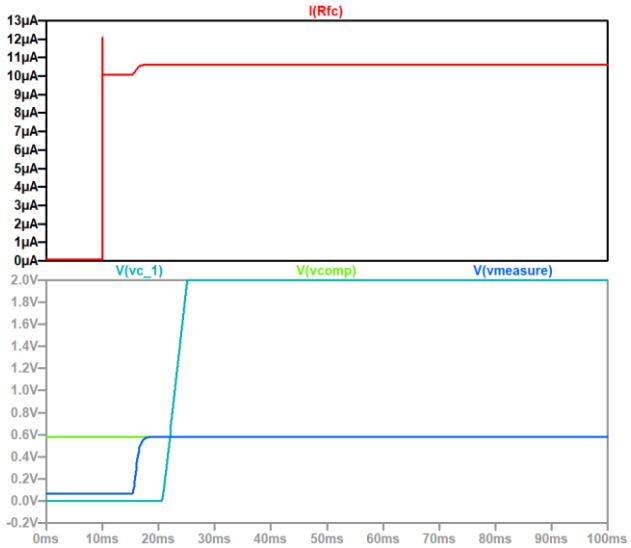

Figure 23. FC current and event detection module for two LFC of 15mM concentration in series.

The development of the Glucose and Lactate Biosensor can be said to have been successful.

5.3 DC/DC Boost Converter

The commercially available LTC3108 DC/DC boost converter has been used to try and amplify the GFC voltage to use it for self-powering purposes. Multiple scenarios have been analyzed, but an important issue has come up every time. The GFC provides too little voltage and current to power the device, and the switch structures are needed to draw current from the GFC. Multiple specific case scenarios (two stacked GFC in series, and two stacked GFC in parallel configuration) have been tried without success. The only way the GFC has elicited a response from the commercially available device is by connecting it, not to the Vout terminal after the switches, but at the node VFC, which presents an ideal scenario of the FC behavior. The reason behind this is that the resistor equivalent after the switches is too low to elicit current from the FC but if a resistor in series is placed to try and generate current, the voltage saturates.

LTC3108 is an ultralow voltage step-up converter and power management, which should be ideal for harvesting and managing surplus energy from extremely low input voltage sources, which is why it has been the chosen component to use. It operates from input voltages as low as 20mV and it presents a fixed Vout option which is the only reason it works when connected to the Biosensor platform since the Vout has been fixed at 3.3V. It provides a complete power management solution for wireless sensing and data acquisition. The used pins functions are as follows [37]:

- The Vstore terminal is the output for the Storage Capacitor or Battery. A large capacitor may be connected from this pin to GND for powering the system in the event the input voltage is lost. It is charged up to the maximum VAUX clamp voltage.
- Vout is the main output of the converter, and its voltage is regulated to a fixed value (3.3V).
- Vldo is a 2.2V low-dropout output.

In *Figure 24,* the circuit of the DC/DC boost converter can be seen to better understand the functionality and where the terminals are, and in *Figure 25*, a study of the power elicited at the vldo and vstore output terminals can be seen, as well as the voltages vstore, vout, and vldo.

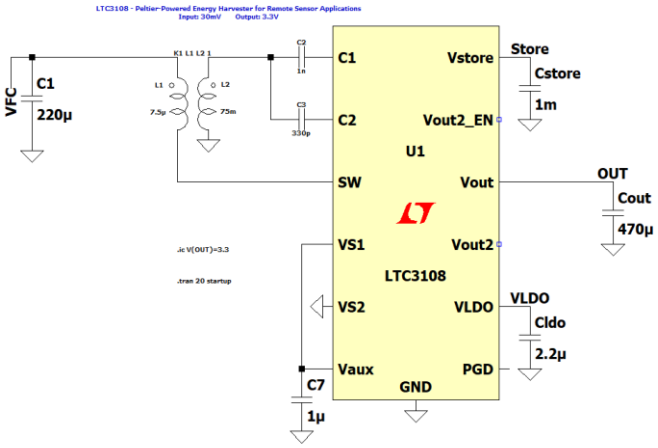

Figure 24. LTC3108 circuit connected to the VFC node.

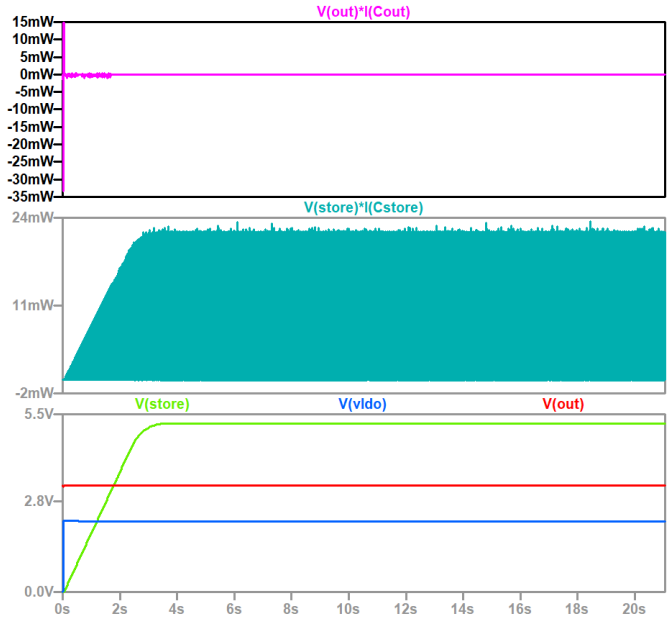

Figure 25. Power at the vldo and vstore output terminals, as well as the voltages vstore, vout, and vldo when connecting the DC/DC converter to VFC with switches.

In *Figure 26 a)*, the graph of the response of the circuit can be seen without the switches, and in *Figure 26 b)* the response when connecting the FC to the DC/DC boost converted at the vout node.

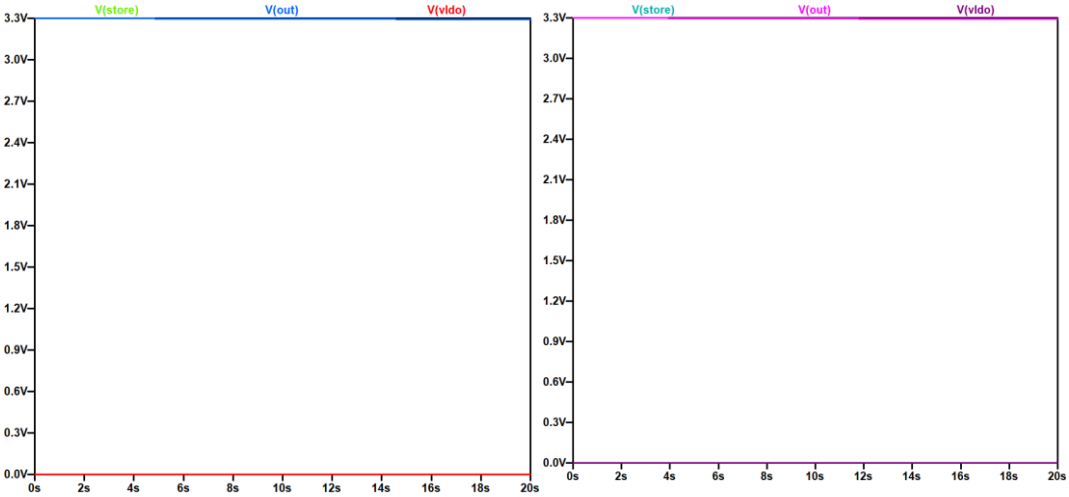

Figure 26. vldo, vstore and vout response with ***a)*** no switches. ***b)*** connecting the DC/DC boost converter to vout instead of VFC.

In *Figure 25*, it can be seen how the BFC connected to the DC/DC converter elicits a response and seems to work when connecting it at the VFC terminal, but this is not a good approximation since it does not consider the actual behavior of the FC taking as a reference ideal values from the look-up table.

Following the literature, a specific case scenario of placing stacked FC to try and solve this issue has been tried without success. In *Figure 27 a)*, it can be seen the response for two GFC of 20mM concentration in a parallel configuration and in *Figure 27 b)*, two in series. A small change in vout can be seen, but it can be appreciated how it does not work.

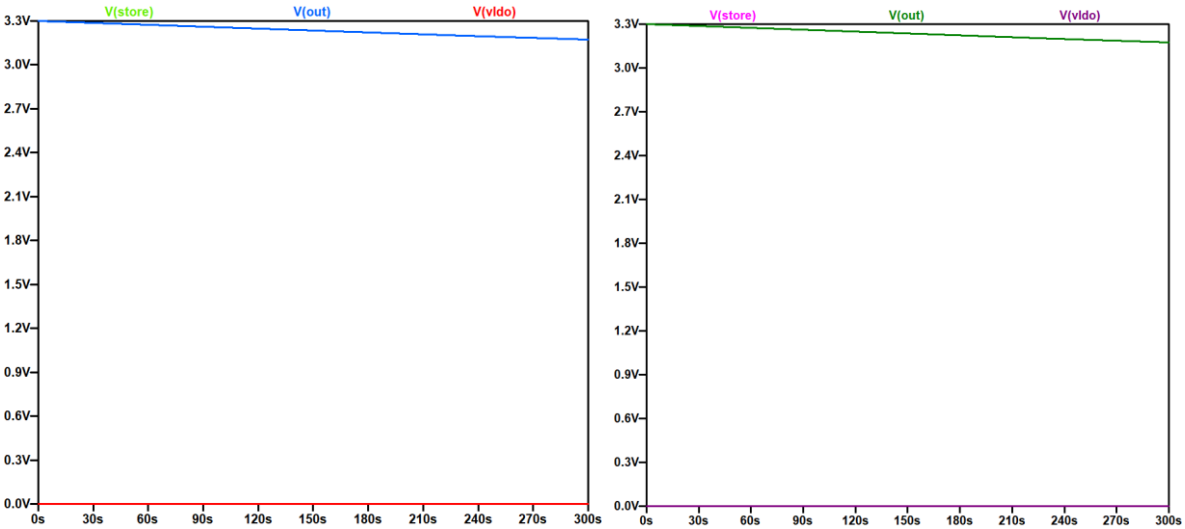

Figure 27. vldo, vstore and vout response with two GFC in ***a)*** parallel with switches***. b)*** in series with switches. Both connecting the DC/DC boost converter to vout instead of VFC.

Even though it is not a good representation, the specific case scenario of using one GFC of 20mM concentration connected to the DC/DC converter to obtain a fixed vout voltage value of 3.3V has been studied. The vout terminal, now named Vout2 to avoid overlapped labels, has been connected to the VDD of the OPAMPS of the biosensor interface electronic platform to see if both modules could work together. Since the voltage has been fixed, no switches are needed because the 3.3V will be generated regardless. Two studies have been performed, one using an ideal current source as the input signal simulating a GFC of 20mM concentration for the biosensor platform, and another using the actual GFC. Both studies can be seen in *Figure 28 a) and b), and Figure 31.*

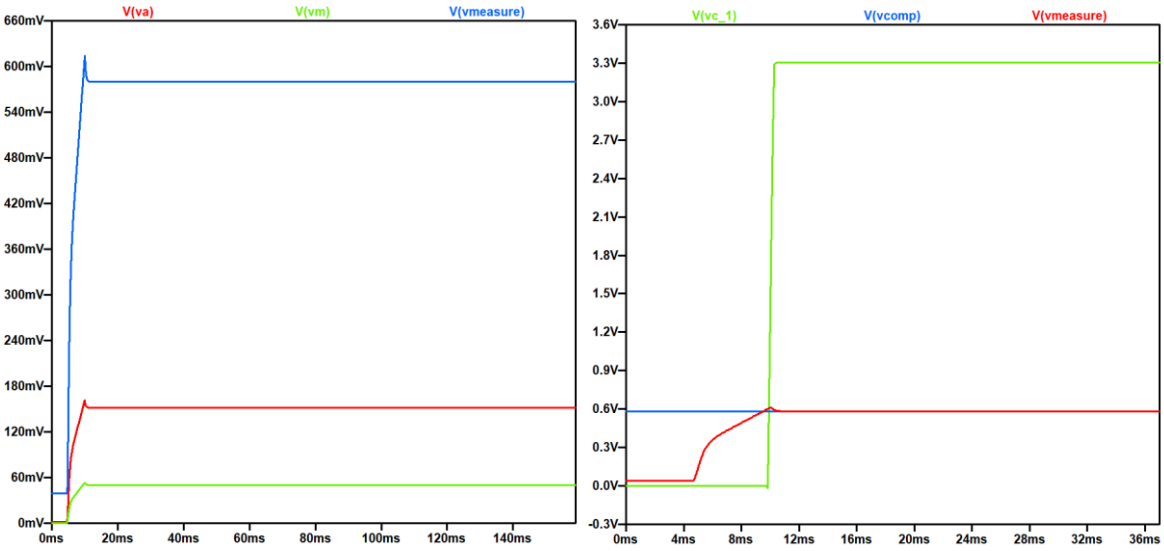

Figure 28. Event detection module for one GFC of 20mM concentration using a GFC connected to DC/DC converted to supply voltage to the instrumentation in the time domain. ***a)*** amplification stage. ***b)*** detection stage.

In *Figure 28* it can be seen how all the OPAMPS of the biosensing platform work with the voltage supplied using the GFC with the LTC3108 at a vout fixed voltage of 3.3V. In the graph on the left, the amplification stage can be observed, and on the right, the detection stage.

In *Figures 29 and 30,* the circuits analyzed to obtain the plots in *Figures 28 and 31,* in which both modules are linked together, one using an ideal current source as an input value for the sensing platform, and the other using a GFC of 20mM concentration, can be seen.

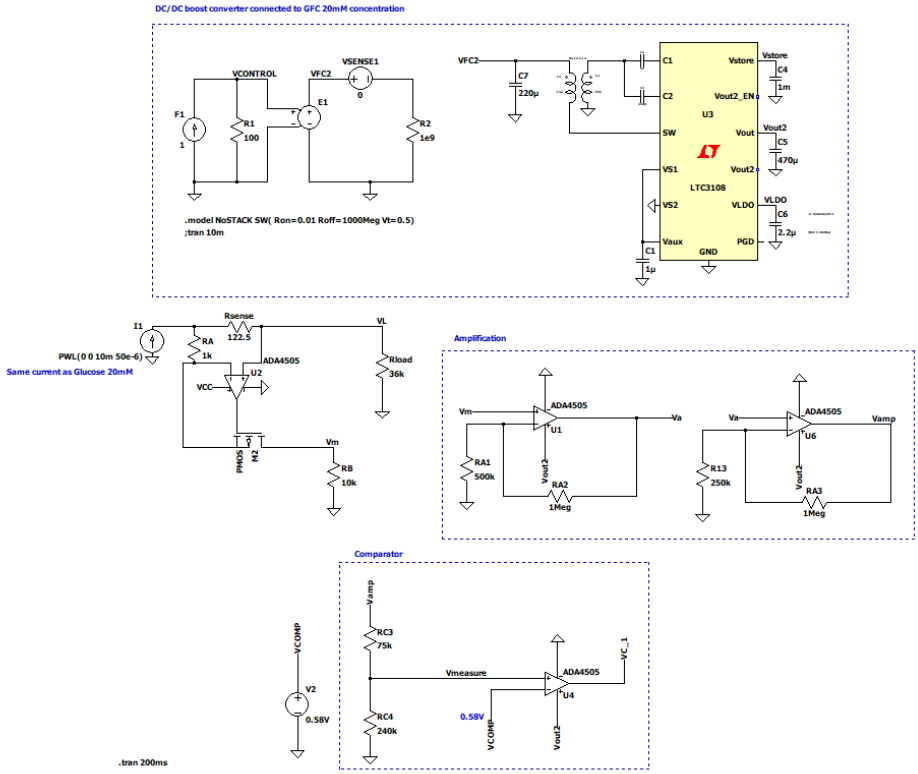

Figure 29. Both modules connected using an ideal current source.

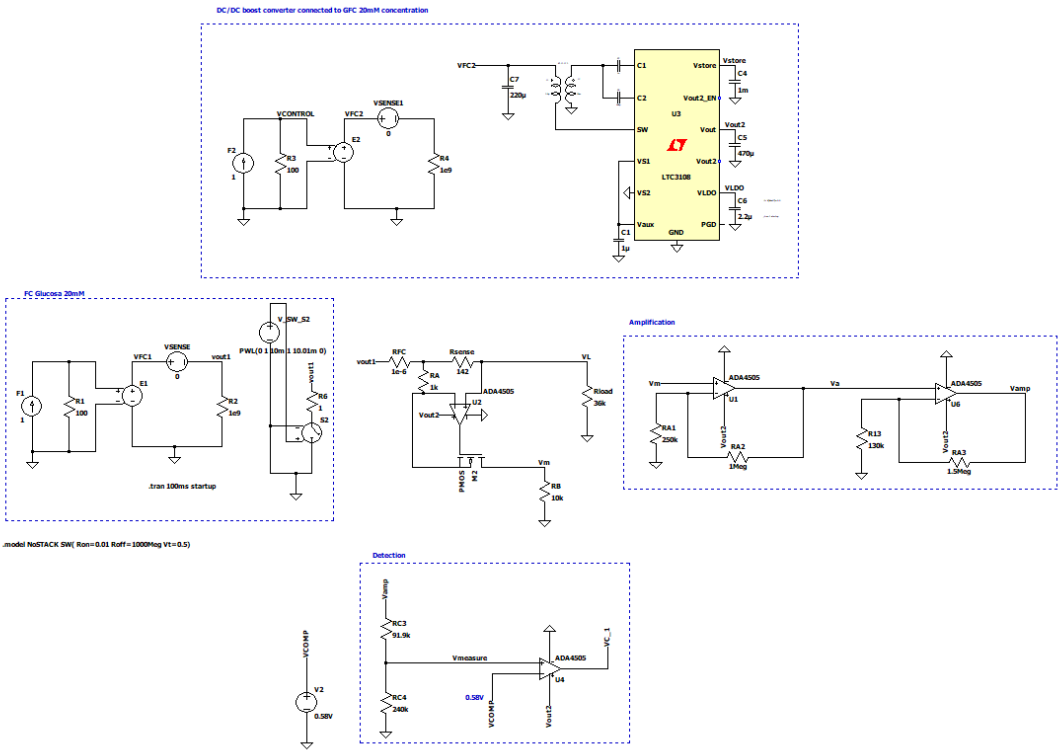

Figure 30. Both modules connected using a GFC of 20mM concentration.

In *Figure 31*, the results obtained when using the GFC of 20mM concentration as the sensing element in the biosensor platform can be seen.

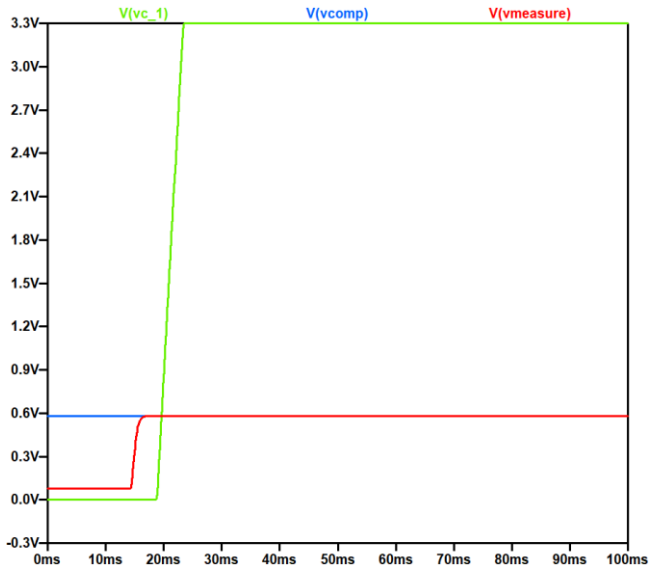

Figure 31. Event detection module for one GFC of 20mM concentration using a GFC connected to DC/DC converted to supply voltage to the instrumentation in the time domain.

It can be seen in *Figure 28 a) and b) and Figure 31*, how the entire circuit works, meaning that the 3.3V at Vout2 (fixed output voltage of the PMU module) is achieved, and is enough to power the instrumentation. The detection takes place and, when comparing it to *Figures 16 and 19* respectively, which use the same values, it can be seen how they match. The only difference is that only a transient analysis has been performed on the latter cases since a dc sweep to see the current at which the comparator activates is not possible because of the LTC3108, which calls for a time domain.

Regardless of this last case study, the main goal has not been completely accomplished since the result obtained are not due to the circuit working properly, but that of using an ideal look-up table and fixing the Vout signal at 3.3V. If more time had been available, the design of a particular DC/DC boost converter could have been accomplished or a solution found.

6. Execution schedule

In the following section, the temporal organization of the different tasks that have been performed to achieve the goals defined at the beginning of this document will be explained. A chronogram has been represented for a clear understanding of the various tasks' timings.

The timings on each activity have been calculated with a small extra time for any inconvenience or unexpected issue.

6.1 Work Breakdown Structure

The main activities of this project, which will be further explained, can be seen in *Figure 32*.

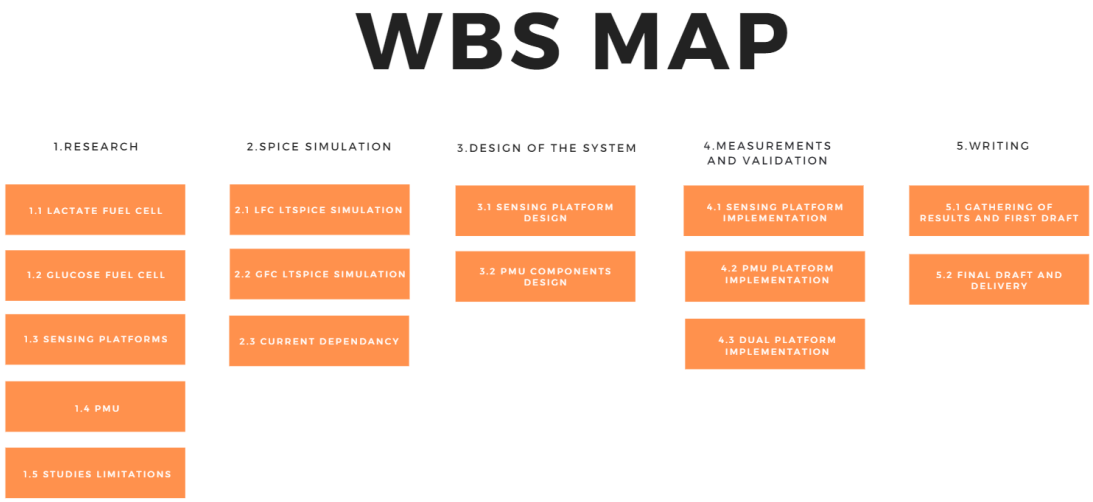

Figure 32. Work Breakdown Structure of the project.

This project's timing and tasks can be divided into five stages:

- *Research*: Both BFCs characterization research to find values in previous studies to understand the FC behavior, as well as an analysis of different sensing platforms on the literature, and examination of PMU instrumentation options to develop a self-powered device. This research allowed a basic understanding of the components limitations to choose appropriate OPAM and DC/DC boost converter components, as well as to gather references for the state of the art and market analysis.
- *Spice simulation*: Simulated GFC and LFC mimicking real-like behavior to use in the design stage, as well as studies of current dependency and working ranges.
- *Design of the system:* Design of both platforms separately and theoretical values calculation.

- *Measurements and validations:* Implementation of the designed platforms with the simulated BFC, error correction, and application of both modules together to have a self-powered biosensor device.
- *Writing:* Gathering of every information and results and writing the Final Degree Project.

6.2 WBS definition and timing

In *Table 4* the main tasks in order with the specified timing have been summarized.

WBS Level	*WBS Code*	*WBS Name*	*WBS Description*	*Number of days*
1	1.1	LFC Research	Research about LFC and their applications.	15 days
1	1.2	GFC Research	Research about LFC and their applications.	15 days
1	1.3	Possible Sensing Platforms Research	Analysis of state-of-the-art Sensing Platforms.	15 days
1	1.4	PMU Research	Study of PMU in self-powered devices.	30 days
1	1.5	Limitations Research	Understanding of the limitations to select the best option.	20 days
2	2.1	LFC LTSpice simulations	Simulation of LFC with values from the literature.	20 days
2	2.2	GFC LTSpice simulations	Simulation of GFC with values from the literature.	15 days
2	2.3	Current Dependency and working ranges study	Current Dependency studies to understand the BFC behavior with Rload and fix a working range.	10 days
3	3.1	Sensing Platform design	Design of an event detection platform, and theoretical analysis of components values.	40 days
3	3.2	PMU components Design	Design of a PMU to increase BFC voltage to power the device.	30 days
4	4.1	Sensing Platform Implementation	Sensing design implementation and error correction.	30 days

4	4.2	PMU Platform Implementation	PMU implementation, analysis of limitations, and ideal implementation.	30 days
4	4.3	Dual Platform Implementation	Implementation of both structures simultaneously to satisfy the main objective.	30 days
5	5.1	Gathering of Results and First Draft	Gathering of all the results obtained (plots, circuits, tables) and First Draft.	30 days
5	5.2	Final Draft	Correction and writing of the Final Draft of the Final Degree Project	30 days

Table 4. WBS definition with Code and description with approximate times

The total completion of the project has taken 360 active days, with tasks starting in March 2020, and ending in June 2021.

6.4 GANTT

To illustrate the schedule of the project, the Gantt chart below has been used, *Figure 33*. It shows the evolution of tasks in orange, with grey areas indicating the non-university significant periods (summer holiday and Christmas).

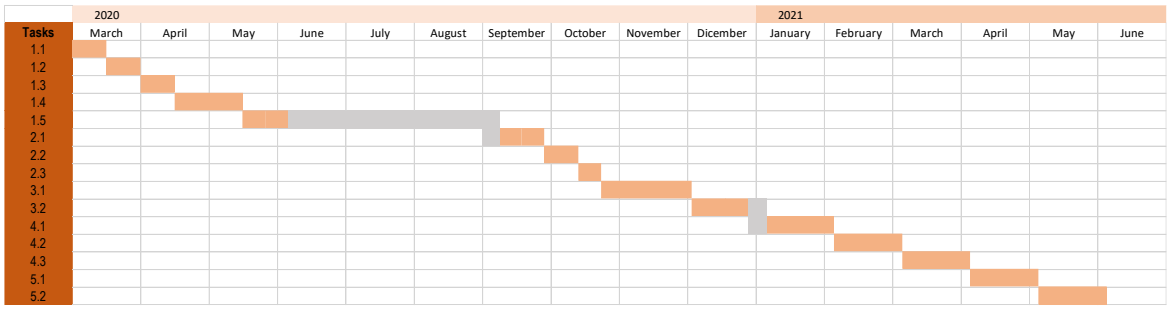

Figure 33. Gantt chart of the tasks.

7. Technical viability

In this section of the document, a SWOT analysis (Strengths, Weaknesses, Opportunities, and Threats) has been performed and the technical specifications and principal features of the designed application have been explained. This Final Degree Project has been considered as a technical project, and as a potentially marketable product if the limitations can be solved as well as the circuits improved.

7.1 Study of the limitations and internal and external analysis

The limitations of this project have already been explained in different parts of this document and, like any other study, it has strengths and weaknesses (internal factors), as well as threats and opportunities (external factors). As stated previously, the field of research of BFC is in expansion, and will most likely grow exponentially as more and more companies try to find more sustainable approaches than batteries to power devices. Moreover, sensors, especially POC devices, are a subject area thoroughly researched and innovated on. This interest in the field is the reason why a SWOT analysis is necessary, to examine all factors concerning the technical viability of the project.

7.1.1 Strengths

The need for precise, accurate, and portable sensors is a reality, as there is a demand for an environmentally friendly approach to PMU. Therefore, the designed platforms, which try to give a response to that demand, can help further the research, or, after a more extensive revision of the project, try to improve upon what exists now on the market, and improve upon this field of study. Moreover, this project has been designed as a low-cost architecture, which, if implemented, could be a selling point of the device.

Another strength this project has is that it counts with the help and resources of the Electronics and Biomedical Engineering Department of the UB, as well as members of the Discrete-to-Integrated Systems research group. They have provided an unmeasurable amount of experience on these types of devices and analysis, which can help eliminate the limitations of this project in the future, to try to implement this self-powered biosensing platform as a prototype.

7.1.2 Weaknesses

The limited experience with building an actual device is an important aspect to consider when trying to think about developing an actual sensing architecture. Time and resources would have to be spent to get to the level where the implementation of the device could be brought to reality,

And another aspect to consider is the lack of equipment to test and develop the components for the device, which could make this implementation difficult to implement with a limited budget and access to materials once the degree has ended.

7.1.3 Opportunities

There is a wide range of companies and research studies working and developing new technology to improve upon BFC, eliminating the limitations their low-current and low-voltage create. If it reached a point in which BFC could be created with improved characteristics, the implementation of the self-powered module could be done more easily, making it a viable option.

Furthermore, due to lack of timing and limited knowledge, a continuous monitoring approach has not been able to be studied, but with more time, and further research, a possible implementation, using the self-powered module, could be created to develop a device that could provide real-time continuous sensing for implantable applications. Moreover, since there is a lack of these types of devices at the moment, if it could be developed it could become a possible market success.

7.1.4 Threats

The main threats this project faces are that universities or small research groups lack the reach big, experienced companies have, which have a consolidated client list and market space, so the lack of infrastructure and influence on this field of study might create a significant difficulty when trying to implement the device.

Another issue that must be considered is the huge amount of restrictive legislation that is tied with the commercialization of a medical device, which can make the development and market launch difficult.

7.2 SWOT analysis

In *Figure 34,* a summary of the information described before can be seen in the SWOT in diagram format.

Figure 34. SWOT analysis of the project.

8. Economic viability

The total cost of this project can be approximated to a certain degree. The cost of labor will be calculated from the estimated salary per hour a Junior Engineer can earn while doing an internship, and Final Degree Project. The computer needed will not be considered since it was already owned, therefore the cost will be 0€, and due to the Covid-19 pandemic, no actual implementation of the BFC took place, meaning the cost is zero as well. The software used and access to bibliographical information were both free since the UB gives free access to multiple platforms where the studies from the state-of-art were found.

This project has taken 360 days to complete, but it can be summarized as 200 hours of the internship and 300 hours of the Final Degree Project.

The total costs can be seen in *Table 5*.

	Units	Price per unit	Total
1. Workers **1.1. Biomedical Engineer student**	1	15€/h·500h	7.500 €
2. Equipment **2.1. Computer**	1	0 €	0 €
3. Licenses **3.1. SPICE Software**	1	0€	0€
			7.500€

Table 5. Table of expenses.

9. Regulations and legal aspects

This project consists of developing a lactate and glucose sensing self-powered device. Although the device has not been produced, medical devices are strictly regulated, and it is necessary to follow the legislation and follow the technical requirements to, in the future, commercialize the product.

9.1 Medical devices

In this first section, general legislation regarding the commercialization of medical devices will be analyzed.

- ISO 13485: Specifies the requirements for a quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements. Such organizations can be involved in one or more stages of the life cycle, including design and development, production, storage and distribution, installation, or servicing of a medical device and design and development [38].
- ISO 14971: Specifies the requirements for the biological evaluation of any material or medical device intended for use in humans shall form part of a structured biological evaluation plan within a risk management process [39].
- ISO 10993: Specifies the general principles governing the biological evaluation of medical devices within a risk management process, and the general categorization of medical devices based on the nature and duration of their contact with the body, among other regulations [40].
- UNE-EN 62366:2009/A1:2015: Specifies requirements for medical devices with emphasis on engineering usability to reduce risk of improper use [41]

9.2 General requirements

Like any other device, it needs to comply and guarantee the general quality, safety, and efficiency features for the device and the manufacturing process.

- ISO 9001: Specifies requirements for a quality management system when an organization needs to demonstrate its ability to consistently provide products and services that meet customer and applicable statutory and regulatory requirements. All the requirements of ISO 9001:2015 are generic and are intended to apply to any organization, regardless of its type or size, or the products and services it provides [42].
- Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales (LOPD-GDD): specifies that any device in contact with a patient must protect the patient's data to guarantee their integrity and confidentiality [43].

10. Discussions and Conclusions

10.1 Fulfilment of Objectives

The main objective of this Final Degree Project has been to implement a self-powering POC type biosensing device, for LFC and GFC measurements. Using the tasks described in the execution schedule, the objectives, and the results obtained in the detailed engineering section, a global evaluation of the limitations and successes of this project has been made.

Taking four out of the five stages explained with the Gantt chart, a specific evaluation has been made (the writing stage has not been considered):

- *Research*

  Both BFCs have been characterized, and the values to later simulate their behavior have been correctly measured. A study of different sensing platform options, their limitations, and the possibility to develop something similar have been performed, as well as an examination of PMU instrumentation possibilities for self-powered applications. A comparative analysis has been developed, and a choice, which later worked, has been chosen.

  It can be said that the objectives and tasks that had been planned for this section of the project have been successfully achieved.

- *Spice simulation*

  The simulation of GFC and LFC mimicking real-like behavior was a success, as well as studies of current dependency and working ranges which were of great use on the event detection platform. This section too has been completed and the secondary objectives met.

- *Design of the system*

  The development of the designed biosensing platform was a success. The resistor values, minimum voltage, and a way to detect the concentration of the sample, measuring the current provided by the BFC to give a valid reading of measurement, were proven to have been correctly constructed in both the design using an ideal independent current source and using BFCs. The design of the PMU was based on the analysis of the promising characteristics of the LTC3108 ultralow voltage step-up converter and power management but was later in the project found to have been lacking since a viable simulation could not be performed.

  The limitations of the design of the PMU have been the main issue of the project, creating difficulties with the implementation and validation stages of this platform.

- *Measurements and validations*

  It is in the implementation of the designed platforms stage that the limitations of this project show in full. The three modules of the BFC biosensor worked adequately, allowing for precise monitoring of the simulated LFC and GFC. It is the PMU module that, as mentioned before, did not properly work, not accomplishing one of the two main goals of this Final Degree Project.

The limitations the BFC presented regarding low-voltage and low-current responses, did not allow for the designed instrumentation to properly start, having an ultra-low current value at the output of the FC which was insufficient to make the DC/DC boost converter work. Some solutions were attempted in the form of multiple stack GFC configurations to try and increase the response, as well as adding a resistor in series to increase the current, but both were unsuccessful.

To understand the connections and how they could be linked together, the output voltage of the PMU module was fixed at 3.3V, to try and see the reaction to it from the Biosensing platform. It worked, proving that if more time and more experience had been at hand, the self-powered applications could have worked.

Therefore, it must be said that the objectives regarding the PMU, beyond just the research and understanding its functions, have not been properly met. Being the most obvious, the fact that the implementation of both platforms at the same time to create a self-powering device for biological sensing of BFC has not been accomplished, only the Biosensing platform working as it should.

10.2 Future opportunities for improvement

As mentioned before, this project started as research about BFC, their applications, and their characteristics. Some of the limitations and problems the proposed design has encountered are linked with the low-voltage, low-current behavior of the FC, meaning that a possible line of study would be finding better materials to build the EFC to improve upon their catalytic redox activity circuit to generate more electric current. This way, the system would not have to deal with this problem since it would be solved at an FC design level. The future of this field relies on finding such a solution since there is a need to find more appropriate ways to harvest the energy extracted from the BFC and design a more stable DC/DC boost converter circuit to implement self-powered characteristics.

Another possible implementation would be to find less invasive means of measurement, taking other fluids such as sweat to analyze glucose and lactate since nowadays, blood is the main, to not say the only, widely available sensing option.

The implications of successfully developing a self-powered sensing device for instant measurements with a POC machine could be a key instrument for the eventual use of this technology to create a self-powered continuously sensing device. This opens the door to the implementation of implantable machines, which could be life-changing for patients, a revolution in clinical settings and out-patient care, and a life-altering event for the medical world as we know it.

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