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ESCUELA TÉCNICA SUPERIOR DE INGENIERÍA INFORMÁTICA

GRADO EN INGENIERÍA DE LA SALUD

MENCIÓN EN INGENIERÍA BIOMÉDICA

Diseño y desarrollo de un dispositivo de estimulación eléctrica para el tratamiento de distrofia muscular de Duchenne.

Design and development of an electrical stimulation device for Duchenne muscular dystrophy's treatment

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Fecha defensa:

Resumen

La distrofia muscular de Duchenne ha estado en el punto de mira de muchos grupos de investigación en todo el mundo. Mientras que ha habido muchos estudios en el campo, especialmente durante la última mitad de siglo, la DMD sigue siendo una enfermedad que reduce la esperanza de vida del paciente que lo sufre drásticamente, a parte de la limitación de movilidad y la constante dependencia de terceros. Sin embargo, muchas pruebas clínicas están siendo organizadas cada día para nuevos métodos para el tratamiento de la DMD, con resultados extraordinarios, las cuáles dan a la comunidad científica esperanzas para que algún día, se encuentre una cura para esta enfermedad. En este proyecto, nos vamos a unir a este movimiento con una aproximación alternativa: electroestimulación.

Palabras clave: Distrofia muscular de Duchenne, electroestimulación, placa de circuito impreso, electromedicina, Arduino

Abstract

Duchenne muscular dystrophy has been in the spotlight of many groups of investigations around the world. While there have been many studies in the field, especially during the last half of the century, DMD is still a disease that still reduces the life expectancy of the patient who suffers it drastically, apart from the limited mobility and constant dependence of others. However, clinical trials for novel methods to treat DMD are being run every day, with astonishing results, which gives the scientific community hope to one day find the definitive cure for this disease. In this paper we are joining this movement by approaching DMD by an alternative method: electrostimulation.

Keywords: Duchenne muscular dystrophy, electrostimulation, printed circuit board, electromedicine, Arduino.

General index

Chapter one

1.Introduction

1.1. Goal of the project

The goal of this project is to develop a prototype of a mobile electrostimulation device as functional as possible, through a non-invasive methodology. To be able to achieve it, we will have to research about the corresponding output signal we need to treat DMD, plus get all the knowledge needed to build both the right circuit structure and software. Although the former's election is not straightforward, meaning that there will be several options to achieve our goal, the selection of elements that will compound the latter will be mostly related to Arduino. This will make the whole project easier, both for the design and the manufacturing part.

Also, as a side goal for this project, we wanted to highlight the importance of both electromedicine and telemedicine, nowadays more than ever, right in the middle of a pandemic. Those research fields have experienced a significant growth in the last decades, and we wanted to show the value of the constant research that is done every day in order to find new treatments for diseases, regardless of if it has or not already one, with always having the goal to improve.

1.2. Motivation

The research for the ideal treatment for Duchenne's muscular dystrophy has been around for more than a half of a century. Young boys, who are more propense to suffer this disease, do not usually live past their teens. Luckily, in the last 50 years, methods to deal with DMD have indeed improved the chances to survive to a relatively high degree (53% during the 1990 through nocturnal ventilation [31].

Nowadays, there is a wide range of treatments which has led us to attain one of the most notable achievements regarding DMD, that is expanding life expectancy to 30 years [32]. And it should be growing as time passes and more research is done in the field.

On the other hand, electrostimulation has been around for a bit longer. The application of electricity for pain treatment dates to thousand years BC: the Ancient Egyptians, and later on the Greeks and Romans, recognised that electrical fishes were capable of generating electric shocks for relief of pain [33]. Many authors consider the 19th century as the "golden age" of electrostimulation. However, this therapy fell in grace during the 20th century, with the rise of analgesic drugs.

Nevertheless, there have been many electro therapies methods, such as TENS (Transcutaneous Electrical Nerve Stimulation), PENS (Percutaneous Electrical Nerve Stimulation) or SCS (Spinal Cord Stimulation). Although being based on the same concept, each one of those has its own speciality. For instance, both TENS and PENS are effective methods for mild or moderate pain and SCS's main use is for treatments for ischemic pain and refractory neuropathic.

The main motivation of this paper is to highlight the perks that electrostimulation has to show in the field of medicine, especially in chronic diseases such as DMD.

1.3. Used tools

a) **Tina-TI.** Tina-TI is a free simulator from Texas Instruments which will allow us to simulate our circuits.

Figure 1: Texas Instrument's Logo (Company's Web)

b) **KiCAD.** KiCAD is an open-source electronics design tool with the capacity to create schematics to later on transform them into printed circuits boards (PCB).

Figure 2: KiCAD's logo (Company's Web)

c) **Arduino.** Arduino is a board which is designed based on an ATMEL microcontroller. Also, it comes with its own software, which we will use to control the board itself.

Figure 3: Arduino's Logo (Company's Web)

d) **TinkerCAD.** TinkerCAD is a free-to-use online 3D modelling programme that allows simulating circuits design, which supports both Arduino's board and software. The latter's language is identical to C++.

Figure 4: TinkerCAD's logo (Company's Web)

1.4. Structure of the paper

This project is divided into four main chapters, one of each addressing a specific topic of the project. In chapter two, we go through all the theoretical bases of DMD that we need to comprehend the disease. Also, we will see how DMD affects several organs of the human body. Finally, a commentary about DMD diagnosis and modern treatments will be discussed, regarding its bases and development in the last years.

In chapter three, like chapter two, we will address the theoretical bases of electrostimulation. We will see all the types of techniques which exist within this field,

such as PENS and TENS, and then we will exhibit several arguments on why electrostimulation therapies can be of major importance. Lastly, we will expose the results of a report article, which has been the main base for this project, about using electrostimulation as an alternative method of treatment.

In chapter four, we will revise all the steps that have been taken during the project's development, looking into both the hardware and software sections. For the hardware parts, all the considered elements which have been put into work will be analysed, highlighting the ones that have been successfully implemented and the ones that have not.

Finally, in chapter five, we will discuss the results of our work, looking into all the requirements imposed during the requirement gathering period of the project that has been successfully achieved, and the ones which, due to a reason or another, has not been possible to fulfil. Several physical proofs will be exhibited of the functionality of the device, followed by a brief commentary about the results.

Chapter two

2.Theoretical bases of DMD

2.1. What is DMD?

Duchenne muscular dystrophy, or DMD for short, is a degenerative muscle disease which is the most common of muscular dystrophies in childhood. This is a result of deletions in the dystrophin gene (DMD; locus Xp21.2), deriving in a progressive muscle degeneration, usually beginning in the proximal limb muscles, and later extending to more distal muscles [1].

DMD rate of affection is 1 in 3600-9300 live male births. Boys who are afflicted by DMD are born healthy, but after the first one and 2 years of life, they start to find difficulties with walking, jumping, or climbing stairs, until they become wheelchair bound by the age 12. Over time, the muscle weakness starts to affect other organs in the body, causing dysfunctions on them. In the next section, we are going to make a brief description of the DMD repercussions of several of these organs [1].

2.2. Organ involvement in DMD

2.2.1. Musculoskeletal

One of the most frequent complications in DMD is neuromuscular scoliosis. This is due to the progressive weakness of truncal muscles, which occurs after the loss of the ability to walk.

Other difficulties such as significant muscle weakness, diminished power and motor agility and decreased bone density can make bone fractures more common in DMD patients.

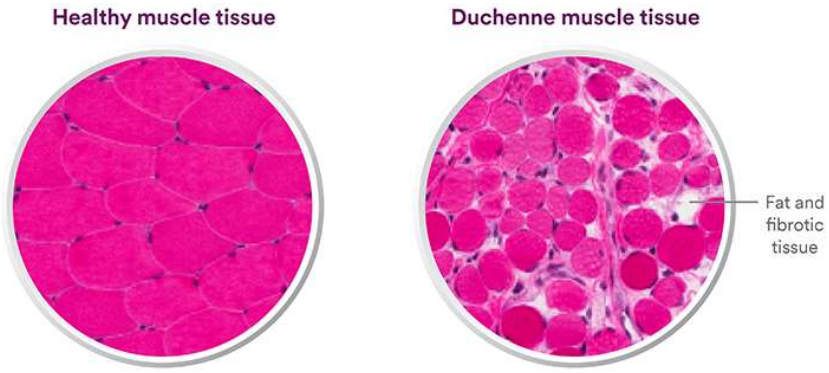

Figure 5: Difference between the muscle tissue of a healthy (left) and a DMD (right) patient. Extracted from Duchenne Muscular Dystrophy. (2021). https://www.sareptatherapeutics.ch.

2.2.2. Cardiac

The involvement of cardiac muscles is inevitable for DMD patients, due to, as in skeletal muscle cells, dystrophin is as required in cardiomyocytes. Pathological alteration of ventricular myocardium in DMD is probably a result of a combined consequence of myocardial wasting and secondary geometric changes, due to decreased systolic function caused by a progressive cardiomyocyte destruction.

Although it is commonly addressed DMD cardiomyopathy as dilated cardiomyopathy (or DCM for short), the way the heart is affected is not always shown by a ventricular dilatation. Many cardiac complications are related to systolic or diastolic decreased

function, but in most of these cases the heart has a thin ventricular wall. Thus, is not entirely correct to address DMD cardiomyopathy to DCM.

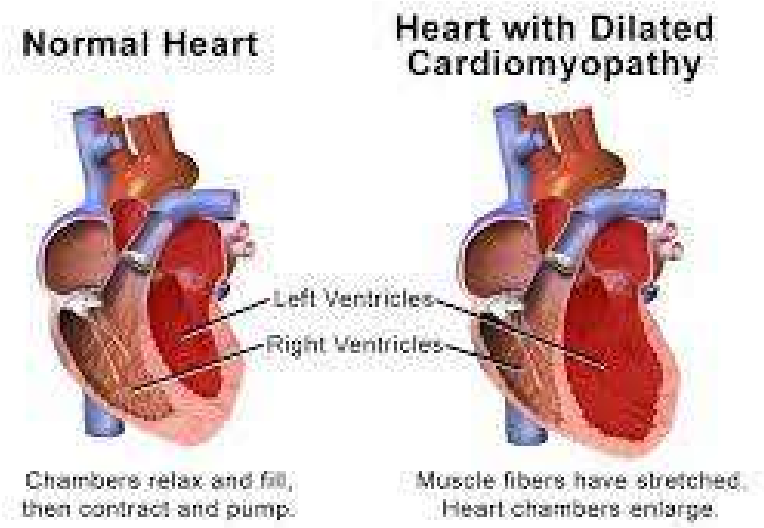

Figure 6: Difference between a healthy (left) and a DCM (right) heart. Extracted from Parent Project Muscular Dystrophy. (2018, 17 October). Care for the Heart. https://www.parentprojectmd.org/care/care-guidelines/by-area/care-for-the-heart/

2.2.3. Neuromuscular

As it was said before, DMD is characterized by a progressive wasting and weakness in muscles, beginning in the proximal limb ones. Those who are affected by DMD, normally children, present at an early age with delayed gross motor development and difficulty climbing stairs or rising from the floor.

It is also known that physical immobility accelerates both the decrease of the bone density and risk of fracture, along with neuromuscular scoliosis and joint contractures, as muscle weakness worsens. In consequence, attenuation of muscle wasting, and prevention of secondary skeletal deformation are primary DMD management goals.

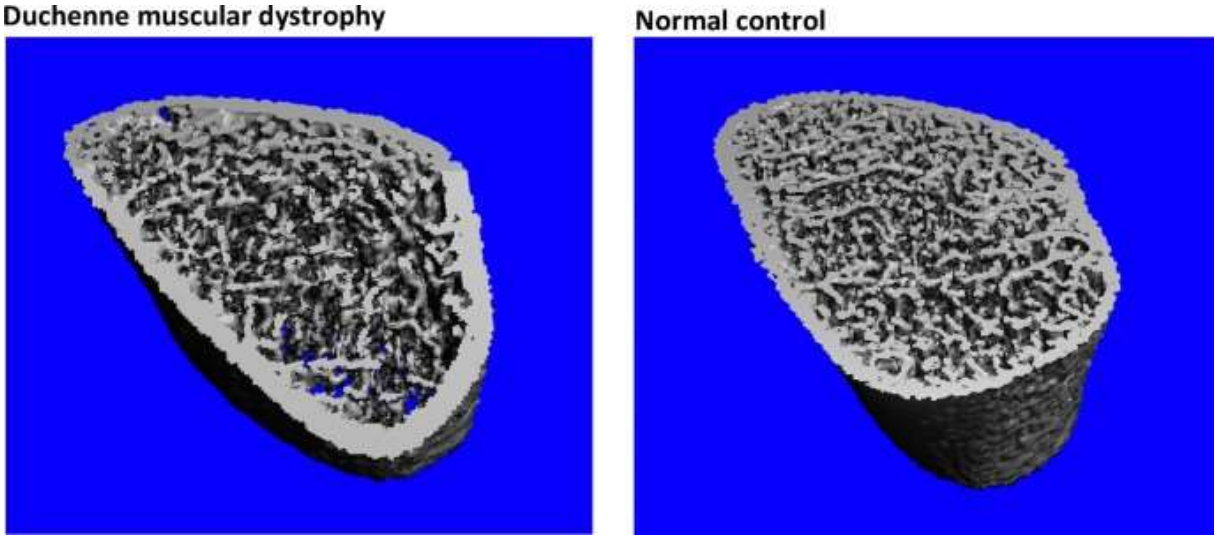

Figure 7: Difference between the trabecular bones of a healthy (right) and a DMD (left) patient. Extracted from Bone microarchitectural alterations in boys with Duchenne muscular dystrophy on long-term glucocorticoid treatment by l., Lam, Tp. & Chan, S.Hs. (2021)

2.2.4. Pulmonary

In DMD, the respiratory status is characterized by a ventilatory insufficiency and sleep-disorder breathing, among other issues. The former is due to weakness of respiratory muscles, which is responsible for major mortality in DMD patients. The progression of neuromuscular scoliosis may result in a significant decrease of lung volume, which can lead to restrictive lung disease.

In the case of sleep apnea (also known as OSA or nocturnal ventilatory insufficiency), is mainly caused by a decrease in strength of respiratory muscle. Some of the effects which the OSA is responsible for is snoring, increased daytime tiredness, headache and drowsiness [1].

2.2.5. Others

Moreover, dystrophin can also be expressed in kidney, retina and CNS (central nervous system), so there can be an increased incidence in neuropsychological problems and neurobehavioral abnormalities, among other issues.

2.3. Diagnosis of DMD

DMD's diagnosis is usually made either after a physical study or a confirmation by molecular genetic testing that examines all 79 exons of the DMD genes. Whether the initial genetic test fails to detect the disease-causing issue, a respective gene sequencing is usually enough to confirm the mutation that provokes the DMD.

It is of major importance to detect the specific mutation of DMD, because the treatment could be individualized in order to get better results.

2.4. Treatments for DMD

Even though there is no cure for DMD yet, there are several treatments, which can at least increase both life expectancy and quality. There are three main therapeutic strategies used currently: gene replacement, muscle growth and regeneration, and reduction of inflammation and fibrosis.

2.4.1. Treatments based on gene replacement

2.4.1.1. Exon skipping

This therapy uses synthetic antisense oligonucleotide sequences to induce skipping of prespecified exons during pre-messenger RNA splicing of the DMD gene. This leads to a restoration of the reading frame and the generation of an internally truncated protein.

With this therapy, Mendel et al [8] revealed significant improvement in walking ability of a great part of the subjects, all of this with histological evidence of the brand-new dystrophin production and restoration of the dystrophin-associated protein complex during the muscle biopsies. Furthermore, side effects of the treatment were not found during the three-year period that the therapy lasted. With these great results achieved, it was concluded that antisense therapies that induce single or multiple exons skipping could potentially be helpful for most dystrophin mutations [10].

2.4.1.2. Stop codon read-through therapy

Between 10 and 15 percent of DMD are caused by point mutations with expression of specific sequences (such as UAA, UGA or UAG) which are not appropriate, leading to premature stop codons. Thus, an arrest in the synthesis of the dystrophin protein is caused.

For this reason, the use of bioavailable drugs designed to overcome premature stop codon mutations (for instance, ataluren) is common in this kind of therapies. The way this substance works is that it binds to the ribosomal RNA subunits and impairs the recognition of premature stop codon. This permits the translation and production of a modified dystrophin protein. Early studies from Finker RS et al reported great success with ataluren, along a high grade of tolerance and safety [11].

2.4.1.3. Gene therapies

One of the biggest perks of gene therapies is, contrary to stop codon therapies, that they can be beneficial for many patients with DMD, regardless of their gene mutations.

Two of the most used proteins for gene transfer studies are Follistatin and *GALGT2*. But due to a recent withdrawal of the latter, a Phase 1 adeno-associated virus (also known as AAV), whose delivery of micro-dystrophin can induce the restoration of muscle protein expression in DMD is being conducted at the Nationwide Children's Hospital. Studies from Okada T. and Takeda S. [13] are also currently being conducted in order to analyse the potential of AAV.

2.4.2. Treatments based on muscle regeneration and growth

2.4.2.1. Cell-based therapies

In this group, we can find a couple of examples related to the transfer of myoblasts and cardiosphere-derived cells. These are:

- The use of myoblasts to transplant them to DMD patients. This technique is still due to investigate its efficacy and most importantly its safety. About thirty million myoblasts will be injected per cubic centimetres in a higher surface of the extensor carpi radialis (ECR) muscle. The contralateral muscle is injected with saline, making it the control. Usually, the results of the therapy, such as muscle strength are determined between three and six months after the transplantation.
- The other main therapy in this group is HOPE-Duchenne (acronym for halt cardiomyopathy progression in Duchenne). It is also a clinical trial, which is in Phase 1 / 2. The main element of this therapy is the use of CAP-1002. It is an investigational product which consists of allogeneic cardiosphere-derived cells

(CDC). The subjects of this therapy are due to receive an infusion of CDC in their active treatment arm, which are going to be directed into each of the three left ventricle cardiac territories (lateral, inferior, posterior anterior). Briggs D. and Morgan JE [14] are currently running research using other progenitor cell populations like inducible pluripotent stem cells.

2.4.2.2. Compensatory upregulation of cytoskeletal proteins

A study in 2016 [15] showed how cytoskeletal proteins, such as utrophin, α-7-β-1 integrin or biglycan, could stabilize the sarcolemma in the absence of dystrophin in *mdx* mice. Also, it was reported that there were significant improvements in the muscle biopsies after the treatment.

Other example of this kind of substances used in this type of therapies is SMT C1100, which is an oral bioavailable molecule which is specifically designed to increase utrophin expression

2.4.2.3. Myostatin

Myostatin, as a negative regulator of muscle growth, has the potential to be another option to treat DMD. In this case, we want to inhibit it, so the muscle growth will be no longer restricted, thus compensating the muscle wasting of the muscular dystrophy.

There are currently running trials using anti-myostatin in order to determine its safety, efficacy and tolerability of new myostatin inhibitors in ambulatory boys diagnosed with DMD.

2.4.3. Treatments based on keeping the calcium homeostasis

2.4.3.1. Rimeporide

It is thought that the characteristic imbalance between the levels of calcium and sodium in muscle cells in patients who suffer from DMD is key in the ongoing muscle damage

[16]. Based on this, the use of Rimeporide, which inhibits the sodium/proton type one exchanger, shows a new way to reduce the waste of muscle.

2.4.3.2. ARM210

This pharmacological therapy, identified by ARMGO Pharma, has shown that it is able to restore normal balance of calcium in the muscle cells. A study in mice with lack of dystrophin, ARM210 has reported that, after correcting the calcium leak, their muscle force and strength has improved significantly [17].

2.4.3.3. AT-300

Finally, we have the AT-300, although being in preclinical study, has shown great outcomes as a modulator of calcium channels, whose goal is to support the restoration of normal levels of calcium in muscle damaged by DMD.

As we have seen, DMD's treatment, as a complex disease that it is, is not trivial. Hundreds and hundreds of studies are running every year in order to eventually find a cure to this disease. In this paper, we decided to join all these alternative treatments with a less known approach: electrostimulation.

Chapter three

3. Theoretical bases of electrostimulation

3.1. Definition

The term electrostimulation is defined in Dorland's Medical Dictionary as: "the application of electricity for therapeutic or experimental purposes". It is not a surprise that the use of electricity could be beneficial for us, due to the evolution of every organism has progressed in the presence of a variety of magnetic and electromagnetic fields, which are naturally originated.

3.2. Types of electrostimulation

As an ever-growing alternative treatment, electrotherapy has been adapted to all kinds of matter through the innovation of more specific types. The most common ones are percutaneous electrical nerve stimulation (PENS or electro-acupuncture) and transcutaneous electrical nerve stimulation (TENS). Although the former is used in several therapies, the latter is the one which we are going to focus on in this paper.

3.2.1. PENS

PENS is the technique which uses needles to deliver current through the skin. In the last decades, it has been used as an alternative therapy to headache [19] and low back pain (LBP) [21] with great success. One of the most notable drawbacks that PENS

has, and TENS do not, is the invasive factor: the mere use of needles, if not used correctly, can lead to infections.

3.2.2. TENS

TENS consists of the delivery of electrical currents across the intact surface of the skin to stimulate (normally through electrodes) the nerves [36]. This type of electrostimulation is usually used as either an independent therapy or as an auxiliary treatment for symptomatic relief of any type of pain. This includes almost any kind of pain, such as acute, malignant, musculoskeletal, nociceptive, or even neuropathic.

3.2.3. SCS

SCS (or Spinal Cord Stimulation) consists of the stimulation of the dorsal columns of the spinal cord with an implanted device with the aim of modifying perception of neuropathic and ischaemic pain [34]. Regarding the latter, it has been suggested that SCS reduces tissue loss and can improve limb salvage in inoperable lower limb ischaemia [35].

3.3. Perks of electrostimulation

Although we have presented electrostimulation as an alternative therapy to DMD, we have chosen this technique among the rest, especially because it has some advantages in opposition to the ones mentioned previously.

3.3.1. Accessibility

In recent years, concepts such as telemedicine have become more notorious. The mere fact of being able to contact your primary care doctor from your house, is something that was unthinkable forty years ago. Furthermore, in the times we are living right now, with the constant menace of COVID-19, avoiding medical places such as hospitals is of major concern in case you do not have any health issue equally or worse than the

COVID-19 itself. So, it is clear that being able to treat any kind of disease from home with the monitoring of a doctor, regardless of the place they are, has become one of the largest concerns of the last ten years.

3.3.2. The "over-the-counter" (OTC) problem

One of the most polemic problems in recent years related to pharmacological products is the "over-the-counter" medicines. No matter how niche some medications are, they eventually become OTC, which can lead to major problems, such as addiction [22]. Furthermore, this kind of behaviour before medications is significantly more worrisome within the pain-reliever group.

On behalf of the electrostimulation devices, there is no such problem. Not only cannot it cause addiction, but they usually are also equipped with controllers to avoid the wrong usage of the device.

3.3.3. Simple and economic

As we will see in the device development section of the paper, this device can be relatively cheap to manufacture. It is true that in the short-term the pharmacological treatments can be less expensive, but in the long term the device will amortize. This is of major importance due to most diseases treated with electrostimulation (such as chronic pains), are meant to last as far as the patient's lifespan. Thus, a treatment that is able to endure long periods of usage will eventually be more economic than any other.

3.4. Results of electrostimulation in recent years

In the last decades, electrostimulation has shown great results in both in therapeutic and experimental issues, being in their majority muscle related. In a less amount, but

with remarkable results, electrotherapy has also been found useful in degenerative diseases, such as Alzheimer's [4] and Parkinson's [5].

3.5. Electrostimulation as a DMD treatment

After establishing all the concepts to know, we may present the main point of this paper: the use of electrostimulation as a DMD treatment.

The inspiration behind this work comes from an article about the possibilities of using low frequency electrical stimulation in children with DMD [30]. It is of major importance to highlight the words "low frequency". In this paper, the authors distinguish two types of electrical stimulation: one with high frequency (30 Hz) and another with low frequency (8 Hz). The former, although it has been studied in another experiment, has not shown results as successful as the latter.

As the other therapies mentioned before, TENS is not either a cure for DMD, but a way of improving the quality of life of the patient, along with their life expectancy. However, there is a huge difference between the genetic therapies and TENS: the accessibility. With the former, the patient is forced to move to a place, usually the hospital, to get their therapy, while in the case of the latter, it gives the patient the opportunity of having the treatment from home. This is of major importance, due to, as we said before, one of the main issues that DMD patients suffer is lack of mobility. Also, TENS therapies are more effective if they are done with a certain degree of constancy, which is provided due to

In the previously mentioned paper, the authors described the possibility of a treatment for DMD using electrostimulation with determined characteristics. Those are going to be our main requirements for the project and will be listed in the next section.

However, before entering the device development part of the paper, we will navigate through those papers and look at the main points of them in order to comprehend the reasons behind why these authors used electrostimulation as a way to treat DMD.

3.5.1. Improvement of maximum voluntary contraction (MVC)

When comparing the maximum voluntary contraction (MVC) between healthy and DMD muscles, it is revealed that the latter was significantly lower than the former. An application of intermittent chronic low frequency (8 Hz) resulted in a notable increase in this value.

Thus, the main goal in this type of therapy is to elicit maximum voluntary contractions (MVC) in order to elevate its value and get as near as possible to the healthy level. In the paper mentioned before, they chose fifteen boys with DMD to test this novel type of therapy.

3.5.2. Treatment methodology

The type of signal used for the treatment was a biphasic asymmetrical waveform, with a phase duration of 290 µseconds and a maximum output of 50 mA on 1 kΩ load. Furthermore, the stimulation must be at 8 Hz as we have told previously) during a period of 1.5 seconds, followed by a rest-period of the same length. The target muscle was their quadriceps femoris muscle, and they were stimulated for three hours, six days a week for a period between seven and eleven weeks. These characteristics will be essential to our work and are the ones that can make it possible.

Every clinical observation reported that those children who retained enough muscle bulk could handle the stimulations better and make the 3-hour routine easier.

3.5.3. Results exposure

The results of the comparison between before and after the ten weeks can be seen in the next graphic:

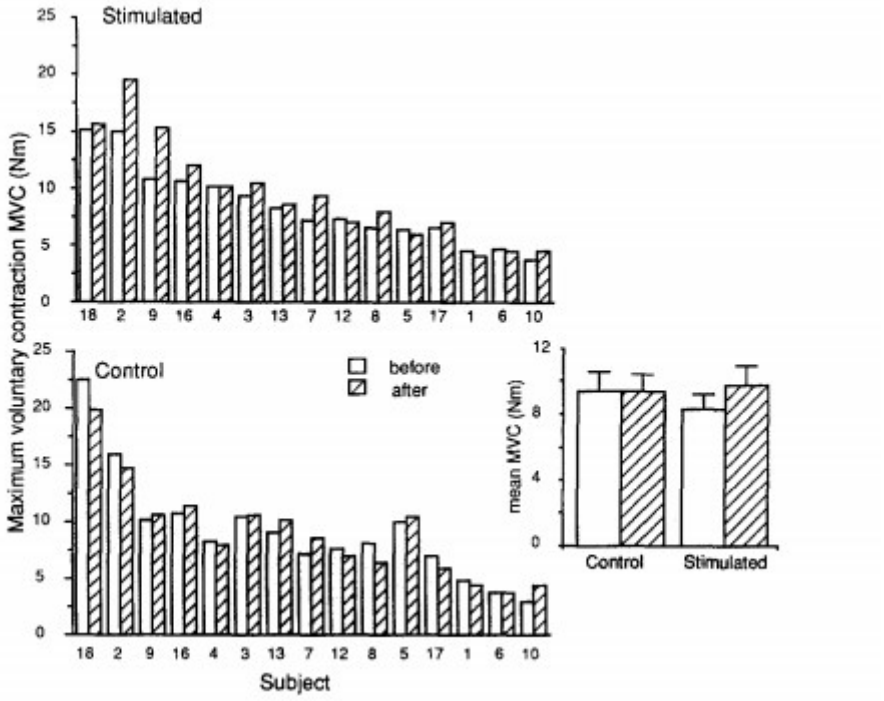

Figure 8: Comparative graphic between before and after the treatment, along with the control results. Extracted from Therapeutic possibilities of chronic low frequency electrical stimulation in children with Duchenne muscular dystrophy, by Scott, O., Hyde, S., Vrbová, G., & Dubowitz, V. (1990)

As we can see, the maximum voluntary contraction (MVC) of most of the children with DMD increases overall, while the control group's one stays the same, as expected.

Chapter four

4. Project development

4.1. Requirements

First, as with every project, we need a set of requirements in order to start our work. Most of them have been already told in this paper, but we are going to repeat them and put them in perspective:

a. Type of waveform. Both sine and square waveforms are the most used in muscle stimulation [23]. In this case, we are looking for a square waveform. The triangle waveform is discarded from the beginning: its periodic peak can potentially burn the skin.
b. Type of symmetry. We are looking for an asymmetric waveform too. This kind of symmetry is used for every kind of electrostimulation treatment, most being in neural-related health issues.
c. Number of phases. The output signal will consist of two phases, which, as we mentioned in the previous point, are going to be of different duration (due to being asymmetric).
d. Phase duration. The duration of the first phase must be of twenty-nine microseconds.

e. Frequency. As we are looking for a low frequency signal, we will set it to 8 Hz (in other words, a period of 125 milliseconds).
f. Amplitude. The ideal amplitude is 50 volts (50 mA in 1 kiloohms). As the goal of this paper is to manufacture a prototype of an electrostimulation device, this requirement will not be part of the main concerns of this project, due to two reasons: (1) as we said, it is a prototype, so it is not meant to be 100% functional, and (2) it is neither meant to be used in anybody, due to safety issues.
g. Electrodes. In the article mentioned before, two carbon rubber electrodes with dimensions 4 x 9.5 centimetres. As we said in the previous point, this device is not meant to be used by anyone, so we are also disregarding this element. However, in order to make the project more realistic, we decided to design an electrode-electrolyte model in the output part of the circuit, in order to get as near as possible to the ideal result. This model will be explained in more detail in the next section.
h. Rest periods. Finally, we have another detail which will be key for the software development. The electrostimulation device, once working, will have two main periods: one "stimulating" period and another "resting" period. Both have the same duration (1.5 seconds)

Other requirements, which have been imposed by us, are more related to the physical part of the project, regarding the size, elements used and software:

a. Desired size. As we want the device to be as mobile as possible, it is important to design it as small as possible, while not disturbing its functionality
b. Software. Arduino will be the software by choice. It is easy to use, free and versatile. The only drawback is that it may interfere with the previous point, but in a first consideration, it is our best election.

Lastly, although these next requirements are not going to be featured in this project (due to being a prototype), they are thought to define the hypothetical final product.

a. The device will have two channels. (for both electrodes)
b. The device will have a screen with all the necessary information portrayed.
c. The device will be terminated once the stimulation programme is finished.
d. The device will notify the user once the stimulation is finished.
e. The device will warn the user in case of any of the next cases happens:
   E1. Any of the lead cables are not properly connected
   E2. The battery is not sufficiently charged.
   E3. The stimulation programme is finished unexpectedly.

Once we have set our requirements, we can continue with the description of the project.

4.2. First attempt

As we said previously, the goal of this project is to be able to design an electrostimulation device which can be used everywhere. In other words, we want to make it mobile.

During the period of designing this device, we came across several options. Below, it is going to describe two of the main options considered, and the reasons why we took one and not the other.

4.2.1. Considered elements

During the first months, we decided to follow a previous work of another student, which worked with a similar device [27].

For this first attempt, the circuit would be compound by several stages, formed each of them by a determined operational amplifier with an assigned function. Those where:

a) A DAC (Digital-Analog Converter), along its correspondent amplifier

b) A high-pass filter

c) An amplifier of isolation

d) An OTA (Operational Transconductance Amplifier).

e) Another amplifier formed by two diodes.

f) And lastly a DC-DC converter.

Also, the device was provided with a potentiometer, which was used to modify the frequency of the output signal.

4.2.2. Hardware development

For hardware development, we started using *TinaTI* as our main design tool. We made sure to follow the structure from our colleague's work [27], and then change the necessary in order to obtain our desired output signal.

At first, all went swiftly: we were setting every stage which was described in the last section.

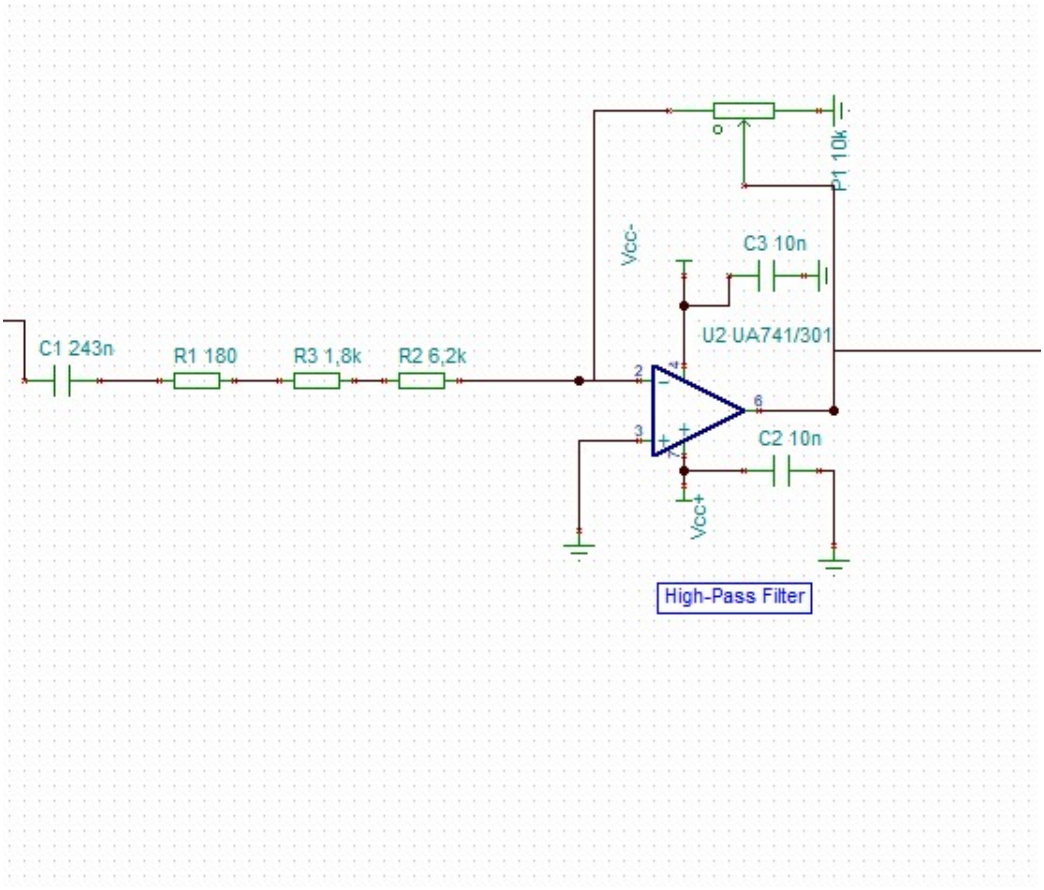

Figure 9: HPF from the first attempt of the electrostimulation device

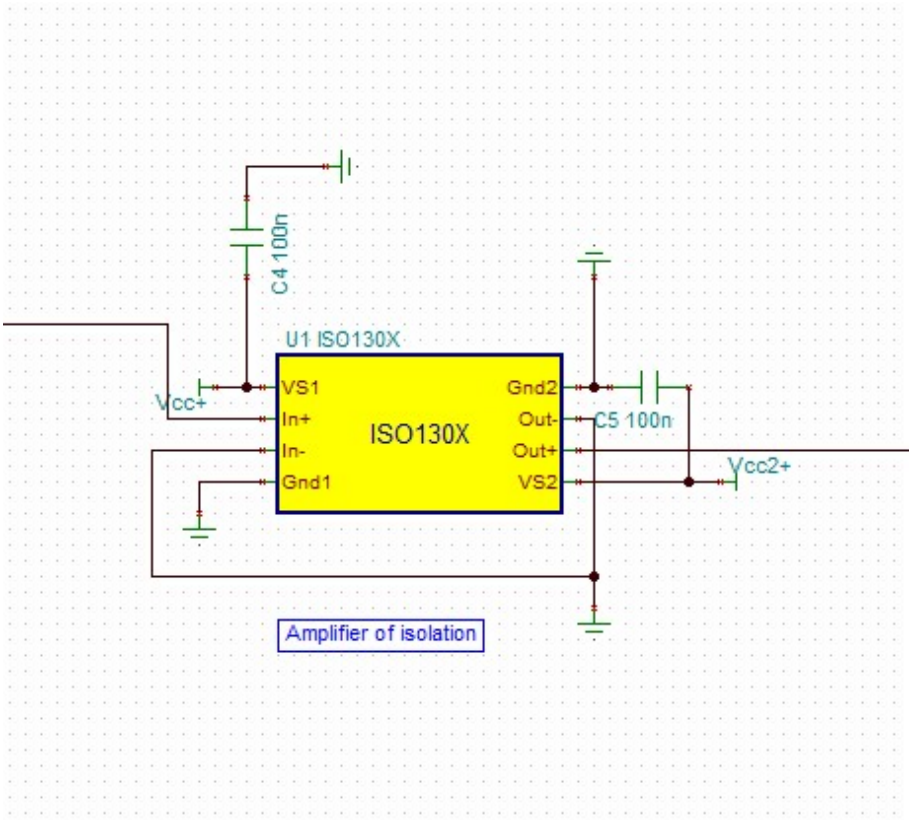

Figure 10: Amplifier of isolation from the first attempt of the electrostimulation device

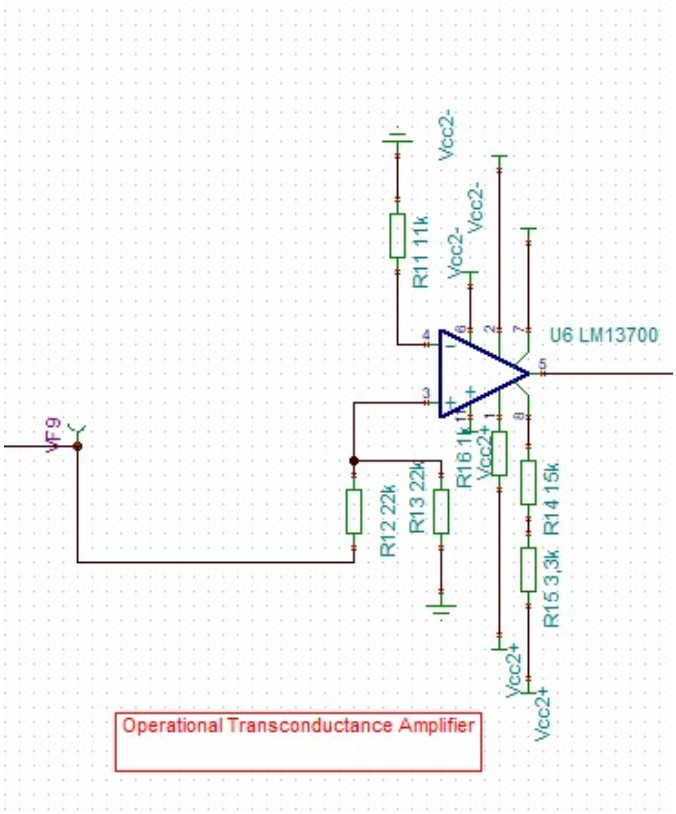

Figure 11: OTA from the first attempt of the electrostimulation device

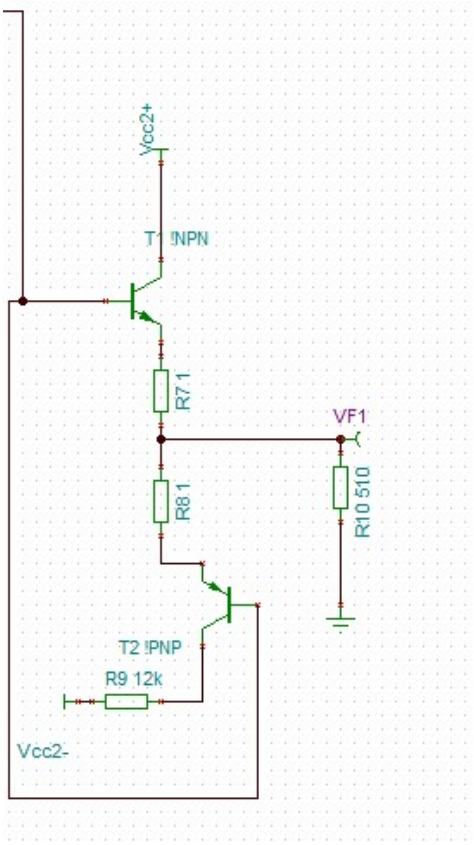

Figure 12: Last stage from the first attempt of the electrostimulation device

Once we had most of the stages of the circuit set, we started to theorize the ways to achieve our main goal: the biphasic asymmetric square waveform. At first, we thought it was feasible: just changing the values of some resistors or capacitors, due to our colleague's outcome signal, was fairly similar to ours. However, we did not take count of one factor: the asymmetry. This issue led us to a dead-end, which made us restart the way to approach the project.

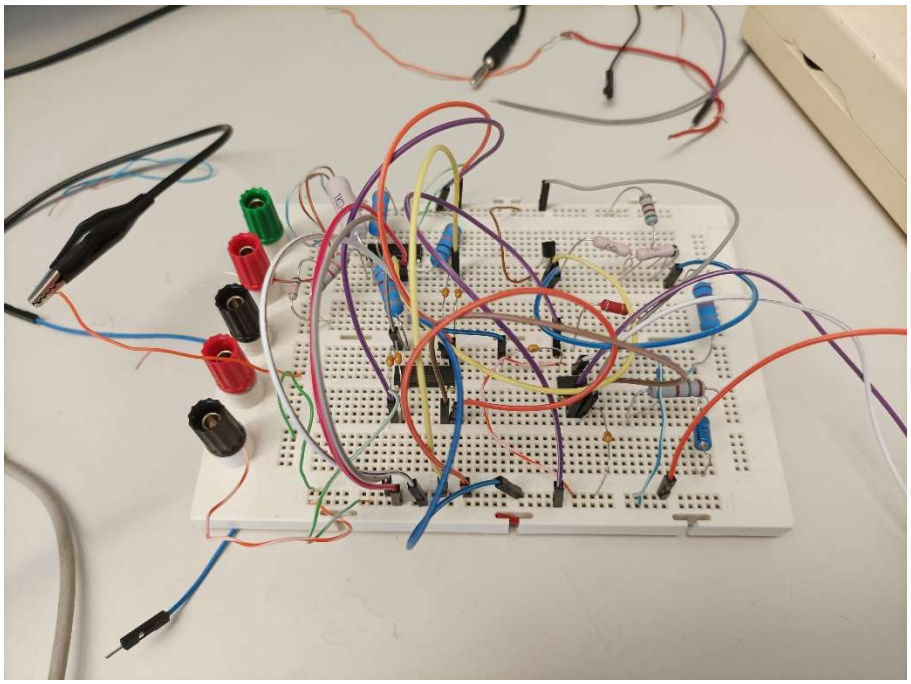

Figure 13: Assembly of the circuit of the first attempt

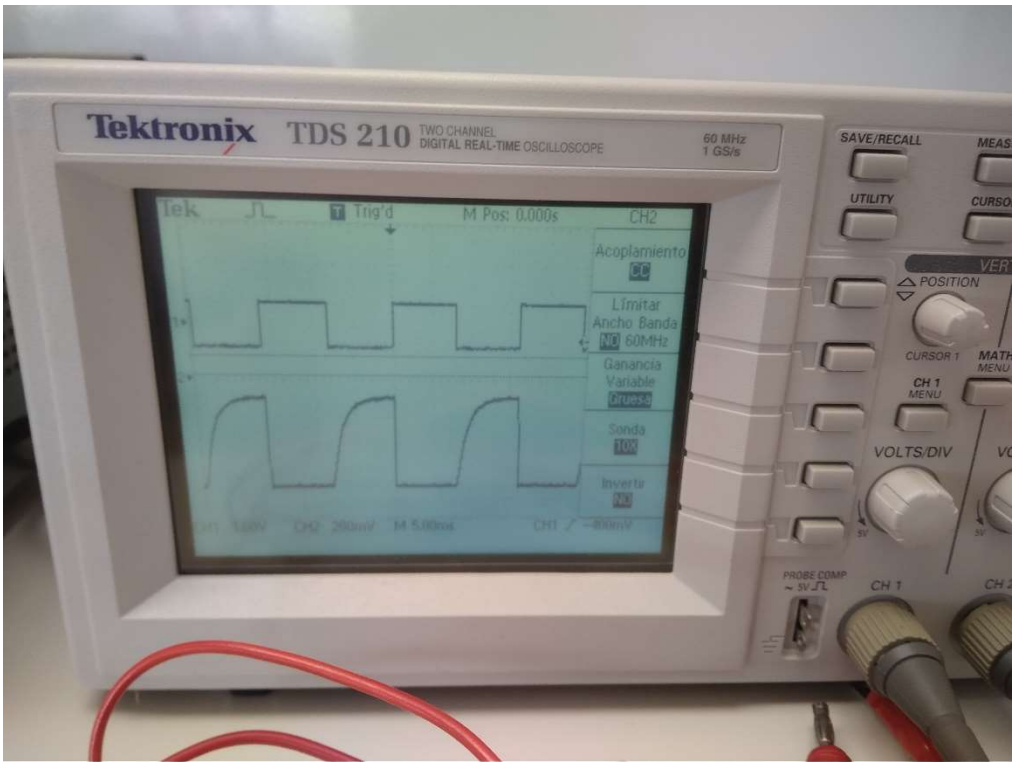

Figure 14: Results of the assembly of the first attempt

4.2.3. Software development

As we did not even get to finish the hardware part of the project in this attempt, this section makes no sense. However, it is important to highlight that, in case this first attempt was successful, the next step would be to use an Arduino Board to control it. Its functionality will be explained in the next section of the paper, belonging to the second attempt of the project, whose software development will remain similar.

4.3. Second attempt

After the first failed attempt, we decided to brainstorm a bit to find a way to get the desired output signal. The result of this insight led us to use a H-Bridge. Furthermore, we decided to use an Arduino USB board to be able to control the circuit easily from a computer. But before continuing with the design of the device, we should clear some definitions in order to be able to better understand the project.

A H-Bridge is a circuit structure formed by 4 switchers. The way it works is simple: depending on which of those switchers are open or close, the current will have a positive or a negative direction. This kind of circuit has been always employed with motors in order to control the direction of its spin. We used one in the next examples to explain how the H-bridges work, but it is important to remember that in the final project the motor is substituted for the actual output, which is the electrodes.

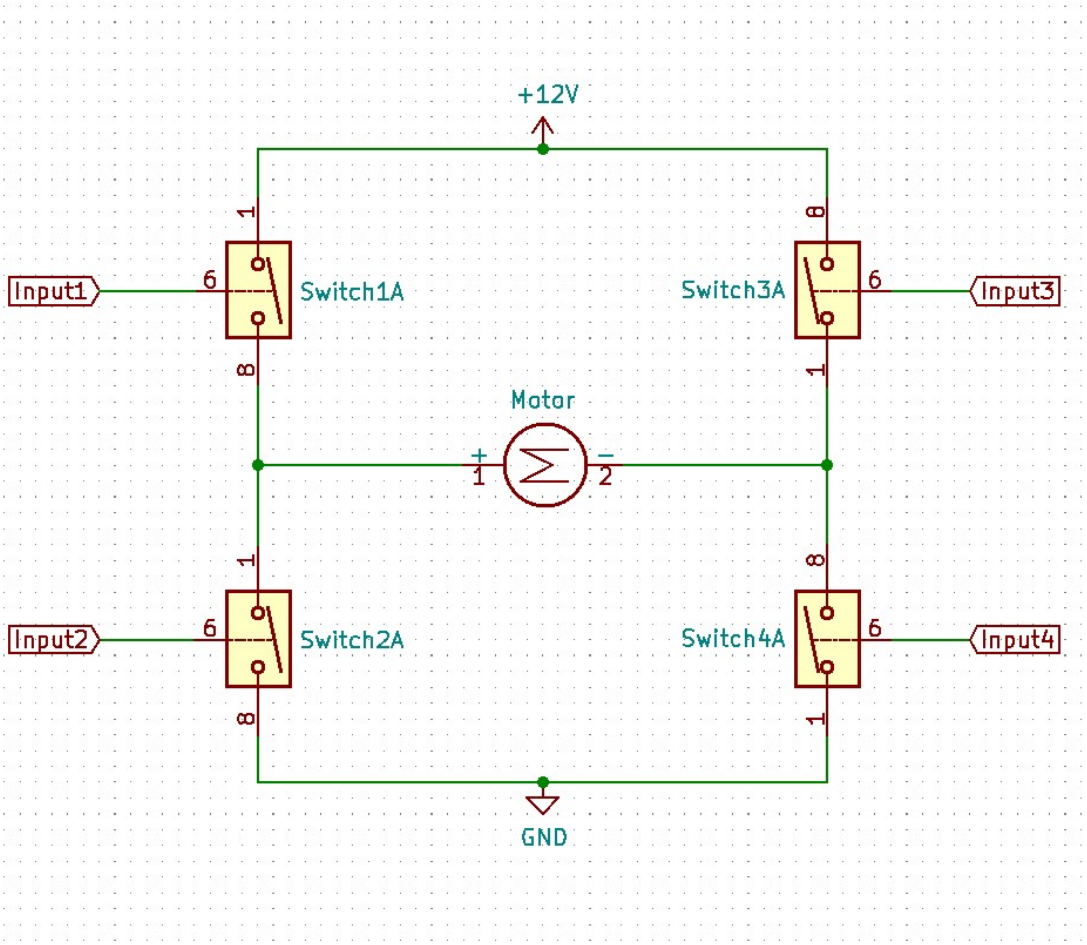

Figure 15: Schematic of a H-bridge with switches

Thus, we have two main cases: (1) the switches one and four are closed (and the other two are open), so the current goes through them, generating a positive spin in the motor, and (2) the switches two and three are closed (and the other two open) letting the current go through the motor in the opposite direction. Both behaviours are graphically described in the figures three, four respectively.

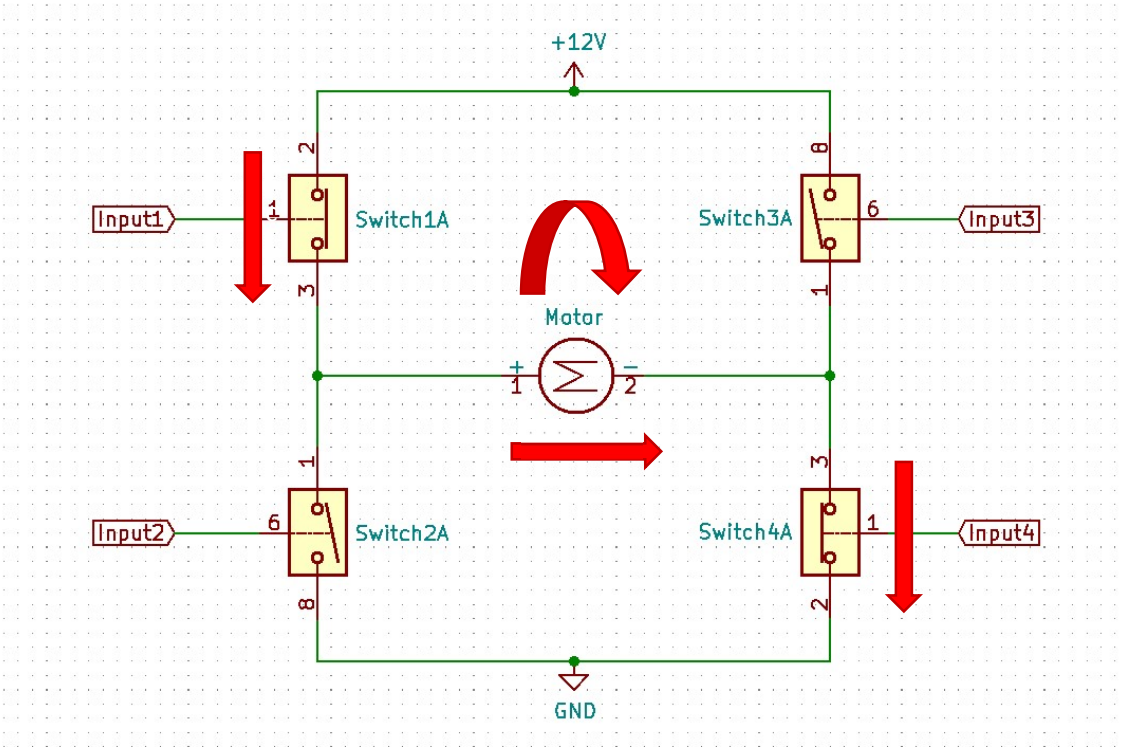

Figure 16: Schematic of the H-bridge in the first case

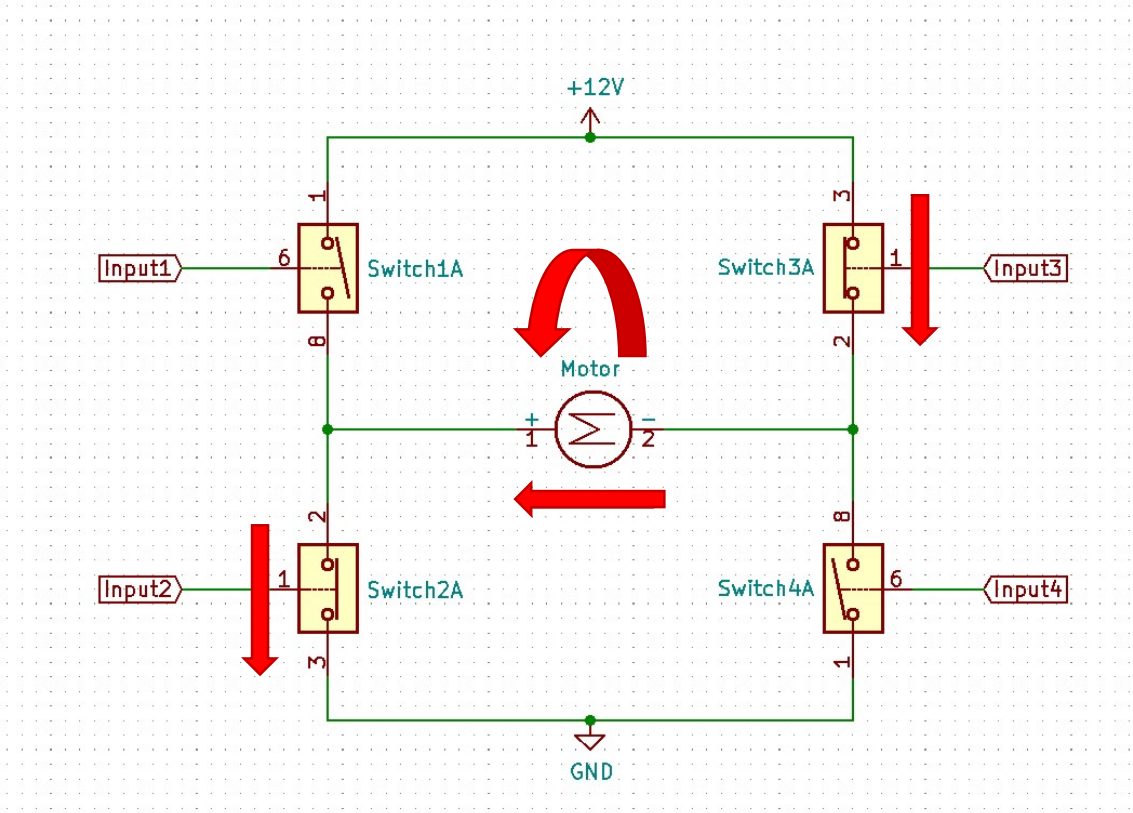

Figure 17: Schematic of the H-bridge in the second case

This kind of structure is mainly used in motor drives to control the movement of the wheels of a car, for instance. The reason why we thought this idea could work was

because of the ability of this structure to generate both positive and negative square signals, which is the main goal of our device.

NOTE: The reader of this paper may be wondering what happens in the case when both switches one and two, or three and four, are closed. Assuming this happens, the whole circuit would break down, which is logically an undesired outcome. The main reason why there was not a further insight of this case is because, as we will see later in this paper, we found a way to eradicate the possibility of this combination.

4.3.1. Considered elements

For this case, we had several options. As we said before, the goal of the H-Bridge is to be able to generate a signal or another depending on the switchers. In order to facilitate the control process of the device, those switchers are going to be MOSFET transistors. However, due to this kind of elements having different types (NPN and PNP), the circuit design is open to a wide variety of options. We decided to go two-and-two with the elements (in other words, two PNP transistors and two NPN transistors), due to this being the most common display.

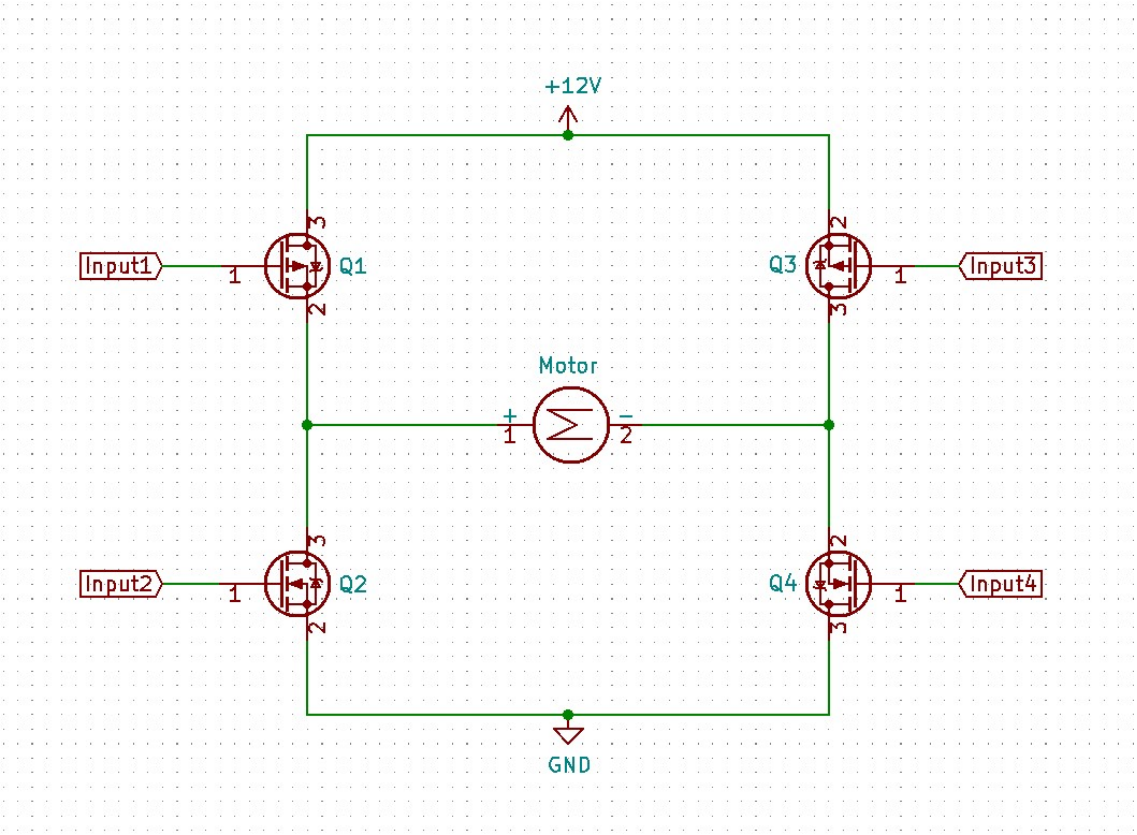

Figure 18: Schematic of the H-bridge with MOSFET transistors

Each one of them will be connected to an output with the corresponding signal. This leads to a potential problem of complexity: a major number of outputs. We must keep in mind that we are going to use an Arduino as a way to control the device, so the design as a whole will be better if we use the least number of variables possible. We will see more in depth the software in its section.

In order to eliminate this problem, we decided to use two extra non-MOSFET transistors, each one-on-one side of the circuit, so we will only need two output signals instead of four.

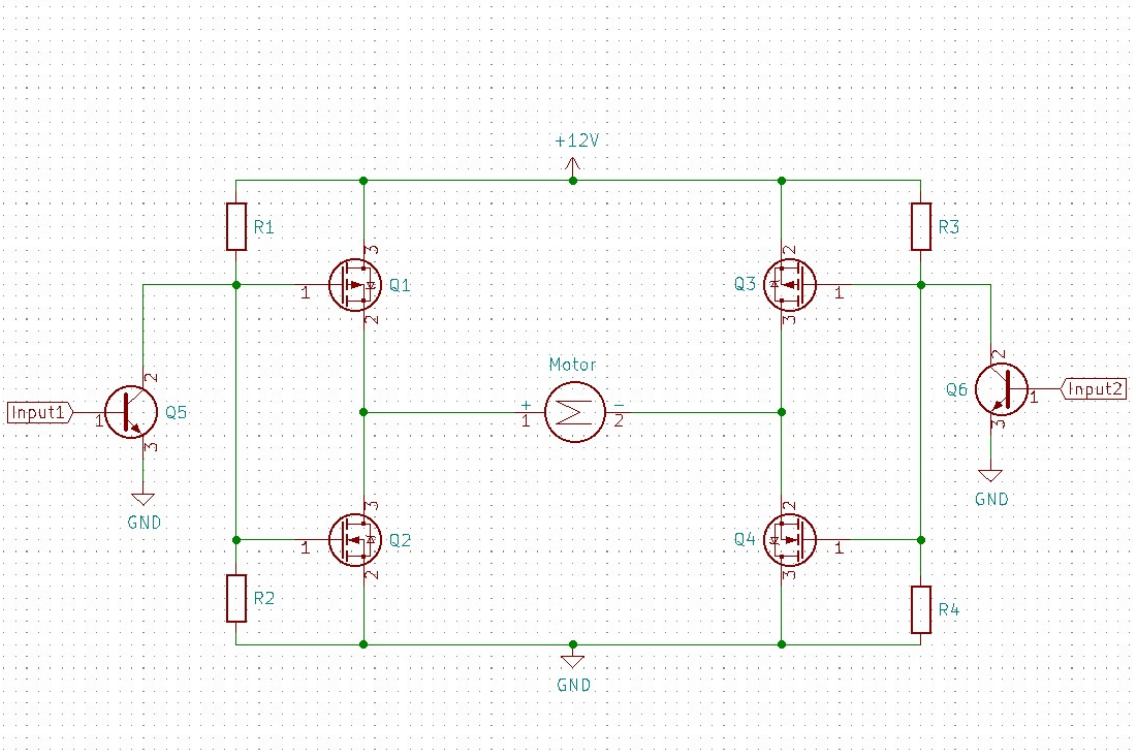

Figure 19: Schematic of the H-bridge with the extra transistors

4.3.2. Hardware development

The development of the hardware during this attempt came significantly easier than the first attempt. The main reasons were the smaller number of elements and the simplicity of the structure.

As with every design process, we started with the blueprints. The program used for this stage of the project was KiCAD. The reasons behind this decision were straightforward: we have easy access to its software; it is simple to use, and it facilitates the transition from blueprints to PCB design.

Another reason we are going to use KiCAD as a way to design the PCB is because it allows us to start a project for an Arduino Shield, which will be our main structure for the project, more easily.

A shield is a printed circuit board (or PCB) which is placed on the Arduino. Both are connected to each other through pins as a way of communication. Its main function is to amplify the capacities of the Arduino [26].

Once we have defined what a shield is, we can continue with the design.

4.3.2.1. Schematic design

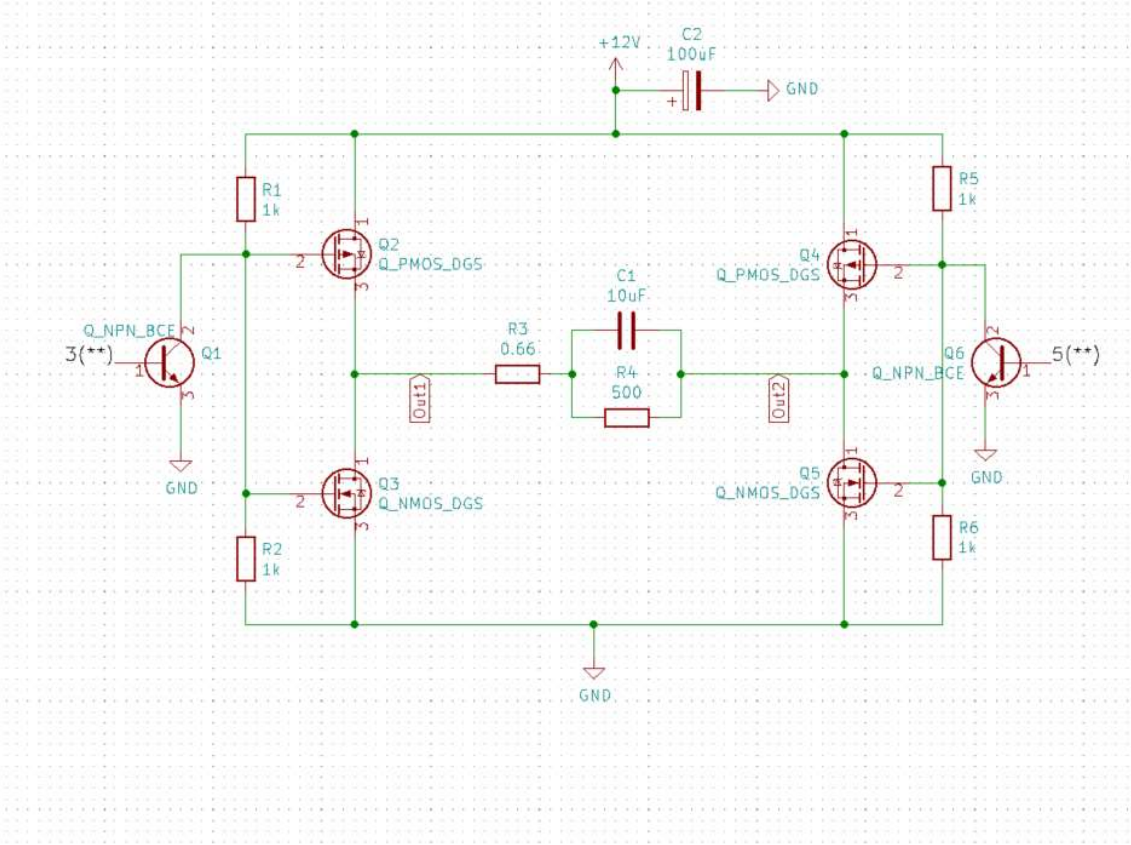

Figure 20: Design of the H-bridge for Low frequency TENS

The reasons behind the usage of transistors have been already explained in the previous section, so now we are going to tackle the rest of elements.

a) Electrode-electrolyte model. As we mentioned in the section of requirements, we are going to use an electrode-electrolyte model in order to make the project more realistic. This model is compounded by one capacitor and a resistor in parallel, followed by a resistor in series. This model was used by the author Wang M. [25] to be able to model electrodes for a tomography. As any model, it is not always faithful to reality, but it will be enough as a reference

b) Auxiliary elements. This section refers to both resistors and capacitors besides the electrode-electrolyte model. The values of them are simply standard in most H-bridges. The only element which has been placed as an extra is the 100uF

capacitor next to the voltage source, whose function is to handle any kind of spikes of voltage that can potentially occur. However, due to several issues when all the components were listed in order to be bought, we could not find this particular component, so for the final project, we used another 10 uF capacitor, just like the electrode-electrolyte model.

c) Pins. As we explained before, as we added a pair of transistors, we are going to need only two pins in order to control the Arduino Board. It is important to highlight which pins we are using, 3 and 5, because those are going to be key in the software section. Finally, we decided to use two output pins to get the desired signal, plus two more to be able to power the H-bridge.

Once we have the design for the H-bridge schematic, we can continue to the footprints.

4.3.2.2. Footprints

Symbol : Footprint Assignments

1	C1	10uF	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
2	C2	100uF	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
3	J1	H-Bridge Supply	Connector_PinHeader_2.54mm:PinHeader_1x02_P2.54mm_Vertical
4	J2	Salida	Connector_PinHeader_2.54mm:PinHeader_1x02_P2.54mm_Vertical
5	P1	Power	Socket_Arduino_Uno:Socket_Strip_Arduino_1x08
6	P2	Analog	Socket_Arduino_Uno:Socket_Strip_Arduino_1x06
7	P3	Digital	Socket_Arduino_Uno:Socket_Strip_Arduino_1x10
8	P4	Digital	Socket_Arduino_Uno:Socket_Strip_Arduino_1x08
9	P5	CONN_01X01	Socket_Arduino_Uno:Arduino_1pin
10	P6	CONN_01X01	Socket_Arduino_Uno:Arduino_1pin
11	P7	CONN_01X01	Socket_Arduino_Uno:Arduino_1pin
12	P8	CONN_01X01	Socket_Arduino_Uno:Arduino_1pin
13	Q1	Q_NPN_BCE	Diode_SMD:D_SMB_Modified
14	Q2	Q_PMOS_DGS	Diode_SMD:D_SMB_Modified
15	Q3	Q_NMOS_DGS	Diode_SMD:D_SMB_Modified
16	Q4	Q_PMOS_DGS	Diode_SMD:D_SMB_Modified
17	Q5	Q_NMOS_DGS	Diode_SMD:D_SMB_Modified
18	Q6	Q_NPN_BCE	Diode_SMD:D_SMB_Modified
19	R1	1k	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
20	R2	1k	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
21	R3	0.66	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
22	R4	500	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
23	R5	1k	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder
24	R6	1k	Capacitor_SMD:C_0805_2012Metric_Pad1.18x1.45mm_HandSolder

Figure 21: Footprint assignment

When choosing the footprints, our main priority was to find the ones which were smaller enough to not make the PCB crowded with elements, but neither too small for the soldering part of the project. Thus, we chose the 0805 series (which have a size of 0.2 x 0.1 mm) for both capacitors and resistors.

However, later in the hardware development, we realised that the transistor's footprint was too large for our project. Luckily, this did not cause any harm, but could have improve the design.

4.3.2.3. PCB design

This section will be straightforward due to, as all elements has been already explained, there are only a few details left to describe.

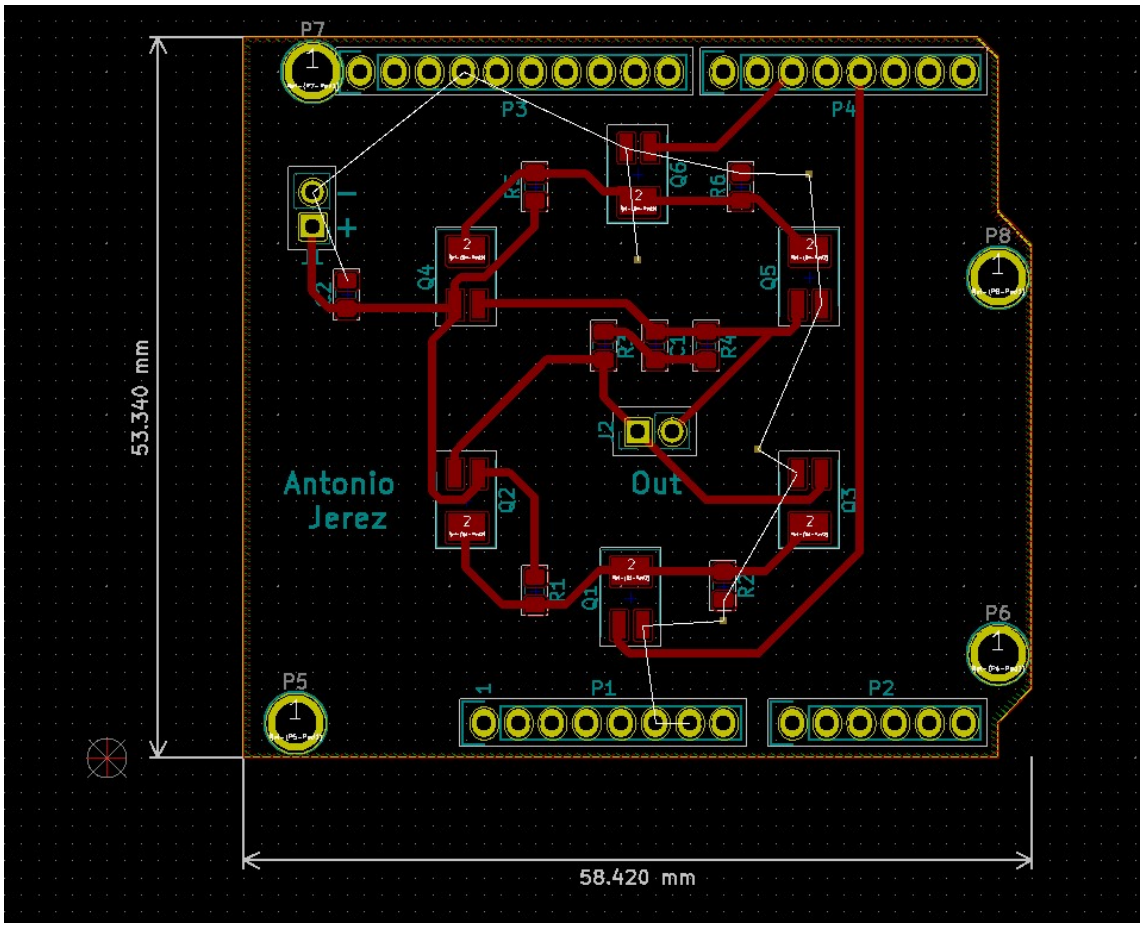

Figure 22: PCB design of the H-bridge

As we can see in the previous figure, the size matches with the Arduino's, which is the main characteristic of an Arduino Shield. In fact, the original PCB was a couple millimetres wider, but we decided to cut them in order to avoid problems with the Arduino's port which is connected to the PC.

Once we have PCB design finished, KiCAD allows us to reproduce it in three dimensions thanks to the tool *3D-View*.

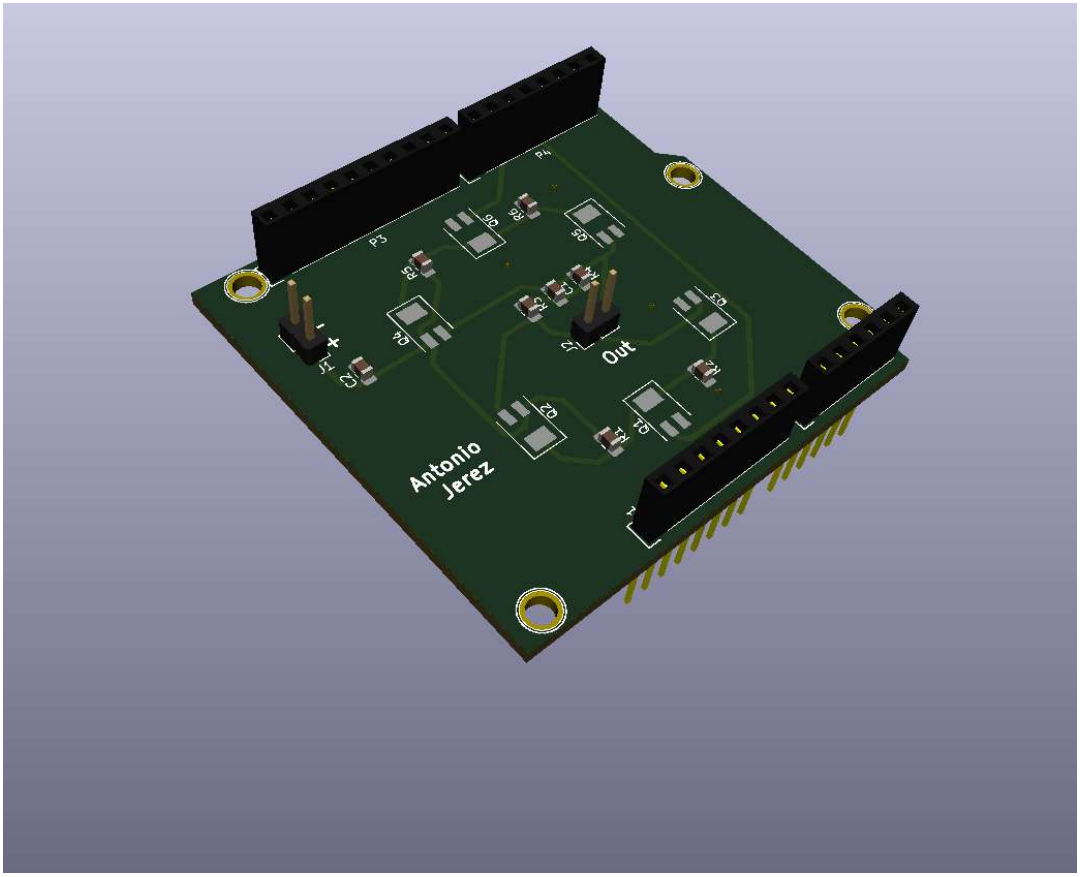

Figure 23: 3D model of the Arduino Shield

Once we had our PCB designed, we downloaded the Gerber archives and sent it to a company which could print them. In this case, we chose multi-cb (www.multi-circuit-boards.eu)

At the same time, we were looking for the components. The chosen company was Mouser (www.mouser.es). Regarding the components, we had no problem searching for them (apart from the 100 uF capacitor).

4.3.3. Software development

As we said several times during this paper, as we are doing an Arduino shield, the more suitable software to use would be the one which comes with the Arduino itself. The language is similar to C++, so it will come with its advantages and drawbacks. However, thanks to the reduction of variables we achieved during the hardware development, the number of variables is low, so it will be much easier for us to develop the software.

Until now, thanks to the H-bridge structure, we are able to get both positive and negative signal outcomes. However, we still need to get the other requirements listed previously, such as frequency, waveform, rest periods, etc.

The way we are going to achieve those achievements is through the software which Arduino uses. Most specifically, we are going to use PWM (Pulse Wide Modulation)

4.3.3.1. What is PWM

PWM is a technique which is possible to control the width of the gate pulses with the help of several mechanisms [28]. With this technique, we will be able to achieve most of the requirements left.

A PWM is principally a unipolar square waveform signal, which with the help of several tools, we will be able to modulate the duration of HIGH and LOW states' times. In other words, we can modulate the duration of its phases. The main tools that are usually used in PWM are two main commands: *analogWrite()* and *analogRead()*. In this project we will use only the former.

Before continuing the development of the project, we have to remember a detail from the hardware development section: the pins. As we said there, pins 3 and 5 were the ones we used to connect the Arduino board with the PCB. The reason behind it is that

those pins are two that can allow PWM. Other pins that can also be used are pins 6, 9, 10 and 11. They are easy to recognise because of the symbol "~" that appears next to the number.

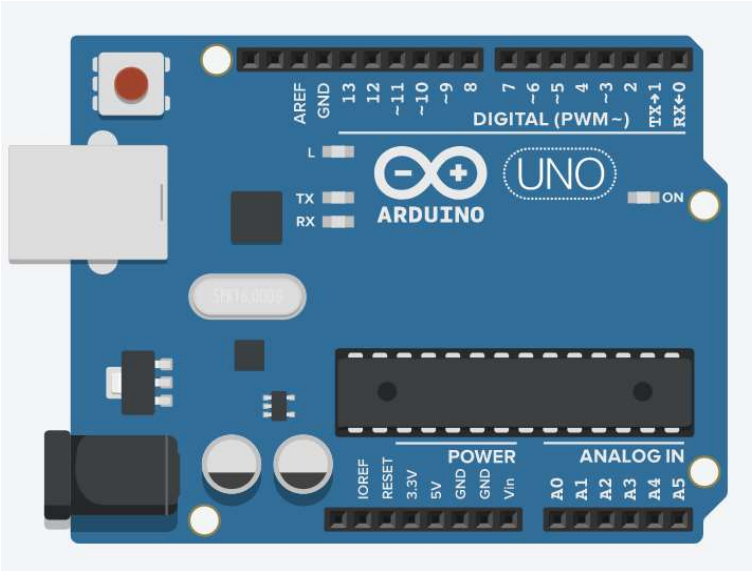

Figure 24: Illustration of an Arduino UNO board

Now that we have understood the definition of PWM, we should continue with the next element of the software, which is related to this technique: duty cycles. But before, it is important to point up one detail of the hardware part of the project. As we have seen, the main goal of the hardware is to get both positive and negative sections of the output signal. Later we will see that most of the requirements left to fulfil are attained thanks to the software. However, there is one left: the amplitude. As we said in the requirement section, this condition is down in the list of our priorities for the project, for the reasons already explained.

Nonetheless, this requirement could be the easiest to achieve, by just changing the voltage source. But again, due to safety concerns, plus both the limited budget and accessibility to compounds that handle high voltages, this requirement is long to be attained in this project.

4.3.3.2. Duty cycles and the *analogWrite()* command

The duty cycle of a signal (normally followed by a percentage) is the amount of time that said signal is at 5 V, which is one of the two possible states of a square waveform in PWM. Some examples for this could be:

- A signal with a 25 % of duty cycle means that during its own period, is only at 5 V the 25 % percent of the time.
- A signal with a 100 % of duty cycle means that during the entire period, is HIGH, or at 5 V.
- A signal with a 0 % of duty cycle means that during the entire period, is LOW, or at 0 V

In our case, we are interested in both the second and third case. The second is due to the necessity of a constant square waveform and we will use the third case for the resting periods, where there is no signal. This technique is truly useful in any kind of project which demands a detailed control of a square waveform, such as ours.

In order to control the duty cycle, we are using the *analogWrite()* command, which allows us to "write" in a pin the duty cycle of the signal we want to emit. This command has two parameters:

- The first is the pin which we want to control. In this case, the only pins that are able to use this command are the PWM's, in other words, pins number 3, 5, 6, 9, 10 and 11.
- The second is the duty cycle. As the Arduino board we are using (Arduino UNO) uses 8 bits, we must put a value between 0 and 256, being 0 the LOW state (or 0 % duty cycle) and 256 the HIGH state (or 100 % duty cycle).

With this tool, we are able to control both the waveform and the rest periods. There is only one main requirement left to achieve: the frequency. This one is a bit tricky,

due to, as we said in previous points, we need to achieve a low frequency (8 Hz). However, with the next tool, we will be able to get a great approximation of it.

4.3.3.3. The *delay()* command

This command is straightforward: the Arduino waits an "x" number of milliseconds before doing the next task. An example would be:

1. taskA;
2. delay(200); // Wait 200 milliseconds
3. taskB;

With this command we will be able to control both the transition from positive to negative waveform and the rest periods.

However, as we mentioned during the requirements section, most of the time lapses we need to attain are around the magnitude of microseconds, so this command is not capable of achieving it. Luckily, there is another command, called *delayMicroseconds()*, which does the same procedure, but in microseconds.

NOTE: The author of this paper acknowledges the existence of the timers, which is a feature of Arduino's software which, with different commands, is also possible to get the same functionality, even in a more efficient way. However, as we are going to see next, we thought the usage of the *delay()* command (and *delayMicroseconds()*) would make the software both easier to build and comprehendible.

Once we have all the tools that we need to build the software, we will explain all the thoughts behind its design.

4.3.3.4. Development of the Arduino program

In this section, it is going to explain the main parts of the code used for this project, which can be found in the Appendix B in the Annex section of the paper.

Variables:

a) *portA*. One of the two pins which we are going to use to control the H-bridge. Its value, as explained at the beginning of this section, is 3. It is an integer variable.
b) *portB*. Same as before, but instead of 3, it is 5. It is an integer variable.
c) *stim*. It is a Boolean variable which will help us to distinguish between stimulation and resting periods.
d) *cycles*. Counter variable which gives us the number of total cycles that the Arduino has already done.

void setup():

In this part, all the variables are set to its respective initial value or in this case, set the states of the pins.

a) *portA*. Thanks to the command *pinMode()*, we are able to set the pins as outputs or inputs. In this case, we are interested in using the outputs. Also, we set the duty cycles of those outputs to 0-
b) *portB*. Same as *portA*.
c) *stim*. We set its initial value as true, due that we want the device to start with a stimulation period.
d) *cycles*. We set its value to 0, as any counter.

void loop():

This part of the code is the one that coordinates the pins in order to attain our output signal.

In the first condition (if (*stim* == true)), is where the stimulating period is working. We write in the *portA* (the positive section of the signal) a 100 % duty cycle square waveform (through the *analogWrite()* command) and to the *portB* a 0 % one. We delay

29 microseconds and invert the states of the pins. In other words, now the *portB* has a 100 % duty cycle square waveform, while *portA* has a 0 % duty cycle one. Then, we add one to the *cycles* counter, meaning that a cycle has finished.

In case the *stim* condition is not fulfilled, the code puts both *portA* and *portB* to 0 % duty cycle and delays 125 milliseconds (which is the equivalent of a period of 8 Hz signal). Again, add one to the *cycle* counter.

Finally, we get to the part which decides if the code is in a resting period or in a stimulating one. The way is done by calculating the module (%) of cycles divided by twelve. The reason why we use twelve is simple. As we said during the requirements section of the project, both resting and stimulating periods have a duration of 1.5 seconds, or 1500 milliseconds. In other words, as our signal has a period of 125 milliseconds, in a whole period, there are 12 cycles, thus that is the reason we use this number.

Then, if the condition is attained, we change the value of the variable *stim* from true to false or vice versa.

Chapter five

5. Verification of the results

As it was mentioned at the beginning of this paper, in this chapter we will discuss the results of the project. In order to do it, it will be divided into two parts: a simulation verification, where we are going to use *TinkerCAD*, and a "real" verification, where we will expose the results of the designed PCB, with the help of an external voltage source and an oscilloscope, both granted by the University of Málaga.

5.1. Simulation verification

Normally, before printing the PCB, we would assemble the circuit in a protoboard in order to be reassured that the design works. However, as we had a failure during the first attempt, we ran out of time, so we skipped that step and went directly to the PCB design.

Nevertheless, as we wanted to be on safe ground, it was decided to find a way to simulate the circuit in the most faithful way. This is when *TinkerCAD* enters the equation.

The greatest utility of *TinkerCAD* is the capacity of be able to simulate with an Arduino board. This, and its visually design, allow it to facilitate the process of simulation.

Next, we will see the schematic assembled in *TinkerCAD* in the Figure 22:

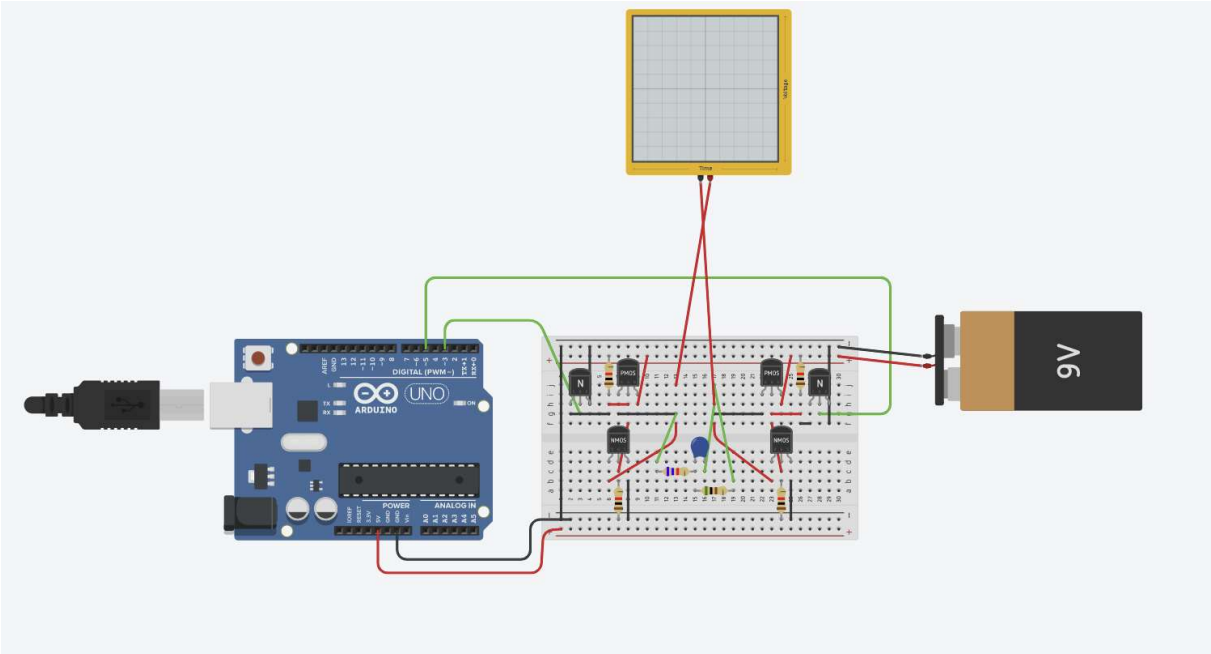

Figure 25: Schematic of the H-bridge

The only difference between this design and the KiCAD one is the voltage source, which here is 9 V, instead of 12. That does not concern us, due to, as it was explained before, changing that parameter only changes the total amplitude of the signal, which is not our main priority.

The way we made the procedure for the simulation was through several iterations. In other words, we will be changing the values of the parameters to be sure that everything is working as intended.

In the first iteration of the simulation, we change the values of the *delay()* commands with these ones:

- For the positive phase of the signal, 40 ms.
- For the negative phase of the signal, 85 ms.
- And for the resting period, 125 ms.

The results are exposed in both Figures 23 and 24.

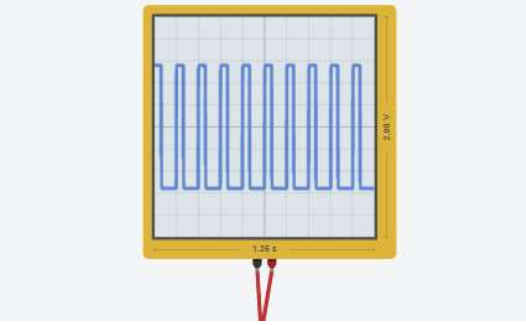

Figure 26: First results of the simulation (125 ms/div)

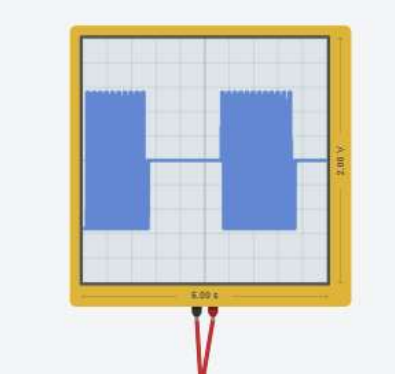

Figure 27: First results of the simulation (500 ms/div)

In Figure 26, we can see that both code and circuit work as intended. It attains the requirements that we prioritise: the biphasic and asymmetry characteristics of our desired signal. Regarding the phases' duration, as we can see, are easy to manipulate, but it presents a problem which we will address later.

In Figure 27, we can also see another of our requirements, the coordination of both stimulating and resting periods. In this case, we managed to set the durations of the periods to 1.5 seconds each.

Now that we know that both the code and the circuit work as intended, a second iteration of the simulation is going to proceed. This time setting the parameters to the real values. Those will be:

- First phase's duration: 29 microseconds
- Second phase's duration: 124 milliseconds (approximately)
- Resting period's duration: 125 milliseconds.

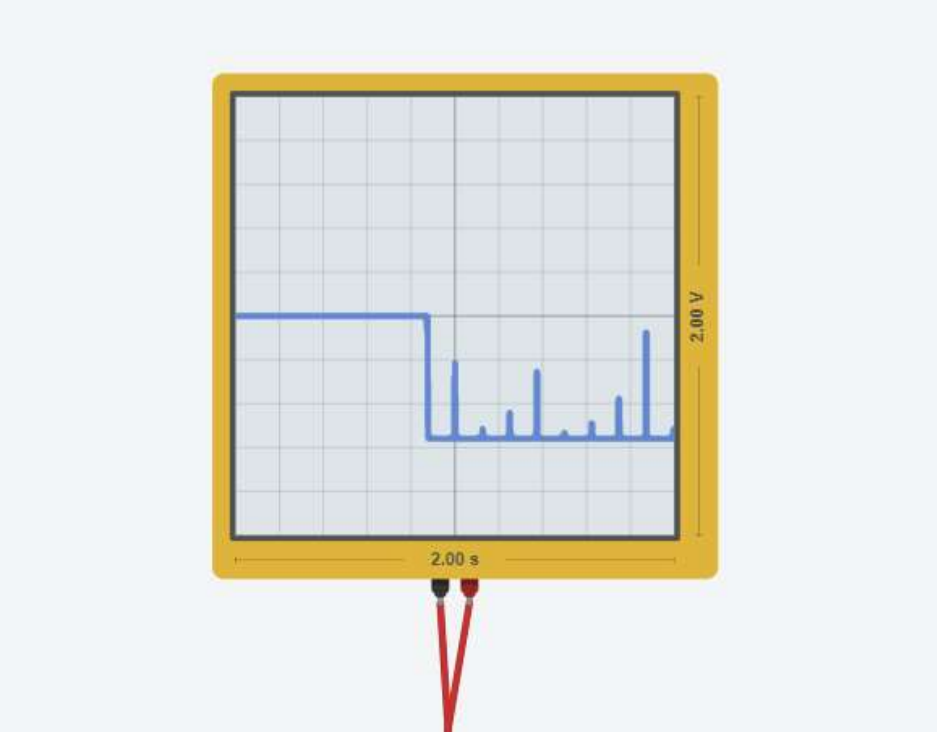

Figure 28: Results of the second iteration of the simulation

As we can see in Figure 28, the output signal starts to behave in an unusual way. This can be due to two main reasons: (1) The simulation software has its limitations, and, as we have used a low value as parameter, the system cannot handle it, or (2) both Arduino board and/or software are the ones that cannot handle the low values.

5.2. Real-time verification

Now that we are mostly reassured that the design works, it is time to prove it with the actual PCB. We used the tools that the Electronic Technology Department disposed us for the project. Those were an oscilloscope, to see the output signal, a voltage supplier and a couple of sensors. In Figure 25 we can see how it was assembled.

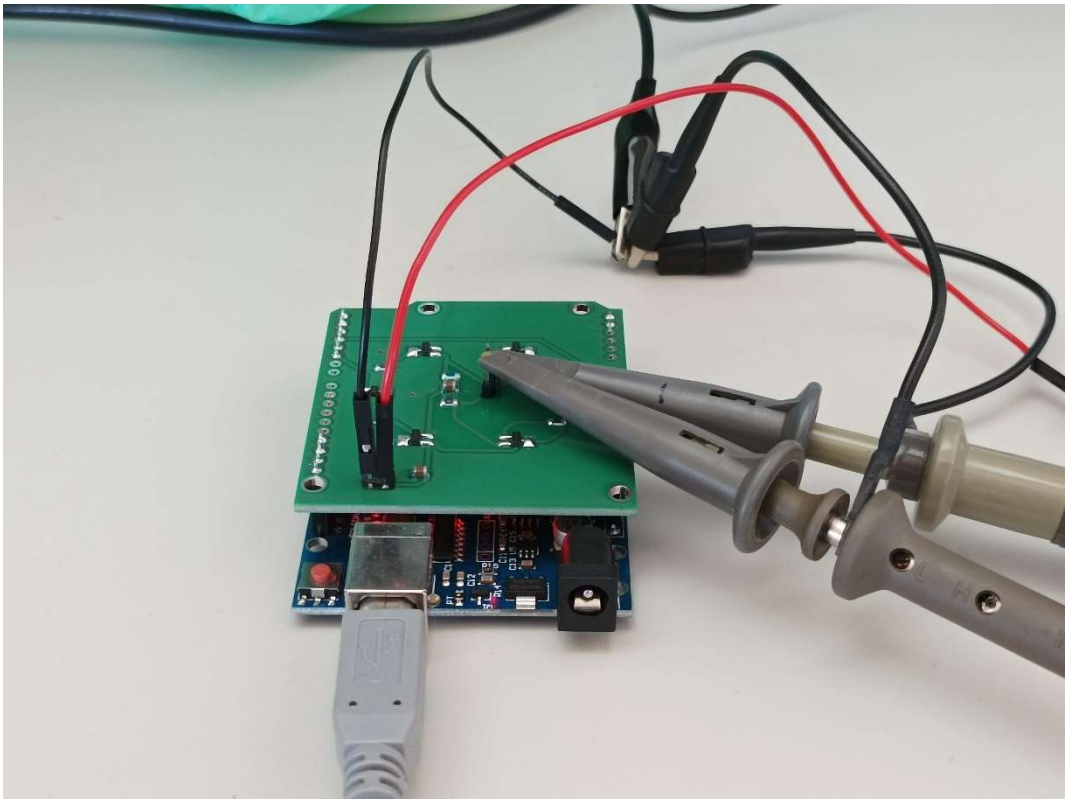

Figure 29: Design PCB assembled with the Arduino Board

The rest of preparations was just to connect the cable to a PC's USB port to link the Arduino board to its software.

In order to maintain the coherency between this trial and the simulations, we set the voltage supplier to 9 V, as we can see in Figure 27.

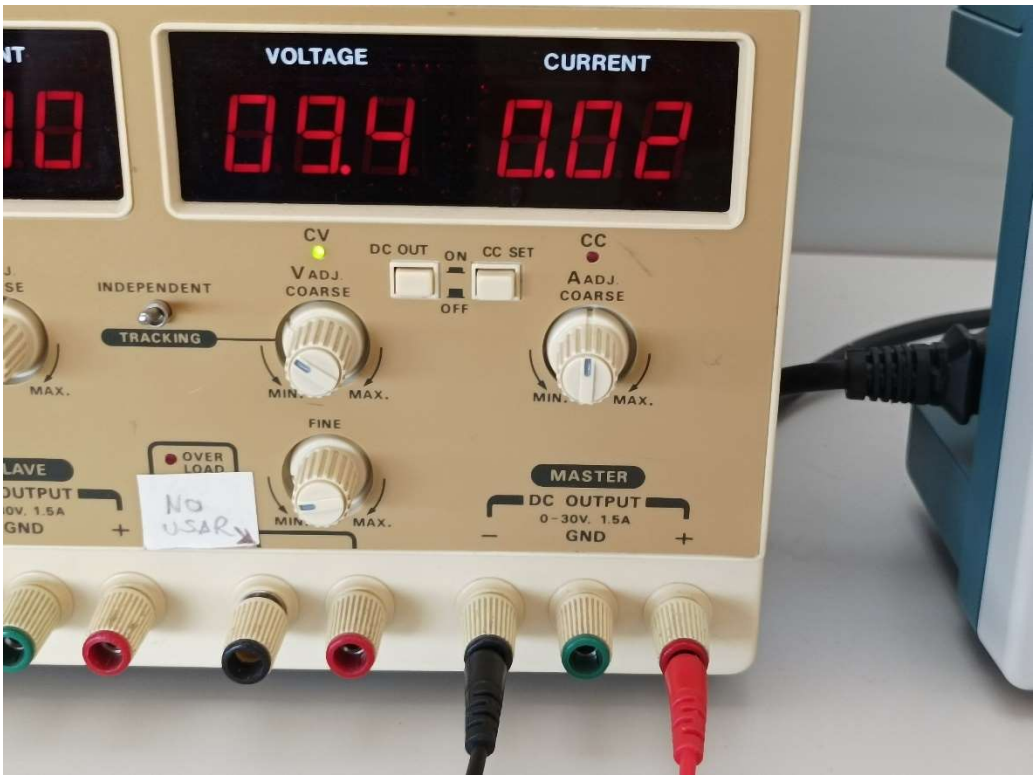

Figure 30: Voltage supplier used for the device

Once everything was prepared, we ran the code and started recording the results. We proceeded in the same way as we did in the simulation verification: through iterations with different values in the parameters.

But first, we must consider an important factor that may affect the verification process. As the trial is being done in the laboratory, the results are not going to be as clean as the ones we got previously. So, in order to get the output that we want to be as faithful to the simulations as possible, we will make a few changes.

To achieve it, we are going to use the settings that are provided by the oscilloscope. Mainly, we will use the coupling setting, so we may see the different characteristics of our signal.

If we set the oscilloscope to CC, we can distinguish different square pulses of the signal, along its resting and stimulation periods. However, we will not be able to see the negative part of the signal.

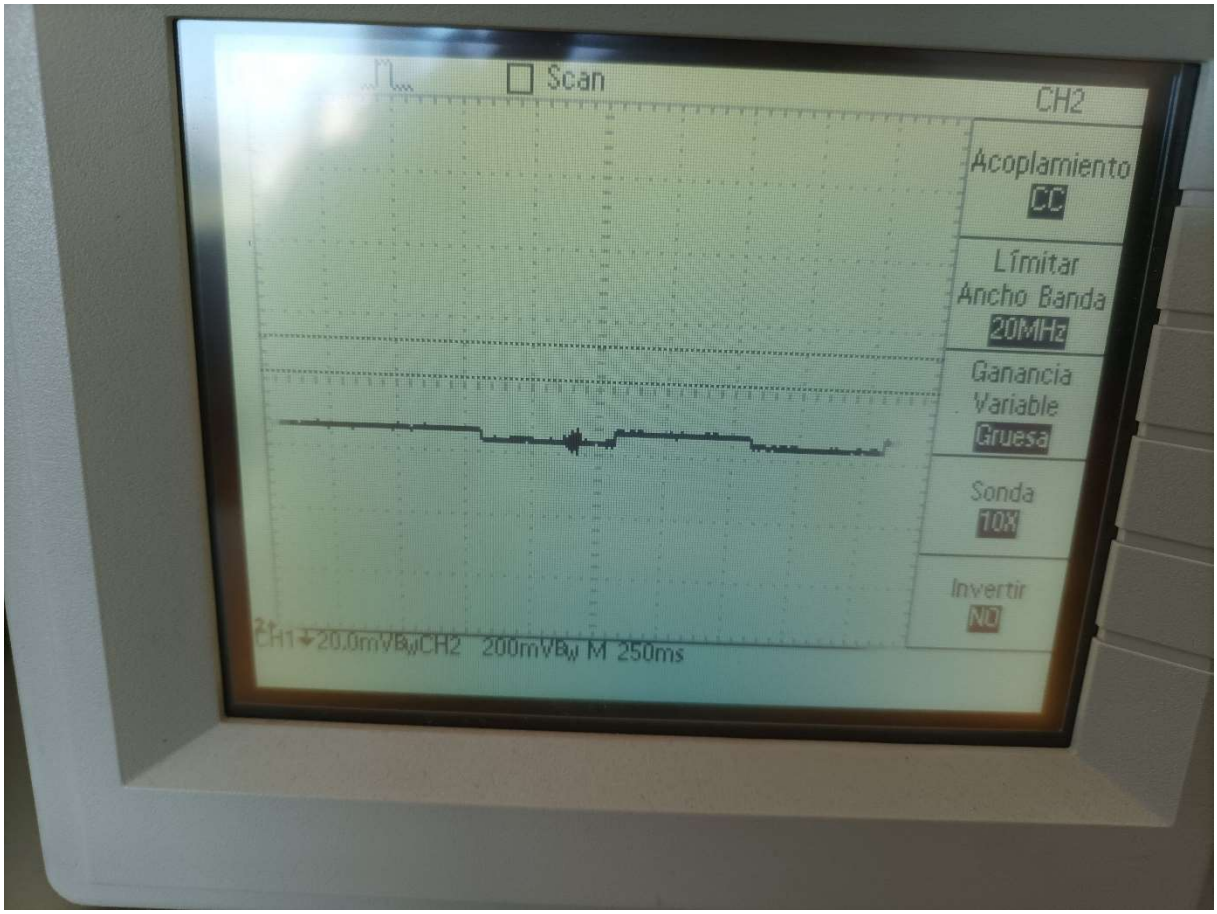

Figure 31: Results of the first iteration: with CC, where we can see the square waveform and both resting and stimulating periods.

Now, if we change to AC, although we will see the signal less clear (like it was filtered), it will be possible to distinguish both negative and positive phases of the output, as well as both resting and stimulating periods.

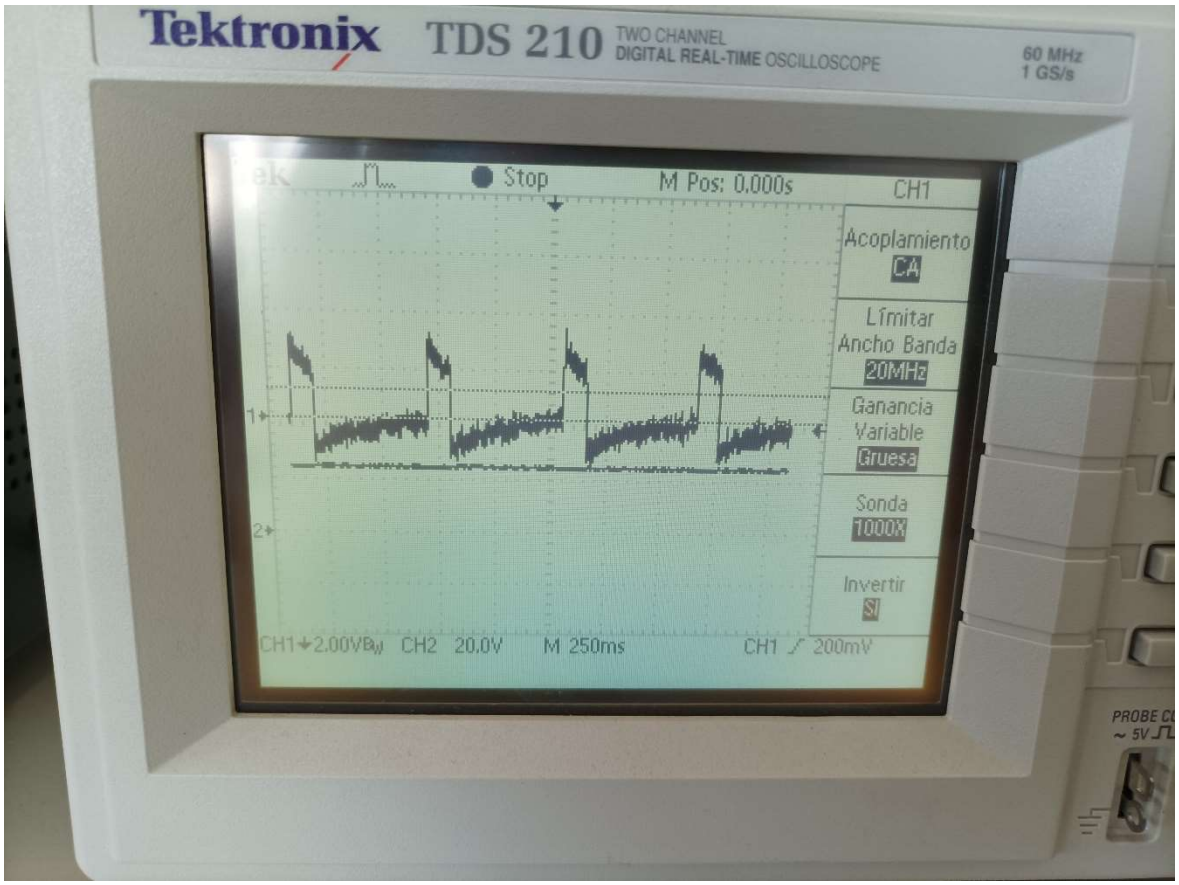

Figure 32: Results of the second iteration: with CA, where we can see both positive and negative phases of the signal.

As we have seen, it is clear that both the device and software are working as intended. However, as this was our first iteration, we were using values for the duration of the phases long enough to appreciate the different characteristics of the signal, so these results, although valid for our verification process, are not final yet.

Following the same behaviour of the simulation, Arduino (or at least the board we are using) is not able to process signals with low values, normally when we use microseconds. In Figure 33, we will see the results when we set the first phase's duration to 6000 microseconds and second one's to 124 milliseconds (which in total corresponds to an 8 Hz signal, approximately).

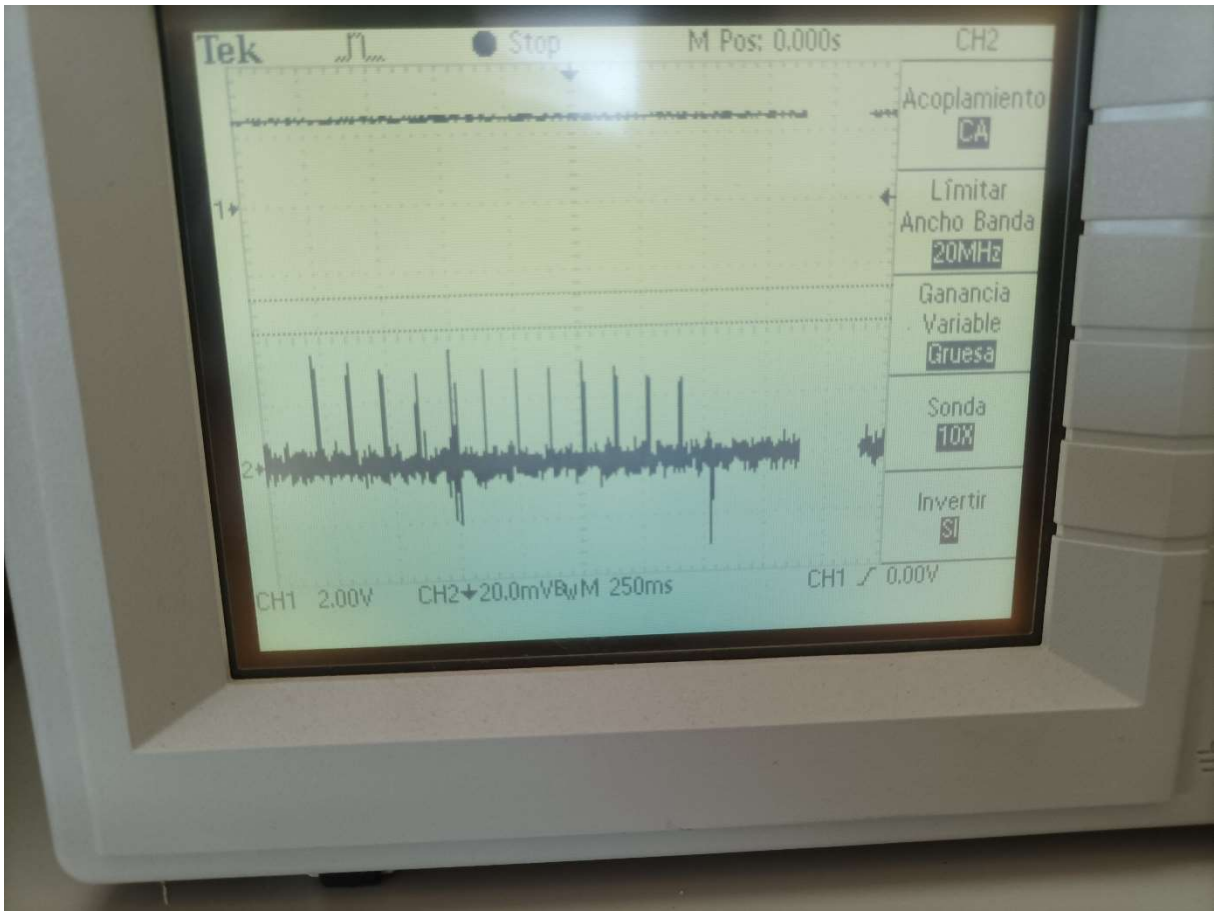

Figure 33: Results of the third iteration

In the last figure we can distinguish the twelve peaks of the first phase which correspond to the twelve cycles of a whole stimulating period. But, as it was mentioned, with such low values in the parameters (not even close to the one that we should use), we cannot even differentiate the square waveforms, although we know that they are.

5.3. Final validation

As a closure for this section, we will see all the requirements that were attained and which not.

Requirement number	Requirement characteristic	Description	Achievement state
1	Waveform	Square	Attained
2	Frequency	8 Hz	Attained
3	Amplitude	50 mA on a load of 1k¡ kiloohms	Not attained
4	Number of phases	Biphasic	Attained
5	Type of symmetry	Asymmetric	Attained
6	Duration of the first phase	29 microseconds	Not attained
7	Rest/Stimulating periods	1.5 seconds	Attained
8	Size	Portable (50 x 50 millimetre)	Attained

Chapter six

6.a. Conclusion and future work lines

As we have seen, this device is far from being clinically functional. However, it is important to remember that there is not that much research made regarding the use of electrostimulation as a treatment of DMD. Furthermore, we must consider that both the budget and the material we have used in this project is far below the necessary for a project of this calibre if we wanted to make it 100 % functional.

Other factors such as electronic security has also difficulted the verification process, due to, as testing it with a real subject was not in the plans since the beginning of the project, it left us to rely on other external measure devices, such as the oscilloscope. Even though the device could be capable of reproducing our desired signal if it was not for the limitations we had, because of the constant noise of the laboratory, we could not record it as faithful as possible to the simulations.

But again, this project was supposed to be a prototype whose main goal, besides the design and development of the device itself, was to highlight the importance of electromedicine nowadays and the wide range of possibilities of alternative therapies, such as electrotherapy, which are full of potential.

In fact, although this project's main concern was DMD, as we explained in the beginning of this paper, electrostimulation has shown even greater results in other chronic diseases, such as Parkinson's or Alzheimer's. Furthermore, as those diseases

are far more common, a larger pool of subjects is available for a more precise study, leading to a possibility of a more efficient design of an electrostimulation device.

Altogether, this project has been a nourishing experience, which has combined all the elements needed for any engineer project: from the lust of innovation and progress to the hard work and persistence to be able to find solutions to the problems during the entire process of design and development of the project.

6.b. Conclusiones y líneas futuras

Como hemos podido comprobar, este dispositivo está lejos de ser clínicamente funcional. Sin embargo, es importante recordar que no hay muchas investigaciones realizadas con respecto al uso de electroestimulación en DMD. Además, debemos tener en cuenta que los presupuestos y materiales empleados en este proyecto son mucho menores a los que habría en un proyecto de este calibre si quisiéramos hacerlo 100 % funcional.

Otros factores como la seguridad electrónica han dificultado el proceso de verificación, debido a que, como el testeo con sujetos reales nunca ha llegado a estar pensado durante ningún momento en todo el proyecto, no hubo otra alternativa que usar otros dispositivos externos de medidas, como puede ser un osciloscopio. Incluso siendo nuestro dispositivo capaz de reproducir la señal deseada, debido al ruido que hay en el laboratorio durante las pruebas, los resultados no eran tan fieles como han sido las simulaciones.

Pero de nuevo, este proyecto estaba pensado ser un prototipo cuyo objetivo principal, más allá del propio diseño y desarrollo de este, era realzar tanto la importancia de la electromedicina hoy en día, como el amplio abanico de terapias alternativas, como la electroestimulación, las cuales tienen un gran potencial.

De hecho, como ya bien explicamos al comienzo de este trabajo, aunque el mayor interés de este proyecto era el tratamiento del DMD, la electroestimulación ha mostrado incluso mayores resultados en otras enfermedades crónicas, como podrían ser el Alzheimer o el Parkinson. Además, siendo estas enfermedades relativamente más comunes que DMD, un mayor pool de pacientes disponibles para las pruebas facilitará la investigación, y así llegar a un diseño del dispositivo más eficiente.

En conclusión, este proyecto ha sido una experiencia que ha fomentado tanto mis habilidades y conocimiento como ingeniero, a través de la combinación de elementos fundamentales en cualquier proyecto ingenieril, como pueden ser el afán por la innovación y el progreso, hasta la persistencia a la hora de buscar soluciones a los problemas que van apareciendo durante el proceso del diseño y desarrollo del proyecto.

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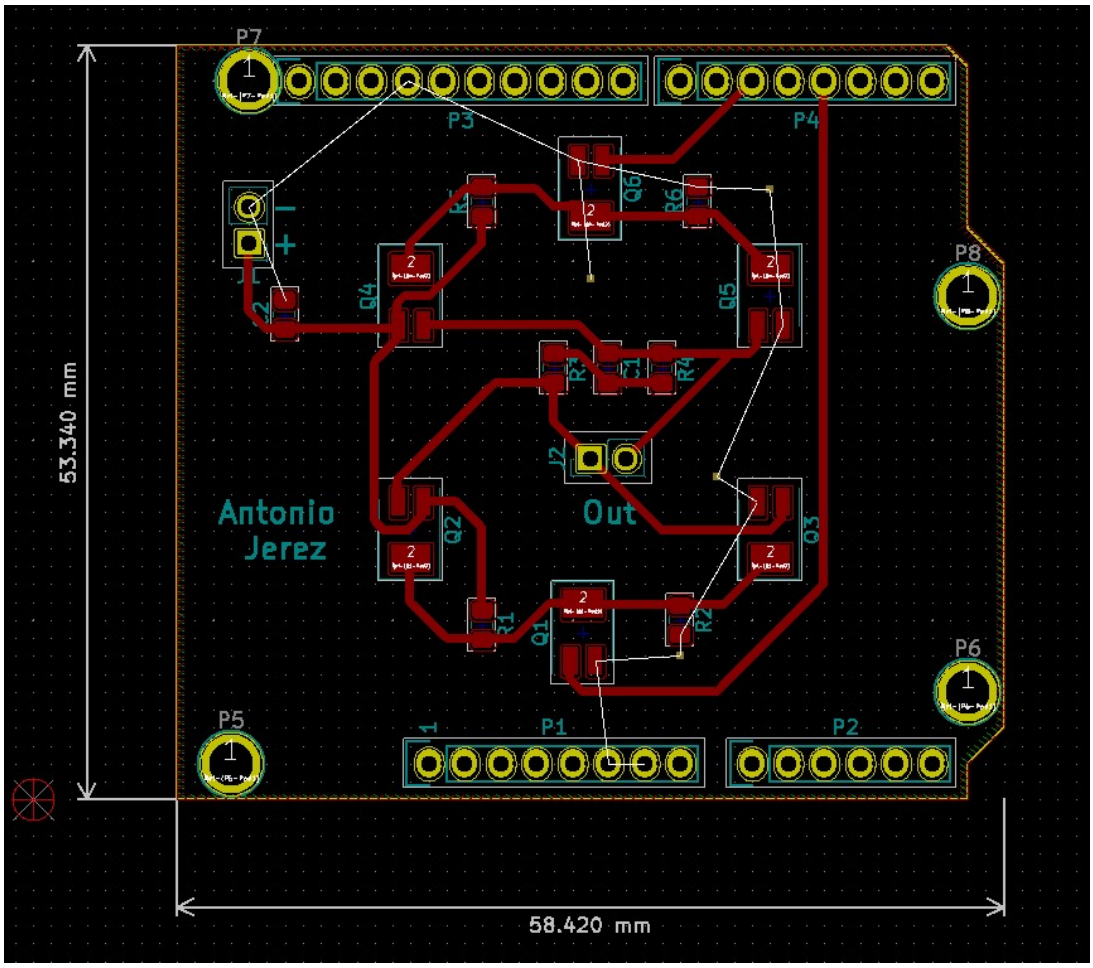
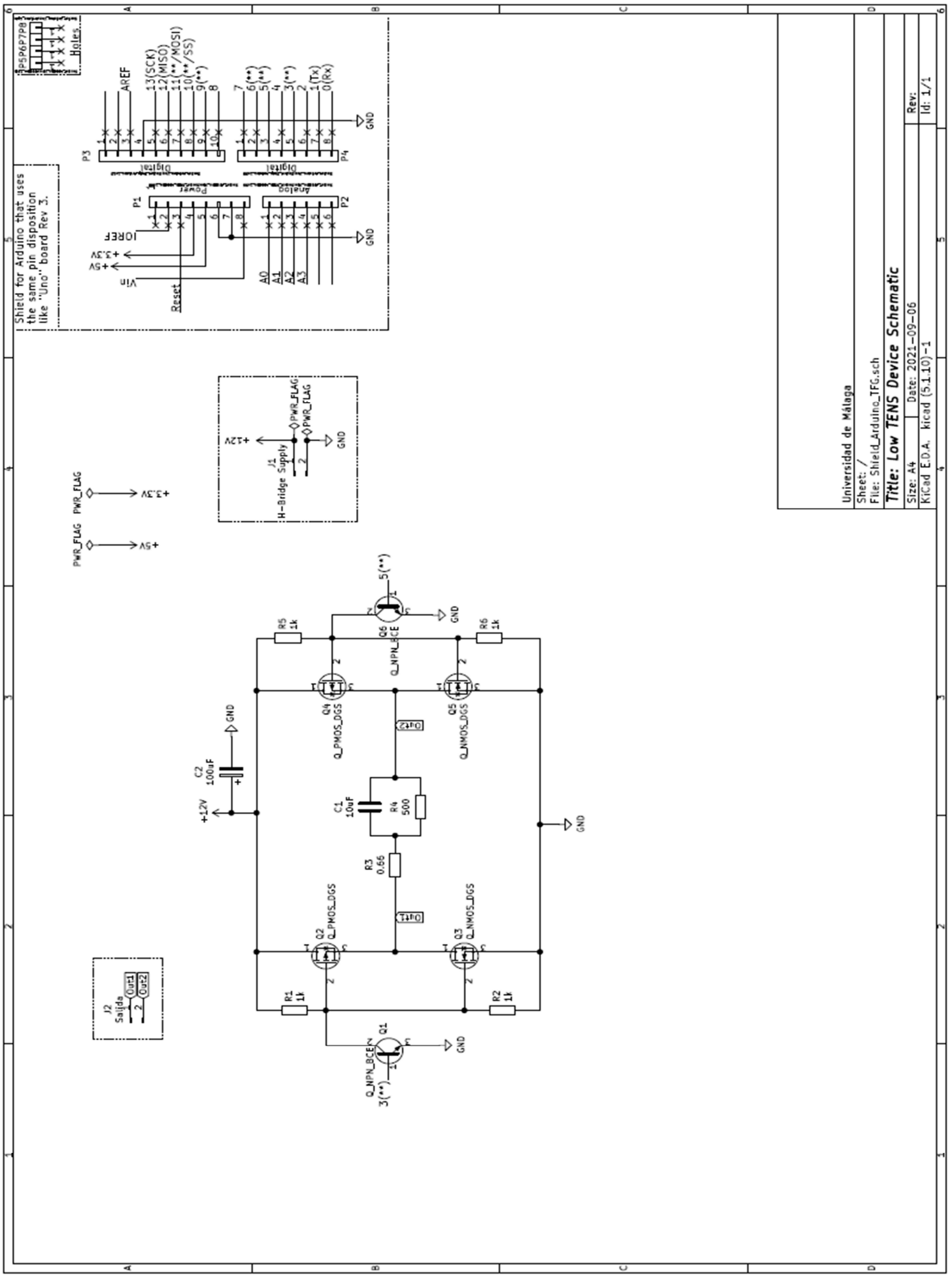
Annex

Appendix A

Annex I: Schematics


P7
P3
P4
P8
P6
P5
P1
P2
Q4
Q5
Q6
Q2
Q3
Q1
R1
R2
R3
R4
R5
R6
C1
J1
J2
Antonio
Jerez
Out
53.340 mm
58.420 mm


Shield for Arduino that uses the same pin disposition like "Uno" board Rev 3.
P5P6P7P8
Notes:
P3
P4
P1
P2
Digital
Analog
Power
AREF
13(SCK)
12(MISO)
11(**/MOSI)
10(**/SS)
9(**)
8
7
6(**)
5(**)
4
3(**)
2
1(Tx)
0(Rx)
IOREF
+3.3V
+5V
Vin
Reset
A0
A1
A2
A3
GND
J1
H-Bridge Supply
+12V
PWR_FLAG
J2
Salida
Out1
Out2
C1
10uF
C2
100uF
R1
1k
R2
1k
R3
0.66
R4
500
R5
1k
R6
1k
Q1
Q_NPN_BCE
Q2
Q_PMOS_DGS
Q3
Q_NMOS_DGS
Q4
Q_PMOS_DGS
Q5
Q_NMOS_DGS
Q6
Q_NPN_BCE
3(**)
5(**)
Universidad de Málaga
Sheet: /
File: Shield_Arduino_TFG.sch
Title: Low TENS Device Schematic
Size: A4
Date: 2021-09-06
Rev:
KiCad E.D.A. kicad (5.1.10)-1
Id: 1/1

Appendix B

Annex II: Software

- arduinohbridge.cpp

```
1 // C++ code
2 //
3 int portA = 3;
4 int portB = 5;
5 boolean stim;
6 int cycles;
7 void setup()
8 {
9   pinMode(portA, OUTPUT);
10  pinMode(portB, OUTPUT);
11 stim = true;
12  cycles = 0;
13  analogWrite(portA, 0);
14  analogWrite(portB, 0);
15 }
16
17 void loop()
18 {
19 if (stim == true){
20
21  analogWrite(portA, 255);
22
23  analogWrite(portB, 0);
24  delayMicroseconds(29);
25
26 analogWrite(portA, 0)
```

```
27
28 analogWrite(portB,255);
29  delay(124);
30  cycles++;
31   }
32 else{
33   digitalWrite(portA, LOW);
34   digitalWrite(portB, LOW);
35   delay(125);
36   cycles++;
37 }
38  if(cycles%12 == 0){
39       if(stim == true){
40            stim = false;
41  }
42  else{
43          stim = true;
44    }
45
46  }
47 }
```

Appendix C

Annex III: List of components

Work units	Unit of measure	Description	Quantity
1	Unit	MOSFET P-CHANNEL 80 V transistor SMD. REF: SI2337DS-T1-BE3	2
2	Unit	MOSFET N-CHANNEL 100 V transistor SMD. REF: SI2392ADS-T1-BE3	2
3	Unit	Thin film resistor 0.2 W 1Kohm 0.1% 10ppm SMD. Size 0805. REF: PTN0805Y1001BST1	4
4	Unit	Current sense resistor 0.665 ohms 1% 100 ppm SMD. Size: 0805. REF: SR732ATTER665F	1
5	Unit	Thin film resistor 500 ohms, 0,05% 5ppm SMD. Size: 0805 REF: TNPU0805500RAZEN00	1
6	Unit	MLCC-SMD Capacitor 25BDC 10 uF 10 % Size: 0805 REF: CGA4J1X7S1E106K125AC	2
7	Unit	BJT NPN bipolar transistor REF: FMMT624TA	2
8	Unit	Pinheaders 2x20 REF: 2-826925-0	1
9	Unit	Arduino Uno R3, microcontroler: ATMega328P, Clock speed: 16 MHz, Flash memory: 32 KB, Operating voltage: 5 V.	1

Appendix D

ANNEX IV: Electronic security

ELECTRONIC SECURITY

Based in the regulation EN 60601-1 and UNE-EN 60601-1—11:2015, which gather the general requirements for basic safety and essential performance of medical electrical equipment and medical electrical systems used in the home healthcare environment. We can distinguish:

According to used protection:

- **Class I**. Medical electrical equipment protected against electric shock by additional protection to basic insulation through means of connecting exposed conductive parts to the protective Earth in the fixed wiring of the installation.
- **Class II**. That medical electrical equipment whose protection do not rely only in basic isolation, but also provides a double isolation system or a reinforced one, with any connection of a protective Earth. Thus, accessible metallic parts cannot be actives with voltage assuming a failure in the basic isolation system.
- **Class III**. Electric device which disposes an internal voltage source, such as a battery, and has a protection against electrical discharges, based in the fact that there are not voltages greater than the maximum tension for low voltage devices (25 V AC or 60 V CC). This type of equipment is supplied with either a battery or a reductor of isolation converter.
- **Internal power supplied**. This type of equipment is not provided by any external electrical connection, but they will be supplied by a battery.

NOTE: The regulations about medical electrical equipment do not recognise Class III devices due to the limitations of the voltage being not enough to ensure the patient's security, although it uses the internal sourced equipment.

According to the level of protection

- Type B. All those electronic devices of Class I, II and III, or with an intern voltage source which supply an adequate grade of protection regarding the liability of the connection to Earth (if applicable).
- Type BF. Those type B devices with an input, or partly, floating circuit, applied to the patient.
- Type CF. Those class I, II or internal power supplied devices which allow a high grade of protection regarding the relation between current leakage and floating inputs.
- Type H. Those class I, II, III or internal power supplied devices which provide protection against electrical discharges comparable to household appliances' ones.

According to the previous classification, this device will be an internal power supply type BF device.

Appendix E

ANNEX V: User guide

USER GUIDE

Although this project's outcome is a prototype, thus it is not going to be used in anybody, we are going to describe briefly how the final product should be use.

1. **Verify the battery's state of the device.**

Before using the device, please verify if it is fully charge.

2. **Connect the lead cables to the device.**

Once your device is fully charged, connect the lead cables supplied to the device.

3. **Connect the lead cables to the electrodes.**

Now connect the opposite end of the previous lead cables to the electrodes.

4. **Place the electrodes.**

Two different electrodes must be placed:

a. The first one should be over the surface of the proximal rectus femoris
b. The second one should be over the surface of the distal part of the same muscle.

5. **Start the stimulation programme.**

Now that everything is ready, choose the stimulation programme and start it. As it is a pre-set programme, changing parameters will not be necessary.

NOTE: As this device is meant to be used in children, its usage requires the presence of any of their parents or legal tutors.

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