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OLLSCOIL NA HÉIREANN, CORCAIGH
NATIONAL UNIVERSITY OF IRELAND, CORK



**DEVELOPMENT OF A BIO-IMPEDANCE MEASUREMENT
SYSTEM FOR BLADDER MONITORING**

Thesis presented by

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for the degree of

DOCTOR OF PHILOSOPHY

UNIVERSITY COLLEGE CORK

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Declaration

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism.

Name: _____

Ardeshir Behrouzirad

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Abstract

The occurrence of disturbance in the control of urine flow and voiding, which leads to involuntary leakage, is called Urinary Incontinence (UI), and it may happen due to several factors such as pregnancy, family background, neurological disorders, etc. It has a negative impact on the social life and also the physical health of patients, highlighting the need for a mechanism to monitor the patient's bladder and warn them during their routine daily activities. For this purpose, the development of a low cost bio-impedance measurement system as a method for bladder monitoring is investigated in this thesis.

Prior to this thesis, the trend in the literature was to identify the correlation between the change of the impedance and the accumulation of urine in the bladder. Categorizing the current challenges and designing a bio-impedance measurement system, this thesis employs a vertical monitoring method, as a feasibility study, to increase the sensitivity of the measurement of impedance variation related to bladder fullness. Also, it employs a separate mechanism with extra sets of electrodes to address the issue of bladder relocation and its impact on the monitoring. The findings of the vertical monitoring method, with around 400 experiments performed on a phantom mimicking the abdomen and bladder, indicated the increased sensitivity of

45% and 52% in the measured impedance for two different urine conductivities, 1 and 2 S/m, respectively, after reaching 60 ml of volume, compared to the conventional horizontal monitoring in bio-impedance measurement. For the extra monitoring mechanism, when the target was relocated, with more than 500 experiments on the phantom, the sensitivity was increased between 1.43 to 4.61 times compared to the conventional horizontal method, depending on the urine conductivity and location of the target. The location of the target was found to be a key factor as the distance of the target to the electrodes recording the impedance change can vary and lead to erroneous outcomes, especially in the case where the bladder is far from the electrodes, due to individual parameters such as the weight or even posture. In summary, the thesis made an impact towards a non-invasive, wearable bio-impedance measurement system for bladder monitoring, by identifying and addressing important issues related to the areas that are still at their early stages.

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Chapter 1

Thesis Introduction: Objectives and Background

1.1 Overview of Bladder Monitoring

The bladder is the organ for accumulation of urine. As the pressure in the bladder increases due to the accumulation, stretch receptors will trigger a set of actions in order to facilitate voiding, although urination will not occur until a voluntary nerve impulse is received [10] (Figure 1.1). A complex neural network plays an important role as a switching circuit to maintain a reciprocal relationship between the reservoir function of the bladder and sphincter function of the urethra. This results in low-pressure filling, continence and periodic voluntary emptying. The frequency of micturition in a person with a bladder capacity of 400 to 600 ml is once every 3 to 4 hours, and the bladder is in a storage phase more than 99% of the time [11–13]. Switching from the storage to the voiding phase is initiated by a conscious decision, which is influenced by the perceived state of bladder fullness and

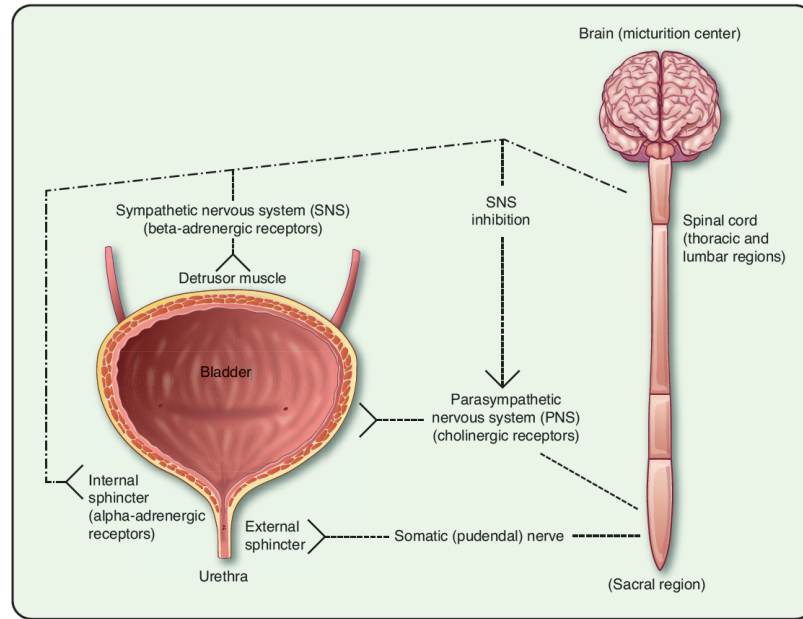


Figure 1.1: *Anatomy of a bladder and its receptors responsible for voiding* [3].

an assessment of the social appropriateness of voiding [12, 13]. However, due to various reasons, the voluntary micturition can be disturbed. The occurrence of disturbance in the control of urine flow and voiding, which leads to involuntary leakage, is called Urinary Incontinence (UI).

It includes voiding or obstructive symptoms such as hesitancy, poor and/or intermittent stream, straining, prolonged micturition, feeling of incomplete bladder emptying, dribbling, and storage or irritative symptoms such as frequency, urgency, and nocturia [3, 14]. Different types of UI are urge urinary incontinence (UUI), stress urinary incontinence (SUI), overflow incontinence and mixed urinary incontinence (MUI) [3]. In general, UI can happen due to several factors such as pregnancy [15–17], obesity [18, 19], increasing age [20, 21], family background [22, 23], neurological disorders [21], etc. In a report published by the World Health Organization (WHO), UI prevalence was found to be from 9.9% to 36.1% and the prevalence rate was higher in older women than older men [24–26]. UI severely and adversely impacts

the quality of lives of people experiencing it, forcing them towards being depressed, socially isolated and anxious [27–29].

Neurogenic bladder (NB), caused by neurological disorders, is the name given to a number of urinary conditions in people who lack bladder control due to a brain, spinal cord or nerve problem [30, 31]. Diseases such as multiple sclerosis (MS) [32, 33], Parkinson’s disease [34] or diabetes [35] can cause damage to the nerves leading to neurogenic bladder. It can also be caused by infection of the brain or spinal cord, heavy metal poisoning, stroke, spinal cord injury or major pelvic surgery [31]. People who are born with problems of the spinal cord, such as spina bifida, may also have this type of bladder problem [31].

It was reported that, in healthy males and females, the intravesical pressure¹ is typically from 50 to 80 cm H₂O, and from 40 to 65 cm H₂O, respectively [30]. In patients whose involuntary urination occurs due to neurogenic reasons, and the sense over bladder-filling is damaged, a high intravesical pressure is very common. Also, due to the lack of control of the bladder muscles, there will be some post-void residual urine (PVR) in the bladder after voiding [36]. Both high intravesical pressure and residual urine can cause urinary tract infection [37], since germs can easily settle on the inner wall of the bladder and cause infections. Also, urinary tract infection encourages the formation of urinary stones. If it remains untreated for a long time, the infection may continue through the ureters into the kidneys. The result is chronic kidney damage, which can lead to kidney failure. The infection can also lead to urinary retention [37]. Complete urinary retention is very painful and occurs when urine can not be released easily and it

¹The pressure recording from a urodynamic catheter placed inside the bladder [30].

leads to significant over-expansion of the bladder. In order to avoid infection from PVR and thickening of the bladder wall due to over-expansion, and its following consequences, regular catheterizing of the bladder is the standard treatment [30]. This can be performed both by a procedure called intermittent self-catheterization² (ISC) and indwelling catheterization³.

Indwelling catheterization increases the risk of other types of infections, so ISC is the preferable and standard method of draining the bladder fully [30]. However, there is no indicator to warn when the bladder is at normal full stage and when ISC should be performed; therefore, it has to be performed 4 to 6 times per day regardless. However, the problem of over expansion of the bladder still exists as the patients bladder could be full between the times of catheterization.

The negative impact on the social life and also the physical health of individuals who are encountering the problem of urine leakage and bladder control highlights the need for a mechanism to perform bladder monitoring to warn the patients in different situations during their routine daily activities.

So, in summary, if there was a device, preferably non-invasive and wearable, acting as an indicator to monitor the state of the bladder and to help to overcome the mentioned issues and prevent the emergence of the consequences, voiding could happen consciously, smoothly and gradually during the day and any risk of further related diseases can be avoided.

In the remainder of this chapter, an outline of the existing work in the area of bladder monitoring is provided. The aims of the thesis are set out

²Catheterization is performed by the trained patient or the caretaker and the catheter is removed after the urine has been drained.

³Catheter is placed permanently in the patient's body.

and the outline for the rest of the thesis can be found at the end of this chapter.

1.2 Methods of Monitoring

There are three approaches for bladder monitoring: 1- Ultrasound (US), 2- Ultra-Wideband (UWB) radar, and 3- Bioimpedance (BI) measurement. First the usage of US will be briefly explored, and the drawbacks of this method will be pointed out. Following that, the usage of UWB radar and later that of BI measurement for bladder monitoring will also be briefly discussed.

1.2.1 Ultrasound

Ultrasound is an inaudible sound at high frequency, which is used to create an image of part of the inside of the body [38, 39]. Medical ultrasound machines use sound waves with a frequency ranging between 2 and 15 MHz and emit and receive acoustic waves from a transducer into and from the body [40, 41]. Receiving the reflected echoes, the transducer transfers the data from the recorded waves, which could be absorbed, scattered, refracted, or diffracted as the wave travels and encounters different tissues, to the image display device [42], for such targets as the bladder.

US has received great attention for use in measuring the bladder volume in order to estimate the amount of urine, and being a clinically standard method, it has been used since 1967 for non-invasive bladder state monitoring [43]. There are three main US methods in this class used for bladder monitoring:

1. A-mode (1D) which is the simplest type of ultrasound sensing that scans and calculates the distance between the anterior and posterior wall of the bladder, hence enabling estimation of the bladder volume.

2. B-mode (2D) which yields an image composed of bright dots representing the ultrasound echoes and the bladder volume is then estimated using different signal and image processing methods.

3. 3D-mode technique which is used to render ultrasound data by accumulating 2D data gathered from different angles on one surface [44].

Among the studies performed from 1967 to present, the B-mode technique was found to be the most prevalent one for bladder monitoring [43, 45–62] with A-mode being used in [63–69] and 3D mode being used in [4, 70–72]. It should be noted that the few studies in the A-mode group were performed with custom designed and non-commercialized devices while the other studies, using the B-mode and 3D mode, were performed with commercial ultrasonic devices.

Among the many devices using the B-mode technique, there are two main methods of monitoring the urine volume from the reconstructed images: the prolate ellipsoid method and the double area method [73, 74]. Devices using the double area method can be used exclusively to detect specific types of issues related to accumulation of the urine in the bladder which is considered a limitation [75]. In the ellipsoid method, first the transverse, anteroposterior, and superoinferior diameter lengths of the bladder will be determined from two-dimensional US images and then the volume will be calculated based on a mathematical formula [73, 74]. Although this method is used in many current US devices [75], the need for a skilled operator to

manually select and measure the three diameters of the bladder is essential. Portable US devices for estimation of bladder urine volume are also available [62,76,77]; however, estimation without visualizations in these devices suffers from lack of accuracy in distinguishing between different structures, such as pelvic cysts and the bladder [75]. Continued until late 2021, the latest study in [4] presents an ultrasonic wearable bladder monitoring device with a 5×5 piezoelectric element array integrated on thin substrates (Figure 1.2). With experiments performed on a pig's bladder placed inside a water tank, the proposed system with the developed algorithm when compared to commercial equipment, had an average error of 24 ml and 29 ml, respectively, from the real volume. Although the authors introduced the usage of an array of transducers which is small in size and suitable for a wearable device, the electronic system required to perform the measurement with the arrays seemed to be hard to implement in a wearable scale and, as for recording the reflected signal, an oscilloscope with 2 GHz sampling frequency was required. Also, the algorithm to reconstruct a 3D image seems to be time consuming. The authors indicated that clinical trials using the developed sensors are planned to determine the volume accuracy of urinary bladders.

During the search for bladder monitoring with ultrasound, two wearable devices were found to be available in the market, namely SENS-U⁴ and DFree⁵ [78, 79] (Figure 1.3). SENS-U, targeted for urinary incontinence in children, consists of four ultrasonic transducers over a peripheral vision of 30° that emits ultrasonic waves upright to the abdominal walls. The bladder's height and volume are determined by measuring the average

⁴More information can be found at the manufacturer website: <https://novioscan.com/how-it-works/>

⁵More information can be found at the manufacturer website: <https://www.dfreeus.biz/how-it-works>

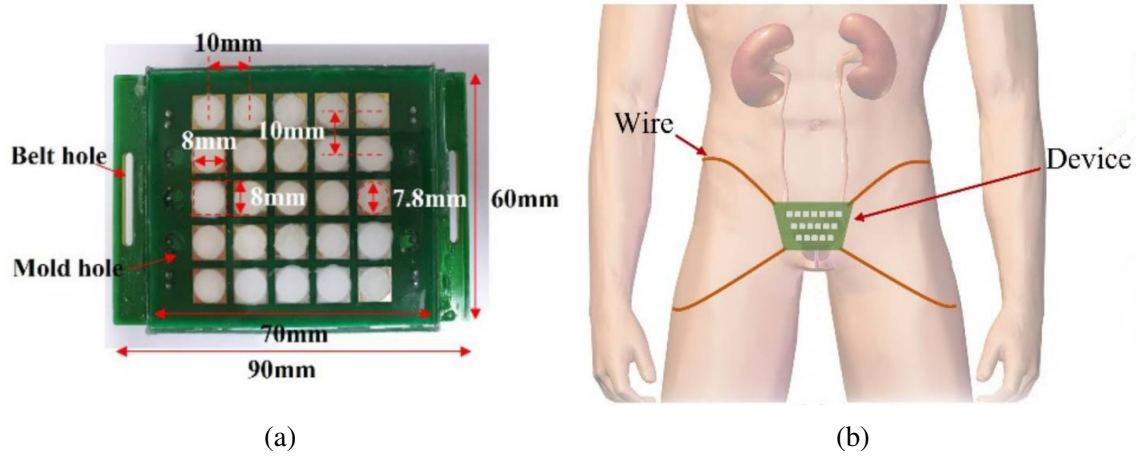


Figure 1.2: Illustration of the wearable urinary bladder scanner system a) Fabricated arrays of US sensors b) conceptualized picture of its placement [4].

anterior-posterior bladder length. It is recommended to modify the SENS-U transducer module for obese children by increasing the field of view and the strength of the ultrasound wave. The focus of the future research will be on reviewing the effect of SENS-U in incontinence training and assessing the level of compliance in children to optimize bladder notifications [44].

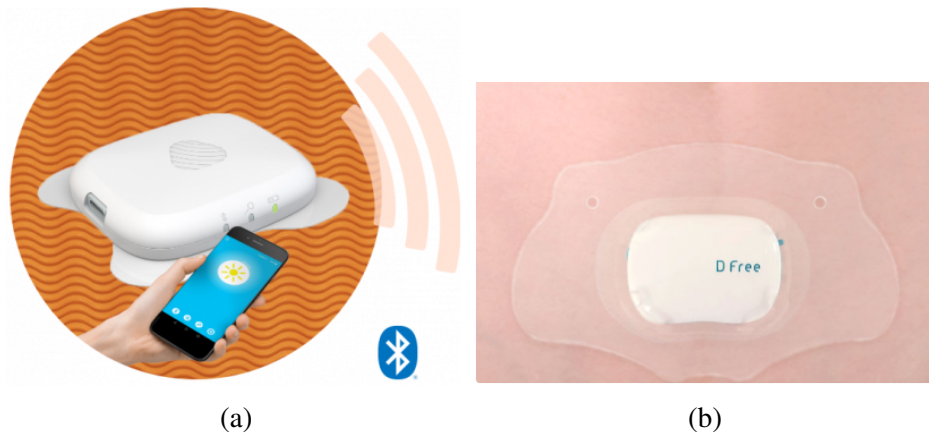


Figure 1.3: Ultrasonic based wearable bladder monitoring devices a) Sens-U, b) Dfree. Images were taken from manufacturer websites (see footnotes 4 and 5, respectively).

DFree supports those who cannot easily get to the toilet without other's help. Although being reported to be the first wearable product for continuous bladder monitoring by their website, Dfree is not a medical de-

vice, meaning it has no diagnostic, preventive or therapeutic applications. To properly detect the bladder volume with it, the sensor should be placed about half an inch above the pubis bone [44], although no technical detail and working mechanism are publicly available.

To summarize this section, US is a promising tools for bladder monitoring; however, one main drawback, is the necessity of a physician for scanning and interpreting the data, specifically in hospitals. As the technology is advancing, the size of the device is moving towards the smaller range, but susceptibility to individual factors and a fixed orientation to scan the bladder are the remaining issues. The cost of the device could be a limiting factor depending on the type of the device whether being a portable/wearable or stationary but, more importantly, is the error rate of bladder state detection due to its intrinsic limitations and sensor placement. Body movement is also a limiting factor that should be considered while using an ultrasound based wearable device [44, 80–82].

1.2.2 Ultra-Wideband Radar

Ultra wide band radar (UWB) is another technology which could be used for bladder monitoring. Being at the early stages, with pilot studies on animals or humans yet to be completed, the technology is a form of microwave imaging that works by emitting a radio pulse into the body within the designated UWB frequency range of 3.1-10.6 GHz [83] and recording reflected and/or transmitted signals by antennas, depending on the dielectric of different tissues. Urine has a high water content and, consequently, a larger relative permittivity than surrounding tissues in the pelvic region, which can be used as a potential factor to detect its volume [84].

The technology has been examined in both simulations and with experimental phantoms of varying complexity [84–91]. Different works have reported the use of various materials to emulate urine: tap water [88], sea water [92], saline based salt water [86, 89], and tomatoes, which are noted to have a 93% water content [93]. In [86], a good match was found between the relative permittivity of 0.5% salt water and urine. However, the properties of urine are being explored, and the conductivity, in particular, spans a potentially wide range of values across the microwave frequency range [91]. Therefore, pending more data about the properties of urine in this frequency range, studies may benefit from examining multiple urine-mimicking solutions to encapsulate a range of expected urine properties. Additionally, the properties of materials such as tap water, sea water, and tomatoes are not fixed and may vary depending on the source, place and time. Thus, the use of saline solutions with different concentrations of salt to mimic varying urine conductivities would provide experimental results that are more repeatable across labs and through time. Aside from notable differences in the pelvic models and phantoms across studies, it is also important to consider the antennas used in the microwave setups. The majority of the works used Vivaldi antennas [85–88, 92–95], while a handful employed bow-tie antennas [87, 89, 96]. In [87], it was found that Vivaldi antennas outperformed bow-tie antennas in terms of differentiating urine volume, likely due to their more directional radiation pattern. With more directional antennas, it is expected that the received signal would have a higher amplitude due to lower scattering loss [91]. However, a trade-off with directional antennas is that a number of antennas and antenna measurement locations may be required

to receive a reflection from the urine, and, indeed, the best placement to receive a reflection may change from person to person and as the bladder fills, which can be another drawback to its use as a wearable device [91].

1.2.3 Bio-impedance Measurement

Impedance measurement has been used for various applications from monitoring biological events for detection of a change in the target condition [97] to monitoring flow of fluid in pipes [98,99]. Impedance measurement is conducted mainly by applying a voltage or current to the target and measuring the variation of current or voltage from the target. The impedance is then calculated from the known applied signal and the measured signal from the target. A more detailed explanation can be found in Chapter 2 regarding the calculation of impedance. The term Bioimpedance (BI) is a broadly applied term when using impedance measurement for body composition and health-care assessment systems [100].

In the early studies (from the 1970's) using BI measurement for bladder monitoring, it was used in an implantable signaling device to help urination happen artificially, in disabled and spinal cord injured patients [101–106]. Those studies started a trend for bladder monitoring. Other studies continued from 2011; since then, development of non-invasive bladder monitoring has received more attention for investigating the possibilities to issue early warning regarding the fullness of the bladder. Indicating the BI measurement was a potential tool, those studies were classified into four categories in this thesis: (i) Clinical trials for proof of concept, (ii) improving the software algorithms used in BI measurement for bladder fullness classification, (iii) exploring optimum set-ups for measurements such as the effect of elec-

trode position and the types of electrodes and, (iv) designing an electronic readout system. Because a BI measurement system for bladder monitoring is a complex system, studies in each of the mentioned categories were conducted together, depending on the researcher's area of expertise. A detailed literature review, from 1969 to 2021 of using BI measurement for bladder monitoring will be presented in Chapter 2 of the thesis. In the next section, the challenges associated with such system are identified based on the literature review, and the aims of the thesis will be stated subsequently.

1.3 Challenges Associated with BI Measurement for Bladder Monitoring

Based on the review of the state-of-the-art, usage of a BI measurement system for bladder monitoring is challenging due to the following issues:

1- ***Accuracy in readings and measurements:*** Suffering from relatively low signal to noise ratio (SNR), is typically the main drawback of the electronic systems. The main step towards achieving a bladder monitoring system is to have an electronic device with low error and high accuracy.

2- ***Issues with the skin-electrode impedance:*** The type of the electrodes that are used to apply and record the signals is important. Wet electrodes have low skin-electrode impedance which eases the required criteria to design an electronic device for bladder monitoring; however, an issue arises when the gel starts to dry out after a certain amount of time, usually one or two hours. The solution would be to either change the electrodes or add extra gel, which means detaching the device. On the other hand, dry electrodes are more comfortable to wear as there is no need for gel and detaching them

is not required; but, they feature higher skin-electrode impedance which makes the design criteria challenging.

3- ***Error caused by location of the bladder***: Apart from the type of electrodes, their role is to be placed on the abdomen as probes to apply and record signals. Their location is going to be fixed on the abdomen; however, due to different postures and positions, the location of the organs and bladder might vary. This may cause an error in the measurement as some of the electrodes may not be covering the area of interest, and, hence, may not be measuring changes of impedance due to the change in urine level in the bladder.

4- ***Urine conductivity, BMI, Shape/Size of the body, Gender, etc.***: Individual parameters play an important role when measuring the impedance of a section of the body. One of the most important factors is urine conductivity. During the day urine conductivity typically changes because of eating and drinking various foods. This means that a certain volume of urine in the bladder can have a different associated impedance, which makes it challenging to monitor the state of a bladder.

1.4 Thesis Aims and Organization

The issues mentioned in the previous section are the challenges yet to be solved in using a BI measurement system for bladder monitoring. The thesis is focused on developing an electronic readout system suitable for bladder monitoring and addressing the issue related to the variation in urine conductivities, and bladder relocation. The aims of this thesis are summarized in four steps:

1- Identifying and understanding the constituent blocks required to perform BI measurement and extracting the electronic design specifications and challenges.

2- Design and implementation of a prototype of a readout system for bladder monitoring based on BI measurement.

3- Proposing and investigating the feasibility of a measurement method to increase the sensitivity of impedance variation related to bladder fullness.

4- Proposing and investigating the feasibility of an extra scanning mechanism to address the impact of a change in location of the bladder.

The thesis is organized as follows:

- Chapter 2 presents a literature review of existing BI measurement systems for bladder monitoring and explains the fundamentals of BI measurement, the electrical behavior of tissue, the electrical model of the tissue under test and the electrode configurations used in this thesis.

- Chapter 3 describes the system level block diagrams and design procedure of the electronic device in order to achieve aim 1 of the thesis. It also introduces the proposed method and an extra scanning mechanism to address the problem of variation in urine conductivity and bladder movement (aims 3 and 4).

- Chapter 4 will present a deeper analysis of the current injection block of the electronic circuit. The performance results of the designed block can be found towards the end of the chapter.

- Chapter 5 describes the data acquisition block and performance results of printed circuit boards (PCB) for the BI measurement system (aim 2). Also, it describes creating a phantom made from a known recipe in the

literature, and experiments performed on the phantom. Those experiments were performed in relation to aims 3 and 4 of the thesis. The results and discussion of those experiments can be found towards the end of the chapter.

- Chapter 6 concludes the work with a summary of the research contributions in this thesis and outlines opportunities for future work.

Chapter 2

Bio-Impedance Measurement: Review, Theory and Fundamentals

2.1 Introduction to Bio-Impedance

Bioimpedance analysis is a broadly applied approach used in body composition measurements and healthcare assessment systems. There is a wide spectrum of utilization of bioimpedance in healthcare facilities such as disease prognosis and monitoring of body vital status [100]. Impedance (Z), from an electrical point of view, is the obstruction to the flow of an alternating current and, hence, is dependent on the frequency of the applied current. It is defined in impedance magnitude ($|Z|$) and phase angle (ϕ). Bioimpedance refers to the electrical properties of a biological tissue, measured when current flows through it. The reason that a current should be applied to the body, and in general a tissue, instead of voltage, is due to the standard IEC60601 [107, 108]. As the impedance of the tissue under test is not known, by applying a voltage there is a chance of damaging the tissue

by unintentionally forcing excessive current through it. In accordance with the standard, this current is limited to 100 μA at low frequency and increases with frequency to 10 mA at 100 kHz [107].

The impedance of the tissue varies with frequency and tissue type, and varies sensitively with the underlying histology. The resistance and the capacitance of tissue are the two basic properties in bioimpedance. Resistance in an aqueous solution, as in a living tissue, is a measure of the flow of ions among its cells. It is the ease or difficulty with which the charged particles can flow. For the purpose of BI, a useful concept for current passing through a capacitance is ‘reactance’ (X_c). Resistance and reactance have the following relationships:

$$\text{Resistance} = R(\text{Ohm}) = \frac{V(\text{Volt})}{I(\text{A})} \quad (2.1)$$

$$\text{Reactance} = X_c(\text{Ohm}) = \frac{1}{2 \times \pi \times f(\text{Hz}) \times C(\text{Farad})} \quad (2.2)$$

When a current is passing through a purely resistive component, the voltage recorded across the resistor will be in phase with the applied AC current. For a capacitor, the voltage recorded across it lags behind the applied current by 90° . When a mixture of resistive and reactive components are present, which is the case for BI as the tissue consists of different types of materials, ϕ is intermediate between 0° and 90° , and depends on the relative contributions of resistance and reactance. The phase ϕ is closer to 0° at lower frequencies and closer to 90° at higher frequencies. Therefore, the impedance of any object, including components or materials with resistive

and capacitive (RC) behavior, can be represented as :

$$\begin{aligned} \mathbf{Z} &= R + jX_c & |Z| &= \sqrt{R^2 + X_c^2} \\ & & \phi &= \tan^{-1}\left(\frac{X_c}{R}\right) \end{aligned} \quad (2.3)$$

Also, considering (2.1), which is Ohm's law, more generally impedance can be represented in magnitude and phase notation:

$$\mathbf{Z} = |Z|\angle\phi \quad \text{where :} \quad |Z| = \frac{|V|}{|I|} \quad \phi = \angle V - \angle I \quad (2.4)$$

Therefore, by measuring the voltage amplitude across the unknown impedance and dividing it by the known applied current amplitude, the magnitude of the impedance can be obtained. To obtain the phase angle of the unknown impedance, the phase difference between the applied current and the measured voltage should be determined.

In the following section, a thorough review of the state-of-the-art, from the early 60's to present, in the area of BI measurement for bladder monitoring is provided.

2.2 Review of BI Measurement Systems for Bladder Monitoring

Urinary tract infection, which can be caused by catheterization leading to UI, is a major problem in paraplegic patients, and all patients eventually develop urinary tract infection which increases the morbidity as well as the mortality [101]. In a study performed on 746 World War Two veterans with spinal cord injury in 1962, the percentage cause of death which was attributed to urinary tract infection was 64%. In order to address this issue

and introduce artificial urination, electrical stimulation was employed [101]. An experiment was performed on fifteen dogs' bladders (invasively) in order to obtain the parameters. The setup was a 4-electrode configuration, with current amplitude and frequency of 5 μA to 1 mA and DC up to 10 kHz, respectively. As it was reported, the aim of the study was to demonstrate the dependency of electro-stimulation of the urinary bladder on the nature, configuration and electrical insulation of the electrodes, as well as upon the individual bladder.

In [102] researchers used an implantable system to measure canine urinary bladder volume. A two-electrode configuration and a frequency of 100 kHz, based on an oscillator-based system was used. They proposed that an implantable bladder-volume system would facilitate setting the time for artificially stimulated urination, and give volitional control of a urination schedule in cases of paraplegic-related urinary retention.

Denniston and Baker [103] have performed a study on six dogs in order to monitor urine accumulation in the bladder non-invasively. Here a four-electrode configuration was used. The applied current had a frequency of 100 kHz and an amplitude of 4 mA. A commercial device originally used for impedance cardiography was used. The results collected from six dogs showed a decrease in impedance in the range of 0 Ω to 2.62 Ω , for stripe-shaped electrodes, and 1.73 Ω to 3.89 Ω in circular-shaped electrodes, per 100 ml infusion of urine into the bladder. Results showed that the abdominal impedance measurement is a promising method of providing a harmless, painless and noninvasive means of monitoring bladder function [103].

In [104–106] an implantable bladder volume monitoring device based on

the impedance measurement of the detrusor muscle was described in order to activate a stimulator to void the bladder. The system also had a feedback loop with a neuro-stimulator to rectify bladder dysfunctions. An algorithm for removing movement artifacts was also proposed.

A study, in [109], by simulation based on the finite element method (FEM), showed that using multiple electrodes instead of two and four electrodes will lead to recording higher impedance variation, due to change of volume. Results showed that placing injection electrodes on the opposite side of the abdomen will give the optimum current distribution for measuring the impedance in their setup. In [110], and [111], studies reported that BI measurement showed a significant inverse relationship with bladder volume.

In [112] a study was performed on 13 patients with spinal cord injuries who were undergoing urodynamic study. An impedance analyzer was used and the applied current had an amplitude of 1 mA at 60 kHz. Instead of regular electrodes, compound electrodes were used, which helped to reduce the contact impedance and increase spatial resolution but have design and reconstruction complexity issue [113–118]. The fluid used to fill each of the patients' bladders was irrigation water. The correlation between the electrical impedance and fluid was negative ($r = -0.7988$). Despite small percentage changes in electrical impedance, impedance measurement showed a significant inverse relationship with bladder volume changes [112].

An implantable impedance measurement system with two electrodes has been introduced in [119]. A voltage controlled oscillator (VCO) was used in order to transfer the data as frequency. An on-chip sine wave generator at 1

kHz was used as the excitation signal. Simulated results on a 7 k Ω resistor showed a 7.5% error in the measurement.

It is worth mentioning that between 2000 and 2010, although some studies were published for other usage of BI measurement for disease diagnosis of the bladder [120, 121] and also a paper where the results were reported not to be satisfactory for bladder monitoring at the time [122], the study in [123] was found to be the first paper published since 2010 which continued research on noninvasive bladder monitoring in patients with the problem of controlling their bladder, and the paper had references to previous papers from 1975 to 2000.

In [123], a clinical and commercialized Draeger measurement device based on electrical impedance tomography (EIT), originally used for lung monitoring, was used for bladder monitoring. The clinical study was performed on nine paraplegic patients, with sixteen electrodes and a current amplitude of 5 mA at 50 kHz, and the aim was to determine whether EIT can be used for non-invasive bladder monitoring. Their results showed that by increasing the fluid volume, impedance decreased in four patients and it increased in five other patients.

The aim of [124] was to assess urinary bladder volume in a noninvasive manner using a system that measures electrical impedance. It was proposed that bladder volume measurement using the electrical impedance method is a good alternative to the US method, for determining the residual urine volume which assists in making a decision regarding the need for catheterization, to void the residual urine. Tested on animals, it was experimentally found that the electrical impedance generated using a sine wave at frequency

of 115 Hz and a current of 0.2 mA was sufficient to measure the continuously changing bladder volume. The study used a two-electrode configuration, on three volunteer women, aged 43 - 55. In this study, instead of calculating the impedance, raw data from voltage recording was used. Results showed that by increasing the fluid volume by 100 ml, the voltage changed linearly by 20 mV.

On the topic of noninvasive bladder monitoring, Li et al. [125] designed a portable BI system, with 4 electrodes, and using 1 mA at 50 kHz. The study was performed first on a known impedance and then on a healthy subject to show the correlation between change of impedance and volume variation in the bladder. The obtained impedance from a known $50\ \Omega$ potentiometer had an error in the measurement with mean of $0.5\ \Omega$ and a variance of $0.0133\ \Omega$. For the human experiment, the subject drank 100 ml of water, lay on the bed and the impedance on his abdomen was measured over a 50 minute duration. The impedance decreased from $11.8\ \Omega$ to $10.2\ \Omega$.

In [126], a matrix of 8×8 custom-made electrodes was used to put on a phantom, mimicking the abdomen area, and an algorithm to enhance the spatial resolution was presented. This was in order to reduce the noise of the reconstructed EIT image for bladder monitoring. The reconstructed image was a 3D image, consisting of various 2D images. Data used in this study was collected both by simulations and phantom experiments and the current had an amplitude of 10 mA at 200 kHz. It was reported that the algorithm can estimate fluid volume within the accuracy of 5 ml.

In 2014, a simulation study for a BI measurement system was performed in order to monitor the bladder of patients with impaired bladder volume

sensation [127]. The study used both image reconstruction, and classification without image reconstruction, to compare the simulated data in these two methods. The same group also published a study which was implemented to use a programming algorithm in order to reduce the impact of variation in urine conductivities on monitoring the bladder [128]. Three different versions of the algorithm were presented, with both single frequency and multi-frequency measurement setups. Both simulation and also in-vitro measurement took place. For simulation, four different levels of signal to noise ratio (SNR) were set: 40, 50, 60 dB, and infinite. These SNRs were chosen since previous studies with a device, called Goe MF II EIT, showed SNR between 42 dB and 156 dB while recording on a dummy phantom. For in-vitro measurements, an Agilent LCR meter was used and an added multiplexer would switch between eight electrodes which were placed on a 30 cm diameter tank as a phantom. Although the results were reported to be promising regarding the algorithm proposed for reducing the impact of different urine conductivities on bladder monitoring, it was mentioned that more experiments were required to also consider other factors such as body posture, body movement, etc.

A brief study for bladder impedance measurement was performed with a commercial and wearable device designed by STM microelectronics [129]. The device was designed to be used for cardiac monitoring and the aim was to see whether it can also be used for bladder monitoring. The abdomen impedance of a healthy subject was measured with a four-electrode configuration and the applied current was $100\text{ }\mu\text{A}$ at 50 kHz. The device was able to measure impedance variations of the abdomen between $15\text{ }\Omega$ and $18\text{ }\Omega$.

Wang et al. [130] conducted a study on twelve healthy male subjects for a noninvasive urination-desire sensing method based on BI spectrum analysis. The Agilent LCR meter used in measurement system provided 0.2 mA current at 50 kHz, which was mentioned to be sufficient to continuously measure the changes during the state of bladder filling. A four-electrode configuration was used for the measurement. Also, a sweep of frequency from 30 kHz to 1 MHz was performed to investigate the impact of different frequencies on the measurements. 1 MHz had both low baseline and variation in impedance due to urine accumulation. On the other hand, 30 kHz had the highest baseline and variation among the measured impedances. The power spectral density (PSD) of the measured BI was investigated in three stages: (i) no sensation of urine, (ii) urgency to void and (iii) discomfort. The oscillation observed in the low frequency bands of PSD had higher amplitude. The range of impedance variation was from 15.5 Ω , for no sensation, to 14.5 Ω for urgency to void.

In [131], an EIT system was designed and tested on four porcine bladders as an ex-vivo experiment and also on six healthy volunteers during bladder filling. An image of the impedance distribution was reconstructed and used to compare four-electrode with sixteen-electrode configurations. Despite measuring with four-electrode configuration, in the measurements with the 16 –electrode configuration, measured impedance increased with increasing the fluid volume.

In 2017, a study was published in order to propose a continuous monitoring wearable device and also to address an issue with the movement of a subject during the measurement [132]. The study used 100 μ A at 50 kHz

as an excitation signal in order to measure the variation in impedance of the bladder and also used the same current at 10 kHz in order to measure the motion artifact. The Impedance obtained at 10 kHz would be subtracted from that obtained at 50 kHz, to reduce the impact of movement on bladder monitoring. Using a signal at 10 kHz was chosen experimentally in that study. The study was performed on a healthy subject. The impedance variation in a standing position from empty to the next voiding moment was reported to be 6.8Ω . Then, a seven-days measurement on the same subject took place. It was reported that the subject immediately should urinate before and after sleeping. The average difference of impedance between the smallest and the largest bladder volume, which is before and after sleeping, was 8.6Ω , with a standard deviation of 3.3Ω .

A study published in 2018 by Dunne et al. [82] showed the effectiveness of using supervised classifiers for electrical impedance-based bladder monitoring. The study was a comprehensive investigation performed in a simulation environment and also it was tested on a body-mimicking phantom. In this study an EIT device (Swisstom Pioneer Set) was used. The current amplitude was set to 5 mA at 50 kHz. A ring of 32 electrodes was used for applying the current and recording the voltages. In the simulation study, four different test cases (TC) were introduced and each TC was repeated with four different levels of SNR, from 20 to 80 dB with a step size of 20 dB. In each TC, the fluid volume in the bladder, the urine/fluid conductivity and the boundaries of the FEM model were varied in order to investigate the performance of the classifiers in different scenarios. As the SNR falls below 80 dB, an error was observed depending on the level of

SNR. For TC4, which was the most realistic scenario including different body shapes of the body, an accuracy of 81.66 % was reported with 70 dB SNR in simulation. The accuracy was defined to be the average of sensitivity and specificity, which means the ability of the classifier to both classify the states of being full, and not full, correctly. At the end, classifiers were also tested on a body-mimicking phantom. Results showed that above 60 dB SNR, all classifiers could classify the state with more than 95% accuracy.

In 2018, a study for bladder volume monitoring was published in order to compare the measurement accuracy of EIT to standard US in healthy volunteers. In this study, four different configurations of electrodes were examined and the results were compared to the measurement results performed by US [81]. The mean deviation from the real fluid volume for standard US was $37 \pm 17\%$ and for EIT, it was reported to be $32 \pm 18\%$. A matrix of electrodes was reported to have the optimal results.

In a very recent study published in 2020, an improved algorithm for BI measurement was introduced [133]. The aim was to introduce a more robust algorithm that is insensitive to different urine conductivities. The improved algorithm, called Focused Impedance Measurement (FIM), was compared with the Global Impedance (GI) measurement algorithm. Here, a phantom was used in order to test the algorithm. A low cost AFE4300¹ impedance measurement device was used for the phantom test with an eight-electrode configuration. The phantom had a cubic shape with 30 cm height, length and width. The overall conductivity of the container filled with saline was set to be 0.217 S/m to emulate the electrical characteristics of the lower pelvis in humans. The conductivity of the saline solutions to imitate urine was

¹More information can be found in the manufacturer website: <https://www.ti.com/product/AFE4300>

1.027, 1.877 and 2.610 S/m. The results showed that using this algorithm, unlike its predecessor, the electrical potentials did not change significantly with constant liquid volumes, indicating its robustness due to changes of conductivity.

In mid 2020, a study was published to assess the feasibility of monitoring the bladder fullness with textile-based bioimpedance spectroscopy [2]. An innovative lab-bench phantom has been designed and fabricated. This phantom was reported to be a step towards a more realistic pelvic phantom which used an ex vivo pig's bladder and skin to connect the electrodes to the phantom and monitor the fullness of the bladder. The measurement was carried out at 5 kHz, with 4 electrodes. A decrease of 7.2 % in the impedance was measured, due to fully filling (350 ml) of bladder with artificial urine, with a conductivity of 2 S/m. The conclusion of the work suggested that the fabricated pelvic phantom is suitable to be used for bladder monitoring experiments, with some limitations, such as less complexity in terms of its behavior compared to real human tissues, the occurrence of physiological phenomena, and body movement.

Table 2.1 summarizes the configuration of the BI measurement system in the different studies.

Table 2.1: Different setups for bladder monitoring with BI measurement method.

Ref.	Year	Number of electrodes	Frequency (kHz)	Current Amplitude (mA)	Subjects	Bladder dysfunction	Monitoring Method	Measured Range of Impedance (Ω)
[101]	1968	4	0 to 10	0.05 to 1	15 dogs	–	Impedance	100 - 600
[102]	1971	2	100	–	1 dog	–	Impedance	150 - 170
[103]	1975	4	100	4	1 dog	–	Impedance	26 - 30
[110]	1983	4	75	0.2	40 individuals	No	Impedance	10 to 20
[111]	1994	4	50	2	10 individuals	Yes	Impedance	5 to 15
[112]	1998	4	60	1	13 individuals	Yes	Impedance	245 - 295
[119]	2000	2	1	–	Simulation	–	Impedance	7000
[122]	2006	4	100	–	1 individual	No	Impedance	10 to 12
[123]	2011	16	50	1	9 individual	Yes	Image-Impedance	10 to 60
[124]	2011	2	0.115	0.2	3 individuals	No	Voltage	–
[126]	2012	64	200	10	Phantom	–	Image-Impedance	–
[125]	2013	4	50	1	1 individual	No	Impedance	10 to 30
[127]	2014	8	50	1	Simulation	–	Image-Impedance	–
[128]	2014	8	50	1	Phantom	–	image-Impedance	–
[129]	2015	4	50	0.1	1 individual	No	Impedance	10 to 15
[130]	2016	4	50	0.2	12 individuals	No	Impedance	12 to 15
[131]	2016	16	50	1	6 individuals	No	Impedance	6 to 21
[132]	2017	3	10, 50	0.1	3 individuals	No	Impedance	10 to 30
[134]	2018	4	50	0.5	1 individuals	No	Impedance	6 % change
[82]	2018	32	50	5	Phantom	–	Impedance-classification	–
[81]	2018	16	50	5	10 individuals	No	Image-Impedance	–
[135]	2019	4	10	1	8 individuals	No	Voltage	–
[136]	2019	2	50	–	1 individual	No	Impedance	375 - 390
[133]	2020	8	50	0.833	Phantom	–	Image-Impedance	–
[137]	2020	4	1 to 100	–	1 individual	No	Impedance	–
[2]	2020	4	5	0.07	Phantom, 3 individuals	No	Impedance	30 - 35

Summary of the Literature Review

As a BI measurement is a complete system, the areas that were mainly addressed in the literature were algorithms and hardware-related studies. Algorithms can be categorized into enhancing the collected data for classifiers in order to detect the state, using mathematical and image processing techniques to increase the robustness of the urine volume detection where the measurement is based on a reconstructed image from an impedance distribution and, posture or movement detection and reducing the generated noise of these artifacts. For the hardware, designing a wearable device with small size, low noise and low power is always challenging, specifically at higher frequencies, such as 100 kHz and above. Although just a few studies reported using such a high frequency, those studies were performed using a commercial instrument that was not wearable, but was suitable for EIT. Custom designed and miniaturized system-on-chip (SoC) EIT devices can be found in the literature for other applications such as breast cancer [138] or respiration monitoring [139], although no miniaturized EIT-related SoC was reported for bladder monitoring.

Regarding the number of electrodes, the use of more than 4 electrodes is related to using EIT and image-based methods for bladder monitoring, but this could be a potential drawback, despite the fact that it provides more information within the body, as wearing more electrodes would be harder to tolerate in the long term, especially as a ring belt around the waist. For most of the studies that are not based on EIT, the use of 4 electrodes is the most common. This configuration will be explained further at the end of this chapter, but a four-electrode setup, compared to a three- or two-electrode

setup, is not sensitive to skin-electrode impedance.

Among the BI measurement systems, the most common selected frequency was 50 kHz. This frequency is considered the standard frequency for body composition estimation, as around this frequency the electrical current starts to pass through the cell [2, 140]. Therefore, most of the studies perform bladder monitoring at this frequency. However, due to the fact that urine is an extracellular fluid, consisting of about 91-96% water with the remainder being inorganic salts, urea, organic compounds, and organic ammonium salts with resistive characteristics [141, 142], usage of a lower frequency below 50 kHz is considered more reasonable [2]. A current amplitude of 1 mA was also common to use within the systems. The main criteria for the current amplitude is to ensure that it is within a safe range at the frequency of interest, so there was no standard or recommended current amplitude that had to be followed, and it depends also on whether the designed system allows this amplitude to be varied. Among all the studies, one common limitation, which mostly was reported by the authors, was the lack of clinical trials. This is a future goal as the research grows, since using a non-invasive BI measurement system for bladder monitoring is a relatively new area with only about one decade of emergence. After the comprehensive review of the existing BI measurement systems for bladder monitoring, next section introduces the electrical behavior of cells and tissue modeling.

2.3 Electrical Behavior of Cells

An electrical model of the cells can create a bridge between electronics and biology in order to obtain impedance information of the cell. This elec-

trical equivalent model, which is made of resistive and capacitive components, will help to investigate the behavior and response of a system required to extract the unknown impedance of a biological tissue. For the rest of this chapter, the term "load" is used to represent the biological tissue/cells with unknown impedance and the instrumentation required to measure the impedance is called the "system". Before proceeding to the equivalent electrical model of the load, introducing some necessary terms follows.

Fat Free Mass (FFM): This is considered as the conducting volume that helps electric current pass through due to the conductivity of electrolytes dissolved in body water.

Total Body Water (TBW): This is the major component of FFM and is equal to 73.2% of FFM in subjects with normal hydration.

Fat Mass (FM): This is considered as a non-conductor of electric charge and is equal to the difference between the body weight (W_{tBody}) and fat free mass (FFM) [143].

2.3.1 Body and Tissue Composition

The human body is divided into five inhomogeneous parts: Trunk, left and right arm, left and right leg. In each part, the body is composed of FM and FFM which consists of bone minerals and body cell mass (BCM). BCM is created by protein and total body water that consists of extracellular fluid (ECF) and intracellular fluid (ICF) [100]. Fluids in ICF and ECF are electrolyte solutions containing primarily Na^+ , K^+ and Cl^- [143]. Depending on the frequency of interest, ECF and ICF, alongside the cell structure, will

contribute to the impedance being calculated [5]; and therefore, to the response and specifications for designing the system to measure the load. Figure 2.1 shows how the current will pass through the tissue based on the frequency. Now the question which rises here is why does a cell, and therefore a tissue, behave like this while it is excited with a range of frequencies? The answer to this question will lead to the electrical behavior of the load and its equivalent electrical model, explained in the following sections.

2.3.2 Conductivity and Permittivity

The resistance of any resistor depends on the geometry and electrical resistivity (ρ) of its constituent material. For example, the resistance of a sample with uniform cross-section is given by:

$$R_{(Ohm)} = \rho_{(\Omega.m)} \frac{L_{(m)}}{A_{(m^2)}} \quad (2.5)$$

Here L is the length, measured in meters, and A is the cross-sectional area of the object, measured in square meters. ρ is a fundamental property of a material that quantifies how strongly it resists electrical current. Inversely, a

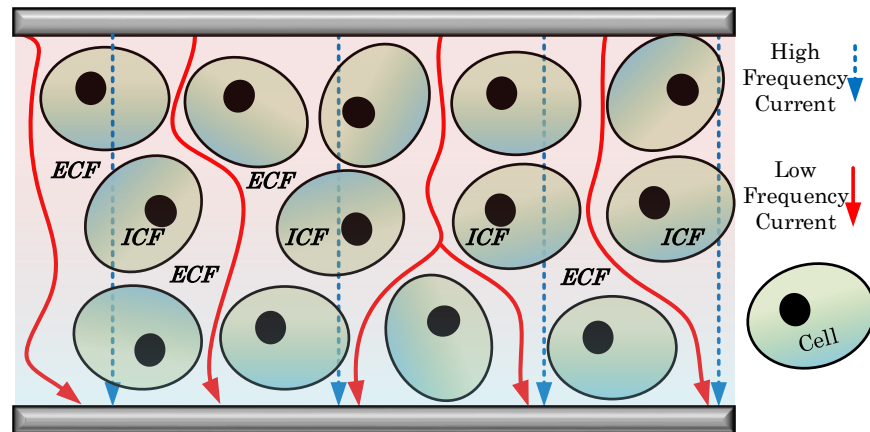


Figure 2.1: Path of current flow for different frequencies through the tissue, redrawn from [5].

term "Conductance" (shown by G) is defined in order to indicate how easily it conducts electrical current. This can be shown by:

$$G_{(S)} = \sigma_{(S/m)} \frac{A_{(m^2)}}{L_{(m)}} \quad (2.6)$$

Where $\sigma_{(S/m)}$ is called the conductivity and is measured in Siemens per meter (S/m). By considering (2.5) and (2.6), the relation between resistance and conductance is:

$$R_{(Ohm)} = \frac{1}{G_{(S/m)}} \quad , \quad \rho_{(\Omega.m)} = \frac{1}{\sigma_{(S/m)}} \quad (2.7)$$

For a parallel plate capacitor, the capacitance is:

$$C_{(F)} = \epsilon \frac{A_{(m^2)}}{d_{(m)}} \quad (2.8)$$

where $d_{(m)}$ is the distance between two plates of the capacitor measured in meters, and $\epsilon = \epsilon_r \epsilon_0$ is the permittivity, $\epsilon_0 = 8.854 \times 10^{-12}$ F/m is the constant permittivity of vacuum and $\epsilon_r = \epsilon / \epsilon_0$ is the relative permittivity, also known as dielectric constant of the material, which is the permittivity relative to that of vacuum and is unitless [6].

In the presence of an electric field, three effects on the charges will emerge which are described below:

Induced dipole polarization [9]: Before the electric field, E , is applied, the positive and negative charges of bound charges are so close together that the macroscopic fields they produce cancel each other. In the presence of E , the positive charges move in one direction and the negative charges in the opposite direction depending of the direction, of E , resulting in a slight

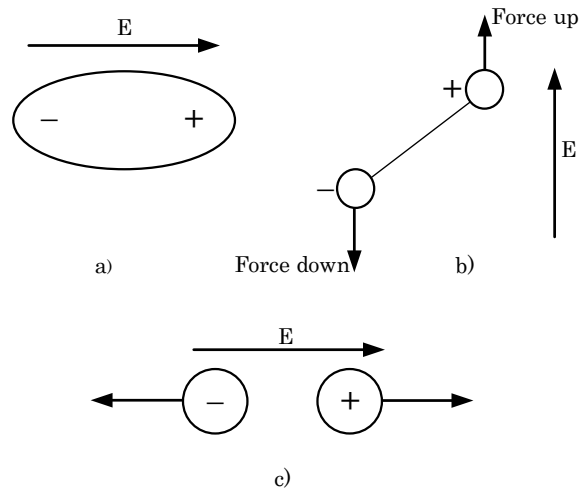


Figure 2.2: Illustration of a) induced dipole polarization b) partial alignment and c) conduction current in the presence of an electric field, E redrawn from [6].

separation of charge. The combination of a positive and a negative charge separated by a very small distance is called an electric dipole. This phenomenon is called *induced polarization*.

Partial alignment [9]: In a biological tissue, the charges are randomly oriented when there is no external E applied. In the presence of E , these charges are forced to also rotate slightly, based on their initial orientation, in order to partially align with the applied E .

Conduction current [9]: Ions, such as K^+ , Na^+ and Cl^- are free charges meaning they are loosely bound and can move between molecules in response to an applied E . The movement of these free charges constitutes a current, which is called a *conduction current*. Tissues with more water content have more free charges than insulating materials, such as fat [6, 9].

Figure 2.2 illustrates the concepts described for the effects of the presence of E on charges. Induced polarization and alignment of electric dipoles are accounted for by the permittivity and conduction current is accounted for by

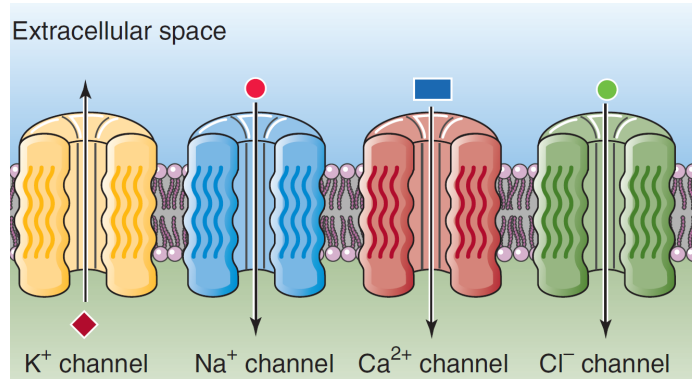


Figure 2.3: Ions passing through channels in a cell membrane to form conduction current [7].

the conductivity [9]. By identifying how ions are responsible for the flow of a current in the presence of E , the next step is to electrically model the tissue under test (i.e. the load).

In the next section, an equivalent circuit model will be presented.

2.3.3 Equivalent Circuit Model of the Load

The current, I , carried by a particular ion varies with applied membrane voltage, V , so there is an I - V relationship for that ion. This suggests that the contribution of each ion, passing through the membrane, to the electrical properties of the cell membrane may be represented by elements of an electrical circuit that has a relatively constant value when V is divided by I . Therefore, this behavior can be modeled by a resistor, called the membrane resistor or R_M [8,9]. Figure 2.3 shows the pathway of ions into a cell. There are different pathways for each ion and all these currents together form the total current passing through channels in a cell. The low conducting membrane of the cell acting as a capacitor [7] is shown in Figure 2.4. This happens because the lipid bilayer of a cell can maintain a separation of charge across its layers of approximately 4 nm [7]. The value of the capacitor can be roughly estimated with (2.8) by considering the dielectric constant of a

biological membrane: $\epsilon_r = 5$. This value for most cell membranes is approximately $1 \mu\text{F}$ in each 1 cm^2 area [7]. Consider a single cell, presented

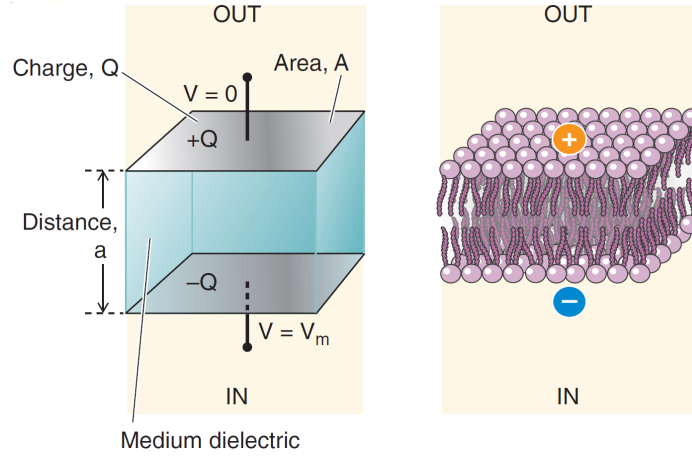


Figure 2.4: Formation of a capacitor in a cell membrane [7].

in Figure 2.5 with its equivalent electrical circuit [8, 144]. R_M and C_M represent the resistor and capacitor in the path of the current from ECF into ICF at the membrane, or in other words, from outside of the cell to inside. Then there is R_i which is a resistive path inside a cell due to ICF [8, 145] and R_E that represents the resistive path due to ECF outside of the cell [8, 145, 146]. Starting from low frequency, resistive paths will conduct the current and, as the frequency increases, the influence of C_M will become significant and increase the current flow through the cell. The model, and the three effects that will emerge when a cell is excited by an electric field, as described in the previous section, complement one another in order to explain how the current flows inside and outside of a cell; and therefore, the tissue. There are more complex models with non-linear elements that are used to explain the equivalent electrical model of a cell and current flow, however; since those elements do not physically exist, they were not considered in this thesis. For the interested reader, more explanation can be found in [9].

The same electrical model can be used for a tissue as it consists of a group

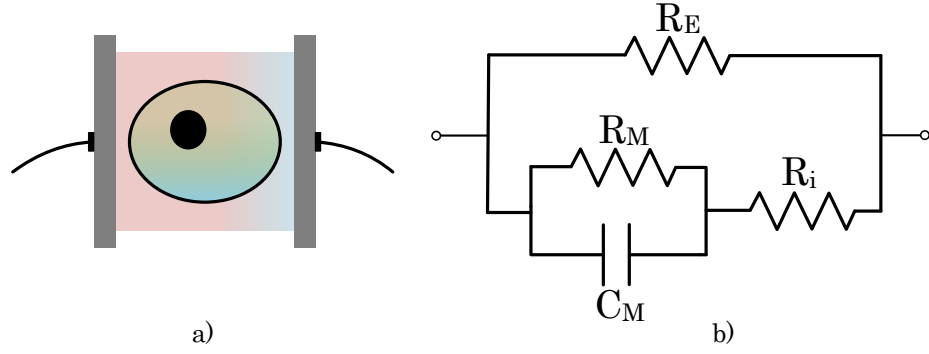


Figure 2.5: a) A single cell excited with E . b) Equivalent electrical model of a single cell [8].

of cells: ECF of the tissue as R_E , membrane of the cells as C_M alongside R_i for ICF resistive path. It should be noted that because C_M is quite large, its impedance will quickly fall as the frequency is increased, thus bypassing R_M . Hence, R_M in the model can be neglected, leading to a simpler model with three components, known as the *Deby model 2R-1C parallel*, which is widely used in the literature for BI measurement [9, 147]. Figure 2.6 shows the two configurations of this model, respectively known as 2R-1C and 2C-1R. The 2R-1C model is mainly used for cells and living tissue. This circuit gives a rough estimate of the behavior of the living tissue both at high frequencies and lower frequencies. In contrast, the 2C-1R model is suitable for higher frequency modelling as the capacitors will block conduction in the lower frequency range [9]. In this thesis, the 2R-1C model is used as the test load in Chapter 5 to test the performance of the designed BI measurement device.

An equation for the equivalent admittance, which is the reciprocal of the impedance, i.e. $Y = 1/Z = G + jB_c$, seen by the system with a 2R-1C load, can be written as follows:

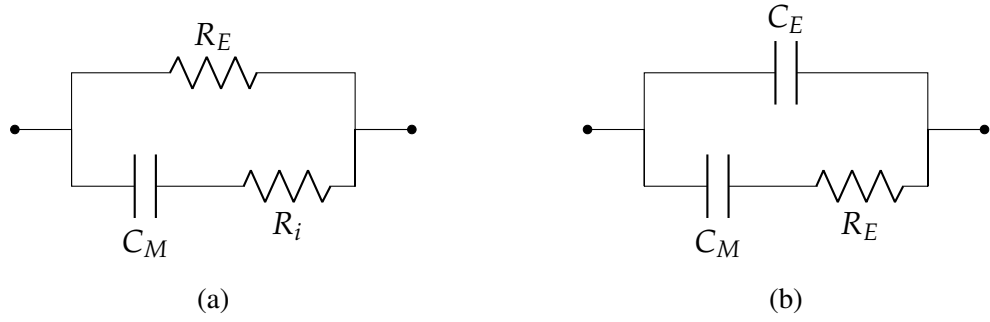


Figure 2.6: Debye equivalent circuit model. a) 2R-1C and b) 2C-1R [9].

$$Y_{Tissue} = G_E + \frac{\omega^2 C_M^2 R_i + j\omega C_M}{1 + \omega^2 R_i^2 C_M^2} \quad (2.9)$$

$$\phi = \tan^{-1} \left(\frac{\omega C_M}{G_E + \omega^2 C_M^2 R_i (1 + R_i G_E)} \right)$$

Where $G_E = 1/R_E$ and $\omega = 2\pi f_{(Hz)}$. Now by substituting $\tau_Y = R_i C_M$ and $\tau_2 = \frac{C_M}{G_E}$ as time constants of the load we have:

$$Y_{Tissue} = G_E + \frac{\omega^2 C_M \tau_Y + j\omega C_M}{1 + (\omega \tau_Y)^2} \quad (2.10)$$

$$\phi = \tan^{-1} \left(\frac{\omega C_M}{G_E \times [1 + \omega^2 \tau_Y \tau_2 (1 + R_i G_E)]} \right)$$

Note that, when $\omega \rightarrow \infty$, then $Y \rightarrow \frac{1}{R_E} + \frac{1}{R_i}$ (which is the conductance two resistors being in parallel) and when, $\omega \rightarrow 0$, then $Y \rightarrow G_E = \frac{1}{R_E}$.

For the impedance of the load we have:

$$Z_{Tissue} = \frac{R_E R_i + \frac{R_E}{j\omega C_M}}{R_E + R_i + \frac{1}{j\omega C_M}} = \frac{1}{Y_{Tissue}} \quad (2.11)$$

The phase of the impedance remains the same as (2.10), but with a minus sign. The basic electrical modeling of the tissue, and its behavior when

excited by different frequencies, has now been outlined. The next section describes different measurement setups for applying and recording the signals, to and from the body, respectively.

2.4 Electrode Configuration

Electrodes play an important role in bioimpedance measurement. Their duty is to deliver current generated by the system to the load, and sense the voltage for impedance calculation. It takes two current-carrying (CC) electrodes to send an electric current through the body, namely a source and a sink. Also, for measurement of the voltage, two electrodes are required, which can be the same as the current carrying electrodes, or two additional electrodes can be used. First, the operation of a single electrode will be described when it is delivering current to the load and, then, different electrode configurations will be discussed.

2.4.1 Electrode-Skin Interface

The charge carriers in the electrode, and in the tissue, are free electrons and free ions, respectively. The electrode is where the exchange of the carriers takes place. Looking at Figure 2.7, the wire from the system is connected to a conductor followed by skin gel. When a metal conductor with free electrons is in contact with a layer of electrolyte gel with free ions, an electric double layer, which is very thin and more or less depleted of charge carriers, is formed at the place of contact [148]. It is in this contact that the conversion and passing of current from electron to ion, or vice versa, takes place [9, 148]. The Ag/AgCl is a very common electrode metal which is

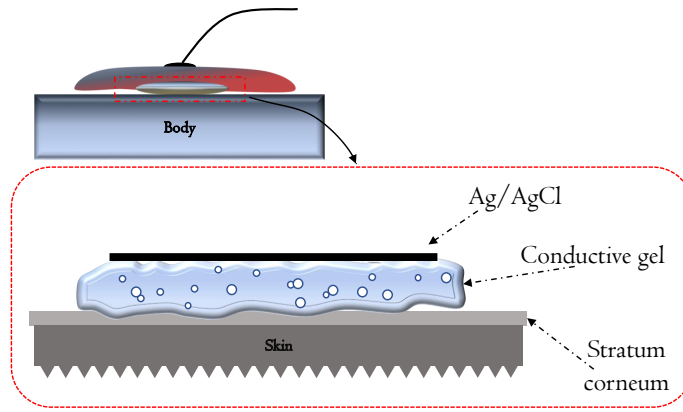


Figure 2.7: *Generic skin surface electrode with sticky contact gel in contact with the skin, redrawn from [9].*

used in biology and can be used as the current-carrying and voltage measurement electrodes, for bioimpedance measurement [9]. Formation of the double layer is illustrated in Figure 2.8.

The metal/electrolyte interface area is called the electrode area (EA). The

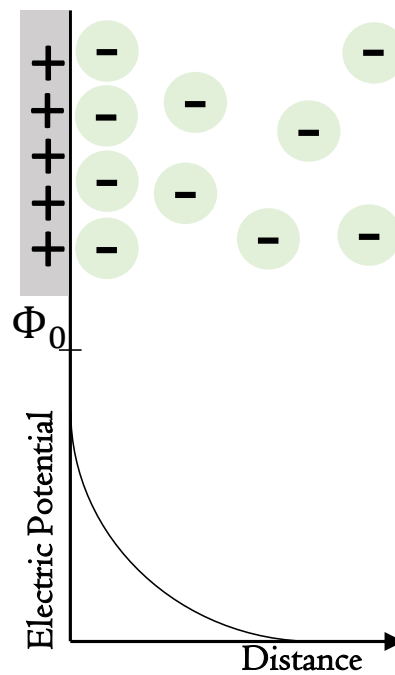


Figure 2.8: *Gouy-Chapman's model of the electric double layer and electric potential as a function of distance from the electrode surface [9].*

electrode area may be a plane area or include a surface roughness or fractal factor. The interface area of the contact medium and the tissue is called the

effective electrode area (EEA) [9]. The contact to the tissue is important because of the following reasons:

- Large EA implies low electrode polarization impedance.
- Large EEA for recording electrodes implies low noise, and an averaging effect, but loss of spatial resolution.

Hence the size of the this area should be taken into consideration for impedance measurement if the application requires good spatial resolution [9].

When an AC current, i , is delivered to a skin-electrode pair, it generates an AC voltage, u , in the electrode plates. The impedance is $Z = u/i$ and it comprises the tissue impedance, the skin impedance and the electrode-electrolyte impedance. In most cases, skin and electrode-electrolyte impedance is a nuisance because it is only the tissue impedance that is of interest. This problem rises if the current applying electrodes are the same as the voltage measurement electrodes [9]. Therefore, to avoid this problem and to measure only the tissue impedance, three- and four-electrode measurement configurations are used, as discussed next.

2.5 Three-Electrode Measurement

Figure 2.9a² shows the principle of the three-electrode measurement approach and the electrical model from skin-electrode to the tissue, as adopted from [149]. R_{EG} , C_D and R_G are the electrode-gel resistance at the interface, the double-layer capacitor and gel resistance, respectively, and R_s and

²The abdomen mannequin image was taken from: <https://www.pinterest.ie/pin/155303887547644784/?mt=login>

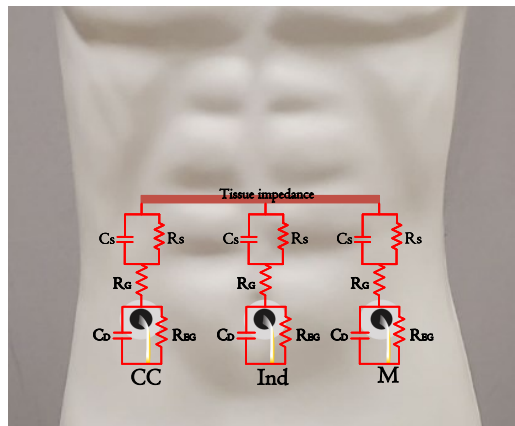
C_s represent the skin impedance [149]. Electrode CC is used to source current into the body. Electrode M is shared between the current injection and voltage measurement phases. Electrode Ind is only used to measure the voltage drop between its position and electrode M. The unwanted impedance of electrodes CC and Ind is omitted in this way. However, as electrode M is used both for current injection and voltage measurement, the skin-electrode impedance still contributes to the measured impedance [9].

2.6 Four-Electrode Measurement

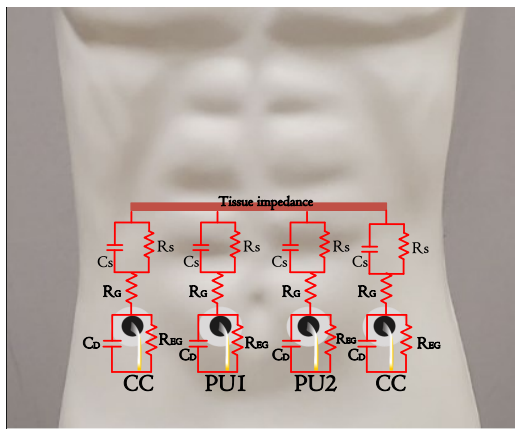
The setup for a four-electrode measurement can be found in Figure 2.9b. If the effect of the skin-electrode impedance of the electrodes themselves is to be reduced, the four-electrode system is preferred [144]. In this setup, the unwanted impedance of the electrodes will not be measured. Considering Figure 2.9b, when the current is applied to the body through one of the CC electrodes, it will pass from the skin-electrode impedance to reach the body and then it will exit through the other CC electrode. The PU electrodes are connected to a high impedance voltmeter to measure the voltage, thus the current "sees" the path of the PU electrodes as an open circuit with very large impedance. Negligible current passes through the skin-electrode impedance of the PU electrodes for this reason and the PU electrodes will essentially only measure the voltage drop due to the current passing through the impedance of the body.

It should be noted that in this configuration if, for instance, the impedance is measured to be 0Ω , this does not necessarily imply a high-conductivity tissue; it could mean that no current is transferring between the CC elec-

trodes and this should be checked.



(a)



(b)

Figure 2.9: a)Three- and b)Four-electrode systems. *PU* is the pick up electrode for voltage measurement and *CC* is the current injection electrode.

2.7 Summary

In this chapter a detailed literature review of the existing BI measurement systems for bladder monitoring was presented. The trend in the studies and the common parameters used to employ BI measurement for bladder monitoring were discussed. Then, BI measurement theory and fundamentals were explained. In order to be able to understand how and why the tissue under test responds to external excitation, an equivalent electrical model of the tissue was also described. It was noted that, at higher frequencies, applied current will pass through both ECF and ICF, while at low frequencies it only tends to pass through ECF. The issue with the presence of skin-electrode impedance was briefly pointed out. It was mentioned that to avoid the unwanted impedance from skin-electrode contacts, a four electrode setup is preferred. This configuration will be used in this thesis to carry out the measurements. In the next chapter, a block diagram of a bioimpedance measurement device, its specification and parameters are introduced and the method to address aims 3 and 4 of the thesis will be outlined.

Chapter 3

System Description, Constituent Blocks and Proposed Method

In this chapter, a block diagram of the BI measurement device for bladder monitoring is investigated and the design parameters of the system are provided. Then, a method of measurement is proposed in order to address aims 3 and 4 of the thesis.

3.1 System Overview

Advances in both analogue and digital electronics have allowed BI measurement instrumentation to evolve, ever since the first systems were introduced. Nowadays, most of the processing loads of systems are being carried out in the digital domain, thanks to advances in the field. However, analogue design is an indispensable part of a system, especially with the requirement to deal with small signal amplitudes at higher speed. These requirements demand that such systems have their precision and accuracy increased and to operate at a higher bandwidth. Early BI measurement systems might only

have been required to operate at lower frequencies but, with advancing technologies and emerging new needs, BI systems are now required to operate in the range of hundreds of MHz, depending on the application. This section introduces the block diagram of a typical BI measurement system extracted from previous studies in the literature. Then, it presents an explanation of each block and discusses some of the general issues involved in the design and implementation of the major functions.

3.2 System Blocks

While there are many different BI measurement system designs; most systems apply currents and measure voltages to assure appropriate safety measures [108, 145], as described in section 2.1. The general structure of the employed BI measurement system is shown in Figure 3.1. The waveform, V_{in} , used in the system, is a sinusoid, and is generated by the waveform generator block. The waveform is fed to a voltage controlled current source (VCCS), which converts the voltage into a controllable current.

If multiplexing is required, then a 2-to-N multiplexer allows the source to be applied to one pair of electrodes at a time. Voltage variation due to the change of impedance of the target under test can be measured using a differential method with an instrumentation amplifier. Then, this voltage is fed to an analog to digital converter (ADC). The ADC will convert the analog signal into digital form and it will send the digital data to the microcontroller. Also, in order to measure the phase, another ADC will sample the applied signal and the samples will be transferred to the microcontroller. From the microcontroller, the data will be sent to a host device, which is a

PC in this thesis, for further processing of data and impedance calculation. More details of each block will now be presented.

3.2.1 Waveform Synthesis

While early BI measurement systems used analog oscillators to produce a reference sinusoidal waveform, recent designs utilize digital waveform synthesis techniques [145]. There are two basic approaches to sinusoidal digital synthesis [145, 150]. The first involves storing all, or part, of a sinusoid in a programmable read only memory (PROM) and sequentially stepping through these stored values. This approach requires the digital host controlling the steps to always be active and to constantly update the next datum to the digital to analog converter (DAC). The second approach is to use a direct digital synthesis (DDS) integrated circuit (IC), which incorporates the function of updating the data inside the IC itself and does not need constant communication between the host and the DDS chip. In both cases,

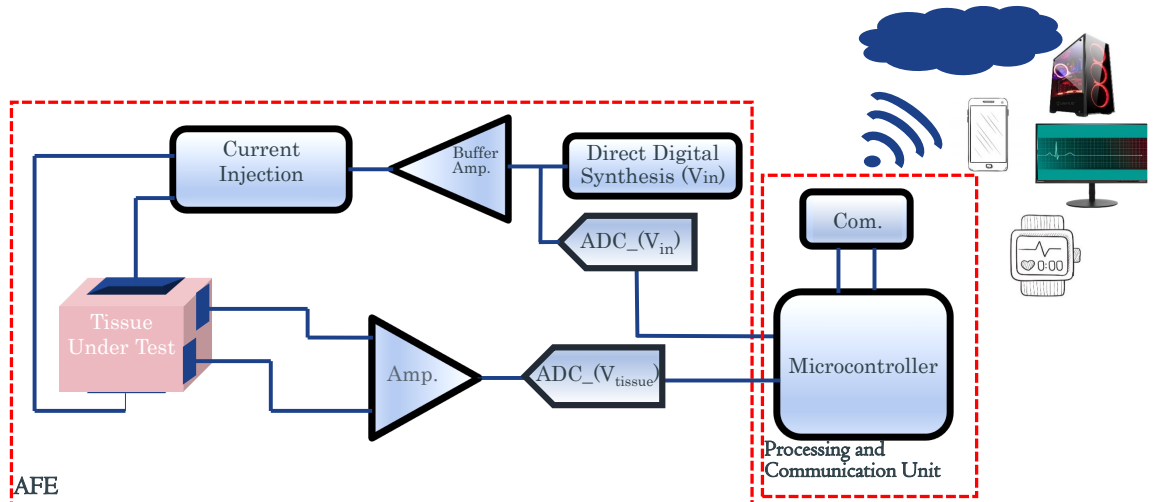


Figure 3.1: Block diagram of the BI measurement system. External ADC-(V_{in}) and ADC-(V_{tissue}) are sampling the input voltage and the voltage from the load under test, being the tissue in the abdomen area.

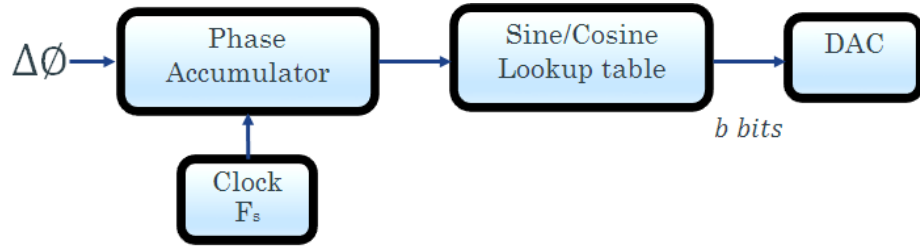


Figure 3.2: Block diagram of a direct digital synthesis circuit.

an analog waveform is produced by feeding the digital samples through a digital-to-analog converter (DAC).

As shown in Figure 3.2, a DDS system is constructed around a sinusoid ROM lookup table [145]. A phase accumulator, and a phase increment ($\Delta\Phi$) input, provide addressing to the lookup table. The size of the phase increment, along with the clock frequency, sets the output frequency. By using a DDS, the frequency can be adjusted by varying the size of the phase increment. However, the limited size of the ROM requires rounding or truncation of the phase value that is used to access values in the ROM, resulting in periodic phase jitter¹ that introduces line spectra (spurs) in the frequency spectrum of the resulting sinusoid [151]. This phase jitter can be removed by restricting the choice of output frequency to those that only require phase values corresponding to entries in the lookup table. To help mitigate the spectral impurity introduced by phase truncation, many DDS chips utilize phase dithering to reduce the coupling between the phase error and the particular point in the sinusoid cycle [150, 151].

The amount of noise in the synthesized waveform after the DAC is a function of different factors such as the resolution of the DAC and the sampling frequency [150]. Considering the noise due to the digital-to-analog

¹The slight movement of a transmission signal in time or phase that can introduce errors and loss of synchronization. More information can be found in <https://pdfserv.maximintegrated.com/en/an/AN377.pdf>

conversion using a DAC, namely the quantization noise, the resulting voltage noise spectral density can be expressed as [145]:

$$v_{NQ} = \frac{A}{2^b \sqrt{12F_s}} \quad V / \sqrt{Hz} \quad (3.1)$$

where A is the peak-to-peak voltage range of the waveform, b is the number of bits of resolution in the DAC and F_s is the sampling rate. Therefore, by increasing the DAC resolution and/or increasing the sampling frequency the noise density is decreased. More information regarding the DDS chips and their detailed functionality can be found in [150, 151]. In this thesis, an integrated DDS chip is used to generate the input voltage to be converted to current. It should be noted that DDS is also a very popular block, mostly used in high frequency communication applications, to generate a reference frequency for the phase-locked loop (PLL) blocks [151]; therefore, the available chips on the market can be power hungry. Considering that the ultimate goal is a wearable device, the power consumption is a factor to be vigilant about, so among the available chips, the one with the lowest power consumption per mega sample per second (MSPS) was used, i.e. an AD9833, with 10 bits of DAC output resolution. The 10-bit resolution has been widely used in the literature for BI measurement applications [137, 147]. Table 3.1 shows the four DDS chips from Analog Devices with their specifications. One point that is worth mentioning is that the performances of the chips are very similar, although their power consumption varies. Packages of available chips other than the AD9833 were not suitable to hand-solder, which was the case in this thesis, so this was another criterion to consider when selecting the DDS chip.

Table 3.1: Low-power DDS ICs available on the market to generate the input voltage controlling the current source. Power consumptions are based on maximum update rate.

Component ID	DAC resolution	Update rate (MSPS)	Power (mW)	Package
AD9833	10	25	14.5	10-MSOP
AD9837	10	16	12.2	10-LFCSP
AD9838	10	16	15.2	20-LFCSP
AD9831	10	25	40	48-TQFP

3.2.2 Current Source

Ideally, a current source should have an infinite output shunt impedance, Z_{Out} , resulting in the current delivered to the load being independent of the load voltage, V_L [145]. Real world current sources, however, have a finite Z_{Out} impedance that is usually characterized as the parallel equivalent of a resistance R_O and capacitance C_{OUT} . Figure 3.3 shows the equivalent model of a practical current source that drives a load, Z_{load} . Due to the existence of finite Z_{Out} , the current I_{load} flowing in the load varies with the changing value of the load. This is made worse as the value of the additional stray or parasitic capacitance is increased. Though not necessarily associated with the current source itself but, rather, due to capacitance between wires and/or the printed circuit board (PCB) traces, this capacitance provides an additional means for current to be shunted away from the load to ground, effectively reducing the output impedance of the current source. In determining the required current source output impedance for a given application, it is essential to consider the impact of this stray capacitance [145].

The current source must be able to deliver current with a desired precision over a specified frequency range to a load impedance. These requirements translate into specifications for the frequency response, output impedance and voltage compliance of the current source. Both the volt-

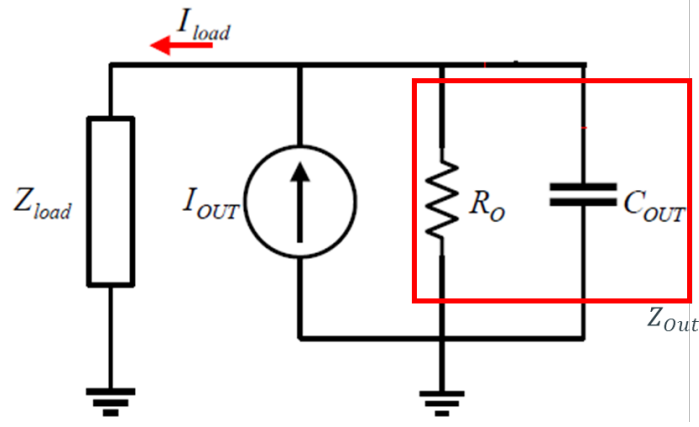


Figure 3.3: Equivalent circuit model of a current source. The output impedance is highlighted within the red box.

age compliance and the output impedance requirements are functions of the expected load impedance. The voltage compliance of the current source should be taken into consideration for the scenario when the maximum current is sourced to a load with the highest possible impedance. The load impedance, which is a function of electrode contact, excitation frequency and the tissue under test, can be within a range from $100\ \Omega$ to $10\ \text{k}\Omega$, with the lower values observed at higher frequencies, and the higher values at lower frequencies [9, 145]. With these currents and impedance ranges, a voltage compliance in the range of a few volts should be considered. The required output impedance is also a function of the load impedance. The error caused by part of the current, generated from the VCCS, passing through the output impedance of the source, $I_{Z_{Out}}$, is given by:

$$I_{Z_{Out}} = \frac{Z_{Lmax}}{Z_{Out} + Z_{Lmax}} \times I_{OUT} \quad (3.2)$$

where Z_{Lmax} is the maximum load impedance. For I_{load} to be accurate within b bits of precision it is required that the error be less than one least significant bit (LSB) or, equivalently, $1/2^b$. Therefore, the output impedance

requirement becomes:

$$Z_{Out} \geq (2^b - 1)Z_{Lmax} \quad (3.3)$$

For instance, a system with 16-bit accuracy with a maximum load impedance of 10 k Ω requires a current source with an output impedance of over 655 M Ω over the frequency range of interest. Another way to consider this is for the systems that should drive a range of load impedances between a minimum and maximum, for example between 1 k Ω and 2 k Ω , then the absolute value for error and, therefore, the output impedance requirement,s will be relaxed. For this scenario, the normalized difference between the current that goes through the maximum load impedance, I_{Lmax} , and minimum load impedance, I_{Lmin} , should be less than $1/2^b$. For the difference between the currents we have:

$$I_{Lmax} - I_{Lmin} = \left(\frac{Z_{Out}}{Z_{Out} + Z_{Lmin}} - \frac{Z_{Out}}{Z_{Out} + Z_{Lmax}} \right) \times I_{OUT} \quad (3.4)$$

and for the required accuracy to be within the b bits, equation (3.5) should be held true:

$$\frac{Z_{Out}}{Z_{Out} + Z_{Lmin}} - \frac{Z_{Out}}{Z_{Out} + Z_{Lmax}} \leq 1/2^b \quad (3.5)$$

In order to visualize the required output impedance of a VCCS for different loads to have b bits of accuracy, Figure 3.4 was generated based on (3.5). The first group of results, showing load impedance ranges from zero to a maximum value, represent the case where the accuracy of the applied current is being maintained within b bits of resolution. The next group shows

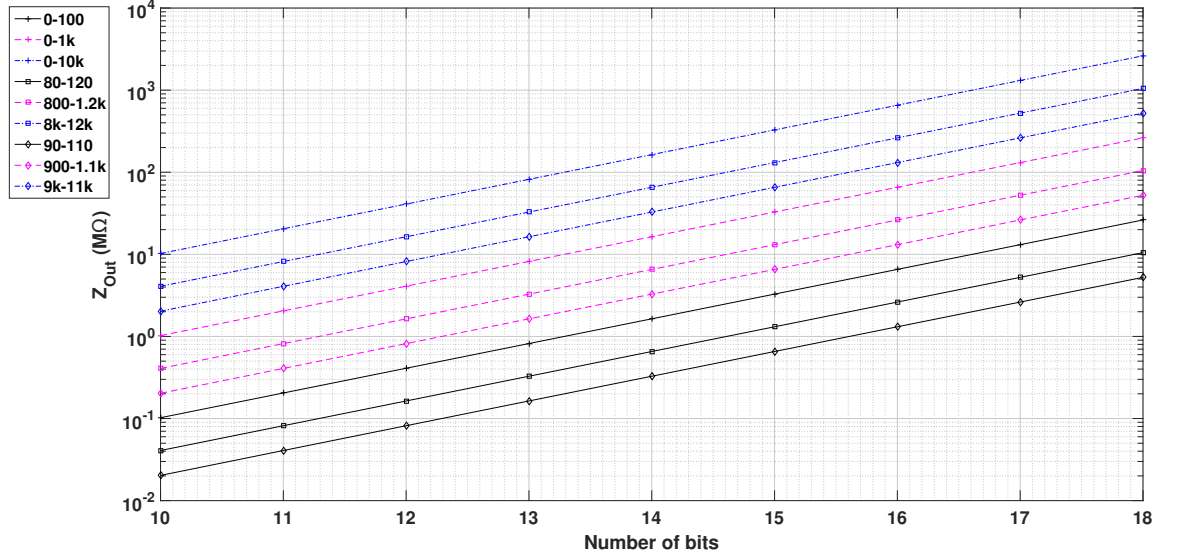


Figure 3.4: Required output impedance for driving different range of loads for b bits of accuracy.

the required output impedance for the case where the load impedance is expected to remain within $\pm 20\%$ of a nominal value (being $100\ \Omega$, $1\ \text{k}\Omega$, and $10\ \text{k}\Omega$), while the last group considers the case where load impedance remains within $\pm 10\%$ of a nominal value. The plot demonstrates the benefit of reduced output impedance requirements over a restricted range of load impedance when a fixed number of bits of resolution is required. For example, a 14-bit system with a load impedance in the range of $0\text{--}1\ \text{k}\Omega$ requires a current source output impedance in excess of $16.38\ \text{M}\Omega$, while, with the same number of bits, for a load impedance within a range of $800\ \Omega\text{--}1.2\ \text{k}\Omega$, an output impedance of only $6.55\ \text{M}\Omega$ is required.

The importance of parasitic and stray capacitances and their impact on degrading the output impedance will now be considered.

Stray capacitance

Stray capacitance, when in parallel with the output of the current source, increases the effective output capacitance of the source and, consequently,

reduces the magnitude of the output impedance. Figure 3.5 shows the capacitive reactance presented by capacitors of various values as a function of frequency. This is to show that if a very large output resistance, even in the order of $G\Omega$ could possibly be achieved, output capacitance will determine the overall output impedance. For example, by assuming an infinite output resistance, obtaining even the modest output impedance of $1\text{ M}\Omega$ at approximately 20 kHz requires a total capacitance of less than 10 pF . At 200 kHz , this value drops to 1 pF and at 2 MHz it drops to 0.1 pF . In a 4-electrode BI measurement setup, the typical stray capacitances can be of the order of 10 pF [145, 152]. If multiplexing between electrodes is required then the parasitic capacitance can be 100 pF or more, thus requiring complex compensation methods to increase the overall output impedance [153, 154].

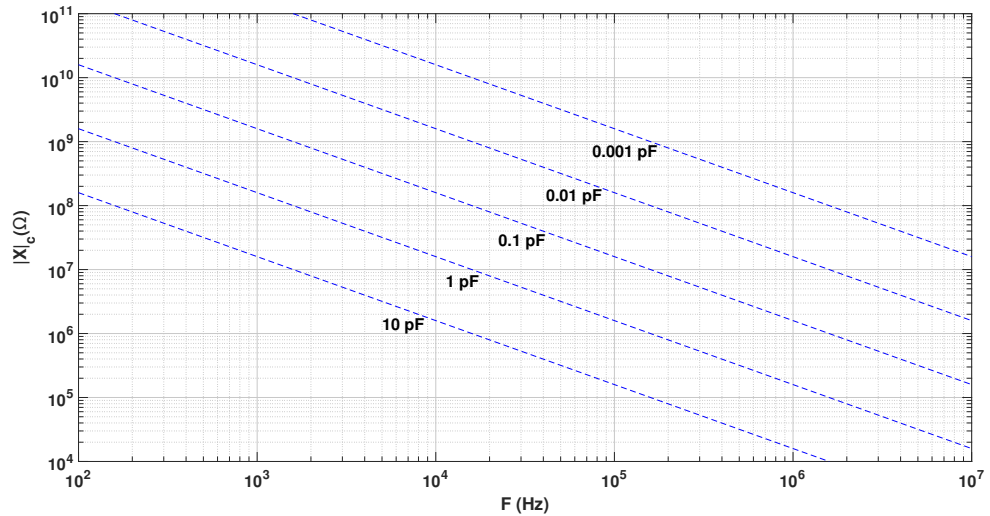


Figure 3.5: Capacitive reactance over different frequencies, forming total output impedance.

3.2.3 Voltage Measurement

In practical implementations, an instrumentation amplifier is used to convert the voltage difference between the two electrodes, recording the signal from

the body as a single-ended voltage. The primary advantage of performing differential measurements is the fact that the voltage difference between a pair of electrodes may be significantly smaller than the voltage between each individual electrode and ground potential, particularly when the electrodes are located near each other on the body. Also, differential measurements cancel out random noise that appears on each electrode. Performing a differential measurement may then result in a reduction in the dynamic range of the voltage signals being measured, which, in turn, reduces the dynamic range requirements for the ADC. However, an important point that should be considered is the common-mode gain of the instrumentation amplifier. If the instrumentation amplifier is ideal, the common-mode gain is zero and the output is determined solely by the differential gain, A_D . However, in a real-world scenario, an instrumentation amplifier will respond to both differential voltage, V_D , and common-mode voltage, V_{cm} , signals and its output is given by:

$$V_o = A_D V_D + A_{cm} V_{cm}$$

where A_{cm} is the common-mode gain of the amplifier. In order to specify how good the instrumentation amplifier is at reducing the effect of V_{cm} and approximating the ideal case, a figure of merit is defined as the common-mode rejection ratio (CMRR), given by:

$$CMRR = 20 \log_{10} \left(\frac{A_D}{A_{cm}} \right)$$

A high CMRR indicates that the differential gain relative to the common mode gain is high; therefore, only the differential signal is being amplified,

and, in most cases, the common-mode signal is being attenuated. In selecting an instrumentation amplifier, a high CMRR at the frequency of interest should be specified, as a low CMRR could cause an error in measuring the differential voltage between the electrodes.

3.3 Parameters of the Device

Considering the blocks described in this chapter and Table 2.1 for the setups used in BI measurement devices in the literature, the overall parameters for the BI measurement device that is to be designed in this thesis is presented in Table 3.2.

Table 3.2: Overall parameters of the BI measurement device.

Parameter	Specification
Frequency range	5 - 50 kHz
Current amplitude	200 μA_{rms}
Number of bits	13
Range of load	10 - 1000 Ω
Number of electrodes	4

It should be noted the range of the load is the total load impedance that the device is going to drive, which is larger than the range of impedances associated with tissue under test, in this case the bladder. The design procedure for the constituent blocks of the system will be explained in chapters 4 and 5, along with their performance. The next section will introduce a proposed method of measurement in order to address aims 3 and 4 of the thesis.

3.4 Proposed Measurement Method

As mentioned in Section 1.3, the impact of bladder location when in different postures and movement could cause an issue in bladder fullness monitoring [127, 128, 131]. This issue has not been addressed fully in the literature. This could be due to the fact that the initial intention and focus for non-invasive bladder motoring by BI measurement, specifically from 2011, was to show that there is a correlation between the accumulation of urine and a change of impedance recorded from an abdomen. Therefore, while pointing out that this change of location would cause errors in identifying the state of the bladder, the issue remained unsolved, to be explored and addressed in future work. Another problem was estimating how much error will this issue cause, on average, for different subjects. Unfortunately, due to the ongoing nature of the research and the limited number of clinical studies, this question still remains unanswered.

Variation in urine conductivity during the day was another important problem, mentioned in Section 1.3, which remains yet to be solved and was only investigated recently, in [133], by proposing an algorithm tested on a phantom. Also, as investigated in a comprehensive study in 2018, variation in urine conductivities would cause an error in monitoring the bladder fullness [82]. In order to address those problems, the current study will present a vertical scanning BI measurement method, performed separately on three different locations, to obtain data. To the best of the author's knowledge, this is the first time that this method is being used to explore the impact of conductivity variation and bladder position on bladder fullness monitoring.

3.4.1 Hypothesis: Vertical Scanning for Urine Level Detection

In the previous studies, electrodes were placed at the same horizontal level, either around the area of interest or just on one side, depending on the number of electrodes used for bladder monitoring. Considering the bladder as a container, when urine starts to accumulate, its level also raises. If the aim is to detect a certain level in the container, then the threshold should be put at a physical level independent of the characteristics of the fluid, such as its conductivity, that will modify the effective impedance. Then the challenge is how to mark the bladder, so when the urine passes a certain volume and/or level, this can be detected and a better sensitivity to the change in impedance due to the urine accumulation is achieved, compared to horizontal monitoring. An intuition about how the current distributes can be helpful to answer this question.

The distribution of the current is a function of electrode placement. In a 4-electrode configuration, by looking at Figure 3.6², and assuming the source electrode is on the left side, the current will be distributed from left to right. The voltage that is being measured to calculate the impedance is also a function of this distribution. As the level of urine starts to rise, it gets closer to the area of dense current distribution, where the current electrodes are placed [5, 107, 123], which is at the same level of the voltage measurement electrodes. However, as the level of urine gets closer and closer to the voltage electrodes, the change in measured impedance will get smaller, as both of those electrodes are being exposed to the same low impedance path through the urine, and by the time the urine level crosses the level of

²The bladder image was generated from a 3D generic model in Solidworks software: <https://www.solidworks.com/domain/design-engineering>

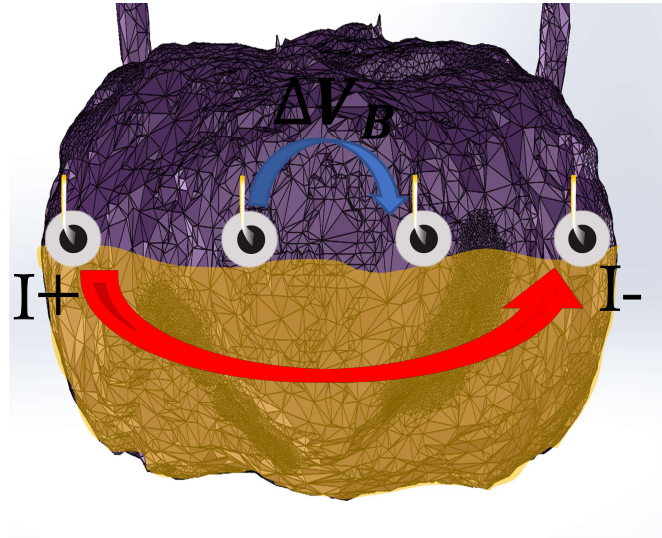


Figure 3.6: *Horizontal placement of electrodes for monitoring the bladder fullness.*

the electrodes, the impedance variation with further filling should be small compared to below this level. To clarify this phenomenon, while the electrodes are placed horizontally, the bladder and urine can be seen as a potentiometer and the two probes are measuring its voltage. As the potentiometer is being tuned towards the lower impedance/resistance the probes will sense lower and lower voltage and therefore, a smaller amount of change. In the urine case, the problem with this placement is that if the urine conductivity changes and the urine becomes less conductive, then it would be even more challenging for the electronic device to sense the small changes associated with the urine accumulation; therefore, it may lead to erroneous state monitoring. This gets even worse if the decision making is based on a fixed level of impedance where, to detect a certain level of urine within the bladder, a fixed impedance is used as a threshold. In order to overcome this problem, a vertical placement of current-applying and voltage-sensing electrodes is proposed. The concept of vertically monitoring the bladder fullness to determine the level of urine, is somewhat similar to the way that

the bladder itself senses the level of urine. As the urine starts to accumulate, in the bladder, its level increases and so does the pressure in the bladder. The bladder has receptors which, based on the amount of stretch and pressure, will trigger the voiding signal. Here, the proposed method is that the level of urine could be sensed and measured as it rises and then a threshold based on this level is set, so that the state can be monitored with increased sensitivity. Again, the example of a potentiometer could be helpful for clarification. Assume that there are two potentiometers in series and that the voltage measurement probes are connected to the top potentiometer. The top potentiometer is controlled by the bottom one, in the sense that its value starts to vary and decrease only when the bottom potentiometer value has reached its minimum value. In this case, the bottom potentiometer value is being changed but no variation, translated to impedance, is being recorded from the probes connected to the top potentiometer. By the time a change in impedance is sensed from those probes, it means the bottom potentiometer has reached its minimum value and that now the impedance value of the top potentiometer started to vary as well. The same principle can be applied for the bladder when monitoring the bladder vertically to sense the change in impedance correlated with urine accumulation.

It should be noted that urine can have the highest conductivity in the pelvic region, with the average conductivity of 2 S/m [2], while the conductivity of the pelvic and abdominal region surrounding the bladder was considered to be homogeneous in various phantom studies and its average was reported to be 0.2 - 0.3 S/m [2, 127, 127]. Therefore, when the bladder is empty, ideally the impedance between the two vertical voltage-recording

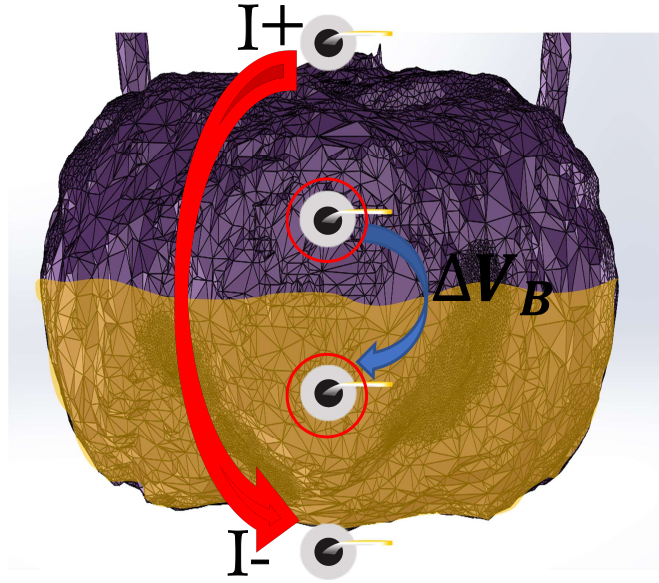


Figure 3.7: Vertical scanning of the bladder. Two inner electrodes that record change in (ΔV_B) as the level of urine rises, are marked in red.

electrodes should not change. As the urine starts to accumulate its surface level will get closer to the first electrode or, in other words the, sensing level. When reaching the first voltage measurement electrode, being the top potentiometer in the this example, then the value of ΔV_B shown in Figure 3.7 should change.

This method can be used as the warning threshold which requires action depending on the situation of the patient. Note that the sudden change in ΔV_B recorded from the electrodes (and, therefore, the impedance), is the signal that urine has reached a certain level. In this case, a threshold is not based on a fixed value of impedance but, rather, on the actual physical level of urine inside the bladder, indicated by observing a steeper change in impedance compared to the previous measurements. This hypothesis and its effectiveness will be examined experimentally on a phantom in Chapter 5.

3.4.2 Scanning of Boundaries

Now, what will happen if the location of the bladder is somehow moved due to different posture or a movement? There should be some mechanism so that, if the electrodes did not cover the normal location of the bladder due to the change in posture, this mechanism takes over the situation and warns regarding the bladder relocation. Figure 3.8 shows an image of the bladder in which extra sets of electrodes are covering each side of the middle electrodes (right and left). Each of those consists of the same four-electrode configuration, two outer electrodes for applying current and two inner electrodes for recording the voltage drop to calculate the impedance; and, therefore, the change that happens due to accumulation.

Since these extra sets of electrodes are covering the abdomen on each side and, as discussed earlier, assuming the conductivity of that area is homogeneous, a similar impedance should be measured at the boundaries if the position of bladder, including the urine inside, has not changed. Now if, the bladder is relocated from its original position, the voltage drop from one side is going to be different, not only from the other set of electrodes, due to the presence of the bladder and urine inside it, in the coverage area of that specific set of electrodes, but also compared to its previous measurement and it should show a bigger change. So, by introducing the side measurements in addition to the main set of measurements, the bladder area is covered and will be monitored to warn whether the location of the bladder has changed.

This hypothesis will also be examined in Chapter 5 and the effect of such relocation will be explored. To the best of the author's knowledge, this is

the first time that this aspect has been studied and addressed in order to propose a solution towards a wearable BI measurement device for bladder monitoring.

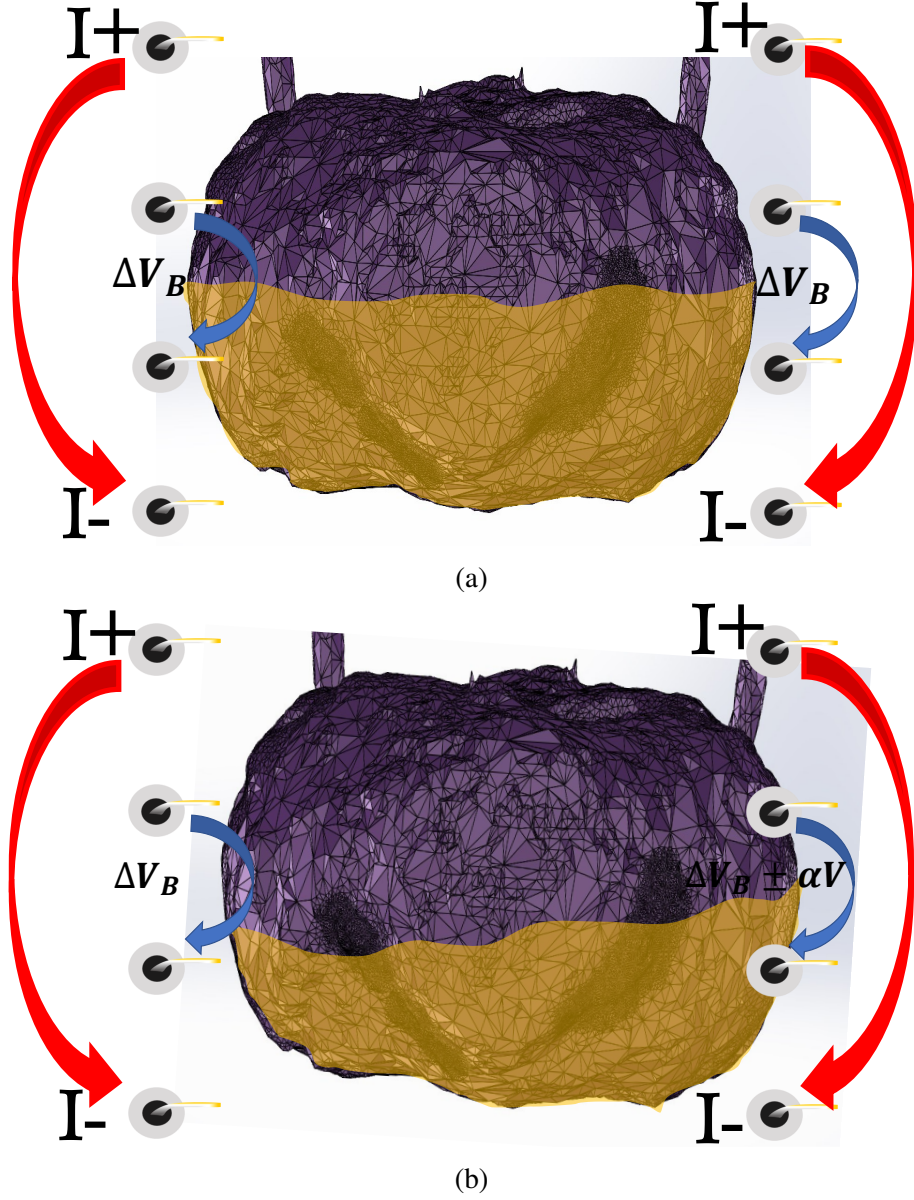


Figure 3.8: Electrodes covering boundaries of the bladder, (a) Bladder is in its original place, (b) Bladder is relocated to the side due to movement and caused a difference in voltage change in comparison to the other side.

3.5 Summary

So, to conclude, the constituent blocks of the BI measurement system were introduced and the overall parameters for the device were provided. Considering aims 3 and 4 mentioned in Chapter 1, a vertical monitoring of the abdomen area, in which the bladder is located, with three sets of electrodes is introduced. The vertical monitoring helps to mark a physical level that can be an indicator of bladder fullness and, when the urine level reaches this point, a steeper change in impedance, compared to previous measurements when the urine level is not as high, may be observed. This might happen regardless of the conductivity of the urine, as it is a comparison between the current measurement state and the previous one. In order to address the problem caused by a change of location of the bladder, the other two sets of electrodes on each side will cover the area underneath them, with the same measurement method. In this case, the bladder is always covered by electrodes that can scan its state and position.

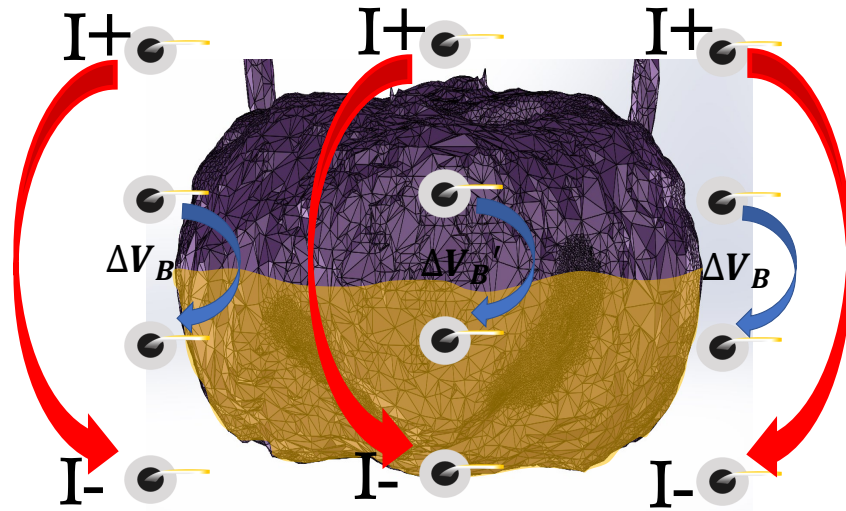


Figure 3.9: Final configuration of the method with three sets of electrodes vertically scanning the bladder area.

Figure 3.9 shows the final configuration for bladder monitoring with three set of electrodes, two sets on the sides and one in the middle.

In the next chapter, the detailed design procedure of the current source block of the BI measurement system is outlined.

Chapter 4

Voltage Controlled Current Source (VCCS) Block: Howland Current Source Design

In the previous chapter, a vertical scanning method with three separate sets of electrodes to monitor bladder fullness and relocation was proposed as a hypothesis. The block diagram of the BI measurement system was shown and briefly discussed. In this chapter, the design procedure of the VCCS block will be explored. This chapter begins with a brief review of the existing VCCS, it then introduces the Howland VCCS, and this is followed by the design procedure and measurement results for the designed Howland circuit. Finally, the conclusion presents a brief summary of the main results.

4.1 Current Source Architectures: A Brief Review

Two main structures for designing a current source for BI measurement were developed over the years; namely Voltage-Controlled and Current-

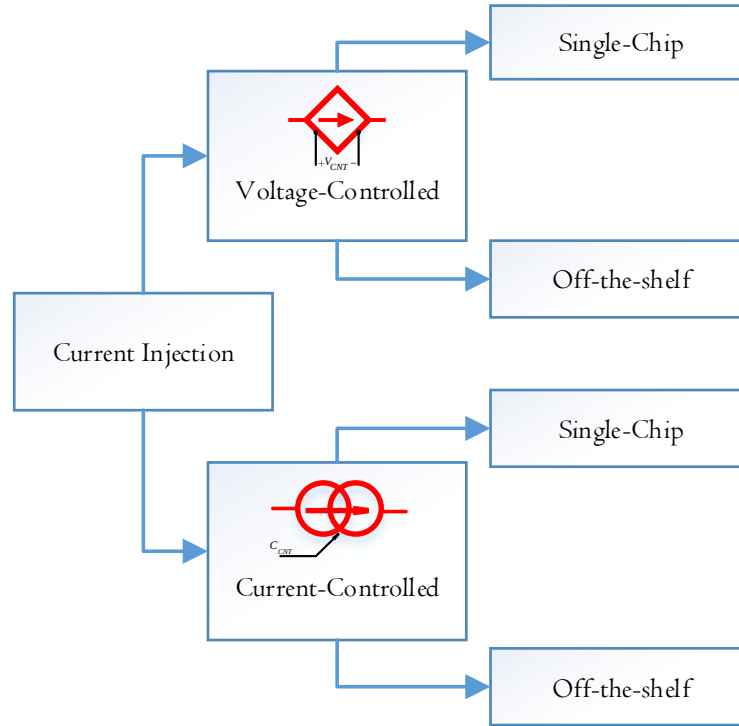


Figure 4.1: *Categories of current source solutions.*

Controlled structures [152]. There are two categories of solution for such structures: single chip or, in other words, application specific integrated circuit (ASIC) designs and off-the-shelf component designs as shown in Figure 4.1. In voltage-based structures, the generation of the output current is dependent on a controlling voltage. In a current-based structure, the output current is generated by an active device with intrinsic current-mode operation, such as Current Conveyors (CC) [152].

A common single-chip solution is the *AD5933* chip¹ [97,152]. Impedance measurement is carried out by exciting the body with a sinusoidal voltage, using a Transimpedance Amplifier (TIA) to convert the current flowing in the unknown impedance/load to a voltage, then using an internal 12-bit analog to digital converter (ADC), along with a Discrete Fourier Transform (DFT) engine to extract the impedance. This IC was used in some BI mea-

¹Information can be found at manufacturer website <https://www.analog.com/en/products/ad5933.html>

surement applications; however, the chip was only able to perform BI measurement with two electrodes, and not with a tetrapolar configuration. However, because of a built-in waveform generator and ADC, it was suitable to be used in off-the-shelf component designs, either as a DDS or when a two-electrode measurement was required [137, 155]. Another common single-chip solution is the *AFE4300*² from Texas Instruments [97]. One of the main advantages of using the *AFE4300* is the fact that it is a tetrapolar, four electrode measurement system. The chip is equipped with a 6-bit digital to analog converter, 10-bit DDS, and a 16-bit, 860 sample per second (SPS), ADC that converts only the peak voltage. It can communicate via a serial peripheral interface (SPI). It is reported that it consumes 100 μA in sleep mode and 970 μA during a BI measurement [156]. There are also other application specific integrated circuits (ASICs) reported in the literature that were used for bio-impedance measurement [157]. As this thesis is focused on the off-the-shelf component solutions, those will not be discussed here, but more discussions regarding the pros and cons of the ASICs can be found in [157]. For the current-based designs, the current conveyor is also popular. The current conveyor generation two (CCII), is a three-port component with two inputs (X, Y) and an output (Z) [158].

Figure 4.2 displays a symbol and a simplified schematic of the usual CCII implementation. The Y input is a high-impedance node, and its voltage is copied to X, the low-impedance node. The input current at the X node is copied to the Z high-impedance output node. To implement a current source with a CCII, an external voltage is connected to the Y node and a resistor R between ground and the X node. Thus, node Z generates the current

²information can be found on the manufacturer website <https://www.ti.com/product/AFE4300>

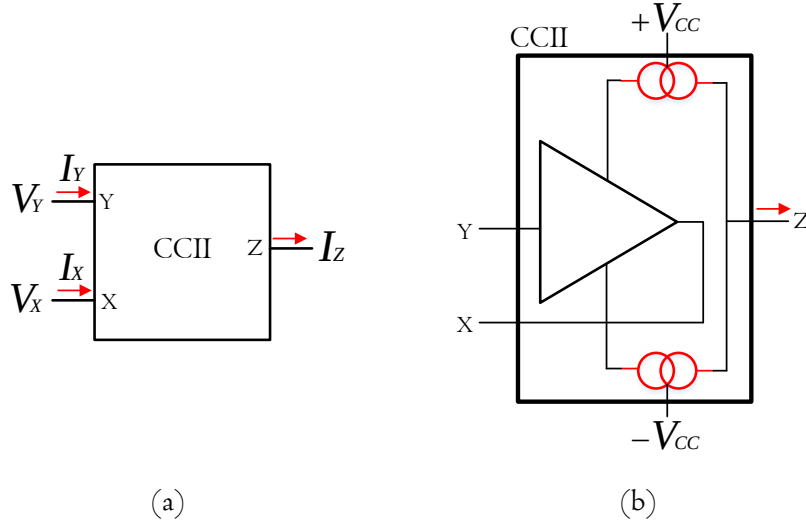


Figure 4.2: Current conveyor: a) symbol. b) simplified schematic.

replicated at node X, providing a large output impedance. The limitations are: first, the mirrored current should be a perfect match of the original current, which usually is a challenge, and second, there is a lack of commercial availability [152]. In this thesis, as discussed in the next section, a popular VCCS structure for the off-the-shelf component solution is employed. This topology is the foundation of the current source block in the BI measurement system. The design procedure for such a topology will be discussed thoroughly and its challenges will be highlighted.

4.2 Voltage-Controlled Current Source: Howland and Tietze Topologies

In bioimpedance measurements, Howland and Tietze typologies are the most used voltage-controlled current sources [159, 160]. Tietze topology [161], as shown in Figure 4.3, uses two operational amplifiers with negative feedback in cascade configuration with six resistors. The output current, I_{load} , and the output impedance, Z_{Out} , for Tietze circuit are given, respec-

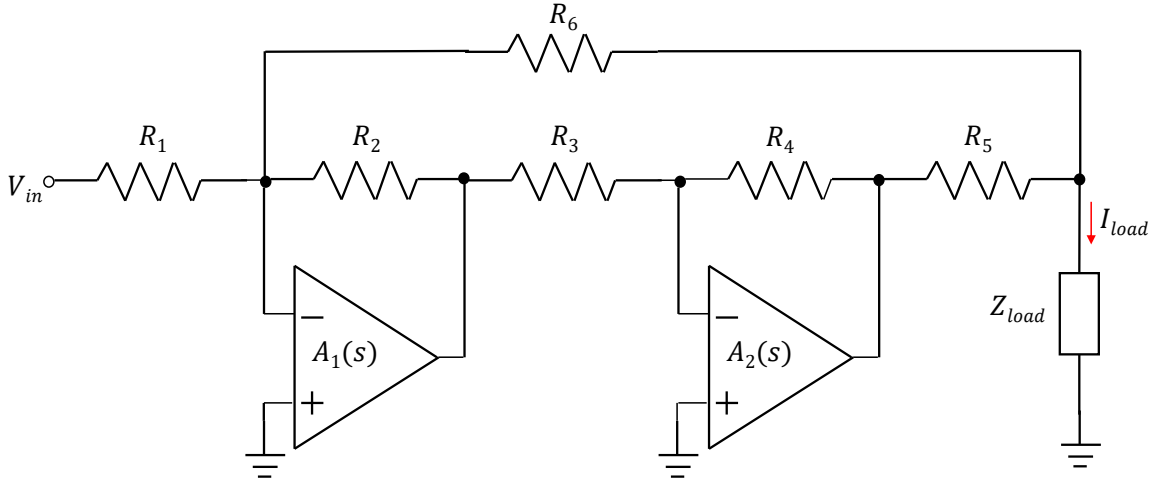


Figure 4.3: Tietze topology as a voltage-controlled current source.

tively [160]:

$$I_{load} = \frac{R_2 R_4 V_{in}}{R_1 R_3 R_5} \quad (4.1)$$

$$Z_{Out} = \frac{R_3 R_5 R_6}{R_2 R_4 - R_3 (R_5 + R_6)} \quad (4.2)$$

In comparison to Howland topology, Tietze uses more components and, selecting the resistors to obtain high output impedance while maintaining the current is challenging. Also, it has less output impedance and its performance is negatively affected when the frequency range is increased more than 1 kHz [159]. Therefore, a VCCS based on Howland topology was selected in this thesis. The Howland current source was first proposed in 1964³ (Figure 4.4a). Although this is an original topology, a comprehensive study in [162] showed its disadvantages and concluded that its performance is low, and that the voltage compliance and CMRR are low.

Within the variants of Howland current source, the Improved Howland circuit (IHW) is the most popular one for BI measurement, due to its sim-

³The study can be found online in http://www.philbrickarchive.org/1964-1_v12_no1_the_lightning_empiricist.htm

plicity and stability [152, 162]. Figure 4.4b shows the IHW circuit. This topology was studied in [162] and it was shown that its performance regarding the voltage compliance, CMRR, and output impedance is better than the original circuit. It should be noted that an important requirement for a current source is to ensure that its output current, which here is applied to the body, has constant amplitude over the frequency of interest. This should be obtained by a high output impedance. Figure 4.5 shows the IHW circuit with a buffered feedback path. This topology has better performance and greater output impedance and it also has superior performance regarding its voltage compliance and CMRR compared to the original Howland current source and the IHW circuit [162, 163]. For these reasons, this modified topology, namely IHW with buffered feedback path, was used in this thesis as the VCCS and the circuit analysis for the rest of the chapter is performed based on it.

The equations for the load current I_{load} can be found by analyzing the circuit as follows. By considering R_1 to R_4 to be equal (for simplicity), the output voltage of the difference amplifier V_{o1} is:

$$V_{o1} = V_{in} + \frac{Z_{load}}{R_a + Z_{load}} \times V_{o1} \quad (4.3)$$

and reforming the equation gives V_{o1} :

$$V_{o1} = \left(1 + \frac{Z_{load}}{R_a}\right) \times V_{in} \quad (4.4)$$

The current in the load can be written as:

$$I_{load} = \frac{V_L}{Z_{load}} = \frac{\frac{Z_{load}}{R_a + Z_{load}} \times V_{o1}}{Z_{load}} \quad (4.5)$$

and substituting V_{o1} from (4.4) into (4.5) gives:

$$I_{load} = \frac{V_{in}}{R_a} \quad (4.6)$$

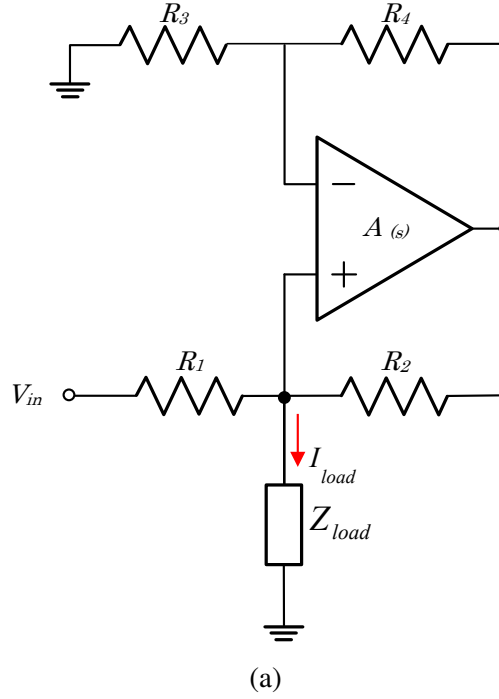
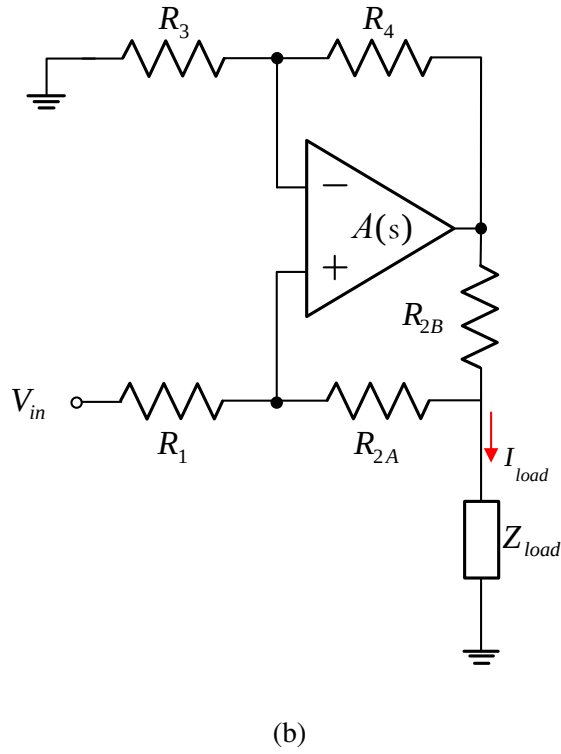


Figure 4.4: VCCS known as a Howland current source a) The original b) Improved Howland current source circuit.

This shows that the current in the load is independent of the value of its impedance. In other words, the current that passes through the load is constant and can only be changed or controlled by changing either or both of the parameters V_{in} and R_a .

To derive the output impedance of this VCCS, V_{in} is set to zero and a test AC voltage source is placed at the output node with parameters of V_x and I_x , giving:

$$I_x = -\left(\frac{R_1}{R_1 + R_2} \times V_x \times \left(1 + \frac{R_4}{R_3}\right) - V_x\right) \times \left(\frac{1}{R_a}\right) \quad (4.7)$$

Now, by reorganizing (4.7), for the output impedance Z_{Out} of the circuit, we have:

$$\frac{V_x}{I_x} = Z_{Out} = \frac{R_a}{1 - \left(\frac{R_1}{R_1 + R_2}\right)\left(\frac{R_3 + R_4}{R_3}\right)} \quad (4.8)$$

To have infinite output impedance, the denominator of (4.8) should be equal to zero. By doing that, for the nonzero values of the feedback resistors, this

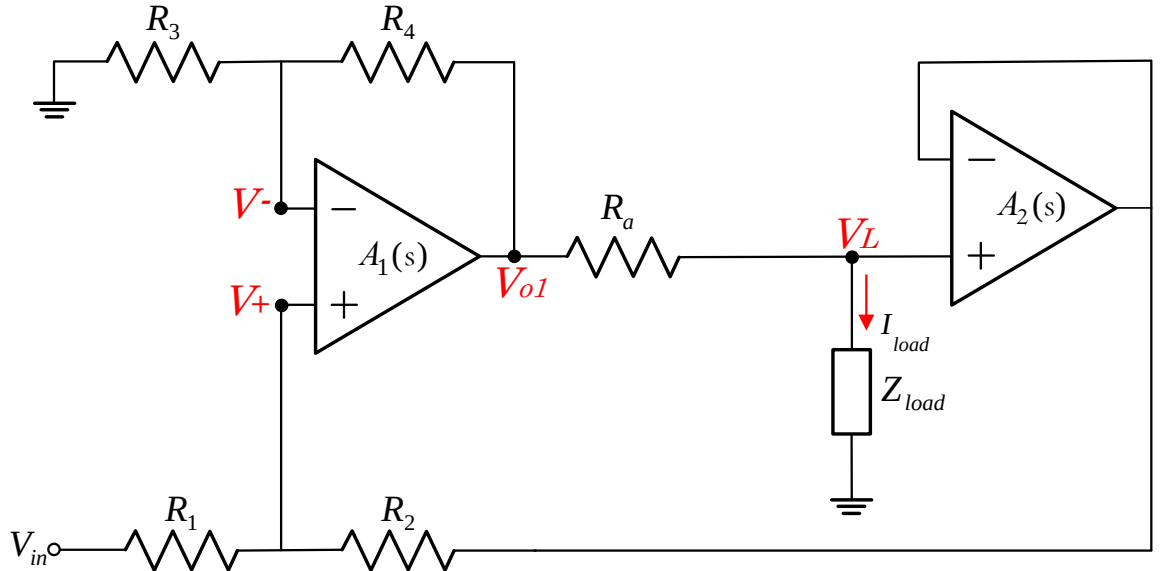


Figure 4.5: Howland current source with buffered feedback path.

gives:

$$R_1(R_3 + R_4) = R_3(R_1 + R_2) \implies R_1 = R_3, R_2 = R_4 \quad (4.9)$$

(4.9) can be rewritten as:

$$\frac{R_3}{R_1} = \frac{R_4}{R_2} \quad (4.10)$$

If (4.10) holds true then Z_{Out} will be infinite, independent of the value of R_a . Considering (4.10) and (4.6), the equations describe an ideal VCCS with infinite output impedance for which the output current can be adjusted by varying the input voltage V_{in} . However, in practice, the components of the buffered IHW circuit have non-idealities. In the next section, the impact of each non-ideality is explored and the final impact on output impedance and output current is shown.

4.2.1 Circuit analysis: Non-Idealities of Buffered IHW Circuit

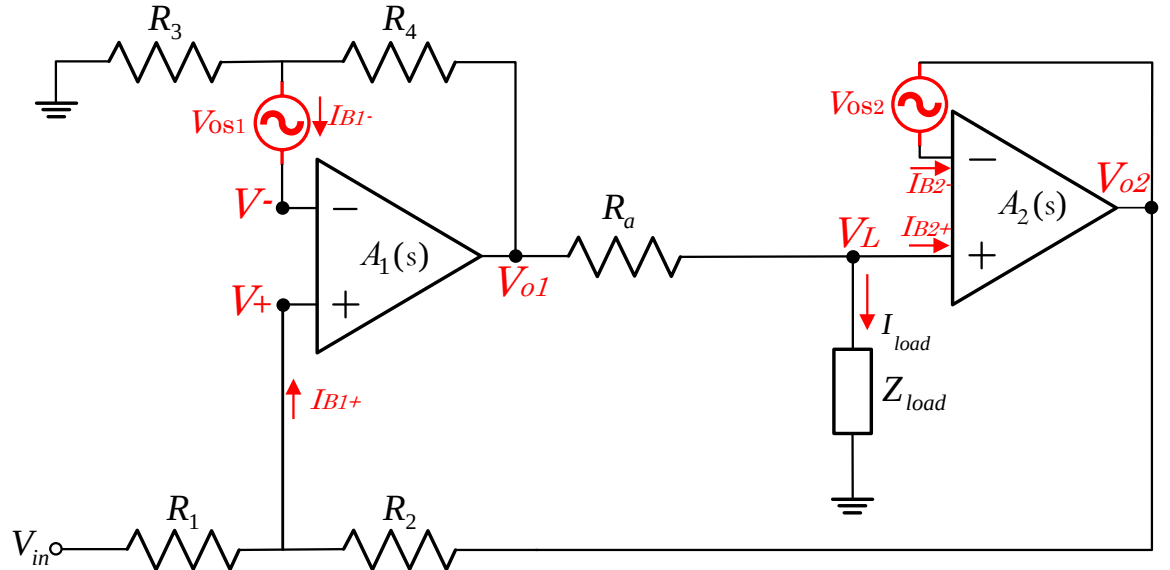


Figure 4.6: Buffered IHW circuit with the non-idealities.

The equations mentioned in the previous section will provide an insight

for the main parameters which can control the current, and how the circuit works ideally. However, from a design perspective, typical non-idealities of the components should be taken into account (Figure 4.6). The first matter that should be noticed is the non-idealities in the feedback resistors, R_1 to R_4 . The values and the amount of mismatch between the resistors are among the main drawbacks of the circuit, if chosen improperly. First, the impact of mismatch is explored as follows.

Resistors have absolute tolerance ΔR represented in percentage in their data sheet. Also, the matching ratio $\frac{\Delta R}{R}$ between the resistors is very important. For instance, if a 1 k Ω resistor with ΔR of $\pm 10\%$ is selected for the feedback resistors, the minimum and maximum values could be 900 Ω and 1.1 k Ω , respectively. The ratio of the component value to its adjacent resistor is also important according to (4.10) and it can affect the output impedance significantly. Taking the worst case scenario in (4.10) and assuming the nominal values of the resistors to be R gives:

$$R_3 = R + \Delta R, \quad R_1 = R - \Delta R, \quad R_4 = R - \Delta R, \quad R_2 = R + \Delta R \quad (4.11)$$

Substituting this into (4.8), it gives:

$$\frac{V_x}{I_x} = Z_{Out} = \frac{R_a}{1 - \left(\frac{R - \Delta R}{2R}\right)\left(\frac{2R}{R + \Delta R}\right)} \quad (4.12)$$

and then it can be shown that Z_{Out} becomes:

$$Z_{Out} = \frac{R_a}{2} \times \left(1 + \frac{1}{\frac{\Delta R}{R}}\right) \quad (4.13)$$

A numerical example can show the importance of good matching, or in other

words, selecting components with the lowest $\frac{\Delta R}{R}$ possible. If, according to (3.5) and Figure 3.4, Z_{Out} should be $10 \text{ M}\Omega$, and for $R_a = 5 \text{ k}\Omega$, then this dictates:

$$\frac{\Delta R}{R} = \frac{\frac{R_a}{2}}{Z_{Out} - \frac{R_a}{2}} \implies \frac{\Delta R}{R} \leq 0.025\% \quad (4.14)$$

As it can be seen, to drive a load in range of $1 \text{ k}\Omega$ and having $Z_{Out} = 10 \text{ M}\Omega$, the feedback resistors should have $\frac{\Delta R}{R}$ below 0.025% . The importance of this value now is clear. From having an ideal infinite output impedance, a significant reduction happens in practice, to the range of $\text{M}\Omega$. Next, the impact of non-idealities of the opamps are explored. It should be noted that, in all the cases below, V_{in} was set to zero for the analysis, unless stated otherwise.

Offset Voltage

Considering equation (4.6), it was mentioned that this equation is true in an ideal scenario. In order to derive a realistic equation for controlling the current that will be applied to the body, superposition is used. At the end, the sum of the outputs due to different inputs and non-idealities will be presented. The first parameter to be considered is the input offset voltage of $A_1(s)$ and then that of $A_2(s)$ will be considered. Looking at the effect of V_{os1} on V_{o1} :

$$V_{o1} = (V_- + V_{os1}) \left(1 + \frac{R_4}{R_3}\right) \quad (4.15)$$

Now, for V_- it can be shown that:

$$V_- = \frac{\left(\left(1 + \frac{R_4}{R_3}\right) \left(\frac{R_1}{R_1 + R_2}\right) \left(\frac{Z_{load}}{R_a + Z_{load}}\right) \right) V_{os1}}{1 - \left(\left(1 + \frac{R_4}{R_3}\right) \left(\frac{R_1}{R_1 + R_2}\right) \left(\frac{Z_{load}}{R_a + Z_{load}}\right) \right)} \quad (4.16)$$

By substituting (4.16) into (4.15) and organizing the equation, it gives:

$$V_{o1} = \left(\frac{\left(\left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \right)}{1 - \left(\left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \right)} + 1 \right) \left(1 + \frac{R_4}{R_3} \right) V_{os1} \quad (4.17)$$

In order to reform and simplify (4.17), it can be considered that:

$$\alpha = \left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \quad (4.18)$$

Then (4.17) can be written as:

$$V_{o1} = \left(\frac{\alpha}{1 - \alpha} + 1 \right) \left(1 + \frac{R_4}{R_3} \right) V_{os1} \implies V_{o1} = \left(\frac{1}{1 - \alpha} \right) \left(1 + \frac{R_4}{R_3} \right) V_{os1} \quad (4.19)$$

Now, V_{o1} is equal to:

$$V_{o1} = \frac{1 + \frac{R_4}{R_3}}{1 - \left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right)} V_{os1} \quad (4.20)$$

Assuming R_1 to R_4 are equal, the above equation reduces to:

$$V_{o1} = \frac{2V_{os1}}{1 - \frac{Z_{load}}{R_a + Z_{load}}} = \left(1 + \frac{Z_{load}}{R_a} \right) 2V_{os1} \quad (4.21)$$

The impact of V_{os1} on the output current being applied to the load is then:

$$I_{load,os1} = \frac{\left(\frac{Z_{load}}{Z_{load} + R_a} \right) V_{o1}}{Z_{load}} \implies I_{load,os1} = \frac{2V_{os1}}{R_a} \quad (4.22)$$

Analyzing the impact of V_{os2} on I_{load} gives:

$$V_L = V_{-,2} = \frac{\left(\left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \right) V_{os2}}{1 - \left(\left(1 + \frac{R_4}{R_3} \right) \left(\frac{R_1}{R_1 + R_2} \right) \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \right)} \quad (4.23)$$

Now, considering R_1 to R_4 to be equal, then I_{load} can be written:

$$I_{load,os2} = \frac{V_L}{Z_{load}} = \frac{\left(\frac{Z_{load}}{R_a} \right) V_{os2}}{Z_{load}} \implies I_{load,os2} = \frac{V_{os2}}{R_a} \quad (4.24)$$

Input Bias Current

Ignoring all other sources of input, the impact of input bias current I_{B1} of $A_1(s)$ will be investigated. Expressions for V_+ and V_- are determined as:

$$V_+ = \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) V_{o1} - (R_1 || R_2) I_{B1+} \quad (4.25)$$

$$V_- = \left(\frac{R_3}{R_4 + R_3} \right) V_{o1} - (R_3 || R_4) I_{B1-} \quad (4.26)$$

Now, as V_+ and V_- are equal, V_{o1} we can be obtained:

$$V_{o1} = \frac{(R_1 || R_2) I_{B1+} - (R_3 || R_4) I_{B1-}}{\left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) - \frac{R_3}{R_4 + R_3}} \quad (4.27)$$

The impact on I_{load} is then found:

$$I_{load,B1} = \frac{(R_1 || R_2) I_{B1+} - (R_3 || R_4) I_{B1-}}{\left(\left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) - \frac{R_3}{R_4 + R_3} \right) (R_a + Z_{load})} \quad (4.28)$$

This reduces to the following, assuming that R_1 to R_4 are equal with a value of R :

$$I_{load,B1} = \frac{R(I_{B1-} - I_{B1+})}{R_a} \quad (4.29)$$

In (4.29), if I_{B1+} is equal to I_{B1-} , then this equation will be equal to zero. What causes a difference between the input bias currents of an opamp is the input offset current. Therefore, this means that if the input offset current of the opamp $A_1(s)$ is relatively low, the impact of this artifact on the output current can be ignored. In other words, the input bias currents of $A_1(s)$ cancel each other out at the output of the system. For the impact of I_{B2} on I_{load} , because the buffer is directly connected to the load, I_{B2} will be drawn directly from the load, giving:

$$I_{load,B2} = -I_{B2+} \quad (4.30)$$

Finite Gain Bandwidth Product

And last, but not least, is the effect of finite bandwidth of the opamps, $A_1(s)$, $A_2(s)$ in the presence of V_{in} . Expressions for V_+ and V_- can be derived:

$$\begin{aligned} V_+ &= \frac{A_2(s)}{1 + A_2(s)} V_{o1} \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) + \left(\frac{R_2}{R_1 + R_2} \right) V_{in} \\ V_- &= \left(\frac{R_3}{R_3 + R_4} \right) V_{o1} \end{aligned} \quad (4.31)$$

Also, referring to Figure. 4.6 gives:

$$V_{o1} = A_1(s)(V_{+,1} - V_{-,1}) \quad , \quad V_{o2} = \frac{A_2(s)}{1 + A_2(s)} \times V_L \quad (4.32)$$

Now, substituting (4.31) into (4.32) for V_{o1} gives:

$$V_{o1} = A_1(s) \left(\left(\frac{A_2(s)}{1 + A_2(s)} \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) - \frac{R_3}{R_3 + R_4} \right) V_{o1} + \left(\frac{R_2}{R_1 + R_2} \right) V_{in} \right) \quad (4.33)$$

Reorganizing the above equation gives:

$$V_{o1} = \frac{A_1(s) \left(\frac{R_2}{R_1 + R_2} \right)}{1 - A_1(s) \left(\frac{A_2(s)}{1 + A_2(s)} \left(\frac{Z_{load}}{R_a + Z_{load}} \right) \left(\frac{R_1}{R_1 + R_2} \right) - \frac{R_3}{R_3 + R_4} \right)} V_{in} \quad (4.34)$$

Now, assuming that R_1 to R_4 are all equal, this gives:

$$V_{o1} = \frac{\frac{A_1(s)}{2}}{1 + \left(\frac{A_1(s)}{2} \right) \left(\frac{(1 + A_2(s)) R_a + Z_{load}}{(1 + A_2(s)) (R_a + Z_{load})} \right)} V_{in} \quad (4.35)$$

Consequently for the impact on I_{load} , this leads to:

$$I_{load, FGB} = \frac{\frac{A_1(s)}{2}}{\left(1 + \left(\frac{A_1(s)}{2} \right) \left(\frac{(1 + A_2(s)) R_a + Z_{load}}{(1 + A_2(s)) (R_a + Z_{load})} \right) \right) (R_a + Z_{load})} V_{in} \quad (4.36)$$

Summation of all Non-Idealities

Now, to sum up, including all the factors in deriving a realistic equation for the error caused by non-idealities of the opamps gives:

$$I_{load} = I_{load, os1} + I_{load, os2} + I_{load, B1} + I_{load, B2} + I_{load, FGB} \quad (4.37)$$

By substituting for each term, the final equation due to the non-idealities⁴ is:

$$I_{load,TnonI} = \frac{\frac{A_1(s)}{2}}{\left(1 + \left(\frac{A_1(s)}{2}\right) \left(\frac{(1+A_2(s))R_a + Z_{load}}{(1+A_2(s))(R_a + Z_{load})}\right)\right) (R_a + Z_{load})} V_{in} + \frac{2V_{os1}}{R_a} + \frac{V_{os2}}{R_a} + \frac{R(I_{B1-} - I_{B1+})}{R_a} - I_{B2} \quad (4.38)$$

It can be seen easily that if the non-idealities of the opamps are zero and the gain-bandwidth product of the opamp is infinite, then equation (4.38) will be reduced to the ideal case in (4.6).

4.2.2 Noise Analysis

In order to analyze the circuit for its noise, shown in Figure 4.7, the contribution of each noise source at node V_{o1} will be calculated and then the sum of all the contributions will be taken as the noise equation for the circuit. After analyzing the circuit, the contribution from each noise source that causes an error for the load current is as follows:

$$\begin{aligned} I_{load,ren1} &= -\frac{e_{n1}}{\left(\left(\frac{R_1}{R_1+R_2}\right)\left(\frac{Z_{load}}{Z_{load}+R_a}\right) - \frac{R_3}{R_3+R_4}\right) (R_a + Z_{load})} \\ I_{load,ren2} &= \frac{e_{n2}}{\left(\left(1 + \frac{R_4}{R_3}\right)\left(\frac{R_1}{R_1+R_2}\right)\left(\frac{Z_{load}}{Z_{load}+R_a}\right) - 1\right) (R_a + Z_{load})} \\ I_{load,rin1} &= \frac{i_{n1}\left(1 + \frac{R_4}{R_3}\right)}{\left(\frac{\left(1 + \frac{R_4}{R_3}\right)\left(\frac{Z_{load}}{Z_{load}+R_a}\right) - 1}{R_2} - \frac{1}{R_1}\right) (R_a + Z_{load})} \\ I_{load,rin2} &= i_{n2} \end{aligned} \quad (4.39)$$

⁴Total nonidealities shown as TnonI in the equation (4.38)

Assuming that R_1 to R_4 are equal to R , and summing up all the noise contributions from the opamps gives:

$$\bar{I}_{load,n1n2}^2 = \frac{4\bar{e}_{n1}^2}{R_a^2} + \frac{\bar{e}_{n2}^2}{R_a^2} + \frac{(R\bar{i}_{n1})^2}{R_a^2} + \bar{i}_{n2}^2 \quad (4.40)$$

For the resistors, the total noise contribution, assuming that all resistors have the same value, is:

$$\bar{I}_{load,R}^2 = \frac{\bar{e}_1^2}{R_a^2} + \frac{\bar{e}_2^2}{R_a^2} + \frac{\bar{e}_3^2}{R_a^2} + \frac{\bar{e}_4^2}{R_a^2} + \frac{\bar{e}_a^2}{R_a^2} \quad (4.41)$$

Therefore, total root mean squared (RMS) noise is:

$$\bar{I}_{load,TN} = \sqrt{\frac{\bar{e}_1^2 + \bar{e}_2^2 + \bar{e}_3^2 + \bar{e}_4^2 + \bar{e}_a^2}{R_a^2} + \frac{4\bar{e}_{n1}^2 + \bar{e}_{n2}^2 + (R\bar{i}_{n1})^2}{R_a^2} + \bar{i}_{n2}^2} \quad (4.42)$$

It can be seen from (4.42) that the voltage noise terms are divided by R_a , which means that increasing R_a decreases the value of the current noise at the load node. This analysis also shows that the contribution of current noise

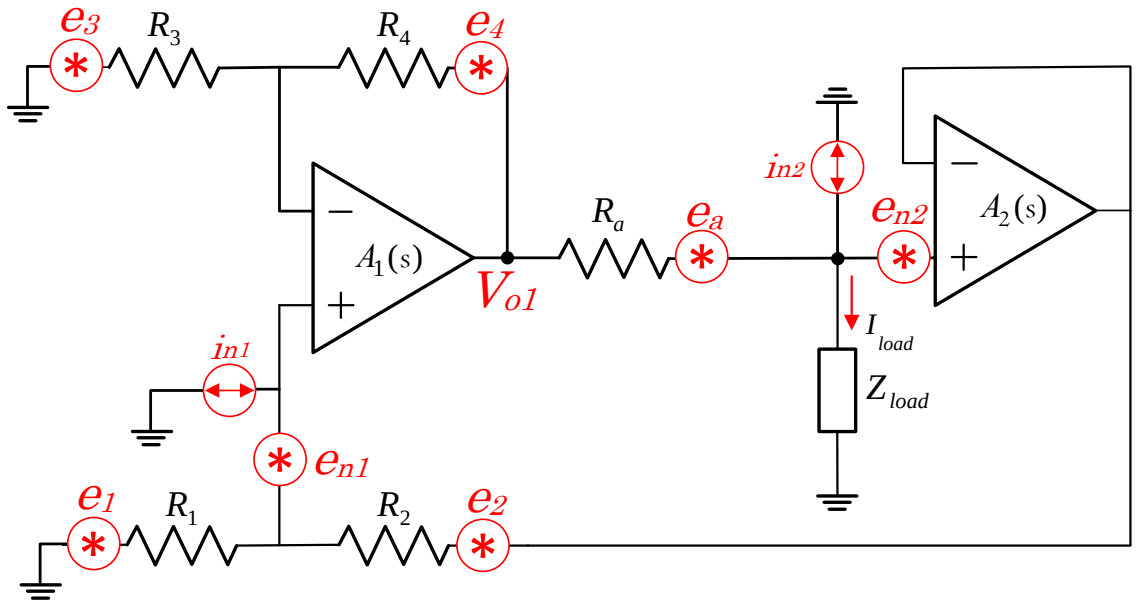


Figure 4.7: The VCCS with noise sources of each component.

of the buffer has a direct impact on the output current.

4.2.3 Stray Capacitance: Impact on Z_{Out}

Apart from all the non-idealities and noise in the circuit, stray, or parasitic, capacitance can cause a significant error in I_{load} or, in other words, in Z_{Out} . Figure 4.8 shows the buffered IHW circuit with the presence of this capacitance, (C_{out}). In this case, the output current is divided between C_{out} and

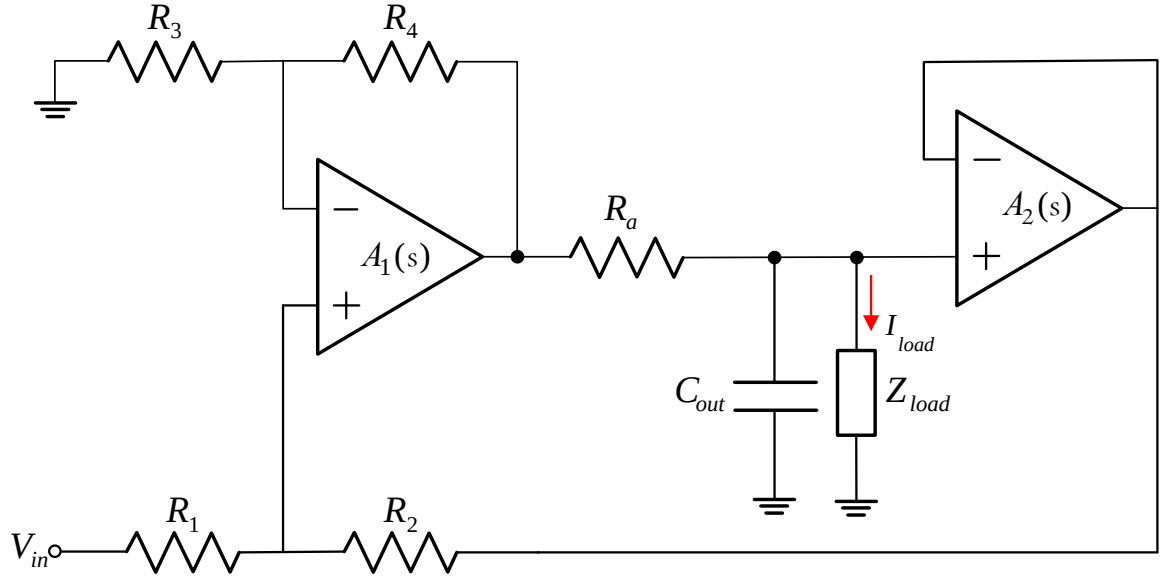


Figure 4.8: Buffered IHW circuit with stray capacitance at the output node.

the load so that, depending on the frequency of operation, the portion of the output current which flows through the load will vary. Because C_{out} is in parallel with Z_{Out} , it will reduce the total output impedance. Therefore, (4.8) should be rewritten:

$$Z_{Out} = \frac{R_a}{1 - \left(\frac{R_1}{R_1 + R_2}\right)\left(\frac{R_3 + R_4}{R_3}\right)} \parallel \frac{1}{sC_{out}} \quad (4.43)$$

For example, as was mentioned previously in the worst case, for a mismatch between the ratio of feedback resistors of the order of 0.02% and C_{out} of

10 pF and $R_a = 5 \text{ k}\Omega$ equation (4.13) gives:

$$Z_{Out} = 2500R_a \parallel \frac{1}{sC_{out}} \implies Z_{Out} = 12.5M\Omega \parallel \frac{1}{2\pi f * 10pF} \quad (4.44)$$

This example highlights the importance of the resistors $\frac{\Delta R}{R}$ and C_{out} together. The higher the value of $\frac{\Delta R}{R}$, the smaller the value of output impedance is achieved. This means if $\frac{\Delta R}{R}$ is increased, the resistive part of Z_{Out} can fall significantly. For C_{out} , it is noticed that as the frequency increases in BI measurement, for a typical parasitic capacitance due to the PCB traces and components, Z_{Out} can also fall significantly, and divert the current that should be applied to the body, into itself. Considering (4.13), (4.38) and (4.42), it can be seen that R_a has an important role in the reduction of variation in the current amplitude, both caused by noise and non-idealities of the circuits and also in increasing the resistive part of output impedance in (4.43). This is apart from the fact that it also controls the amount of current passed through the body, as shown in ideal form in (4.6). These equations dictate that the larger R_a , the less error in the current and the more output impedance the system will have. However, R_a is limited by the supply voltage and the input common range of the circuit and opamps. As R_a is increased, V_{in} should also be increased, to maintain the constant current passing through the body. This can be problematic due to the fact that $A_1(s)$ will go into saturation, as V_{o1} is larger than V_{in} , as shown in (4.4). Therefore, a trade-off here should be taken into consideration, based on the supply voltage and the application of the circuit and the value of R_a .

For the feedback resistors, the absolute values of these have an impact on the bandwidth of the system. Larger values of resistors, in the range of

10 k Ω , will reduce the bandwidth of the current source. However, the main drawback will be the large values for $\frac{\Delta R}{R}$. Although usage of the commercial IC resistors can reduce the effect, the cost is quite high, which can be another potential limitation. Following this thorough analysis, the IHW with a buffered feedback path circuit was manufactured on a PCB. The experimental results of the board are presented in the next section.

4.2.4 Component Selection

In order to select the components, the output impedance, which translates to b-bits of resolution and SNR in the current source, should be first taken into account. Considering (4.13), the IC resistors with the lowest $\frac{\Delta R}{R}$ possible, are the first components to be chosen. Two mismatch ratios were available for the IC resistors used in this thesis: 0.01% and 0.02%. The cost of 0.01% was almost the double of that of the other IC and so, for the feedback resistors, LT5400⁵ grade B (0.02%) with the value of 1 k Ω was selected.

A study performed in 2018, on a realistic pelvic phantom to monitor the bladder fullness with three different classifiers, concluded that if the total SNR of the impedance measurement device is above 60 dB, the classifiers could detect the state of the bladder with very high accuracy, above 95% [82]. The study in [164] indicated that the existing EIT devices have 60 to 80 dB SNR and maximum output impedance between 100 k Ω to 5 M Ω , depending on the device [164]. Unfortunately, no study was carried out to show the acceptable number of bits or SNR required for the current source design at the specific frequency and current amplitude that is used for bladder monitoring. As the study in [82] used a waveform with an amplitude of

⁵More information can be found at manufacturer datasheet at: <https://www.analog.com/en/products/lt5400.html>

5 mA_p (3.53mA_{rms}) at 50 kHz and reported high accuracy with 60 to 80 dB SNR for bladder monitoring, this SNR was taken as a starting point. This suggests that a 490 nA_{rms} to 3.53 μ A_{rms} error in the output current of the VCCS is acceptable.

To select $A_1(s)$ and $A_2(s)$, their high-bandwidth and then low-power consumption should be considered. Then, other parameters that have an impact on the output current, based on (4.38) and (4.42), should be considered. With the advancement of semiconductor technologies there are various options that could be chosen for the off-the-shelf amplifiers and, through various iterations, four different sets were selected and implemented on a PCB, which was designed with Altium Designer⁶. Among the four sets, ADA4807⁷ and AD8065⁸ were selected due to their having the highest bandwidth and low power consumption. Table 4.1 shows the specifications of the selected amplifiers.

Table 4.1: Specifications of the amplifiers used in the VCCS.

Role	ID	Full power bandwidth (MHz)	V _{os} (V)	I _{bias} (A)	V _{noise} (nV/√(Hz))	I _{noise} (fA/√(Hz))	Current Consumption (mA)
A ₁ (s)	ADA4807	30	40	530n	3.1	700	1
A ₂ (s)	AD8065	42	400	1p	7	0.6	6.4

As the aim is to test the device from 5 kHz to 50 kHz, Tables 4.2 and 4.3 indicate the calculated minimum R_a required to obtain a specific output impedance in the presence of parasitic capacitance from 1 pF to 10 pF within b-bits of resolution at 5 kHz and 50 kHz, respectively. In these tables, three categories of the load were considered to be connected to the VCCS: namely

⁶Altium Designer,v2021

⁷More information can be found at manufacturer datasheet at :<https://www.analog.com/en/products/ada4807-1.html>

⁸More information can be found at manufacturer datasheet at: <https://www.analog.com/en/products/ad8065.html>

Table 4.2: Parameters of the VCCS to meet a certain output impedance with b -bits of resolution at 5 kHz.

Load range (Ω)		30 - 100		30 - 500		300 - 600		30 - 1000	
Number of bits		10	13	10	13	10	13	10	13
Output impedance ($M\Omega$)		0.071	0.573	0.48	3.8	0.306	2.45	0.992	7.94
$R_a (\Omega) >$	cp = 1 pF	28.7	233.2	195.2	1750	123.7	1060	409.7	4230
	cp = 5 pF	28.9	252	208	3900	128.7	1600	470.2	CBA*
	cp = 10 pF	29.5	279.7	226.5	CBA*	135.6	4300	576.7	CBA*
$I_{load, TnonI}$ (nA)	$R_a = 2\text{ k}\Omega$	224	224	224	224	224	224	224	224
	$R_a = 5\text{ k}\Omega$	89	89	89	89	89	89	89	89
$I_{load, TN}$ (nA)	$R_a = 2\text{ k}\Omega$	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52
	$R_a = 5\text{ k}\Omega$	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21

* Can not be achieved. This means with the mentioned parameters the output impedance required for having b -bits of resolution is not possible.

Table 4.3: Parameters of the VCCS to meet a certain output impedance with b -bits of resolution at 50 kHz.

Load range (Ω)		30 - 100		30 - 500		300 - 600		30 - 1000	
Number of bits		10	13	10	13	10	13	10	13
Output impedance ($M\Omega$)		0.071	0.573	0.48	3.8	0.306	2.45	0.992	7.94
$R_a > (\Omega)$	cp = 1 pF	29.3	279.7	226.5	CBA*	135.5	4300	518	CBA*
	cp = 5 pF	32.2	2300	785.4	CBA*	236.2	CBA*	CBA*	CBA*
	cp = 10 pF	36.9	CBA*	CBA*	CBA*	3247	CBA*	CBA*	CBA*
$I_{load, TnonI}$ (nA)	$R_a = 2\text{ k}\Omega$	224	224	224	224	224	224	224	224
	$R_a = 5\text{ k}\Omega$	89	89	89	89	89	89	89	89
$I_{load, TN}$ (nA)	$R_a = 2\text{ k}\Omega$	1.65	1.65	1.65	1.65	1.65	1.65	1.65	1.65
	$R_a = 5\text{ k}\Omega$	0.65	0.65	0.65	0.65	0.65	0.65	0.65	0.65

* Can not be achieved. This means with the mentioned parameters the output impedance required for having b -bits of resolution is not possible.

low, mid and full range up to 1 k Ω . In addition, the impact of non-idealities and noise over the mentioned frequency range for two different R_a values is provided. It should be noted that noise and non-idealities are independent of the range of the load and the number of bits required; therefore, they stay the same when those parameters are changed.

4.3 Results

Figure 4.9 shows the manufactured PCB of the IHW circuit with buffered feedback path. The board can be powered up either by an external power supply or the power board shown in Figure 4.9. Each section of the board

is highlighted by red arrows. To measure the amplitude of the load current, an instrumentation amplifier was also included in order to sense the voltage across a known load. This voltage was monitored by an oscilloscope, and then it was divided by the known and previously measured load impedance to obtain the amplitude of the current. The instrumentation amplifier is essential because the probes of the oscilloscope can cause loading on the circuit, thus leading to a potential error in the calculation.

In this version, as the aim was to test the circuit and determine any limitations, R_a was selected to have a nominal value of 2 k Ω and its measured value was 1.978 k Ω . This relatively low value was to ensure that there would be enough voltage headroom for the circuit when connected to higher impedance loads. In a subsequent version, described in Chapter 5, R_a of 5 k Ω was selected as the circuit does not need to drive loads of several k Ω . Based on the specifications of the selected components and with $R_a = 2$ k Ω at 50 kHz, non-idealities and noise generate 225.65 nA_{*rms*} error in the current. The variation in the current due to finite output impedance

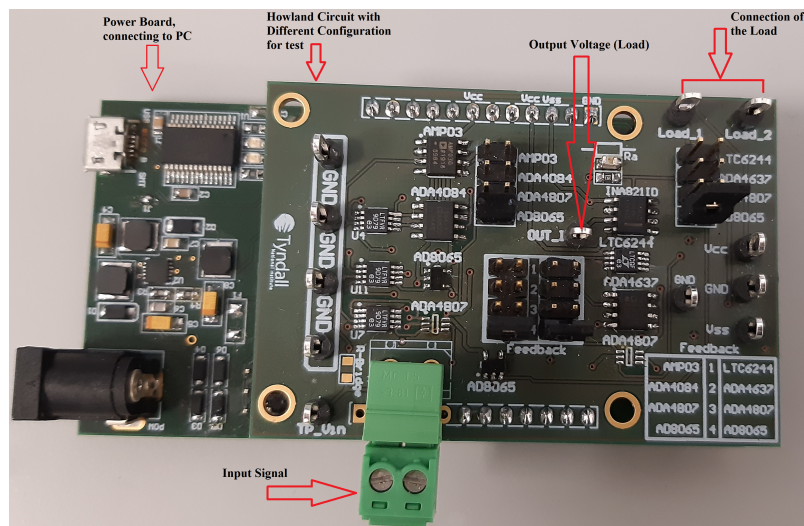


Figure 4.9: *IHW circuit with buffered feedback path on PCB.*

is dependent on the connected load, R_a , and the amplitude of the current applied to the load but, for a full range load and 13 bits, and with $R_a = 2 \text{ k}\Omega$ when the current is $200 \mu\text{A}_{\text{rms}}$, the variation is $353 \text{ nA}_{\text{rms}}$, leading to total of $578.65 \text{ nA}_{\text{rms}}$ error in the current amplitude. This is within the mentioned acceptable error range. With the same parameters and $R_a = 5 \text{ k}\Omega$ the total error would be $419.25 \text{ nA}_{\text{rms}}$. Both of these values also give rise to error voltages less than the least significant bit (LSB) in a 13-bit resolution system. One point that is worth emphasizing is that, although it was stated in Tables 4.2 and 4.3 that a specific output impedance in some scenarios is not achievable, considering the error mentioned in [82], the total generated errors in the current amplitude are well within the acceptable range, as mentioned previously.

For the loads, seventeen different resistors from 50.72Ω to 3250Ω were measured with a precision ohmmeter and used. The circuit was set to provide three different currents with amplitudes of $100 \mu\text{A}_{\text{rms}}$, $200 \mu\text{A}_{\text{rms}}$ and $500 \mu\text{A}_{\text{rms}}$, and the frequency was swept from 1 kHz to 10 MHz. Four different scenarios for parasitic capacitance were considered. Capacitors were also connected to the output of the circuit to mimic the effect of parasitic capacitors. The first experiment was done without any extra capacitor in parallel with the load, so it represents the scenario with the on-board parasitic capacitance only. For the next three scenarios, the values for the capacitors were 47 pF, 100 pF and 220 pF, which can mimic the values for parasitic capacitance when multiplexing is used. In total, 204 experiments and measurements were performed. The board was powered up by $\pm 3 \text{ V}$ supplies and the circuit consumed 7.4 mA. Figure 4.11 through Figure 4.13

show the obtained data from the PCB, for the setups where I_{load} is equal to $100 \mu A_{rms}$, $200 \mu A_{rms}$, and $500 \mu A_{rms}$, respectively. All the data presented here was plotted in MATLAB⁹. The figures represent current amplitude versus frequency, while increasing the load from the nominal value of 50Ω to 3250Ω and also increasing the parasitic capacitance, C_p . It can be seen for each graph that, as the load is increased towards the higher values, the bandwidth is reduced. In order to show all the results, including three current amplitudes and different loads and parasitic capacitances in one graph (for a better comparison) and also to be able to detect the impact of each increment on the bandwidth, Figure 4.10 was plotted in 3D mode. Since the 3250Ω load would make the amplifiers go into saturation when I_{load} is set to $500 \mu A_{rms}$, data from this setup was not shown, as MATLAB requires all the data arrays obtained from the setups to be the same size while plotting in 3D mode; so data from each setup is depicted up to 1968Ω .

This 3D figure shows the -3 dB bandwidth of the current source versus current amplitude, load impedance and parasitic capacitance, so the effect of each of the factors is obvious. All of the -3 dB bandwidths were calculated with data obtained from the PCB. Each surface is related to a parasitic capacitor value, from the top being of i.e. zero Farads to the bottom being 220 pF. It can be seen clearly that with increasing parasitic capacitance, the planes move downward, meaning that the -3 dB bandwidth is falling. As V_{in} is increased, which means increasing the current amplitude, the -3 dB bandwidth also falls. While increasing the load, a maximum -3 dB bandwidth of 1.248 MHz was observed for 50.72Ω with no capacitance connected and a $100 \mu A_{rms}$ output current. A minimum -3 dB bandwidth of 147 kHz was

⁹<https://www.mathworks.com/products/matlab.html>

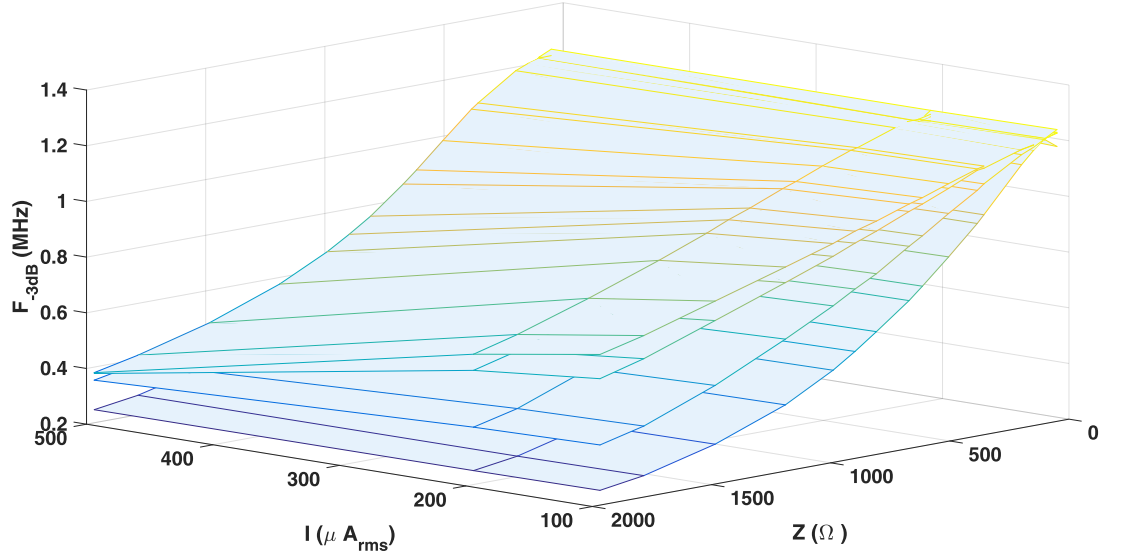


Figure 4.10: -3 dB bandwidth of the improved Howland current source as a function of current and load impedance for four values of parasitic capacitance: 0 (top curve), 47 pF, 100 pF, and 220 pF (bottom curve).

observed for the setup with a 3250Ω load and a parasitic capacitance of 220 pF and a current amplitude of $200 \mu A_{rms}$. The maximum drop in bandwidth, due to increasing load, parasitic capacitance and current amplitude were 88%, 58%, and 44% respectively.

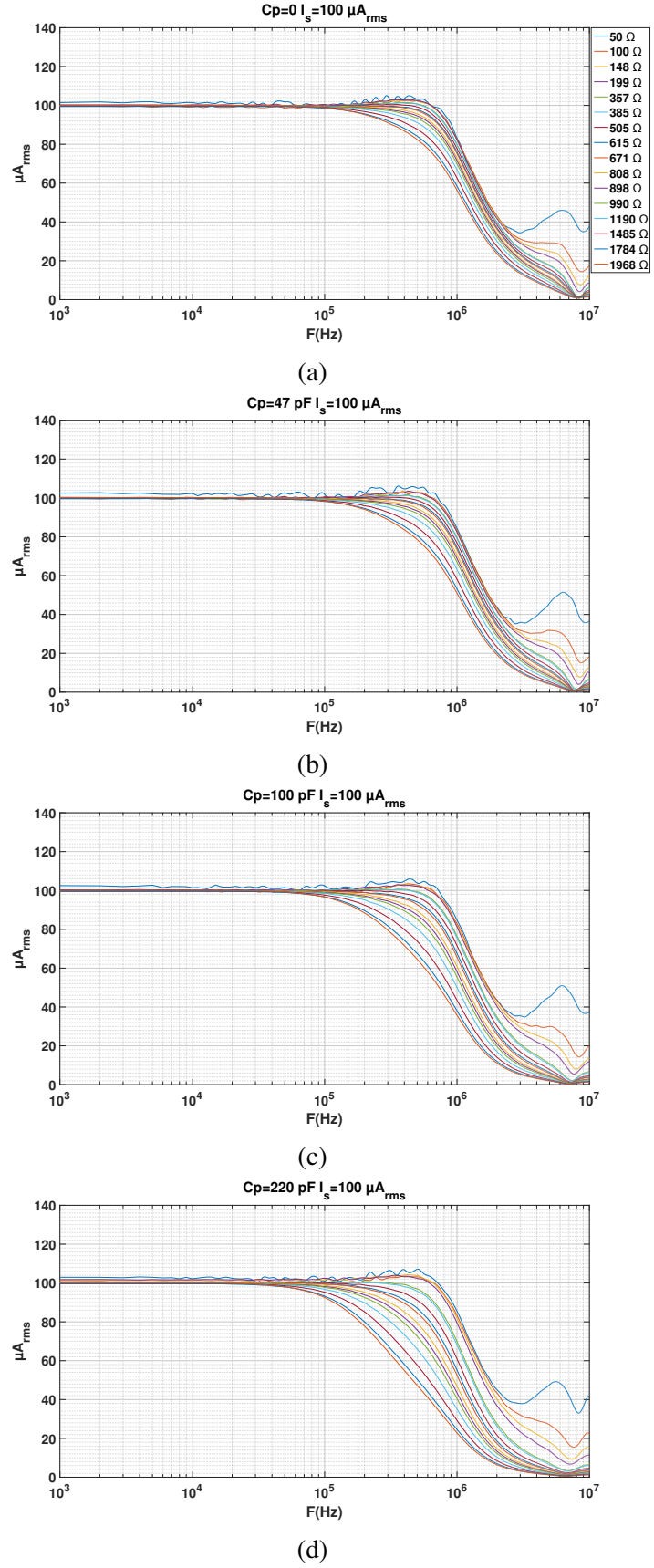


Figure 4.11: Current (I_{load}) vs frequency while varying the loads and parasitic capacitance for $100 \mu A_{rms}$ a) $C_p = 0$, b) $C_p = 47$ pF, c) $C_p = 100$ pF, d) $C_p = 220$ pF.

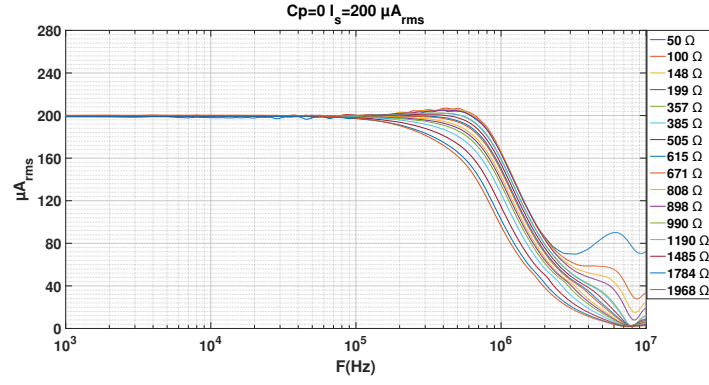
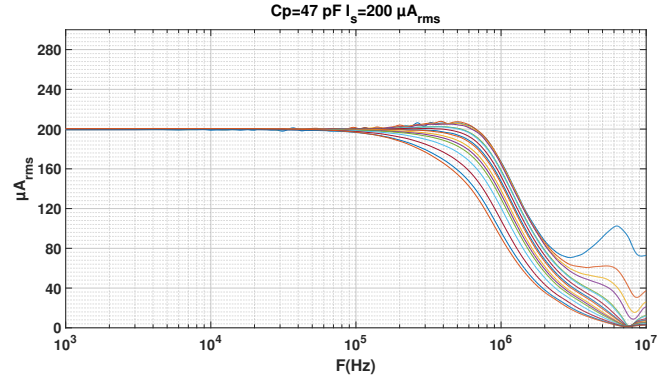
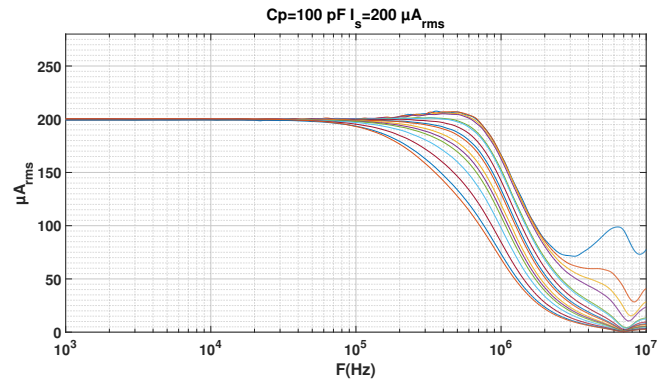
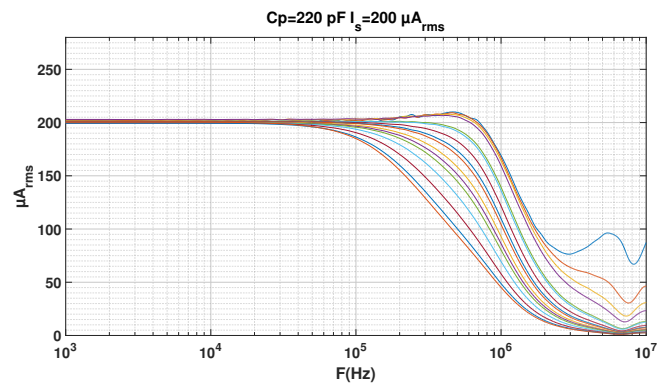


Figure 4.12: Current (I_{load}) vs frequency while varying the loads and parasitic capacitance for $200 \mu A_{rms}$ a) $C_p = 0$, b) $C_p = 47$ pF, c) $C_p = 100$ pF, d) $C_p = 220$ pF.

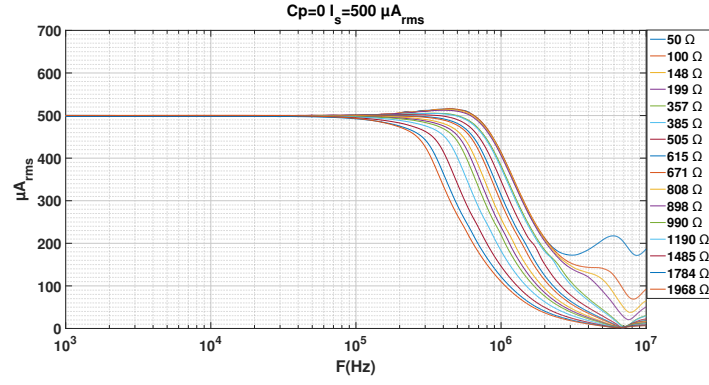
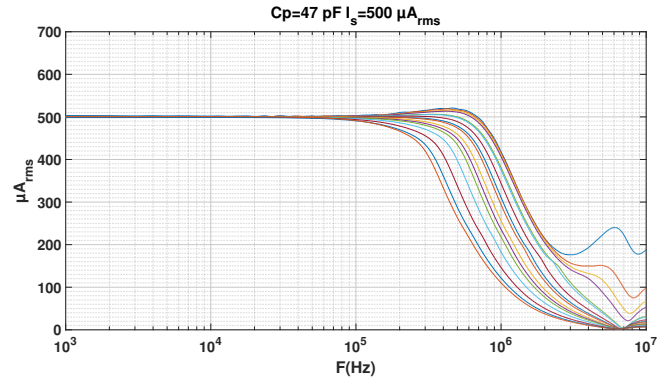
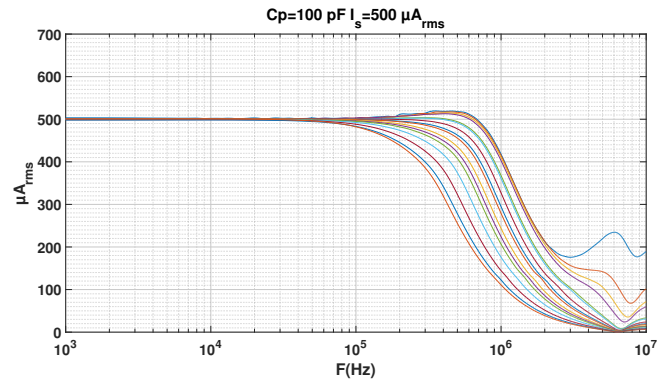
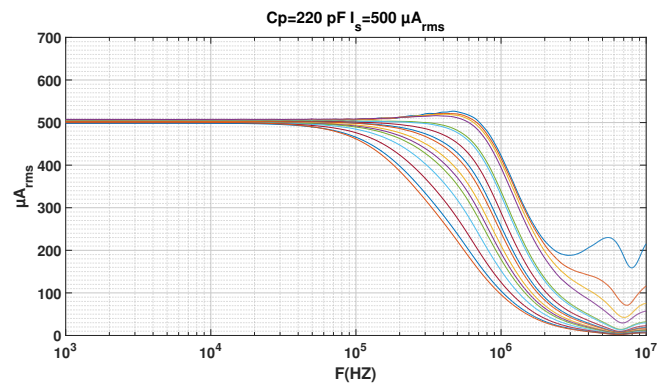


Figure 4.13: Current (I_{load}) vs frequency while varying the loads and parasitic capacitance for $500 \mu A_{rms}$ a) $C_p = 0$, b) $C_p = 47$ pF, c) $C_p = 100$ pF, d) $C_p=220$ pF.

4.4 Chapter Conclusion

In this chapter, a thorough analysis of the IHW current source with buffered feedback path was performed. Equations were derived and the circuit was analyzed in order to investigate its limitation in BI measurement applications. The mentioned architecture was also implemented on a PCB in order to examine its performance and to show the importance of different parameters. Noise and non-idealities had a trivial impact on the performance while the range of the load that is connected to the circuit, parasitic capacitance, and current amplitude were found to be the most important factors, rated in order of their relative impact, that can cause error in the output current, especially at higher frequencies of operation. Larger parasitic capacitance has a detrimental impact on output impedance, causing the current to deviate from its expected value and roll off at higher frequencies as the output impedance starts to drop and the capacitor diverts part of the current. Increasing the current amplitude and the value of the load also significantly reduces the -3 dB bandwidth of the current source. These findings match with the equation provided for V_{o1} earlier in the chapter. Trying to get a higher gain from $A_1(s)$ will cause a drop in bandwidth due to the finite gain-bandwidth product of $A_1(s)$. All of the factors that give a reduction in the bandwidth of the current source mean that, at higher frequencies, the output current is not constant and this will lead to errors when determining an unknown impedance. Therefore, in designing a current source based on the circuit provided here for BI measurement, the target frequency of operation and the range of the load under test are very important and these should be carefully considered.

Chapter 5

Bio-impedance Measurement Device: Results of the Designed System and Phantom Experiments

The design of a VCCS block was examined thoroughly in the previous chapter and, in this chapter, the data acquisition (DAQ) block of the system is explained. The chapter will then review the results of the designed BI measurement system on known loads. Later in the chapter, the agar based phantom used in this thesis is introduced and the experimental results of the proposed method on the phantom, related to aims 3 and 4, is provided. These experiments were carried out by a calibrated and commercial impedance analyzer, Agilent E4980A. Then, the results of the BI measurements carried out using the designed system on the phantom will be shown and the conclusions of the chapter will be presented.

5.1 ADC in the DAQ block: Sampling the Input Voltage and the Voltage of the Tissue Under Test

Two ADCs were used in the designed BI measurement system. One samples the input voltage controlling the VCCS and the second one samples the voltage from the tissue/load under test. This is the voltage that will be sent to the PC, in order to calculate the impedance change due to any variation in the characteristics of the load under test. The ADC that samples the voltage of the load will be called output ADC in this chapter. Considering the frequency of interest being below 50 kHz with 13 bits of resolution, an ADS8860¹ was selected as the output ADC. This ADC had the lowest power consumption amongst other available chips on the market with the same performance specification. The power consumption versus sampling frequency can be found in Figure 5.1².

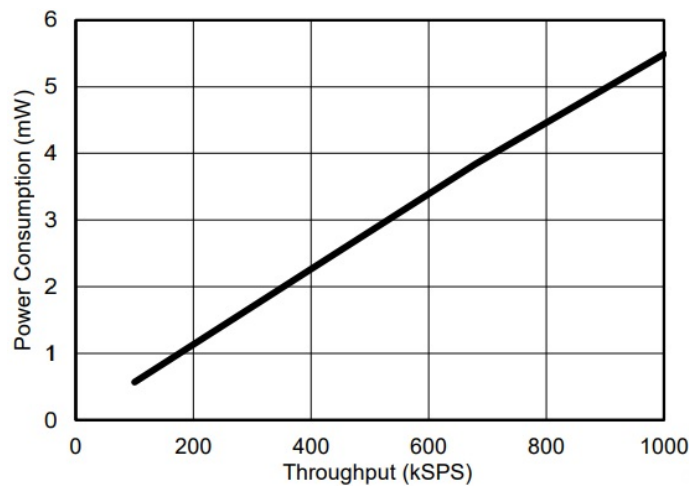


Figure 5.1: Power Consumption vs the sampling frequency of the ADS8860, taken from the datasheet of the chip (see the footnotes in page 97).

The ADC communicates with a microcontroller through the SPI. The

¹More information can be found in the manufacturer datasheet <https://www.ti.com/product/ADS8860>

²Figure was taken from the datasheet of ADS8860

pled data and send it to the PC through a USB cable. For validating the sampling frequency, an oscilloscope was used to measure the output of the CS pin shown in Figure 5.2a, which determines the sampling frequency of the ADC, alongside the clock coming from the microcontroller. Figure 5.3 shows the sampling frequency of the ADS8860, captured on the oscilloscope.

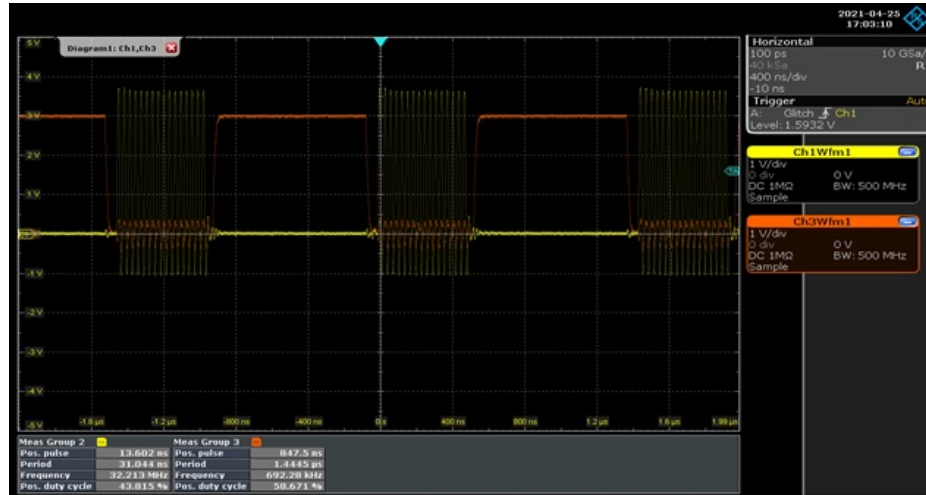


Figure 5.3: Output of the CS pin to the ADC (orange, measurement group 3) and the 32 MHz clock (yellow, measurement group 2). The measured sampling frequency was 692 kHz.

Due to the inherent delay in sending the sets of commands and initializing the tasks in the microcontroller, T_s from equation (5.1) was $1.44 \mu\text{s}$, therefore the sampling frequency was measured to be 692 kHz.

For the ADC which samples the input voltage controlling the VCCS, an ADS7042⁴ with $300 \mu\text{W}$ power consumption was used. Sampling the input voltage, this ADC is used to calculate the phase difference related to the load under test. The sampling frequency due to the timing diagram of the ADC, which can be found in Figure 5.4, and the SPI clock of 8 MHz was calculated as the following:

⁴More information can be found from the manufacturer datasheet <https://www.ti.com/product/ADS7042>

Table 5.1: Specifications of two ADCs used to sample input voltage and the voltage from the load.

ID	Bits	SNR (dB)	Sample rate (kHz)	Max sample rate (MHz)	Dynamic range (V)	Power (mW)
ADS8860	14	93	692	1	3	4
ADS7042	12	70	398	1	3	0.3

5.2 Design of the DAQ Block

In this section the data acquisition block, including the ADC, will be introduced. Figure 5.6 shows the general circuit diagram for the DAQ used here.

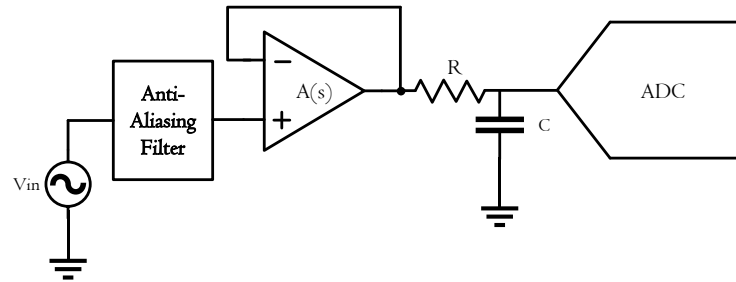


Figure 5.6: Basic topology of a DAQ circuit.

The input of the DAQ system is an analog voltage. As two external ADCs were used in this thesis, for the input voltage and the voltage of the load under test, two DAQ blocks were designed, but the overall design procedure is explained. When developing a DAQ system, it is usually necessary to place a low-pass filter (LPF) or anti-aliasing filter (AAF) before the ADC to rid the analog system of higher-frequency noise and aliases. After the AAF, a buffer amplifier will be essential. This is because the buffer eliminates the loading effect of the AAF block on the input of the ADC. At the output of the buffer amplifier is a charge kickback filter that drives the ADC's input.

This filter can be used as an AAF block, but it is also used to make sure that the charge which is being accumulated on the input capacitor of the ADC is settled at half of a least significant bit of the ADC, before the ADC is switched to the conversion phase. This is a common topology to drive an ADC and more explanation can be found in [165]. As there is an anti-aliasing filter after the input signal, there will be a gain imposed on the signal if the filter is not chosen carefully. Table 5.2 shows the comparison between three common filter types used as anti-aliasing filters. A low-pass Butterworth filter has the maximally flat frequency response in the pass band [166], meaning no gain error will be imposed on the voltage that is being sampled. A second-order Butterworth filter with a cut-off frequency of 50 kHz was designed as the AAF block in this thesis. Shown in Figure 5.7, the implementation is based on the Sallen-Key filter [167, 168]. Table 5.3 shows a comparison between two well-known architectures for a second-order filter, and it can be seen that the Sallen-Key design is not sensitive to component variation at unity gain, which is what is desirable here.

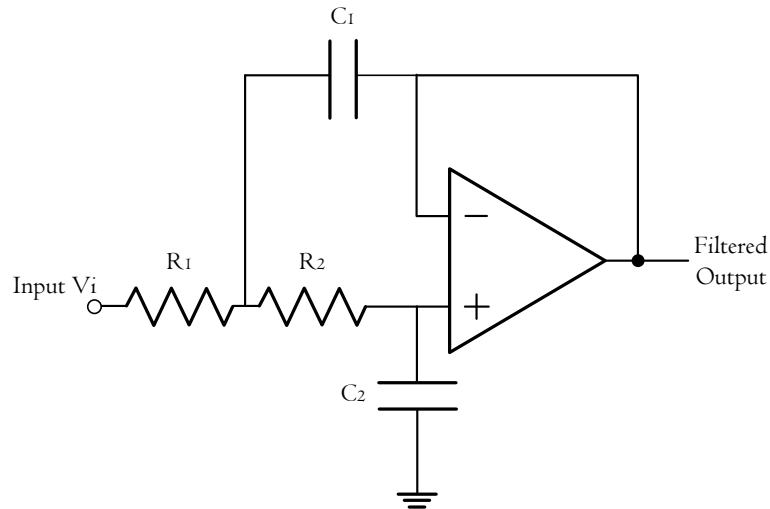


Figure 5.7: Sallen-Key second-order filter architecture.

Although the amplitude of the input voltage of the VCCS is large, in

range of volts ()compared to the signal coming from the load under test, which could be in range of millivolts) and a simpler filter could be used prior to the ADS7042, the same components and second-order Butterworth filter were used to impose the same phase shift on both of the ADC paths so that the difference in final phase calculation was not affected.

Table 5.2: Comparison between filter types [1].

Filter type	Advantage(s)	Disadvantage(s)
Butterworth	Maximum pass-band flatness	Slight overshoot in response to pulse input and moderate rate of attenuation above cut-off frequency
Bessel	Constant group delay, no overshoot with pulse input	Slow rate of attenuation above cut-off frequency
3-dB Chebyshev	Fast rate of attenuation above cut-off frequency	Large overshoot and ringing in response to pulse input

Table 5.3: Comparison for second-order filter architectures [1].

Architecture	Advantage(s)	Disadvantage(s)
Sallen-Key	Not sensitive to component variation at unity gain	High-frequency response limited by the frequency response of the amplifier
Multi-Feedback	Less sensitive to component variations and superior high frequency response	Less simplifications available to ease design

5.3 Measured Impedance with the Designed System

5.3.1 Version 1

Two versions of the BI measurement system were designed and implemented in this thesis. In Version 1 (V1), the input voltage was generated by a signal generator. The DAQ was implemented as a modular part that could be attached to the main board with a VCCS. The reason was to test the performance of the system and, if necessary, change the circuit and components. Also, in this version, the charge kickback filter was used as an antialiasing filter, instead of using a separate second-order Sallen-Key architecture. In order to determine the accuracy and precision, a set of experiments was carried out. It should be noted that, as reported in the literature review section,

the expected range of impedance variation due to the accumulation of urine is roughly from $10\ \Omega$ to $30\ \Omega$. Also, this range was similar to the results of measured impedance from experiments on the phantom, as shown later in the chapter. The experimental setup that was used to test the accuracy of measurements with the designed system is as follows:

- Current Amplitude: $200\ \mu A_{rms}$
- Measured value of the resistors used as the load under test: $10.22\ \Omega$, $11.8\ \Omega$, $12.82\ \Omega$, $15.8\ \Omega$, $18.9\ \Omega$, $23.2\ \Omega$, $30.7\ \Omega$
- Frequency: 10 kHz, 20 kHz, 30 kHz, 40 kHz, 50 kHz
- Repetition of experiments for each set up (shown as N in Figure 5.8):

5

The flow chart for the experiments can be found in Figure 5.8.

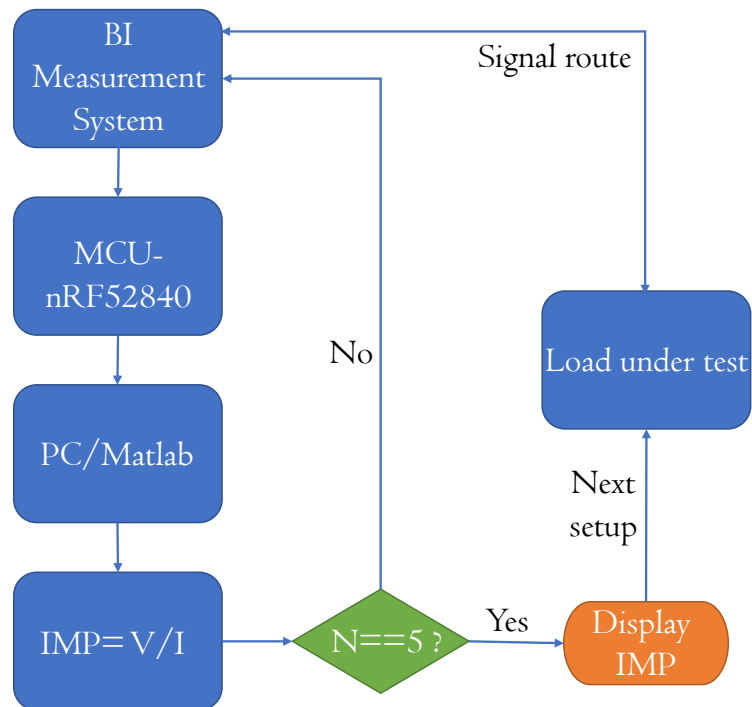


Figure 5.8: Flowchart of the procedure for the experiments.

The nominal values for the resistors were 10, 11, 12, 15, 18, 23 and $30\ \Omega$. The values of these resistors were measured with the Agilent impedance an-

alyzer⁵, which has an accuracy of 0.05%. Each resistor was connected to the designed BI measurement system. A frequency sweep was carried out for each of the resistors. At each frequency, the experiment was repeated five times. This provided a total of 175 measurements. The data for each one of the experiments were digitized by the DAQ block and sent from the microcontroller to Matlab via a serial to USB converter cable. Then, in the PC, a Matlab program was written to read the data sent from the microcontroller. The data was then filtered in order to rid the system of any remaining noise. To obtain the impedance, the RMS value of the recorded voltage of the load under test, divided by the injected current was calculated. This procedure was repeated five times, and then the next frequency was tested. At the end, when the system completed all of the frequency steps, the resistor was removed and the next resistor was connected to the BI measurement system, and this procedure was repeated until the final resistor was connected, which was the 30 Ω resistor. Figure 5.9 shows the PCB layout and a 3D view of the designed system in Altium designer software. The manufactured board and the measurement setups are shown in Figure 5.10. The wire leads that measure the voltage change are connected to VM_+ and VM_- . The lead that applies the current I_+ to the load is connected to *Load_1* and, for I_- , it is connected to *Load_2*, both highlighted in Figure 5.9a.

⁵More information about the device can be found in <https://www.keysight.com/ie/en/product/E4980A/precision-lcr-meter-20-hz-2-mhz.html>

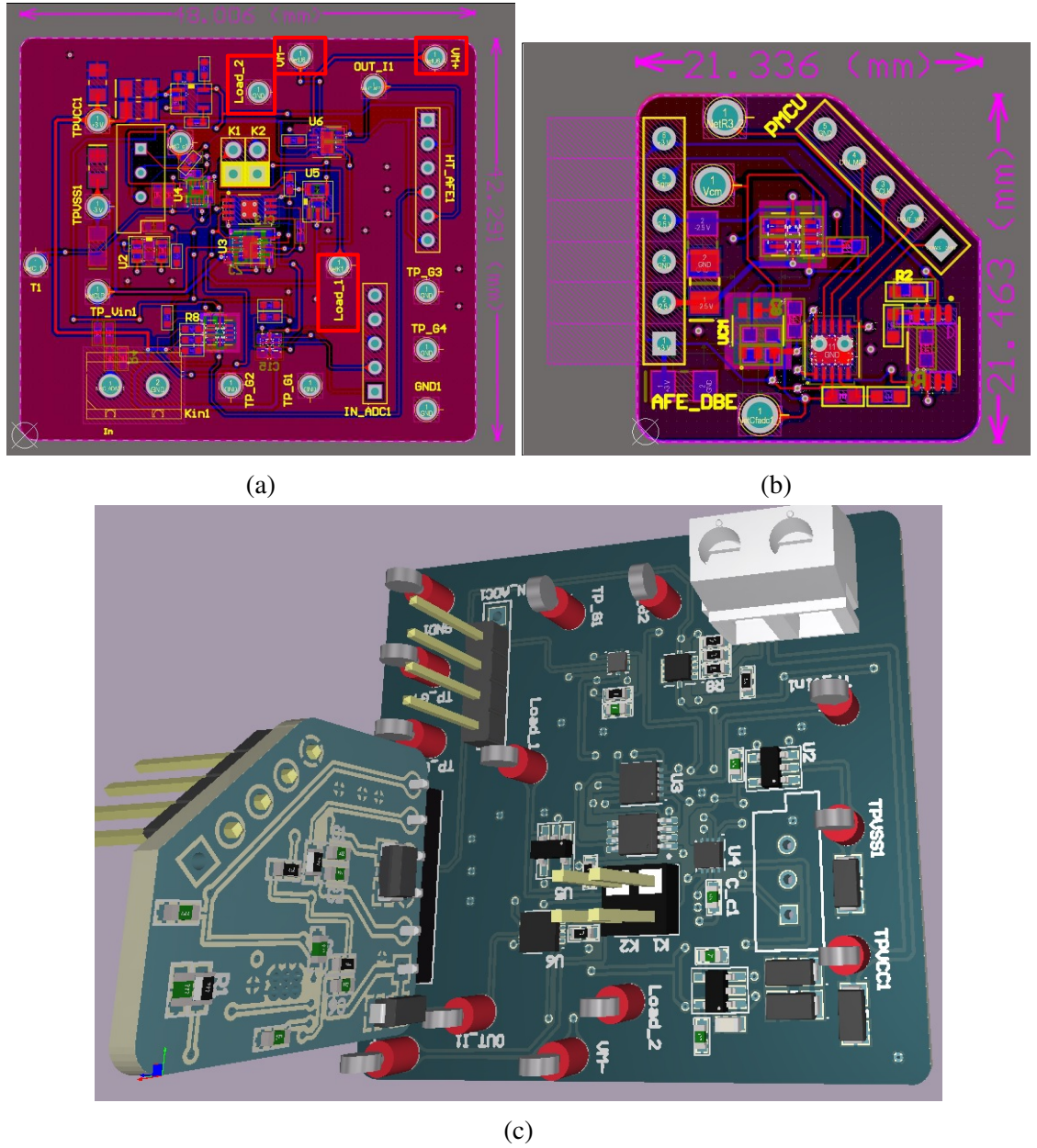


Figure 5.9: PCB of the designed system (V1) a) 2D layout view of the VCCS. Voltage electrodes are connected to VM_+ and VM_- and current electrodes to Load₁ and Load₂, highlighted on the Figure with red rectangle b) 2D layout view of the DAQ circuit including ADS8860 c) 3D model of the BI measurement system.

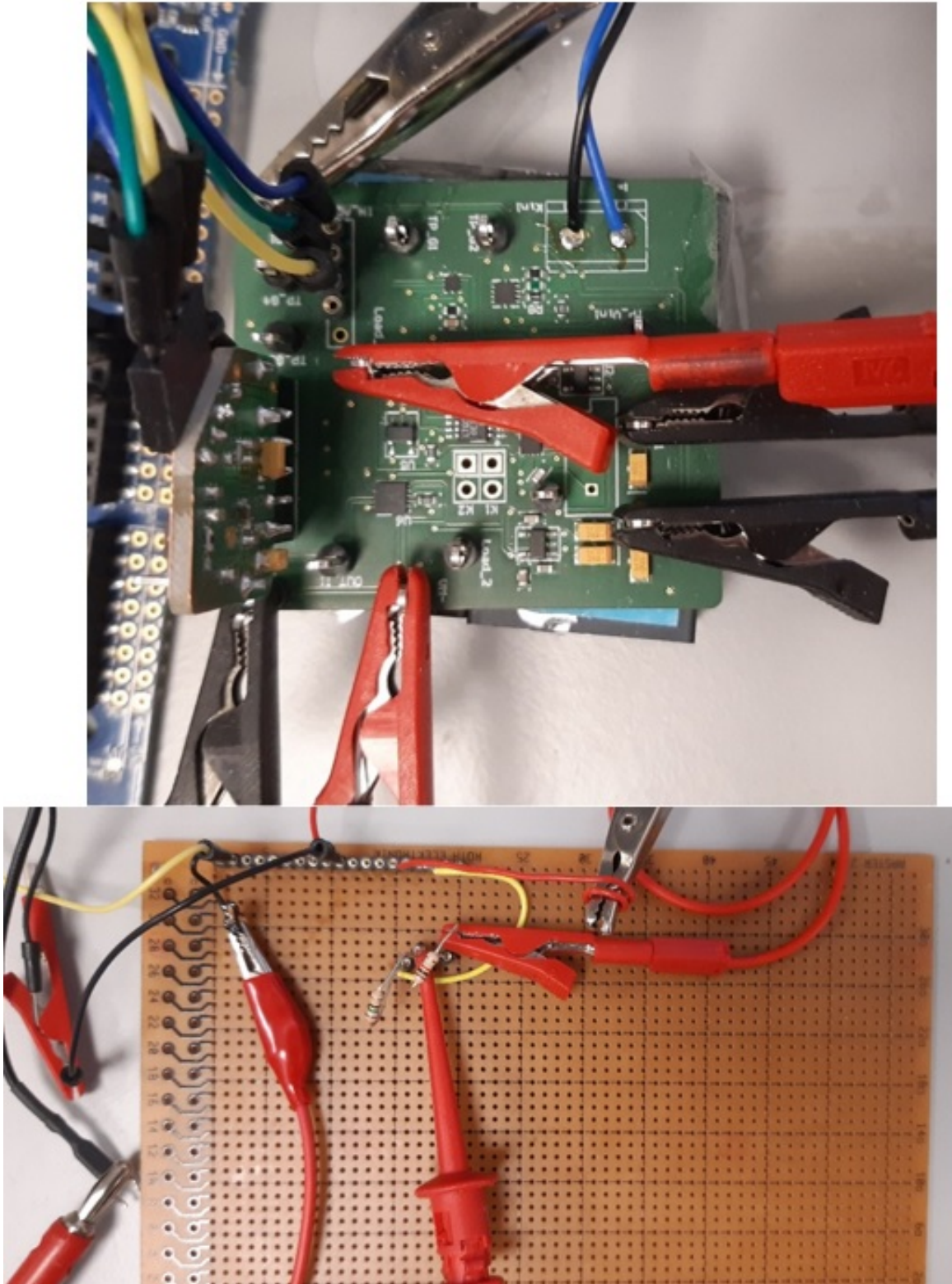


Figure 5.10: The BI measurement system and the setups to measure the accuracy and precision of the VI system.

5.3.2 Results

Table 5.4 shows the data that was obtained in each experiment.

Table 5.4: The measured data points with the BI measurement system. Unit of the presented values of the measurements is Ω .

Measured value by the Agilent device	@ 10 kHz	@ 20 kHz	@ 30 kHz	@ 40 kHz	@ 50 kHz
10.22	10.8	11.05	11.02	11.65	11.12
	10.77	10.88	10.77	10.72	10.93
	11.02	10.95	10.85	10.83	10.89
	10.58	11.15	10.69	10.33	11.02
	10.95	10.53	11.20	10.92	10.71
11.8	12.65	12.45	12.95	12.71	13.21
	12.78	12.71	12.88	13.22	12.68
	12.88	12.83	12.92	13.31	13.14
	12.72	13.22	13.10	12.75	12.78
	13.70	13.50	13.43	13.15	12.83
12.82	14.10	14.18	14.32	14.05	14.29
	13.95	14.33	14.15	13.95	14.38
	14.24	14.22	13.96	14.44	14.27
	14.33	14.25	13.76	14.35	13.86
	13.65	13.82	14.28	14.27	14.56
15.8	17.41	17.37	17.48	17.44	17.61
	17.36	17.22	17.33	17.70	17.55
	17.24	17.49	17.31	17.65	17.42
	17.34	16.95	17.05	17.33	17.52
	17.18	17.56	17.16	17.02	17.21
18.9	20.45	20.38	20.15	20.45	20.66
	20.37	20.41	20.43	20.12	20.51
	20.51	20.13	20.18	20.62	20.18
	20.21	19.93	19.96	19.87	19.65
	19.85	20.31	20.26	20.55	19.93
23.2	25.03	24.93	25.23	25.32	25.12
	24.95	25.05	24.93	24.87	24.93
	25.32	25.10	24.55	24.56	24.85
	24.83	24.77	24.98	24.31	25.32
	24.75	24.58	24.63	24.88	25.02
30.7	32.16	31.95	32.07	32.15	32.90
	32.07	32.06	32.45	32.43	32.65
	32.29	32.22	32.18	32.36	32.42
	32.09	31.90	31.92	32.12	32.25
	32.33	32.08	32.15	32.55	32.03

At each frequency and for each load under test, the experiment was re-

peated five times. For example, for the nominal value of $10\ \Omega$ at frequency of 10 kHz, the values measured by the system, from the first measurement to the fifth, were $10.80\ \Omega$, $10.77\ \Omega$, $11.02\ \Omega$, $10.58\ \Omega$, and $10.95\ \Omega$, respectively. The same is true for the resistor with the nominal value of $30\ \Omega$ for which, at the frequency of 50 kHz, the measured values from the first to the fifth experiments were respectively: $32.90\ \Omega$, $32.65\ \Omega$, $32.42\ \Omega$, $32.25\ \Omega$, and $32.03\ \Omega$.

In order to visualize the performance of the system, the mean value of the impedance measured by the system is shown in Figure 5.11. In this Figure, each dot represents the mean value of the five experiments, provided in Table 5.4 at each frequency for a specific value of the resistor. For example, after the measurements on resistor $10\ \Omega$ were carried out, the mean values of the five measurements over the frequency sweep of 10 kHz to 50 kHz were: $10.82\ \Omega$, $10.91\ \Omega$, $10.90\ \Omega$, $10.89\ \Omega$ and $10.93\ \Omega$, respectively. The same is true for the $30\ \Omega$ resistor, for which the mean values of the measured impedance over the mentioned frequency range were: $32.188\ \Omega$, $32.04\ \Omega$, $32.15\ \Omega$, $32.32\ \Omega$, and $32.45\ \Omega$, respectively. The precise value is also drawn so that a comparison can be made. The precise value represents the value of the resistors as measured by the Agilent impedance analyzer. Those values were mentioned earlier in Section 5.3.1.

In Figure 5.11, it can be seen that there is a difference between the mean values measured by the designed system and the precise values. In order to calibrate this, the difference between each measurement obtained by the designed system and the precise values at different frequencies were calculated. Then, the mean value of the obtained differences was calculated,

which was 1.33Ω , and this was subtracted from all the values. Figure 5.12 depicts the calibrated graph. To quantify the error of the system and show the error before and after calibration, Figure 5.13 is shown. On Figure 5.13a, the error of the mean value from the precise value is shown as a percentage, and Figure 5.13b shows the same error after the calibration procedure is car-

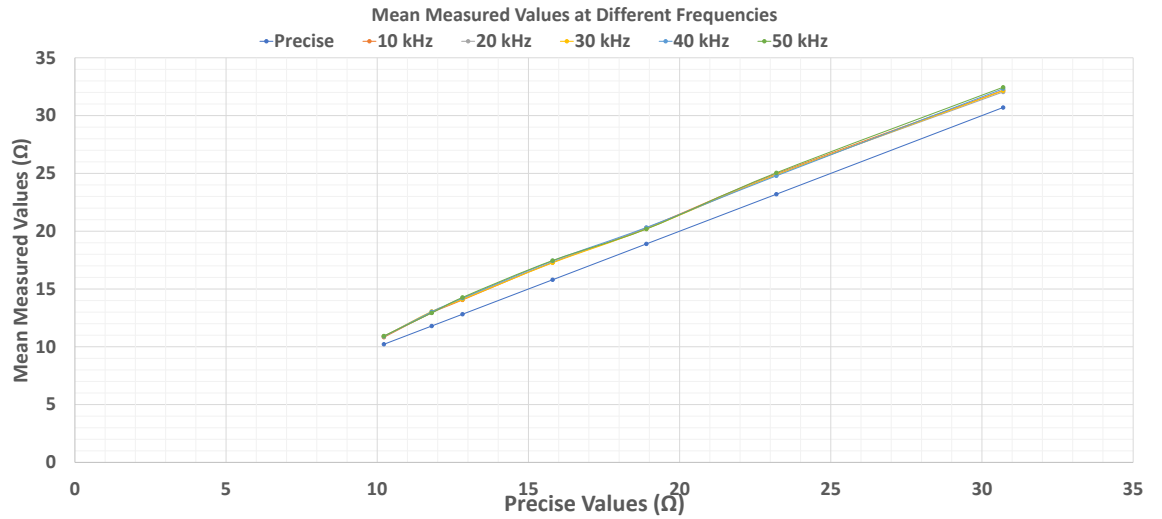


Figure 5.11: Mean value of impedance measured by the designed system at different frequencies before the calibration.

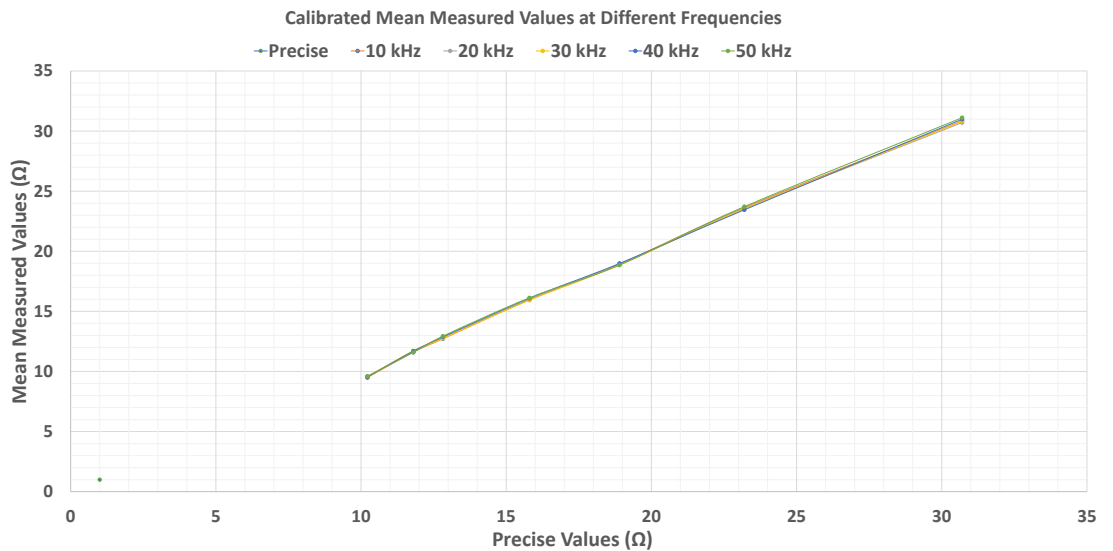


Figure 5.12: Mean value of impedance measured by the designed system at different frequencies after the calibration.

ried out. For example, for the value of $10\ \Omega$ in frequency range 10 kHz to 50 kHz, this error was 6%. For $30\ \Omega$, this error over same frequency range was within 4% to 5.5%.

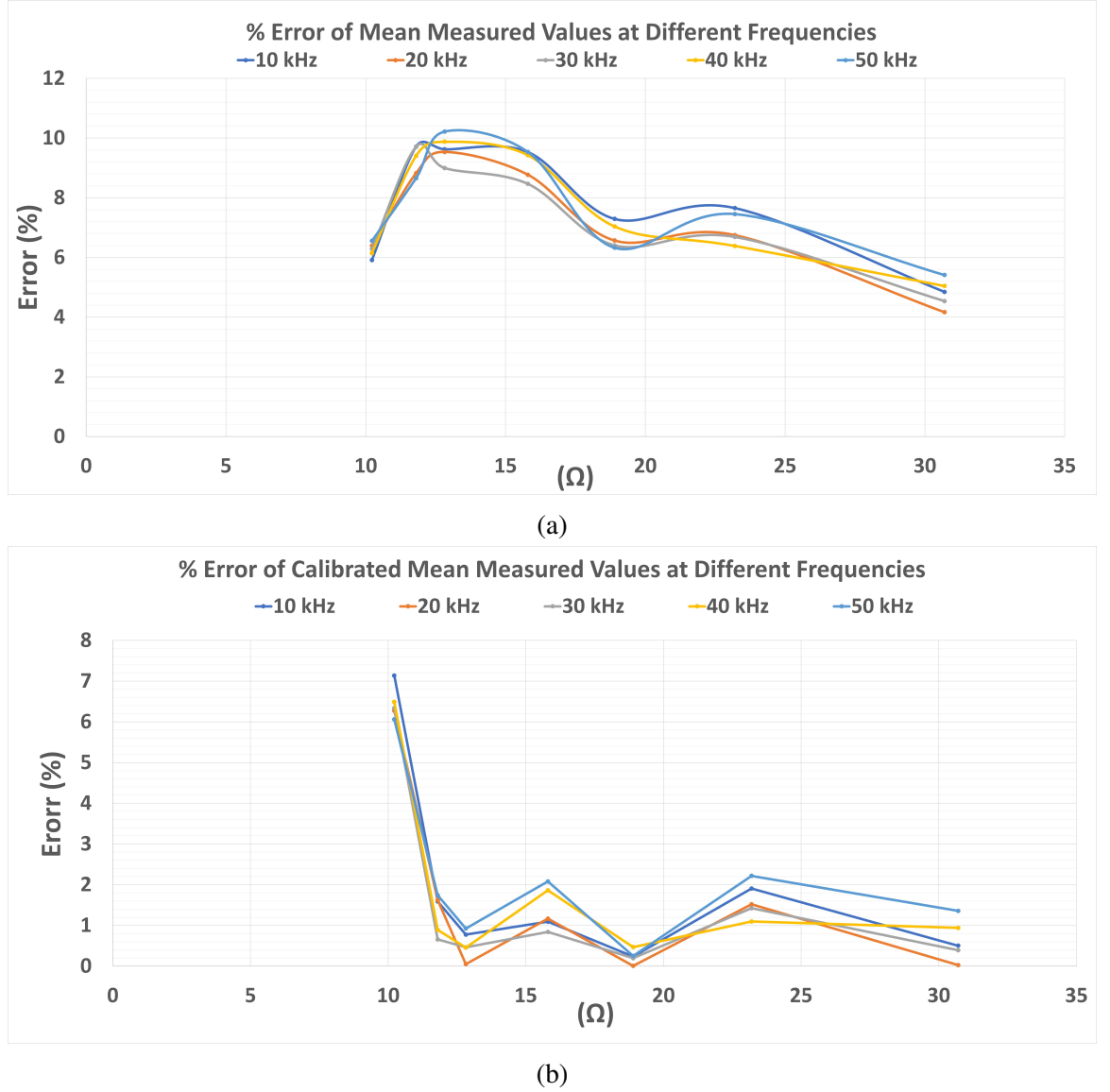


Figure 5.13: Error of mean measured value at different frequencies for different loads a) before calibration b) after calibration

It can be seen that the error after calibration is reduced to maximum of 7% for the $10\ \Omega$ load only and, for the rest of the loads at different frequencies, the error remains well below 2%. It should be noted that the 7% error for the $10\ \Omega$ load is due to the method of calibration, as the mean

of the difference from the precise values over different setups was subtracted from each measurement in Figure 5.11.

The mean value of error after calibration is 0.25Ω . Figure 5.14 shows the measured impedance versus the precise values at each frequency. In these figures, each dot is, in fact, made up of 5 individual measured values, which are so close that they appear to merge into a single datapoint. The standard deviation of the data presented in these figures can be found in Table 5.5. The average of the standard deviation of the system after calibration is 0.21Ω . Therefore, after calibration, the system has an accuracy and precision of $0.25 \Omega \pm 0.21 \Omega$ in the frequency of 10 kHz to 50 kHz.

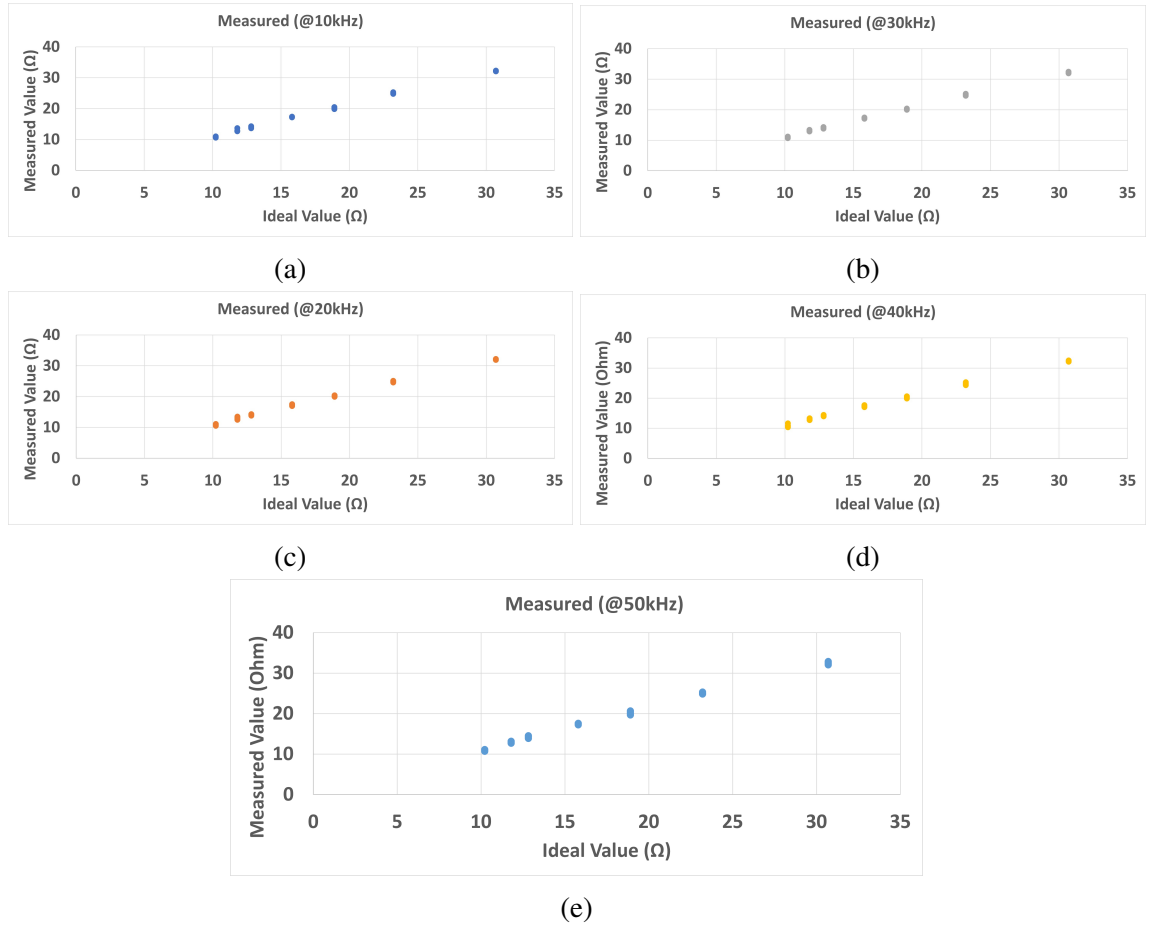


Figure 5.14: Repeated impedance measurement by the system versus the nominal/ideal values at each frequency.

Table 5.5: Standard Deviation of the measured values. Unit of the values is Ω .

Nominal value	@ 10 kHz	@ 20 kHz	@ 30 kHz	@ 40 kHz	@ 50 kHz	Mean value
10	0.15	0.21	0.18	0.43	0.13	0.22
11	0.38	0.37	0.20	0.25	0.21	0.28
12	0.24	0.18	0.20	0.18	0.23	0.21
15	0.08	0.22	0.15	0.24	0.14	0.17
18	0.24	0.18	0.15	0.28	0.37	0.24
22	0.20	0.19	0.25	0.34	0.16	0.22
30	0.11	0.11	0.17	0.16	0.30	0.17
Mean value	0.20	0.21	0.19	0.27	0.22	

5.3.3 Version 2

As was seen in Version one, the system required calibration to reduce the error of the measurements. This was due to the high speed spikes and noise observed on the voltage signal coming from the load under test. In order to eliminate the need for calibration, Version 2 (V2) of the BI measurement system was designed, as shown in Figure 5.15. In this version, the on-board signal generator, AD9833, was used to generate the input signal and the Sallen-Key filter was added before the driving buffer amplifier, as shown in Figure 5.6, to eliminate the high frequency noise. As the clock required for ADCs could also cause cross-talk⁶ and reflection⁷ on the PCB traces, leading to undesired high speed noise on the signal trace, therefore leading to error in the impedance calculation, more care was taken when designing the layout of system and the traces. Figure 5.16 shows the load that was used as a test in order to obtain the performance of V2. This is the 2R-1C model that was introduced earlier in Chapter 2 as the model of the tissue under test. The values for R_i and C_M are 220 Ω and 10 nF, respectively [147]. For R_E , two different resistors, with values of 30 Ω and 68 Ω , were

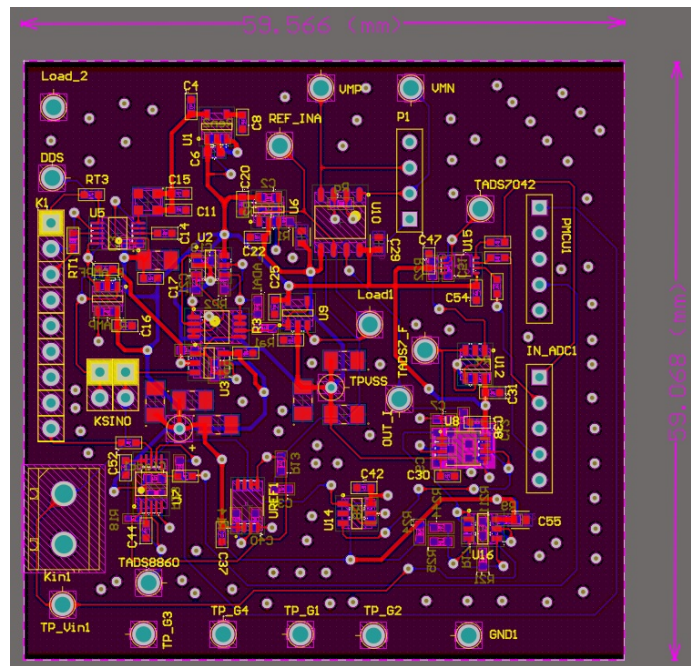
⁶The noise imposed from one trace that carries a high frequency signal to another trace, called the victim trace.

⁷The noise due to reflection of a high frequency signal in a trace back to its source.

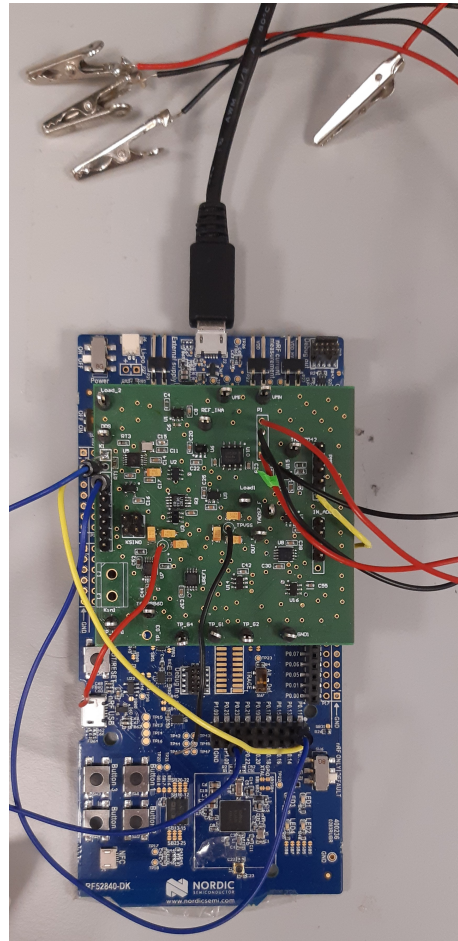
used corresponding to the minimum and maximum range that the device is expected to measure. These values for testing as minimum and maximum were selected based on the experimental results of the BI measurements on the phantom, which is presented in the next section.

Measurement on the 2R-1C model was carried out at two different frequencies, namely 5 kHz and 10 kHz. These frequencies were selected based on a study published in [2] for bladder monitoring. More discussion will be provided in the next section, when introducing the phantom measurement setup. At each of these frequencies and for each value of R_E , measurements were repeated ten times. The rest of the setup was similar to the one used in V1. In total, forty measurements were performed. Table 5.6 shows the mean value of magnitude and phase of the measured impedance, obtained from V2 of BI measurement system. Calculated from Table 5.6 and the measured data, the V2 designed system could achieve an accuracy of $0.3 \Omega \pm 0.15 \Omega$ at the frequency of interest, without any requirement for additional calibration. Table 5.7 summarizes the performance of the Version 2 of the designed BI measurement system compared to other existing BI measurement devices in the literature, which were used for bladder monitoring or general BI measurement application in a small form factor.

5.3. Measured Impedance with the Designed System



(a)



(b)

Figure 5.15: *Version 2 of BI measurement system. a) the layout of the board (with dimension) b) Manufactured BI measurement system mounted on top of the nRF52840 microcontroller development board.*

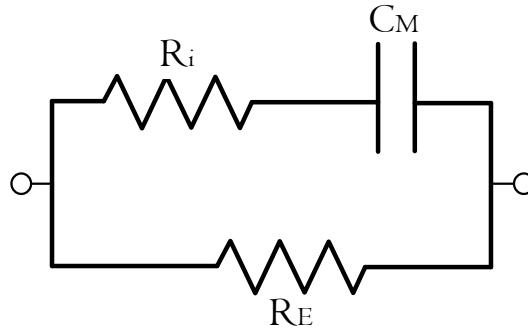


Figure 5.16: The RC model that was used to test the accuracy of the BI measurement system. Values for R_i and C_M are $220\ \Omega$ and $10\ \text{nF}$, respectively. Two values for R_E were used: $30\ \Omega$ and $68\ \Omega$.

Table 5.6: Mean value of the measurements for magnitude and phase of the 2R-1C model. The precise values were measured with an Agilent E4980A, a commercial impedance analyzer.

R_E		5 kHz		10 kHz	
		Mean Value	Precise Value	Mean Value	Precise Value
30 Ω	Magnitude (Ω)	30.06	29.90	30.09	29.83
	Phase ($^\circ$)	-0.78	-0.52	-2.39	-1.02
	Error (Ω)	0.18	—	0.87	—
	Error ($^\circ$)	0.26	—	1.37	—
68 Ω	Magnitude (Ω)	67.69	67.58	67.26	67.16
	Phase ($^\circ$)	-1.79	-1.11	-3.54	-2.17
	Error (Ω)	0.11	—	0.09	—
	Error ($^\circ$)	0.67	—	1.36	—

Table 5.7: Summary of performance of the existing BI measurement devices. SFBI and MFBI stand for single frequency BI measurement and multi-frequency BI measurement, respectively.

Ref.	[129]	[169]	[170]	[171]	[147]	This work
Mode	SFBI	MFBI	MFBI	MFBI	MFBI	MFBI
Design	Commercialized-BodygateWay	Commercialized-BodyStat	Comercialized-Impedimed	Custom	Custom	Custom
Accuracy	0.1 %	2 - 3 Ω	$\pm 1\%$	0.5 Ω	1.5 %, 0.6 Ω std	$0.3 \pm 0.15\ \Omega$
Range (Ω)	0 - 120	20 - 1300	10 - 1100	0 - 54	100 - 1000	10 - 2000 [†]
Frequency (kHz)	50	5, 50, 100, 200	3 - 1000	10 - 120	10 - 100	5 - 50
Power (mW)	88 *	—	—	14.4 **	53	74
Type	Wearable	Portable	Portable	Wearable	Wearable	Wearable
Size	$5.9 \times 5.0 \times 1.64\ \text{cm}$	$27.4 \times 19.5 \times 3.9\ \text{cm}$	$19 \times 13 \times 11\ \text{cm}$	$4.8 \times 3 \times 2\ \text{cm}$	$3 \times 1.8 \times 0.6\ \text{cm}$	$5.9 \times 5.9 \times 0.4\ \text{cm}$

* Calculated based on the information provided in the catalogue.

** Custom designed application specific integrated circuit.

[†] The device is able to drive the upper limit, as discussed in Chapter 4.

5.4 Experiments on Phantom

In this section, a brief overview of different phantoms used for bladder monitoring is given, then the recipe for making the selected phantom is provided. Subsequently, the setups and experiments to measure the variation of impedance due to the change in level of artificial urine inside the phantom are described. Also, the setups and experiments for measuring the impedance variation at different electrode positions, while mimicking the relocation of bladder, are presented. The results of those measurements will be provided subsequently.

5.4.1 Different Phantoms Used for Bladder Monitoring

In a recent study, which was carried out in 2020 [2], it was reported that most of the anthropomorphic pelvic phantoms presented in the literature have been fabricated for radiation therapy dosimetry; hence, the phantom materials used were selected for their radiological properties, rather than their electrical properties. Therefore, the structures for such phantoms are made of materials which are not electrically conductive and cannot be used for measuring variation of impedance. For this thesis, a few electrically suitable phantoms were found in the literature for bladder monitoring. Two of those were created by using agar powder [2, 128] and two were created by using a 3D printed model of the pelvic and the internal organs [172, 173]. For selecting a phantom among the existing ones in the literature, the main criterion is the electrical conductivity, which needs to mimic that of internal organs. As 3D printing of the internal organs was not possible and required extra expertise that was outside of the scope of this thesis, creating an

agar powder based phantom was selected. Although other tissue-mimicking materials can be found in the literature, such as polyvinyl alcohol, gelatin, polysaccharide gels, etc. [2], agar powder phantoms have been widely used in the literature to mimic several organs [2, 174]. This type is cost effective, the preparation procedure is not complex and, also, its electrical conductivity can be adjusted by doping with sodium chloride (NaCl), making it suitable for bladder monitoring applications [2].

5.4.2 Agar Based Phantom: The Recipe

In order to make a phantom which mimics the electrical conductivity of the internal organs in the abdomen area, the recipe and values indicated in [2] were used. That study was carried out to create a phantom which mimics the electrical behavior of internal organs at lower frequencies and to evaluate the ability of textile electrodes to unobtrusively monitor the bladder volume by using BI measurement.

The values which were used to calculate conductivity can be found in Table 5.8.

Table 5.8: Values for electrical conductivity of the different tissues to be mimicked [2].

Tissue Name	Conductivity (S/m)	Percentage (%)	Weighted Conductivity (S/m)
Fat	4.28×10^{-2}	30	1.28×10^{-2}
Colon/Rectum	2.38×10^{-1}	5	1.19×10^{-2}
Muscle	3.37×10^{-1}	50	1.69×10^{-1}
Bone marrow red	1.02×10^{-1}	9	9.18×10^{-3}
Bone marrow yellow	3.08×10^{-3}	6	1.85×10^{-4}
Spinal cord	3.46×10^{-2}	-	-
Internal background			2.03×10^{-1}
Urine	1.75	-	-
Bladder wall	0.211	-	-

The solution that contains the doped agar powder with NaCl is initially

a liquid and, after preparation, it needs to set in a frame/container in order to solidify into a gel, forming the phantom. The frame, which is not electrically conductive, needs to be cut through so that electrodes can be placed on, and be in contact with, the agar phantom. An identical frame without cuts was used to let the liquid settle and form a solid gel. Then, the gel phantom was placed in the final frame, with cuts for the electrodes, for the measurements. Figure 5.17 illustrates the frame for letting the liquid settle and form a gel. This container, in total, can hold up to 1800 ml of liquid.

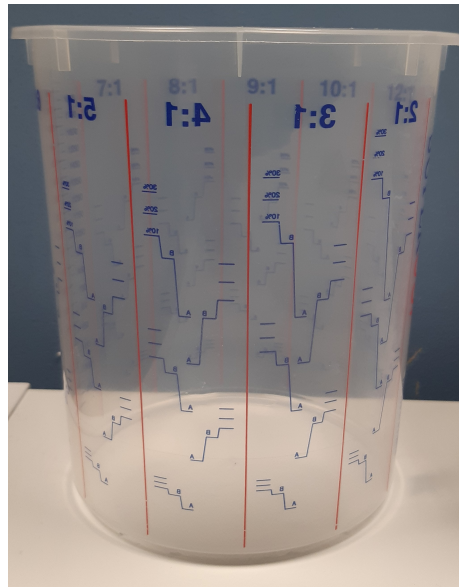


Figure 5.17: The frame/container used for letting the solution set to form a gel. Each section is indicated by its number from 1 to 12.

The diameters, of the container at the top and the bottom are 14.5 cm and 11.5 cm, respectively. The height from the top to the bottom is 16.5 cm. It can be seen that it is marked and vertically divided into twelve equal sections. Each section is indicated with its number, from 1 to 12. For the rest of the chapter, these sections and their related numbers are called positions, for instance, position 1 (P1), position 2 (P2), horizontal position (PH), and so on.

The next step is to prepare the agar solution with the conductivity (σ) of 0.2 S/m, as given in the Table 5.8 for the weighted electrical conductivity of the internal organs in the abdomen area.

To calculate the required molar concentration of NaCl, the following equation can be used [2]:

$$\sigma = \lambda Cl^{-}.[Cl^{-}] + \lambda Na^{+}.[Na^{+}] = (\lambda Cl^{-} + \lambda Na^{+}).x \quad (5.3)$$

where σ is the required conductivity of the solution, λCl^{-} is the molar conductivity of Cl^{-} ($7.63 \times 10^{-3} \text{ S.m}^2.\text{mol}^{-1}$), λNa^{+} is the molar conductivity of Na^{+} ($5.01 \times 10^{-3} \text{ S.m}^2.\text{mol}^{-1}$), and x is the molar concentration of NaCl (mol.m^{-3}). The amount of NaCl needed in grams per liter, is given by [2]:

$$y = M(NaCl).x \quad (5.4)$$

where y is the weight of NaCl (g.m^{-3}), $M(NaCl)$ is the molar mass of NaCl (58.44 g.mol^{-1}) and x is the molar concentration of NaCl calculated from (5.3) and equals 15.9 mol.m^{-3} . Therefore, the weight of NaCl to obtain the required conductivity is 925 g.m^{-3} or 0.925 g.L^{-1} . Knowing this value, the recipe could be found as follows for each 1 L of deionized water [2]:

- 10 g.L^{-1} of agar powder
- 0.925 g.L^{-1} of NaCl

To create the phantom, 1.5 L of deionized water, 15 g of agar powder and 1.39 g of NaCl were used. The weights of the agar powder and the NaCl were measured by a precise and calibrated scale, made by Sartorius⁸, with

⁸Manufacturer website: https://www.pce-instruments.com/english/weighing-equipment/scales-and-balances/lab-scales-laboratory-scales-pce-instruments-laboratory-scale-pce-bsk-310-det_5931266.htm?_list=k&_listpos=1

accuracy of ten thousandths of grams. First, the agar powder was poured into deionized water. Then, the solution was heated to its boiling point and then NaCl was added to the solution. The solution was mixed for five minutes until homogeneous. Then, the solution was allowed to cool to room temperature before pouring into the container, so that the high temperature of the solution would not deform the plastic container. After 45 minutes, it was poured into the container. To create a cavity, or a vacant space, inside the phantom to mimic the bladder into which urine will be accumulated into, a cylindrical tube with a diameter of 4 cm and height of 17 cm was placed inside the solution before gel formation. A mould was used in order to ensure that the cylindrical tube was held at the center of the container. The mould is illustrated in Figure 5.18. After placing the cylindrical tube inside the solution, the container was put inside a fridge, so that the gel could be formed. The tube was removed after this formation, leaving the vacant space inside the agar phantom mimicking a bladder, and the phantom was ready for the experiments. Figure 5.19 shows the final shape of the phantom.

5.4.3 Setups and Results

After the phantom was created, it was time to investigate the proposed method of vertical monitoring. In order to start the experiments, the phantom was moved to the frame where electrodes could be connected to the phantom (Figure 5.20).

Standard gel electrodes used for ECG recording were used, ordered from Promed, Co. Kerry, Ireland. The lead wires connected to the electrodes were repositioned between four different positions, three vertical and one horizontal, for a set of measurements to be carried out. The vertical posi-

tions are at 3, 4, and 5, as shown in Figure 5.20. The horizontal position is the second row, consisting of four electrodes, from the bottom. Electrodes in that row, at each position, were used as the level to indicate a certain amount of fluid inside the phantom was reached, both in vertical and horizontal scanning, as described in Chapter 3. The electrodes are indicated as the following: $A+$, $A-$, $V+$ and $V-$. In the vertical positions, the electrodes $A-$, $V-$, $V+$ and $A+$ are placed at 2.5 cm, 6 cm, 9.5 cm, and

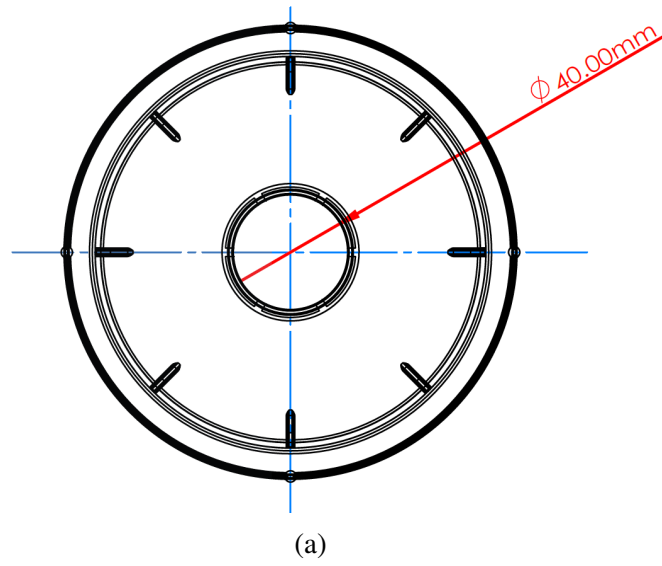
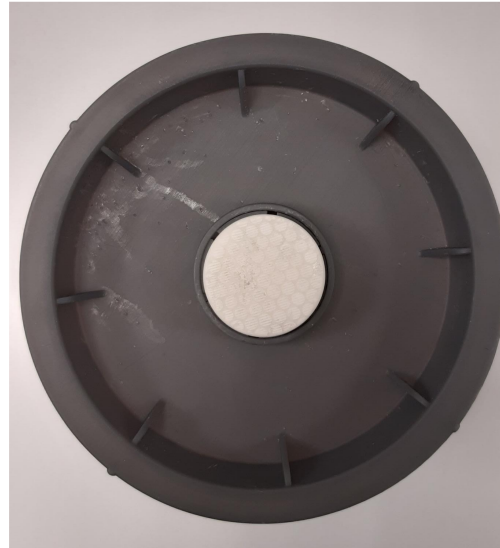


Figure 5.18: The mould used to keep the cylindrical tube firm in its place and in the middle. a) the model b) the fabricated mould holding the cylindrical tube, which is the white object in the middle.

12 cm from the bottom, respectively. $A+$ and $A-$ are the two electrodes which are used to apply the current to the phantom. $V+$ and $V-$ are the two electrodes which obtain the voltage signal. For the horizontal position,

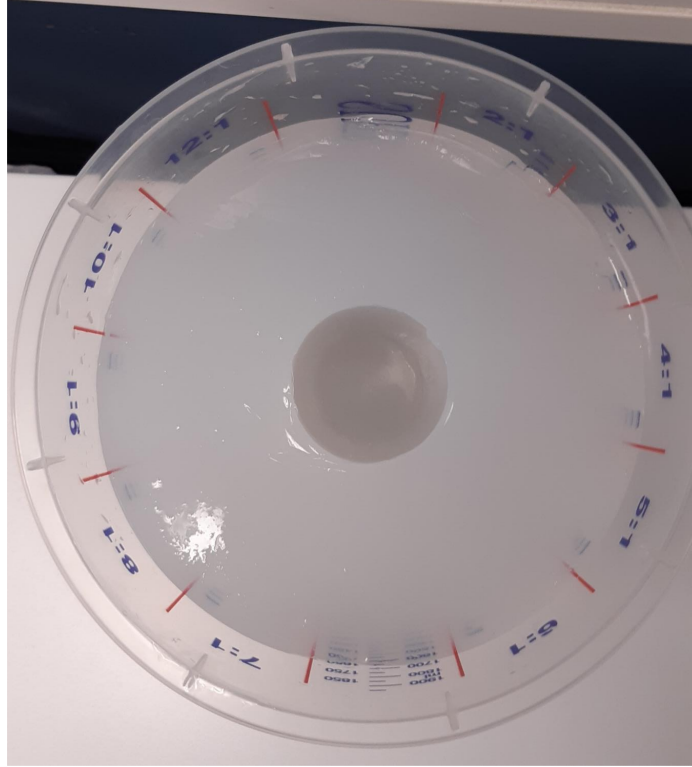


Figure 5.19: Fabricated phantom with a vacant space in the centre mimicking the bladder and the abdomen area.

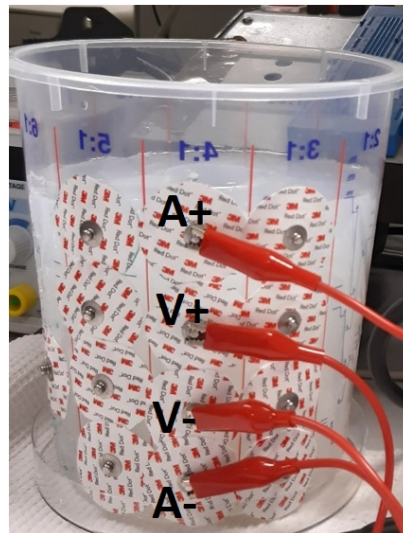


Figure 5.20: Phantom and electrode placement. The current is applied with the electrodes, $A+$ and $A-$ and voltage is recorded from $V+$ and $V-$, at each vertical position (3,4,5) and horizontal.

$A+$ is the left most electrode on the second row from the bottom and $A-$ is the right most electrode on the same row. $V+$ and $V-$ are the two middle electrodes on the same row, from left to right.

After the lead wires are connected to the electrodes, the current is applied to $A+$ and $A-$, the frequency is swept from 1 kHz to 100 kHz and the voltage is measured between $V+$ and $V-$. Then, the impedance data is stored, the lead wires are relocated to the next position, and the same measurements are repeated. The experiment is concluded at the horizontal position. The device that measured the impedance was an Agilent E4980A, which is a commercial impedance analyzer.

Two different electrical conductivities for the artificial urine were used, 1 S/m and 2 S/m [2], to investigate the effect of urine conductivity on the measurements and the method. The artificial urine was made by mixing deionized water and NaCl. The amounts of NaCl required to make the conductivities were determined from the previously mentioned recipe.

The following is the summary of setups used for the experiments:

- Four different positions of electrode placement: three vertical placement, starting from position 5, and one horizontal.
- Horizontal measurements were carried out in the second row from the bottom.
- Two different conductivities of artificial urine: 1 S/m and 2 S/m.
- Eight different volumes of artificial urine for each conductivity were used to carry out the measurements: namely 0, 20, 40, 50, 60, 80, 100, and 120 ml.
- The frequency was swept from 1 kHz to 100 kHz with 1 kHz step.

- The experiments were repeated three times.
- In total, 192 measurement sets were performed.

Before carrying out the experiments, the height of each solution volume poured into the vacant space inside the phantom and, was measured for three times. when adding each 20 ml of solution, the height was raised by 1.5 cm. This means that at a volume of 80 ml, the top of the solution was covering the V — electrode, which is considered the marker.

The collected data points were plotted in Matlab. Figure 5.21 shows the measured impedance over frequency at each position for 1 S/m and 2 S/m solutions, for the last of three rounds. It can be seen from Figure 5.21 that, for both 1 S/m and 2 S/m, a visible decrease in impedance happens after a level of 60 ml, which are the last four lines in each Figure, at vertical positions 3, 4, and 5, although this drop was less for 1 S/m solution. For the horizontal position, the decrease in the impedance value is happening visibly at the lower levels of volume, the lines prior to the 60 ml level.

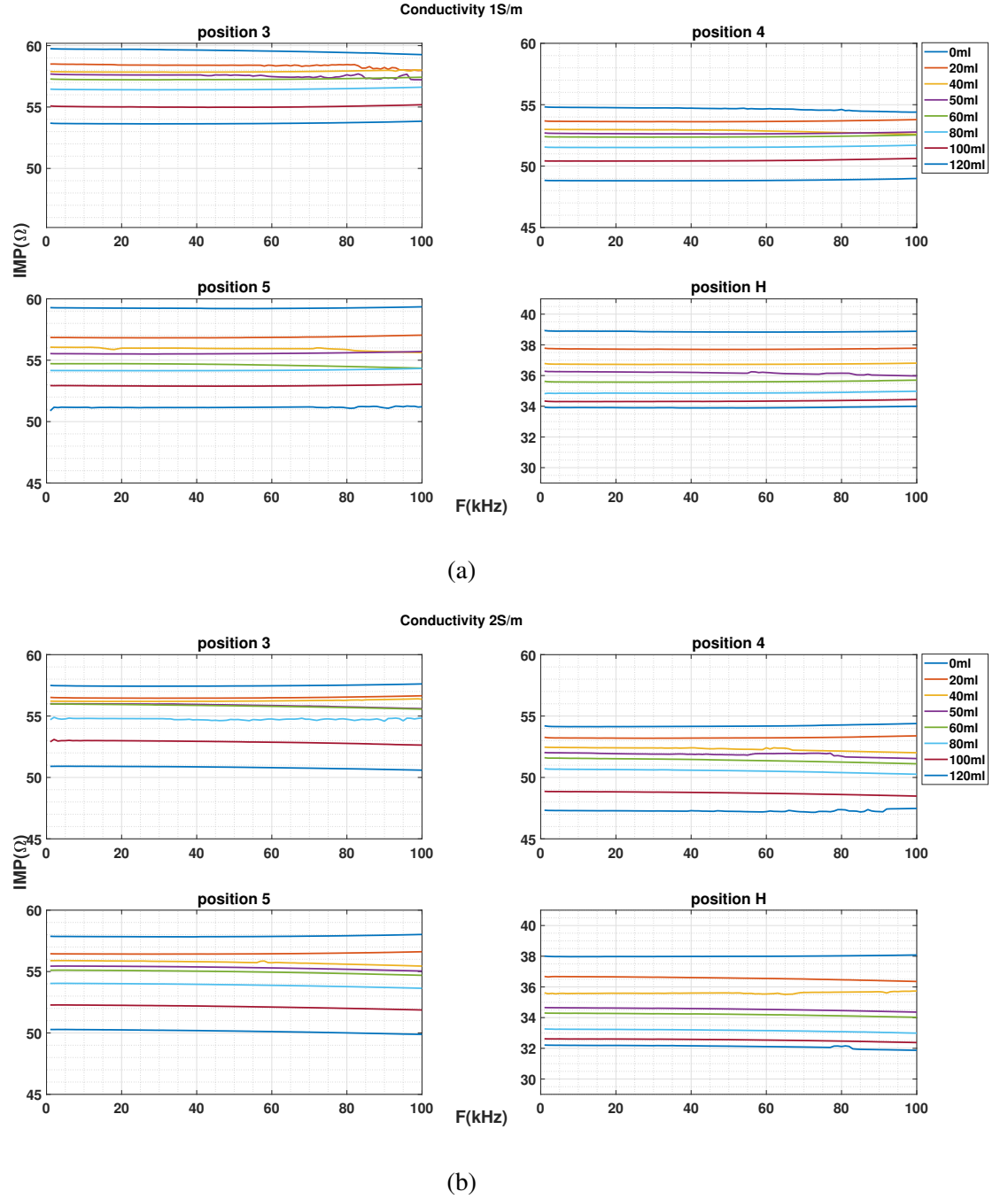


Figure 5.21: The measured impedance over frequency for 4 different positions and for a) 1 S/m b) 2 S/m. Position H is the horizontal position.

In order to have a sense of how much of a drop in impedance was observed at each position when increasing the artificial urine volume, and for a better visual comparison between the vertical positions and the horizontal position, Figure 5.22 was plotted from the data points shown in Figure 5.21.

This Figure shows the impedance over two x axes; one is the volume and the other one is the height at which the electrodes were placed, from the bottom.

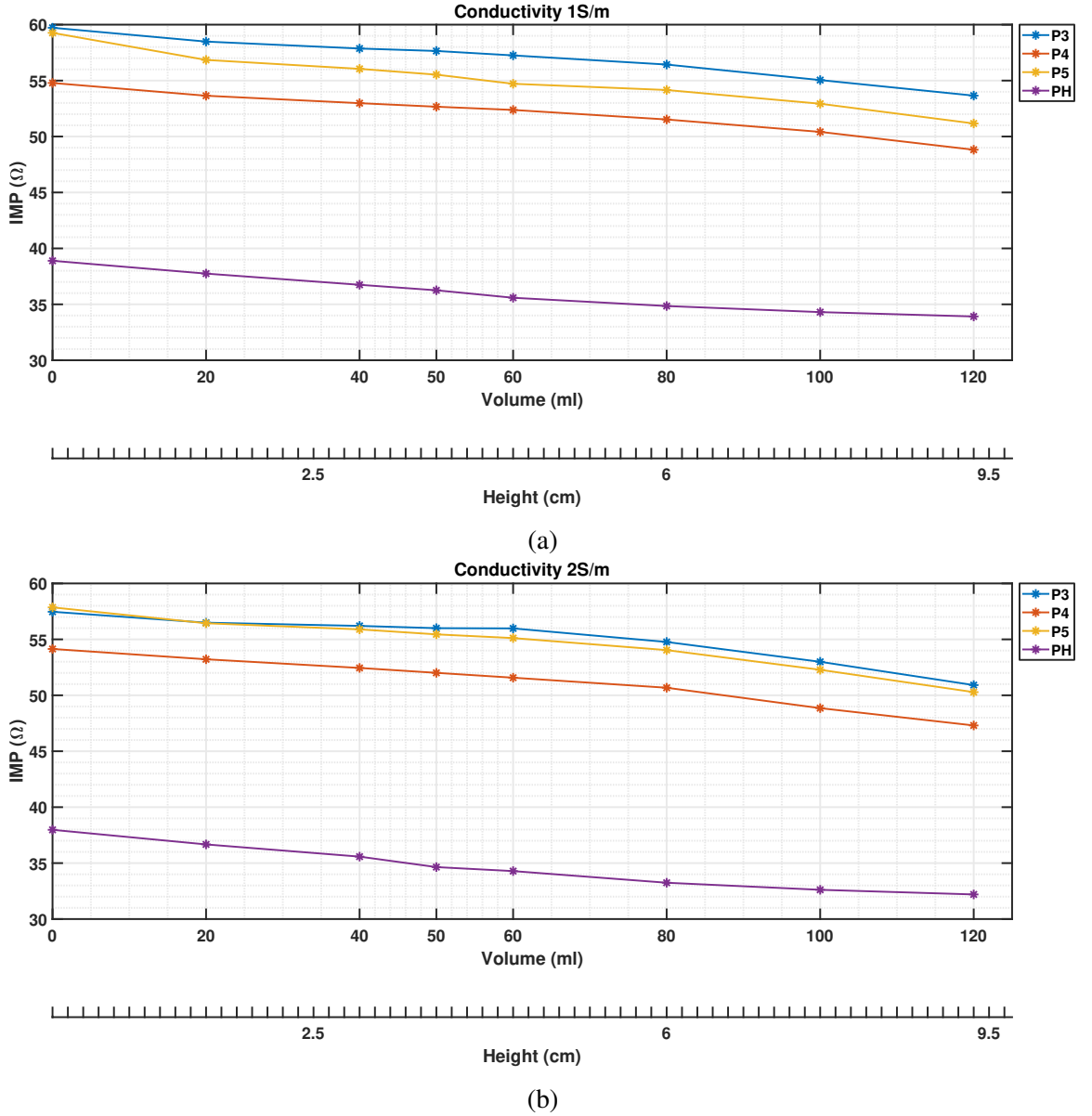


Figure 5.22: The measured impedance versus volume of solution and height of electrodes from the bottom of the phantom for a) 1 S/m b) 2 S/m. P3, P4, P5 and PH stands for the position of the electrodes followed by their number; e.g. position 3 is P3 and horizontal position is PH. Height is the distance of the electrodes from the bottom.

Each datapoint in Figure 5.22 represents an impedance measured at 5 kHz. It should be noted that although the designed BI measurement system has a capability to measure impedance at the frequency range of 5 to 50 kHz (in case future research path requires frequencies in the range of tens of kilohertz) and also, a frequency sweep up to 100 kHz was performed for characterizing the phantom to see whether any substantial change in impedance is observed, data points from 5 kHz were selected for monitoring the amount of urine. The reason is, urine is an extracellular fluid and 5 kHz is considered and tested to be suitable for the purpose of bladder monitoring [2]. It should also be noted that as mentioned earlier in chapter 4, higher frequencies, specially above 100 kHz, will considered to be challenging to design if the aim is to have a wearable device; therefore, higher frequencies were not used in the phantom experiments.

In Figure 5.22a, for instance, the first datapoint on the P3 line represents the measured impedance at 5 kHz from position 3, when no solution was poured inside the phantom, and the value was 59.7 Ω . The second datapoint corresponds to when there is 20 ml of solution with 1 S/m conductivity inside the phantom. This value was 58.5 Ω . Table 5.9 shows the difference in impedance at each position for different volumes for two conductivities of the solution at 5 kHz. In Figure 5.23, the mean of three rounds of repetition of the experiments is shown for each position, and the values of the impedance change is also shown in Table 5.9, in the average section.

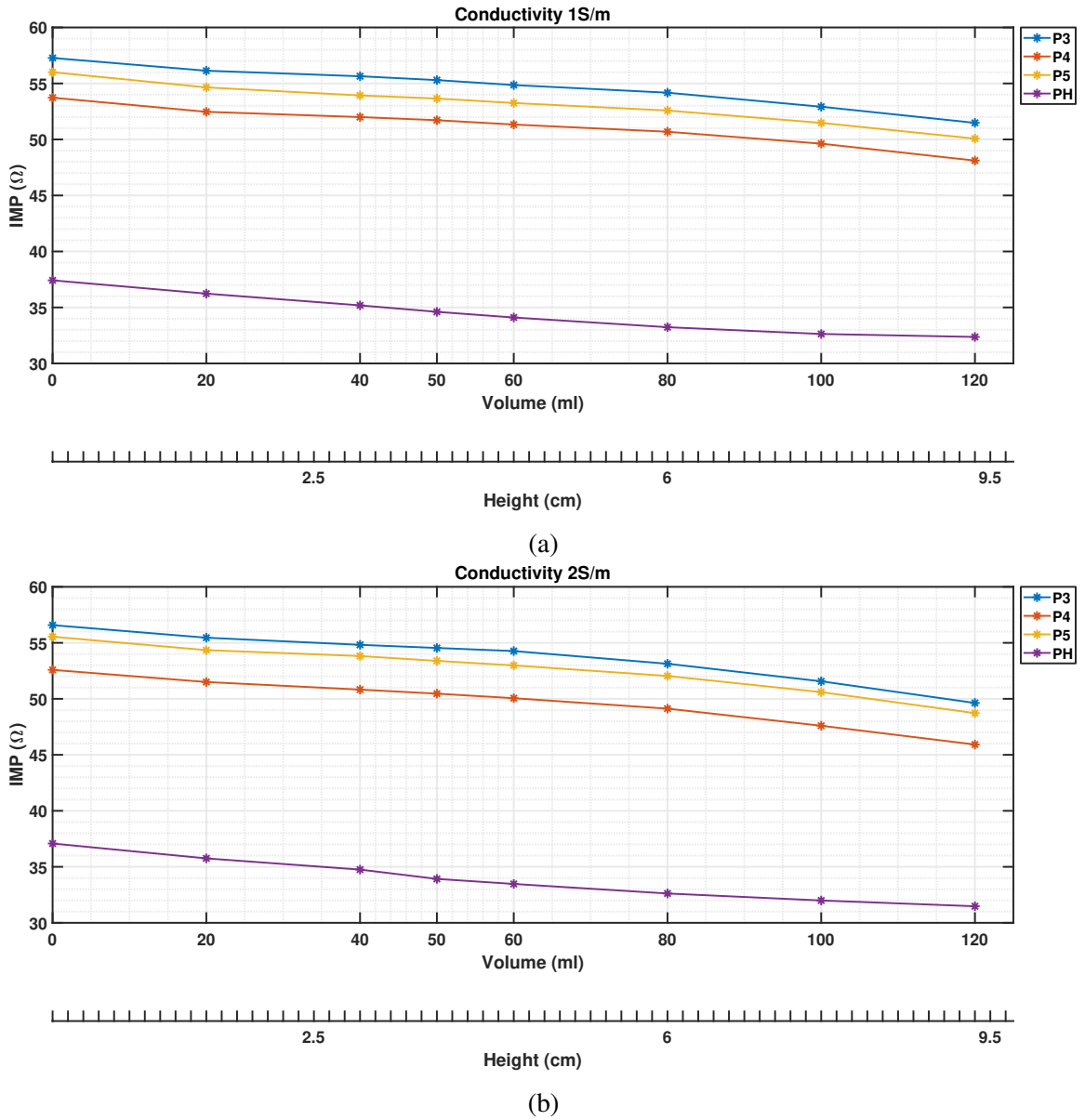


Figure 5.23: The average measured impedance of three repetition versus volume of solution and height of electrodes on a phantom for a) 1 S/m b) 2 S/m.

For the vertical positions, it can be noticed from Figures 5.22 and 5.23 that, as the level of artificial urine rises, the impedance starts to fall and after reaching the 60 ml volume, a steeper drop occurs for further increases. The trend in impedance reduction in the horizontal position is the opposite of the vertical positions. In that configuration, the impedance falls more significantly from the start of pouring the artificial urine in both cases of conductivity, and the variation is slowed down after reaching 60 ml and after

Table 5.9: Impedance drop when the level of artificial urine increases for different volumes. *IMP* stands for impedance in the table.

Conductivity	Repetition	Electrodes Position	IMP Variation from 60 to 80 ml (Ω)	IMP Variation from 80 to 100 ml (Ω)	IMP Variation from 20 to 60 ml (Ω)	IMP Variation from 60 to 120 ml (Ω)
1 S/m	One	3	0.67	0.88	0.67	2.99
		4	0.44	0.83	0.44	2.75
		5	0.76	0.86	0.76	2.71
		H	0.99	0.71	0.99	1.77
	Two	3	0.56	1.49	1.49	3.55
		4	0.60	1.27	1.09	3.33
		5	0.69	1.21	1.04	3.27
		H	0.88	0.55	2.09	1.77
	Three	3	0.82	1.38	1.24	3.60
		4	0.85	1.12	1.27	3.56
		5	0.55	1.23	2.13	3.54
		H	0.75	0.53	2.16	1.68
	Average	3	0.68	1.25	1.28	3.37
		4	0.64	1.06	1.13	3.22
		5	0.67	1.10	1.39	3.18
		H	0.86	0.60	2.13	1.73
2 S/m	One	3	1.04	1.40	1.44	4.06
		4	0.89	1.41	1.18	3.90
		5	0.79	1.25	1.23	3.74
		H	0.77	0.58	2.15	1.76
	Two	3	1.15	1.53	1.62	4.78
		4	1.01	1.35	1.52	4.25
		5	0.93	1.34	1.55	4.20
		H	0.75	0.65	2.30	2.13
	Three	3	1.08	1.80	0.52	5.07
		4	0.89	1.83	1.66	4.26
		5	1.08	1.76	1.33	4.83
		H	1.04	0.64	2.36	2.08
	Average	3	1.13	1.57	1.19	4.63
		4	0.93	1.52	1.45	4.14
		5	0.94	1.44	1.36	4.25
		H	0.85	0.62	2.28	1.99

that, the impedance change is smaller compared to the vertical positions. The trends for change in the impedance at vertical positions and horizontal position can be quantified better in Table 5.9. On average, the change from 60 to 120 ml at vertical position 4 for the 1 S/m conductivity is 3.22 Ω . This change for the horizontal position is 1.73 Ω . This means that the change of impedance at the horizontal position, due to the same change in level of artificial urine inside the phantom, is 45.7% less compared to that of vertical measurement at position 4. For 2 S/m conductivity from 60 to 120 ml, the average of variation at position 4 is 4.14 Ω and, for that of horizontal position, it is 1.99 Ω . This translates to 52% less change in impedance for the horizontal position, compared to vertical position 4.

In order to validate whether there is a statistically significant difference between the impedance change recorded vertically at position 4 and the horizontal position after 60 ml, a paired t-test method was used for both 1 S/m and 2 S/m conductivities. The obtained P-values for both conductivities at the vertical position compared to the horizontal position was below 0.05 (P-value < 0.05). This indicates there is a statistically significant difference for the variation in impedance recorded vertically compared to the horizontal position for both conductivities, with 95% confidence interval.

On average, for 1 S/m solution at position 4, the reduction in impedance is 2.85 times greater after 60 ml than below 60 ml. The value for the horizontal position is the opposite and also less compared to position 4, as the reduction happening below 60 ml is only 1.23 times greater than above 60 ml. For the solution with 2 S/m and at position 4 and the horizontal position, these values are 2.86 and 1.15, respectively. On average, the total

impedance change from pouring the solution inside the phantom to 120 ml for 1 S/m at position 4 was $4.33\ \Omega$ and for the horizontal position it was $3.86\ \Omega$. These values for 2 S/m were $5.69\ \Omega$ and $4.27\ \Omega$, respectively. On average, the difference of impedance change between 1 and 2 S/m conductivity at the horizontal position, when the level of solution was changed from 60 to 120 ml, was $0.25\ \Omega$. For the vertical scanning at position 4, this value was $0.93\ \Omega$. For positions 3 and 5, since the electrodes were placed on the circumference of the phantom, those follow the same trend as position 4, as shown in Table 5.9.

In order to show the reversibility of the method, another three repetitions of the experiments were carried out. The impedance values were recorded from position 4, the middle electrode set, and the horizontal position, to compare the results. After filling the vacant space step by step, as discussed, with 120 ml of solution and performing the measurements at each step, the solution was evacuated step by step, in the same manner as it was poured inside the phantom. The evacuation was performed with a 10 ml syringe. It was confirmed that the capacity of syringe is 10 ml by filling it three times and comparing its content with a 10 ml beaker. Including both conductivities, in total 180 experiments were carried out for the reversibility test. Figure 5.24 shows the average of the three rounds of repetition for two different conductivities.

The grey transparent lines in the Figure 5.24 represent each round of experiments at each position, and the mean is calculated from then. The same trend, as observed previously, can be seen in the reversibility test while in the filling stage, for the vertical positions compared to the horizontal

Table 5.10: Measured impedance drop at vertical position 4 and the horizontal position in the filling and emptying stage.

Conductivity	Electrodes Position	IMP Variation from 60 to 80 ml (Ω)	IMP Variation from 80 to 100 ml (Ω)	IMP Variation from 20 to 60 ml (Ω)	IMP Variation from 60 to 120 ml (Ω)
1 S/m	Filling - 4	0.66	1.30	1.36	3.29
	Emptying - 4	0.56	0.99	0.73	2.54
	Filling - H	0.68	0.64	2.26	1.46
	Emptying - H	0.66	0.28	1.62	1.24
2 S/m	Filling - 4	0.90	1.65	1.31	4.52
	Emptying - 4	0.85	1.32	0.65	3.57
	Filling - H	0.91	0.61	2.72	1.84
	Emptying - H	0.72	0.37	1.63	1.26

position. At position, 4 and reaching back to 20 ml in the emptying stage, a 1.38 Ω difference between the filling and emptying stages was observed in the reversibility test for 1 S/m, and for 2 S/m this value was 1.61 Ω . For the horizontal position these values were 0.86 Ω and 1.67 Ω , respectively. Table 5.10 shows the values of the measured impedance in the reversibility test.

In the next section, the vacant space was relocated to address aim 4 of the thesis.

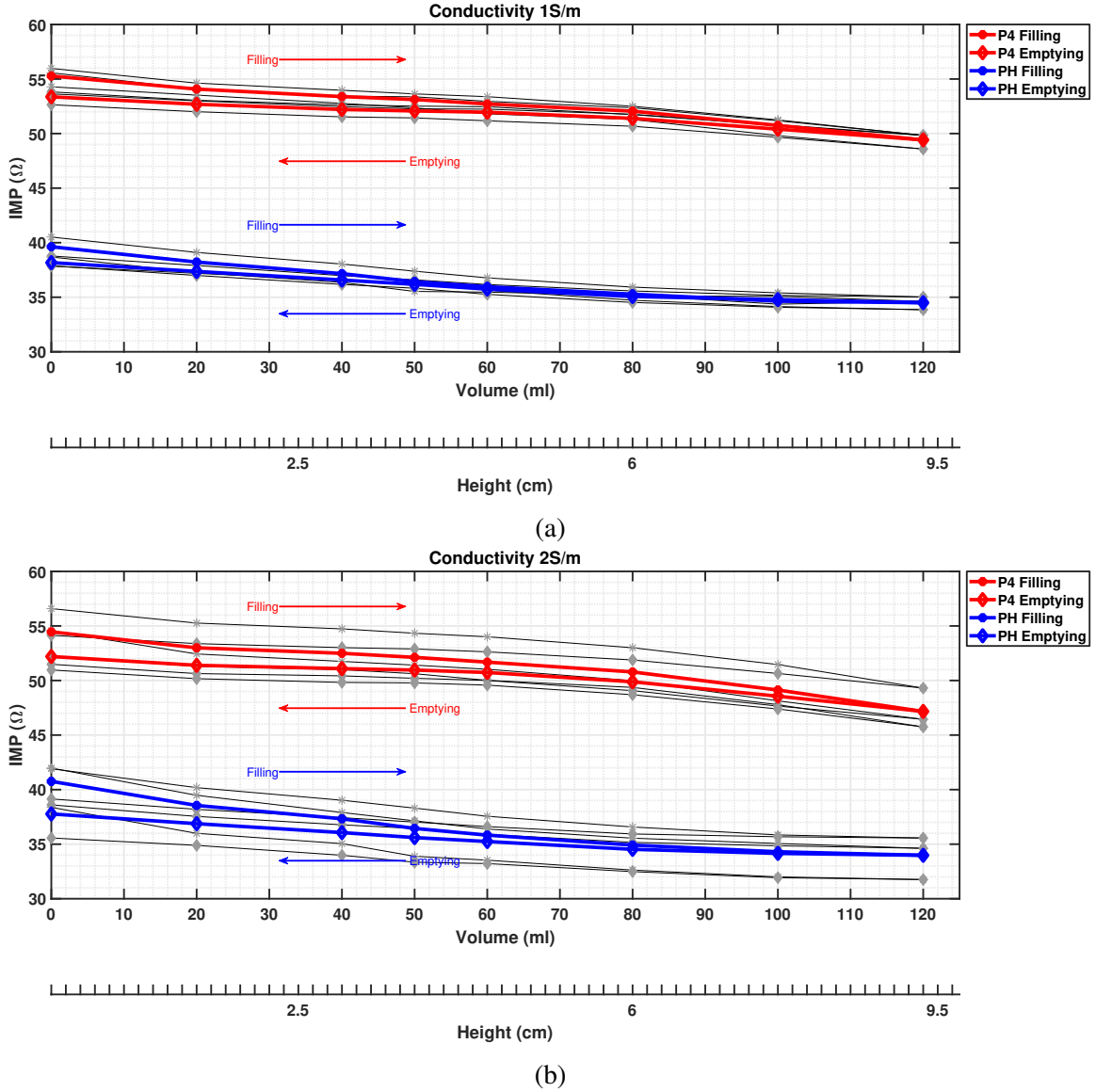


Figure 5.24: The mean measured impedance of three rounds of the reversibility test, versus volume of solution and height of electrodes on the phantom for a) 1 S/m b) 2 S/m. The grey lines represent each specific round of repetition and the mean values, in red and blue lines, were calculated from those.

5.4.4 Effect of Relocation of the Bladder: Setups and Results

To address aim 4 of the thesis, a new set of experiments was designed. The aim was to investigate the impact of bladder relocation and the effectiveness of vertical scanning for bladder monitoring from different locations. Four cases were selected for the experiments. Figure 5.25 shows the top view of setups for different scenarios. The vacant space is indicated by the small orange-coloured circle, which is relocated in the phantom, shown as a blue round object. The electrodes connected to the phantom at each position are shown in black. Because it is a top view, the horizontal placement of electrodes is not shown. Starting from the centre, the vacant space was shifted to the right and, from there, it was rotated 90° anti-clockwise. The solutions with 1 S/m and 2 S/m conductivity were used as the artificial urine. Eight different volumes of the artificial urine were poured into the vacant space at each setup. The values were 0, 20, 40, 50, 60, 80, 100, and 120 ml. The impedance was measured by the impedance analyzer over a frequency range of 1 kHz to 100 kHz. These experiments were repeated in two rounds and, in total, 512 experiments were performed. Figure 5.26 shows the phantom created for the purpose of those experiments. A mould similar to the one shown in Figure 5.18, but with the holder for the cylindrical tube shifted to one side, was ordered and used (Figure 5.27). In this setup, the center point of the vacant space was shifted three centimeter to the side.

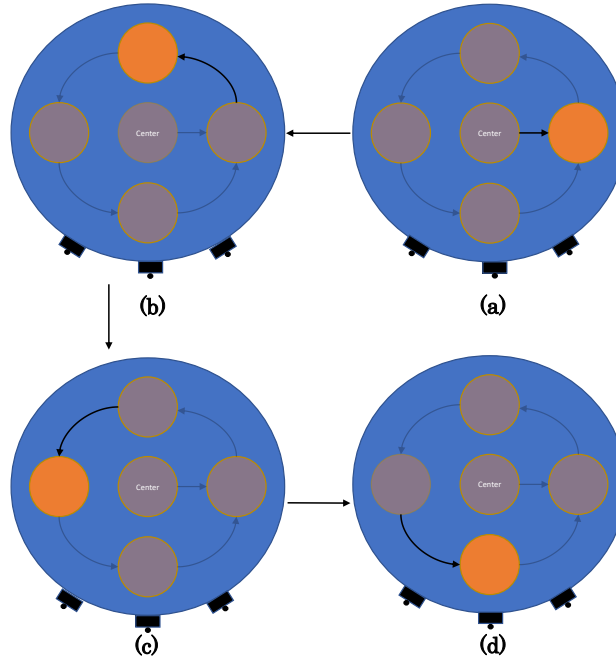


Figure 5.25: Top view of four different scenarios for impact of relocation of the bladder a) shifted to the right side b) rotated far away from the electrodes c) rotated to the left side d) rotated close to the electrodes. The black objects are symbols for the electrodes.

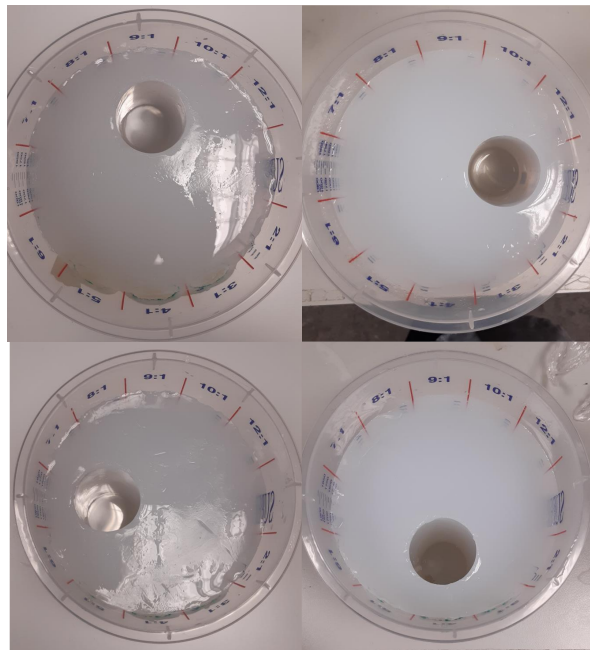


Figure 5.26: Phantom created for BI measurement to investigate the impact of bladder relocation on bladder monitoring.

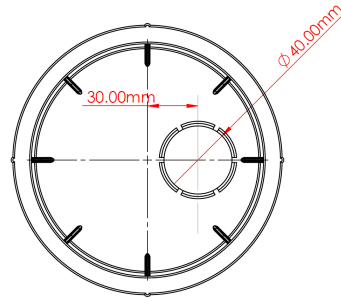


Figure 5.27: A mould used to hold the tube firm and create the vacant space shifted to the side of phantom.

Results

The average of two rounds is shown in Figures 5.28 through 5.31, which present the results of the impedance data at 5 kHz for each of the four scenarios. Similar to the previous section, and as an example, a datapoint on P3 line at 20 ml shows the measured impedance at a frequency of 5 kHz for a specific setup. Table 5.11 shows the measured change in impedance at the mentioned setups for the average of the two rounds, when the volume of artificial urine is increased. The measured impedance at the vertical positions for which the electrodes were closer to the target area, highlighted in light blue in Table 5.11, can be compared to that of horizontal measurements.

For the solution with 1 S/m conductivity, where the location of the vacant space is at the right side and closer to position 3 than the other vertical positions, the impedance fell 1.63Ω and 1.79Ω when the volume was raised from 60 to 80 ml and 80 to 100 ml, respectively. The total change in impedance below and above 60 ml was 2.47Ω and 5.75Ω , respectively. For the horizontal position, the total impedance change below and above 60 ml were 1.60Ω and 0.99Ω , respectively.

At the left location, where the target is closer to the electrodes in position 5, the same trend in impedance reduction for this position compared to the

Table 5.11: Mean of measured impedance change between different volumes, at each electrode position for different location of the vacant space. All locations are referenced to the electrodes, as shown in Figure 5.25.

Conductivity	Location of the Vacant Space	Electrodes Position	IMP Variation from 60 to 80 ml (Ω)	IMP Variation from 80 to 100 ml (Ω)	IMP Variation from 20 to 60 ml (Ω)	IMP Variation from 60 to 120 ml (Ω)
1 S/m	Right	3	1.63	1.79	2.47	5.75
		4	0.98	1.18	1.49	3.52
		5	0.85	0.44	1.05	2.00
		H	0.53	0.51	1.60	0.99
	Far	3	0.27	0.72	0.59	1.44
		4	-0.01	0.03	0.74	0.66
		5	0.40	0.70	0.53	1.46
		H	0.15	0.10	0.85	0.93
	Left	3	0.33	1.21	1.00	2.24
		4	0.81	1.28	1.37	2.99
		5	1.81	3.03	1.90	7.84
		H	1.51	0.67	4.09	2.72
	Close	3	4.67	6.59	6.13	17.60
		4	7.45	10.29	8.24	26.19
		5	4.10	6.54	4.67	17.90
		H	5.70	1.54	18.30	8.33
2 S/m	Right	3	1.92	2.58	2.79	6.83
		4	1.52	1.14	1.32	3.77
		5	0.50	0.69	0.87	2.02
		H	0.43	0.47	1.48	1.02
	Far	3	1.08	-0.14	0.50	1.57
		4	0.01	0.52	0.37	0.59
		5	0.01	0.48	0.66	1.42
		H	0.03	0.41	0.81	0.61
	Left	3	0.77	0.91	1.50	2.33
		4	1.42	1.59	1.86	4.37
		5	2.71	3.91	3.08	10.64
		H	1.40	0.93	5.73	2.78
	Close	3	4.85	9.57	6.71	22.70
		4	8.67	12.01	9.15	31.57
		5	3.62	7.37	4.42	19.81
		H	5.19	2.19	18.96	8.45

horizontal position was observed. Where the vacant space was close to the electrodes as shown in Figure 5.25d, the impedance in all of four positions was changed substantially, compared to the three other locations where the vacant space was shifted to, with position 4 having the greatest amount of change compared to three other positions of electrodes. At a far location, on the contrary, the change in impedance was trivial while the level of the volume of solution was being increased, providing a pseudo flat line in Figure 5.29. When the conductivity of the solution was changed to 2 S/m, similar observations were seen for each scenario shown in Table 5.11.

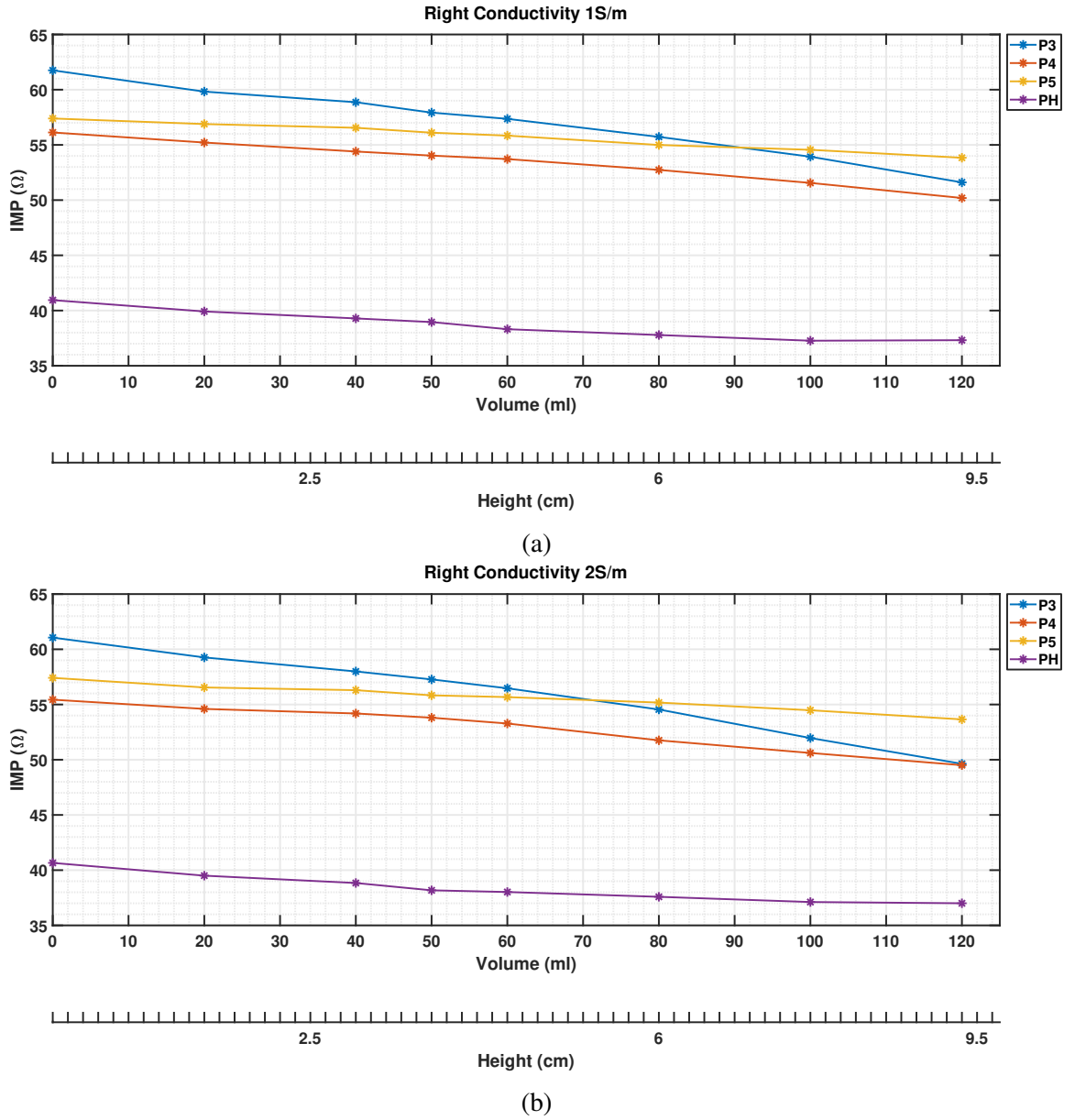


Figure 5.28: Mean measured impedance at four positions when the vacant space is shifted to the far right, as shown in Figure 5.25a. a) conductivity 1 S/m b) conductivity 2 S/m.

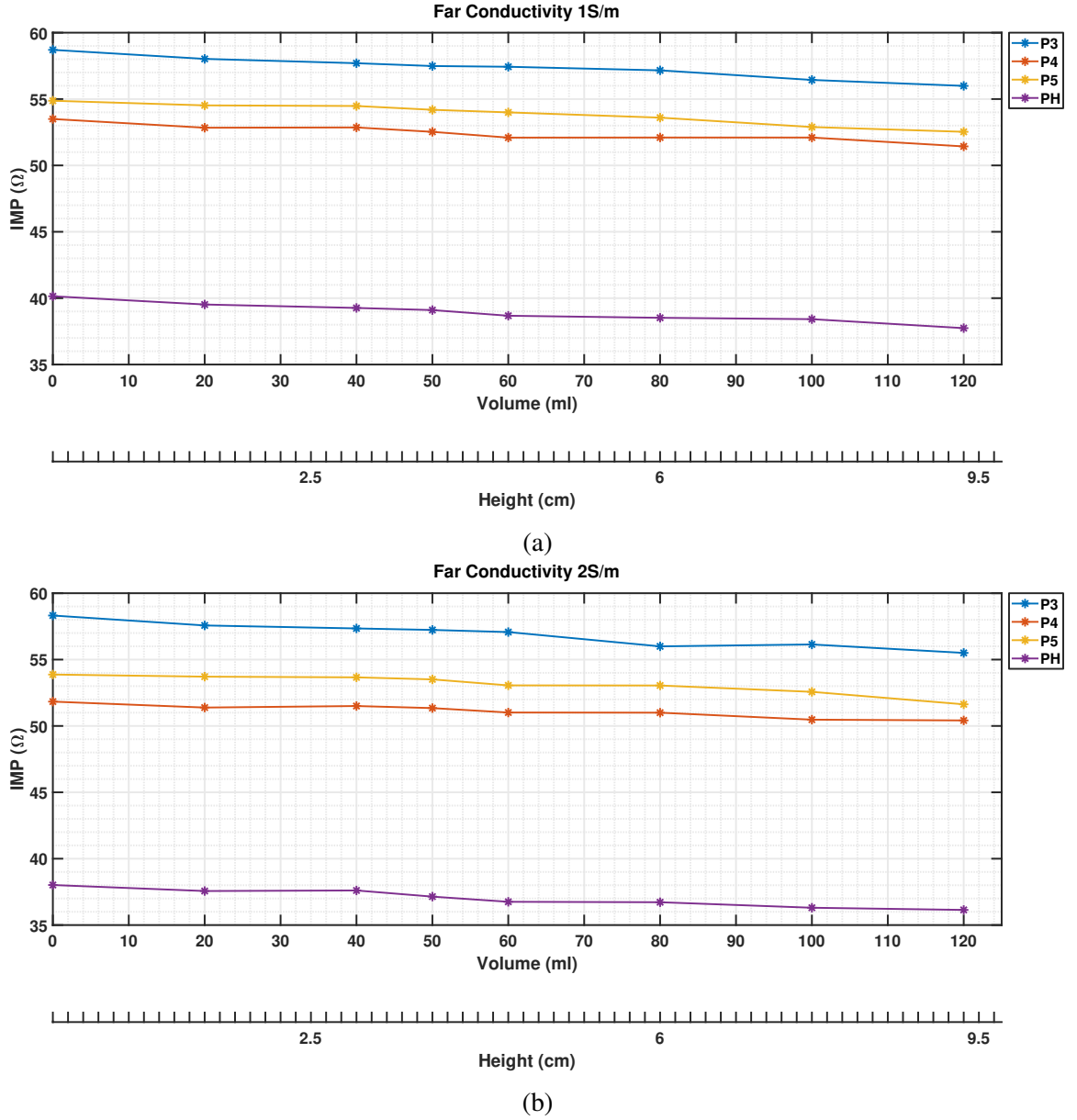


Figure 5.29: Mean measured impedance at four positions when the vacant space was rotated 90° to the back, as shown in Figure 5.25b. a) conductivity 1 S/m b) conductivity 2 S/m.

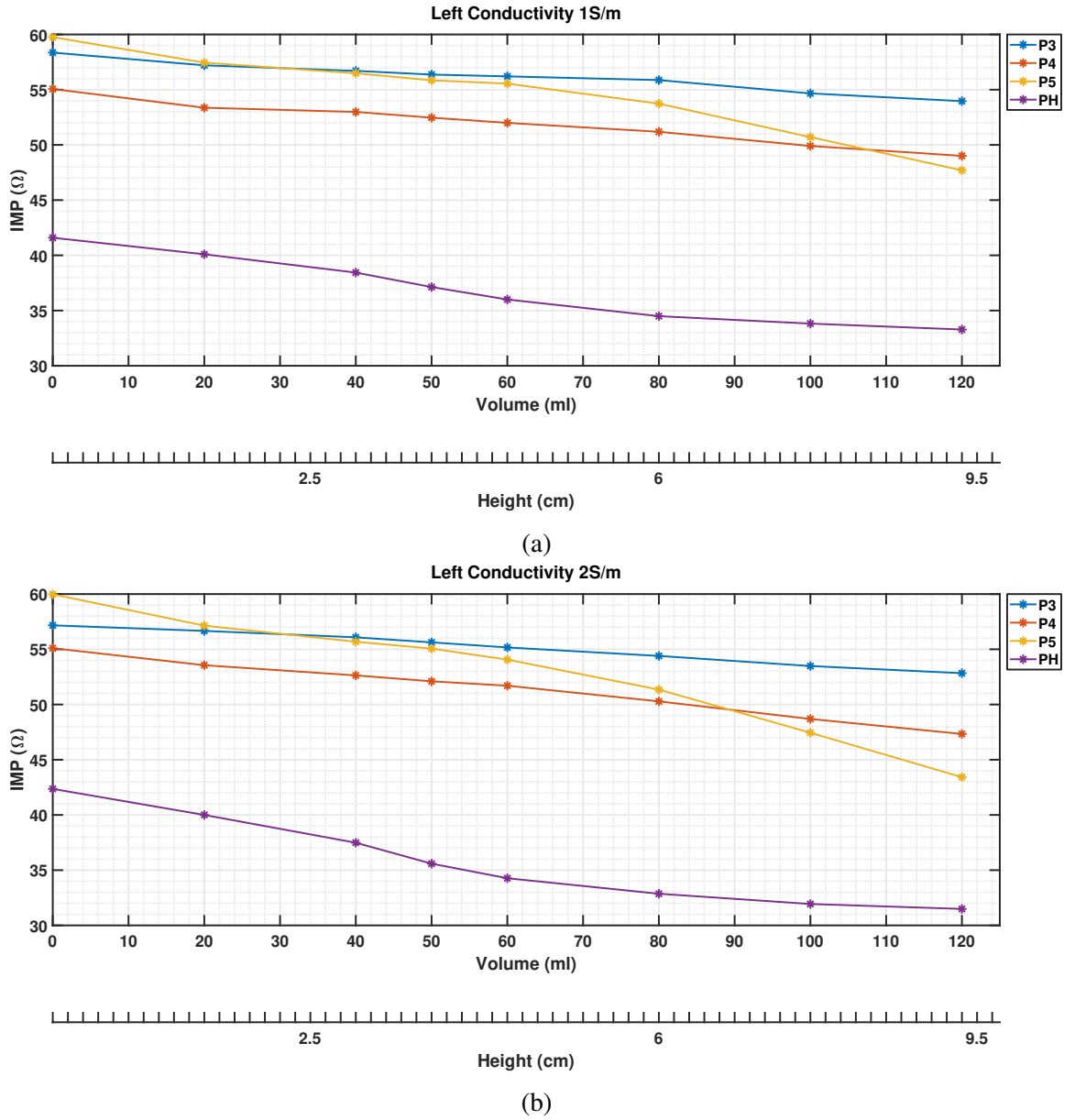


Figure 5.30: Mean measured impedance at four positions when the vacant space was rotated 90° to the left, as shown in Figure 5.25c. a) conductivity 1 S/m b) conductivity 2 S/m.

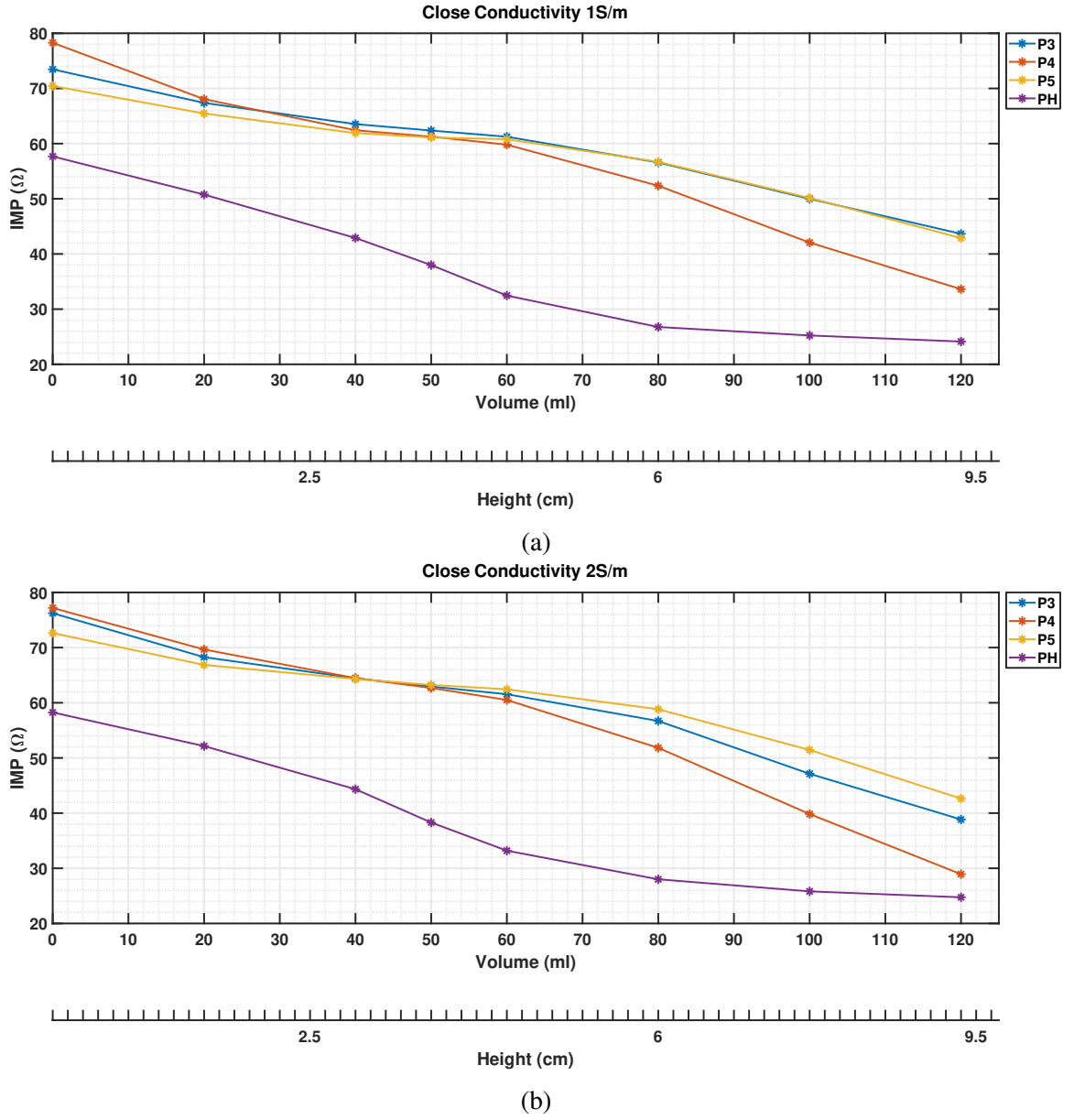


Figure 5.31: Mean measured impedance at four positions when the vacant space was rotated 90° from the left side and was close to electrodes, as shown in Figure 5.25d. a) conductivity 1 S/m b) conductivity 2 S/m.

Test of the Designed Device on the Phantom

As a final test, the designed and manufactured BI measurement system was used to measure the change of impedance at 5 kHz on the phantom with the vacant space in the centre, due to the accumulation of the artificial urine with 1 S/m and 2 S/m conductivities. The results are shown in Figure 5.32. Table 5.12 shows the values of measured variation in impedance with the designed BI measurement device for different volumes, at different positions for both conductivities. At position 4, when the conductivity is 1 S/m, the total change from 60 ml to 120 ml was 3.42 Ω . This value for the horizontal position was measured to be 2.25 Ω . When the conductivity was changed to 2 S/m, at position 4 the change in impedance from 60 to 120 ml was 5.83 Ω . This change in impedance was 1.83 Ω for the horizontal position.

Table 5.12: Impedance drop measured with the designed BI measurement device when the level of artificial urine increases for different volumes.

Conductivity	Electrodes Position	IMP Variation from 60 to 80 ml (Ω)	IMP Variation from 80 to 100 ml (Ω)	IMP Variation from 20 to 60 ml (Ω)	IMP Variation from 60 to 120 ml (Ω)
1 S/m	3	0.59	1.60	1.24	3.72
	4	0.82	0.99	0.95	3.42
	5	1.27	1.26	0.99	3.31
	H	1.12	0.59	2.93	2.25
2 S/m	3	0.84	1.14	1.42	3.69
	4	1.54	2.28	1.77	5.83
	5	0.75	1.38	1.24	3.76
	H	0.85	0.35	2.42	1.83

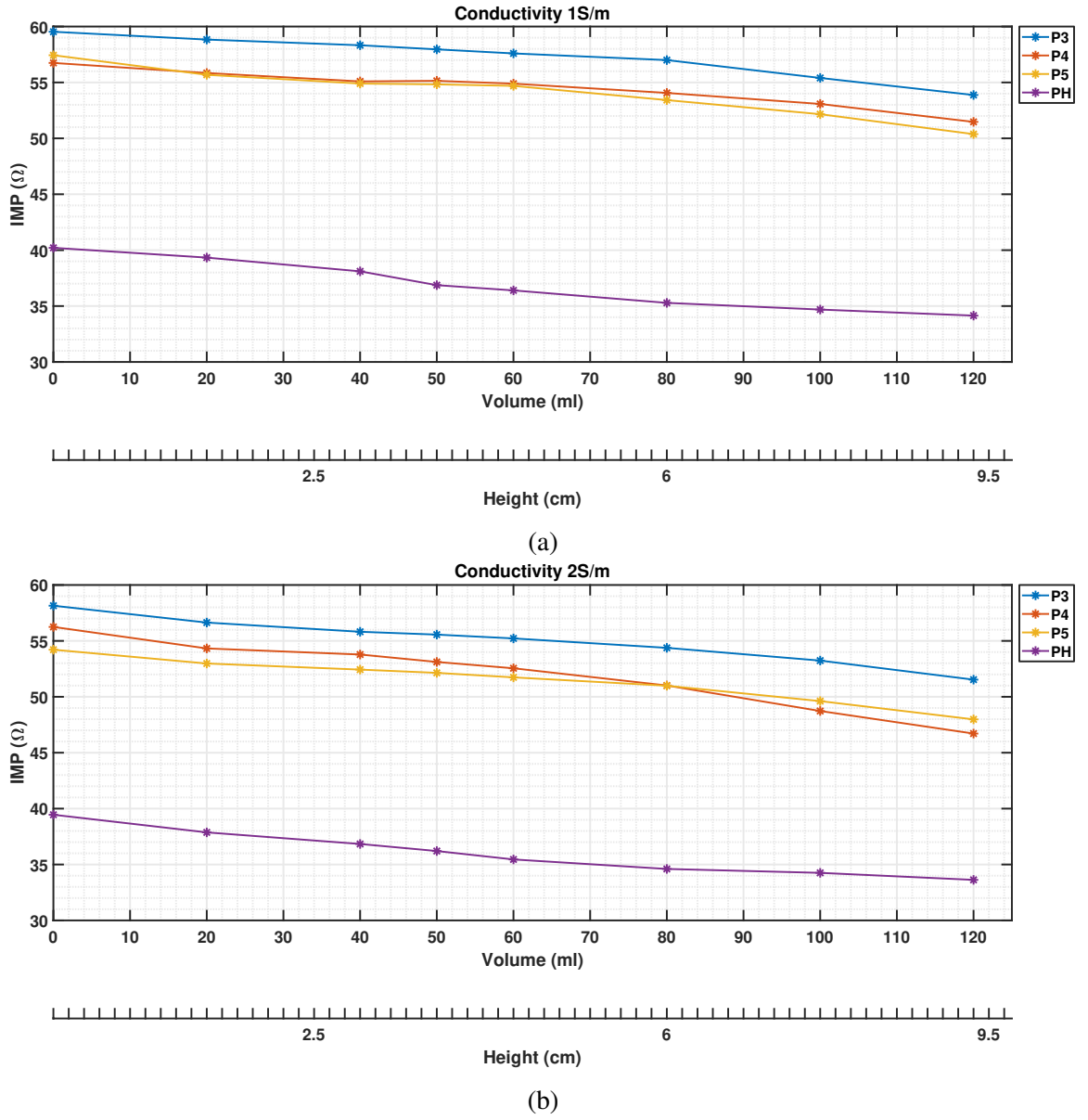


Figure 5.32: Measured impedance with the designed BI measurement system at 5 kHz with conductivity of a) 1 S/m b) 2 S/m.

5.5 Chapter Conclusion

Two versions of a BI measurement system, working in the range of 1 kHz to 50 kHz were developed and verified. The V1 system could measure and distinguish between loads from $10\ \Omega$ to $30\ \Omega$ with an accuracy of $0.25\ \Omega \pm 0.21\ \Omega$ and the error of the measurements was below 2% after calibration. For the V2 system, after the improvements in the design layout and adding a filter, the device was tested with the maximum and minimum range of the load with a 2R-1C model. The accuracy was obtained from forty measurements and was $0.3\ \Omega \pm 0.15\ \Omega$. This translates to less than 0.5% error in the measurements without any calibration, when the change is between 30 and $68\ \Omega$.

The performance of the designed system was shown in Table 5.7 and it was compared to the existing state-of-the-art BI measurement devices. The designed system could have smaller size, but the dimensions were restricted to match the header of the microcontroller board. Also, as the board was hand soldered, the components with larger packages and footprints were selected and, in addition, some space was taken due to the use of test points to measure the performance and debug potential issues with the board. The aim was to also have the microcontroller circuitry on the same PCB but, due to the global supply chain issue of the microcontroller, this was not achievable within the timeframe of the Ph.D. In addition, other possible solutions to shrink the board size are (1) to use more than two layers on the PCB, and (2) to use the components with smaller footprints and packages and outsource the assembly, but it would increase the cost of manufacturing, in addition to the fact that smaller packages were difficult to purchase, again

due to the same reason of a global supply chain issue. This would also considerably delay the delivery time of the board. As a prototype, doing so seemed to be unnecessary. The power consumption of the board is within the range of other existing and similar BI measurement devices, especially compared to the recent study published in late 2020 [147]. It should be noted that this is the active power consumption when the device is doing the measurements, which may only be a small fraction of the time the device is powered up. Although the range of impedance in [147] starts from 100 Ω , and below this range, which is the impedance range for bladder monitoring has not been tested, the error of the system in [147] of 1.5 % translates to 0.8 - 1 Ω error in impedance in the 55 - 65 Ω load range. This would cause error when distinguishing between volumes specially if the electrodes are placed horizontally, as shown in Tables 5.9 and 5.12. The study in [147] did not perform any experiments related to bladder monitoring, although it was reported that their device could be used for this application as it has a low error rate and a small size.

An agar based phantom was fabricated in order to investigate aims 3 and 4 of the thesis. The recipes for creating the phantom and the artificial urine used in the experiments were provided. A vacant space in the center point of the phantom was used to mimic the bladder for storage of the artificial urine. Regarding aim 3 of the thesis, a total of 192 experiments in three repetitions were performed in three vertical positions and one horizontal position. Results indicated that, for the vertical position, passing 60 ml of volume to 120 ml in both 1 S/m and 2 S/m solutions, the fall in impedance is greater compared to the horizontal position, which was shown to be sta-

tistically significant, with a 95% confidence interval. This is the volume that has just reached the bottom of the V_- electrode, the marker. This is in line with the hypothesis explained in Chapter three for vertical scanning compared to horizontal scanning. As the artificial urine level is rising, when it reaches the V_- electrode a lower path impedance is introduced; hence, the greater change in impedance that happens is related to reaching and passing this level for the vertical position, and the opposite happens for the horizontal position. Occurring for both 1 S/m and 2 S/m conductivities, this means that, in the vertical method, the electrode measuring the voltage V_- can be used as a threshold for monitoring the fullness of the bladder with increased sensitivity, compared to the horizontal method. In other words, a steeper change in impedance happens right after the level of interest in the vertical position, in comparison to the smaller change that happens before this level for the horizontal position, for both conductivities. This also has the advantage of allowing the method to be adjustable for monitoring different levels of urine in the bladder while performing vertical scanning.

The results of a reversibility test with a total of 180 experiments showed the same trend. However, there was a difference between the impedance measured prior to pouring the solution into the phantom and after a filling and emptying procedure. This difference could be explained by the fact that, as the solution remains in the vacant space inside the phantom, infusion of ions happens. The more time passes while the solution remains inside the phantom, the longer the difference between values. Due to ion infusion, performing each one set of experiments related to aim 3 and aim 4 was restricted to only eight different volumes from 0 ml to 120 ml, thus; minimiz-

ing this impact, while providing the required data to investigate those aims. As can be noticed from Figure 5.24, the impedance recorded in the emptying stage starts to deviate faster from that of the filling stage after reaching back to 60 ml for both conductivities. At this point, for 1 S/m at position 4, the deviation from the filling stage was 0.7Ω and, at the horizontal position, it was 0.2Ω . For 2 S/m, these values were 0.9Ω and 0.6Ω , respectively. It is worth mentioning that the lower deviation which was recorded for the horizontal position is due to the fact of its lower sensitivity to impedance change at this level.

For aim 4, the investigation of the proposed mechanism when the bladder is relocated, four different scenarios were considered, where the vacant space was shifted to different locations being: right, far, left, and close to the electrodes. Two repetitions and a total of 512 experiments were performed. Results show that, depending on which sets of vertical electrodes are covering the area where the vacant space is shifted to, a change can be observed compared to the other sets. For the 1 S/m sample, where the vacant space is shifted to the right, the total impedance change recorded from position 3, which is vertically covering the area of the vacant space, is 1.63 times greater than position 4 in the middle and 2.87 times greater than position 5, which is covering the left side of the phantom and representing a pseudo-flat line in Figure 5.28. Comparing this to the 1.6Ω reductions in impedance happening below 60 ml at the horizontal position, it is 3.59 times greater. The impedance reduction for 2 S/m are even greater, due to the fact that it is more conductive, leading to more impedance change at the same volume. These values are 1.81 and 3.38 for position 4 and 5, respectively and, com-

pared to the horizontal position, the number is 4.61.

In the far location for both conductivities, the performances at all the positions were similar with a trivial change in impedance, due to the fact that the target is out of reach and, as the current tends to always pass through the minimum impedance path, it does not reach the depth where the target is located. Although, using wider electrodes can be helpful to increase the depth of penetration, with the cost of losing spatial resolution in impedance recording, more study is required for this specific scenario, to test when the bladder gets further from the electrodes due to any change in posture. This can also mean care should be taken using BI measurement for obese patients, where the location of the bladder is farther from the electrodes.

When the target was on the left, the a same trend in impedance change at vertical positions was observed, with position 5 having a large impedance change after 60 ml. In contrast, for the horizontal position, the change recorded below 60 ml was higher compared to the experiments in which the target was located at the right, for both conductivities. This can be explained again by the fact that current tends to flow through a low path impedance. When the location of the target is at the left side, where the A_+ electrode applies current, the low path impedance and any change in the characteristic of the target due to the rising volume is close to the path of current flow. On the contrary, where the target is at the right side, the current has to flow a further distance to reach the target, which would be a high impedance path. Therefore, at the horizontal position and below 60 ml, the change in impedance happening due to the rising volume of the solution on the right side is less than that of the left side. This change of location does not make

an impact for recording the impedance at the vertical positions as the A_+ electrode is always covering the top of the target, which could be taken as another advantage over the horizontal position in these scenarios.

When the vacant space was close to all of the electrodes, a substantial change in impedance was observed for all positions, specifically after 60 ml for vertically positioned electrodes and below 60 ml for the horizontal position, for both of the conductivities. Position 4 had the most total change in impedance, which was 1.5 times greater compared to position 3 and 5 at 1 S/m, and 3.14 times greater than that of the horizontal position. For 2 S/m, this reduction was also in the range of 1.5 times greater compared to all of other vertical positions, and 3.73 times greater than the impedance change at the horizontal position. This also indicates two points: (1) confirmation of using the V_- electrode as the threshold level in vertical scanning at position 4 and (2) where the location of bladder is close to the coverage area of the electrodes, the reduction in impedance due to the increased volume happens at a grater rate at all positions and it is easier to detect. Again, this could be a factor to consider for individuals with different weight.

These findings are in line with the assumption mentioned to address aim 4. If the position of the bladder is relocated due to posture or any other factors, and it is within an accessible range, the vertical scanning method with three set of electrodes, compared to the horizontal measurement, provides a better coverage area.

There are some limitations to the experiments outlined in this chapter for both aim 3 and aim 4:

(1) Although here a vacant space with a maximum capacity of 140 ml was used to imitate the bladder, the full and stretched bladder has the capacity of 400 ml to 500 ml, but a sense of urination will happen at 100 ml to 150 ml [44]. As the method is based on vertically monitoring the accumulation of the volume, the overall response related to the method should not change if the capacity of the vacant space is increased, but more study is required for confirmation.

(2) Indicated in [2], maintenance and storage of a large sized agar based phantom similar to the human body could be challenging. In this thesis, the cooling space required for such an storage was an extra limiting factor. The other option was to dispose of the phantom after each experiment but the preparation of a new phantom would become very costly at such size. If a larger size phantom is used, as the background conductivity and the area of the scanning is the same, there should be no deviation in the trend of impedance change if the experiments were to be repeated.

(3) The relocation of the bladder was performed in a scenario with a 3 cm shift of its centre point. This might not happen in the cases of all individuals, but the experiments provide a good foundation and understanding that such placement of electrodes will be helpful to spot a change in location even in worst case scenarios.

(4) The vacant space that was used here to mimic the bladder was empty and filled with air before performing the measurements. This may not be the case in a human body. The bladder expands as the urine volume is being increased and, there could be some remaining fluid inside the bladder. If a solution with similar but not the same conductivity of phantom is to be poured inside the bladder prior to the measurement to mimic this behavior, the conductivity of the solution should be carefully taken into consideration, as the phantom is prone to ion infusion and the impedance change could be affected. However, the trend in impedance change should be similar to the results of the performed measurements, as discussed earlier in the chapter.

For the final experiment and to test the designed BI measurement system for bladder monitoring with the method discussed here, the phantom with the vacant space in the center was used to monitor the artificial urine accumulation with both conductivities. The same setups for the experiments were used. It should be noted that it would not be possible to measure the impedance at the same time with the Agilent impedance analyzer and the BI measurement device designed in this thesis to compare results of the same experiments. This is because this would increase the time of measurement performed on the phantom by the two systems, thus leading to the issue of the fluid remaining in the vacant space for a long time and the occurrence of ion infusion. However, the results obtained from the BI measurement device designed in this thesis show the same trend in the measurements compared to the results of experiments obtained with the Agilent impedance analyzer, as seen in Figure 5.32 and table 5.12.

Lastly, a comparison of the findings of the thesis to the previously published literature for bladder monitoring, which was performed by BI measurement is discussed. The results of this thesis indicate impedance reduction related to urine accumulation, which is in line with the reports of state-of-the-art studies. Among the recently published research studies after 2011 including EIT, (summarized in Table 2.1) a few used four-electrode configuration for bladder monitoring; therefore, an analogy can be made between this thesis and those studies. Studies in [125, 129, 134] used a BI measurement device on a healthy subject at 50 kHz. The tetra-polar electrode configuration was used horizontally on different subjects to measure the impedance change. In [125], it was mentioned that the subject drank 100 ml of water, similar to 120 ml of volume which was used in this thesis to fill the phantom while, in [129, 134], subjects were asked to drink 1.5 liter of water. The impedance change in the studies were in the range of $2\ \Omega$, except for [134] which reported the impedance change in percentage (6%). However, these studies suffer from the very limited number of subjects and no information was provided regarding the impact of conductivity of the urine, the result of total impedance change that was measured horizontally in this thesis on the phantom shows slightly more change compared to their measurements. In these studies, the subjects lay on a bed, and this might be considered as a potential cause. As seen from the results in Figure 5.29, when the vacant space in the phantom was far from the electrodes, the change in impedance was trivial. When a subject is horizontal on his back, the bladder could move further from the surface of the abdomen, where the electrodes are placed; thus, a smaller change in impedance could

be detected. Another potential reason might be that 50 kHz was used as the frequency of operation. As discussed, at higher frequencies, current can pass through the intracellular fluid of tissues. Assuming the intracellular fluid in tissues does not change significantly within a short period of time, their system might have been affected by the urine accumulated in the bladder alongside with intracellular fluid of the surrounding tissues. Therefore, a less change could be detected, given the amount of urine that is being increased in the presence of intracellular fluid of the surrounding tissues. A combination of both of the causes would also be a possibility.

The study published in 2020 in [2] reported the impedance reduction for urine conductivities of 1 S/m and 2 S/m. On a phantom similar to this thesis, the tetra-polar horizontal measurement showed an impedance change in the range of 3.5Ω , at 5 kHz. However, 350 ml of solution was used as the volume for artificial urine. Considering their filling rate of 1 ml per second and reaching 120 ml, the impedance change appeared to be slightly less than 1Ω . This is less reduction compared to the finding in this thesis. This also might be due to the fact that a larger sized phantom would increase the distance between the electrodes and the target. In addition, a pig's bladder was used for phantom experiments, which could have an impact on the measurement as a complex biological tissue. Their result of total impedance change in percentage (9.7%) was briefly mentioned to be in line with a study in 2006 [122], which reported a 7 to 9% (total of 1Ω at 100 kHz) impedance reduction, on one subject who lay on his back.

In this thesis, it was shown that the proposed vertical measurement provides a greater change in impedance, compared to a horizontal measurement

in a tetra-polar configuration, with 95% confidence interval. Its main advantage is that this significant change happens regardless of the urine conductivity. This specifically is important as low conductive urine makes it difficult to detect and measure the impedance change with electronic devices and to distinguish between a full and not-full bladder.

To summarize the presented thesis, in the next chapter the conclusion of the thesis and its contribution to the state-of-the-art is described.

Chapter 6

Conclusions

6.1 Summary

This chapter summarizes the aims and contributions of this thesis and it suggests a potential future research path for BI measurement systems for bladder monitoring. A complete literature review was carried out leading to four main categories of challenges. Developing a readout device with a low measurement error is crucial to monitor the bladder. As was seen, the variation in impedance was within a small range so even that small errors within a $1\ \Omega$ range can cause a problem in detecting the level of urine in the bladder. Due to the nature of BI measurement and dealing with a dynamic load such as the body, it can be challenging to design a system that can be scaled down to a wearable size, has low power consumption and has high accuracy which is suitable for every individual. To date, this is an ongoing research challenge to maintain or improve the accuracy while moving towards miniaturization and low power consumption, as the circuit complexity, power and noise are always in competition. However, with the

advancement of semiconductors, this becomes more and more achievable. The second challenge is the error that can be caused by using different types of electrodes and the skin-electrode impedance issue. Apart from the fact that the high skin-electrode impedance will put extra demands on the read-out device as part of the dynamic load, and it can vary from one individual to another, the size and shape of the electrodes can also be challenging to select. Very few research papers were found that addressed this issue, and this requires a whole new expertise in electromagnetic simulations and mechanical designs. The third challenge relates to the fact that the bladder location can be changed during different movements/postures. This can negatively affect the monitoring, as the coverage area of the electrodes will be affected if a relocation of the bladder happens and, up to the present, research has not addressed this issue. The final challenge is the individual parameters such as: urine conductivity, BMI, gender, shape of the body, etc. The physical parameters such as gender or weight can affect the design of the readout device, as mentioned previously. However, variation in urine conductivity while monitoring the bladder is another area where very little research work has been carried out, leaving it at an early stage of development.

6.2 Aims and Contributions

Based on the mentioned challenges, This thesis had four aims :

- 1- Identifying and understanding the constituent blocks required to perform BI measurement and extracting the design specifications and challenges.
- 2- Design and implementation of a prototype readout system for bladder

monitoring based on BI measurement.

3- Proposing and investigating the feasibility of a measurement method to increase the sensitivity of impedance change related to urine conductivity.

4- Proposing and investigating the feasibility of an extra scanning mechanism to address the impact of change of location of the bladder on the monitoring.

The followings are the contributions that addressed each of the above aims:

- A current injection block for the BI measurement board was designed and manufactured. More than 200 experiments were performed on this block to extract the bottlenecks of the design for a bladder monitoring BI measurement device. The results were published in [175]:

A. Behrouzirad, P. Sugrue, M. Todorovic, K. G. McCarthy, and P. Galvin, “Analysis and application of a buffered feedback path improved howland current source in bioimpedance measurements,” in 2021 32nd Irish Signals and Systems Conference (ISSC), pp. 1–6, IEEE, 2021.

- Two versions of the BI measurement system with a 4-electrode configuration were designed and manufactured. For V1 with 175 experiments, the system absolute error in measurements was 0.25Ω with standard deviation of 0.21Ω . This version; however, required calibration. A V2 BI measurement system was designed to eliminate noise and the requirement for calibration. Forty experiments were performed and, this time, a more realistic model of the body, the 2R-1C equivalent circuit, was used to determine the performance. For an impedance in the range of 30 to 68Ω , the

error in the measurement was $0.3 \Omega \pm 0.15 \Omega$.

- Carrying out a total of 372 experiments on it, an agar based phantom mimicking the body was created and used in order to investigate aim 3 of the thesis, and a vertical measurement method for monitoring the bladder was proposed. The results, which were shown in Chapter 5, showed an increase in impedance change beyond a certain volume for both conductivities compared to the horizontal position, with 95% confidence interval.

- Four different scenarios were considered and tested with 512 experiments, to address aim 4 of the thesis. The vacant space was rotated to right, far, left, and close positions, as seen in Figure 5.26. These experiments were carried out to address and investigate the impact of bladder relocation. Using two extra sets of electrodes on each side of the middle set of electrodes, this mechanism also showed promising results for being able to detect the impedance change after a certain volume and relocation of the bladder, compared to the horizontal measurement.

6.3 Future Work: Towards A Wearable Bio-impedance System for Bladder Monitoring

The ultimate goal of this research is to develop a wearable bioimpedance measurement system for bladder monitoring. This thesis addressed some of the issues towards this goal. In this section, suggestions for continuing the research and for future work are provided.

Gel electrodes have been used for various applications and, in this thesis, they were also used to apply and record the signals. As a suggestion, the use of different types of electrodes, such as dry or compound electrodes has good potential as a topic of future research in BI measurement for bladder monitoring. Reducing the influence of skin-electrode impedance, compound electrodes with the size and shape similar to [112], while the BI measurement is vertically performed, could provide extra information for bladder fullness monitoring. This electrode type has not received enough attention for medical applications since the year 2000. Even in a review study published recently in 2018, these types were briefly mentioned and references are limited to the 2000's time period [176]. Perhaps this could be explained by the fact that research employing such custom-made electrodes would require expertise in electromagnetic, material and mechanical design and would require multi-disciplinary team work and resources.

One extension of the work that would be interesting to pursue is to observe and validate the current distribution in the body, as described in chapter 3, when vertically measuring the bioimpedance. After such a study, additional factors, such as considering the background area with a com-

plex conductivity rather than homogeneous, could be examined to obtain the current distribution. This could be an interesting topic for researchers in the theoretical and physical field to define and solve partial differential equations related to the body and electrodes. Also here, different types and sizes of electrodes, such as compound electrodes, could be studied and their influence on the current distribution could be investigated.

In this thesis, the proposed method was experimentally examined. The results of the experiments were obtained from testing the method on a phantom, although the method and these results need to be validated in clinical settings. It is suggested that primarily examining the method in a real-world scenario should be carried out by commercially available BI measurement devices such as Impedimed [170], and on a small sample of individuals, similar to [131], which had six subjects.

This thesis was mostly focused on using data obtained at 5 kHz, although the frequency sweep range was 1 to 100 kHz. Testing the method with the same electrode configuration and at higher frequencies with a phantom mimicking the electrical behavior of the body at high frequency could also be investigated for extracting more features to help monitoring the bladder fullness, although a more challenging electronic design would be required for frequencies above 100 kHz and as high as 1 MHz.

Additionally, it would be interesting for future research to consider integration of ultrasound with BI measurement in the device as a complete wearable system. Although this would increase the cost of the device and may be more suitable for use in clinics and hospitals, using ultrasound would provide different and valuable information, such as the a-priori location of the

bladder that, if combined with BI, should result in an accurate monitoring in different real-world scenarios.

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