Integration of Wireless Biosignal Processing with Existing Non-Software Medical Devices

Author: Noel Kelly

Thesis presented in partial fulfilment of

MSc in Software Engineering and Database Technologies

Discipline of Information Technology

National University of Ireland, Galway

Submission: August 2015

Head of Department: Dr. Michael Madden

Thesis Supervisor: Dr. Michael Schukat

Certificate of Authorship

Final Thesis Submission

MSc in Software Engineering and Database Technologies

Discipline of Information Technology

National University of Ireland, Galway

Student Name:	Noel Kelly
Telephone:	0851483316
E-mail:	1noelkelly@gmail.com
Date of Submission:	23-Aug-2015
Title of Submission:	Integration of Wireless Biosignal Processing with Existing Non-Software Medical Devices
Supervisor Name:	Dr. Michael Schukat

Certification of Authorship:

I hereby certify that I am the author of this document and that any assistance I received in its preparation is fully acknowledged and disclosed in the document. I have also cited all sources from which I obtained data, ideas or words that are copied directly or paraphrased in the document. Sources are properly credited according to accepted standards for professional publications. I also certify that this paper was prepared by me for the purpose of partial fulfilment of requirements for the Degree Programme.

Signed: Noel Kelly Date: 23AUG2015

Acknowledgements

To Suzanne for the lack of evenings or weekends as a result of the course and thesis work, thank you for understanding and putting up with it all.

Thanks to the facilitators throughout the two years including the thesis modules and to my classmates who offered their constructive views and feedback.

Thanks to my thesis advisor Dr. Michael Schukat for his help and recommendations throughout this thesis.

Table of Contents

List of Tables

List of Figures

Abstract

The use of medical devices is widespread in an effort to treat a variety of illnesses and disease such as cardiovascular disease and aneurysms. The number one cause of death in the world is cardiovascular disease accounting for 30% of all global deaths. Medical device procedures such as balloon angioplasty using catheters and stents have been developed in an effort to treat cardiovascular diseases such as blocked coronary blood vessels. Implanted non-software medical devices can sometimes fail to perform their intended function and there is often the need for invasive follow up procedures to assess medical device performance. These follow up procedures are often on a periodic basis and as a result potential medical issues may not be detected until the next scheduled follow up. Biosensors could be used to monitor implanted medical device performance or device malfunction. Biosensors could be used with non-software medical devices to continuously monitor device performance. This would allow for immediate detection of device malfunction or the potential need for medical intervention. The use of biosensors has been increasing rapidly in the recent past with a large number of wearable health monitoring devices currently available. With advances in micro systems and wireless communications technologies, there is ongoing development of implantable biosensors to monitor a range of biosignals. This research investigates the integration of a non-software medical device with biosignal processing technology. A proof of concept model is developed depicting an existing non-software medical device integrated with a biosignal processing element.

1. Introduction

1.1 Thesis Statement

Wireless biosignal processing has the potential to be integrated with existing non-software medical devices to monitor their performance.

1.2 General Background

The use of medical devices is widespread. In Ireland in 2010, the medical device sector generated sales in excess of €6 billion (Enterprise Ireland, 2010) while the largest medical device market in the world is the United States which accounts "for nearly 50 percent of the $273 billion global market by sales" (Torsekar & Reed, 2014).

After an initial procedure using a medical device, there is often the need for invasive follow up procedures such as an angiogram to assess device performance (Molyneux et al., 2005). The use of wireless biosignal processing is increasing with improvements in the underlying technology. Hulzink et al., (2011) suggest that advancing technology in wireless devices will improve the quality of healthcare services by providing more opportunities for home or remote monitoring and continuous disease management for patients. Mahfouz, Kuhn, & To, (2013) believe that demand for wireless technology is increasing, eliminating restrictive wiring and allowing patients' greater autonomy and mobility. The growth in wireless medical device technology is enabled by the emergence of reliable low cost wireless technology.

This thesis aims to discover current state-of-the-art in both non-software medical device technology and wireless biosignal processing technology and assess the potential to integrate both technologies.

1.3 Purpose of the Study

The purpose of the study is to investigate the possibility of integrating biosignal processing technology with existing non-software medical devices. This will involve researching the following sub-problems:

Sub-Problem 1: To identify, evaluate and define how biosignal processing is currently used.

Sub-Problem 2: To investigate existing non-software medical device technology.

Sub-Problem 3: To evaluate the possibility of integrating wireless biosignal processing with existing non-software medical devices.

Sub-Problem 4: To develop a proof of concept prototype model depicting an existing non-software medical device integrated with a biosignal processing element.

Researching sub-problems 1 and 2 will identify current state of the art in both biosignal processing and non-software medical device technology. Both areas will be assessed including usage in industry as well as research and development and new concepts will be analysed.

Researching sub-problem 3 will build on the analysis of sub-problems 1 and 2. Sub-problem 3 will assess if both technologies can be integrated.

Researching sub-problem 4 will build on the previous three sub-problems with the aim of delivering a proof of concept prototype model that shows the integration of both technologies.

1.4 Significance of Study

After medical device implantation, there is often the need for follow up consultations / surgeries / procedures to assess device performance. For example, after treatment for cerebral aneurysms, patients often have to undergo invasive cerebral angiography to assess device performance (van der Schaaf et al., 2005). After endovascular coiling, an angiographic follow-up is carried out in all cases as standard practice and depending on results may have to be repeated (Molyneux et al., 2005). Neurological complications such as stroke can occur in high risk patients after or during angiography (Heiserman et al., 1994).

An integrated medical device / biosignal processing element could reduce the need for invasive follow up procedures by continuously monitoring implanted medical device performance. This has the potential to benefit both doctor and patient

for a number of reasons. Removing the requirement of invasive follow up procedures would reduce patient discomfort. The risk of further complications as a result of a surgical procedure would be eliminated. Further complications could cause an increase in hospital stay time or increase the chance of patient death (Waksman et al., 1995). Continuous monitoring of device performance could reduce patient anxiety and concern while also reducing the amount of consultations required between doctor and patient. This could benefit the patient from both a financial perspective and quality of life. It could also free up a doctor to see and help more patients.

1.5 Scope of Study

The thesis will define state-of-the-art technology in both biosignal processing and non-software medical devices. An investigation of the feasibility of integrating wireless biosignal processing with existing non-software medical devices will be conducted. A proof of concept prototype model will be developed depicting an existing non-software medical device integrated with a wireless biosignal processing element.

2. Research Methodologies

The research conducted in this thesis will attempt to address the four strands of investigation described in Section 1.3 (Purpose of the Study). Each of these strands is a separate sub-problem that will be researched as outlined below.

2.1 Critical Analysis of Existing Technologies

A critical analysis of existing wireless biosensor technology (Sub-Problem 1) and existing non-software medical device technology (Sub-Problem 2) will be carried out. This analysis will allow for the evaluation of integrating biosignal processing with existing non-software medical devices (Sub-Problem 3).

2.2 Proof of Concept Prototype Model

Building on the deliverables from Research Method 1, a proof of concept prototype model will be developed depicting an existing non-software medical device integrated with a biosignal processing element (Sub-Problem 4).

3. Success Criteria

The thesis will be considered to be successfully completed after researching the four sub-problems identified in Section 1.3 (Purpose of the Study) and discussed in Section 2 (Research Methodologies) and conclusion of the following:

3.1 Critical Analysis of Existing Technologies

A critical analysis of in-vivo biosignal processing technology and non-software medical device technology including an evaluation of integrating the two technologies.

The first three sub-problems are concerned with the critical analysis of existing technology for both biosignal processing and non-software medical devices and the opportunity to integrate these technologies.

3.2 Proof of Concept Prototype Development

Proof of concept prototype model depicting an existing non-software medical device integrated with a biosignal processing element.

The fourth sub-problem is concerned with integrating biosignal processing and non-software medical device technologies and delivering a proof of concept prototype model depicting the integration of these technologies.

4. Literature Review

This chapter reviews the relevant academic and industry literature available concerning biosginal processing, biosensors and non-software medical devices. The aim of this literature review is to analyse existing wireless biosensor technology, in-vivo biosignal processing technology and non-software medical device technology.

4.1 Medical Device Applications

Blockages can occur in blood vessels due to a build up of plaque on the vessel walls. This build up can reduce or prevent blood flow through a blood vessel and can lead to complications such as heart attacks, stroke and patient death. Treatment for blocked coronary blood vessels in the past required a patient to undergo open heart surgery to bypass the blockage. With advancements in medical device technologies, devices such as catheters and stents were developed that offered minimally invasive treatment alternatives to open heart surgery.

The number one cause of death in the world is cardiovascular disease which accounts for “30% of all global deaths. According to the World Health Organization, worldwide about 17.5 million people die of heart attacks or strokes each year; in 2015, almost 20 million people will die from cardiovascular disease. These deaths can often be prevented with proper health care” (Latré, Braem, Moerman, Blondia, & Demeester, 2011).

A common method of treating cardiovascular disease such as blockages or stenosis in blood vessels is to perform percutaneous transluminal coronary angioplasty. This involves introducing a catheter typically through the femoral or radial artery and routing a catheter through the blood vessels to the blockage site. Treatment types may vary with some surgeons opting for an ordinary balloon catheter known as balloon angioplasty while others may use a catheter with a balloon and stent known as stenting. Radiopaque markerbands are typically positioned next to the balloon area on a catheter. The surgeon can then position the balloon section in the blockage site by aligning the markerbands with the blockage. The balloon is then inflated which compresses the plaque against the arterial wall. A stent may be deployed to ensure the blockage remains open. Some stents may be coated in a drug that prevents restenosis or further narrowing of the blood vessel. The chances of

restenosis can be as high as 40% with balloon angioplasty. Stenting can reduce the chances of restenosis to 25% (Dangas & Kuepper, 2002).

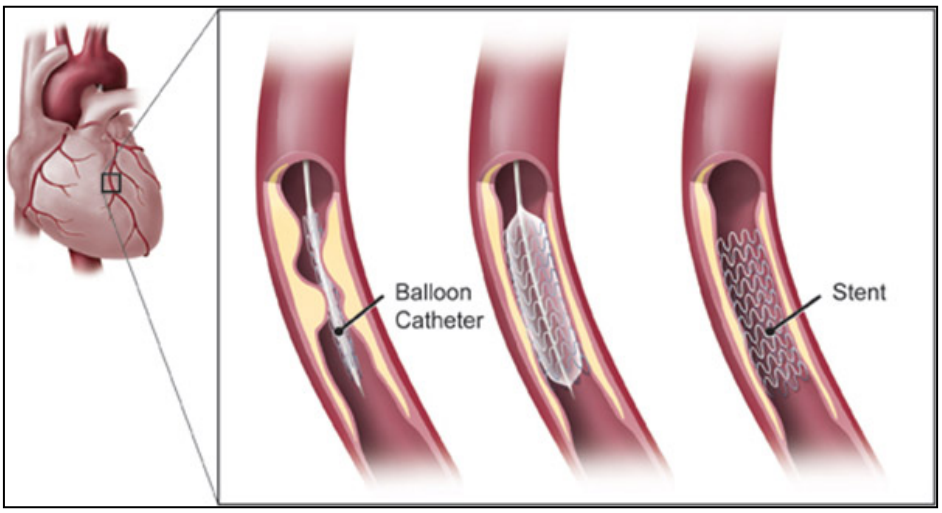

Figure 1. Balloon catheter and stent deployed in vessel (Haan, 2010).

Blood vessel walls can become weaker over time and begin to bulge or leak. This is commonly known as an aneurysm. Cerebral aneurysms can lead to stroke and patient death. Craniotomy and clipping were methods used to treat cerebral aneurysms until the 1990's when endovascular coils where introduced (Molyneux & ISAT Collaborative Group, 2002). A craniotomy involves removing a portion of the skull to gain access to the brain. Clipping can then be performed by placing a clip around the base of the aneurysm to isolate the aneurysm from the flowing blood in the blood vessel. Brisman, Song and Newell (2006) suggest that "detachable coils have been increasingly used as a less physiologically stressful alternative to clipping the aneurysm".

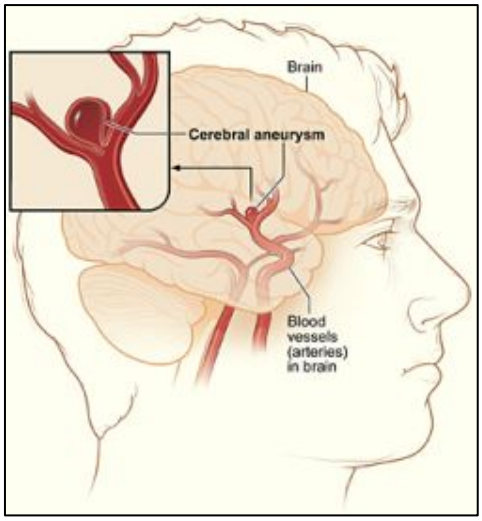

Figure 2. Cerebral aneurysm (Society of NeuroInterventional Surgery, (2014).

Endovascular coiling may be used to treat cerebral aneurysms. Similar to coronary angioplasty, this involves introducing a catheter to a blood vessel and routing it through blood vessels to the target area. A coil is then deposited in the aneurysm which prevents blood from flowing into the affected area.

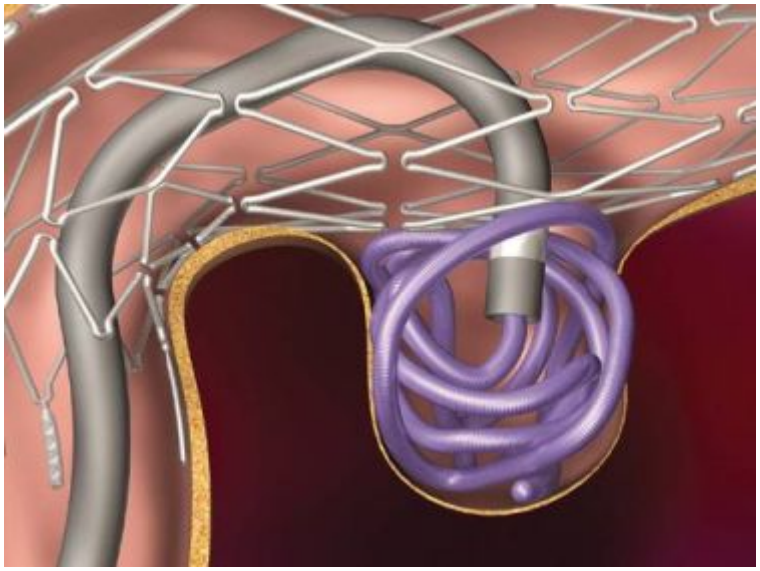

Figure 3. Aneurysm coil (Society of NeuroInterventional Surgery, (2014).

Aortic aneurysms can now be treated using endovascular procedures as an alternative to open surgery. Endovascular aneurysm repair (EVAR) was developed in an effort to reduce the risk of perioperative complications that are associated with open surgical repair. EVAR has reduced in-procedure related adverse events but

during long-term follow up has an increased rate of device-related complications. EVAR has “surpassed open surgical repair in the frequency with which it is performed, both for elective aneurysms and in some centres for ruptured aneurysms as well” (Ouriel, Fowl, Davies, Forbes, Gambhir & Ricci, 2014).

4.2 Medical Device Complications

Brilakis, Karmpaliotis, Patel and Banerjee (2012) state that complication arising from chronic total occlusion intervention can be coronary artery related, cardiac non-coronary or non-cardiac related. Coronary artery related complications include coronary occlusion, coronary perforation and equipment loss or entrapment. Cardiac non-coronary complications include periprocedural myocardial infarction and arrhythmias. Non-cardiac complications include vascular access complications and allergic reactions.

Kresowik et al. (1991) completed a study on patients undergoing angioplasty with the groin (femoral artery) used as the catheter entry site. In the study, 9% of patients were found to have suffered from major vascular complications at the femoral puncture site. A review of femoral or radial access coronary catheterization procedures by Cox et al. (2004) found that 4.8% of patients experienced 1 or more vascular complications. A vascular complication was “defined as the need for surgical repair, transfusion, the development of arteriovenous fistula, pseudoaneurysm, or large hematoma (>8 cm)” (Cox et al., 2004).

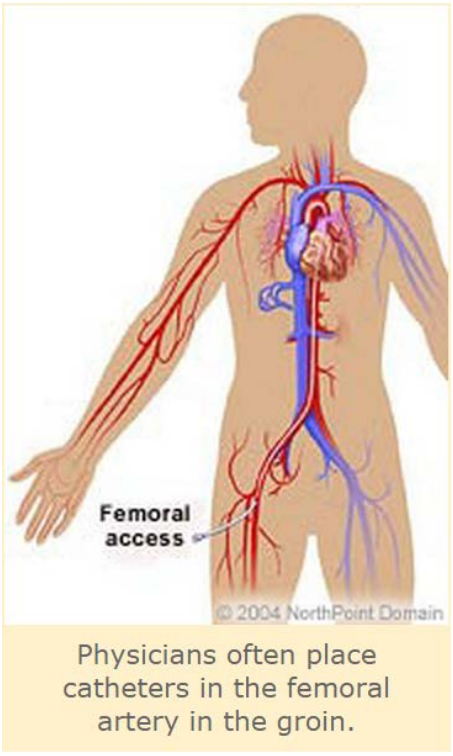

Figure 4. Femoral access for catheter (NorthPoint Domain Inc, 2015).

Polisena, Forster, Cimon and Rabb (2013) assessed adverse events that were reported due to complications with balloon angioplasty procedures. Out of 106 patients, 2 patients suffered from hematoma at the puncture site and 2 patients suffered from contrast reaction. Contract dye is used to detect the blockage area so that the catheter can be routed to the impacted area. Contrast dye is subsequently used after medical device intervention to ensure the successful treatment of the affected area. Polisena et al. (2013) also noted in another study that 21 patients suffered coronary perforation during medical device procedural complications. Although coronary perforation is rare it can be fatal. 13 patients suffered coronary perforation during a coronary balloon angioplasty procedure. 5 patients suffered coronary perforation as a result of guidewire manipulation and 3 patients as a result of stenting. Polisena et al. (2013) noted that.

Pongruangporn, Ajenjo, Russo, McMullen, Robinson, Williams and Warren (2013) assessed complications arising from the use of peripherally inserted central venous catheters over a 31 month period. 162 patients suffered from blood stream infections (BSIs) as a result of the catheter procedure. BSIs were caused by gram-positive bacilli (75%), gram-negative bacteria (13%) and yeast (11%). Pongruangporn et al. (2013) found that multi-lumen catheters increased the risk of BSIs when

compared to single-lumen catheters. This is due to multi-lumen catheters having 2-3 “times more intraluminal surface area for microorganisms to attach to and produce biofilm. This results in increased bacterial growth and increased risk of BSI”. Franco, Abisse, Ruisi, and Abbott (2014) suggest that the incidence of infection as a result of percutaneous procedure is rare. In a study involving over 22,000 cardiac procedures, there was found to be a BSI rate of 0.11%.

Wu, Dai, Kao, Chang and Lou (2015) suggest that patients are confined to bed for several hours and may have to use compression bandages after angioplasty procedures to prevent access site bleeding. Patients may suffer from back, groin and leg pains as a result. Back pain accounts for the 35.8% of complaints after coronary procedures. Wu et al. (2015) suggest that other complication arising from the use of compression bandages include “hematoma formation, followed by bleeding, pseudoaneurysm formation, arteriovenous fistula formation, peripheral arterial thrombosis or embolism, and infections”. Sanborn et al. (2015) suggest that there is a need to define best practices to avoid bleeding after percutaneous coronary intervention (PCI). Bleeding can be an important predictor of adverse events after PCI. Bleeding avoidance may reduce mortality rates after PCI due to a reduction in ischemic events.

Bhat, Teli, Bhat, Akhtar, Meghani, Lafferty and Gala (2012) reviewed complications as a result of transradial coronary interventions. The most frequent complication was radial artery occlusion. Other complications included radial artery perforation and radial artery spasm. Radial artery spasm may lead “to difficult manipulation of intra-arterial catheters or devices, causing pain and discomfort to the patient, sometimes access failure and rarely complete entrapment of the catheter” (Bhat et al., 2012). A benefit of the transradial approach over the transfemoral approach is the reduced incidence of access site bleeding. Major bleeding complications such as fatal bleeding and intracranial haemorrhages are reduced by up to 73% compared to the transfemoral approach (Bhat et al., 2012).

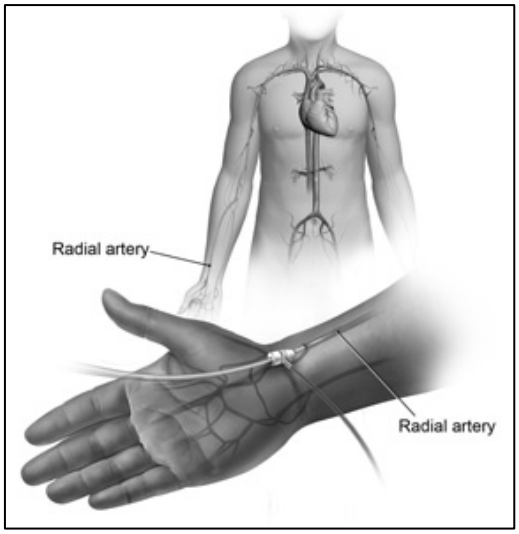

Figure 5. Radial access for catheter (St. Peter's Health Care Services, n.d.).

Chung et al. (2014) studied 72 patients that underwent stent-assisted coil embolisation (SAC) for the treatment of ruptured wide-necked aneurysms. 6.9% of patients developed hemorrhagic complications including rebleeding after partial occlusion of the embolisation and intraparenchymal haemorrhaging. These complications lead to death in 2 cases.

4.3 Biosensors

There was a significant increase in the number of wearable health monitoring devices towards the end of the last decade. These devices ranged from simple pulse or activity monitors to sophisticated implantable sensors. Wearable devices have some disadvantages over implantable devices such as the potential to limit the mobility of a patient and the possibility of causing skin infections contributing to poor health conditions. Darwish and Hassanien (2011) believe that “the range of implantable biomedical devices will increase substantially over the next decade, thanks to improved technology in micro systems technology achieved during the last decade”.

Perumal and Hashim (2014) state that “typically biosensors are comprised of three components: (1) the detector, which identifies the stimulus; (2) the transducer, which converts this stimulus to a useful output; and (3) the signal processing system, which involves amplification and display of the output in an appropriate format”. Some of the different categories of biosensors are shown below in Figure 6.

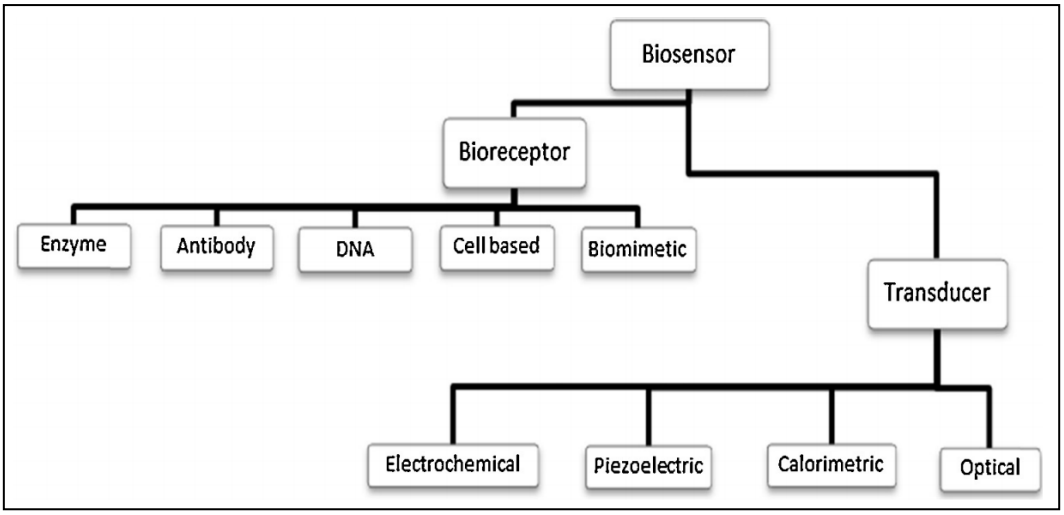

Figure 6. Categories of biosensors (Perumal & Hashim, 2014).

Glucose and lactose electrochemical sensors are already commercially available. Fully implantable glucose sensor prototypes are currently being worked on and have been validated in mice for up to 8 months and in pigs for up to 12 months (Baj-Rossi et al., 2013).

Biosensor systems such as transducers can be used to sense variations in physical or chemical properties. Photodiodes can be used for gene-based analysis for viral detection. Implantable biosensors such as glucose meters can be implanted under the skin and wirelessly monitored (Guiducci et al., 2008).

Bolomey, L., Meurville, E., Ryser, P. (2009) developed a biosensor with two parts; a “sensing node which controls the sensor, performs the digital signal processing and RF data transmission” (Bolomey et al., 2009) combined with a micro-rheometer (Figure 7). The biosensor fits in an 8.4mm diameter cylinder. The size is small enough to allow it to be fully implantable. The authors test the unit at 37°C to mimic *in vivo* conditions.

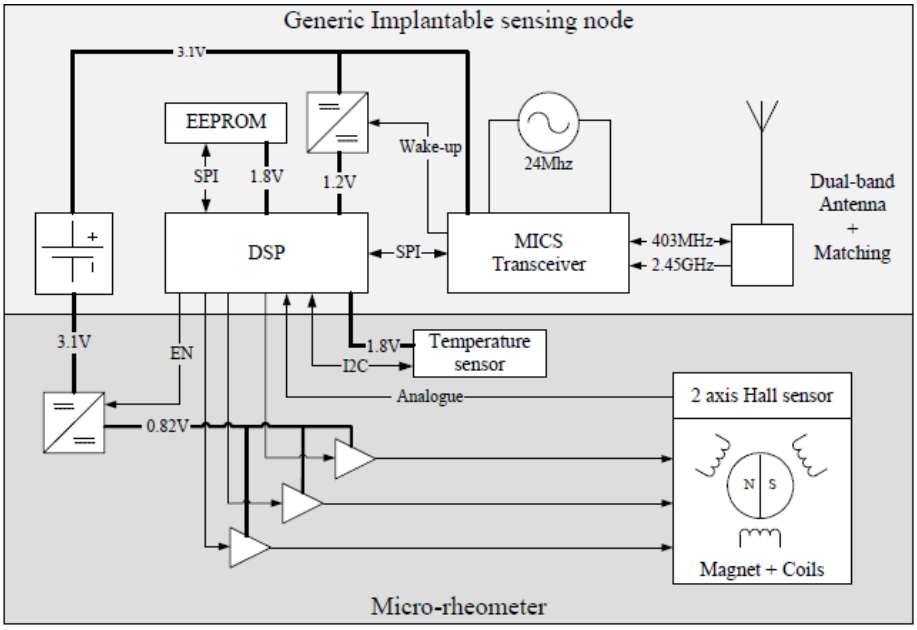

Figure 7. System block diagram (Bolomey et al., 2009).

The life time for taking measurements was found to be 28,500 cycles. The authors successfully demonstrated a potential implantable continuous glucose sensing application taking measurements every 15 minutes. Further work is suggested where modifications can be made to the unit including a smaller transceiver. A biocompatible housing also has to be developed to encapsulate the unit for long term implantation.

Santos, Kumeria, and Losic (2013) discuss the use of nanomaterials for biosensor applications. The use of anodic aluminium (Al) oxide (AAO) is suggested as a basis for nanomaterial biosensor development as it “has a unique set of chemical, optical, mechanical, transport and electrical properties, which include chemical resistance, thermal stability, hardness, biocompatibility and large surface area”. Possible sensing applications include glucose, cholesterol, DNA, blood proteins and viruses (Santos et al., 2013).

Arya, Saha, Ramirez-Vick, Gupta, Bhansali, and Singh (2012) discuss the use of zinc oxide (ZnO) nanostructures and thin films in the area of biosensor applications. These materials can be used to detect antibodies, antigens, myoglobin and haemoglobin. ZnO nanostructures and thin films have attracted interest for use “as materials for biosensors due to their biocompatibility, chemical stability, high isoelectric point, electrochemical activity, high electron mobility, ease of synthesis by diverse methods and high surface-to-volume ratio”.

Kuila, Bose, Khanra, Mishra, Kim, and Lee (2011) suggest there has been extensive research in the area of graphene-based electrochemical biosensors. These biosensors can be used in applications for sensing glucose, NADH, haemoglobin, cholesterol and DNA. Kuila et al. (2011) suggest that graphene is an interesting candidate for biosensor applications as it has a large surface area and excellent electrical conductivity. This allows for rapid electron transfer and "facilitates accurate and selective detection of biomolecules".

Lin and Yan (2012) discuss the used of organic thin-film transistors (OTFT) that use an organic semiconductor for sensing applications and biosensors. The types of applications that OTFT could be used for include sensors for enzymes, glucose, antibody-antigen, dopamine and DNA. Lin and Yan (2012) suggest that sensors will continue to be developed using OTFT as "the organic devices are potentially low cost, highly sensitive, flexible, biocompatible" and easily fabricated.

Chen, Zhou, Peng, and Yoon (2012) discuss the use of polydiacetylenes as biosensors. Research of polydiacetylenes has been carried out on sensing systems for "viruses, microorganisms, bacterial toxins, proteins, organic solvents, surfactants, antigens, pathogens, DNAs, glucose, enzymes, metal ions, anions, membrane interaction, pH" and organic molecules.

Dhand, Das, Datta, and Malhotra (2011) investigate the use of the conducting polymer polyaniline (PANI). This polymer can be used as a transducer material for biosensors and "provides enormous opportunities for binding biomolecules, tuning their bio-catalytic properties, rapid electron transfer and direct communication to produce a range of analytical signals and new analytical applications". PANI can be used for sensing glucose, cholesterol and NADH.

Buenger, Topuz, and Groll (2012) investigate the use of hydrogels, which are hydrophilic polymer networks, as biochemical sensing mechanisms. Buenger et al. (2012) state that "if the polymer network of a hydrogel is endowed with functional groups, hydrogels become responsive to some physical, chemical or biochemical stimuli". Hydrogels can be used in applications for sensing glucose, antibody–antigens and DNA.

Oliveros, Guiseppi-Elie, and Saddow, (2013) discuss the use of silicon carbide (SiC) as a material used in biosensors. SiC has many properties that make it a suitable candidate as a biomaterial or a biosensing substrate. It has high thermal conductivity, high resistance to corrosion, high elastic coefficient and low friction coefficient. SiC

has been used as a coating on stainless steel coronary heart stents and neural probes and has also been “used as substrate material for the construction of myocardial biosensors” (Oliveros et al., 2013).

Kotanen, Moussy, Carrara, and Guiseppi-Elie (2012) describe the use of implantable enzyme amperometric biosensors. This technology measures the level of a biological analyte within the body and “the basic function is to indwell a tissue and to detect, measure and record the levels of a molecule of interest within those tissues”. This biosensor technology is of interest to areas including diabetes care and haemorrhage-associated trauma care (Kotanen et al., 2012).

Tan, Pereles, and Ong (2010) developed a pressure sensor using a ferromagnetic alloy placed on a polycarbonate substrate. The authors suggest the sensor could be used for continuous, long-term monitoring of pressure in flowing fluid with potential applications for long-term implantation. The sensor was tested at a pressure range of 0 to 62kPa and could be used for pressure monitoring in an aneurysm sac where expected pressures are in the range of 0 to 27kPa.

4.4 Wireless Biological Signal Processing

The monitoring of biological signals can give an indication of the health of a person. Biosensors and biosignal processing are concerned with measuring outputs from the human body. Darwish and Hassanien (2011) suggest that continuous monitoring using “implantable body sensor networks will increase early detection of emergency conditions and diseases in at risk patients and also provide a wide range of healthcare services for people with various degrees of cognitive and physical disabilities”.

The growth in wireless medical device technology is enabled by the emergence of reliable low cost wireless technology. Due to the wide array of wireless biosensors currently available and under development, standardisation efforts are underway with the aim of developing wireless technology interfaces and providing a standardised certification process (Mahfouz, Kuhn, & To, 2013).

Hulzink et al. (2011) suggest that advancing technology in wireless devices will improve the quality of healthcare services by providing more opportunities for home or remote monitoring and continuous disease management for patients.

Pawar, Jones, Van Beijnum, and Hermens (2012) state that wireless networking technologies can be broadly categorised as either wireless wide area network (WWAN) technologies or wireless local area network (WLAN) technologies. WWAN provides a "low-bandwidth and high-latency service over a wired geographic area while WLAN technologies such as Wi-Fi provide "a high-bandwidth and low-latency service over a narrow geographic area (Pawar et al., 2012).

Yamashita et al. (2013) develop a biosignal monitoring system that wireless connects with a patient's smart phone using near field communication (NFC) technology. The average power consumption during data logging is 38.1µA. NFC was chosen for the system as "compared with Bluetooth Low Energy or ZigBee, the standby power of NFC is extremely small" (Yamashita et al., 2013).

Steinberg, Kassal, Kereković, and Steinberg, (2015) present a wearable battery-powered potentiostat that performs amperometric electrochemical measurements. The potentiostat is able to wirelessly communicate with mobile devices using NFC or with personal computers using radio-frequency identification (RFID). Steinberg et al. (2015) state that the system can operate "at 13.56 MHz in the high-frequency radio band, and is compliant with the ISO15693 radio-frequency identification (RFID) standard. It is also compatible with Android near-field communication (the NFCv standard)".

Dehennis, Mailand, Grice, Getzlaff, and Colvin (2013) develop a wireless fluorimeter as part of a long-term implantable glucose sensing system. The system is able to wirelessly communicate using NFC. Dehennis et al. (2013) perform an in vivo study of the system where they obtain data "by using a wearable reader system that polls the sensor every 2 minutes via the NFC interface". The implanted sensor transmits data on the fluorescent intensity and temperature. This data is processed using an algorithm and the glucose level is reported back to the subject.

Kim et al. (2015) discuss the development of "thin, lightweight, flexible and ultra-miniaturised NFC devices which could have applications in wirelessly communicating data from biosensors. The devices that are developed have nearly one hundred times less area than conventional NFC devices and are around 100 times thinner and 10,000 times lighter.

Pawar et al. (2012) investigate different methods of acquiring and transmitting data for mobile patient monitoring systems. A mobile patient monitoring system consists of a set of Body Area Networks (BANs) and a Back-End System (BESys).

Pawar et al. (2012) describe a BAN as "a network of communicating devices worn on, around or within the body which is used to acquire health related data and to provide mobile health services to the user. A BAN consists of a Mobile Base Unit (MBU) and a set of BAN devices". The MBU functions such as processing, storage and communications gateway can typically be implemented on a smart phone. BAN devices such as sensors can transmit biosignal data directly to the MBU or there can be an intermediate data acquisition device referred to as a Sensor Front-End (SFE) that can be connected to the MBU via a wired or wireless link depending on the application. The function of the SFE is to digitise and filter the raw analogue biosignals before transmitting data to the MBU. Biosignal data processing can occur locally within the BAN or remotely within the BESys (Pawar et al., 2012).

Zhang et al. (2011) state that "a confluence of advancements in diverse areas of research, including device integration, energy storage, sensor technology, and wireless communications, have facilitated the creation of body sensor networks (BSNs)". The technological advancements that have allowed for the development of BSNs have enabled the possibility of wireless health systems. BSNs are capable of capturing and processing biological data in a continuous, accurate and non-invasive manner. BSNs address some of the weaknesses of typical patient data collection including imprecision and under-sampling (Zhang et al., 2011).

Wu, Chien, Yang, Cheng, and Luo (2011) discuss the use of the Zigbee networking protocol as a wireless communication method for implanted biosensors. The use of a low profile dual band antenna is proposed with a low frequency band of 868 – 928 MHz and a high frequency band of 2.4-2.45GHz. The use of the low frequency band is suggested as it has lower tissue absorption loss and also avoids the resonance frequency of water molecules. The biosensor is placed in fresh ground pork where it is stated that it exhibited "good implanted antenna radiating characteristic, omnidirectional radiation pattern and high measured peak gain at 900MHz/ 2.4GHz, -11.07 and -14.2 (dBi), respectively".

Chou, Chen, Liao, Chen, Huang, and Chou (2015) developed a glucose and PH biosensor system which consisted of an Arduino Mega 2560 microcontroller, XBee modules, a readout circuit, a pH or glucose biosensor and a computer.

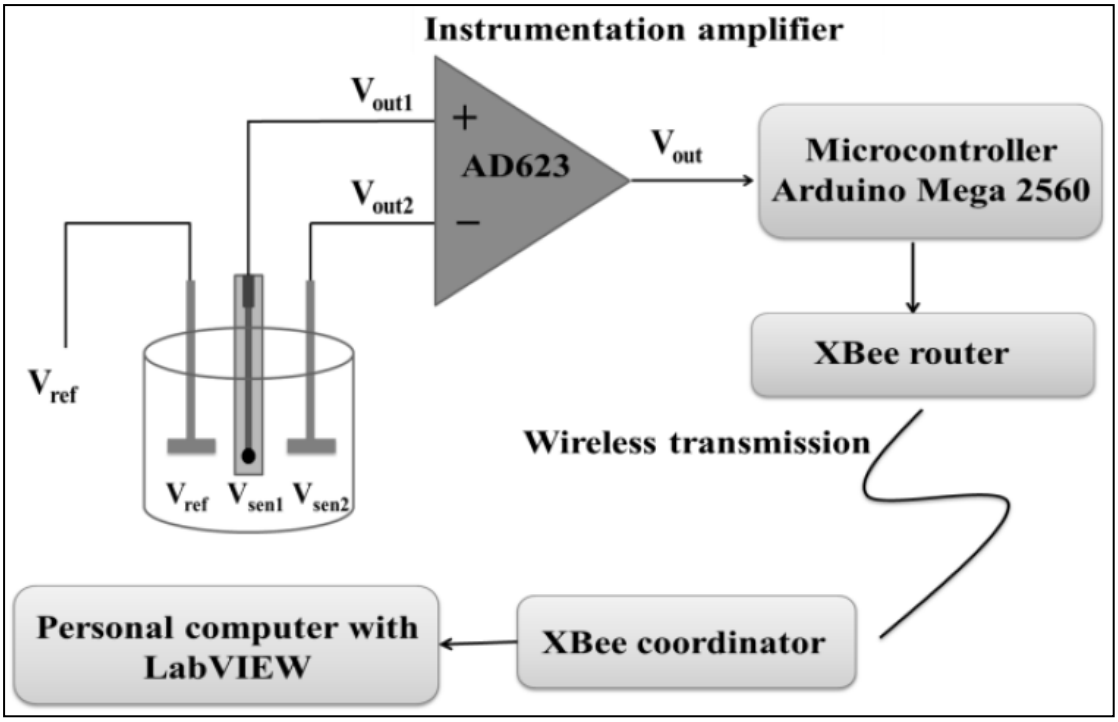

Figure 8. Schematic of system including wireless communication between XBee coordinator and router (Chou et al., 2015).

ZigBee technology is chosen for the wireless communication for the system as the authors suggest it is a standard protocol with advantages such as low cost to implement, low power consumption and low data rate usage for short-range wireless communication. In the system, an XBee router receives and transmits the signals from the sensor to the XBee coordinator. Chou et al. (2015) state that "the underlying layers of the ZigBee technology utilizes the IEEE 802.15.4 standard so that physical layer and media access control layer are defined for low-rate wireless networks in personal area through the IEEE 802.15.4 standard". Palantei et al. (2012) develop a wireless electrocardiograph system to remotely monitor patients' heart rate signals. The sensor system contains the ECG unit, microcontroller with and XBee module and antenna. XBee-Pro 2.4 GHz modules are used for the wireless communication system.

Onunka, Bright, and Stopforth (2013) discuss the use of wireless technologies in the area of wearable biosensors such as EEG data acquisition systems. There is ongoing research into the use of commercially available wireless communication technologies such as XBee and Bluetooth radio networks for biomedical applications. Advantages of these technologies include the low set up cost involved. Onunka et al. (2013) caution that "the long term monitoring effects of bio-signals on human tissues

are also issues that may be addressed in future studies as various adaptations emerge in biosensor networks".

Security of wireless transmissions should also be considered. Communication should be secure so that data cannot be easily intercepted and acquired for malicious intent. Burleson, Clark, Ransford, and Fu (2012) state that "a key problem with fully implanted sensors is that small, infrequent wireless transmissions may pose a greater privacy risk than large or continuous transmissions".

4.5 Biocompatibility

Biocompatibility issues may arise from after implanting devices including adverse physiological reaction due to poor material choice. The shape and size of implantable devices and the material used are all potential sources of inflammation. Baj-Rossi et al. (2013) suggest that "the development of a biocompatible packaging is essential for promoting wound healing, and ensuring prolonged sensor functionality". An implanted sensor should "cause a limited foreign body reaction, and at the same time the contact with biological fluids should not significantly affect sensor performances" (Baj-Rossi et al., 2013).

Baj-Rossi et al. (2013) developed an epoxy enhanced polyurethane membrane to cover a fully implantable biosensor. In-vivo testing was performed where 4 prototype biosensors were implanted in male mice for 30 days. The authors found that the membrane helped to promote "the integration of the sensor with the surrounding tissue, as demonstrated by the low inflammation levels at the implant site" (Baj-Rossi et al. 2013). A cell layer was also observed to have grown on the surface of the biosensor sensing platform. Future research by the authors is suggested to investigate the effect of a cell layer on the sensor and ways to reduce cell adhesion.

Buenger et al. (2012) suggest that hydrogels can be used as a coating on biosensor parts to aid in preventing undesired interaction between the biosensor and biological molecules or cells. Hydrogels are ideal candidates for numerous biological sensing applications as their high water content and hydrophilic nature "is similar to the void-filling component of the extracellular matrix, the natural environment of mammalian cells, and renders them intrinsically biocompatible".

You and Pak (2013) developed a graphene field effect transistor biosensor that was used to detect glucose levels. The biosensor was able to detect glucose in the

range of 3-10 mM which covers the applicable range for diabetes diagnostics. You and Pak (2013) stated that “pure silk fibroin was employed as the substrate material to realize a biocompatible and flexible sensor”. Silk fibroin is a biocompatible material that has been approved by the US Food and Drug Administration (FDA).

Fan, Jeong, Wei, Tan, Lok, and Chun (2005) suggest the use of a ceramic substrate as a carrier for a biosensor chip when discussing the development of an ion-selective field effect transistor biosensor. The biosensor is used to detect pH levels. Fan et al. (2005) state that the “ceramic substrate as a carrier for the biosensor chip can meet both requirements of biocompatibility and chemical resistance”.

Cavallini et al. (2015) developed a prototype of a fully implantable biosensor system including 5 biosensor electrodes, an inductive coil for powering the sensor and an integrated circuit that performed electrochemical measurements.

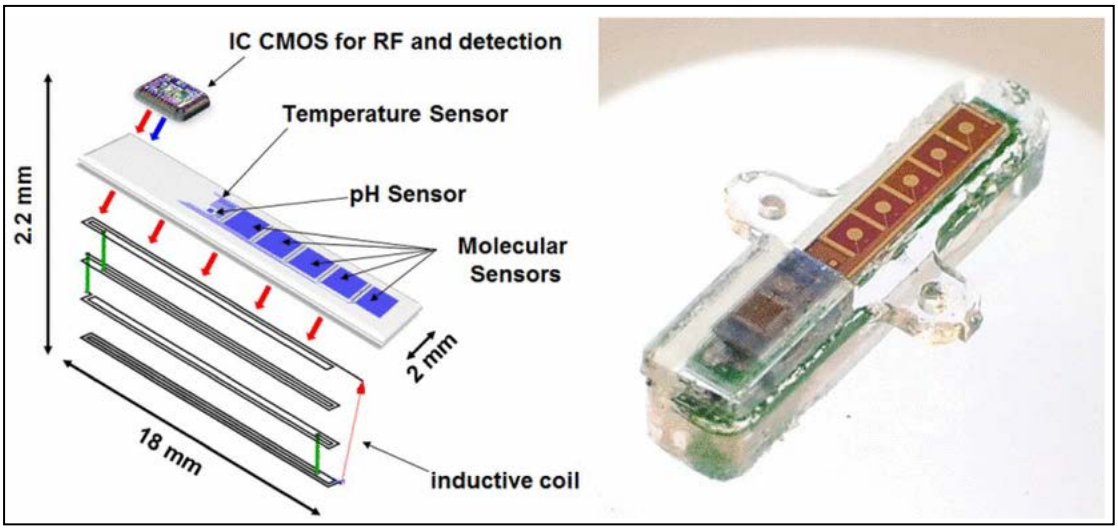

Figure 9. Implantable device (Cavallini et al., 2015).

In an effort to aid in biostability and biocompatibility, enzymes and carbon nanotubes (CNTs) were encapsulated in a chitosan (CHT) matrix before being sealed behind a porous polycarbonate membrane. Cavallini et al. (2015) found that “biocompatibility experiments did not show in vitro cytotoxicity in the considered period of 7 days, while comparison between 7 and 30 days in vivo implantations showed significant reduction of the inflammatory response in time, suggesting normal host recovery”.

4.6 Power Consumption

Hulzink et al. (2011) - concerned with power consumption in miniaturised wireless autonomous devices - propose a platform where power can be scaled to meet an application's needs. Power consumption is directly related to device battery lifetime and size and should be kept as low as possible. The authors propose a new event driven processor system enabling power efficient data processing. A case study is presented using a single lead Electro-Cardiogram (ECG) and positive results are demonstrated with "the lowest energy/sample for ECG heart-beat detection publicly reported" (Hulzink et al., 2011) at the time of publishing.

Zhang et al. (2011) state that as is the case in most wireless sensor networks, wirelessly transmitting sensed data is the largest power consumer in most current BSNs. By performing signal data processing and management at the sensor site and only transferring critical information to an external device, power consumption can be minimised in a system. Farshchi, Pesterev, Nuyujukian, Mody, and Judy (2007) state that the majority of power used by a wireless sensor is used for signal transmission. For systems that use batteries, "the addition of local data-processing capabilities can prolong battery life significantly, due to the elimination of the requirement for constant high-throughput wireless data transmission".

Valdastri et al. (2011) developed a miniaturised fluorescent based wireless sensor for detecting glucose levels. A battery was used to power the device for up to 3 years. Battery replacement would involve a patient going in to a hospital to have the device surgically removed to replace the battery before implanting the device again.

Olivo, Ghoreishizadeh, Carrara, and De Micheli (2013) propose the use of a power delivery system for implanted biosensors where the system is "embedded into a skin patch and located directly over the implantation area, is able to transfer up to 15 mW wirelessly through the body tissues by means of an inductive link". This link is also able to achieve bidirectional data communication. The power delivery system is on a flexible substrate and can be placed in a variety of locations on the body.

Sue and Tsai, (2012) suggest that one of the most critical issues for implantable biomedical devices (IMDs) is the lifetime and stability of the power supply. There is a lot of interest in extracting energy from the human body to overcome these issues. One potential solution is the use of micro-electromechanical systems (MEMSs) based energy harvesters. These micro-energy harvesters could

supply electrical power to IMDs owing to their "tiny size, light weight and recharge-free attributes" (Sue & Tsai, 2012). Padasdao, Shahhaidar, Stickley, and Boric-Lubecke (2013) state that energy harvesting for wearable electronics has been investigated since the mid 1990's. A number of potential sources of energy have been proposed but the focus has been on harvesting human kinetic energy.

The use of solar power as an energy source for implanted devices is discussed by Khan, Singh, Iqbal, and Sharma (2014). Currently, the batteries that are used in pacemakers have a lifespan of about 8-10 years before needing to be replaced due to depleting voltage and power levels over time. Khan et al. (2014) propose the placement of a photovoltaic array beneath the skin. This receives near infrared light (NIR) through the skin and is able to replenish the implanted devices depleted batteries. Simulations show that this arrangement delivers 10-25mW of power for a current range of 6-14mA and is of "sufficient power and voltage to charge the battery of low power implantable cardiac biosensors like pacemaker" (Khan et al., 2014).

Harb (2011) suggests there is ongoing research in energy harvesting from RF, vibration or thermal sources. Energy harvesting has the potential to directly power the application circuit without the need for a battery. There has recently been an interest "in using MEMs to scavenge energy from ambient vibration and transfer it to electrical load". This type of "device is mechanically modelled with the base excitation of an elastically mounted seismic mass moving past a coil" (Harb, 2011).

4.7 Medical Devices with Biosensors

Mohammadi, Chen, Mohamed Ali, and Takahata (2011) investigate the use of platinum embolisation coils with an RF antenna for cerebral aneurysm monitoring. The embolisation coils are able to detect a change in capacitance due to blood flow in the aneurysm area. Testing was carried out by developing a prototype device and aneurysm container. The device was positioned in the aneurysm container and ground meat was placed around it. Saline was introduced to the container and a change in capacitance was noted using a spectrum analyser. The communication between the implanted sensor, external base unit and end user is not investigated.

Ellozy et al. (2004) discuss the use of a pressure sensor attached to a stent used for EVAR. The pressure sensors were hand-sewn onto the stent and repackaged in the delivery sheath. This type of device was implanted in 14 patients. The pressure sensor

consists of “of a piezoelectric membrane, which when actuated by ultrasound waves from a hand-held probe charges a capacitor. Once charged, the transducer measures ambient pressure”. Ultrasound signals are then generated and are relayed to the hand held probe. Data can be downloaded from the probe and exported to a Microsoft Excel file. During follow up visits, it took between 3 and 15 minutes to retrieve data from the pressure sensor. The authors developed an integrated sensor with an existing medical device. Continuous monitoring of the sensor was not achieved and data had to be downloaded from the sensor during follow up visits. One device was found to have ceased functioning at a 2 month follow up visit.

Takahata, DeHennis, Wise, and Gianchandani (2004) integrated two capacitive pressure sensors on each side of a coronary stent. The complete device was capable of monitoring blood flow and pressure by measuring the pressure drop across the two sensors. The authors tested the device by deploying it in a tube and pumping deionised water through the tube. Communication between the implanted device and an external base station or end user was not discussed.

4.8 Summary and Conclusions

The use of medical devices is widespread to treat a variety of diseases and illness such as cardiovascular disease including blocked coronary blood vessels and cerebral and aortic aneurysms. Treatment for these conditions often requires the need for invasive follow up procedures to assess patient health and implanted device performance.

The use of biosensors has been increasing rapidly with a large number of wearable health monitoring devices made commercially available. With the advances in micro systems technologies and wireless communications technologies, there is belief that the use of implantable biosensors will increase over the coming years. Biosensor systems are currently being investigated in applications for assessing levels of glucose, lactose, cholesterol, blood proteins or viruses.

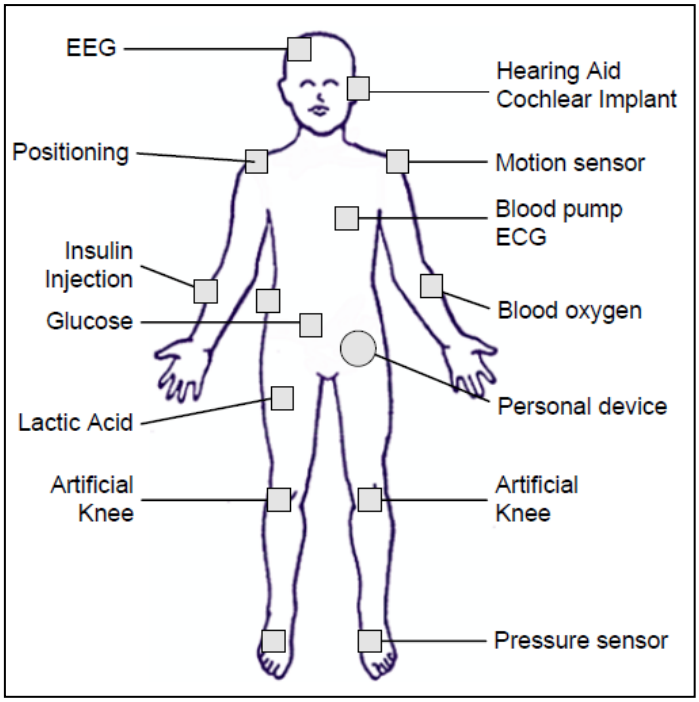

Figure 10. Patient monitoring and biosensor types (Latré et al., 2011).

Guiducci, Schmid, Gürkaynak, and Leblebici (2008) suggest that "the interface between man-made electronic circuits and living organisms will be one of the focal points of future integrated system design". There has been a rapid evolution in bio-electronic interfaces which are following the same trends as conventional silicon-based technology but presently "we are far away from a complete system where a seamless two-way interface exists between the electronic world and the biological system" (Guiducci et al., 2008).

Implanted non-software medical devices can sometimes fail to perform their intended function. Examples of where medical devices fail include cardiovascular stents that fail to keep blood flowing through a blood vessel or aneurysm coils that fail to keep blood from flowing into the aneurysm area. There is also often the need for invasive follow up procedures to check that the implanted devices are functioning as intended. Biosensors could be used in conjunction with implanted medical devices to continuously monitor medical device performance.

The prototype developed in this thesis builds on the work carried out by Mohammadi et al. (2011), Ellozy et al. (2004) and Takahata et al. (2004) discussed in Section 4.7 as the prototype continuously monitors device performance and demonstrates the communication chain between an implanted biosensor, external base

station and end user. If an alert signal or device malfunction is detected, the external base station communicates this immediately to the end user.

5. Case Study

An integrated non-software medical device and wireless biosensor system is feasible with advancing technology. A biosensor is attached to a non-software medical device and deployed with the medical device. Once the medical device is positioned in the required location inside the patient, the biosensor continually monitors for signs of poor device performance and the potential need for medical intervention by a professional.

In the case of implanted cardiovascular stents, a biosensor is deployed with the stent to monitor the device performance. The intention of the stent is to keep the blood vessel open and prevent restenosis. The biosensor continually monitors blood flow at the stent site to ensure that flowing blood is still passing through blood vessel. Blood flow is measured by detecting pressure across the stent site and calculating blood flow. The biosensor is configured to send an alert signal if blood flow at the stent site drops below a certain level. Another type of biosensor that could be deployed with a stent is a capacitance sensor. This sensor is continually monitoring the capacitance at the stent site. If plaque began to form on the stent causing a narrowing of the blood vessel, the biosensor detects a change in capacitance due to the plaque build up and send an alert signal if the capacitance level detected was outside of alert limits.

A capacitance biosensor could also be used in conjunction with aneurysm coils. The intention of an aneurysm coil is to stop blood flow into an aneurysm. If a coil failed to prevent blood from flowing into an aneurysm, the biosensor detects a change in capacitance due to blood flow in the area. If the change in capacitance was outside of alert limits, an alert signal is sent. These implanted biosensors wirelessly communicate to an external system that then communicates an alert message to a medical professional or patient on the status of the device performance.

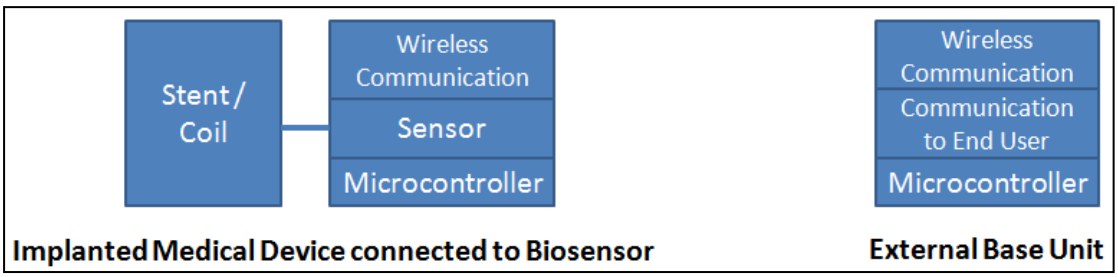

Figure 11. Medical device connected to wireless biosensor system.

This continuous monitoring of the medical device performance could be of great benefit to both the medical professional and the patient. The need for invasive follow up procedures is removed, allowing for more patients to be treated and removing the possibility of complications during the follow up procedure. The infrequent nature of assessing device performance is also replaced with continuous monitoring. This continuous monitoring of medical device performance allows for immediate detection and communication of potential issues with the implanted device. This allows a patient to consult a medical professional as soon as communication is received from the implanted device. With data available from an implanted biosensor, a medical professional can then make a decision on the next course of action to take.

A proof of concept model depicting an implanted biosensor and external base station is discussed in the next section. The proof of concept prototype architecture is detailed in Section 6.3.

6. Proof of Concept Model

6.1 Introduction

This chapter discusses the development of the proof of concept prototype model that depicts an existing non-software medical device integrated with a biosignal processing element. This prototype will show how communication can be achieved from an implanted biosensor to the biosignal processing element and eventually to the intended recipient or end user such as the patient or doctor.

6.2 Real World Device Architecture and Communication

The prototype needs to mimic a real-world potential biosensor/biosignal processing device. An example of this could be an implanted biosensor that is connected to a non-software medical device. The biosensor/biosignal processing device would require a power supply to power the required elements. The sensor could be measuring biosignals such as capacitance, blood flow or heart rate. The sensor continuously monitors for an atypical signal. The implanted biosignal processing element needs to be able to communicate with an external base station. Wireless communication such as radio frequency (RF) communication could be used as a method to transmit data from the implanted biosensor to an external base station. A biosignal processing element continuously reads the signal received from the biosensor. When an atypical signal is received, the biosignal processing element wirelessly transmits a signal to an external base station.

The base station is located externally to the patient in a device located on or near the patient. The base station would require a power supply to power the required elements. The base station is continuously monitoring for an alert signal from the implanted biosensor/biosignal processing device. Once the external base station receives a signal, it processes the signal and if required it can communicate with a doctor or patient. Communication can be send via SMS/email to a doctor or patient detailing the signal received, the potential need for medical intervention and what immediate action may be required.

6.3 Proof of Concept Model Prototype Architecture

6.3.1 Basic prototype design.

The prototype consists of two separate devices. The first device will depict an implanted biosensor and biosignal processing element that is to be integrated to a non-software medical device. This first device uses a sensor to continuously monitor for a signal. When a signal is received it is processed and if required, data is wirelessly transmitted using RF communication. The second device will depict the external base station unit. This device continuously monitors for wireless communication from the implanted prototype device. If an alert signal is received, the external base station can communicate messages to an intended recipient such as a doctor or patient with details of an alert or required action.

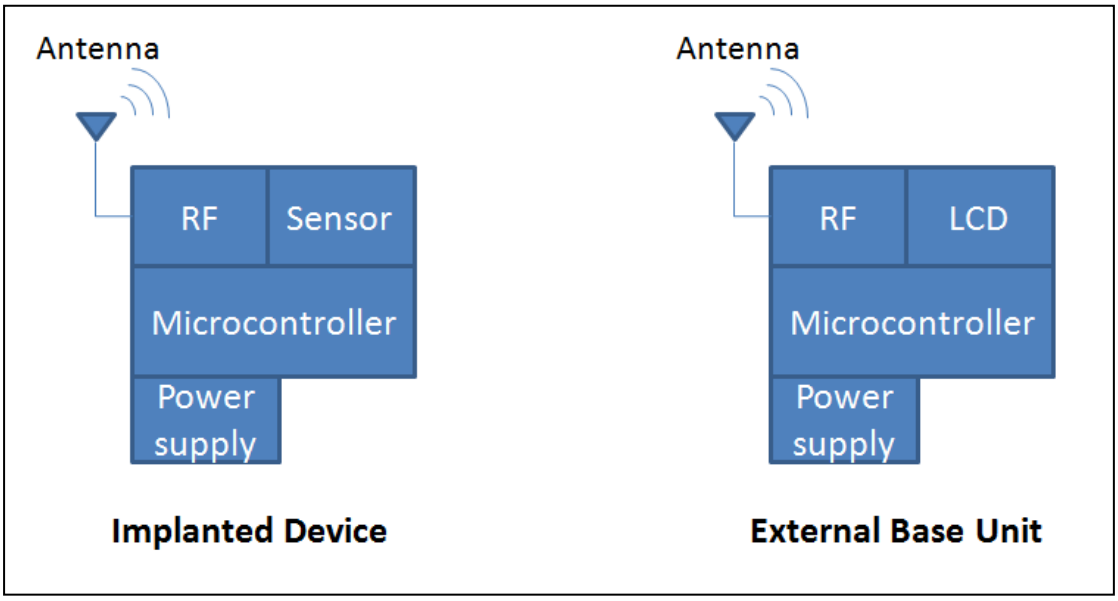

Figure 12. Basic device architecture.

6.3.2 Communication between devices.

A secure wireless communication is required between the implanted device and the base station. To handle the wireless communication for the prototype, XBee series 2 modules are used. These XBee modules can interact via radio frequency (RF) communication using the ZigBee PRO mesh networking protocol.

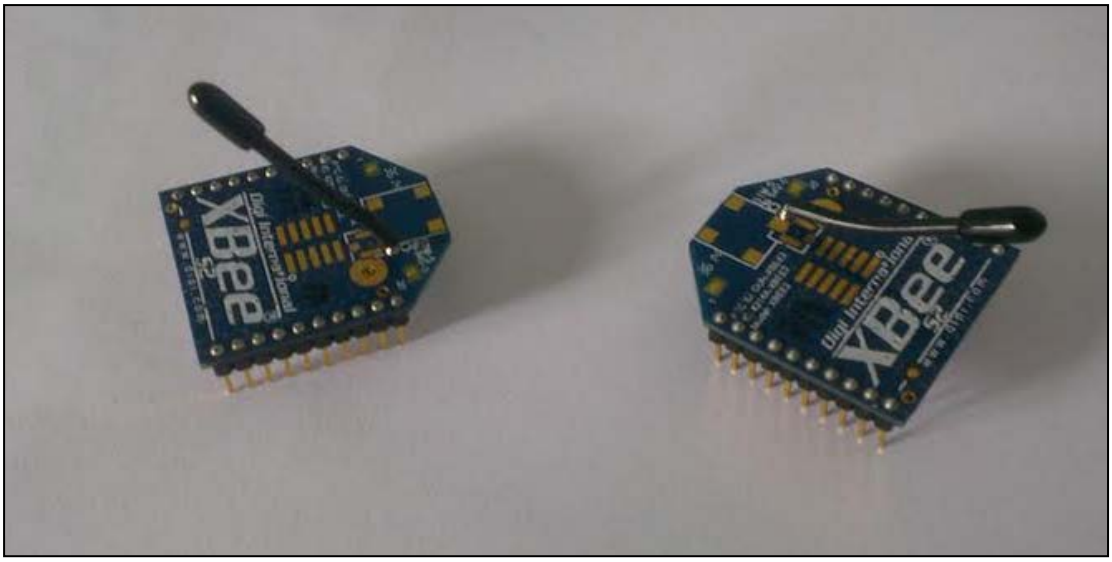

Figure 13. XBee modules.

The XBee modules were configured using an XBee USB adapter and the XBee configuration and test utility software (XCTU). The XBee USB adapter allows for serial communication between the XBee module and the PC.

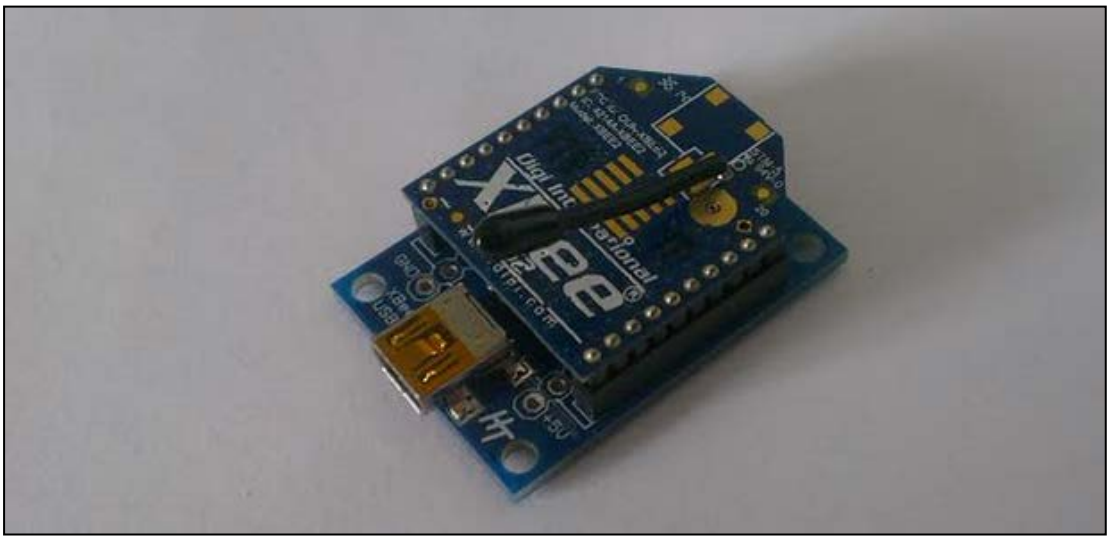

Figure 14. XBee USB adapter and XBee module.

The XBee modules were configured in Application Transparent (AT) mode. When the XBee modules are in AT mode, all serial data that is received by the module is queued up for RF transmission. When a module receives RF data, the data is sent out via the serial interface. One coordinator is required per wireless network. The module that is selected as the coordinator is the device that originally establishes

a network and can connect with other devices such as a router. (Digi International Inc., 2014). For the prototype, one module was configured as a coordinator (Figure 15 below) and the other module was configured as a router (Figure 16 below). The coordinator XBee module was attached to the base unit prototype. The router XBee module was attached to the biosensor/biosignal processing element prototype. The baud rate for both XBee modules was left at the default 9600 bits per second. The baud rate is the rate at which information is transferred over the serial connection. The coordinator router that was attached to the base unit prototype established the network that both XBee modules communicated on. ZigBee networks are known as Personal Area Networks (PANs). Each network has a PAN ID. Both prototype XBee modules were assigned a PAN ID of 3312 which ensured they connected to the same network. The coordinator XBee automatically selected an operating channel (CH) of 19. This CH was then automatically assigned to the router XBee module when it first joined the network. Both XBee modules have Serial Number High (SH) and Serial Number Low (SL) settings as well as configurable settings for Destination Address High (DH) and Destination Address Low (DL). When there are two XBee modules in a network, the destination address of one XBee module should use the serial number values of the corresponding XBee module in a network. The SH and SL of the router XBee module were inputted as the DH and DL for the coordinator XBee module respectively. The SH and SL of the coordinator XBee module were inputted as the DH and DL for the router XBee module respectively. This ensured that both XBee modules were able to communicate over the network. The XBee module configuration settings for the coordinator and router are displayed below in Table 1.

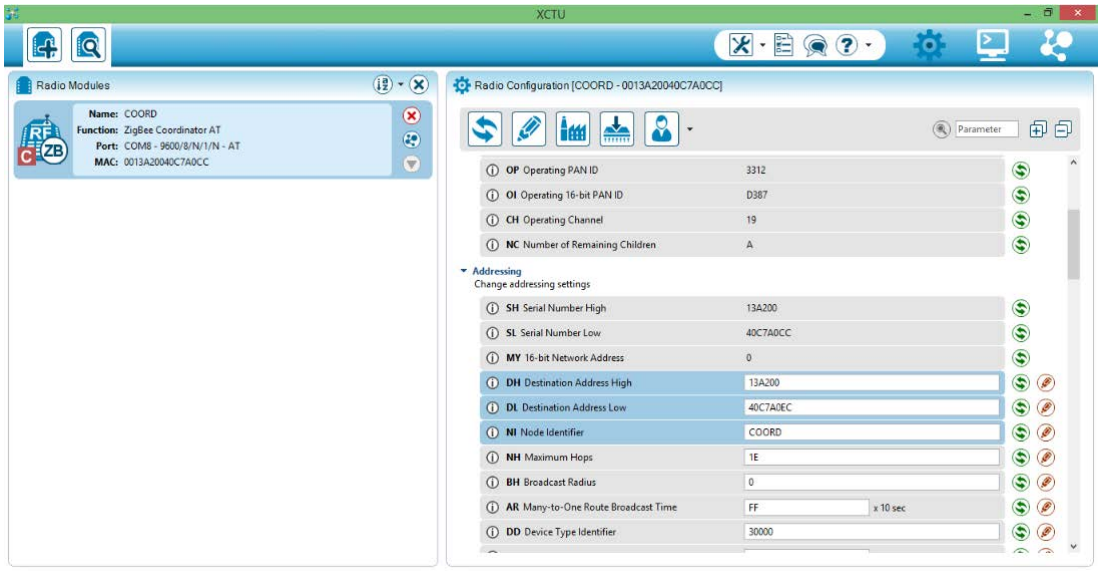

Figure 15. XBee coordinator configuration.

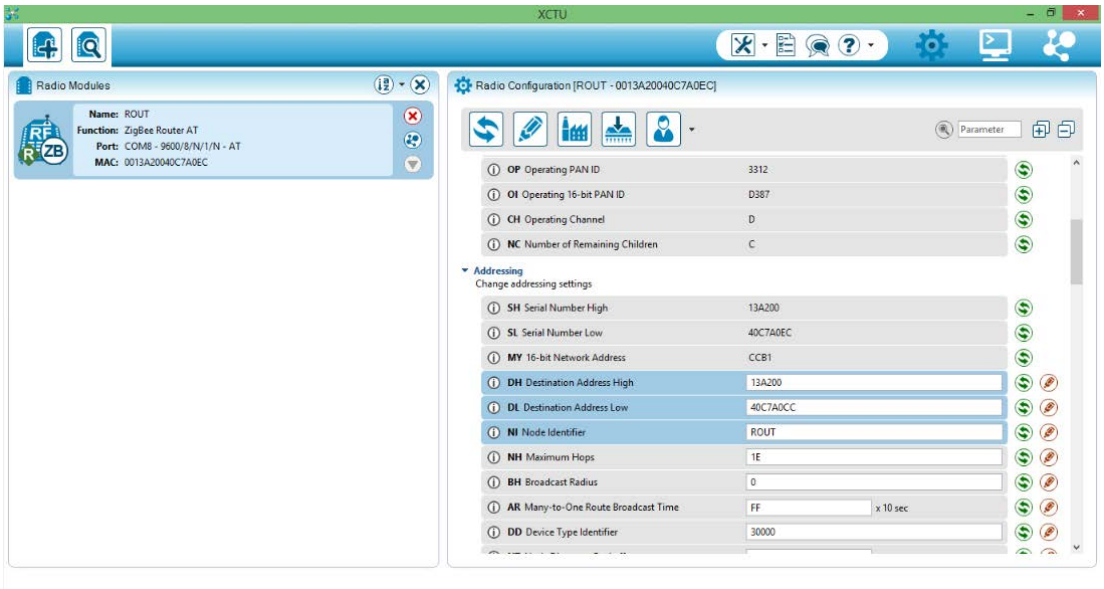

Figure 16. XBee router configuration.

Setting (Changed from Default)	**Coordinator**	**Router**
Function	ZigBee Coordinator AT	ZigBee Router AT
Product Family	XB24-ZB	XB24-ZB
Firmware Version	20A7	22A7
PAN ID	3312	3312
Destination Address High	13A200	13A200

Destination Address Low	40C7A0EC	40C7A0CC
Node Identifier	COORD	ROUT

Table 1. XBee settings.

6.3.3 Biosensor/biosignal processing element.

The biosensor/biosignal processing element prototype needs to continuously monitor for an alert signal and then be able to wirelessly communicate this to a base station (outside of the body). The biosensor/biosignal processing element prototype consists of the following elements: Power supply, Intel Galileo Gen 1 microcontroller, Grove base shield, Grove touch sensor, XBee shield and XBee module.

The Intel Galileo Gen 1 microcontroller is hardware and software pin compatible with Arduino shields the Arduino software development environment. The microcontroller was connected to a 5V power supply.

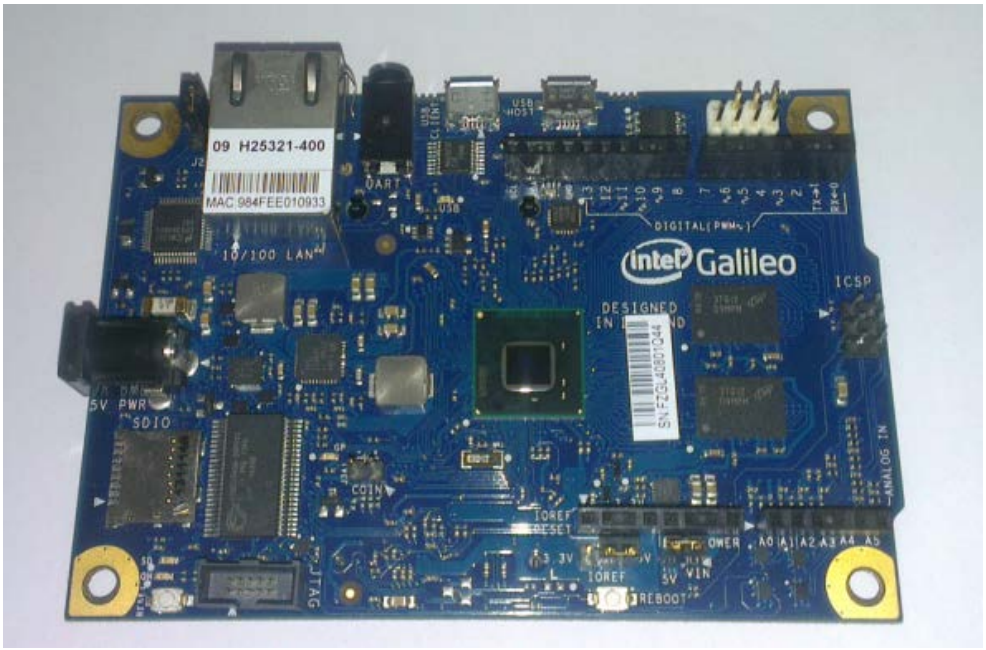

Figure 17. Intel Galileo microcontroller Gen 1.

A Grove base shield was connected to the Intel Galileo microcontroller. This base shield was then connected to the Grove touch sensor.

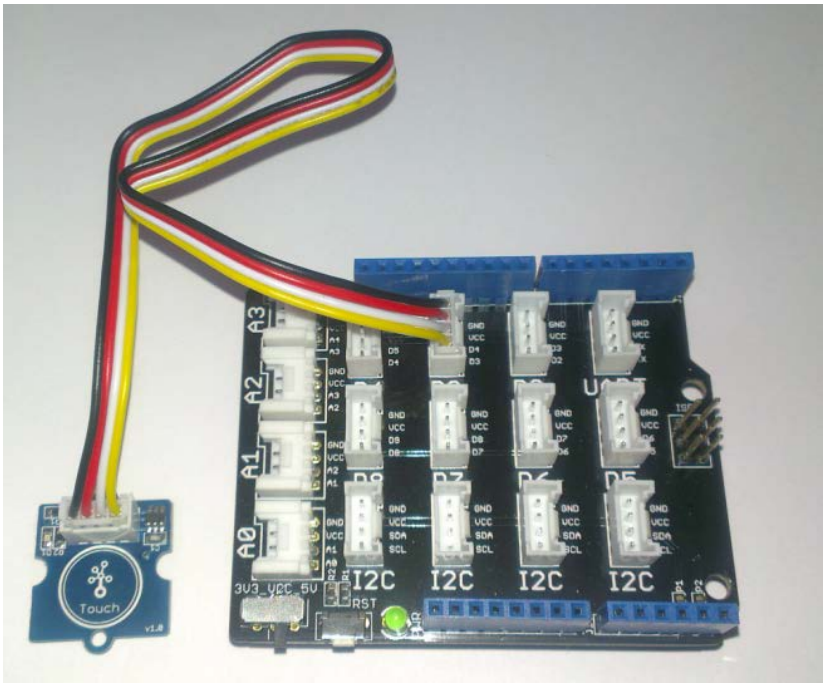

Figure 18. Grove base shield and Grove touch sensor.

An XBee shield was connected to the Grove base shield. An XBee module was then connected to the XBee shield.

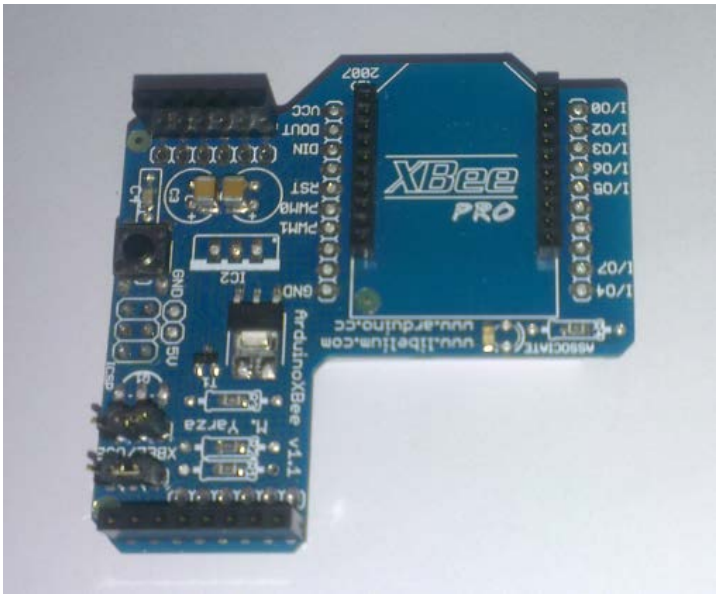

Figure 19. XBee shield.

Code was initially developed for this device with an extra LED on the unit (Appendix A). The code was developed using the Arduino software development

environment. A LED was initially added to the device to confirm that the microcontroller was correctly detecting when the touch sensor was pressed.

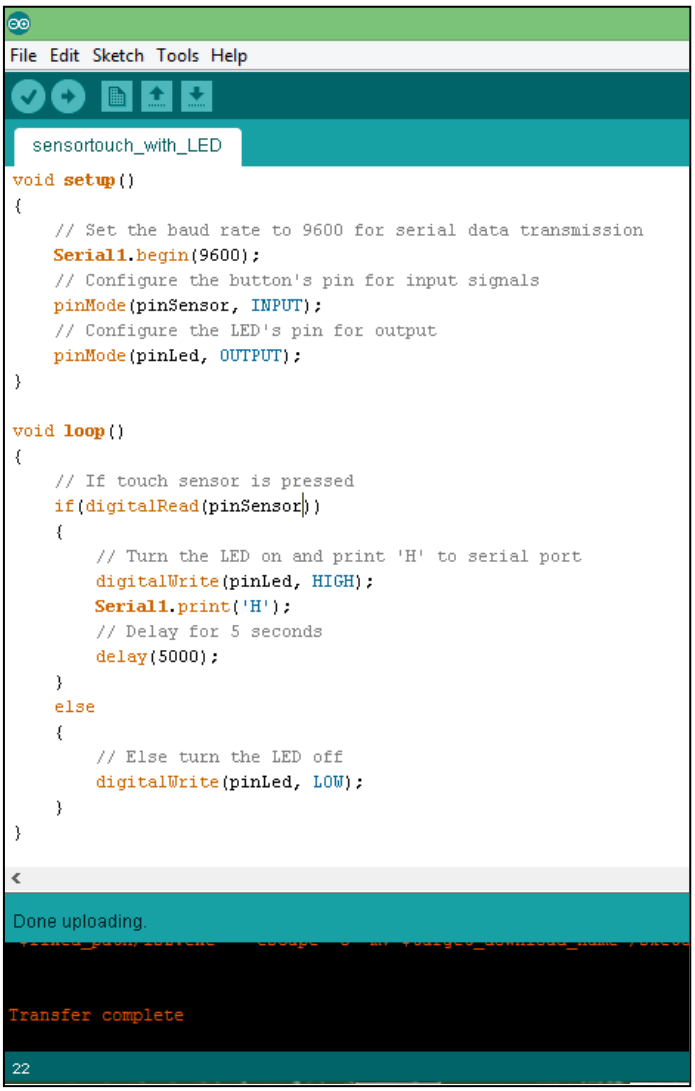

Figure 20. Code for touch sensor with LED uploaded to device.

To ensure the code is correctly uploaded to the prototype, the jumper positions on the XBee shield had to be set to USB mode. The jumpers on the XBee shield are circled in red in Figure 21 below.

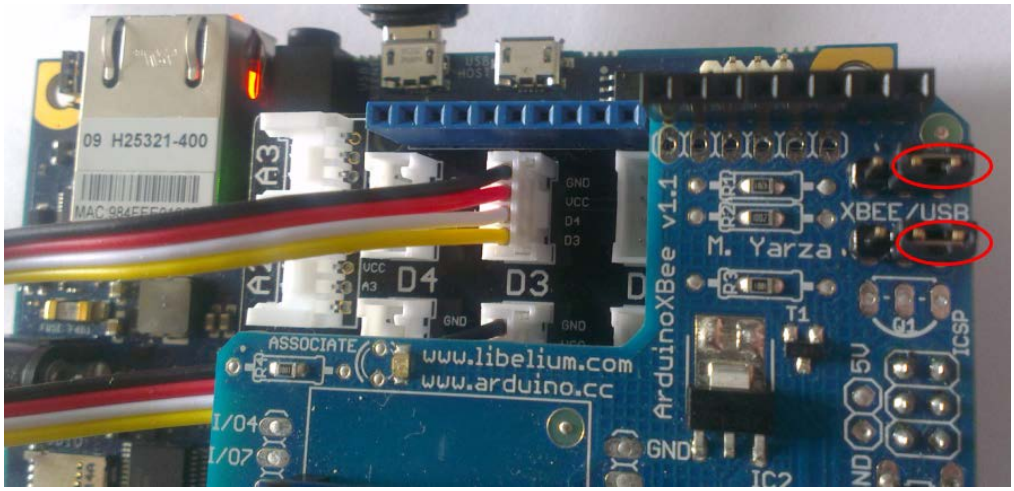

Figure 21. XBee shield with jumpers in USB positions.

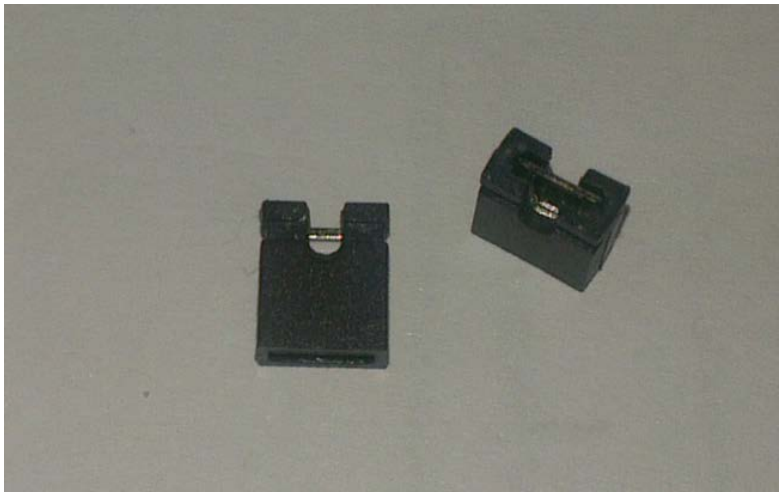

Figure 22. XBee shield jumpers.

The Grove touch sensor can detect a change in capacitance. The Intel Galileo microcontroller continuously monitors for an ‘alert’ signal from the Grove touch sensor. If an ‘alert’ signal is received, the microcontroller needs to send this information to the XBee module that is physically connected to it. The XBee module then transmits the data using RF communication. Figure 23 below shows the prototype in idle mode with no sensor being pressed. Figure 24 shows the touch sensor being pressed and the LED on.

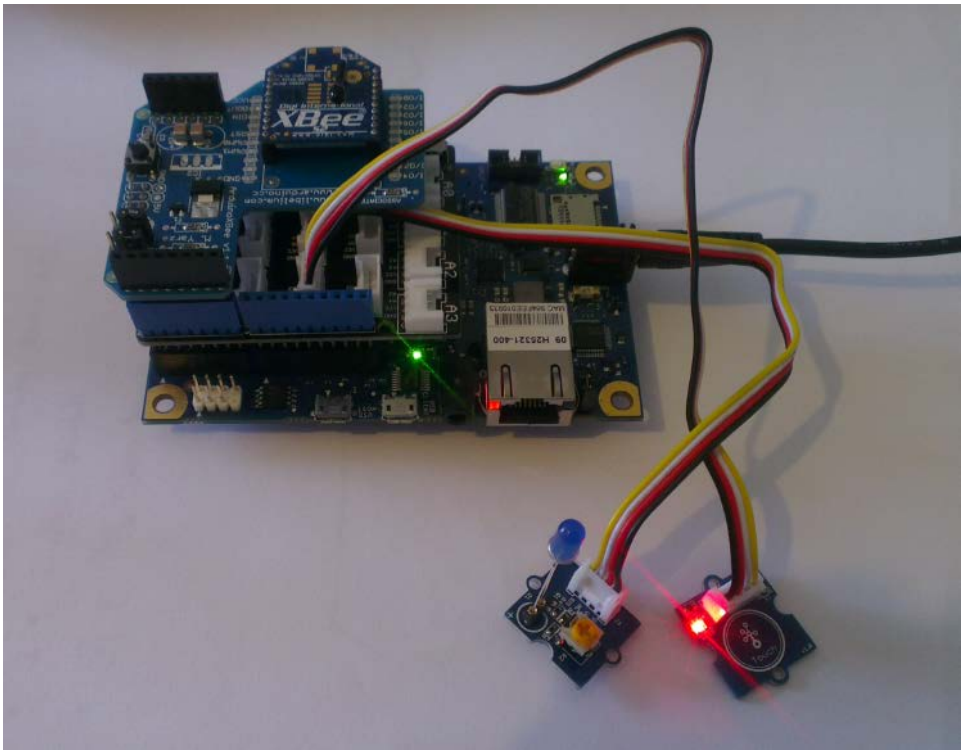

Figure 23. Biosensor/biosignal processing element prototype with LED off.

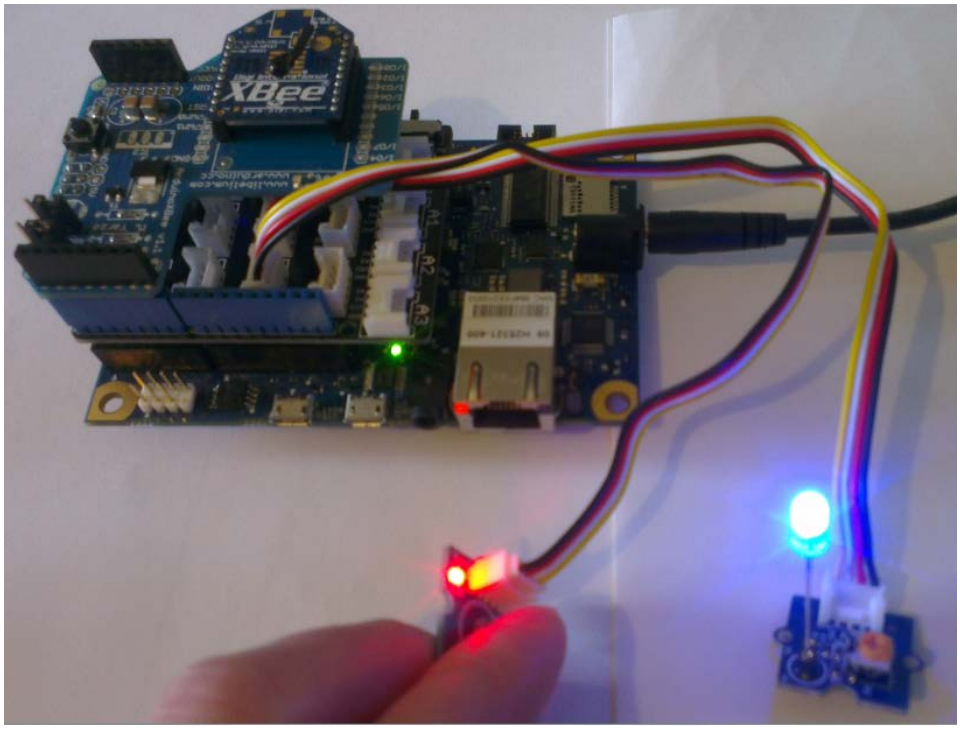

Figure 24. Biosensor/biosignal processing element prototype with LED on.

The code was subsequently updated for this device to remove the LED and is located in Appendix B.

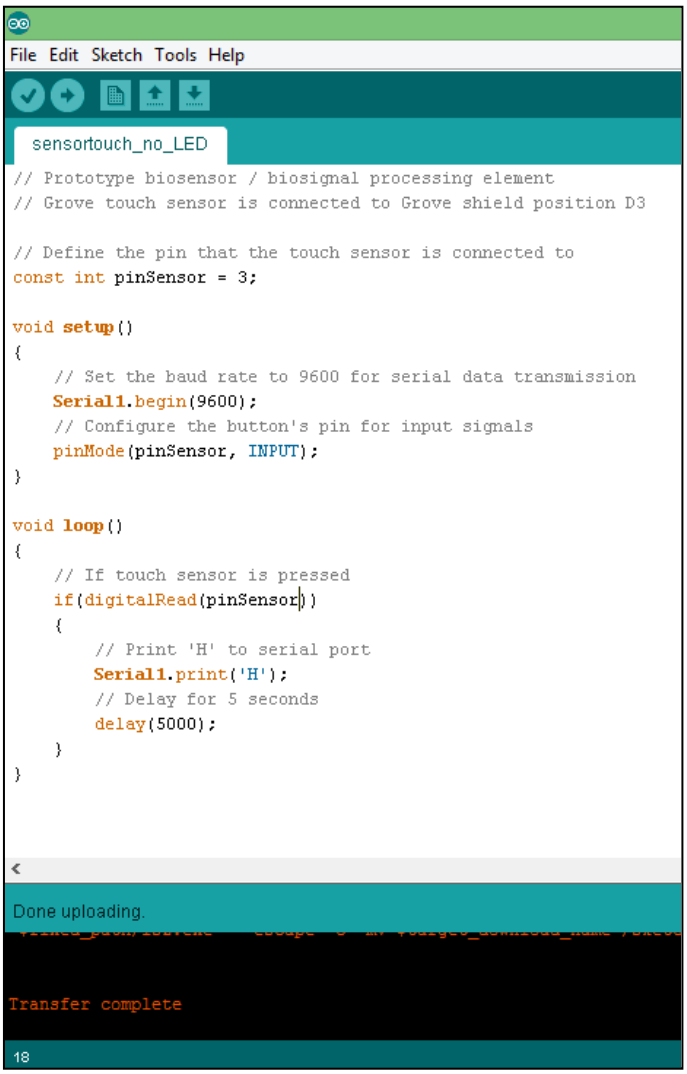

Figure 25. Code for touch sensor without LED uploaded to device.

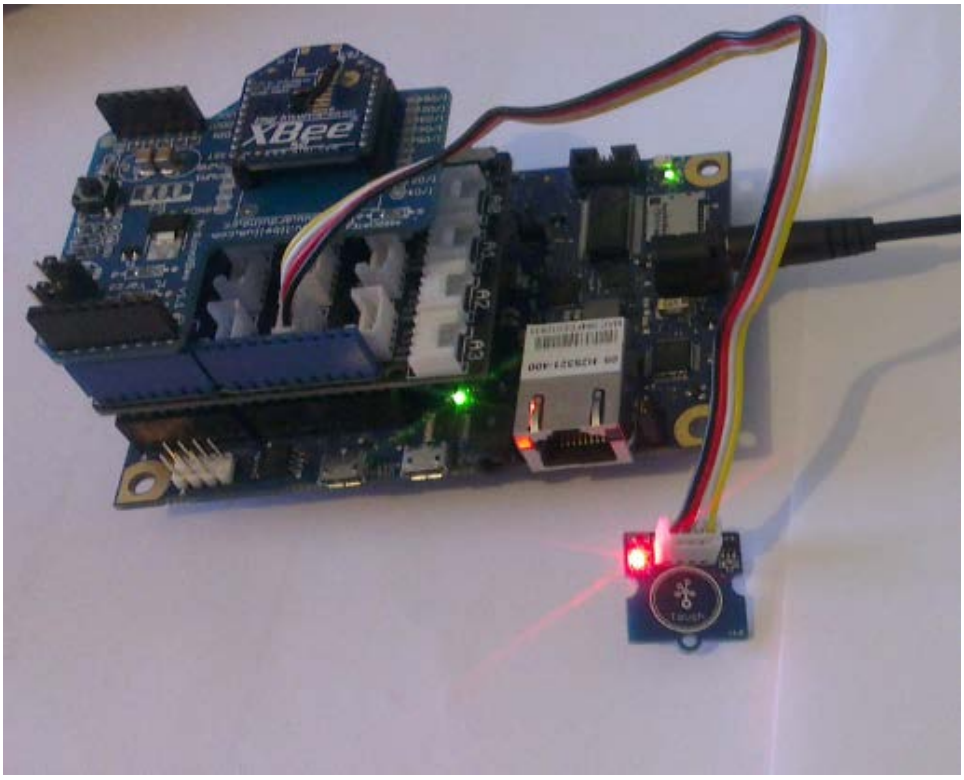

Figure 26. Biosensor/biosignal processing element prototype without LED.

6.3.4 Base station unit.

The base station prototype needs to be able to receive the wireless communication from the internal biosensor and deliver a communication to an intended recipient or end user. The base unit prototype consists of the following elements: Power supply, Intel Galileo Gen 1 microcontroller, Grove base shield, Grove LCD screen, XBee shield and XBee module.

As with the previous device, the microcontroller was connected to a 5V power supply. The Grove base shield was connected to the Intel Galileo microcontroller. This base shield was then connected to the Grove LCD screen. The Grove LCD screen displays a message read when commanded to by the microcontroller. This message can then be read by an intended recipient or end user.

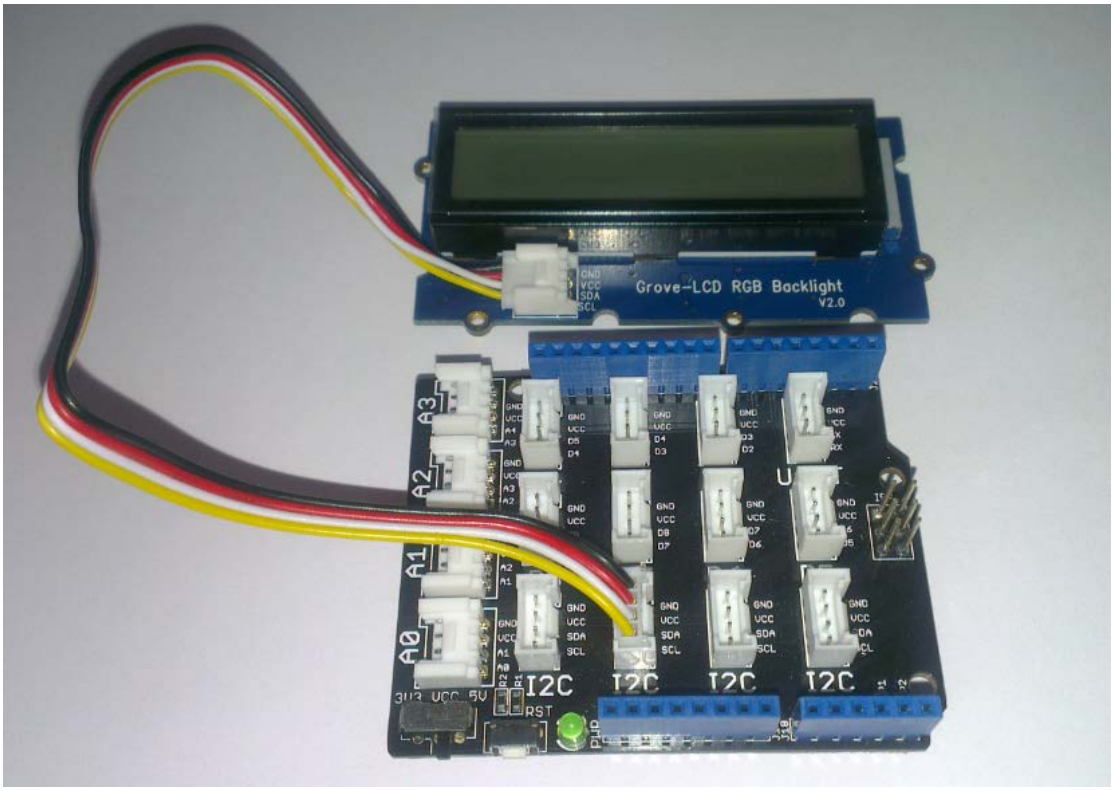

Figure 27. Grove LCD screen.

An XBee shield was connected to the Grove base shield and an XBee module was then connected to the XBee shield. Code was developed for this device using the Arduino software development environment and is located in Appendix C.

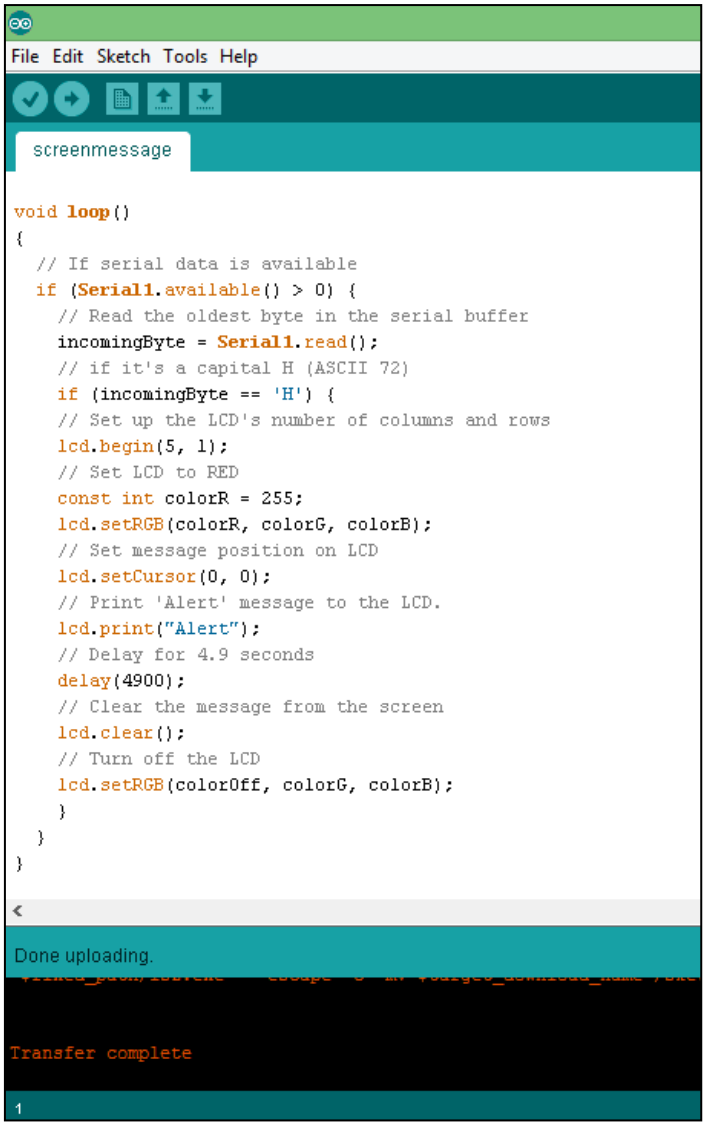

Figure 28. Code for base station.

The XBee that is connected to the microcontroller is configured to receive RF data from the other XBee in the network. The other XBee is located on the biosensor/biosignal processing element prototype. The Intel Galileo microcontroller continuously monitors for an ‘alert’ signal from the XBee module physically connected to it. When the XBee receives RF data, the microcontroller processes the information and if an ‘alert’ signal has been received, an appropriate message is sent to the Grove LCD screen. The LCD screen then displays a message to the user detailing the alert and the appropriate action to take if required.

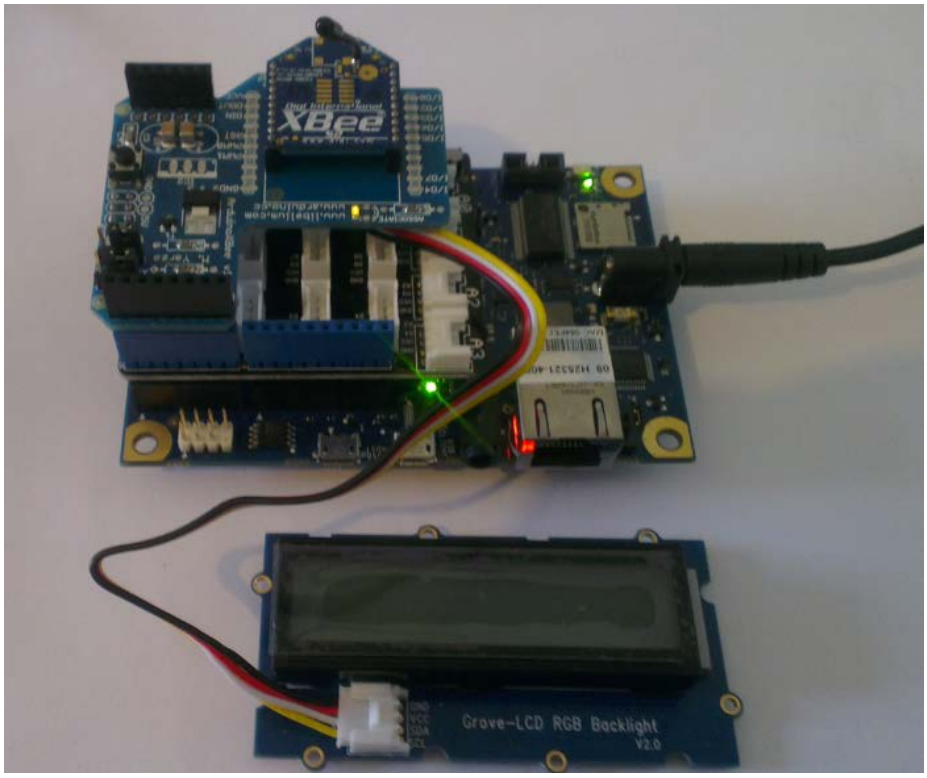

Figure 29. Base station prototype.

6.4 Proof of Concept Model Prototype Interaction

Both devices were connected to separate power supplies that had a supply voltage of 5 volts. The devices were configured as outlined above in Section 6.3. The relevant code was uploaded to each device using the Arduino software development environment.

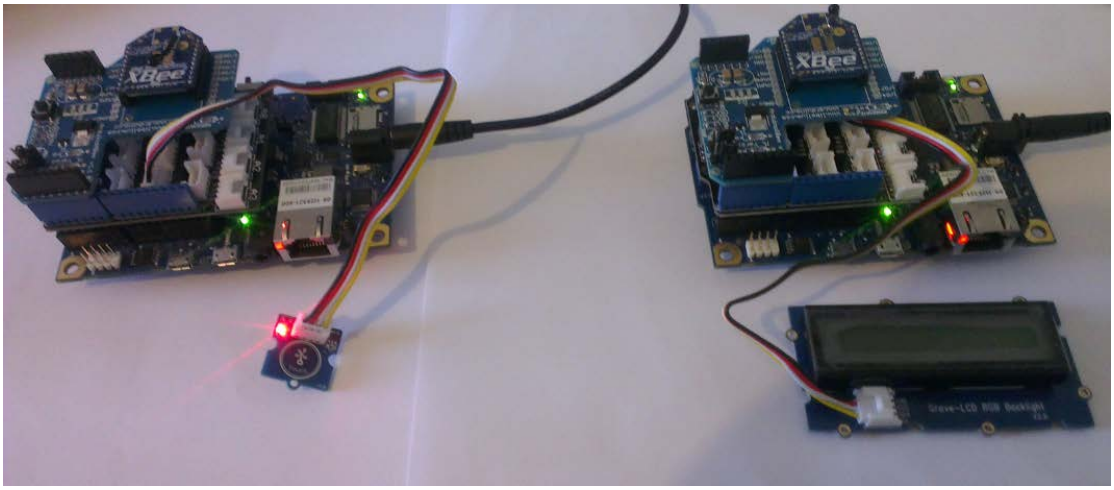

Figure 30. Both devices.

To ensure that both devices communicated to each other, the jumper positions on both XBee shields were set to XBee mode. See Figure 31 below which shows jumper positions on the XBee module circled in red.

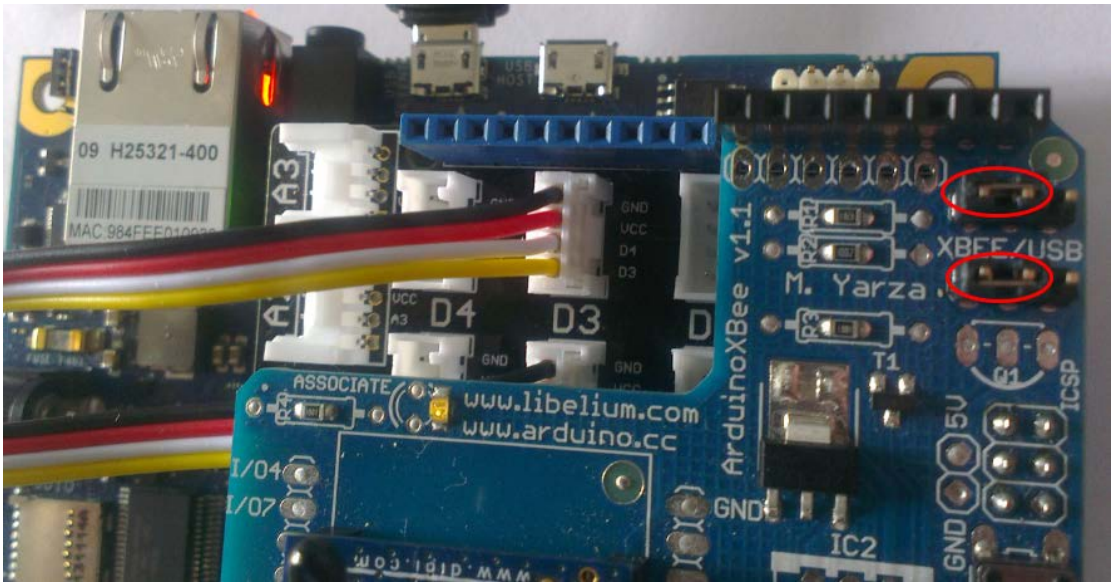

Figure 31. XBee shield with jumpers in XBee positions.

The biosensor / biosignal processing element prototype is continuously monitoring for a change in capacitance in the sensor. The external base unit is continuously monitoring for a signal from the implantable device. When the touch sensor is pressed, the change in capacitance is detected and the microcontroller sends a signal via the XBee RF module.

The XBee RF module on the external base unit receives the signal from the biosensor/biosignal processing element prototype. The incoming data is processed by the microcontroller and a message is sent to the LCD screen. The LCD screen then displays the message.

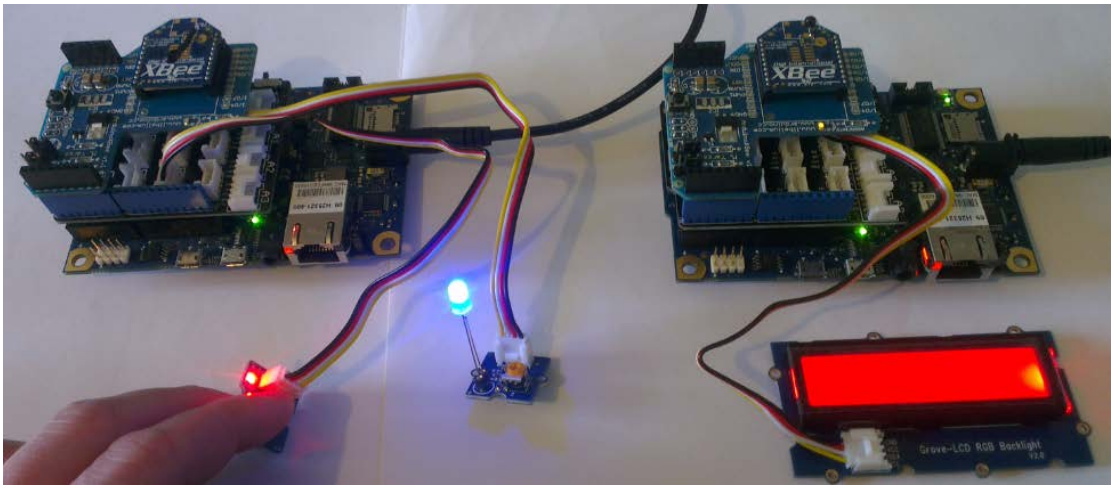

Figure 32. LED attached to biosensor prototype to confirm touch sensor is pressed.

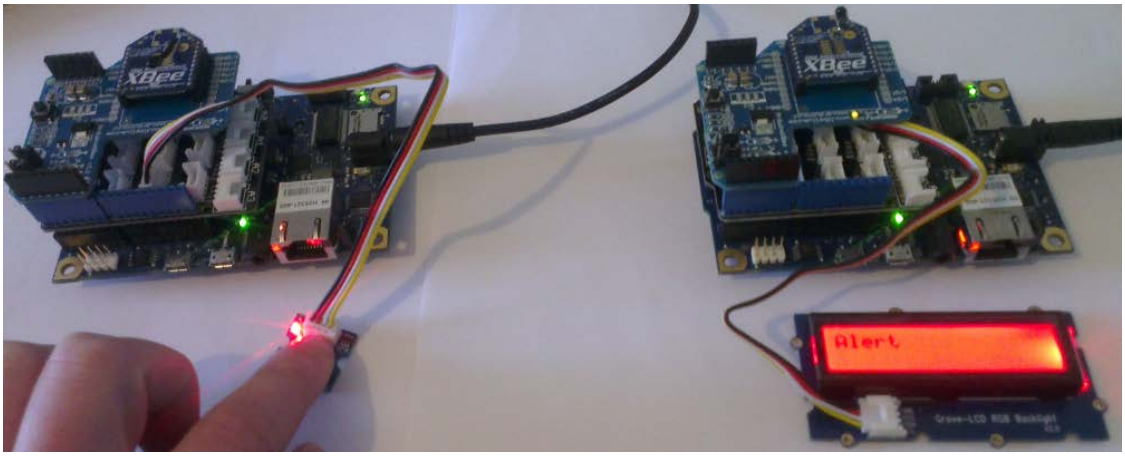

Figure 33. Touch sensor is pressed on device to the left. Signal is sent via RF to base unit (on the right) where 'Alert' message is displayed on LCD screen.

While testing this prototype, the message that was displayed to the Grove LCD screen was 'Alert'. This message and the colour of the LCD screen could be altered if required by updating the code and uploading the new code to the base unit prototype using the Arduino software development environment.

Figure 34. LCD screen with 'Alert' message.

The prototypes devices were placed in separate rooms to check the RF range between the biosensor/biosignal processing element prototype and the base station prototype. A person held the biosensor/biosignal processing element prototype in one room and pressed the touch sensor. There was a person, a solid block wall and over 3 metres between the two XBee RF modules attached to the prototypes. A person located in the second room confirmed the ‘Alert’ message appeared on the base station device when the touch sensor was pressed.

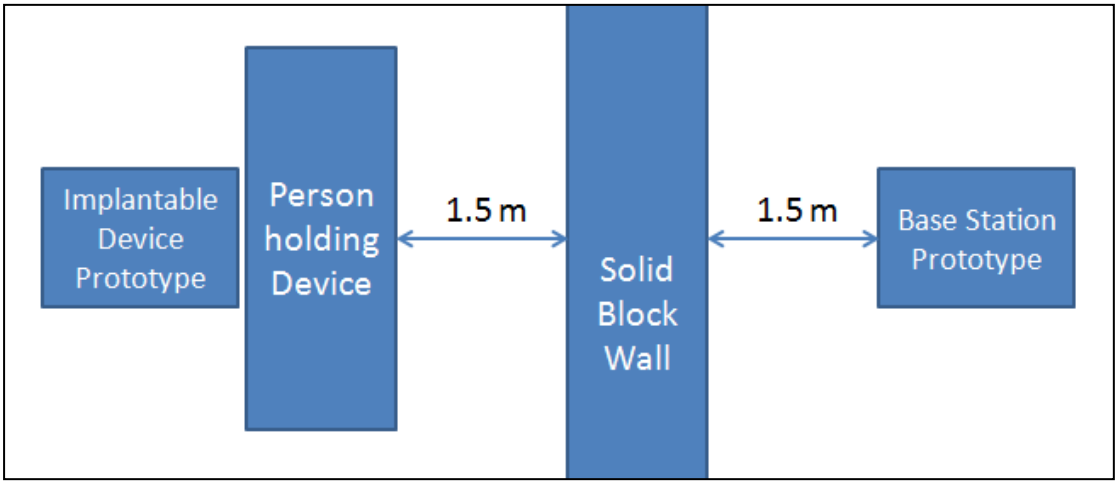

Figure 35. RF transmission through person and block wall.

The response time for the LCD screen to display the ‘Alert’ message after the touch sensor was pressed was also checked. This was to confirm that both XBee

modules and microcontrollers were responding to each other as intended. The touch sensor was pressed at different time intervals to check that both devices were still functioning correctly and communicating to each other after being left idle. See Table 2 below for time intervals. It was noted that each time the touch sensor was pressed, the 'Alert' message on the LCD screen was displayed without delay.

	Date / Time	Time devices left idle	'Alert' message appears?
1	28-Jul-15 14:18	0 minutes	Yes
2	28-Jul-15 17:18	3 hours	Yes
3	28-Jul-15 23:18	6 hours	Yes
4	29-Jul-15 11:18	12 hours	Yes
5	30-Jul-15 11:18	24 hours	Yes

Table 2. Prototype testing after time intervals.

The prototype code was updated to include a check that the biosensor/biosignal processing element prototype was still functioning as intended. This functionality was included in the code in case of device malfunction. Without periodic checks on the implanted device, the user could be unaware that the device is not working. The updated code with additional functionality is located in Appendices D & E. The base station prototype periodically sends data to the biosensor/biosignal processing element prototype. When the biosensor/biosignal processing element prototype receives this specific data, it responds by sending data back to the external base station prototype. If the external base station prototype does not receive any data from the biosensor/biosignal processing element prototype, a message is displayed on the LCD screen informing the end user that communication has been lost.

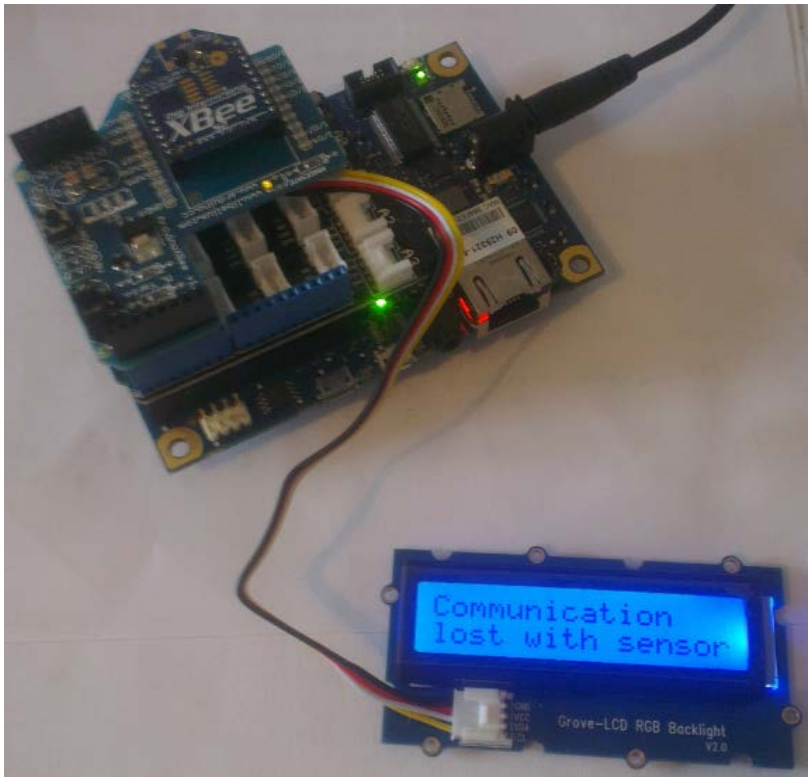

Figure 36. LCD screen with 'Communication lost with sensor' message.

6.5 Prototype Modelling Conclusions

This prototype demonstrates that it is feasible to integrate a biosensor / biosignal processing element with an existing medical device for monitoring purposes. Wireless communication was successfully demonstrated between a biosensor / biosignal processing element and an external base unit using RF communication. When the touch sensor was pressed on the biosensor / biosignal processing element, the attached microcontroller processed the incoming signal. The microcontroller sent the data to the attached XBee RF module and the data was wirelessly transmitted.

The external base unit was continuously monitoring for incoming serial data from the biosensor / biosignal processing element and received the data wirelessly using the XBee RF module attached. The data was processed by the microcontroller and when the ‘alert’ signal was detected, a message was sent to the LCD screen. The LCD screen attached to the microcontroller then displayed an ‘Alert’ message.

This prototype demonstrated the chain of events from a touch sensor being pressed on an implantable device prototype and the wireless transmission of data from that device to a base station prototype. The base station processed the data and

delivered an ‘Alert’ message to the end user. This could correspond to a real-world scenario where a sensor detects an atypical signal and wirelessly communicates to a base station. The base station receives the communication and alerts an end user of a potential issue.

A potential real world scenario of a biosensor attached to a non-software medical device could be a biosensor element measuring capacitance that is attached to an aneurysm coil. An aneurysm coil would typically be a platinum coil that is deposited in an aneurysm in a blood vessel. The intention of the coil is to prevent blood flow into the aneurysm.

Real world chain of events:

1. A biosensor element attached to a coil could be continuously monitoring for blood flow in the aneurysm area or that the coil is not performing its intended function. The biosensor could be measuring capacitance. The biosensor could be configured so that it sends an alert if it detects a capacitance reading outside of the minimum or maximum limits. If blood were to flow into the aneurysm area, a change in capacitance outside of the limits would be detected, triggering the biosensor to send an alert signal wirelessly.

2. An external base station is continuously monitoring for an alert signal. When the base station detects an alert signal, it sends an alert message such as an email or text message to the intended recipient.

Prototype chain of events:

1. The biosensor prototype in this case uses the Grove touch sensor. The microcontroller is continuously monitoring for a signal or change in capacitance from the touch sensor. When a change in capacitance is detected, the microcontroller sends an alert signal via the XBee using RF communication.

2. The external base station prototype continuously monitors for an alert signal. When the XBee receives data via RF communication from the biosensor prototype, the microcontroller detects that it is an alert signal. The microcontroller then sends an ‘Alert’ message to the Grove LCD screen which can then inform the end user that there is an alert condition.

See Figure 12 in Section 6.3.1 for the basic prototype device architecture.

6.6 Prototype Modelling Recommendations

Both devices in the prototype are built with standard off the shelf components which have not been miniaturised. As a result, the biosensor/biosignal processing element is not suitable for implantation. There are many upgrades that could be made to the prototype to ensure that it could be considered for long term implantation.

The assembled dimensions of the Galileo microcontroller, Grove shield, XBee shield and XBee module are 105mm x 70mm x 60mm (L x W x H). These components are common to both prototype devices. The size of this assembly would need to be greatly reduced especially for the implantable prototype.

The microcontroller size would need to be reduced before it could be implanted. The Intel Galileo microcontroller would need to be replaced with a much smaller microcontroller or processing element that would retain the function of the original microcontroller at a fraction of the size.

The sensor type used for the prototype is a standard off the shield Grove touch sensor. This could be replaced with a specialised biosensor that has been fabricated with the intention of being implanted long-term for the monitoring of biological signals. The replacement of the prototype sensor would significantly reduce the size of the device as the associated Grove shield would be removed along with the Grove touch sensor.

Both prototype devices were connected to standard mains 5V power supply. For the implantable device, the potential of energy harvesting should be investigated further to ensure the long-term viability of the device. A battery could replace the power supply for the base station unit if required as the device would be easily accessible for battery replacements as needed. The power consumption of the elements in the devices would need to be assessed to ensure that the prototype does not require more energy than can be supplied.

The wireless communication between the two prototype devices was shown to be effective. The XBee modules and XBee shield are too large to be considered for an implantable device and would have to be miniaturised or replaced. A smaller RF capable element could be sourced or a different technology such as NFC could be considered. As discussed in Section 4.4, Wu et al. (2011) have investigated the use of RF communication using the Zigbee networking protocol while Dehennis et al. (2013) have investigated the use of NFC as wireless communication methods for implantable

biosensors. Security should also be assessed to ensure that data that is transmitted wirelessly cannot be intercepted for malicious intent.

The prototype uses an LED screen attached to the base unit to deliver a message to the end user. This could be updated so that a text message or email is sent to a user when an ‘alert’ signal or communication failure is detected. A more advanced method of contacting the end user may ensure that the ‘Alert’ or communication failure message is received as soon as it is sent. Currently, the prototype relies on a user to be looking at the blank LCD screen and waiting for an message to appear. If the user was not looking at the LCD screen, the message may never be received and further action may not take place.

The biocompatibility of all components in the implantable device would also need to be assessed. The components would need to be made of a material that does not degrade with continuous biological contact and also does not cause any foreign body reactions to the patient.

7. Conclusions and Recommendations

The purpose of the research described in this thesis was to investigate the possibility of integrating biosignal processing technology with existing non-software medical devices. The first sub-problem was to identify, evaluate, and define how biosignal processing is currently used. The current state of the art in biosignal processing and biosensor types were assessed with an emphasis on wireless biosginal processing. Biosensor types that are currently being researched include sensors for glucose, lactose, and cholesterol levels as well as blood proteins and virus detection. It was found that the technology around biosensors and wireless communications is advancing rapidly with research currently taking place in both wearable and implantable biosensors. Wearable biosensors are already on the market and there is belief that a wide array of implantable biosensors will be commercially available in the coming years.

Sub-problem 2 was concerned with investigating existing non-software medical device technology. Existing non-software medical device technology was evaluated in Chapter 4. The use of non-software medical devices was found to be widespread and it was also noted that there was often the need for follow up procedures to assess device performance. Every invasive procedure that is carried out, involves a certain amount of risk, however small, that an adverse event could occur. In the case of angioplasty, patients could develop problems at the catheter entry site or could suffer from issues such as vessel perforation.

In Chapter 4 the possibility of integrating a wireless biosignal processing element with a non-software medical device was evaluated. This was linked to the Sub-Problem 3 objectives of evaluating the possibility of integrating biosignal processing with existing non-software medical devices. It was determined that there is potential for a biosensor/biosignal processing element to be integrated with a non-software medical device. This could remove the need for follow up invasive procedures to assess medical device performance and as a result would remove the potential risk of a patient suffering from an adverse event during an invasive procedure. Other benefits of an integrated biosensor/biosignal processing element with a non-software medical device include the continuous monitoring of device performance and the potential for a medical professional to see and treat more

patients. Continuous monitoring of device performance is advantageous when compared to periodic checkups as potential medical issues can be detected in real-time, communicated to a medical professional and acted on if required. If a medical professional did not have to carry out invasive follow up procedures to assess device performance, it would free up time for that medical professional to carry out more initial procedures.

Sub-problem 4 was to develop a proof of concept prototype model depicting an existing non-software medical device integrated with a biosignal processing element. A proof of concept prototype was developed in Chapter 5 that depicted a biosensor / biosignal processing element that could be integrated with a non-software medical device as well as an external base station prototype. Each device in the prototype used an Intel Galileo microcontroller and XBee RF modules for wireless communication.

The proof of concept demonstrated the chain of events from a touch sensor being pressed on an implantable device prototype to the wireless transmission of data between that device and a base station prototype. The base station processed the data and delivered an ‘Alert’ message to the end user.

Further recommendations on upgrades to the prototype are discussed in Section 6.6. These include updates to the size of the prototype, the sensor type, the power supply and the method of communicating to the end user as well as a recommendation to perform an assessment on device biocompatibility.

References

Arya, S. K., Saha, S., Ramirez-Vick, J. E., Gupta, V., Bhansali, S., & Singh, S. P. (2012). Recent advances in ZnO nanostructures and thin films for biosensor applications: Review. *Analytica Chimica Acta*, *737*, 1–21. http://doi.org/10.1016/j.aca.2012.05.048

Baj-Rossi, C., Kilinc, E. G., Ghoreishizadeh, S. S., Casarino, D., Jost, T. R., Dehollain, C., … Carrara, S. (2013). Fabrication and packaging of a fully implantable biosensor array. In *2013 IEEE Biomedical Circuits and Systems Conference (BioCAS)* (pp. 166–169). http://doi.org/10.1109/BioCAS.2013.6679665

Bhat, T., Teli, S., Bhat, H., Akhtar, M., Meghani, M., Lafferty, J., & Gala, B. (2012). Access-site complications and their management during transradial cardiac catheterization. *Expert Review of Cardiovascular Therapy*, *10*(5), 627–634. http://doi.org/10.1586/erc.12.16

Bolomey, L., Meurville, E., & Ryser, P. (2009). Implantable ultra-low power DSP-based system for a miniature chemico-rheological biosensor. *Procedia Chemistry*, *1*(1), 1235–1238. http://doi.org/10.1016/j.proche.2009.07.308

Brilakis, E. S., Karmpaliotis, D., Patel, V., & Banerjee, S. (2012). Complications of Chronic Total Occlusion Angioplasty. *Interventional Cardiology Clinics*, *1*(3), 373–389. http://doi.org/10.1016/j.iccl.2012.04.006

Brisman, J. L., Song, J. K., & Newell, D. W. (2006). Cerebral Aneurysms. *New England Journal of Medicine*, *355*(9), 928–939. http://doi.org/10.1056/NEJMra052760

Buenger, D., Topuz, F., & Groll, J. (2012). Hydrogels in sensing applications. *Progress in Polymer Science*, *37*(12), 1678–1719. http://doi.org/10.1016/j.progpolymsci.2012.09.001

Burleson, W., Clark, S. S., Ransford, B., & Fu, K. (2012). Design Challenges for Secure Implantable Medical Devices. In *Proceedings of the 49th Annual Design Automation Conference* (pp. 12–17). New York, NY, USA: ACM. http://doi.org/10.1145/2228360.2228364

Cavallini, A., Jost, T. R., Ghoreishizadeh, S. S., Olivo, J., de Beeck, M. O., Gorissen, B., … Carrara, S. (2015). A Subcutaneous Biochip for Remote Monitoring of

Human Metabolism: Packaging and Biocompatibility Assessment. *IEEE Sensors Journal*, *15*(1), 417–424. http://doi.org/10.1109/JSEN.2014.2339638

Chen, X., Zhou, G., Peng, X., & Yoon, J. (2012). Biosensors and chemosensors based on the optical responses of polydiacetylenes. *Chemical Society Reviews*, *41*(13), 4610–4630. http://doi.org/10.1039/C2CS35055F

Chou, J., Chen, R., Liao, Y., Chen, J., Huang, M., & Chou, H. (2015). Dynamic and Wireless Sensing Measurements of Potentiometric Glucose Biosensor Based on Graphene and Magnetic Beads. *IEEE Sensors Journal*, *PP*(99), 1–1. http://doi.org/10.1109/JSEN.2015.2449906

Chung, J., Lim, Y. C., Suh, S. H., Shim, Y. S., Kim, Y. B., Joo, J.-Y., … Shin, Y. S. (2014). Stent-assisted coil embolization of ruptured wide-necked aneurysms in the acute period: incidence of and risk factors for periprocedural complications. *Journal of Neurosurgery*, *121*(1), 4–11. http://doi.org/10.3171/2014.4.JNS131662

Cox, N., Resnic, F. S., Popma, J. J., Simon, D. I., Eisenhauer, A. C., & Rogers, C. (2004). Comparison of the risk of vascular complications associated with femoral and radial access coronary catheterization procedures in obese versus nonobese patients. *The American Journal of Cardiology*, *94*(9), 1174–1177. http://doi.org/10.1016/j.amjcard.2004.07.088

Dangas, G., & Kuepper, F. (2002). Restenosis: Repeat Narrowing of a Coronary Artery Prevention and Treatment. *Circulation*, *105*(22), 2586–2587. http://doi.org/10.1161/01.CIR.0000019122.00032.DF

Darwish, A., & Hassanien, A. E. (2011). Wearable and Implantable Wireless Sensor Network Solutions for Healthcare Monitoring. *Sensors*, *11*(6), 5561–5595. http://doi.org/10.3390/s110605561

Dehennis, A. D., Mailand, M., Grice, D., Getzlaff, S., & Colvin, A. E. (2013). A near-field-communication (NFC) enabled wireless fluorimeter for fully implantable biosensing applications. In *Solid-State Circuits Conference Digest of Technical Papers (ISSCC), 2013 IEEE International* (pp. 298–299). http://doi.org/10.1109/ISSCC.2013.6487743

Dhand, C., Das, M., Datta, M., & Malhotra, B. D. (2011). Recent advances in polyaniline based biosensors. *Biosensors and Bioelectronics*, *26*(6), 2811–2821. http://doi.org/10.1016/j.bios.2010.10.017

Digi International Inc. (2014). *XBee and ZigBee basic concepts*. Retrieved July 21 2015 from http://ftp1.digi.com/support/documentation/html/90001399/90001399_A/Files/XBee-concepts.html#_Toc384719505

Ellozy, S. H., Carroccio, A., Lookstein, R. A., Minor, M. E., Sheahan, C. M., Juta, J., … Marin, M. L. (2004). First experience in human beings with a permanently implantable intrasac pressure transducer for monitoring endovascular repair of abdominal aortic aneurysms. *Journal of Vascular Surgery*, *40*(3), 405–412. http://doi.org/10.1016/j.jvs.2004.06.027

Enterprise Ireland. (2010, June). *Medical Devices*. Retrieved March 07 2015 from http://www.enterprise-ireland.com/en/Source-a-Product-or-Service-from-Ireland/Sector-and-Company-Directories/Medical-Devices-Sector-Profile.pdf

Fan, W., Jeong, Y. W., Wei, J., Tan, B. K., Lok, B. K., & Chun, K. J. (2005). Encapsulation and packaging of biosensor. In *Electronic Packaging Technology Conference, 2005. EPTC 2005. Proceedings of 7th* (Vol. 1, p. 4 pp.–). http://doi.org/10.1109/EPTC.2005.1614372

Farshchi, S., Pesterev, A., Nuyujukian, P. H., Mody, I., & Judy, J. W. (2007). Bi-Fi: an embedded sensor/system architecture for REMOTE biological monitoring. *IEEE Transactions on Information Technology in Biomedicine: A Publication of the IEEE Engineering in Medicine and Biology Society*, *11*(6), 611–618.

Franco, J. J., Abisse, S. S., Ruisi, P., & Abbott, J. D. (2014). Infectious complications of percutaneous cardiac procedures. *Interventional Cardiology*, *6*(5), 445–452. http://doi.org/10.2217/ica.14.53

Haan, L. I. (2010). *Cardiac Stent Info.* Retrieved August 07 2015 from http://www.drliminghaan.com/cardiac-stent-info.html

Harb, A. (2011). Energy harvesting: State-of-the-art. *Renewable Energy, 36*(10), 2641–2654. http://doi.org/10.1016/j.renene.2010.06.014

Heiserman, J. E., Dean, B. L., Hodak, J. A., Flom, R. A., Bird, C. R., Drayer, B. P., Fram, E. K. (1994). Neurologic complications of cerebral angiography. *American Journal of Neuroradiology, 15*(8), 1401-1407.

Hulzink, J., Konijnenburg, M., Ashouei, M., Breeschoten, A., Berset, T., Huisken, J., … Van Ginderdeuren, J. (2011). An Ultra Low Energy Biomedical Signal Processing System Operating at Near-Threshold. *IEEE Transactions on Biomedical Circuits and Systems*, *5*(6), 546–554.

doi:10.1109/TBCAS.2011.2176726

Khan, M., Singh, A. K., Iqbal, S. S., & Sharma, B. B. (2014). A novel SPICE implementation of MPPT technique for implantable solar powered cardiac biosensors. In *2014 9th International Conference on Industrial and Information Systems (ICIIS)* (pp. 1–5). http://doi.org/10.1109/ICIINFS.2014.7036487

Kim, J., Banks, A., Xie, Z., Heo, S. Y., Gutruf, P., Lee, J. W., … Rogers, J. A. (2015). Miniaturized Flexible Electronic Systems with Wireless Power and Near-Field Communication Capabilities. *Advanced Functional Materials*, n/a–n/a. http://doi.org/10.1002/adfm.201501590

Kotanen, C. N., Moussy, F. G., Carrara, S., & Guiseppi-Elie, A. (2012). Implantable enzyme amperometric biosensors. *Biosensors & Bioelectronics*, *35*(1), 14–26. http://doi.org/10.1016/j.bios.2012.03.016

Kresowik, T. F., Khoury, M. D., Miller, B. V., Winniford, M. D., Shamma, A. R., Sharp, W. J., … Corson, J. D. (1991). A prospective study of the incidence and natural history of femoral vascular complications after percutaneous transluminal coronary angioplasty. *Journal of Vascular Surgery*, *13*(2), 328–335. http://doi.org/10.1016/0741-5214(91)90226-K

Kuila, T., Bose, S., Khanra, P., Mishra, A. K., Kim, N. H., & Lee, J. H. (2011). Recent advances in graphene-based biosensors. *Biosensors and Bioelectronics*, *26*(12), 4637–4648. http://doi.org/10.1016/j.bios.2011.05.039

Latré, B., Braem, B., Moerman, I., Blondia, C., & Demeester, P. (2011). A Survey on Wireless Body Area Networks. *Wirel. Netw.*, *17*(1), 1–18. http://doi.org/10.1007/s11276-010-0252-4

Lin, P., & Yan, F. (2012). Organic Thin-Film Transistors for Chemical and Biological Sensing. *Advanced Materials*, *24*(1), 34–51. http://doi.org/10.1002/adma.201103334

Mahfouz, M. R., Kuhn, M. J., & To, G. (2013). Wireless medical devices: A review of current research and commercial systems. In *2013 IEEE Topical Conference on Biomedical Wireless Technologies, Networks, and Sensing Systems (BioWireleSS)* (pp. 16–18). http://doi.org/10.1109/BioWireleSS.2013.6613660

Mohammadi, A. R., Chen, K., Mohamed Ali, M. S., & Takahata, K. (2011). Radio aneurysm coils for noninvasive detection of cerebral embolization failures: A

preliminary study. *Biosensors and Bioelectronics*, *30*(1), 300–305. http://doi.org/10.1016/j.bios.2011.09.033

Molyneux, A. (2002). International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *The Lancet*, *360*(9342), 1267–1274. http://doi.org/10.1016/S0140-6736(02)11314-6

Molyneux, A. J., Kerr, R. S. C., Yu, L.-M., Clarke, M., Sneade, M., Yarnold, J. A., … International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. (2005). International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet (London, England)*, *366*(9488), 809–817. http://doi.org/10.1016/S0140-6736(05)67214-5

NorthPoint Domain Inc. (2015). *Arteriogram*. Retrieved June 28 2015 from http://www.miamivascular.com/handler.cfm?event=practice,template&cpid=23804

Oliveros, A., Guiseppi-Elie, A., & Saddow, S. E. (2013). Silicon carbide: a versatile material for biosensor applications. *Biomedical Microdevices*, *15*(2), 353–368. http://doi.org/10.1007/s10544-013-9742-3

Olivo, J., Ghoreishizadeh, S. S., Carrara, S., & De Micheli, G. (2013). Electronic Implants: Power Delivery and Management. *Proceedings of the Design, Automation & Test in Europe Conference (DATE 2013)*. Retrieved from http://infoscience.epfl.ch/record/185130

Onunka, C., Bright, G., & Stopforth, R. (2013). Investigating the choice factors on the use of XBee/Bluetooth as the communication scheme in EEG sensor networks. In *Robotics and Mechatronics Conference (RobMech), 2013 6th* (pp. 52–57). http://doi.org/10.1109/RoboMech.2013.6685491

Ouriel, K., Fowl, R. J., Davies, M. G., Forbes, T. L., Gambhir, R. P. S., & Ricci, M. A. (2014). Disease-specific guidelines for reporting adverse events for peripheral vascular medical devices. *Journal of Vascular Surgery*, *60*(1), 212–225. http://doi.org/10.1016/j.jvs.2014.04.061

Palantei, E., Baharuddin, M., Andani, A., Nien, K. N., Utami, D., Febriani, A. E. A., … Agus, M. (2012). A 2.5 GHz wireless ECG system for remotely monitoring

heart pulses. In *2012 IEEE Antennas and Propagation Society International Symposium (APSURSI)* (pp. 1–2). http://doi.org/10.1109/APS.2012.6349097

Padasdao, B., Shahhaidar, E., Stickley, C., & Boric-Lubecke, O. (2013). Electromagnetic Biosensing of Respiratory Rate. *IEEE Sensors Journal*, *13*(11), 4204–4211. http://doi.org/10.1109/JSEN.2013.2266253

Pawar, P., Jones, V., van Beijnum, B.-J. F., & Hermens, H. (2012). A framework for the comparison of mobile patient monitoring systems. *Journal of Biomedical Informatics*, *45*(3), 544–556. http://doi.org/10.1016/j.jbi.2012.02.007

Perumal, V., & Hashim, U. (2014). Advances in biosensors: Principle, architecture and applications. *Journal of Applied Biomedicine*, *12*(1), 1–15. http://doi.org/10.1016/j.jab.2013.02.001

Polisena, J., Forster, A. J., Cimon, K., & Rabb, D. (2013). Post-marketing surveillance in the published medical and grey literature for percutaneous transluminal coronary angioplasty catheters: a systematic review. *Systematic Reviews*, *2*(1), 94. http://doi.org/10.1186/2046-4053-2-94

Pongruangporn, M., Ajenjo, M. C., Russo, A. J., McMullen, K. M., Robinson, C., Williams, R. C., & Warren, D. K. (2013). Patient- and device-specific risk factors for peripherally inserted central venous catheter-related bloodstream infections. *Infection Control and Hospital Epidemiology*, *34*(2), 184–189. http://doi.org/10.1086/669083

Sanborn, T. A., Tomey, M. I., Mehran, R., Généreux, P., Witzenbichler, B., Brener, S. J., … Stone, G. W. (2015). Femoral vascular closure device use, bivalirudin anticoagulation, and bleeding after primary angioplasty for STEMI: results from the HORIZONS-AMI trial. *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions*, *85*(3), 371–379. http://doi.org/10.1002/ccd.25663

Santos, A., Kumeria, T., & Losic, D. (2013). Nanoporous anodic aluminum oxide for chemical sensing and biosensors. *TrAC Trends in Analytical Chemistry*, *44*, 25–38. http://doi.org/10.1016/j.trac.2012.11.007

Society of NeuroInterventional Surgery. (2014). *Aneurysms*. Retrieved July 04 2015 from http://snisonline.org/Aneurysms

St. Peter's Health Care Services. (n.d.). *Transradial Cardiac Catheterization*. Retrieved July 12 2015 from http://www.sphcs.org/transradialcardiaccath

Steinberg, M. D., Kassal, P., Kereković, I., & Steinberg, I. M. (2015). A wireless potentiostat for mobile chemical sensing and biosensing. *Talanta*, *143*, 178–183. http://doi.org/10.1016/j.talanta.2015.05.028

Sue, C.-Y., & Tsai, N.-C. (2012). Human powered MEMS-based energy harvest devices. *Applied Energy*, *93*, 390–403. http://doi.org/10.1016/j.apenergy.2011.12.037

Takahata, K., DeHennis, A., Wise, K. D., & Gianchandani, Y. B. (2004). A wireless microsensor for monitoring flow and pressure in a blood vessel utilizing a dual-inductor antenna stent and two pressure sensors. In *Micro Electro Mechanical Systems, 2004. 17th IEEE International Conference on. (MEMS)* (pp. 216–219). http://doi.org/10.1109/MEMS.2004.1290561

Tan, E. L., Pereles, B. D., & Ong, K. G. (2010). A Wireless Embedded Sensor Based on Magnetic Higher Order Harmonic Fields: Application to Liquid Pressure Monitoring. *IEEE Sensors Journal*, *10*(6), 1085–1090. http://doi.org/10.1109/JSEN.2010.2041223

Torsekar, M. P., Reed, M. (2014). US Medical Devices and China's Market: Opportunities and Obstacles. Washington: Office of Industries - U.S. International Trade Commission.

Valdastri, P., Susilo, E., Forster, T., Strohhofer, C., Menciassi, A., & Dario, P. (2011). Wireless Implantable Electronic Platform for Chronic Fluorescent-Based Biosensors. *IEEE Transactions on Biomedical Engineering*, *58*(6), 1846–1854. http://doi.org/10.1109/TBME.2011.2123098

Van der Schaaf, I., Algra, A., Wermer, M., Molyneux, A., Clarke, M., van Gijn, J., & Rinkel, G. (2005). Endovascular coiling versus neurosurgical clipping for patients with aneurysmal subarachnoid haemorrhage. *The Cochrane Database of Systematic Reviews*, (4), CD003085. http://doi.org/10.1002/14651858.CD003085.pub2

Waksman, R., King, S. B., Douglas, J. S., Shen, Y., Ewing, H., Mueller, L., ... & Weintraub, W. S. (1995). Predictors of groin complications after balloon and new-device coronary intervention. *The American journal of cardiology*, *75*(14), 886-889.

Wu, C.-K., Chien, T.-F., Yang, H.-C., Cheng, C.-M., & Luo, C.-H. (2011). A Low Profile Dual Band Antenna for Implanted ZigBee Based Biosensors. In *2011 International Conference on Intelligent Computation and Bio-Medical*

Instrumentation (ICBMI) (pp. 253–255). http://doi.org/10.1109/ICBMI.2011.27

Wu, P. J., Dai, Y. T., Kao, H. L., Chang, C. H., & Lou, M. F. (2015). Access site complications following transfemoral coronary procedures: comparison between traditional compression and angioseal vascular closure devices for haemostasis. *BMC cardiovascular disorders, 15*(1), 34. http://doi.org/10.1186/s12872-015-0022-4

Yamashita, K., Izumi, S., Nakano, M., Fujii, T., Konishi, T., Kawaguchi, H., … Yoshimoto, M. (2013). A 38 #x03BC;A wearable biosignal monitoring system with near field communication. In *New Circuits and Systems Conference (NEWCAS), 2013 IEEE 11th International* (pp. 1–4). http://doi.org/10.1109/NEWCAS.2013.6573637

You, X., & Pak, J. J. (2013). Silk stabilized graphene FET enzymatic glucose biosensor. In *2013 Transducers Eurosensors XXVII: The 17th International Conference on Solid-State Sensors, Actuators and Microsystems (TRANSDUCERS EUROSENSORS XXVII)* (pp. 2443–2446). http://doi.org/10.1109/Transducers.2013.6627300

Zhang, Y., Shakhsheer, Y., Barth, A. T., Powell Jr, H. C., Ridenour, S. A., Hanson, M. A., ... & Calhoun, B. H. (2011). Energy efficient design for body sensor nodes. *Journal of Low Power Electronics and Applications, 1*(1), 109-130. http://doi.org/10.3390/jlpea1010109

Appendix A: Biosensor / Biosignal Processing Prototype with external LED Code

```
// Prototype biosensor / biosignal processing element with LED
// Grove touch sensor is connected to Grove shield position D3
// LED is connected to Grove shield position D7

// Define the pins that the touch sensor and LED are connected
const int pinSensor = 3;
const int pinLed    = 7;

void setup()
{
    // Set the baud rate to 9600 for serial data transmission
    Serial1.begin(9600);
    // Configure the button's pin for input signals
    pinMode(pinSensor, INPUT);
    // Configure the LED's pin for output
    pinMode(pinLed, OUTPUT);
}

void loop()
{
    // If touch sensor is pressed
    if(digitalRead(pinSensor))
    {
        // Turn the LED on and print 'H' to serial port
        digitalWrite(pinLed, HIGH);
        Serial1.print('H');
        // Delay for 5 seconds
        delay(5000);
    }
    else
    {
        // Else turn the LED off
        digitalWrite(pinLed, LOW);
    }
}
```

Appendix B: Biosensor / Biosignal Processing Prototype without external LED Code

```
// Prototype biosensor / biosignal processing element
// Grove touch sensor is connected to Grove shield position D3

// Define the pin that the touch sensor is connected to
const int pinSensor = 3;

void setup()
{
    // Set the baud rate to 9600 for serial data transmission
    Serial1.begin(9600);
    // Configure the button's pin for input signals
    pinMode(pinSensor, INPUT);
}

void loop()
{
    // If touch sensor is pressed
    if(digitalRead(pinSensor))
    {
        // Print 'H' to serial port
        Serial1.print('H');
        // Delay for 5 seconds
        delay(5000);
    }
}
```

Appendix C: External Base Station Prototype Code

```
// Base station prototype

// Include library files
#include <Wire.h>
#include "rgb_lcd.h"

// Declare LCD
rgb_lcd lcd;

// Initally set LCD colours to 0
const int colorR = 0;
const int colorG = 0;
const int colorB = 0;
const int colorOff = 0;
// Declare integer variable
int incomingByte;

void setup()
{
    // Set the baud rate to 9600 for serial data transmission
    Serial1.begin(9600);
}

void loop()
{
  // If serial data is available
  if (Serial1.available() > 0) {
    // Read the oldest byte in the serial buffer
    incomingByte = Serial1.read();
    // if it's a capital H (ASCII 72)
    if (incomingByte == 'H') {
    // Set up the LCD's number of columns and rows
    lcd.begin(5, 1);
    // Set LCD to RED
    const int colorR = 255;
    lcd.setRGB(colorR, colorG, colorB);
    // Set message position on LCD
    lcd.setCursor(0, 0);
    // Print 'Alert' message to the LCD.
    lcd.print("Alert");
    // Delay for 4.9 seconds
    delay(4900);
    // Clear the message from the screen
    lcd.clear();
    // Turn off the LCD
    lcd.setRGB(colorOff, colorG, colorB);
    }
  }
}
```

Appendix D: Biosensor / Biosignal Processing Prototype with Communication Check Code

```
// Prototype biosensor / biosignal processing element with communicat
ion check
// Grove touch sensor is connected to Grove shield position D3

// Define the pin that the touch sensor is connected to
const int pinButton = 3;

// Declare integer variable
int incomingByte;

void setup()
{
  // Set the baud rate to 9600 for serial data transmission
  Serial1.begin(9600);
  // Configure the button's pin for input signals
  pinMode(pinButton, INPUT);
}

void loop()
{
  // If touch sensor is pressed
  if (digitalRead(pinButton))
  {
    // Print 'H' to serial port
    Serial1.print('H');
    // Delay for 5 seconds
    delay(5000);
  }
  if (Serial1.available() > 0) {
    // Read the oldest byte in the serial buffer
    incomingByte = Serial1.read();
    // if it's a capital A (ASCII 72)
    if (incomingByte == 'A') {
      // Print 'B' to serial port
      Serial1.print('B');
    }
  }
}
```

Appendix E: External Base Station Prototype with Communication Check Code

```
// Base station prototype with communication check

// Include library files
#include <Wire.h>
#include "rgb_lcd.h"

// Declare LCD
rgb_lcd lcd;

// Initally set LCD colours to 0
const int colorR = 0;
const int colorG = 0;
const int colorB = 0;
const int colorOff = 0;
// Declare integer variable
int incomingByte;

void setup()
{
  // Set the baud rate to 9600 for serial data transmission
  Serial1.begin(9600);
}

void loop()
{
  // If serial data is available
  if (Serial1.available() > 0) {
    // Read the oldest byte in the serial buffer
    incomingByte = Serial1.read();
    // if it's a capital H (ASCII 72)
    if (incomingByte == 'H') {
      // Set up the LCD's number of columns and rows
      lcd.begin(5, 1);
      // Set LCD to RED
      const int colorR = 255;
      lcd.setRGB(colorR, colorG, colorB);
      // Set message position on LCD
      lcd.setCursor(0, 0);
      // Print 'Alert' message to the LCD.
      lcd.print("Alert");
      // Delay for 4.9 seconds
      delay(4900);
      // Clear the message from the screen
      lcd.clear();
      // Turn off the LCD
      lcd.setRGB(colorOff, colorG, colorB);
    }
  }
  // Print 'A' to serial port
  Serial1.print('A');
  delay(500);
  // Read the oldest byte in the serial buffer
  incomingByte = Serial1.read();
  // if it's a capital B (ASCII 72)
  if (incomingByte == 'B') {
```

```
    // Do nothing, communication is ok
  }
  else {
    // Set up the LCD's number of columns and rows
    lcd.begin(16, 2);
    // Set LCD to BLUE
    const int colorB = 255;
    lcd.setRGB(colorR, colorG, colorB);
    // Set message position on LCD
    lcd.setCursor(0, 0);
    // Print 'Communication failure' message to the LCD.
    lcd.print("Communication");
    lcd.setCursor(0, 1);
    // Print 'Alert' message to the LCD.
    lcd.print("lost with sensor");
    // Delay for 5 seconds
    delay(5000);
    // Clear the message from the screen
    lcd.clear();
    // Turn off the LCD
    lcd.setRGB(colorR, colorG, colorOff);
  }
}
```