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The design and evaluation of discrete wearable medical devices for vital signs monitoring

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Abstract

The observation, recording and appraisal of an individual's vital signs, namely temperature, heart rate, blood pressure, respiratory rate and blood oxygen saturation (SpO_2), are key components in the assessment of their health and wellbeing. Measurements provide valuable diagnostic data, facilitating clinical diagnosis, management and monitoring. Respiratory rate sensing is perhaps the most under-utilised of all the vital signs, being routinely assessed by observation or estimated algorithmically from respiratory-induced beat-to-beat variation in heart rate. Moreover there is an unmet need for wearable devices that can measure all or most of the vital signs. This project therefore aims to a) develop a device that can measure respiratory rate and b) develop a wearable device that can measure all or most of the vital signs.

An accelerometer-based clavicular respiratory motion sensor was developed and compared with a similar thoracic motion sensor and reference using exhalatory flow. Pilot study results established that the clavicle sensor accurately tracked the reference in monitoring respiratory rate and outperformed the thoracic device.

An Ear-worn Patient Monitoring System (EPMS) was also developed, providing a discrete telemonitoring device capable of rapidly measuring tympanic temperature, heart rate, SpO_2 and activity level. The results of a comparative pilot study against reference instruments revealed that heart rate matched the reference for accuracy, while temperature under read (< 1°C) and SpO_2 was inconsistent with poor correlation.

In conclusion, both of the prototype devices require further development. The respiratory sensor would benefit from product engineering and larger scale testing to fully exploit the technology, but could find use in both hospital and community-based

monitoring. The EPMS has potential for clinical and community use, having demonstrated its capability of rapidly capturing and wirelessly transmitting vital signs readings. Further development is nevertheless required to improve the thermometer probe and resolve outstanding issues with SpO_2 readings.

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The last six years have been an experience and a challenge. This now weary author started this journey as an engineer with a passing interest in health technologies and now ends it as biomedical engineer and scientist, having had the opportunity to pass on some of the acquired knowledge to others in the laboratory, lectures, seminars and journals. For this I must humbly express my lasting gratitude.

Before thanking others, first comes regret: I dearly wish that my late mother and father had lived to see this work come to fruition and were able to experience the joy I feel in completing this work. I must hand that baton onto my sister Chris, Sean and my two nephews, Ellis and Ethan.

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Contents

Appendices

Appendix A - 1: EPMS v1 Ear Module Processor Board Schematic

Appendix A - 2: EPMS v1 Ear Module Analogue Board Schematic

Appendix A - 3: EPMS v1 Auxiliary Module Processor Board Schematic

Appendix A - 4: EPMS v1 Auxiliary Module Interface Board Schematic

Appendix A - 5: EPMS v1 Adapter Board Schematic

Appendix B - 1: EPMS v2 Ear Module Processor Board Schematic

Appendix B - 2: EPMS v2 Ear Module Pulse Oximeter Schematic

Appendix B - 3: EPMS v2 Ear Module Skin Resistance and Power Supply Schematic

Appendix B - 4: EPMS v2 Ear Module Bluetooth Board Schematic

Appendix C - 1: EPMS v3 Ear Module Processor and Digital Schematics

Appendix C - 2: EPMS v3 Ear Module Pulse Oximeter Schematic

Appendix C - 3: EPMS v3 Ear Module Skin Resistance and Power Supply Schematic

Appendix C - 4: EPMS v3 Ear Module Bluetooth Board Schematic

Appendix D - 1: EPMS v4 Ear Module Analogue Circuit Schematic

Appendix D - 2: EPMS v4 Ear Module Analogue Circuit Schematic

Appendix E – 1: Ethics Application for the Clavicular Respiratory Sensing Study

Appendix F– 1: Ethics Application for the EPMS Study

Appendix G – 1: Heart Rate Plots from the EPMS Pilot Study

Figures

Tables

Equations

Publications

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The Challenges to Integrating Care via Telehealthcare Device Usage across the Spectrum of End-User Needs. Royal Society of Medicine Conference: Integrated care - how can technology help? Royal Society of Medicine, London, UK.

Glossary

Body Mass Index	Weight in kg, divided by height in metres squared (mass/height^2)
Elderly	Over sixty-five years of age
Morbidity	(i) Displaying disease, infection, or symptoms thereof (ii) The incidence or rate of sickness in a population
Mortality	(i) Subject or susceptibility to death (ii) The incidence or rate of death in a population
Oldest old	Over eighty-five years of age

Abbreviations

ADC	Analogue to digital converter
ADLs	Activities of daily life
AF	Atrial fibrillation
BLE	Bluetooth Low Energy, also known as Bluetooth Smart/v4
BMI	Body Mass Index -
BP	Blood pressure
bpm	Beats per minute (if referring to heart rate)
bpm	Breaths per minute (if referring to respiratory rate)
CAP	Community acquired pneumonia
CAUTI	Catheter-acquired urinary tract infection
CHD	Chronic heart disease
CHF	Congestive heart failure
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
COTS	Commercial off the shelf
CRS	Clavicular respiratory sensor
CT scan	Computed tomography scan
CUHREC	Cranfield University Health Research Ethics Committee
CVD	Cardiovascular disease
DAC	Digital to analogue converter
DBP	Diastolic blood pressure
DSP	Digital signal processing
ECG	Electrocardiography
EEG	Electroencephalography, measurement of the brain's electrical activity
ED	Emergency department
EDR	ECG-derived respiration
emi	Electromagnetic interference
EPMS	Ear-worn personal monitoring system
EWS	Early warning scoring (system)

F	Farads
FUO	Fever of unknown origin
GI	Gastrointestinal
GPIO	General purpose input/output
HAP	Hospital acquired pneumonia
HF	Heart failure
HR	Heart rate
HRV	Heart rate variability
Hz	Hertz (frequency in cycles per second)
HZ	Herpes Zoster
I or i	Electrical current
ICT	Information and communications technology
I/O	Input/output
LED	Light emitting diode
LRTI	Lower respiratory tract infection
LTC	Long term care
MEMS	Micro-electromechanical systems
NHAP	Nursing-home acquired pneumonia
NHS	National Health Service (UK)
PAD	Peripheral artery diease
pcb	Printed circuit board
PPG	Photoplethysmograph
QoL	Quality of life
R	Electrical resistance
RR	Respiratory rate
RSA	Respiratory Sinus Arrhythmia
SaO_2	Blood oxygen concentration
SBP	Systolic blood pressure
SNR	Signal to noise ratio
SpO_2	Blood oxygen concentration measured via pulse oximetry
SR	Skin resistance

SSI	Surgical site infection
TIA	Transient ischemic attack
TRS	Thoracic respiratory sensor
V	Volts
VS	Vital signs
UTI	Urinary tract infection
Z	Electrical impedance

1. Introduction and Literature Review

The research reported in this thesis was inspired by a series of conversations with senior medical professionals, including leading consultants and researchers, who expressed an interest in technologies facilitating the collection of vital signs readings from outpatients and vulnerable individuals in the community, potentially by non-clinical staff or the patients themselves. The remote recording of routine observations, normally taken by hospital-based nursing staff, would greatly assist in timely intervention for improved patient care. To meet this unmet need, a requirement was identified for the provision of a wearable monitoring device that could rapidly and simultaneously capture multiple parameter readings with minimal fuss. With no suitable commercial option available, research into vital signs monitoring and the development of a prototype device was initiated.

This chapter reviews the literature to establish an understanding of medical physiological monitoring and its application, and comprises of sections discussing the vital signs, the clinical aspects of illness, vital signs monitors and telehealthcare. The vital signs (VS) are first defined and examined to uncover the range of normal resting readings in the general adult population and the significance of abnormal readings. Common diseases, infections, their symptoms and the impact of these ailments on morbidity and mortality are then reviewed, providing context for VS monitoring, which is considered next. This looks at a range of commercially available monitors, their application in patient care and considers recent developments in telehealthcare for remote VS monitoring.

The findings from the conclusion of the review helped to frame the aims and objectives that define the work performed and reported in this thesis.

1.1. The Vital Signs

It has been established since ancient times (reviewed by Stewart, 2003) that the observation and assessment of changes in a patient's condition is of great clinical value and can protect them from harm (Ahrens, 2008; Rogers et al., 2008). Vital signs (VS) are a range of physiological measures, ideally taken at regular intervals, that form a key component in monitoring patient's condition (Evans et al., 2001).

The traditional vital signs are temperature, blood pressure (BP), pulse or heart rate (HR) and respiratory rate (RR) which are now well understood and accepted. The relationship between simultaneous measures was first noted and reported by Hunter in 1794 (pulse and temperature). This was followed by further work relating HR, RR and temperature by Cheyne (1818) and Donne (1835). The term 'vital signs' itself originates from an article published in the *Chicago Medical Journal* (1866) by Edward Seguin and William Draper (reviewed by Stewart, 2003).

A number of parameters have been suggested as additional vital signs. Blood oxygen saturation (SaO_2) has been widely accepted as the fifth vital sign; pulse oximetry, a non-invasive method of measuring both pulse rate and blood oxygen saturation, is now routinely used for monitoring the condition of the patient (Tierney Jr et al., 1997; Neff, 1988). In addition to pulse oximetry, Ahrens suggests that capnography (for respiratory and ventilation monitoring) and stroke volume (for heart evaluation) are superior to the traditional measures for rapid clinical assessment

(Ahrens, 2008). Pain and discomfort (Morita et al., 2008), emotional distress (Bultz and Carlson, 2006) and shock index (Zarzaur et al., 2008) have all been proposed for consideration as additional vital signs indicators. Elliott and Coventry propose eight vital signs, adding pain, urine output and level of consciousness to the accepted five, for adequate identification of a deteriorating patient (Elliott and Coventry, 2012). The Glasgow Coma Scale (GCS) is a popular method of assessing an individual's level of consciousness; this scores their optical, auditory, verbal and motor responses to stimuli, giving a standardised classification (Teasdale and Jennett, 1974). The AVPU scale (alert, verbal, painful or unresponsive) fulfils a similar function, facilitating rapid assessment (Kelly et al., 2004). With the exception of the five accepted vital signs, capnography and urine output however, these additional factors cannot be easily quantified via physiological sensors, instead relying largely on observation and introducing subjectivity.

1.1.1 Temperature

The first recorded reference to the importance of body temperature to wellbeing dates ancient Greece (4th century BC) where a high temperature may be portent of disease (reviewed by Pearce, 2002). It would be the early part of the 18th century before Boerhaave, de Haen and Van Swieten started to measure patient's temperatures at the bedside with Fahrenheit's thermometer (reviewed by Stewart, 2003). De Haen observed diurnal variation in healthy patients and that temperature monitoring could help track the progression of an infection. It was Wunderlich's study (1868) of a million readings from the axilla of 25,000 subjects that helped establish a

normal temperature range (36.3 – 37.7°C) for healthy individuals (reviewed by Pearce, 2002.

Environmental effects aside (see *pages 8-9*) there are several factors which influence core body temperature. These include gender, body mass index (BMI), frailty, ADL status and dementia, all of which may indicate a lower core temperature, and the higher temperatures associated with those who are regular users of analgesics (Sund-Levander and Wahren, 2002). Because of these factors and differences in thermoregulation there is both intra- and inter-individual variation in the core body temperature of older people (Güneş and Zaybak, 2008). As there is a temperature gradient of approximately 1°C for every 4 mm of depth between the body surface and the core (Sund-Levander and Grodzinsky, 2009), which is at its warmest in the abdomen, chest and brain, the measurement site is a huge factor in determining both normal and pyrexic values. For diagnostic purposes, an individual's temperature should ideally be evaluated relative to their normal baseline readings taken at a consistent measurement site (Sund-Levander and Grodzinsky, 2009).

Rectal thermometry is considered to be the gold standard in body temperature measurement (Varney et al., 2002) as it provides the closest approximation to true core body temperature. Despite the reported accuracy of rectal measurement, it is clearly not practical in many cases (such as the monitoring device proposed here) and thus other measurement sites must be considered. There is a long tradition of sublingual (oral) temperature measurement, although axillary (armpit), temporal (forehead) and tympanic (ear canal) sensing have gained in popularity.

In comparing oral and axillary measurement in the elderly, oral thermometry was found to offer a more reliable rectal surrogate (Downton et al., 1987). There are number of studies comparing oral and tympanic methods for febrile measurement with some favouring tympanic (Dzarr et al., 2009) and others oral thermometry (Lu et al., 2009). The latter is not without its faults - firstly it requires a compliant patient and secondly, there is the possibility of interference from mouth breathing or the prior ingestion of hot or cold food and drink (Norman, 2000). Additionally there is the suggestion that due to "*the vasoconstriction that accompanies fever*" (Darowski et al., 1991b) and increase in respiratory frequency (Berman and Fox, 1985) oral thermometry may be a less effective febrile detection method; whether this is restricted to respiratory tract infections is not clear.

A study by Dzarr suggests that tympanic thermometry is second only to rectal measurement for fever detection (Dzarr et al., 2009). It is certainly the quickest and most convenient method of body temperature measurement; ease of use is a key factor too as this reduces the probability of operator error. Studies have shown that used correctly (Evans and Kenkre, 2006), a repeatability of ±0.1°C is achievable (Childs et al., 1999). Childs describes best practice is to always use the same ear for measurements as there can be an inter-ear difference of as much as 0.6°C (Childs et al., 1999). Foot temperatures are sometimes monitored, but circulatory problems may limit its potential diagnostic value (Raymann et al., 2007). Axillary and temporal skin temperatures are sometimes used clinically. The former has been identified as relatively ineffective (compared with the methods previously discussed) in fever

detection, while the latter is reported to have a poor predictive capability (Hausfater et al., 2008).

The results of comparative studies, examples from which are shown in *Table 1-1 to Table 1-4*, display clear deviations in both mean and range between the gold standard and alternative measurement sites. These demonstrate that the often quoted 37°C standard is perhaps inappropriate for measures other than core body temperature and relative adjustments should be considered for other measurement sites, which are typically cooler than rectal temperatures. Jensen's comparative study (n = 200, 102 male ,98 females, age range of 18 -93, mean = 56 years old) in *Table 1-1* shows mean differences of –0.62°C (axillary), –0.53°C (sublingual) and –0.34°C (the mean of three tympanic thermometers) to rectal mercury thermometer (Jensen et al., 2000).

	Mean	SD	Range	Mean Difference	SD of difference
Tympanic Core Check	36.92	0.63	35.4 - 39.5	0.54	0.41
Tympanic Diateck	37.17	0.76	34.5 - 39.5	0.29	0.51
Tympanic Genius	37.27	0.68	35.4 39.6	0.19	0.45
Oral Terumo digital	36.93	0.7	34.5 - 39.4	0.53	0.53
Axillary Terumo digital	36.84	0.74	35.0 - 39.2	0.62	0.49
Rectal Terumo digital	37.51	0.57	36.5 - 39.6	-0.05	0.12
Standard Rectal mercury	37.46	0.56	36.4 - 39.5	-	-

(Jensen et al., 2000)

Table 1-1: Temperatures (°C) measured by various medical thermometers - mean differences are measured relative to the standard rectal mercury thermometer's mean

The same trend is apparent in older people; the results of Darowski's study on afebrile patients (n=50) shown in *Table 1-2* again illustrates the variation in range and

mean readings at different measurement sites. Here differences in the mean results of –0.9°C (axillary), –0.6°C (sublingual) and –0.4°C (tympanic) were observed relative to rectal measurement (Darowski et al., 1991b). These results are in broad agreement with Jensen's and may be explained by the relative blood flow, blood temperature and level of cooling in each locality.

Measurement Site	Body Temperature (°C)		
	Range	Mean	Mean ± 2SD
Rectal	36.7 – 37.5	37.2	36.8 – 37.6
Auditory Canal	36.5 – 37.2	36.8	36.5 – 37.1
Sublingual	35.6 – 37.0	36.6	36.1 – 37.2
Axillary	35.5 – 37.0	36.3	35.5 – 37.0

(Darowski et al., 1991b)

Table 1-2: A comparison of temperature measurement sites in fifty elderly afebrile patients.

With regard to the temperatures of febrile patients, Jensen's study also included comparable measurements (n=85) (Jensen et al., 2000). As with the afebrile group, mean differences of –0.64°C (axillary), –0.62°C (sublingual) and –0.38°C (the mean of three tympanic thermometers) were observed compared to rectal mercury thermometer (*Table 1-3*). A further study by Darowski et al investigated the efficacy of different measurement sites in their ability to accurately detect fever in an elderly cohort (n=74) of hospital inpatients who would be considered to have temperatures within the normal range (Darowski et al., 1991a). The results, expressed as percentages, are shown in *Table 1-4*. The temperature thresholds chosen are as suggested in an earlier study (Darowski et al., 1991b) and based upon observation and experimental data. Participants were classified according to their clinical presentations of infection – definite (13), probable (12), possible (32) or no clinical evidence of

infection (17). The findings show that rectal and tympanic are superior to sublingual and axillary in diagnosing fever in a single reading. A mean rectal temperature of 37.5°C was observed in 86% of participants; hence Darowski et al suggest a lower mark of 0.5°C above the notional 37°C norm as a better indicator of fever in the elderly.

Standard compared with:	Mean	SD	Range
Tympanic Core Check	0.64	0.38	-0.2 to 1.7
Tympanic Diateck	0.27	0.49	-0.6 to 1.5
Tympanic Genius	0.24	0.46	-0.8 to 1.8
Oral Terumo digital	0.62	0.61	-0.3 to 2.9
Axillary Terumo digital	0.64	0.48	-0.2 to 2.4
Rectal Terumo digital	-0.05	0.12	-0.3 to 0.4

(Jensen et al., 2000)

Table 1-3: The recorded temperature differences (°C) observed in a range of digital thermometers versus a standard rectal mercury thermometer in febrile patients (n=85)

Infection	Febrile at one or more sites	Rectal > 37.5°C	Tympanic > 37.2°C	Sublingual > 37.0°C	Axillary > 37.0°C
Definite	100	92	92	58	17
Probable	100	80	93	73	14
Possible	81	69	72	47	31
No clinical evidence	71	60	40	47	25
Total	**85**	**73**	**73**	**55**	**25**

(Darowski et al., 1991a

Table 1-4: The percentages of patients regarded as febrile categorised by measurement site from a study on elderly individuals (n=74)

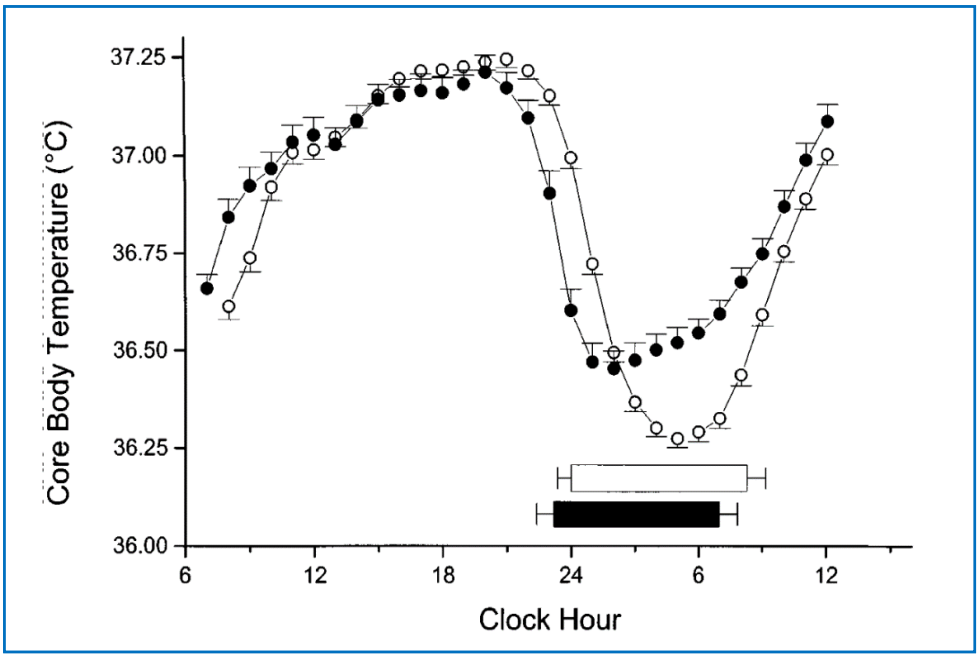
Environmental effects can influence temperature measurement. At a basic level, measurements should ideally not be taken with the subject in a particularly hot, cold

or draughty environment, and the sensor should be allowed to equilibrate in-situ for a short length of time. It should be noted that the patient's measurements taken in Darowski's initial study (Darowski et al., 1991b) followed a twenty-four hour period in a hospital ward at 21-26°C. In a colder environment the readings are likely to be lower, showing a greater deviation from core temperature. Thus when considering body temperatures, however measured, a comparative reading of the ambient temperature should be made as a reference.

Circadian Rhythm and Temperature

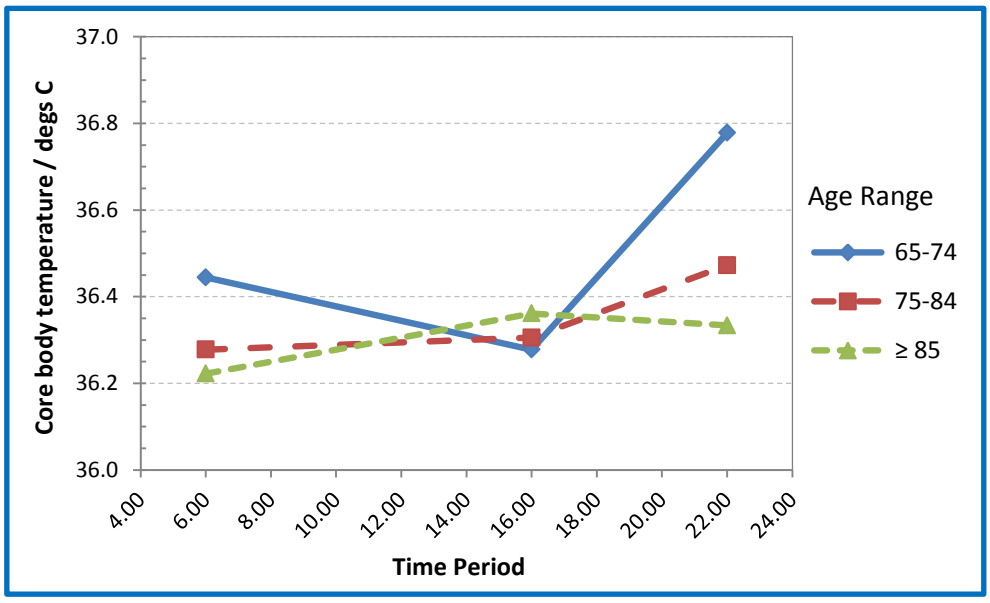
Circadian rhythm is a natural physiological phenomenon involving rhythmic temporal changes in core body temperature every twenty-four hours; thus measurements made in the morning will differ from those made later in the day. When considering the detection of a fever, measurements should, ideally, be referenced to the subject's normal circadian temperature. In healthy adults, the Oxford Handbook of Clinical Medicine quotes a mean daily amplitude variation of 0.5°C, with a minima at 6 am and peaking at 6 pm (Longmore et al., 2009).

In the elderly there is a distinct change in this cycle, which has decreased amplitude and is less stable (Van Someren et al., 2002; Gomolin et al., 2007); this is illustrated in *Figure 1-1* and *Figure 1-2*. The relative difference in the core circadian temperatures of older people (aged 64-81, n =43) to young adults (aged 18 to 30, n=97) are shown in *Figure 1 1*; here a phase difference is apparent between the two groups with the nadir being both earlier and 0.25°C higher in the elderly cohort (Duffy et al., 1998).



(Duffy et al., 1998)

Figure 1-1: The mean recorded core body temperatures (°C) plotted with respect to time for young and older subjects: ● - Older subjects (n=43); ○ - young subjects (n=97).



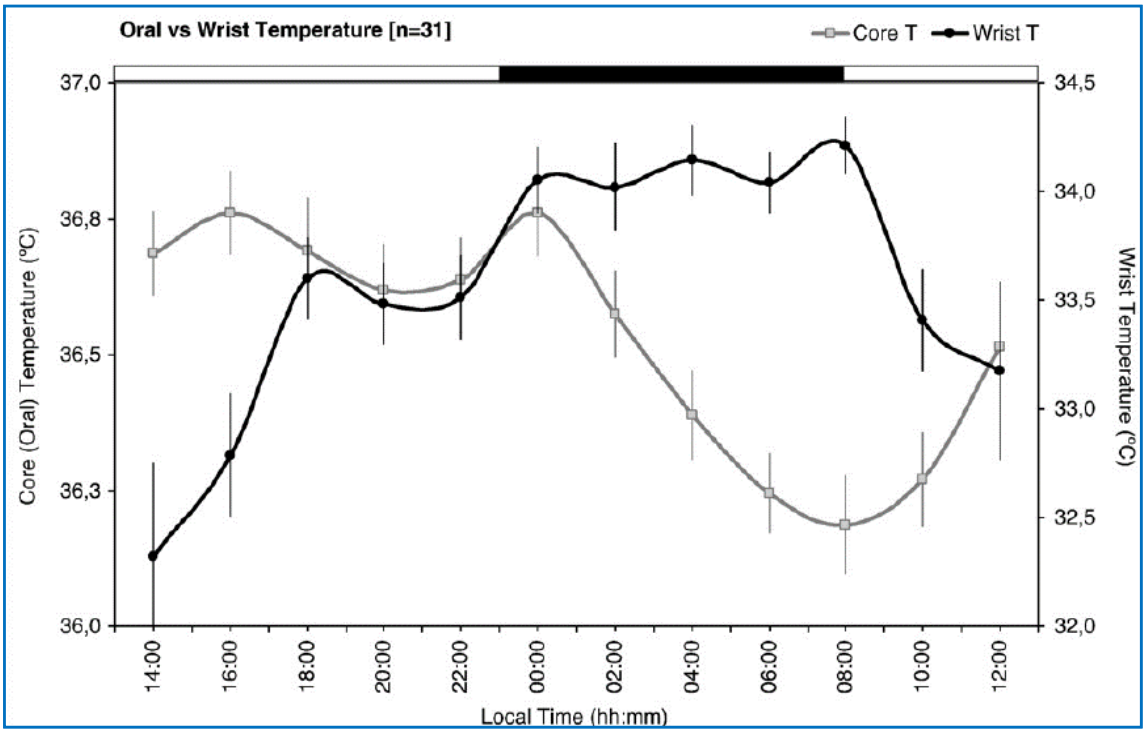
(Gomolin et al., 2005)

Figure 1-2: A graph showing the circadian temperature variation in elderly people

Gomolin's study (Gomolin et al., 2005) found intra-age group variance in the daily temperatures of elderly nursing home residents (n=100) under controlled conditions.

Oral temperatures were taken at 6 am, 4 pm and 10 pm in three groups comprising of participants of 65 to 74, 75 to 84 and over 85 years of age; the results, shown in *Figure 1-2*, demonstrate three times the variation in youngest (0.9°F /0.5°C) to oldest groups (0.3°F /0.17°C) in mean amplitude difference and an opposite trend.

When looking at rectal surrogate measurement sites, direct comparisons are likely to prove difficult due to thermoregulatory, circadian and ambient temperature effects. This is illustrated in *Figure 1-3* by the difference between daily oral and wrist temperatures (Sarabia et al., 2008) where wrist temperatures (taken with a semiconductor sensor placed over the radial artery) are noticeably cooler, have a greater range and a cycle that is almost in anti-phase with reference oral readings.



(Sarabia et al., 2008)

Figure 1-3: The mean daily variation in a study cohort of wrist and oral temperatures

As there is an overlap in the circadian temperature range of up to 0.8˚C (Kräuchi, 2002) and the 1.0˚C rise above the norm indicative of fever, the combined effect must be considered. In conclusion, measurements referenced to the circadian cycle or taken at the same time each day, environmental conditions permitting, should result in an improvement in the determination of fever and reduce false positive outcomes.

1.1.2 Heart Rate

The frequency of the beating heart has long been noted as one of the key vital signs. There is evidence of its diagnostic use in ancient times (BC) by Chinese, Indian, Egyptian and Greek physicians (reviewed by Ghasemzadeh and Zafari, 2011), where an escalating pulse had precedence over temperature as a harbinger of fever (Pearce, 2002). The introduction of watches with a second-hand in the late 17th century allowed accurate pulse rate measurement, in turn driving a demand for suitably equipped watches (reviewed by Stewart, 2003).

Pulse, or pulse rate, is often used synonymously with HR (as in this thesis), but is, strictly speaking, a pulsatile manifestation of arterial blood circulation resulting from heartbeat, with pulse strength and regularity being additional health indicators.

The normal heart rate in adults ranges from 60 to 100 beats per minute (bpm) (Longmore et al., 2009). Mean HR in neonates it is much higher (130 bpm), falling to just below 100 bpm aged 5 years and 85 bpm aged 10, until plateauing at around 70 bpm when at the age of 18 (Fleming et al., 2011). In healthy younger adults HR is typically between 60 and 80 bpm with a resting subject, the frequency diminishing linearly with age at a rate of −0.126 bpm per year (Erikssen and Rodahl, 1979). A

resting HR of below 60 bpm is known as *bradycardia* while that exceeding 100 bpm is referred to as *tachycardia* (Palatini, 1999).

A simple formula (*Equation 1-1*) is often given for calculating maximal heart rate (HR_{max}). Its accuracy is disputed as the sample population in the originating study were aged 65 or less, Tanaka offers instead an alternative formula (*Equation 1-2*) (Tanaka et al., 2001).

Equation 1-1: Maximal HR formula

$$HRmax = 220 - Age$$

Equation 1-2: Tanaka's alternative formula for HRmax

$$HRmax = 208 - (0.7 \times Age\ )$$

Whichever meter is used, many hospitalised febrile individuals are often tachycardic (Marco et al., 1995), which may take them close to a twenty percent safety margin of HR_{max}. This is a noted risk factor in increased HR for coronary heart disease and mortality in middle-aged male subjects (Dyer et al., 1980) and in elderly males, where a heart rate of 81 to 120 bpm is strong predictor of cardiovascular mortality (Palatini et al., 1999).

Before examining how HR may be used diagnostically, it is important to note that there are numerous factors that may determine an individual's reading. In addition to age, these include ethnicity, the circadian cycle, posture, blood pressure, lifestyle factors (such as diet, drinking alcohol and smoking), physical activity, physical fitness, body mass index (BMI), anxiety and mental stress (Valentini and Parati, 2009).

The rise in febrile pulse rate is variously ascribed to be in the order of a 14.4 to 18.0 bpm/deg C (Lyon, 1927) and 8.5 bpm/deg C (Karjalainen and Viitasalo, 1986) rise above basal temperature in otherwise healthy adults, to a difference of 8.8 to 21.6 bpm/deg C between normal and febrile readings (Weinberg et al., 1989). Studies suggest that this is in fact temperature dependent, ranging from 2.9 bpm/deg C if below 39°C and 6.5 bpm/deg C above this threshold (Kiekkas et al., 2007). The range between these figures is quite high and whilst other data is evident, there have not been a significant number of studies in this area. It is possible that factors such as medication, stress or heart rate variability (Stein et al., 1997) are partly responsible. In elderly patients an HR >90 bpm is a strong indicator of infection, especially when combined with a febrile temperature (Pines et al., 2006).

To summarise, resting HR measurement can aid in the diagnosis of coronary heart disease and may be regarded as a measure of cardiovascular wellbeing. It may also assist in the determination of febrile infection, especially in atypical presentations where febrile temperatures are absent.

1.1.3 Blood Pressure

This may be defined as a measure of the pulsatile pressure exerted on the arterial walls by circulatory blood flow (Stroke Association, 2012). Peak, or systolic blood pressure (SBP) occurs as the heart contracts at the end of the cardiac cycle, while the nadir, or diastolic pressure (DBP) arises at the start of the cardiac cycle as the heart relaxes once more. Each measurement therefore consists of a pair of readings and is normally quoted as SBP / DBP (Hypertension Influence Team, 2002). The units used in

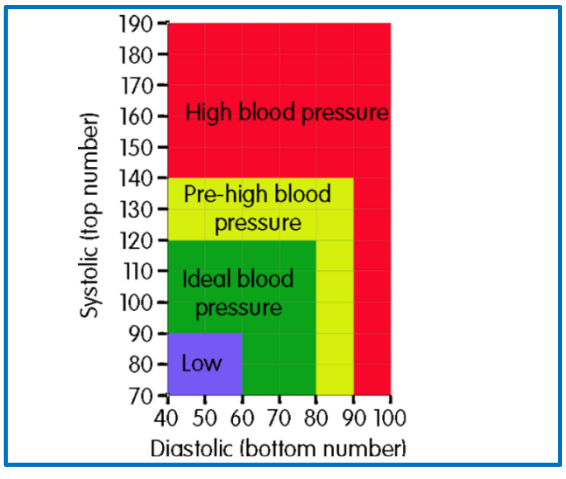
BP measurement, millimetres of mercury (mmHg), relate to pressure readings from a mercury manometer as used in traditional instruments. Though these might be considered archaic they are, nevertheless, retained for modern electronic monitors.

It was not until 1628 that William Harvey concluded that blood circulated around the body in a closed system and was powered by the heart. Blood pressure was first measured by Hales in 1733 after experimenting on a mare, he noted that pressure forced blood to rise nine and a half feet up a narrow glass tube connected to the carotid artery. The first non-invasive device measurement, the sphygmomanometer, was developed by von Basch in 1876, an improved design by Riva-Rocci appearing 20 years later (reviewed by Stewart, 2003).

Non-invasive BP measurement employs an inflatable cuff to temporarily impede arterial blood flow, the cuff pressure providing the two BP readings as air is gradually released and blood flow returns, giving a measurement relative to atmospheric pressure (Pickering et al., 2005). By convention the cuff is fitted to an arm (occluding the brachial artery once inflated) of a seated patient and positioned level with the heart. To ensure accurate BP readings they should be taken in a quiet and temperate environment once the subject has been seated for several minutes and is relaxed. A cuff of appropriate size should be fitted directly in contact with the subject's skin while their arm is relaxed and fist unclenched. Subjects should refrain from talking or crossing their legs while measurements are taken. Ideally readings should be taken consecutively from both arms minutes apart, the higher reading being recorded (Hypertension Influence Team, 2002; British Hypertension Society (BHSOC). 2006; Pickering et al., 2005).

It should be noted that BP readings taken from the arm in supine subjects result in lower DBP readings (around 5 mmHg). Supine readings taken from the thigh (or calf), as may be necessary in hospital, present an increased SBP while DBP may be lower (Kirkendall et al., 1967).

The normal healthy (*normotensive*) resting range of blood pressure in adults is 90/60 to 120/80. Those consistently below this mark are considered to have low BP (*hypotension*). Readings from 120/80 to 140/90 are deemed to be higher than ideal (*pre-hypertension*) while readings beyond 140/90 indicate high blood pressure, also known as *hypertension* (Blood Pressure UK, 2008). *Figure 1-4* shows a standard blood pressure chart of resting readings; in reality this provides a useful guide, but does not account for age and gender. Differences in normotensive BP may be observed between the sexes with males tending to have higher readings. There is also a noticeable increase in BP with age in both sexes as may be seen in *Table 1-5* (Landahl et al., 1986).



(Blood Pressure UK, 2008)

Figure 1-4: A chart showing the ranges and classifications for systolic and diastolic blood pressure

	Males			Females		
Age (years)	No.	SBP (mmHg)	DBP (mmHg)	No.	SBP (mmHg)	DBP (mmHg)
38	-	-	-	369	123±14.4	79±9.1
44	-	-	-	322	124±16.4	81±8.6
50	841	138±20.5	91±12.8	284	133±19.4	84±9.8
54	747	142±20.1	90±11.8	-	-	-
56	-	-	-	298	134±18.8	84±9.1
60	643	144±22.2	88±12.7	-	-	-
62	-	-	-	259	143±19.8	86±10.0
70	362	159±25.0	91±12.6	321	168±25.5	93±13.2
75	234	158±24.5	90±12.4	209	166±22.5	89±12.9
79	130	155±24.6	83±11.3	127	161±22.1	85±9.9

(Landahl et al., 1986)

Table 1-5: Systolic and diastolic blood pressure in adults without antihypertensive treatment – mean readings quoted as BP ± standard deviation

There may be wide deviations in BP over the course of a day. Diurnal variation sees resting readings reach their zenith mid-morning, falling overnight to a low at around 3 a.m. (White, 2007). In addition there are numerous factors that can influence BP; these include diet (Appel et al., 2006) and fitness; physical factors such as posture, activity and exercise; the intake of food ,drink, sodium salts, nicotine, caffeine and alcohol; medical factors such as disease, frailty and the taking of prescribed medication and psychosocial factors like anxiety and mental stress (Carels et al., 1998).

Hypertension is a risk factor for cardiovascular disease and is directly attributable for two-thirds of global stroke cases and half those of ischaemic heart disease (Lawes et al., 2006). Hypertension has two forms - essential hypertension, which accounts for the majority of cases and has no specific cause, and secondary hypertension, which is due to an existing medical condition (Hypertension Influence Team, 2002). Both are

typically asymptomatic and therefore may lie undetected unless BP readings are taken. Sufferers are at an increased risk of ischaemic strokes, where arteries may be blocked due to atherosclerosis (hardening and narrowing of the arteries), or haemorrhagic strokes, where ruptured vessels cause bleeding in the brain (Stroke Association, 2012)

Hypotension, or (abnormally) low blood pressure, can be a health risk. Although considered low compared to the population norm, it may be normal for some individuals and asymptomatic. For others it may lead to dizziness and fainting, which may exhibit when standing after sitting or lying down as the rate of change of circulatory blood flow is unable to match the change in posture (orthostatic hypotension). This may be caused by underlying medical conditions, such as heart disease or anaemia, dehydration, pregnancy, or medication prescribed for other conditions. Trauma-induced (or septic) shock can result in a particularly severe form of hypotension where pressure drops to a point where organ damage may occur, which can be fatal unless promptly treated (PubMed Health, 2014).

In summation, outside of trauma cases in emergency medicine, the greatest application for BP monitoring is in assessing and managing cardiovascular health. This has seen a greatly increased acceptance for home monitoring over the last decade (Parati et al., 2010) with the market well served by a number of manufacturers.

1.1.4 Respiration Rate

Respiration rate (RR), the frequency at which breath is inhaled and exhaled, is considered one of the key vital signs. It is regulated by the medulla in the brain which controls the inspiratory and expiratory muscles that expand and contract to maintain

rhythmic ventilation, ensuring an adequate supply of oxygen to fuel the body while removing carbon dioxide from the system (Braun, 1990).

The basics of respiration, the inspiration of air and its' passage via the lungs into the bloodstream, were understood by physicians in Ancient Greece as long ago as the 4th century BC. It was not until 1687 that this was proved by Hooke who shows that inspired air was essential to life and transformed venous blood to arterial. The discovery of oxygen (Priestley) and carbon dioxide (Black) led to increased interest and understanding of the respiratory system in the 19th century (reviewed by Stewart, 2003).

The normal range for healthy adults is considered to be between 12 and 20 breaths per minute when at rest – a breath every three to five seconds. Febrile infection in the elderly tends to show an increase in resting RR to more than 20 breaths per minute (Marco et al., 1995); a frequency also quoted as marker for sepsis (Nimmo et al., 2006). Rates in excess of 25 breaths per minute may be indicative of lower respiratory tract infections such as pneumonia (Mcfadden et al., 1982); here, the certainty of diagnosis of those presenting with these symptoms is greater if blood oxygen saturation falls below 90% (High et al., 2009).

Rapid breathing (*tachypnea*), which may be accompanied by breathlessness (*dyspnoea*), can be symptomatic of a range of cardiac or respiratory conditions (Janssens and Krause, 2004) such as acute respiratory failure (Ray et al., 2006), respiratory dysfunction in cystic fibrosis patients (Browning et al., 1990), pulmonary hypertension, chronic obstructive pulmonary disease (COPD), asthma (Tobin et al.,

1983) and a predictor of cardiopulmonary arrest if RR exceeds 27 bpm (Fieselmann et al., 1993). Shallow breathing in a recumbent patient (*orthopnoea*), where minimal thoracic movement and inspiratory and expiratory volumes of 250 to 350 mL are observed, could indicate an increase in pulmonary blood circulation (Haldane et al., 1919) and heart failure (Ekundayo et al., 2009).

As so many disparate diagnoses are possible from changes in an individual's breath frequency, it should probably not be considered in isolation but as part of a larger dataset comprising the other vital signs. False positives may result from psychological reactions (Boiten et al., 1994) although it could be argued that anxiety due to 'white coat syndrome' should be reduced if monitored outside a clinical environment.

Whilst monitored in hospital, RR is typically checked and recorded less frequently than the other traditional measures (Cretikos et al., 2008); this is, at least in part, due to a dearth of reliable automatic respiratory rate monitoring equipment (McBride et al., 2005).

1.1.5 Blood Oxygen Saturation

Oxygen from the lungs is absorbed into the bloodstream through small capillaries in the alveolar. Here it reacts with haemoglobin (Hb) in red blood cells to form oxyhaemoglobin (HbO), in which form it circulates around the body via the cardiovascular system until released to fuel metabolic processes. Blood oxygen saturation (SaO_2, commonly known as 'sats') is a measure of the amount of HbO present in the bloodstream or tissue. This is typically 95 to 100% in a healthy individual at rest, with readings of 85 to 94% indicating moderate to mild hypoxia and those

below 85%, severe hypoxia (DeMeulenaere, 2007). This condition may be defined as a deficiency of oxygen in tissue and is not to be confused with hypoxaemia, which refers specifically to low arterial blood oxygen saturation and may be due to environmental or clinical factors. Hypoxia may be as a result of hypoxaemia or unrelated, and even localised, such as in the case of vascular ischaemia where blood flow is impaired or impeded (Samuel and Franklin, 2008).

The measurement of SaO_2 is an invasive procedure involving the collection of a 2 to 3 mL specimen of arterial blood, which is then tested in the laboratory or introduced as a sample to an automated blood gas analyser (Trulock, 1990). A non-invasive proxy of SaO_2 may be conveniently taken using a pulse oximeter, which employs optical sensing to determine the ratio of HbO to total haemoglobin and provides a capability for continuous measurement. SaO_2 measurements taken with a pulse oximeter are known as SpO_2 readings (Philips Medical Systems, 2003)

Stimulated by the production of early photocells in the 1930s, Matthes introduced what might be recognised as the first (pulse) oximeter just before the outbreak of World War Two in Germany (reviewed by Severinghaus, 2007). Parallel research activities in England, Germany and the United States was driven by aviation medicine and the interest in high-altitude flight and pressurized cabins, as hypoxaemia was a frequent issue for pilots and aircrew (reviewed by Mendelson, 1992). Millikan, to whom the naming of the oximeter must be credited, developed a lightweight ear oximeter for use by pilots in 1942; this was then developed by Wood and Geraci, who overcame the requirement for individual calibration. Aoyagi's patent application

describing the design of an oximeter was first disclosed in 1974, the first commercial devices appearing in the 1980s (reviewed by Severinghaus, 2007).

In conclusion, modern pulse oximeters, offering pain-free and non-invasive measurement, have greatly facilitated the rapid assessment of blood oxygenation. Although the most recently accepted of the vital signs, SpO_2 measurement has been universally adopted in the care of critically ill patients (Jubran, 2015), recommended for primary care (Schermer et al., 2009) and the self-management of COPD (MacNab et al., 2015).

1.2 Disease and Infection

The threat of disease and infection to mortality and morbidity is next assessed, together with the symptoms that may aid detection, diagnosis and ultimately, the treatment of patients.

1.2.1 Disease

This might best be defined as an internal condition where the body's normal functional abilities are impaired, whether due to infectious agents, environmental factors (Emson, 1987) or inherited genes (Flint et al., 1993). Examples include many cardiovascular conditions, cancer, COPD, asthma and diabetes mellitus.

Cardiovascular Disease and Heart Conditions

Stemming from a narrowing and hardening of the arteries (atherosclerosis), cardiovascular disease (CVD) describes a family of related conditions with common risk factors. These include coronary heart disease (CHD), angina, hypertension, strokes and transient ischaemic attacks (TIAs, also known as mini strokes), diabetes mellitus,

chronic kidney disease, peripheral arterial disease (PAD) and vascular dementia, with sufferers of one condition being predisposed to develop one or more of the others (Department of Health, 2013). Atherosclerosis typically affects the great arteries supplying the heart (coronary artery), brain (carotid) and legs (peripheral) and is irreversible. It is caused by thickening plaque that lines the coronary and carotid arteries. This may break down or rupture, blocking an artery and stifling the flow of blood to the heart or brain and triggering a heart attack (CHD) or stroke respectively, which may damage or kill affected tissue in these organs and can be fatal (British Heart Foundation, 2014a).

Risk factors for atherosclerosis are many: age, gender, familial genetics, high SBP, high cholesterol levels, kidney disease, diabetes mellitus and lifestyle (poor diet, lack of exercise, obesity, smoking and excessive alcohol consumption), the latter of which may add to the risk burden unless behavioural change is successful (Rydén et al., 2007; Department of Health, 2013). It is asymptomatic, unless hypertension is apparent, and may go unnoticed until angina or claudication (pain from PAD - restricted blood flow to the legs) is diagnosed or the subject suffers a stroke or heart attack. The condition is irreversible, but may be treated with pharmaceuticals or a range of surgical procedures to reduce its effects. These involve angioplasty and the use of stents to widen arteries and thus improve blood flow or a coronary bypass using a healthy blood vessel (British Heart Foundation, 2014a).

In addition to CHD there are a range of other heart conditions. These include congenital heart disease (defects developed in the womb), inherited heart conditions (genetic abnormalities), heart failure (HF) and arrhythmias (British Heart Foundation,

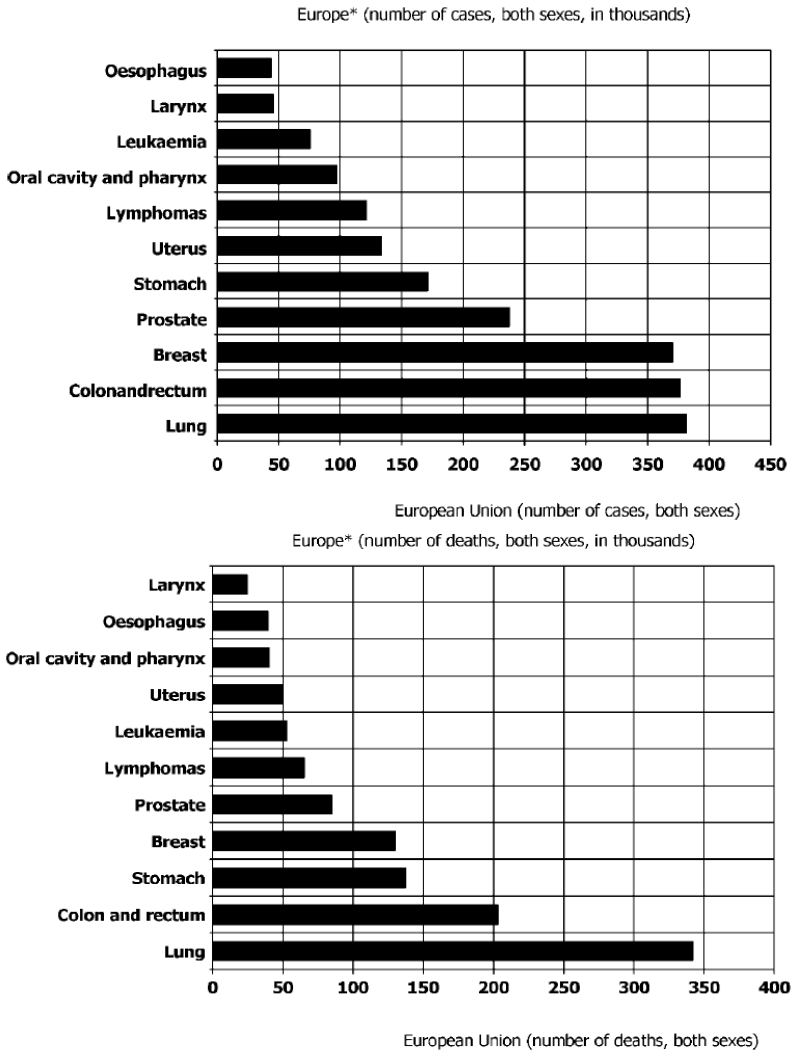
2014b). HF results from a weakened or damaged heart that is no longer able to pump blood around the body and may be caused by CHD, previous heart attacks (*myocardial infarctions*) and cardiomyopathy, a disease of the heart muscle. (National Heart Foundation of Australia, 2012). It shares risk factors with CVD, with symptoms including breathlessness, fatigue (Royal College of Physicians, 2010) and rapid weight loss (Ho et al., 1993). Arrhythmias, such as atrial fibrillation or AF, are caused by a disruption of normal heart rhythm where HR may be irregular, or the pacing bradycardic or tachycardic, due to abnormalities in the electrical system that drive the heart. It may be asymptomatic, though can present with palpitations or breathlessness, and can be detected with an electrocardiograph (ECG) (Mitchell, 2015).

Cancer

This is caused by genetic mutations following normal cell division that can cause abnormal cancer cells to grow, multiply and cause malignant tumours (neoplasms). These can grow quickly, invading and damaging surrounding tissue and organs and spreading to other parts of the body. There are more than 200 different forms of cancer, which may be specific to certain parts of the body or gender (such as prostate cancer in men and cancer of the uterus in women. There are many potential causes including age, familial history, exposure to carcinogens (cancer-causing materials), infection and lifestyle (diet, obesity and smoking), the risks differing depending on cancer type. (Cancer Research UK, 2014).

Figure 1-5 shows the number of cancer cases and deaths in Europe during 2002 for leading types of cancer. Lung, colorectal and breast cancers were the most common by a significant margin. By comparing the number of cases and deaths a measure of the

relative mortality of the respective conditions may be obtained. Of those shown in the two charts, the mortality rates of lung and oesophageal cancer were particularly high, with breast and prostate cancers having the best survivability (Boyle and Ferlay, 2005).



(Boyle and Ferlay, 2005)

Figure 1-5: The number of cancer cases and deaths in Europe in 2002

Symptoms can largely depend upon the type of cancer, but can include the appearance of lumps (breast and testicular), a persistent cough (lung), breathlessness (leukaemia) and passing blood (bladder, cervical and colorectal). Diagnosis may involve testing for markers in blood or tissue samples and medical imaging (e.g. ultrasound, x-

ray, CT scan or MRI) (Cancer Research UK, 2014). Treatment would vary according to the type of cancer, but could include prescribed drugs, surgery to excise the tumour, radiotherapy and chemotherapy (Cancer Research UK, 2014), a side effect of which is a reduction in the number of white blood cells (neutropenia). This can leave patients extremely vulnerable to infection (CDC, 2014).

Respiratory Diseases

These cover a host of conditions, including asthma, chronic obstructive pulmonary disease (COPD) and emphysema. Taken together with infections which impact the respiratory system (pneumonia and influenza), these are one the leading cause of death in the elderly (Meyer, 2004). Statistics for 2001-2002 (see *Table 1-6*) show the differences in impact between asthma and COPD on an average health district within the NHS. Here COPD is responsible for 20% more general practice consultations, 66% more hospital admissions and 5.33 times the number of inpatient bed days than asthma, which translates to an annual COPD hospital cost of £587 million. Data from health authorities in Merseyside shows that 12.5% of all emergency hospital admissions were COPD related (British Lung Foundation, 2003).

	Hospital Admissions	Inpatient Bed Days	GP Consultations
Chronic bronchitis, emphysema & COPD	680	9,600	14,200
Asthma	410	1,800	11,900

(Data from British Lung Foundation, 2003)

Table 1-6: The impact of respiratory disease on an average UK health district (2001–2002)

Asthma is a debilitating condition with both hereditary and environmental risk factors; it causes a chronic inflammatory response that obstructs the airways and leads

to bouts of dyspnoea, coughing and wheezing (Todo Bom and Mota Pinto, 2009). With appropriate treatment, which includes anti-inflammatory drugs and bronchodilators, the effects, though severe, are reversible (Longmore et al., 2009). An estimated 6.5% to 17% of older people suffer from bronchial asthma, some of whom display late-onset with no apparent symptoms up to the age of 65 (Lindner et al., 2007). Asthma and COPD both display similar fixed airflow obstruction and consequently asthma may be under diagnosed; careful observation and analysis should reveal distinct differences in characterisation (Di Lorenzo et al., 2008).

COPD is a progressive and irreversible pulmonary disease caused by an abnormal inflammatory response following prolonged exposure to airborne environmental toxins, such as the gases, volatile compounds and particulates found in tobacco smoke (Ramsey and Sullivan, 2004). This leads impairment to inhalation and exhalation and increasingly severe dyspnoea. Chronic bronchitis, a persistent cough with excess sputum caused by abnormalities in the mucus glands of the large airways, and emphysema, which sees the progressive decline and destruction of the alveoli, are both forms and causes of COPD. Sufferers can gain some respite through oxygen therapy; this may be used "on demand" to aid recovery from bouts of breathlessness or long term in the case of a chronic condition. Oxygen is normally supplied in the form of a small portable gas cylinder or by an oxygen concentrator depending on the severity of a patient's condition (British Lung Foundation, 2003).

There are a number of approaches to diagnosis; these may involve lung function testing using spirometry, medical imaging (chest x-ray or CT scan) or arterial blood gas analysis (Rabe et al., 2007). SpO_2 monitoring may be used in the home to detect

worsening symptoms or exacerbations where bronchodilators, supplementary oxygen or hospital admission may be required (Decramer et al., 2012).

1.2.2 Infection

Infection results from transmissible pathogenic microbial agents - bacteria, viruses, fungi and protozoa. These may be airborne, passed via close personal contact or contact with infected material, animals or insects (NIH, 2009), entering the body via the respiratory or digestive systems, abrasions to the skin or through the urinary tract, where they multiply and affect the host (World Health Organization, 2001). Presentation can differ greatly, with latent effects or rapidly developing symptoms, with varying degrees of severity that may last days, months or a lifetime (NIH, 2009).

	Bacteria	Fungus	Protozoa	Virus
Athlete's foot		▲		
Common cold				▲
Diarrheal diseases	▲		▲	▲
Flu				▲
Genital herpes				▲
Meningitis	▲			▲
Pneumonia	▲	▲		▲
Shingles				▲
Sinusitis	▲	▲		
Skin diseases	▲	▲	▲	▲
Strep throat	▲			
Tuberculosis	▲			
Urinary tract infection	▲			
Vaginal infection	▲	▲	▲	

(NIH, 2009)

Figure 1-6: Some common diseases and infections and their microbial causes

Figure 1-6 shows the microbial sources of a number of common infections, some of which have multiple causation. In these cases the symptoms and treatment may be quite different.

Pneumonia

Pneumonia is an acute lower respiratory tract infection (LRTI) that normally presents with fever and chest or respiratory complications (Longmore et al., 2009) and of all the infectious diseases, is the leading cause of death (Garibaldi, 1985; Calverley et al., 2011). In its various forms (e.g. community acquired - CAP, hospital acquired - HAP, nursing-home acquired - NHAP), pneumonia has a particularly high morbidity in vulnerable groups. These include patients with diabetes (Ehrlich et al., 2010), COPD (Restrepo et al., 2006; Calverley et al., 2011), the immunocompromised (Couch and Englund, 1997; Camps Serra et al., 2008) and the elderly, pneumonia the most commonly reported lethal infection in older people (Gelfand, 1995).

There are a number of microbes that are commonly responsible for infection. These are typically bacteria such as *Streptococcus pneumoniae*, responsible for up to 58% of CAP and 30% of NHAP cases, *Haemophilus influenza*, up to 14% of CAP and NHAP cases, *Staphylococcus aureas*, MRSA and enteric Gram-negative bacteria. Viral infections may account for up to 42% of acute LRTIs with up to 32% of hospital admissions being due to *influenza*, *parainfluenza* (PIV) and *respiratory syncitial virus* (RSV) (Janssens and Krause, 2004). These are serious enough pathogens in their own right and a cause of significant seasonal morbidity with up to 90% of all deaths being in the elderly (Thompson et al., 2003), but can cause further complications, including functional decline and frailty (Barker et al., 1998) and secondary infections, which can

lead to pneumonia (Fleming and Elliot, 2005). Selective vaccination of the at-risk groups affords some protection against pneumococcal infection if treated every five to ten years and influenza, if given annually (Janssens and Krause, 2004; Lim et al., 2009).

The elderly are more predisposed to pneumonia due to a number of age-related changes; these include decreased mucociliary clearance caused by reduced lung and chest wall elasticity and poorer cough reflex, in turn leading to increased microbial colonisation of the respiratory tract which is exacerbated by a weakening immune response (Fung and Monteagudo-Chu, 2010). The risk of hospitalisation from CAP increases substantially with age until the eighth decade of life, those of 60 years-of-age or over account for 81.2% of all cases (Fung and Monteagudo-Chu, 2010).

Diagnosis may use vital sign monitoring, chest x-rays, urea, electrolyte, liver function and blood tests, followed by an array of biological assays to determine the nature of the infection, bacterial, viral or fungal. Treatment is dependent on these findings, which can help in delivering targeted medication. For bacterial infections oral antibiotics are preferred for all but severe cases, where intravenous medication is given. The less common viral infections are treated with appropriate antiviral agents (Mandell et al., 2003; Lim et al., 2009).

Skin Infections

Skin and soft tissue infections cover a range of conditions that may result from microbial infection. These range from the mild, such as athlete's foot and *Herpes simplex virus* (HSV) to severe, as with the microbial colonisation of wounds or decubitus ulcers (Stevens et al., 2005). The more severe outcomes can be a

consequence of infectious agents entering the body via cuts, abrasions, abscesses, wounds, ulcers, intravenous drug use or animal bites or scratches, cats being the main offender (Laube, 2004; Stevens et al., 2005; DiNubile and Lipsky, 2004). Polymicrobial colonisation of infected sites is not uncommon and can lead to unpleasant complications such as *Necrotising fasciitis*, a destructive infection resulting in rapid deep tissue necrosis (Scheinfeld, 2005).

Diabetics are particularly susceptible to infection, most commonly in the feet or lower legs (Joshi et al., 1999; Lipsky et al., 2010) leading to a risk of gangrene, *Necrotising fasciitis*, amputation and death (Joshi et al., 1999). Immunocompromised patients are also vulnerable to severe infection (DiNubile and Lipsky, 2004; Perfect and Schell, 1996) as are the elderly (Gavazzi and Krause, 2002; Laube, 2004). Skin and tissue infections are common in older patients and could be due to a number of factors, e.g. sun damage, vascular disease and infected wound sites (Webster, 2001). Some have multiple skin conditions with varying degrees of severity. Age-related changes to the skin's structure such as a thinning epidermis, diminishing cell turnover rate and a reduction in blood flow and perspiration, all affect susceptibility to damage and prolong wound healing. This, together with a decrease in the water-binding capacity of the epidermis and the function of the eccrine and sebaceous glands – leading to dry skin – all play a part in the propensity for infection. (Laube, 2004).

Decubitus ulcers (pressure sores) are a particular problem for the frail or bedridden; two-thirds of cases occur in those aged 70 years or older, often as a consequence of hospitalisation. These can develop when tissue becomes compressed for long periods,

reducing local blood flow and increasing ischemic cell death through the accumulation of toxins and leading to ulceration and necrosis of skin and tissue (Bansal et al., 2005).

Surgical site infections (SSIs) are another common source of infection and are considered a "major cause of morbidity and mortality" (Owens and Stoessel, 2008). SSIs are defined as infections arising within 30 days of a patient undergoing a surgical procedure (Owens and Stoessel, 2008) and occur in up to 17% of surgical patients who are up to six times more likely to be readmitted to hospital than their infection-free counterparts, adding to healthcare costs (Weigelt et al., 2010; Humphreys, 2009). These are examples of nosocomial (hospital-acquired) infections, which also include bloodstream infections (BSIs) (Karchmer, 2000), and occur as a result of clinical intervention or hospital admission and occur in 5 -10% of outpatients in the UK. Members in the aforementioned groups would be especially vulnerable to nosocomial infection (Breathnach, 2009).

Symptoms may be determined, at least in the first instance, by the monitoring of a patient's vital signs for signs of fever (Stevens et al., 2005). Infected patients are at a risk of sepsis, which can lead to organ failure and fatality unless promptly diagnosed and treated (Nimmo et al., 2006).

Urinary Tract Infection

Urinary tract infections (UTIs) are relatively common in the adult population and describe the pathogenic infection of the urinary tract, bladder, kidneys or the urine itself (Foxman, 2003). They are most common in women, with around 40% of those over 18 years experiencing at least one outbreak in their lifetime (Hooton, 2000;

Medina-Polo et al., 2015), which compares to an estimated 0.07% in men (Ulleryd, 2003). Around a quarter of women are likely to suffer reoccurrence (Foxman, 1990), the likelihood of which may be determined by the type of infecting organism and sexual behaviour (Foxman et al., 2000).

Uncomplicated infections - those occurring in a "normal genitourinary tract with no prior instrumentation" (Foxman, 2003) - are largely due to pathogens (commonly from rectal flora) entering the urinary tract, with *Escherichia Coli* being responsible for around 80% of cases (Ronald, 2003; Hooton, 2000). Complicated infections may occur as a result of abnormalities in the urinary tract or from clinical interventions (such as catheter use), the etiology being different to uncomplicated UTIs with a higher risk of polymicrobial colonisation (Hooton, 2000; Ronald, 2003). With almost two-thirds of patients receiving intensive care using urinary catheters (Tominaga et al., 2014), research has shown that as many as 75% of catheterised patients can suffer with asymptomatic bacteriuria if a device is in-situ for a few days (Cove-Smith and Almond, 2007) and that catheter-acquired UTIs (CAUTIs) alone account for a third of all nosocomial infections (Tominaga et al., 2014). Acute infections can lead to sepsis and can be life threatening (Bjerklund Johansen et al., 2014).

UTI is seen as a complication of diabetes with a marked increase in prevalence and in certain types of bacteria compared with non-diabetics (Ronald, 2003; Yu et al., 2014). Other vulnerable groups with an increased susceptibility and risk include the immunocompromised, those with injuries to the spinal cord, with a permanent bladder catheter, recurrent UTI, multiple sclerosis patients and pregnant women (Foxman, 2003; López and Cortés, 2012).

The greatest prevalence, and potential for morbidity, is in older people. UTIs in the elderly are the most common of nursing-home acquired infections (Garibaldi, 1999) and cause of sepsis and fever in hospitalised patients, having a mortality of up to 33% (Tal et al., 2005). A number of age-associated physiological changes increase the likelihood of UTIs. These factors include increased reduced urine flow rate, greater residual urine volumes (Gavazzi and Krause, 2002), bacterial colonisation of the skin, effects of dementia and the side effects of medication. Gender specific causes include a high intra-vaginal (alkaline) pH in post-menopausal women which can lead to increased pathogenic bacterial adhesion, and hypertrophy of the prostate in men (Cove-Smith and Almond, 2007).

Symptoms can vary widely, from the frequency of passing water and an abnormal appearance of urine in milder cases to discomfort, fever and confusion in the most severe. Treatment is dependent on the nature of the diagnosed infection, which may be achieved via the use of urine dipstick tests and blood and urine assays (Gibson and Toscano, 2012).

Fever and the Febrile Response

Once thought to be brought on by an excess of yellow bile (one of the four humours) by physicians in ancient Greece or even demonic possession in the Middle Ages, fever results from pathogenic microbial infection (Mackowiak, 1998). The classic febrile response is an adaptive physical reaction to infection resulting from a complex of trigger responses and controlled by the hypothalamus. The most obvious physiological effect is a rise in core temperature (from 1 to 4°C above the norm (Blatteis, 2003) as the body's thermostatic setting is temporarily increased (Hasday et

al., 2000). This is typically accompanied by increases in perspiration, respiration and pulse rate – three of the four vital signs commonly used as an aid to diagnosis.

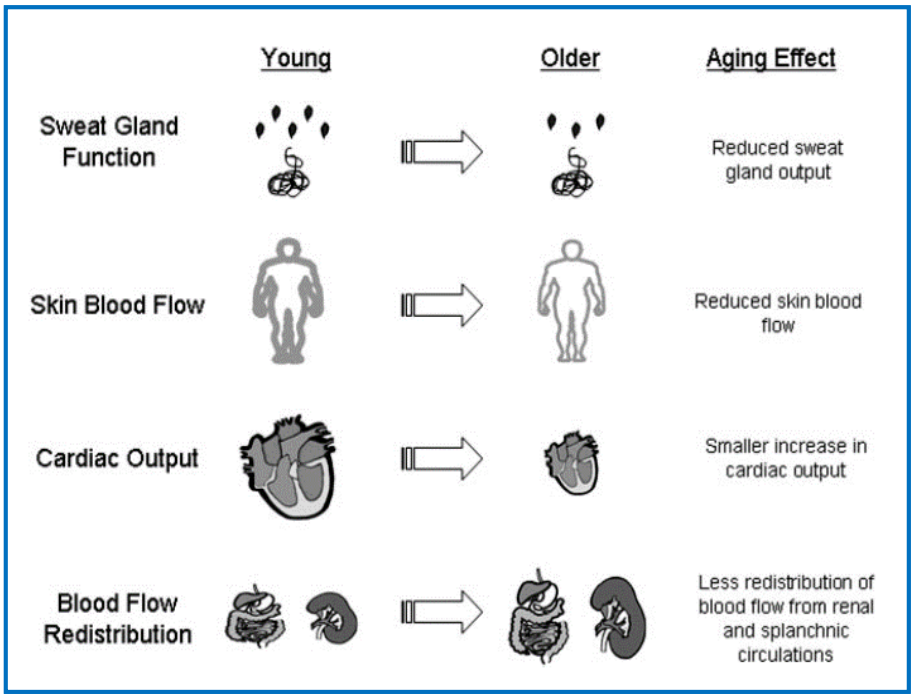
Fever is normally described as having three distinct phases as it runs its' course: At onset blood concentrates in the body's core leading to chills, shivering and a rise in core temperature; the second phase sees an equilibrium in heat loss and production as the temperature plateaus before the final phase, in which cutaneous vasodilation (leading to a redistribution of blood from the core) and sweating cause heat loss and a return to normal core temperatures (Aiyagari and Diringer, 2007; Romanovsky et al., 2005). Febrile episodes are not, arguably, harmful to the host and may be seen as beneficial to the greater immunological response (Blatteis, 2003). The elevated temperatures when febrile have been suggested to reduce mortality with some infectious agents (e.g. CAP and *E-coli*) (Aiyagari and Diringer, 2007), but may be prove detrimental to those with brain injury or severe neurological insults. The unpleasantness of fever may be treated by antipyretic drugs; this can have a protective effect for brain injuries but may prolong recovery from some infections, e.g. rhinovirus and varicella (Mackowiak, 1998; Blatteis, 2003; Aiyagari and Diringer, 2007).

Fever in the Elderly

The febrile response is typically less pronounced in the elderly (Berman et al., 1987; Sund-Levander and Grodzinsky, 2009). In many reported cases there is little change in core temperature in the elderly despite the subject displaying other symptoms of infection (Norman, 2000). Arguably, both healthy adults (Kiekkas et al., 2007) and the healthy elderly (Darowski et al., 1991b) typically have core temperatures ranging from 36.5°C to 37.5°C – a nominal 37°C. A core temperature of one degree or more above

the norm is widely considered to be hyperthermic and thus, indicative of fever (Mackowiak, 1998).

Studies show changes in thermoregulation in the elderly compared with their younger counterparts, but little difference in body core temperature between the two groups (Kenney and Munce, 2003). Thermoregulatory changes find older individuals more prone to suffer the effects of cold and heat stress as their ability to regulate body temperature is blunted. The normal response to cold stress, vasoconstriction and shivering, occurs at lower temperatures (< 1°C) – leading to an increased risk of hypothermia - a core body temperature of less than 35°C (Lien, 2002).



(Kenney and Munce, 2003)

Figure 1-7: A summary of age-related changes in thermoregulation during heat stress

With heat stress, the normal control mechanisms show a diminished response (*Figure 1-7*) - cutaneous blood flow, sweating, and cardiac output are all reduced,

which would appear to suggest the elderly are at an increased risk from hyperthermia, however the ability to maintain core temperature is not usually unduly compromised (Kenney and Munce, 2003).

Temperature assessment alone may not be sufficient for classifying febrile infection, leading to a late or incorrect diagnosis (Varney et al., 2002). Analysis of this in combination with respiration, pulse rate and skin resistance, the other characteristic responses, should facilitate early detection of infection and improve positive prediction.

Aging and Infection

The over sixty-fives are more predisposed to infection, the seriousness of which increases with age (Weinberger et al., 2008). The source of infection may be endogenous or exogenous microbes, but it has a far greater chance of progressing to a stage where the elderly host will require hospitalisation (Yoshikawa, 1981). Gavazzi and Krause note a general susceptibility of infection that is typically three times greater than the general population of contracting community-acquired pneumonia, extending to twenty times for urinary tract infection (Gavazzi and Krause, 2002) and three times higher for nosocomial infections (Yoshikawa, 1981). Frequently reported ailments include upper and lower respiratory tract infections (Janssens and Krause, 2004), pneumonia, influenza, urinary tract infections, soft tissue infections, sepsis (Schmader, 2001) and a range of gastrointestinal infections (Gelfand, 1995). Treatment can be complicated by adverse reactions to drugs, especially antibiotics which may cause gastrointestinal intolerance in the form of nausea and diarrhoea (Gavazzi and Krause, 2002).

Immunosenescence

The deterioration of the immune system with age is known as immunosenescence; this decline in the immune response results in an increased susceptibility to infection. Whether this is due to a general deterioration in the host defence system, a decline in a number of specific mechanisms or a combination of both of these factors is unclear (Gavazzi and Krause, 2002). Telomere shortening, where the repetitive DNA that stabilise and protect the ends of chromosomes (known as telomeres) shorten with and ultimately prevent replication, is one cited aging mechanism (Aubert and Lansdorp, 2008). Another is a decline in the production of immunity-promoting naive T cells as the aging thymus gradually atrophies and becomes increasingly adipose (Grubeck-Loebenstein, 2010). There is also evidence to suggest that persistent infections such as *cytomegalovirus* (CMV) can cause chronic stimulation of the immune system over time, and that accelerated immunosenescence may be due to an individual's immunological history (Pawelec et al., 2010).

Vaccination can be an important weapon in protecting the elderly from infection; vaccines for influenza and pneumonia are routinely given to those with comorbid conditions who are particularly vulnerable. The attenuated immune response in an aging population however presents challenges for vaccine developers (Chen et al., 2009). As vaccines tend to be less effective this may necessitate changes to formulations, plus additional therapies such as boosting thymic output for an enhanced immune response (Aspinall et al., 2007). An increase in immunity duration may also be achieved by regular booster vaccinations (Kaml et al., 2006).

1.2.3 Comorbidity

Comorbidity, the presence of other morbid conditions in addition to and independent of a primary disease, is a complication at any age and an added threat to vulnerable groups in which the prevalence and severity of comorbidities are greater (Wedding et al., 2007). It is a particular issue for elderly patients; an Irish study of the national pharmacy claims database of patients aged 70 years or older (n=316,928) reported 27% of the sample population with two chronic conditions, 19% with three comorbidities and 14% with four or more (Naughton et al., 2006). Another based on a review of literature on the MEDLINE database published between 1990 and 2002 puts the prevalence of 'multimorbidities' in 55 to 74 year-olds at 60% (Fortin et al., 2005), whilst the findings of an Australian survey of returns from general practitioners puts the incidence in the over 75 age group at 83% for two or more comorbid conditions (Britt et al., 2008).

Those suffering from one or more common long-term conditions, such as diabetes mellitus, cancer, heart disease or COPD, face an increased risk of mortality from infection; examples include pneumonia, which may be both difficult to detect and particularly perilous to COPD patients (Garibaldi, 1999), and the danger posed by soft tissue infections to diabetics (Joshi et al., 1999). Comorbidity (especially COPD, cardiovascular disease and chronic heart failure) can also be problematic for elderly surgical patients as it may cause complications, delays or even prevent procedures and leads to a higher post-operative mortality rate (Roche et al., 2005). Comorbid patients are more predisposed to suffer cumulative deficits, leading to frailty and adversely affecting their activities of daily living (ADLs) and quality of life. There are also

complications with treatment; many may be too vulnerable to undergo radio- or chemotherapy, or may suffer side effects from prescribed drugs (Gijsen et al., 2001).

1.2.4 Disease, Infection and Mortality

An examination of the leading causes of death in the general population shows a range of common conditions. *Table 1-7* shows the top fifteen causes of death in the United States from 2006; this is a comprehensive list that includes non-clinical data.

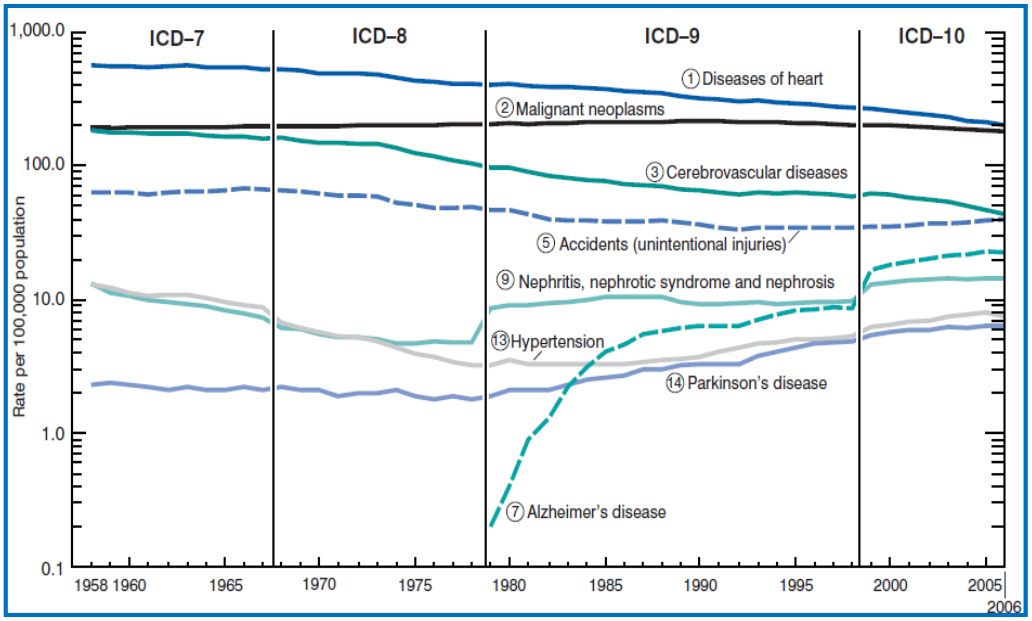
Rank	Disease/Infection
1.	Diseases of heart (heart disease)
2.	Malignant neoplasms (cancer)
3.	Cerebrovascular diseases (stroke)
4.	Chronic lower respiratory diseases
5.	*Accidents (unintentional injuries)*
6.	Diabetes mellitus
7.	Alzheimer's disease
8.	Influenza and pneumonia
9.	Nephritis, nephrotic syndrome and nephrosis (kidney disease)
10.	Septicaemia
11.	*Intentional self-harm (suicide)*
12.	Chronic liver disease and cirrhosis
13.	Essential hypertension and hypertensive renal disease (hypertension)
14.	Parkinson's disease
15.	*Assault (homicide)*

(Heron et al., 2009)

Table 1-7: The fifteen leading causes of death in the United States in 2006

When historic data is considered and compared, trends in population mortality may be observed - this is apparent in *Figure 1-8*, which shows the changes in reported causes of death from 1958 to 2006. Here the gradual reduction in deaths from heart

and cerebrovascular conditions (strokes) and increases in mortality from Alzheimer's and Parkinson's diseases may be seen (Heron et al., 2009). When historic data is considered and compared, trends in population mortality may be observed - this is apparent in *Figure 1-8*, which shows the changes in reported causes of death from 1958 to 2006. Here the gradual reduction in deaths from heart and cerebrovascular conditions (strokes) and increases in mortality from Alzheimer's and Parkinson's diseases may be seen (Heron et al., 2009).



(Heron et al., 2009)

Figure 1-8: The age adjusted death rates for leading causes of death: USA, 1958 - 2006

UK-based studies show gender differences in the leading causes of mortality. *Table 1-8* ranks death rates in the over fifties (Ashton et al., 2010), showing heart disease (1st) and strokes (2nd) as the greatest risks. Neoplasms (3rd) show males more likely to suffer lung cancer than their female counterparts, where breast cancer is a threat.

Rank	Males	Females
1	Ischaemic heart diseases	Ischaemic heart diseases
2	Cerebrovascular disease	Cerebrovascular disease
3	Malignant neoplasm: trachea, bronchus and lung	Malignant neoplasm: breast
4	COPD, bronchitis, emphysema	Pneumonia
5	Malignant neoplasm: stomach	Malignant neoplasm of colon

(Ashton et al., 2010)

Table 1-8: The leading five causes of mortality in men and women over fifty years of age in England, 2005

Cause of Death in Males	No.	Cause of Death in Females	No.
Neoplasms	76512	Circulatory system diseases	71773
Circulatory system diseases	69420	Neoplasms	68532
Respiratory system diseases	33364	Respiratory system diseases	37168
Miscellaneous conditions	14786	Miscellaneous conditions	24782
Digestive system diseases	11735	Mental and behavioural disorders	24148
Mental and behavioural disorders	11709	Digestive system diseases	12784
External causes	10500	Nervous system diseases	11575
Nervous system diseases	9325	External causes	6309
All causes, aged 20 years and over	**237351**	**All causes, aged 20 years and over**	**257071**

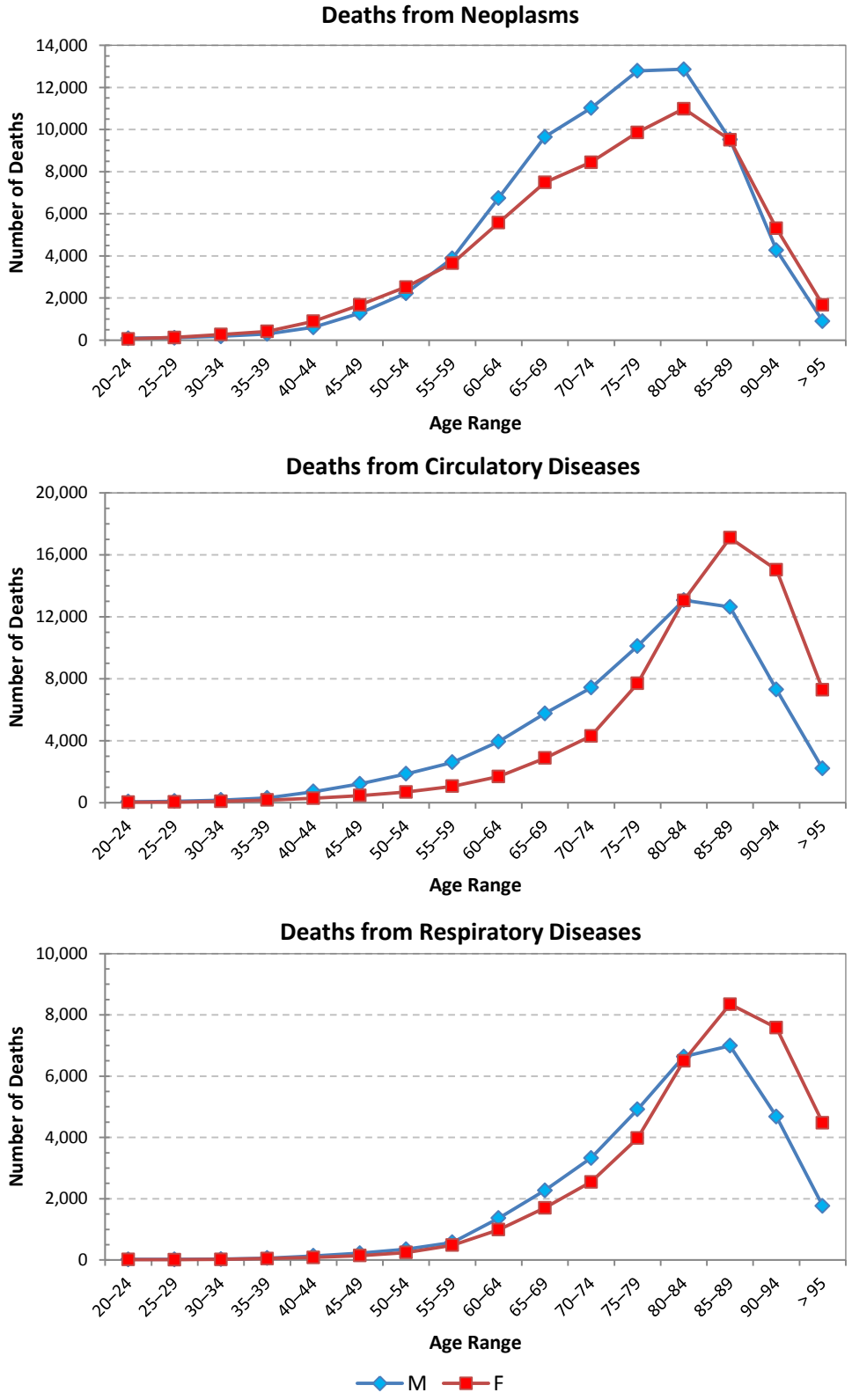
(Office for National Statistics, 2013)

Table 1-9: The leading causes of death in the male and female adult population (aged 20 years or older) in England and Wales, 2012

Table 1-9 shows 2012's statistics and rankings for the leading causes of death in the wider adult (20 years or older) population (Office for National Statistics, 2013). These data show cancer (1st), heart and cardiovascular disease (2nd) and respiratory disease (3rd) as the main risks to males; that for females is similar though the ranking of cancer

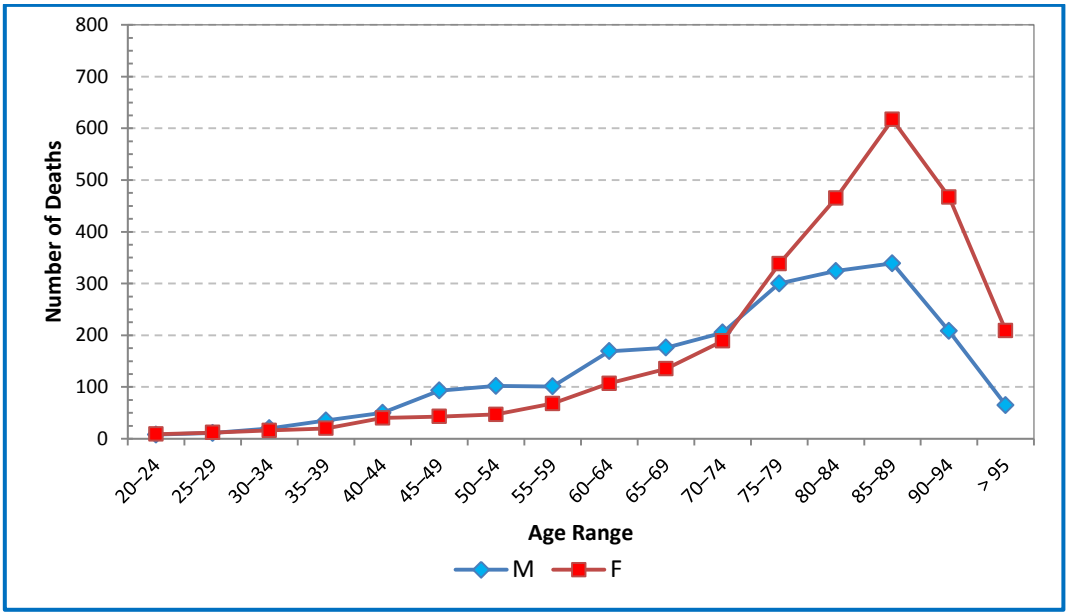
and cardiovascular diseases are reversed. The study also reveals that the likelihood of females dying from mental disorders is more than twice that of males. In examining the three leading causes of death, age must be considered in addition to gender. Plots for each showing the age distribution for both genders are presented in *Figure 1-9*.

Although there are differences between the death rates for each gender, it can be seen that there is a substantial increase in death rates with advancing years from the age of around 50 to 55. In the case of neoplasms (cancers) mortality rates are comparable up to age of 55 years when the male trajectory increases significantly until reaching a zenith at 80, then returning to comparable levels to the female figures at age 85 and beyond. Male deaths from circulatory (cardiovascular) diseases show a steady increase from the age of 35 to a peak at 80 years, whereas the rate of female deaths start to increase from 40 to 50 years then escalating and exceeding the male figures when peaking aged 85. Mortality for respiratory diseases are broadly similar between the sexes, the rates reaching parity by 80 years after which female deaths greatly outstrip those of males.



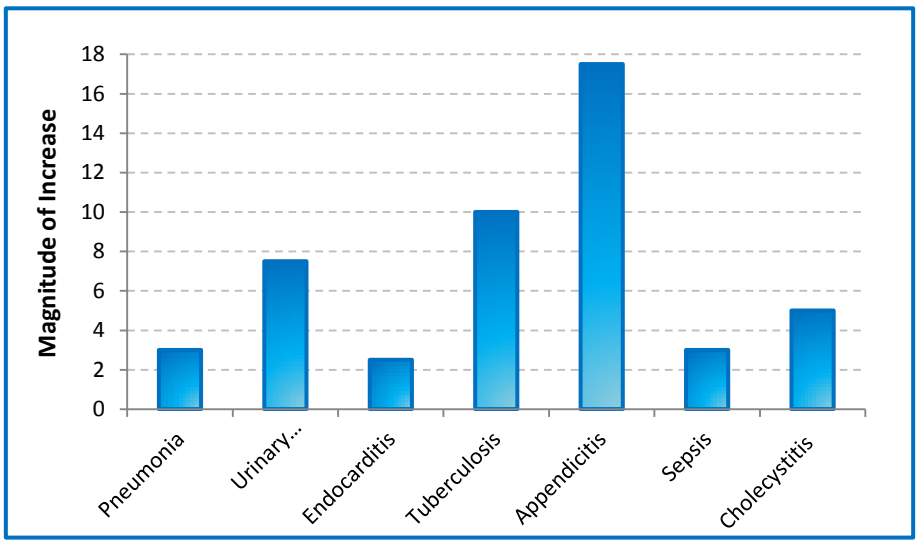
(Office for National Statistics, 2013)

Figure 1-9: The three leading causes of death in adults (of 20 years or older) in England and Wales by age and gender, 2012.



(Office for National Statistics, 2013)

Figure 1-10: The number of deaths from infectious diseases in adults (of 20 years or older) in England and Wales by age and gender, 2012.



(High, 2004; Yoshikawa, 1997)

Figure 1-11: Relative mortality in older adults vs. young adults with the same diagnosis

It is clear from *Figure 1-10* that infection in the elderly (over 65 years), as with other conditions, has a significantly higher mortality rate than the general population (Office for National Statistics, 2013) – typically around nine times higher than in patients aged 25 to 44 years of age (Mouton et al., 2001). The relative mortality of some of the

leading infectious diseases in younger and elderly patients is depicted in *Figure 1-11* (Yoshikawa, 1997; High, 2004).

1.2.5 Summary

This section reviews the nature of disease and infection and the differences between them. It examines their causation, risk factors, impact, prevalence, morbidity, mortality and the range of methods employed in their diagnosis and management.

Many diseases lead to the development of long term conditions, with many sufferers having comorbidities. This, together with the consequences of ageing (such as immunosenescence), can leave many individuals increasingly vulnerable to infection, which has a significantly higher mortality rate in these groups.

With the exception of hypertension, where BP readings provide a valuable indicator, many diseases rely on methods other than VS monitoring for diagnosis. While abnormal HR, RR or SpO_2 readings may be indicative of a heart or respiratory condition, more specific diagnostic tests (e.g. ECG, lung function tests etc.) are required to determine the precise nature of a patient's condition, although VS monitoring does have a place in condition management.

VS monitoring can be effective in the determination of infection, especially those with a febrile presentation. Rather than relying on an elevated temperature however, this should be considered in combination with the other VS for a more certain diagnosis – especially with elderly patients. This can also help in the diagnosis of respiratory infections, pneumonia and sepsis.

1.3 Vital Signs Monitoring

In considering electronic health monitoring and its applications, it is clear that this is a diverse environment with a wealth of products from many manufacturers and vendors, with systems ranging from condition-specific devices such as glucometers (for diabetics monitoring their blood sugar levels) to vital signs monitors for general healthcare applications. Here, the next sections examine vital signs monitoring devices, which signs provide the best diagnostic information for a range of different medical conditions and how the monitoring is performed for the best patient benefit.

1.3.1 Monitoring Devices

These were developed in response to a need for assistive devices or instruments as a means of establishing verifiable vital signs readings in clinic, rather than relying on subjective observations. Whilst originally designed for clinical use, many products are now freely available in the high street and are purchased for home use by those managing a morbid condition and the "worried well" (Amies, 1996).

Temperature

Braun and Omron are well known digital thermometer brands, both supplying a range of products for medical temperature measurement. Together with numerous other brands, they produce non-contact (IR) forehead sensing devices as well as ear, oral, rectal and axillary thermometers (see *Figure 1-12*). While many of these allow readings to be stored, examples such as the Braun PRT2000 have age-adjusted thresholds for fever prediction in young children (Braun GmbH., 2015).

(OMRON Corporation, -)

Figure 1-12: The Omron Eco Temp Smart digital medical thermometer

Heart Rate

This might be measured with a pulse oximeter or if more detail is required, via electrocardiography, which can display and record the heart's electrical activity. The latter is more likely to be used in hospital, in the form of a bedside unit, where it is used as a diagnostic tool to determine heart conditions such as CVD, heart failure and arrhythmias (World Health Organization, 1981).

For a more thorough analysis, patients may be asked to wear a Holter monitor (*Figure 1-13*) for 24 to 48 hours to record continuous ambulatory ECG readings. This device, named after its inventor, N.J. Holter (1914 – 1983), an American physicist (Ioannou et al., 2014), is a small wearable battery-powered ECG with a high capacity memory. It is able to capture heart signal transients acting as markers for heart disease while the subject goes about their normal daily life. Manufacturers include GE Healthcare, Philips Healthcare and Welch Allyn Inc. (Welch Allyn Inc., 2012), all of whom provide software applications to quickly identify anomalies and aid diagnosis.

(Welch Allyn Inc., 2012)

Figure 1-13: Welch Allyn's HR-100 Holter monitor for ambulatory ECG recording

Many fitness monitoring products (fitness trackers) provide HR measurement capability, with examples available from manufacturers such as Garmin, Fitbit, Withings and Jawbone. There are also numerous smartphone apps that use the built-in camera and flash (LED) to produce a crude photoplethysmograph (pulse waveform) from which HR is derived.

Blood Pressure

Digital blood pressure monitors see widespread use in hospitals GP surgeries and increasingly, in the home for improved management of hypertension (Padfield, 2010). The majority of devices employ an inflatable pneumatic cuff worn around the arm or wrist to temporarily occlude blood flow during the measurement process (Babbs, 2012). Leading manufacturers include Braun, Omron and A&D Medical, all of whom produce a range of wrist and arm cuff-based devices featuring battery operation, digital displays and data recording facilities. Over the last few years wireless-enabled

devices have appeared, both from established brands and newcomers such as Cardio and Withings (*Figure 1-14*). These integrate the electronics and batteries within the cuff design, using a smartphone to wirelessly control operation, then display, archive and chart readings (Withings, 2015b).

(Withings, 2015b)

Figure 1-14: A wireless-enabled blood pressure monitor by Withings

Readings taken in clinic provide but a snapshot of a patient's true blood pressure and are prone to the effects of "white coat hypertension", in which readings may be elevated by as much as 12% to 50% due to anxiety and stress (Owens et al., 1999). Ambulatory blood pressure monitoring (ABPM) addresses this by taking a series of readings over a 24 hour period, the frequency of which may be up to every 15 minutes during the day and 30 minutes at night (Schächinger and Langewitz, 1997). Data may be analysed to establish an individual's normal readings, their range, identify variability, overnight dipping and any markers for CVD (Schächinger and Langewitz, 1997; Grossman, 2013). This has provided more reliable and realistic results, reducing

white coat effect and revealing a patient's underlying readings for an improved diagnosis. UK clinical guidelines recommend ABPM in the management of hypertension (White and Maraka, 2012).

Respiration Rate

Capnography is the standard method of measuring RR in anesthetised, intensive care and trauma patients. The exhalatory in-line sensors may be fitted to a ventilator, endotrachael tube or mouthpiece and connect to a host monitor to display real-time data. Smiths Medical, Nonin, Covidien and Masimo (Masimo Corp., --c) all provide hand-held or bedside monitoring systems. A recent innovation (c.2008) is Masimo's acoustic respiration rate sensor (Macknet et al., 2007; Masimo Corp., --a) which sticks to the side of the neck of patients and detects respiratory sounds (*Figure 1-15)*.

(Masimo Corp., --a)

Figure 1-15: Masimo's acoustic respiration rate sensor (RRa)

There are few dedicated RR sensors on the market, many choosing to use an estimation calculated from HR. The most common of the commercially available sensors are thoracic band-based systems for medical use (Thought Technology Ltd., -;

Vernier Software & Technology, 2009) and wearable fitness bands that incorporate similar technologies (see Zephyr Technology, 2012).

Blood Oxygen Saturation

This is measured with a pulse oximeter. These are widely available with in excess of 450 models (plus accessories) reported on Amazon's UK website, with examples priced from £12.99 (Amazon.co.uk, 2015) and finding use in the home. They are typically offered in three main forms: (i) a fingertip model with integrated sensor and display, plus (ii) hand-held and (iii) bedside models with separate sensor probes, examples of which are presented in *Figure 1-16*. Leading manufacturers include Nonin, Covidien (Nellcor), Smiths Medical and Masimo.

(Covidien, 2015)

Figure 1-16: A range of pulse oximeter sensor probes from Nellcor (Covidien)

These sensors are frequently incorporated into fitness products such as the wrist-band devices offered by Withings, Fitbit and others (Withings, 2015a).

1.3.2 Multi-Parameter Monitoring Devices

The majority of vital signs monitors read no more than two parameters (e.g. a blood pressure monitor records HR and BP and a pulse oximeter, HR and SpO_2), hence several different devices may be required if all five vital signs are to be measured. Bedside patient monitors found in hospital however are often capable of measuring all five of the vital signs (Infinium Medical Inc., -), with some examples providing additional physiological data for (ECG-based) cardio (Koninklijke Philips Electronics NV, 2010) and (capnograph-based) respiratory diagnostics (Covidien, 2013). Probes connect to the side or rear of the instrument, which may contain plug-in modules to accommodate different sensor types. The probes are attached to the patient for continuous monitoring and provide valuable data, although the subject is effectively tethered to the bed by the umbilical cables. Therefore these are used primarily with bed-bound patients requiring constant monitoring, such those in intensive care.

An example of a modern bedside monitoring system is shown in *Figure 1-17*. These typically have a large colour LCD display with the key readings (e.g. HR, SpO_2, BP, RR and temperature etc.) shown prominently in a large font, being clearly visible from several feet away, together with signal waveforms (on some models) from ECG, SpO_2 and capnograph sensors. A command button or touch screen user interface allows alarm thresholds to be set, diagnostics performed and (on some models) the preferred display screen selected. Although normally mains-powered, many systems are capable of battery operation to facilitate patient transfers.

(Infinium Medical Inc., -)

Figure 1-17: The Infinium Omni II, an example of a modern bedside patient monitoring system

Systems better suited to ambulatory patients are also becoming available. These may be smaller units, with reduced capability, or make use of wireless sensors that connect to suitably equipped bedside monitors (Koninklijke Philips Electronics NV, 2013). Other developments use networked monitoring systems that connect to a central server to provide integrated patient care and management capabilities, allowing remote access to vital signs readings (Covidien, 2014).

1.3.3 Vital Signs as an Aid to Diagnostics and Condition Management

The review presented in sections *1.1* and *1.2* details the vital signs and shows how they may be employed in aiding the diagnosis and management of a range of medical conditions. *Table 1-10* provides a summary of which signs best benefit patient

monitoring for those conditions discussed in section *1.2* and for general fitness and wellbeing.

Condition	Temp	HR	BP	RR	SpO_2	Other
CVD		X	X	X		Weight Loss
Cancer				X		Imaging
COPD and Asthma		X		X	X	Spirometry
Pneumonia	X	X		X	X	
Febrile Infection	X	X		X	X	Perspiration
Sepsis	X	X	X	X	X	Delirium
Fitness and Wellbeing	X	X	X	X	X	

Table 1-10: The use of vital signs in the diagnosis and management of disease and infection as determined from this literature review.

The findings suggest the following points:

- Temperature monitoring is best for employed for determining infection and wellbeing.
- HR, and the detection of bradycardia and tachycardia, can be useful for managing CVD, respiratory conditions and general fitness, with an increase above normal levels aiding in the diagnosis of infection.
- BP is most effective in CVD management and monitoring general fitness, but can be useful in diagnosing sepsis.
- RR has the widest range of applications in monitoring heart, respiratory conditions (including lung cancer), infection and fitness.
- SpO_2 is at its most effective in monitoring respiratory conditions, fitness and infection.

Of the other signs mentioned only perspiration sensing as a marker for febrile infection could realistically be incorporated into a non-invasive VS monitor. This would take the form of skin resistance sensing and is reviewed in the following paragraphs. Bathroom scales and spirometers (Medical International Research, 2015) are available with Bluetooth wireless links, the data from which would complement the physiological readings.

Skin Resistance

Electrical skin resistance (SR) is a well-known stress marker; this may be due to psychological or physiological causes (Strauss et al., 2005), such as infection (see *section 1.2.2, p36*), and is perhaps best recognised as one of the prime measures used in lie detectors or polygraph testing. Skin provides evaporative cooling through sweat and therefore this mechanism should be apparent with a febrile subject, even though the elderly may show a diminished response (Kenney and Munce, 2003). The effects of dermal aging in elderly individuals include a thinning epidermis and reductions in blood flow, the water-binding capacity of the stratum corneum and sweat gland function, all contributing to an increased dryness of the skin (Laube, 2004).

SR changes according to the level of local skin hydration or sweating and falls as hydration increases. Dry skin has a typical resistance in the order of a few hundred thousand Ohms, although it is clear that the response can be quite different between individuals where a number of factors, including skin type, diet, medication, age, hydration level and environmental conditions, may come into play (Hume, 1966). Measurement sites display different characteristics; this is largely due to local sweat gland density which differs considerably around the body as shown in *Table 1-11*

(Wilke et al., 2007). The key determinants in the electrical evaluation of sweat are sweat rate and concentration, the latter of which is inversely proportional to resistance (Licht et al., 1957). The specific ratios between the major (ionic) constituents of sweat (see *Table 1-12*) and the rate of sweat production are also likely to be measurement site dependent (Patterson et al., 2000). Therefore, in order for meaningful comparisons to be made, this should be consistent for any set of tests.

Region	Wilke et al, 2005	Sato et al, 1989	Fiedler et al, 1968	IFSCC Monograph, 1999
Palms	644	600 - 700	620 ± 120	370
Forearm	134	108	225 ± 25	155
Abdomen	127	-	190 ± 5	-
Upper arm	90	108	150 ± 20	-
Armpit	68	~100	400 ± 50	90 - 200
Thigh	57	-	120 ± 10	80
Face	59	181	360 ± 20	175
Chest	20	-	175 ± 30	-
Back	-	64	160 ± 30	60 – 100

(Wilke et al., 2007)

Table 1-11: Sweat gland density (per cm2) measured by direct (Wilke) and indirect (Fiedler, IFSCC) counting

Organic Compounds (mEq/L)		Inorganic Compounds (mEq/L)	
Sodium	15 - 60	Lactic acid	17 - 330
Potassium	3 - 8	Urea	3 - 7
Chloride	15 - 60	Amino acids	0.7 – 1.5
Calcium	0.1 – 1.0		
Sulphate	0.4 – 1.8		
Trace Elements			
Iron, magnesium, copper, phosphate, iodide, fluoride			
pH			
4.5 – 7.1			

(Licht et al., 1957)

Table 1-12: The basic composition of sweat from healthy subjects

1.3.4 Vital Signs Monitoring

Although there is variation between individuals, the baseline readings for healthy adults fall within a broadly similar range. Deviation from an individual's normal baseline values could indicate illness or infection (Harries et al., 2009) while a return to normal values may suggest an improving condition or recovery. Readings that may be considered normal for the adult population however, can differ from values considered normal in the elderly leading to increased patient risk (Wolf, 2007).

When used as part of the screening process during triage, vital signs monitoring can assist in decision making when prioritising critical treatment (Cooper et al., 2002). Following initial triaging, monitoring frequency is dependent upon patient condition. Emergency hospital admissions or those in critical care may be subject to continuous monitoring of at least one parameter in extremis, extending to every 15 to 30 minutes if less acute (Evans et al., 2001). For lower risk emergency admissions two-hour

intervals are not unusual (especially during busy periods) while inpatients outside of intensive care are usually monitored every four hours, within a one-hour window (Johnson et al., 2014). Checking for abnormalities in the vital signs prior to discharge from a hospital's emergency department has been shown to result in a reduced risk of readmission (Domagala, 2009).

There are however some practical issues which must be considered if reliable measurement is to be achieved:

1. The frequency and timing of readings are often ultimately determined by routine rather than driven by clinical need (Zeitz and McCutcheon, 2006).
2. With observation-based assessment, inter-observer variability should be taken into account as there may be an element of subjectivity in reported results (Edmonds et al., 2002).
3. Once recognised, abnormal VS should be reported promptly allowing for timely clinical intervention - delays may be critical for effective patient care (Cioffi et al., 2006)..

These are areas where intelligent electronic monitoring systems with appropriate alarm settings may offer a demonstrable advantage.

1.3.5 Early Warning Scoring Systems

A measurable deterioration in a patient's vital signs is frequently apparent six to eight hours prior to suffering cardiopulmonary arrest (Schein et al., 1990; Franklin and Mathew, 1994; Hillman et al., 2001). All too often, suboptimal care, whether due to organisational failure, inexperienced staff, insufficient clinical knowledge, inadequate

training or resource issues, has led to avoidable mortality (McQuillan et al., 1998; Smith and Poplett, 2002; NCEPOD, 2005; Massey et al., 2008). In particular, there have been issues with poor clinical practice where changes in observations and vital signs have not been noted, recognised or acted upon (Franklin and Mathew, 1994; NPSA, 2007).

Regular observation and monitoring (four hourly or less) should detect deteriorating vital signs inside the six to eight hour window for an improved outcome. In an effort to ensure best practice and improve outcome a number of innovative practices were introduced, including ALERT training and EWS systems. ALERT (Acute Life-threatening Early Recognition and Treatment) training was established to provide a one-day course for healthcare professionals in the management of critically ill adult patients (Smith et al., 2002). In effort to standardise patient monitoring and the response to changes in condition, the Early Warning Scoring (EWS) systems were born (Morgan and Wright, 2007). These aggregate weighted VS readings and observations to provide a score that may be used to track changes in patient condition and trigger the appropriate clinical response if predetermined thresholds are exceeded.

EWS systems, in their various forms, have found widespread use. Whilst they may vary in the number of parameters scored and their relative weightings, they all employ a track and trigger system (TTS). The ViEWS (VitalPAC EWS) system collected readings (VS and GCS) on PDAs (personal digital assistants) running VitalPAC software and wirelessly linked to a database (Prytherch et al., 2010). The MEWS (Modified EWS) system was designed for routine bedside monitoring and uses weighted measures of temperature, heart rate, respiratory rate, systolic blood pressure and level of

consciousness (Subbe et al., 2001). More recently, the NEWS (National EWS) system has been introduced and is being rolled out across the NHS (Royal College of Physicians, 2012).

The NEWS physiological parameters and their weightings are shown in *Figure 1-18*. It is based upon the five vital signs together with level of consciousness, which in this case uses an AVPU (alert/verbal/painful/unresponsive) responsiveness score - a simplified version of the GCS that tests a patient's response to verbal and painful stimulation (Kelly et al., 2004). Each parameter is scored according to where a reading falls in the ranges shown in the table, higher scores exhibiting a greater patient risk. These scores are then aggregated for an overall measure of patient condition (*Figure 1-19*), with a score of 5 or above, or 3 on a single parameter, being flagged as a medium risk and a result of 7 or above as a high risk (Royal College of Physicians, 2012).

PHYSIOLOGICAL PARAMETERS	3	2	1	0	1	2	3
Respiration Rate	≤8		9 - 11	12 - 20		21 - 24	≥25
Oxygen Saturations	≤91	92 - 93	94 - 95	≥96			
Any Supplemental Oxygen		Yes		No			
Temperature	≤35.0		35.1 - 36.0	36.1 - 38.0	38.1 - 39.0	≥39.1	
Systolic BP	≤90	91 - 100	101 - 110	111 - 219			≥220
Heart Rate	≤40		41 - 50	51 - 90	91 - 110	111 - 130	≥131
Level of Consciousness				A			V, P, or U

(Royal College of Physicians, 2012)

Figure 1-18: The NEWS scoring system assessment chart.

NEW scores	Clinical risk
0	Low
Aggregate 1–4	
RED score* (Individual parameter scoring 3)	Medium
Aggregate 5–6	
Aggregate 7 or more	High

(Royal College of Physicians, 2012)

Figure 1-19: The clinical risk thresholds of the aggregated NEWS scores

NEWS SCORE	FREQUENCY OF MONITORING	CLINICAL RESPONSE
0	Minimum 12 hourly	• Continue routine NEWS monitoring with every set of observations
Total: 1-4	Minimum 4-6 hourly	• Inform registered nurse who must assess the patient; • Registered nurse to decide if increased frequency of monitoring and / or escalation of clinical care is required;
Total: 5 or more or 3 in one parameter	Increased frequency to a minimum of 1 hourly	• Registered nurse to urgently inform the medical team caring for the patient; • Urgent assessment by a clinician with core competencies to assess acutely ill patients; • Clinical care in an environment with monitoring facilities;
Total: 7 or more	Continuous monitoring of vital signs	• Registered nurse to **immediately** inform the medical team caring for the patient – this should be at least at Specialist Registrar level; • Emergency assessment by a clinical team with critical care competencies, which also includes a practitioner/s with advanced airway skills; • Consider transfer of Clinical care to a level 2 or 3 care facility, i.e. higher dependency or ITU;

(Royal College of Physicians, 2012)

Figure 1-20: The NEWS standardised clinical response, in which monitoring frequency and the scale of response track patient risk.

Different risk factors trigger an appropriate response depending on the severity of a patient's NEWS score. *Figure 1-20* shows the NEWS clinical response chart; it should be noted that the observation frequency is proportional to the level of risk (Royal College of Physicians, 2012).

Any EWS system depends on regular and complete sets of patient data; gaps in a dataset compromise effectiveness and diminish reliability. Adherence to a standardised monitoring protocol is essential if EWS is to be of any clinical value (Day and Oldroyd, 2010; Ludikhuize et al., 2012). With appropriate implementation EWS systems have consistently demonstrated their value in improving hospital mortality figures (Green and Williams, 2006; Moon et al., 2011) and have been reported to be superior to clinical judgement alone in detecting critical illness (Fullerton et al., 2012).

1.4 Telemedicine and Telehealth

Telemedicine, a term that first appeared in the 1970s, may be considered as the "delivery of health services via remote telecommunications" (Moore, 1999). Today, it perhaps more accurately describes the application of information and communications technology (ICT) to enable the delivery of healthcare services at a distance, rather than face-to-face. It encompasses a range of interactive video, audio, imaging and data services on a number of platforms (e.g. mobile devices, computers, tele- and videoconferencing etc.) to facilitate remote monitoring and consultation, whether clinician-clinician or patient-clinician, to aid the diagnosis, treatment and prevention of disease or injury. The term lacks a definitive definition, as illustrated by a 2007 study

that found no less than 104 in peer-reviewed publications (Sood et al., 2007). The WHO definition is widely used and cited (World Health Organization, 2010).

Telehealth is seen by some as an umbrella term incorporating telemedicine together with the remote provision of non-clinical services such as health research and education (Cochrane Library, 2010). As with telemedicine, the precise definition is unclear, the two terms being frequently confused and used interchangeably and synonymously (World Health Organization, 2010). For consistency the telehealth term is used throughout this thesis.

1.4.1 Classification

There are three main classes of telehealth services, (i) store and forward, (ii) interactive and (iii) remote monitoring. Store and forward facilitates the capture and sharing of digital medical images and clinical audio, video and observation data. Rather than being transmitted in real-time, data is stored and subsequently forwarded to clinicians (who may be specialists) for assessment. Interactive telehealth describes real time remote audio/video instead of face to face consultation, whether patient to clinician or clinician to clinician. Lastly, remote monitoring, as the name suggests, involves use of sensors and monitoring devices for the collection of physiological and clinical data (Cochrane Library, 2010). This is also known as telemonitoring.

1.4.2 Telemonitoring

This was pioneered by NASA following work by Grams et al (Grams and Jin, 1989) who in 1980 developed a portable stand-alone medical decision support system for life support activities during space missions (Hatcher and Heetebry, 2004). In the years

that followed, many researchers proposed, built and reported results from studies on wireless ambulatory vital signs monitoring systems. Examples include AMON, a wrist-worn vital signs monitor (Anliker et al., 2004), MOPET, a sophisticated fitness monitor (Buttussi and Chittaro, 2008), SMART, a belt worn vital signs monitoring system (Curtis et al., 2008), MUSE, a multi-sensor wireless system for the continuous monitoring of congestive heart failure patients (Anand et al., 2011) and Ellingson's vital signs and biomedical monitoring system (Ellingson et al., 2006) shown in *Figure 1-21*.

(*Ellingson et al., 2006*)

Figure 1-21: An example of an ambulatory physiological monitoring system for EEG, HR, RR, temperature, bioimpedance and BP.

For the most part these were rather unwieldy and not designed with the user in mind, which is perhaps understandable, as their intention was to demonstrate proof of concept or new sensing techniques.

With advances in the electronics industry over the last two decades, such as highly integrated chips with superior performance, low power chip designs and compact component packaging for semiconductors, passives and connectors alike, telemonitoring devices, as with commercial ICT and audio/video products, have become smaller and more capable. Together with the advent of rapid prototyping through the widespread use of CAD for electronic and mechanical design, economic fast-turnaround prototype pcb production and assembly and 3D printing, has driven down the development time and costs of bringing a device to a pre-clinical trials stage.

Technological advances have led to numerous new design studies, examples including a flexible pcb sensor patch for ECG and temperature measurement (Chang et al., 2008); a real-time vital signs monitor for astronauts (Fei et al., 2010); an ear-worn cardiac monitor providing an estimation of mean arterial BP (Winokur et al., 2012); the AIRBEAT system, a sensor patch for monitoring HR, activity and motion (Li and Kim, 2012). It has also seen the launch of a number of commercial telemonitoring devices such as SensiumVitals®[1], a single-use sensor chest patch providing HR, RR and axillary temperature (*Figure 1-22*); Lifetouch[2], a similar patch-based device and the EQ02

[1] *Sensium Healthcare, London, UK*

[2] *Isansys Lifecare Ltd., Abingdon, Oxfordshire, UK*

LifeMonitor[3], a thoracic belt-mounted device capable of monitoring ECG, HR, RR, SpO_2, motion and temperature.

(Sensium Healthcare, 2015)

Figure 1-22: The SensiumVitals sensor patch, a self-adhesive disposable wireless monitoring device.

Interest generated in telemonitoring and personal healthcare has led to the announcement of the Qualcomm Tricorder X-Prize in 2014, a *"$10 million global competition to stimulate innovation and integration of precision diagnostic technologies, helping consumers make their own reliable health diagnoses anywhere, anytime."* (XPRIZE, 2015). Ten finalists have been announced, the project teams having to demonstrate and trial their devices with the winner being announced early in 2016.

[3] *Equivital, Hidalgo Ltd., Cambridge, UK*

1.5 Conclusions

The importance of vital signs measurement has long been understood (Stewart, 2003). In the healthcare sector it is an essential tool in maintaining wellbeing, aiding diagnosis and managing morbid conditions (Evans et al., 2001; Ahrens, 2008; Rogers et al., 2008). The preceding literature review in this chapter defines the vital signs and establishes what they may convey. It then examines common diseases and infections to determine where VS monitoring may have the greatest benefit, investigates VS monitors and their application in clinic, and finally appraises telemedicine and telemonitoring.

Knowledge of the normal range of readings is a prerequisite if VS measurement is to serve any diagnostic purpose. Once established, abnormal readings may be identified and their significance deliberated (Harries et al., 2009). As there are a variety of confounding factors that may cause temporary changes in VS readings (such as circadian effects (Longmore et al., 2009), anxiety, use of medication, smoking and the consumption of alcoholic or caffeinated drinks (Pickering et al., 2005; Valentini and Parati, 2009)), plus the possibility of atypical patient presentation, careful consideration is necessary before judgement is made. Regular monitoring can help minimise these problems however, revealing underlying normal levels and aiding identification of anomalies. This has great value in general fitness monitoring and condition management, where small changes over time may be significant.

Examination of the etiology, diagnosis and morbidity of common diseases and infections helps in understanding how and where VS monitoring may prove beneficial. Cancer, cardiovascular and respiratory diseases were identified as the leading causes

of death in the UK's adult population (Office for National Statistics, 2013), with many, particularly with elderly individuals, suffering from the added complication of comorbid conditions. This group, together with the elderly and immunocompromised, where found to be especially vulnerable to infection, the consequences of which are more severe with an increased mortality rate (Garibaldi, 1999; Joshi et al., 1999).

With few exceptions, diagnostic power may be improved by the combined assessment of multiple vital signs (Domagala, 2009; Royal College of Physicians, 2012). HR and BP monitoring can identify risk factors for cardiovascular disease (tachycardia and hypertension), with regular measurement benefitting condition management (Pickering et al., 2005). The latter is also true for respiratory disease, where routine SpO_2 measurement can warn of a worsening condition and hypoxaemia (Decramer et al., 2012). For cancer patients, the application for VS monitoring is not disease diagnosis itself, but rather that of infection in the immunosuppressed undergoing chemotherapy (CDC, 2014). VS monitoring is especially effective in the diagnosis of febrile infection, where an elevated temperature (Blatteis, 2003), HR (Kiekkas et al., 2007) and RR (Marco et al., 1995) may be observed in typical presentations. It is also a valuable tool in the diagnosis of atypical presentations of fever (seen in elderly patients), sepsis, respiratory infections and pneumonia, where a reduced SpO_2 level may be observed (High et al., 2009). Infection was identified as an area where regular VS monitoring could prove beneficial, especially to vulnerable individuals.

Outside of hospital VS measurement generally involves the use of multiple devices, typically a thermometer for temperature, a BP monitor for BP and HR and a pulse oximeter for HR and SpO_2. Examples of each are readily available from a number of

vendors and manufacturers. Ambulatory heart and BP monitors are also in widespread use in specialist secondary care (hospital) for cardiovascular assessment. While RR monitoring can yield valuable clinical data, unlike the other VS, readings are not routinely taken outside of a hospital setting as there are few commercial sensors available (McBride et al., 2005).

Hospital-based VS measurement may be performed with multiple devices or dedicated bedside systems capable of the simultaneous monitoring of multiple or all VS. These readings assist in triage and form the basis of Early Warning Scoring (EWS) systems, which employ aggregated scoring of routine observations as part of standardised patient care. This allows abnormal readings to be rapidly identified and reported, enabling a targeted clinical response (Royal College of Physicians, 2012).

Telemonitoring brings the benefits of ICT to medical devices for remote monitoring at the point of care, allowing a subject's VS to be captured and uploaded for assessment and storage. The recent emergence and coalescence of wireless technologies, low-power processor chips, lithium batteries and miniature components driven by the consumer electronics market has made the design of compact VS telemonitoring devices viable. This has seen the development of a number of commercial devices, none of which meet the requirements detailed in this chapter's introduction for the routine 'one-shot' collection of multiple VS observations in the community.

In conclusion:

- Regular and routine VS monitoring facilitates the identification of abnormal readings, aids diagnosis, condition management and forms part of standardised patient care in hospital.
- While cardiovascular conditions are well served, VS monitoring as an aid to the diagnosis of infection (i.e. temperature, HR, RR and SpO_2) was identified as a potential application that could be of particular benefit to vulnerable groups.
- There is a need for non-invasive, discrete and wearable respiratory sensors such that a direct measure of respiratory rate may be easily obtained for routine clinical assessment.
- Outside the hospital environment, multiple devices are required in order to obtain a full set of VS readings. There is an unmet need for a non-invasive, discrete wearable telemonitoring device capable of rapidly and simultaneously acquiring routine VS measurements in the community, from where data may be transferred to a host platform for display, analysis and storage.

1.5.1 Aim and Objectives

Following the conclusions, the aim and objectives of the research are as follows:

Aim:

To design, build, test and demonstrate the operation of prototype wearable non-invasive physiological monitoring devices capable of measuring respiratory rate and other vital signs.

Objectives:

- To design a prototype respiratory sensor.
- To carry out a pilot study of a prototype respiratory device on healthy subjects in order to compare the device to reference devices.
- To design a prototype wireless multisensor device that can simultaneously measure VS readings.
- To carry out a pilot study of a prototype multisensor device on healthy subjects in order to compare it to references devices.
- To test the telemonitoring capability of the multisensory device.

2 Device Specification and Sensor Selection

2.1 Introduction

The selection of appropriate physiological sensors is critical to the successful operation of the devices outlined in the aim and objectives of this thesis. This chapter first defines the specifications and design criteria of the two monitoring devices and then determines the optimal sensing options. Each monitoring device's key features are considered; these include measurement range, physical characteristics, how the device might be best employed and operational requirements. With these factors in mind, the sensors are then reviewed and assessed to facilitate selection for the proposed device designs. Here criteria such as transduction method and technologies, method of application and usability, resolution and accuracy, ease of interfacing and cost are evaluated, scored and aggregated to aid sensor selection. Finally, the sensor arrangement and placement of the devices are examined to produce outline designs of the prior to device prototyping.

2.2 Respiratory Sensor

From *section 1.1.4* it is clear that the sensor must measure resting RR at frequencies extending beyond the normal physiological range (12 to 20 bpm) to provide any diagnostic potential. Therefore the measurement range may be set at 4 to 30 bpm (or better), to an accuracy of at least 1 bpm mirroring that of a commercial device (Masimo Corp., 2010). The sensor's response, including averaging effects, should ideally not be delayed by more than three or four breaths.

Physically, the chosen solution should ideally be small, minimally invasive, comfortable to wear and unobtrusive. It should take little power (a few milliwatts), require little additional signal conditioning circuitry and have the development potential for wireless applications.

2.3 Multisensor Device

The simultaneous measurement of a range of physiological parameters in a single discrete device would help expedite routine patient monitoring and improve the diagnostic power of assessment compared to conventional methods, whether in clinic or the community. The proposed multisensor device should incorporate appropriate sensors to facilitate these measurements and store or transmit the readings for appraisal. It should enable snapshot readings to easily be taken, several times a day (or as directed by a physician) rather than being worn for long periods or broadcasting real-time data.

The device should be compact, easy to fit when required and easy to use - potentially by the patients themselves. Ideally, it should not encumber the wearer by requiring anything to be worn under clothing, be frequently adjusted or place any expectation on them to perform any specific exercises in order to acquire readings. These should be taken without causing distress or anxiety (eliminating white coat effect).

The unit should be battery powered with sufficient capacity to operate for at least 30 minutes a day, the batteries being easily changed or recharged as required. This would enable a minimum of six readings to be taken daily, allowing around five

minutes per reading, in line with typical clinical practice for inpatients (Johnson et al., 2014). The device should be capable of wireless data transfer to a host PC, tablet or smartphone, whether for real-time or archived readings. This should be included in the power budget.

As cardiovascular monitoring is already well served the device may be better employed in the detection of infection and disease management. It should therefore incorporate as many of the vital signs sensors as practically possible, but in view of the proposed application and difficulties of integration, blood pressure monitoring will be omitted. Skin resistance (SR) measurement however will be considered.

2.4 Sensor Specification and Selection

This section investigates physiological sensing techniques to determine those best suited for use with the proposed monitoring devices. Temperature, HR, RR and SR sensors are each assessed in turn, compared and scored against a range of measures; these include reliability, linearity, ease of interfacing, ease of use and cost. The aggregate value for each class of sensor demonstrates the degree of suitability for the application.

2.4.1 Temperature Sensing

There are many types of temperature sensors, only some of which are in common use for medical thermometry. These must be capable of measuring from around 34°C (hypothermic) to 42°C (hyperthermic) to an accuracy of ±0.2°C (Braun GmbH., -). Ignoring mercury/spirit glass thermometers and liquid crystal adhesive sensors, which

must be dismissed as they have no electrical output, the choice is between thermocouples, thermistors, semiconductor sensors and infrared pyrometers.

Thermocouples

These temperature probes are composed of two dissimilar metals that are joined (e.g. welded) at one end; when the junction is heated a thermoelectric voltage is produced across the open circuit ends due to the Seebeck effect. The magnitude of this voltage produced at a specific temperature depends on the Seebeck coefficients of metals used. Connecting thermocouple terminals directly to a monitoring device (via metallic conductors) introduces secondary thermocouple junctions that can affect the resulting output. If these are maintained at the same temperature however, there is no undue output distortion and compensation can be applied to determine the temperature at the probe's junction. The traditional method of achieving this was to place secondary junctions in an ice bath to provide "cold junction" compensation (CJC). As this is impractical in most cases, secondary junctions should be thermally matched and their temperature monitored using a thermistor to provide CJC; the probe temperature being calculated as a product of the thermoelectric output and CJC temperature (Horowitz and Hill, 2001. The process is simplified by dedicated chips (e.g. Linear Technology's LTK001 and Analog Devices' AD595), some with on-board temperature compensating sensors, that provide a compensated and linearised (mV/°C) output

Thermistors

Thermistors come in a variety of forms, but all work on the principle that a change in temperature results in a corresponding change in the device's resistance. They are

offered with both positive (PTC) and negative temperature coefficients (NTC) where the resistance is respectively proportional or inversely proportional to temperature, and either in component form or that of a temperature probe. NTC devices are widely used for temperature sensing, including medical applications whereas PTC devices employ their inherent self-heating effects to limit current for circuit protection as 'resettable' fuses (Horowitz and Hill, 2001).

Semiconductor Temperature Sensors

Semiconductor sensors such as the AD590[4] and the LM335A[5], are forms of diodes that regulate current (1μA/K) and voltage (10mV/K) respectively, and provide an output relative to absolute zero (Horowitz and Hill, 2001. Thus the LM335A has an output (its breakdown voltage) of 3.07V (+34°C) to 3.13V (+40°C) at physiological temperature ranges.

IR Pyrometers

The sensing element in an IR pyrometer is a micro-thermopile that detects radiated IR emissions of an object (wavelength ≈ 10μm). The thermopile comprises of an array of thermocouples connected in series to produce a thermoelectric voltage which is amplified and filtered to give a voltage output, or digitised and processed for a digital output. Unlike the other sensors mentioned here, detection relies on radiated heat energy rather than heat conduction or convection; hence the sensor may be used for non-contact temperature measurement (Wotiz 2012).

[4] *Analog Devices, Norwood, MA, USA*

[5] *National Semiconductor, Santa Clara CA, USA*

Sensor Comparison

This section compares the attributes of thermocouples, thermistors, semiconductor temperature sensors and IR pyrometers for use in medical thermometry.

Accuracy and Resolution

Thermocouples tend to have relatively poor accuracy (≥ ±1°C depending on the type and whether on standard or special limits (Park, 2005)), due in part to the polynomial linearisation used (Texas Instruments Inc., -). Thermistors are amongst the most accurate temperature sensors available with highly stable medical-grade devices offering ≤±0.1°C accuracy (Measurement Specialties, 2011). For all their convenience semiconductor devices have a relatively poor accuracy, e.g. ±0.5°C for the premium-grade AD590M (Analog Devices Inc., 1997). IR pyrometers, as used in tympanic membrane (ear) thermometers, have an accuracy of around 0.5°C (better once calibrated) and high resolution (≤ 0.1°C) (N. V. Melexis SA, 2008).

Response Time

The response time of a temperature sensor is related to its thermal mass and thermal conductivity of the packaging of the sensing element. The thermopile has little thermal mass and provides a faster response from radiated IR rather than heat conduction or convection.

Contact v Non-Contact

Thermocouples, thermistors and semiconductor sensors require good surface contact for reliable and accurate temperature measurement. IR pyrometers are designed for non-contact measurement and work very effectively if the target is within the focal range and viewing angle of the detector.

Linearity

Thermocouples and thermistors have a non-linear response that may be corrected by using a 'best-fit line', look-up table or applying the appropriate equation. This is likely to produce significant measurement errors unless the approximation is very close to the original response. This also affects resolution which will also be non-linear, the acceptability of which depending on the relative differences in the V/deg C ratio at the points of interest. Semiconductor temperature sensors and IR pyrometers have linear outputs across their ranges and are therefore more attractive.

Interfacing

Raw thermocouple outputs are in the order of tens of microvolts per degree Celsius and require amplification and specific signal conditioning, which includes CJC. Thermistors require either a constant current source or a potential divider circuit if used with a voltage supply, whereas semiconductor sensors tend to need a single resistor. IR pyrometers are available voltage or digital outputs, the latter being either pulse width modulated (PWM) to simulate an analogue voltage or two-wire serial bus interface.

Cost

When representative sensors of a suitable performance, size and accuracy are considered, semiconductor sensors[6] offer the most cost effective solution. Thermistors[7] and IR pyrometers[8] are next with thermocouples[9] proving the most expensive option.

[6] *£0.86 for a LM335A– RS part no. 714-7917*

[7] *£2.25 for ±0.2˚C accuracy over a 0-70˚C range – RS part no. 629-8708*

[8] *£8.75 for an MLX90615 – Future Electronics*

2.4.2 Heart Monitoring

There are a number of methods currently in use and under development. Some of these provide a wealth of data for use in cardio-diagnostics, whilst others produce a basic measure of heart rate (HR). They should be capable of measuring rates from around 30 bpm extending to a maximal rate of 250 bpm, to an accuracy of ±1 bpm (Smiths Medical International Ltd., 2009). The sensors and their sensing methods are discussed in the following sections:

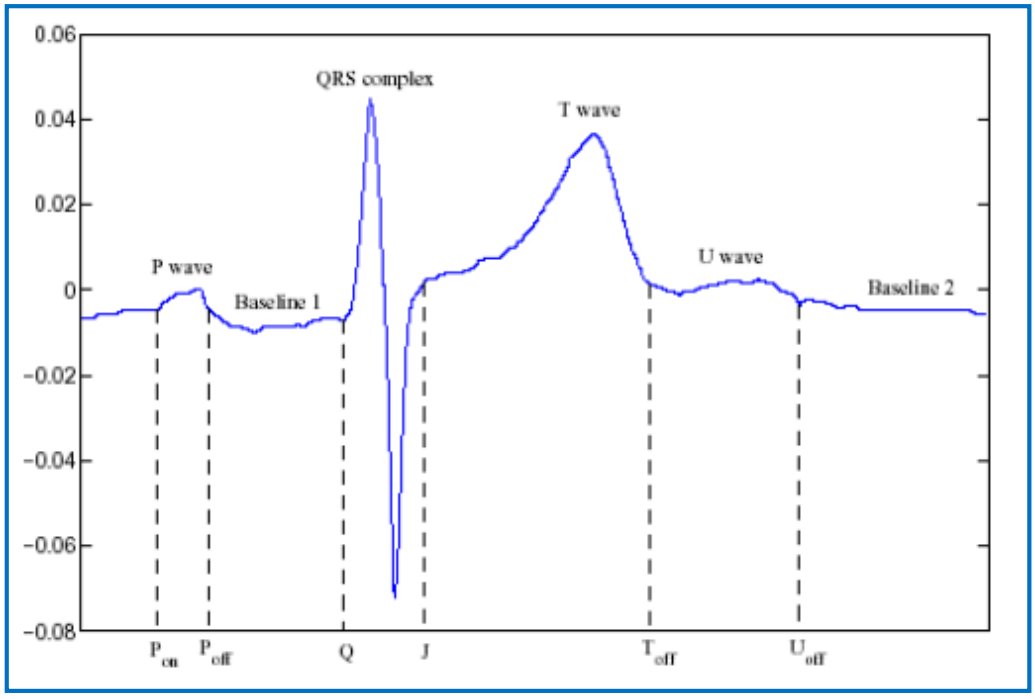
Electrocardiography

Electrocardiography (ECG or EKG) is a measure of differential (skin) potential over time across the body, of the order of a millivolt, as the cardiac muscle expands and contracts with each heartbeat (Pocock and Richards, 1999). This is measured at various points of the body, typically around the chest, using adhesive electrodes. Fitness monitors tend to display heart rate using a simple two electrode system whilst medical grade devices, whether bedside monitors or ambulatory systems, utilise multiple electrodes (from three to as many as twelve) to provide detailed cardiac data from the ECG waveform. This can be used for cardio-diagnostics, where the differential potentials from pairs of electrodes can be used to provide detailed electrocardiograms characterised by the peaks and troughs of six points, labelled P, Q, R, S, T and U (see *Figure 2-1*), of the cardiac cycle, or for simple HR monitoring based upon beat-to-beat (R-R) intervals.

ECG signal conditioning requires relatively high-gain amplification with good common-mode rejection to minimise dc effects and separate the signal from

[9] *£9.89 for a K-type ¼" copper disc probe – RS part no. 621-2287*

background noise. A range of (analogue) filters are then applied to the amplified response to limit the signal bandwidth to 0.05–100 Hz (Alberti, 2008). Further processing, perhaps using digital techniques, is required to reject or reduce electromagnetic interference (emi), conducted noise from mains electricity (typically 50 or 60 Hz with higher frequency harmonics), baseline drift due to electrode contact noise and motion artefacts prior to digitisation. A key point in ECG interface design is patient safety, thus steps must be taken to electrically isolate the electrode connections from potentially harmful currents or provide current-limiting protection (Company-Bosch and Hartmann, 2003).



(Cheah and Kumar, 2008)

Figure 2-1: An ECG waveform produced by a normal healthy heartbeat.

Impedance Cardiography

This is non-invasive method used in cardiac output monitoring. It employs two or more thoracic electrodes to measure changes in bioimpedance due to haemodynamic

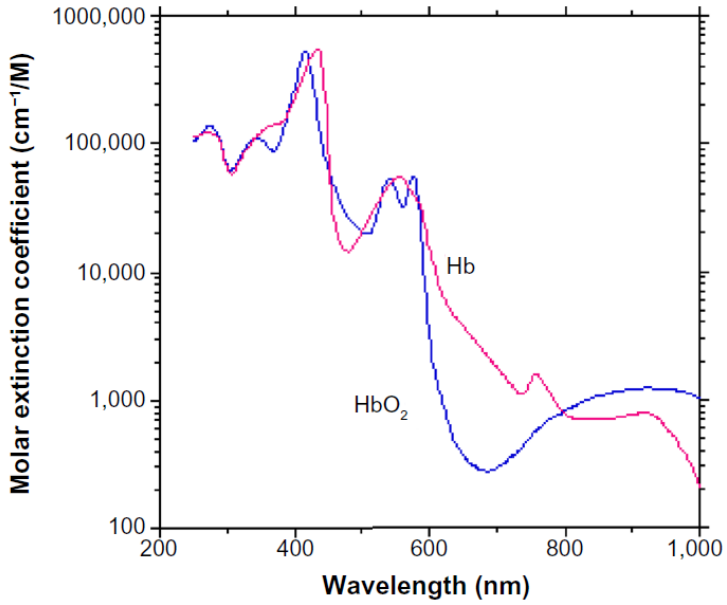
plethysmography of the heart or surrounding vasculature to provide a measure of cardiac output as well as other parameters such as stroke volume. In operation, a high frequency ac source (typically in the order of hundreds of microamps to a few milliamps) is applied across a pair of excitation electrodes with the resulting voltage appearing at a second pair of electrodes being measured; the amplitude of this voltage being bioimpedance dependent.

The development of this sensing technique is based upon Nyboer's work on impedance plethysmography (Nyboer et al., 1950), which followed earlier pioneering research first reported by Atzler and Lehmann on the measurement of thoracic impedance). After being commissioned by the National Aeronautics and Space Administration (NASA) to produce a non-invasive cardiovascular monitor for astronauts, Kubicek produced the first true impedance cardiograph (Kubicek et al., 1966), publishing the comparative results to standard invasive methods. Although this measurement method has undergone significant further development it is generally considered to have insufficient accuracy, largely due to critical electrode placement and a poor signal-to-noise ratio (SNR), for use in clinical practice (Kuper, 2004), though studies have demonstrated the potential for this technology (Thangathurai et al., 1997; Bour and Kellett, 2008; McFetridge-Durdle et al., 2008).

Photoplethysmography (PPG)

This is an optical spectroscopic technique that detects volumetric changes in blood flow from which HR, SpO_2 and blood perfusion may be measured and is more commonly known as pulse oximetry Tissue and haemoglobin absorb different wavelengths of visible and near infrared (NIR) light depending on the level of blood

oxygenation as depicted in *Figure 2-2*. The absorption of oxygenated haemoglobin (HbO_2) is strongest in the infrared (IR) band and reduced haemoglobin (Hb) in red light, therefore wavelengths with the greatest departure from the isobestic point (that of equal absorption at 800 nm) are chosen for the maximum differential absorption. Wavelengths of 660 nm (Hb) and 915 – 940 nm (HbO_2) are commonly used with LEDs providing the light source (Jalan et al., 2006).

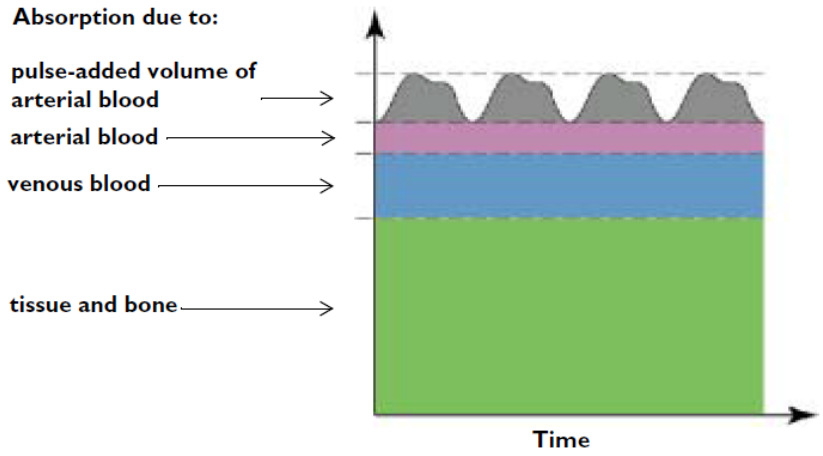


(Nitzan et al., 2014)

Figure 2-2: The absorption spectra of oxygenated (HbO_2) and reduced haemoglobin (Hb)

Light absorption in perfused tissue follows the Beer-Lambert law in that the concentration of an absorbent material may be determined from the intensity of light transmitted through it given the light's intensity, wavelength, path length and the absorption characteristics at the emitted wavelength (Sinex, 1999). Light is absorbed in the red and IR bands by bone, tissue and venous blood to produce a DC response, the magnitude of which is relative to level of absorption. Variations in the absorption of arterial blood with the systolic phase of each heartbeat produces a small AC response

reflecting pulse frequency (*Figure 2-3*) which provides an indirect measure of HR; this appears in superposition with the larger DC response (Philips Medical Systems, 2003).



(Philips Medical Systems, 2003)

Figure 2-3: The relative absorption characteristics of perfused tissue

In operation the two emitters are turned on and off alternately and thus can be measured with a single detector. The SpO_2 is calculated from the ratio between the HbO_2 and total haemoglobin measurements and is expressed as a percentage (Moyle, 2002). As the LEDs can be relatively power hungry, the pulse frequency and duty cycle (the relative time that the LED is on or off) may optimised for power saving in portable devices.

Sensor probes are usually clipped on to fingers or toes, although ear lobe sensing is sometimes used in cases where subjects have poor circulation in their extremities. These are examples of transmissive sensors where the detector measures the amount of light transmitted through tissue from parallel-mounted opposed emitters. Reflectance oximeters, as the name suggests, measure the amount of light reflected from the surface of skin and tissue and are typically applied on the forehead above the temporal artery (Fernandez et al., 2007). Some reports suggest that reflectance

oximetry is superior and more reliable than fingertip sensing in certain clinical environments (Schallom et al., 2007).

Seismocardiography

Contact accelerometers have been successfully used for HR measurement by detecting cardiac thoracic motion (Phan et al., 2008), a method that has been termed *seismocardiography* (Dinh et al., 2011). Although this method has been successfully demonstrated, care must be taken in the separation of the HR signal from the respiratory response, motion artefacts and noise sources.

Other Methods

Electronic blood pressure (BP) monitors (also known as sphygmomanometers) usually use oscillometric methods (Raamat et al., 2010) and are able to record HR over the BP measurement period. This is calculated from the period between pulse wave oscillations in cuff pressure once the cuff has been inflated. Due to its very nature this can only provide periodic snapshot readings and therefore cannot be considered for any form of continuous monitoring.

Sensor Comparison

This section compares ECG, impedance cardiography, PPG and seismocardiography sensing for use in HR monitoring.

Reliability

ECG and PPG are in widespread use and offer reliable measurement with the former having better performance, being less affected by motion artefacts. Impedance and seismocardiography are less developed and prone to a variety of problems such as

motion artefacts, accuracy of positioning and high SNR; this makes them less suitable for use in the proposed monitoring device.

Ease of interfacing and data processing

There is little to choose between the sensing methods in this respect. They all require significant signal conditioning, filtering and signal processing to extract a viable signal from background noise from which HR can be calculated.

Ease of use

PPG is the easiest method to use, especially from the subject's perspective, as the sensor may be clipped on or fixed in place with adhesive material. The other methods all necessitate a certain amount of preparation before any data can be collected. ECG and cardiothoracic impedance monitoring are both electrode-based (whether single-use disposable or sprung metallic contacts), requiring clean skin and gel to ensure good electrical contact. The accelerometer used in seismocardiography must be securely fixed to the thorax (with an adhesive pad). For electrode-based or motion sensing there may be problems with the consistency of positioning and adhesive or electrode integrity.

Costs

The cardiothoracic accelerometer is potentially the most expensive of the sensors considered here and requires consumable sticky fixing pads. The electrode-based sensing methods may need disposable contacts, but would require conductive gel and alcohol wipes. If assembled from discrete LEDs and photodiodes, PPG sensing is relatively low cost in parts terms (two LEDs and a photodiode costing approximately £1

to £2[10]). The cost of the associated interface circuitry however, though relatively inexpensive, must also be considered, together with computational costs.

2.4.3 Respiratory Monitoring

There are possibly more sensors and methods for respiratory monitoring than all the other vital signs combined. Some have been adopted for clinical use, but there is little evidence to suggest the development of monitoring products for the home market. Some of the key sensing methods and technologies are discussed in the following sections.

Direct Sensing Methods

Capnography is perhaps the most common clinical respiratory monitoring technique, being used in the observation of anaesthetised patients and in ventilators, and is widely considered to be the gold standard. A capnograph measures changes in carbon dioxide concentration levels in breath, usually via infrared absorption, to provide diagnostic respiratory data. A pneumotachometer (also known as a pneumotachograph) may also be used to monitor respiratory flow and breath volume (Mandal, 2009).This typically employs a differential gas flow sensor that may be used for direct oral measurement or mask-mounted for continuous monitoring. Cranfield Health's Single Metal Oxide Sensor – Gas Analyser system (SMOS-GA), otherwise known as the "Breathotron" (Walton et al., 2014) utilises a similar, but simpler (and less expensive) monitoring method, in which a mass flow sensor is fitted to the outlet

[10] *RS Components Ltd, Corby, Northants, UK*

of a modified respirator mask. Neither of these is particularly discrete, being relatively invasive, or suited to continuous ambulatory monitoring.

Another method employs one or more temperature sensors, typically thermistors, mounted in a nasal cannula such that respiratory temperature changes can be detected. These devices must have a low thermal mass and sufficient sensitivity such that the sensor's dynamic response can accurately track the convection effects of nasal respiratory airflow. Ease of use has led to some clinical adoption although accuracy is a concern and the relationship to flow rate only semi-quantitative (Farre et al., 1998); nevertheless they have shown some success in the detection of sleep apnoea events (Farré et al., 2004) and wireless sensors have been demonstrated (Jovanov et al., 2001. A pyroelectric polymer (PEP) based respiratory sensor has been developed and validated against standard methods (Brookes et al., 2003) reportedly with notable success. Although the device relies on directly sampled breath, it is small enough to integrate into a miniaturised system. As of January 2015 there is little evidence to suggest the device has been commercialised.

Thoracic Band-Based Sensing Methods

There are a number of non-invasive sensing methods that measure physiological changes with respiration via a thoracic band. Of the commercial devices, Vernier[11] offer a belt-mounted system (Vernier Software & Technology, 2009) using a pressure sensor attached to a pneumatic chest band. There are a number of devices reported that utilise a similar mounting, e.g. chest bands featuring piezoelectric tension/strain sensors plus chest and back-mounted tri-axial accelerometers (Khoo et al., 2008) and

[11] *Vernier International Inc., Sarasota, Florida, USA*

bi-modal ultrasound transducer (Lanatà et al., 2006). Another method which has grown in popularity is respiratory inductance plethysmography (RIP); this employs an elastic belt containing coiled wire which is energised by an AC current to generate a weak magnetic field. Respiratory changes in thoracic cross-sectional area produce fluctuations in the magnetic field, causing measurable frequency variations in the excitation (Mazeika and Swanson, 2007). Two independent bands are typically used, one around the chest and another around the abdomen, giving a measure of normal respiration and airway obstruction that is reportedly less prone to spurious signal artefacts than impedance measurement methods (Cohen et al., 1994). However effective, once again these are relatively cumbersome and not especially discrete.

One approach to simplify the mounting of a diverse range of sensors is to incorporate them into a wearable garment to which a compact monitoring system may be attached. One such example uses both an ECG-derived response (EDR) and piezo plethysmograph sensors on the thorax and abdomen in to measure respiration in a 'bioshirt' (Nam et al., 2005). This method is, arguably, an improvement over a chest-band for respiration sensing if multiple physiological parameters are to be monitored.

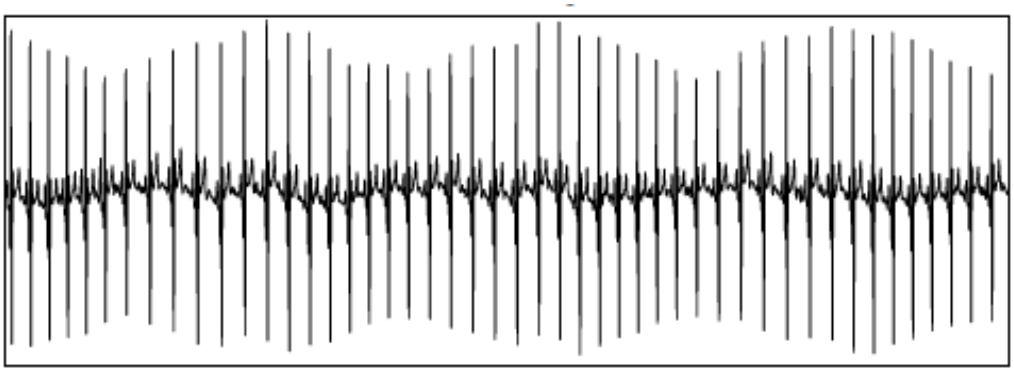
Impedance Pneumography

Electrical impedance pneumography (EIP) uses pairs of conventional ECG electrodes placed upon the thorax or abdomen to measure respiratory changes in conductivity (Lahtinen et al., 2009). A high-frequency AC current of low amplitude (typically a milliamp or less at a frequency above 20 kHz (Baker, 1989) is passed between the electrodes, producing a measurable impedance-dependent voltage that rises on inhalation and falls on exhalation. The resulting waveform is prone to distortion due to

interference from cardiac output and motion artefacts (Wilkinson and Thanawala, 2009) and sensitive to electrode positioning (Seppä et al., 2007; Lahtinen et al., 2009).

Estimation from Heart Rate Variability

ECG-derived respiration monitoring (EDR) employs a range of signal processing techniques to provide an estimation of respiratory rate from an ECG waveform. It is based upon rhythmic beat-to-beat heart rate variability (HRV) caused by respiratory modulation of the heart (Porges and Byrne, 1992). One method analyses an ECG's R-wave amplitudes (see *Figure 2-4*) and extracts the underlying respiratory modulated response from the signal envelope to provide a measure of breath frequency (Mazzanti et al., 2003; Bailon et al., 2006; O'Brien and Heneghan, 2007; Cysarz et al., 2008).

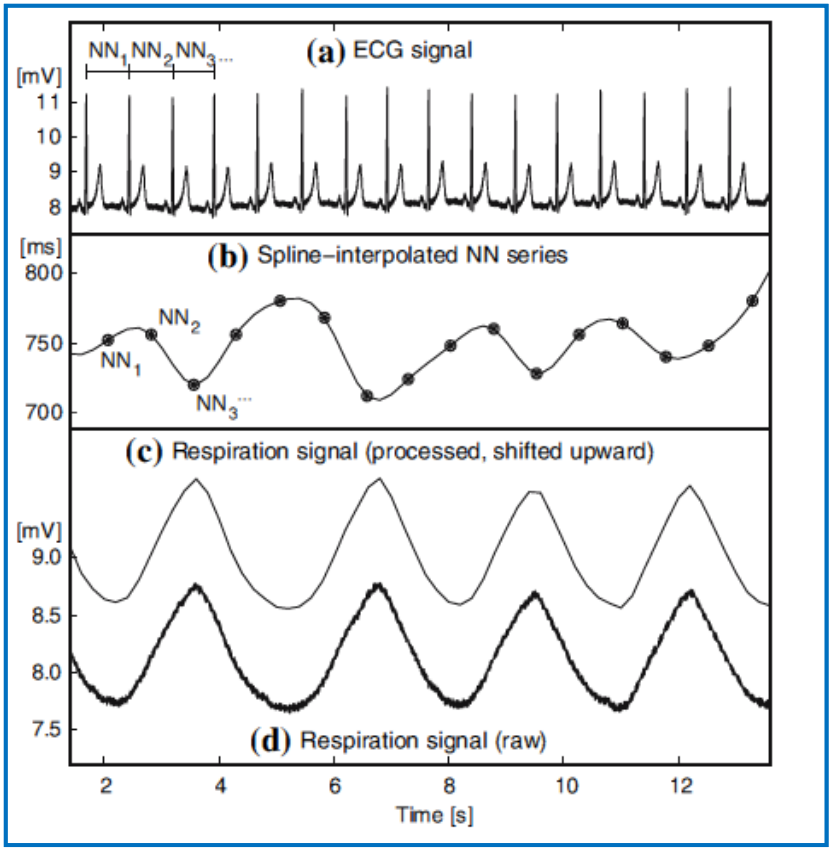


(O'Brien and Heneghan, 2007)

Figure 2-4: An ECG trace showing respiratory-induced amplitude changes in the QRS envelope

Another approach is based upon HRV monitoring, specifically that due to respiratory sinus arrhythmia (RSA) (Bernardi et al., 2001). Here, periodic changes in the ECG's R-R interval may be observed as this is shorter during inspiration and longer in exhalation. A surrogate respiratory signal with a bandwidth of approximately 0.15 to

0.8Hz (Yasuma and Hayano, 2004) may be extracted from the ECG waveform by comparing the periods of successive R-waves and applying a range of signal processing techniques, an example of which is shown in *Figure 2-5* (and reported by Cysarz et al., 2008; Schäfer and Kratky, 2008; Tiinanen et al., 2010). RSA is most prominent in the young and diminishes with both age and fitness, thus it may be less effective in elderly individuals (Yasuma and Hayano, 2004).



(Schäfer and Kratky, 2008)

Figure 2-5: An ECG trace showing R-R intervals (a) plotted as a time interpolated series (b)and the extracted respiratory signal (c& d)

With appropriate filtering and signal processing, respiration may also be determined from the photoplethysmograph (PPG) waveform of a pulse oximeter

(Leonard et al., 2003; Clifton et al., 2007), although in Vegfors' fibre-optic IR sensor it is suggested that there may be some latency in the response (Vegfors et al., 1993).

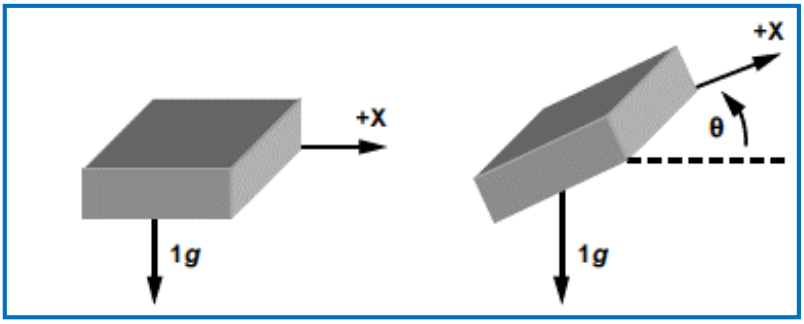
Respiratory Motion Sensing

Another option is that of directly measuring respiratory thoracic movement with single or multi-axis accelerometers. These are electromechanical transducers that are sensitive to acceleration forces and thus, motion relative to gravity ($1g = 9.81\ ms^{-2}$) – to which they are normally calibrated. Developments in fabrication and the growth of micro-electromechanical systems (MEMS) technology have seen a significant reduction in the size and cost of devices over the last 10 to 15 years (Walter, 2007) to the point that they are becoming ubiquitous. Today, the ubiquitous accelerometer is commonly found in vehicles (land, sea and air), hard disk drives, mobile phones, tablet PCs, computer gaming controllers and many other products and devices where orientation, motion or vibration sensing is required.

Static measurements can provide a measure of incline where the device's plane is measured relative to gravity. Here, the initial position shown in *Figure 2-6* gives an output equivalent to +1g – a rotation of 90°= 0g and 180° = -1g. An intermediate angle (θ), as shown in the right–hand diagram, may be calculated as follows:

Equation 2-1: Accelerometer tilt angle calculation

$$\theta = sin^{-1}\left(\frac{accelerometer\ output\ (g)}{gravity\ (g)}\right)$$



(Fisher, 2010)

Figure 2-6: Basic gravimetric tilt sensing with a uniaxial accelerometer

Dynamic measurements can be used to determine the nature of motion that the accelerometer is experiencing. Both the magnitude and frequency of the signal are of interest, providing amplitude range, angular motion, velocity (acceleration divided by time) and, with the application of frequency domain analysis, key frequency components (from vibration or motion) from a single signal which may be used to characterise a response.

A study by Reinvuo comparing single-axis accelerometers with HRV-derived respiratory measurements from a blood pressure sensor gave passable results (Reinvuo et al., 2006). Phan investigated respiratory and cardiac monitoring using a biaxial device (two orthogonal axes) (Phan et al., 2008). In their experiments the sensor was sited approximately over the heart. Whilst this successfully captures both cardiac and respiratory waveforms, they are superimposed and must be separated both from each other and from extraneous noise. Hung's study also uses a biaxial device upon the thorax, this time summing the two outputs to give a composite signal; a dynamic adaptive filter was then applied to clean the waveform which showed correlation to a reference RIP sensor (Hung et al., 2008).

Use of a triaxial accelerometer (having three orthogonal axes) would appear to offer advantages over uniaxial or biaxial sensing as all three planes may be considered; hence a respiratory signal is not dependent upon the orientation of the sensor (Bates et al., 2010). Anmin's work, which employed a triaxial accelerometer as an inclinometer upon the diaphragm muscle below the xiphoid, suggests composite waveforms may also be considered and that with appropriate signal processing interference from non-respiratory motion artefacts may be reduced (Anmin et al., 2009).

Acoustic Sensing Methods

A number of acoustic sensing methods and devices have been reported. Masimo's[12] Rainbow Acoustic Sensor has recently become commercially available. The sensor is incorporated into a self-adhesive neck-worn pad and senses the characteristic inspiratory and expiratory sounds from which respiratory frequency is extracted. Clinical trials have shown favourable performance when compared to a standard capnograph (Macknet et al., 2007; Masimo Corp., --b).

Corbishley reports on the development of a miniaturised acoustic sensor (Imperial College, London) monitoring tracheal sounds; these are caused by turbulent respiratory airflow and may be detected as wideband white noise on the skin surface (Corbishley and Rodríguez-Villegas, 2008). This reportedly requires relatively high sampling rates (11.050 kHz) and a sophisticated algorithm to resolve the respiration signal from background noise; speech, swallowing, heartbeat and musculoskeletal

[12] *Masimo Corp, Irvine, California, USA*

motion. Proposed future developments included integrating signal processing with the sensor assembly, although it would appear that this was not pursued.

Sensor Comparison

Although direct aspiratory sensing using flow or temperature sensors would likely prove effective, it is relatively invasive and will not be considered here. In the following sections thoracic band, thoracic impedance, respiratory motion sensing and estimation of RR from HRV are compared.

Reliability

With a resting and compliant subject all four monitoring methods should be reliable assuming the sensors are fitted correctly and extraneous motion is minimised. All should perform satisfactorily with subjects standing, sitting or supine (providing the sensors are not disturbed), as demonstrated with a triaxial accelerometer (Chan et al., 2013). Thoracic bands and estimation from HRV are the most established in clinical practice while the other methods are still rooted in research.

Ease of interfacing and data processing

Accelerometers used in respiratory motion sensing offer the easiest electrical interface, irrespective of whether analogue or digital outputs are available as negligible additional signal conditioning is required. Impedance pneumography employs the same techniques as those used in seismocardiography (with different electrode positioning and excitation parameters) and suffers from motion and cardiac artefacts, which must be minimised or removed. Thoracic band interfacing rather depends upon the transduction method used, but would nevertheless require analogue signal conditioning and digital signal processing to extract respiratory rate. The process of

extracting RR readings by estimation from HRV is detailed in section *2.4.3 (page 90*) and may be achieved algorithmically.

Ease of use

Where an HR sensor is already in use, estimation of RR from HRV places the least burden on the user as it piggy-backs on an existing sensor. Thoracic band sensing, by its very nature, requires that the subject fits one (or two) belts around their torso to capture sympathetic respiratory motion; hence there is a reasonable degree of preparation prior necessary before measurement can take place, proving unwieldy and likely to be unpopular with test subjects. In comparison fitting a respiratory motion sensing accelerometer is far more straightforward and is relatively unobtrusive, although a degree of preparation is still necessary. A consideration of the issues with impedance sensing may be found in *section 2.4.2 (page 81)*.

Costs

The thoracic sensing band has the highest associated cost which is essentially the one-off cost of the sensor. The respiratory motion sensing accelerometer has the second highest one-off cost, but also adds consumables in the necessity for sticky adhesive pads. Impedance pneumography would prove cheaper, requiring consumables such as disposable contact electrodes, conductive gel and alcohol wipes. Estimation of RR from HRV would appear to have no associated impact, aside from development, though there is the potential for a small increase in computational cost and power budget.

2.4.4 Skin Resistance Monitoring

In its simplest form, skin resistance (SR) can be measured using either of the circuits shown in *Figure 2-7*. Here, resistance is calculated from Ohm's Law using a simple circuit where a constant dc excitation voltage or current is applied across electrodes contacting the skin and the resulting circuit current or voltage measured. In either case the circuit current should be kept to a maximum safe level of no more than 1 – 2 mA and below 1V (Sutherland et al., 2009). It should be noted that in practice potential dividers and amplifiers would be employed in additional signal conditioning circuits.

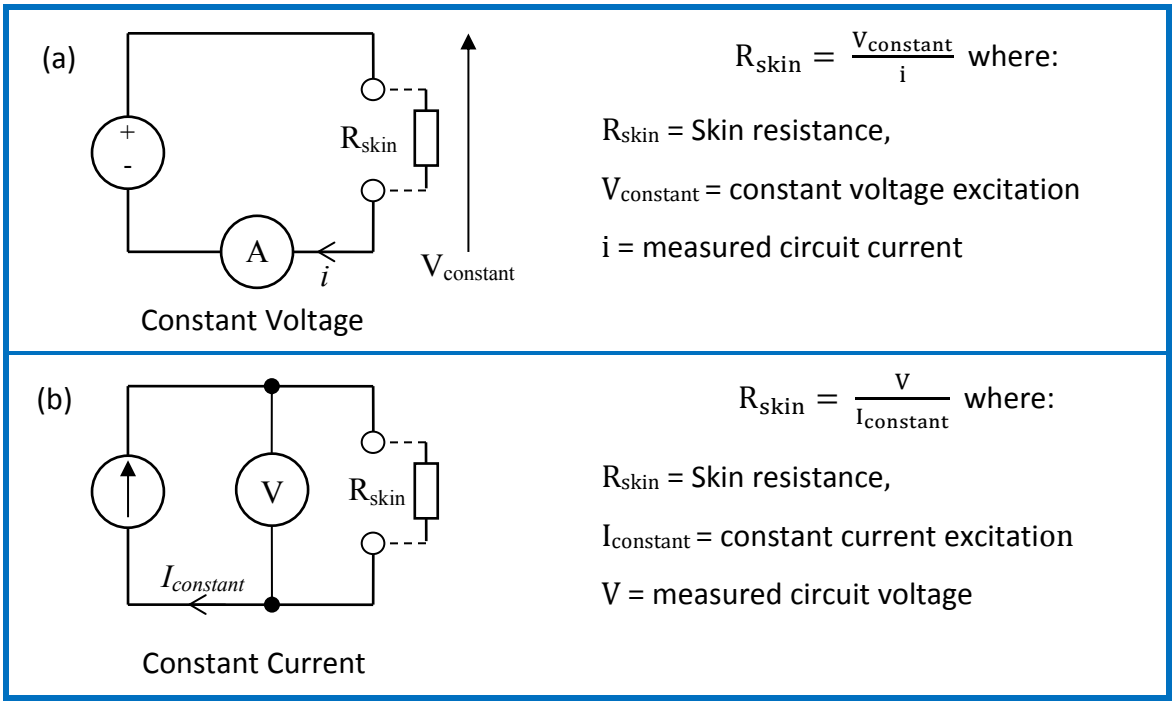


Figure 2-7: Two basic skin resistance measurement circuits using (a) constant voltage and (b) constant current techniques, resistance is calculated from the ratio of the constant and measured values.

The simple circuits described should produce a measurable difference between dry skin and that moistened by sweat. Both resultants are quoted as a resistance with units of Ohms (Ω), but should perhaps more correctly be considered as a conductance

(G), a reciprocal measure of conductivity (G = I/V from Ohm's Law) quoted in Siemens (S) or Mhos (or Ohm spelt backwards with an inverted Ω symbol) in older literature. Strictly speaking, as skin has capacitance and thus reactance or resistance (X_C) to an alternating voltage or current source, this might be considered when taking measurements and reference should be made to impedance rather than resistance. Impedance (Z) may be described as the voltage to current ratio in the frequency domain and comprises of both resistive and reactive components, the former having no frequency dependence and the latter (capacitive reactive component) given by $X_C=1/2\pi fC$ (where the variables are capacitance C and frequency f). This has little significance at frequencies nearing DC (zero Hz) as the 'capacitor' does not conduct, reactance tends to infinity and the resistive component dominates. Impedance is often quoted as admittance (Y), its reciprocal form, which is also measured in Siemens.

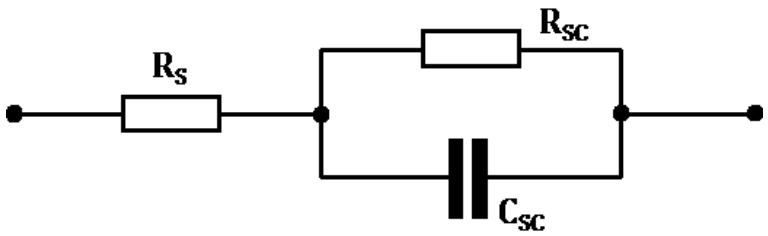
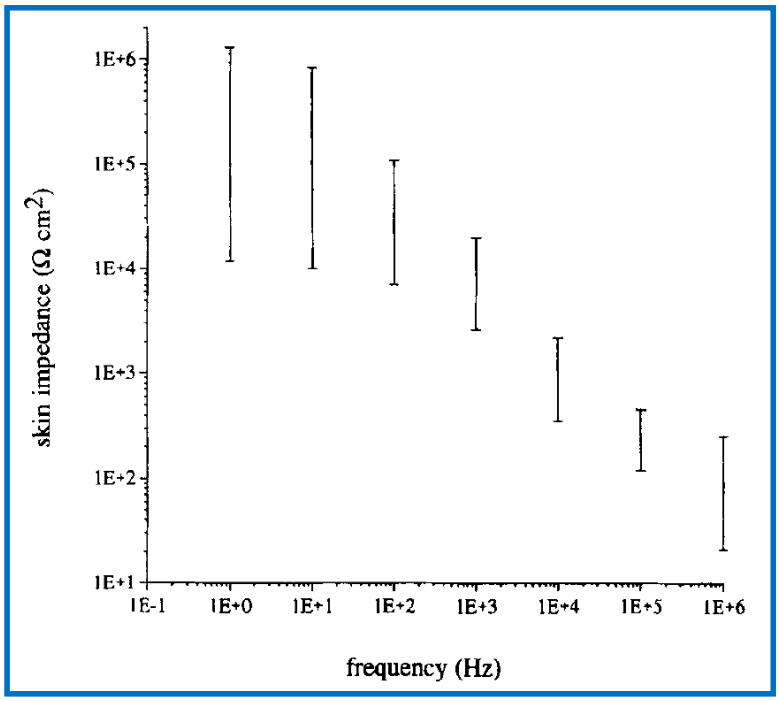


Figure 2-8: A basic equivalent circuit model of skin impedance, with R_{SC} and C_{SC} representing the stratum corneum and R_S, deeper tissue

Skin impedance can be modelled by a simple two terminal network as shown in *Figure 2-8*. The *stratum corneum* may be characterised by a resistor (R_{SC}) and capacitor (C_{SC}) in a parallel circuit, which is in series with a resistor (R_S) representing deeper internal tissue. Typical values quoted range from 10^4 to 10^6 Ω cm^{-2} for R_{SC}, l to 50 nF cm^{-2} for C_{SC} and 100 to 200 Ω cm^{-2} for R_S (Prausnitz, 1996), to 25 to 500kΩ cm^{-2} (R_{SC})

and 10 to 30 nF cm^{-2} (C_{SC}) (Montagu, 1964). Therefore, at DC and low frequencies R_{SC} dominates until the falling reactance of C_{SC} takes over at high frequencies as depicted in *Figure 2-9*. Whatever the measurement frequency may be, as both components are area dependent, the intra-electrode spacing is an important factor to consider.



(Prausnitz, 1996)

Figure 2-9: Ranges of skin impedance shown as a function of frequency

Irrespective of the parameter of interest, it is electrode properties that are the key to successful measurement. The skin-electrode impedance should be minimised, particularly at DC and low frequencies, such that it does not compromise measurement; thus the electrode material, form and application of conductive aqueous gel must all be considered (Rosell et al., 1988). Inter-electrode spacing might ideally be of sub-centimetre order, but should be consistent. As skin is far from homogenous in terms of measured impedance (Horton and VanRavenswaay, 1935), sweat gland density (Wilke et al., 2007) and sweat rate (Licht et al., 1957), the

measurement site must be carefully chosen. Those areas prone to interference from electro-muscular and cardiorespiratory activity should, where possible, be avoided.

Sensing Method

This requires two skin-contacting electrodes, the choice being between wet (silver/silver chloride electrodes and hydrogel) or dry (gold) contacts. The other key concern is the choice of dc excitation for basic skin conductance measurement or ac for true skin impedance/admittance.

Electrodes

Whilst silver/silver chloride electrodes and hydrogel undoubtedly give good results, as seen with ECG measurements, location and inter-electrode spacing are important for reproducibility, and they must be replaced after use. Gold electrodes, whether with surface or sprung contacts, may be used dry but are less likely to provide optimal results without the use of a gel electrolyte (Neuman, 1999). They may however be mounted with fixed spacing in a sensing probe or upon a monitoring device and would not require replacement, only cleaning.

Excitation

Basic SR measurements using dc excitation are adequate for sweat detection. Although impedance measurements with ac excitation would also return viable results and provide supplementary data, the additional circuitry and software overhead adds significantly to the design burden with little additional benefit.

2.4.5 Sensor Selection

Having investigated the sensing methods in each category, these are now discussed and scored to determine the preferred option in each case. A relative scoring system is

used, in which extremely poor performance is scored at zero and excellent performance at ten.

Temperature Sensing

In considering the factors discussed in *section 2.4.1 (pages 78-80)* and their influence on sensor selection, the four sensor types were scored by the author based upon the evidence presented. The results are shown in Table 2-1. Thermistors and IR pyrometers stand out as the best overall options for physiological temperature measurement, with the IR device scoring highest due to several clear advantages. As a good thermal coupling may not be guaranteed, non-contact thermometry offers improved reliability and reproducibility. IR sensors with integral signal conditioning also provide a linear response and digital or analogue outputs for ease of interfacing. A survey of available IR pyrometers determined that the MLX90615 from Melexis offered the optimum solution (chiefly package size and availability) for the proposed monitoring device. This has four terminals for a digital (I^2C) or pulse width modulated output housed in a small 5mm diameter (TO-46) package with the lens aperture uppermost and pin contacts below (N. V. Melexis SA, 2008).

Property	Thermocouple	Thermistor	Semiconductor	IR Pyrometer
Resolution at physiological temperatures	6	10	3	9
Ease of interfacing	4	7	8	9
Fast response time	8	8	7	9
Linearity	4	5	8	9
Non-contact performance	6	6	6	9
Costs *(lower scores indicate higher costs)*	4	7	9	5
Total	**32**	**43**	**41**	**50**
	53.3%	**71.7%**	**68.3%**	**83.3%**

Table 2-1: Temperature sensor scoring

Heart Rate Monitoring

Following on from section 2.4.2, the four monitoring methods discussed were assessed for use with the proposed monitoring device and scored accordingly (see *Table 2-2*). For reliable monitoring the well-established ECG and PPG methods are the preferred options. There is not too much to choose regarding the ease of interfacing and data processing as all methods have their own particular issues. From the user's perspective PPG is the easiest to use as there is no preparation required. If integral LEDs and detector are assumed, the lowest costs are for PPG; there are also no associated consumables.

The aggregated scores demonstrate that PPG sensing offers the best all round solution for HR monitoring, being cheap, easy to use and reliable. It is also

advantageous in that it provides the potential for simultaneous SpO_2 monitoring if suitable algorithms are applied.

Property	ECG	Impedance	PPG	Accelerometer - Seismocardiology
Reliability	9	6	8	4
Ease of interfacing and data processing	7	6	6	7
Ease of use	6	4	9	7
Costs *(lower scores indicate higher costs)*	6	6	9	5
Total	**28**	**22**	**32**	**23**
	70.0%	**55.0%**	**80.0%**	**57.5%**

Table 2-2: Heart rate sensor scoring

Respiratory Rate Monitoring

The four monitoring methods discussed in *section 2.4.3* were assessed and scored accordingly (see *Table 2-3*). There is little to choose between the sensing methods in terms of reliability (see *page 95*) and ease of interfacing and data processing; here the two thoracic methods show a slight advantage. For ease of use and costs, thoracic motion sensing and estimation from HRV easily outscore the other methods. The latter method in particular is easy to use and without cost if a PPG or ECG signal is already available.

The results show that estimation of respiratory rate from HRV derived from a PPG waveform offers the best overall potential sensing method as no additional circuitry is required. There are potential problems with the method as discussed (see *section*

2.4.3, page 90); hence the thoracic motion sensor offers a viable option for discrete indirect respiratory sensing.

Property	Estimation from HRV	Thoracic Band	Thoracic Motion	Impedance
Reliability	7	8	7	6
Ease of interfacing and data processing	5	5	7	5
Ease of use	9	6	8	5
Costs *(lower scores indicate higher costs)*	10	5	7	8
Total	**31**	**24**	**28**	**24**
	77.5%	**60.0%**	**70.0%**	**60.0%**

Table 2-3: Respiratory rate sensor scoring

Skin Resistance Sensing

After consideration the points raised were scored according to perceived values, the results being shown in the following tables. Although gold electrode performance is likely to prove inferior to silver/silver chloride, this is outweighed by the convenience offered by the former in a fixed installation; without the need for disposable parts, consumables or constant maintenance. The main drawback of silver/silver chloride electrodes however is the use of a water-based electrolyte gel upon the surface of the skin; this renders any such measurement of skin water content meaningless. This is shown in *Table 2-4*.

Property	Silver/silver chloride	Gold contacts
Convenience and practicality	3	10
Contact performance	9	7
Costs *(lower scores indicate higher costs)*	3	9
Total	**15**	**26**
	50.0%	**86.6%**

Table 2-4: SR electrode scoring

Property	dc	ac
Performance	9	9
Benefit	8	9
Ease of interfacing	8	4
Total	**25**	**22**
	83.3%	**73.3%**

Table 2-5: SR excitation scoring

Table 2-5 compares dc and ac excitation for SR measurement. Both methods will deliver results, but producing a dc output and measuring the resulting response considerably reduces circuit complexity. There is no clear benefit to be gained from ac excitation and impedance sensing for this application.

2.5 Device Placement

The physical positioning of the devices on the human body can be critical to successful and reliable measurement. In considering the sensors, the selected HR (PPG) and SR sensors must be in direct skin contact (the former with well perfused tissue), while the RR sensing accelerometer must be closely coupled to the body and the IR pyrometer in close proximity to a measurement site reflecting core temperature or a reliable proxy thereof. Focussing first on temperature, rectal and skin measurement can immediately be ruled out on the grounds of inconvenience and ineffectiveness respectively, eliminating a wrist-worn solution. Oral measurement may also be excluded as though temperature readings would be assured, HR, RR and SR would certainly not. Temporal measurement remains a possibility (using a headband or hat), but would need to maintain perfect skin contact throughout the measurement period which may prove impractical. Having eliminated other temperature measurement sites, only the axilla and ear remain as viable options.

2.5.1 The Axilla Option

The preferred solution would be a device with multiple integral sensors. In this instance this would be unachievable as a wireless or umbilical axillary temperature sensor would be necessary – probably in the form of a thermistor. This would however allow a multisensor device to be located upon the thorax and attached either to a thoracic band or directly via an adhesive backing. A number of extant telemonitoring systems, such as those offered by Sensium Healthcare and Hidalgo Ltd. (see section 1.4.2, p66-67), employ similar wearable sensing solutions. These are effective in a role

requiring continuous or longer-term (on demand) monitoring, but do not lend themselves to discretely acquiring periodic readings as proposed in this thesis.

An alternative concept considered employed a small multisensor device attached to the clavicle and sited next to the throat (as depicted in *Figure 2-10*). This featured skin-contacting reflectance pulse oximetry and SR sensors on the underside, and incorporated a tri-axial accelerometer to monitor clavicular respiratory motion. Temperature would be measured either in the axilla or, if accurate placement above the carotid artery was achievable, via an integral IR pyrometer. Whilst there was some merit in this idea, it would be unlikely to provide meaningful temperature readings and would be relatively unwieldy in use. This was therefore eliminated for multisensor monitoring, but formed the basis for the proposition of a clavicular respiratory sensor.

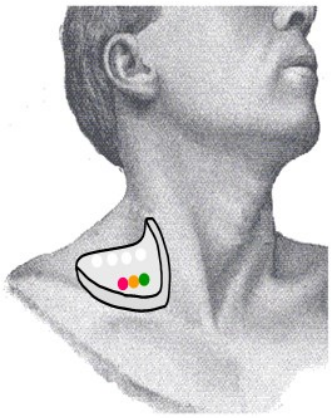


Figure 2-10: An original design concept for a multisensory monitoring device sited upon the clavicle

2.5.2 The Ear Option

An ear-based system would appear advantageous for the proposed multisensor device. It would provide access for tympanic temperature measurement and a pulse oximeter ear clip for HR, SpO_2 and estimated RR measurement. SR could prove to be

more difficult however unless good skin to electrode contact is achievable. The location would certainly facilitate discrete measurement, being easily accessible for taking readings and meeting the requirement for periodic monitoring set out in *section 2.3 (p74)*. As this appeared superior to the clavicular option, the Ear-worn Personal Monitoring System (EPMS) was selected for further development.

2.6 Conclusions

In this chapter the design specifications for the respiratory and multisensor devices were established and the VS sensing options reviewed to aid sensor selection. Finally, the optimal placement of the multisensory device was discussed.

- Both proposed devices would need to be small, consuming little power and capable of VS measurement extending beyond the normal ranges.
- The respiratory monitoring device should be capable of measuring RRs from 4 to 30 bpm, require minimal signal conditioning and the response not delayed by more than three or four breaths.
- The multisensory device should allow the simultaneous collection of multiple VS readings. It should facilitate the recording of 'snapshot' measurements taken several times a day and wirelessly transmitted to a host device. It should be easy to fit and use by non-clinical staff or patients and need only be worn when taking readings.
- Infection monitoring and disease management were identified as potential applications. As BP measurement would present difficulties with device integration

and was of less diagnostic value, it was dropped from the multisensor device's list of requirements with SR sensing being considered for inclusion.

- IR pyrometers were chosen for temperature sensing, having good resolution, a fast response, linear output, non-contact performance and digital interface.
- PPG sensing was selected for its clear advantage over other HR sensing methods, being reliable, well proven, easy to use and presenting the potential for simultaneous SpO_2 monitoring if appropriate signal processing was applied.
- RR estimation from HR variability was the most attractive RR measurement option as it extracted readings directly from an HR sensor waveform, albeit with additional signal processing load. While this was suitable for the multisensory device, respiratory motion sensing accelerometers, the next best option, were chosen for development as an independent RR sensor.
- Measurement sites for the multisensory device were narrowed down to a clavicular or ear-worn solution. The ear was chosen as it enabled tympanic temperature measurement and HR, SpO_2 and RR sensing via a pulse oximeter ear probe and satisfied the requirement for accessibility, facilitating discrete periodic monitoring.
- Clavicular sensing was chosen for the wearable RR sensor, where an accelerometer would monitor respiratory clavicular motion.

3 Materials and Methods

This chapter details the materials used and methods applied during the design and manufacture of the prototype devices. The former reviews component selection and the equipment used over the course of the project, the manufacturers or suppliers being listed as footnotes. The materials section describes the design philosophy of the electronics and circuit board layouts, the assembly methods employed in circuit construction and the design and construction of the system enclosures.

3.1 Materials

The materials used in this project are described in the following sections where they have been separated into appropriate categories for clarity and convenience.

3.1.1 Components

The architecture of the Ear-worn Personal Monitoring System (EPMS) is shown in *Figure 3-1;* this depicts the processor core, the basic functional blocks and connectivity.

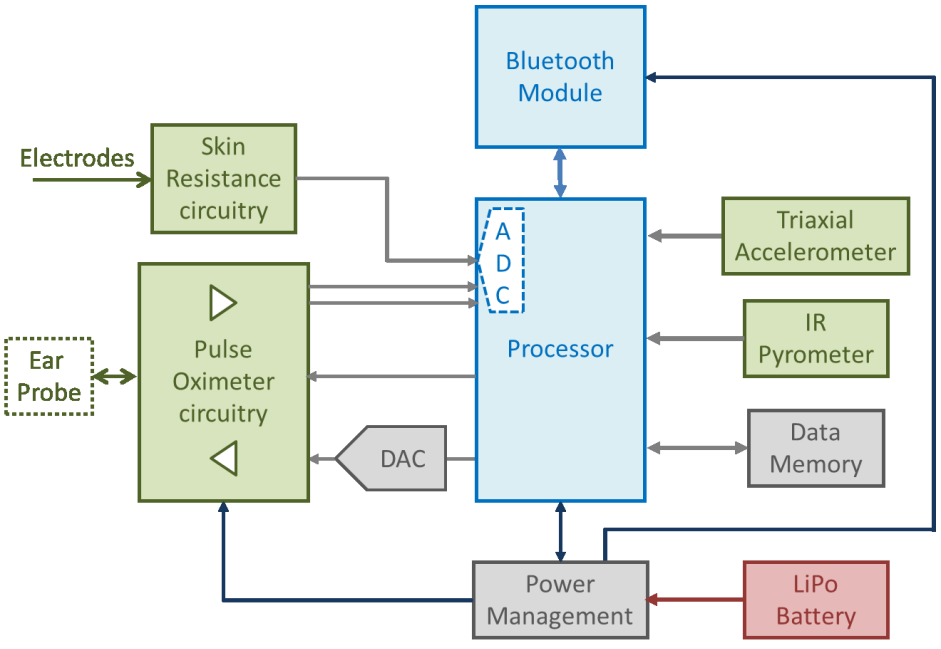


Figure 3-1: The general arrangement of the EPMS device

As the ear-worn device necessitated a compact design, the preferred power source would be a small lithium battery. This offered a nominal terminal voltage of 3.7V which would be regulated to provide a +3.3V single-rail voltage supply, thus setting the systems' operating voltage.

The choice of processor was critical to EPMS performance, especially regarding computational resources. Selection of the Atmel and ARM devices was largely influenced by computational performance, familiarity with the chip family and access to design and debugging tools. Amplifiers used in signal conditioning and drive circuits were selected for their analogue performance, namely single supply operation, rail-to-rail input and output, low noise and minimal input/output offset. For other components the criteria for selection were dominated by power budget and board space, both of which were at a premium. Preference was given to low-power devices in small surface mount packages and chips with integrated functionality.

A critical factor in component selection was availability, particularly with new or recently introduced devices such as those used in the ultimate version of the EPMS (v4). The majority of the electronic components were sourced from RS Components[13] and Premier Farnell[14]. Low capacity lithium polymer (LiPo) batteries were supplied by Cool Components Ltd.[15] and Proto-PIC.co.uk[16]. The BQ51050 wireless power

[13] *RS Components Ltd, Corby, Northants, UK*

[14] *Premier Farnell plc, Leeds, UK*

[15] *Cool Components Ltd. London, UK*

[16] *Relchron Ltd, Kirkcaldy, Fife, Scotland)*

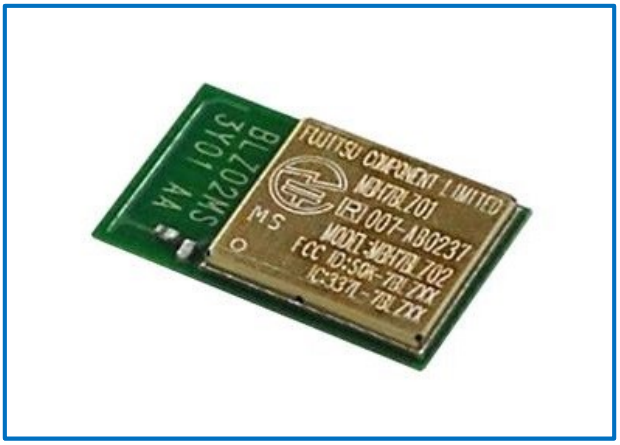
receiver/LiPo charger and AFE4490 integrated analogue front end pulse oximeter chips[17] were sourced from Digi-Key[18].

Wireless Modules

Rather than designing wireless transceivers using one of the many available chipsets and discrete components, a decision was made to use commercial off-the-shelf (COTS) modules with integral antennae. Using proven technology helped in reducing development time and cost, providing a reliable platform and enabling the author to concentrate on other aspects of the project.

Being one of the larger components, size was a key factor in module selection. The ATBZ-24-A2 ZigBee modules[19] used in EPMS v1 were sourced from Digi-Key, as were the RN-41 and RN-42 Bluetooth modules[20], used in EPMS v1 and v2 respectively. The Bluetooth Low Energy (BLE - also known as Bluetooth v4.0 and Bluetooth Smart) device on EPMS v3 was a Bluegiga BLE112 Bluetooth Smart Module[21] sourced from Mouser[22]. The final version of the EPMS (v4) used Fujitsu MBH7BLZ02-109004 BLE modules[23] (see *Figure 3-2*) from YEG[24].

[17] *Texas Instruments, Dallas, Texas, USA*
[18] *Digi-Key Corporation, Thief River Falls, MN, USA*
[19] *Atmel Corporation, San Jose, CA, USA*
[20] *Roving Networks, Los Gatos, CA, USA*
[21] *Bluegiga Technologies Oy, Espoo, Finland*
[22] *Mouser Electronics Inc., High Wycombe, Buckinghamshire, UK*
[23] *Fujitsu Ltd., Tokyo, Japan*
[24] *Young Electronics Group, High Wycombe, Buckinghamshire, UK*



(Mouser Electronics Inc., 2013)

Figure 3-2: The Fujitsu MBH7BLZ02 Bluetooth low energy (BLE) wireless module.

3.1.2 Sensors

Reusable pulse oximeter ear probes and a reference finger probe (part numbers 3078 and 3044 respectively, both by Smiths Medical[25] were obtained from Pulmolink[26]. MLX90615 infrared pyrometers[27] were supplied by Future Electronics[28]. ADXL330 and ADXL345 triaxial accelerometers[29] were sourced from Premier Farnell.

3.1.3 CAD and Printed Circuit Boards

Some initial prototype circuits were constructed on stripboard where they could be iteratively tested and modified to achieve the desired performance prior to committing the design to a printed circuit board (pcb).

[25] *Smiths Medical International Ltd., Ashford, Kent, UK*

[26] *Pulmolink Ltd., Charing, Kent, UK*

[27] *Melexis Microelectronic Systems, Ieper, Belgium*

[28] *Future Electronics Ltd., Egham, Surrey, UK*

[29] *Analog Devices, Norwood, MA, USA*

The majority of the schematic capture and circuit layout for the designs were performed using Easy-PC v15[30]. The final version of the EPMS (v4) was designed using version 8.0 of Pulsonix EDA[31], a more sophisticated package from the same software stable. In both cases, libraries were created for components, or modified as necessary, to facilitate manual assembly as in the author's experience larger component pad sizes are required than those for automated volume production.

All printed circuit boards were produced by pcb-pool.com[32] from uploaded pcb CAD design files rather than CAD-generated photoplot and NC (numerically controlled) drill files during postprocessing. The majority of the boards were fabricated from standard 1.6 mm thick FR4 glass-epoxy laminate clad with 35µm copper. All were finished in a green soldermask coating with the pads in electroless nickel gold (ENIG) for improved surface mount assembly; component legends on both sides of the boards (in white) aided component identification. A stainless steel solder paste mask was supplied with the EPMS v4 boards and was used during board assembly.

3.1.4 Equipment

Most of the board assembly was performed using hand soldering techniques with a Weller WP80 soldering iron and WD1000 soldering station[33], with a range of tips. Soldering was performed with 0.46mm diameter low melting point (179°C - 62% Tin

[30] *Number One Systems, Tewkesbury, Gloucestershire, UK*

[31] *Pulsonix, Tewkesbury, Gloucestershire, UK)*

[32] *trading as Beta LAYOUT Ltd., Shannon, Co. Clare, Eire*

[33] *Weller Tools GmbH, Besigheim, Germany*

(Sn), 36% Lead (Pb), 2% Silver (Ag) Alloy) solder wire[34], with 0.8mm width desoldering braid[35] used to clean up surface mount solder joints. A set of SMD tweezers[36], specifically designed for use with surface mount devices, facilitated the handling and manipulation of small components during the assembly process.

EPMS v4 boards were part-assembled using hot air reflow techniques using a Tenma 21-10135 heating plate[37] and Duratool D01841 hot air surface mount rework station[38]. Chip Quik SMD4300TF tacky solder flux[39] and Multicore SN62RA10BAS86 solder paste[40] were used during board assembly.

Assembly and rework was greatly aided by the use of a binocular headband magnifier with LED illumination[41] giving a magnification of x3.5. Inspection was also aided by the use of a Duratool BW1008-500X digital USB microscope[42].

Circuitry was powered by a Thandar TS3021S bench power supply[43] whilst under development. The majority of the testing was performed using Tektronix DMM870[44]

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[34] *Multicore, Henkel AG & Company, KGaA, Dusseldorf, Germany, (Premier Farnell part number 419503)*

[35] *ITW Chemtronics, Kennesaw, GA, USA (Premier Farnell part number 957203)*

[36] *part number 5-050, BERNSTEIN-Werkzeugfabrik Steinrücke GmbH, Remscheid, Germany; supplied by RS Components*

[37] *Premier Farnell, part number 2064552*

[38] *Premier Farnell, part number SD01694*

[39] *Chip Quik Inc., Mashpee, MA, USA (Premier Farnell part number 1850221)*

[40] *Multicore, Henkel AG & Company (Premier Farnell part number 149968)*

[41] *RS Components, part number 534-2400*

[42] *Premier Farnell part number 2319418*

[43] *Thurlby Thandar Instruments Limited, Huntingdon, Cambridgeshire, UK*

[44] *Tektronix Inc., Beaverton, OR, USA*

and Metrix MX24B[45] multimeters, a Tektronix TDS 210 digital oscilloscope and PicoScope 2105 USB oscilloscope[46]. A variety of probes and test leads were made using 2mm and 4mm connectors from laboratory stock to facilitate circuit testing.

3.1.5 Medical Devices

A Microplus V002-MS03 digital hand-held spirometer[47] with disposable mouthpieces was used to collect lung function data for the respiratory sensor pilot study (chapter 4).

A Braun ThermoScan IRT 4520 ear thermometer[48] was purchased from Amazon, together with a stock of disposable lens filters, for use as a reference in EPMS testing. Once placed in the ear and triggered, measurement was completed in around five seconds and readings presented on a small display.

An Oxi-Pulse 20 digital handheld pulse oximeter from Smiths Medical (supplied by Pulmolink Ltd.) was used as a reference for the EPMS. This displayed two-digit SpO_2 readings in large numerals with HR below, together with an indication of blood perfusion and pulse strength as LED bar graphs (*Figure 3-3*), and featured *"patented Serial Autocorrelation"* to minimise noise and motion artefacts. A D9 sub-miniature connector at the top of the device accepted a range of standard sensor probes.

[45] *AEMC Instruments, Foxborough, MA, USA*

[46] *Pico Technology, St. Neots, Cambridgeshire, UK*

[47] *Cardinal Health, Dublin, OH, USA*

[48] *Kaz Inc., Southborough, MA, USA*

Figure 3-3: The Oxi-Pulse 20 digital handheld pulse oximeter – shown here fitted with a finger probe.

3.1.6 Cellular Phones and Tablets

A variety of mobile handsets were used in this project. Initial work with the EPMS v1 and v2 designs used the author's Sony Ericsson W995, running the Symbian operating system. As Apple were the only manufacturer initially supporting Bluetooth v4, an iPhone 4S was obtained to aid in the development of the EPMS v3. Subsequent development of the EPMS v3 and v4 was performed with a Nexus 7 tablet running version 4.4.4 of Google's Android operating system (known as *"KitKat"*). This had the benefit of a larger screen which facilitated testing during trials of the EPMS v4 device.

3.1.7 Software

All embedded software for the Atmel AVR and ARM processors and mobile phone applications software (Symbian, Apple iOS and Android) used in the ear-worn

monitoring devices was kindly written by Paul Knight, a fellow doctoral student and professional software engineer.

3.2 Methods

This section describes the methods applied in the design and assembly of the project's prototype electronic systems and device enclosures.

3.2.1 Circuit Design

Before starting each design or design revision, key components were shortlisted and comprehensively reviewed. Having determined and selected the optimum component fit, which considered factors such as specification, package type, availability and prior experience of a device, component details from manufacturers' datasheets were added to CAD libraries. The schematic design was initially sketched out before detail was added and the design expanded across multiple sheets into functional blocks for clarity. Careful attention was paid to application notes, connectivity details and electrical specifications provided on product datasheets for interfacing details, passive component values and circuit connectivity. Decoupling capacitors (100nF) were added on a one-per-chip basis with a few more (1 to 10µF) around the circuit for power smoothing. Where necessary, prototype circuits were first constructed on stripboard to confirm operation before being added to a schematic.

3.2.2 Circuit Layout

Both Easy-PC and Pulsonix EDA are integrated packages, thus ensuring direct translation of the schematic design to the respective circuit layout utilities whilst maintaining complete design integrity. The majority of the pcbs were designed with

four electrical layers; the two outer layers for signal tracks (facilitating modification if required) and the inner layers providing power and ground connectivity in the form of air-gap power planes. This allowed tighter component placement, more room for signal routing and had the added benefit of reducing system noise.

Major components were placed on an oversized outline of the target board outline then moved and rotated to give the optimum track routing paths and minimise inter-layer connecting via holes. The remaining components were then added using both sides of the board, again keeping track lengths short wherever possible. The board was then manually routed with components being rotated and repositioned as necessary to accommodate tracks, via holes and minimise board space. Every effort was made to keep analogue signal tracks away from high-speed digital lines, especially clock signals, to minimise the possibility of crosstalk. With routing complete, components and tracks were carefully 'nudged' to allow the board outline to be adjusted to its' minimum size.

Track widths and clearances (typically ≥0.20 mm) were kept well within the limitations of the pcb manufacturer's guidelines to maximise yield and facilitate manual modification if required. It was decided not to use blind or buried inter-layer (via) through-holes to keep costs down, reduce design or manufacturing errors and simplify testing.

A critical point of the layout process was to keep the overall board size as small as possible without compromising the requirement for hand assembly, which placed constraints upon the component packages used as the smallest parts are only realistically compatible with automated assembly methods. This ruled out the use of

ball grid array (BGA) and other similar chip packages, in which a high-density pad matrix is sited on the underside of a chip, and 0402 (1.0mm x 0.5mm) and 0201 package (0.6mm x 0.3mm) passive parts. On a proven design intended for volume production, use of more than four electrical layers, blind and buried via holes and smaller components could save valuable board space for a more compact design.

3.2.3 Hand Assembly of Circuit Boards

The bulk of the circuit boards used in this project were hand assembled with a temperature controlled Weller soldering iron and low melting point solder wire. Whereas conventional through-hole component assembly was straightforward, assembly of many of the surface mount components proved to be a challenge due to their size, pin pitch and packing density. In all cases, the build order was (i) surface mount chips, (ii) surface mount passives and (iii) connectors, through-hole components and wires.

Prior to surface mount chip assembly, a single corner pad on each device's pcb footprint was lightly tinned with solder. A chip was then introduced and aligned with the pcb pads and the tinned pad carefully reheated to solder the pin flat to the board. A second pin diagonally opposite the first was then soldered to stabilise the device on the pcb ready for the next step. Where the pin pitch was greater than 1.0mm, the chip's remaining pins could then be soldered individually with a fine soldering bit. Devices with a pin pitch less than 1.0mm pin were subjected to drag soldering and solder braid clean-up. Here, liquid solder flux was applied to the chip's pins and the wetted (tinned) tip of a soldering iron dragged along one face at a time to create

solder joints. As the pins were often bridged with excess solder, this was removed by applying solder braid and a tinned iron as required.

Surface mount passive components, which included resistors and capacitors in 0603 (1.6mm x 0.8mm), 0805 (2.0mm x 1.25mm) and 1206 (3.2mm x 1.6mm) package formats, and small three to five-pin discrete semiconductors, were soldered using a similar technique as that used for chip assembly and assembled after the chips had been mounted. A single pad in each component footprint on a circuit board was first tinned with solder. Components were then offered up to their correct locations with SMD tweezers, the value, orientation and alignment checked and the tinned pads reflowed flat to the board. Having reflowed a number of components, the remaining pads were then soldered. Excess solder or solder bridges were removed with solder braid as before.

Once the surface mount components had been assembled boards were visually inspected for solder bridges and bad joints with the binocular headband magnifier and USB microscope. Connectors and through-hole components were then fitted, soldered and the circuit re-inspected.

3.2.4 Hot Air Reflow Assembly of Circuit Boards

The Fujitsu MBH7BLZ02-109004 BLE module and BQ51050, AFE4490 and ADXL345 chips necessitated a different approach for assembly on to the EPMS v4 boards as each had one or more component pads on the underside of the device that were inaccessible for hand soldering. As a result, hot air reflow soldering, either by direct

(from above with the Duratool rework station) or indirect heating (from below using the Tenma hot plate), was the method of choice for prototype board assembly.

Before attempting to assemble the EPMS v4 board, direct and indirect assembly methods were trialled on scrap pcbs using obsolete or surplus components. Indirect heating was found to give reasonably consistent results for components with higher pin counts and allowed simultaneous soldering of all parts (using solder paste) of one side of the board. Direct heating was reasonably effective for soldering larger parts, but the air jet tended to disturb smaller parts and blow them off their pads – especially where smaller-bore nozzles were used. Reducing the airflow was not a viable option as it necessitated a reduction in temperature to prevent the rework station overheating; the reduced heat proving insufficient for effective reflow soldering. This experience demonstrated that the Duratool device was best used for the targeted reflow of larger devices or the removal of specific small components.

An immediate problem with using the Tenma hot plate was that the EPMS v4 board was too small to sit upon the stand above the heating nozzle without a special holder. This was fashioned from a thin sheet of brass to which the pcbs were secured with twisted loops of tinned copper wire threaded through the board's four corner mounting holes. This enabled boards to be safely positioned over the heating plate's nozzle for effective indirect reflow soldering (*Figure 3-4*).

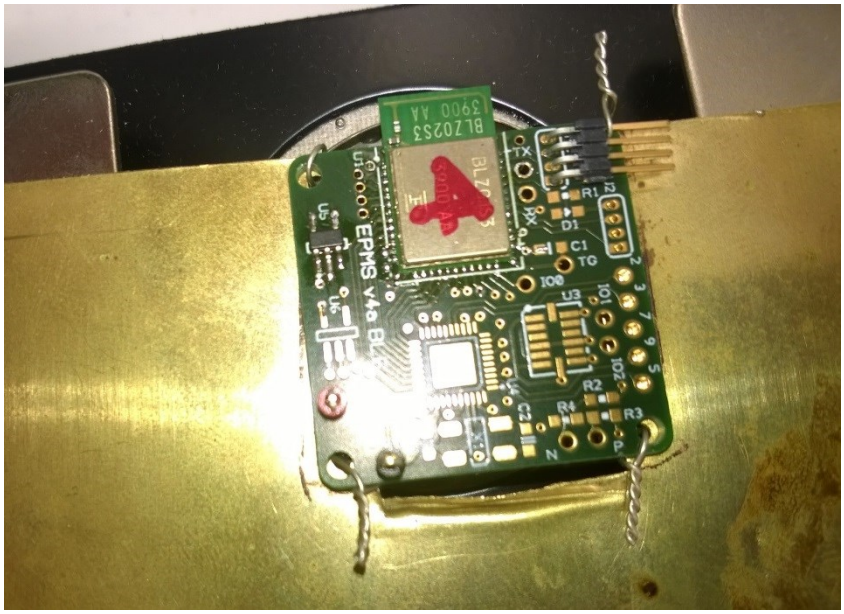


Figure 3-4: An EPMS v4 pcb wired on to the holder and positioned over the Tenma hot plate for reflow soldering.

A number of approaches were tried including pre-tinning pads and screen printing solder paste. As successful mounting of the MBH7BLZ02 BLE module was likely to be the most difficult and present the greatest risk this was attempted first. The component pads on the board were pre-tinned using a soldering iron and solder wire, solder flux applied around the tinned pads and the device was positioned ready for soldering. The board was then fixed to the brass holder, arranged on the heating plate and reflow soldered using temperature profiles suggested on the device's datasheet.

Before any further parts were added, test leads were temporarily attached to the board, voltage levels probed and an attempt was made to program the BLE module. This proved unsuccessful demonstrating poor connectivity; with no way of adding solder paste for reflow and little or no exposed pad area to aid manual soldering, no effective remedial action was possible. Thus the board was reflowed on the hot plate

and the module removed for inspection which showed a number of contacts had not been soldered correctly – most likely due to inconsistent tinning.

As a result wires were soldered directly to the BLE module's power pins and SWD programming port and a test program uploaded. This output a 1Hz square wave on all of the uncommitted general purpose input/output (GPIO) terminals allowing signals to be monitored on the circuit board with an oscilloscope to demonstrate connectivity. Solder flux was distributed around the tinned pads on the board once more and solder paste added to those pads where the solder joints had been of poor quality. After reflowing on the heating plate the board was tested once more, this time returning square waves signals of the correct voltage threshold on the GPIO pins confirming successful assembly.

With further experimentation it was found that carefully pre-tinning the pads on the BLE module with a soldering and "buttering" the pcb pads with solder paste produced the most consistent results. With a voltage regulator added for system power (U5), programming header and test leads added, boards were programmed with the 1Hz GPIO test code and before any other board assembly took place. Here, the remaining pads were prepared with solder paste and flux, the components carefully positioned and reflow soldered using the holder on the heating plate. The boards were then inspected and poor quality joints and solder blobs were reworked with the Duratool hot air rework station or manually with a soldering iron and solder braid.

3.2.5 Enclosure Design and Production

With the EPMS v1 and v3 designs this was very much an afterthought as the circuitry was initially developed for bench testing. As a consequence the enclosures were designed around the boards and might be considered less than aesthetically pleasing. Conversely, the EPMS v2 and v4 board outlines were designed from the outset to fit enclosures arising from design studies.

EPMS v1 Enclosure Fabrication

This design consisted of two separate modules communicating over a ZigBee wireless network, one worn on the ear and the other carried about a subject's person. After noting board dimensions and making allowances for wiring a design was sketched out and then transferred (drawn) onto sheet styrene of various thicknesses[49]. Pieces were cut out using a craft knife and tinsnips and glued together with solvent-based adhesive (EMA Plastic Weld Cement). Having test fitted the pcbs, the enclosures were rubbed down and spray painted with primer, black paint and finished with a coat of protective acrylic varnish. A length of heat-formed plastic rod serving as an ear-hook and pulse oximeter ear probe clip were then glued to the rear of the ear enclosure with two-part epoxy resin adhesive to complete fabrication.

3D CAD

The author had hoped to use Autodesk CAD software[50] to design enclosures; it soon became apparent however that the investment in time to gain sufficient expertise to produce the required designs would be prohibitive. Therefore, A fellow doctoral

[49] *sourced from Squires Model and Craft Tools, Bognor Regis, West Sussex, UK*

[50] *Autodesk, Inc., San Rafael, CA, USA*

student and professional 3D CAD user, David Sziroczak, assisted by producing the 3D CAD drawings and data files using Catia software[51] from the author's original design sketches.

3D Printing

This technology has found an application in rapid prototyping and proved its worth over the course of this project. Casings were printed on the School of Engineering's Dimension Elite 3D printer[52] in white ABS (acrylonitrile butadiene styrene) plastic, the printed object being formed by building up successive thin layers of plastic in an additive printing process.

Stereo lithography (.STL) files were generated from the native 3D CAD and uploaded to the printer's host PC where the print settings were adjusted for high resolution output (0.254 mm layer thickness) and the cases printed, which took three to six hours per unit. Any voids were printed with sacrificial filler material (polylactic acid, a form of polyester commonly known as PLA) to support and maintain the ABS parts' structural integrity over the printing process. On completion parts were placed in a tank of hot concentrated sodium hydroxide solution for several hours to dissolve the PLA, then rinsed with copious water.

The outer finish on the 3D-printed parts was quite poor, having a pronounced step of around 0.2 mm on most curved or angled surfaces. These were rubbed down with various grades of wet and dry paper to achieve a smoother and more pleasing finish.

[51] *Dassault Systèmes, Vélizy-Villacoublay, France*

[52] *Stratasys Ltd., Eden Prairie, MN, USA*

Assembly

Holes in cases (e.g. for pulse oximeter sensor cables and USB connector access) were made using a range of small drill bits held in a pin vice, needle files and scalpels. IR pyrometers were glued into ear probes with a PVA adhesive (for ease of removal) and tested prior to the probe being glued to the case. Solvent-based (EMA Plastic Weld, sourced from a local model supplies shop) and two-part epoxy adhesives were used to glue parts together.

3.3 Conclusions

- The component selection criteria, design philosophies and assembly techniques employed successfully delivered a series of prototype systems.
- The circuit design and layout methods employed resulted in the production of good quality pcbs with very few errors and proved to be extremely reliable.
- Assembly of the BLE module and smaller surface mount devices on EPMS v4 proved to be especially challenging. This required significant experimentation and effort to achieve a good yield with quality solder joints and suggests that subcontract manufacture may have been a better option.
- 3D printing proved to be ideal for EPMS case manufacture as this allowed the rapid prototyping of complex shapes that would have been too costly or inefficient using conventional methods.

4 Clavicular Respiratory Sensor

4.1 Introduction

Respiratory rate is one of the key vital signs with a wide diagnostic potential (Cretikos et al., 2008). Unlike temperature, HR, BP or SpO_2 however, there are few dedicated sensing devices available and accepted for medical use. Outside of the hospital environment it is underutilised, largely due to a dearth of reliable automatic monitoring equipment (McBride et al., 2005).

This chapter reports the use of accelerometers to monitor respiratory motion. Whereas thoracic sensing has been the subject of a number of studies (including Reinvuo et al., 2006; Phan et al., 2008; Bates et al., 2010; Hung et al., 2008), clavicular respiratory motion sensing is described here for the first time. The findings of a pilot study comparing RR readings derived from clavicular and thoracic motion with those from an expiratory breath flow reference sensor are presented and discussed. This work was reported in the journal *Physiological Measurement* (Pitts et al., 2013)

4.2 Materials and Methods

This section documents the materials used in the construction, design and calibration of the sensors and the protocols and analytical methods employed in this pilot study.

4.2.1 Respiratory sensors

A sensor circuit board (18 x 15 x 3mm) was designed around the ADXL330 accelerometer[53] (Analog Devices Inc., 2007), a tri-axial device which benefits from

[53] *Analog Devices Inc., Norwood, MA, USA*

nano-scale MEMS (Micro Electro Mechanical System) technology to produce a small 4mm x 4mm monolithic package (*Figure 4-1*). A number of boards were assembled; each attached to a 2.5m four-core screened connecting cable and wrapped in non-allergenic surgical tape to provide insulation and protection. For data validation, a mask-mounted AWM720 mass flow sensor[54] was used to measure exhalatory breath flow (as reported in Walton et al., 2014).

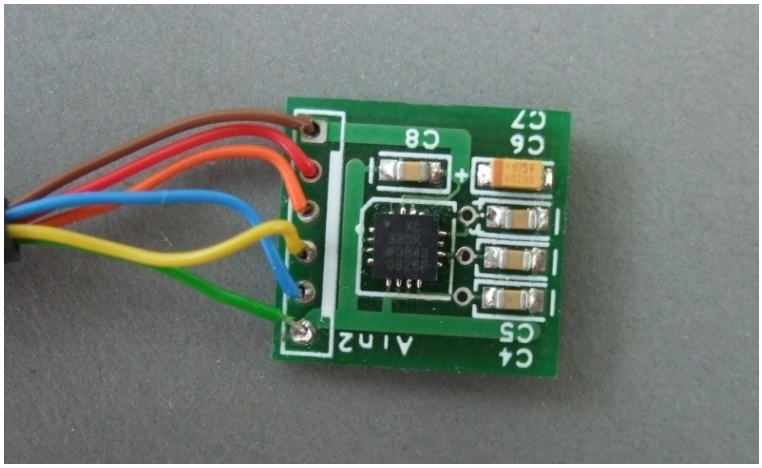


Figure 4-1: The tri-axial accelerometer boards designed for and used in the respiratory monitoring study.

Filters and Interfacing

Working with the RR specified in *section 2.2* of 4 to 30 bpm, this equated to a frequency range of 0.067 to 0.5Hz. A feedback capacitor value of 470nF was chosen to limit the 3db signal bandwidth to approximately 10Hz on each axis, requiring a sample rate of at least 20 Hz to meet the Nyquist rate. A 10Hz cut off was chosen as this would attenuate high frequency transients and mains electricity-derived electromagnetic interference (emi), which is prevalent at frequencies of 50/60Hz and its higher harmonics, leaving lower frequencies unaffected. At this experimental stage it was

[54] *Honeywell Sensing and Control, Golden Valley, MN, USA*

considered more practical to use software filters during post-processing; the hardware filters being optimised as part of future sensor development.

With reference to *Figure 4-2*, capacitors C4, C5 and C6 combine with internal 32kΩ resistors to form bandwidth-limiting low-pass filters for each output. The 3db point of the filter (i.e. half power) is given as:

Equation 4-1: Accelerometer low-pass filter formula

$$f_{3db} = \frac{1}{2\Pi\left((32\times10^{3})\times C_f\right)}$$

With a C_f value of 470nF (instead of the 220nF shown in *Figure 4-2*), this gives us:

Equation 4-2: Accelerometer low-pass filter calculation

$$f_{3db} = \frac{1}{2\Pi\left((32\times10^{3}).(470\times10^{-9})\right)} = 10.58 \cong 10\ \text{Hz}$$

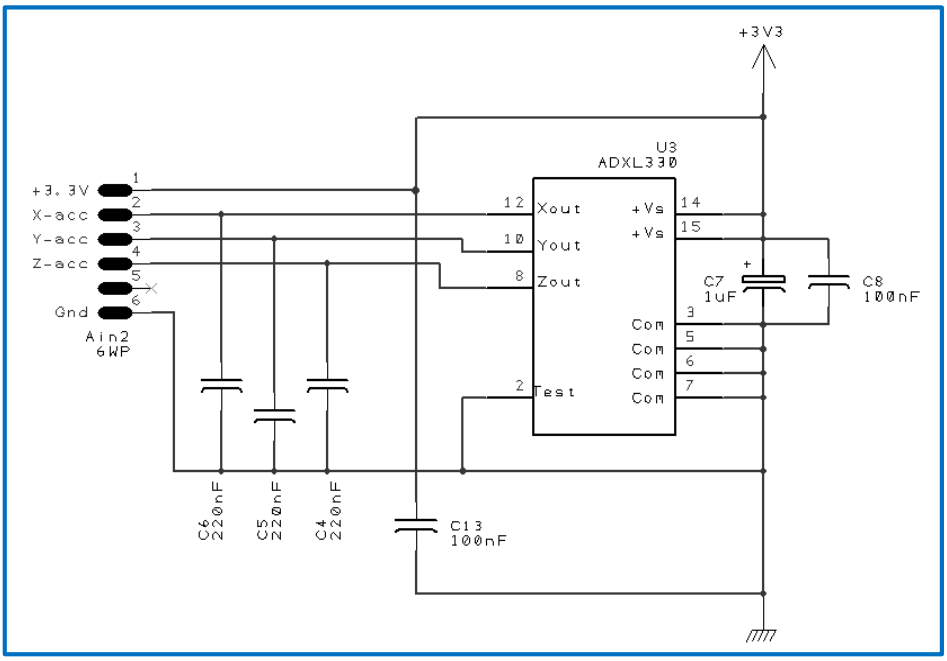


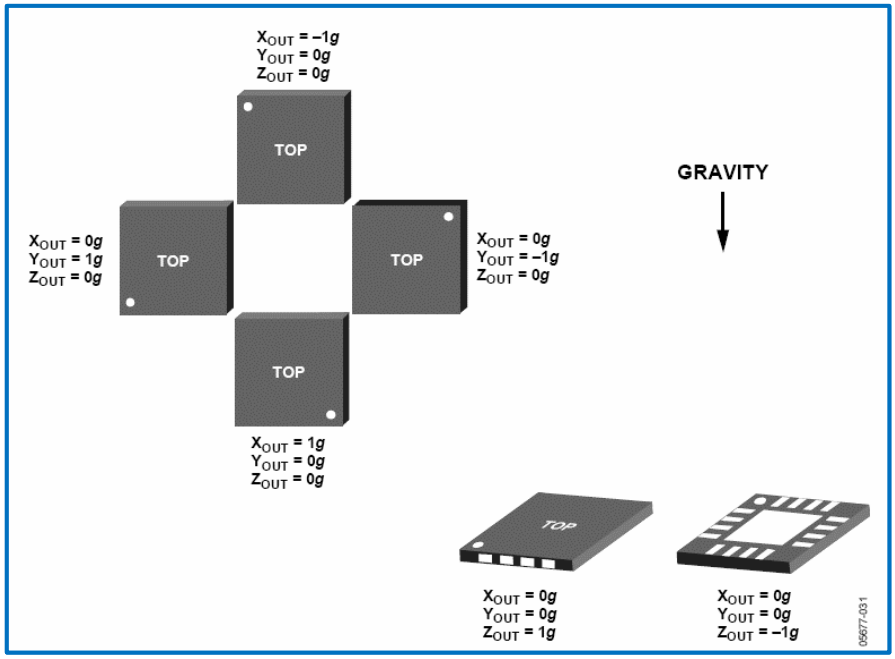
Figure 4-2: A schematic of the triaxial accelerometer circuit showing filter capacitors C4-C6.

A basic interface board providing power distribution for the sensors (+3.3V for accelerometers and +10V for the mass flow sensor), and connectivity to a data logger was designed and assembled. No additional signal conditioning or amplification was applied. Data acquisition was provided by a Cranfield CardCorder system[55]; 12-bit data was acquired using 0-5V (accelerometers) and 0-10V input ranges (AWM720) at 100 samples per second, well above the Nyquist rate, on each signal channel.

4.2.2 Calibration

Accelerometers are normally calibrated with reference to gravity, therefore 1g equates to an acceleration of a nominal 9.81 ms^{-2}. Output signals from the ADXL330 are ratiometric and therefore proportional to the supply voltage. For the 3.3V supply voltage, sensitivity is an effective 330mV/g with a full scale output of ±990mV at ±3g. The output swings about a centre of zero g, which is specified at half the supply, 1.65V in this instance. This gives a full scale output span of 0.66V to 2.64V.

[55] *formerly produced by Cranfield Impact Centre Ltd., Cranfield, Bedford, UK*



(Analog Devices Inc., 2007)

Figure 4-3: The gravimetric response of the ADXL330 in all three axes.

The static gravimetric output responses for all three accelerometer axes are shown in *Figure 4-3*. A two-point calibration was applied to the accelerometers by rotating each axis in turn with respect to gravity upon a true horizontal surface (confirmed by spirit level) with the aid of an engineer's square. This provided voltage readings corresponding to positive and negative gravity (± 1g) which were entered and stored in the logger's setup software for each respective input.

Reference Sensor

The AWM720 mass flow sensor data was recorded as a pure voltage for translation into standardised litres per minute (SLPM) in post-processing. Because of the non-linear relationship, a calibration curve was produced (*Figure 4-4*) from the data (*Table 4-1*) provided on the manufacturer's product datasheet (Honeywell International Inc., 2008) and an equation derived to give an estimation in SLPM.

Equation 4-3: Honeywell AWM720 flow sensor linearisation

$$Breath\ SLPM\ =\ e^{(Breath\ mV-886.89)/776.93}$$

Flow (SLPM)	Output (mV)
1	1000
25	2990
50	3820
75	4300
100	4580
150	4860
200	5000

Table 4-1: The AWM720 flow sensor voltage output for different levels of flow in standardised litres per minute (SLPM)

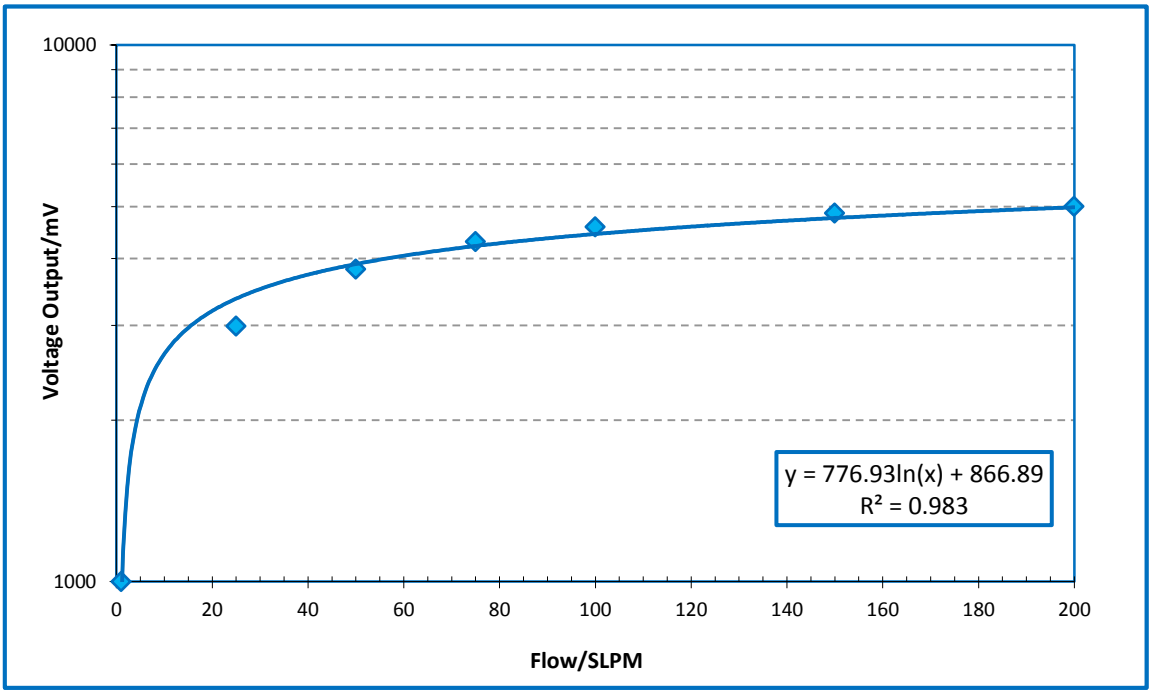


Figure 4-4: A plot of the AWM720 sensor's calibration table data showing curve fitting

4.2.3 Study Participants and Assay Description

After ethical approval (from Cranfield University Health Research Ethics Committee – CUHREC) and full consent had been obtained (see for *Appendix E* for details), eight healthy volunteers aged 24 to 55 years old (i.e. non-smokers, free from any respiratory condition or infection and not taking any medication in the days prior to or during the study period) were recruited for the study. Five were male (volunteers 01, 02, 04, 07 and 12) and three female (volunteers 06, 08 and 11). Each was asked to attach two motion sensing accelerometers with non-allergenic surgical tape – one to the left clavicle, the other, over the sternum along the sagittal plane along the line of the fifth rib (see *Figure 4-5*); the latter to provide reference data to determine how clavicular measurement might compare with the form of thoracic sensing used in other studies (including those by Phan et al., 2008; Bates et al., 2010).

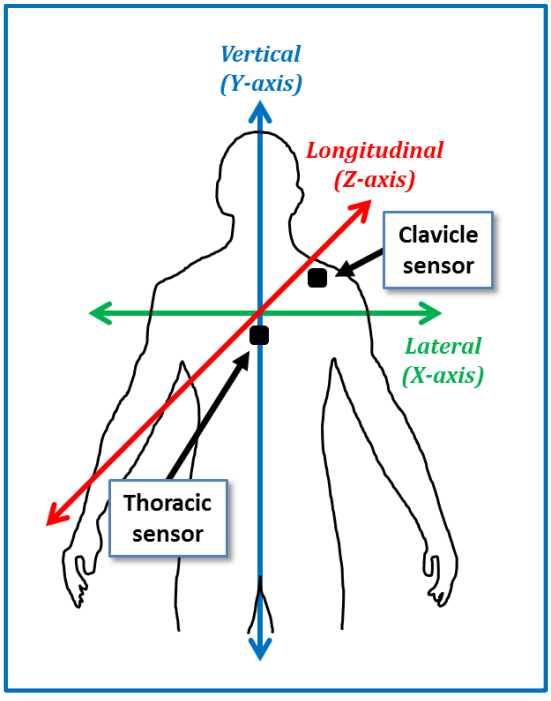


Figure 4-5: Diagram showing the locations of the motion sensors and their orientation on the body with respect to gravity

Both sensors were positioned with the same basic orientation (facilitating cable routing), giving a nominal resting output of x (lateral) =0g, y (vertical) =-1g and z (longitudinal) =+1g on the sensors' axes with respect to gravity with a standing volunteer; the offsets being removed during offline data processing. Volunteers were then fitted with a breath monitoring mask, the headstall being adjusted to provide a secure yet comfortable fit. Several minutes were allowed for acclimatisation prior to initiating each experiment.

Tests commenced with the volunteers standing and breathing normally. After two minutes of normal breathing, volunteers were asked to vary their breathing patterns, taking random short, long, shallow and deep breaths for a further 90 seconds, following which, they were asked to provide a full and deep outbreath and resume normal breathing for the last 30 seconds of the experiment. This provided a four-minute recording of a range of breathing patterns allowing direct comparison between the sensors. Participants were asked not to speak over this period and refrain from excessive movement, remaining as still as reasonably possible.

Data was uploaded serially (RS232) immediately after each test in an ASCII text CSV file format and backed up on a network drive provided by the University.

4.2.4 Spirometry

As the sensing methods in the study were based upon thoracic and clavicular motion, reference spirometry readings were taken to establish whether there was any relationship with motion data. Each participant was asked to take a deep breath and

blow into a hand-held spirometer[56] with full expiratory effort for three comparative readings from which the means were calculated. Four parameters, FVC, REV1, FER and PEF (see *Table 4-2* for details), were recorded for six of the eight volunteers.

Parameter	Meaning / Units	Description
FVC	Forced Vital Capacity (L)	Full forced expiratory volume
FEV1	Forced Expiratory Volume in one second (L)	Volume measured in the first second of full forced expiration
FER	Forced Expiratory Ratio (%)	FEV1/FVC, the percentage of FVC exhaled in the first second
PEF	Peak Expiratory Flow (Ls^{-1})	Peak flow rate at full forced expiration

Table 4-2: A glossary of the spirometry terms used and parameters measured in the study

4.2.5 Data analysis

MATLAB software[57] was used for data processing, analysis and visualisation. A series of scripts were written to automate data importation and signal processing tasks.

The raw accelerometer data was essentially sinusoidal with a DC offset (from static gravitational forces) and exhibited significant signal noise (*Figure 4-6*). The DC offset was first removed by applying a DC blocking filter; a 5-pole low-pass Butterworth filter (Butterworth, 1930) was then applied to remove signal noise. This was selected for its flat response in the pass band rather than the additional ripple and sharper cut-off transition of a Chebyshev or the flat phase response of a Bessal filter (Horowitz and Hill, 2001). A cut-off frequency (-3dB point) of 0.5 Hz, equivalent to a RR of 30 bpm,

[56] *Microplus V002-MS03, Cardinal Health, Dublin, OH, USA*

[57] *Mathworks Ltd., Natick, Massachusetts, USA*

was found experimentally to provide a sufficiently clean signal for effective peak detection, whilst preserving waveform shape.

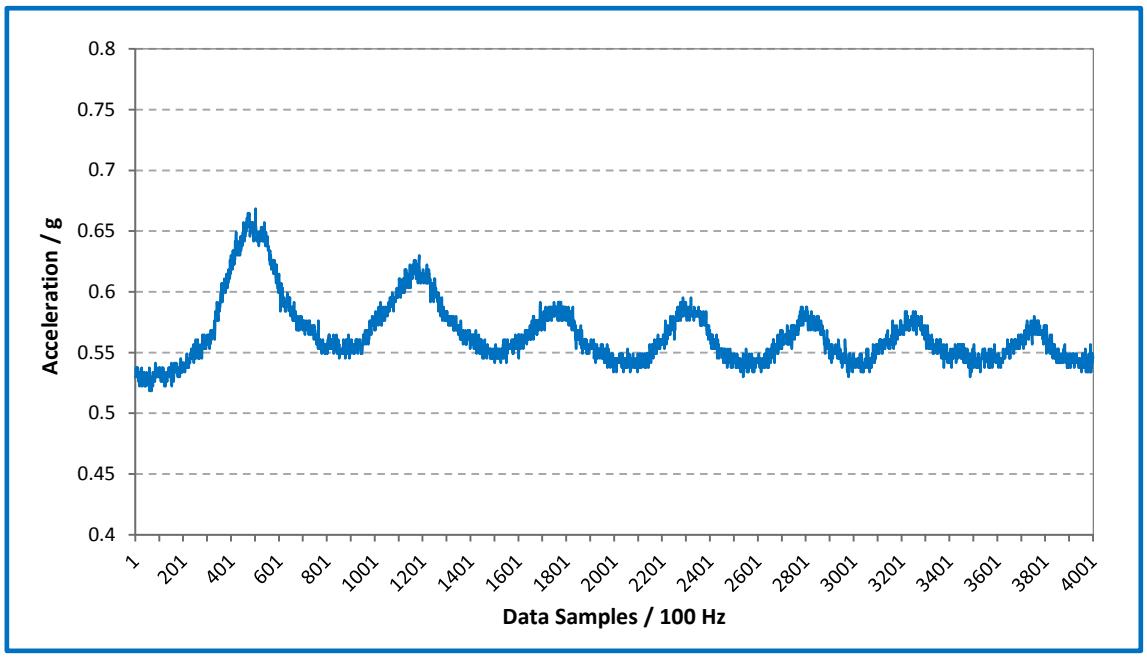


Figure 4-6: An example of raw clavicular accelerometer data (study participant 012)

Signal processing of the reference data was limited to unit conversion (to SLPM) and the removal of signal noise with a 5-pole low-pass Butterworth filter once again. A higher cut-off frequency of 2.5Hz was selected as this was found to preserve the shape of the waveform, in which each breath displayed a fast rise time with a slower decay *(Figure 4-7)*. Ideally, both the accelerometer and reference flow sensor data would have the same cut-off frequency to minimise any phase shift or time delay issues. With the cut-off frequencies closely matched however, any phase issues were considered negligible compared to the flow sensor peak rounding had both sensors been filtered at the lower frequency or accelerometer signal noise at the higher frequency.

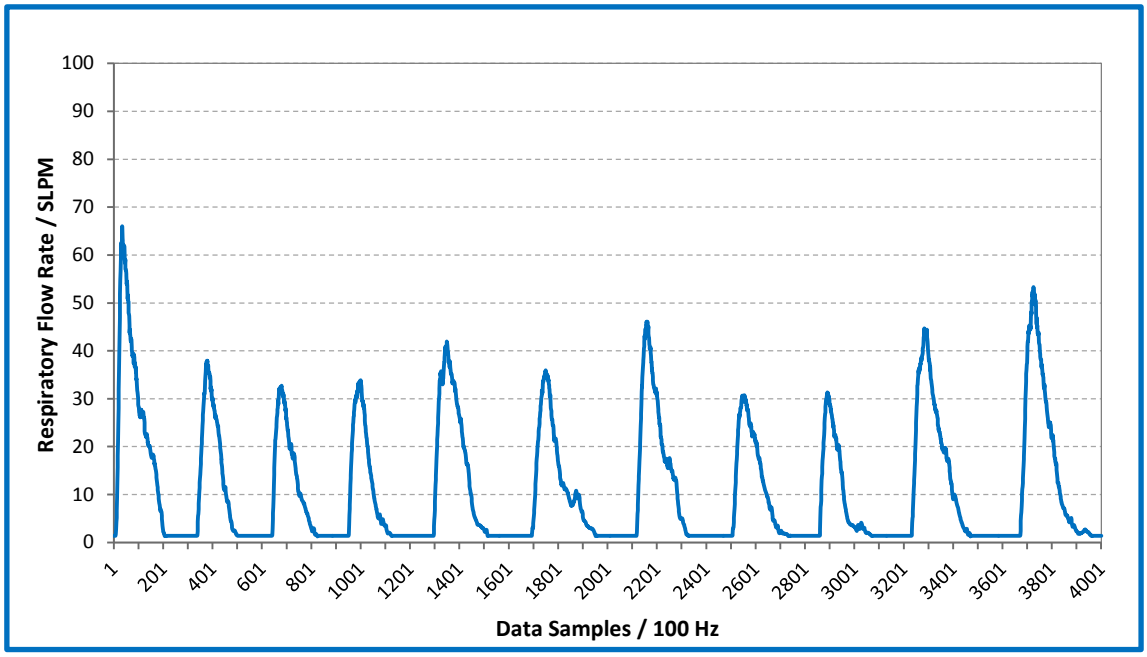


Figure 4-7: An example of raw flow sensor data (study participant 012)

Scripts for peak detection used MATLAB's 'findpeaks' function with threshold filters for magnitude (relative to the waveform mean) and periodic time (±150 samples) to eliminate false peaks. Breath periods were then extracted and exported to MS Excel for plotting and statistical analyses.

An estimation of the mean minute volume, a standard measure of exhalatory breath in a one minute period, was calculated for each participant from the flow sensor signal in MATLAB to provide an indication of ventilatory condition. This was achieved by summing the areas of each outbreath over the study period (using the trapezium rule) and dividing the resultant by four for the mean minute reading.

To assess the agreement between the CRS and TRS median respiratory rates regression and Bland-Altman (difference) plots were computed. The Bland-Altman plot is a method of data plotting used in analysing agreement between two different techniques of measurement, one of which may be a reference method or gold

standard, by calculating the mean difference between the two methods of measurement (the bias) and 95% limits of agreement as the mean difference (1.96 SD) (Altman and Bland, 1983). It is expected that the 95% limits include 95% of differences between the two techniques of measurement.

4.3 Results

This section presents the results from the pilot study and includes comparative sensor data, plots and statistical analyses.

4.3.1 Comparison of Clavicular and Thoracic Motion Responses

An example of an individual's resting breath-by-breath clavicular respiratory responses are shown in *Figure 4-8*. The dominance of the amplitude response in the longitudinal (Clav fZ) and lateral (Clav fX) axes was clearly defined with a regular phase relationship between all axes, albeit that the lateral axis was inverted.

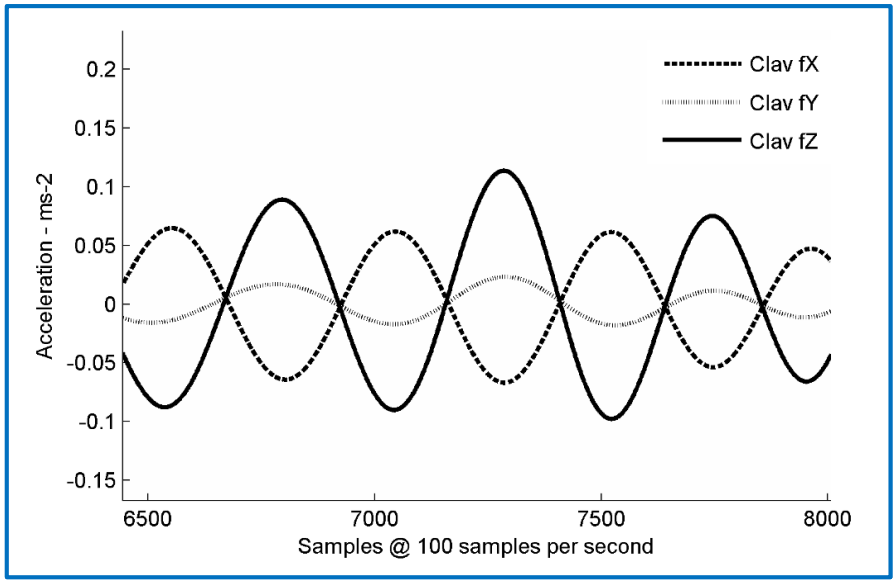


Figure 4-8: Tri-axial clavicular sensor motion following the application of a DC block and low-pass Butterworth filter

On inhalation and following thoracic expansion, this translated to three-dimensional clavicular motion that showed slight upward (vertical) displacement accompanied by pronounced forward (longitudinal) and outward (lateral) movement, with a reversal on exhalation as the chest contracted.

The thoracic sensor demonstrated a similar three dimensional motion as it tracked chest expansion. Again the dominant signals were in the longitudinal (Thor fZ) and lateral (Thor fX) axes (*Figure 4-9*), but their magnitude was less than the corresponding clavicular axes (0.075 ms^{-2} versus 0.2 ms^{-2} peak to peak) and comparable with the weak vertical (Clav fY) response. In addition a slight irregularity in relative phase was observed between the three thoracic axes on most datasets. Analysis of data from the two motion sensors demonstrated that clavicular respiratory sensing (CRS) was superior to thoracic sensing (TRS) in terms of signal amplitude (typically double), phase relationship and consistency.

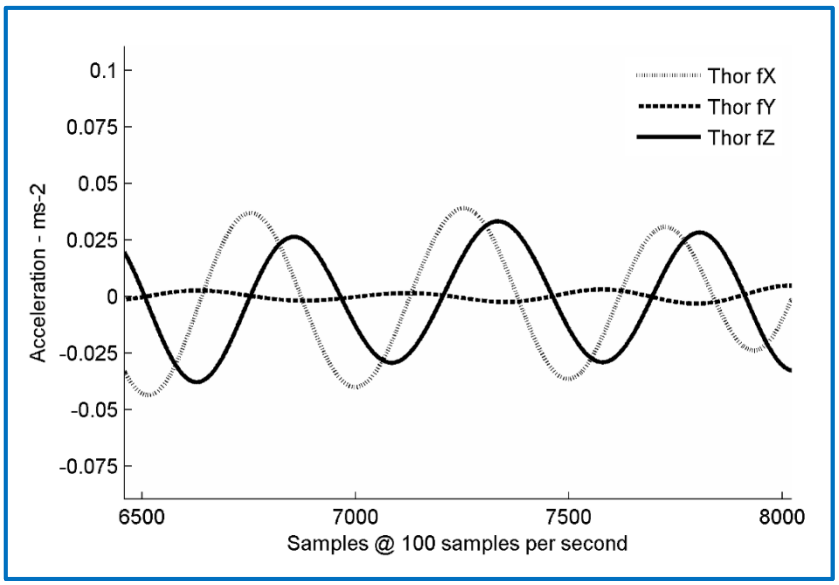


Figure 4-9: Tri-axial thoracic sensor motion following the application of a DC block and low-pass Butterworth filter

4.3.2 Comparison of Motion and Reference Waveforms

A series of time-history graphs were plotted of volunteer's respiratory responses to establish the temporal alignment of the respiratory motion signal peaks with the reference. It was found that the clavicular sensor's longitudinal (Z) axis produced the best overall agreement. An example of this may be seen in *Figure 4-10* where the alignment (between clavicular peaks and the rising edge of the reference) of individual breaths, inhalation and exhalation phases and inter-breath periods are shown.

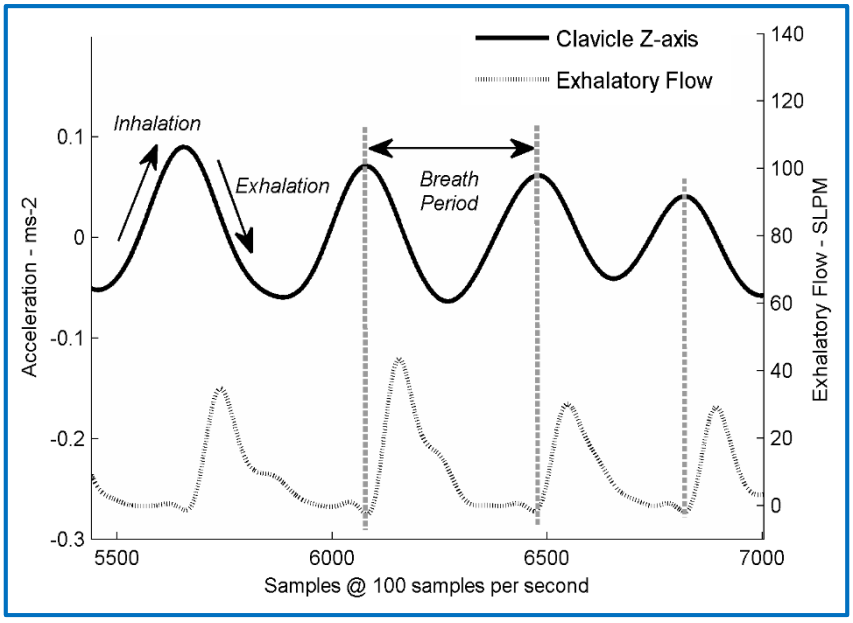


Figure 4-10: Respiratory periods measured by clavicular motion and exhalatory breath flow showing alignment of the two traces.

An example of the breath-by-breath differences observed during the mixed-breathing phase is shown in *Figure 4-11*. Here, the relative depth of two consecutive breaths can clearly be seen and may be characterised from the duration, area and amplitude of each breath pulse, all of which are shown to be proportional to breath volume.

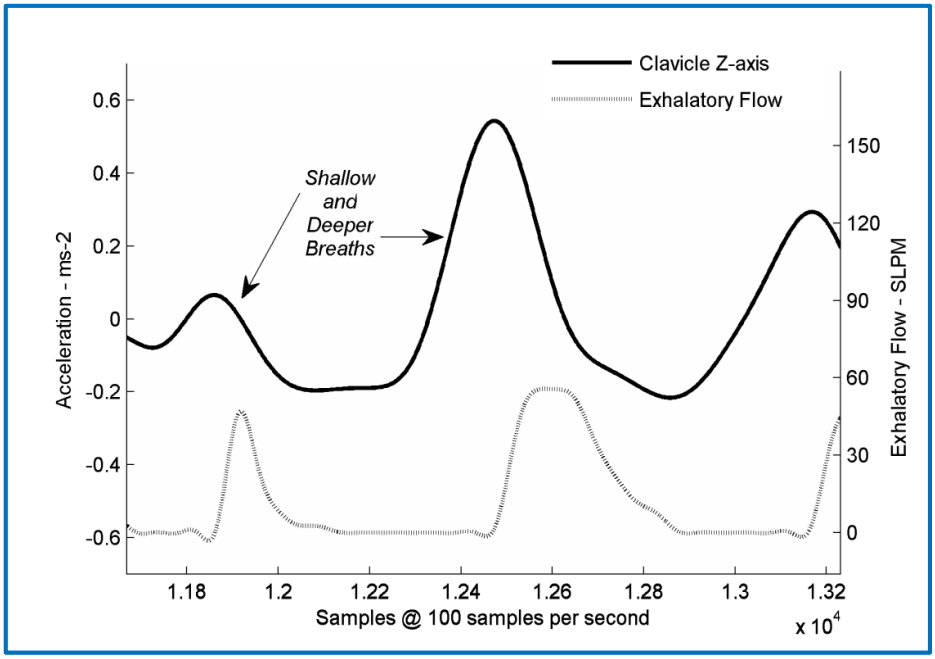


Figure 4-11: Respiratory depth measured via clavicular motion and exhalatory breath flow; differences in magnitude and area may be observed between the two breaths

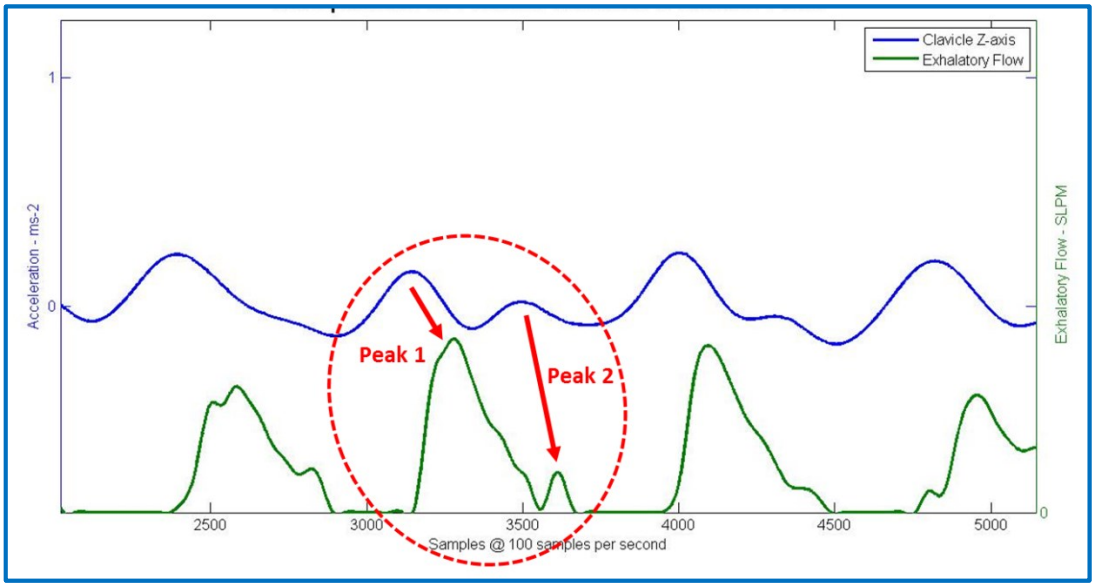


Figure 4-12: Occasional double-peaks observed in the data from one volunteer, the reasons for which were unclear

Figure 4-12 shows the occasional double-peaks observed in a single breath in the data from one volunteer. Whilst the clinical significance of this is unknown and has not

been investigated as part of this research project, it is nevertheless interesting as the effect is undoubtedly real, being evident in motion and exhalatory flow traces. It does however pose a problem for peak detection if the magnitudes of the secondary pulses are above those of the cut-off threshold and approximate shallow breaths. The double peak may result in the detection of two breaths rather than one.

4.3.3 Spirometry

Spirometry readings are presented in *Table 4-3* with the exception of the results for two volunteers, which were not recorded. All FER values are of the normal range of approximately 80% (Pearce, 2011).

Volunteer	FEV1	FVC	FER	PEF	Minute Volume (L)	Tidal Volume (mL)
001	-	-	-	-	8.73	598
002	3.64	4.56	79.33	629.00	6.67	569
004	4.20	5.15	81.00	710.33	6.39	573
006	2.46	3.05	80.67	345.67	4.04	212
007	-	-	-	-	6.33	727
008	2.65	2.99	88.00	263.67	2.92	288
011	2.84	3.57	79.00	344.00	7.03	892
012	4.51	5.66	79.67	679.33	11.90	797

Table 4-3: The means of three replicate measures of study participant's spirometry readings shown with their calculated minute and mean tidal volumes

Minute Volumes

With typical resting values in the range of 6 to 10 L (US Navy, 2005), five of the volunteers fall within the normal range. However, the results from volunteers 006 and 008 (4.04 and 2.92 L respectively) appear lower and 012 (11.9 L) slightly higher than the norm. Mean tidal (single breath) volumes were calculated by dividing the minute

volumes by the mean median RRs from exhalatory flow (see *Table 4-4*) for each volunteer. This is normally given as 6 – 12 mL\kg of body mass (Grossbach et al., 2011) giving a median figure of around 600 mL for a mass of 70kg (Walpole et al., 2012). Although weights were not taken in the study, the estimated volumes for subjects 006 and 008 appear unusually low which may be indicative of poor mask sealing.

4.3.4 Respiratory rate analysis

The peak-to-peak periods were extracted from each respective dataset and entered into an MS Excel spreadsheet. These were converted to instantaneous RRs (60 seconds/breath-periods) and the resulting data plotted to show raw and processed readings over the study period. The relationship between breath periods and RR is shown in *Figure 4-13*. It can be seen that small changes or measurement errors in breath periods have a significant effect on RRs at normal physiological ranges.

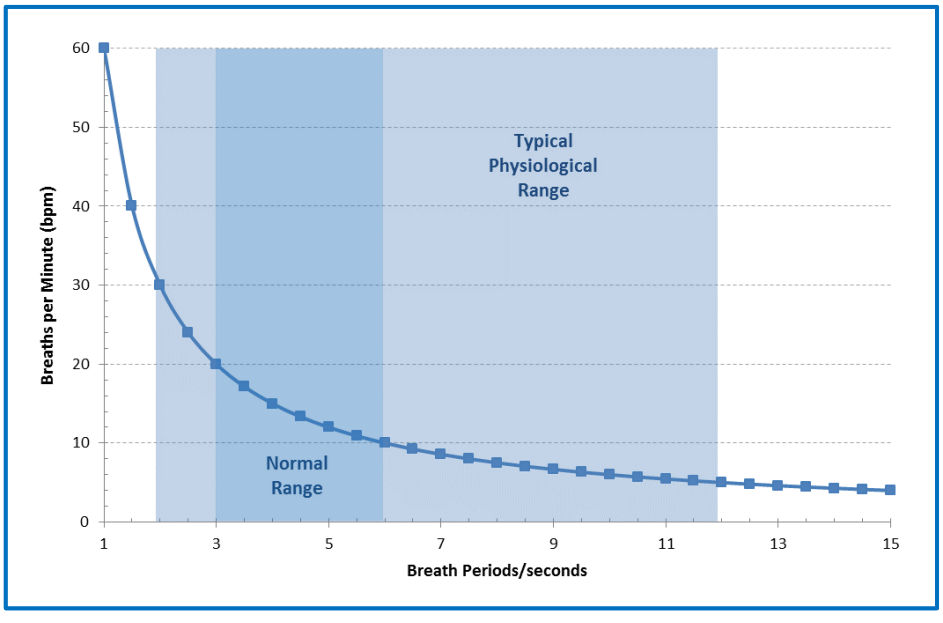


Figure 4-13: The relationship between breath periods and breaths per minute (bpm) over the typical physiological range

Instantaneous Respiratory Rates

These were calculated for each tabulated breath period and plotted as a series of graphs, one for each of the participants, as shown in *Figure 4-14*. Each graph shows the reference expiratory flow RR (*Ref*), CRS x- and z-axes RRs (*CRS_X* and *CRS_Z*) and TRS z-axis RR (*TRS_Z*) plotted against consecutive breath numbers over the study period.

Some discrepancies in the agreement between and the total number of peaks in the reference and accelerometer responses were observed. Occasional small extraneous peaks in breath flow were almost certainly due to volunteers talking as noted during study sessions; one peak was removed from a dataset where the time correlation was clear. Instances of missing peaks following a full outbreath may be explained by imperfect mask sealing on some volunteers.

Median Filtered Respiratory Rates

Displaying instantaneous RRs could be considered impractical for real-world use due to “jitter” from normal inter-breath variation, thus additional processing was applied to moderate breath frequency. Here the median value of a sample window of five ordered consecutive breaths was used; this method was chosen as intermittent high or low readings have a reduced influence on results, but rate changes that occur over a number of (>3) readings are preserved. Graphs showing the results of a five-sample median filter for each study participant are presented in *Figure 4-15*.

Figure 4-14: A comparative plot of instantaneous breath-by-breath RRs for each of the eight study participants

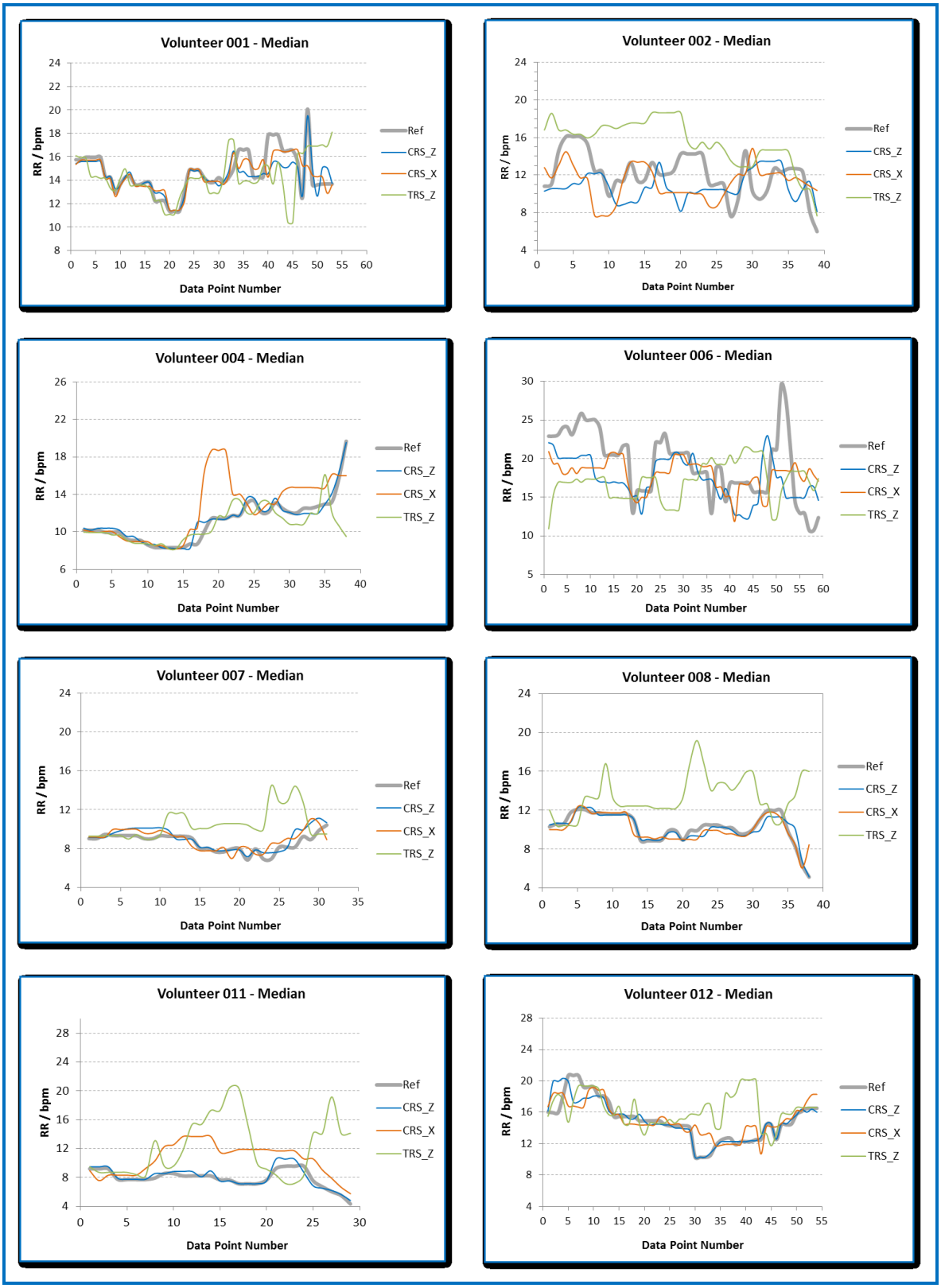


Figure 4-15: A comparative plot of ordered five-sample median filtered RRs for each of the eight study participants

Study Mean Respiratory Rates

Table 4-4 shows the mean instantaneous and mean median RRs for each study participant giving the respective figures for the reference, CRS x and z axes and TRS z-axis. It can be seen that the results for subject 001 are quite closely matched throughout while the others show clear discrepancies. Results for the z-axis clavicle sensor appear the closest to the reference.

Volunteer No.	Reference RR	CRS-X RR	CRS-Z RR	TRS-Z RR	Median Reference RR	Median CRS-X RR	Median CRS-Z RR	Median TRS-Z RR
001	14.84	14.54	14.57	14.50	14.59	14.46	14.34	14.24
002	12.45	11.31	11.25	15.13	11.72	11.20	10.80	15.35
004	11.63	12.70	11.42	11.05	11.14	12.66	11.29	10.68
006	19.31	17.47	17.42	16.92	19.05	17.90	17.32	17.12
007	8.84	8.65	9.13	10.94	8.71	8.96	9.11	10.45
008	10.35	10.38	10.29	14.95	10.14	10.00	9.93	14.06
011	8.90	11.11	8.71	13.82	7.88	10.89	8.08	12.54
012	14.72	15.38	14.89	16.27	14.93	15.07	14.86	16.32

Table 4-4: The means of breath-by-breath and five-breath median RRs from the study for each participant

Statistical Analysis

The mean median RR data from *Table 4-4* was used to prepare regression and Bland-Altman plots of the CRS x and z and TRS z-axis against the reference, showing relative performance.

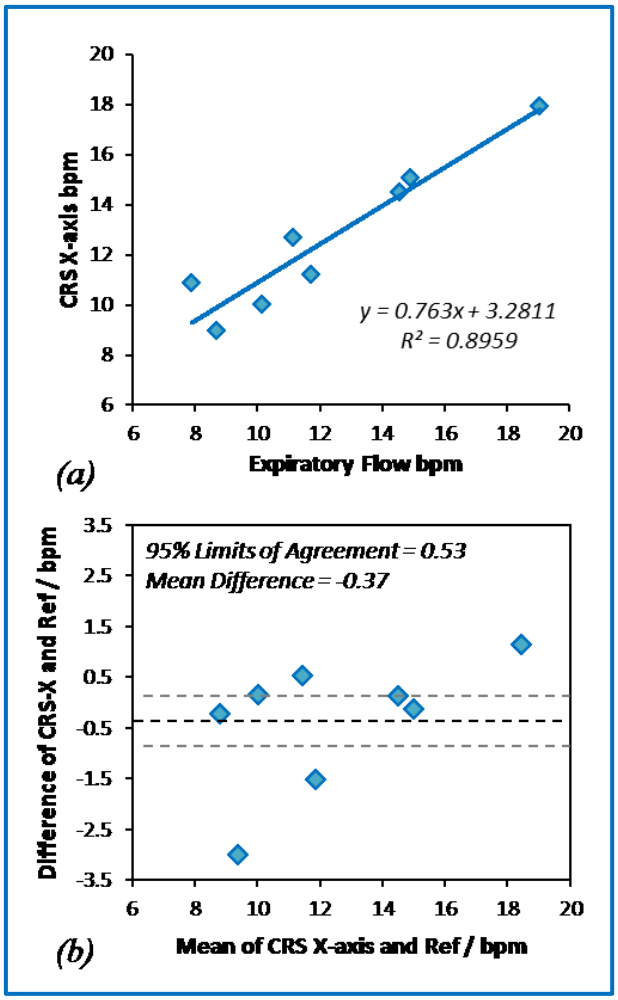


Figure 4-16: Regression of the means of the CRS X-axis median RRs against the reference (a) and Bland-Altman plots of the means and difference of the paired readings (b).

Figure 4-16 shows comparative plots of the CRS x-axis and the reference. The regression plot shows a relatively tight grouping around the trend line giving a coefficient of determination (R^2) of 0.896 ($p < 0.001$). The Bland-Altman plot shows a small mean bias (-0.37) with four outliers outside of the limits of agreement. The largest errors point to underestimation in the lower ranges, but with a general tendency to overestimate

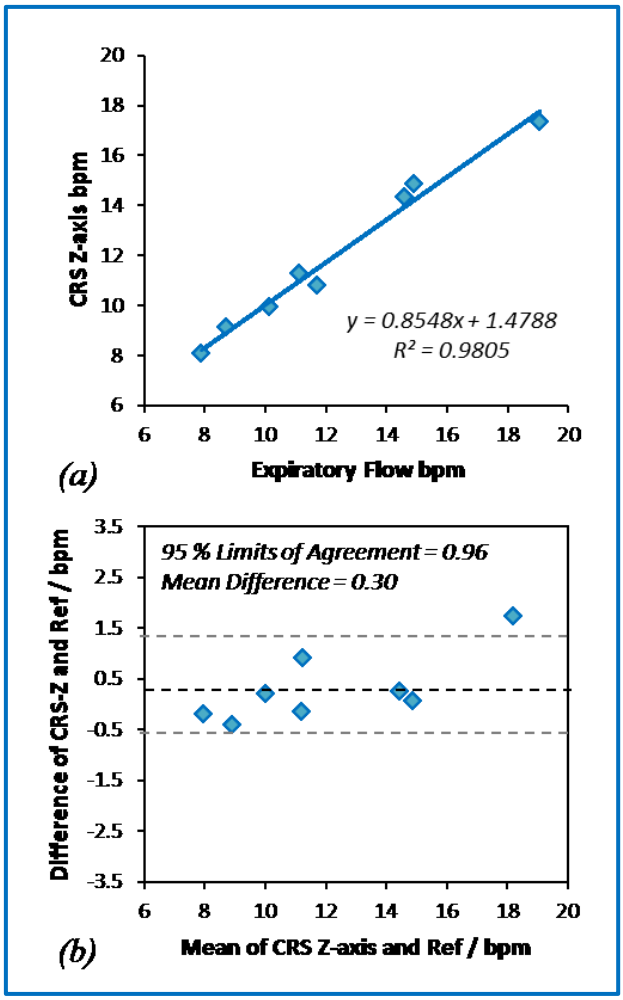


Figure 4-17: Regression of the means of the CRS Z-axis median RRs against the reference (a) and Bland-Altman plots of the means and difference of the paired readings (b).

Comparative plots of the CRS z-axis and the reference are shown in *Figure 4-17*. The tight grouping around the trend line in the regression plot gives an R^2 value of 0.981 ($p < 0.001$). The Bland-Altman plot shows a smaller mean bias (0.30) than the CRS x-axis with a single outlier and, with most of the points below the mean bias line, a propensity for underestimation.

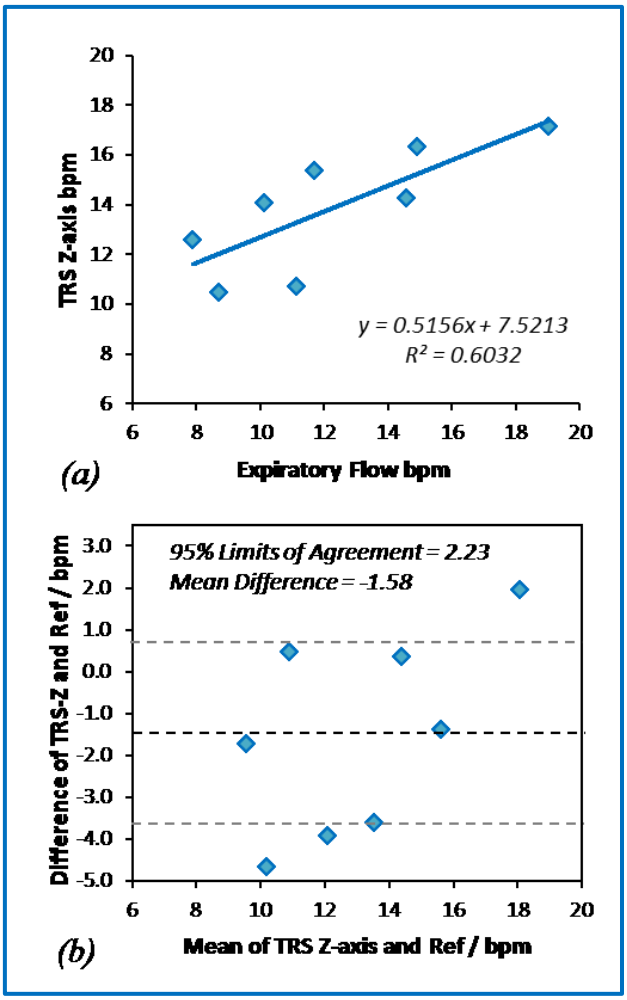


Figure 4-18: Regression of the means of the TRS Z-axis median RRs against the reference (a) and Bland-Altman plots of the means and difference of the paired readings (b).

Figure 4-18 shows comparative plots of the TRS z-axis and the reference. The regression plot shows a relatively loose grouping around the trend line with $R^2 = 0.603$ ($p < 0.023$). The Bland-Altman plot shows the greatest mean bias (-1.58) of the three plots presented here. The limits of agreement too are the highest of the set (2.23) with three outliers. There is noticeable greater scatter and as with the CRS x-axis plot, the largest errors point to underestimation in the lower ranges and overestimation at higher frequencies.

4.4 Discussion

The pilot study reported here produced encouraging results and has successfully demonstrated that CRS can ably track resting RRs. Clavicle sensor signals were of superior amplitude and signal to noise ratio than those from the thoracic device, giving notably superior RR readings using relatively basic signal processing techniques with the longitudinal (Z) axis providing the best results.

Precise sensor positioning upon the clavicle was not found to be particularly critical, a feature that should reduce user error and facilitate use by non-clinical staff and in home monitoring. Optimal operation would require compliant subjects, which should not present any more of a problem than with other vital sign measurements of resting patients. Any non-respiratory motion-induced artefacts could be minimised by considering composite or angular waveforms (Anmin et al., 2009), an activity monitoring algorithm (Mathie et al., 2004) applied to qualify the respiratory data or the sample window size increased, whether for signal averaging or a median filter as used here. Alternatively the types of algorithms employed in more sophisticated pulse oximeters to suppress motion artefacts (Moyle, 2002) could be adopted.

Additional and missing peaks were observed in the study datasets, some of which were caused or masked by non-respiratory motion. With good sensor to clavicle coupling, CRS RRs compared well with the reference. Two volunteers experienced problems with poor sensor adhesion, a key factor for optimal performance, causing inadequate coupling, which was reflected in the data. This was generally more of a problem with male participants due to body hair; this may be easily addressed by local hair removal, use of alcohol wipes and more resilient surgical tape. The estimated

minute and tidal volumes suggest that mask sealing was an issue for two volunteers, the masks (medium and large sizes) being incorrectly sized and causing leakages.

The signal processing techniques employed were relatively simple and straightforward compared to those in many medical devices. Rather than having to process analogue and acquire waveforms in a host device this would allow the use of small, relatively basic and low-cost microprocessors for on-board data processing. This would offer embedded algorithms and digital output, practical devices being available in wired USB-powered or wireless (battery powered) formats. Power requirements would be very low, so many hours of wireless operation would be possible with a small battery unless continuous real-time wireless monitoring was required.

4.4.1 Comparison with Other Methods

Clavicular respiratory sensing is less intrusive than direct monitoring methods, such as capnography and nasal thermometry, that measure exhalatory flow and more convenient and discrete than thoracic band-based measurement. Being motion-based, it does not suffer from the contact resistance, electrical noise and interference, arrhythmia-induced or treatment-related problems seen with ECG or impedance respiratory sensing methods employing electrodes to capture thoracic electrical activity (Malik, 2004). The estimation of RR via EDR or RSA from ECG or PPG signals does not offer the accuracy or range suggested by the CRS in this study. Whereas the CRS was sampled at 100 Hz, a rate that could be increased for improved temporal resolution, as the accuracy of the EDR and RSA methods are dependent upon the ratio between HR and RR; as this narrows accuracy suffers. A study by Wu estimating RRs

derived from ECG and PPG waveforms gave mean errors of 0.85 ±0.53 bpm and 1.46 ±1.12 bpm respectively (Wu et al., 2010), both significantly inferior to the CRS figures (0.30 ±0.70 bpm). When compared with Cysarz's findings (Cysarz et al., 2008), clavicular respiratory sensing appears superior at lower RRs (<10 bpm) and has better potential for accurately detecting higher RRs (>20 bpm).

4.4.2 Respiratory Depth

The study shows that the magnitude of the accelerometer waveform is proportional to that of respiratory motion. This is of clinical interest as it offers a potential means of monitoring respiratory effort and has seen interest by researchers investigating respiratory flow in sleep apnea (Dehkordi et al., 2012). Shallow breathing, where minimal thoracic movement may be observed, could indicate orthopnoea in a recumbent patient (Haldane et al., 1919). Changes in breath depth, where this becomes shallower over time for example, could be of value for monitoring progressive dyspnoea (Longmore et al., 2009). It also facilitates the detection of Cheyne-Stokes respiration and apneas and may assist in the early detection of acute exacerbations of COPD and asthma (Maitre et al., 1995).

4.4.3 Study Limitations

A few limitations were apparent in this pilot study, the greatest being the number of participants. A larger study group would address this, having greater statistical power, and could include the investigation of postural influences upon RR readings. It would also help to determine the device's accuracy and bias across a wider range of frequencies. A more thorough assessment of ventilatory condition involving

spirometry, body mass index (BMI) and thoracic measurements would help build an understanding of the relationship between respiratory depth and signal magnitude. This would provide calibration data for the estimation of tidal and minute volumes.

4.4.4 Applications

This pilot study demonstrates that clavicular respiratory motion sensing is superior to thoracic sensing and offers a viable and convenient method for the non-invasive monitoring of respiratory rate. Whilst this in itself is of value, especially outside of clinical settings, the possibility of simultaneous measurement of respiratory depth significantly enhances the devices' potential as a practical diagnostic or monitoring device (Folke et al., 2003). Use of such a discrete respiratory monitor could benefit dyspnoea sufferers as it could help promote patient compliance for breathing exercises by offering valuable feedback and encouragement (Gavish, 2010). For home-based patients, whether elderly or suffering from long-term conditions such as COPD, the regular monitoring of RR depth and breathing patterns with a device such as the CRS, could be of great clinical value. When combined with pulse oximetry and other vital signs in a telemonitoring system, it could provide an early warning of acute exacerbations, a worsening condition or the onset of severe respiratory infection. These enhancements, together with further waveform and multi-parameter analysis, may yield useful data in characterising respiratory patterns as an aid to diagnosis (Tobin et al., 1983; Dellweg et al., 2008).

4.5 Conclusions

The work reported in this study meets two of this thesis' stated objectives:

- A novel prototype respiratory sensor (CRS) was designed and produced.
- A pilot study of the prototype respiratory device on healthy subjects was completed in order to allow comparison with a reference device.

Results from the study demonstrate the following points:

- When compared with the reference, the longitudinal (z) axis gave the most consistent results in both the clavicular and thoracic sensors.
- The mean study results demonstrate that clavicular sensing (R^2 = 0.981, p <0.001, mean bias = 0.30, limits of agreement = 0.96) was superior to thoracic measurement (R^2 = 0.603, p <0.023, mean bias = -1.58, limits of agreement = 2.23) when compared with the reference, with which it had an excellent agreement.
- The CRS (z-axis) study data gave a mean error of 0.30 ±0.70 bpm, meeting the desired 1 bpm accuracy.
- It was observed that the magnitude of the accelerometer response was proportional to respiratory depth, offering the potential for further study into the viability of the method for the estimation of tidal volume.
- Clavicular respiratory sensing has demonstrated its potential for development as a discrete wearable RR sensor.

5 Development of an Ear-worn Personal Monitoring System (EPMS)

5.1 Introduction

Having established that ear thermometry was the best proxy for core body temperature it was apparent that this was the preferred temperature measurement site. With pulse oximetry selected as the preferred HR monitoring method and the availability and acceptance of ear probes for sensing, by logical progression the optimal arrangement for simultaneous multiple-sensor vital signs monitoring was an ear-worn device. In choosing the ear as a monitoring site this facilitated access for periodic monitoring and saved users from having to undress to fit the sensing device. Over the course of the project there were four major design iterations; these are referred to here as EPMS v1 to v4, with EPMS v4 being the final incarnation of the design.

This chapter describes the engineering of the prototype EPMS designs. The four main sections cover the sensor design and installation, electronic systems and initial tests, concluding with a discussion. Details of the key aspects of the sensor and system designs are reported, these include schematics of sub-circuits, control system flowcharts, the specifics of circuit operation, CAD images of the board designs, the particulars of sensor installations and system enclosures. The results of initial testing are then presented, providing an indication of sensor and system performance. The differences between evolutions of the device design are also highlighted and discussed.

5.2 The Sensors

This section reports the development of the sensors for the EPMS device, with the temperature, pulse oximeter, accelerometer and SR sensing each covered in turn. The pulse oximeter design is covered in particular detail, showing the basic design criteria and the theory of operation.

5.2.1 Temperature Sensing

The Melexis MLX90615 was housed remotely in an in-ear probe such that the sensor lens was aimed at a subject's inner ear. In the EPMS v1 this was encapsulated (epoxy resin) inside a modified audio earpiece whereas a 3D-printed hollow conical probe was used in the other designs. The design of the latter was modelled on that of a Braun Thermoscan ear thermometer, having similar overall dimensions with the exception of probe length – this was shortened slightly to minimise the potential for injury or discomfort. In all cases the sensor was connected to a +3.3V power supply and the host circuits' I^2C serial bus, the connections being made directly to a pcb by short wires (40 to 60mm long).

Sensor calibration was not required, the quoted resolution being 0.02°C with an accuracy of ±0.5°C over the physiological temperature range. The emissivity was left at the factory setting of 1.0 - equivalent to that of a perfect black body. Emissivity of human skin is typically quoted as 0.96 to 0.98 (Boylan et al., 1992); as this is close to the pre-set value there was little to be gained by changing the setting.

5.2.2 Pulse Oximeter

This consists of the sensor probe (described in the next paragraph) and accompanying circuitry. The circuitry itself may be broken down into two distinct sections, drive control and signal conditioning, which are necessarily interdependent and described in the sections on *pages 160 a*nd *161* respectively. The control systems employed in the prototype devices are described in the section from *pages 162-165*.

Ear Clip Probe

All designs used a standard off-the-shelf Smith's Medical reusable pulse oximeter ear clip probe (part number 3078), which was worn on the ear lobe. As delivered, cables were terminated with a D9 sub-miniature male connector. These used a standard pinout employed by Nellcor[58], Masimo[59], Nonin[60], Smiths Medical and other leading device manufacturers (see *Table 5-1*).

9 pin D-Sub male connector	Function	Details
2	LED A	LED Drive input
3	LED B	LED Drive input
5	Photodiode Anode	Sensor output
7	Ground	Sensor/cable shield
9	Photodiode Cathode	Sensor output

(Markandey, 2010)

Table 5-1: Standardised pulse oximeter probe pin connections, as used by Nellcor (Covidien) and many other leading manufacturers

[58] *Covidien plc, Dublin, Ireland*

[59] *Masimo Corporation, Irvine, CA, USA*

[60] *Nonin Medical, Inc., Plymouth, MN, USA*

In this configuration the two (red and infrared) LEDs were connected in an inverse parallel configuration requiring two connections to a drive circuit which alternately switches polarity to illuminate the LEDs, e.g. an H-bridge. The remaining connections accommodate the photodiode (more correctly a PIN diode) connections and a shield for the sensor cable and pcb which must be grounded. For installation into the prototype devices, cables were significantly shortened (to less than 100mm), the braided screens pigtailed with a ground wire and the individual wires soldered directly to the circuit boards. With the EPMS v1 the clip was glued to the ear module enclosure; as fitting the device to the ear was found to be rather difficult, the clip was left free on subsequent designs where it could be easily clipped onto the earlobe.

Smith's Medical were contacted on several occasions regarding technical and calibration data for the ear probe, but unfortunately this was not forthcoming.

Drive Control Overview

The drive control sets the illumination intensity of the probes LEDs and the pulse repetition frequency. Instantaneous drive current could exceed 100mA per LED (with this equal to *[drive voltage - LED forward voltage] / LED series resistance* and assuming typical values of [3.3V – 1.5V] / 15Ω), though the mean ac current was considerably less. Thus components with appropriate power ratings were used. This allowed a range of tissue thicknesses and skin tones to be accommodated with transmissive sensing.

An H-bridge LED driver circuit, a common feature of pulse oximeter designs employing inverse parallel LEDs (Markandey, 2010; Texas Instruments Inc., 2010; Texas Instruments Inc., 2013), was used in all of the EPMS variants. In the case of EPMS v1 to

v3 this used discrete components whereas in EPMS v4 it was on-chip in a dedicated integrated device. This allowed control of both LED drive (via digital-to-analogue converters - DACs) and switching. Once enabled, the LEDs were cycled at the chosen pulse frequency – IR ON, both OFF, red ON, both OFF – such that only one LED was illuminated at any time, the OFF periods providing reference ambient light levels (*Figure 5-1*). The clock frequency of the LED drive for the EPMS v1 to v3 was 500 Hz and 1000 Hz for EPMS v4; the sampling rate for the four quartiles being 125 Hz and 250 Hz respectively.

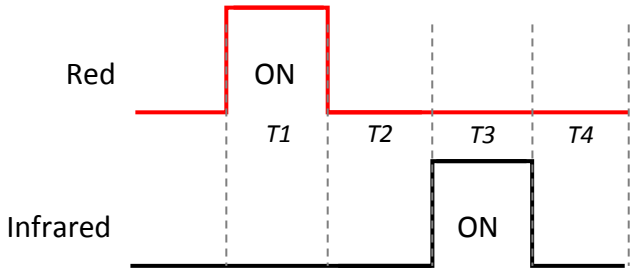


Figure 5-1: Pulse Oximeter LED switching timing diagram shown with equal switching periods (T1 – T4)

Signal Conditioning Overview

Signal conditioning for the photodiode employed a transimpedance amplifier to convert the diode's small photocurrent to a voltage, and rail-to-rail input and output op-amps to filter and amplify the signal prior to analogue to digital conversion. The circuit designs used in EPMS v1 to v3 were based around discrete components under digital control while the EPMS v4 used integrated analogue and digital circuits in a dedicated chip for essentially similar signal conditioning provision.

Control System

This is a critical part of any pulse oximeter design and encompasses control of the LED drive and signal conditioning using feedback to control dynamic system behaviour, and signal demultiplexing.

As the LEDs may have different adsorption characteristics, independent adjustment of their light intensity is required. In addition, as the power budget is limited, it is important that LED light intensity is optimised, balancing the signal response and LED drive. Another key feature is to turn off or reduce intensity of one or both LEDs when no viable target (i.e. tissue) is present to save energy.

Feedback from the digitised photodiode response allows dynamic adjustment of LED drive under software control to achieve the desired results. A flowchart of the control system is shown in *Figure 5-2*. In an initial "standby mode", the red LED alone is pulsed at low frequency and moderate intensity, with test readings taken. With the ear clip not in use there would be no apparent absorption whereas a change in adsorption could indicate tissue is present. In this case the red and IR LEDs are turned on, monitored and adjusted for optimum performance such that data sampling can begin if viable. If the adsorption levels during sampling suggest the clip has been removed (i.e. minimal absorption) the system enters standby once more, whereas, if the signal levels exceed predetermined boundaries (e.g. poor perfusion, sensor fitting or motion artefacts) the LEDs are "retuned".

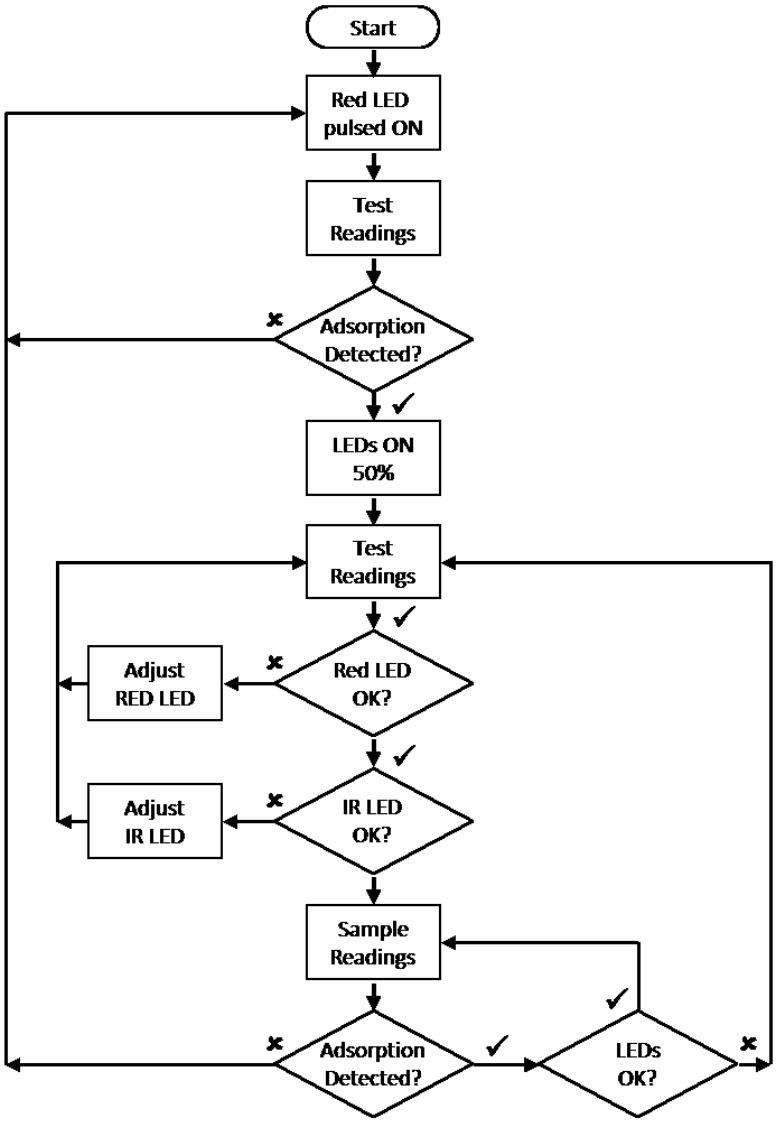


Figure 5-2: A flowchart showing pulse oximeter LED drive control and adjustment

As there are two LEDs and a single photosensor, this presents a composite output of red, IR and ambient (reference) signals. These must be demultiplexed (separated) before anything useful can be achieved. This may be performed in software, hardware or a mixture of both techniques; however, the critical point in all cases is that the timing of the LED switching and sample acquisition are in lockstep. While this alone may suffice for software methods, it should be noted that the host microprocessor or microcontroller must also simultaneously process the signals, acquire data from other

sensors and manage system-level functions. Performance is therefore dependent upon the micro's computational power and specification. A hardware solution, which is relatively straightforward, takes the burden away from the embedded software, but adds to the component count and circuit space requirements. For lower performance micros, a compromise between both methods employing software-controlled analogue switching could present the best option.

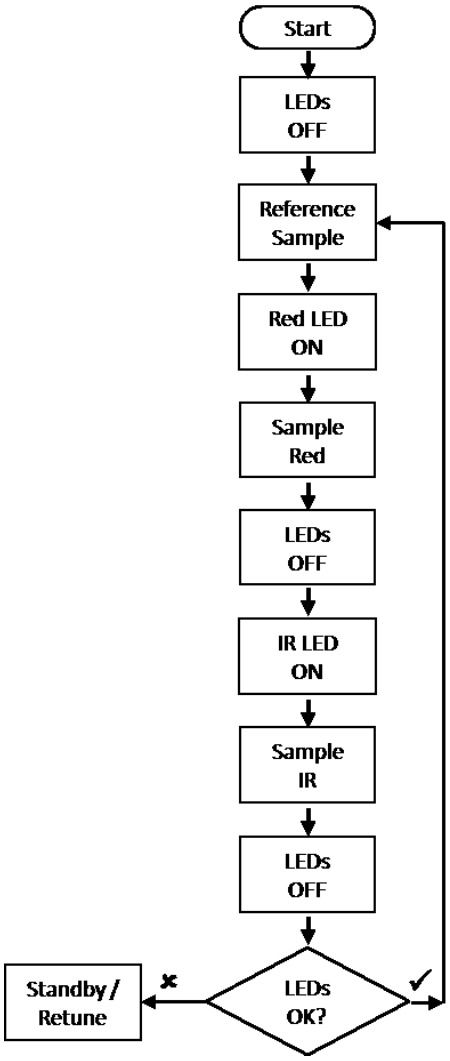


Figure 5-3: A flowchart showing the relationship between pulse oximeter LED control and sample acquisition

Figure 5-3 shows the basic sampling algorithm with the sample intervals sequenced with the LED control timing (see also *Figure 5-1*). A reference sample, taken with both LEDs turned off, gives an indication of the ambient light levels and provides a useful baseline indicator.

Filtering and Signal Processing

The demultiplexed signals have both a dc and ac component - and a degree of noise in superposition. These must be separated to produce clean PPG waveforms for HR and SpO_2 calculation. A resting HR of 60 bpm equates to a frequency of 1Hz and an HRmax of 240bpm to 4Hz, thus a form of filter is required with a pass band ranging from around 0.5Hz to 4Hz.

The question of the method of choice is the same as that for signal demultiplexing. Digital filtering, using the onboard processor, requires a relatively high performance device and may not be sensible or even possible on lower specification micros. At higher sample rates, such as the 250 Hz used in the ultimate prototype here, the computation required places a high demand on the processor. If this is to be performed in real-time, the computational requirements necessary may demand the use of dedicated digital signal processing (DSP) chips.

Analogue (hardware) filters, especially in multipole form, are very efficient at attenuating higher frequencies, but not so effective at frequencies approaching dc. The preferred option here therefore is to combine the techniques giving the best of both without placing undue load on the embedded processor.

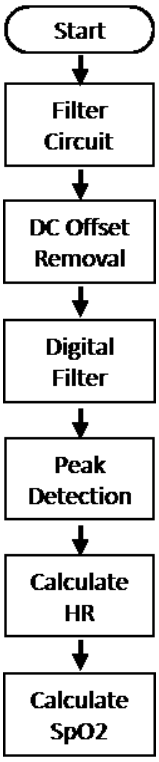


Figure 5-4: A diagram of the filter and digital signal processing chain

The basic outline of the filter chain is shown in *Figure 5-4*. A low-pass (active or passive) analogue filter was first employed to remove higher frequencies (e.g. >5Hz) before a final stage of digital filtering using an infinite impulse-response (IIR) was applied to clean the final signal. The EPMS v4, with an ARM (Cortex-M0) processor and dedicated signal conditioning chip, employed a 5Hz IIR low-pass multipole digital filter.

Heart Rate

HR may be calculated from either the filtered red or IR waveforms, or both, giving a self-checking option. A peak detection algorithm first determines the waveform's peaks, then either counts the number of inter-peak samples, multiplying this by the sample period or measuring the inter-peak interval to give an instantaneous measure of HR (60 \ peak-to-peak period) in bpm. As the instantaneous reading is unstable due to HRV and RSA additional processing is necessary to return a stable indication of HR.

There are a number of methods of achieving this. Although the methods and algorithms used in commercial devices are not published, being commercially sensitive and closely guarded, available details suggest the use of moving averages and in some instances, look-up tables of historic data to counter motion artefacts (Moyle, 2002).

Regarding moving averages, there is a question of the size of the sampling window and the effect this has upon the processed data – too short and the result may be unduly affected by transients, too long and a time delay is introduced. A median filter provides the best of both narrow and wide sample windows without the need for sample weighting. This takes a number of samples which are then ordered, the result being the middle value in the ordered list. Most transients tend to fall above or below the middle value and do not influence results unless reflected in several consecutive readings (suggesting they may be real), whereas an average value would be affected. It also offers a rapid response as the sample window may be relatively short (Bernholt et al., 2006). A 5-sample moving median filter was used initially, however this was extended to 9 samples to reduce jitter.

Blood Oxygen Saturation

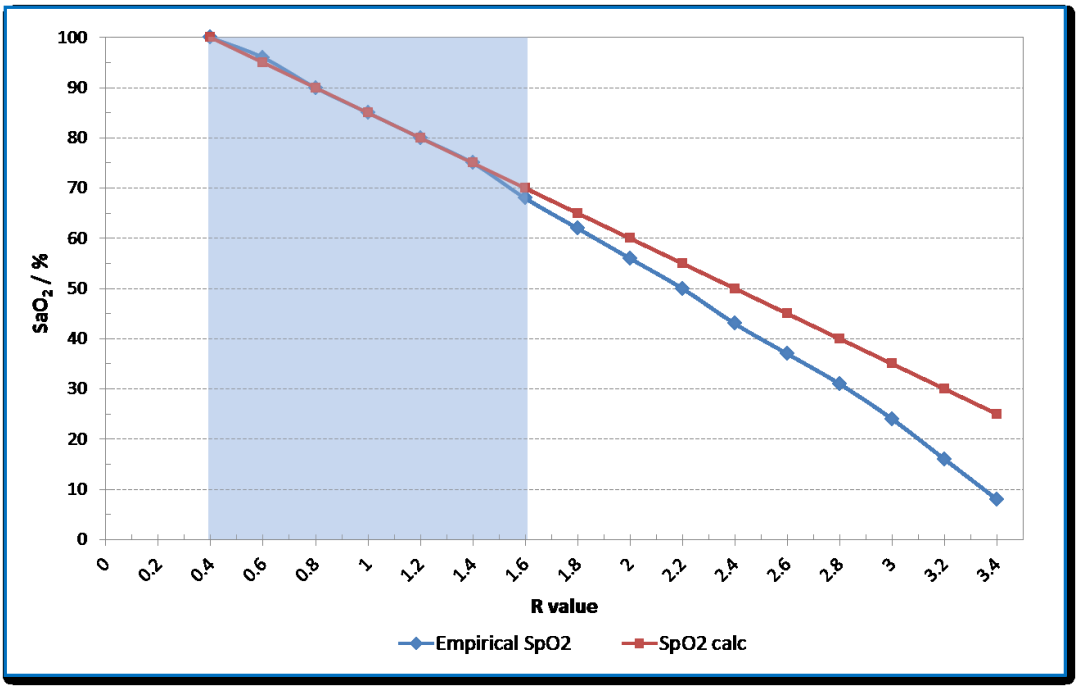
This may be calculated from well-perfused tissue's relative absorption of red and IR light, where oxyhaemoglobin (HbO) has a greater absorption in IR than in red light and deoxyhaemoglobin (Hb) a greater absorption in red light than IR. This may be expressed in terms of an absorption ratio (R) as shown in *Equation 5-1*:

Equation 5-1: Absorption ratio equation for the calculation of blood oxygen saturation

$$Absorption\ Ratio\ (R) = \frac{(Red\ AC)/(Red\ DC)}{(IR\ AC)/(IR\ DC)}$$

Where Red AC and IR AC are the amplitudes of the AC signal components and Red DC and IR DC the amplitudes of the DC component in the respective waveforms (Rusch et al., 1996; Moyle, 2002). Absorption ratios are referenced to a look up table to produce corrected SpO_2 values, the data for which was derived from real clinical measurements of healthy subjects. Here absorption ratios or SpO_2 readings (perhaps involving multiple probes) are referenced to SaO_2 measurements from a blood gas analyser while study volunteers breathe a hypoxic (nitrogen-oxygen) gas mixture. The mixture's ratio is adjusted to provide an SaO_2 range of around 70 to 100% in subjects under close medical supervision. Regression and Bland Altman plots determine the relationship for each probe against the reference and provide calibration data (Smiths Medical PM, 2006).

A plot showing the relationship between the absorption ratio (R) and SaO2 values is presented in *Figure 5-5*; this is based on empirical data (Webster, 1997; Reddy et al., 2008). The graph shows a calibration curve that is almost linear for saturation levels of 75% to 100%, but non-linear below this threshold. As the linear portion approximates the physiological range of clinical interest a linear approximation may be used. This is shown overlaid in *Figure 5-5* with *Equation 5-2* giving the derived formula:



(Reddy et al., 2008)

Figure 5-5: Empirically-derived and calculated SaO_2 for a range of R values, with those of normal clinical interest (70% to 100%) highlighted

Equation 5-2: A linear approximation equation for the estimation of blood oxygen saturation values for a given absorption ratio, R.

$$SpO_2 = 110 - 25R$$

(Rusch et al., 1996)

5.2.3 Accelerometer

A low-power triaxial accelerometer was used on all design variants, an ADXL330 on EPMS v1 and an ADXL345 (both from Analog Devices) on subsequent devices. The ADXL330 chip has a measurement range of ±3g and a sensitivity of a nominal 330 mV/g (being dependent on the supply voltage and thus ratiometric) on each of its three analogue voltage outputs, swinging around a centre (zero g) voltage of 1.65V (Analog Devices Inc., 2007). The ADXL345 provided a digital interface to an I^2C serial bus and

offered a programmable 10-bit measurement range of ±2, 4, 8 or 16g. Other features included activity/inactivity monitoring and single/double tap detection; the former was in EPMS v4 as part of the power management system to awaken the processor from sleep mode after a period of inactivity (Analog Devices Inc., 2008).

5.2.4 Skin Resistance

The skin resistance sensing circuit consisted of tinned copper or gold contact electrodes connected to the basic potential divider and amplifier circuit shown in *Figure 5-6*. This connected to the potential divider formed by resistors Rh, Rl and Rn; high values were chosen for Rl and Rn (680kΩ) while Rh (10kΩ) provided a resistance path between the negative electrode and ground, offering shock protection from external sources. The probes themselves were connected in parallel with Rl, thus the resultant was a product of the two resistances. This minimised skin current flow to a maximum of 4.8μA with shorted probes (with a terminal voltage of 47mV). Clamping diodes on EPMS v4 offered additional protection to overvoltage conditions.

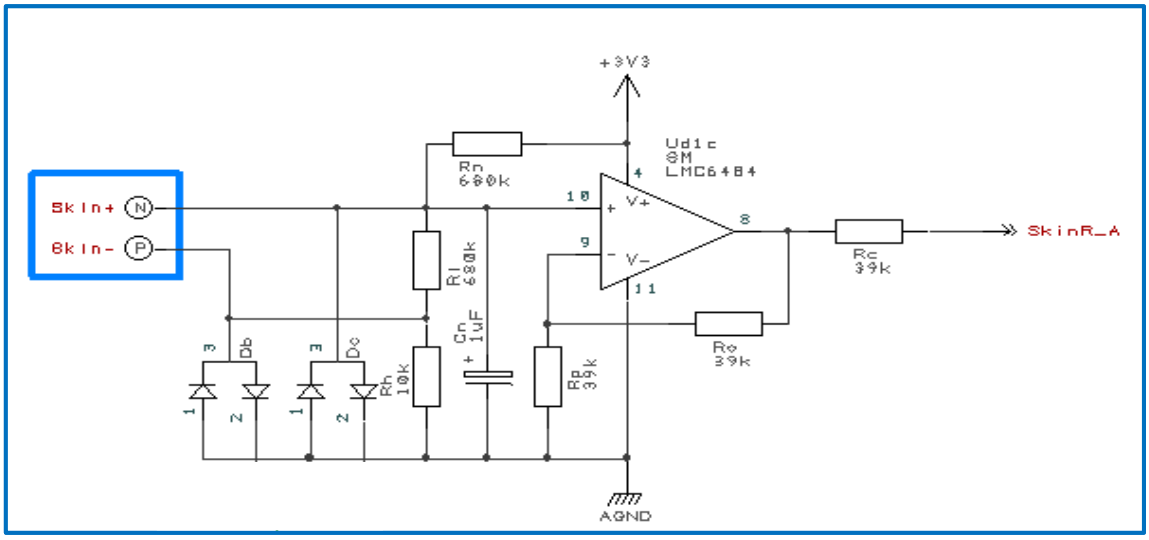


Figure 5-6: A drawing of the skin resistance sensing circuit from the EPMS (v4) schematic.

Equation 5-3: Skin current calculation

$$I_{skin} = \frac{Vcc}{Rn + Rh\left(Rl + {R_{skin}}/{Rl.R_{skin}}\right)}$$

$$Where\ Vcc = 3.3V,\ Rl\ and\ Rn = 680k\Omega\ and\ Rh = 10k\Omega$$

Equation 5-4: Skin terminal voltage

$$V_{skin} = \frac{Vcc.\left(Rh + \left(Rl + {R_{skin}}/{Rl.R_{skin}}\right)\right)}{Rn + Rh\left(Rl + {R_{skin}}/{Rl.R_{skin}}\right)}$$

The output from the potential divider connected to the non-inverting input of an op-amp configured in non-inverting mode. Here the voltage gain (A_V) was set by the ratio of resistors Ro and Rp (each 39 kΩ). The resulting amplifier output voltage was proportional to SR.

Equation 5-5: SR amplifier voltage gain

$$A_V = 1 + \frac{Ro}{Rp} = 1 + \frac{39k\Omega}{39k\Omega} = 2$$

SR sensing was tested on EPMS v1 using thin wires glued to the pulse oximeter clip which gave mixed results due to poor skin contact and adhesion to the clip. The circuit was included on all other variants, but not connected to skin electrodes.

5.3 System Designs

The design details of the four iterations of the evolving EPMS device are described here, with both circuit and system operation being reported (with reference to the full circuit schematics presented in *appendices A to D*).

5.3.1 EPMS v1

Initial investigations suggested that ZigBee technology (ZigBee Alliance, 2009), with its mesh networking capability, would provide an ideal platform for connecting a range of physiological and environmental sensors to form a personal network. The design used two separate modules communicating over a ZigBee wireless data link, one worn on the ear acquiring physiological signals and the other carried by the subject acting as a Bluetooth gateway (*Figure 5-7*).

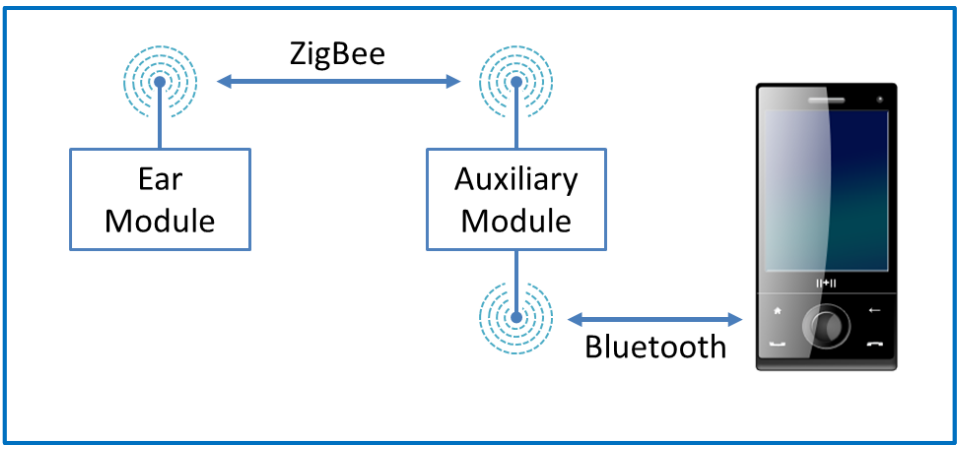


Figure 5-7: The arrangement of the EPMS v1 wireless communications

ATBZ-24-A2 Zigbee modules were chosen as a basis for the design. These are compact low-power 2.4GHz ZigBee wireless (IEEE 802.15.4) modules with integrated antennae incorporating a programmable Atmel ATmega1281V microcontroller and associated support circuitry (Atmel Corporation, 2009). The micro's control and

input/output (I/O) pins were accessible via terminals around three of the device's sides; these were used to connect power and peripheral devices to the ear (see *Appendix A-1*) and auxiliary module (*Appendix A-3*).

The ear and auxiliary modules comprised two pcbs, one hosting the ZigBee module (*Appendices A-1 and A-3*, *Figure 5-10a, b* and *Figure 5-11a, b*) and the other the analogue and interface circuitry (*Appendices A-2 and A-4*, *Figure 5-10c, e* and *Figure 5-11c, e*). The system circuit boards are shown in *Figure 5-8*, with the ear unit in its intended application in *Figure 5-9*.

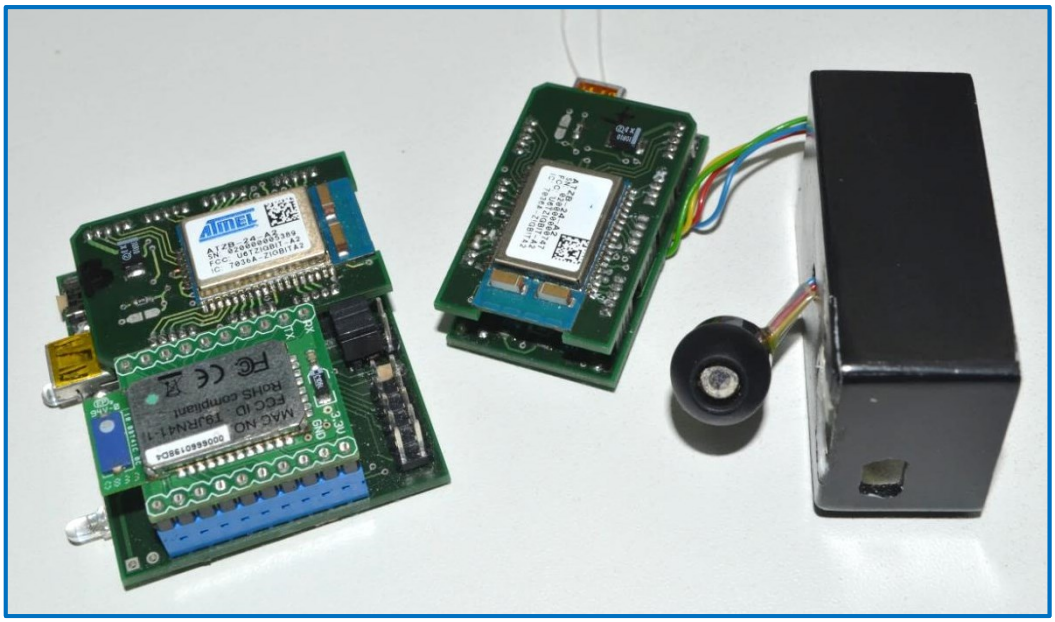


Figure 5-8: The EPMS v1 system showing the Auxiliary Unit on the left (with the RN-41 Bluetooth module nearest) and the Ear Unit, thermometer probe and enclosure to the right

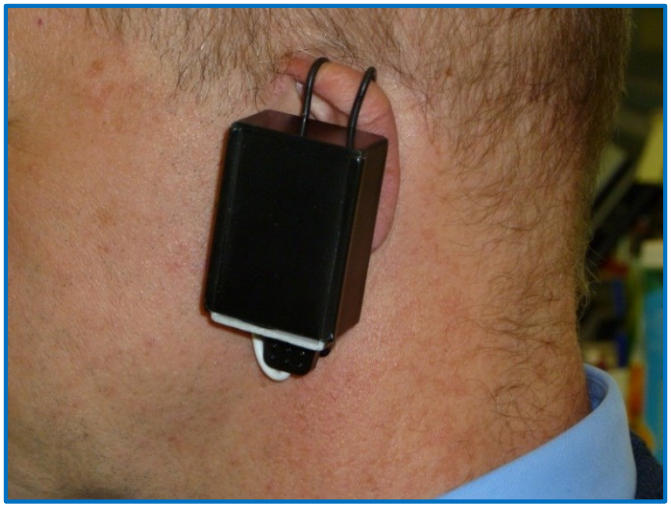


Figure 5-9: The ear-worn component of the initial EPMS v1 prototype device

Ear and auxiliary module digital circuit description

As many of the usual microcontroller support components (e.g. crystals, power rail decoupling etc.) were on-board the module, this helped simplify circuit design. The SPI serial bus was used as a high-speed interface to an FM25H20ds 2Mbit flash memory chip[61] for local data storage and the I2C bus to connect a DS1337 real time clock[62] and the MLX90615 IR pyrometer. The serial busses and I/O pins were connected to sockets S1 to S5 and S7 to S12 respectively, to provide breakout for the accompanying interface board. The JTAG (Joint Test Action Group) programming port was brought out to another socket (JT1) to facilitate programming and in-system debugging. A status LED was added (GPIO8), together with decoupling capacitors and pull-up resistors to the I2C bus and reset pin. The pcb layout used surface mount components on both sides of the board which had a cutaway beneath the ZigBee antenna to minimise wireless signal attenuation.

[61] *Cypress Semiconductor Corporation, San Jose, CA, USA*

[62] *Maxim Integrated, San Jose, CA, USA*

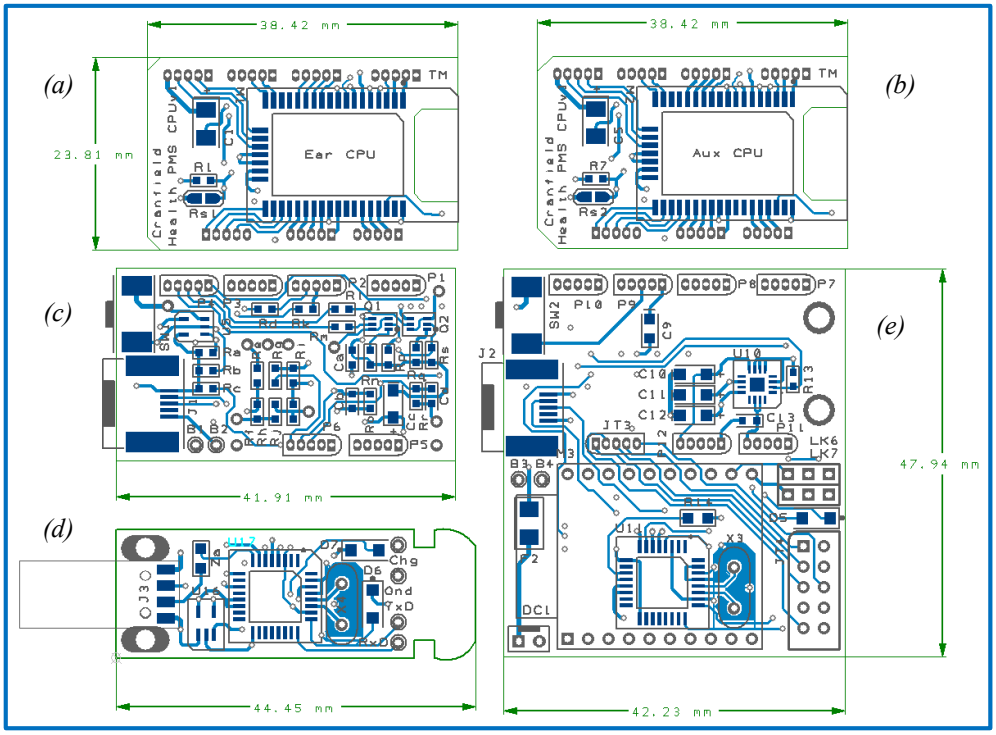


Figure 5-10: EPMS v1 CAD of the pcbs' top layer showing the (a) ear unit processor, (b) auxiliary processor, (c) ear unit interface, (d) adapter/charger and (e) auxiliary interface

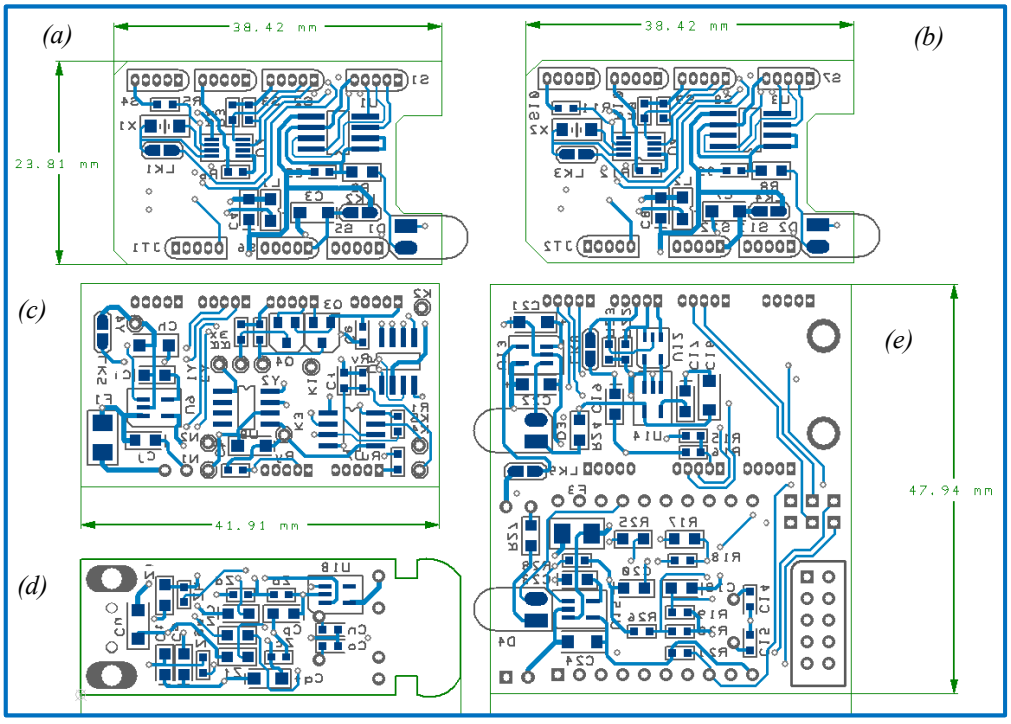


Figure 5-11: EPMS v1 CAD of the pcbs' bottom layer showing the (a) ear unit processor, (b) auxiliary processor, (c) ear unit interface, (d) adapter/charger and (e) auxiliary interface

Ear module interface circuit description

The interface (*Appendix A-2*) contained the power supply and signal conditioning for the pulse oximeter and SR sensor. The board was provided with mating headers (P1 to P5) connecting to the I/O pins from the ATBZ-24-A2 Zigbee module on the digital board.

The pulse oximeter LED drive was provided by a pair of PBSS2515YPN NPN/PNP dual transistors[63] in an H-bridge arrangement, the maximum current being set by resistors (10 - 20Ω) on the NPN emitters. The bases of the NPN transistors were connected to the outputs of an MCP4822 dual-channel SPI 12-bit DAC[64], providing independent control of LED light intensity. The PNP bases were connected via header P4 to pulse outputs on GPIO3 and GPIO4 on the ZigBee module for LED switching.

The pulse oximeter probes photodiode output was connected to one half of a dual op-amp (*U7a*) configured as a transimpedance amplifier, thus converting the output current to a voltage. The output (*DACoff*) was fed via header P6 to an ADC input (*ADC in1*) to give a reading of the DC offset voltage, and to the other half of the op-amp (*U7b*) where the signal was filtered and amplified with the output passing to the ADC (*ADC in2*). The composite signal was demultiplexed in software to give separate signals for the red and IR LEDs from which HR and SpO_2 were derived.

The unit was powered from a small lithium polymer (LiPo) 3.7V battery which fed a TPS73233 low dropout voltage regulator[65], giving a 3.3V output to power the system.

[63] *NXP Semiconductors Netherlands N.V., Eindhoven, The Netherlands*

[64] *Microchip Technology Inc., Chandler, AZ, USA*

[65] *Texas Instruments, Dallas, TX, USA*

The regulator itself was controlled by a simple logic circuit combining a push-button switch and two GPIO lines (*Power_Hold* and *Power_Cntl*) with a 74AHC1G00 two-input NAND gate[66]. Both NAND inputs were normally held high by pull-up resistors (to the battery voltage) holding the output low and disabling the regulator output; either input going low sent the output high and turned power on. The push button and *Power_Cntl*, an input to the microcontroller, shared one input while *Power_Hold*, an output, occupied the other. Pressing and holding the switch caused the output logic to change state, turning on the regulator and powering the rest of the circuitry. With the power on the processor booted up, read the *Power_Cntl* pin and pulled *Power_Hold* low, holding power on, irrespective of the state of the other NAND input. Pressing and holding the switch with power on initiated a safe shutdown.

A simple battery monitor was added by feeding the output of a potential divider connected between the battery's positive terminal and ground into an ADC input (ADC in0). This gave a half-scale output such that a fully charged battery (approximately 4.2V) would read 2.1V and around 1.8V when discharged. This enabled the unit to be automatically turned off should the battery voltage reach levels (i.e. <3.0V) where it would suffer damage or degradation of performance.

In addition to JTAG for debugging, the TTL-level *TxD* (transmit data) and *RxD* (receive data) of the ATBZ-24-A2's UART (Universal Asynchronous Receiver Transmitter) were taken to a mini-USB socket. This was connected to the Programming

[66] *NXP Semiconductors, Nijmegen, Netherlands N.V.*

Adapter/Charger board (*Appendix A-5*), featuring an on-board serial to USB converter and USB-powered LiPo charger.

Auxiliary module interface circuit description

This (*Appendix A-4*) shared features such as the system power supply and control logic and battery monitor with the ear module interface, but included a number of additional circuit blocks which are described next:

An ADXL330 tri-axial accelerometer's voltage outputs connected through header *P12* to the ATBZ-24-A2's ADC inputs (*ADC in1* to *3*) for activity or gravimetric orientation monitoring.

The *TxD* and *RxD* lines from the microcontroller's UART were taken to a 6-pin header for jumper selectable wired (via a serial to USB converter and mini-USB socket) or wireless Bluetooth communication. The FT232BL integrated serial to USB transceiver chip[67] converted the (3.3V) TTL-level serial data to USB 1.1 and 2.0 compliant standards, facilitating communication with a host PC for test and development. Alternatively, the RN-41 Bluetooth module[68] converted the serial data to a Bluetooth v2.1 compliant radio signal for wireless communication. As this was relatively power hungry the module was powered by its own switchable TPS73233 voltage regulator and enabled under software control.

A charger circuit for the unit's LiPo battery was also included. This was based around a MAX1555 single-cell charger chip[69] which managed battery charging

[67] *Future Technology Devices International Limited, Glasgow, UK*

[68] *Roving Networks, Los Gatos, CA, USA*

[69] *Maxim Integrated, San Jose, CA, USA*

according to discharge level, limiting charge current to 100mA. The circuit was powered from by the +5V USB supply when connected.

Adapter/charger circuit description

This combined the serial to USB converter and LiPo battery charger circuit blocks with a USB type-A connector producing an external USB communications adapter (using another FT232BL chip) and battery charger (MAX1555) for the ear module (*Appendix A-5*). This may be seen in the board layouts in *Figure 5-10d* and *Figure 5-11d* and the photograph in *Figure 5-12*. The adapter plugged directly into a PC USB port with a mini-USB lead hard-wired to four contacts on the pcb. The USB data link saw limited use during system testing. However, with the USB cable replaced by a battery connector, the adapter was used as a convenient means of charging numerous small LiPo cells over the course of the project.

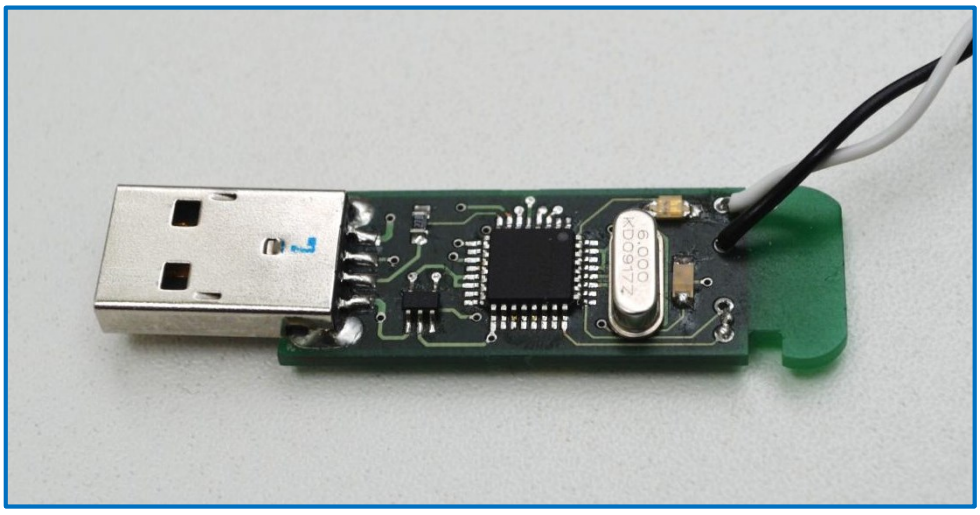


Figure 5-12: The USB adapter/LiPo charger, shown here with a wired battery charger lead

Enclosure Fabrication

This was essentially an afterthought to facilitate handling, testing and system demonstration, the boards being designed for evaluation of the electronic systems

without regard for packaging. As no suitable off-the-shelf enclosures were available, these were fabricated by hand from sheet polystyrene (see *section 3.2.5, page 125* for details) to produce cases for the ear (48 mm x 34 mm x 23 mm, plus the ear hook and pulse oximeter clip) and auxiliary modules (53 mm x 48 mm x 24 mm).

5.3.2 EPMS v2

It became apparent that despite increasing interest and use of ZigBee, its application in portable medical monitoring devices would be compromised by poor market penetration and low uptake by mobile device (smartphone and tablet) manufacturers - notwithstanding the mesh network capability had many advantages. Bluetooth technology meanwhile was becoming a standard feature. It was thus decided to dispense with ZigBee and redesign the EPMS circuitry for a Bluetooth-enabled single-box solution incorporating a number of improvements over EPMS v1.

Circuit schematics may be found in *Appendices B-1 to B-4* while a 3D CAD representation of the pcbs (*Figure 5-13*) and photographs showing the system's general arrangement (*Figure 5-14*) and the system in its casing (*Figure 5-18*) follow:

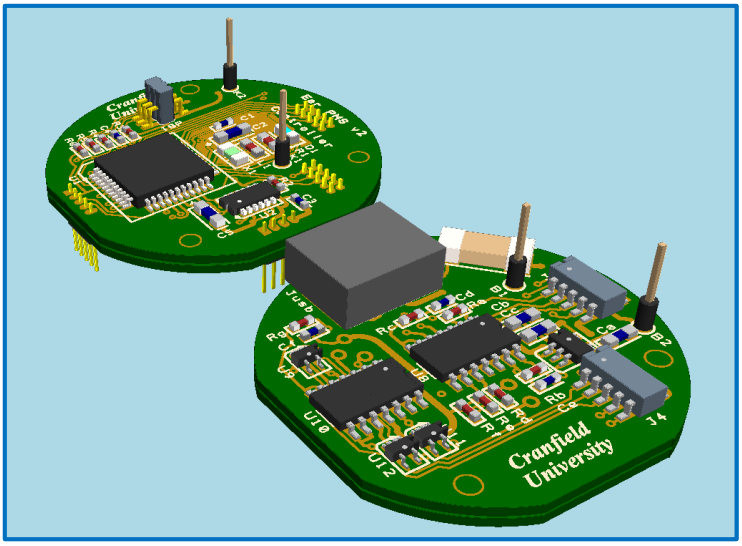


Figure 5-13: 3D CAD representation of the EPMS v2 digital (left) and interface boards (right)

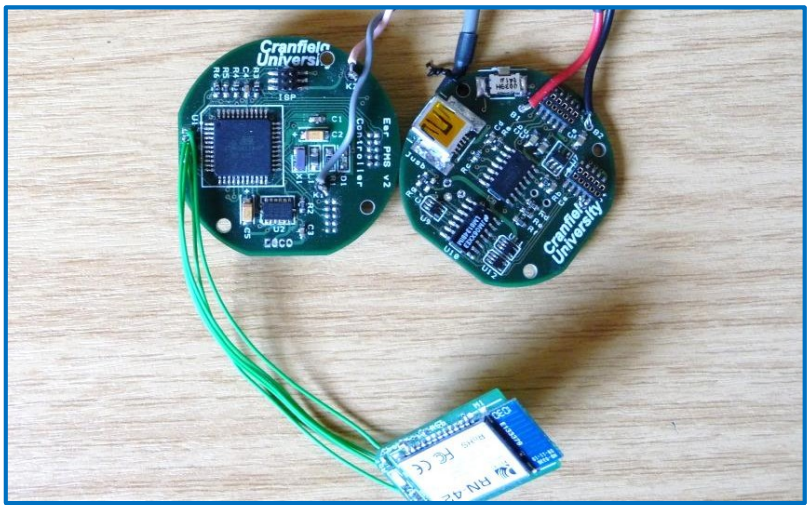


Figure 5-14: The EPMSv2 digital (left) and interface boards (right) that form the top and bottom of a two-board stack (shown separated), with the Bluetooth board below.

EPMS v2 digital board description

A dedicated ATmega1284P microcontroller[70] was chosen for the design (*Appendix B-1*), offering superior performance to the Atmel-powered ZigBee module due to lack

[70] *Atmel Corporation, San Jose, CA, USA*

of software overhead reserved for wireless control. As this was from the same processor family this offered continuity for the embedded code.

The microcontroller's I^2C bus accommodated both the MLX90615 temperature sensor and an ADXL345 tri-axial accelerometer, from which an alarm output was connected a microcontroller I/O pin. As with the EPMS v1 the SPI bus was connected to an FM25H20ds 2Mbit flash memory chip and MCP4822 dual-channel 12-bit DAC, and also, together with *Reset*, to a 6-pin ISP (In-System Programming) header, which facilitated device programming and served as a debugging aid.

Additional features included a 32.768 kHz crystal which was connected to the micro's PC6 and PC7 terminals as a reference for the micro's on-board real time clock and for power saving low frequency operation in standby. Two 10-pin headers, J1 and J2, connected power and I/O to the mating interface board. Two pairs of serial I/O lines from the micro's UART provided serial communication links to the outside world - RxD0/TxD0 connecting to a mini USB socket for connection to the adapter/charger board and RxD1/TxD1 (via wires to the *Jio* solder pads) to the Bluetooth board.

With this design the pulse oximeter's LED drive circuitry (*Appendix B-2*) was relocated to the digital board (*Figure 5-15* and *Figure 5-16*), largely to provide more space for components and track routing on the interface board. It employed the same H-bridge transistors as EPMS v1, but with an op-amp buffer (U4a and b) on each DAC output and a 2N3904 NPN transistor buffering the two TTL pulse outputs for improved drive characteristics.

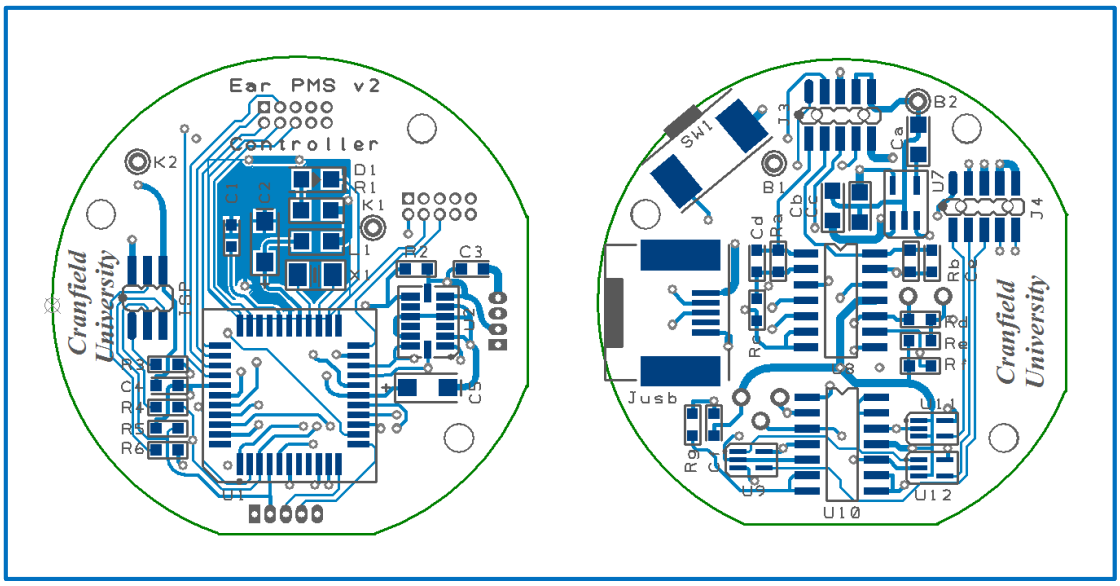


Figure 5-15: CAD layout of the top of the EPMS v2 digital (left) and analogue board (right).

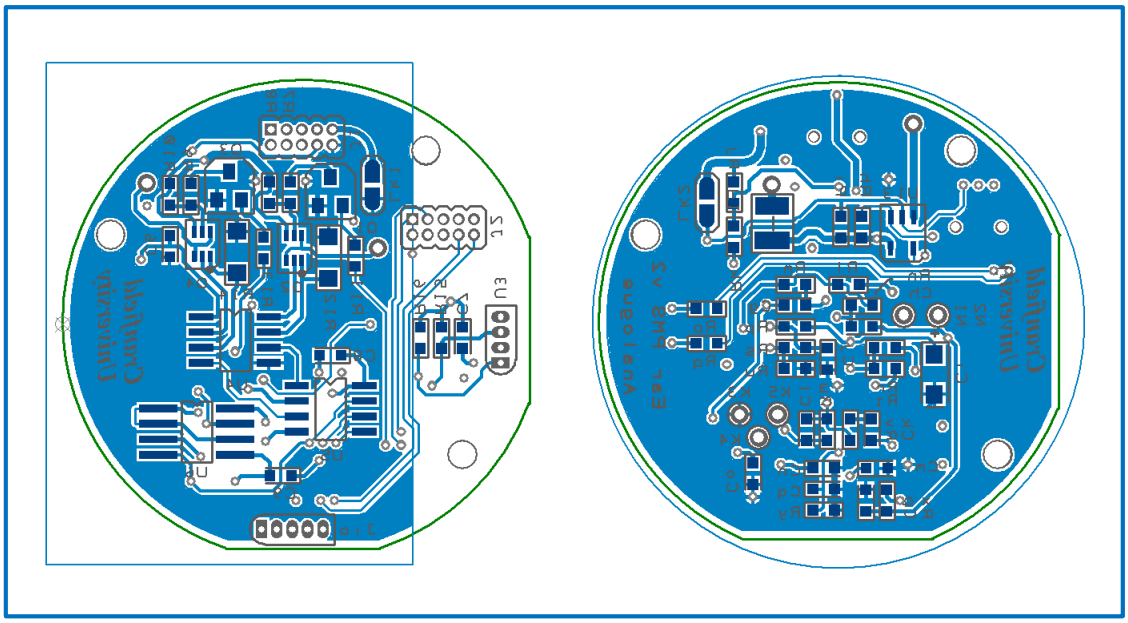


Figure 5-16: CAD layout of the bottom of the EPMS v2 digital (right) and analogue board (left) shown mirrored.

EPMS v2 interface board description

The design of the interface board (*Appendices B-2 and B-3*) built on the experience gained with EPMS v1 and included the pulse oximeter signal conditioning, power supply and the SR sensing circuits used previously.

Pulse oximeter signal conditioning differed substantially from that in EPMS v1 in that it used hardware demultiplexing to split the composite signal into its separate components. One of the amplifiers in a quad op-amp package (*U10a*) formed a transimpedance amplifier, converting the photodiode current to a voltage; this was then buffered by another op-amp stage from the same quad package (*U10d*). The output then split into two, connecting to a pair of 74LVC1G66 single-pole analogue switches[71] configured as sample and hold circuits (*U9* and *U12*). These were synchronously and alternately switched (i.e. the respective enable pins cycled) by the microcontroller in lockstep with the pulse oximeter LEDs to produce independent red and IR signals, which were fed to separate buffer amps (*U10b and U10c*). These outputs were AC coupled and a fixed offset, *Vref*, (derived from the voltage divider network on op-amp *U8b*) introduced (+1.65V) before the signals passed to a final gain stage (op-amps *U8a* and *U8d*) and the ATmega1284P's 10-bit ADC for digitisation.

EPMS v2 Bluetooth board description

This comprised of the RN-42 Bluetooth module and a few basic components (*Appendix B-4* and *Figure 5-17*), which were all assembled on the same side of the pcb. A pull-up resistor on the RN-41's PIO7 pin set the baud rate at 9600 while PIO5 connected a status LED via a series resistor. Connections to the digital board for power, RxD1, TxD1 and Reset were made using a short length of 1.27mm pitch ribbon cable.

[71] *NXP Semiconductors, Nijmegen, Netherlands N.V.*

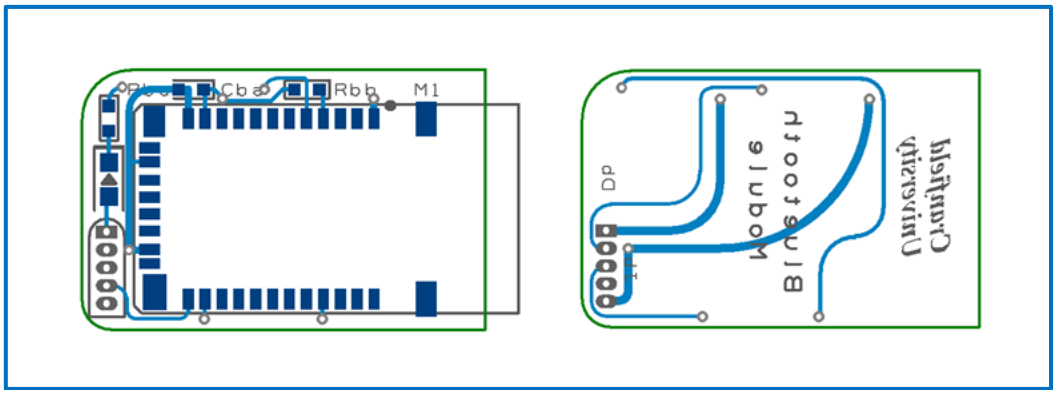


Figure 5-17: CAD layout of the EPMS v2 Bluetooth board (bottom shown mirrored on the right)

Enclosure Design

This was based upon a conceptual design study by Cranfield MDes students for a 3D-printable casing for an ear-worn monitoring device incorporating an in-ear temperature sensing probe (Umeh et al., 2011). The 3D-CAD of the original version had a number of issues, not the least of which was holes in the 3D mesh and inadequate wall thickness, rendering it was unprintable. These problems were corrected and the design modified by an experienced 3D-CAD operator, David Sziroczak, a fellow doctoral student, to better accommodate the system's pcbs and battery. With a diameter of 50 mm and thickness of 20 mm (less the ear probe) the printed case proved to be a tight fit for the boards and wiring (*Figure 5-18*).

Figure 5-18: The EPMS v2 with its 3D-printed enclosure

5.3.3 EPMS v3

Building on EPMS v2, this introduced new ideas and components in a two-board solution and was intended primarily as a technology demonstrator. However, over the course of the debugging phase it was decided that an enclosure was required. This was quickly developed using 3D printing to rapidly produce a prototype enclosure to facilitate system demonstration.

A key element of the design was the adoption of the Bluetooth Low Energy (BLE) (also known as Bluetooth v4 or Bluetooth Smart) in place of Bluetooth v2.1 for wireless communication. This offered significant savings in power (see *Table 5-2*) and board space over the older RN-42. A Bluegiga BLE112 Module[72] was chosen as it was one of the most compact devices available at the time of purchase (late 2012).

[72] Bluegiga Technologies Oy, Espoo, Finland

The circuit schematics may be found in *Appendices C-1 to C-4.* A 3D CAD representation of the main boards (*Figure 5-19*) and a photograph showing the system's circuit boards and enclosure (*Figure 5-22*) follow:

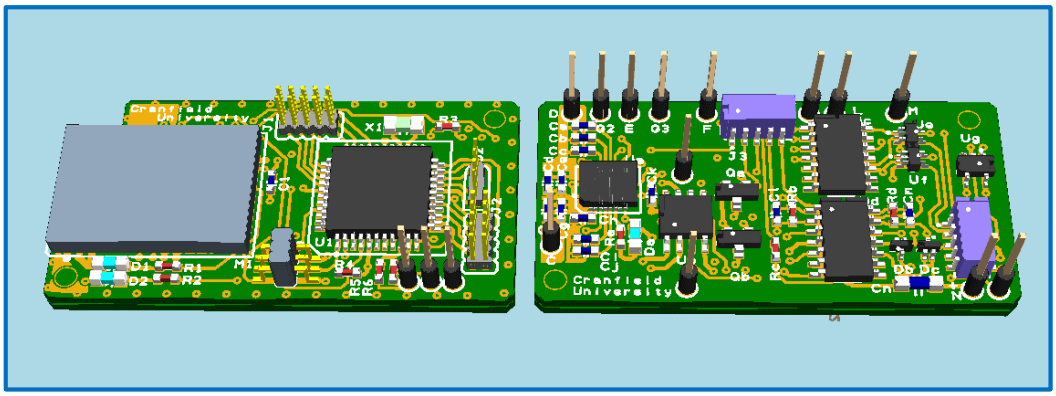


Figure 5-19: 3D CAD representation of the top sides of the EPMS v3 Processor / BLE (left) and analogue interface boards (right)

EPMS v3 digital board description

This was broadly similar to the EPMS v2 design, the key difference being the Bluegiga BLE-112 module in place of the Roving Networks RN-42 for Bluetooth v4 compliant wireless communication. The cut-out beneath the BLE-112's antenna and ground-linked via holes around the board edge (see pcb layouts in *Figure 5-20* and *Figure 5-21*) follow the pcb layout guidelines in the manufacturer's datasheet (Bluegiga Technologies Oy, 2011).

The ATmega1284P microcontroller's I^2C bus connected to the IR pyrometer and ADXL345 triaxial accelerometer, from which an alarm output was connected to a microcontroller I/O pin. The SPI bus connected to a flash memory chip and dual 12-bit DAC, and also, together with *Reset* once more, to a 6-pin ISP header (ISP) for device programming and debugging.

Two 10-pin headers, J1 and J2, connected power and I/O to the mating interface board. The two UART channels provided serial I/O for communication links. Here, RxD0/TxD0 were tracked to pads on the PCB (labelled A and B respectively) to which the USB adapter/charger board (described previously) could be connected. RxD1, TxD1, CTS1 and RTS1 were linked to the BLE-112 module (*Appendix C-4*), the additional lines providing hardware "handshaking" to improve data throughput.

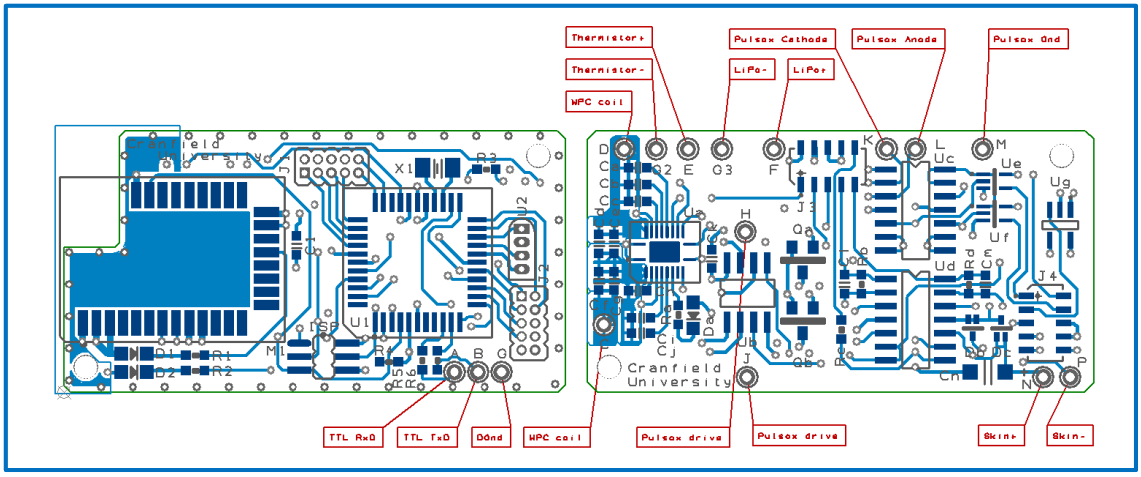


Figure 5-20: CAD layout of the top of the EPMS v3 digital (left) and analogue interface boards (right).

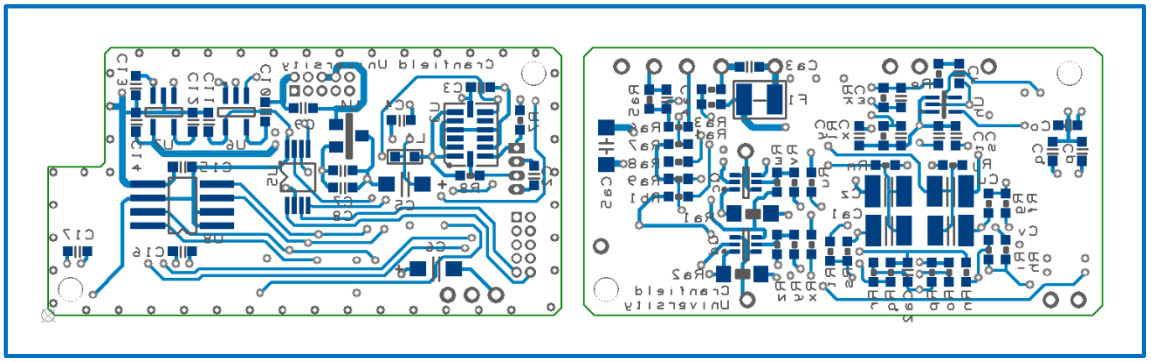


Figure 5-21: CAD layout of the bottom of the EPMS v3 digital (left) and analogue interface boards (right) shown mirrored.

EPMS v3 interface board description

Much of the circuitry will be familiar from the EPMS v2 design, although there were some significant detailed differences with the power supply in particular.

The pulse oximeter's LED drive circuitry (*Appendix C-2*) was moved to the interface board, but was otherwise the same as that used in EPMS v2. Signal conditioning followed that in the previous design, the only specific differences being the capacitors in the filter network before the final gain stage (Cl, Cm, Cu and Cv) which were of a polyphenylene sulphide (PPS) rather than multilayer ceramic (MLCC) construction for improved signal filtering.

Instead of a single voltage regulator for the system, the design employed multiple devices independently enabled under software control (*Appendices C-3 and C-4*) as part of a power management system. The microcontroller drew its power (*Vcc* on the schematic) from a ZMR330FTA +3.3V linear voltage regulator[73] which was always "on", the microcontroller entering a sleep mode when the system was inactive, running from the 32 kHz crystal clock. Three TPS73233 regulators provided power for the digital (*Vdd*), analogue *(+3V3*) and BLE module (*Vdd Blue*) and were enabled by the microcontroller as required.

Another addition to the board was the potential for wireless battery charging, the technology relying on inductive coupling for power transfer between a compatible target (receiver) and host (transmitter). This was based around the bq51050B single-chip Qi-compliant wireless power charger (WPC) receiver (Texas Instruments) which only required a few additional passive components and a special charging coil

[73] *Diodes Incorporated, Plano, TX, USA*

optimised for the application[74]. The design was based upon specified criteria and application notes in the product datasheet (Texas Instruments Inc., 2012a) and evaluation module documentation (Texas Instruments Inc., 2012b). As low capacity batteries were being used (110 to 165 mA/h) the maximum charge current was set to 100 mA to keep the charge rate below the 1C threshold. A provision for battery temperature monitoring was afforded by the inclusion of a thermistor to be mounted next to the battery.

Enclosure Design

As originally conceived, the circuit boards were intended as a proof of concept design to evaluate the BLE-112 and wireless charging on the test bench. Apart from this and an effort to generally minimise board space, the size and shape of the boards had not been considered important. It was however subsequently decided that encasing the boards would allow more realistic evaluation of the core sensing technology whilst communicating over a BLE wireless data link.

The key criteria determining the enclosures internal dimensions were the pcbs (48 mm x 25 mm x 13 mm overall when stacked), battery (30 mm x 18 mm x 4 mm), wireless charging coil (38 mm x 38 mm x 2 mm), plus accommodation for the bulky pulse oximeter ear probe cable and other wiring. A series of design sketches were made to ascertain the maximal internal dimensions of the casing (approximately 52 mm x 39 mm x 14 mm) which were passed to an experienced 3D CAD designer (David Sziroczak) to produce the design drawings. The resulting design was larger than

[74] *Wurth Elektronik, Niedernhall, Germany*

anticipated so the charging coil was omitted in an effort to slim down the design, the battery being charged externally with the USB adapter/charger.

The final enclosure design consisted of a 3D-printed box and lid with internal mating flanges (see *Figure 5-22*), the lid having an integral ear probe for the temperature sensor as per the EPMS v2 and pulse oximeter cable entering through a small hole in the base. A box-mounted pivoting hook fabricated from 1/8" copper tubing covered in heat-shrink tubing was used to hold the unit in place on a subject's ear. This proved adequate for the task.

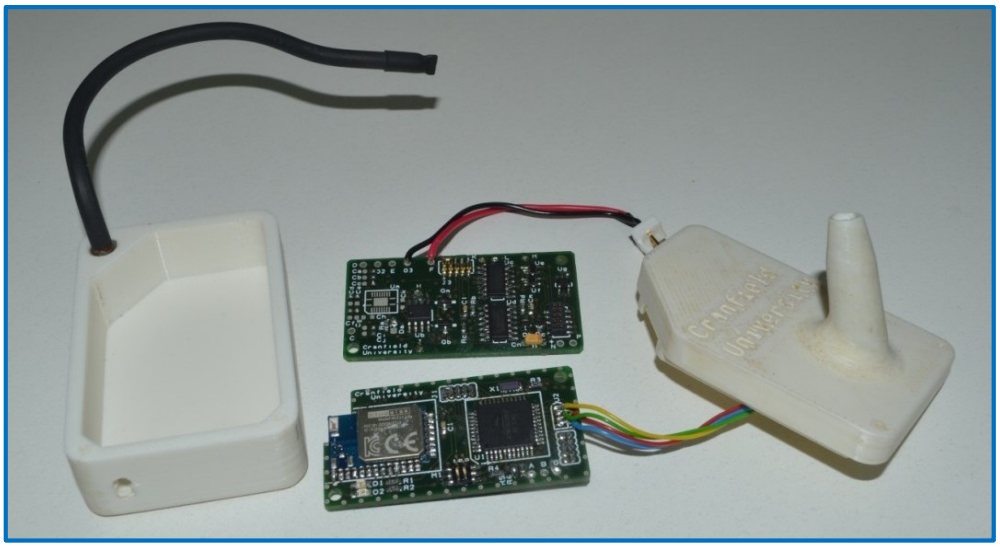


Figure 5-22: The EPMS v3 circuit boards and enclosure with ear hook.

5.3.4 EPMS v4

This was a departure from earlier variants being based around early examples of newly announced devices (mid 2013), namely the MBH7BLZ02 BLE wireless module[75] and AFE4490 single-chip integrated Analogue Front-End (AFE) for pulse oximeters[76].

[75] *Fujitsu Component Ltd., Tokyo, Japan*

[76] *Texas Instruments, Dallas, Texas, USA*

These components allowed the bulk of the design to be fitted onto a single double-sided circuit board measuring 30 x 30 mm and promised a reduced power budget. A second single-sided board provided an onboard battery charging capability, with USB and wireless charging options being designed.

The circuit schematics may be found in *Appendices D-1 and D-2*, while a 3D CAD representation of the main boards (*Figure 5-23*) and a photograph showing the system's circuit boards and enclosure (*Figure 5-24*) follow:

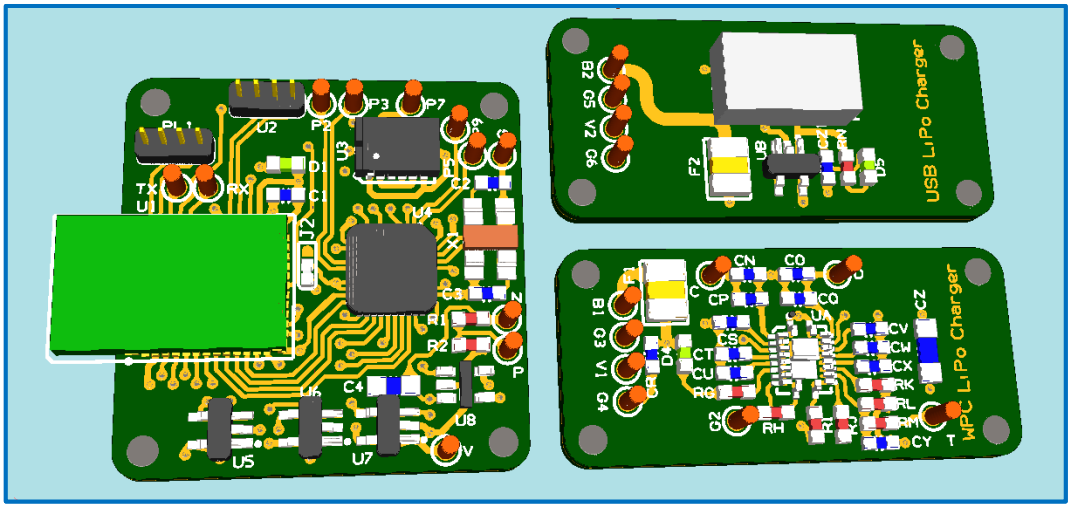


Figure 5-23: 3D CAD representation of the top of the EPMS v4 core circuitry (left) and battery charging boards (right) with the USB LiPo battery charger uppermost.

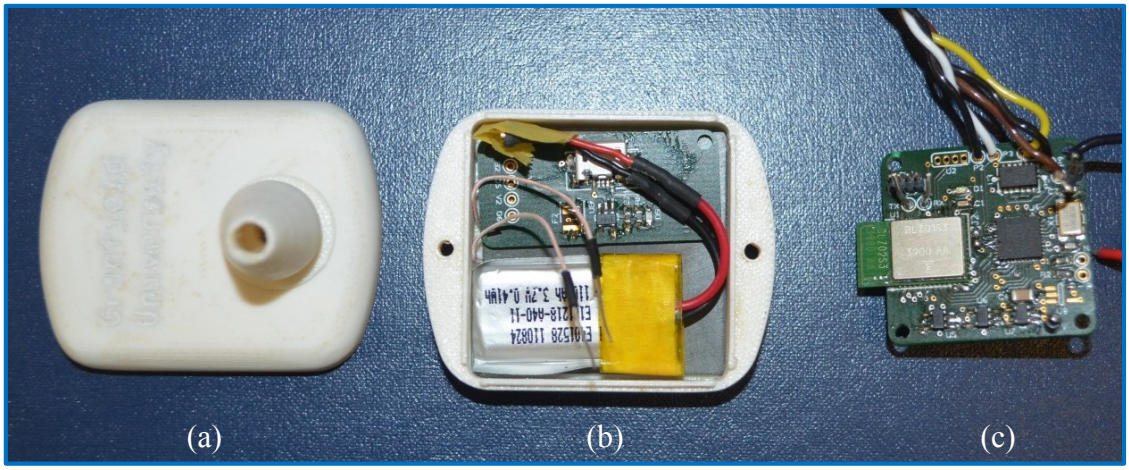


Figure 5-24: EPMS v4 prototype showing (a) the lid with ear probe, (b) the enclosure base, battery and charger board, and (c) main board showing the BLE module on the left and central AFE4490 pulse oximeter chip

EPMS v4 board description

The MBH7BLZ02 BLE wireless module, at 15.7 x 9.8 x 2.0 mm, is the smallest of all those used over the course of this project. It is based around an nRF51822 chip[77], which incorporates a 32-bit ARM Cortex-M0 processor with onboard RAM (16kB), flash (256 kB), flexible I/O and BLE wireless, the module adding an integrated antenna and ancillary support components. As this provided superior computational power to the Atmel ATmega1284P microcontroller, the MBH7BLZ02 assumed the dual roles of processor and wireless data link. The module was positioned along a board edge with the antenna overhanging as suggested in the manufacturers' design guidelines (Fujitsu Component Limited, 2014). This may be seen in *Figure 5-23* through to *Figure 5-26*.

[77] *Nordic Semiconductor ASA, Oslo, Norway*

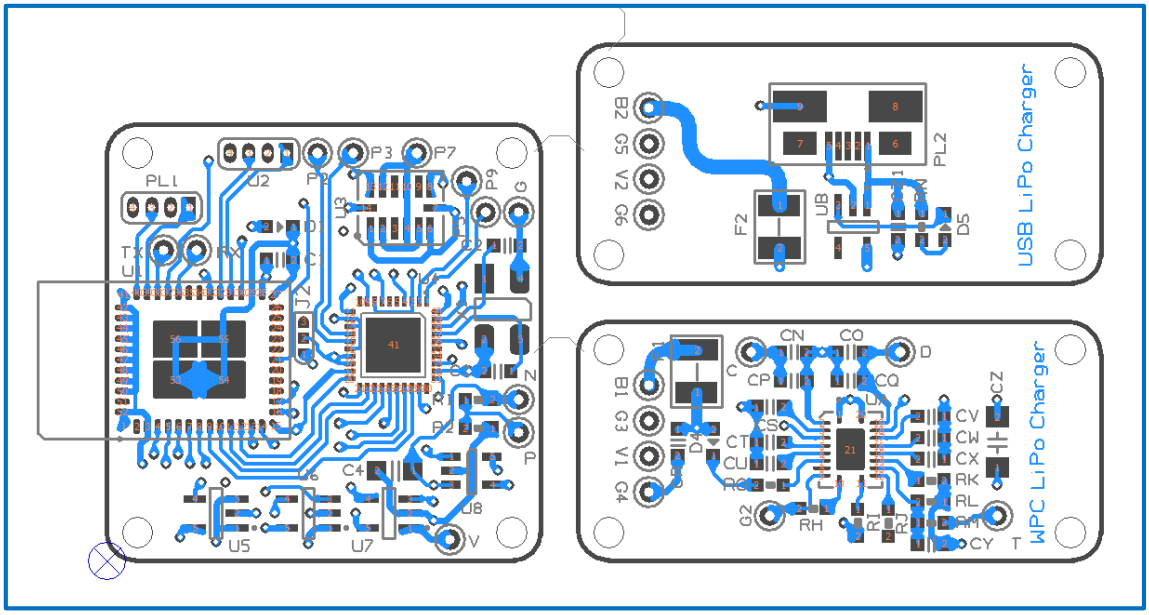


Figure 5-25: CAD layout of the top of the EPMS v4 core circuit (left), USB charger (top right) and wireless charger boards (bottom right)

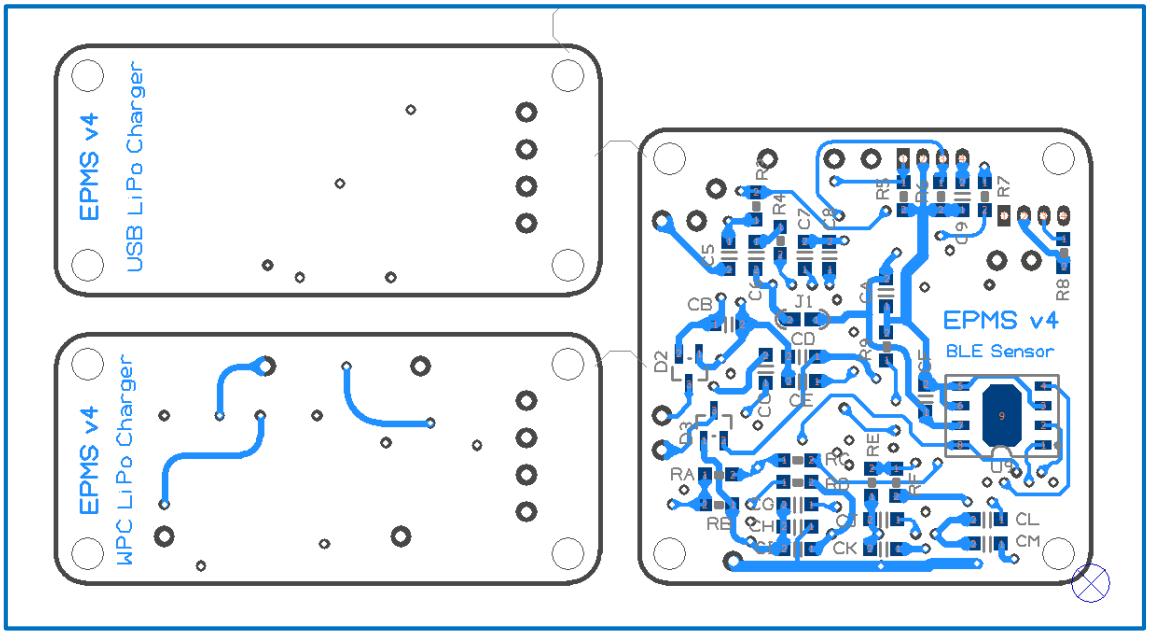


Figure 5-26: CAD layout of the bottom of the EPMS v4 core circuit (right), USB charger (top left) and wireless charger boards (bottom left)

As the MBH7BLZ02's I/O pins were software configurable, these were first designated for general I/O or serial bus connectivity. As before the IR pyrometer and

ADXL345 triaxial accelerometer were connected via I^2C (*GPIO28 and 29*) while the higher speed SPI bus (*GPIO17 – 19*) connected the flash memory and the AFE4490 pulse oximeter chip. TTL-level serial I/O was provided (*GPIO9 and 11*) as a debugging aid, the data lines being tracked to pads on the pcb. A dedicated Serial Wire Debug (SWD) port (*PL1 header*), a feature of ARM Cortex processors, was used for in system programming and debugging.

The AFE4490 incorporates all the features required for pulse oximetry sensing, combining on-chip LED drivers, programmable signal conditioning, a 22-bit ADC and software configurable registers in an integrated "front-end" for connection to a host microsystem. This saved two quad and one dual op-amp, three sample and hold circuits, a dual-channel DAC, H-bridge transistors and numerous passive components when compared with the EPMS v3 design - only a handful of capacitors being required for filtering and decoupling purposes. In addition to the SPI bus, connections were made to system *Reset*, three control lines (*AFE_Enb*, *AFE_Rdy* and *AFE_Diag*) and two alarm outputs (*PD_Alm* and *LED_Alm*). An external 8 Mhz crystal ensured synchronous operation.

The power supply was arranged similarly to that in the EPMS v3 design. Three TPS73233 were used, one (*U5*) was permanently enabled and powered the MBH7BLZ02 and accelerometer (*Vcc*), with the others enabled under digital control. One of these (*U6*) powered the digital circuitry (*Vdd*) and the other (*U7*) the analogue circuitry and the oximeter LED drive of the AFE4490 (*+3V3*). The power management was arranged such that the system would power off the *Vdd* and *+3V3* supplies after a period of inactivity and enter sleep mode (consuming approximately 50 µA), from

which it could be awoken via accelerometer motion sensing by a signal on the MBH7BLZ02's GPIO5 interrupt pin.

On-board Battery Charger

The design included options for on-board wireless (bq51050B chip) or USB charging (MAX1555). These were produced on separate pcbs with identical footprints and fixing centres, the USB charger acting as insurance in case of problems with the wireless option. The wireless charger design was almost identical to that used in EPMS v3, having only minor detail differences. The USB charger was essentially the same as that employed in the charging adapter (see *section 5.3.1, page 179*), but included a micro USB socket to connect to an external USB power source.

Enclosure Design

The main electronic systems were laid out on a single pcb with minimal dimensions, offering more flexibility in the enclosure design. The internal dimensions of the casing had to be at least 38.5 mm for the wireless charging coil, being ample for the systems board (29 mm x 29 mm x 7 mm, with the BLE antenna extending 6 mm from one face), battery charger board (35 mm x 16 mm x 6 mm – the latter being the height of the USB version) and battery (approximately 30 mm x 17 mm x 4 mm). Thus the case was designed around the charging coil with a solid area at the top and bottom for fixing screws resulting in the design shown in *Figure 5-24*. The casing's lid accommodated the in-ear temperature probe which was engineered with multiple parts facilitating the optimisation of the sensor's position and incorporated a 'snap on' mounting point for attaching off the shelf ear hooks for Bluetooth earpieces. The probe itself was modelled on that used in the v2 device, being around a millimetre longer and having a

reduced diameter (0.5 mm) over its length. The pulse oximeter cable entered the case via a small hole in the base of the case's bottom section, passing close to one of the fastening screws.

The final design measured 50 mm x 41 mm x 18 mm, less the ear probe, being the most compact of the four design studies. As with EPMS v2 and v3, the CAD was prepared by David Sziroczak and 3D-printed using the University's facilities.

5.4 Results

This section reports the results of initial system testing and examines both sensor and system-level operation, comparing the relative performance of the four EPMS designs.

5.4.1 Temperature

The EPMS v1 typically reported temperatures of around 31°C, up to 6.5°C below normal core body temperature when tested on a healthy individual. Mounted on a short length of cable and by no means uncomfortable, this proved difficult to fit with any consistency and had a tendency of quickly becoming dislodged after a few minutes use. The v2 design employed a conical ear probe in which the sensor's lens was located in the tip, the aperture giving an unobstructed field of view. This proved to be a more reliable fit than the v1 model and could be worn for up to 30 minutes without becoming dislodged or causing discomfort. Typical readings however were in the range of 32°C to 34.5°C. Readings from the EPMS v3 device were no better than its predecessor (32.5°C to 34.5°C) and although the probe was a snug fit, it was not comfortable.

The final design (v4) showed a marked improvement in performance in showing test readings ranging from 34.5°C to 36.5°C, much closer to those of normal core body temperature. The fit of the probe (see *Figure 5-27*), being slightly slimmer than the preceding versions, was good although it display a propensity to disengage from the ear canal after some minutes of continuous use.

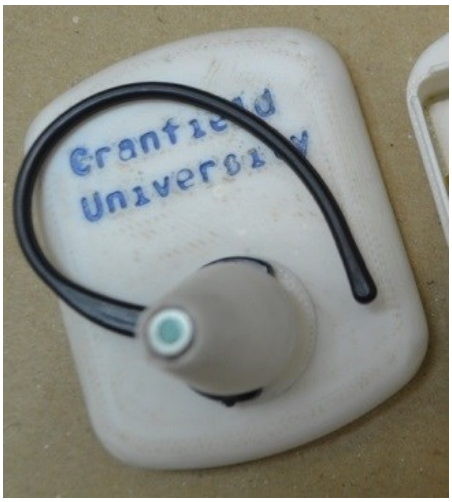


Figure 5-27: A photograph showing the lens of the IR thermometer mounted in the aperture of the EPMS v4 sensor probe

There was a notable increase in recorded temperatures with each evolution of the EPMS design, with v4 approaching nominal body temperature. The reason for the discrepancies was unclear; test readings of skin temperatures, though understandably lower than the body norm, appeared more consistent and comparable than those from the ear. Although the EPMS had only been trialled by the author at this stage, this suggested that the probe design may be responsible for the measurement errors.

5.4.2 Pulse Oximeter

The first design demonstrated that it was possible to acquire HR readings from the PPG signals, though not reliably. Processor performance proved insufficient for the

effective real-time control of data acquisition and signal processing tasks required in obtaining robust and stable signal waveforms, making SpO_2 measurement impossible.

The EPMS v2 and v3 pulse oximeter circuits were essentially the same in both execution and performance. The combination of a higher performance microcontroller, buffered H-bridge control and a redesigned signal chain with sample and hold (S&H) circuits providing a more robust PPG signal. The addition of S&H circuits helped in reducing processor load, which in turn allowed the application of more sophisticated digital signal processing techniques for improved signal integrity. This made for better peak detection for the determination of beat-to-beat periods for HR calculation. Although much improved compared to EPMS v1 the variations in DC offset of the red and IR waveforms meant that realistic SpO_2 calculations were not viable.

The introduction of the AFE4490 chip and ARM processor in the final EPMS v4 design gave superior results to those achieved with the previous designs. *Figure 5-28* shows exemplar raw (unfiltered) red and IR waveforms, displaying the degree and nature of the superimposed noise. The post-filtered waveforms are presented in *Figure 5-29* and demonstrate the effectiveness of the filtering techniques in presenting clean pulsatile signals, the IR response being characteristically larger than that red waveform. This facilitated peak detection and extraction of the beat-to-beat periods from the IR response used in HR calculation.

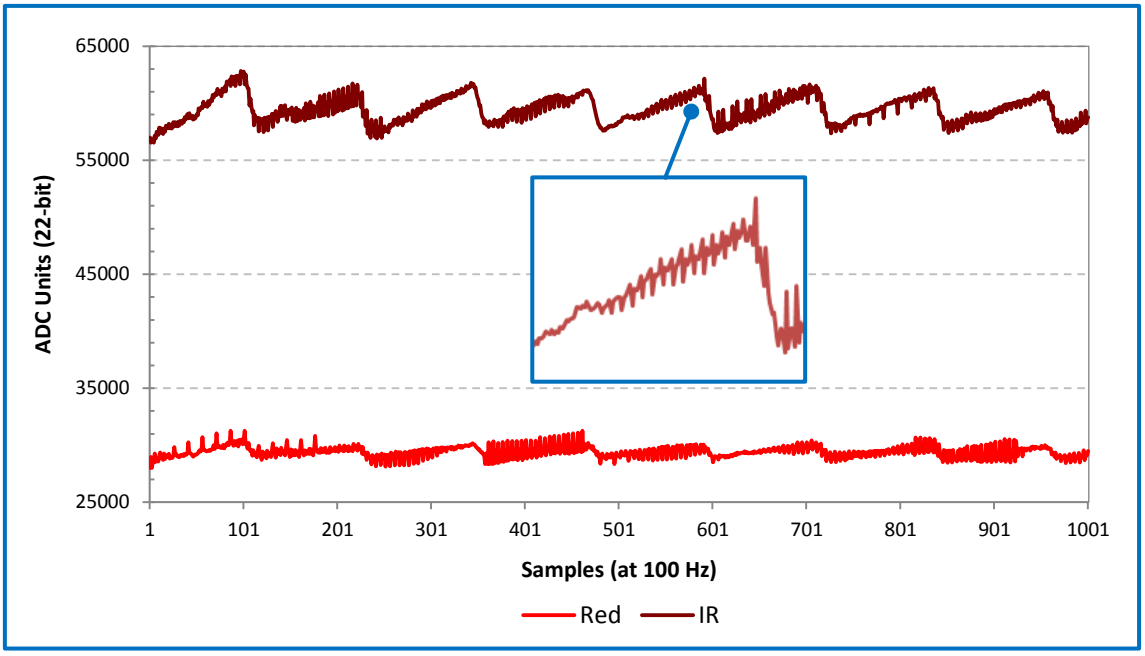


Figure 5-28: Raw SpO_2 red and IR signal waveforms with a close up of a single peak inset.

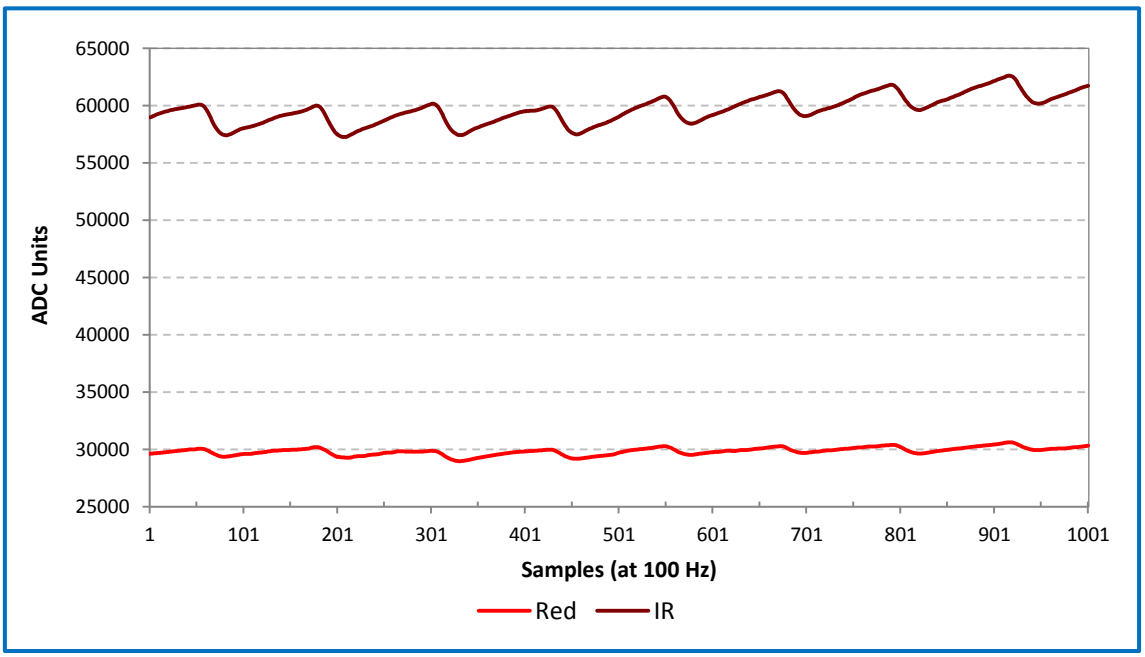


Figure 5-29: SpO_2 red and IR signal waveforms post filtering showing wide DC separation.

Although the filtering of the AC component of the PPG signals was successful significant DC drift was routinely observed, an example of which is presented in *Figure 5-30*. The main causes of this were found to be motion artefact and changes in

ambient light levels, the latter being a particular problem with ear probes which do not incorporate a light shield, unlike finger probes. In addition to the relatively slow drift, rapid changes in the DC response were also frequently observed (*see Figure 5-31*). While the 22-bit ADC values of the AC component ranged from 2000 to 12000 that of the DC drift could range from 10,000 to 200,000 (over time). With EPMS v1-3 poor signal stability in the DC response prevented any meaningful calculation of SpO_2 values. Although this was much improved in EPMS v4, extraction of robust SpO_2 data proved extremely challenging with R values from 0.97 to 1.02 being returned from differential absorption (*Equation 5-1*) during bench tests. R values of 0.6 to 0.4 would typically be expected for SpO_2 readings of 95% to 100%; those recorded equated to SpO_2 levels of around 85%. At this time it was unclear whether this was due to systematic errors or incorrect calibration.

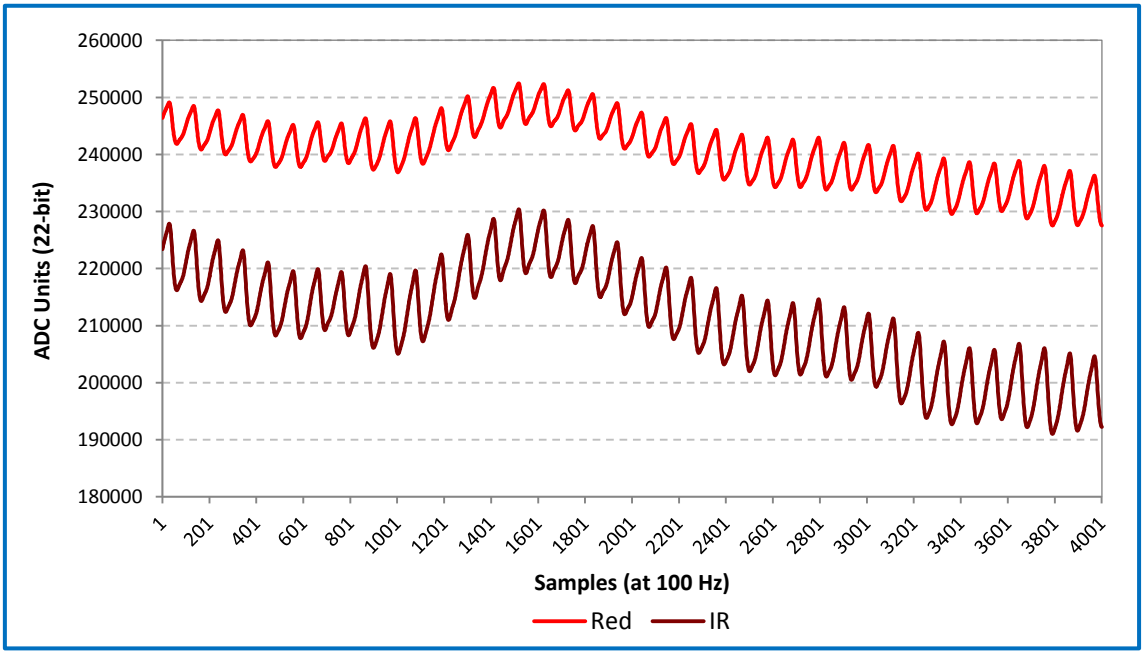


Figure 5-30: Filtered PPG signals showing DC drift over a 40 second period (EPMS v4), the drift being of greater magnitude than the AC response.

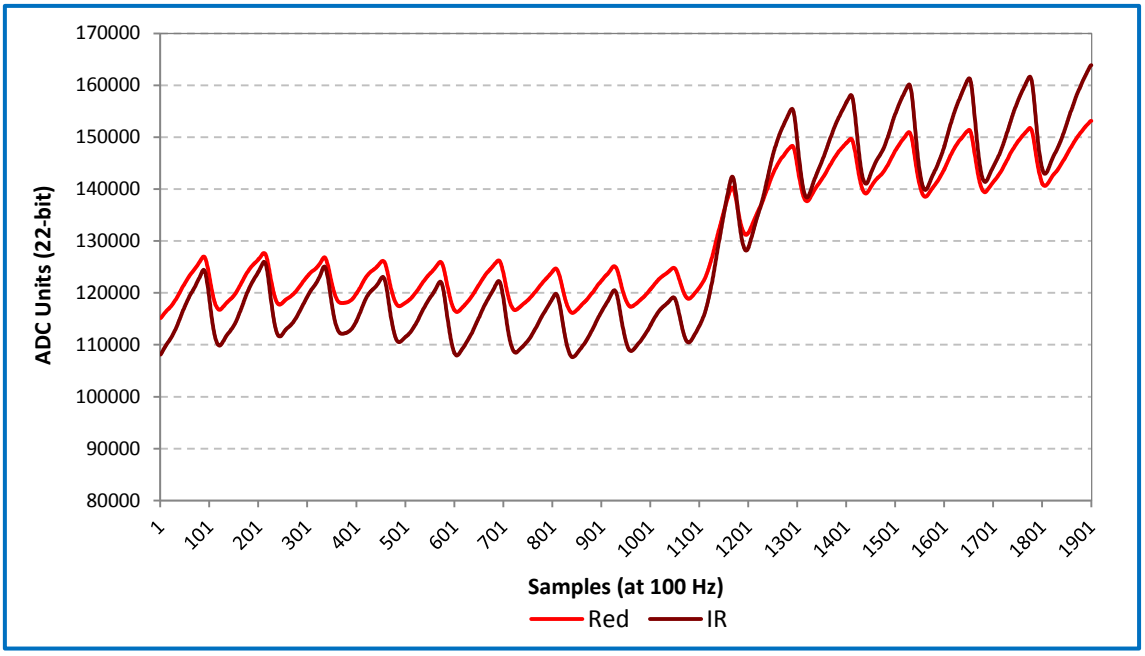


Figure 5-31: Rate of change of DC drift observed in the PPG signals (EPMS v4), the two signals are almost superimposed.

5.4.3 Accelerometer

On all variants the static gravimetric readings proved reliable in all axes; this was confirmed using a flat surface (confirmed in two planes with a spirit level) and engineers square. With the first three variants the outputs were combined (taking the square root of the sum of the squares) to give a measure of relative activity. In addition to this function the EPMS v4 successfully employed the accelerometer's threshold-triggered alarm output to wake the system from a low-power sleep mode (initiated after 30 seconds of inactivity).

5.4.4 EPMS System Level Performance

This section considers the system level performance of the four EPMS designs and examines power consumption, battery charging and wireless communications performance.

Power Consumption

In all cases, the wireless system and pulse oximeter were responsible for drawing the majority of circuit current in the EPMS systems. That used by the remaining circuitry (where low power operation was a key design criterion) differed between designs, but nevertheless may be considered as relatively insignificant. The power budget for the pulse oximeter circuitry, though essentially similar in the first three versions and using a dedicated chip in EPMS v4, was dependent upon the LED drive current, pulse frequency and duty cycle and therefore nominally the same for a given level of tissue illumination. Therefore, it can be seen that system power consumption is directly related to the properties of the respective wireless devices.

As EPMSv1 and v2 use Bluetooth v2 modules, one may anticipate that these would be expected to be less energy efficient than the BLE examples used in the EPMSv3 and v4 designs. This is borne out in the module manufacturers' published current consumption data which was used to calculate the power consumption figures (while operating with a +3.3V supply) shown in *Table 5-2*.

EPMS	Module	Standby/Sleep (mW)	Connected (mW)	Receive (mW)	Transmit (mW)
v1	**RN-41**	0.825 - 8.25	26.4 – 99.0	116 – 198	99 - 330
v2	**RN-42**	0.086	39.6 – 82.5	132 - 165	132 - 165
v3	**BLE-112**	0.71 – 2.97	-	83	92 - 119
v4	**MBH7BLZ02**	0.017	-	54 - 79	29 - 76

Table 5-2: Manufacturer's quoted power consumption for the Bluetooth modules used in this project when running from a +3.3V power supply.

The operating power for the EPMS devices operating from a +3.7V bench power supply (simulating a LiPo battery) are given in *Table 5-3* . This shows power

consumption in sleep mode, whilst in standby and whilst attempting to pair with Bluetooth devices and whilst operational, using the pulse oximeter and broadcasting Bluetooth data.

The figures for EPMS v1 reflect the simultaneous use of ZigBee and Bluetooth radios and combine the readings of the two system components. As a proof of concept demonstrator little effort was made to establish sleep mode operation (as indeed was the case with EPMS v2 and v3). The power figures are therefore understandably high. The EPMS v2 benefits from ZigBee omission and an improved Bluetooth v2 module (RN-42) to show substantial power savings, but is still considerably down on the BLE-equipped EPMS v3 and v4 units. The main difference between these devices is the level of power efficiency offered by the more recent MBH7BLZ02 BLE module.

EPMS	Sleep Mode (mW)	Standby/Pairing (mW)	Operating Mode (mW)
v1	-	218	275
v2	-	89	155
v3	-	33	70
v4	< 1	11	52

Table 5-3 : Typical EPMS power consumption when powered from +3.7V bench power supply.

Battery Charging

A dedicated USB-powered LiPo battery charger (see *section 5.3.1, page 179*) was designed to externally charge system batteries. These were connected to a mating polarised connector (as wired to the pcbs) attached via a length of cable to the USB charger. This successfully charged a range of different LiPo batteries, with capacities from 30 to 360 mA/h, the charge rate and time being capacity and charge status

dependent. The unit was used throughout the development program and specifically with EPMS v1 to v3.

EPMS v3 included a prototype design for a wireless battery charger using Texas Instrument's bq51050B chip. Difficulties in the assembly of the device prevented testing which was abandoned in favour of progressing the design and development of EPMS v4. This included options for on-board wireless or USB charging - a prudent decision as it transpired. During the design phase the wireless charging circuit was reviewed and minor modifications made. It then became apparent that many of the key details listed in the manufacturer's reference designs (Texas Instruments Inc., 2012a; Texas Instruments Inc., 2012b) were in direct contradiction. Although sample boards were assembled, seemingly successfully this time, testing was postponed in light of the aforementioned findings to focus on other aspects of the project. Thus the USB charger was used with the intent of revisiting the wireless charger as time permitted.

Wireless Systems

Aside from differences in their respective power budgets, the pairing or connection times and ranges of the wireless systems must be considered. The time for a host (e.g. a smartphone or tablet) to connect to an active EPMS device was found to shorter with the BLE-equipped EPMS v3 and v4 (typically 1 – 2 seconds), though no connectivity problems were experienced with either wireless system. The operating range of the Bluetooth systems exceeded 10m whereas BLE was limited to around 10m, both more than adequate for the intended application. Initial ranging problems experienced with the initial EPMS v4 prototype (limited to 2m) were found to be due to the loss of two

small passive components necessary for tuning the BLE module's integral antenna. It became clear that this had occurred during pcb assembly and rework and thus additional care was taken when assembling other boards.

5.5 Discussion

From an initial proof of concept demonstrator, the iterative design of the EPMS culminated in the fourth and final version of the device, an evolution which offered a marked improvement in performance together with a reduction in size. This was made possible by a combination of the availability of newer highly-integrated chips and the experience gained in designing, building and testing successive devices.

5.5.1 EPMS Devices

The initial EPMS v1 acted as an initial demonstrator to prove the concept of a multi-sensor ear-worn monitoring device. It was clear from the outset that a two-box solution was not ideal and thus would require extensive optimisation. The decision to use ZigBee was based upon the requirement for a compact ear-worn unit powered by a single small LiPo battery, ZigBee offering low power operation (compared to Bluetooth) and the provision for the development of local wireless mesh networks for further physiological sensors. Although this initially appeared to be a good solution, the ear unit needed to connect to a host mobile device to manage the acquisition and display of sensor readings; this posed a problem as there were no ZigBee-equipped mobile devices on the market. This necessitated the use of a second body-worn unit acting as a ZigBee hub that also included Bluetooth to communicate with a host mobile

device. Here, case size was less of an issue allowing the use of a larger battery to power the two wireless systems.

Sensor performance was not as good as had been hoped, but established the feasibility of the application. The potential of the ear temperature sensor was clear despite the poor probe design. Pulse oximeter performance was impeded by that of the processor, which was lacking the computational power required to both control signal acquisition and perform digital signal processing on real-time signals. The degree of variability in the PPG waveforms prevented SpO_2 calculation, though verifiable HR readings were achieved - albeit without any degree of consistency.

Lessons learned with the design of EPMS v1 strongly influenced the design of the next development, EPMS v2. This eliminated ZigBee and was based around a standard Atmel ATmega microcontroller offering improved performance. The use of a new lower-power Bluetooth module (RN-42) allowed the design to fit onto two stacked pcbs and a Bluetooth daughter board with relatively small footprints. The design also introduced 3D printing to produce the case which featured an integral ear probe to house the ear temperature sensor.

EPMS v2 performance was superior to its predecessor at sensor and system level. Temperature readings were closer to the 37°C norm, but still around four degrees short. HR readings were encouragingly more consistent and seemingly accurate (compared to a reference pulse oximeter) although once again the SpO_2 readings were not obtainable, the excessive variability in DC levels making reliable calculations impossible. The unit did however deliver substantial power savings allowing extended

operation. The case design, with its integral ear probe, was more compact, comfortable to wear and aesthetically pleasing than the hand-crafted system enclosures fabricated for EPMS v1.

EPMS v3 was conceived as a technology demonstrator, introducing BLE and wireless charging to an EPMS v2 based design. The 3D-printed case could not be considered small or attractive, but nonetheless was functional if somewhat uncomfortable to wear. Sensor performance was (unsurprisingly) comparable to EPMS v2, but with an operating power just less than half of that of the previous design.

EPMS v4 saw a number of new developments incorporated, with a BLE module featuring an ARM processor and dedicated pulse oximeter signal conditioning chip. The revised designed saved a number of chips which led to a considerable reduction in overall board space on the main system pcb. The case was designed around a compact wireless charging coil to accommodate the main system and battery charger pcbs, a LiPo battery and system wiring and had a reduced wall thickness compared to previous designs. This proved to be the smallest of the EPMS devices and demonstrated superior sensor and system performance.

Temperature readings were by far the closest to a 37°C norm, being around 1.5°C below the mark, while the probe afforded a good degree of comfort for the user. HR readings were a good match to a reference pulse oximeter and though the SpO_2 results were the best yet attained, the R values obtained gave an estimated SpO_2 reading of around 85% using the standard method of calculation. A larger sample size would be

required to ascertain whether the problem with readings was a functional or arithmetic error, or a calibration issue.

5.5.2 Practical Issues

Efforts to reduce device size led to problems and delays with board assembly and testing, which required a significant level of manual dexterity in handling, soldering and checking the small components employed. A range of assembly techniques were evaluated before being used on the prototype pcbs as, at least initially, surface mount assembly tools were not available, pcb assembly having previously been sent out to sub-contract manufacturers. As this couldn't provide the level of flexibility required for device development, some basic surface mount assembly equipment was purchased allowing assembly in the laboratory. Whilst this helped improve yield, it was an imperfect solution as discovered during testing where many solder joints had to be carefully reflowed, prolonging board and system testing. It became clear that only professional-level equipment could provide the reliability and quality required when working with the latest chip technology and packaging.

5.6 Conclusions

The work reported in this chapter meets one of this thesis' stated objectives:

- A novel prototype wireless multisensor device that can simultaneously measure VS readings was designed and produced.

In addition, the following conclusions may be made:

- The project saw the evolution of four iterative designs for the EPMS device; each demonstrated an improved performance and, with the exception of EPMS v3, a reduction in size.
- All EPMS devices were able to measure HR, the reliability and suggested accuracy improving with each evolution of the device's design.
- SpO_2 measurement was not viable with EPMS v1 -3, the signal waveform being insufficiently robust and the computational load for signal processing too high. Improved signal conditioning and processor performance in EPMS v4 provided readings, which were lower than expected. This was caused by DC drift in both red and IR signals, whether from ambient light effects, motion artefacts or other sources, which affected the differential absorption calculations.
- Temperature readings were consistently lower than body temperature. These ranged from 31°C (EPMS v1) to 34.5 - 36.5°C (EPMS v4).
- The use of 3-D printing was found to be an efficient and cost-effective solution for case production, proving superior to traditional methods.
- The maximum system power consumption, with active wireless transmission and pulse oximeter drive, showed a dramatic improvement from EPMS v1 (275 mW) to EPMS v4 (52 mW).
- Wireless communication proved successful on all design variants and gave an operating range of ≥ 10m from a host mobile device. Connection times (around 1 – 2 seconds) were noticeably shorter with the BLE-equipped EPMS v4 and v4.

6 EPMS Trials on Healthy Individuals

6.1 Introduction

Data captured by the EPMS during bench testing and during device demonstrations gave an insight into system performance, but was limited to use by one individual - the author – and insufficient replicate measures or rigour. It was therefore important to trial the device on a wider population to determine how readings compared with reference measurements, gain calibration data and capture feedback on usability.

This chapter reports the methods and findings resulting from a pilot study using the EPMS (v4) and reference devices to monitor the vital signs of a number of healthy subjects. It describes the devices used in the study and the study methods, detailing the study protocol, the study participants, inclusion criteria and the data analysis techniques employed. The results are grouped by VS parameter (HR, SpO_2 and temperature) and presented as both individual readings and mean datasets. These are shown in tabular form and as time history, linear regression, Bland-Altman and frequency distribution plots. Observations and feedback on the usability of the EPMS are also included before a final discussion where the results are analysed and the device's overall performance is considered.

6.2 Materials and Methods

This section reports the materials and methods employed in the execution of the trials performed with EPMS v4 on healthy subjects.

6.2.1 Materials

Details of the devices used in the study are shown in this section. These include the EPMS, mobile devices, reference medical devices and a description of the EPMS support 'app'.

EPMS device

Two EPMS v4 devices were produced for the study, labelled '3' and '4', each identifiable via a unique Bluetooth MAC (media access control) address transmitted with each dataset. Ultimately all experiments were conducted with device '3'. The ear probe, enclosure and oximeter clip were thoroughly cleaned with antiseptic medical wipes prior to use to minimise any hygiene risks to study participants and ensure a clean optical sensor path for optimal performance.

Mobile Devices

Second generation Google Nexus 7 tablets and a Motorola Moto G smartphone, all running version 4.4.4 of the Android operating system (also known as "KitKat") for BLE compatibility, were used to interface with the EPMS device. All study sessions were conducted with the same Nexus 7 tablet.

EPMS Support Software

This app was provided by Paul Knight and developed with the assistance of the author to facilitate both the execution of the EPMS study and to provide a demonstration platform for the device.

On starting the app the user was invited to connect to an EPMS v4 device, an operation that typically took around a second to complete. Once connected, the main

display screen was launched; this displayed real-time vital signs readings from the EPMS and controlled device and data connectivity. A connection to the University's wireless network was confirmed prior to the commencement of a study session.

The display screen (see *Figure 6-1*) presented real-time EPMS data in numeric and graphical formats, this being updated every second. HR (bpm), SpO_2 (%), temperature (°C) and battery status (ADC units) were displayed numerically; the latter as raw hexadecimal ADC values where 540_H represented a low battery (3.7V) and indicated that the EPMS should be recharged. A further data field to display blood pressure data from third-party BLE monitors was reserved for use in Paul Knight's PhD project.

A ten-minute parameter-selectable time history window allowed readings of HR, SpO_2, temperature and activity level to be displayed graphically. All traces were overlaid on a common display, each ascribed a different colour to aid identification and scaled relative to normal ranges - the Y axes scales and labels not being shown for clarity and to avoid a cluttered and confusing display. By default all four traces were displayed, but could be selected or deselected by tapping on the appropriate tick box. A separate bar chart displayed instantaneous activity level.

A test ID field allowed each test to be logged against a unique identifier, simplifying data management. Once connected wirelessly to the internet, the 'Send Email' button sent the last 60 seconds of acquired data to the author's university email account.

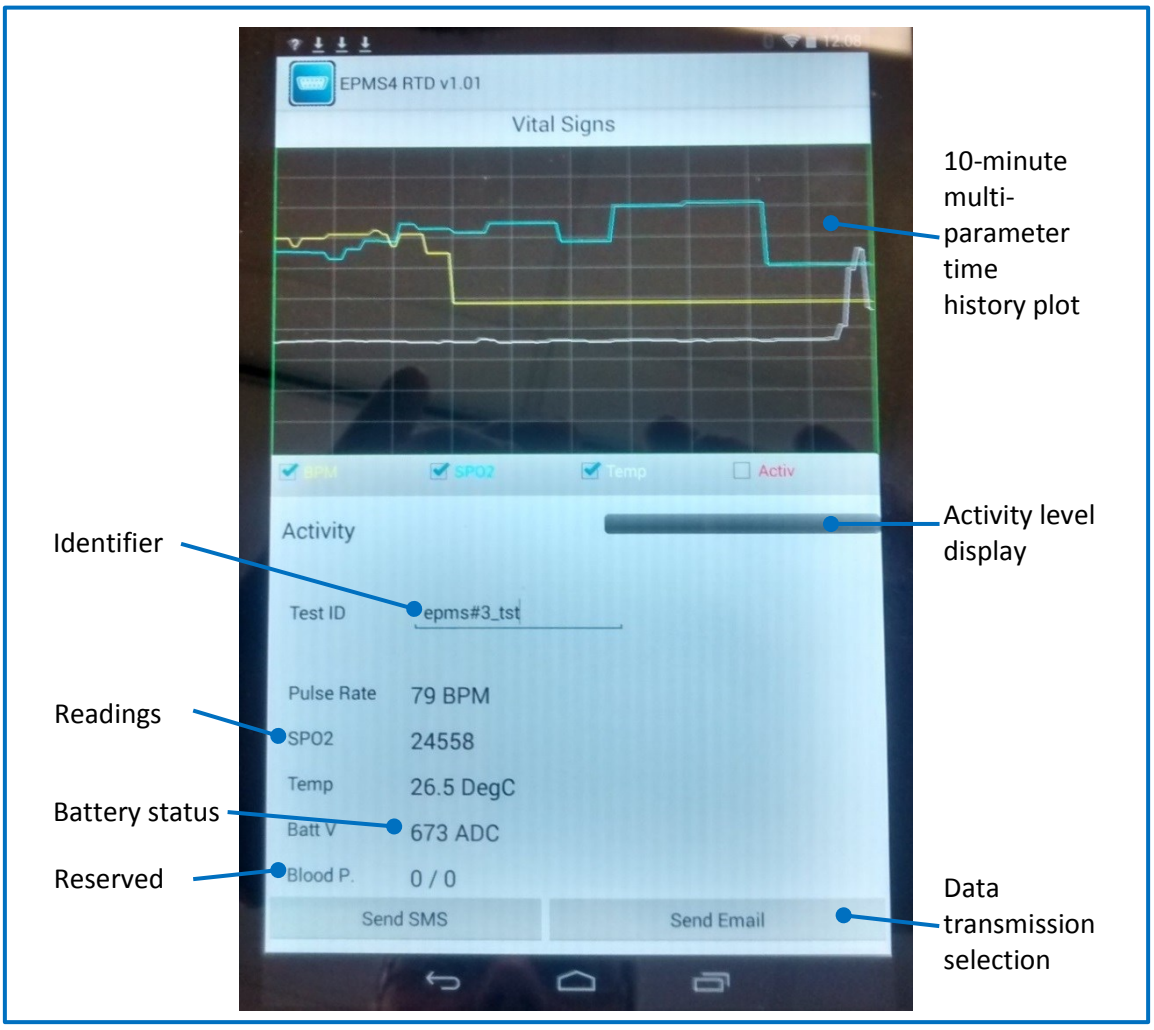


Figure 6-1: The main display page of EPMS support software running on a Nexus 7 tablet showing time history and instantaneous numeric data

Reference Devices

A Smiths Medical Oxi-Pulse 20 digital handheld pulse oximeter (and 3078 ear probe) provided reference readings of HR and SpO2. The manufacturer's data for the former (Smiths Medical International Ltd., 2009) specified an HR measurement range of 30 – 254 bpm with an accuracy of ±1 bpm (for a finger probe assuming minimal motion and good blood perfusion) and a range of 70 – 100% for SpO_2 (to ±2.5 %). It should be noted that although a capability to measure an oxygen saturation of 100% was claimed, in actuality the reading displayed was limited to 99% as only two significant figures are displayed.

A Braun ThermoScan IRT 4520 ear thermometer was used to take reference temperature readings (see *section 3.1.5*). The ear thermometer's user manual (Braun GmbH., - quoted an overall measurement range of 34 – 42.2°C with an accuracy of ±0.2°C between 35.5–42°C and ±0.3°C outside this range. Repeatability was quoted as ±0.14°C.

Both reference units were fitted with new batteries prior to the commencement of the study; these were checked and replaced as necessary before each trial.

6.2.2 Methods

This section documents the methods employed in this study. It provides details of the study participants, the study protocol, data handling and the analysis methods employed.

Ethics

This study was subject to approval from Cranfield University Health Research Ethics Committee (CUHREC), which was applied for and granted (reference no. 02/12, 17/09/2014). All participants gave fully informed written consent prior to joining this study. For the patient information sheet, study consent form and CUHREC approval, please see *Appendix F*.

Study Participants

After ethical approval (from CUHREC) and full consent had been obtained, 8 volunteers (6 male and 2 female) aged 18 to 65 years old were recruited for the study. The inclusion criterion was for individuals who would consider themselves to be in

good health and were not taking medication in the days prior to the study period. A test schedule was agreed with each participant prior to commencing the study.

Each subject was assigned a test identifier (see *Table 6-1*) which was used throughout the study. The study was conducted over a two-month period with up to five datasets being collected from each participant, though it can be seen that only subjects H and S provided a full dataset and subject G only one. Wherever possible data from individual subjects was sampled over the course of a week (subjects F, H and S), though this proved inconvenient in some cases (subjects N and R). Two participants (subjects E and O) were able to provide sample readings over a single day.

Subject ID	Gender	Age	Datasets	Notes
E	Male	40-50	4	Data collected over a single day
F	Male	50+	4	-
G	Male	20-30	1	-
H	Female	50+	5	Reference pulse oximeter finger probe used
N	Male	30-40	3	-
O	Female	30-40	2	Data collected over a single day
R	Male	20-30	2	-
S	Male	40-50	5	-

Table 6-1: Details of the EPMS study participants (n=8) showing their age range, gender, the number of datasets collected and study notes.

Assay Description

On joining the study consent forms were collected and subjects were asked to choose (and retain) an anonymising test identifier (A to Z) using a 'lucky dip' method. To aid study data management a unique test identifier was used to reference readings

and observations recorded in the author's laboratory notebook and entered in the EPMS App's Test ID field before each test. This took the form:

Exp_[*Subject ID*] [*Day Number*] [*Session Number*];
e.g. *Exp_A11*

Where the Subject ID was the anonymised subject identifier (A-Z), the Day Number indicated which of the subject's five test days were being reported (1-5) and the Session Number, which of the four daily test sessions the data related to.

The study was conducted in (private) offices or conference rooms to minimise participant anxiety and prevent observation by third parties in accordance with CUHREC guidelines. Room temperature in all cases was a comfortable 20-23°C. On arrival and having completed any formalities, subjects were invited to sit down and place the EPMS in their right ear and reference pulse oximeter ear clip on their left ear such that several minutes of resting readings could be taken concurrently. As the reference oximeter did not have a recording facility, four HR and SpO_2 readings were noted at 15 second intervals in the author's laboratory notebook. Upon completion, the last 60 seconds of EPMS data was sent to the author's University email account. A stopwatch app on the author's mobile phone was used to synchronise the oximeter readings with the EPMS such that they fell upon the mid-quartile points of the recorded dataset. Participants were then asked to remove the EPMS and reference oximeter probe and take three replicate ear temperature measurements (in the same ear as the EPMS) with the reference ear thermometer, which were once more noted in the author's laboratory notebook.

Readings were only viewed by the author. Study participants were not shown their readings and they were not discussed; this was to reduce bias and 'white coat' effect and to satisfy the requirements of the Ethics Committee.

Data Analysis

All noted data was anonymised and entered in a spreadsheet held electronically on a secure University server. Anonymised EPMS data was emailed to the author's university email account in an embedded comma separated variable (CSV) format. The header contained the Test ID, a time and date stamp, the device's unique BLE identifier and battery status, with the column headings and data shown in *Figure 6-2*. Each EPMS dataset comprised of 60 seconds of readings collected at one second intervals, each line of data featuring HR (bpm), SpO_2 (expressed as the R value x 25000), ear temperature (°C) and activity level (a dimensionless value). This was imported into MS Excel with the resultant files being held on the same secure server.

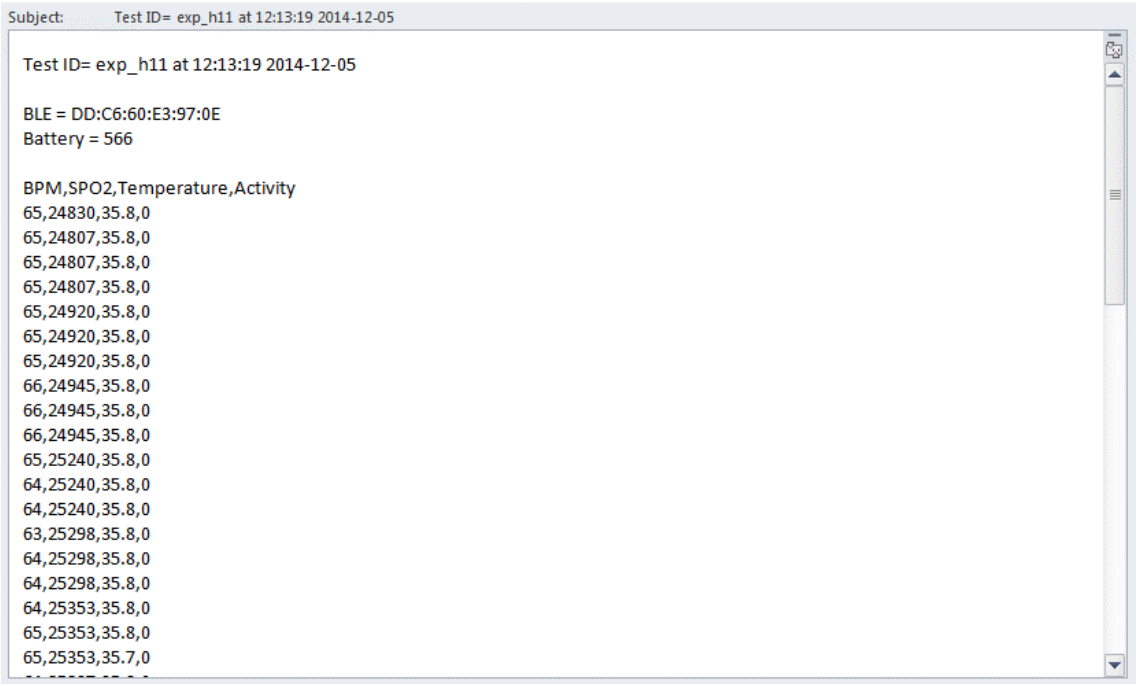


Figure 6-2: An example EPMS data email (exp_H11: subject H, dataset 1) showing the test and device (BLE) identifiers, battery status and physiological study data in CSV format

Separate files were created for each study subject's data with each EPMS dataset having its own worksheet with others being used for reference and statistical data. Tabulated HR, temperature and activity level readings required no conversion, whereas SpO_2 readings were converted into R values and estimated SpO_2 readings (see *Equation 5-2*). All calculations, statistical analyses and graphs were produced in MS Excel[78]. Descriptive statistical data (minima, maxima and mean values) and comparative plots of EPMS and reference data were produced for each of the study datasets and for each of the three studied parameters. Regression and Bland-Altman plots (Altman and Bland, 1983) were then prepared from the paired mean reference and EPMS readings from each test session to establish the degree of correlation and

[78] *MS Office Professional Plus 2010, Microsoft Corp., Redmond, WA, USA*

bias. Histograms showing the frequency distribution of the differences in paired readings were also produced for each of the three vital signs monitored.

6.3 Results

These are ordered and presented by vital signs. They compare readings from individual EPMS and reference datasets and their means to establish the correlation, bias and validity of the measurements, and thus the performance of EPMS. With reference to *Table 6-1*, it should be noted that different numbers of datasets were collected from volunteers, reflecting their availability and willingness in participation.

6.3.1 Heart Rate

Subject HR data is presented in *Table 6-2*. This shows the minimum and maximum recorded readings (and thus the ranges) for each test subject across their respective datasets with both the EPMS and reference pulse oximeter. It can be seen that the EPMS has the same range of readings as the reference (53 – 87 bpm v. 54 – 87 bpm), spanning the nominal healthy range of 60 – 90 bpm. The overall means (67.235 v. 67.869 bpm) are also very closely matched. *Figure 6-3* displays the subject dataset's HR characteristics graphically.

Subject	Datasets	EPMS HR (bpm)			Reference HR (bpm)		
		Min	Max	Mean	Min	Max	Mean
E	4	53	66	58.750	54	66	59.563
F	4	61	79	66.942	62	74	67.313
G	1	58	75	64.817	60	71	65.250
H	5	58	76	66.180	57	74	67.300
N	3	62	87	76.100	63	84	75.750
O	2	68	87	76.567	70	87	77.500
R	2	57	70	63.625	62	68	64.875
S	5	58	76	64.903	59	73	65.400
Overall	**26**	**53**	**87**	**67.235**	**54**	**87**	**67.869**

Table 6-2: Study subject heart rate (HR) data showing the minima, maxima and means for EPMS and reference data collected from each participant

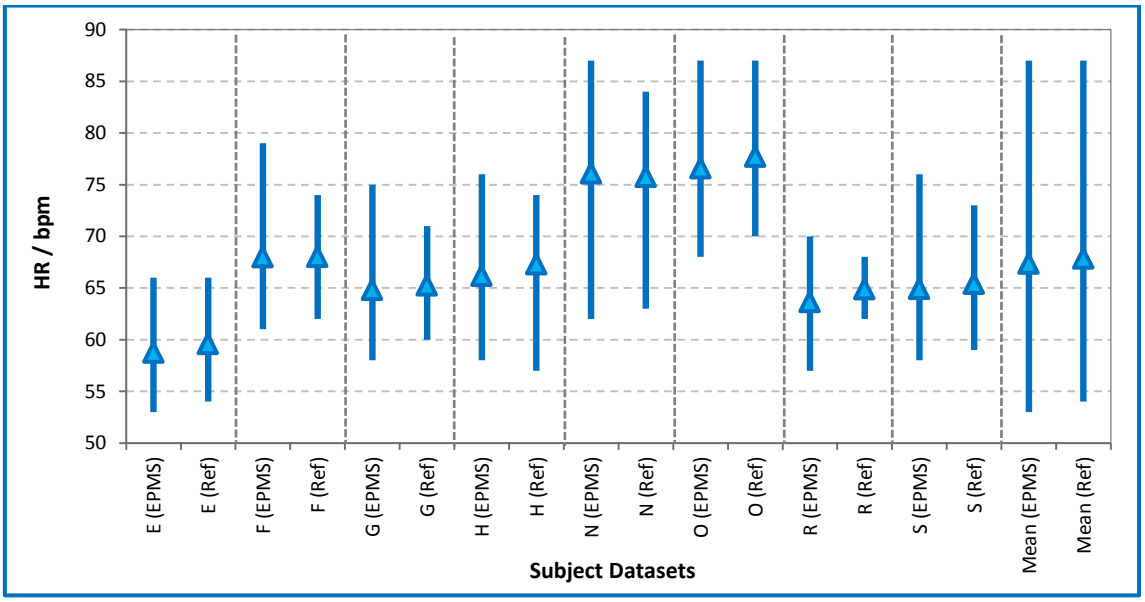


Figure 6-3: A plot showing the paired range and means of EPMS and reference HR readings of subject datasets

Analysis of HR Data

Plots were prepared from each set of subject data. These comprised of 60 seconds of continuous time history EPMS data with reference data superimposed at the four mid-quartile points; the means of the EPMS data in each quartile (labelled Q1 to Q4)

were also added to provide a direct comparison with the reference data and to assist in identifying trends. The scaling on the Y-axes was fixed for all plots according to the established recorded minimal and maximal limits (50 – 90 bpm) to facilitate comparison. The complete set of plots from the study may be found in *Appendix G*.

Subject's HR plots may be classified by the degree of deviation observed in the respective responses, having minimal, moderate or significant variation. This is illustrated in the following example figures:

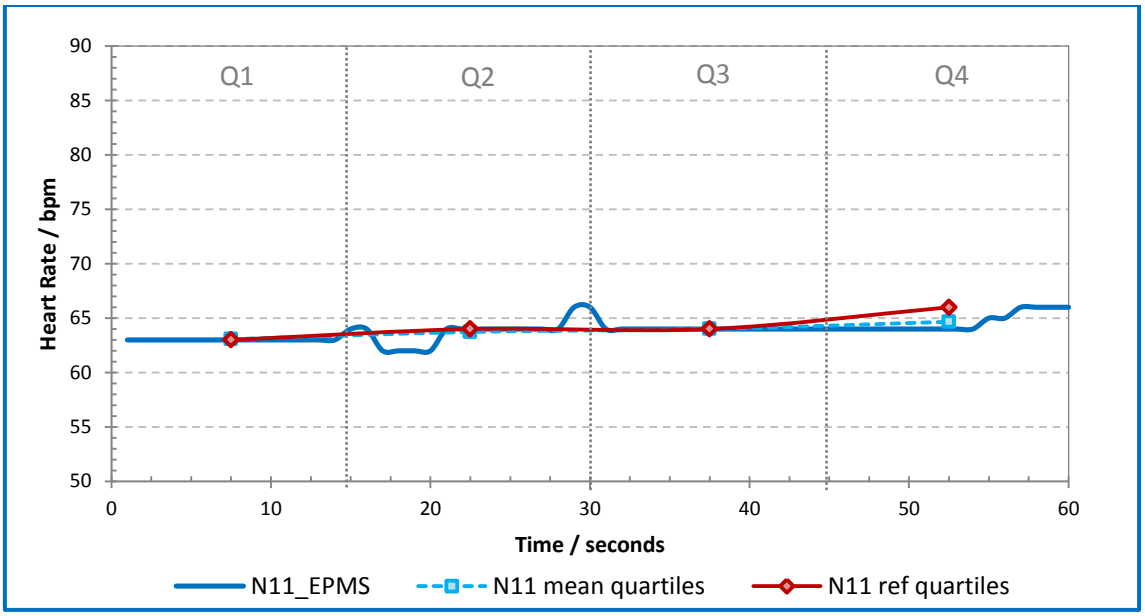


Figure 6-4: A comparative plot of EPMS and reference HR data showing minimal deviation (subject N, dataset exp_N11).

Figure 6-4 illustrates an example of minimal deviation as observed in 5 of the 26 datasets (19.23%). Here there is little variation in the EPMS data, which closely tracks the reference in all four quartiles.

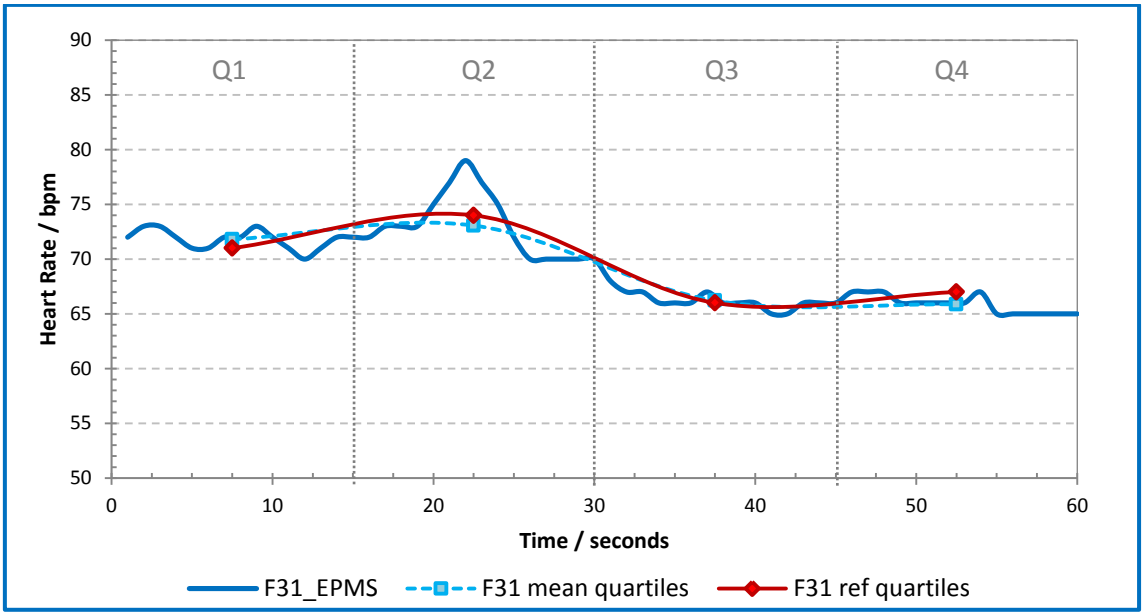


Figure 6-5: A comparative plot of EPMS and reference HR data showing moderate deviation (subject F, dataset exp_F31).

Figure 6-5 shows moderate deviation. In this instance there is some variation in the EPMS response, but it nevertheless tracks the reference quite closely in most quartiles. This trend was observed in 16 of the datasets (61.53%), which was by far the most common pattern.

Figure 6-6 illustrates an example of significant deviation as observed in 5 of the datasets (19.23%), matching the number observed with minimal deviation. Here there is variation in both the EPMS data and the reference, which does not track the EPMS as well. There is a suggestion of a time lag (approximately 10 seconds) between the two traces, something that was also observed on other plots and by the author over the course of the study. The mean EPMS quartiles in this example show a relatively 'flat' response due to the nature of the distribution of the original EPMS data.

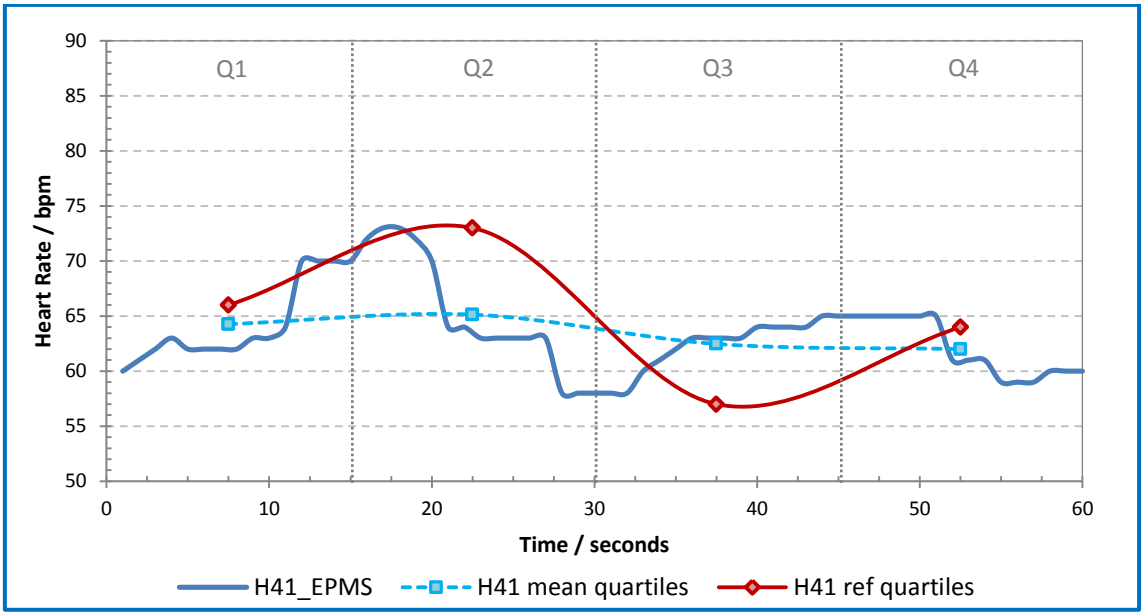


Figure 6-6: A comparative plot of EPMS and reference HR data showing significant deviation (subject H, dataset exp_H41).

In order to explore the nature of the relationship between the EPMS and reference pulse oximeter further, HR data was collected for a full five minutes from subject S – the EPMS providing continuous readings and with reference readings taken every 10 seconds. The results are presented in *Figure 6-7* which shows the EPMS and reference readings plotted on common axes together with a measure of the activity level (using a second Y-axis on the right of the graph). The latter was plotted to help determine whether there was any change in either HR response that may be due to motion artefact.

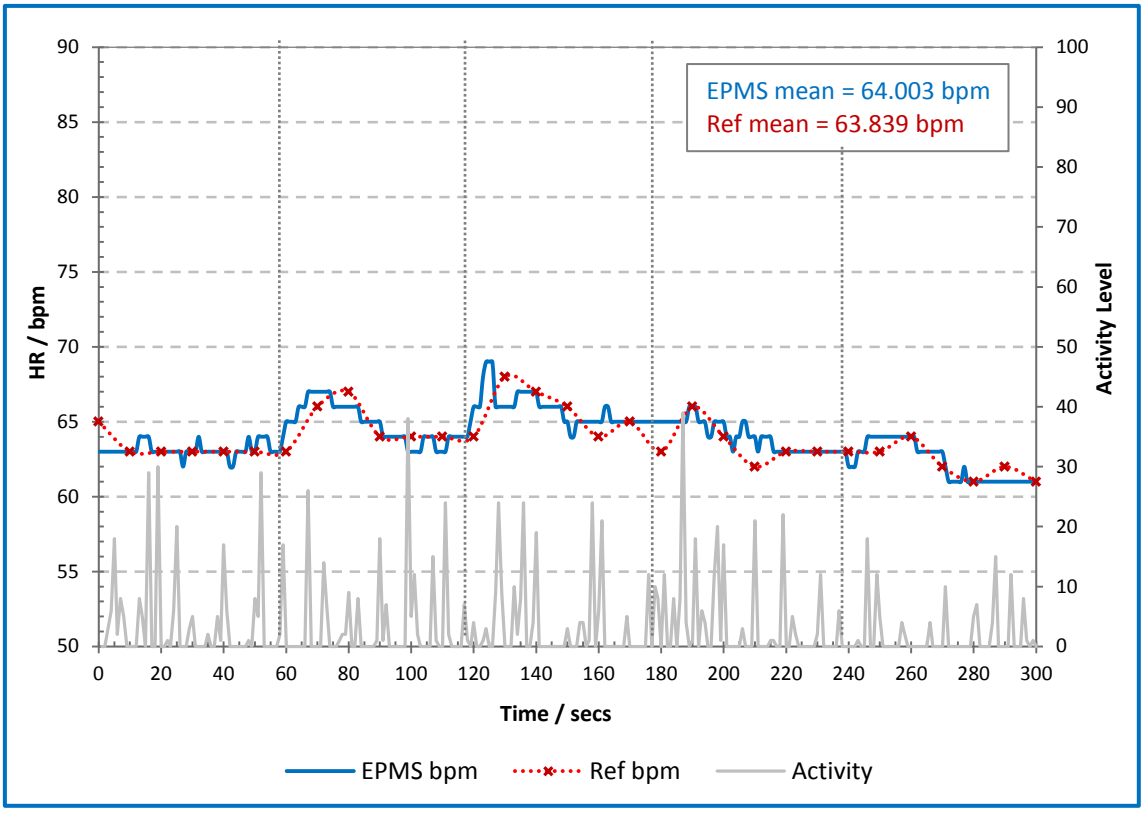


Figure 6-7: A comparative time history plot (subject S) showing five minutes of continuous EPMS and reference pulse oximeter HR data (taken every 10 seconds).

The EPMS and reference traces show a close relationship, but provide further evidence for an apparent 'phase lag' between the two devices. *Figure 6-7* shows the EPMS peaking several seconds before the reference at 65, 125 and 245 seconds. The range of the readings however is extremely close (EPMS = 61 – 69 bpm, reference = 61 – 68 bpm) with a difference of only 0.164 bpm between the means of the two datasets (EPMS mean = 64.003 bpm, reference mean = 63.839 bpm).

Regarding motion artefact, a change in the EPMS reading of 1 bpm may be observed coincident with activity peaks at 40, 100, 160 and 190 seconds and in the reference at 160 and 190 seconds. Conversely however, there is no change in the EPMS response following the activity peaks at 220 seconds and 290 seconds.

Analysis of the Mean HR Datasets

The mean HR readings in each of the study datasets are shown in *Table 6-3*. The means of the EPMS and reference readings provide the data for the correlation plot in *Figure 6-8*, while the means and differences (EPMS minus the reference) of the paired data were used to produce the Bland-Altman plot in *Figure 6-9*.

Dataset	EPMS	Ref	Mean	Diff
E11	55.567	55.750	55.658	-0.183
E12	64.567	65.250	64.908	-0.683
E13	56.767	58.000	57.383	-1.233
E14	58.100	59.250	58.675	-1.150
F11	68.800	67.000	67.900	1.800
F21	65.867	67.500	66.683	-1.633
F31	69.233	69.500	69.367	-0.267
F41	63.867	65.250	64.558	-1.383
G11	64.817	65.250	65.033	-0.433
H11	64.333	66.750	65.542	-2.417
H21	70.517	70.750	70.633	-0.233
H31	68.000	68.000	68.000	0.000
H41	63.467	65.000	64.233	-1.533
H51	64.583	66.000	65.292	-1.417
N11	63.867	64.250	64.058	-0.383
N21	81.300	81.750	81.525	-0.450
N22	83.133	81.250	82.192	1.883
O11	70.900	71.000	70.950	-0.100
O12	82.233	84.000	83.117	-1.767
R11	63.350	63.750	63.550	-0.400
R21	63.900	66.000	64.950	-2.100
S11	65.450	65.500	65.475	-0.050
S21	63.200	63.750	63.475	-0.550
S31	59.333	60.750	60.042	-1.417
S41	64.400	65.000	64.700	-0.600
S51	72.133	71.500	71.817	0.633
Means	**67.235**	**67.869**	**67.552**	**-0.633**

Table 6-3: The study HR EPMS and reference readings means and differences (bpm).

A linear regression plot of the paired means of the EPMS and reference readings was prepared to establish the degree of correlation between the two sets of data. This is presented in *Figure 6-8* and shows an almost linear relationship with the data points distributed fairly evenly about the trend line, to give a coefficient of determination (R^2) value of 0.980 (P <0.001). This indicates a strong correlation.

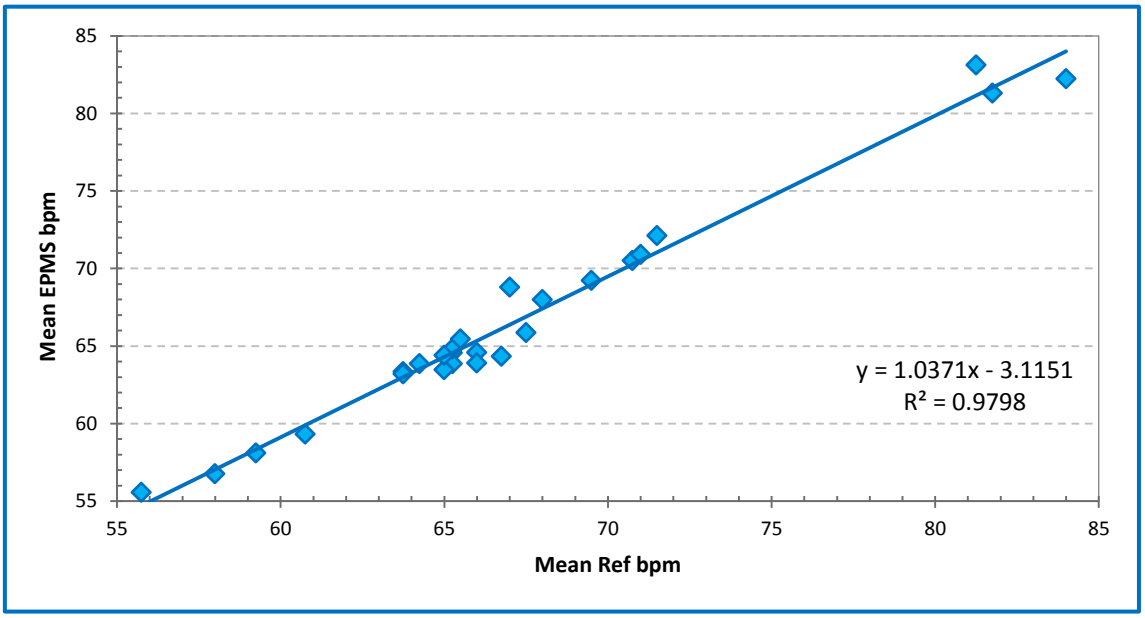


Figure 6-8: A linear regression plot of the 26 paired mean EPMS and reference HR readings for each dataset showing correlation.

Figure 6-9 shows a Bland-Altman plot comparing the means and differences in the paired data to highlight any bias. The mean bias (difference) is close to zero and relatively small (-0.633), with half of the data points falling close to the mean bias line. The distribution suggests a general tendency for the EPMS to underestimate at heart rates below 67 bpm and overestimate slightly at thresholds above and beyond this, giving a small proportional error. All but two of the data points (F11 and N22) fall within the limits of agreement (±1.96 x the standard deviation of the differences between the datasets).

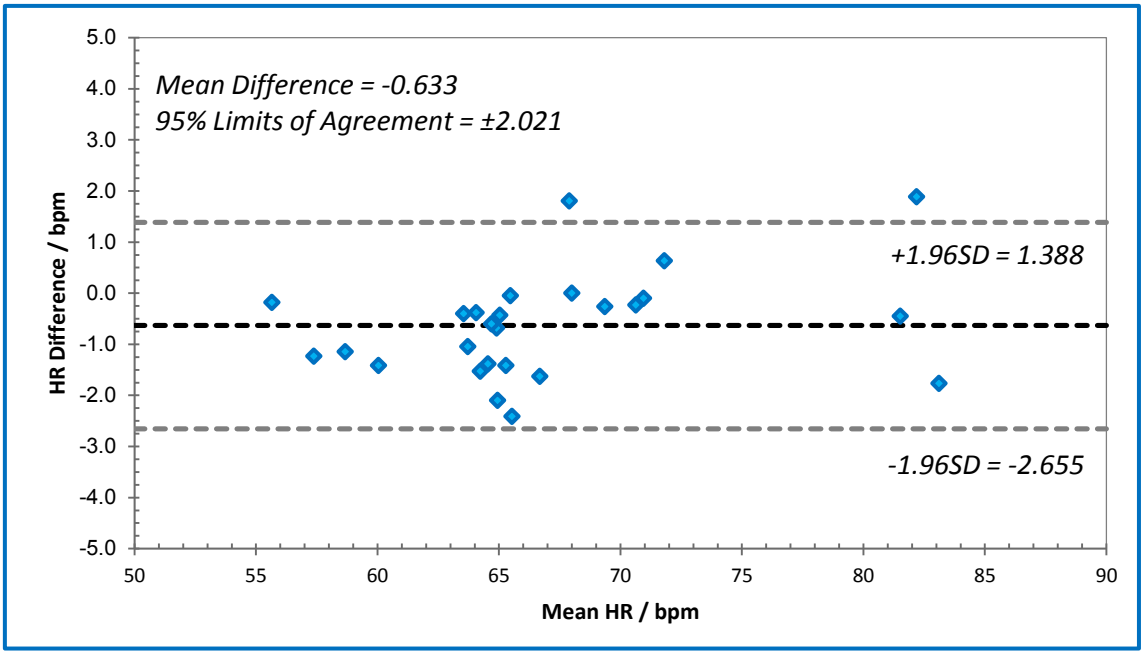


Figure 6-9: A Bland-Altman plot of the means and differences of the paired mean EPMS and reference HR readings.

Figure 6-10 provides a frequency distribution plot of the differences in the datasets. It can be seen that 13 of the datasets (50%) fall within 0.5 bpm of the reference while all fall with a range of ±2.5 bpm.

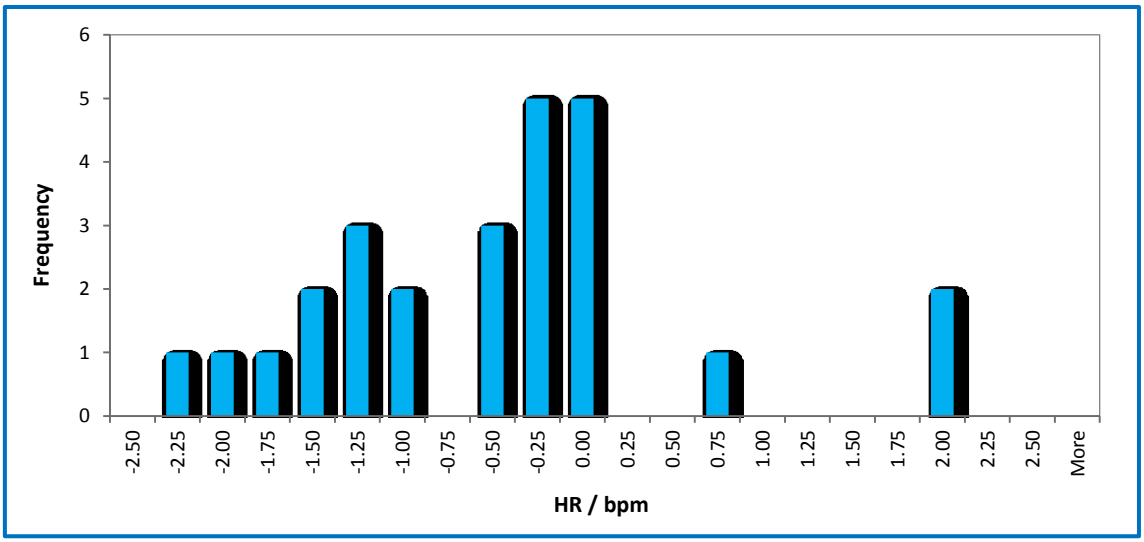


Figure 6-10: A distribution plot of the mean differences in HR readings between the study datasets.

6.3.2 Blood Oxygen Saturation

Subject SpO_2 data is presented in *Table 6-4*. This shows the minimum and maximum recorded readings (and thus the ranges) of EPMS R values and estimated SpO_2 readings together with reference readings for each test subject across their respective datasets. The R values were calculated by dividing raw EPMS readings by 25000, while an estimated SpO_2 value was calculated using the empirically derived formula described in *Equation 5-2*.

Subject	Datasets	EPMS R values			EPMS SpO_2 (%)			Reference SpO_2 (%)		
		Min	Max	Mean	Min	Max	Mean	Min	Max	Mean
E	4	0.958	1.025	0.994	84.378	86.040	85.156	96	98	97.125
F	4	0.985	1.019	0.996	84.535	85.363	85.056	95	98	96.625
G	1	0.979	1.050	1.018	86.036	88.533	86.884	99	99	99.000
H	5	0.950	1.070	1.006	83.262	86.261	84.860	96	98	97.000
N	3	0.943	1.046	0.984	83.852	86.417	85.398	95	99	97.083
O	2	0.964	1.068	1.018	83.289	85.912	84.547	98	99	98.500
R	2	0.979	1.092	1.034	82.700	85.537	84.138	95	99	97.500
S	5	0.928	1.040	0.996	84.012	86.799	85.099	96	99	97.600
Overall	**26**	**0.928**	**1.092**	**1.006**	**82.700**	**88.533**	**85.142**	**95**	**99**	**97.554**

Table 6-4: Study SpO_2 data showing the minima, maxima and means for EPMS calculated R values, estimated SpO_2 values and reference readings.

It is immediately apparent that the estimated EPMS SpO_2 values fall some way short of the reference pulse oximeter readings, though the ranges between the minima and maxima are broadly similar. All reference measurements were within the healthy range (>95%) whereas as those from the EPMS were less than <90%.

Analysis of SpO_2 Data

This follows the same approach as that employed with HR analysis in section *6.3.1*. It compares continuous EPMS time history data with reference at the four mid-quartile points. Again, the means of the EPMS data in each quartile (Q1 to Q4) were also added to provide a direct comparison with the reference. The scaling on the Y-axes was fixed for all plots according to the established recorded minimal and maximal limits (80 – 100%) to facilitate comparison.

Subject's SpO_2 plots were classified by the degree of deviation observed in the reference, as illustrated in the following example figures:

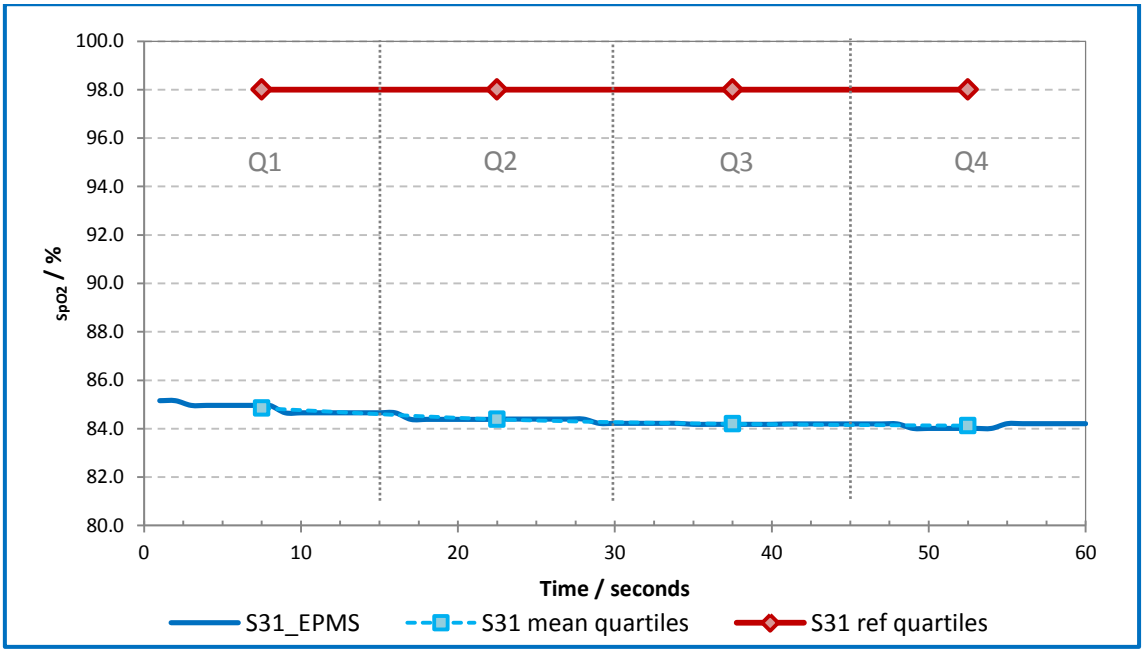


Figure 6-11: A comparative plot of EPMS and reference HR data showing no deviation in the reference (subject S, dataset exp_S31).

Figure 6-11 shows an example SpO_2 plot, the most noticeable thing in which initially is the difference in the scale of the readings between the EPMS and the reference. The other thing of note however is the unwavering reference reading. It might therefore be

expected that there is little variation in the accompanying EPMS trace. This was observed in 21 of the 26 datasets (80.77%).

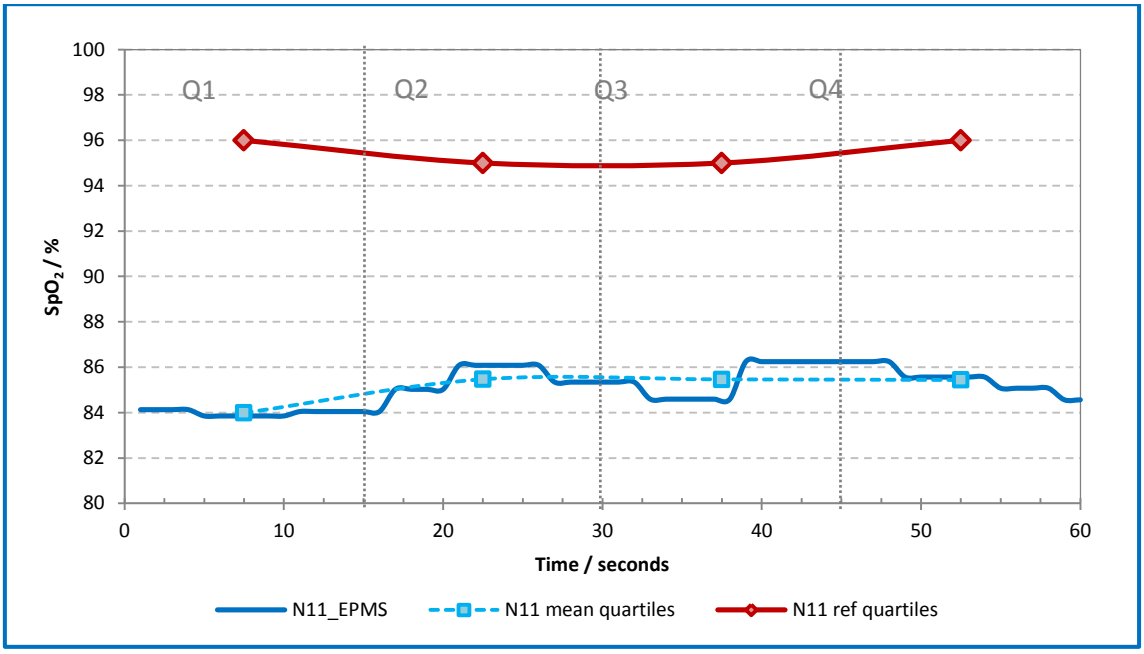


Figure 6-12: A comparative plot of EPMS and reference HR data showing slight deviation in the reference (subject N, dataset exp_N11).

Figure 6-12 shows an example of an SpO_2 plot where there is variation in the reference reading, something that should be echoed in the corresponding EPMS data and was indeed observed in 5 of the datasets. Here there is greater variation than in the previous example although there is a suggestion it may be inversely proportional.

Analysis of the Mean SpO_2 Datasets

The mean HR readings in each of the study datasets are shown in *Table 6-5*. The means of the EPMS and reference readings provide the data for the regression plot in *Figure 6-13*, while the means and difference of the paired data were used to produce the Bland-Altman plot in *Figure 6-14*.

Dataset	EPMS	Ref	Mean	Diff
E11	84.970	97.000	90.985	-12.030
E12	85.029	97.000	91.015	-11.971
E13	85.634	96.500	91.067	-10.866
E14	84.989	98.000	91.495	-13.011
F11	85.065	95.500	90.283	-10.435
F21	84.983	98.000	91.491	-13.017
F31	85.227	98.000	91.614	-12.773
F41	84.951	95.000	89.975	-10.050
G11	86.880	99.000	92.940	-12.120
H11	84.426	97.250	90.838	-12.824
H21	85.041	97.750	91.395	-12.709
H31	84.883	96.000	90.442	-11.117
H41	85.005	97.000	91.003	-11.995
H51	84.946	97.000	90.973	-12.054
N11	85.090	95.500	90.295	-10.410
N21	85.791	98.750	92.271	-12.959
N22	85.313	97.000	91.157	-11.687
O11	84.846	99.000	91.923	-14.155
O12	84.249	98.000	91.125	-13.751
R11	84.548	99.000	91.774	-14.452
R21	83.728	96.000	89.864	-12.272
S11	85.126	98.000	91.563	-12.874
S21	84.803	99.000	91.901	-14.197
S31	84.388	98.000	91.194	-13.612
S41	85.523	96.000	90.761	-10.477
S51	85.654	97.000	91.327	-11.346
Means	**85.142**	**97.554**	**91.348**	**-12.412**

Table 6-5: The study SpO_2 EPMS and reference readings means and differences (%).

A linear regression plot of the paired means of the EPMS and reference SpO_2 readings is presented in *Figure 6-13* and shows the data points distributed evenly about the trend line, but very poor correlation with an R^2 value of 0.020 (P = 0.489).

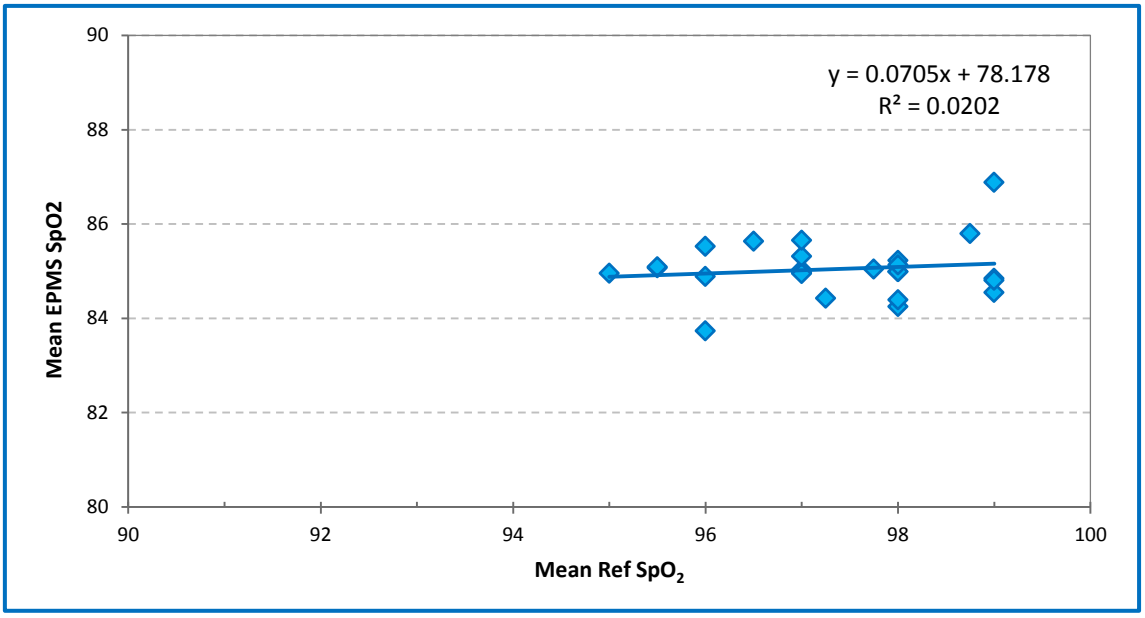


Figure 6-13: A linear regression plot of the 26 paired means EPMS and reference SpO_2 readings for each dataset showing correlation.

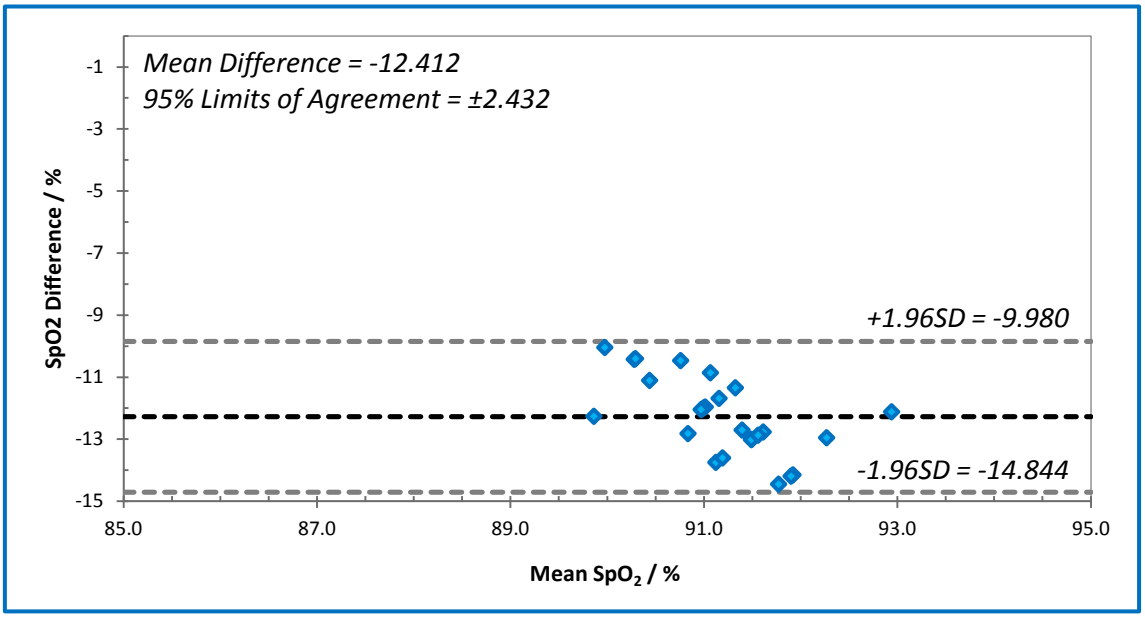


Figure 6-14: A Bland-Altman plot of the means and differences of the paired mean EPMS and reference SpO_2 readings.

Figure 6-14 shows a Bland-Altman plot comparing the means and differences in the paired data. The mean bias is large (-12.412), reflecting the discrepancies in the magnitudes of the readings. All of the data points fall within the limits of agreement

with the distribution suggesting the error to be inversely proportional to the means of the readings.

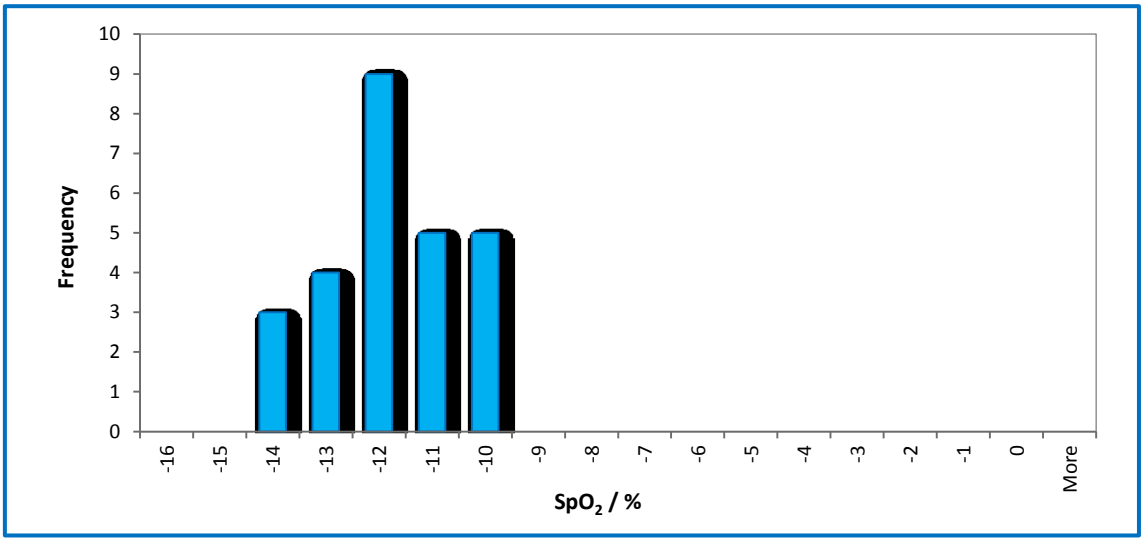


Figure 6-15: A distribution plot of the SpO_2 mean differences in the study datasets.

Figure 6-15 shows a histogram displaying the frequency distribution of the differences in the datasets; this clearly highlights that the EPMS SpO_2 under reads by -12% in the majority of the datasets.

6.3.3 Temperature

This section first investigates the repeatability of the replicate readings taken with the reference tympanic thermometer and then compares these with the EPMS.

Reference Temperature Data

Table 6-6 shows the replicate reference temperature readings from the study cohort together with the range and means from each of the study sessions. The first replicate gave the highest reading on 23 occasions (88.5%) with readings equal to or above 37°C being observed in all three replicates on only four occasions (O12, S31, S41 and S51). Mean temperatures of this mark were only recorded consistently by subjects

O and S (O11, O12, S31, S41 and S51), while the mean readings for subject R (< 36.0°C) were significantly cooler than the established norm. The mean temperature measurement was 36.707°C with a mean variation of 0.238°C. The widest range observed was 0.7°C (Subject R, dataset R21).

Subject	Datasets	Replicate Readings (°C)			Range and Means (°C)	
		1	2	3	Range	Mean
E	E11	**37.1**	36.9	36.9	0.2	36.967
	E12	**37.1**	37.0	37.0	0.1	37.033
	E13	**36.8**	**36.8**	36.7	0.1	36.767
	E14	36.7	36.7	**36.8**	0.1	36.733
F	F11	**37.1**	36.8	36.8	0.3	36.900
	F21	**37.2**	37.0	36.8	0.4	37.000
	F31	**37.1**	36.9	36.9	0.2	36.967
	F41	**36.9**	36.7	36.7	0.2	36.767
G	G11	36.4	36.4	36.4	0.0	36.400
H	H11	**37.0**	36.8	36.7	0.3	36.833
	H21	**36.7**	36.6	36.4	0.3	36.567
	H31	36.4	36.4	**36.5**	0.1	36.433
	H41	**36.8**	36.5	36.4	0.4	36.567
	H51	**36.7**	36.5	36.2	0.5	36.467
N	N11	**36.8**	36.7	36.6	0.2	36.700
	N21	**37.0**	36.8	36.8	0.2	36.800
	N22	**37.1**	36.8	36.8	0.3	36.900
O	O11	**37.1**	36.9	37.0	0.2	37.000
	O12	**37.4**	37.1	37.1	0.3	37.200
R	R11	**36.1**	36.0	35.8	0.3	35.967
	R21	**36.1**	35.9	35.4	0.7	35.800
S	S11	**36.9**	36.7	36.7	0.2	36.767
	S21	**36.9**	**36.9**	36.8	0.1	36.867
	S31	**37.3**	37.2	37.1	0.2	37.200
	S41	**37.5**	37.4	37.4	0.1	37.433
	S51	**37.4**	37.3	37.2	0.2	37.300
				Means	**0.238**	**36.707**

Table 6-6: Replicate study temperatures (°C) showing the range and means of the reference ear thermometer readings. High readings are shown in bold.

A Comparison of Temperature Data

Subject HR data is presented in *Table 6-8*. This shows the minimum and maximum recorded readings for each test subject across their respective datasets with both the EPMS and reference ear thermometer. Random instances were observed of zeroes being recorded by the EPMS, no more than two instances in any given dataset. These were manually replaced in affected spreadsheets by the means of the two surrounding values.

Subject	Datasets	EPMS Temperature (°C)			Reference Temperature (°C)		
		Min	Max	Mean	Min	Max	Mean
E	4	35.5	36.3	35.822	36.7	37.1	36.875
F	4	35.7	36.3	35.898	36.7	37.2	36.908
G	1	35.5	36.0	35.545	36.4	36.4	36.400
H	5	34.7	35.9	35.431	36.2	37	36.574
N	3	35.6	36.0	35.769	36.6	37.1	36.800
O	2	36.5	36.7	36.592	36.9	37.4	37.100
R	2	35.0	35.2	35.122	35.4	36.1	35.883
S	5	34.6	36.4	35.718	36.7	37.5	37.113
Overall	**26**	**34.6**	**36.7**	**35.737**	**35.4**	**37.5**	**36.707**

Table 6-7: Study subject temperature data showing the minima, maxima and means for EPMS and reference data collected from each participant

The EPMS readings were noticeably lower than the reference (overall means showing 35.737 versus 36.707°C) although the overall spans were the same (2.1°C). The mean variation was 0.214°C, proving better than the reference (the lowest subject mean variation being N and O at 0.1°C and G the highest with 0.5°C). Results followed the same general trend as the reference with subject O recording the highest mean

temperature and subject R the lowest. Differences may be noted in the mid-rankings however.

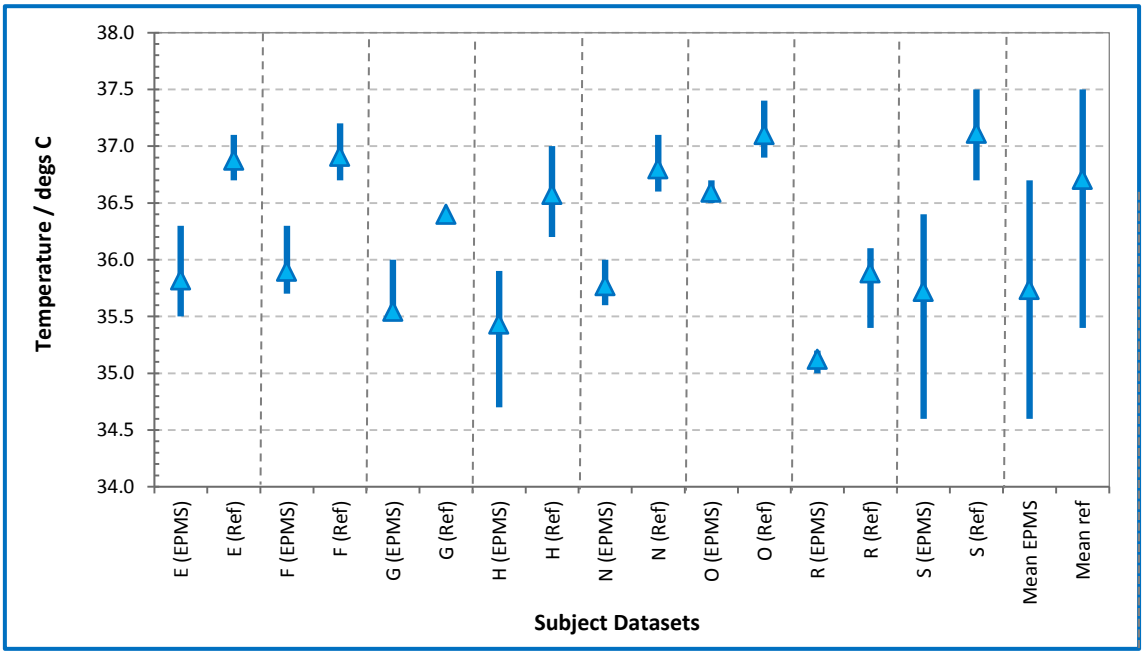


Figure 6-16: A plot showing the range and means of readings of the study subject's temperature datasets.

Figure 6-16 displays the subject dataset's temperature profiles graphically. This demonstrates there was no overlap between the measurement methods on an individual dataset whereas there was substantial overlap between the dataset means.

Analysis of Temperature Data

Plots were prepared from each set of subject data. These comprised of 60 seconds of continuous time history EPMS data with the means of the three replicate reference readings (complete with error bars) superimposed. The scaling on the Y-axes was fixed for all plots according to the established recorded minimal and maximal limits (34 – 38°C) to facilitate comparison.

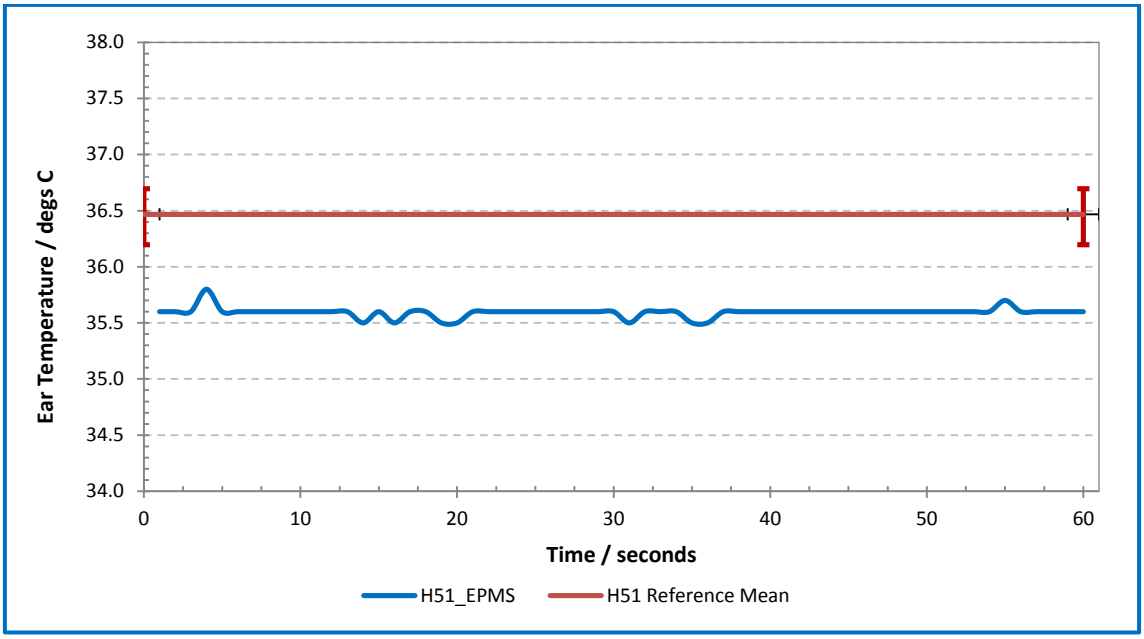


Figure 6-17: A comparative plot of EPMS and reference temperature data (subject H, dataset exp_H51).

Figure 6-17 shows a typical example of the recorded temperature data. It can be seen that there is little variation in the EPMS temperature reading over the measurement period (0.3°C), which closely compares with the range of the reference observations (0.5°C in this example). Though stable, there is however a marked difference in the recorded temperatures in all datasets with the EPMS consistently under-reading.

Analysis of the Mean Temperature Datasets

Table 6-8 shows the means of the EPMS and reference readings for each dataset and the means and differences of the paired readings used in the following regression (*Figure 6-18)* and Bland-Altman plots (*Figure 6-19)*.

Dataset	EPMS	Ref	Mean	Diff
F11	35.800	36.900	36.350	-1.100
F21	36.203	37.000	36.602	-0.797
F31	35.792	36.967	36.379	-1.175
F41	35.797	36.767	36.282	-0.970
G11	35.545	36.400	35.973	-0.855
H11	35.790	36.833	36.312	-1.043
H21	34.900	36.567	35.733	-1.667
H31	35.380	36.433	35.907	-1.053
H41	35.490	36.567	36.028	-1.077
H51	35.593	36.470	36.032	-0.877
N11	35.600	36.700	36.150	-1.100
N21	35.931	36.800	36.365	-0.869
N22	35.777	36.900	36.338	-1.123
O11	36.557	37.000	36.778	-0.443
O12	36.627	37.200	36.913	-0.573
R11	35.123	35.967	35.545	-0.843
R21	35.120	35.800	35.460	-0.680
S11	35.490	36.767	36.128	-1.277
S21	34.643	36.867	35.755	-2.223
S31	35.913	37.200	36.557	-1.287
S41	36.200	37.433	36.817	-1.233
S51	36.343	37.300	36.821	-0.957
Means	**35.727**	**36.782**	**36.255**	**-1.055**

Table 6-8: The means and differences of study EPMS and reference temperature readings (°C).

A linear regression plot of the paired means of the EPMS and reference SpO_2 readings was prepared to establish the degree of correlation between the two sets of data. This is presented in *Figure 6-18* and shows the most of the data points distributed evenly about the trend line, but with two significant outliers (H21 and S21) which reduce R^2 to 0.448 ($P < 0.001$).

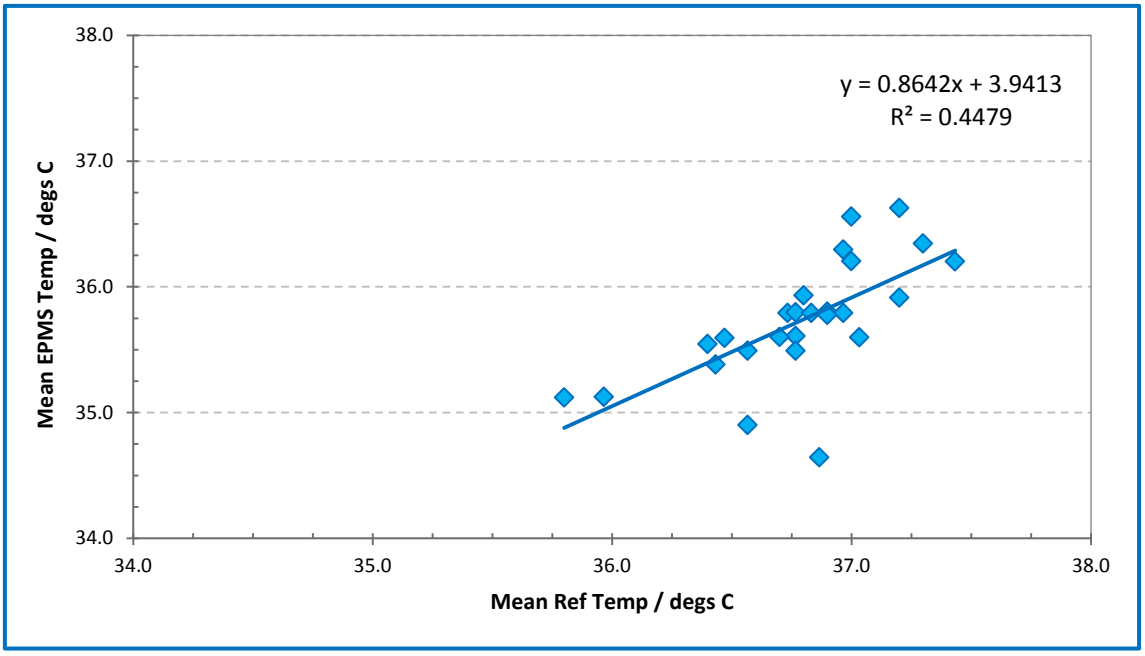


Figure 6-18: A linear regression plot of the 26 paired mean EPMS and reference temperature readings for each dataset showing correlation.

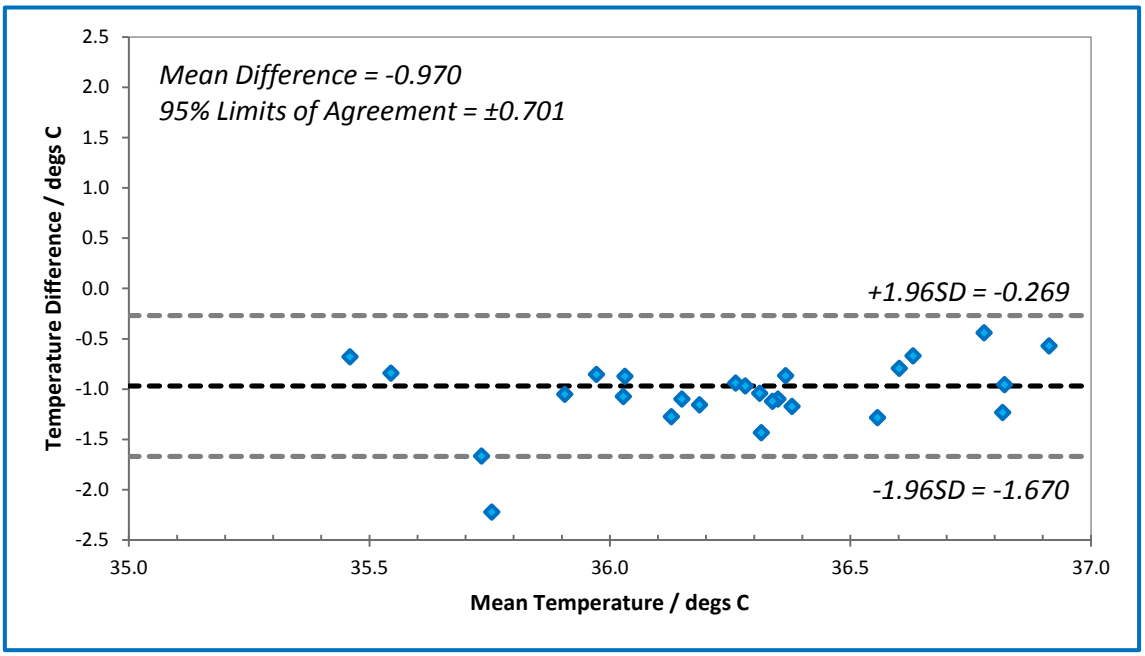


Figure 6-19: A Bland-Altman plot of the means and differences of the paired mean EPMS and reference temperature readings.

Figure 6-19 shows a Bland-Altman plot comparing the paired means and differences of the temperature data. The mean bias is small and close to zero (-0.970), with most

of the data points falling close to the mean bias line. With the exception of an outlier (S21) all data points fall within the limits of agreement, though one is on the line of the lower limit (H21) and another (O11) quite close to the upper limit. The even distribution of the data suggests minimal bias.

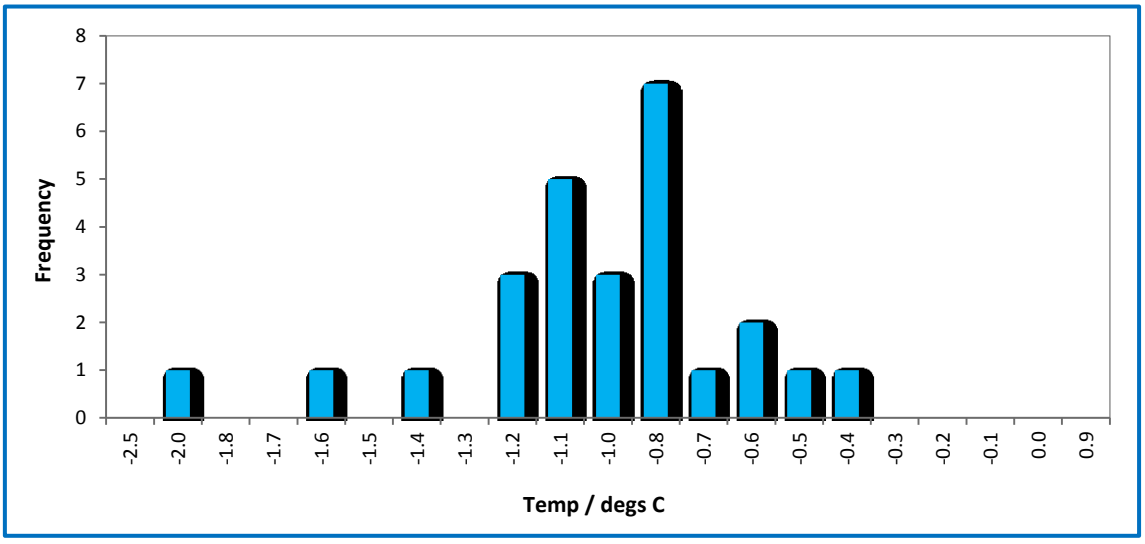


Figure 6-20: A distribution plot of the mean differences in temperature readings of the trial datasets.

Calibration

Figure 6-20 shows a histogram displaying the frequency distribution of the temperature differences in the datasets. This shows that an EPMS error of -0.8°C was most common with H21 (-1.667 °C) and S21 (-2.223 °C) skewing the mean error. With these points removed the mean error falls from -0.970 to -0.890°C. If this is added to the EPMS readings as a compensation factor, the resulting regression (*Figure 6-21*) and Bland-Altman plots (*Figure 6-22*) show a notable improvement. The revised R^2 value increases to 0.659, confirming improved correlation, while the modified mean bias is effectively zero (-0.091°C) with all points evenly distributed along the mean bias line and, with a single exception, constrained within tighter limits of agreement (±0.470°C).

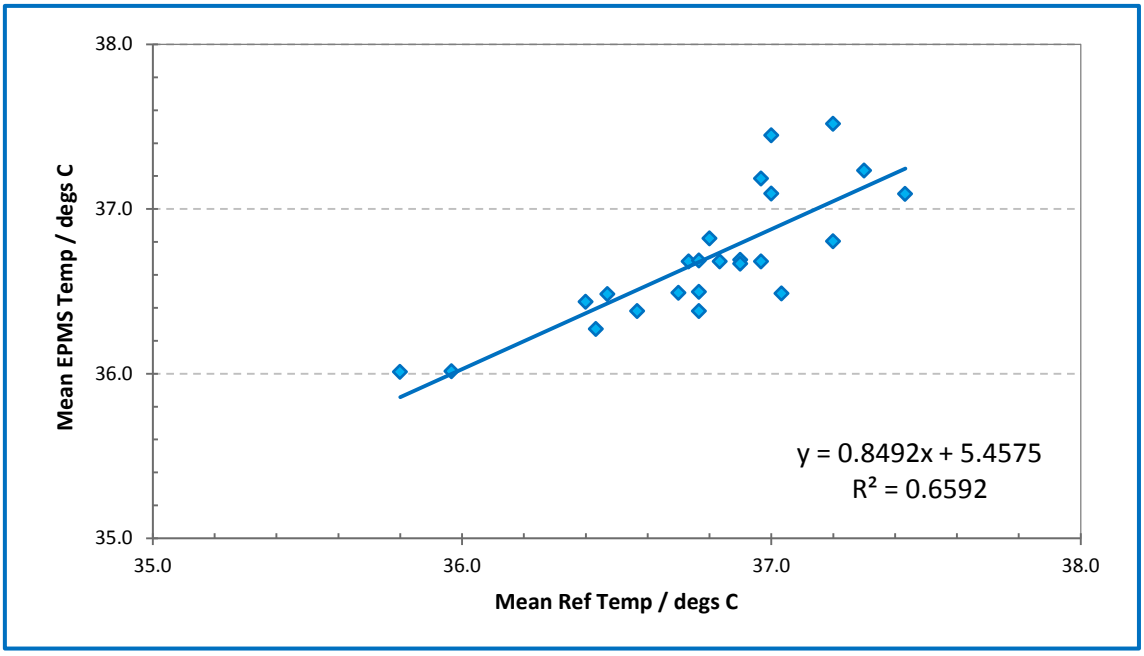


Figure 6-21: A linear regression plot of the paired mean EPMS and reference temperature readings with H21 and S21 removed and an EPMS compensation factor of +0.890°C added.

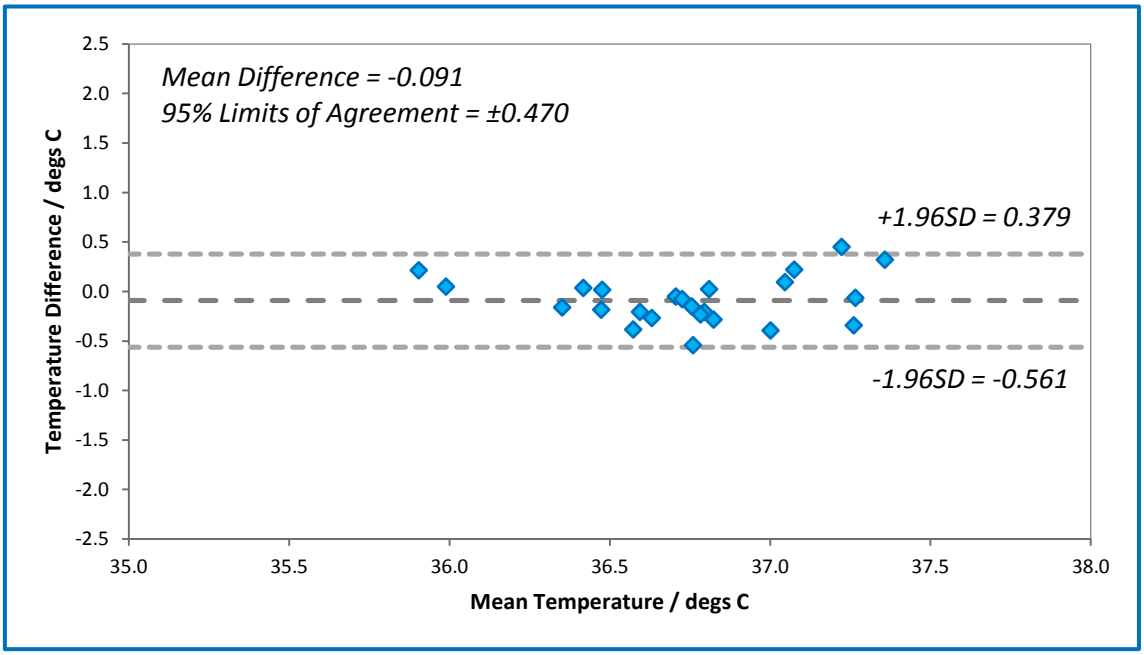


Figure 6-22: A Bland-Altman plot of the means and differences of the paired mean EPMS and reference temperature readings post-compensation.

The frequency distribution plot presented in *Figure 6-23* demonstrates the effect of the temperature compensation. The removal of the two outliers and addition of the

+0.89°C offset results in a reduced range of readings spanning from -0.547 to +0.447°C centred around zero.

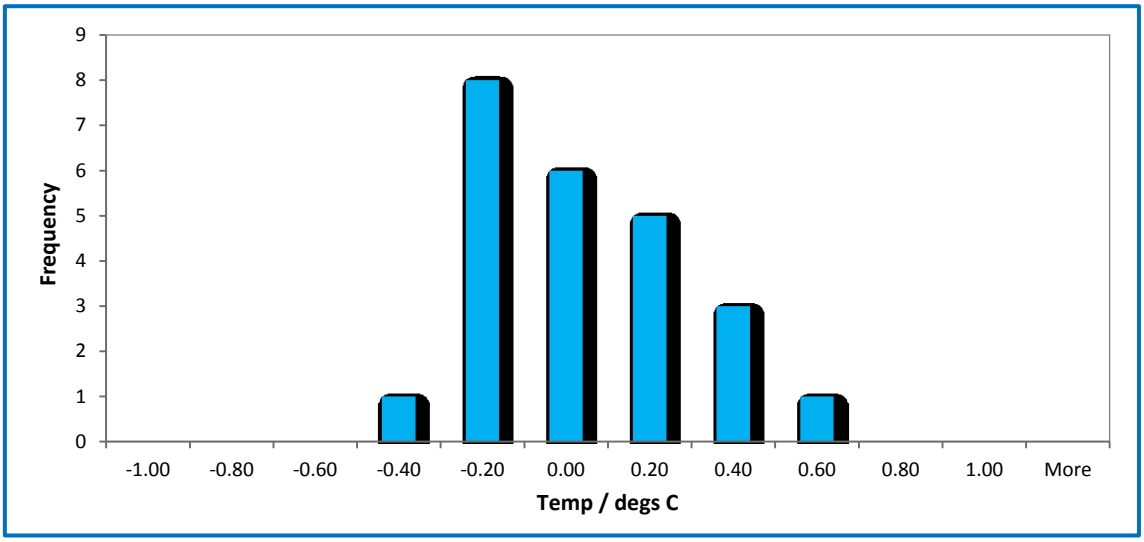


Figure 6-23: A distribution plot of the mean differences in compensated temperature readings from the trial datasets.

6.3.4 Usability

The EPMS and software performed well throughout the trials with no technical issues to report. None of the participants reported discomfort when wearing the device although two experienced some problems with the fit of the ear probe. Most experienced initial problems in fitting and securing the device's pulse oximeter clip on their ear lobes without dislodging the ear probe.

Something immediately apparent was the difference in equilibration times between the EPMS and the reference pulse oximeter, an observed throughout the study. The EPMS was significantly more responsive, being faster in acquiring readings and reacting to changes, thus appearing slightly less stable. Acquisition time from attaching the ear clip was consistently less than five seconds with up to a further 10 seconds for

readings to stabilise. The reference took between 10 and 20 seconds to initially acquire readings from its ear probe (which it sometimes failed to do) with a stabilisation time of around 10 seconds. This caused issues with the reference device, frequently requiring the probe to be re-sited or the unit power cycled to reinitialise sample acquisition. These difficulties led to a finger probe being used with subjects H (all datasets) and F (dataset F41) which offered improved reliability over the ear probe.

6.4 Discussion

Analysis of the study results show mixed success in that the EPMS provides excellent HR, promising temperature and poor SpO_2 data. These will be discussed in turn in *sections 6.4.1 to 6.4.3.*

6.4.1 Heart Rate

The results demonstrate excellent correlation between the EPMS v4 design and reference as seen in individual datasets and the mean data. This is borne out by the difference in the means of the datasets (-0.633 bpm), which is well within the quoted accuracy (±1 bpm) of the reference instrument and comparable to figures reported for commercial monitors (Iyriboz et al., 1991; Dawson et al., 2011). As the optical sensing elements are the same in the EPMS and the reference, this demonstrates that the filtering, signal processing and peak detection algorithms employed are capable of extracting accurate beat-to-beat periods from which a measure of HR can be calculated. This would also provide a good platform for expanding the device's capability to measure respiratory rate (Clifton et al., 2007) and mental stress (Srinivas et al., 2007), both of which may be extracted from heart rate variability.

As reported, there was a noticeable difference in acquisition time between the EPMS and reference pulse oximeter. This would appear to demonstrate the essential differences in the processing of beat-to-beat frequencies, the EPMS employing an nine-sample moving median whereas the reference would appear to use a moving average with a relatively wide (or dynamic) sampling window– hence the extended equilibration time. This supposition is further reinforced by the time lag between the devices' data presented in *Figure 6-7* and observed in many of the datasets (an example of which is shown in *Figure 6-6*). If the sampling window is too short, whether time or sample-based, the resulting readings may appear unstable. Too wide however and lower readings can be over emphasised, damping the response and eliminating detail, while introducing a temporal offset in displayed data (Jennings et al., 1981).

The most likely reason for employing a wide sampling window is to minimise the influence of motion artefacts on displayed data. Although resting rather than ambulatory measurements were recorded during the study, the degree of motion determined from the EPMS' activity level scoring was investigated. There was little evidence however to support this contributing to changes in recorded HR data in either the reference or EPMS results.

The differences observed between readings would appear to be primarily due to the different data processing techniques employed. The EPMS, with its rapidity of response, is arguably better able to track dynamic HR in a resting subject than the reference, which provides a good measure of the underlying mean. If the EPMS has a place in periodic patient assessment, rapid acquisition and equilibration are key attributes for successful operation. In the case of HR measurement, the study amply

demonstrates that a one minute sampling window has proved to be sufficient to deliver a representative measure of a subject's mean HR.

6.4.2 Blood Oxygen Saturation

The performance of the SpO_2 sensing was disappointing though not unexpected. There was no correlation between the EPMS and the reference (*Figure 6-13*, R^2 = 0.020), suggesting inconsistency and considerable variation, and a large mean difference (*Figure 6-14*, bias = -12.412).

Sources of Error

First and foremost, sensor and hardware errors may be ruled out as four examples of the EPMS v4 design exhibited the same problem, the connections to the AFE4490 oximeter chip closely following those of reference designs. There was little variation in the EPMS response (or the reference data for that matter) in any of the dataset's individual time history plots, suggesting noise was not the problem. The study results are suggestive of two problems, which may be related: (i) inconsistency and (ii), the scale of the difference in the readings.

Section 5.4.2 reports the issues experienced with SpO_2 derivation which had been problematic from the outset. The magnitude and rate of change of DC offset in the red and IR waveforms defeated attempts to resolve a viable saturation reading in the first three EPMS variants as the signals were too erratic, ambient light and motion artefacts being mostly responsible. The additional processing power and improved digital signal processing in EPMS v4 improved stability although it was still prone to DC drift effects.

It was noted that the R value (red/IR absorption ratio) returned after performing the calculation given in *Equation 5-1* was close to unity, whereas a value of 0.4 to 0.6 would be expected for SpO_2 levels above 95%. Applying the formula in *Equation 5-2* gave an estimation of SpO_2 for a given R value, the EPMS giving readings of approximately 85%. Although this was low it wouldn't have been a problem had there been good correlation with the reference, as it would have allowed a compensation factor to be calculated from the study data to effect calibration. The degree of inconsistency observed between EPMS and reference readings demonstrates the problem is not an arithmetic one, but is related to variability in the original waveform's DC voltage component.

The R value is a ratio of the AC:DC ratios of the red and IR signals (*Equation 5-1*), which comprise of a small AC response on a large and variable DC offset. Thus it is clear that the minimisation of DC drift is essential for robust SpO_2 measurement and critical for the future development of the EPMS device.

On examination (post trial) a number of differences were found between the AFE4490 product datasheets used in the original design (Texas Instruments Inc., 2013) and that most recently published (Texas Instruments Inc., 2014) – the list of documented revisions being two pages long. Of particular interest were changes to the control registers of the PPG signal's second internal gain stage, where new features have been introduced. These directly affect the DC offset and facilitate control of an 'ambient cancellation scheme' in which ambient light readings are used to provide dynamic DAC offset adjustments to the PPG second gain stage, thus maintaining an

even DC threshold. The ambient light readings could also be used to rapidly adjust LED drive levels to the same end.

Another possibility is to evaluate in-ear sensing with a side-facing reflective sensor mounted on the device's ear probe. This would have dual benefit of reduced motion artefact and the elimination of most ambient light, directly addressing two of the biggest complications in SpO_2 monitoring.

6.4.3 Temperature

The results of the study show mixed success for temperature measurement, but nevertheless demonstrates the EPMS' potential. EPMS ear temperatures were remarkably stable, showing little variation in any of the datasets and returning a marginally better mean range than the reference (0.214°C versus 0.238°C). The device was found to consistently under read by a mean of -0.970°C, the range of errors being from -0.443°C to –2.223°C. This compares with the stated accuracy of ±0.2°C of the reference ear thermometer (Braun GmbH., -) which, although challenging, demonstrates the exacting requirements for medical thermometry.

As two of the EPMS temperature readings (H21 and S21) were below 35°C and stood out in *Figure 6-18* (and *6-19*) there was a case for considering them as outliers and ripe for removal. With these exceptions removed the mean difference improved to -0.890°C. Adding this to EPMS temperature readings as a compensation factor zeroed the offset and improved both correlation (*Figure 6-21*, R^2 = 0.659 as opposed to 0.448) and bias (*Figure 6-22*). Had the grouping on the regression plot (*Figure 6-21*) been tightly aligned to the trend line and R^2 close to unity, there would be some

justification for applying the compensation factor to adjust temperature calibration. The range and degree of variability however are too great for this to be viable, demonstrating the problem is not one of calibration but design.

Sources of Error

With any IR thermometer a clear optical path is critical for accurate measurement; though this was nominally provided by the EPMS probe, the path may still be impeded by hair and cerumen (ear wax) to give low readings (Gallimore, 2004; Doezema et al., 1995). As there was no specific provision for ensuring subjects' ear cleanliness during the trial (a deficiency of the study) there remains the probability that this may have been a factor with some readings. In addition, as EPMS temperature readings were collected prior to those of the reference ear thermometer, the degree and distribution of cerumen in the ear canal may have changed between the two sets of readings.

Although the sensor has a calibrated digital output its quoted accuracy is given as ±0.5°C, which could account for some of the error. Skin emissivity is close to unity (see *section 5.2.1*) and therefore unlikely to be responsible for errors of this magnitude.

A more likely culprit is the design of the probe itself. As this was made from rigid ABS there was no compliance to accommodate ear canals of different shapes and sizes, therefore affecting the fit and aim of the sensor. Although the viewing angle was relatively generous (100° to 50% thermopile signal) and unobstructed by the ABS probe housing itself (see *section 5.4.1, p197*), the lens may not be pointing directly at the tympanic membrane, but rather the wall of the ear canal itself. This hypothesis is supported by feedback from the study and research describing the range of cross-

sectional areas, curvature, lengths and temperature profiles of the adult ear canal (Arsenault and Ducharme, 2001; Braun GmbH., -). This could be largely addressed with a redesigned probe.

6.4.4 Usability

There were no technical concerns, with the EPMS performing flawlessly for the study's duration and from the operator's perspective the system proved to be easy to use for data collection. The EPMS was consistently faster than the reference pulse oximeter in acquiring and presenting stable HR and SpO_2 readings, possibly a result of the differences in the signal processing methods employed.

From a user's perspective however, restrictions placed upon the study by the Ethics Committee, though understandable and necessary, prevented the use of direct feedback from the host tablet as a fitting aid, instead relying on verbal instruction from the investigator. The tablet would have provided the necessary affirmation that the device was correctly seated for reliable measurement. This compromised usability in the author's opinion despite attracting little negative feedback.

Some participants found the EPMS' pulse oximeter clip was difficult to fit, requiring the use of both hands, a degree of manual dexterity and in one instance, a mirror. Ideally the clip should be eliminated and incorporated into a redesigned in-ear probe providing a better and more comfortable fit for a wide cohort of users.

Probe Design

The fit of the in-ear thermometer probe was not ideal; some participants found the diameter to large and experienced slight discomfort. As the probe was made from rigid

ABS there was no compliance to accommodate ear canals of different shapes and sizes (see *section 6.4.3, page 249*). The probe would benefit from a slight extension (no more than 5 mm), a general reduction in diameter (to produce a concave form with a gradual taper from the sensing tip) and a degree of flexibility. A thin layer of compliant material (e.g. a soft hypoallergenic silicone) could also be incorporated, ensuring an improved fit and providing improved user comfort.

6.5 Conclusions

The work reported in this study meets two of this thesis' stated objectives:

- A pilot study of the prototype EPMS on healthy subjects was carried out in order to allow comparison with a reference device.
- This provided a representative test of the device's telemonitoring capability.

Results from the study demonstrate the following points:

- The EPMS' HR readings showed an excellent agreement with those from the reference pulse oximeter in terms of overall range (53 – 87 bpm v. 54 – 87 bpm), means (67.235 bpm v. 67.869 bpm), with a strong relationship (R^2 = 0.980, p <0.001, mean bias = -0.633, limits of agreement ±2.021 bpm). The mean measurement error (mean bias) compared favourably with the ±1 bpm accuracy quoted for the reference.
- The SpO_2 readings were disappointing and showed a poor relationship between the EPMS and reference readings. This was apparent from the discrepancies in overall range (82.70 – 88.53% v. 95 – 99%), means (85.142% v. 97.554%) and lack

of correlation (R^2 = 0.020, p = 0.489, mean bias = -12.412, limits of agreement ±2.432%). The magnitude of DC drift, whether from ambient light effects or motion artefacts, was identified as the cause of the poor SpO_2 readings. The AFE4490 pulse oximeter signal conditioning chip is suspected to be (at least in part) responsible, something that changes to the silicon relating to DC offset control in recent revisions might attest to.

- The temperature readings recorded by the EPMS were lower than the reference. This was evident in the overall range (34.6 – 36.7 ˚C v. 35.4 – 37.5 ˚C) and means (35.737 ˚C v. 36.782 ˚C). The regression and Bland Altman plot data (R^2 = 0.448, p <0.001, mean bias = -0.970, limits of agreement ±0.701 ˚C) demonstrated a clear (but weak) relationship between the datasets which, even allowing for compensation, did not provide the level of accuracy required for medical thermometry.
- Evidence suggests that problems with the EPMS' temperature measurement are due to the profile and design of the in-ear probe. Its shape is unable to accommodate the variety of shapes and sizes of ear canals and thus although the IR pyrometer's lens has an unobstructed view, it may not be pointing at the tympanic membrane.
- The BLE wireless system worked flawlessly, broadcasting real-time EPMS data to a host tablet for the duration of the study.

- If developed as a product, the EPMS has the potential to extend routine VS monitoring into the community where it could greatly benefit the wellbeing of vulnerable individuals.

7 Conclusions and Recommendations

7.1 Conclusions

This research was prompted by an unmet need identified by senior medical professionals for community-based routine VS monitoring as an aid to wellbeing in vulnerable groups. The literature review uncovered the importance of VS monitoring in supporting health and wellbeing, and its use in the diagnosis and management of disease and infection. It underpins hospital care as part of EWS track and trigger systems, but there is no mechanism for routine monitoring and reporting in the community. The review also identified a paucity of respiratory sensors and a need for devices capable of one-stop simultaneous VS monitoring, whether for use by healthcare professionals or patients in the community. This helped define the aim and objectives of this project which led to the development of the CRS and EPMS devices.

7.1.1 CRS

The pilot study demonstrated the potential of clavicular respiratory sensing and its superiority to a similar thoracic sensor in measuring respiration rate. The device is minimally intrusive, especially when compared to direct exhalatory monitoring, providing a response based upon respiratory motion without out the need for thoracic belts. The study also revealed the potential for monitoring respiratory depth (tidal volume) from the relative magnitude of the response. Although further research is required to quantify the relationship, this feature would increase its clinical value.

A commercialised version of the CRS, particularly if a patient's ventilatory condition can be resolved, could find use in the management of chronic respiratory conditions

(e.g. COPD). If paired with a pulse oximeter (perhaps in an integrated package), it could offer an excellent assessment of respiratory efficiency by examining RR and estimated tidal volume versus blood oxygen saturation.

7.1.2 EPMS

The EPMS demonstrated its capability in capturing a set of readings, when worn for no more than two minutes, and wirelessly uploading these to a host mobile device. A pilot study established that HR readings were comparable with industry standards and closely matched the reference, although temperature and SpO_2 measurement was less successful.

Temperature readings were a typically a degree lower than the reference, though stable. The use of temperature compensation was investigated but ruled out as the range of readings was too great with some participants. It became clear that the problem was with design of the in-ear probe and a failure to account for a range of different ear canal shapes and sizes, thus measuring the temperature of the ear canal rather than the tympanic membrane.

Problems with DC drift had prevented SpO_2 measurement in early variants of the EPMS, and although the final version was much improved the readings were still unsatisfactory. The study readings were low (by around 12%), but a correction factor could have been used had correlation with the reference been acceptable. Unfortunately this was not the case, there being no discernible correlation between the two methods.

Development Program Issues

The direction of the research was driven, at least in part, by interests in securing research funding and commercialising the EPMS device. In hindsight, from a purely academic perspective, some of the time spent on these activities may have been more effectively used in resolving some of the identified issues, e.g. refining SpO_2 signal processing offline and developing an algorithm for the estimation of RR from the RR signal using MATLAB.

Potential EPMS Applications

This section discusses some example applications where the EPMS could provide real patient benefit if successfully deployed.

Monitoring Infection in the Elderly

With the general increase in life expectancy in most of the developed world the elderly population is increasing with an estimated 500 million, or seven percent globally, aged sixty-five or older. These numbers are predicted to further increase over the next few years with the 'oldest old' (at 85 plus) showing the most rapid rise (Kinsella and He, 2009). As a group the elderly are more likely to suffer from chronic long term conditions and many will suffer the misfortune of comorbidities (Fortin et al., 2005; Britt et al., 2008). This leaves them at an increased risk of infection, the consequences of which may be severe (Garibaldi, 1999; Gijsen et al., 2001). If the burden of frailty is added (Fillit and Butler, 2009), it is apparent that older people are especially vulnerable.

It is those aged over sixty-five that place the heaviest demand on healthcare resources, occupying as much as 65% of available hospital beds for acute care (Philp,

2007). Regular vital signs monitoring of the vulnerable elderly, whether in the community or care setting, would help in the management of chronic long term conditions and could reduce hospital admissions (Goodwin et al., 2010). The timely identification and treatment of infection would also be more certain if more vital signs readings were available.

This is an area where a discrete monitoring device such as the EPMS, that can easily and rapidly capture multiple vital signs, could find use in general practice, care institutions or in the home.

Post-operative and Outpatient Care

The literature review revealed the incidence of nosocomial infections, including those in post-operative patients (Owens and Stoessel, 2008; Weigelt et al., 2010). These are at an increased risk of infection, as indeed are the immunocompromised such as patients undergoing chemotherapy (CDC, 2014). Whilst monitored regularly in hospital, once released as an outpatient it is the non-expert patient or their family who typically assesses their wellbeing and whether to seek medical assistance.

Given access to an EPMS or similar device upon release, outpatients could self-monitor their vital signs. This could help in detecting the early signs of infection, providing evidential readings to assist clinicians in their diagnoses. It would assist in early intervention, improving the outcome for patients and reducing the number of readmissions due to severe infection.

7.1.3 Summary

The work reported in this thesis has successfully achieved the aim and objectives set out in *section 1.5.1*, namely:

- A novel accelerometer-based prototype sensor (CRS) monitoring clavicular respiratory motion was designed and developed.
- A pilot study comparing the performance of the CRS and a reference device on healthy subjects was carried out, showing outstanding agreement. This also revealed the potential for the estimation of tidal volume via the magnitude of the breath response.
- A novel prototype ear-worn wireless multisensor device (EPMS) was iteratively designed and developed to simultaneously measure VS readings. This combined tympanic thermometry and pulse oximetry sensing in a single ear-worn wireless-enabled device for the first time.
- A pilot study comparing the performance of the prototype EPMS and reference devices on healthy subjects was completed. This demonstrated that HR monitoring performance was comparable to industry standards, but temperature readings were a degree below reference readings and SpO_2 measurement was poor.
- The EPMS successfully demonstrated its capability in successfully and reliably capturing a set of readings when worn for no more than two minutes. The telemonitoring facility worked flawlessly, broadcasting real-time EPMS data to a host tablet over a maximum range of 10 metres.
- The EPMS meets the identified unmet need for a device capable of routine remote VS monitoring in the community.

7.2 Recommendations

Here the future development of the CRS and EPMS is discussed, establishing the nature of any further work that would be necessary prior to successful exploitation. The final section discusses the field of personal VS monitoring and proposes the application of a personalised EWS system for use with personal monitoring devices in the community.

7.2.1 CRS

The device used in the pilot study was a triaxial accelerometer with analogue outputs. The use of both triaxial accelerometers and gyros may be worthy of investigation, the gyro providing angular acceleration for a measure of rotational clavicular respiratory forces. The CRS would benefit from the addition of an on-board microcontroller running embedded signal processing algorithms. This would include a digital or wireless interface to external devices such that respiratory readings could be displayed and archived.

The pilot study revealed a relationship between signal magnitude and respiratory depth, providing the potential of calculating an estimation of tidal volume. Further research is recommended to better understand this relationship. A future study involving the CRS, spirometry and physical measurements may offer a method of quantifying respiratory depth together with estimations of tidal and minute volumes for a more complete ventilatory assessment of patients, including indirect quasi-real time monitoring.

7.2.2 EPMS

Although the EPMS has been shown to perform well, SpO_2 monitoring aside, usability would be greatly improved and ambient light effects be reduced if the pulse oximeter ear clip could be omitted. The study provides prima facie evidence for a redesign of the in-ear thermometer probe for improved accuracy and user comfort. Ideally, this would feature an integrated side-facing reflectance pulse oximeter sensor, with the probe itself being re-profiled for an improved fit in the ear canal for enhanced accuracy in temperature sensing.

A critical area of focus is to get to the bottom of the problems encountered with SpO_2 measurement. This might be resolved by fitting the latest version of the AFE4490 signal conditioning chip and modifying the signal processing software accordingly (see *page 247*). The HR readings were very encouraging, suggesting that the waveform is robust and peak detection returning accurate beat-to-beat periods. This raises the possibility of investigating heart rate variability (HRV) analysis to determine whether an estimation of respiratory rate can be reliably extracted. Another area for future study is the analysis of HRV to determine mental stress.

On the engineering front, the testing and evaluation of the wireless charger should be completed. Use of this technology would allow the case to be sealed (IP68), facilitating cleaning and simplifying day to day charging. With capital investment, the size of the circuitry and case could be much reduced to suit a range of different form factors and reduce costs.

Usability

The fit of both the in-ear probe and the pulse oximeter clip presented challenges for some test subjects, partly due to design issues and partly from a lack of software feedback offering confirmation that the EPMS was correctly seated. The latter issue was largely a result of an Ethics Committee's stipulation that subjects should not be able to view their VS readings, the necessary feedback being available from the host tablet. Problems with the profile of the ear probe affected both user comfort and measurement accuracy, both of which require demand a redesigned probe. Elimination of the ear clip would also simplify device fitting, thus it is proposed that the pulse oximeter sensor is integrated within the ear probe.

7.2.3 Personal Monitoring Systems- A Proposal

Whether using the EPMS or other monitoring devices to acquire vital signs and physiological data, this should be considered as just one part of a monitoring system. A sensing device paired with a mobile platform is just the start as the host, being a powerful internet-enabled wireless computer, has the potential to provide a range of additional benefits, acting as a health hub. This allows apps providing appointment and medication reminders, medical information services and teleconsultations to be added and potentially integrated with vital signs monitoring and data services. Whether for personal use or community use by a healthcare professional, this could greatly benefit the management of long-term conditions in the community. For best effect, the apps would connect to servers at a monitoring centre and be accessible by healthcare professionals allowing them to view and assess patients' vital signs data and update prescriptions as necessary.

Personal EWS

Early Warning Scoring (EWS) systems have been shown to greatly improve patient outcome in hospital. With regular monitoring this could be rolled out into the community. It is the author's belief that to be truly effective the scoring should be based upon relative rather than absolute measures, essentially providing a personal EWS system (PEWS).

Regular home monitoring allows an individual's normal resting readings to be established; these would act as a datum for PEWS scoring which would be assessed relative to these marks. *Table 7-1* shows an example of the PEWS chart, which includes the five vital signs and weight (as a marker for heart disease and frailty) instead of an AVPU consciousness score. Here only the highest score in each category uses absolute measures while others are within a range of the norm. The availability of BLE-equipped bathroom scales (available from Salter, Fitbit, Withings etc.) facilitates measurement which could be controlled via a mobile device. Normal readings could be continually assessed and the indices adjusted to account for changes in condition and medication. PEWS chart values could also be adjusted (with clinical approval) to more appropriately reflect individual patient condition and better address risk.

	PEWS Scores						
Parameter	**3**	**2**	**1**	**0**	**1**	**2**	**3**
Temp (°C)	35.5.5	-1.0	-0.5	norm	+0.5	+1.0	38.5
HR (bpm	50	-20%	-	norm	+10%	+20%	100
RR (bpm)	<8	-4	-	norm	+4	+8	>25
SBP	<80	-30	-20	norm	+20	+40	>190
SpO_2 %	<85	-10	-5	norm	-	-	-
Weight (kg)	-3	-2	-1	norm	-	-	-

Table 7-1: The proposed scores for a personal early warning scoring (PEWS) system for community-based monitoring

Table 7-2 presents a proposition for a PEWS risk and response chart. Modelled on that currently implemented in the NEWS system (Royal College of Physicians, 2012), this matches risk and response. The system is based on the supposition that daily vital signs readings are routinely taken via a tablet or smartphone, where PEWS scores are calculated, and uploaded together with the physiological data to a central server for storage and assessment.

A score of zero suggests good health and attracts little attention. A score between one and four raises the level of risk, which would still be classified as low, would result in an increase in measurement frequency and the status being flagged a monitoring centre. The patient would also be prompted to complete a brief online health assessment, providing qualitative feedback to back up the quantitative data. Entering the medium risk category (a score 4 – 7) would trigger a teleconsultation with a healthcare professional (telephone or Skype video call) to allow a direct assessment of a patient's condition; this could mean the patient is asked to change their medication,

visit their GP or admitted to hospital. A score of seven or above, or three on a single parameter, indicating the patient is at high risk, could result in a home visit from healthcare professional or admission to hospital.

PEWS Score	Risk	Frequency	Response
0	LOW	Daily	Readings routinely uploaded to server
1-4		4-6 hours	Readings uploaded; patient prompted to complete online health assessment; flagged at monitoring centre
4-7	MEDIUM	2-4 hours	As above; teleconsultation with health professional
>7	HIGH	Real time	As above; visit from health professional or ambulance sent to admit patient to hospital
>3 in any category			

Table 7-2: The proposed PEWS risk and response chart

An integrated system such as proposed here would benefit the delivery of healthcare in the community, whether based in the home or a care facility. It would provide a targeted response for outpatients, vulnerable individuals and the elderly based upon clinical need, for improved outcomes, reduced hospitalisation and better quality of life while maintaining independence.

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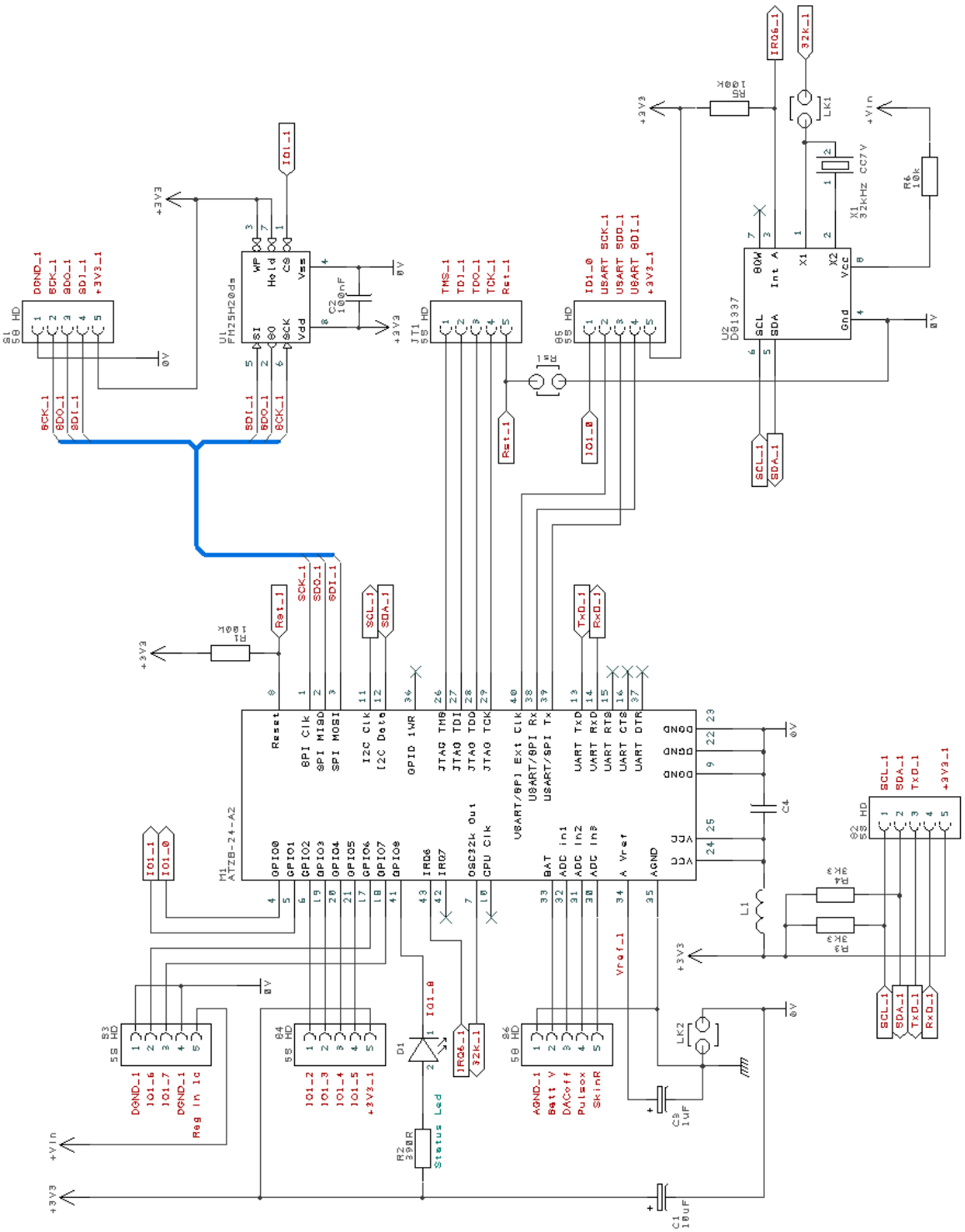
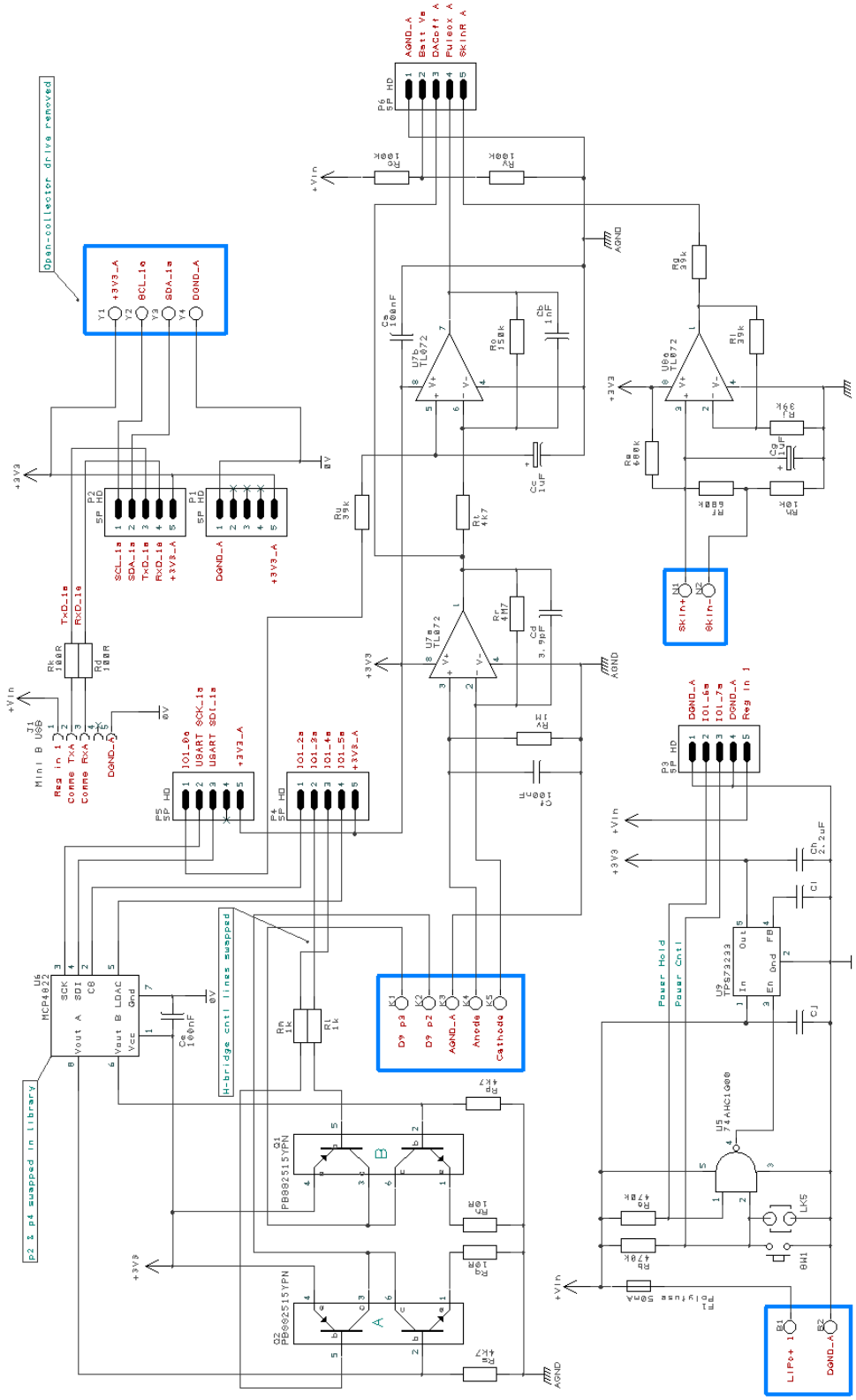
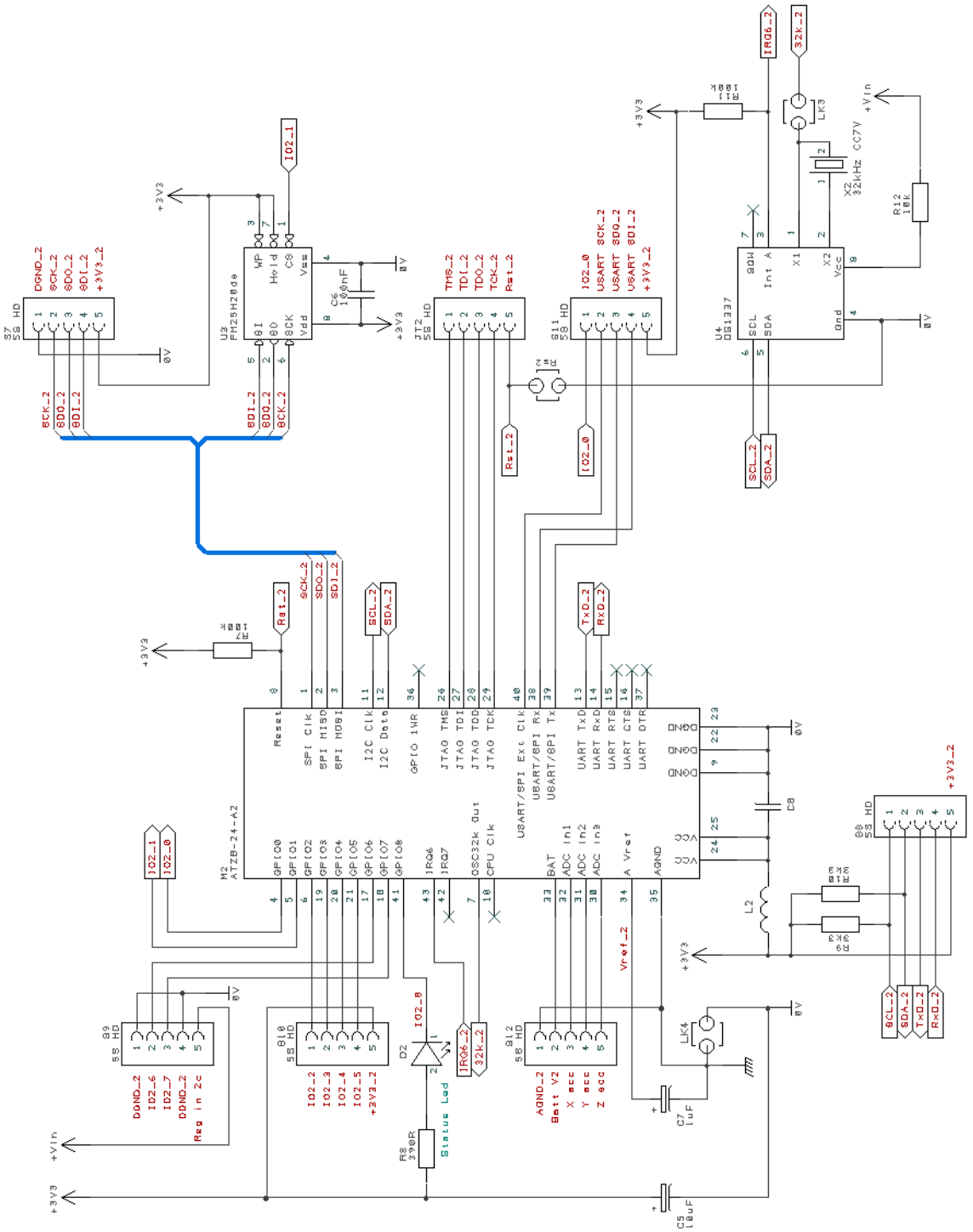
Appendix A - 1: EPMS v1 Ear Module Processor Board Schematic



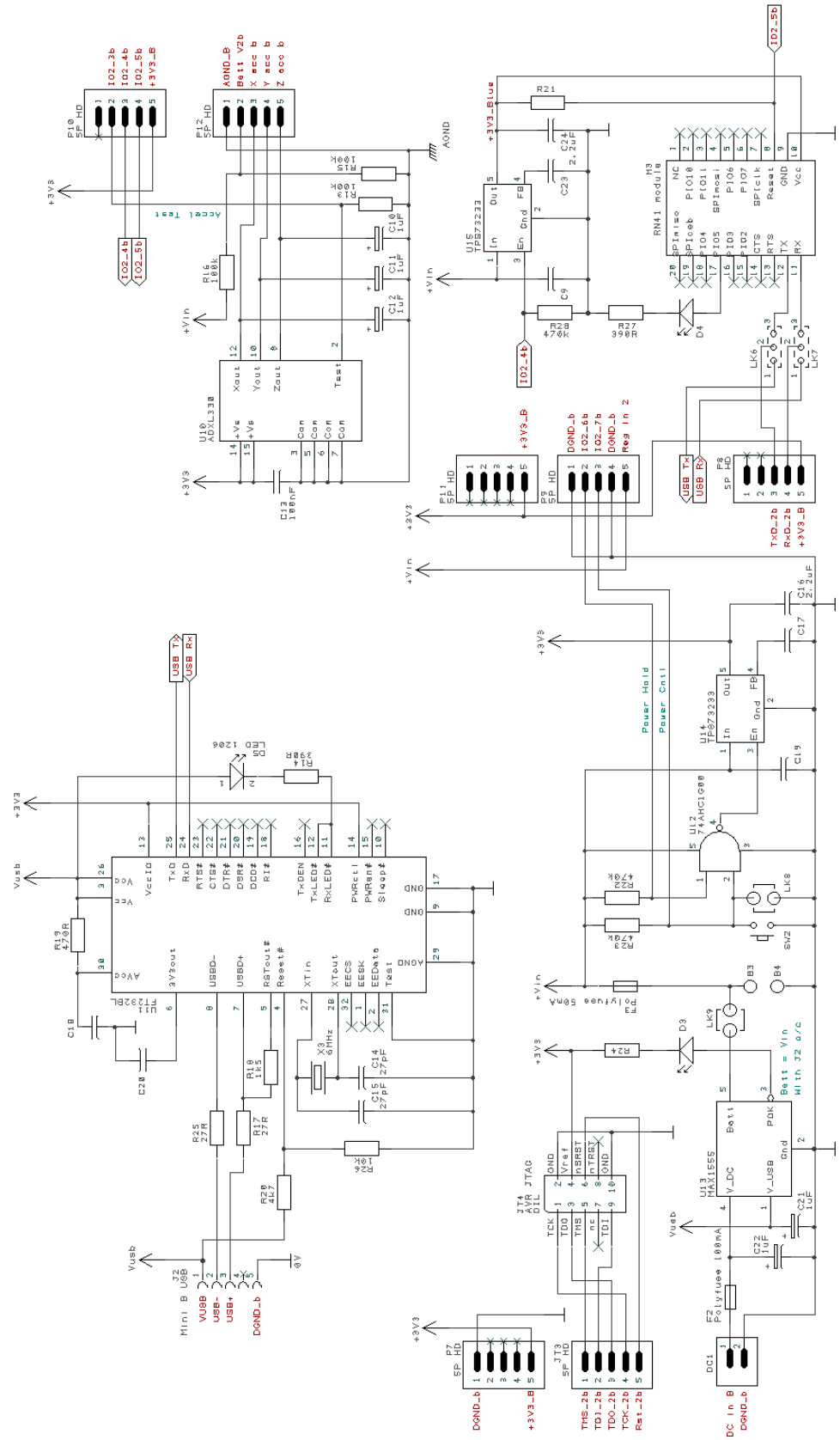
Appendix A - 2: EPMS v1 Ear Module Analogue Board Schematic



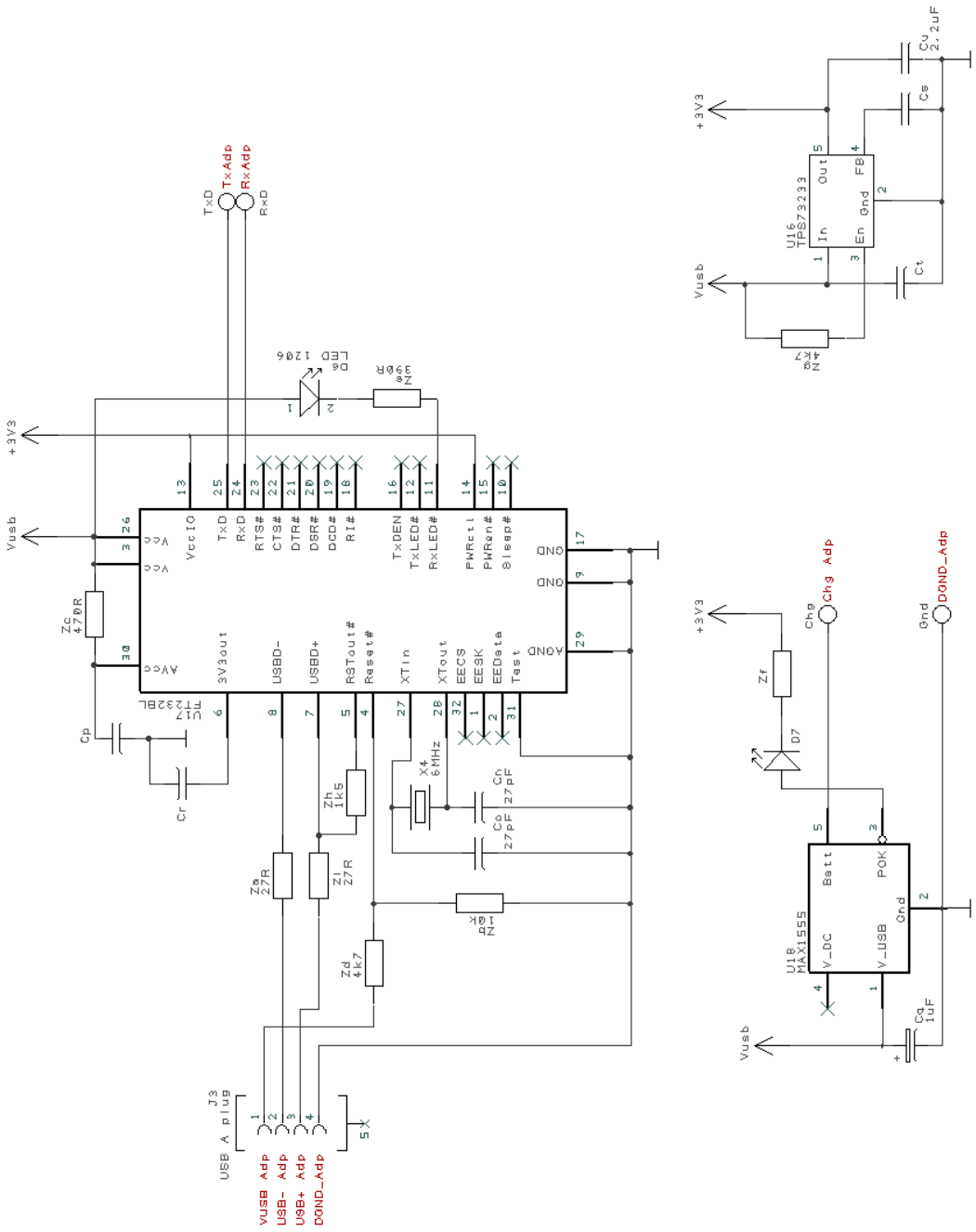
Appendix A - 3: EPMS v1 Auxiliary Module Processor Board Schematic



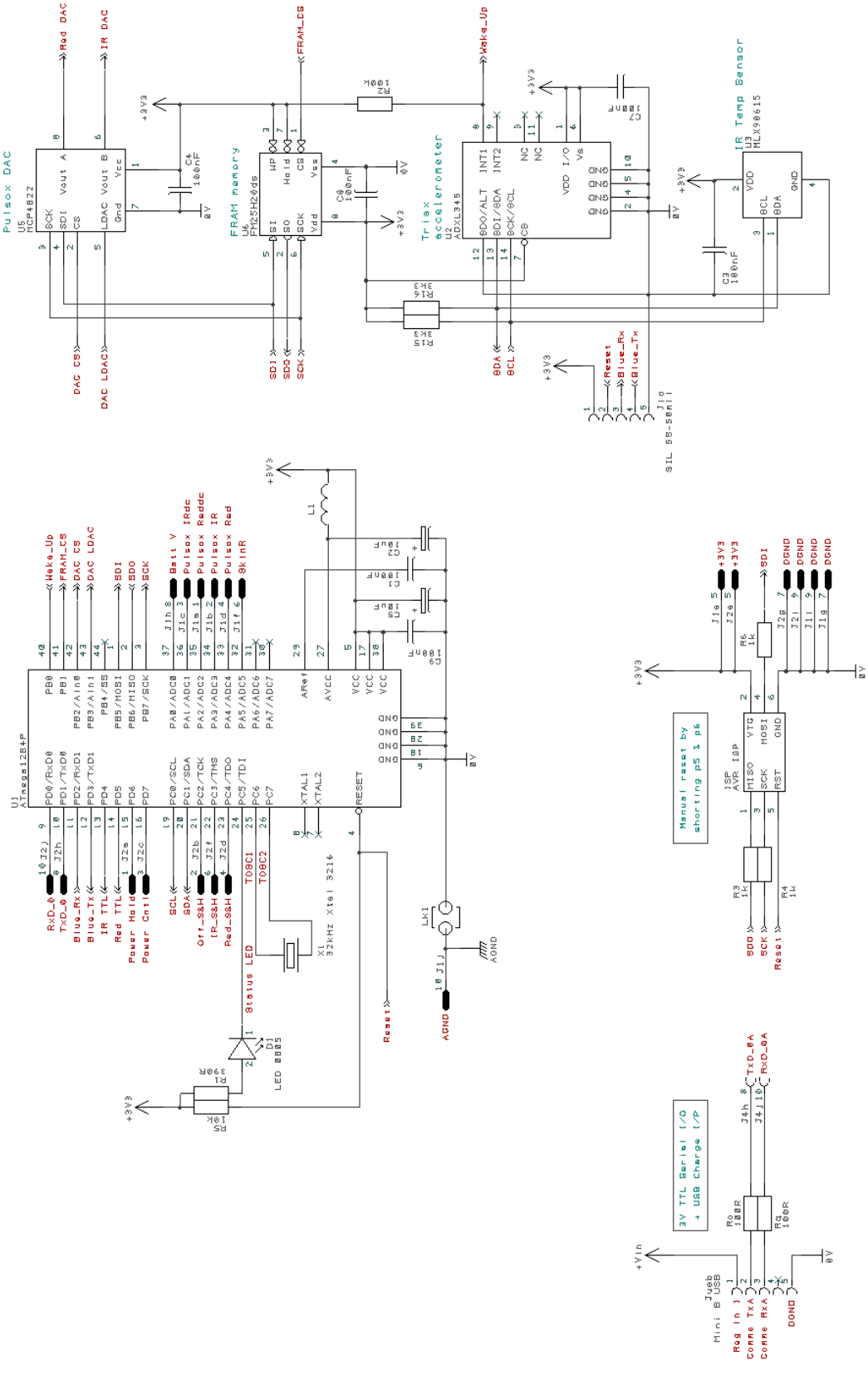
Appendix A - 4: EPMS v1 Auxiliary Module Interface Board Schematic



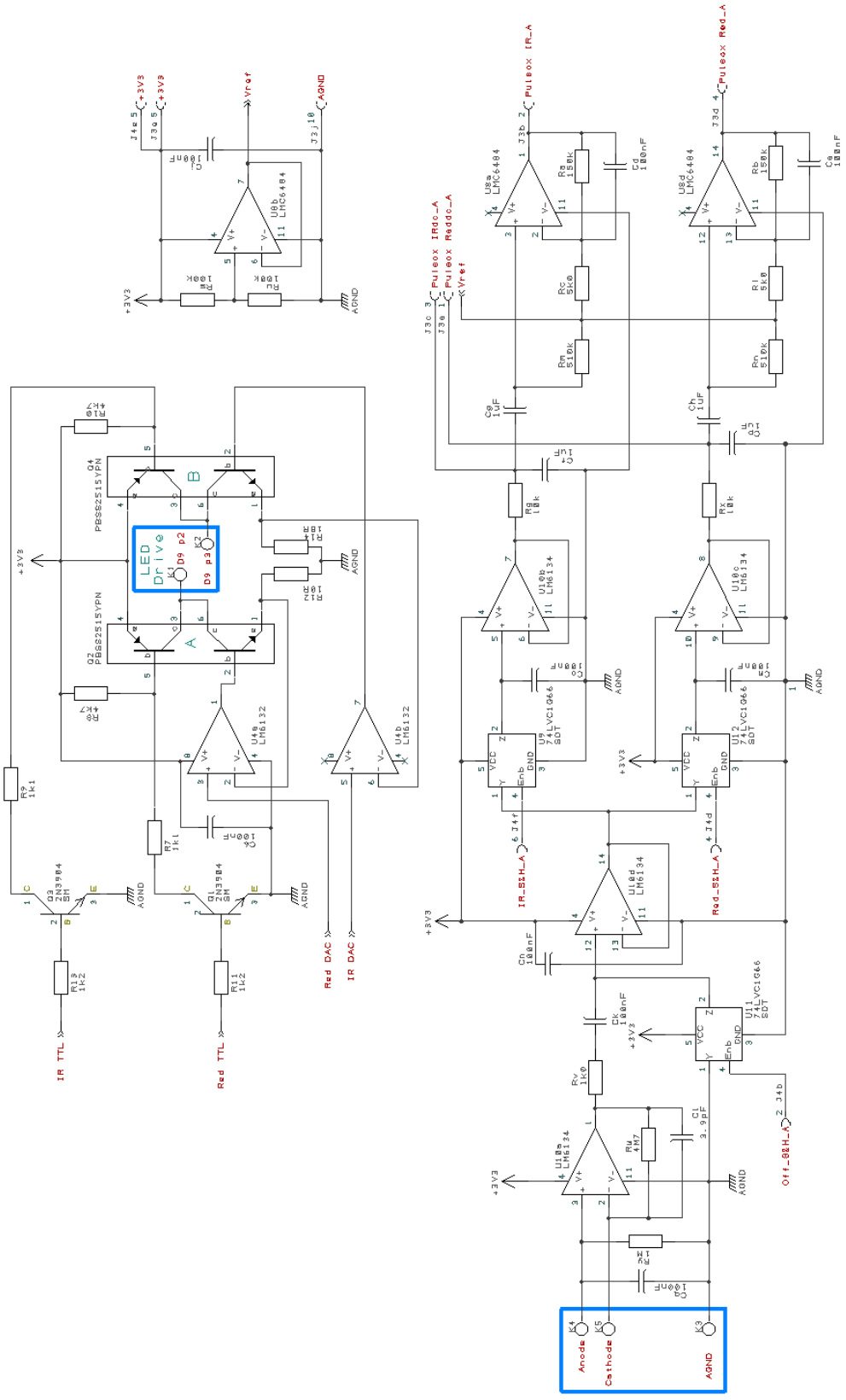
Appendix A - 5: EPMS v1 Adapter Board Schematic



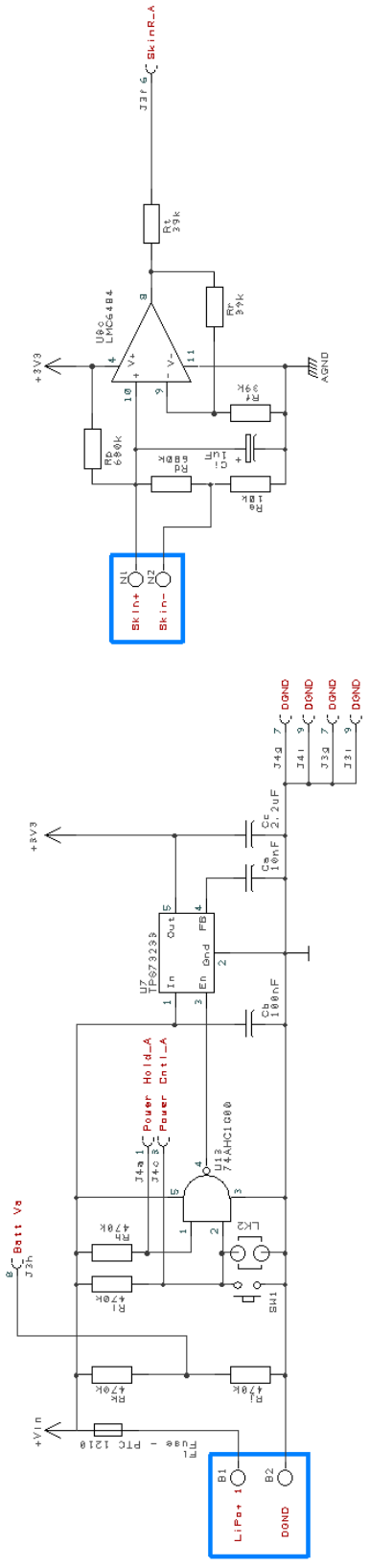
Appendix B - 1: EPMS v2 Ear Module Processor Board Schematic



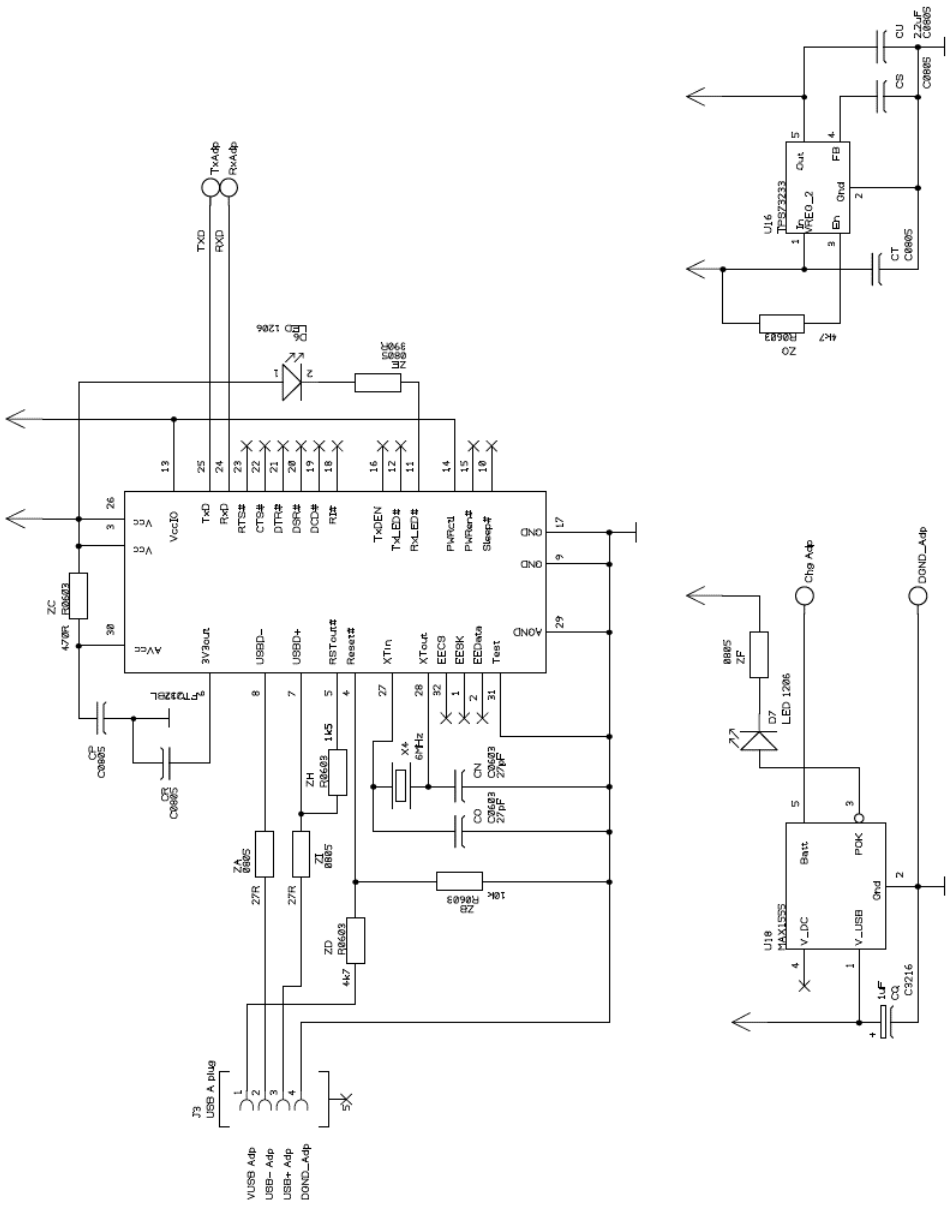
Appendix B - 2: EPMS v2 Ear Module Pulse Oximeter Schematic



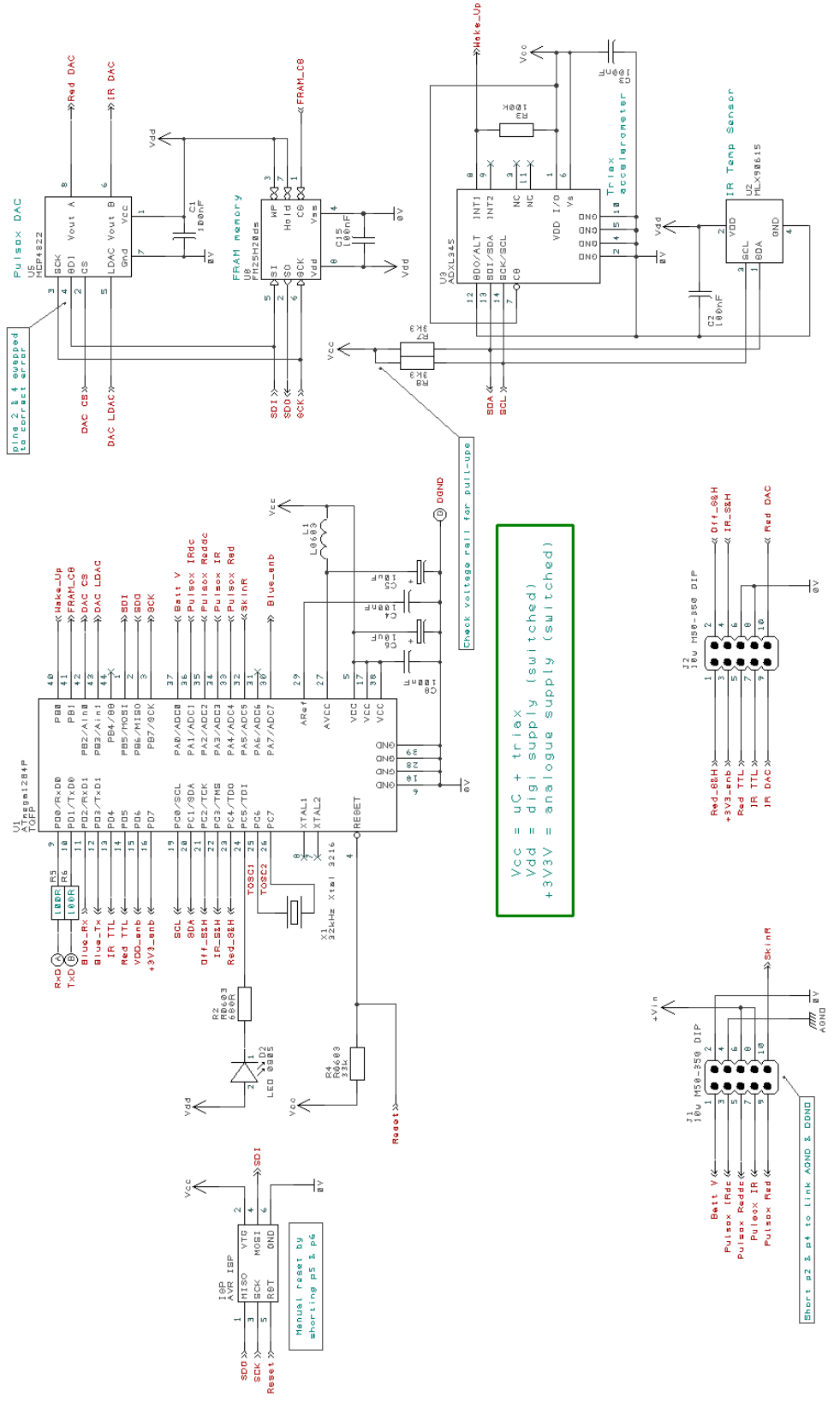
Appendix B - 3: EPMS v2 Ear Module Skin Resistance and Power Supply Schematic



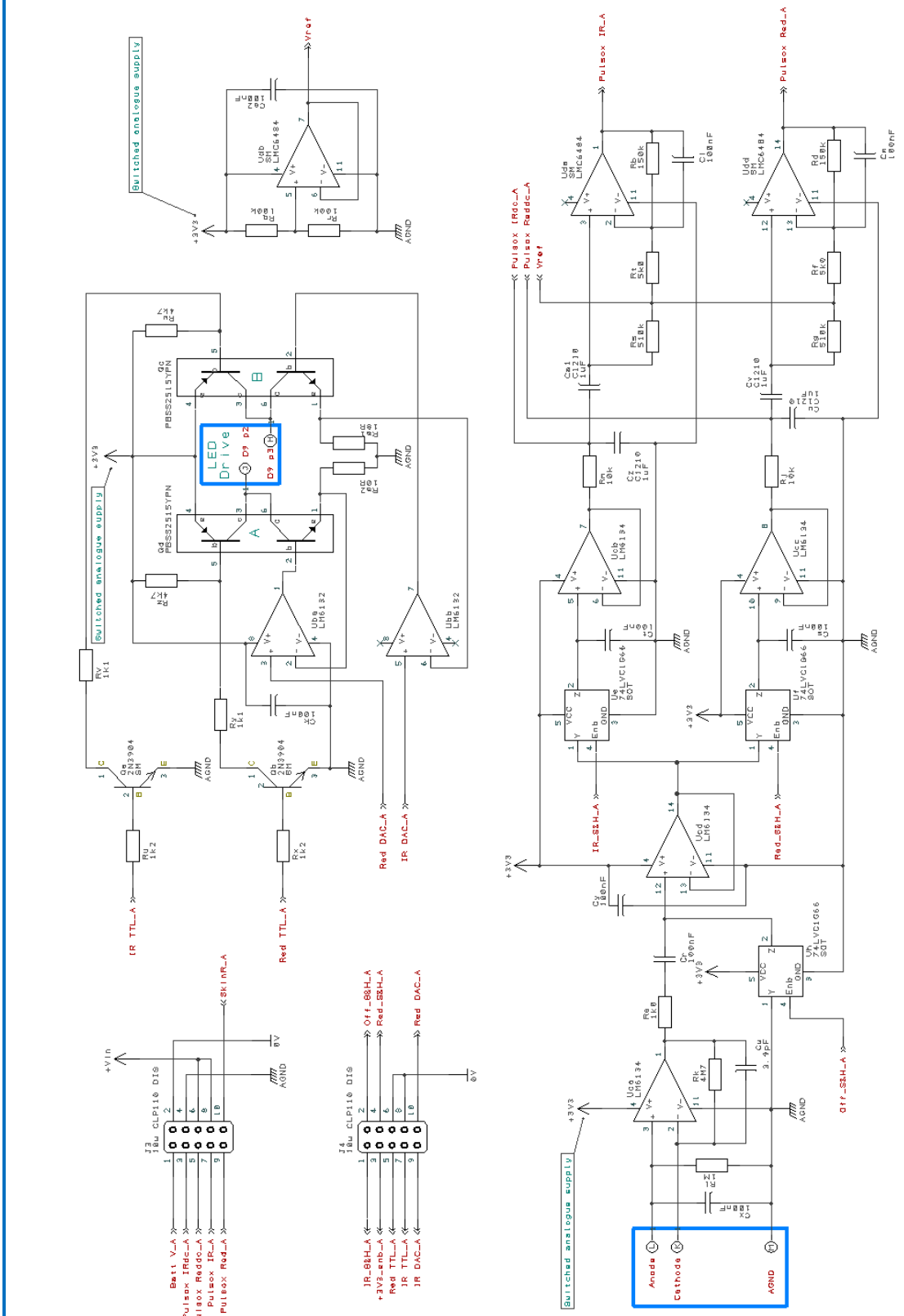
Appendix B - 4: EPMS v2 Ear Module Bluetooth Board Schematic



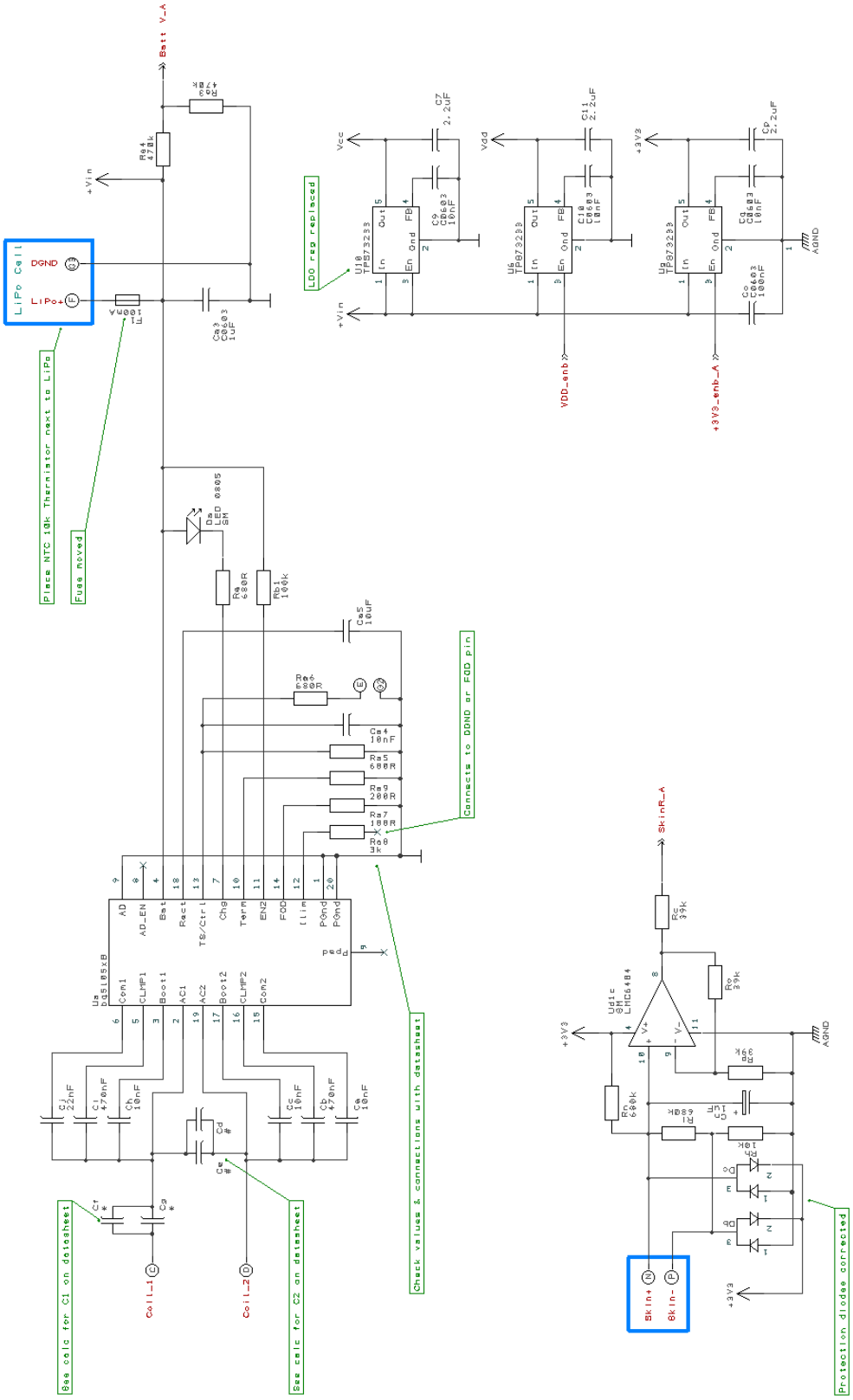
Appendix C - 1: EPMS v3 Ear Module Processor and Digital Schematics



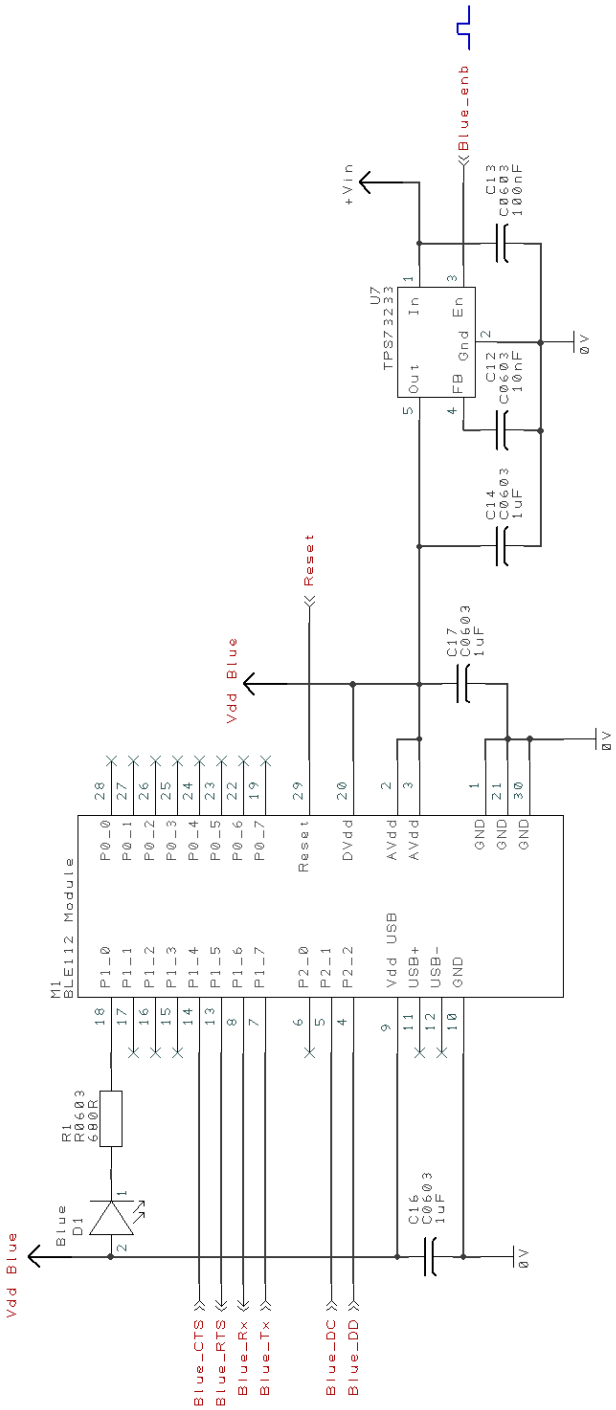
Appendix C - 2: EPMS v3 Ear Module Pulse Oximeter Schematic



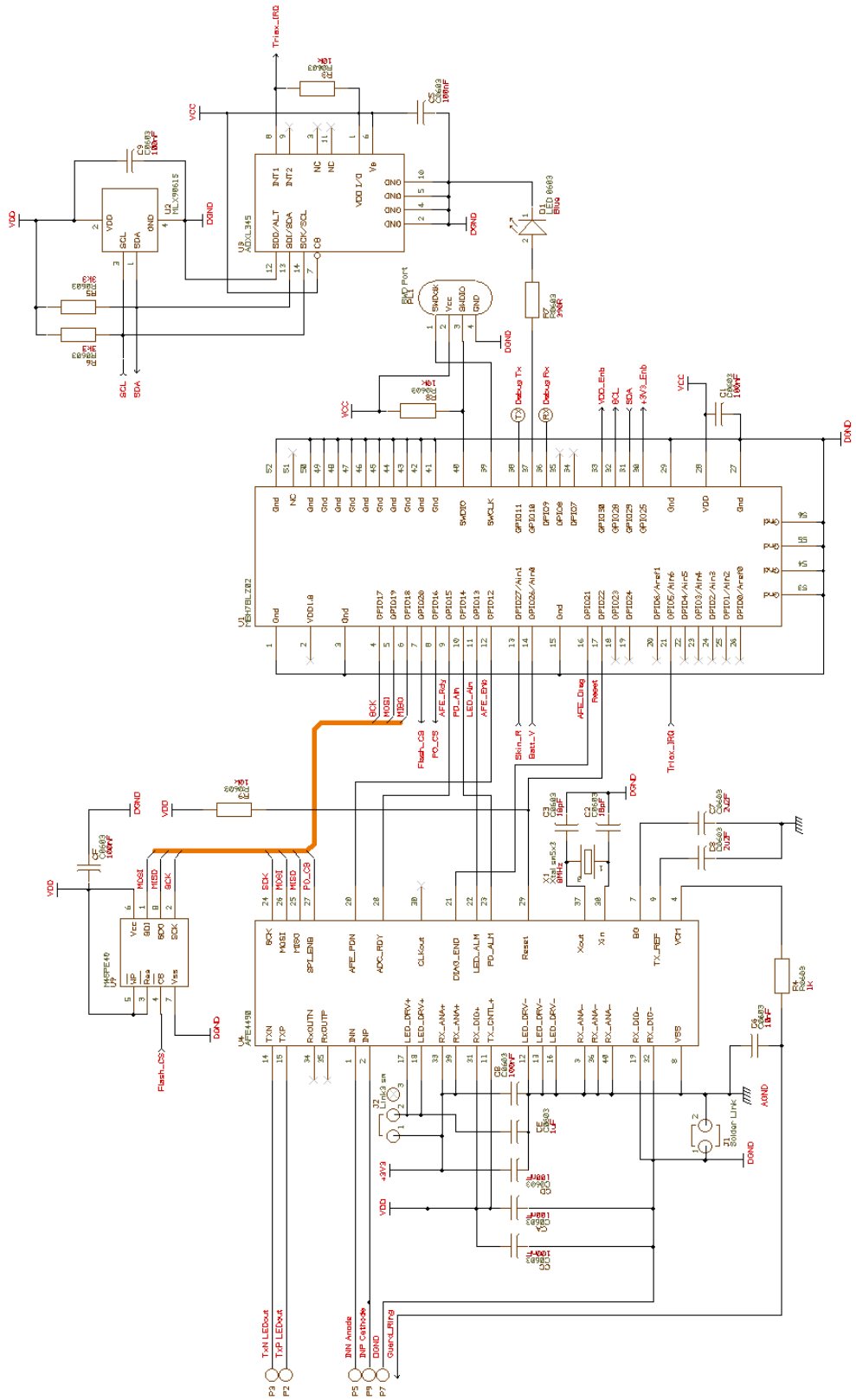
Appendix C - 3: EPMS v3 Ear Module Skin Resistance and Power Supply Schematic



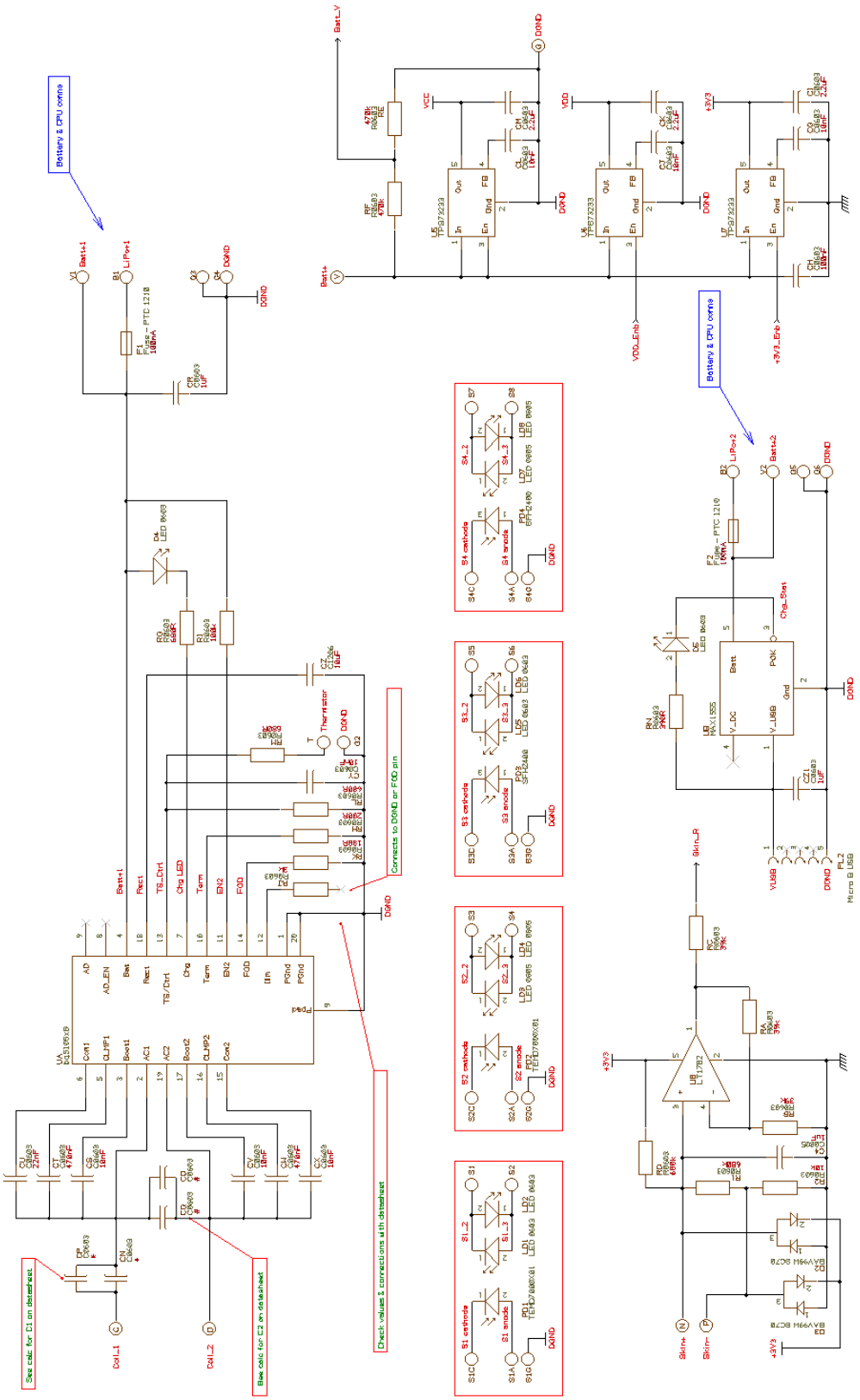
Appendix C - 4: EPMS v3 Ear Module Bluetooth Board Schematic



Appendix D - 1: EPMS v4 Ear Module Analogue Circuit Schematic



Appendix D - 2: EPMS v4 Ear Module Analogue Circuit Schematic



Cranfield University Health Research Ethics Committee Approval Form

CUHREC Ref:03/10
To be completed by committee secretary

Principal Investigator: Dave Pitts
Title of Study: Assessing the use of a clavicle-mounted triaxial accelerometer for respiratory monitoring

Before submitting the ethics approval form, please ensure you have completed all sections and provided all supporting documents.

The following list should be checked, completed and submitted with your application:

Document	Enclosed? Delete as applicable	Version/date	Checked by CUHREC
Completed Approval Form	Yes	DGP100728 EF / 28-07-2010	☐
Full Study Protocol	Yes	DGP100728 SP / 28-07-2010	☐
Volunteer Information Sheet*	Yes	DGP100708 SIS / 08-07-2010	☐
Volunteer Consent Form*	Yes	DGP100728 VCF / 28-07-2010	☐
Patient Information Sheet*	N/A		☐
Patient Consent Form*	N/A		☐
Invitation Letters/E-mails*	Yes	DGP100728 SVE / 28-07-2010	☐
Investigator Signatures	Yes	30/07/2010	☐

* - must be presented on headed paper

(Please read the guidance document 'CUHREC Application Process and Requirements for Approval' carefully before completing this form)

Checked by:

Principal Investigator

Signature_____ Date_____

Administrator

Signature_____ Date_____

Investigator Details

Principal Investigator Staff

If student please justify

Name: Dave Pitts

Department: Health

E-mail: d.g.pitts@cranfield.ac.uk Tel: 07775 884782

Investigator 2 Student

Name: Mitesh Patel

Department: Health

E-mail: mitesh.patel.s06@cranfield.ac. Tel: (01234) 75 8306

Investigator 3 Staff

Name: Prof. Richard Aspinall

Department: Health

E-mail: r.aspinall@cranfield.ac.uk Tel: 01234 758343

External Collaborator / Investigator

Name:

Address:

E-mail: Tel:

(Any further information can be submitted on a separate sheet)

What is the proposed start date and duration of this project?

Start date: (DD/MM/YY) 16/08/10

Proposed duration: Years 3 Months

Short Description of Study

This study is designed to ascertain whether respiration rate can be measured non-invasively with an accelerometer motion sensor via clavicle movement.

Aim(s) of Project

The aim of this project is:

1. To test and validate the hypothesis of measuring respiration rate from clavicle motion.

2. To examine whether it is possible to determine deep and shallow breaths by analysing the period, amplitude and slope of the clavicle sensor signal. This will be validated against the response of a Breathotron's flow sensor.

Project Background – Scientific Justification

An increased respiration rate is a well-established marker of febrile and pulmonary infection; e.g. a rate of 25 breaths per minute is a strong indicator of pneumonia (McFadden, J.P., Price, R.C., Eastwood, H.D., & Briggs, R.S. 27-2-1982 Br.Med.J. (Clin.Res.Ed) 626-627). This is normally measured using a device such as a capnograph, which monitors breath, or by observation.

Ambulatory respiration sensors are available but, for the most part, are based upon an expanding chest band or derived from a multi-electrode electrocardiograph response. Neither of these methods are ideal; one can be quite cumbersome whilst the other requires the electrodes have good electrical contact and reasonably accurate placement.

An accelerometer is capable of detecting and measuring small dynamic changes in movement and in a triaxial form, if the vector product is considered, it should be possible to operate with the device in any orientation. Such a configuration should facilitate use as a respiration sensor if placed upon an area of the body that experiences respiratory movement. The clavicle is ideal for such; its proximity to the carotid artery opens up the future possibility of a discrete multiple-sensor device giving additional pulse and oximetric measurements.

The knowledge obtained from this study will be used to develop this technology further for use in medical monitoring.

Section 2 - Recruitment

NOTE: You must include a copy of invitations (e-mails/letters) to be used for recruiting within this study along with your volunteer information sheet and consent form

Volunteer population

Where will volunteers be recruited? Internally: ☒ Externally: ☐

Internal

Schools: Health ☒ SAS ☐ SOE ☐ SOM ☐ Shrivenham ☐

Population: Staff ☒ Number Students ☒ Number

Total number required: 8

External

NHS ☐ General Public ☐ Other ☐

If other, please specify

Number required:

NRES Approval

Will your study require NRES approval? (e.g. NHS linked projects) No

If yes, state which committee:

Will the University be required to act as sponsor for this application? No

Information and consent

Is written consent required for this study? Yes

If no, please state why:

If yes, please answer the questions below.

How will volunteers find out about the study? (Mark all that apply)

E-mail ☒ Advert ☐ Clinician ☐

How will volunteers be informed about the study? (Mark all that apply)

Information sheet ☒ Personal discussion ☒

Will there be at least 24 hours between invitation and consent? Yes

If no, please state why:

Who will be responsible for taking consent?Dave Pitts

Briefly describe the consent process: After reading the Study Information Sheet, contacting and then discussing the experiment with the Principal Investigator, those wishing to particpate will be asked to sign a consent form.

Volunteer payment

Will volunteers be paid for participation? No

If yes how much?

Section 3 - Sample / volunteer requirements

NOTE: You must include a full study protocol

Does your study involve: (Mark all that apply)

Collection of human samples	☐	
Intervention/activity	☒	
Participation in an activity	☒	
Questionnaire completion	☐	
Other Physiological measurements	☒	Please specify

Human sample collection
For each volunteer:

Blood ☐ Volume ml Number Frequency

Urine ☐ Volume ml Number Frequency

Saliva ☐ Volume ml Number Frequency

Other ☒ Briefly Explain Physiological measurements (respiratory rate and lung volume), please see the Study Protocol (DGP100728 SP) for details

Other ☐ Briefly Explain

Other ☐ Briefly Explain

Sample Use

How will the samples be collected? Sensors will be monitored and data recorded on a data logger, spirometer results will be entered on a spreadsheet.

Will the samples be anonymised? Yes

If no please state why:

How and where will the samples be stored? No physical samples will be taken; electronic data will be held for subsequent analysis

How will the samples be used? See above

Will remaining samples be destroyed at the end of the study? No

Who will be responsible for destruction of the samples? N/A

If samples will not be destroyed please explain why: No physical samples will be taken; electronic data will be held for subsequent analysis

NOTE: You must include in your protocol all measurements etc. that will be undertaken on the samples, including any external measurements

Volunteer population

State any specific inclusion or exclusion criteria for this study:

Inclusion criteria: Healthy adults aged 18-65 years old

Exclusion criteria: Those with any form of respiratory condition

Intervention/Activity

What will the volunteers be asked to do? Include all measures for minimising risk in this activity: (1) Blow into a spirometer (2) Attach motion sensors to clavicle and chest using non-allergenic tape; they may choose to use a private room and have a colleague of the same gender assist them (3) wear a clean face mask fitted with a flow sensor to monitor respiration

How long will the subject involvement be within the study as a whole? approximately 15 minutes

NOTE: You must include copies of any questionnaires etc. to be used

Section 4 - Data Protection

Will the PI be responsible for the following?:

Consent form storage: Yes

Electronic data storage: Yes

Duration of data storage: Yes

If you answered no to any of the above explain why:

Where will consent forms be kept? In a locked filling cabinet in the Academic Office of the Vincent Building.

If data is to be stored electronically where will it be stored? The data will be stored on a password protected Cranfield networked server. The data will not contain any personal information about the volunteers but will be stored according to a random volunteer number.
The data obtained from the study must be stored securely in a password protected file and this should be auditable, so please provide exact locations for data storage. If this changes, please inform CUHREC

Will data be stored for 5 years or less? Yes

If no, please state why:

Signatures

Principal Investigator ..... Date .....

Investigator 2 ..... Date .....

Investigator 3 ..... Date .....

External Investigator ..... Date .....

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Study Protocol

Assessing the use of a clavicle-mounted triaxial accelerometer for respiratory monitoring

1. Summary

This study will recruit volunteers in order to assess the efficacy of using a low-cost accelerometer motion sensor, as commonly found in Nintendo Wii hand controllers and mobile phones, to measure clavicle movement from which respiratory rate may be derived. Data from a clavicle sensor, a secondary thoracic sensor and a mask-mounted flow sensor, as used in Cranfield Health's Breathotron, will be recorded simultaneously on a data logger for later analysis. It is hoped that the clavicle sensor will be able to monitor respiration rate and give an indication of breathing depth; this will be validated against the flow sensor data. It is envisaged testing each volunteer will take approximately 15 minutes.

The knowledge obtained from this study will be used to develop this technology further for use in medical monitoring and diagnostic devices.

2. Background Information

An increased respiration rate is a well-established marker of febrile and pulmonary infection; e.g. a rate of 25 breaths per minute is a strong indicator of pneumonia *(McFadden, J.P., Price, R.C., Eastwood, H.D., & Briggs, R.S. 27-2-1982 Br.Med.J. (Clin.Res.Ed) 626-627)*. This is normally measured using a device such as a capnograph, which monitors breath, or by observation.

Ambulatory respiration sensors are available but, for the most part, are based upon an expanding band worn around the chest or derived from a multi-electrode electrocardiograph response. Neither of these methods are ideal; one can be quite cumbersome whilst the other requires the electrodes have good electrical contact and reasonably accurate placement.

An accelerometer is capable of detecting and measuring small dynamic changes in movement and in a triaxial form, if the vector product is considered, it should be possible to operate with the device in any orientation. Such a configuration should facilitate use as a respiration sensor if placed upon an area of the body that experiences respiratory movement. The clavicle is ideal in this respect; its proximity to the carotid artery opens up the future possibility of a discrete multiple-sensor device giving additional temperature, pulse and oxygen saturation measurements.

3. Study Objectives

The objectives of this experiment are twofold:

a) To test and validate the hypothesis of measuring respiration rate from clavicle motion.

Cranfield UNIVERSITY

b) To examine whether it is possible to determine deep and shallow breaths by analysing the period, amplitude and slope of the clavicle sensor signal. This will be validated against the response of a Breathotron's flow sensor.

4. Materials

Study Information Sheet
Consent Form
Clean spirometer sampling tubes
Clean Breathotron sampling masks
Non-allergenic sticky tape

5. Subject Inclusion and Exclusion Criteria

Volunteers can be either male or female between the age of 18 and 65. Those with respiratory problems, e.g. asthma, chest infections, hay fever etc., are ineligible for this experiment.

6. Volunteer Recruitment

Volunteers will be recruited from Cranfield Health (both staff and students), using email. The maximum of eight volunteers will be recruited.

6.1 **Recruitment and Admission**

Volunteers will be informed about the opportunity to participate in this research study in which they will be required to be fitted with motion sensors and a breath sampling mask. Interested applicants will be given the Study Information Sheet and Consent Form. If the volunteer has any queries regarding the study, they can ask the Principal Investigator.

6.2 Volunteers are under no obligation to join the study if they do not wish to do so. If, after reading these documents they wish to join the study, they will sign the Consent Form. ExperimentsThey may withdraw at any time.

6.3 The suitability of Volunteers will be checked against the study selection criteria (Section 6).

6.4 Once the documents have been successfully completed, the Volunteer will be deemed to have been admitted to the study.

6.5 The results obtained from this study may be used in a peer reviewed publication.

7. Study Method

Eight volunteers will be recruited for this experiment.

On arrival in the Electronics Laboratory, the Volunteer will be asked to blow into a spirometer to provide reference breath volume data. They will then be asked to attach

Study Protocol Version 2, 28/07/2010 *DGP100728 SP*

one accelerometer motion sensor to their clavicle and a second centrally to their chest using non-allergenic tape; sensor orientation will be as directed by the investigators. Volunteers may prefer privacy when fitting sensors, thus they may choose to use a private room and have a colleague of the same gender assist them. Once fitted, the sensors will be connected to a data logger and checked to ensure correct operation.

The volunteer will be asked to wear a face mask fitted with a flow sensor to monitor respiration; this will be adjusted to provide a tight but comfortable fit. The masks will have been cleaned prior to the experiment (see relevant SOP for cleaning procedure). This will not be removed for the duration of the experiment. The sensor will be then connected to a data logger and checked to ensure correct operation.

The volunteer will be asked to sit and breathe normally for around five minutes. During this time they will be asked periodically to take deeper breaths. On completion, they will remove the mask and sensors and be free to leave. It is anticipated the experiment will take approximately 15 minutes overall to complete.

8. Discontinuation
Volunteers can leave the study at any time without giving a reason.

9. Confidentiality
All data will be anonymised.

10. Data Analysis
Results obtained from the experiment shall be subjected to analysis using the software package Matlab, and/or Microsoft Excel.

11. Ethical Statement
Ethical approval will be obtained from the Cranfield University Health Research Ethics Committee.

STUDY INFORMATION SHEET

Assessing the use of a clavicle-mounted triaxial accelerometer for respiratory monitoring

The purpose of this document is to provide you (the Volunteer) with enough information to assist you in making a decision to take part in this study. If this document does not answer your questions to your satisfaction, please do not hesitate to contact the Principal Investigator (Dave Pitts).

Introduction
An increased respiration rate is a well-established marker of febrile and pulmonary infection. This is normally measured using a device such as a capnograph (as used by anaesthetists) or by observation. This study is designed to ascertain whether respiration rate can be measured non-invasively with a low-cost accelerometer motion sensor via clavicle movement.

Recruitment Criteria
You must be a healthy adult aged 18 to 65 years old. Those with respiratory problems, e.g. asthma, chest infections, hay fever etc., are ineligible for this experiment.

What you will be asked to do
If you decide to take part in the study, you will be asked to do the following:

a) You will be asked to blow into a spirometer to provide reference breath volume data.
b) You will be asked to attach one accelerometer motion sensor to your clavicle and a second centrally to your chest using non-allergenic tape. You may choose to use a private room and have a colleague of the same gender assist you with this. Once fitted, the sensors will be connected to a data logger and checked to ensure correct operation.
c) You will be asked to wear a clean face mask fitted with a flow sensor to monitor respiration; this will be adjusted to provide a tight but comfortable fit. The sensor will be connected to a data logger and checked to ensure correct operation
d) You will be asked to stand and breathe normally for around five minutes. During this time you will be asked periodically to take deeper breaths.
e) On completion, you will remove the mask and sensors and be free to leave.

It is anticipated the experiment will take approximately 15 minutes overall to complete.

If at any time you feel any discomfort, please inform one of the investigators, and the experiment will be terminated.

You are under no obligation to join the study if you do not wish to do so. You may withdraw your participation in the study at any point without reason. Data collected from this study will be stored on a personal computer on a password protected Cranfield networked server. The data will not contain any personal information about the volunteers but will be stored according to a random volunteer number. The results of this study will be published in a peer-reviewed journal and may form part of Dave Pitts' PhD.

There is no payment for taking part in this study.

If you are unhappy with the manner in which you have been treated, or the experiment has been conducted, please do not hesitate to contact the Head of School, Prof Joe Lunec (j.lunec@cranfield.ac.uk, +44 (0)1234 758300).

Volunteers expressing interest will need to sign a Consent Form.

Contact Information

Dave Pitts
Research Fellow
Cranfield Health
Vincent Building
Cranfield University
Cranfield
Bedfordshire
MK43 0AL

Telephone: 07775 884782
E-mail: d.g.pitts@cranfield.ac.uk

Prof Richard Aspinall
Professor of Translational Medicine
Cranfield Health
Vincent Building
Cranfield University
Cranfield
Bedfordshire
MK43 0AL

Telephone : 01234 758343
Fax: +44 (0) 1234 758380
E-mail: r.aspinall@cranfield.ac.uk

Sample Volunteer E-Mail

Dear Colleague,

I would like to invite you to take part in a study investigating the use of a motion sensor placed upon the clavicle to monitor respiration rate.

Volunteers can be either male or female between the ages of 18 and 65. Those with respiratory problems, e.g. asthma, chest infections, hay fever etc., should not apply to participate in this experiment.

You would be asked to blow into a spirometer to provide reference breath volume data, then attach motion sensors to your clavicle and chest, and wear a face mask fitted with a flow sensor to monitor respiration. Once seated, the sensors would be connected to a data logger and you would be asked to breathe normally for around five minutes. During this time you will be asked periodically to take deeper breaths.

On completion, you would be able to remove the mask and sensors and be free to leave. It is anticipated the experiment will take approximately 15 minutes overall to complete.

Further details are available in the attached Study Information Sheet. If you are interested in participating in the study please contact me.

Yours Sincerely,

Dave Pitts MSc
Research Fellow
Cranfield Health
Vincent Building
Cranfield University
Cranfield
Bedfordshire
MK43 0AL

email: d.g.pitts@cranfield.ac.uk
Tel: 07775 884782

email: d.g.pitts@cranfield.ac.uk
email: r.aspinall@cranfield.ac.uk

Centre: Cranfield University, Cranfield campus.
REC Reference Number:
Volunteer Identification Number for this study: .....

CONSENT FORM

Title of Project: ***Assessing the use of a clavicle-mounted triaxial accelerometer for respiratory monitoring***

Name of Researcher: *Dave Pitts*

(Please tick box)

1. I confirm that I have read and understood the information sheet that has been provided for the study named above. I can confirm that I have been given opportunity to ask questions regarding the study, and that they have been answered to my satisfaction. ☐
2. I understand that my participation in this study is entirely voluntary, and I am free to withdraw my consent at any time without giving any reason. My legal rights shall not be affected. ☐
3. I understand that data (results) acquired during this study may be looked at by authorized individuals (project supervisors) from Cranfield University and may be used in a peer-reviewed article. I give my consent for these individuals to access my records. ☐
4. I agree to take part in the above-mentioned study. ☐

.....	.....	.....
Name of volunteer	**Date**	**Signature**
.....	.....	.....
Researcher	**Date**	**Signature**

Original (to be filed) ☐ Volunteer Copy ☐ (please tick)
Version 2 Date: 28/07/10 *DGP100728 VCF*

Cranfield Health

Vincent Building
Cranfield University
Cranfield
Bedfordshire
MK43 0AL
England
T: +44 (0)1234 756300
F: +44 (0)1234 756380
www.cranfield.ac.uk/health

7th March 2011

Dear Dave

Project Reference No 03/10: Assessing the use of a clavicle-mounted triaxial accelerometer for respiratory monitoring

Thank you for your letter regarding the possible extension of this study.

I am able to confirm that an extension to your study can now be granted by Chairman's action until the 16th August 2011.

Yours sincerely

S C Morgan

Dr Sarah Morgan
Vice-Chairman,
Cranfield University Health Research Ethics Committee

The Queen's Anniversary Prizes
For Higher and Further Education
2007

Cranfield UNIVERSITY

Cranfield University Health Research Ethics Committee Approval Form

CUHREC Ref:02/12
To be provided by CUHREC administrator

Principal Investigator: Selim Cellek
Title of Study: Validation of an Ear-Worn Vital Signs Monitoring Device

Before submitting the ethics approval form, please ensure you have completed all sections and provided all supporting documents.

The following list should be checked, completed and submitted with your application:

Document	Enclosed? Select as appropriate	Version/date	Checked by CUHREC
Completed Approval Form	Yes	DGP140812 EF (12/08/14)	☐
Full Study Protocol	Yes	DGP140812 SP (12/08/14)	☐
Volunteer Information Sheet*	Yes	DGP140812 SIS (12/08/14)	☐
Volunteer Consent Form*	Yes	DGP140812 VCF (12/08/14)	☐
Patient Information Sheet*	N/A		☐
Patient Consent Form*	N/A		☐
Invitation Letters/E-mails*	Yes	DGP140812 SVE (12/08/14)	☐
Investigator Signatures	No		☐

* - must be presented on headed paper

(Please read the guidance document 'CUHREC Application Process and Requirements for Approval' carefully before completing this form)

Checked by:

Cranfield UNIVERSITY

CUHREC Administrator

Signature_____ Date_____

Cranfield UNIVERSITY

Section 1 : Investigator Details and Study Background

Principal Investigator Staff

Name: Dr Selim Cellek

Department: SOE

E-mail: s.cellek@cranfield.ac.uk Tel: (01234) 758319

Investigator 2 Staff

Name: Dave Pitts

Department: SOE

E-mail: d.g.pitts@cranfield.ac.uk Tel: 07775 884782

Investigator 3 Staff

Name:

Department: SOE

E-mail: Tel:

External Collaborator / Investigator

Name:

Address:

E-mail: Tel:

(Any further information can be submitted on a separate sheet)

What is the proposed start date and duration of this project?

Start date (DD/MM/YY): 01/09/14

Proposed duration: 0 Years 6 Months

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Short Description of Study **[max 200 characters]**

This study is designed to validate vital signs readings taken by Cranfield Health's Ear-worn Personal Monitoring System (EPMS)

Aim(s) of Project **[max 500 characters]**

The EPMS is able to take simultaneous readings of core body temperature, heart rate(HR), blood oxygen saturation (SpO2), skin conductivity and activity level via integrated sensors. The aim of this study is to validate EPMS temperature, HR and SpO2 readings of participants against those from reference devices to determine the veracity of the system's performance. Volunteers would be expected to take a number of daily representative measurements over the course of the study whilst keeping a study diary to record various details that may be relevant to the recorded physiological data.

Project Background – Scientific Justification **[max 1500 characters]**

Vital signs (VS) are a range of physiological measures, traditionally temperature, blood pressure, pulse and respiratory rate, which form a key component in monitoring patient condition. Although there is variation between individuals, the baseline readings for healthy adults fall within a broadly similar range. Deviation from an individual's normal basal values could indicate illness or infection.

Emergency hospital admissions or those in critical care may be subject to continuous monitoring of at least one parameter or assessed every 15 to 30 minutes initially, extending to a period of every four hours. During triage, VS monitoring can assist in decision making when prioritising critical treatment. Checking for VS abnormalities prior to discharge has been shown to reduce the risk of hospital readmission.

Outside of the hospital environment, observations are rarely taken. Typically, each parameter requires the use of a separate monitoring device and careful adherance to a manufacturer's guidelines to ensure correct use and reliable readings. The EPMS is intended for use by those without clinical skills or knowledge for the simultaneous monitoring of multiple parameters, greatly facilitating the measurement process. By taking daily samples at regular intervals, an individual's normal baseline readings may be captured. This offers the potential for diagnostic use in much the same way as a nurse's observations; hence the onset of a febrile infection may be detected.

EPMS readings are transmitted wirelessly via Bluetooth to a paired internet-enabled mobile platform (smartphone or tablet etc.) where they are displayed and may be uploaded and stored on a remote server. On a fully-fledged commercial system, this would be available for clinical assessment where an individual's VS trends could analysed by a clinician or intelligent clinical algorithm for signs of infection - something that could be of value for long-term care or vulnerable groups.

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Section 2 : Recruitment

NOTE: You must include a copy of invitations (e-mails/letters) to be used for recruiting within this study along with your volunteer information sheet and consent form

Volunteer population

Where will volunteers be recruited? Internally: ☒ Externally: ☐

Internal

Schools: Health ☐ SAS ☒ SOE ☒ SOM ☐ Shrivenham ☐

Population: Staff ☒ Students ☒ Total number required: 25

External

NHS ☐ General Public ☐ Other ☐

If other, please specify

Total number required:

NRES Approval

Will your study require NRES approval? (e.g. NHS linked projects) No

If yes, state which committee:

Will the University be required to act as sponsor for this application? Yes

Information and consent

Is written consent required for this study? Yes

If no, please state why:

If yes, please answer the questions below.

How will volunteers find out about the study? (Mark all that apply)

E-mail ☒ Advert ☐ Clinician ☐ Other ☒ Please specify Personal contact

How will volunteers be informed of the study details? (Mark all that apply)

Information sheet ☒ Personal discussion ☒

Will there be at least 24 hours between invitation and consent? Yes

If no, please state why:

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Who will be responsible for taking consent?Dave Pitts

Briefly describe the consent process: Having read the study information sheet and met with the investigators, subjects will be invited to give their written consent and join the study. They are under no obligation to join the study if they do not wish to do so. Consent will be taken by an investigator at least 24 hours prior to participation in the study. They may withdraw at any time.

Volunteer recompense

Will volunteers be recompensed for their time? No

If yes, how

Section 3 : Sample / volunteer requirements

NOTE: You must include a full study protocol and any other relevant documentation.

Does your study involve: (mark all that apply)

Collection of human samples	☐ Complete section 3A
Intervention	☐ Complete section 3B
Participation in an activity	☒ Complete section 3C
Questionnaire completion	☒ Complete section 3D
Other	☐ Complete section 3E

Inclusion / Exclusion criteria

State any specific inclusion or exclusion criteria for this study:

Inclusion criteria: 18-65 year old adults who consider themselves to be in good health

Exclusion criteria: Those not meeting the inclusion critria or develop an illness prior to joining the study

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Section 3A : Human sample collection, storage and use
For each volunteer:

Blood	☐	Vol	ml	Frequency	Total No.
Urine	☐	Vol	ml	Frequency	Total No.
Saliva	☐	Vol	ml	Frequency	Total No.
Other	☐	Give details			
Other	☐	Give details			
Other	☐	Give details			

How and where will the samples be collected?

Will the samples be anonymised? Yes

If no please state why:

How and where will the samples be stored? *All samples should be appropriately labelled, including unique CUHREC identifier.*

How will the samples be used?

Will remaining samples be destroyed at the end of the study? Yes

Who will be responsible for destruction of the samples?

If samples will not be destroyed please explain why:

NOTE: You must include in your study protocol all measurements etc. that will be undertaken on the samples, including any measurements made in external laboratories.

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Section 3B : Intervention

What will the volunteers be asked to do? Include all measures for minimising risk in this activity:

How long will the subject involvement be within the study as a whole?

Section 3C : Activity

What will the volunteers be asked to do? Include all measures for minimising risk in this activity: Allow their vital signs to be measured non-invasively with prototype and reference instruments. Readings will only be seen by Investigators

How long will the subject involvement be within the study as a whole? 10 to 40 mins a day for 5 days

Section 3D : Questionnaire [you must include copies of your questionnaire]

Has the questionnaire been validated? : Yes
If yes, please give details : Trialled by University staff

How will the questionnaire be administered? : Completed by investigator

Section 3E : Other

What will the volunteers be asked to do? Include all measures for minimising risk in this activity:

How long will the subject involvement be within the study as a whole?

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Section 4 : Data Protection

Will the PI be responsible for the following?: Anonymisation of subject identifiable data : Yes Consent form storage: During study Yes Post study Yes Project data storage: During study Yes Post study Yes If you answered no to any of the above explain why:

How will consent forms be stored? In a locked drawer/filing cabinet If non-anonymised data is to be stored electronically where will it be stored? All electronically held data will be anonymised The data obtained from the study must be stored securely in a password protected file and this should be auditable, so please provide exact locations for data storage ie named computer. If this changes, please inform CUHREC.

For how long will data be stored ? 5 Years If less than 5 years, please state why: Who will be responsible for data destruction ? Dr Selim Cellek (PI)

Section 5 : Signatures

Principal Investigator ..... Date .....

Investigator 2 ..... Date .....

Investigator 3 ..... Date .....

External Investigator ..... Date .....

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Study Protocol

Validation of an Ear-Worn Vital Signs Monitoring Device

1. Summary

Cranfield's Ear-worn Personal Monitoring System (EPMS) is able to take simultaneous readings of core body temperature, heart rate (HR), blood oxygen saturation (SpO2), skin conductivity and activity level via integrated sensors. The aim of this study is to validate EPMS temperature, HR, SpO2 and skin conductivity readings of participants against those from reference devices to determine the veracity of the system's performance. Volunteers would be expected to take a number of daily representative measurements over the course of the study whilst keeping a study diary to record various details that may be relevant to the recorded physiological data.

The knowledge obtained from this study will be used to develop this technology further for use in medical monitoring.

2. Background Information

Vital signs (VS) are a range of physiological measures, traditionally temperature, blood pressure, pulse and respiratory rate, which form a key component in monitoring patient condition [1]. Although there is variation between individuals, the baseline readings for healthy adults fall within a broadly similar range. Deviation from an individual's normal baseline values could indicate illness or infection [2]. Values considered normal for the adult population however can differ from those in the elderly, leading to increased patient risk [3].

Emergency hospital admissions or those in critical care may be subject to continuous monitoring of at least one parameter or assessed every 15 to 30 minutes initially, extending to a period of every four hours [1]. When used as part of the screening process during triage, VS monitoring can assist in decision making when prioritising critical treatment [4]. Checking for VS abnormalities prior to emergency department discharge has been shown to result in a reduced risk of readmission [5].

Outside of the hospital environment, whether as an outpatient, member of an at-risk group, in long term care or normally healthy, observations are infrequently or rarely taken. Typically, each parameter requires the use of a separate monitoring device and careful adherance to a manufacturer's guidelines to ensure correct use and reliable readings. The EPMS is intended for use by those without clinical skills or knowledge and can simultaneously monitor multiple parameters, greatly facilitating the measurement process. By taking daily samples at regular intervals, an individual's normal baseline readings may be captured - with allowances made for the circadian cycle. Measurements made relative to the adjusted circadian baseline have the potential for diagnostic use in much the same way as a nurse's observations; hence the onset of a febrile infection may be detected.

EPMS readings are transmitted wirelessly via Bluetooth to a paired internet-enabled mobile platform (smartphone or tablet etc.) where they are displayed and uploaded and stored on a remote server. On a fully-fledged commercial system, this would be available for clinical assessment where an individual's VS trends could analysed by a clinician or intelligent clinical algorithm for signs of infection - something that could be of value for long-term care or vulnerable groups.

1. *Evans, D., Hodgkinson, B. & Berry, J. 2001. Vital signs in hospital patients: a systematic review. International journal of nursing studies, 38, 643-650.*
2. *Harries, A. D., Zachariah, R., Kapur, A. Et al 2009. The vital signs of chronic disease management. Transactions of the Royal Society of Tropical Medicine and Hygiene, 103, 537-540.*
3. *Wolf, L. 2007. How Normal are "Normal Vital Signs"? Effective Triage of the Older Patient. Journal of Emergency Nursing, 33, 587-589.*
4. *Cooper, R. J., Schriger, D. L., Flaherty, H. L., et al. 2002. Effect of vital signs on triage decisions. Annals of Emergency Medicine, 39, 223-232.*
5. *Domagala, S. E. 2009. Discharge Vital Signs: An Enhancement to ED Quality and Patient Outcomes. Journal of Emergency Nursing, 35, 138-140.*

3. Study Aims

This study is designed to validate vital signs readings taken by the EPMS by comparison with reference devices.

4. Subject Inclusion and Exclusion Criteria

a) Study population:
Volunteers should be adults between the ages of 18 and 65 and will be recruited from Cranfield's staff and student population. Numbers will be limited to a maximum of 25 subjects.

b) Specific inclusion and exclusion criteria:
The study is looking to recruit individuals who would consider themselves to be in good health and are free from infection at the time of joining the study.

c) Recruitment process:
Subjects will be invited to join the study by email and personal contact. They will be supplied with a copy of the study information sheet and will meet with the investigators who will address any questions or concerns they may have.

d) Consent process:
Having read the study information sheet and met with the investigators, subjects will be invited to give their written consent and join the study. They are under no obligation to join the study if they do not wish to do so. Consent will be taken by an investigator at least 24 hours prior to participation in the study. They may withdraw at any time.

5. Study Methodology

a) Study Details
Prior to the commencement of the study the investigators will agree a test schedule with each participant, who will then be required to attend the study at appointed times (between one and four times a day, as agreed with each volunteer) for the duration of the experiment. Each subject will select a study number to preserve their anonymity.

The study will be held in a small room or office that offers privacy for study participants. On the volunteer's arrival the Investigator will complete a study questionnaire after asking a series of simple questions (piloted by a number of Cranfield Staff). These include basic demographic data (gender and age range) and factors that may cause temporary changes to or influence an individual's normal readings. The latter questions relate specifically to the hour preceding a monitoring session and require nothing more than yes/no answers. Clarification will be given where necessary:

- Has the Volunteer had a caffeinated/alcoholic drink?
- Eaten a meal or snack?
- Smoked a cigarette?
- Exercised? *(other than normal walking)*
- Taken medication?
- Felt unwell? *(includes headaches, colds, aches and pains)*

Records will be held by the Investigator and updated upon each test session.

Volunteers will then be asked to sit down and fit the EPMS (instruction will be given) which will be worn for up to five minutes to take resting readings. Comparative readings of HR and SpO2 (with a reference pulse oximeter probe upon an ear lobe or finger) will be taken by an investigator.

Once the EPMS readings have been completed, Volunteers will be asked to take up to three temperature measurements using a reference ear thermometer equipped with disposable hygienic filters. Once all measurements have been recorded participants are free to leave.

Readings will only be viewed by the investigators, not the subject, and not discussed.

It is anticipated that each monitoring session will take around ten minutes.

Volunteers can leave the study at any time without giving a reason.

b) Study administration
All recorded data will be anonymised and held electronically, where it will be stored on a password-protected Cranfield server.

6. Data Analysis
A range of statistical methods will be employed in the analysis of anonymised study data using Matlab, Microsoft Excel, Statistica or other similar software packages.

7. Dissemination of information
The results obtained from this study will be used internally to validate and refine the EPMS design. They may also form part of Dave Pitts' PhD study and appear in in peer-reviewed journals and other publications.

8. Ethical issues arising
This is explicitly a comparative study to determine the accuracy of a new vital signs monitoring device against reference instruments. Thus, the volunteers will not be shown or told their readings as this may cause anxiety or lead to misdirected research on the internet. The investigators are not trained clinicians and are neither able nor willing to make any diagnostic judgements.

EPMS data is transmitted wirelessly via Bluetooth Smart technology (also known as Bluetooth Low Energy or BLE) to a mobile device for display and for uploading to a Cranfield server. Each device is paired with a host phone or tablet providing an element of security. Further protection is provided by the fact that only the EPMS App running on the host, which controls the EPMS, is able to decode the data blocks into anything meaningful. The password-protected Cranfield server hosting the data (managed by Cranfield's IT Dept.) offers secure storage.

9. Data protection issues
Consent forms will be stored in a locked filing cabinet. All other data will be anonymised. Records of names v. volunteer reference numbers will not be taken. Study data will be held electronically, where it will be stored on a password-protected Cranfield server. The principal investigator will be responsible for the data and its storage.

STUDY INFORMATION SHEET

Validation of an Ear-Worn Vital Signs Monitoring Device

The purpose of this document is to provide you (the Volunteer) with enough information to assist you in making a decision to take part in this study. If this document does not answer your questions to your satisfaction, please do not hesitate to contact the Principal Investigator (Dr Selim Cellek).

Introduction
Cranfield's Ear-worn Personal Monitoring System (EPMS) is able to take simultaneous readings of core body temperature, heart rate (HR), blood oxygen saturation (SpO2), skin conductivity and activity level via integrated sensors. The aim of this study is to validate the EPMS against comparative readings from reference devices and test system performance. Volunteers would be expected to take a number of daily representative measurements over the course of the study and answer a few simple questions to provide a log of details that may influence readings.

Recruitment Criteria
You must be an adult aged 18 to 65 years old who considers themselves to be in good health and is free from infection at the time of joining the study.

What you will be asked to do
If you decide to take part in the study, you will be asked to do the following:

a) Select a random study number. This preserves your anonymity.
b) On arrival at the study location, a small private room or office, the Investigator will complete a study questionnaire after asking a series of simple questions. These include basic demographic data (gender and age range) and those factors that may cause temporary changes to or influence an individual's normal readings. The latter questions relate specifically to the hour preceding a monitoring session and require nothing more than yes/no answers. Clarification will be given where necessary:
    - Have you had a caffeinated/alcoholic drink?
    - Eaten a meal or snack?
    - Smoked a cigarette?
    - Exercised? (other than normal walking)
    - Taken medication?
    - Felt unwell? (includes headaches, colds, aches and pains)

    Records will be held by the Investigator and updated upon each test session.
c) You will be asked to sit down and fit the EPMS (instruction will be given) which will be worn for up to five minutes to take resting readings.
d) Comparative readings of HR and SpO2 (with a reference pulse oximeter probe upon an ear lobe or finger) will be taken by an investigator.
e) You will then be asked to take up to three temperature measurements using a reference ear thermometer equipped with disposable hygienic filters.

Readings will only be viewed by the investigators and not discussed. Once measurements have been taken you are free to leave.

It is anticipated that each monitoring session experiment will take approximately 10 minutes to complete. There may be up to four daily sessions over five days. The investigators will agree a schedule with each participant prior to them commencing the study.

If at any time you feel any discomfort, please inform one of the investigators, and the experiment will be terminated.

You are under no obligation to join the study if you do not wish to do so. You may withdraw your participation in the study at any point without reason.

Anonymised data collected from this study will be stored on a password-protected Cranfield networked server. This will not contain any personal information about you (other than your age range and gender) and will be stored according to a random volunteer number. The results will be used internally to validate/refine the EPMS design, may be used in peer-reviewed publications and form part of Dave Pitts' PhD study.

Volunteers expressing interest will be asked to sign a Consent Form.
There is no payment for taking part in this study.

If you are unhappy with the manner in which you have been treated, or the experiment has been conducted, please do not hesitate to contact the Head of the Centre for Biomedical Engineering, Dr Charles Wainwright (c.wainwright@cranfield.ac.uk, +44 (0) 1234 758354).

Contact Information

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Dr Selim Cellek
Reader in Translational Medicine
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SATM
Conway House
Cranfield University
Cranfield
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E-mail: s.cellek@cranfield.ac.uk

Volunteer E-Mail

Dear Colleague,

I would like to invite you to take part in a validation study of an ear-worn vital signs monitoring device (EPMS). Volunteers should be between the ages of 18 and 65, in good general health and not suffering from infection at the time of joining the study.

You would be asked to assist the investigator in completing a simple study questionnaire and carrying out non-invasive measurements of your temperature, heart rate and blood oxygen saturation between one and four times a day for five days (by agreement) with the EPMS and commercial reference devices. Each monitoring session should take around 10 minutes.

Further details are available in the attached Study Information Sheet (ref. DGP140812 SIS, dated 12th August 2014). If this does not answer your questions, please do not hesitate to contact me by email or telephone to arrange a meeting discuss the study in more detail.

Yours Sincerely,

Dave Pitts
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Conway House
Cranfield University
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MK43 0AL

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email: d.g.pitts@cranfield.ac.uk
email: s.cellek@cranfield.ac.uk

Centre for Bio-Medical Engineering: Cranfield University, Cranfield campus.
REC Reference Number: 02/12

CONSENT FORM

Title of Project: *Validation of an Ear-Worn Vital Signs Monitoring Device*

Name of Researcher: *Dave Pitts*

	(Please tick box)
1. I confirm that I have read and understood the information sheet *(ref. DGP 140812, dated 12th August 2014)* that has been provided for the study named above. I can confirm that I have been given opportunity to ask questions regarding the study, and that they have been answered to my satisfaction.	☐
2. I understand that my participation in this study is entirely voluntary, and I am free to withdraw at any time without giving any reason. .	☐
3. I understand that anonymised data (results) acquired during this study may be looked at by authorized individuals from Cranfield University and may be used in a peer-reviewed publication and/or PhD thesis. I give my consent for these individuals to access my records.	☐
4. I agree to take part in the above-mentioned study.	☐

.....	.....	.....
Name of volunteer	**Date**	**Signature**
.....	.....	.....
Researcher	**Date**	**Signature**

Original (to be filed) ☐ Volunteer Copy ☐ (please tick)
Version Date: 12/08/2014 *DGP140812 VCF*

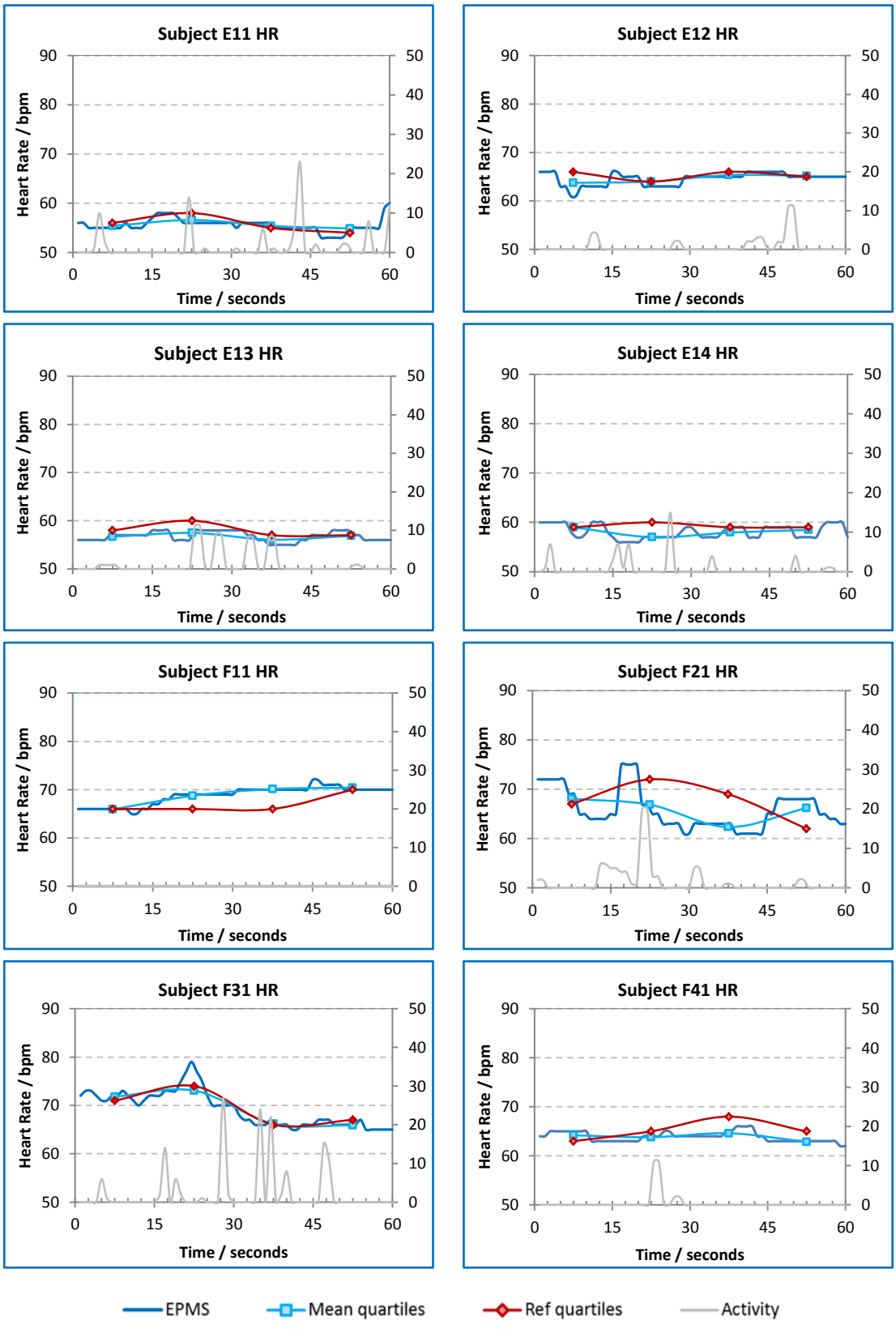
From: Bevan, Ruth
Sent: 17 September 2014 09:42
To: Pitts, Dave
Cc: Cellek, Selim
Subject: CUHREC Approval

Hi Dave
Just to let you know that your CUHREC application has been fully approved and the study can go ahead.

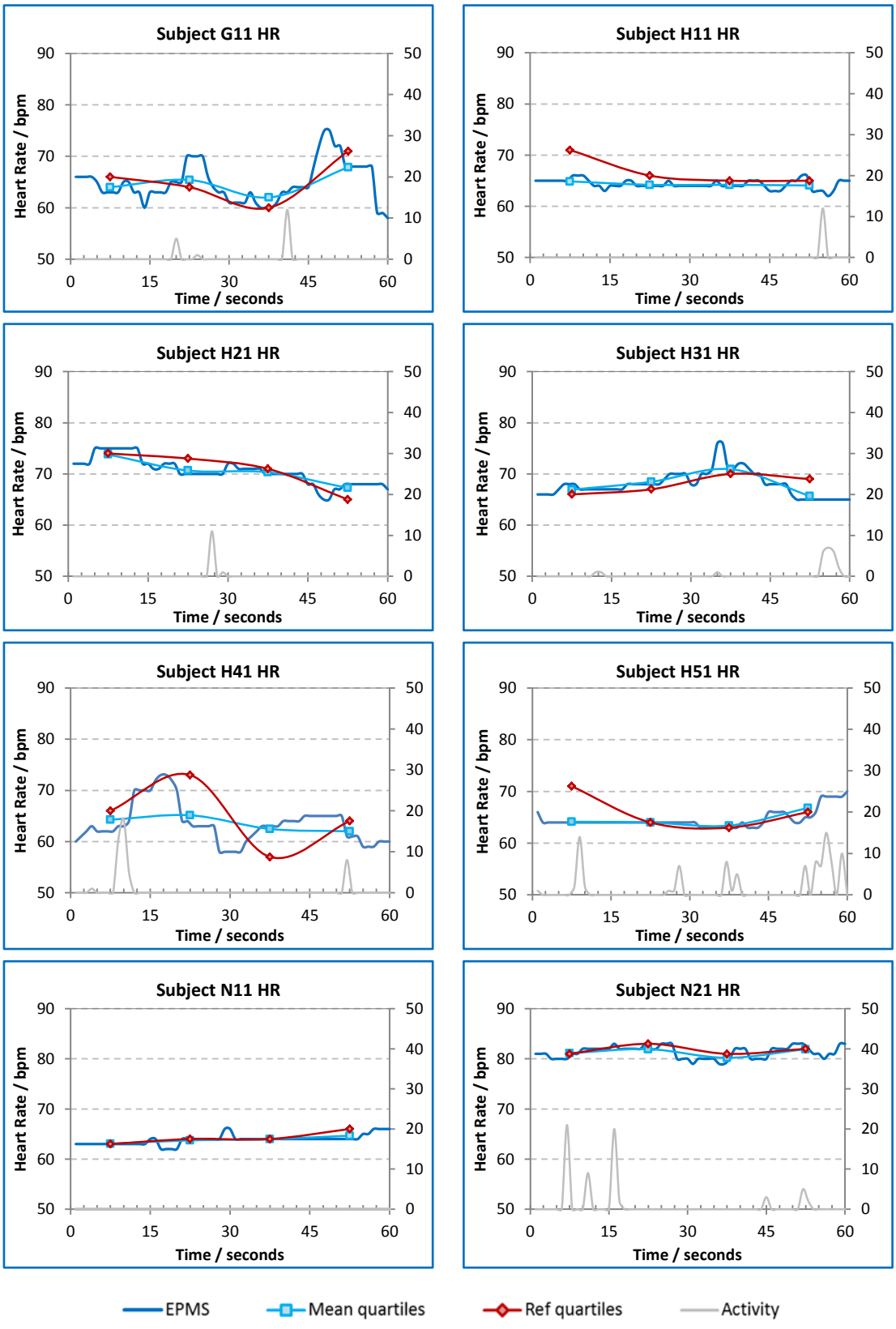
I am out of office at the moment on medical leave so will forward a formal letter of approval in due course.

Best Regards
Ruth

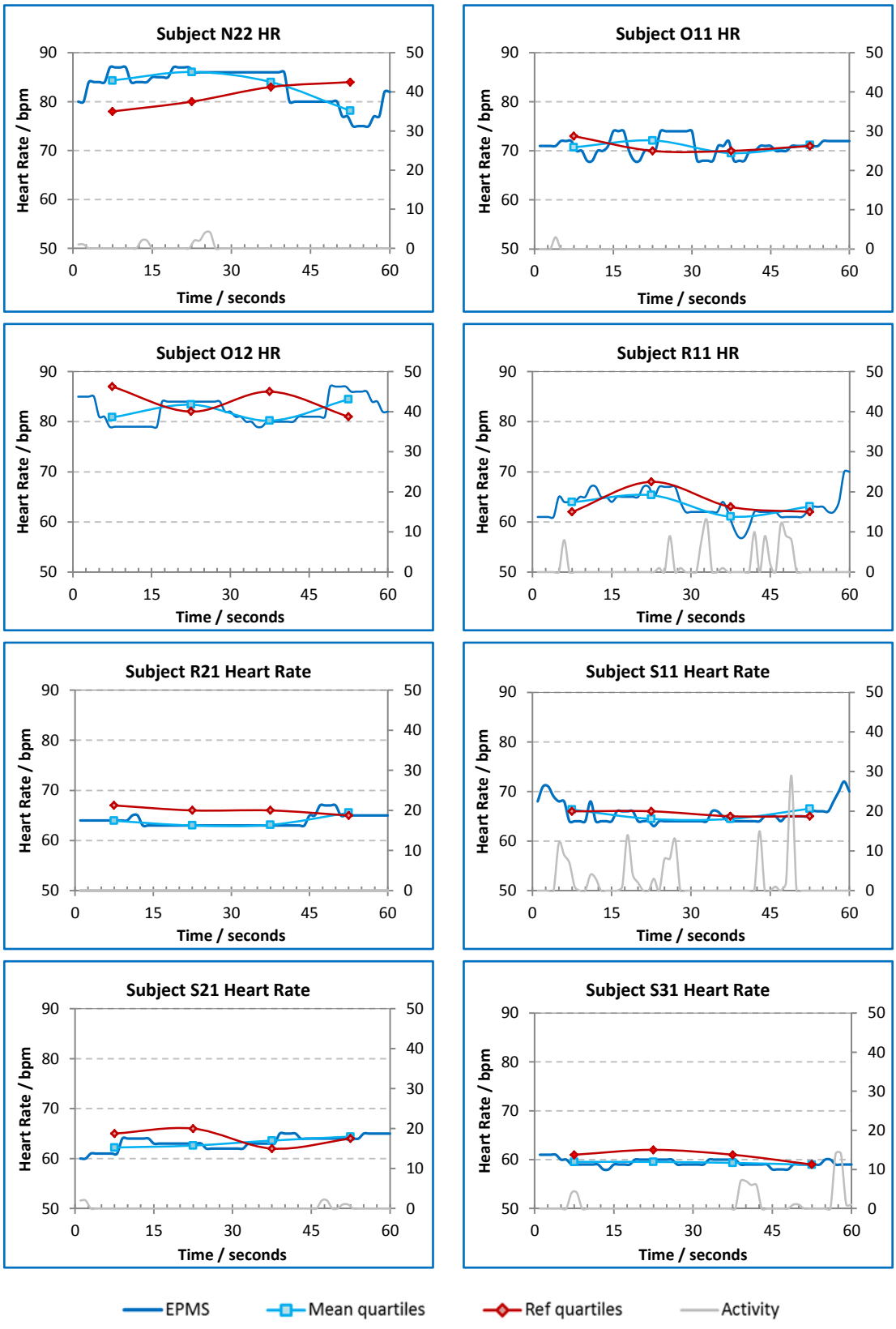
EPMS Pilot Study – Heart Rate Plots



EPMS Study – Heart Rate Plots



EPMS Study – Heart Rate Plots



EPMS Study – Heart Rate Plots