FETAL QT INTERVAL DETECTION FROM ABDOMINAL ECG SIGNALS BY USING ITERATIVE INDEPENDENT COMPONENT ANALYSIS

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FETAL QT INTERVAL DETECTION FROM ABDOMINAL ECG SIGNAL BY USING ITERATIVE INDEPENDENT COMPONENT ANALYSIS

Prenatal cardiac monitoring is an aspect of utmost importance in early detection of fetal distress. Currently, electronic fetal heart monitoring is used on the majority of pregnancy episodes in the developed world to identify risk situations for both mother and fetus. Fetal heart monitoring also provide valuable parameters such as fetal heart rate (FHR), fetal RR and fetal QT (FQT) interval. This study focuses on the systematic methods for accurately locating the fetal QRS complexes and estimating the QT interval in non-invasive fetal electrocardiogram (NIFECG) signal from a single lead abdominal recorded electrocardiogram (ECG). NIFECG signals are usually corrupted by many interfering sources. Most significantly, by the maternal ECG (MECG), whose amplitude usually exceeds that of the fetal ECG (FECG) by multiple times. The presence of additional noise sources further affects the signal-to-noise ratio (SNR) of the FECG. The methods included four steps. In step one, the autocorrelation function was used to detect and remove the maternal QRS (MQRS) complex from the abdominal FECG signals. Then, a filtering method used to pre-process and remove noise from the signals. After the pre-processing the obtained FECG signals, the fetal R-peaks (FR-peaks), fetal RR and FHR were determined by a stationary wavelet transform. Finally, an Iterative Blind Source Separation Method approach was implemented in order to determine the FQT intervals. It was shown, that the NIFECG can allow accurate estimation of the FQT interval, which opens the way for new clinical studies on the development of the fetus during the pregnancy. The single lead FHR detection is particularly useful. This dissertation addresses the current aspects of NIFECG analysis and provides future suggestions to establish NIFECG in clinical settings.

Keywords: Non-Invasive, Fetal Electrocardiogram, Iterative ICA, Fetal Heart Rate, Fetal QT Interval

PENGESANAN SELANG QT JANIN DARIPADA SISTEM ABDOMEN ELEKTROKARDIOGRAM DENGAN MENGGUNAKAN ANALISIS *ITERATIVE INDEPENDENT COMPONENT*.

Pemantauan jantung pranatal adalah satu aspek yang sangat penting dalam pengesanan awal klinikal janin. Ketika ini, pemantauan jantung janin elektronik digunakan pada kebanyakan proses kehamilan di dunia maju untuk mengenalpasti situasi berisiko bagi ibu dan janin. Pemantauan jantung janin juga menyediakan parameter yang berharga seperti kadar denyutan jantung janin, RR janin dan selang QT janin. Kajian ini memfokuskan kepada kaedah sistematik untuk mencari *QRS complexes* janin dan menganggarkan selang QT dengan menggunakan hanya satu elektrod dalam isyarat elektrokardiogram janin (NIFECG) yang tidak invasif dari elektrokardiogram (ECG) yang direkodkan. Isyarat NIFECG biasanya terganggu oleh pelbagai sumber. Kebanyakannya, oleh ECG ibu kerana amplitudnya berkali ganda melebihi ECG janin (FECG). Kehadiran sumber bunyi tambahan selanjutnya memberi kesan pada nisbah isyarat hingar FECG. Kaedah ini melibatkan empat langkah. Pada langkah pertama, fungsi autokolerasi digunakan untuk mengesan dan menyingkir *QRS complex* ibu dari isyarat FECG abdomen. Kemudian, kaedah penapisan digunakan untuk pra-proses dan mengeluarkan gangguan dari isyarat. Selepas pra-pemprosesan isyarat FECG yang diperoleh, puncak R janin, RR janin dan kadar denyutan jantung janin ditentukan oleh gelombang kecil boleh ubah. Akhir sekali, *Iterative Blind Source Separation Method* diterapkan untuk menentukan selang QT janin. Telah ditunjukkan, bahawa NIFECG dapat memungkinkan anggaran tepat untuk selang QT janin, yang mampu membuka jalan untuk kajian klinikal baru mengenai perkembangan janin semasa kehamilan. Pengesanan FHR menggunakan hanya satu elektrod amat berguna. Disertasi ini juga membincangkan aspek-aspek terkini mengenai analisis NIFECG dan menyediakan cadangan masa depan untuk pembentukan NIFECG dalam pengaturan klinikal.

Kata kunci: Tidak invasive, elektrokardiogram janin, *Iterative ICA*, kadar denyutan jantung janin, selang QT janin.

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LIST OF SYMBOLS AND ABBREVIATIONS

s	:	Second
V_{in}^{-}	:	Negative electrical input
V_{in}^{+}	:	Positive electrical input
⊕	:	Positive terminal
⊖	:	Negative terminal
µV	:	micro Volt
$CTh.$	:	Correlation threshold
f_0	:	Interference frequency
fs	:	Frequency Sampling
Hz	:	Hertz
i.e	:	That is
k	:	Iteration index
kHz	:	kilo Hertz
ms	:	milli second
mV	:	milli Volt
q	:	Block size
r	:	Radius
Wr	:	Window of duration
ω_0	:	Digital angular frequency
ABDECGDB	:	Abdominal and Direct Fetal Electrocardiogram Database
ACC	:	Accuracy
ADS	:	Abdominal signal
AECG	:	Abdominal electrocardiogram
AHA	:	American Heart Association

ANS	:	Autonomic nervous system
ANSI	:	American National Standards Institute
AV	:	Atrioventricular
Avg_FECG	:	Average FECG
Avg_FHR	:	Average of FHR
bpm	:	Beats per minute
BSS	:	Blind Source Separation
CHD	:	Congenital heart defect
CTG	:	Cardiotocography / Cardiotocograph
DDB	:	Daisy Database
DWT	:	Discrete Wavelet Transform
ECG	:	Electrocardiogram/Electrocardiography
EFM	:	Electronic fetal monitoring
EMG	:	Electromyogram
EP	:	Evoke Potential
FCTG	:	Fetal cardiotocograph
FECG	:	Fetal ECG
FECGSYNDB	:	Fetal ECG Synthetic Database
FHR	:	Fetal heart rate
FHRV	:	Fetal variability rate fetal
FMCG	:	Fetal magnetocardiography
FN	:	False negative
FP	:	False positive
FPO	:	Fetal pulse oximetry
FQRS	:	Fetus QRS
FQT	:	Fetal QT

FR-peaks	:	Fetal R-peaks
FSE	:	Fetal scalp electrode
FST	:	Fetal ST
GND	:	Ground electrode
HDR	:	Heart rate detection
HR	:	Heart rate
HRm	:	HRm
ICA	:	Independent Component Analysis
*i*ICA	:	Iterative Independent Component Analysis
MECG	:	Maternal ECG
MHR	:	Maternal Heart Rate
MQRS	:	Maternal QRS
NIFECG	:	Non-invasive fetal electrocardiogram
NIFECGDB	:	Non-invasive Fetal Electrocardiogram Database
PCA	:	Principal component analysis
PCDB	:	PhysioNet/Computing in Cardiology Challenge Database
PCG	:	Phonocardiogram
PCinC2013	:	Physionet/Computing in Cardiology Challenge 2013
PLI	:	Power line interference
PPV	:	Positive predictive value
RMSE	:	Root means square error
SA	:	Sinoatrial
SE	:	Sensitivity
SECG	:	Fetal scalp ECG
SNR	:	Signal-to-noise ratio
SQI	:	Signal quality index

STAN	:	ST Segment Analysis
SWT	:	Stationary Wavelet Transform
TP	:	True positive
VCG	:	Vectocardiogram
πCA	:	Periodic component analysis

LIST OF APPENDICES

CHAPTER 1: INTRODUCTION

1.1 Background and Motivation

The most common and severe birth defects recorded are heart defects, which are also the leading cause of birth defects related to death. This defect can disrupt the growth of the baby as the disability may be so slight that the baby looks healthy for years after birth, or can be so severe that his or her life is in danger.

Every year, more than 32,000 infants, roughly one in 125-150 babies are born with some form of congenital heart defect (CHD) (Association, 2004). This defect is the leading cause of death related to disability and is also the most commonly recorded birth defect. In 2015, 2.65 million deaths were estimated worldwide, equivalent to 7,200 per day where 98% occur in low and middle income countries, with more than 45% during the *intrapartum* (occurring during the act of birth) period (Behar, 2016; Lawn et al., 2011). This estimation does not show any changes since *The Lancet* published a similar stillbirth series. Figure 1.1 shows the estimated stillbirth rate in selected countries in 2015. Early detection and more effective abnormal fetal health conditions may help obstetric and paediatric cardiologists determine the proper prescription of medication, or to take necessary precautions during delivery or after birth (Sameni, 2008).

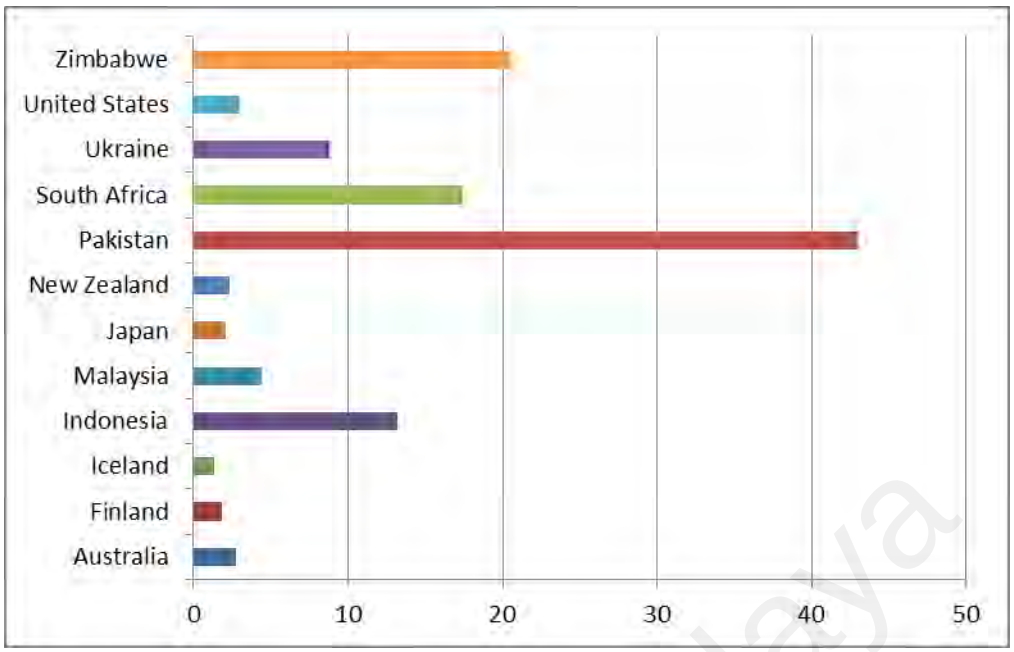

Figure 1.1: Estimated stillbirth rate per 1000 births in 2015 for selected countries (Association, 2016).

Early detection of fetal defects is a very important aspect of the prenatal heart monitoring process. In most developed countries; the fetal heart monitoring process is performed electronically throughout the duration of the pregnancy. In this process, the risk for both mother and fetus will be identified through the commonly used method, analysis of FHR, which was developed more than 50 years ago and has become widely available by the mid-1970s (Clifford, Silva, Behar, & Moody, 2014). This manner of monitoring is a very important process and is expected to resist the possibility of adjacent or congenital conditions that may lead to fetal/newborn morbidity or death.

Fetal heart monitoring has many advantages. Apart from being used to diagnose and monitor CHD fetuses, it is also used to improve the diagnosis of other heart-related pathologies such as anaemia, growth restriction and hypoxia. These kinds of complications can occur any time during pregnancy until birth and has a long-term effect on newborn health if prolonged exposure is present for example cerebral palsy is associated with cerebral hypoxia and birth complications. When the mother progressively decides to postpone her first pregnancy, there is a higher risk to fetal

health (Andersen, Wohlfahrt, Christens, Olsen, & Melbye, 2000). Indeed, improving efficacy and reducing prenatal monitoring costs in risky pregnancies is a priority for both developed and undeveloped nations.

Cardiotocography (CTG) is a common procedure used for perinatal assessment of the developing heart and fetal health. With the CTG that uses ultrasound, FHR can be analysed. CTG is the most widely available surveillance device in the obstetric field. However, CTG only provides information on the mechanics of the fetal heart and has limited predictive value. CTG interpretations are also subjective and have fewer consensuses among experts/guidelines on its interpretation. Other than that, CTG is only performed under expert guidance which results in the recording to take place for a short term only. This situation results in problems arising in the use of CTG. When detecting pathological patterns, the condition has led to a high false positive rate (Nelson & Gailly, 1996). As a result, instead of decreased perinatal morbidity/mortality, CTG is responsible for the increase in instrumental vaginal deliveries and unnecessary obstetric interventions that is caesarean delivery (Ayres - de - Campos & Bernardes, 2010).

Current techniques have various limitations. This situation motivates researchers to strive in searching for alternative methods in the fetal monitoring process over the last few decades. Study conducted focuses on NIFECG (see Figure 1.2), which underlies several studies and has the potential to provide prenatal diagnostic information (Behar, Andreotti, Zaunseder, Oster, & Clifford, 2016; Clifford et al., 2014; T. F. Oostendorp, 1989; Pieri et al., 2001; Sameni & Clifford, 2010). The NIFECG is an alternative to Doppler's ultrasound recording, which can provide more accurate estimates of FHR as well as additional information related to the fetal heart electrical activity that can be obtained through a study on FECG morphology. NIFECG has several advantages such There is a difference between NIFECG and CTG, where NIFECG is measured using a

regular ECG surface electrode attached to the maternal abdomen. This method of recording effort gives a great advantage to the monitoring process where NIFECG is an appropriate technique for monitoring the presence of pregnancy risk. Among these benefits are low relative costs, due to NIFECG's long term recording capabilities and does not require expert oversight during data collection.

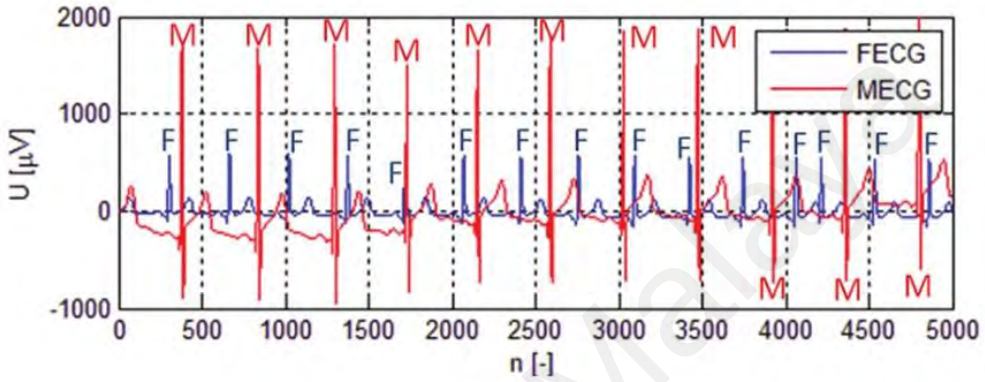

Figure 1.2: Sample of NIFECG signal contains both FECG and MECG and also contaminated by noise (Martinek & Žídek, 2012).

Despite its advantages such as it can be performed at earlier stages of the pregnancy, the NIFECG still has its drawbacks. The NIFECG signals are usually disturbed by many interfering noise sources. Apart from noise sources, the most noticeable FECG signal disorder is by the MECG whose amplitude is usually greater than FECG. Low SNR of the resulting FECG causes the extracting process which is the method for separating FECG from the abdominal electrocardiogram (AECG) measurement and further detection of the FQRS complex is a challenging task. Various efforts in the literature have been made and the focus is placed on the problem of separating the canonical source (Clifford et al., 2014; Sameni & Clifford, 2010), but slow progress has been made. Due to the lack of available random clinical trials little is known about the nature of the NIFECG signal and the true diagnostic value. Despite its remarkable potential, the actual diagnostic value of the current NIFECG approach has not been demonstrated until now. As a result, its use in clinical practice is limited.

1.2 Problem Statement

Fetal heart monitoring is not only useful for diagnosing and monitoring CHD fetuses, but it also may improve the diagnosis of other heart-related pathologies such as hypoxia, growth restriction and *anemia*. Such complications can happen prior to or during birth and may have long lasting effects on the newborns health; if exposure is prolonged (e.g. cerebral palsy is related to cerebral hypoxia and birth complications). As mothers progressively decide to postpone their first pregnancy, there is a higher risk for the fetal health (Fretts, Schmittdiel, McLean, Usher, & Goldman, 1995). Indeed, increasing the effectiveness and reducing costs of prenatal monitoring on risk pregnancies is a priority for both developed and underdeveloped worlds.

The standard technique for perinatal assessment of the developing heart is the CTG. Despite being the most available mean of surveillance, CTG only provides time averaged mechanical information about the fetal heart. Furthermore, CTG's interpretation is subjective and lacks consensus amongst experts/guidelines on its interpretation. These problems in CTG's usage have led to high false-positive rates in the detection of pathological patterns (Nelson & Gailly, 1996). Therefore, instead of producing a decrease in perinatal morbidity/mortality, CTG was made accountable for an increase in unnecessary obstetric interventions (e.g. *cesarean* delivery) and in instrumental vaginal deliveries (Ayres - de - Campos & Bernardes, 2010).

Limitations on the current techniques have instigated the pursuit for alternative fetal monitoring methods over the last few decades. Particularly, because of its potential to furnish prenatal diagnostic information, the so-called NIFECG (see Figure 1.2) has become the focus of several studies (Sameni & Clifford, 2010). Due to its higher temporal, frequency, and spatial resolution, the NIFECG enables the monitoring of

FQRS complexes in a beat-to-beat manner. Therefore, the use of sophisticated FHR/FHRV techniques is possible.

FHRV parameters provide important indices in determining the functional state of the ANS and have been associated with diverse pathological conditions such as hypoxia as the deprivation of an adequate oxygen supply for a complete review (Hutter & Jaeggi, 2010) and growth restriction (Hoyer et al., 2009). Beyond FHR and FHRV information, the FECG may allow a deeper characterization of the electrophysiological activity (i.e. heart electrical conduction) by means of morphological analysis of FECG's signal waveform. Such a morphological analysis provides additional insights that cannot be obtained through CTG. In contrast to CTG, NIFECG can be measured using regular ECG surface electrodes attached to the maternal abdomen. This straightforward recording scheme provides considerable advantages regarding the recording effort, which makes NIFECG a suitable technique for the ubiquitous monitoring of risk pregnancies. Amongst those benefits is the non-requirement of an expert supervision during data collection1, consequent long-term recording capability of NIFECG

Despite many interesting theoretical frameworks, the robustness of most of these methods has not been quantitatively evaluated sufficiently and little progress has been made in their use. This is mainly due to three factors: (i) the lack of gold standard databases with expert annotations; (ii) the underdeveloped methodology for assessing the algorithms and (iii) the absence of open source code makes the re-implementation of the original algorithms prone to errors, and makes objective benchmarking difficult if not impossible.

The non-observance of these aspects leads to the undesired suppression of fetal peaks, either when MECG temporal overlap occurs (lack of trust in model) or partial

suppression of the FECG due to noise overestimation (remember that the FECG is treated as noise).

In this work, those topics were further explored, particularly regarding the MECG/FECG modelling. Therefore, two aspects are further explored: (i) the creation of the MECG template/model and (ii) the varying presence of measurement noise.

Unfortunately, non-invasively recorded FECG signals are usually corrupted by many interfering noise sources, most significantly by MECG whose amplitude is usually much greater than those of the FECG. The generally low SNR of the resultant FECG makes the extraction (i.e. methods for separating the FECG from AECG measurements and subsequent detection of the FQRS complexes a challenging task. This thesis focuses on the systematic methods for accurately locating FQRS complexes and estimating the QT interval in a NIFECG signal from a single lead abdominal recorded ECG. The method includes four steps. Beginning with the step one, the autocorrelation function was used to detect and remove the MQRS complex from the abdominal FECG signals. Then, a filtering method was used to pre-process and remove noise from the signals. After pre-processing the obtained FECG signals, the FR-peaks, fetal RR and FHR were determined by the stationary wavelet transform. Finally, an Iterative Blind Source Separation Method approach was implemented to determine the FQT intervals.

1.3 Objectives

- To develop on the systematic methods for accurately locating the FQRS complexes and estimating the QT interval in NIFECG signal from a single lead abdominal recorded ECG.
- To develop the systematic methods for accurately locating the FQRS complexes and estimating the QT interval in NIFECG signal from a single lead abdominal recorded ECG.

- To analyses and compare existing NIFECG extraction in different methodologies, approaches and their application.
- To propose and implement an improved method to detect the FECG from the composite abdominal signal.
- To analyse the changes in beat-to-beat variability in fetal heart rates of the fetus.
- To determine an estimation of the median QT interval for each recording in the NIFECG signals.

1.4 Contribution and Impact

This thesis focuses on the signal processing techniques that can be used to extract clinically relevant information from the NIFECG. Two features are of interest in this work: FHR and FQT interval. For successful extraction of both features it is necessary to accurately detect the FQRS location. This is because the FHR is directly derived from the FQRS location, and QT measurement techniques use the QRS location as an anchor point. Thus, a large part of this thesis is concerned with implementing and benchmarking techniques for FQRS detection. A particular emphasis is given to the methodology for tuning and assessing these algorithms. Following the work on FQRS detection is the estimation measurement of the FQT from the AECG.

1.5 Thesis Outline

This dissertation consists of five chapters.

Chapter 1 provides a general overview of this dissertation and discusses the background of the study, objectives and problem statement. **Chapter 2** presents the literature review about the clinical backgrounds on the NIFECG and factors that may influence the fetal cardiac activity are described. Further in **Chapter 2**, the current technical state-of-the art on prenatal monitoring is presented. Also in this chapter, an overview on the NIFECG signal processing is provided, database and tools and ECG

signal quality. **Chapter 3** is the methodology used in the study, details on which algorithms were used and the various processes involved. In **Chapter 4**, presents the results and discusses the finding of the FQRS detection, analysing of the heart rate variability of the fetus and determination of QT interval estimation. **Chapter 5** presents the conclusion to the study, and highlights the problems encountered in the study.

1.6 Summary

This chapter introduced the reader to the main message, aim, and objectives of this dissertation.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

This chapter discusses various findings from the literature review on the topics relevant to this research. This chapter provides background information on the current clinical state of fetal monitoring. With that in mind, this chapter provides information about the fetal development that is relevant for fetal monitoring. Meanwhile, it is also describes some complications that may benefit from novel monitoring techniques. The background information on current approaches to interpreting the available information about the fetal heart also presented. MECG suppression / FECG extraction is presented throughout where the method of choice is discussed extensively. Further in this chapter, the techniques to perform and evaluate FQRS detection, FHR estimation, and FECG morphological analysis are showed.

2.2 Fetal Heart Physiology

According to a study conducted, the duration of a normal pregnancy is around 40 weeks or 280 days. Pregnancy is counted from the first day of a woman's last period, not the date of conception, which generally occurs two weeks later. This period is in accordance to the normal menstrual cycle. There is also a longer period of pregnancy as in Germany, where the duration of pregnancy is recorded between 37 - 42 weeks. During this pregnancy, some changes occur to the mother as well as the fetus. It will be explained briefly in several sections of this chapter.

The first system, that starts to function in the embryo are the cardiovascular system. The process of heart development begins with the formation of the main tube, which will then be separated into four cardiac chambers and pairs of arterial trunks. This main tube will eventually form the adult heart (Moorman, Webb, Brown, Lamers, & Anderson, 2003). The diagram below (Figure 2.1) describes several stages of heart

development during pregnancy. The heart is the first organ to function in the process of vertebrate embryos formation. This system will only work by the end of the third week of development.

In the first two trimesters of pregnancy, frequency of fetal movement is observed. Frequency is estimated every four minutes between weeks 8 – 20 of gestation (J. G. Stinstra, 2001a). From week 20 – 30 of gestation the frequency is estimated every five minutes (J. G. Stinstra, 2001a). The cells that form the conduction system have a very advanced strength in rhythmicity and spontaneous flow that is more advanced than the liver. However, ventricles and atria have a spontaneous contractual inherent power of any neural influence (für Statistik, 2004). The fetal heart begins to hit before the conduction system or nervous system is established. This is due to the isolated cardiac cells that contract rhythmically when viewed in the culture, and from the observation of the human heart that continues to beat even when removed from the body (as in heart transplant surgery). Fetal development last for 40 weeks and during this period, several complex systems are developed, such as nervous, gastrointestinal, respiratory, circulatory systems, and so forth. The formation of the cardiogenic cord is the first sign of cardiac development. This can be used to form two angled *endocardial* tubes to make one heart tube.

2.2.1 Early Development of the Heart

Endocardial tubes (Day 19): These thin-walled, endothelial tubes develop from condensations of *splanchnopleuric* mesoderm in the cardiogenic region of the *trilaminargerm* disc. The cardiogenic region is cranial to the neural plate.

Embryonic folding (begins Day 20): Lateral and cephalic folding of the *trilaminargerm* disc over the course of several days brings the *endocardial* tubes together and tucks them ventrally in the thoracic region at the base of the yolk sac. This

process also brings the septum *transversum* into its adult position inferior to the heart. Figure 2.1 below shows the development stages of the fetal heart.

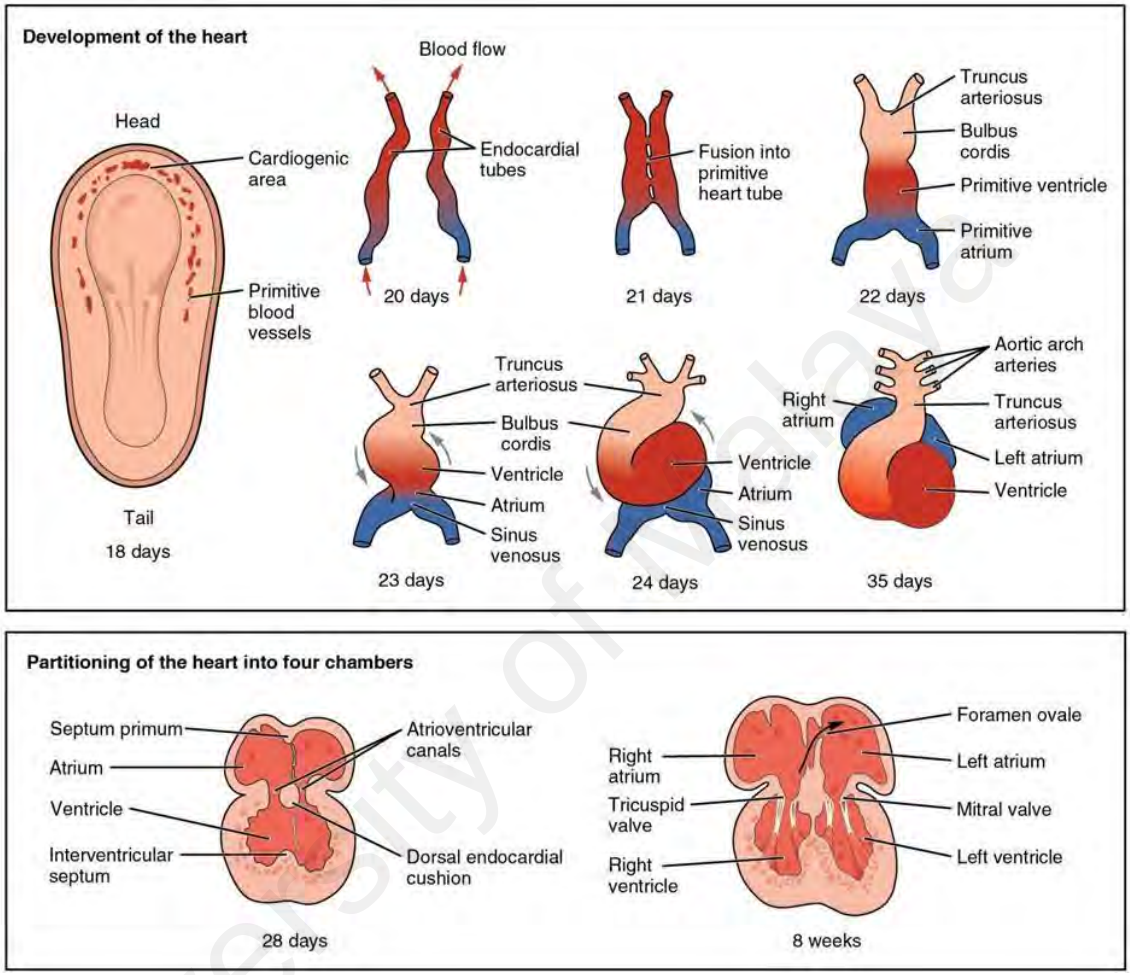

Figure 2.1: Development stages of the fetal heart (College, 2013).

The blood vessels: Composed of the aorta, pulmonary artery, and vena cava (inferior and superior branches). The blood vessels transport fetal blood outside the fetal heart and back to it. Additionally, and present only during fetal life, the *ductus arteriosus* connects the main pulmonary artery to the descending aorta, which transports the majority of blood flow towards the fetal lower body and the placenta.

The placenta: The placenta is an organ that carries out three important functions in the fetal cardiovascular system such as (i) interface between the fetal and maternal systems; (ii) execution of many of the functions for the fetus that the lungs will later assume in extra uterine life; and (iii) metabolic exchange. In other words, the placenta is fundamental for the fetus since it brings in oxygen and nutrients whilst removing waste products (Rychik, 2004).

The umbilical cord: The umbilical cord is composed of the umbilical vein and two umbilical arteries. The former transports oxygen rich blood from the placenta to the fetus whilst the latter transports deoxygenated blood from the fetus to the placenta. In addition, the *ductus venosus*, which is present only during fetal life, connects the umbilical vein (after it enters into the fetal abdomen) with the inferior vena cava just as it enters the right atrium (Menihan & Kopel, 2007). Figure 2.2 shows the anatomical structure of the fetal cardiovascular system.

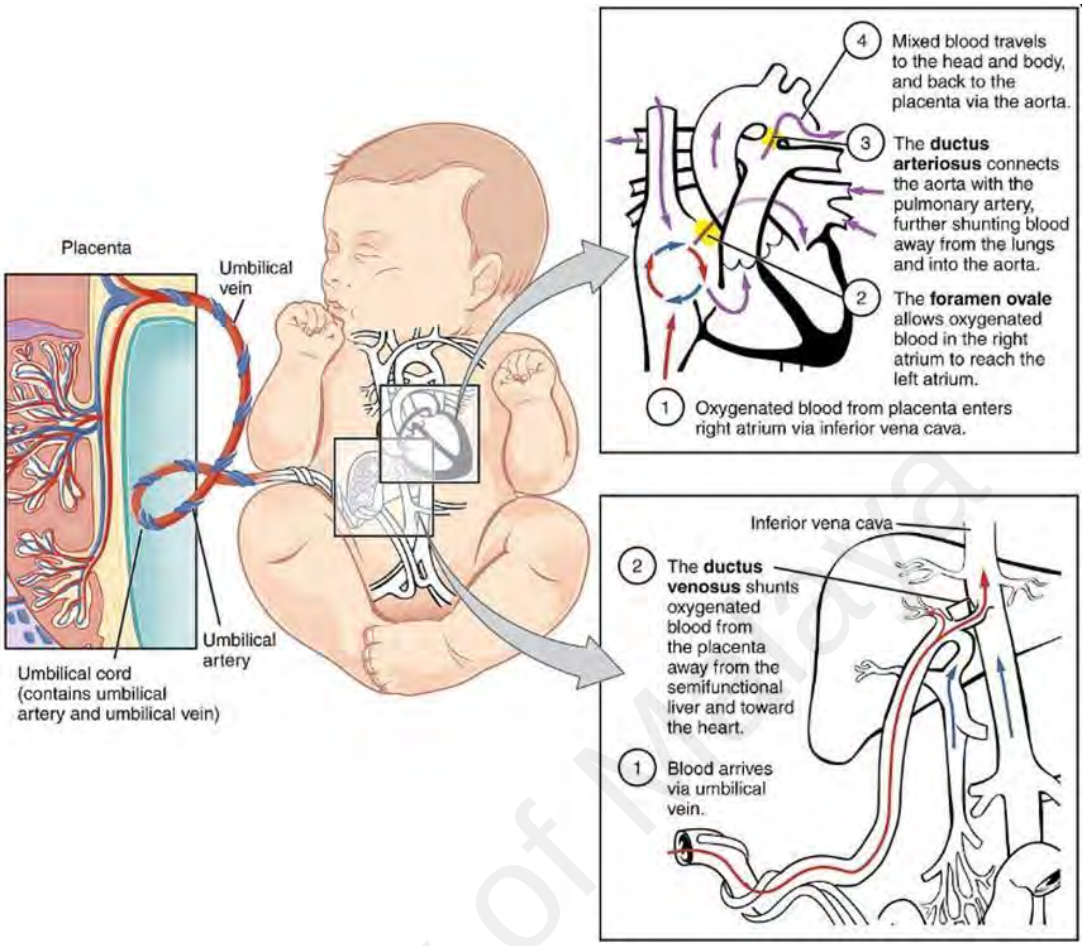

Figure 2.2: Anatomical structure of the fetal cardiovascular system (Blackburn, 2014).

Fetal heart begins beating approximately at the fourth week of pregnancy with a frequency of about 65 beats per minute (bpm). This frequency increases during gestation up to 140 bpm before delivery. The main function of the fetal heart is to pump oxygenated blood from the placenta to the organs and, in turn, to carry carbon dioxide back to placenta where the exchange between mother and fetus is maintained. The exchange is not limited to blood gases only, but includes all substances such as nutrition and fetus's waste products (Gibb & Arulkumaran, 2017).

Fetal heart development affects FECG signals recorded from the mother's abdomen. The fetus's movement and position along with heart development affects the orientation, strength and non-stationary characteristics of the FECG.

2.3 Fetal-Maternal Compartments

In the womb, the fetus will be completely surrounded by several anatomical layers. These layers can be found in *vernix caseosa* and amniotic fluid with different electrical conductivities, the highest and lowest electrical conductivity.

These layers also have enormous influence on recorded FECGs. These layers are the interface of the surface electrode as well as the inner tissue. This condition is caused by subcutaneous fat and the skin in the maternal abdomen compartments having a poor conductivity, which is estimated to be about ten times smaller than muscle tissue (T. F. Oostendorp, 1989). This conductor called volume conductor, which is formed by these different tissues, and layers, which the fetal cardiac signal propagates to the surface of the maternal body. This conductor is not a firm conductor because it is influenced by the ever-changing geometric shape and electrical conductivity over the duration of the pregnancy (Brace & Wolf, 1989). Especially during the 20th week of gestation and onward, there is an increase in volume in amniotic fluid, placenta and fetus itself. At this time, ECG and MECG can be recorded from external electrodes. Between weeks 28 to 32 of gestation, very low layers of *vernix caseosa* conductivity will form. This condition makes the recording process extremely difficult because the very low conductivity of *vernix caseosa* conducts the electrically shields on fetus. However, for normal pregnancies (non-premature delivery), the layers slowly dissolve in the 37th to 38th week of pregnancy. Figure 2.3 below shows the maternal fetal heart that affects electrical conductivity.

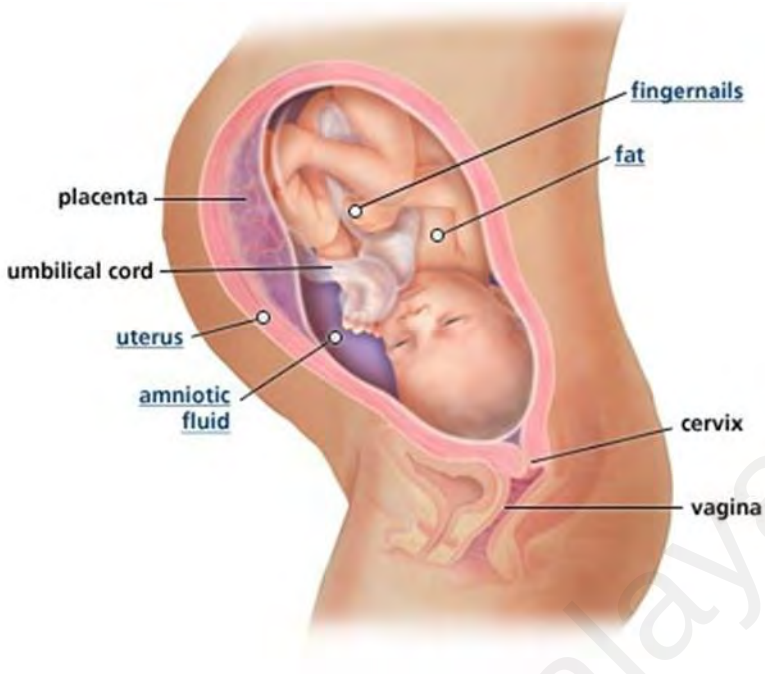

Figure 2.3: The major fetal-maternal compartment that influence fetal cardiac surface potentials (J. G. Stinstra, 2001b).

2.3.1 Fetal Presentation

The presentation of the fetus influences the fetal cardiac signals recorded from the maternal body surface over different leads. During the first two trimesters of pregnancy the fetus does not have a specific presentation and moves about a lot. By the middle of the third trimester the fetus commonly settles in a head down position known as the vertex presentation, which is more appropriate for birth (Roche & Hon, 1965). However, the fetus may also settle in other less probable presentations. There are basically three positions that the fetus can be in; breach, shoulder and arm, and cephalic (head first). Breach means the baby is coming feet or buttock first which only happens in about 3% of births. The rest presentation is the shoulder and arm position, which means that the baby is laid sideways which only, happens in less than 1% of births. The most common position for birth is head first (cephalic). Cephalic presentation is considered normal and occurs in about 97% of births (Suzuki & Yamamuro, 1985).

The difference in movement in utero is due to the increase of fetal size. In the Figure 2.4, the difference in fetal performances during delivery is shown along with their respective prevalence. The closer to birth time, the fetus will be in vertex position, which is 96.8% down to the birth channel. However, as shown in the Figure 2.4 there are six different ways a baby could be facing while head down which are:

1. Occiput Posterior - head facing mother's tummy (sunny side up)

2. Occiput Anterior - head-facing mother's back

3. Occiput Transverse - head facing mother‟s side

4. Sacrum Anterior - the buttocks face anteriorly

5. Sacrum Posterior - the buttocks face posteriorly

6. Mentum Anterior/Posterior - Face presentations according to the position of the chin.

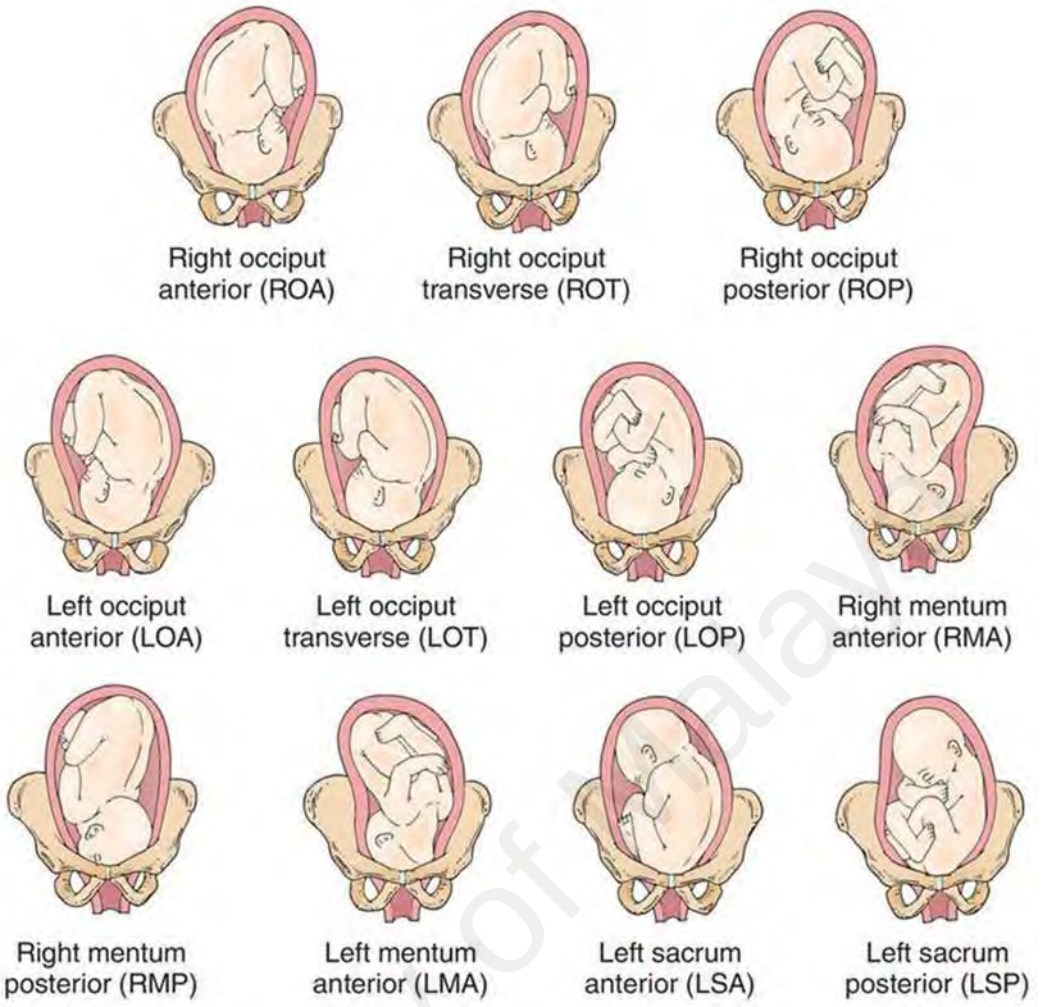

Figure 2.4: Different ways of fetal presentation (Suzuki & Yamamuro, 1985).

2.4 Electrical Activity of the Fetal Heart

The heart is the muscular organ of the circulatory system that constantly pumps blood throughout the body. Approximately the size of a clenched fist, the heart is composed of strong cardiac muscle tissue that is able to contract and relax rhythmically throughout a person's lifetime.

The heart has four separate compartments or chambers. The upper chamber on each side of the heart, the atrium, receives and collects blood coming to the heart. The atrium then delivers blood to the powerful lower chamber, called the ventricle, which pumps blood away from the heart through powerful, rhythmic contractions.

The human heart is actually composed as two pumps in one. The right side receives oxygen poor blood from various regions of the body and delivers it to the lungs. In the lungs, oxygen is absorbed in the blood. The left side of the heart receives oxygen rich blood from the lungs and delivers it to the rest of the body. Figure 2.5 indicates the pumping system of the heart.

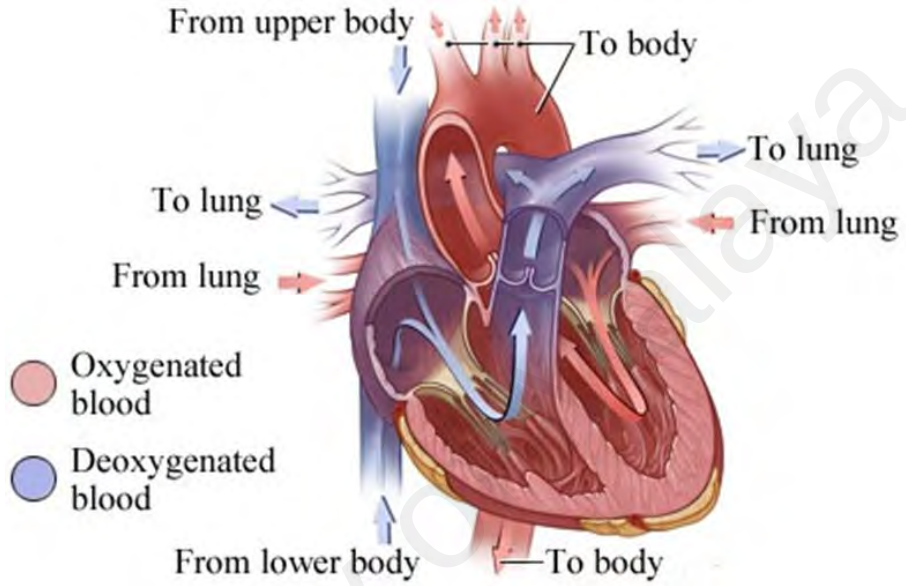

Figure 2.5: Pumping system of the heart (Blackburn, 2014).

Systole: The contraction of the cardiac muscle tissue in the ventricles is called systole. During systole, the ventricles contract and forces blood to exit the chambers and enter their respective arteries, thereby leaving the heart. The left ventricle empties into the aorta and the right ventricle into the pulmonary artery. The increased pressure due to the contraction of the ventricles is called systolic pressure.

Diastole: The relaxation of the cardiac muscle tissue in the ventricles is called diastole. When the ventricles relax, they make room to accept the blood from the atria. The decreased pressure due to the relaxation of the ventricles is called diastolic pressure.

2.4.1 Electrical Conduction System

While the mechanical function of the fetal heart differs from an adult heart, its beat-to-beat electrical activity is rather similar (Sameni & Clifford, 2010). The heart possesses an underlying activation structure that serves the mechanical function of the heart as pump. As oxygen is supplied to the fetus by the placenta, the need for pumping blood through the lungs is not present. *Postnatally*, the left ventricle of the heart is pumps blood to the body and the right ventricle pumps blood to the lungs. In the fetus, both ventricles operate together and both pump blood to both the body and the lungs. For this purpose an additional connection is present between atrial, the foramen oval, and the *ductus arteriosus* links the outgoing vessels of both ventricles.

Not all *myocardiac* cells in the heart show the same response to activation. Generally, two classes of cell responses are distinguished, being the slow and fast response. The *myocardiac* cells that display the slow response lack the fast opening of sodium channels. These cells, however, have the property of generating a brief action potential after the last one ended and are the pacemakers of the heart. In the posterior wall of the right atrium, a cluster of cells is found labelled the *sinoatrial* (SA) node. These cells are the first to trigger an action potential in the heart. The subsequent depolarization spreads through both atria, depolarizing the *myocardiac*cells. However, this activation front is not able to continue into the ventricles as the tissue separating ventricles and atria cannot conduct the depolarization front. The only pathway through which the activation front can spread from atria to ventricles is through the *atrioventricular* (AV) node. This node is located in the lower posterior wall of the right atrium and connects to the ventricular septum. The AV node also consists of cells showing the slow response and the depolarization front is conducted slowly through this node. At the other end of the AV node the depolarization front enters the His bundle, which later on branches into a left and a right bundle and ends in the Purkinje fibres.

These bundles consist of specialized *myocardiac* cells with a high conduction velocity for the depolarization front. Thence, the depolarization front travels along these bundles and initiates a depolarization front from within the ventricular walls. From here the depolarization front spreads from within to the inner and outer surface of the ventricular muscle. After the depolarization phase, in the repolarization phase all cells return to their resting state (J. G. Stinstra, 2001a).

The time it takes to return to the resting state depends on the duration of the action potential. Once in rest, the cells in the SA node are the first ones to generate another action potential and the process repeats itself. Figure 2.6 below shows the conduction system of the heart.

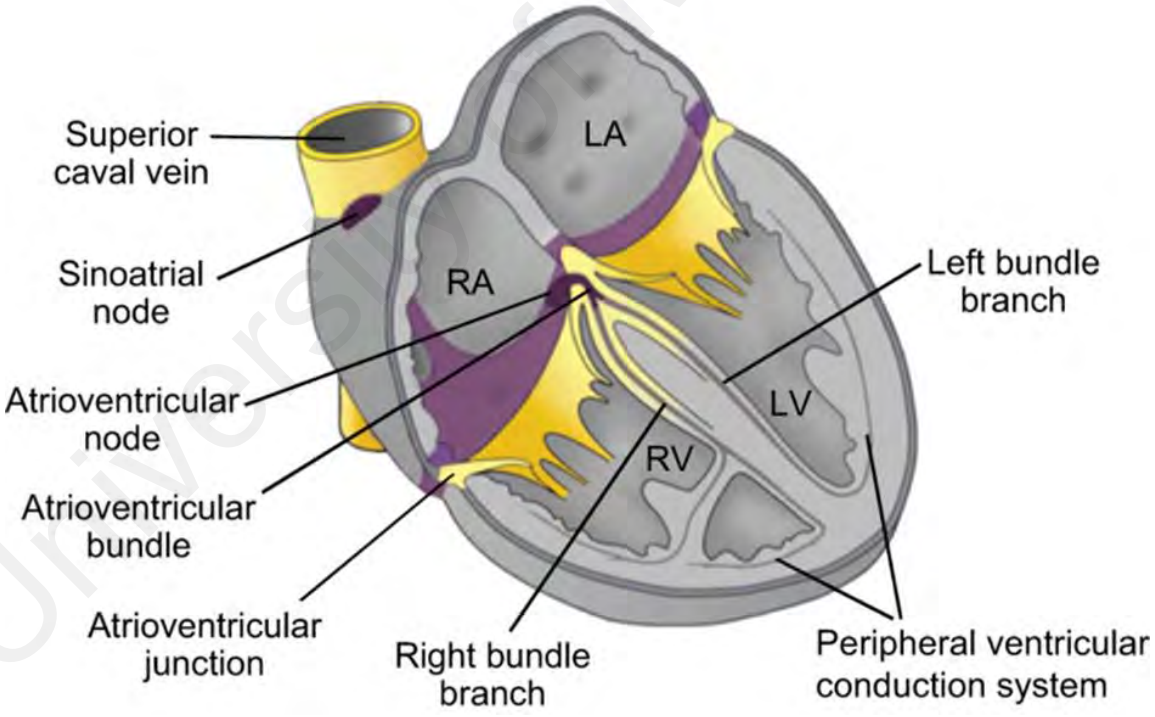

Figure 2.6: Conduction system of the heart (Blackburn, 2014).

The stage wise activation pattern results in the PQRST complex when measured with an ECG. The name of the complex dates back to Einthoven (1908), who labelled the subsequent peaks in the electrocardiogram alphabetically starting with P. The first wave encountered is the P-wave, which is the spreading of the depolarization front through

the atria. In the next 50 ms no signal is measured as it takes some time for the depolarization front to travel through the AV node.

As only a small number of *myocardiac* cells take part in the AV conduction the signal is too small to be measured. Subsequently, the ventricles are depolarized, which results in the QRS complex. In the meantime the atria are repolarized; however, this repolarization is obscured by the depolarization of the ventricles. Finally, the ECG shows a T-wave, which corresponds to the repolarization of the ventricles. Figure 2.7 shows the activation sequence. In this figure show the anatomy of the fetal heart and illustrate the activation sequence, resulting in the typical PQRST-waveform seen in fetal ECG.

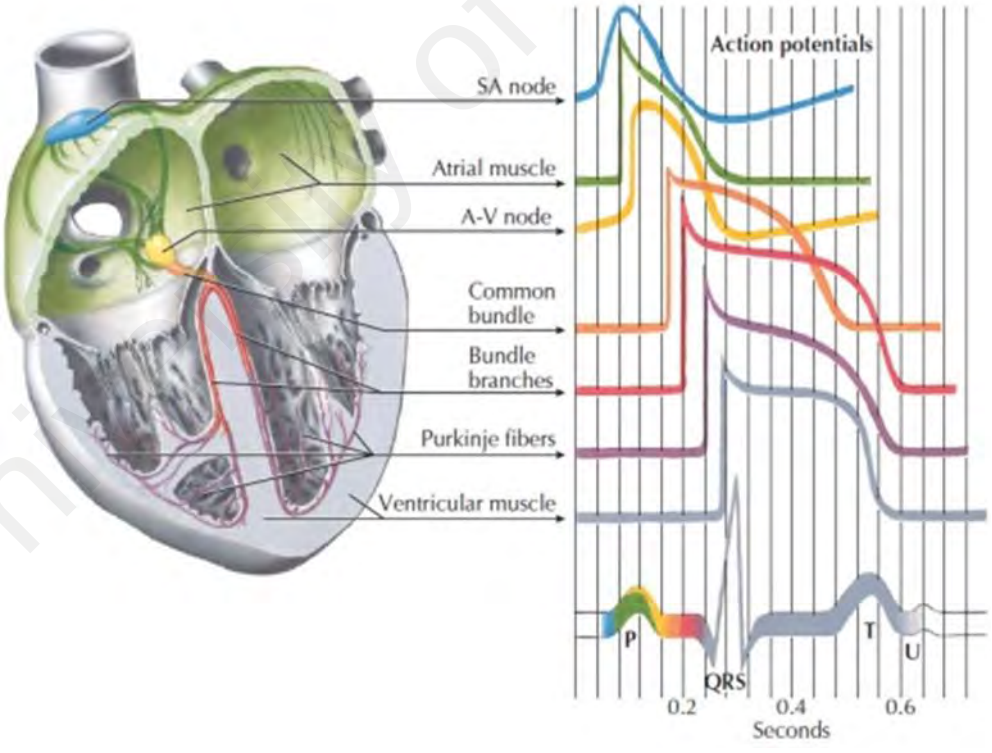

Figure 2.7: The anatomy of the fetal heart (Suzuki & Yamamuro, 1985).

Similar to the ECG analysis, the FECG allows for a deeper interpretation of the heart's electrical activity than merely assessing its rhythmic changes. This is realized by

performing a morphological analysis over the so called PQRST complex (see Fig. 2.8). This evaluation suffers from similar limitations as the FHR/FHRV analysis, i.e. the lack of standards. Additionally, FECG analysis is rarely used in clinical practice. Several FECG features have been studied in the context of fetal monitoring (Symonds, Chang, & Sahota, 2001). Between those features: width and shape of the QRS complex, R/S ratio by using fetal vectocardiogram (VCG), P-wave morphology (inversion, notching, and disappearance), PR interval, QT interval and ST segment. The reader is referred to (Behar, Andreotti, et al., 2016) for an overview on available morphological features. In this work, focus was on the following metrics that have initially shown promising results (Behar, Andreotti, et al., 2016):

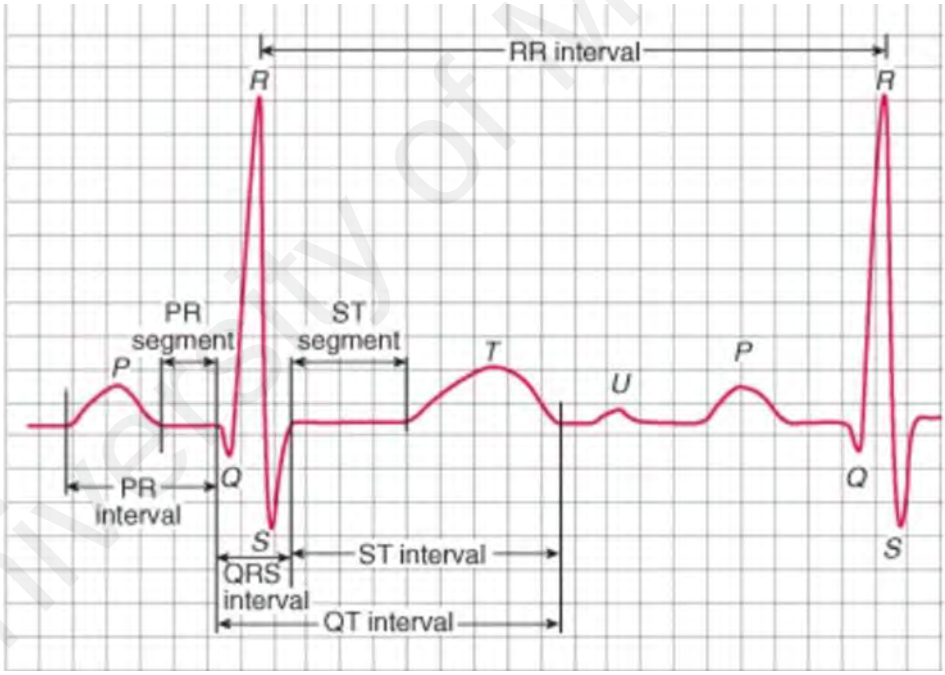

Figure 2.8: Typical PQRST sequence (Blackburn, 2014).

Fetal QT (FQT) segment: Adults' changes in the QT interval are associated with myocardial ischemia, cardiomyopathy, and sudden cardiac death amongst several other conditions. Thus, the FQT interval is of much interest in the monitoring of fetal hypoxia. In a study by (Oudijk et al., 2004), a significant shortening of the FQT interval has been shown to be associated with *intrapartum* hypoxia resulting in metabolic

acidosis, whereas in normal labour none of such changes occur. In Behar (Behar, 2016) and in (Behar, Zhu, et al., 2016), the authors showed the possibility to automatically recover the FQT from NIFECG recordings. Three clinicians manually annotated the FQT from invasive and non-invasive recordings of 22 labouring women. The annotations were fused, and the errors between reference and automated detection were found to be in a similar range to adult QT analysis.

Fetal ST (FST) segment: it is believed that an elevation of the FST segment and T-wave identifies hormone induced fetal heart muscle responding to hypoxia, where a deviation from the baseline indicates a pathological response (Amer-Wåhlin et al., 2002). For this reason, fetal monitoring could greatly benefit from FST analysis. However, the ST segment delineation involves the detection of the end of the T-wave and J-point, which even in adult ECG is a challenging task. Due to the considerably lower amplitudes and surrounding noise, the FST is hardly attainable. An alternative is to use the fetal T/QRS (FTQRS) ratio (as follows) as a proxy for the FST elevation.

Fetal T/QRS (FTQRS) ratio: FTQRS was demonstrated to be a proxy for the ST segment using animal models by (Greene, Dawes, Lilja, & Rosén, 1982), where the authors examined 10 chronically instrumented fetal lambs at 115 days to term. The study showed that the normal FTQRS ratio was lower than 0.30, whereas it was in the range of 0.17 - 0.59 for eight of the lambs after inducing hypoxia and reverted to normal with *normoxia*. However, studies by (Belfort et al., 2015) suggest that the FTQRS as proxy for the FST level is either not accurate enough, or that it does not provide meaningful information for fetal monitoring.

Regarding the difficult task of segmenting the largely unexplored FECG beats, the duration of such intervals highly depend on the gestational age and projection of the fetal heart that is electrode configuration, and should be taken into consideration. Since

no standard is available for morphological analysis, clinical considerations from the current studies have to be analysed with caution. (Symonds et al., 2001) concluded in 2001 that, "The issue of the value of current use of the FECG morphological characteristics and time intervals for the prediction of fetal compromise remains promising but unresolved". As (Behar, Andreotti, et al., 2016) pointed out: 15 years later the problem remains unresolved.

2.5 The Fetal Heart Monitoring

There are two ways of recording the electrical activity of the fetus. These are direct electrocardiography (during gestation from the scalp of the fetus) and indirect electrocardiography (from the mother's abdomen). Since it is difficult to record continuously using the direct (invasive) method, the indirect (non-invasive) method has been available as optional equipment to CTG since 1974 (T. Oostendorp, Van Oosterom, & Jongsma, 1989).

One of the undisputed advantages of the non-invasive method is the fact that the fetus does not receive any energy, which allows for the performance of long term studies. Application of a traditional external probe without implementing the modern filtration technology only enables the recording of the R-R interval, i.e. the time segment between the individual heartbeats of the fetus. This technique cannot be used to detect the complete FECG curve.

Abdominal recorded signals are an alternative to CTG fetal monitoring, as they represent a method for fetal surveillance that is non-invasive, provides clinically significant information concerning the well-being of the fetus through the analysis of the FHR and the morphology of the FECG, and moreover, can also be used for long term monitoring. However, the fundamental problem is that abdominal signal (ADS) represents a multi-component signal containing several other disturbing components of

high amplitudes be-sides the low amplitude FECG. Moreover, the FECG overlaps with them in the spectral domain. Figure 2.9 below shows the abdominal ECG interferences.

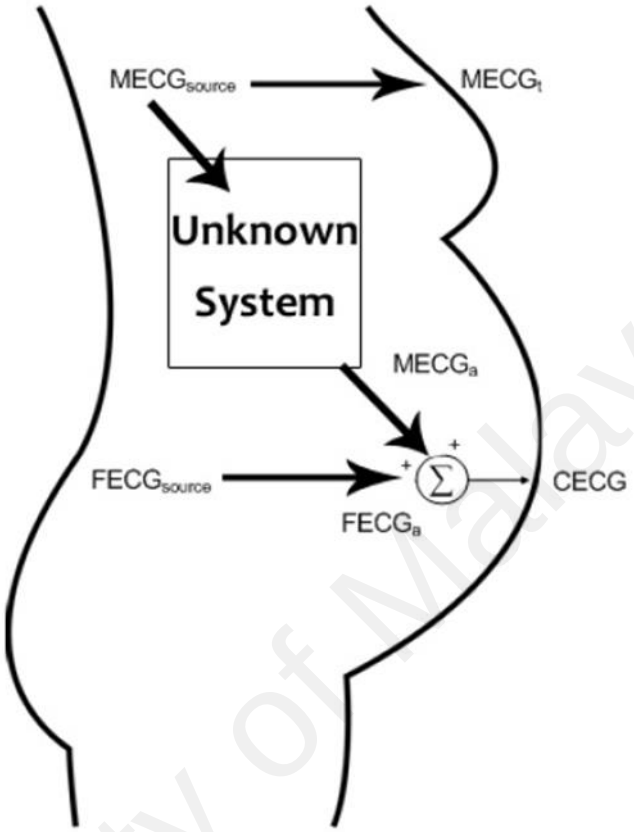

Figure 2.9: Abdominal ECG recording and the interferences (Blackburn, 2014).

2.5.1 Artefacts of Fetal ECG

The use of the gentler (non-invasive) external method brings about a number of problems. There is a great degree of noise interfering with the FECG signal, which consequently becomes unreadable for further evaluation (diagnosis). Above all, the FECG signal gets contaminated to a great extent by the MECG signal, characterized by a much higher amplitude (Martinek & Žídek, 2012).

There are a series of other, non-cardiac sources of interference occurring during the FECG extraction. Among the perturbing bio-signals, the MECG and the power line interference (PLI) are clearly the main sources of disturbance. The *transabdominal*

FECG R-peak amplitude is about 10 μV, while the amplitude of the QRS complex of the MECG shows a range for the amplitude of 0.5 to 1 mV (Peters et al., 2001).

Also, PLI is one of the most common and unwanted types of noise encountered in bio-potential measurements. It is always present in biomedical recordings and high magnitude interference can bury and degrade low voltage (power) signals like the FECG, for example. The source of the noise is the ac line and there are different ways in which the interference enters the recordings: i) magnetic induction; ii) displacement currents; and iii) unbalanced electrodes impedances which give rise to the *potential divider effect,* that are common mode interference is converted into differential mode interference voltage which is amplified (Spinelli, Mayosky, & Pallás-Areny, 2006).

Other disturbing signals, which must be considered, are the electronic noise (introduced by amplifiers, etc.), the slow baseline wander of signals (mainly due to electrode skin interface), and the myoelectric crosstalk from abdominal muscles, and, in particular during labour, the uterine contractions. Figure 2.10 below shows the ECG signal with baseline drift and 60 Hz power line interference.

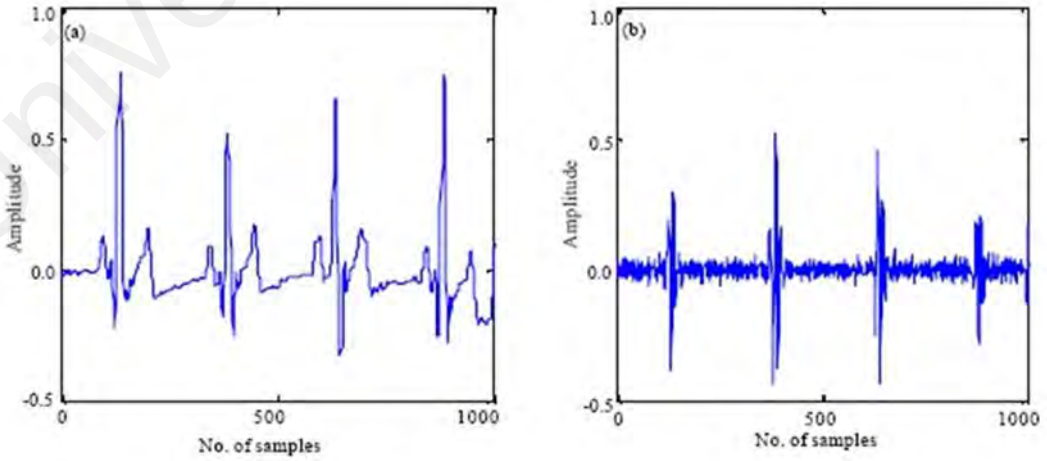

Figure 2.10: Abdominal ECG signal with baseline wander (left) and power line interference (right).

The large amplitudes of these noise sources hide the *transabdominal* FECG and a simple high pass filtering of ADS for FECG extraction cannot be applied due to the overlapping spectra of the FECG and of the noise components. Also, the application of a filter may introduce some unwanted phase distortion to the FECG. Moreover, the amplitude of the FECG depends on the electrode configuration and varies among subjects due to the different body weight and size of the mother, as well as due to the different positions of the fetus. In addition, the recording quality of the FECG changes with time, especially with the appearance of the *vernix caseosa* during the last three months of pregnancy, when the R-peak of the FECG is hardly detectable (T. Oostendorp et al., 1989). Thus, it is desirable to eliminate as much noise as possible during recording in order to apply uncomplicated software algorithms for further cleaning of the FECG signal. Figure 2.11 below shows the methods of FECG recording and processing.

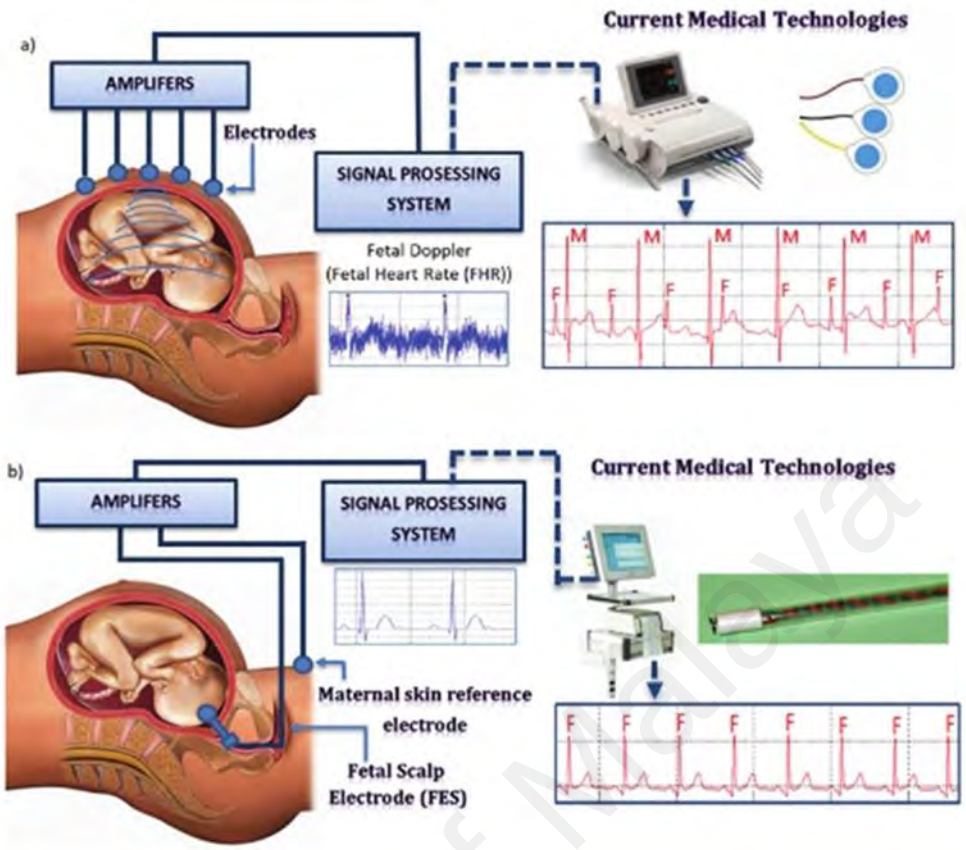

Figure 2.11: The fetal ECG monitoring and signal processing. (a) Non-invasive; (b) Invasive (Martinek & Žídek, 2012)

2.5.2 Non-Invasive Fetal Electronic Monitoring

Non-invasive monitoring is conducted during pregnancy, labour, prenatal visits, non-stress test, and contraction stress test. For this procedure, the ultrasound transducer is attached to the maternal abdomen. It sends the fetal heart sounds in forms of electrical signals to the computer. The rate and pattern of the fetal heartbeat will then be shown on the screen, printed on paper, and analysed. This procedure has a greater vision for fetal safety and more significantly, long term monitoring of the FHR can be achieved using innumerable signal-processing techniques. It is completely non-invasive, low power consumption, and can be used over continuous periods of time.

The fetal monitoring process can be performed with various non-invasive methods. The fetus in the womb can be safely developed because mechanically the fetus is protected from the outside world. This directly causes all fetus-related information to be

limited. There are various forms of information that can be obtained in the form of signals. These signals are taken through the maternal abdominal wall. Examples of information include: i) fetal heart bioelectric activities that cause electric potential and magnetic field; and ii) a fetal heart mechanical activity that produces acoustic vibration.

In general, the signal from the mother is a strong signal. These maternal signals normally will overlap and mix with fetal signals, which are too weak in amplitude. There are several types of detection methods in electronic fetal monitoring (EFM) used to detect these fetal signals. Among them are fetal pulse oximetry (FPO), fetal scalp electrode (FSE), fetal magnetocardiography (FMCG), Non-Invasive fetal electrocardiography (NIFECG), phonocardiogram (PCG) and continuous wave Doppler-shift ultrasound based on fetal cardiotocograph (FCTG). Table 2.1 lists the summary of the available technique of EFM that presents their advantages and disadvantages (Behar, Andreotti, et al., 2016).

Table 2.1: Available techniques in fetal heart monitoring.

Method	Technique	Anterpartum	Intrapartum	Other descriptions
FCTG	Non-Invasive	≥20 *wg*	/	- Mechanic / acoustic - Smoothed HR time series - Trained expert required during recording - No beat-to-beat data and cardiac function descriptor limited to HR - Only short time capable - FHR available on window averages - Active method (ultrasound irradiation) - Prone to maternal/fetal HR confusion - Sensible to fetal/maternal movement - Thousands of dollars

FMCG	Non-Invasive	≥20 *wg*	X	- Magnetic - Multichannel (>20 channels) - High SNR for FECG make analysis easier - Expert personnel required during recording - Only short term capable due to size and cost - Expensive
FPO	Invasive	X	/	- Optic - Single channel only - Application possible after rupture of membranes - Estimate for fetal oxygen saturation available - Usability often questioned - Hundreds of dollars
FSE	Invasive	X	/	- Electric - Single channel only - Application possible after rupture of membranes - Thousands of dollars
NIFECG	Non-Invasive	≥20 *wg*	/	- Electric - FHR and possibly morphological analysis - Low SNR for FECG - Presence of *vernix caseosa* severely reduces SNR (Week 28-37 of gestation) - No skilled personnel required during recording - Long term monitoring - Low cost
PCG	Non-Invasive	≥28 *wg*	X	- Mechanic / acoustic - Lowest SNR of all methods - Requires expert to locate fetus - Sensitive to surrounding and gastrointestinal noises - Hundreds of dollars

wg = numbers of weeks of gestation

2.6 Electrode configurations

Data collection for NIFECG needs to be done with caution. Priority should be given to the electrode position during recording. To date, there is no specific standard for the determination of the position of the abdominal electrode. This is also similar for adult electrocardiographs, where the signal morphology is much too dependent on the lead configuration used. For the AECG database, before electrode placement, the recording should not be done easily. Although it may choose to use the lead system and can be permanently stored, it also depends on maternal and *girt's* size. The position of the fetus is uncertain as well. For this reason, optimal electrode placement for general purpose is impracticable (Agostinelli et al., 2015).

Before proceeding, the terminology used in this work is defined as based on the recommendations of the American Heart Association (AHA) (Arena et al., 2007). Bio-amplifiers usually make use of differential amplifiers, thus there are two main electrical potential inputs (V^{+}_{in} and V^{-}_{in}). As input to the amplifier, one generally has two active electrodes, one connected to the positive terminal (V^{+}_{in} henceforth graphically shown as $\oplus$) and another to the negative terminal (V^{-}_{in} depicted as $\ominus$). In addition, a reference electrode (here termed as ground electrode – "GND") is used to improve common mode (unwanted noise) rejection. Take, for instance, Einthoven"s lead II, the positive, negative, and ground electrodes are located on the left leg, right arm, and right leg respectively. The negative electrode can physically exist (as in Einthoven"s lead II) or be calculated as the average of some (or all) leads, as in Wilson's central terminal. When this electrode physically exists, the derivation is often referred to as *bipolar*, when otherwise it is referred as *unipolar*. However, the use of this historical nomenclature that is *bipol*ar and *unipolar* is discouraged by the AHA since all leads are effectively *bipolar*, thus, the term *unipolar* is described as lacking in precision (Arena et al., 2007).

In literature, various efforts have been made in standardizing the configuration or placement of electrodes during the recording process. Examples of configuration are as in Figure 2.12. Through this figure, it is clear that some authors focus only on the usual fetal performances. The performance depends on the vertices, waist or shoulders. This method also can minimize the complexity of the application by reducing the number of leads used and targeting the normal position of fetal head and thorax. In addition, there are methods that can maximize the opportunity to get FECG signals by covering most of the abdomen (Agostinelli et al., 2015). During the recording process, the position and distance of the electrode plays a very important role in the imposition of SNR, FECG and MECG power. More information can be obtained if the electrode is located near each other in the differential scheme. As a result, the electromyogram (EMG) noise (muscle crosstalk) and FECG have higher power, while MECG power is generally smaller.

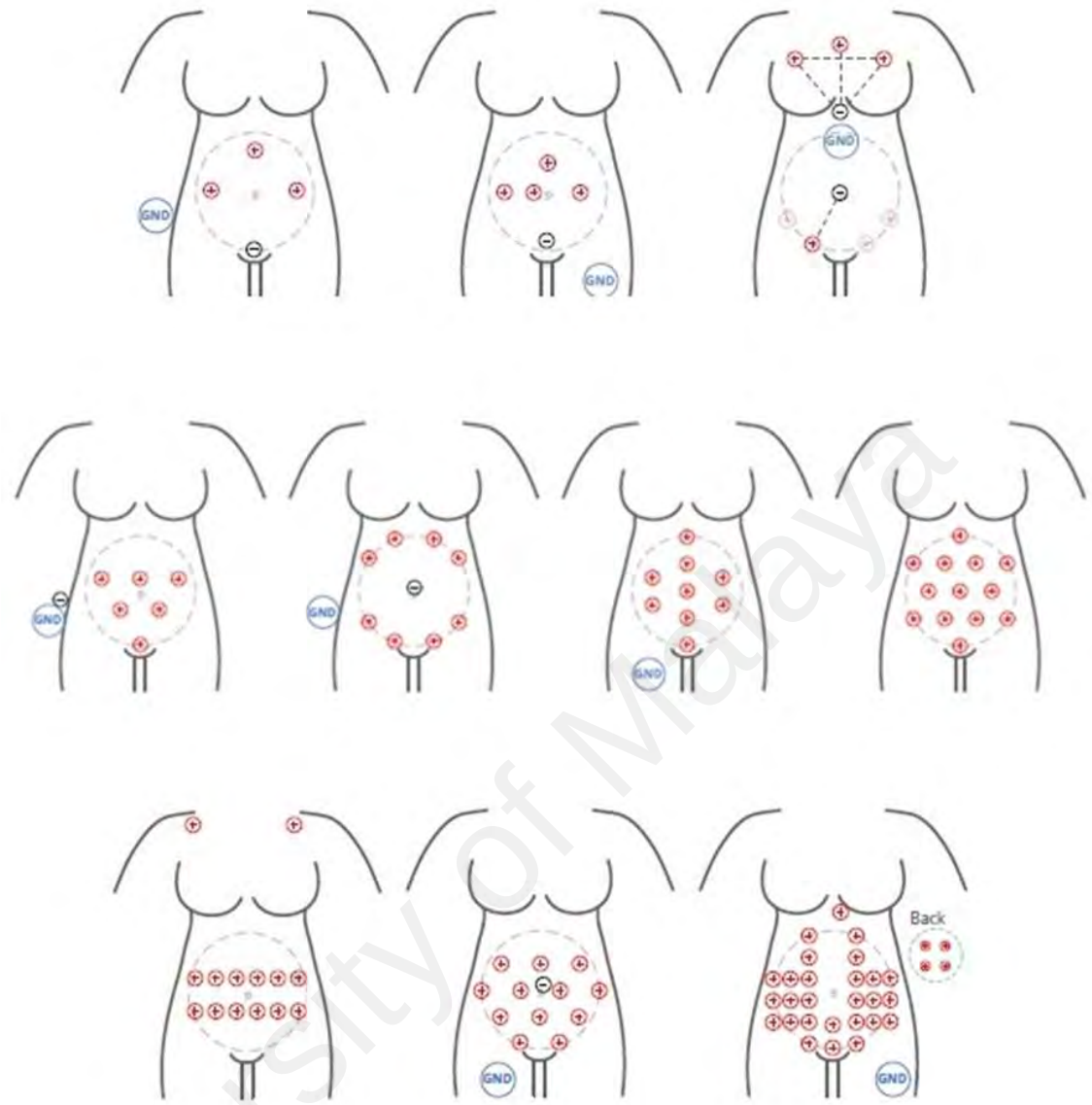

Figure 2.12: Different electrode configurations present in the literature (F Andreotti, 2011).

An issue to be considered in designing the electrode configuration is the patient's condition. Although more and more electrodes are used to increase power consumption, attention should be given towards patient comfort. Similarly, with the issue of distinguishing between MECG and FECG signals. Usually, increasing the need for hardware and the addition of leads outside the abdomen makes it easy to distinguish between the signals; it still gives them a sense of discomfort. In addition, in applying the NIFECG, consideration should be made regarding the location of the common ground

and negative electrodes. The ground electrode is recommended as it reduces the normal mod interference while increasing the relative contribution of signalling significance (Martens, Rabotti, Mischi, & Sluijter, 2007).

2.7 Available NIFECG Database

2.7.1 Public Database

When analysing FECG, the important thing is to use the high quality database such as low noise and accuracy of FHR. This database has two types that are known as invasive and non-invasive. Both types of data have their own advantages and disadvantages.

Database for the non-invasive method has advantages because it could use a number of electrodes hence the recording process is easier because it can be done at any time and at any stage of pregnancy. However, various disorders that limit good and reliable results such as low SNR FECG distract the use of this method. With these advantages that exist, (Clifford et al., 2014), researchers have formed a partnership and formed a body to develop signal processing techniques in their effort to recover the FECG of non-invasive recording.

In contrast, invasive has advantages in terms of quality when recording data, in which the electrodes are connected directly to the skin of the fetus. It can only be achieved by using a special electrode called intrauterine during labour (Genevier, Deans, Carter, & Steer, 1995). This method can only be carried out during delivery and this means that this method has a very limited recording time. This shows the complexity that must be taken during the data recording process.

Increased research and interest in the field of NIFECG has led to the creation of a data platform requirement that could assist researchers in using and comparing the

methods they use. These researchers use existing data to see the results of their extraction/detection process. Over the last two decades, several databases have been created and are freely available. To date, there are five publicly available databases that can be used to evaluate NIFECG extraction algorithms' performance. All databases are summarized as below in Table 2.2:

Table 2.2: Summary of the existing open databases

Database	NR	NF	Fs (Hz)	RA	Duration (minutes)
DDB	1	1	250	No	0.17
NIFECGDB	55	1	1000	No	Varying
ADFECGDB	5	5	1000	Yes	5
PCDB	447	>10[a]	1000	Yes	1
FECGSYNDBD	1750	9[b]	1000	Yes	5

NR: Number of records

NF: Number of fetuses

Fs: Sampling Frequency

RA: Reference annotation available (Yes/No)

[a] An unknown number of additional subjects were used in the hidden test dataset.

[b] Only nine different VCG are used in the FECGSYN simulator, but an unlimited number can be defined and generated.

i. The Daisy Database (DDB) (De Moor, De Gersem, De Schutter, & Favoreel, 1997)is not so much a database, but a single unrepresentative snippet of data. It consists of eight ECG channels (5 abdominal and 3 thoracic) from a single fetus, lasting 10 s, sampled at 250 Hz, without reference annotations. This dataset is part of a database

known as SISTA (Signals, Identification, System Theory and Automation) of the Department of Electrical Engineering of the Katholieke Universiteit Leuven, Belgium. Although this recording is often used, it is unrepresentative as it is a particularly clean and short set of recordings.

ii. The Non-invasive Fetal Electrocardiogram Database (NIFECGDB), available on PhysioNet (Goldberger et al., 2000), has been prepared for Physionet by the Digital Signal Processing Group of the Electronic Engineering Department, ETSE Escuela Técnica Superior de Ingeniería, University of Valéncia, Spain. The signals were recorded at 1 kHz, including 55 multi-channel AECG recordings taken from a single subject (21–40 weeks of gestation) and recorded using a g.BSamp Biosignal Amplifier. The g.BSamp is a stand-alone analogue biosignal amplifier with 16 channels and two independent grounds which was manufactured by GTech GMBH Medical Engineering, Austria. No reference annotations were available. Each record has 2 thoracic and 3 or 4 abdominal signals.

iii. The Abdominal and Direct Fetal Electrocardiogram Database (ABDECGDB) available on PhysioNet (Goldberger et al., 2000) was acquired in the Department of Obstetrics at the Medical University of Silesia, Poland. Sampling rate for this database was 1 kHz with 5 minutes of recordings (four abdominal channels and the fetal scalp ECG (SECG)) from five women in labour (38–41 weeks of gestation) and with reference FQRS annotation derived from the SECG. Data were recorded using the KOMPOREL fetal monitoring system (ITAM, Zabrze, Poland).

iv. The 2013 PhysioNet/Computing in Cardiology Challenge Database (PCDB) (Silva et al., 2013) consists of 447 minutes of data from five different databases (including the NIFECGDB, ABDECGDB and simulated data using the FECGSYNDB). FQRS reference was provided to a subset of the PCDB, the remaining reference was

kept as hidden test set. Data were resampled at 1 kHz. This database represents the largest publicly available dataset to date. Each record has four abdominal channels and no maternal reference. The open training set has reference FQRS available while the closed validation and test sets had restricted access to the reference annotations to facilitate independent testing. In this respect, it is a unique database, which prevents over tuning of parameters. Data and references for set A (training set), are still available and the platform is still open for scoring annotations for the recordings of set B (validation set.)

v. The Fetal ECG Synthetic Database (FECGSYNDB) (Behar, Andreotti, et al., 2016; Goldberger et al., 2000) includes 1750 five minutes realistic simulations of abdominal mixtures sampled from 34 channels (32 abdominal and 2 MECG channels), totalizing to 145.8 hours of multichannel data and 1.1 million fetal peaks. The FECSYNDB comprised of seven different cases of physiological events, for ten different maternal fetal heart dipoles' arrangements, at five noise levels. The seven different cases of physiological events were considered and simulated as describe below in Table 2.3:

Table 2.3: Seven different cases of physiological events for FECGSYNDB.

Case	Descriptions
Baseline	Abdominal mixture (no noise or events)
0	Baseline (no events + noise)
1	Fetal movement + noise
2	MHR / FHR acceleration / decelerations + noise
3	Uterine contraction + noise
4	Ectopic beats (for both fetus and mother) + noise
5	Additional NI-FECG (twin pregnancy) + noise

Each combination was simulated five times for statistical purposes, hence combined into a total of 10 (simulated pregnant) × 7 (cases) × 5 (SNR levels) × 5 (repetition) = 1750 synthetic signals simulations produced. The data was generated using the FECGSYNDB simulator (Behar, Zhu, et al., 2016).

Until now, there is no existing database known to contain any data that have relevant clinical information or data from more than one subject. There is also no standard measurement procedure published for any databases.

2.7.2 Latest Technology: ST Segment Analysis (STAN)

The modern and most recent technique utilized for detecting fetal ST segment changes is called the STAN system (ST segment analysis) of the FECG signal (Martinek et al., 2015), which was developed by a Swedish medical device company. The STAN system has the ability to directly diagnose the fetus under threat from hypoxia, which enables physicians to confirm pathological conclusions and suspicions by ST segment analysis. STAN works in parallel with the valuable information about

the fetus from CTG tracing and fetal heart rate. It helps the clinician to detect signs of hypoxia and also the fetus condition during the stress of labour.

STAN is made to monitor any changes during the ST Event. A normal ST waveform will show sufficient fetal oxygen supply. STAN automatically detects significant changes in the ST intervals. Hypoxia happens during the increase of the T-wave amplitude of the ECG. STAN creation is also helpful in making decisions related to the labour process. It will also help decrease fetal injury and mortality rates. STAN will also provide continuous fetal wellbeing information during labour. However, STAN also does have a few limitations. STAN can only be used in clinical practice after 32 weeks of gestation. STAN requires the attachment of a fetal scalp electrode; any contraindications to the use of such an electrode would preclude its use to give reliable results.

2.8 Non-Invasive Fetal Electrocardiogram Extraction Methods

2.8.1 Fetal QRS Detection

Analogous to the analysis of adult electrocardiography, the FQRS complexes obtained from FECG signals provide the first interesting feature, which can be directly linked to clinical diagnostic information. The primary feature that any algorithm must extract from the AECG signal mixture is the FQRS complex location. This peak detection is used for computing the FHR, detecting rhythm abnormalities, or as an anchor point for extracting features from the FECG waveform. Ascertaining the location of the FQRS is simplified by first separating the FECG from the AECG, and several approaches have been suggested in the literature. These include: Principal Component Analysis (PCA), Independent Component Analysis (ICA), or Periodic Component Analysis (πCA) which makes use of the ECG's periodicity. In essence, these approaches are a form of blind source separation (or in the case of semi-blind source), which aim to

separate the underlying statistically independent sources into three categories: MECG, FECG and noise. Other techniques, which are operate in lower dimensions that are using a lower number of, or single, abdominal channel, and include Adaptive Filtering, Template Subtraction and Kalman Filltering.

During the Physionet/Computing in Cardiology Challenge 2013 (PCinC 2013) several participants made use of this strategy, including some open source entries available at Physionet (Clifford et al., 2014), and proposed an adapted implementation of the Pan and Tompkins algorithm. Another relevant source of FQRS detection methods is the Open-Source Electrophysiological Toolbox (OSET), which includes a maxima search algorithm. Other examples of this strategy are Matched Filters, Slope-detection, supervised machine learning using the ESN algorithm, Wavelet Transform. A comprehensive overview on those methods can be found in (Kohler, Hennig, & Orglmeister, 2002; Taylor et al., 2003).

Aside from the PCinC 2013, there is to date no study evaluating the performance of those FQRS detectors against each other known to the author. Some authors separate the FQRS procedure performed after FECG extraction (see Figure 2.13) into "FECG enhancement" and "FQRS detection" steps. However, in this work, the pre-processing performed to enhance the fetal peaks (i.e. feature extraction) is regarded as part of the FQRS algorithm.

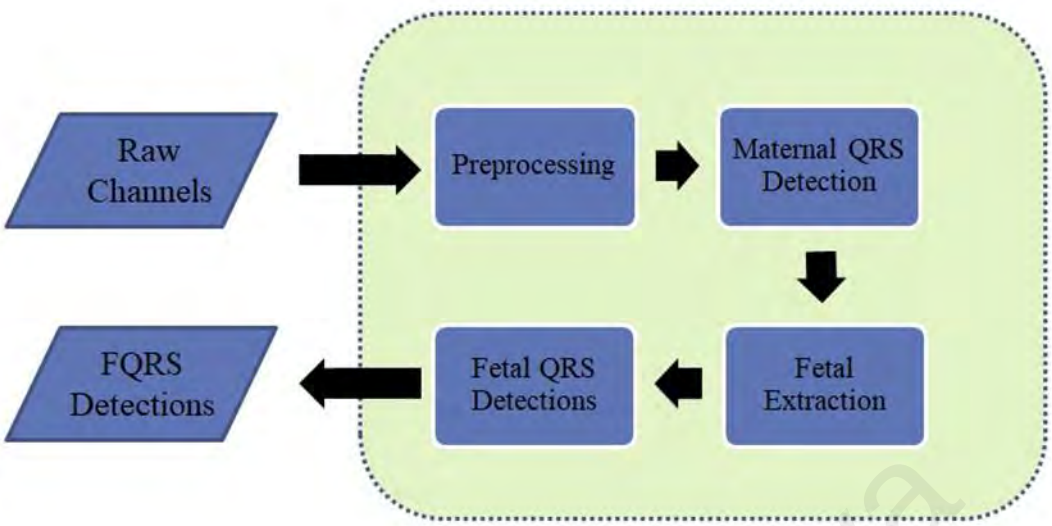

Figure 2.13: Signal processing work flow for NIFECG extraction.

2.8.1.1 Merging multichannel fetal QRS detections

Most FQRS detectors available in the literature make use of a single extracted FECG channel. However, real applications usually make use of multi-lead systems (as discussed in Section 2.5.2). In order to profit from this higher data dimensionality, one can either select/merge the available FECG channels that is prior to FQRS detection, or select/merge the different FQRS detections available. In any case, some sort of metric for fetal signal quality that is signal quality index (SQI) has to be applied to determine which lead(s) to use. Typical measures to take into consideration: (i) the morphology of the FECG signal, such as a kurtosis as *peakedness* measure; and (ii) the pseudo-periodicity of the FQRS detections that is RR interval regularity.

Therefore, performing the selection/merge after the FQRS detection occurs is advantageous since the regularity metric for each FECG channel is then available. While the selection of one single FQRS source to represent the whole measurement may work in short datasets, it is sub-optimal for long term recordings due to the varying nature of the fetal signal's SNR. Therefore, adaptive fusion of the information contained in multiple FQRS detections is a more attractive solution. One solution is to adaptively

for example on every few seconds chooses the lead with the best SQI, the so-called lead switching approach. An-other option is to use weighted or majority voting to obtain consensus detections. Such approaches have often been for merging the results of different QRS detectors/classifiers (Ghaffari, Mollakazemi, Atyabi, & Niknazar, 2015) and for producing consensus from annotations provided by different experts (Clifford et al., 2014).

2.9 Detection performance / Standard Statistic

In order to report FQRS detection statistics different measures were proposed in the literature. The main goal of these metrics is to assess the accuracy and precision of the obtained FQRS in order to present the accuracy of FQRS detections more clearly measures presented in the American National Standards Institute (ANSI) (Benitez, Gaydecki, Zaidi, & Fitzpatrick, 2000), can be used. Particularly, the number of true positive (*TP*) denotes correctly detected peaks, false negative (*FN*) being existing peaks which were not detected and false positive (*FP*) non-existent peaks that were falsely detected can be reported. Differing from the adult norm of 150 ms acceptance interval between detection and reference annotation, a window of 50 ms is usually applied to account for the higher FHR (Fernando Andreotti et al., 2014; Behar, Johnson, Clifford, & Oster, 2014). Based on these absolute numbers, the following summary metrics can be used:

$$Se = \frac{TP}{TP + FN} \tag{2.1}$$

$$PPV = \frac{TP}{TP + FP} \tag{2.2}$$

Where sensitivity (*Se*) measures the percentage of actual FQRS complexes that were correctly identified and positive predictive value (*PPV*) defines the proportion of detected peaks that corresponds to FQRS peaks. Once again, these measures can be condensed into two FQRS detection accuracy measures, namely accuracy (*ACC*) (E. C. Karvounis, Tsipouras, Fotiadis, & Naka, 2007) and the *F1* score (Behar et al., 2014):

$$ACC = 100 \cdot \frac{TP}{TP + FN + FP} (\%) \tag{2.3}$$

$$F1 = 2 \cdot \frac{PPV \cdot Se}{PPV + Se} = 100 \cdot \frac{2 \cdot TP}{2 \cdot TP + FN + FN} (\%) \tag{2.4}$$

ACC is simply the percentage of the correctly detected peaks, over all detected and un-detected peaks, while *F1* provides the harmonic mean between *Se* and *PPV*, therefore summarizing those measures in one score. Despite some criticism, the latter measure is particularly suitable for situations when the average of rates is desired (Behar, Andreotti, et al., 2016; Sasaki, 2007).

From equation (2.3 and 2.4) one can observe that *FN* and *FP* play a symmetric role in penalizing the accuracy measure *F1*. The *F1* statistic is an average of the *Se* and *PPV*, thus providing a good summary metric. The *F1* measure is a harmonic mean and is suited for situations when the average of rates is desired as opposed to an arithmetic mean (Sasaki, 2007).

The overall statistics were calculated by averaging the *F1, Se,* and *PPV* (respectively) obtained from each individual record that is computing the gross average statistics.

The performance of the algorithms was also evaluated in terms of the FHR. FHR can be derived from the RR interval time series and compared with the reference trace HR derived from the reference annotations. At any given time, the extracted FHR was said to match the reference FHR if it was within +5 bpm. The corresponding FHR measure is denoted HRm. The tolerance of +5 bpm was motivated by the industrial standards (Instrumentation, 1998).

2.9.1 Fetal Heart Rate Estimation

The FHR is the most often used parameter in clinical routine to evaluate the fetal health state. This parameter is usually obtained through the Doppler ultrasound or using the STAN monitor during the *intrapartum* period. Since accurate FQRS are a pre-requirement but are generally faulty for example missing detections, the attained FQRS needs to be pre-processed before further analysis (presented in Section 2.8.1).

2.9.2 Pre-processing the fetal heart rate

Despite one's best effort on obtaining accurate detections, FQRS are usually imperfectly identified. These inaccuracies may have physiological, pathological or technical origins (Peltola, 2012). For instance, according to (Clifford, Azuaje, & McSharry, 2006), the *fiducial* markers should always be set on the onset of the P-wave rather than on the R-peaks, since this is a more accurate marker of the SA node stimuli. However, the R-peaks are considerably simpler to detect, particularly in the NIFECG case. Aside from this technical difficulty, several other aspects should be considered. (Peltola, 2012) presented an overview on available methods for pre-processing HR tachograms, while (Clifford, 2002) provided a more in-depth analysis of available methods.

The RR series obtained from ECG recordings usually functions to the number of heart-beats instead of time which is usually in bpm. Some of the common difficulties

encountered when analysing FHRV such as these may have a technical for example detection jitter, missing detections or uneven sampling or a pathophysiological origin for example ectopic beats. Different pre- processing methods are available in the literature to treat each of these events. Despite being an interesting research topic, such techniques to process heart rate series exceed the scope of this work.

2.9.3 Fetal heart rate statistics

Similar to the *F1* accuracy metric presented for FQRS detections, the heart rate detection rate (HDR) has been often applied in adult Heart Rate detection. HDR assesses the percentage of the Heart Rate values within +5 bpm tolerance (Instrumentation, 1998) of the reference HR annotations (regarded as *TP* estimates) (Behar, Andreotti, et al., 2016). On the fetal case, this tolerance was modified to +10 bpm to reflect the higher FHR (accelerations and decelerations of the FHR are usually defined by changes greater than 15 bpm (Blackwell, Grobman, Antoniewicz, Hutchinson, & Bannerman, 2011). HDR results (in percentage) are given by dividing the number of *TP* by the total number of measured FHR estimates (Fernando Andreotti, Trumpp, Malberg, & Zaunseder, 2015), that is similar to Equation 2.5, as follows:

$$HDR = 100 \cdot \frac{TP}{TP + FN + FP}(\%) \tag{2.5}$$

2.10 Fetal ECG Morphological Analysis

In Section 2.4 the three major parameters used in fetal morphological analysis were clarified, namely the FQT, FST and the FTQRS. Due to the lack of standards for FECG morphological analysis, there are several aspects of this evaluation that require further investigation. In this section, focus is put on the signal processing tools that enable the derivation of these morphological features. Further on, metrics on how to evaluate the accuracy of such estimated measures are proposed.

The first aspect to be regarded is the bandwidth used while extracting the NIFECG signal, since it can deform the fetal signal, for example the T-wave. Throughout this work the signal bandwidth was configured as recommended by the American Heart Society for adult ECG (Arena et al., 2007). Similarly, the extraction method used (see Section 3.3.1) is expected to have an impact on those parameter estimates.

Another important consideration is whether the morphological features should be obtained on a beat-to-beat basis or on an averaged FECG template. The first option is obviously more attractive; however, due to the usually low SNR of the fetal signal it is impractical, making the use of averaged FECG beats imperative. As an example, even though direct FSE recordings comprise of a much higher FECG SNR, commercial equipment such as STAN still makes use of this averaging procedure.

Alternatively, if simulated data is used, distance measures such as the MSE or SNR between the fetal reference and extracted signals could be applied (Behar, Andreotti, et al., 2016).

2.11 Summary

In this chapter, overviews on the main pathophysiological influencing factors to the fetal heart activity were presented. The current antepartum clinical standards for interpreting the cardiac activity of the fetus were introduced. The state-of-the-art on techniques for prenatal diagnostic (i.e. data acquisition) is presented. Particular focus is put on the NIFECG technique's signal acquisition and processing methods to enable its analysis. In this chapter, current prenatal diagnostic techniques were presented and the benefits from NIFECG clearly stated. Further, an overview on NIFECG extraction algorithms was provided. Lastly, the metrics to assess FQRS, FHR, and FECG morphology parameters were presented. In the next chapter, novel methods are proposed to deal with the limitation of current techniques.

CHAPTER 3: METHODOLOGY

3.1 Introduction

In this chapter, the aim is to propose and implement an improved method to detect the FECG from the composite abdominal signal and to produce an estimate of the median QT interval for each recording in the test set. In FECG extraction, enhancement and heart rate variability analysis, a new method for single channel FQRS is presented based on the combination of filtering techniques such as the Notch Filter and Wavelet decomposition, and Autocorrelation Function. In this work, only a single abdominal lead signal has been utilized to extract the FHR. For determination of FQT Interval estimation, the extraction of the FQT from the NIFECG output by the Physionet Challenge 2013 is studied by referring to the annotations provided by Physionet. A notch filter that removes power interferences at 60 Hz was applied. The signals were then data segmentations before applying the iterative blind source separation technique.

3.2 Non-invasive Fetal Electrocardiogram Extraction Methods

3.2.1 Database

The data set used was obtained from the MIT NIFECGDB (Goldberger et al., 2000) which contains 55 multi-channel AECG recordings, taken from a single subject between the 21 to 40^{th} gestational weeks with varying signal noise ratio. Every recording included two thoracic signals and three or four abdominal signals, with a synchronized sampling rate of 1 kHz, and the 16-bit resolution was applied. This data set was used for FECG detection in other studies as well (Ghaffari et al., 2015).

3.2.2 Proposed method for FHR monitoring

So far, various methods (Kohler et al., 2002) have been used to remove the disturbances resulting from the maternal heart and abdominal noise. This unwanted disturbance is removed to extract the fetal heart signal component in the fetal QRS

complex detection process. This work proposes a method using only one electrode recording from the maternal. In addition, the proposed method allows identifying not only the FQRS complexes but also the MQRS, thus monitoring both FHR and Maternal Heart Rate (MHR). Figure 3.1 outlines the components and signal flow of the study approach. Apart from filtering the data, the solution consists of two major steps: step 1, detection of MQRS and step 2, detection of FQRS in the remaining signal. These major blocks are discussed in greater detail in the upcoming sub-sections, with a greater elaboration on the latter.

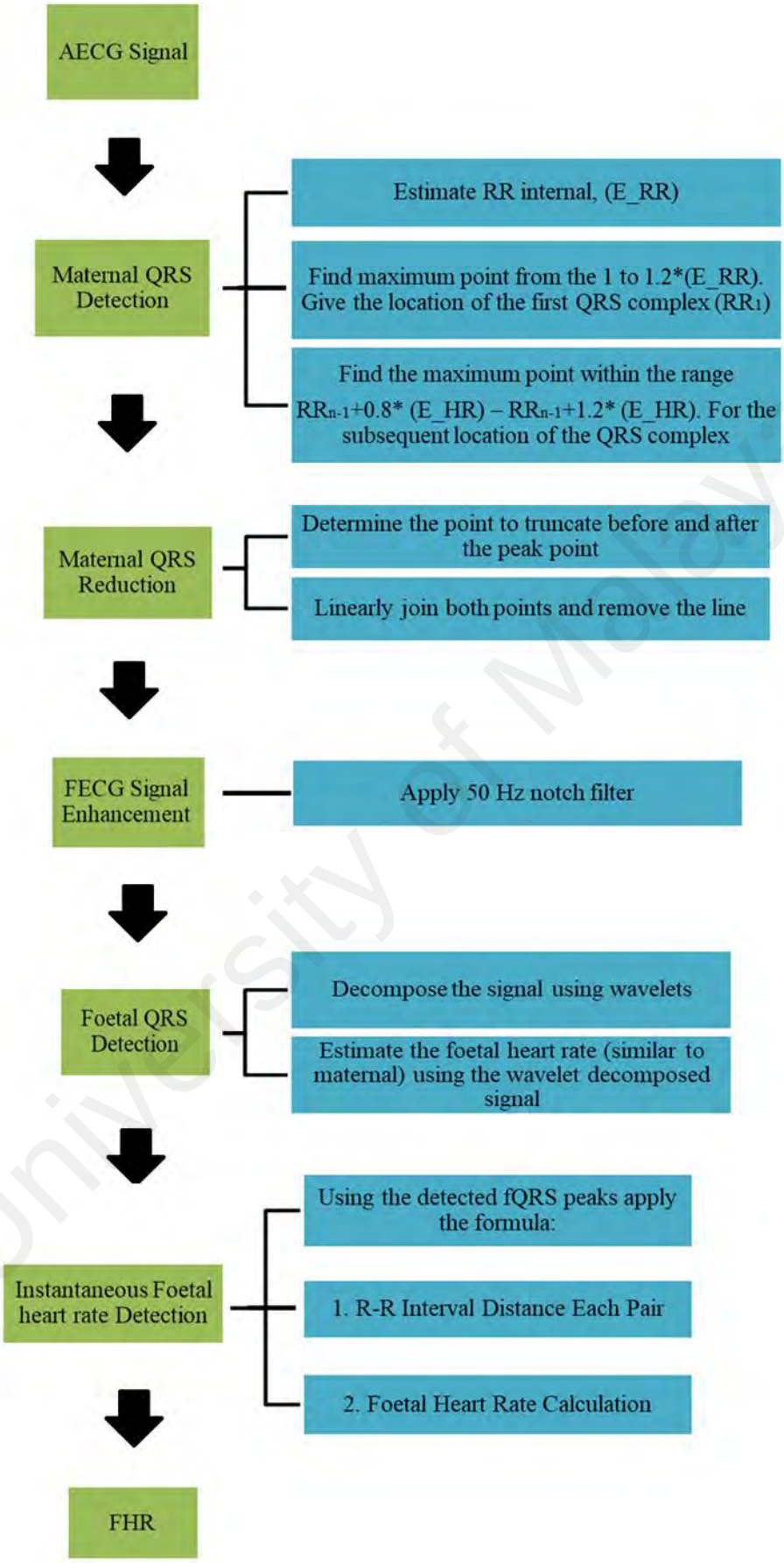

Figure 3.1: Schematic flow of the processing stages.

3.2.2.1 Maternal QRS Detection and Reduction

There are numerous methods that have been proposed to find the QRS complex. However, most of them require the determination of the threshold value (Herry, Frasch, Seely, & Wu, 2017) or are rather complicated. In this study, a method that first estimates the R-R interval was used before attempting to find it on the assumption that the QRS complex has the highest amplitude. The R-R interval was then estimated using the autocorrelation function. In general, a peak can be found when the signal matches itself after a certain shift in the time domain which actually corresponds to the R-R interval. This is not the true R-R interval as the R-R interval may vary across the different QRS complexes. Thus, the first peak may probably be indicative of the shortest possible R-R interval. It is a good estimation of the R-R interval.

The first QRS complex was obtained by finding the maximum point of the segment of data (1- 1.2* estimated RR interval). This estimation is based on the percentage of FECG signal which less than 20% of MECG (M. A. Hasan, Reaz, Ibrahimy, Hussain, & Uddin, 2009). The subsequent QRS complex is expected to fall within (0.8-1.2 E_RR) from the previously found QRS complex. Thus, the maximum point is found within this segment. This process was repeated until all the QRS locations have been found.

Once the peak value of the QRS complex has been determined, it is imperative to determine the width of the QRS complex so that it can be removed. Figure 3.2(a) shows the typical QRS complex that has been determined. Figure 3.2(a) is split into two different signals; one 100 samples before the peak to the peak and the other from the peak to 100 samples after the peak which can be seen in Figure 3.2(bi). Each of this data is sorted from biggest to smallest. First, the threshold was determined using the 50 smallest values. The maximum and mean value of this 50 smallest value was found. The threshold is given by the formula (3.1). From Figure 3.2(bii), it is seen where the

threshold intersects the graph and the value that indicates how many points before the maximum point is indicative of the starting point for the QRS complex. This whole process was repeated on the other set of data to find where the QRS complex ends. Then the starting point to the ending point of the QRS complex was linearly interpolated to remove the QRS complex as can be seen in Figure 3.2(c).

$$Threshold = Maximum + (Maximum - Minimum) \tag{3.1}$$

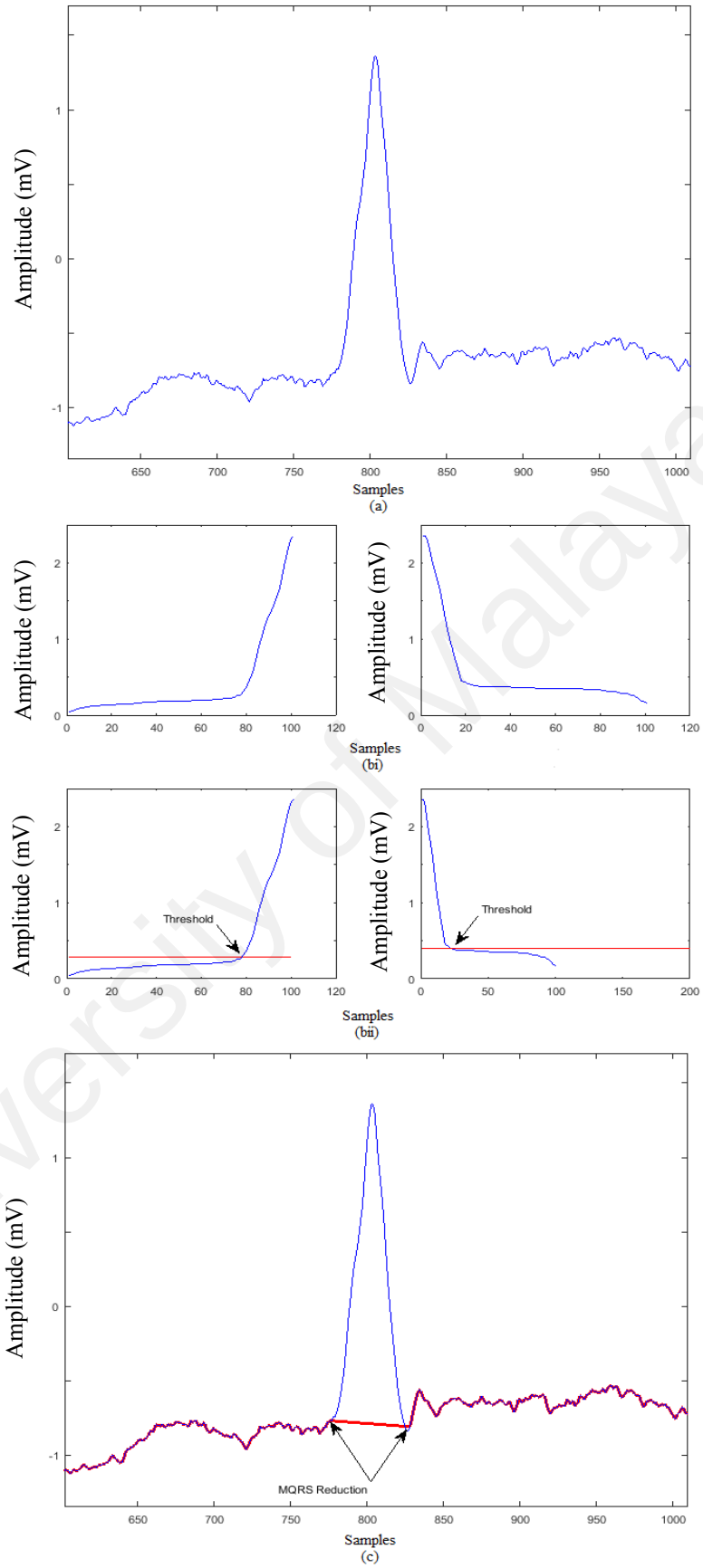

Figure 3.2: Reduction process of MQRS complexes. (a) Original signal; (b) Moving point method; and (c) MQRS reduction.

3.2.2.2 Fetal QRS Detection

The bandwidth for the FECG is between 0.05-100 Hz. In the abdomen list, the maximum amplitude of QRS will swing according to the type of recording. For maternal recording, the QRS amplitude will normally oscillate from 100 to 150 μV, while for fetal recording will oscillate up to 60 μV (E. C. Karvounis et al., 2007). In order to achieve better FQRS detection, other noises in the same frequency range should be removed. This was done by applying the 50 Hz notch filter to the MQRS removed signal.

The next step involved enhancing the signal by increasing the signal to noise ratio. Decomposing the signal using wavelet transform did this. Although wavelet transform was used to decompose the FECG signal, most of them applied Discrete Wavelet Transform (DWT) (Kahankova et al., 2017). DWT has a problem where the occurrence of the QRS complex is not localized as the DWT downsampled the signal as it moves to a different decomposition level. Stationary Wavelet Transform (SWT) does not have this problem, as it is the wavelet coefficients that are upsampled as it moves to a different level (Ng & Raveendran, 2009). The FQRS complex frequency range corresponded with the decomposition at level 3 (approximately 63-125 Hz) and level 4 (approximately 31-63 Hz). However, in this study, level 3 was used at level 4 may be contaminated with the residual MQRS complex as well as 50 Hz noise. The 4th order *Daubechies* wavelet was used here as it had been commonly used in other studies (Hassanpour & Parsaei, 2006).

In order to find the FQRS complex, a similar method, as in finding the MQRS, was applied to the level-4 Stationary Wavelet Transform decomposition. The heart rates which in bpm were extracted from R-R intervals of an ECG signal. The R-R intervals are the time in ms and calculated the distance between two consecutive ventricular

contractions of the ECG signal. The R-R interval distance between the two points of the FQRS candidate will give the FHR. By using this distance method, the detection of normal and very high FHR will be achieved. Each signal will go through this process and it will be filtered separately. After few processes, a set of FQRS locations can be determined for each channel.

In order to validate the effectiveness of the algorithm, the actual location of the QRS complex was determined visually from the raw abdominal ECG data. This location was to determine the FHR which was used as a comparison with the proposed algorithm to determine its performance.

An average of FHR (Avg_FHR) can be calculated by using the value of R-R interval obtained in Figure 3.3. To calculate the FHR, the formula used for this process is as below:

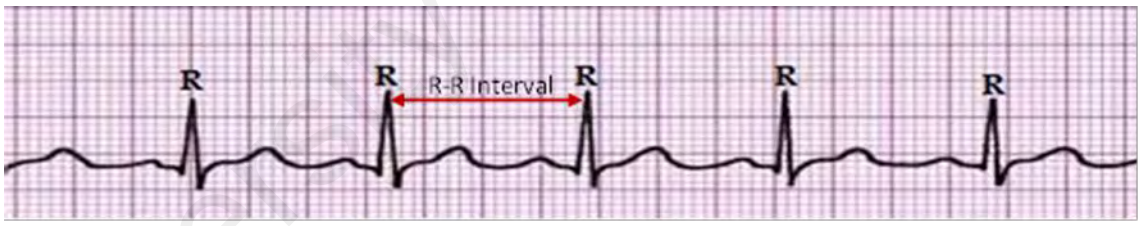

Figure 3.3: R-R Interval for Heart Rate Variability.

Heart Rate Calculation:

i) R-R Interval Distance Each Pair (3.2)

$$R\text{-}R = loc\_FQRSn - (loc\_FQRSn\text{-}1)$$

ii) Fetal Heart Rate Calculation (3.3)

$$FHR\ (FHR) = [(Sampling\ Rate) / (R\text{-}R\ Interval)]\ X\ 60$$

3.2.3 Performance Evaluation

Four different types of measurements were used to evaluate the effectiveness of the FR-peaks detection process. The equations used to calculate them are shown in equation 3.4 to 3.7 (E. C. Karvounis et al., 2007). They are composed of Sensitivity, *Se,* (3.4), Positive Diagnostic Value, *PDV*, (3.5), Accuracy, *Acc,* (3.6) and Overall Performance, *Per,* (3.7).

$$Se = \frac{TD}{TD + FN} X\ 100 \tag{3.4}$$

$$PDV = \frac{TD}{TD + FP} X\ 100 \tag{3.5}$$

$$Acc = \frac{TD}{TD + FN + FP} X\ 100 \tag{3.6}$$

$$Per = \frac{TD - (FP + FN)}{TD} X\ 100 \tag{3.7}$$

In this study, False Negative (*FN*) has a direct connection with *Se* in translating a probability of FR-peaks discovery. Meanwhile, *PDV* was used in determining the presence of False Positive (*FP*) where it gave the FQRS probability that is found FQRS. Next, the *Acc* is a metric in the process of summarizing all positive and negative diagnostic values for the proposed method. In summary, *TD* is a true detected (FR-peaks correctly detected), *FP* is a false positive (artefacts detected as FR-peaks), and FN is a false negative (FR-peaks are not detected by the proposed method). This *FN* and *FP* will be determined after stage 3 in the methodology.

3.3 Determination of Fetal QT Interval Estimation

3.3.1 Study Design

QT interval abnormalities in newborns are associated with hypoxia, maternal selective *serotonim* reuptake inhibitors during pregnancy (Dubnov, Fogelman, & Merlob, 2005), heart block, and sudden infant death syndrome (Degnan, 2013). This study sought to validate measurement of the FQT interval in term labouring women using data Set A from PCinC2013. General signal processing process flow for this study is as in Figure 3.4.

Figure 3.4: The flow of estimation of FQT interval.

3.3.1.1 Database

Data were provided by the PCinC2013 (Goldberger et al., 2000). Data for the challenge consists of a collection of one minute FQRS recordings. Each recording contains four non-invasive abdominal leads. Though the sampling frequency is the same 1000 Hz for all recordings, the instrumentation varied and had differing frequency responses, resolution, and configurations. Noise, artefacts, EMG, power line interference and baseline wandering affected signals. The 447 records used in the challenge were drawn from five data collections Table 3.1. For this study, the algorithm was developed using a training set, Dataset A (75 records), that was used as a training set which included non-invasive FECG signals, as well as reference annotations marking the locations of each FQRS complex (by marking the time of R events). Sets A and the reference annotations for set A, remain freely available ("Noninvasive fetal ECG: the PhysioNet / Computing in Cardiology Challenge 2013,"). Figure 3.5 shows a

short excerpt of a record from set, A which include four simultaneous non-invasive fetal ECG signals, acquired using electrodes placed on the mother's abdomen, containing both the fetal and the maternal ECGs. The maternal QRS complexes (not marked) are larger than the fetal QRS complexes (marked in blue).

Table 3.1: FECG database reference.

Database Name	N records
Abdominal and Direct FECG (1)	25
Artificially Generated FECGs (2)	20
Non-Invasive FECG (3)	14
Ukraine Non-Invasive FECG	340
Private Scalp FECG Database	48

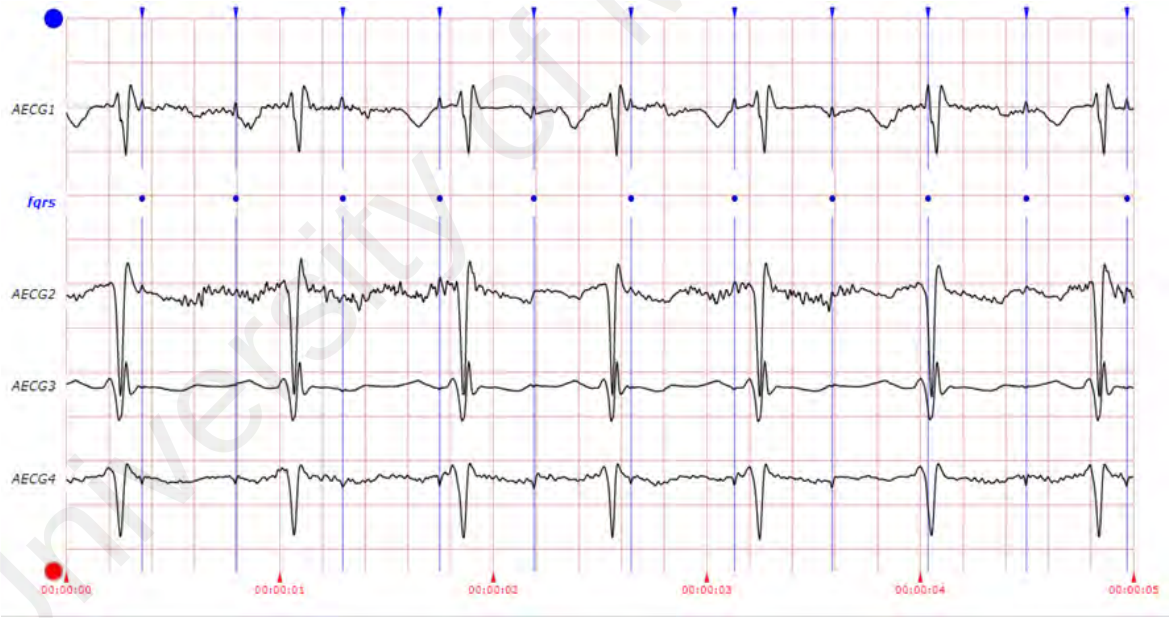

Figure 3.5: A five seconds excerpt of one minute record from the challenge training set.

The reference annotations used for the challenge were revised during the competition. Gold standard (reference) FECG R-peaks (FR-peaks) time series was expertly annotated from a SECG recorded simultaneously with an AECG. During the first phase of the challenge, preliminary scores were based on reference QRS

annotations derived by the authors of the respective datasets. During the later stages of the challenge, the original annotations were replaced by a set of crowd-sourced reference annotations, derived by applying a novel probabilistic voting algorithm (Silva et al., 2013) to multiple sets of manual annotations and those made by the open-source entries in Phase 1. Out of the five events, Event 3, the reference QT durations were also derived by applying the probabilistic voting algorithm to manual annotations done by seven observers. The challenge was to produce a set of annotations (FQRS complex locations) that matches the non-disclosed references as closely as possible. The FQRS complex locations were annotated by marking the R events. Figure 3.6: shows the sample of annotation for data "a01m.mat".

t0	b0	RR (sec)	b1	t1
0:00.000	[0]	0.355	N	0:00.355
0:00.355	N	0.439	N	0:00.794
0:00.794	N	0.501	N	0:01.295
0:01.295	N	0.454	N	0:01.749
0:01.749	N	0.441	N	0:02.190
0:02.190	N	0.455	N	0:02.645
0:02.645	N	0.485	N	0:03.130
0:03.130	N	0.457	N	0:03.587
0:03.587	N	0.449	N	0:04.036
0:04.036	N	0.461	N	0:04.497
0:04.497	N	0.471	N	0:04.968
0:04.968	N	0.459	N	0:05.427
0:05.427	N	0.459	N	0:05.886
0:05.886	N	0.463	N	0:06.349
0:06.349	N	0.460	N	0:06.809
0:06.809	N	0.460	N	0:07.269
0:07.269	N	0.467	N	0:07.736
0:07.736	N	0.462	N	0:08.198
0:08.198	N	0.453	N	0:08.651
0:08.651	N	0.461	N	0:09.112
0:09.112	N	0.471	N	0:09.583

Figure 3.6: Annotation for fetal R-R interval location.

The algorithm starts with the pre-processing of the FECG signals. Pre-processing is intended to reduce possible power-line interference from each channel using a simple

Notch filter. For power-line noise removal, a Notch filter at 60 Hz is applied, since the origin of the data is unknown.

3.3.2 Algorithm

3.3.2.1 Notch Filter

The ECG signal has been a major diagnostic tool for the cardiologists and provides almost all the information about the electrical activity of the heart. Therefore, care should be taken while doing the ECG filtering, such that the desired information is not distorted or altered in any way. Although researchers to reduce the power-line noise have suggested many methods, filtering introduces an unacceptable ringing effect especially after the QRS complexes.

A major source of interference in ECG signals is the 50/60 Hz power-line frequencies. The 60 Hz frequency components can be removed by using a Notch filter. A very simple approach to filter power-line interference is to create a Notch filter with zeros on the unit circle in the z domain at the specific frequencies to be rejected. If f_o is the interference frequency, the angles of the (complex conjugate) zeros required will be $\pm f_o/f_o(2\pi)$; the radius of the zeros will be unity. The sharpness of the notch may be improved by placing a few poles near or symmetrically around the zeros and inside the unit circle. But the increased transient response time results in a ringing artefact. The general, more sophisticated filters can be constructed by having a narrower notch but it is not possible to design the notch to remove the noise without causing ringing (Reddy, 2002). Therefore, a combination technique was proposed to filter out 60 Hz power line interference in this study.

(a) ***The Notch Filter Design and Characteristics***

The filter is designed taking care that lesser ringing effect is introduced and the desired information is not altered in any way. The transfer function of notch filter at a

digital angular frequency ω_0 can be designed by pole-zero placement method and can be represented in the z domain as:

$$H(z) = \frac{(z - e^{j\omega_\circ})(z - e^{-j\omega_\circ})}{(z - re^{j\omega_\circ})(z - re^{-j\omega_\circ})} \tag{3.8}$$

A complex conjugated pair of zeros lies on the unit circle at the notch frequency ω_o, a pair of complex-conjugated poles position at the same angle as the zeros, but at a radius r. The radius r determines the notch bandwidth. When radius r approaches unity, amplitude response becomes an ideal filter. The transfer function can also be represented as:

$$H(z) = \frac{1 - 2\cos\omega_\circ z^{-1} + z^{-2}}{1 - 2r\cos\omega_\circ z^{-1} + r^2 z^{-2}} \tag{3.9}$$

For r=0.95 the transfer function of the 60 Hz notch filter is:

$$H(z) = \frac{1 - 1.2856z^{-1} + z^{-2}}{1 - 1.2213z^{-1} + 0.9025z^{-2}} \tag{3.10}$$

3.3.2.2 Blind Source Separation

Over the past decade blind source separation (BSS) has received much research attention because of its potential applicability to a wide range of problems, spanning disciplines as diverse as communications, geophysical exploration, airport surveillance and biomedical signal processing (Barros, Mansour, & Ohnishi, 1998). In biomedical signal processing, BSS has been successfully applied to a wide variety of applications such as the extraction process for FECG.

The BSS problem can be written as $X(t) = MS(t)$, where $X(t) = \{x1(t),.....xnc(t)\}$ is the time series data from nc number of recorded channels; $S(t) = \{s1(t),.....sns(t)\}$is the unknown ns number of sources; M is an unknown nc X ns constant mixing matrix.

(a) ***Independent component analysis***

Independent component analysis (ICA) is a sub-type of BSS techniques, and ICA can be applied successfully to biomedical signal processing with the assumption of the independence of sources (Naik & Kumar, 2011). There are various algorithms based on ICA to separate out the statistically independent components of the signal. Important work related to FECG extraction with ICA is done in (Asha, Paul, & Kavana, 2014; De Lathauwer, De Moor, & Vandewalle, 2000).

ICA represents a solution for the extraction of the set of signals based merely on their mixtures. ICA assumes a linear combination of sources (called components):

$$X = AS \tag{3.11}$$

where X is a mixture of source signals, A is the mixing matrix that characterizes environment through which source signals pass, and , S is the source signals.

BSS based on ICA has been successfully applied to the Evoke Potential (EP) analysis (Jung et al., 2001; Makeig et al., 2002; Vigário, 1997). The ECG is of considerably higher amplitude than that of EP, which is typically obscured by the background, processes and requires the averaging of a large number of single-trial responses to become visible. The sample of the resulting simulated EP in shown in Figure 3.7, which is used in Electroencephalogram signal processing. This EP response consisted of a combination of two half-sinusoids.

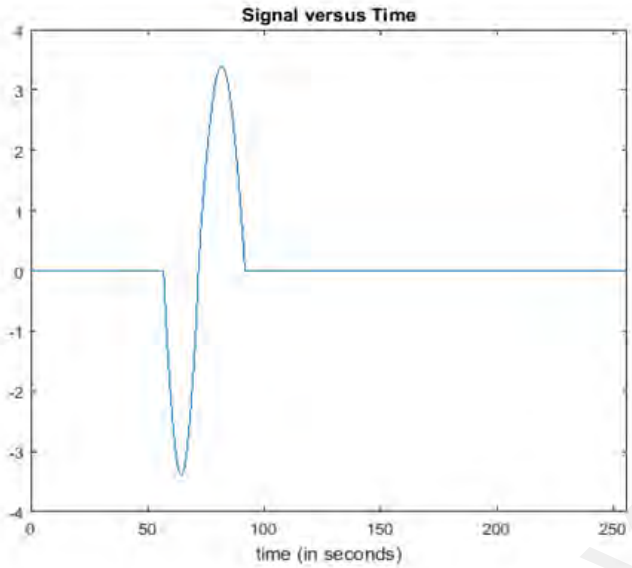

Figure 3.7: Artificial signal typically seen in an auditory EP.

3.3.3 Estimation of Fetal QT Interval

At the first stage, the pre-processing process will filter out the noise. Notch filter of 50 Hz has been used. In this work, FQRS annotation has been given by Physionet. After detected the FQRS, it followed with the data segmentation process. It will segment a bit in front and behind for all FQRS and stacks them together and also line them. This process is done because all of FQRS must have the same or similar shape. But since FECG is a weak signal, the outside noise will influence and make them not in it shape. So, to make them in a line and average across them, the noise must be removed.

It is known that noises can be positive or negative. In this process, it will take all average and make a lot of noise to be zero. In this way, the beautiful FECG signal can be found. Only then, the FQT can be determined.

However, when use data segmentation, averaging is only can take one wave instead of 10, 15 or more. Here, the *i*ICA will be used. This *i*ICA will throw and process by BSS, where the signal will be trimmed and cleaned up. So, the individual FQT can be detected clearly for each and every pulses.

3.4 Summary

In summary, all the procedures stated above were conducted to obtain the outcomes. For FHR detection, the proposed algorithm first detects and removed the MQRS complex from the abdominal FECG recordings. Then, the signal is decomposed using stationary wavelet transform to enhance the FQRS complex. By using the R-R interval, the FHR can be computed. This is compared with the FHR obtained through visual observation of the raw abdominal FECG signal. While for determination of FQT Interval estimation, the extraction of the FQT from the NIFECG output by the Physionet Challenge 2013 is studied by referring to the annotations provided by Physionet. A notch filter that removes power interferences at 60 Hz was applied. The signals were then data segmentations before applying the iterative blind source separation technique. The next chapter will present the results and data analysis from all the trials that were conducted.

CHAPTER 4: RESULTS AND DISCUSSION

4.1 Fetal Electrocardiogram Analysis

To investigate further the effectiveness of the described method for estimation of the FECG from the abdominal ECG signal, it was applied to NIFECGDB from Physionet. The MATLAB m - files were used to execute the proposed method. All processes through this method retained all the original features of FECG.

Figure 4.1 highlights a segment of the "ecgca748" signal recording at 22nd gestational weeks plus 1 day. Ch1 – Ch2 are thoracic signals, and Ch3 - Ch5 are abdominal signals.

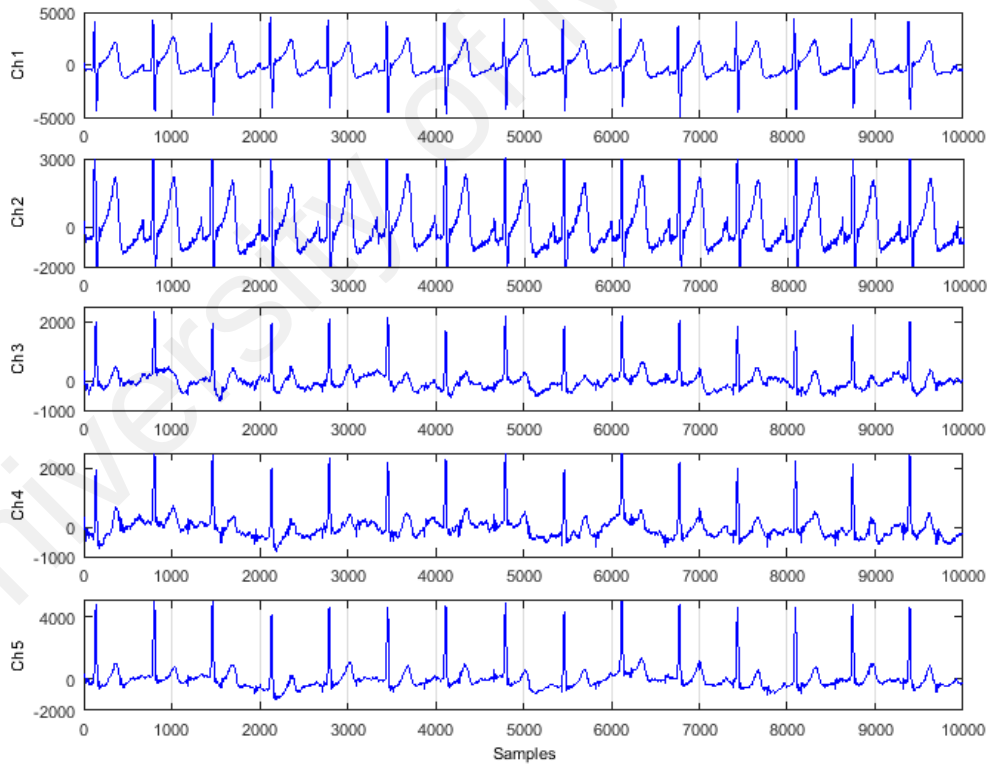

Figure 4.1: A segment (5 seconds) of the "ecga748" signal recording at 22 gestational weeks plus 1 day in the MIT database. Ch1-Ch2: Thoracic signals. Ch3-Ch5: Abdominal signals.

The suggested methodology was implemented on the AECG leads. In this study, thoracic leads were not necessary and were implemented to the Channel 3 to Channel 5 abdominal signals one by one. Despite the background noise being very strong, the FECG signals still estimated clearance where FQRS complexes were clearly visible, and the result is shown in Figure 4.2. There are three steps in this study, which are the suggested methodology is implemented on the AECG leads. In this study, thoracic leads are not necessary and have implemented to the Channel 3 to Channel 5 abdominal signals one by one. Despite the background noise is very strong, the FECG signals are still estimated clearance where FQRS complexes are clearly visible, and the result is shown in Figure 4.2. There are three steps in this study which are: i) MQRS detection; ii) MQRS reduction; and iii) FQRS detection.

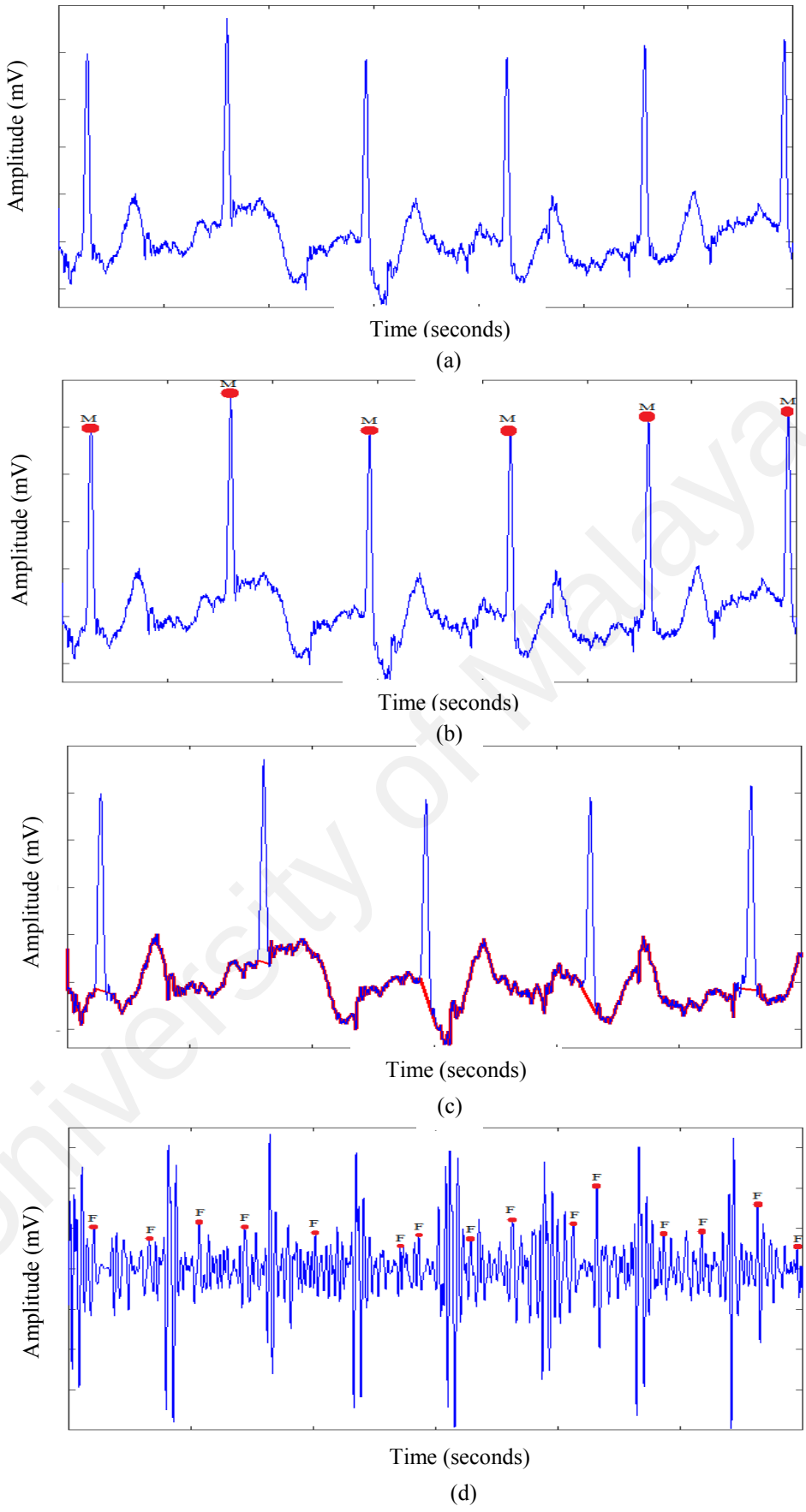

Figure 4.2: Channel 3 "ecga748" MIT 3 seconds Non-invasive Fetal ECG database, (a) Raw Abdominal signal Channel 3; (b) Candidates of MQRS; (c) MQRS reduction; and (FQRS candidate.

Figure 4.2 shows 3 seconds of the FHR monitoring of signal Ab-748 for Channel 3, where the original signal, MQRS detection/reduction, and the detected FQRSs candidates are displayed. Figure 4.2(b) shows the candidates for MQRS complexes. It goes with Figure 4.2(d), which shows the candidates for FQRS complexes. Finally, Figure 4.2(c) shows the result of the MQRS reduction.

During the FHR monitoring, all dataset will go through to a few processes till lastly succeed to calculate the fetal heartbeat. Firstly, a comparison has been made on average FHR obtained for computational result, visual result and least error (by 1 bpm and 5 bpm) result. From here, it can be seen that, the result for these three types of parameter will show the error for every single of candidate R-R interval for computational and visual result. The result will show in percentage.

The entire sample of the Physionet dataset was used to verify the proposed method in the FQRS detection process. It should be noted that FECG estimates using this proposed method only use segments of a single abdomen. Validation of reasonable FECG estimates that needed to meet certain conditions such as maternal ECG components, were eliminated. Repetitive R wave fetal protruding in the final waveform, and fetal pulse rates can be extracted accurately from the resulting waveform at the end of the process.

The percentage of success of the proposed method was based on the success of the FHR detection process found. This percentage plays an important role in the FECG extraction method. It is because FHR detection is an important prerequisite for the FECG parameter extraction process. It is very helpful for clinicians to know the condition of the fetus. In addition, it can also help to improve the quality of the FECG extraction process.

As mentioned, the proposed methodology has been applied to the Channel 3 to Channel 5 abdominal signals in Figure 4.1 one by one. It can be seen that the FECG was estimated from the abdominal signal successfully. Then a selection process will be run to select one of the best channels. The best channel through this selection process needs to have a good quality signal so that the subsequent analysis process can be done. From the 55 dataset, Channel 3 has been selected for 27 times. The percentage of the channel selection is shown in Figure 4.3.

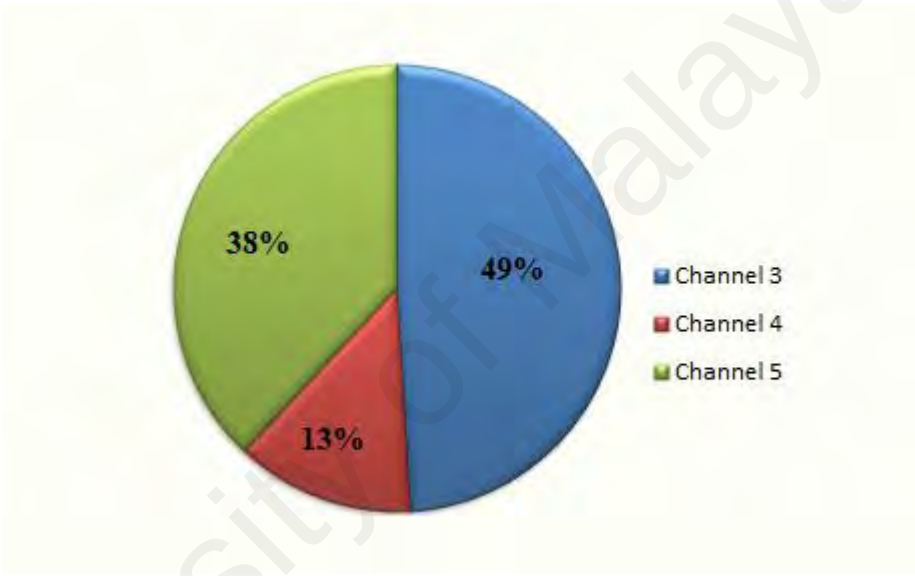

Figure 4.3: The percentage of best channel selected.

Average of FHR (Avg_FHR) can be calculated by using the value of R-R interval obtained. FHR can be calculating by using the equation stated in (3.4) and (3.5). For clarity, Figure 4.4 displays the average FHR for all analysis. In this figure, it can be seen that the average FHR for three types of analysis is about the same.

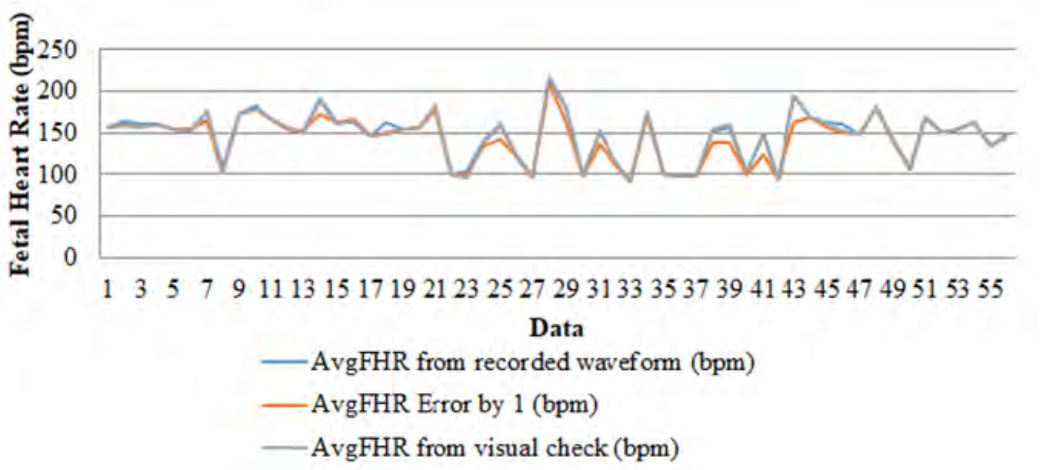

Figure 4.4: Average fetal heart on each analysis for all dataset.

While doing the analysis, few datasets were very easy to detect the FQRS and some were not due to the morphology of FECG. A total of 30 out of 55 datasets was graded as Class A data based on a parameter which set by us. It showed that these 30 datasets have at least averages that differ by ≤ 1 bpm with a minimum score of 0.6 and differed by ≤ 5 bpm with a minimum score of 0.8. Out of the 29 datasets, there are 5 best datasets where FQRS found 100% in 2 or 3 channels. The dataset are ecga244, ecga444, ecga649, ecga748 and ecga826. The determining parameter to classify each dataset is in Table 4.1.

Table 4.1: Parameter used to classify dataset.

Classes	Parameter	Total (dataset)
A	Accuracy is 100%	29
B	Accuracy is ≥95% & ≤99%	4
C	Accuracy is ≥90% & ≤94%	9
D	Accuracy is ≥85% & ≤89%	5
E	Accuracy is ≥80% & ≤84%	2
F	Accuracy is ≤79% ; else	6
N	Error cannot be defined as visual cannot see	-

Extensive computer simulations and experiments were performed on NIFECGDB. But due to limited space, only several typical results were carried out. The summarization of obtained result is shown in Table 4.2.

Table 4.2: Evaluation of the method proposed using the fetal ECG database from the Physionet.

Dataset No.	AvgFHR from recorded waveform (bpm)	AvgFHR from visual check (bpm)	TP (recorded)	TD (visual check)	FN	FP	Acc (%)	Class
ecga102	157	157	26	26	0	0	100	A
ecga154	165	165	26	26	0	0	100	A
ecga192	161	161	26	25	1	1	96	B
ecga445	160	160	26	26	0	0	100	A
ecga748	155	155	25	25	0	0	100	A
ecga811	153	153	25	24	1	1	96	B
ecga876	174	176	28	25	3	3	89	D
ecga900	108	108	17	16	1	1	94	C
ecga274	172	172	28	28	0	0	100	A
ecga300	165	165	27	27	0	0	100	A
ecga649	166	166	27	27	0	0	100	A
ecga323	155	155	26	26	0	0	100	A
ecga902	152	152	25	21	4	4	84	E
ecga986	104	104	30	30	0	0	100	A
ecga997	162	162	26	24	2	2	92	C
ecga848	163	163	26	26	0	0	100	A
ecga368	146	146	23	23	0	0	100	A
ecga410	163	163	26	26	0	0	100	A
ecga826	155	155	25	25	0	0	100	A
ecga571	156	156	25	25	0	0	100	A
ecga880	184	184	27	25	2	2	93	C
ecga115	99	99	16	15	1	1	94	C
ecga252	103	103	16	15	1	1	94	C
ecga816	140	140	22	20	2	2	91	C
ecga308	160	160	25	25	0	0	100	A
ecga621	120	120	19	17	2	2	89	D
ecga864	98	101	28	20	8	8	71	F
ecga127	217	229	26	19	7	7	73	F
ecga384	180	182	29	25	4	4	86	D
ecga436	99	98	25	19	6	6	76	F
ecga699	153	160	30	20	10	10	67	F
ecga868	118	118	22	15	7	7	68	F
ecga998	93	93	15	15	0	0	100	A

ecga392	173	174	27	27	0	0	100	A
ecga416	102	102	16	16	0	0	100	A
ecga776	99	98	16	14	2	2	88	D
ecga968	98	98	17	16	1	1	94	C
ecga896	152	153	23	23	0	0	100	A
ecga595	158	158	24	24	0	0	100	A
ecga629	103	103	17	14	3	3	82	E
ecga659	149	149	23	23	0	0	100	A
ecga515	95	95	16	14	2	2	88	D
ecga711	195	195	28	26	6	6	79	F
ecga244	169	169	27	27	0	0	100	A
ecga290	166	166	24	24	0	0	100	A
ecga733	161	161	26	25	1	1	96	B
ecga585	148	148	22	20	2	2	91	C
ecga597	181	181	29	29	0	0	100	A
ecga886	143	143	23	23	0	0	100	A
ecga444	106	107	25	24	1	1	96	B
ecga840	169	169	28	28	0	0	100	A
ecga746	151	151	25	25	0	0	100	A
ecga771	154	154	25	25	0	0	100	A
ecga473	163	163	28	26	2	2	93	C
ecga906	135	135	22	22	0	0	100	A

From Table 4.2, the comparison of average FHR obtained from computational result, and visual result. The success rate for obtaining reasonable estimates of the FHR data using the proposed method ECG was almost 90% (49/55) and 6 were not detected such as “ecga127”, “ecga436” and “ecga699”. Although using the same dataset, in Table 4.2 it can be seen that the method proposed by the authors is one of the best methods when compared to other methods.

Moreover, the results showed having closely related to the gestational week, the relatively high success rate at 22–29 and 33–40 gestational weeks. For the failing estimation of the FECG, the records were associated with lower quality of SNR. There may be several significant factors related to records such as the position of the fetus, gestational age and type presentation (breech or cephalic). When the gestation age is in the range of 24 to 34 weeks, there is a *vernix caseosa* effect that will make the FECG

amplitude lower. Consequently, there is a very important aspect to be assessed in the future, which is the collection of FECG signal needs to comply with the FECG standard signals.

Based on the data in Table 4.2, a comparison of FHR analysis of the recorded dataset, visual checking and differed by ≤ 1 bpm was done. The overall accuracy of the system was observed to be around 100 % with error difference of 1 bpm. This value shows that the proposed method is good enough for detecting the FHR. In the table displayed, the average FHR between two types of analysis varied around 146 bpm.

There are three quantitative result and indices of test performance that were calculated. Table 4.3 shows the summarization amounts of true FQRS (*TP* FQRS), *TD* FQRS*, FNs* and *FPs*, which were obtained by the computational result, which compared the FQRSs obtained by manually resulting. The FECG recording of Non-invasive Physionet was processed and selected abdominal lead samples included a total of 1165 FR-peaks of which 38 were not detected (3.3%), 38 were false detection (3.3%) and 1127 (96.7%) were correctly detected. The average number of *Se* counts was 96.4%, *PDV* (96.4%) and *Acc* (93.6%). Meanwhile, the calculation for the overall performance of the methodology, *Per* is 92%.

Table 4.3: Evaluation results for real-time FHR extraction using PhysioNet Database.

No. of record	TP FQRS	Method Results			Parameters (%)			
		TD FQRS	FN	FP	Se	PDV	Acc	Per
49	1165	1127	38	38	96.4	96.4	93.6	92.0

4.1.1 Proposed Methodologies for Heart Rate Variability Analysis

The suggested methodology is to extract the FHR from the AECG signal. This methodology is designed so that it is used especially with the presence of a limited number of AECG leads. For example, when the wearable devices were employed in some cases, a single lead selection would improve the accuracy in all used leads. This proves that the proposed methodology can be implemented by just using a single lead. This methodology can also be implemented only if this lead carries a strong FECG interference.

Table 4.4 shows several methods for the process of extracting FHR that has been used in the literature by using various databases. Through this table, it can be seen the performance level of each proposed method. The evaluation of the study uses different datasets, as there was no benchmark for the database. Therefore, the comparison between the methods cannot be carried out directly. It should be noted that all these studies were conducted using the real AECG recording without the involvement of any simulation signal. In addition, the analysis process of these methods does not use thorax leads and only used a small number of recorded leads. While Table 4.5, shows several methods for the process of extracting FHR that has been used in the literature by using same type of database. Based on the results, it can be concluded that the proposed methodology yields the best result and excellent performance; plus can be comparable to other methods.

Table 4.4: Summary of existing methods with different database.

Author	Description	Dataset	Accuracy (%)
Pieri et al., (Pieri et al., 2001)	Matched Filter	400 records (3 abdominal leads)	65
Karvounis et al. (E. Karvounis, Papaloukas, Fotiadis, & Michalis, 2004; E. C. Karvounis, Tsipouras, & Fotiadis, 2009; E. C. Karvounis et al., 2007)	Time-frequency analysis	10 long records (3 abdominal leads)	97.35
	Complex Wavelet	15 records (3 abdominal leads)	99.5
	Phase-space	13 long recording (3 abdominal leads)	94.45
Martens et al., (Martens et al., 2007)	PCA & matched filter	20 long recording	85
Ibrahim et al., (Ibrahimy, Ahmed, Ali, & Zahedi, 2003)	Statistical analysis	5 records (1 abdominal leads)	89
Azad et al., (Azad, 2000)	Fuzzy approach	5 records (3 abdominal leads)[a]	89
Hasan et al., (M. Hasan & Reaz, 2012)	Neural network	10 records	93.75
Behar et al., (Behar et al., 2014)	Echo state neural Network [ESN]	11 records (28 abdominal leads)	90.2
Ghaffari et al., (Ghaffari et al., 2015)	Time Frequency analysis	69 records (4 abdominal leads)	83.62
This Study	**Filtering Method**	**49 records (3-4 abdominal leads)**	**93.6**

Table 4.5: Summary of various methods using the same database.

Author	Method	Successfully found FHR	Success Rate (%)
Pu et al.(Pu, Han, Liu, & Jiang, 2017),	Combination Vector	33	60
Wei et al.(Wei, Xueyun, & Hongxing, 2013),	Adaptive Comb Filter-Resampling	43	78.1
Zheng et al.(Zheng, Liu, He, Ning, & Cheng, 2010),	Adaptive Comb Filter	29	52.7
This Study	**Filtering Method**	**49**	**90**

The FQRS detection process is at a critical stage in the methodology suggested by the authors, which directly affects the performance of this method. After the MECG component removal, error detection will often occur in the remaining ECG signal. This situation will occur when the fetus component is in a very weak condition or when the background noise is very strong. From the observation, FECG's estimation failure in the PhysioNet database recording is due to difficulties or failure to find FQRS complexes in the abdominal waveforms by the naked eye. Similarly, FECG's estimation failure occurred due to the difficulty in detecting FQRS in residual signals. In addition, the scalp signal will also be damaged if the amplitude of the noise is large. It happens because the reference point is not available for the period when the noise appears. Multiple channels fusion could be considered as a good solution for improving the R peaks detection. In the future, in the next research stage is planning to detect the R peaks using multichannel AECG signals occur.

In the selection best channel process in all locations of FQRS, it does not necessarily lead to the best results. To date, there is no suggestion or prediction of better criteria. Possibly, the best way is to simultaneously take all the contributions to find the existence of FQRS for all leads.

4.2 Estimation of Fetal QT Interval

4.2.1 Algorithm Parameters

To validate the measurement of the FQT interval, the parameter values used were as follows: notch filters between 50 and 60 Hz, q = 8, Wr = 100 - 400 ms post stimulus and CTh = 0.15. Also, the convergence criterion ε was set in terms of the estimate improvement between successive iterations, and the algorithm was assumed to converge when the absolute difference between successive iterations resulted in 1/NRF value changes of less than 10^{-3}, i.e.,

$$\varepsilon = \left| \frac{1}{NRF_k} - \frac{1}{NRF_{k-1}} \right| < 10^{-3} \tag{4.1}$$

Where, k represents the iteration index. This study desired a relatively large value for the maximum number of iterations to allow the algorithm to converge, and the $k_{\max}$ =2 are used.

4.2.2 Evaluation with Abdominal ECG recordings

The performance of the *i*ICA procedure on actual recordings from normal subjects is depicted in Figure 4.5, where show examples of single-trial Av_FECG before and after *i*ICA processing, respectively of signal “a15m.mat”. These plots illustrate the effectiveness of the proposed technique in enhancing individual components in single trials for N100 components, without destroying the average response. In Figure 4.6 shows an example of the Av_FECG from “a15m.mat”, when data from all 600 samples

are superimposed. The FQRS complex is clearly visible against the noisy background between 100 and 400 ms after stimulus onset. The components extracted out of the entire Av_FECG waveform after *i*ICA processing is shown in the same figure. Overall, the peaks in the FQRS complex are much sharper, and the waveform outside that latency range is practically flat, thus giving an enhanced view of the N100 components.

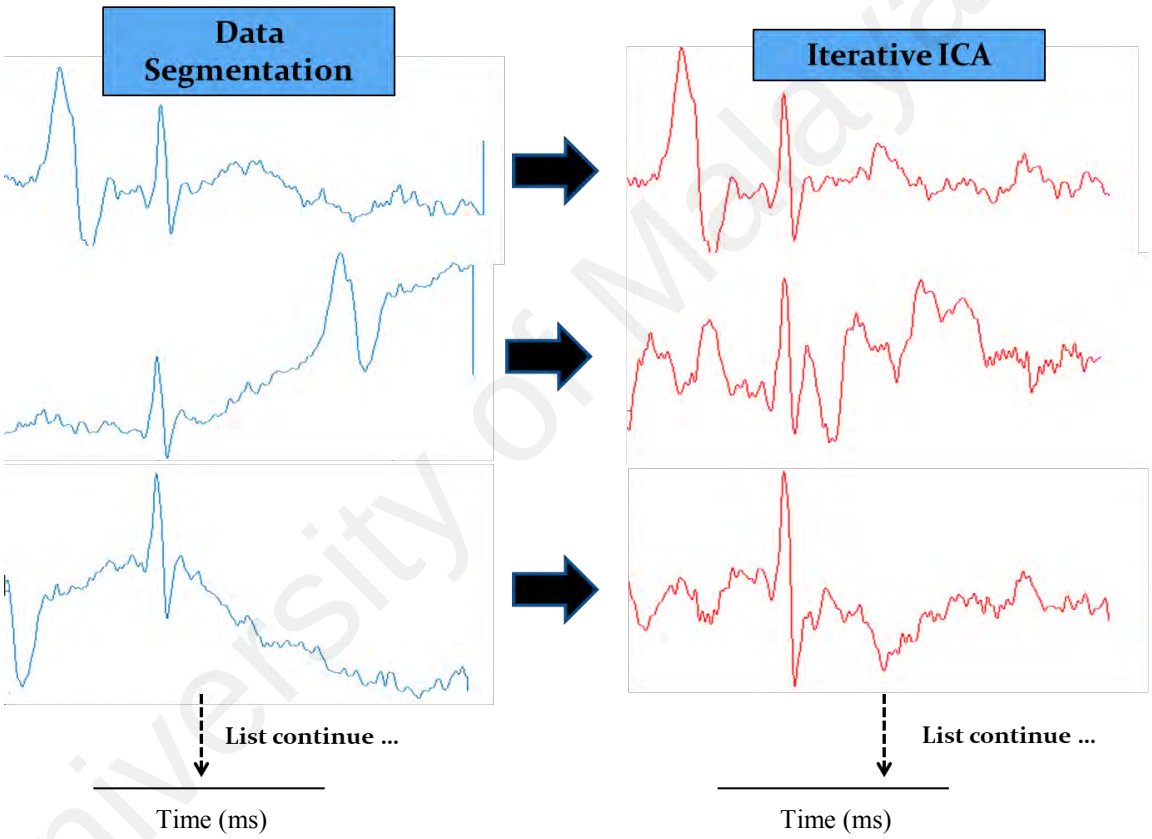

Figure 4.5: Examples of single trial for N100 components Avg_FECGs before and after *i*ICA processing.

4.2.3 QT Interval Evaluation

The QT interval is defined as the time interval between the Q wave onset and the end of the T wave in the heart's electrical cycle. In 1920, Bazett (Kawataki, Kashima, Toda, & Tanaka, 1984) mentioned there is a relationship between the QT length and the heart rate has been established in adults and although such a relationship has not been studied in fetuses, it is reasonable to assume that the QT length be modulated by the FHR (even

if differently than for adults). Three annotators on adult ECG annotated the data using the modified Physionet Lightwave interface has found the root means square error (RMSE) is 16.07 ms.

Since the RR interval annotation is provided, this means that the QT interval estimation is straightforward process. The Q position was located as the first maximum before the R wave and the T position are located at a minimal value between 100 ms and 400 ms from the position of the Q wave as seen in Figure 4.6 for the signal of "a15m.mat". In this signal, the QT length was found to be in the interval 173-323 ms and the magnitude of the FQT estimation error obtained 12.25 ms.

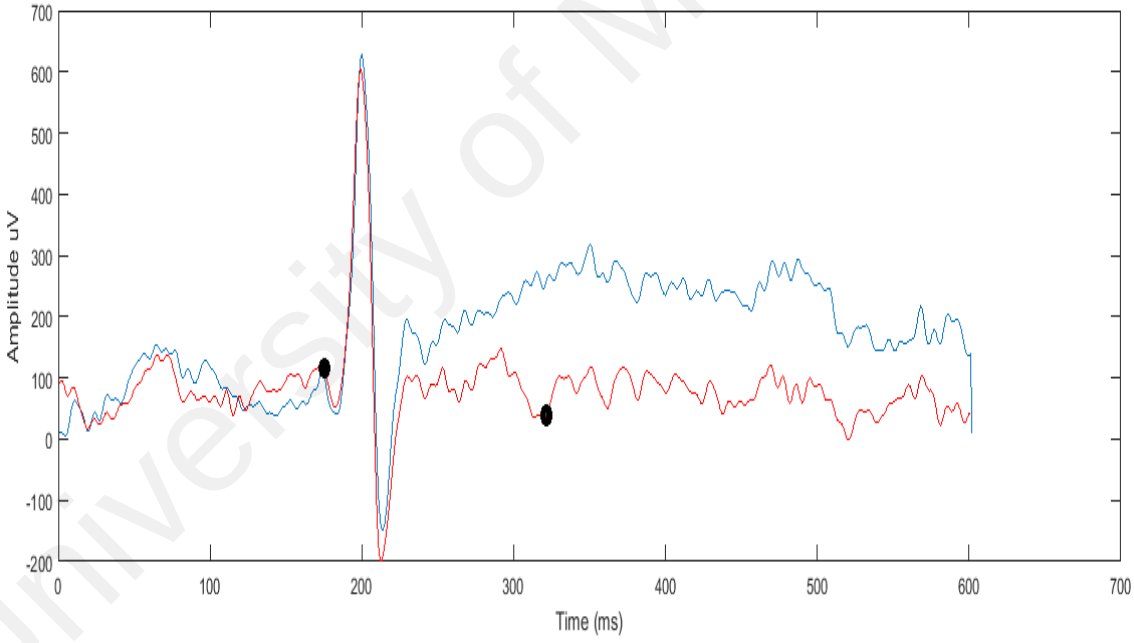

Figure 4.6: Fetal QT estimation. The fetal QT length is marked in black.

The entire sample of the dataset was used to verify the proposed method in the FQT estimation process. Extensive computer simulations and experiments were performed on PCinC 2013 Set A. But due to limited space, only several typical results were carried out. The summarization result is shown in Table 4.6 which obtaining reasonable estimation of FQT interval. This proposed method succeeded to detect 30 out of 75

reasonable estimation of FQT. The table also displayed the average of QT length to be in the interval 173-341 ms and the magnitude of the FQT estimation error obtained at 12.95 ms.

Table 4.6 : Evaluation of the method proposed using the PCinC2013 database Set A from the Physionet.

Data	QT Interval (ms)	RMSE (ms)
a01	185-340	12.45
a03	168-335	12.92
a04	178-323	12.04
a07	160-342	13.49
a10	181-320	11.79
a12	170-330	12.65
a13	178-328	12.25
a15	173-323	12.25
a16	178-362	13.56
a17	165-332	12.92
a20	180-344	12.81
a22	170-334	12.81
a23	198-357	12.61
a24	178-338	12.65
a25	170-340	13.04
a41	178-362	13.56
a44	184-339	12.45
a49	174-360	13.64
a52	178-338	12.65
a53	160-345	13.6
a54	176-356	13.42
a56	160-345	13.6
a57	155-322	12.92
a58	172-345	13.15
a60	168-355	13.67
a61	175-340	12.85
a64	158-335	13.3
a70	178-360	13.49
a71	172-355	13.53
a72	178-335	12.53
Average QT Interval 173-341 ms RMSE = 12.95 ms		

The results obtained show that the advantage of the new method is twofold: it can extract individual components out of the entire FECG signal, and also provide enhanced estimates of these components in each single trial. With actual recordings, the *i*ICA procedure was able to show responses in single trials, which are typically difficult to see due to low SNR. In the corresponding Av_FECG, the FQRS peaks became sharper, and the waveforms outside the region of interest became flatter, thus giving an overall enhanced view of the N100 component. However, in situation that FECG signal are really weak, the detection results of the proposed method seem not good. Further development needed to improve the performance of the present method.

4.2.4 Proposed Methodologies for QT Estimation Analysis

The average of QT length in this study was in the interval 173-341 ms. The RMSE between all corresponding averaged was 12.95 ms, which compares to an RMSE of 12.8 ms observed in (Behar, 2016) even uses different datasets since there was no benchmark for the database.

A number of published studies have attempted to extract the FQT (and other ECG morphology based quantities) from the NIFECG or FMCG (Abboud, Barkai, Mashiach, & Sadeh, 1990; Brambati & Pardi, 1980; J. Stinstra et al., 2002; Taylor et al., 2005). Table 4.7 shows the published studies of extraction the FQT, which can be used as reference for any of the time interval measures. However, these studies did not validate their measurements with invasive data and thus they did not prove that the algorithms that they used for NIFECG extraction did not distort the QT length.

Table 4.7: Reference FQT interval based on published studies.

Parameters Name	Definition	Description	Interval (ms)
QT Segment	Duration between Q onset and end of the T wave	i.(n = 412, wg: 16–42) ii.(n = 21, wg: 32–41), iii.(n = 11, wg: 24–41)	149–339 ms 207–338 ms 233–329 ms

n = number of record used

There is no gold standard for the FQT interval, given the inability to adhere standard electrodes to the fetal precordium. Validation using the SECG is a reasonable approach; however it would be useful to validate the FQT interval with ECG data measured immediately after birth. Such data would also provide information on whether the QT interval changes at delivery. Despite the fact that one of the principal advantages of the NIFECG is its ability to perform antenatal monitoring, the study focused on measurements performed at birth. This is because this is the only alternative for obtaining a QT reference by using the SECG (other than using magnetocardiography, which is expensive and would prohibit the use of the NIFECG monitor). However, it is important to mention that the accuracy in estimating the FQT from the NIFECG will likely be lower if the gestational age was significantly lower, since the fetal heart would be smaller and the NIFECG signal to noise ratio may therefore be lower.

Since the extraction and study of morphological parameters from the NIFECG is a nascent field, it is difficult to say whether the error reported in this study is low enough to be considered acceptable for FQT monitoring. However, it is less than that quoted for adult ECG studies and thus demonstrates a promising application.

4.3 Summary

In this chapter, the algorithms developed throughout this work were presented. This chapter proposed a systematic method for determining the FHR, fetal RR and QT interval from maternal abdominal ECG. These methods performed well even some channels of original AECG signals were seriously polluted by noises. However, in situations that FECG signal are really weak, even could not be visually identified, the detection results of the proposed method seem not good. An extensive noise filtering is necessary and a filtering method in this work seems to be not sufficient for very noisy data. At the same time, further development by incorporating the artificial intelligence methods will facilitate to improve the performance of the present method.

CHAPTER 5: CONCLUSION AND RECOMMENDATION

5.1 Introduction

In this work, several relevant aspects regarding the NIFECG research were addressed. A variety of different approaches have been proposed in the literature to extract fetal signals from AECG. In this study simple, automatic, and effective schemes are developed for the use in signal processing of fetal ECG waveforms generated from single lead non-invasive abdominal recordings. Analysis of signals recorded from single lead ECG is a convenient solution to allow FECG monitoring in a non-clinical environment. Minimal abdominal detecting electrodes are used, and the method is simple to operate, even by the mothers themselves. Therefore, it can be used in the normal home care environment.

5.2 Limitations

The real data used in these experiments are from the NIFECG Database from MIT-BIH PhysioBank. The real FECG signals are highly contaminated by MECG and noise, and the extraction of the FECG is a challenging issue. The proposed method can obtain reasonable estimates of FECG signals for approximately 90% of the abdominal signals in this database, which seems to be a promising result. The 96.7% positive prediction implies that the algorithm detects almost all existing peaks, and the missed peak detection is resulted because of non-existing peaks in the original abdominal signal. This may occur due to misplacement of leads on the abdomen of the mother or due to the fetus position.

Applications of the proposed method on different data sets may be useful for further validation and also to investigate potential clinical implications. Moreover, the method proposed here can be applied only for single fetus signals recorded from the mother's abdomen. To detect twins' signals, the algorithm should be modified in some

way. Therefore, the future work will focus on the development of such modified algorithms to extract twins' FECG signals.

5.3 Contribution of research

Aside from the produced simulated data, a large private clinical study was carried out in partnership with the Obstetrics & Gynaecology Department and Technical Department (Obs. Central), UMMC. This exploratory study enabled further insights on the nature of the FECG signal (particularly during delivery). Moreover, the data supplied important information on the recording technique. This exploratory study enabled further insights on the nature of the FECG signal (particularly during delivery). Throughout the development of this work, it can increase knowledge and understanding of CTG. This method is used in all clinics and hospitals in Malaysia, in monitoring the condition of infants in the womb. Future works on the clinical front should aim at generating a large randomized trial, to conclusively confirm FECG's clinical relevance in prenatal monitoring.

5.4 Future works

There are number of statistics that should be reported when assessing the performance of any NI-FECG extraction algorithm; classical statistics for QRS detection algorithm assessment should include: *Se, PPV*, *Acc*, and *F1* computed with a tolerance of 50 ms around the reference annotations. These statistics reflect the performance of the algorithm in extracting the FQRS from the abdominal mixture and should also be reported at different stages of pregnancy. Although the NIFECG can be recorded from 20 weeks onward (Peters et al., 2001), the *vernix caseosa* forms around the 28^{th}-32^{nd} week and dissolves in 37^{th}-38^{th} week in normal pregnancies (Stinstra, 2001b), theoretically limiting successful NIFECG recording during this time period. To

what extent the *vernix caseosa* influences accurate FECG extraction is to be further quantified.

In addition to reporting statistics on FQRS detection, it is necessary to report the performance of the algorithms in terms of FHR (i.e. after any smoothing has been performed to compute the FHR from the detected FQRS), since ultimately the FHR is used in clinical practice. Statistics could also be grouped by HRV range or events (e.g. accelerations/decelerations): in clinical practice, physicians are interested in rapid variations of FHR; as such algorithms should be evaluated in their capacity to adapt to highly variable FHR rather than when there is no event (and thus less non-stationary).

In the current literature, very little work has been done in reconstructing the FECG morphology from the extracted NIFECG signal. In this thesis a number of points were highlighted that, if addressed, could push the research forward. The effect of the baseline frequency on FQT extraction is yet to be determined. It is known that for adults a high baseline frequency will distort the T-wave morphology, negatively affecting the QT estimation. However, the baseline wander is rather substantial on the abdominal recordings and needs to be heavily removed. The trade-off between least QT distortion and good baseline removal needs to be studied.

It was shown, in Chapter 4, that QT can be extracted from both the source and observation domain. However, number of challenges associated with the two approaches need to be tackled; while working in the source domain, is QT affected by the BSS transform? While working in the observation domain, which abdominal channel should be selected? In particular, the abdominal channel selection when working in the observation domain is likely to have an important impact on the measured QT due to the associated projection and QT dispersion.

5.5 Conclusion

In summary, this thesis focused on the processing of the ECG recorded from a set of abdominal sensors recorded on pregnant women, and the extraction of clinically relevant information from this signal. Indeed, NIFECG offers many advantages over the alternative fetal monitoring techniques, the most important one being the opportunity to enable morphological analysis of the FECG, which is an instrumental in determining whether an observed FHR event is physiological or pathological feasible during delivery. Measurement of the QT could also be used before giving birth to identify whether any drugs the mother takes will prolongs the QT of the fetus during the pregnancy.

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LIST OF PUBLICATIONS AND PAPERS PRESENTED

Manap, F. A., Ng, S. C., & Abdul Wahab, A. K. (10 April 2019). A Review on Non-Invasive Fetal Electrocardiogram Signal Processing to Analyse Crucial Data and its Future Directions. *EURASIP Journal on Advances in Signal Processing*. (*ISI – Indexed Under review*)

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