Non-invasive fetal electrocardiogram classification using spatial correlation

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Abstract

In Europe and many developed countries the preterm birth rate is generally 5-9 %, and in the USA it has even risen to 12-13 % in the last decades. Preterm birth is the major cause of neonatal mortality in developed countries. Premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development. The cause for premature birth is in many situations difficult to determine; many factors appear to be associated with the occurrence of premature birth, making the prevention of premature birth a challenging proposition. Fetal monitoring can support the physician in making the often vitally important decision whether or not to induce labor artificially.

Nowadays, the most common used technique for fetal monitoring is cardiotocography (CTG). However, information from Doppler CTG alone is not sufficient for making important decisions regarding the treatment of the fetus and the mother in case of fetal distress. The predictive value of the CTG can be increased when it is combined with ST analysis of the electrocardiogram (ECG) of the fetus. The STAN® device (Neoventa, Sweden) uses this combination by attaching a single spiral electrode to the fetal scalp to obtain the fetal ECG (fECG) and to perform ST analysis. The major drawback of the STAN® device is, however, its invasiveness. It can only be performed when the fetal membranes are ruptured and sufficient cervical dilatation is present.

In order to get a better insight into the fetal condition during pregnancy, it would be advantageous to develop a method for fetal monitoring that operates non-invasively, and provides additional information with respect to the CTG.

In collaboration with the Eindhoven University of Technology, at the Máxima Medisch Centrum in Veldhoven, The Netherlands, researchers have developed an algorithm to obtain the fECG from the abdominal recordings for singleton pregnancies. The algorithm is capable of estimating the maternal ECG (mECG) and subtracting it from the abdominal recordings, but due to the low signal to noise ratio (SNR), the signals remaining after subtraction of the mECG are often not suitable for extracting the fECG.

Additionally, at the moment, the calculation time of the algorithm is too long to permit online fetal heart rate detection. A solution to decrease the calculation time significantly could be by excluding several abdominal signals for further analysis. The main goal of this project was therefore to reduce the calculation time of the fECG extraction by excluding a number of abdominal signals from further analysis. In order to achieve this, the abdominal signals need to be screened in order to assess their quality. In this report, a technique is presented that classifies the abdominal recordings based on their spatial correlation. The technique is referred to as the classification of fetal ECG signals using spatial correlation (CLASC).

CLASC considers a priori knowledge on the abdominal electrode configuration and fetal heart activity. It obtains a two dimensional representation of the fetal vectorcardiogram (fVCG) by using a patient-tailored vectorcardiography approach to spatially combine the abdominal fECG signals. However, due to the low SNR of the abdominal fECG recordings, this fVCG representation is significantly corrupted by noise. However, in spite of the low SNR, the fVCG can be once used to locate the positions of the fetal R-peaks and to define individual fECG complexes. These ECG complexes can, in turn, be enhanced by averaging the detected ECG complexes, synchronized on their R-peaks. The resulting average ECG complexes can be used
to obtain an fVCG, again using the patient-tailored vectorcardiography approach mentioned before, with increased signal to noise ratio. This fVCG, since it originates from averaged ECG complexes, is referred to as the average VCG (AVCG).

By projecting the AVCG onto the lead vectors that indicate the electrode positions, and comparing the resulting projected fECG signals to the originally determined average fECG complex, the fECG signal exhibiting the lowest correlation can be identified. This signal is subsequently considered to contain the least useful, mutual fECG information and is therefore classified in the last position and omitted from further processing.

From the remaining average ECG complexes, the process (i.e. calculation of the AVCG, projecting this AVCG onto the lead vectors, and omitting the signal with lowest correlation) described above is repeated until full classification of the abdominal recording is achieved by CLASC.

By limiting further processing and analysis of the abdominal fECG signals to the best (e.g. four) signals, calculation times can be decreased significantly, while only a limited amount of fECG information is lost.

In order to assess the performance of the fetal R-peak detection of CLASC, it is compared to a widely spread technique called principal component analysis (PCA). In general, CLASC significantly outperforms PCA on abdominal recordings with a large SNR, but is beaten by PCA on low SNR recordings, albeit marginally.

The classification part of CLASC is compared to an average visual selection (AVS) which is an average of the visual selection by multiple researchers in the MMC. In general, when both techniques define the best four fECG signals, at least 3 out of four are the same. The advantage of using CLASC is that it operates fast, automatically, and always produces the same results, in contrast with the visual selection, which is dependent of the observer.

So as a general conclusion, although CLASC should be enhanced in the future, it already performs quite accurate and fast, and takes a huge step towards future online beat-to-beat heart rate detection and fECG extraction from abdominal recordings.
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## Abbreviations

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<th>Description</th>
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<tbody>
<tr>
<td>NICU</td>
<td>Neonatal intensive care unit</td>
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<tr>
<td>MMC</td>
<td>Máxima Medisch Centrum</td>
</tr>
<tr>
<td>OHC</td>
<td>Obstetric high care</td>
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<tr>
<td>CTG</td>
<td>Cardiotocography</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<tr>
<td>fECG</td>
<td>Fetal electrocardiogram</td>
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<tr>
<td>TU/e</td>
<td>University of technology Eindhoven</td>
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<tr>
<td>mECG</td>
<td>Maternal electrocardiogram</td>
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<tr>
<td>CLASC</td>
<td>Classification of fetal electrocardiogram signals using spatial correlation</td>
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<tr>
<td>VCG</td>
<td>Vectorcardiogram</td>
</tr>
<tr>
<td>fVCG</td>
<td>Fetal vectorcardiogram</td>
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<tr>
<td>AVCG</td>
<td>Average fetal vectorcardiogram</td>
</tr>
<tr>
<td>AV</td>
<td>Atrioventricular</td>
</tr>
<tr>
<td>SA</td>
<td>Sinoatrial</td>
</tr>
<tr>
<td>CVO</td>
<td>Combined ventricular output</td>
</tr>
<tr>
<td>WAMES</td>
<td>Weighted averaging of maternal electrocardiogram segments</td>
</tr>
<tr>
<td>SNR</td>
<td>Signal to noise ratio</td>
</tr>
<tr>
<td>BPM</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>NEMO</td>
<td>Non-invasive electrophysiological monitor for obstetrics</td>
</tr>
<tr>
<td>AVS</td>
<td>Average visual selection</td>
</tr>
<tr>
<td>CD</td>
<td>Classification difference</td>
</tr>
<tr>
<td>I.V.</td>
<td>Interobserver variability</td>
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<td>PCA</td>
<td>Principal component analysis</td>
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1. Introduction

Birth is something every human being has in common. If one seeks the definition of the word “birth”, the free online dictionary will describe it as “The emergence and separation of offspring from the body of the mother”. However, when a mother is asked exactly the same question, she will often describe it with the words “happy”, “miracle” and sometimes also “painful”.

Birth normally occurs between 37 and 42 weeks of gestation, calculated from the beginning of the last menstruational period. When birth takes place before the 37th week of gestation, the baby is considered premature. In Europe and many developed countries the preterm birth rate is generally 5-9 %, and in the USA it has even risen to 12-13 % in the last decades. Key factors contributing to this increase include a rise in the number of pregnancies in women over age of 35 and the growing use of assisted reproduction techniques, leading to an increase in the number of twin and higher orders of multiple births.

In terms of gestational age, 5% of preterm births occur at less than 28 weeks (extreme prematurity), 15% at 28-31 weeks (severe prematurity), 20% at 32-33 weeks (moderate prematurity), and 60% at 34-36 weeks (near term) [1]. Preterm birth is the major cause of neonatal mortality in developed countries. Premature infants are at greater risk for short and long term complications, including disabilities and impediments in growth and mental development. Significant progress has been made in the care of premature infants, but not in reducing the prevalence of preterm birth. The cause for premature birth is in many situations difficult to determine; many factors appear to be associated with the occurrence of premature birth, making the prevention of premature birth a challenging proposition.

Babies born before 32 weeks of gestation are often not able to survive without help and have to be monitored. Besides these severe premature babies, also babies with a weight below 1 kg and babies with serious disorders of vital functions have to be admitted in a neonatal intensive care unit (NICU) of a hospital. In the Netherlands, ten hospitals are equipped with such a NICU, including the Máxima Medical Center (MMC) in Veldhoven. The MMC also has an obstetric high care (OHC) unit, where women with complicated pregnancies can be monitored.

The decision to deliver a baby prematurely due to fetal distress is often a difficult balance between the benefits and risks of continued life in utero, the neonatal risks of extrautero life, and the risks to the mother of continuing the pregnancy. The survival rate of prematures increases severely from 26 to 30 weeks of gestation. However, intervening too late could result in fetal brain damage due to a lack of oxygen. Fetal monitoring can support the physician in making the often vitally important decision whether or not to induce labor artificially.

The task of obstetric care is to secure a safe delivery for mother and child. Nowadays, the most common used technique for fetal monitoring is cardiotocography (CTG). CTG is a technical means of recording (-graphy) the fetal heart rate (cardio-) and the uterine contractions (-toco-) during pregnancy, typically in the third trimester. Simultaneous recordings are done by two separate transducers, one for the measurement of the fetal heart rate and a second one for the uterine contractions. Each of the transducers may be either external or internal.

External measurement means taping or strapping the two sensors to the abdominal wall. The heart ultrasonic sensor, based on the Doppler effect, then overlays the fetal heart. The pressure-sensitive contraction transducer, called a tocodynamometer (toco), measures the tension of the maternal abdominal wall - an indirect measure of the intrauterine pressure.
Internal measurement requires a certain degree of cervical dilatation, as it involves inserting a pressure catheter into the uterine cavity, as well as attaching a scalp electrode to the child's head to adequately measure its heart rate. Besides the need to have cervical dilatation, another major disadvantage of the scalp electrode is the need to screw the scalp electrode in the fetal scalp. In particular, mothers' concerns about pain or harm to the baby from needle electrodes, the risk of viral transmission, and the risk of serious scalp infection must be considered. In the Netherlands, each year, on average one fetus dies due to complications of the scalp electrode [2]. However, internal measurement is more precise, and might be preferable when a complicated childbirth is expected.

When the CTG was introduced in the late 1950’s [3,4], it was assumed that electronic fetal monitoring would identify fetuses affected by intrapartum asphyxia by detecting specific patterns in the heart rate variability, resulting in early intervention and a reduction in cerebral palsy. However, since every fetus shows heart rate variability, it can be difficult to distinguish asphyxiated from healthy fetuses using CTG alone. This lack of diagnostic information has caused abnormal CTG patterns to be missed and, as a result, babies to suffer from intrapartum asphyxia, as well as normal CTG patterns to be mistaken for signs of hypoxia, leading to unnecessary interventions. Since it is a physician who interprets the CTG, the CTG interpretation suffers from both intra- and interobserver variability.

The predictive value of the CTG can be increased when it is combined with ST analysis of the electrocardiogram (ECG) of the fetus. The STAN® device (Neoventa, Sweden) uses this combination by attaching a single spiral electrode to the fetal scalp and a skin electrode to the upper leg of the mother (used as the ground electrode) to obtain the fetal ECG (fECG), and to perform ST analysis. Due to the use of a fetal scalp electrode, this can only be done during cervical dilatation. The STAN® device is used on a large scale and has shown to reduce both the operative delivery rate for presumed fetal distress and the cord artery metabolic acidosis rate [5].

Additional information on the condition of the fetus can be obtained by performing a fetal scalp blood sampling. Again, since this is an invasive technique, this can only be done during labor. In case of an abnormal CTG, the fetal scalp can be cleansed and pierced to obtain a small sample of blood. The pH level of the fetal blood sample can be considered as an indirect measurement of the oxygen supply to the fetus. In general, a low pH value suggests a low oxygenation of the fetus, which is an indication of fetal distress. However, the physician has to be careful to draw conclusions from the pH level of the blood sample, since it needs to be interpreted in the context of each individual labor. Also, a sample of the blood in the umbilical cord (microblood sampling) could lead to additional information on the condition of the fetus, including chromosomal abnormalities, blood disorders, metabolic disorders and infections.

As stated before, the major drawback of the STAN® device and the fetal blood sampling is their invasiveness. They can only be performed when the fetal membranes are ruptured and sufficient cervical dilatation is present. The blood sampling method and the microblood sampling suffer from the additional drawback that in case of fetal distress, a decision has to be made immediately and no time is available to await laboratory tests results.

For the reasons stated above, it would be advantageous to use a technique for performing early diagnostics in a non-invasive way. The only technique that can perform diagnostics non-invasively throughout the entire pregnancy is the Doppler CTG method. However, as mentioned above, the Doppler CTG has shown poor specificity in case of fetal distress as well as considerable intra- and interobserver variability [6]. Information from Doppler CTG alone is not sufficient for making important decisions regarding the treatment of the fetus and the mother in case of
fetal distress. In order to get a better insight into the fetal condition during pregnancy, it would be advantageous to develop a method for fetal monitoring that operates non-invasively, and provides additional information with respect to the CTG. In collaboration with the Eindhoven University of Technology (TU/e), the MMC has developed a system, called NEMO (Non-invasive Electrophysiological Monitor for Obstetrics), which uses electrophysiological recordings from the maternal abdomen to determine uterine activity, fetal heart rate, and the fECG. Because it is non-invasive, the NEMO system can be used throughout the entire pregnancy.

The first fECG measurement, by means of electrodes placed upon the maternal abdomen, took place about 100 years ago, but only in the last 25 years, mainly due to the revolution in modern electronic techniques, researchers are able to process the abdominal recordings in order to extract the fECG from the recording. However, abdominal fetal electrocardiography has not yet been implemented in hospitals around the world due to the large difficulties in this extraction. The abdominal recordings are a mixture of various components such as the fECG, the maternal ECG (mECG), the electrical activity of the abdominal muscles and uterus, power line interference, and noise. The low amplitude of the fECG with respect to amplitude of these unwanted components makes the extraction process difficult.

At the MMC in Veldhoven, researchers have developed an algorithm [7] that is capable of estimating and subtracting the mECG from the abdominal recordings, but due to the low amplitude of the fECG, the signals remaining after subtraction of the mECG are often still not suitable for extracting the fECG. Additionally, at the moment, the calculation time of the algorithm is too long to permit online fetal monitoring. A solution to decrease the calculation time significantly could be by simply excluding several abdominal signals for further analysis. This approach can be justified by noting that in most cases, some abdominal electrodes record less fECG than others, depending on the orientation of the fetus in the uterus and the position of the abdominal electrodes.

In order to enable online fECG recordings in the future, the main goal of this project is to reduce the calculation time of the fECG extraction by excluding a number of abdominal signals from further analysis. In order to achieve this, the abdominal signals need to be screened in order to assess their quality. In this report, a revolutionary technique will be presented that classifies the abdominal recordings based on their spatial correlation. The technique is referred to as the classification of fetal ECG signals using spatial correlation (CLASC).

The correlation between the different abdominal fECG signals can be explained by the fact that all fECG signals originate from the same source, i.e. the fetal heart. More specifically, in a simplified model, the electrical activity of the fetal heart can be represented by a single electrical field vector that varies both in amplitude and orientation over time. The time path of this field vector during one heartbeat is referred to as the vectorcardiogram (VCG). In addition, in the model, each ECG signal originates from the projection of the fetal VCG (fVCG) onto the vector that indicates the position of the recording electrode with respect to a reference electrode. The VCG is discussed in more detail in chapter 2.

CLASC obtains a two dimensional representation of the fVCG by using a patient-tailored vectorcardiography approach to spatially combine the abdominal fECG signals, utilizing knowledge on the positions of the abdominal electrodes. However, due to the low signal to noise ratio of the abdominal fECG recordings, this fVCG representation is significantly corrupted by noise. In addition, as opposed to the
definition of the VCG above, in this case the calculated fVCG representation contains the electrical activity of multiple heart beats, instead of a single one. Once calculated, the fVCG representation is used to locate the positions of the fetal R-peaks and to define individual fECG complexes. These ECG complexes are, in turn, enhanced by averaging ECG complexes, all synchronized on their R-peaks. The resulting average ECG complexes can be used to obtain an fVCG, again using the patient-tailored vectorcardiography approach mentioned before, with increased signal to noise ratio. This fVCG, since it originates from averaged ECG complexes, is referred to as the average VCG (AVCG).

This AVCG can be projected onto the lead vectors that indicate the electrode positions. By comparing the resulting projected fECG signals to the originally determined average fECG complex, the fECG signal exhibiting the lowest correlation with the other abdominal fECG signals can be identified. This signal is subsequently considered to contain the least useful, mutual fECG information and is therefore classified in the last position and omitted from further processing.

From the remaining average ECG complexes, the process (i.e. calculation of the AVCG, projecting this AVCG onto the lead vectors, and omitting the signal with lowest correlation) described above is repeated until full classification of the abdominal recording is achieved by CLASC.

By limiting further processing and analysis of the abdominal fECG signals to the best (e.g. four) signals, calculation times can be decreased significantly, while only a limited amount of fECG information is lost.
2. Physiology

In this chapter, the basic physiology of the heart will be discussed. First, the adult heart will be discussed followed by the discussion of the VCG and the ECG. Next, the fetal heart will be discussed as well as the abdominal recording of the fECG.

2.1 The human heart

The human heart is located in the chest, behind the sternum and between the lungs inside the pericardium [8]. The pericardium comprises two parts: the fibrous pericardium, made of dense fibrous connective tissue, and a double membrane structure (parietal and visceral pericardium) containing a serous fluid to reduce friction during heart contractions. The center of the heart is located about 1.5 cm to the left of the midsagittal plane (although sometimes it is on the right, which is called dextrocardia). The size of an average adult heart is about that of a fist, and it weighs around 250 to 300 grams. Directly above the heart are the great vessels: the superior and inferior vena cava, the pulmonary artery, pulmonary vein, and the aorta. The aortic arch is located behind the heart. In figure 1, a sketch of the human adult heart is shown.

The walls of the heart are composed of cardiac muscle, called myocardium. This myocardium has striations similar to skeletal muscle. The heart has four chambers; the upper chambers are called the left and right atria, and the lower chambers are called the left and right ventricles. The atria form one unit and the ventricles another. This has special importance to the electric function of the heart, which will be discussed later. A wall of muscles called the septum separates the left atrium and ventricle from the right atrium and ventricle. The left ventricle is the largest and strongest chamber in the heart. The heart is oriented so that the anterior aspect is the right ventricle while the posterior aspect shows the left atrium (see figure 1). The heart also has four valves; the tricuspid valve between the right atrium and ventricle, the mitral valve between the left atrium and ventricle, the pulmonary valve between the right ventricle and the pulmonary artery and, finally, the aortic valve in the outflow tract of the left ventricle.

The main function of these valves is to prevent backflow of blood.

![Figure 1: The human heart](image)
The main function of the heart is to pump blood around the entire body. Blood returning from the systemic circulation enters the heart in the right atrium from where it goes through the tricuspid valve to the right ventricle. It is then ejected through the pulmonary valve to the lungs where the blood will be re-oxygenized. Oxygenated blood returns from the lungs to the left atrium, and from there through the mitral valve to the left ventricle. Finally blood is pumped through the aortic valve to the aorta and the systemic circulation can begin again.

2.2 Electrical activation of the heart

In the heart muscle cell, or myocyte, electric activation takes place by means of the same mechanism as in the nerve cell - that is, from the inflow of sodium ions across the cell membrane. This sodium inflow causes the occurrence of an action potential which is a transient alteration of the transmembrane voltage (or membrane potential) in the excitable myocyte. The inward flow of sodium ions increases the concentration of positively-charged cations in the cell and causes depolarization; a change in the sign of the transmembrane potential.

The amplitude of the action potential in the heart is the same as for the nerve and muscle cells: about 100 mV. The duration of the cardiac action potential is, however, two orders of magnitude longer than that of nerve or skeletal muscle cells. After cardiac depolarization, a plateau phase follows, and thereafter repolarization takes place. As in the nerve cell, repolarization is a consequence of the outflow of potassium ions. The duration of the action potential is about 300 ms, as shown in figure 2.

![Figure 2: Electrophysiology of the cardiac muscle cell.](image)

Associated with the electric activation of cardiac muscle cell is its mechanical contraction, which occurs a little later. An important distinction between cardiac muscle tissue and skeletal muscle is that in cardiac muscle, activation can propagate from one cell to another in any direction. As a result, the activation wavefronts are of a rather complex shape. The only exception is at the boundary between the atria and ventricles, which the activation wave normally cannot cross due to the presence of a nonconducting barrier of fibrous
tissue. Only along a special conduction system, called the atroventricular node (A.V. node), can propagation of the activation wavefronts from the atria to the ventricles take place.

For each heartbeat, the activation wavefront originates in the sinus node (sinoatrial or SA node), which is located in the right atrium at the superior vena cava. This SA node has the shape of a crescent and is about 15 mm long and 5 mm wide (see figure 3) and consists of specialized muscle cells that function as self-excitatory, pacemaker cells. They generate an action potential at the rate of about 70 per minute.

Because the heart is effectively a syncytium, a compact collection of cardiac muscle cells interconnected by contiguous cytoplasmic bridges, the cardiac muscle cells are electrically coupled and impulses from the SA node spread rapidly through the walls of the atria, causing both atria to contract, and to the AV node. In the AV node, the impulses are delayed for about 0.1s before spreading to the walls of the ventricle. This delay ensures that the atria empty completely before the ventricles contract. Directly after the AV node, the so called bundle of His (named after W. His, Jr., 1863-1934) conducts the signals, before splitting into two bundle branches (left and right) along each side of the septum. Finally, the signals travel through the Purkinje fibers (named after J. E. Purkinje, 1787-1869) that diverge to the inner sides of the ventricular walls. Once the signals are within the ventricular region, the conduction process takes place at a high speed compared to the previous parts of the conduction path.
So basically, cardiac contractions originate from the propagation of an action potential through the cardiac tissues. The front of these action potentials causes the occurrence of numerous electrical dipoles. By superpositioning these electrical dipoles, for each point in time, the electrical activity of the heart can be modeled as a single electrical field vector, originating in the heart. The time path of this electrical field vector during a single cardiac contraction is called a vectorcardiogram (VCG).

### 2.3 The electrocardiogram

The impulses generated during the heart cycle are conducted through body fluids to the skin, where they can be detected by electrodes and recorded as an electrocardiogram (ECG). In fact, these ECG recordings are nothing more than the projection of the VCG onto the lead vector indicating the electrode position. As a consequence, all ECG recordings need to be spatially correlated to each other. In figure 4, a VCG is shown together with the three so called Einthoven projections [9]. In figure 5, a closer look is taken into the ECG and its nomenclature.

![Figure 4: The VCG is shown in green. The biggest loop represents the QRS complex, and the two smaller loops the P and T wave. When the VCG is projected onto the 3 lead vectors shown in blue, the ECG complexes are obtained. These particular projections are referred to as the Einthoven I (above), Einthoven II (left), and Einthoven III (right) leads.](image_url)
As stated in section 2.2, the electrical activation of the heart starts at the SA node, after which the depolarization wave propagates along the atrial walls to the AV node. This process is represented in the ECG complex by the P wave. The depolarization wave then travels further through the ventricular walls, represented by the QRS-complex.

Since the ventricular repolarization wave is oriented from the outside of the heart inwards, its direction is opposite from that of the ventricular depolarization wave. As a result, the depiction of the repolarization wave, which has opposite electrical sign, in the ECG (T-wave) has the same direction as the depiction of the QRS complex. The repolarization of the atrial walls is not visible in the ECG complex since it occurs simultaneously with the depolarization of the ventricles and has a small amplitude.

2.4 The abdominal fetal electrocardiogram

In this section, a closer look will be taken into the anatomy of the fetal heart and the propagation of the electrical signals from the fetal heart through the various tissues of the maternal abdomen to electrodes on the maternal abdomen.

2.4.1 The fetal heart

In the adult heart, the left and right ventricles eject the same output to the peripheral circulation, but the left ventricle generates a much higher pressure. In order to do so, the mass of the left ventricle greatly exceeds that of the right ventricle. Because of this greater mass and wall stress, the left ventricle is less compliant than the right one. This lesser compliance and greater ejection pressure enables the left ventricle to exert a great effect on the filling and ejection of the right ventricle (much more than the other way around). Therefore, the left ventricle is considered to be the dominant ventricle in the adult circulation.

In the fetus, gas exchange occurs in the placenta and not in the lungs, so only a small amount of blood needs to flow to the lungs for nutritional and metabolic needs. For this reason, the fetal heart has a slightly different anatomy from the adult heart, as can be seen in figure 6. There exist connections between the atria, called the
foramen ovale, and between the outgoing vessels of both ventricles, called the ductus areriosus. The ductus diverts blood away from the lungs to the descending aorta and umbilical-placental circulation. Mielke and Benda [10] reported that about 45% of the combined ventricular output (CVO) passes through the ductus. A second method to shunt blood away from the lungs is by permitting a right-to-left flow across the foramen ovale to the left atrium and ventricle.

Due to these shunting mechanisms, the interaction of the two ventricles in the fetal heart is quite different from that in the adult heart. The systolic pressure in the two ventricles is the same since they eject into the same ventricular bed, but they do not eject the same amount of blood. In fact, in utero, the right ventricle ejects about 55% of the CVO. Thus, the mass of the right ventricle is somewhat greater than that of the left, and both the diastolic and systolic interactions are much different. In the fetus, the right ventricle is thought to significantly constrain left ventricular filling and is considered the dominant ventricle because of its greater volume load.

![Figure 6: Anatomy of the fetal heart.](image)

This assumption has been verified by various researchers by calculating the spatial VCG directly after birth, arguing that the fetal heart works exactly the same immediately after birth as before birth [11,12]. Recently in the MMC, this theory has even been tested and confirmed on fetuses during the pregnancy at 21 weeks of gestation (Appendix A).

### 2.4.2 Propagation of the electrical signals to the abdominal electrodes

When the ECG is recorded from adults, the electrical impulses of the heart have to travel through the body tissues and the skin to the electrodes. In the case of the recording of the fetal ECG, by means of electrodes placed on the maternal abdomen, the electrical impulses have to travel through various fetal and maternal tissues before reaching the electrodes. The fetoabdominal anatomy is depicted in figure 7.
Physiology

As can be seen in figure 7, the fetus is enclosed in a system of shells, each with a different structure and with different electrical characteristics. The fetal tissue and the amniotic fluid are considered to be a good conductor, while the maternal skin and the subcutaneous fat are both poorly conducting, about a factor 10 less than the muscle tissue. The conductivity of the placenta is considered to be less than the amniotic fluid, but may be larger than that of the other tissues in the maternal abdomen. Since the poorly conducting maternal skin and subcutaneous fat layer form the interface between the abdominal ECG leads and the rest of the maternal abdomen, they have a profound influence on the fetal ECG measurements. In addition, between the 28th and 32nd week of gestation, the vernix caseosa (an isolating layer that forms around 28 weeks and starts to shed around 32 weeks) will be a considerable obstacle for the measurement of the fetal ECG [14]. The vernix caseosa is largely composed of a combination of oily and waxy matter called sebum and shedded fetal skin and lanugo hair [15]. It serves several purposes: moisturizing the infant’s skin, facilitating the passage of the baby through the birth canal and it functions as a physical barrier to the passage of bacteria. The conductivity of this layer is however very low, making it very difficult to detect the fetal ECG between week 28 and 32.

As a consequence of all the layers shielding the fetus from the outside world, the fECG signal recorded by the electrodes typically has a small amplitude and is disturbed by various electrophysiological signals and noisy interferences.

The most significant electrophysiological signal disturbing the fECG signal is the maternal ECG (mECG) [16]. The amplitude of the maternal ECG signal is 3 to 15 times higher than that of the fetal ECG (the fetal QRS complex peak-to-peak amplitude ranges from less than 5 µV to 60 µV depending on the electrode location, fetal position and gestational age, while the maternal abdominal ECG amplitude can easily reach 100µV). Another biological interference of the electrode signals is the mother’s respiration and electromyographic (EMG) signals due to movement of the mother and uterus contraction.

One of the main noisy components of the signal is the 50 Hz powerline signal, which can easily be filtered out with a combination of a bandstop filter and a low-pass filter (to filter the harmonics). Additional filtering can be used to filter out the baseline wander. There are also other non-physiological disturbances such as motion.
artefacts, thermal noise due to the electronic equipment, and noise caused by badly attached electrodes.

An abdominal fECG recording is shown in figure 8. The dotted vertical lines each indicate a fetal R-peak.

![Figure 8: An abdominal recording of the fetal ECG in the 24th week of gestation. The vertical lines indicate the positions of the fetal R-peaks. Note that the peak-to-peak amplitude of the fetal ECG is much lower than that of the mother ECG. In this particular recording, the fetal R-peaks can be detected visually, after only removing the powerline interference and the baseline wander. However, in most cases, it is more difficult and sometimes even impossible to detect the fetal R-peaks visually before the removal of the mECG, and sometimes even after the mECG is removed.](image)
3. Signal Processing

The goal of this chapter is to present a new method to classify the fECG signals referred to as the classification of fetal ECG signals using spatial correlation (CLASC). First, the maternal ECG and partial noise removal will be discussed, followed by an additional pre-screening step. Next, a fast and convenient way to calculate the fVCG from the fECG will be presented, followed by a detailed presentation of the CLASC method.

3.1 Maternal ECG and partial noise removal

The CLASC algorithm operates on abdominal signals in which both noise and the maternal ECG component are already suppressed. Therefore, in this section, a short summary of the pre-processing of the raw abdominal signals will be given. The theory of suppressing the undesired signals from the abdominal signals is based on the previous work of Vullings et al.. Readers desiring a more extensive discussion on the filtering techniques discussed in this section are therefore referred to [7].

As stated before, the main noisy non-physiological component of the recorded abdominal signals is the 50 Hz powerline signal. Since the signals of interest are in the range of 2 Hz to 80 Hz [17], a combination of a fourth order Butterworth bandstop filter, set to filter out frequencies between 48 and 52 Hz, and a fourth order Butterworth low-pass filter with a cut-off frequency of 90 Hz filters the powerline disturbances and any additional high frequency noise. The baseline wander of the signals is filtered using a fourth order Butterworth high-pass filter with a cut-off frequency of 1.5 Hz. All filters are applied in both forward and backward directions to compensate for phase shifts.

When the non-biological disturbances are filtered from the abdominal data, the next step is the removal of the maternal ECG signal. This is done by calculating a linear prediction of each separate wave in the mECG, referred to as the weighted averaging of mECG segments (WAMES). WAMES operates by dynamically dividing the mECG complex in separate segments and generating an estimate for each individual segment. Each estimate is hereby obtained by the linear combination of time-shifted, offset compensated, and scaled corresponding segments in preceding mECG complexes.

3.2 Pre-screening

The filtering techniques presented in section 3.1 perform well in most occasions. However, even though most of the noisy components and physiological interferences are filtered from the abdominal signals, artefacts sometimes remain. These artefacts originate from movement or from inaccuracies in the mECG removal. In order to filter these artefacts from the signals, before the data is analysed further, a fast and simple screening of the data is performed. The main goal of the pre-screening is to make the CLASC more robust by removing these artefacts, which could lead to errors during further analysis beforehand.

Each of the signals measured by an abdominal electrode (lead) is first divided into half-overlapping intervals with length 1s. By limiting the length of the intervals to 1s, only a small amount of data will be deleted when an interval has to be deleted, meanwhile ensuring the removal of the complete artefact.
Next, for each interval and each lead, the standard deviation is calculated. For each time interval, the standard deviations of the individual leads are then summed and compared to the average summed standard deviation (i.e. averaged over all intervals). When the summed standard deviation of a specific time interval is more than 1.5 times the average summed standard deviation, the data in the specific time interval is excluded for further analysis, due to the possible presence of an artefact. The threshold value of 1.5 is chosen to exclude all the intervals that could possibly disturb further analysis, while at the same time retaining enough data to perform further analysis. Note that when an interval is excluded from further analysis, it does not necessarily imply that an artefact or maternal ECG residue is present in the interval, but rather that the data in the considered interval could decrease the robustness of the main algorithm.

In order to preserve the time information of the data, the excluded intervals are not omitted, but set to zero.

An example of a fetal ECG recording before and after the pre-screening can be seen in figure 9.

Figure 9: In the upper figure, the data from eight different abdominal electrodes is depicted after filtering, but before the pre-screening. In the lower figure, that same dataset is pre-screened.
### 3.3 Calculating of the vectorcardiogram

The current standard for the calculation of the VCG from ECG signals, the inverse Dower matrix method, uses a fixed linear combination of the standard 12 lead ECG to calculate the VCG [18]. This technique is considered to be accurate and useful in clinical application for adult patients [19]. However, the main downside of this technique is that it uses a fixed, numerical description of a matrix $D$ (the Dower matrix) that maps the 12-lead ECG onto the VCG. Since the Dower matrix $D$ represents the electrode positions, this approach assumes that all the electrodes have to be placed in the same formation on each patient. Additionally, the geometry and conductive properties for all patients are assumed to be equal, as a result of which the application of the inverse Dower matrix method does not lead to accurate VCG calculations for patients whose geometry and conductive properties differ from the standard.

In this report, the abdominal fECG is recorded by means of eight electrodes, so the Dower matrix $D$ has to be modified for the fetus. This way, it would nevertheless still be a fixed, numerical approach.

In the fetal case however, there is no such thing as standard geometry and conductivity, since the position of the fetal heart with respect to the abdominal electrodes, the amount of amniotic fluid, placental position, and abdominal fat vary for each patient and each recording. Therefore, the inverse Dower matrix method does not lead to accurate results in the fetal case and needs to be modified further in order to be useful in the estimation of the fetal VCG.

The theory presented by Vullings et al. [20] uses a patient-tailored calculation of the VCG from the ECG signals. It operates by determining the joint probability distribution, using Bayesian probability theory, for both the VCG and a scaling matrix that models the attenuation at each recording site. This probability function is based on a simplified model of the relation between the VCG and the cutaneous ECG.

#### 3.3.1 Bayesian vectorcardiography

**One-dimensional ECG**

The electrical field generated by the cardiac tissue can be considered as a rotating electrical field vector $\vec{s}(t)$ with variable amplitude, as explained in section 2.2. The potential $V(t)$ at the cutaneous surface is determined by:

$$V_i(t) \propto \frac{\vec{r}_i \cdot \vec{s}(t)}{|\vec{r}_i|}.$$  \hspace{1cm} (1)

Where the medium is considered infinite and the surface position for electrode $i$ with respect to the heart is defined by $\vec{r}_i(t)$.

In the case of bipolar electrodes, the potential difference $V_{ij}$ between two cutaneous surface positions can be expressed as

$$V_{ij}(t) \propto \left(\frac{\vec{r}_i}{|\vec{r}_i|^3} - \frac{\vec{r}_j}{|\vec{r}_j|^3}\right) \cdot \vec{s}(t) .$$  \hspace{1cm} (2)
\[
\alpha \propto \left( \frac{\tilde{r}_i - \tilde{r}_j}{|\tilde{r}_i|} \right) \cdot \tilde{s}(t).
\]  

(3)

If the surface positions are close to each other, the distance between the heart and each of the electrodes can be approximated to be the same, and eq. (3) can be approximated by

\[
V_q(t) \approx \left( \frac{\tilde{r}_i - \tilde{r}_j}{|\tilde{r}_i|} \right) \cdot \tilde{s}(t).
\]  

(4)

**Multi-dimensional ECG**

The two dimensional representation of the positions of \(N\) cutaneous electrodes with respect to each other can be expressed in a \([N \times 2]\) matrix \(D\) where each row represents the electrode’s position with respect to a reference electrode \(D_i = \tilde{r}_i - \tilde{r}_{ref}\). The \([N \times 2]\) ECG \(V\) can then be written as

\[
V = \alpha DS + H. \quad (5)
\]

With \(S\) a \([2 \times T]\) matrix representing the VCG, \(H\) a \([N \times T]\) matrix representing noise in the ECG complexes, \(T\) the number of samples in a single cardiac cycle, with the ECG signal sampled at 1 kHz, and \(\alpha\) a diagonal scaling matrix for which the elements are related to the heart electrode distances \(|\tilde{r}_i|\).

The simplification shown in eq. (5) is only valid when the heart-electrode distances are the same for every electrode. By placing the electrodes in a circle-like position around the reference electrode, the heart-electrode distances are more or less the same for every electrode and the simplification can somewhat be justified.

Since in eq. (5), both \(S\), \(\alpha\) and \(H\) are unknown, some additional steps need to be taken in order to assess the VCG \(S\) from this formula. By applying statistical analysis, the VCG can be determined when only the ECG signal \(V\), the electrode positions \(D\), and noise variance \(\Sigma\) are known (i.e. \(H\) is assumed to be Gaussian distributed with zero mean and variance \(\Sigma\)). However, for this method to work, additional assumptions on statistical independencies need to be made. In the remainder of this section, these assumptions will be made explicit.

**Statistical analysis**

When the noise \(H\) is assumed to have a Gaussian probability distribution with zero mean and variance \(\Sigma\), the joint probability distribution of \(S\) and \(\alpha\), given \(V, D, \Sigma\) can be expressed using the theorem of Bayes:

\[
p \{S, \alpha | V, D, \Sigma\} = p \{S, \alpha | D, \Sigma\} \frac{p \{V | D, S, \alpha, \Sigma\}}{p \{V | D, \Sigma\}}. \quad (6)
\]

Considering \(p(V|D, \Sigma)\) a normalization term, assuming \(\alpha\) and \(S\) statistically independent from each other

\[
p \{S, \alpha | D, \Sigma\} = p \{S | D, \Sigma\} p \{\alpha | D, S, \alpha, \Sigma\}. \quad (7)
\]
and assuming no prior knowledge on $S$, in other words assigning $p(S|D,\Sigma)$ a uniform distribution, eq. (6) can be written as

$$p(S,\alpha|V,D,\Sigma) \propto p(\alpha|D,\Sigma) p(V|D,S,\alpha,\Sigma).$$

The terms on the right hand side of eq. (8) are referred to as the prior probability distribution and likelihood, respectively. The prior probability distribution $p(\alpha|D,\Sigma)$ can be simplified by noticing that $\alpha$ is independent of $D$ and $\Sigma$ and by furthermore assuming the elements $\alpha_i$ on the diagonal of $\alpha$ to be independent (this is not exactly true, but is assumed for mathematical simplification).

$$p(\alpha|D,\Sigma) = \text{const.}$$

Combining the assumption of Gaussian noise with the assumption that the rows of both $H$ and $V$ are statistically independent, the likelihood can be written as:

$$p(V|D,S,\alpha,\Sigma) = \prod_i \exp \left[ -\frac{1}{2\sigma_i} \left( \overline{V}_i - \alpha_i \overline{D}_i S \right) \left( \overline{V}_i - \alpha_i \overline{D}_i S \right)^T \right].$$

Here, $\sigma_i$ is the variance of the $i$th row of $H$ ($\Sigma = \sigma I$ is assumed). Moreover, $\overline{V}_i$ is a time vector describing the ECG signal recorded at position $\overline{D}_i$, yielding that $\overline{V}_i$ is a $[1 \times T]$ vector and $\overline{D}_i$ is a $[1 \times 2]$ vector.

Substituting Eq. (9) and (10) in (8), leads to a joint posterior probability distribution for $S$ and $\alpha$:

$$p(S,\alpha|V,D,\Sigma) \propto \prod_i \exp \left[ -\frac{1}{2\sigma_i} \left( \overline{V}_i - \alpha_i \overline{D}_i S \right) \left( \overline{V}_i - \alpha_i \overline{D}_i S \right)^T \right].$$

The optimal VCG estimate is in this case equal to the maximum likelihood solution and can be assessed by integrating Eq. (11) over $\alpha$ and determining for which $S$ the hence obtained probability distribution is maximal. However, the required integral is impossible to evaluate analytically, and hence, other approaches must be explored to approximate the optimal solution for the VCG. By employing variational interference [21], in factorized form known as mean field theory [22], and applying an iterative process, $\overline{D}_i S$ can be estimated by $U$ and the VCG estimate $\hat{S}$ can be calculated as

$$\hat{S} = (D^T D)^{-1} D^T U = D^* U,$$

with $D^*$ the Moore-Penrose pseudoinverse of $D$. This iterative process and the definition of $U$ is described in more in detail in [20].
3.3.2 Application of the Bayesian approach

The method described in the previous section is a convenient and easy way to calculate the VCG from a multi-dimensional ECG signal and is therefore used in this report. However, small modifications are implemented in order to comply with the specific demands in this research. Also, in this report, the calculated VCG representation contains the electrical activity of multiple heart beats, instead of a single one.

The most important modification is the definition of the electrode position matrix \( D \). Instead of working in all 3 spatial dimensions as is done in [22], the positions of the electrodes are expressed in only two dimensions (the coronal plane, as can be seen in figure 11). This leads to a loss of spatial information, but drastically simplifies the calculation of the VCG, making it more robust and less susceptible to errors. The 2D representation of the electrodes can also be somewhat justified by stating that at the moment, only 2D representations of the VCG are used in clinical practice.

The positions of the electrodes in this report are defined in Cartesian coordinates, with the reference electrode placed in the origin, by measuring the positions on the maternal abdomen. The matrix \( D \), representing the electrode positions, is then scaled in order to function properly.

To test this, the eight lead ECG signals are replaced by random noise. Obviously, the estimated VCG has to be a cloud of datapoints in the shape of a symmetrical disc. The result of the VCG calculation method can be seen in figure 10. Clearly, the resulting VCG is a random, circular cloud of points.

![Figure 10: Calculation of the VCG from an eight lead signal containing only Gaussian noise. The result is as expected a random cloud of data points in the shape of a symmetrical disc. The x and y directions are defined as shown in figure 11.](image)

3.4 Classification of fetal ECG using spatial correlation

In this section, CLASC will be presented. CLASC exploits the spatial correlation of the abdominal leads, and operates by first detecting the fetal R-peak locations in the individual fECG signals, and then by classifying the fECG signals. CLASC classifies the fECG signals by their amount of useful, mutual fECG information. Obviously, the
noise level of the individual fECG signals is a major criterion, but also the position of the abdominal electrode with respect to the fetal orientation influences the amount of mutual information. For example, an electrode whose lead vector is orthogonal with respect to the principal axis of the fetal heart may record no useful information for future fECG complex calculations, even though it might have a low noise level.

The abdominal recordings are performed by 8 electrodes placed in a circular configuration around a reference electrode in the center (see figure 11). The figures used in this section to visualize the used techniques, are based on an actual 90 second long abdominal recording performed at 24 weeks of gestation.

### 3.4.1 Fetal R-peak detection

At the start of CLASC, the abdominal fECG signal is filtered once more by the filter presented in section 3.1, in order to filter any noise which may be added to the signal during the removal of the mECG from the abdominal recordings. The signal is then screened as explained in 3.2 in order to remove any parts of the signal that could lead to errors in the algorithm. The first step in the classification of the individual abdominal fECG signals is investigating an intelligent method to detect fetal R-peaks and fECG complexes in the abdominal data.

Even after suppression of most of the biological and non-biological interferences (as explained in section 3.1), it can be difficult to detect the fECG directly from the 8 individual recordings since the fECG has very low amplitude, often smaller than the remaining noise level. Because of this often very low signal to noise ratio (SNR), additional information is necessary to detect the fECG in the signals. This extra information can be derived from the positions of the electrodes, which are placed in a specific formation, as shown in figure 11. The electrodes are placed in such a way as to cover as much uterine surface area as possible.

![Figure 11: The electrode configuration and definition of the coordinate system. The eight electrodes are placed in two curves around the reference electrode in the middle. An additional ground electrode is placed on the side of the mother's abdomen, but is not depicted here.](image)

After filtering and prescreening the signal, instead of analyzing the eight ECG signals individually, the fetal information contained in the fECG signals is combined in a two
dimensional representation of the fVCG. This representation can be calculated by utilizing the spatial correlation of the eight abdominal fECG signals and the patient-tailored vectorcardiography approach presented in section 3.3. In figure 12 and 13, respectively, the abdominal recording (after removing both physiological and non-physiological interferences) and the calculated two dimensional representation of the fVCG are shown.

Figure 12: The abdominal recording used in this section. The 90s long recording (only a 15s long part of the data is shown for reasons of clarity) was performed at 24 weeks of gestation on a healthy woman with an uncomplicated singleton pregnancy.

Figure 13: The abdominal recording presented in figure 12 is used to calculate the 2 dimensional representation of the fVCG. Since the SNR of the fECG recordings is usually low, the fVCG representation usually represents itself as a scatter plot in which most points in the plot will be focused near the origin of the axis system.

Due to the relatively low SNR of the fECG recordings, the fVCG representation usually represents itself as a scatter plot in which most points in the plot will be focused near the origin of the axis system. However, as the QRS complexes of the fECG generally entail the parts with the largest amplitude, for all points near the origin it can be assumed that they do not belong to a QRS complex. Since the fVCG representation was calculated in order to increase the SNR of the QRS complexes
(and in particular in the small interval around the R-peak), the points near the origin can be omitted. In general, the average time length of a QRS complex is around 40 ms [23], which corresponds to 10 percent of the length of a heart-beat cycle of 400 ms or 150 beats per minute (BPM). By only retaining the top 5 percent of the scatter plot (i.e. the points with the largest distance from the origin of the scatter plot), both most of the noise and the P and T loops are deleted from the fVCG, while the high amplitude part of the QRS loops (i.e. the short interval around the R-peak) is retained.

Note that in order to delete anything but the QRS loops from the fVCG, the obvious choice would be to omit 90% of the points. However, since the amplitude of some parts of the QRS complex are below the noise level and/or the amplitude of the P and T waves, in the remaining 10 percent, noise and/or parts of the P and T wave could still be present.

The remaining points of the fVCG representation are then approximated by an ellipse, fitted by means of a least-squares approach (appendix B) and then projected upon the principal axis of the fitted ellipse. The polarity of this projection is determined by the positive direction of the principle axis. For this, the two intersections (A and B in figure 14) of the fitted ellipse and the principal axis are studied: the direction, associated to the point (A or B) that is furthest away from the origin, is considered positive. In figure 14, the fitted ellipse is shown in red and the positive direction of the principle axis in blue.

Once the projection of the fVCG on the principle axis is calculated (shown in figure 15), the fetal R-peaks can be detected using a peak-detection algorithm [24]. The detected peaks are indicated with a red circle in figure 15.

![Figure 14](image-url)

*Figure 14: In this figure, the two dimensional representation of the fVCG is depicted after omitting 95% of the data points. The remaining 5% is then approximated by an ellipse shown in red. From this fitted ellipse, the principle axis and its direction can be determined (shown in blue).*
Figure 15: The remaining data points of the fVCG representation are projected upon the principle axis. $V_{PA}$ stands for the amplitude in the direction of the principle axis. By applying a peak detection algorithm, the fetal R-peaks can be detected. They are represented by red circles.

Once the positions of the fetal R-peaks in the projection on the principle axis are known, the average heart rate can be calculated. In this particular case, the average heart beat is 154 BPM.

The location of the fetal R-peaks in the projection provides valuable information on the position of the fetal R-peaks in all the 8 individual leads, even though the positions of the fetal R-peaks in the 8 leads do not necessarily all coincide with the detected R-peaks in the projection on the principle axis. The detected R-peak locations however, can still function as a trigger for identifying individual fECG complexes, since for each independent fECG signal they correspond to a specific point in the cardiac cycle.

3.4.2 Classification of the fECG signals

The individual fECG complexes are enhanced by averaging fECG complexes, all synchronized on this trigger. The resulting average fECG complexes can then be used to obtain an fVCG, again using the patient-tailored vectorcardiography approach presented in section 3.3, however, this time with increased SNR. This fVCG, since it originates from averaged fECG complexes, is referred to as the average fVCG (AVCG).

In figure 16, the average fECG complexes and the AVCG are shown. The eight average fECG complexes are depicted conform the position of their corresponding abdominal electrodes as indicated in figure 11, surrounding the AVCG in the center. They are all depicted on the same vertical and horizontal scale.
Signal Processing

Figure 16: The eight average fECG complexes are depicted conform to the position of their corresponding abdominal electrodes. Both vertical and horizontal scales are the same for all eight ECG complexes. These average fECG complexes are used to calculate the AVCG by applying the patient-tailored vectorcardiography approach. The AVCG is depicted in the center.

FECG signals which do not contain any valuable fetal information or with a very low SNR (for example when an electrode is not attached properly to the abdomen), are also used to calculate the AVCG.

CLASC then projects the AVCG onto the 8 lead vectors that indicate the abdominal electrode positions. Since the AVCG is in fact a spatial combination of all the fECG signals, by comparing the resulting projected AVCG signals to the originally determined average fECG, the spatial correlation of the fECG signal with the other seven fECG leads can be visualized. The signal exhibiting the lowest correlation is considered to contain the least useful, mutual fECG information and is therefore classified in the last position and omitted from further processing. In figure 17, the eight projections of the AVCG and the original average fECG complexes are shown together, as well as the AVCG. In this particular example, the projections correspond very well to the original average fECG complexes, however, this is not always the case. The fECG signal exhibiting the lowest correlation factor in this example is signal 5.
Figure 17: The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.

From the remaining average ECG complexes, the process (i.e. calculation of the AVCG, projecting this AVCG onto the lead vectors, and omitting the signal with lowest correlation) described above is repeated until full classification of the abdominal recording is achieved by CLASC.
4. Data acquisition

All the measurements in this report are performed in the MMC in Veldhoven. After approval of the Medical Ethics Committee of the MMC, pregnant women were asked to participate in the study by their gynaecologist. Healthy women above 18 years of age and with an uncomplicated singleton pregnancy were included after giving informed consent.

The abdominal measurements started around 14 weeks of gestation, since it was expected that the fetal heart rate could be obtained from abdominal recordings at the earliest between 14 and 18 weeks of gestation. Following this first recording, additional recordings took place at least every four weeks until the time of birth. Around week 24 of gestation as well as near term, additional recordings were made since important fetal developments are expected in these periods. Thus, abdominal recordings were made around 14, 18, 22, 24, 26, 30, 34, 36, 38, 40, 41 and 42 weeks of gestation. However, for some women, not all the measurements were performed due to various reasons.

The measurements were performed using 10 Ag/AgCl electrodes placed on the maternal abdomen in a specific configuration, as can be seen in figures 11 and 18. Eight measurement electrodes are placed in two curves around the upper region and lower region of the uterus. Due to this specific configuration, the entire uterine area can be monitored and the chance of measuring a fetal ECG signal is maximized. Note that not all electrodes may record the fECG.

In the center a reference electrode and on one of the sides of the abdomen a ground electrode are placed. Each of the eight abdominal signals is obtained by measuring the voltage difference between the recording electrode and the reference electrode. Before placing the self adhesive electrodes on the abdomen, the skin was prepared by gentle scrubbing of surface skin and cleaning it with alcohol in order to minimize impedance between the skin and the electrodes.

The abdominal signals are recorded by the NEMO system (Non-invasive Electrophysiological Monitor for Obstetrics), shown in figure 18. NEMO is a class II medical device (IEC 60601,type BF), developed by the MMC in cooperation with the TU/e and Maastricht Instruments and approved for medical practice by the Medical Technical Service Department of MMC. The device comprises of an 8-channel amplifier, a 20-bit ADC and a panel PC. The signals are sampled at a frequency of 1 kHz and stored on the panel PC for off-line analysis. The recording time varies from one recording to the next, but in general, until 36 weeks of gestation, around 45 minutes of data was recorded and around 30 minutes from week 36 onwards.
Figure 18: The NEMO system used to perform the abdominal recordings (Picture taken by Bart van Overbeeke).
5. Results and discussion

In this section, the performance of CLASC will be assessed in three distinctive ways. First of all, CLASC will be tested on an artificial ECG signal, both with and without added random noise. One of the benefits of using this artificial signal is that the number of ECG complexes and the positions of the R-peaks in the data set can be determined visually. Since the ECG signal is artificial, and all the signals contain about the same amount of ECG information, the focus of the testing will be on the peak detection part of CLASC, rather than the classification part.

In the second part of this chapter, a 90s long abdominal fECG recording performed at 34+4 weeks of gestation will be used to test both the peak detection and the classification of CLASC. The performance of the classification will be assessed by replacing fECG signals by Gaussian noise and testing whether or not CLASC can correctly identify these signals. The classification of CLASC is also compared with a visual classification by various researchers at the MMC.

In the final part of this chapter, a longitudinal study of an uncomplicated pregnancy will be performed. The classification of CLASC will again be compared with a visual classification performed by various researchers at the MMC.

The performance of the peak detection part of CLASC is assessed by the sensitivity SE and the positive predictive value PPV, representing the percentage of fetal QRS complexes detected correctly. SE and PPV are defined in the following way:

\[
SE = \frac{TP}{TP + FN} \times 100\%,
\]

\[
PPV = \frac{TP}{TP + FP} \times 100\%.
\]

with TP representing the number of correctly detected R-peaks (true positives), FN the number of undetected R-peaks (false negatives), and FP the number of falsely detected R-peaks (false positives).

In sections 5.1 and 5.2, some ECG signals are replaced by random noise, so they should be classified in the last position(s) yielding the use of these signals an objective way of evaluating the performance of CLASC. However, in section 5.3, actual fECG recordings are used, and none of them are replaced by Gaussian noise, making it more difficult to evaluate the performance of the classification. The only objective way that could shed some light on the performance is by comparing the SNR of the signals. However, since the detected R-peaks are not always detected correctly, and some R-peaks are missed, the calculation of the SNR of the signals is considered not trustworthy. Additionally, the SNR only compares the amplitude of the detected fetal R-peaks with the rest of that same signal, ignoring spatial correlations, while CLASC compares a signal’s complete average total fECG complex with the seven other average fECG complexes.

In order to overcome the problem of not having a golden standard for evaluating the performance of CLASC, a visual selection of the abdominal fECG signals is performed by various researchers in the MMC. Due to the expertise of the researchers in the MMC in the field of fECG extraction, and since the pattern recognition capabilities of the human brain are considered to be superior over computers, this approach should enable assessment of the performance of CLASC.
The 5 researchers who performed the visual selection are all connected to this project in some degree, and classified the signals without knowing the output of the CLASC method. They classified the individual signals by assigning weights to them, ranging from a weight of 8 for the best fECG signal to 1 for the signal containing the least amount of useful and mutual information. For each signal, the results of all the researchers are averaged, and the interobserver variability is defined as the standard deviation of the average weights. The average weight of the signals, together with the interobserver variability is referred to as the average visual selection (AVS).

The AVS is compared quantitatively with CLASC’s classification by defining a term called classification difference $CD$

$$CD = \frac{1}{8} \sum_{i=1}^{8} \left| P(CLASC)_i - P(AVS)_i \right|.$$

Here, $i$ represents the number of the ECG signal, $P(CLASC)_i$ the weight of signal $i$ calculated by CLASC, and $P(AVS)_i$ the weight of signal $i$ determined by AVS. The total interobserver variability is represented as a single number by averaging the interobserver variability of the individual fECG signals.

Additionally, CLASC and AVS are compared graphically as can be seen in figure 19. The data used to make this figure is fictive and only serves as an example. In this figure, for each of the 8 fECG signals, the weight assigned to the signal by CLASC and AVS are visualized by, respectively, the left and the right bar. For both CLASC and AVS, the three best and the three worst ECG signals are represented by respectively green and red bars. The orange bars represent the signals classified in positions 4 and 5. The interobserver variability of the individual ECG signals is represented as a black error bar.

Figure 19: Graphical comparison of the classification of CLASC and AVS for each fECG signal. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads. The data used in this figure is fictive and only serves as an example.
5.1 Artificial Signals with and without noise

The focus of this section is to test the R-peak detection part of the CLASC method on an artificial 8 lead ECG signal, both with and without added Gaussian noise. However, for reasons of completeness, also the classification of the abdominal leads will be discussed briefly.

The artificial ECG signals are fabricated by using a principal component analysis (PCA; discussed in detail in section 5.3) on an actual abdominal 8 lead ECG recording followed by a peak detection algorithm to detect the maternal R-peaks in the principal component. Then, for each of the 8 signals, the R-peaks are aligned and an average ECG complex is calculated. Note that this is an average maternal ECG complex and it therefore has better SNR properties than a fetal ECG complex. Finally, for each of the ECG signals, each detected ECG complex is replaced by the average ECG complex and the signal is normalized. The resulting artificial ECG signals are shown in figure 20.

One of the benefits of using this artificial signal is that the number of ECG complexes and the positions of the R-peaks in the data set can be determined visually. The artificial signal has a length of 90 seconds and contains exactly 109 ECG complexes which correspond to an average maternal heart rate of around 73 BPM.

5.1.1 Artificial signal without noise

First, CLASC will be tested on the original artificial signal. The artificial signals and the detected R-peaks (indicated by the vertical red dotted lines) are shown in figure 21. Exactly 109 R-peaks are detected, at the correct locations. This leads to a PPV and SE of 100%. The resulting average ECG complexes and the AVCG are shown together in figure 22.
The final, and most important part of CLASC, classifies the leads. However, since this is an artificial signal, all the leads contain more or less the same amount of ECG information. Still, for reasons of completeness, the resulting classification calculated by CLASC is given (starting with the best ECG signal): 7, 8, 5, 1, 6, 2, 4 and 3.
5.1.2 Noisy artificial signals

The question that presents itself after evaluating CLASC on the original artificial signal is whether or not the algorithm is still able to detect the R-peaks when Gaussian noise is added. In order to give some sort of insight into the noise level of the signals, the SNR is calculated for each of the 8 ECG signals by defining the SNR as the ratio between the root mean square amplitude of the R-peaks and the root mean square of the complete signal:

$$SNR = \frac{\sqrt{\frac{1}{M} \sum_{m=1}^{M} V^2 (R_{peak}(m))}}{\sqrt{\frac{1}{N} \sum_{i=1}^{N} V^2 (i)}}$$ \tag{16}

$V$ is the amplitude of the signal, $R_{peak}(m)$ is the position of the $m^{th}$ R-peak, $M$ is the number of R-Peaks and $N$ is the number of samples in the signal.

Two abdominal 8 lead ECG recordings were fabricated to test CLASC by adding Gaussian noise to each individual artificial ECG signal, equalizing the SNR for all individual ECG signals. In the first recording, the SNR of the individual ECG signals is about 2.5 and in the second set, the SNR is decreased further to 1.5. The exact SNR values of the individual signals in both recordings are depicted in table 1. Since, in this report, the noise added to artificial signal is random noise, a simple filter at the start of CLASC could dramatically increase the SNR. However, since the goal of this chapter is to test the peak detection part of the CLASC method, the signals are not filtered at the start of the algorithm.

Table 1: The SNR for the 8 ECG signals, both before and after adding random noise.

<table>
<thead>
<tr>
<th>Lead</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>6.12</td>
<td>5.87</td>
<td>5.46</td>
<td>6.17</td>
<td>5.95</td>
<td>5.73</td>
<td>3.96</td>
<td>5.63</td>
</tr>
<tr>
<td>SNR = 2.5</td>
<td>2.55</td>
<td>2.49</td>
<td>2.52</td>
<td>2.53</td>
<td>2.48</td>
<td>2.52</td>
<td>2.52</td>
<td>2.46</td>
</tr>
<tr>
<td>SNR = 1.5</td>
<td>1.48</td>
<td>1.49</td>
<td>1.51</td>
<td>1.52</td>
<td>1.49</td>
<td>1.49</td>
<td>1.51</td>
<td>1.51</td>
</tr>
</tbody>
</table>

Analyzing the ECG signals with SNR of 2.5, CLASC detects exactly 109 peaks at the correct locations, leading to a PPV and a SE of 100%. Both the signals and the detected R-peaks (indicated by the vertical red dotted lines) are shown in figure 23.
Figure 23: Gaussian noise is added to each of the artificial ECG signals, reducing the average SNR to about 2.5. The signals are depicted together with the detected R-peaks, indicated by the red dotted vertical lines. Only 15 seconds are shown for reasons of clarity.

For the ECG signals with a SNR of 1.5, the algorithm detects all the 109 R-peaks at the correct location, but two false positive R-peaks are detected too. The SE is therefore again 100%, while the PPV has decreased to 98.20%. The ECG signals and the detected R-peaks are shown in figure 24. One of the false positive peaks can be seen around 4500 ms. Note that in the ECG signals with a SNR of 1.5, it is difficult to detect the R-peaks visually.

Figure 24: Gaussian noise is added to each of the artificial ECG signals, reducing the average SNR to about 1.5. The signals are depicted together with the detected R-peaks, indicated by the red dotted vertical lines. Only 15 seconds are shown for reasons of clarity.

The next step in CLASC is to classify the ECG signals. Therefore, the for each ECG signal, the average ECG complex is calculated, after which the 8 average ECG complexes can be used to calculate the AVCG. The resulting average ECG complexes and AVCG can be seen in figure 25 and 26 for, respectively, the ECG signals with SNR 2.5 and 1.5. In these figures, also the projections of the AVCG onto the lead vectors that indicate the electrode positions are depicted in red. Due to the
The calculated average ECG complexes, and consequently also the average VCG, are noisy as well.

Again, for reasons of completeness, the classification of the leads is presented: the signal with SNR 2.5 is ordered in the following way (starting with the best lead): 7, 8, 5, 1, 6, 2, 4, and 3. This classification is the same as the one CLASC found before noise was added to the artificial signal. Thus CLASC does not seem to be influenced by the added noise. The signal with a SNR of 1.5 is ordered in 5, 7, 8, 1, 6, 2, 4, and 3. As a result from the added noise, the classification thus changed slightly. Nevertheless, still the same three signals are classified in the first three positions, although in a different order, and the last 5 signals are classified in the same order as before.

Figure 25: The average ECG complexes and AVCG of the artificial ECG recording with a SNR of 2.5. The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.
5.1.3 Different noise levels

In this section, besides the peak detection part of CLASC, also the classification of the signals will be tested. For this, again, the artificial ECG signals will be used and a different amount of Gaussian noise is added to each of these artificial signals. The SNR of the individual ECG signals is shown in table 2.

Table 2: The SNR for the 8 ECG signals, both before and after adding random noise.

<table>
<thead>
<tr>
<th>Lead</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>6.12</td>
<td>5.87</td>
<td>5.46</td>
<td>6.17</td>
<td>5.95</td>
<td>5.73</td>
<td>3.96</td>
<td>5.63</td>
</tr>
<tr>
<td>Noise added</td>
<td>4.51</td>
<td>4.03</td>
<td>3.52</td>
<td>3.06</td>
<td>2.49</td>
<td>2.03</td>
<td>1.51</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Since the goal of this chapter is to test the CLASC method, the signals are again not filtered at the start of the algorithm. CLASC detects all 109 peaks at the correct locations, leading to a PPV and SE of 100%. The ECG signals are presented in figure 27 together with the detected R-peaks (indicated with the vertical red dotted lines).
Results and discussion

Figure 27: Gaussian noise is added to each of the artificial ECG signals, leading to a different SNR for each signal. The signals are depicted together with the detected R-peaks, indicated by the red dotted vertical lines. Only 15 seconds are shown for reasons of clarity.

To classify the ECG signals, the average ECG complexes are calculated followed by the AVCG. In figure 28, the average ECG complexes as well as the calculated AVCG are shown, together with the projection of the calculated AVCG on the eight leads. Comparing the projections with the average ECG complexes leads to following classification: 1, 3, 5, 4, 6, 2, 7, and 8.

Figure 28: The average ECG complexes and AVCG of the artificial ECG recording with a different SNR for each signal. The eight average IECG complexes (black) are depicted together with the projections of the IVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.
The classification of the ECG signals presented by CLASC does seem to be influenced by the SNR of the individual signals. However, even though lead 2 has the second best SNR, it is not classified as the second best ECG signal. This is because CLASC does not simply compare the SNR of the individual ECG signals, but rather studies the spatial correlation of the individual signals with the rest of the ECG signals. In particular, the SNR only compares the amplitude of the fetal R-peak with the rest of that same signal, while CLASC compares for each signal the complete average fECG complex with the seven other complete average fECG complexes.

5.1.4 Replacing signals with random noise

In this section, the artificial ECG signals presented in section 5.1.2 with a SNR of around 2.5 are used. However, this time, four ECG signals (1, 3, 5 and 7) are replaced by random noise. In order to test the peak detection algorithm, the signals are not filtered at the start of the algorithm. CLASC detects all 109 peaks at their correct locations, together with an additional false positive, leading to a SE of 100% and a PPV of 99.10%. The ECG signals as well as the detected R-peaks are shown in figure 29.

![Figure 29: Gaussian noise is added to each of the artificial ECG signals, reducing the SNR to about 2.5, and signals 1, 3, 5, and 7 are replaced by Gaussian noise. The signals are depicted together with the detected R-peaks, indicated by the red dotted vertical lines. Only 15 seconds are shown for reasons of clarity.](image)

The average ECG complex for each ECG signal and the AVCG are then calculated. The results can be seen in figure 30.
Results and discussion

Figure 30: The average ECG complexes and AVCG of the artificial ECG recording with a SNR of 2.5. Signals 1, 3, 5, and 7 are replaced by Gaussian noise. The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.

In figure 30, it can be seen that the average ECG complexes of signals 1, 3, 5, and 7 resemble random noise, as expected. The signals are ordered in the following way (starting with the best lead): 4, 6, 2, 8, 5, 3, 1 and 7. The CLASC classification thus functions as expected, since the four leads containing only noise are considered to contain the least amount of useful, mutual information. However, looking only at the signals classified in the first four positions, their order is different from what would be expected from section 5.1.2. (excluding signals 1, 3, 5, and 7 leads to 8, 6, 2, and 4). This can be explained by noting that CLASC uses spatial correlation to classify the leads. If, for example, signal 7 had a high spatial correlation with signal 8, replacing signal 7 with noise would imply that signal 8 will lose some level of spatial correlation with the AVCG, and thus also with the projection of AVCG on his lead. This could lead to a change of order in the classification.

Taking a closer look at figure 30, and in particular to signals 1 and 5, the calculated average ECG complex looks like random noise, except at the point where in the other leads the R-peaks are depicted. At exactly this point, a significant peak can be seen in both signal 1 and 5.

This can be explained by noticing that the R-peaks are detected in a one dimensional signal (the projection of the AVCG on the principle axis of the fitted ellipse), which basically is a superposition of all 8 ECG signals. The peaks are detected using a peak detection algorithm, defining local maxima in this one dimensional signal as R-peaks. These maxima therefore do not necessarily correspond to the real R-peak locations found in the individual ECG signals, but rather correspond to maxima in the superposition. Averaging over all these maxima can therefore lead to a peak, even in a signal containing nothing more than random noise.
5.1.5. Conclusions

In table 3, the results of this section are presented. Clearly, CLASC is able to detect all R-peaks in the artificial signal, even when four signals have a SNR of 2.5, and the other four no longer contain any valuable information on the ECG since they are replaced by Gaussian noise. However, when the SNR decreases to 1.5, and when four signals are replaced by Gaussian noise, additional false peaks were detected, decreasing the PPV.

<table>
<thead>
<tr>
<th>Artificial Signal</th>
<th>SE (%)</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Noise</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>SNR 2.5</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>SNR 1.5</td>
<td>100</td>
<td>98.20</td>
</tr>
<tr>
<td>Different SNR</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>4 signals random noise</td>
<td>100</td>
<td>99.10</td>
</tr>
</tbody>
</table>

The classification part of CLASC performs also as expected. When four signals were replaced by random noise, CLASC classified them in the final four positions.

The SNR of the individual ECG signals does seem to influence the classification. However, even though in section 5.1.3, signal 2 has the second best SNR, it is not classified as the second best ECG signal. This is because CLASC does not simply compare the SNR of the individual ECG signals, but rather studies the spatial correlation of the individual signals with the rest of the ECG signals. Moreover, the SNR only compares the amplitude of the fetal R-peak with the rest of that same signal, while CLASC compares for each signal the complete average fECG complex with the seven other complete average fECG complexes.

5.2 Fetal signals with and without noise

In this section, the algorithm is tested on an actual abdominal fECG recording, both before and after a few ECG signals are replaced by random noise. The fECG signal is a 90 seconds recording performed at 34+4 weeks of gestation.

Since it is often difficult to detect fetal R-peaks visually in these recordings, an algorithm was written to calculate the SE and PPV of the peak detection part of CLASC. In short, this algorithm compares the length of each RR interval with the median of the seven neighboring RR intervals. This median entails a smoothened version of the beat-to-beat RR intervals and serves as a reference signal for assessing whether the fetal R-peaks are detected correctly.

Several types of incorrect RR intervals may occur. During fetal R-peak detection, CLASC may have failed to detect R-peaks, or detected them at the wrong place. In figure 31, a 90s long artificial maternal ECG signal is depicted, together with the recorded fetal RR intervals. In this figure, the arrows numbered 1, 2 and 3 indicate, respectively, 1 missing R-peak, 5 missing R peaks, and a shifted R-peak.
The algorithm defines an R-peak as a true positive (correctly detected R-peak) when the time distance to its preceding R-peak (RR interval) diverges less than 20 percent from a multiple $n$ of the median RR interval $\bar{RR}$ (i.e. $RR \in [(n-0.2)\ \bar{RR}, (n+0.2)\ \bar{RR}]$). In case of missing R-peaks, this approach ensures that the first peak detected after the missing peak(s) is not incorrectly classified as a false positive. As an example, in figure 31, for the first fetal R peak after the gap indicated by arrow two, the preceding RR interval is 5051 ms and the median 830 ms. 20 % of 830 ms is 166 ms, so in order to be considered as a true positive, the RR interval can not diverge more then 166 ms from a multiple of 830. In this particular case, this multiple is 6, and since the RR interval lies within [4814, 5146], the peak after the gap is considered a true positive. The multiple 6 indicates that $6 - 1 = 5$ peaks are missing.

When the RR interval diverges more than 20 percent from a multiple $n$ of the median RR interval $\bar{RR}$, it is an indication for a falsely detected R-peak (false positive). Such a false positive is indicated by arrow three in figure 31. The preceding RR interval is 511 ms, and the median is 804. Since the RR interval does not lie between 643.6 ms and 964.4 ms, the R-peak will be considered as a false positive.

The number of undetected R-peaks (false negatives) is assessed by the algorithm by calculating the ratio of the RR interval and the median. The gaps indicated by arrows 1 and 2 in figure 31 will therefore account for respectively 1 and 5 missed R-peaks. Afterwards, an additional visual check is performed to ensure the algorithm produces accurate results.

5.2.1. Fetal signal

When CLASC is evaluated on the real abdominal fECG recording, depicted in figure 32, it detects 177 fetal R-peaks and has a SE of 85.71% and a PPV of 99.36%. From the average RR interval, an average heart rate of 137 BPM is calculated. The average ECG complexes and the AVCG, calculated by CLASC, are both shown in figure 33, together with the projection of the AVCG onto the lead vectors that indicate the electrode positions. Comparing the projections of the AVCG with the average fECG complexes, CLASC orders the leads in the following way: 1, 7, 2, 8, 6, 3, 5 and
4. The AVS leads to the following classification: 1, 7, 2, 8, 6, 3, 4, and 5. The CD and the total interobserver variability are respectively 0.4 and 0.70. The small values of both the interobserver variability and CD indicate a large correlation between AVS and CLASC. This can also be seen in the graphical representation in figure 34. Both methods define the same three signals as the most useful (signal 2, 7 and 8), and place the same three signals in the lowest positions (3, 4 and 5).

Figure 32: A 90s long abdominal fECG recording performed at 34+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure 33: The average fECG complexes and AVCG of a real abdominal recording after 34+4 weeks of gestation. The eight average fECG complexes (black) are depicted together with the projections of the IVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.
Figure 34: Graphical comparison of the classification of CLASC and AVS for a fECG recording performed at 34+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.

5.2.2. Replacing fECG signals with Gaussian noise

In this section, the classification part of CLASC will be further evaluated by replacing a few fECG signals by random noise. First, the two best classified ECG signals 1 and 7, according to CLASC, are replaced. CLASC, now, detects 149 peaks with a SE of 72.48% and a PPV of 90.76%. The average heart rate is estimated at 136 BPM. This small decrease can be explained by the lower number of detected R-peaks. CLASC then calculates the average ECG complexes and the AVCG. They are shown in 35, together with the projection of the AVCG onto the lead vectors that indicate the electrode positions. CLASC updates the classification order of the fECG signals into: 8, 2, 6, 3, 5, 4, 1 and 7. The signals were also classified by AVS, leading to following classification: 2, 8, 6, 3, 4, 5, 7, and 1. The CD and the interobserver variability are respectively 0.7 and 0.83 in this test. The small values of both the interobserver variability and CD indicate a large correlation between AVS and CLASC. This can also be seen in the graphical representation in figure 36. Both methods present the same top 3, and they both place signals 1 and 7 (random noise) in the last two positions.
Secondly, when the fECG signal of lead 8 is also replaced by random noise, the SE and PPV of the peak detection part of CLASC decrease to respectively 64.08 % and 68.04%, and an average heart rate of 132 BPM is found. This lower average heart rate can again be explained by the smaller number of detected R-peaks.
The average fECG complexes and AVCG calculated by CLASC can be seen in figure 37, together with the projection of the AVCG onto the lead vectors that indicate the electrode positions.

CLASC updates the classification order of the fECG signals into: 3, 2, 4, 6, 5, 1, 8 and 7. The signals were also classified by AVS, leading to following classification: 2, 6, 3, 5, 4, 1, 7, and 8. AVS gives the final three leads (1, 7 and 8) the same weight, so they are placed in random order.

The CD and the interobserver variability are respectively 1.15 and 0.48 in this test. The three signals containing nothing but random noise are placed in the last three positions for both methods. The first three however are not the same. The comparison of CLASC and AVS is visualized in figure 38.

Figure 37: The average fECG complexes and AVCG of a real abdominal recording after 34+4 weeks of gestation. Signals 1, 7 and 8 are replaced by Gaussian noise. The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.
Figure 38: Graphical comparison of the classification of CLASC and AVS for a fECG recording performed at 34+4 weeks of gestation. Signals 1, 7 and 8 are replaced by Gaussian noise. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.

In order to study the working boundaries of CLASC, also fECG signal 3 is replaced by Gaussian noise. The SE and PPV of CLASC drop further to respectively 37.04% and 53.55%, and an average heart rate of 131 BPM is found. In figure 39, the AVCG and the average fECG complexes are shown, together with the projections of the AVCG onto the lead vectors that indicate the electrode positions.

CLASC classifies the signals in the following order: 2, 4, 6, 5, 1, 3, 7, and 8. The signals were also classified by AVS, leading to following classification: 2, 6, 5, 4, 7, 3, 1, and 8. AVS gives the leads 1 and 8 the same weight, so they are placed in random order. The CD and the interobserver variability are respectively 1 and 0.79 in this test.

Once more, both CLASC and AVS placed the signals containing nothing but noise in the last positions. The first three however are not the same. The comparison of CLASC and AVS are visualized in figure 40.
Results and discussion

Figure 39: The average fECG complexes and AVCG of a real abdominal recording after 34+4 weeks of gestation. Signals 1, 7, 8 and 3 are replaced by Gaussian noise. The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.

Figure 40: Graphical comparison of the classification of CLASC and AVS for a fECG recording performed at 34+4 weeks of gestation. Signals 1, 7, 8 and 3 are replaced by Gaussian noise. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.

Finally, when also fECG signal 2 is replaced by random noise, the SE and PPV of the peak detection part of CLASC drops below 30 % and an error message will be returned by CLASC, stating that the average heart rate has dropped to an implausible BPM (in this case 49 BPM), indicating that the resulting classification could be erroneous. In this particular case, CLASC has indeed difficulties calculating
the average fECG complexes and fVCG as can be seen in figure 41, and returns an erroneous classification: 8, 5, 6, 1, 4, 2, 7, 3. This classification would indicate that fECG signal 8 (which contain nothing more than Gaussian noise) contains the most fECG information. Nevertheless, in some cases, CLASC is even able to identify the signals containing only noise, even when 5 out of 8 signals are nothing more than random noise.

Figure 41: The average fECG complexes and AVCG of a real abdominal recording after 34+4 weeks of gestation. Signals 1, 7, 8, 3 and 2 are replaced by Gaussian noise. The eight average fECG complexes (black) are depicted together with the projections of the fVCG on the eight leads (red) conform to the position of their corresponding leads. Both vertical and horizontal scales are equal for all 8 depicted ECG complexes.

5.2.3. Conclusions

In table 4, a summary of the results of this section is presented.

Table 4: Summary of the results presented in this section. I.V. = interobserver variability. The signals containing nothing but random noise are indicated in red. The AVS of the fECG signal containing 5 signals containing nothing but random noise is not given, since CLASC failed in this particular test.

<table>
<thead>
<tr>
<th></th>
<th>SE (%)</th>
<th>PPV (%)</th>
<th>CD</th>
<th>I.V. Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>No noise</td>
<td>85,71</td>
<td>99,36</td>
<td>0,40 0,70</td>
<td>CLASC AVS 1 7 2 8 6 3 5 4</td>
</tr>
<tr>
<td>2 Gaussian noise signals</td>
<td>72,48</td>
<td>90,76</td>
<td>0,70 0,83</td>
<td>CLASC AVS 8 2 6 3 5 4 1 7</td>
</tr>
<tr>
<td>3 Gaussian noise signals</td>
<td>64,08</td>
<td>68,04</td>
<td>1,15 0,48</td>
<td>CLASC AVS 3 2 4 6 5 1 8 7</td>
</tr>
<tr>
<td>4 Gaussian noise signals</td>
<td>37,04</td>
<td>53,55</td>
<td>1,00 0,79</td>
<td>CLASC AVS 4 2 6 5 1 7 3 8</td>
</tr>
<tr>
<td>5 Gaussian noise signals</td>
<td>&lt;30</td>
<td>&lt;30</td>
<td></td>
<td>CLASC AVS 8 5 6 1 4 2 7 3</td>
</tr>
</tbody>
</table>
From table 4, it can be seen that when more signals are replaced by random noise, both the SE and the PPV of the peak detection part of CLASC decrease. Also the CD between CLASC and AVS tends to increase, but still indicates a large correlation between CLASC and AVS.

Even though the CD increases, CLASC does identify the signals containing nothing but noise correctly, since it places them in the last positions. Not until 5 signals are replaced, leaving only three signals which contain fECG, CLASC gives an erroneous classification. But, since the SE and PPV have dropped below 30%, leading to an implausible average fetal heart rate, CLASC prompts a message indicating that the classification of the fECG signals could be erroneous.

So as a general conclusion, it can be stated that both the SE and the PPV drop when more signals are replaced by random noise, but even when four signals are replaced, CLASC is still able to identify them. When a fifth signals is replaced, CLASC does not always perform correctly, and warns the user that the result may be erroneous.

5.3 Longitudinal study

In this section, the CLASC method is tested on nine abdominal fECG recordings performed during an uncomplicated pregnancy. The recordings were performed in the 14th, 18th, 21st, 24th, 26th, 30th, 34th, 36th and 38th week of gestation. In order to assess the peak detection performance of CLASC, both the SE and the PPV are compared to that of a blind source separation technique called principal component analysis (PCA). PCA involves a mathematical procedure that transforms the 8 correlated fECG signals $V$ into a number of uncorrelated signals called principal components. The first principal component accounts for as much of the variability in the data as possible, and each succeeding component accounts for as much of the remaining variability as possible. The principal components are calculated using the covariance method [25]. In this method, the fetal ECG signals $V$ are multiplied with an orthonormal transformation matrix $P$ such that the resulting sources $S_{PCA}$ are uncorrelated:

$$ S_{PCA} = P^T V. $$

(17)

Here cov($S_{PCA}$) is constrained to be a diagonal matrix because the rows of $S_{PCA}$ are assumed to be uncorrelated. Because $P$ is defined as an orthonormal matrix, it holds that $P^T = P^{-1}$. And thus

$$ cov(S_{PCA}) = E[S_{PCA}S_{PCA}^T] $$

(18)

$$ = P^T E[VV^T]P $$

(19)

$$ = P^T \text{cov}(V)P $$

(20)

with E the expected value. Since cov($S_{PCA}$) is a diagonal matrix, eq. (19) is in fact an Eigenvector problem:

$$ P \text{cov}(S_{PCA}) = \text{cov}(V)P. $$

(21)

By solving the Eigenvector problem of eq. (21), the orthonormal transformation matrix $P$ can be determined and, using eq. (17), the sources $S_{PCA}$ assessed. The source
that represents the fECG is then selected from the principal components by visual inspection.

5.3.1 Conclusions

The performance of the peak detection part of CLASC and of PCA is presented in table 5.

Table 5: Comparison of the performance of the fetal R-peak detection of CLASC and PCA. G.A. stands for gestational age.

<table>
<thead>
<tr>
<th>G.A.</th>
<th>CLASC SE (%)</th>
<th>CLASC PPV (%)</th>
<th>PCA SE (%)</th>
<th>PCA PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14+4*</td>
<td>32.94</td>
<td>37.25</td>
<td>35.00</td>
<td>45.45</td>
</tr>
<tr>
<td>18+0</td>
<td>46.43</td>
<td>52.70</td>
<td>53.98</td>
<td>57.55</td>
</tr>
<tr>
<td>21+4</td>
<td>84.13</td>
<td>86.52</td>
<td>85.56</td>
<td>59.69</td>
</tr>
<tr>
<td>24+4</td>
<td>81.70</td>
<td>89.93</td>
<td>67.35</td>
<td>58.41</td>
</tr>
<tr>
<td>26+4**</td>
<td>98.85</td>
<td>93.48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30+4</td>
<td>85.54</td>
<td>63.96</td>
<td>89.71</td>
<td>53.17</td>
</tr>
<tr>
<td>34+4</td>
<td>95.10</td>
<td>99.43</td>
<td>95.61</td>
<td>98.99</td>
</tr>
<tr>
<td>36+4</td>
<td>86.91</td>
<td>78.15</td>
<td>85.29</td>
<td>64.93</td>
</tr>
<tr>
<td>38+0</td>
<td>86.79</td>
<td>72.44</td>
<td>68.25</td>
<td>51.81</td>
</tr>
</tbody>
</table>

*CLASC indicates an implausible average heart rate, indicating an erroneous classification is possible.
**The maternal mECG subtraction did not perform correctly.

As indicated in table 5, the recording performed at 14+4 weeks of gestation leads to an implausible average fetal heart rate, and CLASC prompts a message indicating that the classification could be erroneous. When also the recording performed at 26+4 weeks of gestation is omitted from further analysis (the reasons are mentioned later), it can be seen that the PPV of CLASC is higher than that of PCA on the recordings performed after 21 weeks of gestation. In most recordings after 21 weeks of gestation, also the SE of CLASC is higher, sometimes even significantly, as for example in the recording performed at 38+0 weeks of gestation. In the 14th and 18th week of gestation, both the techniques perform poorly, leading to low SE and PPV values. The PCA performs better in these recordings, although marginally.

The performance of the classification part of CLASC is assessed in the same way as in section 5.2: by determining the AVS, and calculation of CD and the interobserver variability. The recording performed at 34+4 weeks of gestation and the graphical comparison of CLASC and AVS are depicted, respectively, in figures 42 and 43. All other recordings performed during the pregnancy and their graphical comparison between CLASC and AVS are shown in appendix C.

The results of the comparison between CLASC and AVS are summarized in table 6.
Results and discussion

Figure 42: A 90s long abdominal fECG recording performed at 34+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure 43: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 34+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Table 6: Summary of the comparison between the classification of CLASC and AVS. In this table, I.V. stands for interobserver variability.

<table>
<thead>
<tr>
<th>G.A.</th>
<th>CD</th>
<th>I.V.</th>
<th>Classification</th>
<th>CLASC</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>AVS</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>14+4*</td>
<td>1,67</td>
<td>2,15</td>
<td>CLASC</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>8</td>
<td>7</td>
<td>5</td>
<td>6</td>
<td>AVS</td>
<td>1</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18+0</td>
<td>2,17</td>
<td>1,77</td>
<td>CLASC</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>AVS</td>
<td>5</td>
<td>1</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21+4</td>
<td>1,63</td>
<td>1,23</td>
<td>CLASC</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>AVS</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24+4</td>
<td>0,99</td>
<td>0,71</td>
<td>CLASC</td>
<td>7</td>
<td>8</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>AVS</td>
<td>7</td>
<td>8</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26+4**</td>
<td></td>
<td></td>
<td>CLASC</td>
<td>AVS</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30+4</td>
<td>2,00</td>
<td>1,03</td>
<td>CLASC</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>7</td>
<td>8</td>
<td>AVS</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>8</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>34+4</td>
<td>0,63</td>
<td>0,52</td>
<td>CLASC</td>
<td>1</td>
<td>7</td>
<td>2</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>AVS</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>36+4</td>
<td>2,19</td>
<td>1,55</td>
<td>CLASC</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>8</td>
<td>AVS</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>8</td>
<td>3</td>
<td>4</td>
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</tr>
<tr>
<td>38+0</td>
<td>1,58</td>
<td>2,51</td>
<td>CLASC</td>
<td>7</td>
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<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td>AVS</td>
<td>6</td>
<td>2</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

*CLASC indicates an implausible average heart rate, indicating an erroneous classification is possible.

** The maternal mECG subtraction did not perform correctly.

From table 6, it can be seen that for the recordings performed at 14+4 and 38+0 of gestation, the CD is lower than the I.V., indicating that the classification of CLASC is within the interobserver variability, and thus performs similar as a human expert. For recordings performed at 24+4 and 34+4 weeks of gestation, the CD is less than 1, indicating a good correlation between AVS and CLASC. The CD of the recordings performed at 18+0, 21+4, 30+4, and 36+4, is larger: between 1,58 and 2,17. However, when only the four best signals are used for further analysis, 3 out of four signals will be the same.

So in general, when the four signals containing the largest amount of useful, mutual information are chosen by CLASC and AVS, at least three out of four signals will be the same.

The advantage of using CLASC is that it operates fast, automatically, and always produces the same results, in contrast with AVS, which is dependent of the observer.

As stated before, the recording performed after 26+4 weeks of gestation is not used to analyze the performance of CLASC. The reason for this is that the mECG component was not extracted correctly for this recording. The recording is depicted in figure 44. Clearly, in lead 3 to 6, large ECG complexes are visible, but, according to the RR-intervals, the average heart rate of these ECG complexes is about 72 BPM. This indicates that these peaks could originate from the mother instead of the fetus. After comparing the signals with the original abdominal recording, it became undoubtedly clear that they are indeed maternal ECG complexes. Still, the fECG complexes are also present in the signals, for example in lead 7 in figure 44. One of the fECG complexes is circled in blue.

When CLASC analyses this particular recording, it disregards the small fECG complexes, and incorrectly identifies the mECG complexes as fECG, since it is designed to function on recordings where the mECG signals are already extracted. However, since CLASC calculates an implausible average fetal heart rate, (about 72 BPM), it will prompt a message that indicates that the results may be erroneous.
Results and discussion

For these reasons, the results of CLASC on this particular recording are not used in this report.

Figure 44: A 90s long abdominal fECG recording performed at 26+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. An fECG complex is circled in blue in signal 7.
6. Conclusion

The goal of this study was to enable online recordings of the fECG in the future, and thus, to reduce the calculation time of the fECG extraction. By limiting processing and analysis of the abdominal fECG signals to the best (e.g. four) signals, calculation times can be decreased significantly, while only a limited amount of fECG information is lost.

In order to achieve this, the abdominal signals need to be screened to assess their quality. In this report, a technique is presented that classifies the abdominal recordings based on their spatial correlation. The technique is referred to as the classification of fetal ECG signals using spatial correlation (CLASC). This correlation between the different fECG signals can be explained by the fact that all fECG signals originate from the same source, i.e. the fetal heart.

In order to assess the quality of the fECG complexes in the signals, these complexes need to be detected first. In contrast to the most widely used blind source separation techniques known from the literature (principal component analysis PCA and independent component analysis ICA), CLASC does this by considering a priori knowledge on the abdominal electrode configuration and fetal heart activity.

The performance of the peak detection of CLASC was first assessed on an artificial ECG signal, both with and without added random noise. CLASC was able to detect all R-peaks in all the artificial signals, even when four signals had a SNR of about 2.5 and the other four were replaced by Gaussian noise. However, depending on the SNR of the signals, CLASC sometimes detected a small number of false R-peaks.

In a second test, the performance of CLASC’s peak detection was tested on a 90s long abdominal fECG recording performed at 34+4 weeks of gestation. Again, some fECG signals of the recording were replaced by random noise. As expected, an increase in the number of replaced signals led to a decrease in the peak detection performance.

Finally, the performance of the technique was compared with that of PCA on 8 abdominal recordings, performed at different times during an uncomplicated, singleton pregnancy. The results of this comparison indicated that in week 14 and 18 of gestation, both methods perform poorly, with PCA performing marginally better. From week 21 onwards, CLASC identifies more fetal R-peaks correctly, and in most cases, also misses less fetal R-peaks.

As a general conclusion, it can be stated that in signals with a high SNR (higher gestational age), CLASC outperforms PCA, while for the lower SNR (lower gestational age), PCA functions better than CLASC, albeit marginally.

In order to assess the performance of the classification by CLASC, the problem of not having a golden standard for evaluating the performance of CLASC was overcome by having various researchers in the MMC perform a visual selection of the abdominal fECG signals. Due to the expertise of the researchers in the MMC in the field of fECG extraction, and since the pattern recognition capabilities of the human brain are considered to be superior over computers, this approach should enable assessment of the performance of CLASC. To assess the performance of CLASC’s classification, both artificial ECG signals and actual abdominal fECG recordings were used. When four out of eight artificial ECG signals were replaced by random noise, and noise was added to the remaining four leads until they had a SNR of 2.5, CLASC was able to identify the signals containing no ECG information. Also, evaluation of CLASC on artificial ECG signals with different SNR levels revealed that
the SNR of the individual ECG signals influences CLASC’s classification, but that ordering the signals by decreasing SNR does not lead to the same classification as presented by CLASC. This is because CLASC does not simply compare the SNR of the individual ECG signals, but rather studies the spatial correlation of the individual signals with the rest of the ECG signals. In particular, the SNR only compares the amplitude of the fetal R-peak with the rest of that same ECG signal, while CLASC compares for each signal the complete average fECG complex with the seven other complete average fECG complexes. When CLASC was evaluated on a real abdominal fECG recording, it classified the signals consistently with the MMC researchers. Only after having replaced 5 fECG signals by noise, and thus, leaving only 3 signals containing fECG, CLASC’s performance deteriorated. However, because CLASC detected an implausible average fetal heart rate for this situation, it prompted a message indicating that the classification of the fECG signals could be erroneous. Evaluation of CLASC on various recordings performed throughout the pregnancy of an uncomplicated, singleton pregnancy revealed that in general, CLASC and the visual selection by experts show a large correlation. In particular, when comparing the four signals containing the biggest amount of useful, mutual information, at least three out of four signals are the same for CLASC and the visual selection. The advantage of using CLASC over a visual selection is that it operates fast, automatically, and always produces the same results. This is in contrast to the visual selection, which is dependent of the observer.

To sum up, in this report, a new technique called CLASC was presented. This technique uses spatial correlation to detect individual fECG complexes in the fECG signals, and to classify the fECG signals. It performs accurate and fast, and takes a huge step towards future online extraction of beat-to-beat heart rate and fECG from abdominal recordings.
7. Technology assessment and recommendations

Nowadays, the most common used technique for fetal monitoring is CTG. However, information from Doppler CTG alone is not sufficient for making important decisions regarding the treatment of the fetus and the mother in case of fetal distress. The predictive value of the CTG can be increased when it is combined with ST analysis of the ECG of the fetus. The STAN® device uses this combination by attaching a single spiral electrode to the fetal scalp and a skin electrode to the upper leg of the mother (used as the ground electrode) to obtain the fECG, and to perform ST analysis. The major drawback of the STAN® device is its invasiveness. It can only be performed when the fetal membranes are ruptured and sufficient cervical dilatation is present. Therefore, it would be advantageous to develop a technique for performing early diagnostics in a non-invasive way.

In collaboration with the TU/e, the MMC has developed a system, called NEMO, which uses electrophysiological recordings from the maternal abdomen to determine uterine activity, fetal heart rate, and the fECG. Because it is non-invasive, the NEMO system can be used throughout the entire pregnancy. The algorithm produced by the researchers at the MMC is capable of estimating the mECG and subtracting it from the abdominal recordings, but due to the low SNR, the signals remaining after subtraction of the mECG are often not suitable for extracting the fECG. Additionally, at the moment, the calculation time of the algorithm is too long to permit online fetal heart rate detection. In this report, a fast and robust way to classify the fECG signals was presented. By limiting further processing and analysis of the abdominal fECG signals to the best (e.g. four) signals, calculation times can be decreased significantly, while only a limited amount of fECG information is lost. Thus, CLASC takes a huge step towards future online extraction of beat-to-beat heart rate and fECG from abdominal recordings. However, before abdominal fECG recordings can actually replace the Doppler CTG in clinical practice, several steps need to be taken. First, some steps which could enhance the performance of CLASC will be presented, afterwards, some more general steps are stated.

- At the moment, CLASC obtains a two dimensional representation of the fVCG by using a patient-tailored vectorcardiography approach to spatially combine the abdominal fECG signals. Next, this fVCG is approximated by an ellipse. It may be advantageous to study the effects of another fitting method (i.e. geometric in which the mean orthogonal distance between the ellipse and each data point is minimized) or to expand this approach to the third dimension. Perhaps, approximating the representation of the fVCG by some sort of universal fVCG template instead of an ellipse may lead to better results.

- Once CLASC detects the individual fECG complexes, they are enhanced averaging the fECG complexes, synchronized on their R-peak. This approach was chosen since it is fast and robust. However, the fECG complexes could be enhanced even more using the same technique that is at the moment used in the extraction of the mECG from the abdominal recordings (WAMES [7]). The downside of implementing this technique is that the calculation time will increase, making CLASC less fast.

- At the moment, the mECG component can be extracted from the abdominal recordings in most cases. However, sometimes, the extraction fails, which could lead to errors in further analysis. Thus, the mECG extraction method should be made more robust.

- In this report, a step towards decreasing the calculation time of the fECG extraction is presented. However, even though it sounds plausible that the
calculation time decreases significantly when the amount of data is cut in half, its effect should still be researched. Furthermore, because the entire algorithm is written in Matlab, calculation times can be decreased even more when by rewriting it in another computer language such as C++.

- In order to minimize patient discomfort, the number of abdominal electrodes should be reduced. Since CLASC identifies the abdominal electrodes which record the best fECG signals, performing CLASC on a large amount of abdominal recordings could lead to a better understanding of the correlation between electrode position and quality of the recorded signal.
References

2. Quote of prof. dr. G. Oei, gynocolyst at the MMC
Appendices

Appendix A: Article on the physiology of the fetal heart

This article is submitted for publication in the journal of the American medical association.

Electrical axis of the human fetal heart in early pregnancy – insights into fetal electrocardiography

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3Eindhoven University of Technology, Department of Applied Physics, Eindhoven, the Netherlands
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5Máxima Medical Center, Department of Obstetrics and Gynecology, Veldhoven, the Netherlands

It is generally assumed that the fetal heart is adapted to its antenatal circulation by increased mass of the right ventricle. In terms of the electrocardiogram, this adaptation reveals itself by an electrical axis pointing towards the right ventricle, as opposed to an axis pointing towards the left ventricle for adults. So far, this assumption about the electrical axis has never been verified on human fetuses. Using novel non-invasive technology, we managed to determine the electrical axis of the human fetal heart in-vivo and show that this axis is indeed adapted to the fetal circulation, providing insights into fetal electrocardiography.

Analysis of the electrocardiogram (ECG) of preterm born infants can have significant relevance for establishing a strategy for treatment of the newborn. However, clinical interpretation of the newborn's ECG is complicated due to the absence of adequate knowledge of what constitutes a normal ECG for these ages. These days, it is generally assumed that, due to the different circulation in fetal life as opposed to the adult circulation, the fetal heart is adapted to its intrauterine environment. This adaptation yields an abundance of cardiac muscle in the right ventricle. Accordingly, the mean electrical axis of the fetal ventricles is assumed to point to the right-anterior-inferior octant. This assumption has been verified by various researchers through assessing the spatial vectorcardiogram (VCG) of neonates directly after birth, hypothesizing that the axis directly after birth is the same as before birth [1,2].

With recent progresses made in the treatment of fetal congenital heart diseases [3,4,5], the extrapolation of neonatal ECG standards to the fetus is becoming more important. This extrapolation, however, calls for a verification of the above-mentioned assumption that the mean electrical axis of the fetal ventricles generally points towards the right-anterior-inferior octant. To the best of our knowledge, such a verification has not hitherto been attempted, due to inadequate and insufficient technological means. Building on a novel method for fetal ECG and VCG extraction from non-invasive electrophysiological recordings on the maternal abdomen [6,7], we conceived a method to determine the electrical axis of the fetal heart (i.e. ventricles and atria). In this report we briefly discuss the method and present the result of the electrical axis determination for a single fetus at 21 weeks of gestation, relative to the simultaneously determined mean electrical axis of the mother.
Materials and Methods

The in-vivo measurement discussed in this paper forms part of a larger study conducted at the Máxima Medical Center (Veldhoven, the Netherlands) in which for about 50 pregnant women, longitudinally across the pregnancy, the fetal ECG is recorded from the maternal abdomen. The measurement discussed here was performed on a healthy primigravida mother, 28 years of age, with a singleton pregnancy of 21+4 weeks of gestation and who has given informed consent. Delivery took place at 41+0 weeks of gestation by means of vacuum extraction due to slow progression of labor. The fetus was a healthy female, 3630 grams of weight, and normal 1 and 5 minute Apgar scores. Simultaneously with the fetal ECG recordings, also an ultrasonic recording was performed, as depicted in Figure 1.

The abdominal fetal ECG signals are obtained with 8 adhesive electrodes on the maternal abdomen and are processed to remove the interferences and artifacts from, among other factors, respiration and the maternal ECG (also indicated in Figure 1). Subsequently, the fetal ECG signals are further enhanced by averaging several consecutive ECG complexes. Finally, the fetal VCG is estimated by a method referred to as patient-tailored vectorcardiography [7]. This method is an extension of the commonly known method proposed by Dower [8] and involves an automated, patient specific estimation of the ECG signal conduction, yielding an improved accuracy in VCG estimation.

In order to visualize the fetal VCG in the fetal frame of reference, the estimated spatial VCG is rotated to compensate for the fetal orientation, which is assessed from the simultaneously performed ultrasound recording.

![Figure 1: Methodology for assessment of the electrical axis of the fetal heart. The electrical axis is obtained in two steps. In the first step, the fetal ECG is recorded from the maternal abdomen (upper left photo) and processed by successive filtering, removal of the maternal ECG, enhancement of the fetal ECG, and estimation of the fetal VCG (right panel). In the second step, the fetal VCG is rotated towards the fetal frame of reference, obtained from the ultrasound image (bottom left) to enable assessment of the electrical axis of the fetal heart.](image_url)
Results

In Figure 2a and 2b the results of the determination of the mean electrical axis of the fetal heart are shown. In these figures, the fetal VCG and the mean electrical axis of the ventricles are plotted together, the mean electrical axis being defined as the direction in which the VCG exhibits the maximum amplitude. The VCG potential along the x-axis of the plot, referred to as $V_x$, constitutes the potential along the vector pointing normal to the frontal plane, from the posterior side to the anterior. The axis indicated with $V_y$ points from the right to the left and the $V_z$ axis points from the inferior side of the fetus to the superior side. The direction in which the QRS loop evolves over time is indicated as well.

To facilitate assessment of the fetal VCG and its associated mean electrical axis, the result of the fetal heart is depicted alongside a mean electrical axis for the adult maternal heart. The maternal heart VCG is obtained here from the same recording as the fetal VCG. In the maternal ECG removal step, referred to in the Materials and Methods section (and in Figure 2), the maternal ECG is therefore not just removed but stored for later use in maternal VCG determination.

The fetal VCG, more clearly than the maternal VCG, also shows that the direction of the electrical axis of the atria (i.e. the direction of the maximum P-wave amplitude) conforms to the electrical axis of the ventricles. The reason that the P-wave is not that clear in the maternal VCG is the non-standard electrode configuration that is used to assess the maternal VCG (see Figure 1).

In Figure 2c and 2d the frontal view of the fetal and adult VCG’s are shown again, together with their projections on the Einthoven triangle [9]. The data files presented in this report will be made available at www.nemohealthcare.com.
Discussion

The results in Figure 2a and 2b indicate that the direction of the mean electrical axis of the fetal ventricles is, indeed, as assumed for many years, towards the right-anterior-inferior octant. In addition, the results indicate that full adaptation of the fetal heart to the larger mechanical load in the right ventricle can be seen at least as early as 21+4 weeks of gestation.

This larger mechanical load of the right ventricle originates from the larger ejection volume of this ventricle, as opposed to the left ventricle. As both ventricles, due to the ductus arteriosus, eject to the same vascular bed, systolic pressure in both ventricles has to be the same [10]. Bearing this in mind, the direction of the electrical axis of the fetal atria, at first sight counter-intuitive due to the location of the sinoatrial node in the right atrium, can also be explained. Because only one-third of venous return flows through the foramen ovale from the right to the left atrium [10], the right atrium has to eject about twice as much blood to the right ventricle as the left atrium has to eject to the left ventricle.

The results in Figure 2c and 2d show that the alternative direction of the fetal mean electrical axis has direct consequences in fetal electrocardiography. The projections of the fetal and adult VCG onto the Einthoven triangle [9] indicate that clinical interpretation of the fetal ECG should be made differently from clinical interpretation of the adult ECG.

It can be concluded that our results verify existing assumptions on the electrical axis of the fetal heart, opening new research opportunities in the as yet uncharted field of fetal electrocardiology. When normal values for the fetal ECG can be established, diseases like bundle branch block, typically originating in the fetus around 18-20 weeks of gestation, can be diagnosed and treated early [3]. In addition, interpretation of the fetal ECG for assessment of fetal distress [11] could presumably improve with better knowledge on the electrical axis of the fetal heart.

Conclusion

In this report the authors have shown in-vivo that the healthy fetal heart, as assumed and proven in neonatal studies, is indeed adapted to its alternative circulation by increased mass of the right atrium and ventricle, already as early in pregnancy as 21 weeks. The presented methodology can be a valuable basis for the field of fetal cardiology.
References


Appendix B: Ellipse fit

The ellipses are fitted in the two-dimensional plane using a least squares approach. In this approach, the ellipse is described in the conic equation:

\[ f(x, a) = a_1x^2 + a_2xy + a_3y^2 + a_4x + a_5y + a_6 = 0 \]  

(B1)

By assessing the value of the conic equation \( f(x, a) \) for each point \( x_i = (x_i, y_i) \) in the scatter plot, for given ellipse parameters \( \tilde{a} \), the deviation from the expected value (i.e. zero) can be determined. That is, for given \( \tilde{a} \), the ellipse is fully described and only for points \( x_i \) that lie exactly on the ellipse the conic equation of eq. (B1) will equal zero. Any deviation in the conic equation for \( x_i \) will therefore yield a measure for the error of the ellipse fit. By minimizing the summed square of this error \( \varepsilon \):

\[
\sum_{i=1}^{T} \varepsilon_i^2 = \sum_{i=1}^{T} \left( a_1x_i^2 + a_2x_iy_i + a_3y_i^2 + a_4x_i + a_5y_i + a_6 \right)^2
\]

(B2)

the optimal estimate \( \hat{a} \) for the ellipse parameters can be expressed.
Appendix C: Longitudinal study

In this appendix, the recordings performed during an uncomplicated, singleton pregnancy are shown. Additionally, the comparison between the classification of CLASC and AVS is depicted graphically for each recording.

Figure C1: A 90s long abdominal fECG recording performed at 14+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C2: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 14+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
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Figure C3: A 90s long abdominal fECG recording performed at 18+0 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C4: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 18+0 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C5: A 90s long abdominal fECG recording performed at 21+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C6: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 21+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C7: A 90s long abdominal fetECG recording performed at 24+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C8: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 24+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C9: A 90s long abdominal fECG recording performed at 30+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C10: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 30+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C11: A 90s long abdominal fECG recording performed at 34+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C12: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 34+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C13: A 90s long abdominal fECG recording performed at 36+4 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C14: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 36+4 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.
Figure C15: A 90s long abdominal fECG recording performed at 38+0 weeks of gestation. Only 15 seconds are shown for reasons of clarity. The vertical red dotted lines indicate a fetal R-peak detected by CLASC.

Figure C16: Graphical comparison of the classification of CLASC and AVS for the fECG recording performed at 38+0 weeks of gestation. The weight assigned to the fECG signals by CLASC and AVS are depicted, respectively, by the left and right bars, conform the position of their corresponding leads.