Chapter 2

Literature Survey

2.1 Autonomic Nervous System

The autonomic nervous system (ANS) is a subcomponent of the central nervous system and is responsible for involuntary functions. Figure 2.1 shows that the autonomic nervous system consists of two functionally opposite systems, the sympathetic and the parasympathetic.

The parasympathetic (vagal) nervous system and the sympathetic nervous system, each working in opposing directions to maintain a balanced state of control over internal organs. Parasympathetic restricts or slows down how organs function and the sympathetic increases or speeds up the same organs.


Specific to the heart, parasympathetic input modulates heart rate on a time scale of a few seconds (mostly in tune with respiration) while sympathetic input tends to act on a slower time scale, typically around 30 seconds. During inhalation, the sympathetic nervous system takes control and increases heart rate to take advantage of the extra oxygen in the lungs. During exhalation, parasympathetic dominates, lowering the heart rate. At rest, both the parasympathetic nervous system and sympathetic nervous systems are active, but the parasympathetic will overshadow the sympathetic (at least in a healthy, well rested individual). In order to create an ideal state within the body and in response to the many forms of external stimulation, this balance between the two branches of the ANS is constantly being adjusted.

All the body functions that are not conscious or under the control of the will—for example, the circulation, digestion excretion, gland function and smooth activity—are regulated by the autonomic nervous system. This system is not anatomically well defined, however, but it does function as a unit.

The autonomic nervous system consists of two purely motor systems working in opposition, the sympathetic and the parasympathetic systems. Nerve impulses conducted through one of the systems stimulate activity in an organ in one direction, and those conducted through the other system evoke the opposite effect. For example, the pupil of the eye is dilated by the sympathetic system and contracted by the parasympathetic. There is thus a state of equilibrium, or homeostasis, in the activity of the organ.

The sympathetic nervous system consists of, among other things, sympathetic ganglia, which are located along each side of the spinal column. From here sympathetic fibers lead to the viscera, blood vessels and skin. When stimulated by the sympathetic systems, the vessels contract, the heart rate increases, the peristaltic activity of the intestine is decreased, the uterus contracts, secretion by the sweat glands is stimulated, and secretion by the glands of the digestive organs is inhibited. The parasympathetic nerve fibers run in certain cranial nerves (e.g., the vagus nerve) and in certain spinal nerves (Figure 2.1) [5].

2.2 Heart Rate Variability

Heart rate variability is due to change in the ECG signal time period. This variation in heart rate time period is controlled by autonomic nervous control system developed in the body. Slow
developing disease affecting respiratory and cardiac system can be monitored in the HRV power spectrum. This power spectrum can be used as a health signature to identify the health system condition [3].

Heart rate is a variable signal and provides a balance between the sympathetic and parasympathetic nervous systems. The heart rate variation may contain indicators of present disease, or warnings about impending or future cardiovascular diseases. These indicators may be present at all times or may occur at random during certain intervals in the time scale. It is difficult and time consuming to pinpoint these abnormalities in huge cardiac data.

Heart rate variability (HRV) constitutes a tool for assessing the activities of the autonomic nervous system (ANS). In this work, we have proposed a computer based analytical system to find the heart rate and analyzed it to obtain HRV Power-spectrum for investigation of the autonomic nervous system (ANS) during fetal gestational development. We have designated indices based on the HRV power-spectra power values (= areas under the power-spectrum plot between spectral peaks) and frequency shift of the peaks from their normal frequency values. We have shown the efficacy and sensitivity of these indices to differentiate between normal and abnormal growth of fetus. Thus we have demonstrated how effectively these HRV power-spectral indices can enable advance diagnosis of fetus autonomic nervous system.

We have demonstrated how effectively Spectral analysis of the HR fluctuations provides quantitative amplitude and estimate of the cardiac ANS activity. Finally, we have composed an integrated index made up of these power-spectral indices, to facilitate distinguishing and diagnosing fetal autonomic neuropathy in terms of just one index or number.

The sympathetic outflow to the peripheral blood vessels is directed by vasomotor center which is in the brain stem. Figure 2.2 indicates the control of heart rate by the sympathetic and parasympathetic nervous system.
2.2.1 Heart Rate Variability as a Measure of Autonomic Nervous System Function

Under steady state conditions, the specific oscillations of the heart rate reflect the beat-to-beat autonomic control of SA node activity. The SA node, which is the dominant pacemaker of the heart, is enervated by both sympathetic and parasympathetic nerves. Sympathetic nerve activity increases the heart rate, while parasympathetic nerve activity slows it. Clinically measured variations of the heart rate have shown modulations at low, medium and high frequency. These oscillations are of cardiovascular origin and are pseudo periodical. They repeat themselves in time, with a period which oscillates around a certain mean value even when no rhythm disturbances are present. These oscillations are now recognized as physiological rhythms, representing neurocardiac regulation of blood pressure and heart rate.

Changes in blood pressure in normal healthy persons show spontaneous oscillations of the heart rate in a narrow range around 0.1 Hz known as the Traube-Hering-Mayer (THM) waves. It has been established that these HR oscillatory waves are generated by the blood pressure control system, that causes switching on-off of the baroreceptor reflex. The frequency oscillations of the heart rate (HR) reflect neuroregulatory activity. In this context, the heart rate variation (HRV)
power spectrum has been studied, and provides a noninvasive measure of the autonomic nervous system function. Studies have documented the repeatability of HR power density at rest and its alterations due to mental loading, orthostatic stress, forced respiration, post-myocardial infarction as well as following heart transplant, to help autonomic tone [4].

2.3 Measurement of Heart Rate Variability

HRV analysis methods can be divided into time-domain, frequency-domain, and nonlinear methods. In the following chapters these methods are discussed. Denotations and definitions for HRV parameters in this work and in the developed software follow the guidelines given in [6].

Heart Rate Variability (HRV) measurements analyze how these RR intervals, which show the variation between consecutive heartbeats, change over time. The strategy of obtaining the data for the HRV analysis is shown in Figure 2.3. This flow chart summarizes individual steps used when recording and processing the ECG and Doppler ultrasound signal in order to obtain data for HRV analysis.

Figure 2.3: Flow chart summarizing individual steps used when recording and processing the ECG and Doppler ultrasound signal in order to obtain data for HRV analysis (modified from Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, “Heart rate variability Standards of measurement, physiological interpretation, and clinical use,” European Heart Journal 17, pp 354–381, 1996).
Figure 2.4 shows the HRV of a typical 34 wk of gestation, BMI23.3 normal weight mother fetus. HRV analysis provides a quantitative marker of the autonomic nervous system (ANS) because the regulation mechanisms of HRV originate from the sympathetic and parasympathetic nervous systems [7]. To date, many researchers and engineers have made contributions to discover information which could be applicable to hospitals. In the last fourteen years, over 3000 articles have been published about HRV. These articles observe relationships between HRV and blood pressure, myocardial infarction, nervous system, cardiac arrhythmia, diabetes, respiration, renal failure, gender, age, fatigue, drugs, smoking, alcohols, and so on. Various medical disciplines also have been researching HRV [6]-[8].

2.3.1 Time Domain Analysis

For time series analysis, time domain measures are commonly used. Many measures can be extracted from the original RR interval signals to show the changes in the ANS. Simple time domain variables that can be calculated include the mean NN interval, the mean heart rate, the difference between the longest and shortest NN interval, the difference between night and day heart rate, and so forth.

- **Statistical Methods:**

The simplest variable to calculate is the standard deviation of the NN intervals (SDNN), that is, the square root of variance. Since variance is mathematically equal to total power of spectral analysis, SDNN reflects all the cyclic components responsible for variability in the period of recording. Other commonly used statistical variables calculated from segments of the total monitoring period include SDANN, the standard deviation of the average NN intervals calculated over short periods, usually 5 minutes, which is an estimate of the changes in heart rate due to
cycles longer than 5 minutes, and the SDNN index, the mean of the 5-minute standard deviations of NN intervals calculated over 24 hours, which measures the variability due to cycles shorter than 5 minutes. The most commonly used measures derived from interval differences include RMSSD, the square root of the mean squared differences of successive NN intervals, NN50, the number of interval differences of successive NN intervals greater than 50 ms, and pNN50, the proportion derived by dividing NN50 by the total number of NN intervals [6].

- **Geometric Methods:**

  The series of NN intervals also can be converted into a geometric pattern, such as the sample density distribution of NN interval durations, sample density distribution of differences between adjacent NN intervals, Lorenz plot of NN or RR intervals, etc. The geometric shape is classified into several pattern-based categories that represent different classes of HRV (for example, elliptic, linear, and triangular shapes of Lorenz plots). Most geometric methods require the RR (or NN) interval sequence to be measured on or converted to a discrete scale that is not too fine or too coarse and permits the construction of smoothed histograms. Most experience has been obtained with the length of the bins of approximately 8 ms long (precisely 7.8125 ms=1/128 seconds), which corresponds to the precision of current commercial equipment.

  The HRV triangular index measurement is the integral of the density distribution (that is, the number of all NN intervals) divided by the maximum of the density distribution. Using a measurement of NN intervals on a discrete scale, the measure is approximated by the value:

  \[
  \frac{\text{(Total number of NN intervals)}}{\text{(Number of NN intervals in the modal bin)}}
  \]

  which is dependent on the length of the bin, that is, on the precision of the discrete scale of measurement. Thus, if the discrete approximation of the measure is used with NN interval measurement on a scale different from the most frequent sampling of 128 Hz, the size of the bins should be quoted. The triangular interpolation of NN interval histogram (TINN) is the baseline width of the distribution measured as a base of a triangle approximating the NN interval distribution (the minimum square difference is used to find such a triangle).

  The major advantage of the geometric methods lies in their relative insensitivity to the analytical quality of the series of NN intervals. The major disadvantage of the geometric methods is the need for a reasonable number of NN intervals to construct the geometric pattern. In practice, recordings of at least 20 minutes (but preferably 24 hours) should be used to ensure the correct performance of the geometric methods, i.e. the current geometric methods are
inappropriate to assess short-term changes in HRV. The variety of time domain measures of HRV is summarized in Table 2.1. Since many of the measures correlate closely with others, the following four measures are recommended for time-domain HRV assessment: SDNN (estimate of overall HRV); HRV triangular index (estimate of overall HRV); SDANN (estimate of long-term components of HRV), and RMSSD (estimate of short-term components of HRV) [6]-[8].

Table 2.1: Selected time domain measures of HRV ((modified from Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, “Heart rate variability Standards of measurement, physiological interpretation, and clinical use,” European Heart Journal 17, pp 354–381, 1996).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Units</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Statistical Measures</strong></td>
<td></td>
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</tr>
<tr>
<td>SDNN</td>
<td>ms</td>
<td>Standard deviation of all NN intervals</td>
</tr>
<tr>
<td>SDANN</td>
<td>ms</td>
<td>Standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording</td>
</tr>
<tr>
<td>RMSSD</td>
<td>ms</td>
<td>The square root of the mean of the sum of the squares of differences between adjacent NN intervals</td>
</tr>
<tr>
<td>SDNN index</td>
<td>ms</td>
<td>Mean of the standard deviations of all NN intervals for all 5-minute segments of the entire recording</td>
</tr>
<tr>
<td>SDSD</td>
<td>ms</td>
<td>Standard deviation of differences between adjacent NN intervals</td>
</tr>
<tr>
<td>NN50 count</td>
<td></td>
<td>Number of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; three variants are possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer</td>
</tr>
<tr>
<td>pNN50</td>
<td>%</td>
<td>NN50 count divided by the total number of all NN intervals</td>
</tr>
<tr>
<td>CVRR</td>
<td></td>
<td>Ratio standard deviation of normal RR intervals value to mean of</td>
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</table>
such intervals.

<table>
<thead>
<tr>
<th>Geometric Measures</th>
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</thead>
<tbody>
<tr>
<td>HRV triangular index</td>
</tr>
<tr>
<td>TINN</td>
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</table>

### 2.3.2 Frequency Domain Analysis

Various spectral methods for the analysis of the tachogram have been applied since the late 1960s. Power spectral density (PSD) analysis provides the basic information of how power (variance) distributes as a function of frequency. Independent of the method employed, only an estimate of the true PSD of the signal can be obtained by proper mathematical algorithms.

Methods for the calculation of PSD may be generally classified as nonparametric and parametric. In most instances, both methods provide comparable results. The advantages of the nonparametric methods are: (a) the simplicity of the algorithm used (fast Fourier transform [FFT] in most of the cases) and (b) the high processing speed. While the advantages of parametric methods are: (a) smoother spectral components that can be distinguished independent of preselected frequency bands, (b) easy post processing of the spectrum with an automatic calculation of low- and high-frequency power components with an easy identification of the central frequency of each component, and (c) an accurate estimation of PSD even on a small number of samples on which the signal is supposed to maintain stationarity. The basic disadvantage of parametric methods is the need of verification of the suitability of the chosen model and of its complexity (that is, the order of the model) [7].

The RR interval time series is an irregularly time-sampled signal. This is not an issue in time domain, but in the frequency-domain it has to be taken into account. If the spectrum estimate is calculated from this irregularly time-sampled signal, implicitly assuming it to be evenly sampled, additional harmonic components are generated in the spectrum. Therefore, the RR interval signal is usually interpolated before the spectral analysis to recover an evenly sampled signal from the
irregularly sampled event series. In the frequency-domain analysis power spectral density (PSD) of the RR series is calculated. Methods for calculating the PSD estimate may be divided into nonparametric [e.g. fast Fourier transform (FFT) based] and parametric [e.g. based on autoregressive (AR) models] methods. The PSD is analyzed by calculating powers and peak frequencies for different frequency bands. The commonly used frequency bands are very low frequency (VLF, 0-0.04 Hz), low frequency (LF, 0.04-0.15 Hz), and high frequency (HF, 0.15-0.4 Hz). The most common frequency-domain parameters include the powers of VLF, LF, and HF bands in absolute and relative values, the normalized power of LF and HF bands, and the LF to HF ratio. Also the peak frequencies are determined for each frequency band. For the FFT based spectrum powers are calculated by integrating the spectrum over the frequency bands. The parametric spectrum, on the other hand, can be divided into components and the band powers are obtained as powers of these components. This property of parametric spectrum estimation has made it popular in HRV analysis [6]-[8].

**Spectral Components in Short-term recordings:** Three main spectral components are distinguished in a spectrum calculated from short-term recordings of 2 to 5 minutes VLF, LF, and HF components. The boundaries of the bands are defined differently by different authors. The bands with most commonly employed boundaries are the following.

- **HRVPS Low Frequency (VLF) Band (0.00-0.04 Hz)**
  In this band, variations are related to temperature regulation of the body, the vasomotor control and the rennin-angiotensin system, with the center-of-frequency at 0.04 Hz. This is an ill defined band, modulated by the influence of both parasympathetic and sympathetic systems. A very low frequency band (VLF) ≤ 0.04 Hz is described with the influence of mainly the sympathetic system.

- **HRVPS Mid Frequency (LF) Band (0.04-0.15Hz)**
  This band consists of variations related to the arterial blood pressure control system, with the center-of-frequency at 0.1 Hz. It is influenced by parasympathetic and sympathetic systems. Increase in vagal activity augments peak LF power, or energy content of the HRV wave form in this frequency range. Conversely, parasympathetic blockade diminishes LF power, especially in the supine position.

Interventions which increase sympathetic activity (e.g., passive tilting, standing, mental and physical stress, sympathomimetic agents, baroreceptor unloading with nitro-glycerine infusion
and coronary occlusion) are known to increase the LF component. The magnitude of the power in this band decreases monotonically with age; it is increased by standing when the sympathetic system is activated. It is not influenced by breathing, when the respiratory rate is above nine breaths per minute. In supine position, its magnitude is mainly dependent on parasympathetic system.

- **HRVPS High Frequency (HF) Band (0.15-0.4 Hz):**

  Variations related to respiration are associated with parasympathetic activity, with the center-of frequency at 0.25 Hz, which varies with the respiratory rate. This band is mediated solely by the parasympathetic system. The magnitude of the power in this band is more in the supine than the standing position. There is a linear decline in the power of this band up to the age of 30 years, and does not change thereafter.

  The distribution of the power and the central frequency of LF and HF are not fixed but may vary in relation to changes in autonomic modulations of heart period. The physiological explanation of the VLF component is much less defined, and the existence of a specific physiological process attributable to these heart period changes might even be questioned. The non harmonic component, which does not have coherent properties and is affected by algorithms of baseline or trend removal, is commonly accepted as a major constituent of VLF. Thus, VLF assessed from short-term recordings (≤5 minutes) is a dubious measure and should be avoided when the PSD of short-term ECGs [3, 4].

  The measurement of V LF, LF, and HF power components is usually made in absolute values of power (ms²), but LF and HF may also be measured in normalized units (n.u.) which represent the relative value of each power component in proportion to the total power minus the VLF component. The representation of LF and HF in normalized units emphasizes the controlled and balanced behavior of the two branches of the autonomic nervous system. Selected frequency domain measures of HRV are summarized in Table 2.2.
Table 2.2: Selected frequency domain measures of HRV [(modified from: Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, “Heart rate variability Standards of measurement, physiological interpretation, and clinical use,” European Heart Journal 17, pp 354–381, 1996).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Units</th>
<th>Description</th>
<th>Frequency Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analysis of Short-term Recordings (5 min)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5-min total power</strong></td>
<td>ms²</td>
<td>The variance of NN intervals over the temporal segment</td>
<td>Approximately ≤0.4 Hz</td>
</tr>
<tr>
<td>VLF</td>
<td>ms²</td>
<td>Power in very low frequency range</td>
<td>≤0.04 Hz</td>
</tr>
<tr>
<td>LF</td>
<td>ms²</td>
<td>Power in low frequency range</td>
<td>0.04-0.15 Hz</td>
</tr>
<tr>
<td>LF norm</td>
<td>n.u.</td>
<td>LF power in normalized units</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>LF/(total power-VLF) x 100</td>
<td></td>
</tr>
<tr>
<td>HF</td>
<td>ms²</td>
<td>Power in high frequency range</td>
<td>0.15-0.4 Hz</td>
</tr>
<tr>
<td>HF norm</td>
<td>n.u.</td>
<td>HF power in normalized units</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>HF/(total power-VLF) x 100</td>
<td></td>
</tr>
<tr>
<td>LF/HF</td>
<td></td>
<td>Ratio LF [ms²]/HF[ms²]</td>
<td></td>
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<tr>
<td><strong>Analysis of Entire 24 Hours</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total power</td>
<td>ms²</td>
<td>Variance of all NN intervals</td>
<td>≤0.4 Hz</td>
</tr>
<tr>
<td>ULF</td>
<td>ms²</td>
<td>Power in the ultra low frequency range</td>
<td>≤0.003 Hz</td>
</tr>
<tr>
<td>VLF</td>
<td>ms²</td>
<td>Power in the very low frequency range</td>
<td>0.003-0.04 Hz</td>
</tr>
<tr>
<td>LF</td>
<td>ms²</td>
<td>Power in the low frequency range</td>
<td>0.04-0.15 Hz</td>
</tr>
<tr>
<td>HF</td>
<td>ms²</td>
<td>Power in the high frequency range</td>
<td>0.15-0.4 Hz</td>
</tr>
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2.3.3 Nonlinear Analysis

It is realistic to presume that HRV also contains nonlinear properties because of the complex regulation mechanisms controlling it. The interpretation and understanding of many nonlinear methods is, however, still insufficient. One simple and easy to comprehend nonlinear method is
the so called Poincare plot. It is a graphical presentation of the correlation between consecutive RR intervals. The geometry of the Poincare plot is essential. A common way to describe the geometry is to fit an ellipse to the graph. The ellipse is fitted onto the so called line-of-identity at 45° to the normal axis. The standard deviation of the point’s perpendicular to the line-of-identity denoted by SD1 describes short-term variability which is mainly caused by respiratory sinus arrhythmia (RSA). The standard deviation along the line-of-identity denoted by SD2 describes long-term variability [7].

The analysis of Poincare plot can be performed in a qualitative manner (visual), by assessing the figure formed by its attractor, which is useful for showing the degree of complexity of RR intervals or quantitative, by adjusting the ellipse of the figure formed by the attractor, from which three indexes can be obtained: SD1, SD2 and SD1/SD2 ratio. SD1 represents the dispersion of points perpendicular to the line of identity and it seems to be an index of instantaneous recording of beat-to-beat variability; the SD2 represents the dispersion of points along the line of identity and represents the HRV in long-term records; the relationship of both (SD1/SD2) shows the ratio between the short- and long-term variations of the RR intervals.

The qualitative analysis (visual) of the Poincare plot is performed through the analysis of the figures formed by the plot attractor, which were described by Tulppo et al. [9] who classified them as follows: (a) Comet-shaped figure, on which an increase in the dispersion of beat-to-beat RR intervals is observed with increase in RR intervals, characteristic of a normal plot; (b) Torpedo-shaped figure, with a small global beat-to-beat dispersion (SD1) and without increasing the long-term dispersion of RR intervals; (c) Complex or parabolic figure, on which two or more distinct ends are separated from the main body of the plot, with at least three points included in each end. Selected nonlinear measures of HRV is summarized in Table 2.3

<table>
<thead>
<tr>
<th>Nonlinear Measures (Poincare plot)</th>
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</thead>
<tbody>
<tr>
<td>SD1 ms The standard deviation of Poincare plot perpendicular to the line-of-identity</td>
<td></td>
</tr>
<tr>
<td>SD2 ms The standard deviation of Poincare plot along the line-of-identity</td>
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</tbody>
</table>
2.4 Historical Review of Early Work

The most studied parameter of fetal physiology is the fetal heart rate (FHR). In fact, the identification of various fetal heart rate patterns has provided obstetricians with a very valuable tool for assessing fetal well-being. Typical changes in FHR patterns are known to reflect hypoxia or asphyxia, as well as sympathetic and parasympathetic activity.

Fetal and neonatal HRV is an important area of investigation, and it might provide early information about fetal and neonatal distress and identify those at risk for sudden infant death syndrome. Most of the preliminary work in this field was carried out in the early 1980s before more sophisticated power spectral techniques became available. Insight into autonomic maturation in the developing fetus also might possible through the proper applications of these techniques. Fertile area of research is the use of HRV techniques to explore the role of autonomic nervous system alterations in disease mechanisms, especially those conditions in which sympathovagal factors are thought to play important role. Recent work suggests that alterations in autonomic innervations to the developing heart might be responsible for some forms of long QT syndrome. Fetal HRV studies in pregnant mother with this disorder are certainly feasible and might be very informative.

In physiological conditions of healthy subjects, heart cycles are not of the same length, due to many influences on sympathovagal balance, among which respiratory and circadian changes are the most prominent. These subtle differences between consecutive R-R intervals on electrocardiogram are called heart rate variability. HRV has been studied for several years, with an increasing interest in understanding its mechanisms and its clinical utility in diseases. Historically, its clinical interest emerged in 1965 when Hon and Lee showed a well-defined clinical application of HRV in the monitoring area of fetal distress.

Heart rate variability (HRV) refers to the beat-to-beat alterations in heart rate. Under resting condition, the ECG of healthy individuals exhibits periodic variation in R-R intervals. This rhythmic phenomenon, known as respiratory sinus arrhythmia (RSA), fluctuates with the phase of respiration—cardio-acceleration during inspiration, and cardio-deceleration during expiration. RSA is predominantly mediated by respiratory gating of parasympathetic efferent activity to the heart: vagal efferent traffic to the sinus node occurs primarily in phase with expiration and is absent or attenuated during inspiration. Atropine abolishes RSA. Reduced HRV has thus been used as a marker of reduced vagal activity.
V. Kalakutskij et al. [10] in 2002, confirmed method of an estimation of a fetus condition includes abdominal ECG registration, correlation processing of the received data, fetal R-R intervals allocation, estimation of distribution parameters and diagnostic index calculation, describing activity of sympathetic nervous system of fetus. This technique is used in real-time mode and serves as an approach to the problem of fetal stress diagnostics by means of maternal abdominal ECG processing.

In, 2004, Rajendra Acharya U et al. [11] showed an analysis based on heart rate variability in normal subjects of various age group using the various time domain, frequency domain and nonlinear parameters. The results show that, with aging the heart rate variability decreases. In this work, the different linear and nonlinear parameters evaluated show a particular range for various cardiac abnormalities. And the results of these were subjected to ‘t’ test with more than 89% confidence interval giving excellent ‘p’ values in all cases.

In, 2006, Janusz Jezwski et al. [12] compared Doppler ultrasound and direct electrocardiography acquisition techniques for quantification of fetal heart rate variability, and showed that evaluation of the acquisition technique influence on fetal well-being assessment cannot be accomplished basing on direct measurements of heartbeats only. The more relevant is the estimation of accuracy of the variability indices, since analysis of their changes can significantly increase predictability of fetal distress.

In 2007, Maya David et al. [13] showed an estimation of fetal autonomic state by time-frequency analysis of fetal heart rate variability and confirmed that there is a neural organization during the last trimester of the pregnancy, and the sympathovagal balance is reduced with the gestational age.

In 2008, Akimune Fukushima et al. [14] showed analysis based on the time-domain and frequency domains of heart rate variability using fetal magnecardiography enable an evaluation of fetal autonomic nervous system (ANS) activity. The result show that sympathetic nervous activity increased with gestational age in the normal pregnancy group.

Monica Healthcare’s clinical specialist Karnie Bhogal and research fellow Indu Asanka Jayawardane [15], in 2009, highlights some of the problems with Doppler ultrasound (cardiotocogram (CTG)) in monitoring obese mothers, and how by using the technology of abdominal fetal electrocardiogram (ECG) monitoring, the quality of care in relation to fetal heart rate (FHR) monitoring to this cohort can be improved. A study of 120 pregnancies, ranging from
a body mass index (BMI) of 18 to 44, showed that obesity did not affect the success rate of the FHR data.

In 2009, Meldijana Omerbegovic et al. [16] introduced a Heart rate variability non-invasive monitoring of autonomic nervous system function special measurements, based on time and frequency domain analysis. The results show that, heart rate variability gives many parameters that are related to the functioning of two branches of autonomous nervous system: sympathetic and parasympathetic system. Many observational and controlled clinical studies have shown reduced heart rate variability in different pathological conditions, so that it could be a useful tool in risk stratification after acute myocardial infarction, or coronary artery disease, in diabetic autonomic neuropathy, endocrine diseases, neurologic and psychiatric diseases.

In 2009, Luiz Carlos Marques VANDERLEI et al. [17] showed the HRV indexes are obtained by analyzing the intervals between consecutive R waves, which can be captured by instruments such as electrocardiographer, digital-to-analog converter and the cardio-frequency meter, from external sensors placed at specific points of the body. The results show that, changes in the HRV patterns provide a sensible and advanced indicator of health involvements. Higher HRV is a signal of good adaptation and characterizes a healthy person with efficient autonomic mechanisms, while lower HRV is frequently an indicator of abnormal and insufficient adaptation of the ANS, provoking patient’s poor physiological function.

In 2010, a group of experiments performed to investigate whether anxiety during pregnancy can be linked with the autonomic nervous system via different heart rate variability parameters, confirmed that the ANS modulation is slightly influenced by the anxiety level, but not as strongly as hypothesized before. The work was performed by Joachim Taelman et al. [18] at Katholieke Universities Leuven, Belgium and universities van Tilburg, The Netherlands.

In 2011, Janusz Jezewski et al. [19] introduced a novel technique for fetal heart rate estimation from Doppler ultrasound signal. Results suggest that proposed method for fetal heart rate determination on a beat-to-beat basis offers a high accuracy of the heart interval measurement enabling reliable quantitative assessment of the FHR variability, at the same time reducing the number of invalid cardiac cycle measurement.

In 2011, Akimune Fukushima et al. [20] have demonstrated developmental activity of the autonomic nervous system (ANS) of the normal fetus and intrauterine growth restriction (IUGR) cases using fetal magnetocardiography (FMCG). The results show that, the value of CVRR in the
normal pregnancy group displayed a slight increasing trend with gestational age. However, no such trend was observed in the IUGR group. The development of fetal ANS activity in IUGR cases might differ from that observed in the normal pregnancy group, and this may facilitate early detection of IUGR.

In 2013, Sumana Panja et al. [21] have evaluated the physiological responses to non–invasive cardiovascular autonomic function tests (cardiovascular reflexes, including heart rate response tests and blood pressure response tests) in normal pregnancy and compared them with non-pregnant controls. The observations serve to corroborate that the cardiovascular indices in pregnant women are significantly altered in comparison to non-pregnant women, thus highlighting the importance of cardiovascular monitoring during pregnancy.

### 2.4.1 Mathematical Technique for FECG Extraction

The assessment of FHR variability (FHRV), especially when short-term variability is concerned, requires a very accurate detection of fetal heartbeats [22]. There are only few available technologies that can achieve this required beat-to-beat accuracy; most of them are based on fetal magnetocardiography. The maternal abdominal ECG signal is a superposition of the cardiac electrical signal of the mother and the cardiac electrical signal of the fetus. Due to the indirect measurement and the differences in cardiac size, the fetal contribution is smaller by at least one order of magnitude. Furthermore, there are many additional noise sources, such as maternal muscle activity, uterine contractions, external electrical interference etc. As measurement and amplification techniques improved, fetal electrocardiography became more feasible and popular [1, 2]. Figure 2.5 shows the maternal ECG, consisting of the ECG signal of both the mother and the fetus. The FECG signal can be observed as small spikes within the maternal ECG, surrounded also by experimental noise.

![Figure 2.5: Result of FECG experiment (bandwidth 0.05 Hz - 300Hz); sampling rate, 1.25 MS/s Abdominal leads recording, F: Fetal influence, M: Maternal influence.](image)
The aim of the mathematical techniques is to extract the fetal component from a maternal ECG signal such as the one shown in figure 2.5 and provide a clean FECG time series that can be further analyzed in search for possible abnormalities. The techniques that can be found in the literature are numerous. We will very briefly review in this section the most commonly found ones. Most of these approaches are evaluated using simulated maternal ECG signals or/and a very small data set of real recordings. To begin with, we note that a significant number of studies found in the literature report the implementation of the complex continuous wavelet transform for the extraction of the fetal heart rate, for example [23]. In particular, in this work a complex continuous wavelet transform is applied in order to extract the wavelet-based features of the fetal cardiac signal so that the normal cases can be easily distinguished from the abnormal ones and fetus well-being during pregnancy.

Another method to monitor fetal heart rate patterns is by studying the fetal heart rate variability. It has been shown that heart rate variability is an important marker for the fetal well-being. Various methods have been therefore used to analyze the fetal heart rate variability, in particular concerning variables from both the time and the frequency domain. A promising approach is the so-called independent component analysis (ICA). ICA is a method for retrieving independent hidden signals from a multi-channel observation. Results suggest that in proposed system maternal ECG suppressed effectively and the FHR can be obtained accurately and conveniently. The ICA technique separates a set of signals into a set of other signals, assuming that the original signals are non-redundant (for example, the signals may be mutually statistically independent or de-correlated). It was reported that the results by ICA were more satisfactory than those by classical methods like adaptive noise cancellation and blind source separation methods for extraction of fetal ECG [24].

In 1975, Bernard Widrow et al. [25] introduced the concept of adaptive noise cancelling, an alternative method of estimating signals corrupted by additive noise or interference. The method uses a “primary” input containing the corrupted Signal and a “reference” input containing noise correlated in some unknown way with the primary noise. The reference input is adaptively filtered and subtracted from the primary input to obtain the signal estimate. Baseline drift and 50Hz interference are clearly present in the primary input, obtained from the abdominal lead. The interference is so strong that it is almost impossible to detect the fetal heartbeat. The inputs obtained from the chest leads contained the maternal heartbeat and a sufficient 50Hz component
to serve as a reference for both of these interferences. In the noise canceller output both interferences have been significantly reduced, and the fetal heartbeat is clearly discernible.

To finish our brief review, we note below the use in the literature of methods such as:

- Independent component analysis [24]
- ECG Feature Extraction Based on multi-resolution Wavelet Transform [26]- [28]
- A real-time QRS detection algorithm [29,30]
- Wavelet Transform & ECG [31]
- Wavelet Based Peak Detection [32]
- Discrete wavelet transform [28, 33].