Chapter-3
Theoretical Background for HRV and Echocardiogram.

The chapter includes:
- HRV indices, their variations in different disease conditions and pathophysiology of the variation in the indices
- Brief introduction of ECG signal
- Algorithm to acquire R-R interval from ECG signal and HRV simulator.
- Basic echocardiogram techniques
- Echocardiogram indices for the study

3.1 Study of HRV analysis and related indices.
The Heart rate variability is a significant index that directly relates to the physiology of heart. [3]

The HRV parameters that determine the cardiac performance assessment are
1) Heart Rate
2) Heart Rate variability (HRV)
3) Normalized power in LF band (0.0Hz -0.15Hz)
4) Normalized power in HF band (0.15Hz -0.4Hz)
5) Total power
6) Sympatho vagal balance (HF/LF power ratio)
7) Orthostatic ratio

1) Heart Rate:
Heart rate at rest is known as basal heart rate. Basal heart rate of a normal healthy person is 60 beats per minute. Heart rate goes on increasing with age. Diabetic subjects are observed to have higher basal heart rate. With increasing duration of prevailing diabetes heart rate increases. Higher basal heart rate indicates the extra load on heart. The average value of diabetic subjects with different durations of prevailing diabetic conditions may be higher than as 84 bpm. [3], [5], [6] and [10]

2) Heart Rate Variability:
The heart rate varies as the demand from the body increases. If there is change in the parameters that control the heart rate, the heart rate varies so as to maintain homeostasis i.e. the condition of equilibrium within the different body parameters. If the body performs some physical activity heart rate should increase. Such capability of varying the heart rate is heart rate
variability. Heart rate variability reduces with age. The heart rate variability reduces by 4.6 beats per minute (0.07 beats per second) per year. [3] The heart rate variability is measured in SDNN which is defined as standard deviation of NN intervals in milliseconds. [6] SDNN is high in case of a normal subject. The typical average value is 47 in case of a normal subject and is 15 in case of diabetic subject. [3] In case of diabetic subjects the heart variability reduces. Longer the prevalence of diabetes, lower the heart rate variability.

Every decade of prevailing diabetes, HRV is reduced. HRV is measured by SDNN i.e. standard deviation of N-N intervals. (The R-R interval is defined as N-N intervals. Actually starting point of electrical activity is P event i.e. the atrial depolarization. But it is possible to locate and measure R interval due to the highest rate of change in amplitude. Hence N-N interval can be considered as R-R interval.)

FFT or Auto Regressive (AR) analysis gives three prominent frequency bands of range 0-0.04 Hz, 0.04-0.15 Hz and 0.15 to 0.4 Hz that are called as Very Low Frequency (VLF), Low frequency (LF) and High Frequency (HF) band. AR analysis is preferred over FFT bands analysis because it provides smoother spectral components that are independent of preselected frequency bands. The bands of diagnostic interest are LF and HF band. Unlike heart rate and heart rate variability, the frequency bands do not vary with age. The power variations in the two bands provide a noninvasive sympathetic measure of the autonomic dysfunction. Alterations due to mental stress, orthostatic stress, assessment post myocardial infarct, heart transplant surgery, evaluation of cardiac function after bypass etc. can be characteristic feature. [3] Auto regressive band is used to record the data as the technique filters out unwanted frequencies.

3) Normalized LF power:

The power in these spectra represent the baroreceptor control in LF band, sympathetic hormone drives the heart to respond to the increase in the demand of blood supply initiated from change in physical or mental conditions. Parasympathetic hormone controls and inhibits the increase in the heart rate. Increase in sympathetic power augments this band. Every frequency spectrum represents the normalized power spectral density from the respective band in the HRV analysis report. This power is around 50 Normalized Units (NU) in case of normal subjects, decreased in diabetic
patients. The Extent of decrease is related to the prevailing cardiac performance. In case of hypertensive cohorts, the power in enhanced as it is associated with sympathetic activity. In case of diabetic and hypertensive cohorts, this power depends upon the dominance of hypertensive or diabetic disease conditions. [3]

4) **Normalized HF power**
The power in this band for normal subjects is around 52 Normalized Units (NU). It is found that the parasympathetic power solely dominates this band. Parasympathetic band varies with variation related to respiration around 0.25 Hz. This error is called respiratory sinus arrhythmia (RSA). The subjects are requested to deep breath during the ECG was acquired so that RSA in eliminated. The power is much higher in case of diabetic cohorts and highest in case of diabetic cohorts with myocardial ischemia/infarction. [3]

5) **Total Power**
The total power is the sum of power in all the frequency bands. Since there is deterioration of neuron conduction in prevailing diabetic condition, total power is reduced in diabetic subjects and highly reduced in case of diabetic cohorts with myocardial ischemia/infarction. [3]

6) **Sympatho-vagal balance**
The ratio of LF/HF power is defined as the sympatho-vagal balance. The value of this index is observed to be higher in normal subjects that the diabetic subjects. [3]

7) **Orthostatic stress index**
The ratio of difference of sympatho vagal balance in supine position and sitting position to sympatho vagal balance in supine position is defined as the orthostatic stress index. This index represents the hormonal balance of sympathetic to parasympathetic power. In case of normal subjects, this power is more than one indicating the parasympathetic power on little higher side. As the body demands are changed the orthostatic balance also changes as per the requirement. This value is retained back after the body the demand is fulfilled. The orthostatic stress index value for normal subjects is higher than unity. The diabetic subjects have the ratio values that tend to reduce with more prevalent diabetic conditions. Lower values of orthostatic index signify the inability of heart to pump more blood as per the demand of the body. As a compensatory mechanism, the basal heart rate increases and heart rate variability is observed to be reduced. [3]
3.2 **Detail of data acquisition methodology for HRV analysis.**

Since Sir Williams Einthoven invented Electrocardiogram in 1902, it has been the most widely used, noninvasive quick and effective diagnostic tool to recognize the cardiac rhythm and electrophysiology studies. The Lead 12 system gives the details of the electrical impulse conduction in all different parts of the heart. For the HRV analysis required for the study Lead II ECG that maps the electrical activity of the left ventricle was sufficient. ECG waveform using 12 leads is shown in figure 3.1.a. The diagram shows the portion of the heart shown by different leads. The corresponding waveform of a normal heart is shown in the 3.1.b. [27], [31] and [4]

![Figure- 3.1-A- Portion of the heart viewed by the corresponding leads.](image)

![Figure- 3.1-B- ECG waveforms of different leads. Figure adapted from www.physionet.com](image)
Lead II ECG is also shown in the same diagram below. For the lead II ECG, the left and right ventricles window is available. The leads are applied to both the hands and the left leg. [27], [28] and [29]

Lead II ECG is acquired for 3-5 minutes (128 samples or more). To catch all the details, a sampling frequency of 500 samples/sec is used. The signal acquisition is through disposable surface electrodes. ECG amplifier is used. The acquired signal is interfaced with LABVIEW software interface. The signal generated is read into a MATLAB program though a Microsoft Excel file. The MATLAB program implements the QRS detector using Pan-Tompkins’s algorithm. [26] The Details of the algorithm are discussed below.

3.3 QRS detector using Pan-Tompkins’s algorithm.

ECG signal is superimposed by different types of signals like -

1) Supply frequency interference  
2) Muscle artifact  
3) Baseline wander  
4) T-wave interference

The band pass function is realized through a design of a low pass filter and the high pass filter.

The low-pass filter is described by the formula:

\[ y(n) = 2y(n-1) - y(n-2) + x(n) - 2x(n-6) + x(n-12) \]

And the high pass filter is described by the formula:

\[ y(n) = y(n-1) - \frac{y(n-2)+x(n)-2x(n-6)+x(n-12)}{32} \]

The low pass filter removes the supply frequency interference (50 Hz), the baseline wander which is a low frequency and the T-wave interference. The T-wave is due to atrial repolarization that overlaps the QRS wave. The high pass filter used to remove the muscle noise interference.

The derivative filter is used to detect the QRS peak. Since this part of the ECG signal has the highest slope, the detection is possible through derivative filter. This
is followed by a square filter that converts the negative spectral amplitudes to positive and also enhances the high frequency component.

\[ y(n) = \frac{2x(n) + x(n - 1) + x(n - 3) + 2x(n - 4)}{8} \]

Moving window integration is used to incorporate the changes in the signal as the samples of the signal move ahead. The window size is directly related to the sampling rate. The sampling rate of the signal is 500 samples /second and the window size 75. The algorithm is shown in figure-6.2.

\[ y(n) = \frac{x(n - (N - 1)) + x(n - (N - 2)) + x(n - (N - 3)) + x(n)}{N} \]

A temporal location of the QRS is marked from the rising edge of the integrated waveform. In the last step two thresholds are adjusted. The higher of the two thresholds identifies peaks of the signal. The lower threshold is used when no peak has been detected by the higher threshold in a certain time interval. In this case the algorithm has to search back in time for a lost peak. When a new peak is identified (as a local maximum – change of direction within a predefined time interval) then this peak is classified as a signal peak if it exceeds the high threshold (or the low threshold if we search back in time for a lost peak) or as a noise peak otherwise. In order to detect a QRS complex the integration waveform and the filtered signals are investigated and different values for the above thresholds are used. To be identified as a QRS complex, a peak must be recognized as a QRS in both integration and filtered waveform.

The changes in the waveform are shown step by step in figure 3.3 subfigures a-f denote the changes due to each signal transformation. The X axis in all the waveforms from 3.3-(a-f) shows the time scale. The Y-axis is represented by voltages from 3.3-(a-e). The 3.3-f wave form represents the digitized state from presence or absence of pulse. The R-R peak in figure-e is observed to be matching the peak of the integrator i.e.3.3-e.

The R-R interval difference is stored and read as input to the simulation software used for HRV analysis as explained in the next section as shown in Figure-3.2.
Figure 3.2 Pan Tompkins Algorithm adapted from [26]
3.4 Simulation software

Once the QRS is detected, a text file is created by the difference of successive R-R intervals. This is file that is stored as *.txt. An open source software simulation code Kubios simulator developed by PHYSIONET organization is used as HRV analysis tool. It reads from the RR interval sample and provides linear and nonlinear HRV analysis findings. [28]

As per the problem definition the parameters that can correlate with echocardiogram are to be found out from the HRV findings. For that study of echocardiogram and the findings from the echocardiogram is necessary.

The typical simulated report is shown in figure 3.4. The HRV indices in time domain, frequency domain and nonlinear analysis are shown in the report. Name of the input *.txt file, the duration of ECG data acquisition, the duration of the window if part of the file is selected is specified. The order of auto regressive analysis, factorization the detrending methods if used are specified. The nonlinear results are not shown in the figure because they are not used in the results analysis.
3.5 Study of Echocardiogram as a diagnostic modality
Since the early 1950s, ultrasound use in medicine has been the basis for several procedures that are widespread in today’s clinical practice. The principal application is in the field of medical imaging. Medical ultrasound imaging relies on the same principles as sonar or radar units. The ultrasound probe produces a (pulsed) acoustic pressure field. When the ultrasound signal is incident upon an elastic medium, the signal returns back without penetrating. This delay represents lowest intensity in grey scale. Depending upon the density of the target velocity of
the reflected signal is modified. The field propagates through the tissue and is partially reflected and scattered due to the inherent inhomogeneity of most tissues. The backscattered signal is received by the same probe and converted into a grey scale image of the organ. The probe of the ultrasound has a transmitter and a receiver in one assembly so that the organ mapping does not vary spatially. Since the ultrasound signals cannot pass from the bone, the probe is placed suitably to get suitable view. [5] and [32]

Medical ultrasound is a non ionizing radiation has several advantages over other popular imaging modalities as Magnetic Resonance Imaging (MRI), X-ray and Computed Tomography (CT). At first, unlike X-ray and CT, ultrasound is a non ionizing radiation and hence practically harmless to the human body. Computational complexity needed for the image creation is comparative less because ultrasound systems work at frame rate of 100 frames/sec. This makes ultrasound the standard tool for diagnosis of disease based on organs dynamics, as it is in echocardiography. Further advantages connected with ultrasound systems are their cost effectiveness and reduced size, making their availability possible even in small local low budget ambulatories. This is instead not the case for X-ray, CT and MRI, whose installation, besides relevant costs, requires extended dedicated areas. In Figure 3.5, a standard ultrasound imaging system is illustrated.

Figure 3.5: External parts of an ultrasound imaging system figure adapted from [32]
The finite bandwidth of the transducer and the non-negligible width of the acoustic beam, along with the characteristic granular texture referred to as speckle noise. All these factors result in low spatial resolution. This affects the interpretation of ultrasound frames highly ambiguous and subjective, even for expert physicians, thereby limiting their diagnostic reliability. The quality of image is reduced as compared to that of X-ray, CT or MRI. [32] and [5]

In figure 3.5 the shows a short axis slice of the left ventricle is represented from 2 Dimensional echocardiography and cardiac MRI it is evident how ultrasound image interpretation is difficult. [5] Improving the quality and diagnostic reliability of medical ultrasound has always represented a continuous challenge for many scientists working in the field. The efforts are mainly spent in two directions:
1) Improving the acquisition modality itself, by designing new transducers, more sophisticated beam-forming, etc.
2) At a post processing step with suitable signal and image processing tools.

![Figure 3.6: Images from MRI and 2-D echocardiography imaging system figure adapted from [32]](image)

The research literature on the above mentioned approaches is available. The proposed doctoral research suggests a novel approach to the above mentioned challenge.

HRV analysis can be effective tool that guides the echo cardiologist to conduct the diagnostic study. Also it proves to be sufficiently high potential research domain. The echo cardiologist’s time and effort can be saved and HRV can be an early diagnostic tool guiding the echo cardiologist as to what area of the investigation needs to be focused thoroughly.
HRV is the only diagnostic tool that detects the functional deterioration of the heart at preclinical stage. The same can be verified for whether the changes are visible in the 2-D Echocardiogram. Since echo cardiogram gets the information about the functional, structural and haemo-dynamic performance of the heart, the test is gives a more clear cardiac assessment. Establishing the correlation indices, the cardiac assessment will be more effective and specific.

3.6 Data acquisition from echocardiogram.

Detail of data acquisition methodology for echocardiogram.

The echocardiogram gives the structural, functional, mechanical and hemodynamic information of heart. The prevalence of diabetes deteriorates the functioning of the heart. In the earlier prevalence of diabetes, slow deterioration is expected to be surfaced showing increased heart rate, decreased heart rate variability, reduced orthostatic stress index. In the echocardiogram studies it is expected to find correlation with reduced ejection fraction. [3]

Continuous reduced performance of heart may cause reduced blood supply to heart wall which results into reduced wall velocity and clinically symptoms of fatigue, breathlessness difficulty to perform strenuous task etc. can be visible. [3]

The report of echocardiogram states the numerical value of left ventricle ejection fraction in percentage. The ratio value of the same can be compared from orthostatic stress index.

The changes in the volume of left ventricle during systole and diastole give information about the ability of left ventricle to expand and contract. Also the time gap information relates to the ability of the left ventricular contraction and expansion as response to the electrical repolarization and depolarization of the left ventricle due to changes in the ECG signal. [32]

The echocardiogram image shown in figure 3.7 shows the 2- chamber epical window view in the upper part of the image. The M-mode echocardiography at the section mentioned shows the wall thickness at ventricular systole and diastole. The X-axis mentions the time scale. The thickness in mentioned for posterior wall, ventricular cavity and Intraventricular septum wall. [73] The velocity for posterior and Intraventricular walls is given by the formula –
Posterior wall velocity = \( \frac{PWT_{sys} - PWT_{dia}}{PWT_{sys} * \Delta t} \)

Where, \( PWT_{sys} \) is posterior wall thickness at systole, \( PWT_{dia} \) is posterior wall thickness at diastole. \( \Delta t \) is time elapsed between systole and diastole.

Figure 3.7 Echocardiogram showing 4-chamber view in M-mode. Figure from research database.

Intra ventricular wall velocity = \( \frac{IVT_{sys} - IVT_{dia}}{IVT_{sys} * \Delta t} \)

Where, \( IVT_{sys} \) is Intraventricular wall thickness at systole and \( IVT_{dia} \) is intra-ventricular wall thickness at diastole and \( \Delta t \) is time elapsed between systole and diastole.

The contractility of left ventricle can be measured by the formula,

Contractility of left ventricle = rate of change of left ventricular volume during diastole and systole.

\[ \text{Contractility of left ventricle} = \frac{LVID_{sys} - LVID_{dia}}{LVID_{sys}} \]