Chapter 1
Introduction to Non-Invasive Biomedical Signals for Healthcare

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Abstract With the advancement of medical science, new healthcare methods have been introduced. Biomedical signals have provided us with a deep insight into the working of the human body. Invasive biomedical signaling and sensing involve inserting sensors inside the human body. Non-invasive biomedical signals such as electroencephalogram (EEG), electromyogram (EMG), electrocardiogram (ECG), electrooculogram (EOG), phonocardiogram (PCG), and photoplethysmography (PPG) can be acquired by placing sensors on the surface of the human body. After the acquisition of these biomedical signals, further processing such as artifact removal and feature extraction is required to extract vital information about the subject's health and well-being. In addition to conventional signal processing and analysis tools, advanced methods that involve machine and deep learning techniques were introduced to extract useful information from these signals. There are several applications of non-invasive biomedical signal processing, including monitoring, detecting, and estimating physiological and pathological states for diagnosis and therapy. For example, detection and monitoring of different types of cancer, heart diseases, blood vessel blockage, neurological disorders, etc. In addition, biomedical signals are also used in brain control interfaces (BCI), Neurofeedback and biofeedback systems to improve the mental and physical health of the subjects.

1.1 Introduction to Biomedical Signals

With the advancement in technology in recent years, the biomedical industry has radically grown. Real-time health monitoring is now possible using smart sensing technologies. Biomedical signals are the records of physiological events including

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neural activities, cardiac rhythms, and tissue imaging [1]. Biomedical signals can be divided into two categories depending upon the source of energy for measurement, active and passive biomedical signals. In active biomedical signals, the source of energy for measurement is driven by the subject himself. There are further two types of signals in the active category i.e., electrical such as EEG, ECG, etc., and non-electrical signals such as blood pressure, temperature, etc. In passive biomedical signals, the source of energy for measurement is from outside the subject such as X-Ray, MRI, etc. Biomedical signals can also be divided into sub-categories depending upon the nature of the signals such as electrical, mechanical, and chemical biomedical signals. Electrical biomedical signals originate from neural cells such as EEG, from muscles such as EMG and ECG, and other sources such as EOG. Like electrical biomedical signals, strong magnetic field from outside the subject's body can also be used to scan different organs of the subject. These scans are known as MRI scans. These include motion and displacement signals, pressure and tension, blood flow signals, etc. Another category of biomedical signals is the chemical signals which measure the chemical change in the subject's body such as PPG, level of glucose, blood oxygen levels, etc. Mechanical biomedical signals such as blood pressure and phonocardiogram can also be measured. Furthermore, there are acoustic biomedical signals as well such as PCG and respiratory sounds. Optical biomedical signals include endoscopy while there are thermal biomedical signals as well such as the heatmap of the subject.

In this chapter, the focus will be on electrical and magnetic biomedical signals which are recorded by the sensors placed outside the subject's body. These biomedical signals are then used for the diagnosis and monitoring and progression of various diseases. The improvements in signal processing methods and electronics have encouraged the use of biomedical signals for prognosis and diagnosis.

Sensors of different types are used to measure and record biomedical signals. Some sensors are implanted or inserted inside the subject to record these signals e.g., implanted EEG and endoscopy. While some sensors record these signals from outside the subject's body e.g., MRI, and X-Ray. The recorded signals are used for the improving people's health. Engineers have developed many devices that process these signals and present the results in an easy-to-understand way. Heart rate monitoring devices have enabled us to examine irregularities in the beating rhythms of the heart [2]. Body glucose monitoring devices help diabetic patients to monitor and manage their blood sugar levels without any help and supervision from healthcare providers. Emotiv MN8 is a wearable device that monitors brain activities to measure stress and attention.

In this chapter, a brief introduction to important biomedical signals followed by their acquisition techniques will be provided. Afterwards, processing and analyzing these signals will be discussed followed by the application of these signals for rehabilitation such as brain-computer interface (BCI) and neurofeedback & biofeedback systems. Finally, a brief conclusion of this chapter will be provided.

1.2 Invasive and Non-Invasive Procedures

Biomedical signals can be divided into two types depending upon the nature and procedure of signal acquisition. In the invasive method of obtaining biomedical signals, sensors are inserted inside the human body. In other words, invasive tests are performed by penetrating the body using medical tools [3]. On the other hand, the non-invasive technique of acquiring biomedical signals does not involve any skin breaking. These tests are performed by placing sensors on the surface of the human body from outside the skin [4].

Non-invasive methods are much simpler and have low risk. No surgery is required for the placement of sensors. Once the sensors are placed, the collected data is processed to get the required information. These techniques are cheaper and user-friendly and involve low risk which makes them more acceptable to the subject instead of invasive techniques. One of the main advantages of using a non-invasive method over an invasive method is that, for an invasive method, a professional specialist is required to perform the procedure. While in the case of non-invasive techniques, scientists have developed many user-friendly devices which can be worn by the subject themselves with minimal supervision and the data can be easily recorded [5].

Both invasive and non-invasive techniques have some advantages and disadvantages. One of the main disadvantages of non-invasive methods is their low signal-to-noise ratio (SNR). To overcome this problem, the data is recorded under specific conditions to avoid noise and enhanced noise removal procedures are applied before using the data for analysis. Non-invasive methods generally yield less information rather than invasive techniques. Invasive sensors can be of different types such as single electrodes or multi-electrode arrays (MEA) [6]. Depending upon the type of the sensor, more precise information can be collected. For example, if the brain signals are recorded by inserting sensors inside the brain, the resulting information will be much more reliable, precise, and detailed rather than trying to collect the same data from outside the scalp of the subject. At the same time, invasive techniques are more laborious and have a higher risk factor.

Invasive methods require trained professionals to insert sensors inside the body by operations or by inserting the sensor into a body opening. For example, for bone conduction hearing devices, surgery is performed to implant a device inside the skin of the subject and for endoscopy, a long tube with a camera is inserted to examine the inside of the subject's body. Similarly, EEG can be collected invasively where EEG electrodes are surgically implanted on the surface or inside the brain. On the other hand, the non-invasive method includes X-rays, MRI, ECG, EEG, etc. In terms of biomedical signaling, EEG is one of the examples, in which the signals can be recorded in both invasive and non-invasive ways. The invasive EEG will have high spatial resolution and fewer artifacts with more risk while non-invasive EEG will have high temporal resolution with more artifacts and less risk.

1.3 Non-Invasive Biomedical Signals

1.3.1 Electroencephalography (EEG)

EEG is an electrophysiological signal that records brain activity in terms of electrical potentials. It is a non-invasive technique to record the potential differences formed by the ionic currents between the brain neurons [7]. In 1875, Richard Canton performed the first neurophysiological recordings of animals. In 1924, Hans Berger a German psychiatrist recorded the first EEG of human subjects.

To record the EEG signals, the sensors, also known as EEG electrodes, are placed over the scalp of the subject at specific locations. Reference electrodes are required to record EEG data. EEG data for the required site is then collected as a potential difference between the two electrodes. These reference electrodes are generally placed beside the ear of the subject. EEG activity is quite small, measured in microvolts. The location of EEG electrodes is governed by international standards such as 10–5, 10–10, and 10–20 systems among which the international 10–20 system of electrode placement is most used as shown in Fig. 1.1. This system of electrode placement is designed in such a way that the distance between the electrodes is either 10% or 20% of the total front-to-back or left-to-right distance of the skull [8].

The human brain is divided into four different lobes based on its location and tasks that it performs. The frontal lobe is responsible for concentration, attention, working memory, and executive planning. The temporal lobe is responsible for language and memory, object recognition, music, and facial recognition. The parietal lobe is responsible for problem-solving, attention, and association. The occipital lobe controls visual learning and reading [9].

EEG is a complex time-series non-stationary signal which represents the electrical activity of the brain. The EEG signal varies from 0.1 to more than 100 Hz and can be decomposed into different frequency bands such as delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–100 Hz). Each frequency band represents some specific physiological functions. Delta frequency band represents sleep, unawareness, deep unconsciousness, and complex

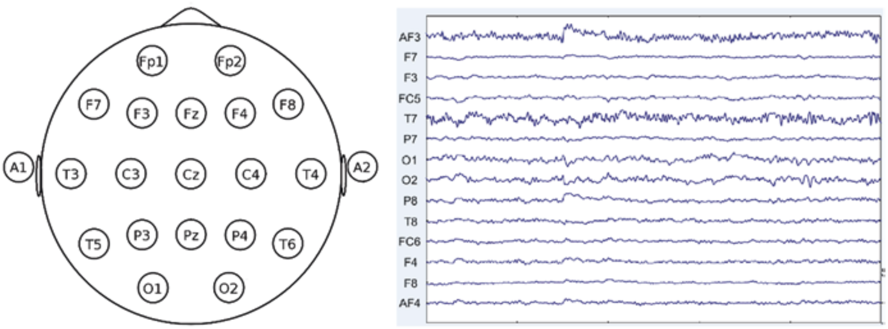


Fig. 1.1 International 10–20 system of EEG electrodes placement and 14 channel EEG data

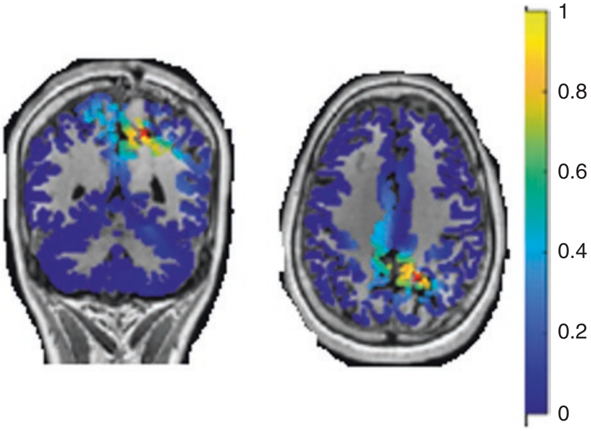
problem-solving abilities of the brain. Theta frequency band represents the deep states, creativity, distractibility, anxiety, and depression. Alpha frequency band represents memory recall, alertness, peacefulness, relaxation, and meditation. The beta frequency band represents the thinking, alertness, attention, focus, and excitement of the subject. The Gamma frequency band represents the learning, problem-solving cognitive capabilities, and mental sharpness of the subject [9].

EEG electrodes are very sensitive and are prone to noise and have low SNR. Due to this, the EEG recordings are taken very carefully in silent rooms. Many artifacts still manage to appear into the recordings. Filtering and artifact removal techniques are utilized to remove such noises from the data. This extra procedure makes the EEG system complex and computationally expensive. The main advantage of EEG is its high temporal resolution, and the most important limitation of non-invasive EEG is its poor spatial resolution. The EEG is recorded non-invasively, by using electrodes placed over the scalp, however, the actual brain activity occurs several centimeters below the electrodes. This means that the cortical current must travel through different resistances including the scalp itself to be detected by the electrode. This causes distortions and noise at the scalp level. Therefore, for non-invasive EEG acquisition, source localization is one of the primary steps in which the actual source of EEG in the brain is identified based on the surface EEG recording.

Event-related potentials (ERPs), also known as event-related voltage or evoked potentials coming from EEG data are time-locked to sensory, motor, and cognitive events. ERPs can be used to classify and identify perceptual, memory, and linguistic processes. ERPs originate from synchronous activations of the neuronal population during some specific task or information processing. The ERPs are usually observed by averaging EEG signals. Averaging makes the ERPs less effective to background noise in the EEG data and thus it can extract vital information about the event-related activity which is otherwise difficult to differentiate in the ongoing EEG activity.

The human brain can develop different neurological and physiological diseases. Different techniques can be used to modulate EEG signals to enhance cognitive performance of subjects. Music can be used to regulate EEG signals to achieve calmness and relieve stress [10]. On the other hand, EEG can be used for the diagnoses of neurological diseases such as epilepsy, Parkinson's disease, multiple sclerosis, and Alzheimer's disease. The most common use of EEG is to diagnose epilepsy [11] in which brain activities become abnormal. This can cause seizures and loss of awareness for some time. On the other hand, EEG is also used for diagnoses and cure of many physiological disorders such as depression, post-traumatic stress disorder (PTSD), attention deficit hyperactivity disorder (ADHD), and autism. Different applications of EEG include but are not limited to diagnosing and checking the status of brain injury, brain infections, tumors, etc. EEG can also be used to identify the reason for symptoms such as syncope, memory loss, confusion, or seizures. EEG is also used to diagnose sleep disorders in which the EEG recordings must be taken while the subject is sleeping to analyze any disorders.

Fig. 1.2 Sample MEG scan



1.3.2 Magnetoencephalography (MEG)

MEG is a brain imaging technique that measures tiny magnetic fields inside the subject's brain. Superconducting detectors and amplifiers (SQUIDs) are highly sensitive devices that are used to detect magnetic fields of the brain without the emission of magnetic field or radiation. It generates a magnetic source image (MSI) to classify the specific part of the brain that is causing seizures.

Some of the advantages of MEG are its non-invasive nature, sensitivity and accuracy, and safety. MEG can also record the brain activities when it is actively functional. MEG can be used to either detect the brain's impulsive activity like a seizure or for mapping motor, sensory areas, memory, vision, and other functions of the brain. Due to the high sensitivity of the devices, the imaging is done in a specially designed shielded room with a video and intercom system to communicate with the subject and technicians. Electrodes are placed over the scalp of the subject while the head of the subject will remain in the helmet like MEG scanner. Movement of the head during the test may cause noise or artifacts in the recorded image so it is important to remain still during the test. While the technician may ask the subject to move certain body parts to measure the response in the brain. The sample MEG scan can be seen in Fig. 1.2.

MEG scan can be used by doctors to identify the source of seizures in the brain and determine if the subject requires seizure surgery or not. Generally, MEG is accompanied by EEG and magnetic resonance imaging (MRI) which creates an anatomical image of the brain.

1.3.3 Electromyography (EMG)

EMG is used to diagnose the health of muscles and motor neurons that controls the contraction of those muscles [12]. Muscles contract when the motor neurons from the brain send electrical signals to them. The EMG activity is directly proportional

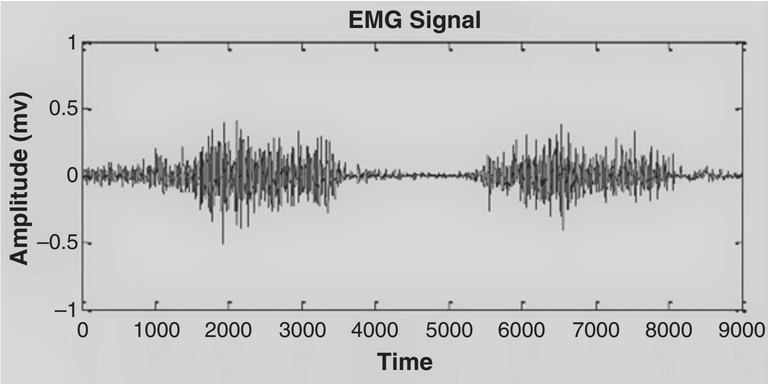


Fig. 1.3 Sample EMG signal

to the number of contracted muscles as well as the strength of the contracted muscle. Generally, the range of the electrical signals captured by the electrodes is in microvolts. Non-invasive sticky electrodes are placed near the muscles over the skin to record their electrical activity. EMG is a process of translating these electrical activities into graphs.

The non-invasive nature of EMG allows us to monitor physiological processes without affecting movement patterns. To prepare the skin for high-quality EMG recordings, the area must be cleaned, and any residual makeup or dirt must be removed. To get valid and reliable EMG data, EMG electrodes are placed over the muscle group of interest. This requires a certain level of anatomic knowledge. To collect the EMG data, a reference electrode is required. EMG data for the required site is then collected as a potential difference between the two electrodes. The recommended reference sites are elbow, hip, and collar bones. Figure 1.3 shows an example of an EMG signal. The noise can be induced in EMG recordings from the surrounding power sources. To minimize such noises, the distance between the EMG sensors and the amplifier is kept minimum [13].

EMG is used to diagnose several muscle and nerve disorders. It is used to test if the muscle correctly responds to the nerve signal or not. Some of the common problems diagnosed by the EMG test are muscle weakness, muscle cramps, numbness in arms, legs, hands, feet, or face, and muscle paralysis [14]. Facial EMG (fEMG) is used for the detection of facial emotions.

1.3.4 Electrocardiography (ECG)

ECG is a test that is performed to check the electrical activity and rhythm of the heart. A heart specialist might recommend taking an ECG test to check any unusual activity in the heartbeats of the subject. Sticky sensors are placed over the skin of the subject which detect the electrical activity produced by the contraction and expansion of the heart muscles [15]. The detected electrical activities are then recorded, and a graph is plotted. The doctor or the heart specialist then looks at these graphs to find any unusual behavior of the heart.

ECG can be carried out in many ways. Generally, several sticky ECG electrodes are placed on the arms, legs, and chest of the subject. These electrodes are connected by the ECG machine via wires. Figure 1.4 (a) displays a sample ECG signal. The duration of the test is normally around 5 min after which the subject is free to go. There are three types of ECG tests. A resting-state ECG in which the subject must be lying down while the electrodes record the ECG signals. In stress ECG, the subject is required to do some exercise such as running on a treadmill. In an ambulatory ECG test, a small portable and wearable machine is used to monitor the ECG for a longer period such as a day or more [16]. The selection of the ECG test type is based on the suspected heart problem and is recommended by the heart specialist. For example, if the heart problem symptoms appear during a workout or some physical activity, a stress ECG test might be conducted while if the symptoms are unpredicted or random, an ambulatory ECG test will be more suitable [17]. In the case of ambulatory ECG tests, the machine records and stores the collected data which can be later accessed by the specialist once the test is complete.

ECG devices record the electrical activities of the heart. These electrical activities are generated due to the contractions of the beating heart. The ECG machine records and prints or displays the electrical activity and rhythm of the subject on a graph. The spikes in the ECG graph represent one complete heartbeat. Each heartbeat is composed of several spikes in which the first peak is a P wave which represents contracting atria, the largest one known as the R or QRS complex, occurs due to the contracting of ventricles. Before and after the QRS complex, inverted peaks can be seen which are known as Q and S waves respectfully. The last spike is the T wave which occurs because of the relaxation of ventricles again as shown in Fig. 1.4 (b). There should be regularity in the spikes of ECG data. The distance between these spikes represents heart rate. Irregularities in these spikes can be a sign of a problem. Abnormalities in these rhythms indicate some heart disorders such as arrhythmia often known as heart attack which causes damage to the heart due to the lack of oxygen to the heart muscles. Similarly, the distance between the spikes should not be too short, or too long. If the spikes are too close, it can be a sign of tachycardia. Other tests might be required to confirm any heart problem.

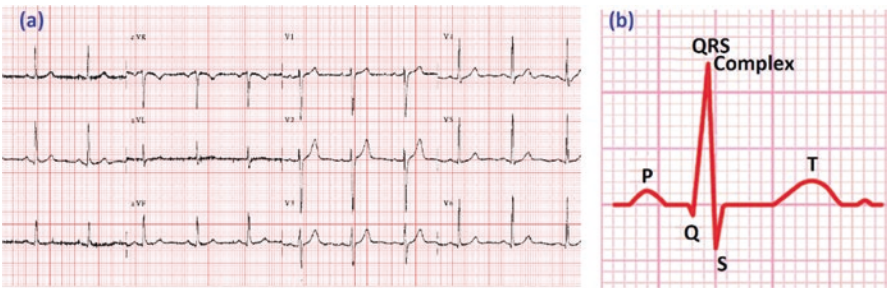


Fig. 1.4 (**a**) Sample ECG signal (**b**) Components of ECG signal

Due to the non-invasive nature of the ECG test, there is very little risk in performing the ECG. During the stress ECG, the subject is required to be monitored all the time and if the subject feels unwell, the test is immediately stopped. The removal of sticky electrodes might cause some discomfort, and, in some cases, a mild rash can be felt after the removal of the electrodes.

ECG is often performed along with other tests to diagnose potential heart problems such as chest pain, palpitations, dizziness, and shortness of breath. If the subject feels irregularities in the heartbeat or the heart beats too slowly or quickly, it is possibly due to arrhythmias. Coronary heart disease can occur if there is any blockage in the blood supply of the heart. This can happen due to the build-up of fats in the blood vessel connected with the heart. If the supply of blood is suddenly stopped, it might cause a heart attack. Thickened walls of the heart might cause cardiomyopathy.

1.3.5 Electrooculography (EOG)

EOG measures the resting potential between the front and the back of the human eye. Due to the neurons and ion channel, the back of the retina creates a negative pole. The EOG measures this potential difference by placing pair of electrodes near the eye (up and down or right and left) [18]. The electrodes are divided into two groups: horizontal and vertical electrodes. The horizontal electrodes are placed near the outer edges of the eyes. The vertical electrodes are placed above and below the eyes. A ground electrode is placed on the forehead as shown in Fig. 1.5 (a). This arrangement of EOG electrode placement allows us to examine the full movement of the eye. The movement of the human eye will change the effective distance between the poles and the electrodes. One electrode will become nearer to the negative side of the retina while the other will become nearer to the positive side. This change can be sensed by the electrodes as an electrical activity and hence can be recorded and plotted.

The potential difference changes with the change in the exposure to light. EOG is used to evaluate the efficiency of the pigment epithelium. In this test, a subject

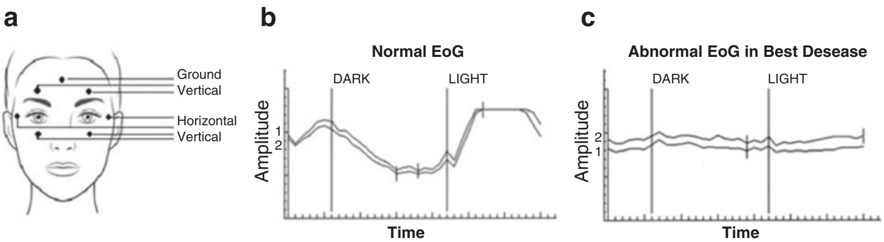


Fig. 1.5 (**a**) EOG electrode position, (**b**)Normal EOG signal, (**c**) Abnormal EOG signal with Best disease

with EOG electrodes is requested to sit (resting state) in a dark room with his/her eyes open. In this phase, the subjects adapt to the darkness in such a way that their EOG voltage decreases at the start and reaches a minimum value after some time. Then the lights in the room are turned on and the subject remains sitting there for another several minutes. In this phase, the EOG voltage will increase and eventually reaches a maximum point. Once the subject adapts to the lighting condition, the voltage will decrease again. The comparison of voltages in the dark and light phases is known as Arden Ratio (AR). Generally, the AR should be around 2.0, if the AR decreases to 1.8 or less, there are chances that the subject has the best disease, which is an inherited retinal disease causing macular degeneration and may cause loss of central vision, as well as the ability to perceive colors and details [19]. Figure 1.5 (b) shows a normal EOG signal while Fig. 1.5 (c) displays an abnormal EOG signal with the best disease where AR is less than 1 [20].

Due to its non-invasive nature, portability, cheap price, and low risk of EOG, its applications are limitless [21]. The application of EOG in the diagnoses of diseases related to human eyes is just one example. Other applications of EOG include Human-Computer Interface (HCI). Many EOG-controlled assistive devices are available such as controlling wheelchair-using eye movement, video games controlled by eyes, etc.

1.3.6 Phonocardiogram (PCG)

PCG measures and plots the sounds and murmurs generated by the heart of the subject using a machine known as a phonocardiograph. The machine has a sensor that is placed over the chest of the subject to detect the sound and murmurs coming from the heart. These sounds are recorded, plotted on the screen, and can be listened to directly using a headphone. Figure 1.6 displays an example of PCG recording. The high resolution of phonocardiography makes this procedure very useful. These sounds and plots are then listened to or viewed by the specialist to diagnose any heart disease [22].

From ancient times, it is known that the heart makes a sound while beating. Robert Hooke proposed the idea of developing an instrument to record these sounds back in the seventeenth century. In the 1930s and 1940s, phonocardiography monitoring and recording equipment were developed. In the 1950s, the PCG was standardized in the first conference held in Paris [23]. NASA used the PCG system made by Beckman Instruments to monitor the heartbeat of astronauts in space.

The vibrations made by the opening and closure of the beating heart valves, and the movement of heart walls generates sounds. PCG records two sounds in each heartbeat. The first sound appears at the closure of atrioventricular valves during systole while the second sound appears at the end of systole when aortic and pulmonary valves close. PCG is used for recording subaudible echoes and murmurs of the heart. On the other hand, a stethoscope is unable to detect such minor sounds. Hence a stethoscope cannot be used for a more precise diagnosis of heart disease.

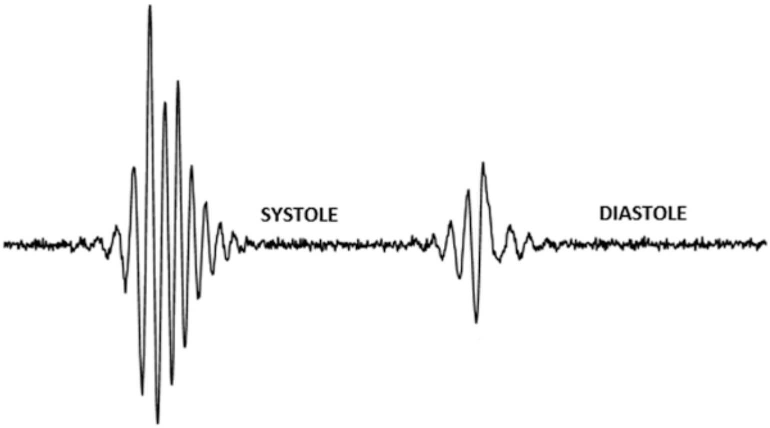


Fig. 1.6 Sample PCG Signal

Some of the common uses of PCG are the detection of the rheumatic valvular lesion in which the valves of the heart are possibly damaged or not functioning well. The murmur of the aortic stenosis can also be detected using PCG in which the high pressure of blood through small openings of the aortic valve causes turbulence and hence cause intense vibrations. The non-invasive nature of PCG is very beneficial to diagnose several diseases related to the heart with a very low factor of risk. The murmur of mitral and aortic regurgitation in which the blood flows backward from the mitral and aortic valves during systole and diastole can also be detected by using PCG. Similarly, it is also used to detect the murmur of mitral stenosis in which the pressure difference causes difficulty while the blood passes from the left atrium to the left ventricle [24].

1.3.7 Photoplethysmography (PPG)

PPG is a simple, non-invasive, and low-cost procedure, commonly used for monitoring heart rate. In PPG, a light source generally in the infrared range is used with a photodetector over the skin of the subject to measure the volumetric alterations of blood flows. The light is emitted on the tissue by the light source which is reflected and measured by the photodetector. This measurement is proportional to the volumetric variation of blood circulation. Recently, wearable PPG devices have been introduced. Depending upon the type of the device, these can be worn on different parts of the body such as the forehead, earlobe, forearm, fingertip, and ankle [25].

Several factors may affect the response of PPG such as the geometry of the sensors being used, the intensity of the light source, ambient light, and photodiode sensing power. Other than that, the oxygen concentration and organ characteristics can also change the PPG recordings. Similarly, some cardiovascular factors may also alter the PPG readings. This is the reason that different PPG devices are designed to use in different parts of the body. The basic working of PPG is shown in Fig. 1.7 (a). One of the main advantages of PPG over traditional heart monitoring devices such as ECG is its cheap cost and simplicity. Instead of using multiple electrodes on the chest and other body parts in the case of ECG, a single PPG sensor is required to monitor heart rate.

A PPG signal has two parts, a pulsatile or AC component which is due to the heartbeats and causes synchronous variations in blood volume. The other part is the DC component which is superimposed on the AC component. The DC component of PPG is due to respiration and thermoregulation [26]. A sample PPG signal is shown in Fig. 1.7 (b).

Portable and wearable PPG devices have the potential for early detection of cardiovascular diseases. PPG devices are widely used in various clinical applications. Some of the common applications of PPG are monitoring blood pressure and oxygen saturation, heart rate, respiration, vascular assessment, arterial diseases or compliance and aging, microvascular blood flow, thermoregulation, and orthostasis [27, 28].

1.3.8 Magnetic Resonance Imaging (MRI)

MRI generates a three-dimensional anatomical image of the required organ of the subject. The non-invasive and high-resolution MRI allows the specialists to examine the organs, tissues, and skeleton system of the subject and diagnose several diseases. The working principle of MRI is that it detects the change in direction of the rotational axis of protons found in the living tissues using powerful magnets and radiofrequency [29]. Physicians can differentiate different types of tissues from the magnetic features of the MRI image. Figure 1.8 shows an MRI machine and an MRI image of a muscle.

To get an MRI image, the subject is placed inside a large tube-like magnet. The magnetic field aligns the water molecules inside the body for a fraction of time while radio waves are used to create a cross-sectional image of these aligned

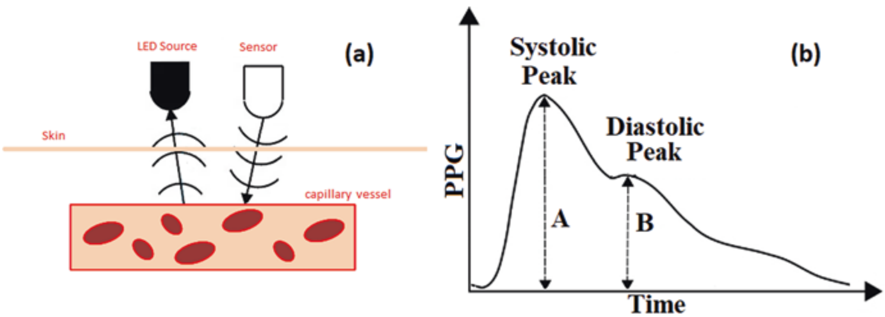


Fig. 1.7 (**a**) PPG sensor working principle (**b**) Sample PPG signal

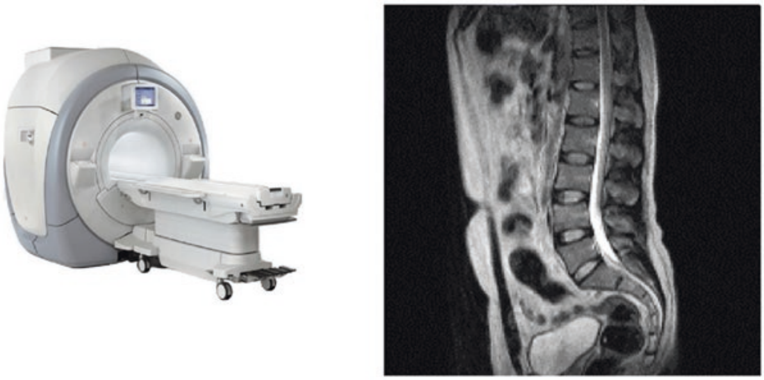


Fig. 1.8 MRI Machine and Sample MRI image of a muscle

molecules. Sometimes, gadolinium is injected as a contrast material into the vein in the hand of the subject to enhance a variety of details. To ensure the best quality of the image, the subject must not move otherwise the MRI image might get blurred.

MRI of different body parts can be taken to diagnose different disorders. MRI of the brain might be required for the detection of stroke, tumors, or disorders in the spinal cord. In the 1990s, functional MRI (fMRI) was invented which is a non-invasive brain imaging technology. fMRI can detect brain activities by measuring changes in the blood flow within a specific part of the brain. This can be used to analyze the function of different brain regions. fMRI can detect which parts of the brain are activated during specific tasks such as lifting the leg and even just thinking about something. fMRI is being used by researchers to diagnose, better understand, monitor, and treat several diseases such as post-concussion syndrome, schizophrenia, tumors, etc.

MRI of the heart can be used to examine the working of the heart, functionality of heart chambers, and magnitude of damage after heart disease or blockages in the blood vessels of the heart. Similarly, MRI of internal organs such as kidneys, uterus, liver, etc. can be used for the detection and examination of tumors or abnormalities in them. It can also be used for the detection of breast cancer.

An MRI machine contains very strong magnets, the metal in the body of the subject might be dangerous. Metals that are not attracted to the magnets can still modify the MRI image. So, it is required to remove any metal item before taking the test [30]. Other than that, a doctor might avoid taking MRI if the subject has some kidney or liver problem and/or the subject is pregnant or breastfeeding [31].

1.4 Biomedical Signal Processing

Biomedical signal processing deals with extracting significant and useful information from the biomedical signals for medical purposes [32]. As the non-invasive techniques of the biomedical signal acquisition have a low peak signal-to-noise ratio (PSNR), advanced signal processing methods are developed and used to extract the required user information. A full-time check on patients' heartbeat, blood pressure sugar levels, and neural activity can extensively improve medical diagnosis. This monitoring is not only used to know the status of the patient's body but also to diagnose diseases in the body. With the help of biomedical signal processing, biologists can develop methods for the detection, monitoring, and cure of diseases. Proper processing and analysis of biomedical signals can provide numerous advantages in the field of medicine. The four steps involved in the processing of signals are:

1.4.1 Signal Acquisition

The first step is a signal acquisition which deals with capturing a signal from the subject. A hardware device is used to capture biomedical signals from the subject body. Analog signals are recorded and transformed into digital signals.

1.4.2 Signal Visualization and Annotation

Visualizing the recorded biomedical signals gives significant information which can effectively boost the analyzing procedures. Currently, periodograms and spectrograms are used for visualization and analyses [33]. A periodogram determines the frequency spectrum of a biomedical signal and is the most used tool for visualization. A spectrogram is a visual representation of signal strength over time at various frequencies. A spectrogram is a 2-dimensional graph where the color represents the signal strength. Modern tools e.g., MATLAB, LABVIEW provide built-in apps to visualize and analyze the data in time as well as a frequency domain.

1.4.3 Artifacts Removal and Preprocessing

Artifact Removal is a preprocessing step that involves removing any artifact, error, or noise from the recorded data before processing and analysis of biomedical signals. Different biomedical signals have different types of noise. For example, power line noise can be found in PCR and EEG data. In ECG data, baseline wanders artifact can be found which is a low-frequency data superimposed on the recorded ECG signal. Similarly in MRI data, motion artifacts and external magnetic field artifacts are very common. In addition, the noise can be found in the recorded biomedical signals due to faulty or improper use of the acquisition instrument such as dislocation of electrodes/sensors. Noise in the recorded signals might also be found in the acquisition that does not follow the standard procedures while recording the data such as recording from unclean skin, unwanted movements of body parts while recording, interference of electrodes, and impedance from power sources. Non-invasive biomedical signal acquisition techniques often yield low PSNR. These artifacts or noise can interfere with the diagnostic system and may result in improper classification or detection of diseases. Different artifact removal methods are available based on the type of artifacts in the signals [34]. Some artifacts or noise such as powerline interference and DC component in the recording can be removed by using the filtration method. To remove more complicated artifacts or noise, many filtration and machine learning models are available. After that, various preprocessing steps are implemented which include dealing with missing values, data normalization, outlier removal, etc. before using the recorded biomedical signal.

1.4.4 Feature Extraction

Feature extraction is a process in which raw data is used to extract useful information that can be processed by machine learning or deep learning models. The model uses these features to classify the data. Raw data is not useful until feature extraction is done. Features can be extracted manually as well as automatically. Feature extraction is generally based upon the required classification. For instance, Nawaz et al. [35] provided a comparison between different methods for feature extraction for the classification of emotions using EEG data. For manual feature extraction, Fast Fourier transform (FFT) is widely used in biomedical signal processing [36]. The FFT involves the conversion of a time domain signal into a frequency domain signal. FFT can achieve high efficiency because a smaller number of calculations are required to evaluate a waveform. For automatic feature extraction, the wavelet scattering method is used which creates the representation of a signal into a function called waves. A wavelet can acquire both local as well as temporal spectra. Two types of wavelet transformation, discrete and continuous wavelet transforms are often considered while extracting features automatically [37]. Discrete wavelets transform gives back data of equal length as that of input while the continuous transform returns an array with high dimensions data as compared to the input. Other than these methods, statistical feature extraction also plays an important role in the signal analysis [38]. Some commonly used statistical features are mean, variance, skewness, and kurtosis.

In Fig. 1.9, we can see all the steps and observe that after feature extraction we can use these features for multiple purposes. Medical diagnoses are made very easy with visualization and manipulation of features using digital tools. Machine learning is used to identify various patterns in the signal which can lead to major discoveries.

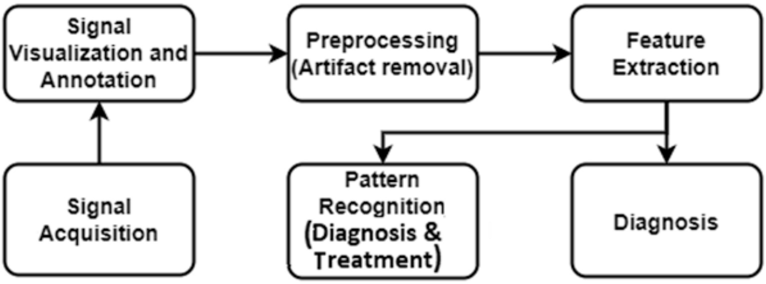


Fig. 1.9 Flow of biomedical signal processing

1.5 Machine Learning in Biomedical Signal Analysis

After the first mathematical modeling of neural networks in, machine learning was invented. In 1943, Warren McCulloch published a paper in which he mathematically mapped decision-making and thought processes in human cognition [39]. Alan Turing proposed a "Turing Test" in 1950 which can classify any system to be intelligent or unintelligent [40]. The idea behind this test is that a machine can be considered intelligent if it can convince humans that the machine is also a human. After this point, many machine learning models and processes started to appear, and a new era of smart and intelligent machines was started.

Machine Learning (ML) enables software and applications became more efficient in predicting outcomes and results using trained data. The concepts of machine learning are used in various fields like health care, finance, marketing, new developments in cyber security, and other significant fields [41]. Machine learning has proven its application in various domains, and it is also widely used in biomedical signal processing and healthcare. It can be beneficial in extracting, analyzing, and visualizing various signals as well as for the detection and classification of biomedical signals such as ECG, EMG, EEG, etc. [42]. Deep neural networks (DNN) have enabled us to achieve more accurate and robust results of detection and classification of biomedical signals. Applications of DNN in biomedical signal processing includes classification of ECG signals [43], brain tumor classification [44], missing data prediction in ECG signals [45], and many more. Convolutional Neural networks (CNN) have also played an important role in this filed such as drowsiness detection [46], detection of congestive heart failure [47], classification of EEG data listening to different kinds of music [48], EEG signal classification for emotion recognition [49] etc.

With the advancement in medical science and the increase in environmental pollution, many new diseases have been detected. Some mild intensity of diseases can be cured by simple over the counter medicines. But other diseases require proper diagnoses, clinical surgeries, and treatments. To correctly cure any disease, proper diagnoses must be carried out for which correct evaluation of symptoms and biomedical signals from the human body is required. Machine Learning may assist in making the right decision for the diagnosis and treatment of diseases. To develop automated symptoms and disease diagnostic systems, the contribution of machine learning is very important, e.g., for the segmentation of skin lesions, tumors, cancer cells, etc. Normal practice is the observation by radiologists or other specialists that puts a high burden on them in terms of time and cost and it also results in inter and intra-rater variability. Hence developing automated systems using machine learning can decrease the burden on radiologists and specialists.

After analysis, the next step is a prediction of the right treatment for the patients. This prediction could be challenging if developers have not designed an intelligent system. Machine learning allows the development of efficient and reliable systems for the prediction of diseases as well as medicines. For analysis and diagnosis of disease in the human body, different models of machine learning can be used. There are two main types of machine learning algorithms, supervised and non-supervised learning models. In supervised learning models such as support vector machine (SVM), naïve Bayes (NB), and K-nearest neighbor (KNN), the models are trained on a labeled dataset containing the ground truth. The dataset provided to the model contains data from diseased and healthy subjects. The model is trained in such a way that once it is trained, it can predict that either the subject has the disease or not. In medical science, the availability of labeled datasets is very limited as it requires a lot of time and effort by healthcare professionals and specialists. To overcome such problems, unsupervised ML models such as K-means, Gaussian mixture, and neural networks can be trained without the need for the labeled dataset. These models extract features from the non-labeled dataset and classify them based on those features extracted [50].

The impact of ML cannot be denied in health care and medicine because of its capability for disease detection, management, and treatment [51]. Disease diagnosis through machine learning techniques can reduce the risk of losing patients' life. Advanced algorithms are used nowadays for a prior diagnosis of epilepsy, heart attack, and other fatal diseases. It is now easy to handle big data through ML as many advancements and modifications have been made. The processing, analyzing, and characterizing of biomedical signals is now done efficiently using ML approaches. Biomedical signals such as MRI, (CT), (PET), whole slide images (WSIs), ECG, EEG, EMG, etc. are very important and significant for analyzing and determining the current condition of some diseases in the human body. The diagnosis of diseases in a traditional way in which health specialists visually inspect the biomedical signals can induce a risk of human error and ambiguities. ML methods remove these limitations providing low-risk systems. Signal feature extraction is one of the techniques in ML that provides systematic visualization of biomedical signals. Modern ML methods provide advantages in noise reduction, artifact removal, and early detection of diseases. ML can be used for the classification and clustering of biomedical signals and images. For small dataset, classical ML is used and optimized by following the conditions that suit microcontrollers that are inbuilt into biomedical signal processing devices. This requires the correct selection of ML algorithms that are done by experts in ML.

1.6 Brain-Computer Interface BCI)

Research and advancements in BCI began in the 1970s by Jacques Vidal at the University of California, Los Angeles (UCLA). He published his studies of controlling external objects using EEG signals in 1973 and stamped the name brain control interface [52]. Cogent Negative variation (CNV) was a major part of his publications. He calculated the evoked electrical activity of the cerebral cortex from the skull using EEG [53]. In 1988, Farwell and Donchin [54] added another achievement in establishing direct communication between a computer and the brain of an individual. After these initial establishments, a lot of progress was made by developers. In 1990, research was done on bidirectional adaptive BCI controlling computer buzzers. These studies and research opened the path for the concept of BCI technologies to restore brain functionality.

The brain-computer interface, often called the brain interface machine, provides a direct communication door between the brain's electrical activity and an external device [55]. The physical implementation of the BCI ranges from non-invasive to invasive methods [56]. BCI system acquires brain signals from the subject, processes these signals which might contain preprocessing such as noise reduction, feature extraction according to the application of BCI, and classification of the brain signals into useful commands, and returns a feedback information to the subject as per application to enhance certain brain functions.

There are a lot of applications of BCI in medical, educational, and other fields which makes it an important topic for research and development. The medical application can be divided into 3 parts, prevention, detection, and rehabilitation. In prevention, BCI techniques are used to prevent a subject from certain diseases or habits such as smoking and alcohol. This is done by first training a subject specific classifier that learns the EEG pattern of smoking and neutral cue and then the subject is asked to deactivate their real-time EEG activity patterns of smoking cue calculated using a previously constructed classifier [57]. The possible loss of function and decrease in alertness level resulting from smoking and or alcohol drinking can be prevented. Similarly, in detection, BCI can be used for forecasting and detecting health issues such as abnormal brain structure. Diseases such as stroke can be detected before time so that the subject can gather proper medical help. Rehabilitation is another important medical application of BCI in which the subjects who suffer from mobility disorders after strokes and other traumatic brain disorders can be trained to regain their previous level of these functions by helping to guide activity-dependent brain plasticity using EEG to indicate to the current state of brain to the subject and enable the subject to subsequently lower abnormal activity [58]. EEG-based BCI uses brain signals to control robotic arms, artificial limbs, wheelchairs, and other prosthetic devices [59]. The BCI approach allows the disabled individual to use their limbs and voice once again to communicate with the world [60].

The applications of BCI are not limited to the medical field but smart environment such as smart homes, safer transportation, and brain-controlled home appliances is also a major use of BCI [61]. The use of BCI to monitor the stress and attention of the driver and assist drivers during transportation in reducing the risk of accidents on roads [62]. Furthermore, marketing and advertisements have also been an interest of researchers. BCI-based advertisement is being implemented in which the attention and watching activity of the subject is analyzed and the most effective advertisements are displayed to the audience.

Moreover, in the educational field, BCI techniques such as neurofeedback training are being used to enhance the performance of the subject's brain including improvement in alertness, focus, and cognitive skills of the subject. The entertainment industry is also using BCI to enhance the user's involvement in games. BCI is being used to control toys and video games that attract more and more users to try and use them. BCI is being used in security as well, where cognitive biometrics (such as brain signals) are used as sources of identity information, reducing vulnerabilities and the chance of being hacked [63].

BCI techniques have some challenges that need to be resolved for user acceptance. The usability of BCI has certain challenges such as the training process which is necessary to discriminate between classes. In the training process, the subject is taught to use the system as well as control the brain feedback signal. After training, the BCI system would be able to classify or do certain functions as per the subject's requirements. Noise in the recordings of brain activities can reduce the performance of the BCI system. For this, the subject must be careful while using BCI. Time consumption also played an important role in the acceptability of BCI in normal life as the training process can be very long. Other than that, there are a few technical issues such as the non-linearity of the brain signals. Thus, the noise or artifact removal process is computationally expensive.

1.7 Neurofeedback & Biofeedback Systems

Hans Berger, a German researcher was the first to use EEG devices on human subjects in the 1920s, by attaching electrodes to the scalp and measuring the produced currents [64]. After this, in the 1950s and 1960s, a method of altering brain activities was formulated by Dr. Joseph Kamiya and Dr. Barry and they called it Neurofeedback [65]. The main concept behind this system is that if a subject is offered a simple reward system, he/she can control their brain waves. Dr. Kamiya used a simple bell sound based on the subject's EEG as a reward to achieve an alpha state.

Biofeedback has been found in ancient times where Indian Yogis used to practice similar yoga and transcendental meditation [66]. The modern biofeedback was first documented in 1969. The concept behind this is the feedback formalized by cybernetics during World War II [67]. Biofeedback instruments deployed modern electronic technologies in the field of psychiatry.

In the biofeedback treatment method, self-regulation of the bodily process is achieved by monitoring some aspect of the physiological functioning of the subject using electronic devices, and feedback is provided to the subject, generally in the form of audio or video, so that the subject can learn to alter that function in some way. Some subjects used biofeedback training to control heartbeat and body temperature [68]. Similarly, biofeedback training can be used to train subjects to gain control over blood pressure, skin temperature, and electrical activities of the brain.

In EMG biofeedback, electrical changes in specific muscle groups are converted into electrical signals and displayed to the subject. Similarly, thermal biomedical signals use skin temperature as feedback to train the subject to control blood flow and blood pressure. Electrodermal (EDR) biofeedback measures skin conduction and uses it as feedback to reduce the sympathetic tone of the subject [69].

Some of the common applications of biofeedback include the treatment of headaches, Cardiovascular disorders including hypertension, cardiac arrhythmias, and Raynaud's disease. Neuromuscular rehabilitation such as spasmodic torticollis, blepharospasm, and chronic pain can also be achieved by using biofeedback training [70]. Similarly, gastrointestinal disorders can also be treated using biofeedback methods [71].

Neurofeedback training is a non-invasive form of therapy used to regulate brain waves. This process has been found helpful in the treatment of various neurological disorders and psychological disorders. In neurofeedback training, EEG signals are used to detect brain activities of the subject and real-time feedback is provided to the subject to improve certain functions of the brain. Neurofeedback training is also widely used to improve brain activity to obtain cognitive and behavioral improvements [72]. Alpha neurofeedback training can be used for cognitive enhancement of healthy subjects [73]. Other applications of Neurofeedback training include improvement in cognitive processing speed and executive functions [74], decreasing anxiety [75], treatment of epilepsy disorder and ADHD [76], improvement in artistic performance [77], and improvement in intelligence testing and psychological assessments [78].

1.8 Conclusion

In this chapter, a brief introduction to non-invasive biomedical signals for healthcare is provided. Biomedical signals are the recordings of the physiological activities occurring inside a human body. These signals can be recorded from different parts of the body such as the brain, heart, eyes, etc. The use of biomedical signals has enabled professionals to get a deep insight into the working of different body parts of the subject. Non-invasive biomedical signals are usually very prone to noises. This requires some extra preprocessing steps before using the signals for analysis. First, the data is recorded with a lot of care to minimize the noise. The recorded data is then visualized, and artifact removal methods are implemented which remove the signals not associated with the activities of the observed body part. Once the signal is cleaned, the features are extracted. These features are then fed to machine learning algorithms for the analysis of different diseases and disorders. Non-invasive biomedical signals have been used to detect and prevent various diseases and disorders. ECG and PCG have been used for the detection of heart-related diseases. Similarly, EEG can be used for early diagnoses of neurological and psychological disorders. The applications of non-invasive biomedical signals are not only limited to the cure and prevention of diseases, but these signals can also be used for the improvement and betterment of human cognitive and physical health. EEG can be used to improve the cognition and mental health of the subject. PPG can be used to monitor blood pressure, heart rate, and oxygen saturation in the blood. Applications of non-invasive biomedical signals such as neurofeedback and biofeedback training enabled us to enhance mental and physical health.

1.9 Teaching Assignments

1. Describe different types of biomedical signals.
2. Differentiate between invasive and non-invasive acquisition procedures of biomedicals signals with examples.
3. Explain different steps involved in Biomedical signal processing.
4. What are features and what is meant by feature extraction?
5. Briefly describe Brain Computer Interface and what are its applications.
6. What is biofeedback therapy?
7. What are the benefits of Biofeedback?
8. Explain how Neurofeedback training works.
9. What is neurofeedback training used for?

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