## 1.3 OBJECTVIES OF BIOMEDICAL SIGNAL ANALYSIS

The representation of biomedical signals in electronic form facilitates computer processing and analysis of the data. Figure 1.32 illustrates the typical steps and processes involved in computer-aided diagnosis and therapy based upon biomedical signal analysis.

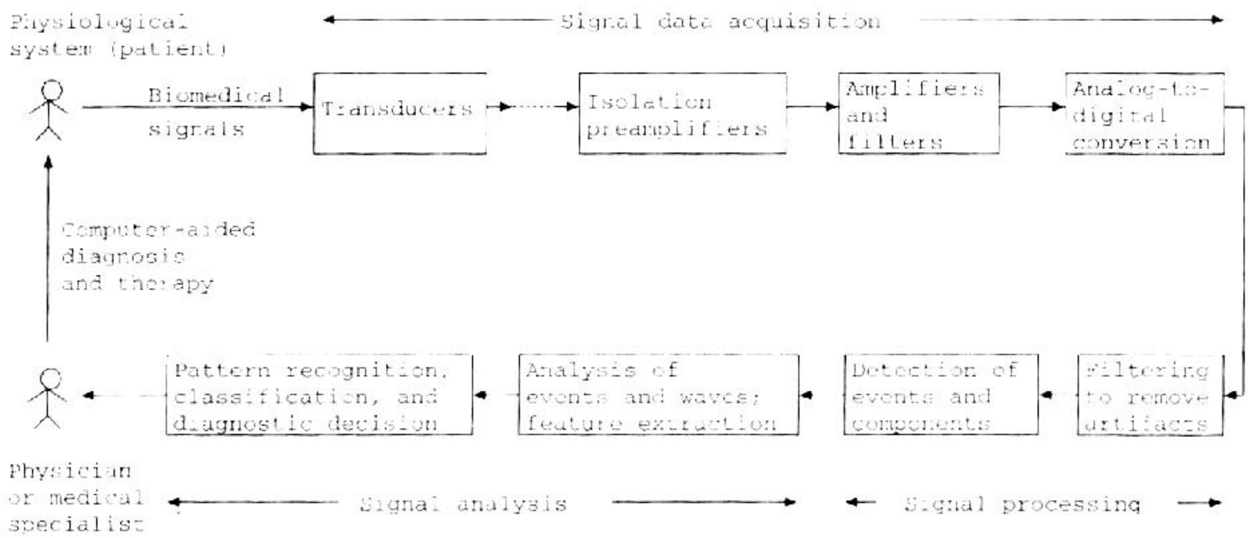


*Figure 1.32 Computer-aided diagnosis and therapy based upon biomedical signal analysis*

The major objectives of biomedical instrumentation and signal analysis [17, 13, 10, 11, 12l are:

- *Information gathering* - measurement of phenomena to interpret a system.
- *Diagnosis* - detection of malfunction, pathology, or abnormality.
- *Monitoring* - obtaining continuous or periodic information about a system.
- *Therapy and control* - modification of the behavior of a system based upon the outcome of the activities listed above to ensure a specific result.
- *Evaluation* -objective analysis to determine the ability to meet functional requirements, obtain proof of performance, perform quality control, or quantify the effect of treatment.

Signal acquisition procedures may be categorized as being invasive or noninvasive, and active or passive.

**Invasive versus noninvasive procedures:** Invasive procedures involve the placement of transducers or other devices inside the body, such as needle electrodes to record MUAPs, or insertion of catheter-tip sensors into the heart via a major artery or vein to record intracardiac signals. Noninvasive procedures are desirable in order to minimize risk to the subject. Recording of the ECG using limb or chest electrodes, the EMG with surface electrodes, or the PCG with microphones or accelerometers placed on the chest are noninvasive procedures.
Note that making measurements or imaging with x-rays, ultrasound, and so on, may be classified as invasive procedures, as they involve penetration of the body with external1y administered radiation, even though the radiation is invisible and there is no visible puncturing or invasion of the body.

**Active versus passive procedures:** Active data acquisition procedures require external stimuli to be applied to the subject, or require the subject to perform a certain activity to stimulate the system of interest in order to elicit the desired response or signal. For example, recording an EMG signal requires contraction of the muscle of interest, say the clenching of a fist; recording the VAG signal from the knee requires flexing of the leg over a certain joint angle range; recording visual

ERP signals requires the delivery of flashes of light to the subject. While these stimuli may appear to be innocuous, they do carry risks in certain situations for some subjects: flexing the knee beyond a certain angle may cause pain for some subjects; strobe lights may trigger epileptic seizures in some subjects. The investigator should be aware of such risks, factor them in a risk - benefit analysis, and be prepared to manage adverse reactions.

Passive procedures do not require the subject to perform any activity. Recording of the ECG using limb or chest electrodes, the EEG during sleep using scalp-surface electrodes, or the PCG with microphones or accelerometers placed on the chest are passive procedures, but require contact between the subject and the instruments. Note that although the procedure is passive, the system of interest is active under its own natural control in these procedures. Acquiring an image of a subject with reflected natural light (with no flash from the camera) or with the natural infra-red (thermal) emission could be categorized as a passive and non-contact procedure.

Most organizations require ethical approval by specialized committees for experimental procedures involving human or animal subjects, with the aim of minimizing the risk and discomfort to the subject and maximizing the benefits to both the subjects and the investigator.

**The human -instrument system:** The components of a human –instrument system [17, 13, 10, 11, 12l are:

- *The subject or patient*: It is important always to bear in mind that the main purpose of biomedical instrumentation and signal analysis is to provide a certain benefit to the subject or patient. All systems and procedures should be designed so as not to unduly inconvenience the subject, and not to cause any harrn or danger. In applying invasive or risky procedures, it is extremely important to perform a risk -benefit analysis and deterrnine if the anticipated benefits of the procedure are worth placing the subject at the risks involved.

- *Stimulus or procedure of activity:* Application of stimuli to the subject in active procedures requires instruments such as strobe light generators, sound generators, and electrical pulse generators. Passive procedures require a standardized protocol of the desired activity to ensure repeatability and consistency of the experiment.
- *Transducers:* electrodes, sensors.

- *Signal-conditioning equipment:* amplifiers, filters.

- *Display equipment:* oscilloscopes, strip-chart or paper recorders, computer monitors, printers.

- *Recording, data processing, and transmission equipment*: analog instrumentation tape recorders, analog-to-digital converters (ADCs), digital-to-analog converters (DACs), digital tapes, compact disks (CDs), diskettes, computers, telemetry systems.

- *Control devices*: power supply stabilizers and isolation equipment, patient intervention systems.

The science of measurement of physiological variables and parameters is known as biometrics. Some of the aspects to be considered in the design, specification, or use of biomedical instruments [17, 13, 10, 11, 12l are:

- *Isolation of the subject or patient* – of paramount importance so that the subject is not placed at the risk of electrocution.

- *Range of operation* - the minimum to maximum values of the signal or parameter being measured.

- *Sensitivity* - the smallest signal variation measurable. This determines the resolution of the system.

- *Linearity* -desired over at least a portion of the range of operation. An nonlinearity present may need to be corrected for at later stages of signal processing.

- Hysteresis – a lag in measurement due to the direction of variation of theentity being measured. Hysteresis may add a bias to the measurement, and should be corrected for.

- *Frequency response* -represents the variation of sensitivity with frequency. Most systems encountered in practice exhibit a lowpass behavior, that is, the sensitivity oft he system decreases as the frequency of the input signal increases. Signal restoration techniques may be required to compensate reduced high frequency sensitivity.

- *Stability* - an unstable system could preclude repeatability and consistency of measurements.

- *Signal-to-noise ratio (SNR)* - power-line interference, grounding problems, thermal noise, and so on, could comprornise the quality of the signal being acquired. A good understanding of the signal-degrading phenomena present in the system is necessary in order to design appropriate filtering and correction procedures.

- *Accuracy* - includes the effects of errors due to component tolerance, movement, or mechanical errors; drift due to changes in temperature, humidity, or pressure; reading errors due to, for example, parallax; and zeroing or calibration errors.

## 1.4 DIFFICULTIES ENCOUNTERED IN BIOMEDICAL SIGNAL ACQUISITION AND ANALYSIS

In spite of the long history of biomedical instrumentation and its extensive use in health care and research, many practical difficulties are encountered in biomedical signal acquisition, processing, and analysis [ 17, 13, 10, 11, 12l. The characteristics of the problems, and hence their potential solutions, are unique to each type of signal. Particular attention should be paid to the following issues.

**Accessibility of the variables to measurement:** Most of the systems and organs of interest, such as the cardiovascular system and the brain, are located well within the body (for good reasons!). While the ECG may be recorded using limb electrodes, the signal so acquired is but a projection of the true 3D cardiac electrical vector of the heart onto the axis of the electrodes. Such a signal may be sufficient for rhythm monitoring, but could be inadequate for more specific analysis of the cardiac system such as atrial electrical activity. Accessing the atrial electrical activity at the source requires insertion of an electrode close to the atrial surface or within the atria.

Similarly, measurement of blood pressure using a pressure cuff over an arm gives an estimate of the brachial arterial pressure. Detailed study of pressure variations within the cardiac chambers or arteries Over a cardiac cycle would require insertion of catheters with pressure sensors into the heart. Such invasive procedures provide access to the desired signals at their Sources and often provide clear and useful signals, but carry high risks.

The surface EMG includes the interference pattern of the activities of several motor units even at very low levels of muscular Contraction. Acquisition of SMUAPs requires access to the specific muscle layer or unit of interest by insertion of fìne-wire or needle electrodes. The procedure carries risks of infection and damage to muscle fìbers, and causes pain to the subject during muscular activity.

An investigator should assess the system and variables of interest carefully and determine the minimal level of intervention absolutely essential to the data acquisition procedure. The trade-off to be performed is that of integrity and quality of the information acquired versus the pain and risks to the subject.

**Variability of the signal source:** It is evident from the preceding sections that the various systems that comprise the human body are dynamic systems with several variables. Biomedical signals represent the dynamic activity of physiological systems
and the states of their constituent variables. The nature of the processes or the variables could be deterministic or random (stochastic); a special case is that of periodicity or quasi-periodicity.

A normal ECG exhibits a regular rhythm with a readily identifìable waveshape (the QRS complex) in each period, and ùnder such conditions the signal may be referred to as a deterministic and periodic signal. However, the cardiovascular system of a heart patient may not stay in a given state over signifìcant periods and the waveshape and rhythm may vary over time.

The surface EMG is the summation of the MUAPs of the motor units that are active at the given instant of time. Depending upon the level of contraction desired (at the volition of the subject), the number of active motor units varies, increasing with increasing effort. Furthermore, the fìring intervals or the fìring rate of each motor unit also vary in response to the level of contraction desired, and exhibit
stochastic properties. While the individual MUAPs possess readily identifìable and simple monophasic, biphasic, or triphasic waveshapes, the interference pattern of several motor units fìring at different rates will appear as an almost random signal with no visually recognizable waves or waveshapes.

The dynamic nature ofbiological systems causes most signals to exhibit stochastic and nonstationary behavior. This means that signal statistics such as mean, variance, and spectral density change with time. For this reason, signals from a dynamic system should be analyzed over extended periods of time including various possible states of the system, and the results should be placed in the Context of the correspondjng states.
Inter-relationships and interactions among physiological systems: The various systems that compose the human body are not mutually independent; rather, they are inter-related and interact in various ways. Some of the interactive phenomena are compensation, feedback, cause-and-effect, collateral effects, loading, and take-over of function of a disabled system or part by another system or part. For example, the second heart sound exhibits a split during active inspiration in normal subjects due to reduced intra-thoracic pressure and decreased venous return to the left side of the heart [41 l (but not during expiration); this is due to normal physiological processes. However, the second heart sound is split in both inspiration and expiration due to delayed right ventricular contraction in right bundle-branch block, pulmonary valvular stenosis or insufficiency, and other conditions [4ll. Ignoring this interrelationship could lead to misinterpretation of the signal.

**Effect of the instrumentation or procedure on the system:** The placement of transducers on and connecting a system to instruments could affect the performance or alter the behavior of the system, and cause spurious variations in the parameters being investigated. The experimental procedure or activity required to elicit the signal may lead to certain effects that could alter signal characteristics. This aspect may not always be obvious unless careful attention is paid. For example, the placement of a relatively heavy accelerometer may affect the vibration characteristics of a muscle and compromise the integrity of the vibration or sound signal being measured. Fatigue may set in after a few repetitions of an experimental procedure, and subsequent measurements may not be indicative of the true behavior of the system; the system may need some rest between procedures or their repetitions.

**Physiological artifacts and interference:** One of the pre-requisites for obtaining a good ECG signal is for the subject to remain relaxed and still with no movement. Coughing, tensing of muscles, and movement of the limbs cause the corresponding EMG to appear as an undesired artifact. In the absence of any movement by the subject, the only muscular activity in the body would be that of the heart. When chest leads are used, even normal breathing could cause the associated EMG of the chest muscles to interfere with the desired ECG. It should also be noted that breathing causes beat-to-beat variations in the RR interval, which should not be mistaken to be sinus arrhythmia. An effective solution would be to record the signal with the subject holding breath for a few seconds. This simple solution does not apply in long-term monitoring of critically iIl patients or in recording the ECG of infants; signal-processing procedures would then be required to remove the artifacts.

A unique situation is that of acquiring the ECG of a tetus through surface electrodes placed over the mother's abdomen: the maternal ECG appears as an interference in this situation. No volitional or extema1 control is possible or desirab1e to prevent the artifact in this situation, which calls for more intelligent adaptive cancellation techniques using multiple channels of various signals [62].

Another example of physiological interference or cross-talk is that of muscle contraction interference (MCI) in the recording of the knee-joint VAG signal [63]. The rectus femoris muscle is active (contracting) during the swinging movement of the leg required to elicit the joint vibration signal. The VMG of the muscle is propagated to the knee and appears as an interference. Swinging the leg mechanically using a mechanical actuator is a possible solution; however, this represents an unnatural situation, and may cause other sound or vibration artifacts from the machine. Adaptive filtering using multi-channel vibration signals from various points is a feasible solution [63].

**Energy limitations:** Most biomedical signals are generated at microvolt or millivolt levels at their Sources. Recording such signals requires very sensitive transducers and instrumentation with low noise levels. The connectors and cables need to be shielded as well, in order to obviate pickup of ambient electromagnetic (EM) signals. Some applications may require transducers with integrated amplifiers and signal conditioners so that the signal leaving the subject at the transducer level is much stronger than ambient sources of potential interference.

When external stimuli are required to elicit a certain response from a system, the level of the stimulus is constrained due to safety factors and physiological limitations. ElectricaI stimuli to record the ENG need to be limited in voltage level so as to not cause local bums or interfere with the electrical control signals of the cardiac or nervous systems. Auditory and vis!1al stimuli are Constrained by the lower thresholds of detectability and upper thresholds related to frequency response, saturation, or pain.

**Patient safety:** Protection of the subject or patient from electrical shock or radiation hazards is an unquestionable requirement of paramount importance. The relative levels of any other risks involved should be assessed when a choice is available between various procedures, and analyzed against their relative benefits. Patient safety concerns may preclude the Use of a procedure that may yield better signaIs or results than others, or require modifications to a procedure that may lead to inferior signals. Further signal-processing steps would then become essential in order to improve signal quality or otherwise compensate for the initial loss.

## 1.5 COMPUTER-AIDED DIAGNOSIS

Physicians, cardiologists, neuroscientists, and health-care technologists are highly trained and skilled practitioners. Why then would we want to use computers or electronic instrumentation for the analysis of biomedical signals? The following points provide some arguments in favor of the application of computers to process and analyze biomedical signals.

- Humans are highly skilled and fast in the analysis of visual patterns and waveforms, but are slow in arithmetic operations with large numbers of values. The ECG of a single cardiac cycle (heart beat) could have up to 200 numerical values; the corresponding PCG up to 2,000. If signals need to be processed to remove noise or extract a parameter, it would not be practical for a person to perform such computation. Computers can perform millions of arithmetic operations per second. It should be noted, however, that recognition of waveforms and images using mathematical procedures typically requires huge numbers of operations that could Iead to slow responses in such tasks from low-level computers.

- Humans could be affected by fatigue, boredom, and environmental factors, and are susceptible to committing errors. Long-term monitoring of signals, for example, the heart rate and ECG of a critically ill patient, by a human observer watching an oscilloscope or computer tracing is neither economical nor feasible. A human observer could be distracted by other events in the surrounding areas and may miss short episodes or transients in the signal. Computers, being inanimate but mathematically accurate and consistent machines, can be designed to perform computationally specific and repetitive tasks.

- Analysis by humans is usually subjective and qualitative. When comparative analysis is required between the signal of a subject and another or a standard pattern, a human observer would typically provide a qualitative response. For example, if the QRS width of the ECG is of interest, a human observer may remark that the QRS of the subject is wider than the reference or normal. More specific or objective comparison to the accuracy of the order of a few milliseconds would require the use of electronic instrumentation or a computer. Derivation of quantitative or numerical features from signals with large numbers of samples would certainly demand the use of computers.

- Analysis by humans is subject to inter-observer as well as intra-observer variations (with time). Given that most analyses performed by humans are based upon qualitative judgment, they are liable to vary with time for a given observer, or from one observer to another. The former could also be due to lack of diligence or due to inconsistent application of knowledge, and the latter due to variations in training and level of understanding. Computers can apply a given procedure repeatedly and whenever recalled in a consistent manner. It is further possible to encode the knowledge (to be more specific, the logic) of many experts into a single computational procedure, and thereby enable a computer with the collective intelligence of several human experts in the area of interest.

- Most biomedical signals are fairly slow (lowpass) signals, with their bandwidth limited to a few tens to a few thousand Hertz. Typical sampling rates for digital processing of biomedical signals therefore range from 100 Hz to 10- 20 kHz. Sampling rates as above facilitate on-line, real-time analysis of biomedical signals with even low-end computers. Note that the term "real-time analysis" may be used to indicate the processing of each sample of the signal before the next sample arrives, or the processing of an epoch or episode such as an ECG beat before the next one is received in its entirety in a buffer. Heartrate monitoring of critically ill patients would certainly demand real-time ECG analysis. However, some applications do not require on-line, real-time analysis: for example, processing a VAG signal to diagnose cartilage degeneration, and analysis of a long-term ECG record obtained over several hours using an ambulatory system do not demand immediate attention and results. In such cases, computers could be used for off-line analysis of pre-recorded signals with sophisticated signal-processing and time-consuming modelling techniques. The speed required for real-time processing and the computational complexities of modelling techniques in the case of off-line applications both would rule out the possibility of performance of the tasks by humans.

One of the important points to note in the above discussion is that quantitative *analysis* becomes possible by the application of computers to biomedical signals. The logic of medical or clinical diagnosis via signal analysis could then be objectively encoded and *consistently* applied in routine or repetitive tasks. However, it should be emphasized at this stage that the end-goal of biomedical signal analysis should be seen as computer-aided diagnosis and not automated diagnosis. A physician or medical specialist typically uses a significant amount of information in addition to signals and measurements, including the general physical appearance and mental state of the patient, family history, and socio-economic factors affecting the patient, many of which are not amenable to quantification and logistic rule-based processes. Biomedical signals are, at best, indirect indicators of the state of the patient; most cases lack a direct or unique signal pathology relationship [31] l. The results of signal analysis need to be integrated with other clinical signs, symptoms, and information by a physician. Above all, the *intuition* of the specialist plays an important role in arriving at the final diagnosis. For these reasons, and keeping in mind the realms of practice of various licensed and regulated professions, liability, and legal factors, the final diagnostic decision is best left to the physician or medical specialist. It is expected that quantitative and objective analysis facilitated by the application of computers to biomedical signal analysis will lead to a more accurate diagnostic decision by the physician.

**On the importance of quantitative analysis:**

"When you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind: it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of science."

-Lord Kelvin (William Thomson, 1824- 1907) [64]

**On assumptions made in quantitative analysis:**

"Things do not in general run around with their measure stamped on them like the capacity of a freight car; it requires a certain amount of investigation to discover what their measures are ...What most experimenters take for granted before they begin their experiments is infinitely more interesting than any results to which their experiments lead."

-Norbert Wiener (1894 -1964)

## 1.6 REMARKS

We have taken a general look at the nature of biomedical signals in this chapter, and seen a few signals illustrated for the purpose of gaining familiarity with their typical appearance and features. Specific details of the characteristics of the signals and their processing or analysis will be dealt with in subsequent chapters.

We have also stated the objectives of biomedical instrumentation and signal analysis. Some practical difficulties that arise in biomedical signal investigation were discussed in order to draw attention to the relevant practical issues. The suitability and desirability of the application of computers for biomedical signal analysis were discussed, with emphasis on objective and quantitative analysis toward the end goal of computer-aided diagnosis. The remaining chapters will deal with specific techniques and applications.