Theme 11. Biosignals analysis. Methods of biosignals processing. Visualization of biomedical data. Processing and analysis of medical images

Every living cell, organ, or organism generates signals for internal communication or to make itself known to the outside world. In general, we may express this situation as a biological process that generates some output, and in some circumstances we might even be interested in offering this process an input signal to examine its response.

Such biological signals can have a different nature:

- electrochemical, for example, the depolarization of a cell, which is the result of flows of ions, that pass the cell membrane, such as Ca++, Na+, or Cl-;
- mechanical, for example, the respiration, set in motion by thoracic muscles and resulting in airflows and pressures;
- biochemical, for example, blood gas values such as pO_2 or pCO_2;
- hormonal, for example, the release of oxytocin during labor.

Living organisms are composed of different functional systems. In the human body there exist, for example, the nervous system, the cardiovascular system, the musculosceletal system, the digestive system, and the immune system. These systems employ physiological processes such as blood circulation and breathing in the case of cardiovascular system.

Biosignals are signals that quantify the physiological processes. They can be measured as physical quantities such as temperature or pressure, electrical quantities such as currents and voltages and biochemical quantities such as concentrations.

The clinical need for the monitoring of biosignals arises from the fact that diseases and dysfunctions in the biological processes cause changes that usually degrade their performance. Such changes lead to pathological processes – a rise in the body temperature during an infection for example. Also nonpathological changes in the status of the body can cause changes in the physiological processes. For example, physical strain increases the heart rate and blood pressure whereas talking causes irregularities in the breathing rhythm. The nonclinical biosignal monitoring solutions, such as fitness monitors, concentrate on such nonpathological changes in the biosignals.

Biosignals are used for transmission of the information about a patient. In most instances we deal with transmission situations 1 or 5 indicated above (theme 1). The received signal ***s*** is sometimes very distorted by the transmission channel in the body if ***s*** must pass different tissues on its way to the transducer. An example of a signal ***s*** that passes many tissue layers before it reaches the transducer is the fetal ECG (Fig. 8.1). In the first three months of pregnancy this signal is too weak to be detected, and during labor it is much distorted by the uterine and abdominal muscles. On top of the foetal signal, the maternal ECG (which can be considerably larger in voltage than the

foetal ECG) is also superimposed. The intervals between foetal heart beats can reveal information about possible foetal distress during birth.

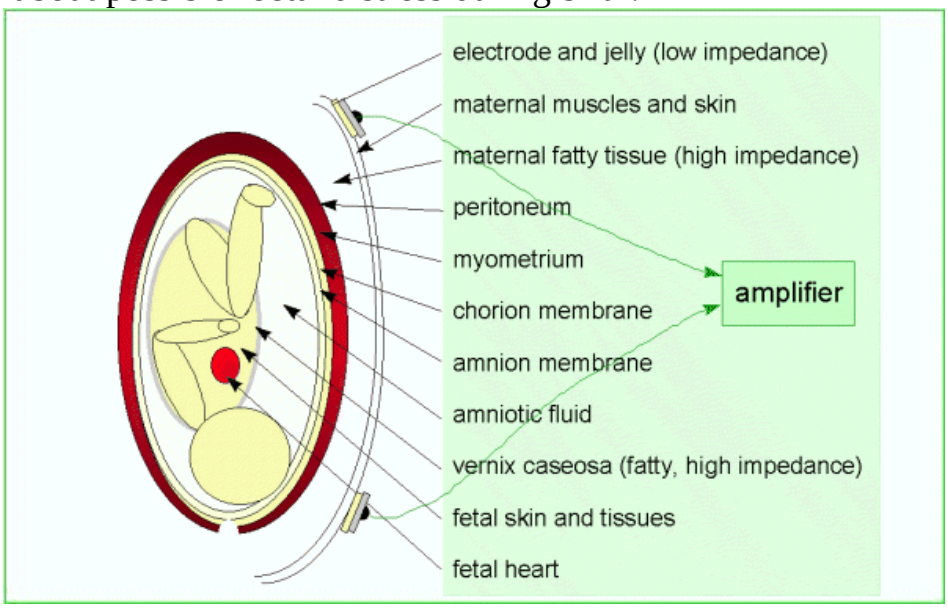

Fig. 8.1. An example of a signal transmission

There are many other examples of situations in which information is transmitted from the sender to the receiver by means of temperatures, mass, electric current, hormones, biochemical parameters, DNA, and so forth.

In general, we may conclude that **from the viewpoint of information and communication, patients and organs can be considered as time-varying *processes* that generate signals *s* that are of interest for determining or monitoring the state of the process**.

Unfortunately, the signals are often distorted or the processes cannot be approached closely enough to be able to record the signals with a high enough fidelity.

There are four stages of biosignals processing. They are represented on the Fig. 8.2.

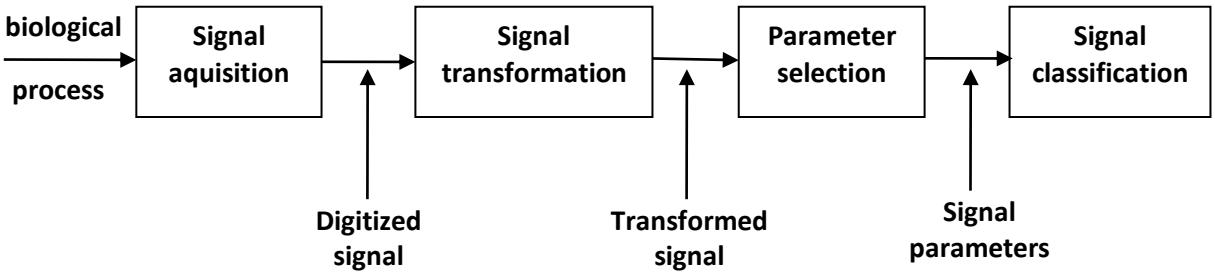

Fig. 8.2. The four stages of biosignal processing

Before being able to digitally process a real world signal, this signal has to undergo a process commonly known as ***Analogue to Digital Conversion***. This

process may be further divided into two different stages, respectively, called ***sampling*** and ***quantification***. *Sampling* is the process through which the original signal has its value measured in several time instants. *Quantification*, on the other hand, relates to the process through which the value of each sample is approximated by one out of a finite set of integer values.

Biosignals classification

Biological signals of clinical interest, generally called biomedical signals, can, when in digital form, be subdivided and grouped *according to their sampling scheme*. Based on this criterion, the following groups of signals can be identified:

1. Temporally sampled signals, i.e., measurements of a single variable, or of a group of variables, over time. Examples of these kind of signals are digital records of ECG, EEG, EMG, EOG, SaO2, MEG, NCS and others;
2. Spatially sampled signals, i.e., measurements of a single variable in many different space locations, all made in the same time instant. Examples of these kind of signals are digital X-ray images (bi-dimensional sampling) and CT scans (tri-dimensional sampling);
3. Spatially and temporally sampled signals, i.e., measurements of a single variable in different space locations, and made in several time instants. A simple example of this kind of signal is ecography.

The second group of signals, identified by a common sampling scheme, is usually called an ***image*** (or a volume, for tri-dimensional data), while the third group may also be called a ***movie***. Thus, we will reserve the term signal to refer exclusively to those biological signals that can be associated with a temporary sampling scheme.

It is also possible to classify biomedical signals, generally known as biosignals, *with respect to their generation mechanisms*. We may have:

1. ***Bioelectric signals***. These signals are electric potentials generated by nerve and muscle cells. They can be measured by placing the tip of a micro-electrode inside the cell. However, instead of measuring single cell bioelectric signals, which always require an invasive procedure, it is easier to measure the spatially averaged value of the bioelectric signal of a group of cells. This non-invasive procedure, which can only be used if the group of cells is either close to the skin, or close to an easily reachable inner surface of the body, can be simply done by placing a surface electrode over the group of cells. That is precisely what is done in scalp EEG measurements. Due to the ease of construction of appropriate measurement devices (transducers), which normally relates to a low cost signal acquisition procedure, this kind of signal is quite popular in biomedicine.
2. ***Bioimpedance signals***. Some physiological processes produce changes in the impedance of tissues inside the human body. This impedance can be measured by applying a small alternating current to the tissue and measuring the voltage

it produces across the same tissue. The frequency used (from 50 kHz to 1 MHz) minimizes electrode and cell polarization problems, and the current densities used (from 20 μA to 20 mA) produce negligible tissue damage. Example: Thoracic Electrical Bioimpedance.

3. ***Bioacoustic signals***. Some physiological processes generate acoustical noise. Examples are the flow of blood in the heart or in the blood vessels, and the flow of air in the lungs. Sounds are also generated in the joints, in the digestive tract, and in contracting muscles. All these sounds are important to biomedicine. Since the sound waves propagate inside the human body, they can be conveniently measured at the surface (skin), using appropriate transducers (microphones and accelerometers).
4. ***Biomagnetic signals***. All time-varying electric fields produce magnetic fields. The small electric fields produced in the human body are no exception. The tiny magnetic fields generated in the human body, especially those of the brain, are useful in biomedicine. Their measurement requires expensive and high-tech equipment.
5. ***Biomechanical signals***. Some body functions produce motion and displacement, pressure and tension, and flow of liquids. These biomechanical signals are also important to biomedicine. Well known examples are the systolic and diastolic blood pressure measurements. Due to their nature, most of these signals do not propagate to other parts of the human body. Thus, their measurements have to be performed usually in situ.
6. ***Biochemical signals***. These kind of signals are the result of measurement of some chemical quantity, usually a concentration of a molecule or of an ion. Examples of biochemical signals are the acidity (pH), and the partial pressures of oxygen (pO_2) and of carbon dioxide (pCO_2) measured in the blood or in the respiratory system. Note that these kind of signals change very slowly over time.
7. ***Biooptical signals***. Some physiological processes also produce changes in the transmission and reflection of light in tissues and fluids. A well known example is the change in color of the blood (from red to blue) that shows up when its oxygen content is lowered.

As previously stated, digital processing of a biosignal can only take place if the signal has been previously submitted to a sampling (over time) and quantification process known as Analogue to Digital conversion (AtoD). This process always requires the following equipment:

- ***A transducer***, normally followed by an amplifier, to convert the biosignal to a sizable voltage potential (a few volts).
- ***An analogue to digital converter***, to sample and quantify the signal. The analogue to digital conversion amounts to substituting the signal s(t) that evolves continuously over time, by its samples s(nT), with a spacing of T s

between samples, and to replace the value of these samples by the nearest output level of the quantifier. The number of possible output levels of the quantifier is usually a power of two, say 2b, meaning that its output signal can be represented by an integer with b bits (binary digits).

In order to lose as little information as possible in the analogue-to-digital conversion, special care must be taken while choosing the sampling period T and the number of bits b of the converter. The sampling period is chosen based on the frequency content of the biological signal being converted; the higher the frequency components present in the signal, the smaller the sampling period must be. A useful rule of thumb is to set the sampling period between one fourth to one tenth of the inverse of the highest frequency present in the signal. The number of bits of the converter has to be chosen according to the dynamic range of interest of the signal; the higher the dynamic range, the higher should be the number of bits. Table 8.1 presents the frequency and dynamic ranges of some common biosignals.

Table 8.1.

Frequency and dynamic ranges of some common biosignals

Biosignal	Type of electrodes	Frequency content	Dynamic range
Action potential	Microelectrodes	100 Hz – 2 kHz	80 dB (10μV – 100mV)
Electro-oculogram (EOG)	Surface electrodes	dc – 100 Hz	54 dB (10μV – 5 mV)
Surface electroencephalogram (S-EEG)	Surface electrodes	0,5 – 100 Hz	60 dB (1μV – 1 mV)
Surface electromyography (S-EMG)	Surface electrodes	2 – 500 Hz	40 dB (50μV – 5mV)
Electrocardiogram (ECG)	Surface electrodes	0,05 – 100 Hz	30 dB (0,1 – 10 mV)

Scenarios

Different scenarios can be depicted where the utilization of an agreed upon digital interchange signal format may be fundamental to the success of the underlying applications. Examples of these scenarios may be:

- ***Long-term patient follow up***. In order to assess the evolution of a patient disease (e.g. epilepsy) it is necessary to store exams made over extended periods of time (months or even years). Digital storage of these exams, say, on CDROMs, requires much less space and cost than its storage on paper, as was traditionally done in the past. Also, the digital storage of information eases and speeds up the comparison of different exams. On the other hand, consistent technology evolution and backward compatibility, together with well

established open formats for signal archive, are essential to ensure correct data retrieval over the years.

- ***Telemedicine***. In order to be able to transfer patient exams between two hospitals, or between a hospital and a remote location, it is absolutely necessary that sites involved agree on a common exchange format. This is equally important for real time data exchange (e.g. when a surgeon performs an operation remotely), and for off-line data transfer (e.g. when a hospital requests the patient's exams stored in another hospital).
- ***Medical research***. In order to analyze the effects of an experimental therapy, of different environmental conditions, etc., it is usually necessary to analyze and compare large volumes of medical records and exams of several groups of patients, made over an extended period of time. In most large scale tests of this kind, exams are performed on different locations, possibly with different brands of equipment. To be able to process the raw exam data coming from different locations, it is convenient that a single storage format be used in all locations. At the very least, compatible formats should be used in all locations so that simple conversion between formats may be easily achieved.

Digital monitoring

Medical monitors evolve with the development of digital signal processing (DSP) technology, which has the advantages of miniaturization, portability, and multi-parameter monitoring that can track many different vital signs at once.

These typically include

- *pulse oximetry* (measurement of the saturated percentage of oxygen in the blood, referred to as SpO_2, and measured by an infrared finger cuff),

- *ECG* (electrocardiograph of the QRS waves of the heart with or without an accompanying external heart pacemaker),

- *blood pressure* (either invasively through aninserted blood pressure transducer assembly, or noninvasively with an inflatable blood pressure cuff), and

- *body temperature* through an adhesive pad containing a thermoelectric transducer.

In some situations, other parameters can be measured and displayed, such as *cardiac output* (via an invasive Swan-Ganz catheter), *capnography* (CO_2 measurements, referred to as $EtCO_2$ or end-tidal carbon dioxide concentration), *respiration* (through a thoracic transducer belt, an ECG channel or via EtCO2, when it is called AWRR or airway respiratory rate), etc.

Besides the tracings of physiological parameters along time (X axis), digital medical monitors have automated numeric readouts of the peak and/or average parameters displayed on the screen, and high/low alarm levels can be set, which alert the staff when some parameter exceeds of falls below the level limits, using audible signals.

Digital monitoring has created the possibility, which is being fully developed, of integrating the physiological data from the patient monitoring networks into the emerging hospital electronic health record and digital charting systems, using appropriate health care standards which have been developed for this purpose by organizations such as IEEE and HL7. This newer method of charting patient data reduces the likelihood of human documentation error and will eventually reduce overall paper consumption. In addition, automated ECG interpretation incorporates diagnostic codes automatically into the charts. Medical monitor's embedded software can take care of the data coding according to these standards and send messages to the medical records application, which decodes them and incorporates the data into the adequate fields.

Automated ECG interpretation (Fig. 8.3) is the use of artificial intelligence and pattern recognition software and knowledge bases to carry out automatically the interpretation, test reporting and computer-aided diagnosis of electrocardiogram tracings obtained usually from a patient.

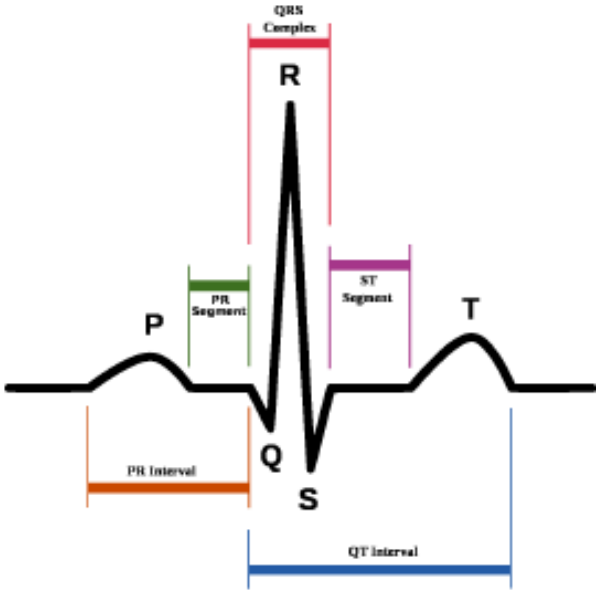

Fig 8.3. Basic signal features of time and amplitude which are measured and form the basis for automated ECG analysis

Phases

1. A digital representation of each recorded ECG channel is obtained, by means of an analog-digital conversion device and a special data acquisition software or a digital signal processing (DSP) chip.

2. The resulting digital signal is processed by a series of specialized algorithms, which start by conditioning it, e.g., removal of noise, baselevel variation, etc.

3. Feature extraction: matemathical analysis is now performed on the clean signal of all channels, to identify and measure a number of features which are important for interpretation and diagnosis. This will constitute the input to AI-based programs, such as the peak amplitude, area under the curve, displacement in relation to baseline, etc., of the P, Q, R, S and T waves, the time delay between these peaks and valleys, heart rate frequency (instantaneous and average), and many others. Some sort of secondary processing such as Fourier analysis and wavelet analysis may also be performed in order to provide input to pattern recognition-based programs.

4. Logical processing and pattern recognition, using rule-based expert systems, probabilistic Bayesian analysis or fuzzy logics algorithms, cluster analysis, artificial neural networks, genetic algorithms and other techniques are used to derive conclusions, interpreation and diagnosis.

5. A reporting program is activated and produces a proper display of original and calculated data, as well as the results of automated interpretation.

Applications and future perspectives

Signal interchange formats can play a decisive role in the development of signal archive and communication systems (SACS) for many different clinical applications. Real world clinical systems and applications dealing with digital biosignal and its exchange and storage support are growing everyday in number and complexity.

SIGIF is an example of a basic infrastructure of one of such systems developed in a clinical neurophysiology environment. In this application, an integrated access to different types of information used in neurophysiology (clinical and demographics, biosignal, multimodal medical imaging, etc.) is obtained through a multimedia distributed database called LINE. For the biosignal storage, SIGIF was used with an identifier which linked signal files to the patient information, and from this, to all other information available in the system. With this graphical environment clinicians can easily perform cross-analysis procedures or make use of several visualization/analysis applications on-line, each one in a different window. Features such as zooming into a particular pair of signals, measurement of amplitude, phase, delay, frequency or other biosignal values, computation of brain mappings of a particular EEG epoch, manipulation of MRI images with false color or histogram equalization, supported search for cases with similar characteristics, and many others, are readily available through this kind of applications.

As another example, EDF is the basic piece for exchange of sleep polygraphic and other registrations between different users from many different countries. In the European Biomed I project IMPROVE, e.g., EDF is used to store and exchange biosignals in critical care environments involving 12 groups from 11 countries. In the Telecardio project, which aims at providing a complete remote ECG monitoring system in different scenarios, the SIGIF format is also used. It covers primary care to central hospital co-operative ECG analysis based on ISDN technology, on-call ECG home monitoring over normal phone lines and mobile monitoring units (for ambulances, or other situations) based on GSM technology.

Many other examples of applications could be given to show situations where open data formats for biosignal are important. The future of this technology is now being prepared and many challenges are to be faced. In the near future, with the emergence of new techniques that link several types of information, questions arise on how to perform the archive and interchange of these data sets. These questions have direct implications not only for the problem of storing (exchanging) individual types of information (biosignals, multi-modality medical images, digital video, etc.), but also on the needed referential data for the linkage procedures. This may constitute one of the next major challenges for biosignal support formats. Another fundamental challenge faced by people working in this field will be the inclusion, at the healthcare middleware infrastructure level, of the functionalities needed for the manipulation of

biosignals. Three different middleware families are now actors in this field: the already referred HL7; the CEN's "Hospital Information System Architecture (HISA)" standard (CEN/TC251/PT-013)[18]; and the CORBA-Med from the CORBA consortium. Although some work was already done in the first of these families, no significant results are known to have had success. The other two families are now undergoing strong development efforts and will most probably become important Hospital information infrastructures in the near future.

Medical Image Processing

Medical imaging is the general name for the widely-used techniques developed in order to create images of the human body for medical purposes. As acquired images could involve the complete human body, they can span it partially. Medical imaging data is used for revealing normal or abnormal physiological and anatomical structures. Medical imaging techniques are also employed in diagnosis and treatment planning processes of patients suffering from many health problems. Professionals from field of medicine make use of medical imaging data in order to guide or avoid medical intervention. Image processing is a subfield of signal processing, for which the input signal is an image and the outputs are again an image and/or various parameters defining the characteristics of the image and applied operations. Medical image processing is applied on the images acquired by medical imaging techniques, such as CT, Ultrasonography, PET, SPECT, MRI, fMRI and NMR spectroscopy. Medical images are post-processed for many purposes, such as denoising, restoration, segmentation, registration, and 2D/3D visualization.

Quantitative analysis of medical images is crucial for diagnosis and prognosis stages of many diseases and abnormalities. Quantification of radiographic information includes various features such as linear measurements, estimation of cross section and surface areas, volume quantization, estimation of tissue density, monitoring tumor growth, verification of treatment, and comparison of patient's data with anatomical atlases. Medical image data is exposed to degradations and/or deformations during data acquisition processes. For instance, MRI intensity inhomogeneities occur subject to RF coil imperfections or problems associated with acquisition sequences. Hence, quantification of medical image information for analysis requires sequential application of several image processing operations. These operations can be classified in three main groups which are smoothing and restoration of images, segmentation of images, and registration of images. Each step of this workflow necessitates user interaction at varying levels. Manually operating, semi-automated and even automated systems receive numerical, vectorial or optional inputs from the user, defining the instantaneous or future behavior of running operations. Diversity in the number of user interaction points may cause complete or partial failure of the operations, or irregularities or instabilities in the acquired results. Even if the processes are completed and reasonable results are obtained, sets of these results depending on different users and/or different time instants may have high standard deviation values.

Control questions

1. What is the nature of biological signals?
2. Which stages of biosignals processing do you know?
3. What is a process Analogue to Digital Conversion?
4. How are biosignals classified?
5. Which equipment is used for a process Analogue to Digital Conversion?
6. What is Digital monitoring?
7. What are applications and future perspectives of biosignals processing?
8. What is Medical Image Processing?

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