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BIOMEDICAL ENGINEERING RESEARCH AND EDUCATION IN HUNGARY

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Abstract

Biomedical Engineering is a relatively new interdisciplinary science. This paper presents the biomedical engineering activity, which is carried out at Budapest University of Technology and Economics and its partner institutes. In the first part the main goals and the curriculum of the Biomedical Engineering Education Programme (BMEEP) is presented. The second part of the paper summarizes the most important biomedical engineering researches carried out mostly in the Biomedical Engineering Laboratory of BUTE university.

Keywords: education, biomedical systems, physiological models, image analysis, signal processing, detection algorithms.

1. Introduction

Biomedical engineering education in Hungary started in 1995, after a comprehensive investigation of similar European programme [1], as a joint programme of three universities: Budapest University of Technology and Economics, Semmelweis University of Medicine, and University of Veterinary Sciences. It is the first high-level comprehensive education form in Hungary that grants an MSc Biomedical Engineer diploma. Over 150 students have already completed their studies and obtained MSc degree in biomedical engineering.

2. Objectives of the Biomedical Engineering Education Program

The objective of the Biomedical Engineering Training is to educate specialists with a second diploma who have – in addition to their engineering, medical or biological background – a high-level interdisciplinary theoretical and practical knowledge and ability to it, thus, they can be employed in wide range of biomedical engineering fields, both of theoretical and practical nature. The Biomedical Engineering Education Program (BMEEP) sets out to meet these diversified needs by imparting wide horizon of basic knowledge, majoring in special fields and deepening experience in the fields selected by students [2]. BMEEP prepares students for the following activity fields:

1. Design, manufacture, installation, and operation of biomedical equipment. Measuring techniques of physiological processes, computer-aided analysis of biomedical signals.
2. Research, development, testing, and manufacture of medicines, agents and medication substances. Development of pharmaceutical procedures.
3. Bioengineering examination of accidents, orthopedic cases, rehabilitation and sport activities. Preparation of development trends. Design and manufacture of medical auxiliary materials and appliances.
4. Assurance of instrumental and measurement technological background of biomedical research. Development and operation of routine laboratory large equipments, technologies, automated analysers and robots.

3. Curriculum of Biomedical Engineering Training

Training comprises 6 semesters, spending the first five with education and the last one with preparing the diploma work.

Engineering and medical students are allowed to take part in the training during the last 3 semesters of their basic training. Precondition of admission for external specialists is the valid university diploma. Students pursuing their basic education simultaneously obtain a parallel training in the first 3 semesters with a partial loading. In the following two semesters, students study at full loading. Diploma work is prepared in the last semester.

The number of contact hours during the training makes 1080 in total, equalling 108 credit points. Preparing the diploma work gives 22 credits.

Training starts with obligatory basic subjects, which are differentiated according to the student's engineering or medical background. Special subjects can be chosen optionally out of the ones announced in the curriculum, in a prescribed obligatory number of hours or credits. Further on, common training and specialization according to the major will be carried out. Possession of the basic diploma is mandatory at the beginning of the 4th semester. Two global exams are carried out at the end of the 3rd and 6th semester. The preparation and successful presentation of the diploma work is the last condition of obtaining the diploma. A more comprehensive presentation of the curriculum can be found in [3].

Most of the Biomedical Engineering diploma holders work in medical and pharmaceutical research institutes, university clinics, medical instrumentation developing companies, medical information centers, etc.

4. Biomedical Engineering Research Activity

Research and development related to the biomedical engineering, are the main activities in the Biomedical Engineering Laboratory. The main research areas of the last years are presented below.

4.1. Computer-Aided Identification of Physiological Systems

Dynamic characteristics of a physiological system in the time domain are described by means of a differential equation or a differential equation system. According to preliminary information on the system, two extreme cases of identification may be distinguished. If the structure of the mathematical model is known, that is, how many compartments are needed to model the physiological system, and how they are related, it is a parameter assessment [4]. For a tested system of unknown structure, the problem is termed system identification. Most problems are situated between these two extreme cases. The compartment model of the clearance test is described generally by a linear differential equation system of first order. Evaluation of the test consists essentially of determining parameters, and then solving this differential equation system. For the computer evaluation of clearance-like tests, the algorithm is relying on the least square principle, developed by D.W. Marquardt. Our computer program is based on this algorithm and has been applied, among others, to evaluate liver-flow tests made with colloid 198 Au. The test relies on colloids of a given particle size being screened out of the plasma by RES (reticulo-endothelial system) cells of the organism. Most of these cells are found in the liver, but there are some in the spleen and the medulla. The structure of the mathematical model of the test is a so-called mammilary system of four components.

4.2. Diabetic Management and Blood Glucose Control

Symbolic computation has been applied to design a procedure for blood glucose control of diabetic patients under intensive care. The used model has been verified and tested in clinical environment. From the engineering point of view, the treatment of diabetes mellitus can be represented by outer control loop to replace the partially or totally failing blood glucose control system of the human body. We have used symbolic computation to design multivariable model control based on the state-space representation of a verified nonlinear model. To simulate the insulin-glucose interaction in human body, a two-compartment model was employed, which was verified by parameter estimation technique based on clinical test data. Insulin injection was given to the test person and the glucose concentration of blood has been measured in time. According to the results, the system is expected to provide a useful help to the control of blood glucose level in diabetics under intensive care, and to the optimization process of diabetic administration [5, 6].

4.3. Remote Patient Monitoring and Diagnostic System

The goal of this research project was to develop a patient monitoring system supporting remote access of the patient information. The traditional patient monitoring systems do not support the remote access (i.e. through internet connection) to the managed patient information. The remote access to the system makes possible the implementation of several useful services:

- patients can be monitored by their doctors through the internet;
- remote diagnostic systems can be connected to the monitoring system to process the patients' data.

The remote patient monitoring system is developed by the collaboration of the Department of Informatics, Széchenyi István University and the Department of Control Engineering and Information Technology, Budapest University of Technology and Economics (DCEIT-BUTE).

The structure of the system is shown in *Fig. 1*.

The system integrates a local patient monitoring system shown at the left hand side of the figure. This subsystem is responsible for the data acquisition. This system had been developed previously at the DCEIT-BUTE in the framework of the INCO/Copernicus Project (INCO 960161) with the collaboration of the University of Munich, University of Vienna, University of Prague, and University of Wroclav [7, 8].

The data are extracted from the local monitoring system by a data access server which transfers them to the data converter server. The role of the data access server is to increase the portability by isolating the other parts of the system from the local patient monitor. If somebody wants to use the remote patient monitoring system with other local patient monitor, the data access server has to be modified only.

The internal data representation of the system is standardized: all the system components exchange the information in the same format. The format of the internal data representation is defined based on international standards in order to make easy the interconnection of the remote patient monitor to other medical information systems such a HIS. The responsibility of the data converter server is to convert the binary data (from the data access server) to the standard internal representation.

The external interface of the system is supplied by a web server. The system stores the patient data in an SQL data base to provide access to the historical patient data as well.

Many free software components are integrated to the remote patient monitor in order to reduce the cost and the time of the development.

The core remote patient monitoring system has been already implemented. Currently we are working on the development of diagnostic systems to connect them to the remote patient monitor.

4.4. Automated System for Analysing Cardiac Ultrasound Images

Ultrasound echocardiography is a widely used clinical technique, but the images obtained using the current technology, are still processed manually with semiautomated methods. In contrast to this, the newly developed system works in an automated way, first obtaining a series of long and short axes views of the heart synchronized by the ECG in real time, then processing them offline. After the detection of the internal edges of the left ventricle, the system determines the short/long axes areas, diameters, calculates the volume of the left ventricle frame by frame and, based on this, the ejection fraction for each cardiac cycle [9].

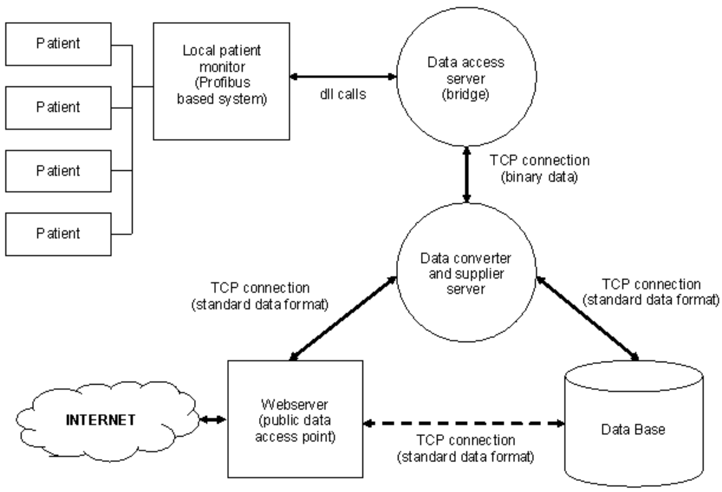

Fig. 1. Structure of the remote patient monitoring and diagnostic system.

4.5. Event Recognition and State Classification to Detect Brain Ischemia by Means of EEG Signal Processing

EEG is an electric signal, which is the spatial sampling of an electric field around the active neurons of the brain. In general, we observe both temporal and spatial characteristics of this signal ensemble. Due to its origin from nerve cells, it is strongly correlated with the primary component of the metabolic activity of these cells: oxygen supplied by cerebral blood flow. Physiological inputs modify the state of the brain, what is reflected in parametric changes based on the EEG. The available processing methods are automatic event recognition or state classification, or semi-quantitative human observation. Two series of animal experiments were carried out with cats and rats, where the occlusion of the middle cerebral artery was used as a model of the ischemic damage. For human registrations, data were collected during open-heart surgery and carotid endarterectomy; in these cases the observation of the neurologist served as reference. Three different methods for event recognition were developed:

- wavelet-based semi-quantitative spectral analysis;
- automatic detection by AR model fitting and observation of dominant frequency and peak power shifts;
- multi-channel activity correlation method based on the eigenvalue representation of a correlation matrix [10].

On the other hand, two classification methods were developed:

- using a distance measure derived from the Karhunen-Loéve transform;
- discriminant analysis using multi-channel autoregressive model parameters [11].

4.6. Single-channel Hybrid ECG Segmentation

Our new system presents a time domain single-channel ECG segmentation method based on beat type and a priori morphological information. The proposed hybrid method combines the advantages of several well-known ECG signal processing techniques with several new solutions. The denoising of the ECG signal is provided by a wavelet-based filter [12]. The R-peaks are detected on a differential basis. A new adaptive beat isolator was developed, which separates the samples belonging to individual ECG beats. The separated beats are classified by a neural network, which can currently distinguish the normal sinus rhythms, ventricular and premature atrial contractions. We used a modified version of the PLA algorithm, which produced the linear approximation of the beat. The rule-based morphological segmentation is carried out by individual segmentation units specific to the beat type. The test and evaluation of the system were carried out using reference ECG databases. The segmentation precision was over 90%.

4.7. Detection of Breathing Disorders Like Apnea and Hypopnea

The most common breathing disorder is the apnea, which means the lack of breathing for certain amount of time. Episodes of apnea can happen commonly during sleep, but also at intensively cared patients and new-born babies. Frequent episodes of apnea can disturb the normal breathing process and can cause the development of metabolic, organic and nervous disorders. The diagnosis of apnea has several standardized steps, including the detection of apnea and its milder version (hypopnea), the determination of their type (central vs. obstructive) and the calculation of frequency. The applied signal processing methods evaluate the respiration signals and provide over 80% apnea detection accuracy. The determination of event type is provided only by the off-line analysis of multi-channel signal assays (e.g. polysomnography). We developed a new neural-network based apnea/hypopnea detection method, which uses the sophistically preprocessed nasal airflow signal as network input. We tested two-hour-long airflow excerpts of 16 different patients. The entire detection precision was over 90% [13].

4.8. Molecular Biology Studies with DNA-chips

This topic is focused on a DNA-sequencer system for translation of genetic information into protein-structure. Several problems have been studied in this domain:

- making electronic DNA-chips, developing new electronic hybridization and immobilization methods with polipirrol-copolimerization and with tiol-sub-groups on gold-monolayer;
- tumor development and propagation, several methodological questions, such as producing reference-RNA for microarray analysis and describing a simple recovery method of cyanine dye labelled nucleotide triphosphates;
- monitoring mRNA-expression changes and chromosomal aberrations in specific tumor-tissues and to build up a database.

Using spotted cDNA-chips it performs Comparative Genomic Hybridization and mRNA-expression monitoring examinations on metastatic lung and hepatocellular tumors and multiplex cancers associated with sclerosis tuberosa, MEN-syndrome and adrenal gland adenomas. The main goal is to gain insights and to determine genes and pathways playing role in metastasis-development and multiplex cancer development [13].

4.9. Evaluation of the Cry of Normal Hearing and Hard of Hearing Infants

Is there any difference between the cry of a normal hearing and a heard of hearing infant? What is the earliest time in the infant's life when these differences are manifested? These are the questions to answer during the investigations. The recently developed technique consists of four steps: recording, pre-processing, processing, and evaluation. Recording was performed in a quiet room, at 44100 Hz sampling frequency, the distance between the microphone and the mouth of the infant was 1 meter. Pre-processing phase contains an intelligent segmentation of stationary signal parts. The processing phase consists of extracting statistic information on the strength of the speech chorus from the clarified signal. FFT is applied to obtain the spectrum of the statistical signal. In order to perform the evaluation, the fundamental frequency of the cry has to be determined. The fundamental frequency is not the most dominant one, but the lowest useful component in the spectrum of the infant's cry. This frequency differs from infant to infant, and in most cases is situated between 400Hz and 600Hz. The fundamental frequency is determined using the Fourier transformation spectrum called cepstrum. The diagnosis of the infant cry is based on the following criterion: the dominant frequency of the normal hearing infant is an odd multiple of its fundamental frequency, while those of hard of hearing ones are even multiples [15].

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