

UNIVERSITY OF SZEGED
FACULTY OF SCIENCE AND INFORMATICS
DEPARTMENT OF EXPERIMENTAL PHYSICS

Improvement and application of examination methods in automated processing of neurocardiological fluctuations

PhD dissertation theses

Written by:
Norbert Csík

Supervisor:
Dr Zoltán Gingl
senior lecturer

SZEGED
2012

Introduction

Electrocardiogram (ECG) and blood pressure curve are the most widely applied biological signals in constitution of cardiological diagnosis. Quantifiable consequences can be drawn upon their characteristics and fluctuations about the patient's condition, neurological state, medical history or hidden hereditary disease.

One of the most important problem - and most difficult at the same time - of ECG analysis is the efficient automated identification of QRS-complexes, specifically R-peaks that compose the basis of examinations.

Samples derived from invasive measurings or animal experiments include often stochastic features; they may contain signal errors, scale- and morphological changes, baseline fluctuations or local overloading that can make the interpretation of evalutaion more complicated. In addition, morphology of informative events can depend on the individual, the position of measuring point, the disease or the medical history. In this case the processing of samples is carried out manually through point by point data recording.

A number of detection methods and preprocessor kernels are known in the field of automated evaluation. Their efficacy can be limited almost only by the noise on the signal and the extreme diversity of ECG forms.

The object I proposed to one part of my work is to improve an adaptive peak finder method including a new nonlinear filter system that is less sensitive to noises and can be apply to automated typify fluctuations of human and animal ECG records.

Herein I introduce the application of the developed method with regard to three research areas.

- I examine the characteristics of derived TWLI parameters that are known predictive in LQT-syndrome;
- I develop such an evaluation module that is appropriate to automated record of ECG ST-elevation curve derived from ischemic precondition and which contains new algorithms to identify the convenient measuring points;
- I adapt mentioned method to animal (rabbit) ECG samples hereby establishing an efficient device in investigation of fluctuation parameters from pharmacological animal experiments

R-peaks are followed in time by blood pressure maximums that are well-measurable biological signal as well.

In other part of my work I improve and extend the application of EDAQ530 device (an open source measuring device serving educational and research purposes already introduced in education). I make said device capable of continuous monitoring of ECG fluctuations and blood pressure dynamic on plethysmographic grounds.

New and open source application of mentioned device together with instrument can now serve demonstrational, educational and research demands not only in the field of technology but in informatics and medical science as well.

New scientific results

1. During my work I developed such a QRS-detector for human ECG analysis that is suitable for effective and informative beat-to-beat assay of irregular (ST-elevation) samples including artefactums and noises.

I compared well-known preprocessor kernels of literature; then being attentive to its applicability I defined a new preprocessor transformation. I developed a segmentator algorithm on the basis of the features of the result signal which can identify R-peaks while estimates the limits of events even in case of near by signal error (potentialjump). Providing selective features to the detector I improved a method based on adaptive sample reconstruction. I tested the complete algorithm on clinical and international database to reveal the limits of its efficiency and validity. I adopted it successfully for analysing invasive samples of ST-elevation including numerous QRS. We found that the attainable 'beat to beat' analysis held more essential information on ST-elevation compared to well-known methods of literature grounding for only few measuring points [1].

2. I examined theme asuring protocol of ST-elevation and the manual beat-to-beat measurements. Based on it I improved new, automated methods to localize informative points of ST-elevation.

I defined two new procedures besides the original method to choose the measuring points taking into

consideration the morphological changing in time of the signal and the baseline fluctuation of the whole sample. I implemented and tested each algorithm in the course of clinical practice reducing stochastic properties of ST-elevation curve recorded beat to beat by the original method [1].

3. I executed the adaptation of my algorithm on animal samples comparing human and animal (rabbit) ECG-samples which allowed effective and automated examination of widely used biomarkers and fluctuations reflecting nervous system function.

In the course of my work I examined the local scale factors differences typifying the QRS segments in ECG samples of both species. I modified by simulations some of the kernel sizes of the peak detector according to animal samples keeping its robust behavior. I obtained that more corrections were necessary when processing such ECG signals that were modified artificially at a significant degree (for example AV-blocked heart). In reference to a number of research sub-projects we applied the implementation mainly to generate repolarization markers. In this context I examined the TWLI parameter which was dedicated to a kind of possible LQT indicator by Jan Nemec, Joseph B Hejlik, Wing-Kuang Shen and Michael J. Ackerman without providing reliable results in animal samples where the animals were artificially TdP sensitized. Analyzing human records it was revealed that the cubic spline-based baseline correction that we applied during the

original procedure was not applicable for intense baseline fluctuation [2-7, 10-15].

4. I made an EDAQ 530 measuring device (that was developed at University of Szeged for educational and research purposes) capable of photoplethysmographic measuring, observing and demonstrating of fluctuations upon neurocardiological parameters.

In pursuance of elaboration I improved an application which was capable of monitoring blood pressure while recording signal and analysing continuously the fluctuations of the sample.

I evolved a peak finder algorithm referring to blood pressure curve with adaptive threshold making possible to observe time development of frequent diagnostic parameters according to ECG signals by variable size of the kernel. Mentioned measuring instrument with the relevant software both have open source attribute, only the hardware stands in but at a relatively low cost. Therefor the appliance with its new complementarity can become a popular device not only for students with interests towards technology or informatics but towards biology and medicine as well [8].

Papers on which the thesis is based

- [1] SASI V. – UNGI I. – BENCSIK P. – Csík N. – GINGL Z. – UNGI T. – FERDINANDY P.: Precondition effect of repeated occlusions during elective coronary intervention. *Cardiologia Hungarica* 2007; 37:A50.
- [2] FARKAS S. A. – RUDAS L. – MAKRA P. – Csík N. – LEPRÁN I. – FORSTER T. – CSANÁDY M. – PAPP J. Gy. - VARRÓ A. – FARKAS A.: Biomarkers and endogenous determinants of dofetilide-induced Torsades de Pointes in α_1 -adrenoceptor-stimulated, anaesthetized rabbits. *British Journal of Pharmacology* 2010; Vol. 161, P. 1477-1495.
- [3] FARKAS A. – FARKAS S. A. – RUDAS L. – LEPRÁN I. – OROSZ Sz. – Csík N. – FORSTER T. – CSANÁDY M. – PAPP J. Gy. – VARRÓ A.: Basal vagal nerve activity does not predict susceptibility to dofetilide-induced torsade de pointes in anaesthetized rabbits. *Journal of Molecular and Cellular Cardiology* 2006; Vol. 40, Iss. 6. P. 984.
- [4] OROSZ Sz. – FARKAS A. – MAKRA P. – Csík N. – LEPRÁN I. – RUDAS L. – VARRÓ A. – FARKAS S. A.: Repolarization-related ECG parameters do not predict the proarrhythmic activity of dofetilide. *Journal of Molecular and Cellular Cardiology* 2007; Vol. 42, Iss. 6. P. S6.
- [5] VINCZE D. – FARKAS S. A. – RUDAS L. – MAKRA P. – Csík N. – LEPRÁN I. – FORSTER T. – CSANÁDY M. – PAPP J. Gy. – VARRÓ A. – FARKAS A.: Relevance of anaesthesia for dofetilide-induced torsades de pointes in alpha1-adrenoceptor-stimulated rabbits. *British Journal of Pharmacology* 2008; Vol. 155, P. 75-89.
- [6] FARKAS S. A. – MAKRA P. – Csík N. – OROSZ Sz. – SHATTOCK J. M. – FÜLÖP F. – FORSTER T. – CSANÁDY M. – PAPP J. Gy. – VARRÓ A. – FARKAS A.: The role of the $\text{Na}_+/\text{Ca}_{2+}$ exchanger, I_{Na} and I_{CaL} in the genesis of dofetilide-induced torsades de pointes in isolated, AV-blocked

rabbit hearts. British Journal of Pharmacology 2009; Vol. 156, P. 920-932.

- [7] FARKAS A. – FARKAS S. A. – Vincze D. – MAKRA P. – Csík N. – LEPRÁN I. – VARRÓ A. – RUDAS L.: Examination of the role of the sympathetic nervous system in the proarrhythmic activity of dofetilide. Journal of Molecular and Cellular Cardiology 2007; 42:S7
- [8] Csík N.: Real-time monitoring of frequent cardiovascular parameters on plethysmographic base. A Magyar Tudomány Ünnepe, AGTEDU 2011, 354-360. o.

Other papers and conference talks

- [9] GINGL Z. – MAKRA P. – RUDAS L. – ZÖLLEI É. – Csík N.: Spectral analysis problems of heart rate and blood pressure fluctuations. Fluctuations and Noise Letters 2007; Vol.7, P. 143-150.
- [10] FARKAS A. – FARKAS S. A. – MAKRA P. – Csík N. – LEPRÁN I. – VARRÓ A. – RUDAS L.: Examination of the role of the autonomic nervous system in the proarrhythmic activity of dofetilide in Na-pentobarbital-anaesthetized rabbits. Cardiologia Hungarica 2007; 37:A15
- [11] OROSZ Sz. – FARKAS A. – MAKRA P. – Csík N. – LEPRÁN I. – VARRÓ A. – FARKAS S. A.: Repolarization characterizing ECG variables do not predict the proarrhythmic activity of dofetilide in Na-pentobarbital-anaesthetized rabbits. Cardiologia Hungarica 2007; 37:A23
- [12] Vincze D. – FARKAS S. A. – MAKRA P. – Csík N. – LEPRÁN I. – RUDAS L. – FARKAS A.: Examination of the relationship between the autonomic effects of intravenous anaesthetics and proarrhythmic activity of dofetilide in anaesthetized rabbits. Cardiologia Hungarica 2007; 37:A29

- [13] FARKAS S. A. – Csík N. – MAKRA P. – OROSZ SZ. – FORSTER T. – CSANÁDY M. – PAPP GY. – VARRÓ A. – FARKAS A.: The effect of verapamil and lidocaine on the QT/RR variability and on the genesis of dofetilide-induced torsade de pointes. *Cardiologia Hungarica* 2008; 38:B13
- [14] FARKAS S. A. – Csík N. – MAKRA P. – OROSZ SZ. – FORSTER T. – CSANÁDY M. – PAPP GY – VARRÓ A. – FARKAS A.: The effect of verapamil and lidocaine on the QT/RR variability and on the genesis of dofetilide-induced torsade de pointes. *Magyar Kardiológusok Társasága* 2008. Évi Tudományos Kongresszusa, Balatonfüred.
- [15] FARKAS S. A. – MAKRA P. – Csík N. – OROSZ SZ. – FORSTER T. – CSANÁDY M. – PAPP J. GY. – VARRÓ A.– FARKAS A.:The role of the $\text{Na}_+/\text{Ca}_{2+}$ exchanger in the genesis of dofetilide-induced torsades de pointes ventricular tachycardia. *A Magyar Kísérletes és Klinikai Farmakológiai Társaság és a Magyar Élettani Társaság* LXXII. Vándorgyűlés 2008, Debrecen.
- [16] Csík N.: Automatic processing of the ST-elevation. *A Magyar Tudományos Akadémia Szegedi Területi Bizottsága, Fiatal Kutatók Pályázata*, II. helyezés, 2009.
- [17] Csík N.: Effective detection of events in human ECG. *A Magyar Tudomány Ünnepe AGTEDU* 2006, 317.-321.o.
- [18] Csík N.:ST-eleváció meghatározása emberi EKG-ban. *A Magyar Tudomány Ünnepe AGTEDU* 2007, 219.-224.o.
- [19] Csík N.: Nonlinear filter system for detection of events in human ECG. *A Magyar Tudomány Ünnepe AGTEDU* 2009, 493.-498.o.