SESSION XIV

PHYSIOLOGY MEETS ENGINEERING

Friday (September 17, 2021; 9:00 – 11:55)

Chair:

Prof. Teresa Malecka-Massalska
Department of Human Physiology, Medical University in Lublin, Lublin, Poland

Assoc. Prof. Teodor Buchner
Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

DETAILED SESSION XIV SCHEDULE

Opening lectures (Friday, September 17, 2021; 9:00 – 9:50; *virtual stream A*)

S14.L1 TISSUE ELECTRIC IMPEDANCE MEASUREMENTS: FROM PROPER UNDERSTANDING OF PHYSICS TONE TO NEW FUTURE IN CLINIC. **T. Buchner** (Faculty of Physics, Warsaw University of Technology, Warsaw, Poland).

S14.L2 ELECTRICAL PARAMETERS OF BIOLOGICAL SYSTEMS (ECIS TECHNIQUE) IN THE STUDY OF THE CHEMOPREVENTIVE AND THERAPEUTIC POTENTIAL OF SUBSTANCES OF BIOLOGICAL ORIGIN. **M. Prendecka-Wrobel[1], A. Kociubinski[2]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Faculty of Electrical Engineering and Computer Science, Department of Electronics and Information Technology, Lublin University of Technology, Lublin, Poland).

Oral presentations (Friday, September 17, 2021; 9:55 – 10:45; *virtual stream A*)

S14.L3 MACHINE LEARNING FOR PREDICTING THE OCCURRENCE OF SYMPATHETIC BURSTS BASED ON THE NONINVASIVE RECORDING OF CARDIOVASCULAR PARAMETERS. **B. Paleczny[1], R. Seredynski[1], A. Siennicka[1], A. Kotwica[2], R. Zygala[2], M. Pondel[2], M. Sinski[3], J. Lewandowski[3], B. Ponikowska[1]** ([1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland, [3]Medical University of Warsaw, Warsaw, Poland).

S14.L4 MALE REPRODUCTIVE FUNCTION UNDER CONDITION OF TREATMENT WITH GOLD ANOCOMPOSITES. **O. Kaleinikova[1], S. Ukrainska[1], V. Sribna[1], Y. Kuziv[2], A. Vinogradova-Anyk[3], I. Karvatskiy[3], T. Voznesenskaya[1], T. Blashkiv[1], N. Kutsevol[2]** ([1]Bogomoletz Institute of Physiology, NAS of Ukraine, Kyiv, Ukraine, [2]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, [3]Bogomoletz National Medical University, Kyiv, Ukraine).

S14.L5 STABILIZATION OF PHYSIOLOGICAL FUNCTIONS OF CELLS IN THE ECIS ELECTRODE SYSTEM METALLIZED WITH CHROMONIKELIN AND COPPER. **M. Prendecka-Wrobel[1], A. Kociubinski[2], T. Malecka-Massalska[1]** (Department of Physiology, Medical University of Lublin, Poland; Lublin University of Technology, Faculty of Electrical Engineering and Computer Science, Lublin, Poland).

Session summary

Poster session (Friday, September 17, 2021; 11:05 – 11:55; *virtual stream C*)

S14.P1 ASYMMETRIC PROFILE OF SPONTANEOUS SEQUENTIAL CHANGES OF BLOOD PRESSURE COUPLED WITH MONOTONIC CHANGES OF SUCCESSIVE HEARTBEATS IN UNRESTRAINED NORMOTENSIVE RATS. **S. Zajaczkowski, T.H. Wierzba** (Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S14.P2 IMPAIRED BLOOD PRESSURE REGULATION IN SHR RATS ASSESSED BY DETAILED ANALYSIS OF MONOTONIC RUNS OF BLOOD PRESSURE AND HEART RATE. **T.H. Wierzba, K. Malinowski, G. Redlarski** (Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S14.P3 HOW DATA SCIENCE MAY SUPPORT PHYSIOLOGICAL EXPERIMENTS? A REVIEW OF EXAMPLES AND POSSIBILITIES. **A. Siennicka[1], B. Paleczny[1], R. Seredynski[1], M. Pondel[2], M. Wyciszkiewicz[1], T. Okupnik[1], B. Ponikowska[1]** ([1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland).

S14.P4 CARDIAC AND NON-CARDIAC SOURCES OF T WAVE MORPHOLOGY. **K. Rams[1], M. Ozimek[1], M. Andrzejewska[1], T. Buchner[1]** ([1]Faculty of Physics, Warsaw University of Technology, Warsaw, Poland).

S14.P5 HEART RATE DYNAMICS IRREVERSIBILITY AND INFORMATION FLOW IN TYPE 1 LQTS PATIENTS UNDER BETA BLOCKER TREATMENT. **M. Andrzejewska, M. Ozimek, J.J. Zebrowski, K. Rams, T. Buchner** (Faculty of Physics, Warsaw University of Technology, Poland).

S14.L1

TISSUE ELECTRIC IMPEDANCE MEASUREMENTS: FROM PROPER UNDERSTANDING OF PHYSICS TO NEW FUTURE IN CLINIC

T. BUCHNER

Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

Attempting to answer a seemingly simple question: how fast is the ECG signal? We ran at many interesting contradictions, concerning the physical nature of biopotential. What does actually change in tissue when the biopotential propagates to the electrode? This area, shared between clinicians, (electro)physiologists, neurophysiologists, bioengineers, electrochemists and biophysicists is a real Tower of Babel, where each specialty speaks its own language. Solving the riddle of biopotential by means of a new molecular biopotential theory seems to simplify our understanding of bioelectrical phenomena on systemic level. Basic phenomena, which constitute a foundation for propagation of biopotentials are outlined. The unequivocally believed volume conductor theory is opposed on anatomical basis. Relation between conductance an polarization is shown, with its crucial consequence: the relation between biopotential propagation and impedance spectrum. Some consequences concerning clinical applications are drawn: various patophysiological states have altered conductance response: from epilepsy, tumors (and other states of pronounced angiogenesis), arrhythmogenic myocardial scars to extravascular lung water and ventillation- perfusion ratio. Caveats, which also exist, include impedance cardiography and total body water measurements, which are very promising and quite widespread, but constantly suffer from poor measurement model. What is provoking in this theory is its simplicity, which allows its wide usage: from basic science to clinical intuition, which supplements the diagnosis. It is tempting to conclude, that if we change the paradigm, the full diagnostic power of impedance methods will be unleashed.

Author for correspondence: Teodor Buchner (buchner@if.pw.edu.pl)

S14.L2

ELECTRICAL PARAMETERS OF BIOLOGICAL SYSTEMS (ECIS TECHNIQUE) IN THE STUDY OF THE CHEMOPREVENTIVE AND THERAPEUTIC POTENTIAL OF SUBSTANCES OF BIOLOGICAL ORIGIN

M. PRENDECKA-WROBEL[1], A. KOCIUBINSKI[2]

[1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Faculty of Electrical Engineering and Computer Science, Department of Electronics and Information Technology, Lublin University of Technology, Lublin, Poland

The thesis of the presentation is based on literature reports indicating possible therapeutic and chemopreventive activity of substances of biological origin and the probability of showing the character of these effects using selected electrical parameters, i.e. impedance, resistance and cell membrane capacity. Therapeutics and chemopreventive substances work in various ways including induction of apoptosis of pathologically altered cells. This group of biological substances includes antioxidants, vitamin A, fungal extracs and lycopene among others. Compared to other methods of for e.g. cancer prevention, chemoprevention is associated with lower costs, no invasiveness and utilization of easily accessible natural components, which is very important from both social and economic perspective. And the potential of medical fungi has not been fully used in chemoprevention yet. Literature reports say that medical fungi include a series of bioactive substances, which have been used mainly in textile and paper industry so far. In the face of new technical possibilities and assuming, that changes in the electrical properties of cells precede changes on the biochemical level, it would be very interesting to examine the character and dynamics of changes leading to desirable therapeutic or chemopreventive effects. It is possible with monitoring of selected electrical parameters i.e.: impedance, resistance and capacity of cell membrane in real time after application of chosen bioactive compounds to the examined cell lines. Resistance is a physical quantity describing relations between electric current voltage and strength in direct current circuits. It is commonly depicted with letter R and its SI unit is Ω (ohm). In direct current circuits resistance is directly proportional to voltage between the extremes of the conductor and inversely proportional to the strength of electric current but this correlation, known as the Ohm's Rule, is only valid in certain ranges of voltage value. Impedance is a quantity characterizing the correlation between electric current voltage and strength in alternate current circuits (opposite to resistance where direct current circuits are used). It is described as a complex function, which, for alternate current with frequency ω is expressed using the following formula:

$Z(\omega) = R(\omega) + iX(\omega)$, where $X(\omega)$ is reactance, which can be also transcribed as:

$Z(\omega) = |Z|e\text{-}j\varphi$, where φ is phase shift between current voltage and strength.

Electric capacity is considered, to be a physical quantity equal to the ratio of charge collected on the conductor to the potential of the conductor. Understanding the interaction of cells with biological substances and reflecting these changes in electrical parameters is a fascinating and hugely promising challenge.

S14.L3

MACHINE LEARNING FOR PREDICTING THE OCCURRENCE OF SYMPATHETIC BURSTS BASED ON THE NONINVASIVE RECORDING OF CARDIOVASCULAR PARAMETERS

B. PALECZNY[1], R. SEREDYNSKI[1], A. SIENNICKA[1], A. KOTWICA[2], R. ZYGALA[2], M. PONDEL[2], M. SINSKI[3], J. LEWANDOWSKI[3], B. PONIKOWSKA[1]

[1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland, [3]Medical University of Warsaw, Warsaw, Poland

The development of the microneurography technique in the 1960s was a milestone for autonomic neuroscience. Microneurography includes the percutaneous insertion of the needle-like microelectrode into the peripheral nerve, which enables direct intraneural recording of sympathetic outflow to the vasculature of the muscles (muscle sympathetic nerve activity, MSNA) in conscious humans. However, it is a technically demanding procedure characterized by a high ratio of failed attempts and prolonged recordings (>1 h) are contraindicated due to safety reasons. These limitations can be overcome by employing machine learning (ML) to retrieve the MSNA signal from physiological correlates of MSNA (i.e. total peripheral resistance) recorded simultaneously and noninvasively. We attempted to use ML to reconstruct the occurrence of MSNA bursts from the cardiovascular parameters recorded simultaneously and noninvasively. The 10-minute recording of the following signals: (1) multi-unit MSNA (raw and integrated), (2) arterial blood pressure waveform (recorded by the Nexfin monitor), (3) III-lead limb ECG, and (4) hemodynamic variables derived from the blood pressure waveform (systolic, diastolic, and mean blood pressure and total peripheral resistance), collected from a healthy volunteer was used. The Gradient Boosting (XGBoost) algorithm was employed for the prediction of the MSNA bursts occurrence. The recording was divided into two sets: the training set (60% of the whole recording), and the test set (40%). The Gradient Boosting algorithm accurately predicted the occurrence of 71.8% of the MSNA bursts in the test set. The preliminary results obtained with the non-optimized algorithm are encouraging and suggest that it is feasible to reconstruct the occurrence of the MSNA bursts from the simultaneous noninvasive recordings of the cardiovascular parameters, at least with moderate accuracy.

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Author for correspondence: Bartlomiej Paleczny (bartlomiej.paleczny@umed.wroc.pl)

S14.L4

MALE REPRODUCTIVE FUNCTION UNDER CONDITION OF TREATMENT WITH GOLD NANOCOMPOSITES

O. KALEINIKOVA[1], S. UKRAINSKA[1],V. SRIBNA[1], Y. KUZIV[2], A. VINOGRADOVA-ANYK[3], I. KARVATSKIY[3], T. VOZNESENSKAYA[1], T. BLASHKIV[1], N. KUTSEVOL[2]

[1]Bogomoletz Institute of Physiology, NAS of Ukraine, Kyiv, Ukraine, [2]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, [3]Bogomoletz National Medical University, Kyiv, Ukraine

Recently, it has been proved that polymers with a dextran core and grafted polyacrylamide chains dextran-polyacryl-amide (D-PAA) are effective in photodynamic chemotherapy, which gives confidence in the prospect of drug-nanosystem. This study aim is to evaluate the influence of a five-time treatment of polymers with a dextran core and grafted polyacrylamide chains dextran-polyacrylamide (D-PAA and D-PAA(PE)), as well as gold nanoparticles in the composition of such polymer matrices on the male reproductive function in mice. Experiments were carried out with the use of adult male albino Albino mice (weighing 25–30 g). We used an „uncharged" star-shaped polymeric matrices of D-PAA (dextran-polyacrylamide) and „charged" D-PAA(PE) (dextran-polyacrylamide polyelectrolyte). Hydrodynamic dimensions of both types of macromolecules are 70–80 nm. The size of the Au nanoparticles loaded in D-PAA, 2–5 nm, and the nanosized gold synthesized in D-PAA(PE) has sizes 4–11 and 16–20 nm. Au nanoparticles have a spherical shape. The obtained data indicate the disorder of the reproductive function of males under the conditions of five times intravenous treatment with gold nanoparticles in the polymer matrix D-PAA(PE), namely - there are significant changes in the viability and death of cells of different generations of spermatozoa and an increase in pre- and postimplantation embryonic mortality and a decrease in the number of live fetuses per female. Whereas, under the conditions of such administration, the introduction of D-PAA and D-PAA(PE), as well as AuD-PAA, no significant changes were observed in: 1) sperm and abnormal sperm forms (%); 2) spermatocytes (primary) and spermatids (%); 3) living, apoptotic and necrotic testicular cells (spermatocytes (primary)) and in the epididymis cells (spermatozoa); as well as in: 4) pre- and post-implantation mortality of embryos; and 5) the number of live newborns (pups).

Author for correspondence: (svetlanamavr@ukr.net)

S14.L5

STABILIZATION OF PHYSIOLOGICAL FUNCTIONS OF CELLS IN THE ECIS ELECTRODE SYSTEM METALLIZED WITH CHROMONIKELIN AND COPPER

M. PRENDECKA-WROBEL[1], A. KOCIUBINSKI[2], T. MALECKA-MASSALSKA[1]

[1]Department of Physiology, Medical University of Lublin, Lublin, Poland,
[2]Lublin University of Technology, Faculty of Electrical Engineering and Computer Science, Lublin, Poland

Looking for an alternative to the currently used one gold, currently used in measuring plates for testing the electrical parameters of cells in the system ECIS. This work focuses on the interesting materials such as chrome nickel and copper. The aim of the conducted research was to determine the effect of chromonikelin and copper on the growth of cell culture during *in vitro* testing. In addition, specifying under what conditions the use of a given material will be sufficient and will open up new development paths. As part of the research work, chromonikelin and copper comb capacitors on biocompatible substrates were designed and manufactured. Metallization layers were deposited by magnetron sputtering on various materials. In the experiment cells from the mouse fibroblast line - NCTC clone 929 [L cell, L-929, strain L derivative] (ATCC® CCL-1™) from the American Type Culture Collection were used. During the cultivation, cell impedance measurements were performed and recorded. The best results were obtained on polycarbonate substrates, meeting all the defined requirements, incl. biocompatibility and resistance to chemical solutions used during technological works. The designed geometry of the comb capacitors was obtained by the photolithography process. Preliminary results of measurements on the plates have shown that it is possible carrying out the cultivation on chromonikelin and copper electrodes. No problems with proliferation and viability of cells were observed on the test plates. The obtained results make it possible to assess the possibilities of using chromonikelin and copper in various biotechnological applications.

Author for correspondence: Monika Prendecka-Wrobel (monika.prendecka-wrobel@umlub.pl)

S14.P1

ASYMMETRIC PROFILE OF SPONTANEOUS SEQUENTIAL CHANGES OF BLOOD PRESSURE COUPLED WITH MONOTONIC CHANGES OF SUCCESSIVE HEARTBEATS IN UNRESTRAINED NORMOTENSIVE RATS

S. ZAJACZKOWSKI, T. H. WIERZBA

Department of Physiology, Medical University of Gdansk, Gdansk, Poland

An intriguing physiological phenomenon is occurrence of short periods of monotonic beat-to-beat changes of systolic blood pressure (SBP, increasing or decreasing runs) accompanied by unidirectional runs of RR intervals (RRi deceleration or acceleration). The study was performed to assess the occurrence of spontaneous sequential changes in BP coupled with monotonic changes of intervals of successive heartbeats (RR intervals; RRi) in rats in resting conditions. The experiments were performed on unrestrained male Wistar rats (N=11, 300–350 g). ECG and systolic blood pressure (SBP) were recorded continuously at sampling rate 1.5 kHz. Sequences of 3 to 6 unidirectional changes of SBP and RRi were identified. Proportion of the SBP sequences coupled to the monotonic changes of RRi time-series was taken as an index of baroreflex sensitivity (BRS). Sequences of SBP increase or decrease were analyzed separately. Two types of SBP sequences were discriminated: the concordant, in which SBP and RRi changed in the same direction (considered the baroreflex effect), and the opposite, where changes of SBP coincided with inverse changes in RRi (regarded as a feed-forward cardiovascular setting). Proportion of the baroreflex-related (concordant) SBP sequences to all SBP sequences were taken as baroreflex efficacy (BEI). SBP was 134 ± 5 mmHg and HR 181 ± 6 bpm. The sequences of an increase of SBP involved 10.1% of all cardiac cycles and were more frequent than its declining (7.4%). RRi prolongation sequences (10.5%) were less frequent than those of RRi shortening. Proportion of RRi sequences coupled with SBP-increase sequences was about 69% higher in the feed-forward sequences (^SBP and ¡RRi than in the concordant ones (^SBP and ^RRi). In contrary, the feed-forward sequences of SBP decrease (¡SBP and ^RRi) occurred less frequent than the opposite ones (¡SBP and ¡RRi). Spontaneous variability of SBP and RRi have a well-determined irregularity. More frequent attempts to adjust high blood pressure are coordinated with an increased reflex control against its reduction. Analysis of the beat-to-beat fluctuations of SBP and RRi revealed non-random pattern of spontaneous hemodynamic oscillations. It is recommended, in light of non-uniform profile of sequential beat-to-beat changes of RRi and SBP, that the sequences of either an increase or a decrease of SBP should be analyzes separately.

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Author for correspondence: Stanislaw Zajaczkowski (stanislaw.zajaczkowski@gumed.edu.pl)

S14.P2

IMPAIRED BLOOD PRESSURE REGULATION IN SHR RATS ASSESSED BY DETAILED ANALYSIS OF MONOTONIC RUNS OF BLOOD PRESSURE AND HEART RATE

T.H. WIERZBA, K. MALINOWSKI, G. REDLARSKI

Department of Physiology, Medical University of Gdansk, Gdansk, Poland

Spontaneously hypertensive rats (SHR) represent experimental model corresponding to human hypertension of mostly neurogenic background. Observation of spontaneous fluctuations and coherence between major hemodynamic variables such as systolic blood pressure (SBP) and heart rate (HR) offers an advanced insight to the regulatory aspects of hypertension. The study was performed to compare the occurrence of spontaneous sequential changes in SBP coupled with monotonic changes of intervals of successive heart cycles (RR intervals; RRi). ECG and systolic blood pressure (SBP) were recorded at sampling rate 1.5 kHz in previously instrumented (insertion of arterial line, ECG electrodes) conscious male spontaneously hypertensive rats (SHR; n=7; 306–344 g), and their respective control (WKY; N=7; 302–355 g). Sequences (Seq) of 3 to 6 unidirectional changes of SBP and HR were identified. Proportion of the SBP sequences coupled to the HR (cSeq) ones was taken as an index of baroreflex sensitivity (BRS). Two types of cSeq were discriminated: the concordant, in which SBP and HR changed in the same direction (interpreted as a feed-forward baroreflex setting), and the opposite (considered the baroreflex effect), where changes of SBP coincided with inverse changes in HR. Proportion of the baroreflex related SBP sequences to all cSeq sequences were taken as baroreflex efficiency (BEI). SHR exhibited higher SBP and lower HR than WKY (191 vs. 135 mm Hg; 307 vs. 319 beats/min). Compared to the WKY control, in SHR rats: 1) frequency of runs of an increase of SBP was higher, while occurrence of sequential SBP decrease was lower; 2) higher frequency of HR acceleration with lower deceleration runs was observed; 3) higher BEI of an increase of SBP, and lower BEI for a SBP decrease was found. In SHR the latency between the beginning of an increase of SBP and the onset of the following monotonic HR runs was prolonged. BRS was reduced in either cSeq of an increase and a decrease of SBP. Our data indicate profound regulatory dysfunction in SHR rats. The observed regulatory profile reflects reduced chance for the reflex correction of an increase in blood pressure, with impaired counter-regulatory defense against its decrease. Moreover, an increased phase shift between the HR and SBP reflex responses may promote sudden critical cardiovascular incidents.

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Author for correspondence: Tomasz H. Wierzba twierzba@gumed.edu.pl

S14.P3

HOW DATA SCIENCE MAY SUPPORT PHYSIOLOGICAL EXPERIMENTS? A REVIEW OF EXAMPLES AND POSSIBILITIES

A. SIENNICKA[1], B. PALECZNY[1], R. SEREDYNSKI[1], M. PONDEL[2], M. WYCISZKIEWICZ[1], T. OKUPNIK[1], B. PONIKOWSKA[1]

[1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland

Nowadays, scientific research in the field of life sciences, including human physiology, is carried out with the use of numerous devices (such as monitors of blood pressure, ECG, muscle tension analysers, pulsoximeters, breathing gas analysers etc.), which are able to collect data in digital form. As a result of an enormous sensitivity and accuracy of the measurements performed during each physiological examination, single test or experiment can serve as a source of huge amounts of data. At the same time, the classic approach to experiments and analysis based on statistics (comparison of values before and after the intervention, correlation analysis) excludes taking full advantage of the amount of collected digital information. During a cooperation with specialists in the field of data science, we decided to transfer some solutions based on modern methodology of large data-sets analyses to physiological experiments in the field of autonomic regulations of cardiovascular and respiratory systems at rest as well as during an exercise, which are carried out within the Department of Physiology and Pathophysiology of WMU. The attempts which were made to date show that data science (including methods such as collective clustering, neural networks, association rules, machine learning, deep learning and related) can be widely used in analyzing physiological data, which may include: forming predictions (eg. predicting a missing signal from another signal or predicting changes of signals based on their initial values and changes registered during first seconds of the examination) proposing more precise methods of signal filtering and many other applications.

Acknowledgements: This presentation results from a project: HeartBIT_4.0 - Application of innovative Medical Data Science technologies for heart diseases. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement number 857446.

Author for correspondence: Agnieszka Siennicka (agnieszka.siennicka@umed.wroc.pl)

S14.P4

CARDIAC AND NON-CARDIAC SOURCES OF T WAVE MORPHOLOGY

K. RAMS, M. OZIMEK, M. ANDRZEJEWSKA, T. BUCHNER

Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

When the morphology of the ECG is analyzed, there is often a tendency to interpret the observed symptoms as a sole result of electric activity of cardiac muscle, and to treat all the factors that modify the ECG as environmental noise, even if it is a symptom itself, as for pericarditis or P pulmonale. In order to circumvent these opinions we have performed a thorough analysis of patients in THEW database - Holter ECG, 200 Hz sampling, 24 h signals. Study group consists of 235 patients: 125 healthy, 86 w/LQTS1, 21 w/LQTS2, 2 w/LQTS3. Gender ratio was close to 0.5 with 129 females, and 106 males. We started from a detailed analysis of QT/RR relationship and we found that the idea of restitution: i.e the dominant role of the APD/DI relation on the whole QT and RR dynamics does not hold, as each of signals may exhibit a certain extent of its own dynamics. Of special importance are the QT increases at increasing HR, which correspond to the negative QT(RR) regression slope (Baranowski, Buchner, *European Heart J* 2003). They may appear as isolated islands in QT-RR plot. It is an open question whether this discrepancy may be interpreted as a symptom of ischemia (J.M. Starobin, Y.B. Chernyak, US patent 6,361,503). We also show, that the amplitude of the T wave does not directly follow the amplitude of the QRS, so these two variables are to some extent statistically independent. This means, that the T wave possesses a different source of information, not necessarily related to both the interval and the amplitude of the QRS. This well corresponds to the clinical value of T-wave axis, both in CAD patients (Scherer *et al*., *Scand Cardiovasc J* 2009) and in population with high prevalence of Chagas disease (Moraes *et al*., *Am J Cardiol* 2018). Postural changes of ST-T may even mimic myocardial ischemia (Lachman *et al*., *Circulation* 1965). The question of the origin of the observed changes, their relation to the position of the body and their potential clinical correlates is a matter of an ongoing study.

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Author for correspondence: Teodor Buchner (teodor.buchner@pw.edu.pl)

S14.P5

HEART RATE DYNAMICS IRREVERSIBILITY AND INFORMATION FLOW IN TYPE 1 LQTS PATIENTS UNDER BETA BLOCKER TREATMENT

M. ANDRZEJEWSKA, M. OZIMEK, J.J. ZEBROWSKI, K. RAMS, T. BUCHNER

Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

There is a big question of statistical independence in physiological timeseries: which physiological variables can be treated as independent sources of clinical data and which just mimic each other. Another question concerns time-irreversibility: is the studied signal a sum of responses to some unknown stimuli? In such a case the time symmetry of the signal is broken due to signal causality constraint. We decided to answer this question on a big database of Holter recordings. Two databases from the THEW Project were used to provide the RR, QT and the DI intervals: E-HOL-03-0202-003 (202 ECG of healthy individuals) and E-HOL-03-0480-013 (480 ECGs of the Long QT Syndrome patients forming 4 subgroups by genotype). In this paper, we analyze only the LQTS1 patients - this is the most frequent type of the long QT syndrome. We limited the study group to age subgroup 18–50 years obtaining 84 (42 women) ECGs for the healthy and 65 (45 women) cases for the LQTS1 case (Ozimek *et al*., 2021). The results show, that with $p < 0.01$ both irreversibility and information flow shows no response to beta blocker treatment. This result indirectly shows, that the key factor, which determines such quantities of the signal as its irreversibility and information flow is the parasympathetic nervous system, at least in LQTS 1 patients. Typically, the role of sympathetic nervous system in baroreflex is emphasized, note, however, that for Anrep *et al*. regulation of right atrium pressure was the method to set the vagal tone in dog experiments (Anrep 1936). Hence, we support the opinion on a dominant role of parasympathetic over sympathetic mechanisms, expressed by Karemaker and Wesseling (Cardiovasc Eng, 2008).

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Author for correspondence: Malgorzata Andrzejewska (malgorzata.andrzejewska.dokt@pw.edu.pl)