REVIEW

of the dissertation work for the degree "Doctor of Science."

Author of the dissertation: Assoc. Prof. Eng. Galya Nikolova Georgieva - Tsaneva, PhD

Dissertation topic: "HYBRID APPROACHES FOR BUILDING A DIGITAL TWIN OF HEART RATE VARIABILITY"

Member of the scientific jury: Prof. DSc Eng. Ivo Tsvetanov Iliev

1. Relevance of the problem developed in the dissertation work in scientific and applied scientific terms.

The quality of the modern medical diagnostic process, in addition to the knowledge, skills, and experience of the medical staff, is directly dependent on the level of its hardware and instrumentation. A permanent trend in the development of medical technology is the application of the latest technological achievements. The goal, on the one hand, is to obtain maximum volume and diagnostically reliable information, and, on the other, to achieve an optimal treatment effect with gentle application. In the modern diagnostic process, more and more attention is paid to prevention and the early detection of symptoms, which is associated with continuous monitoring of key parameters and processes in the patient's natural living environment, without restricting their daily activities. Heart rate variability (HRV) is an important vital sign indicator, providing information about autonomic regulation, physiological stress, fatigue, and the body's adaptive mechanisms. The research in the dissertation is aimed specifically at building a digital twin of HRV, combining analysis, modelling, and data protection, with applications in intelligent monitoring and personalised.

2. Degree of knowledge of the state of the problem and creative interpretation of the literary material.

The review section presents an in-depth literature review, evidence of creative interpretation of the results achieved, and directions for future development in the dissertation's subject area.

The focus is on aspects directly related to the content of the individual chapters in the dissertation, such as:

- Methods for filtration, detection, simulation and assessment of physiological states based on modern approaches for analysis and processing of electrocardiographic (ECG) and photoplethysmographic (PPG) signals;
- Specific requirements and methods for the protection of cardiological data in telemedicine applications;
- Differentiation of physiological states in athletes and when performing activities related to serious physical exertion.

A total of 235 literary sources are cited, the majority of which are from the last ten years. All sources are cited in an appropriate place in the text and adequately support the author's thesis.

At the end of the review chapter, conclusions are drawn regarding: (1) - the sensitivity of PPG and ECG signals to noise and motion artifacts, the strong individual physiological variability between different individuals, as well as the lack of integral indicators that would unite linear and nonlinear HRV metrics into a single analytical framework; (2) - The limitations in long-term prediction of autonomic adaptation related to the lack of validated digital twins tested in real conditions.

3. Correspondence of the chosen research methodology and the set goal and tasks of the dissertation with the contributions achieved.

As a result of the analysis and conclusions regarding the current state of research in the field of the dissertation, its main goal has been defined: Development and research of an integrated hybrid methodological framework for processing, analysis, modelling and protection of cardiological signals, based on a combination of classical mathematical and modern AI approaches, supporting the construction of a digital twin of heart rate variability in IoT environments.

Seven tasks have been defined for implementation, which correspond to the set goal. The overall presentation clearly shows the systematic approach to solving specific tasks, including:

- Theoretical analysis and reasoned assessment of achievements, as well as unsolved problems in the field;
- Synthesis and research of a hybrid methodological framework for processing, analysis, modelling, and data protection, based on modern AI approaches, to build a digital twin of HRV.
- Analysis of the results obtained and optimization of the developed methods and algorithms to achieve the necessary reliability.

4. An analytical description of the content and assessment of the credibility of the material on which the contributions of the dissertation are based

The presentation of the activities related to the implementation of the formulated tasks covers 5 chapters of the dissertation. At the beginning of the dissertation, the overview section discusses theoretical statements related to two of the main methods for HRV analysis, namely, those based on registered ECG and PPG signals. The individual aspects of both the signal parameters and the superimposed interference are examined in detail, especially under conditions of free movement of the subject under study. Various methods for removing interference and subsequent analysis of the filtered signals to identify characteristic areas (R-peak, pulse-wave maximum) are considered. As a natural continuation, methods for assessing heart rate variability are presented. In addition to the classical methods in the time and frequency domains, some heuristic methods are also presented, such as the Poincaré method in the two-dimensional and spatial domains, analysis of graphic repetitions, quantitative analysis of repetitions, the Hurst exponent and analysis of long-term dependence, fractal and entropy analysis of heart rate variability, etc. It should be noted that, aside from the traditional methods, the others are mainly tested as components of scientific research and still lack significant clinical application. Further in the same chapter, methods and approaches for simulating cardiological signals are presented - physiological cell models, generative AI, stochastic, generative neural, etc., noting that although with a high degree of reliability, there are still certain challenges in terms of modeling realistic motion artefacts, as well as the lack of holistic simulation frameworks that would allow adaptation of parameters in real time in response to load, stress, thermoregulation and peripheral perfusion. All this limits the incorporation of HRV simulations into digital twins of autonomic regulation. Regarding the protection of cardiological data, the literature review concludes that combining cryptographic techniques with digital watermarking methods appears to be an effective strategy for increasing security.

The number of publications in the first chapter is 5.

In the second chapter of the dissertation, developments aimed at reducing interference that affects the detection of characteristic regions in biomedical signals are presented. The focus is on PPG analysis. The processing algorithms are (1) a multifactorial wavelet-based method for adaptive noise reduction in PPG signals, including DWT with different bases, decomposition levels and threshold rules, and (2) a real-time PPG noise reduction algorithm, designed for integration into portable and low-power devices, based on standard digital procedures. Regarding the detection of maxima (P-peaks) in PPG, a hybrid wavelet-based method using time-frequency signal transformation, derivatives, the zero-crossing method, DWT and threshold processing is presented, as is a method based on integrating DWT with two types of neural networks - CNN and LSTM. The total number of publications under the second chapter is 5.

A separate chapter of the dissertation is devoted to the mathematical modelling of HRV, PPG and ECG signals. Regarding HRV, a Gaussian-based model is used to generate varying heart rhythms by summing a limited number of Gaussian functions (typically 3 or 4). Further development of the model introduces fractality into the simulated HRV series using a modified Hosking algorithm with a time-varying Hurst exponent. Regarding the PPG signal, the Gaussian model for describing the pulse waveform is combined with statistical temporal modelling using the ARIMA method, which is designed to reproduce the long-term non-stationarity and circadian dynamics of real recordings. The model is upgraded to a variant designated as Deep-SimPPG by including a GAN-amplifier to add morphological and noise dynamics, maximising the similarity of the synthesised signal to the real one. The final part of the chapter presents a nonlinear simulation model of ECG signals, based on Gaussian Mesa Functions (GMF) for the morphological description of P, QRS and T waves and a chaotic Rössler attractor for modelling the variability of RR intervals. The model can be considered complex, given the possibilities for the controllable formation of cardiac cycle morphology and the physiologically reliable reproduction of the non-stationary and fractal dynamics of heart rhythm. All proposed models and methods for HRV analysis and classification have been experimentally validated on real and/or synthesised data and evaluated using standard quantitative measures. The results show stable, deterministic behaviour of the models under different conditions, including in the presence of noise characteristic of these types of signals. The number of publications under the third chapter is 6.

In the fourth chapter of the dissertation, a model for the cryptographic protection of cardiological data is presented to address the need to protect data during transfer between a real subject and its virtual digital twin. Its essence consists of the sequential application of: (1) wavelet transform; (2) hybrid cryptography in two steps - symmetric encryption (AES) applicable to large volumes of data and asymmetric encryption (RSA) used for the secure management and exchange of symmetric keys; (3) digital watermarking containing data about the subject under study. Results from the experimental validation of the proposed cryptographic model on eight real ECG signals of a specified duration, exhibiting diverse morphological characteristics and amplitude-time variations, are presented. Validation was also performed with respect to the compression algorithm to reduce the data volume to the diagnostically important sections of the signals, as well as the influence of watermarking on the diagnostic quality of the transferred data after their recovery in the receiving tract. Part of this chapter presents an analysis and specific solutions for implementing a principle for protecting cardiological data, based on the concept of region-aware security. This formulation implies the need for preliminary detection of diagnostically significant regions in the registered signals. Number of publications on chapter four – 3

The last chapter of the dissertation unifies the methodology and algorithms presented in the previous three chapters into a common conceptual implementation of an HRV digital twin. The studies were conducted with athletes at time points before physical exertion, during training, and 2 (in some cases 12) hours after training. The emphasis is on the real-time algorithmic identification of physiological states and the formulation of interpretable indices for clinical telemonitoring using wearable devices. The informativeness of more than 20 HRV-related parameters (indices), both independently and in various multi-vector combinations, has been statistically assessed. For example, the developed adaptive multi-index method for automatic detection and signalling of physiological risk, implemented as a hybrid system for analysis and decisionmaking, as well as the three new indices FDTI, RDTI, and PDTI for assessing the body's fatigue/stress after physical/mental exertion. The obtained results are appropriately illustrated. The number of publications under this chapter is 6.

5. Scientific and/or applied scientific contributions of the dissertation work

The author's claims regarding the significance of the results achieved in the dissertation are formulated in three categories of contributions - scientific, scientific-applied and applied. Scientific contributions predominate, which directly corresponds to the scope of the synthesised algorithms and methods for pre-processing and detection of peak values in ECG and PPG signals. The presented AI approach, integrating wavelet decomposition, a CNN–LSTM architecture and a mechanism for detecting P-peaks, as well as simulation models for HRV, PPG and ECG signals (especially the GMF–Rössler model), can be characterised as discovering new patterns, identifying cause-and-effect relationships and dependencies related to improving methods for analysing and processing biomedical signals using modern technological solutions.

As a significant scientific and applied contribution, I would highlight the introduction of the three integral indices — FDTI, RDTI, and PDTI — as measurable criteria for assessing athletes' fatigue, short-term recovery, and long-term adaptation.

The applied contribution is definitely in the complex approach, combining methods for processing and analysing PPG/ECG, simulating HRV, protecting data during transfer, and in general, the concept of implementing an HRV-digital twin, allowing for personalization in tracking the current state and predicting changes in athletes' physical exertion.

In general, I accept the contributions, with the exception of the statement of argumentation for "PPG-based interval series as a practical alternative to ECG in remote monitoring and wearable systems", mainly because the research and analysis of ECG signals (real and from databases) predominate, without a sufficient assessment of the correlation between results with ECG and PPG.

Taking into account the authorship of the publications and the fact that Assoc. Prof. Georgieva is the first author in all but one, I believe that the formulated contributions correctly reflect her significant share in the achieved results.

6. Assessment of dissertation publications

The total number of publications is 25, of which 14 are refereed and indexed in world-renowned databases, with scientific information, including IF or SJR (6 with Q1, 2 with Q2, 4 with Q3 and 2 with Q4), and 10 have been presented at international and national scientific conferences, as well as in 1 chapter of a monograph. At the time of submission of the materials, 71 citations of the publications on this dissertation work have been noted, 52 of which are in SCOPUS and 19 in other publications.

The publication activity assessed according to the criteria for acquiring the scientific degree "Doctor of Science" shows that under indicator G, the excess is more than 4 times, and under indicator D, it is more than 5 times.

7. Using the results of the dissertation work in scientific and social practice

No data on the implementation of scientific achievements in practice has been presented. No direct economic effect has been indicated.

8. Evaluation of the compliance of the abstract with the requirements

The abstract is 93 pages long and comprehensively and reliably reflects the content of the individual parts of the dissertation, as well as the author's contributions. In its preparation, the requirements for preparing abstracts for dissertation works have been met.

9. Opinions, recommendations and remarks

On the content of the separate chapters:

Chapter Two:

1. As stated, one of the goals of preprocessing is to preserve the shape of the primary PPG signal as much as possible. After processing, the signal in Fig. 2.1 differs from those in Figs. 2.4 and 2.5. With such a highly differentiated signal after filtration, peak detection can be implemented with a simple threshold detector, but the probability of false recognition in the presence of movements is also high.
2. Regarding the presented validation results of the proposed wavelet-based detection method (Table 2.2), it is not clear whether the analysed 6 records are from an annotated database or from volunteers. If it is the second option, how were the markers' local positions determined?

Chapter Three:

1. On page 75, the clarification on the use of more Gaussian functions should refer to formula 3.4, not 3.8.
2. Table 3.3 has unexplained parameters, e.g. TP as a parameter in frequency analysis, as well as corresponding units of measurement ms^2 related to frequency.
3. Point 3.1.6 - it is not clear how reference limits are defined when generating a simulated signal, given that fundamental parameters (reference values) are initiated in the simulation algorithm itself?
4. Page 97 - an analysis is presented in terms of speed, but not the consumption for executing the algorithms, which is important when executing from a mobile/wearable device.

Chapter Four:

1. The presentation would benefit from describing how the beginnings and ends of diagnostically important segments, the so-called fiducial points, are determined.

2. How will HRV be determined if only P, QRS, T are transmitted?

Chapter Five:

1. In point 5.1.1, it is noted that the signals are recorded using an ECG Holter. In the next point, Poincaré analysis is performed on PPG signals. Is this correct?

2. Does merging data from 10-minute recordings of 22 athletes, conducted under uncontrolled conditions for recognition of physiological states, and analysed using HRV and fractal analysis with AI algorithms, not suppress significant individual HRV changes that would clearly manifest in independent analysis?

3. When a potential risk is detected, pre-processing is applied, including detrending and removal of atypical RR intervals. Does this not eliminate potential arrhythmias that may indicate risk?

CONCLUSION

The dissertation presented here is undoubtedly relevant and aims to address a number of problems related to methods, approaches, and specific implementations for remote monitoring of cardiac activity using wearable devices. The specificity of such research is associated with increased requirements for the overall conceptual implementation, including sensors, hardware, data transmission interfaces, and algorithms for processing, storing, and protecting sensitive information. In this case, an innovative approach is presented and justified in detail, based on the synthesis of a digital twin of heart rate variability, an important indicator of athletes' physiological state. The volume of work performed exceeds many times the minimum required for such a dissertation. The approach to solving the defined tasks is of significant scientometric value and of proven scientific and scientifically applied nature. The author has demonstrated high potential and experience in theoretical and experimental analysis, statistical processing and practical implementations. I find the publication activity to be entirely sufficient for popularising the results achieved, and the number and location of citations for individual works are evidence of their relevance and significance. The questions and recommendations raised are intended to improve understanding of the specific subject and to assist the author in future scientific research.

I support the dissertation work and propose that Assoc. Prof. Dr Eng. Galya Nikolova Georgieva - Tsaneva be awarded the scientific degree "Doctor of Sciences" in Scientific Field: 5.2 Technical Sciences, Professional Field:

Electrical Engineering, Electronics and Automation, Specialty: 02.21.02 Elements and Devices of Automation and Computing.

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Prof. Ivo Iliev