The Method of Computer Modeling of Heart Rhythm based on the Vector of Stationary and Stationary-related Random Sequences

Petro Onyskiv [a], Iaroslav Lytvynenko[a], Volianyk Oleksandr[b], Grigorii Shymchuk[a] and Volodymyr Hotovych[a]

[a] *Ternopil Ivan Puluj National Technical University, 56, Ruska Street, Ternopil, 46001, Ukraine*
[b] *Institute of telecommunications and global information space, Kyiv, Ukraine*

Abstract
The article discusses a method of computer modeling of the rhythm of an electrocardiosignal based on a mathematical model in the form of a vector of stationary-correlated random sequences. This computer modeling method allows for the formation of implementations of the vector rhythm of the cardio signal (components of the vector of stationary-correlated random sequences) for different types of electrocardiosignals, both in the norm and with various types of rhythm pathologies. Based on the obtained statistical information in the form of estimates of correlation functions of vector components, modeling of the rhythm of electrocardiosignals was carried out. The accuracy of the computer modeling by the proposed method was studied.

Keywords
Computer modeling, vector of stationary random sequences, electrocardiosignal, heart rhythm

1. Introduction

Automated diagnostic systems allow studying the state of the human cardiovascular system, and the effectiveness of such systems largely depends on their components, including hardware and software tools. It is known that the process of automated diagnosis based on such systems involves processing the electrocardiosignal (ECG) signal in two stages. At the first stage, diagnostic information is obtained based on the analysis of the morphological features of the patient's ECG. This involves analyzing the shape and amplitude of diagnostic zones of the ECG. At the second stage, information is obtained based on the analysis of rhythm characteristics, i.e., the temporal relationships between the durations of diagnostic zones (segments) of the ECG. The development of technical tools based on models and methods that allow processing and modeling the ECG rhythm is of great interest because this information allows assessing the adaptive-regulatory capabilities of the cardiovascular system, as well as the psycho-emotional state of the patient. To develop new models and methods in medicine, in addition to well-known databases of biological signals such as https://physionet.org/, more and more tools are being used to create new databases of modeled signal realizations [1]. Additionally, knowledge bases are being formed, for example, based on the application of ontologies, knowledge bases in medicine, including for traditional medicine. In the vast majority of cases, databases are used to test created methods and verify new mathematical models, so creating them is an important task.

CITI'2023: 1st International Workshop on Computer Information Technologies in Industry 4.0, June 14–16, 2023, Ternopil, Ukraine
EMAIL: rasegas21@mail.com (P. Onyskiv); iaroslav.lytvynenko@gmail.com (I. Lytvynenko); wonderage2018@gmail.com (O. Volianyk); gorych@gmail.com (G. Shymchuk); gotovych@gmail.com (V. Hotovych)
ORCID: 0000-0002-9717-4538 (P. Oniskiv); 0000-0001-7311-4103 (I. Lytvynenko); 0000-0001-9137-7580 (O. Volianyk); 0000-0003-2362-7386 (G. Shymchuk); 0000-0003-2143-6818 (V. Hotovych)

2. Analysis of recent research

There are many developed automated diagnostic systems for processing electrocardiosignals (ECGs) that analyze the rhythm of the signal. Known systems use artificial intelligence and machine learning algorithms [2,3]. In such systems, the ECG is processed and a diagnostic conclusion is formed based on the training of neural network algorithms. Stochastic mathematical models have found wide application in some systems [4,5]. Mathematical models that allow for variability and rhythmic variability are presented in works [6,7], and these approaches to building mathematical models are possible through the use of a vector of cyclic rhythmically related random processes. New diagnostic features are proposed based on these new mathematical models and methods of rhythm processing [14]. Mathematical models in the form of cyclostationary signals for processing ECGs are considered in works [8-13]. ECG modeling is presented in works [14-16].

The existence of a significant number of mathematical models [18-26] and methods for processing ECGs [37-43] emphasizes the importance of evaluating diagnostic characteristics of morphological nature. However, rhythm analysis methods have been less widely applied, since not all mathematical models take into account the stochasticity and variability of the rhythm. This is due to the insufficient level of development of mathematical models and methods of rhythm analysis, which would allow for the consideration of both the stochastic nature of the signal, as manifested in the morphological and rhythmic features of the ECG [31-36]. Part of computer realisation of models is presented in works [25, 26, 36, 37, 43-45]

3. Mathematical model of the rhythm of the electrocardio signal

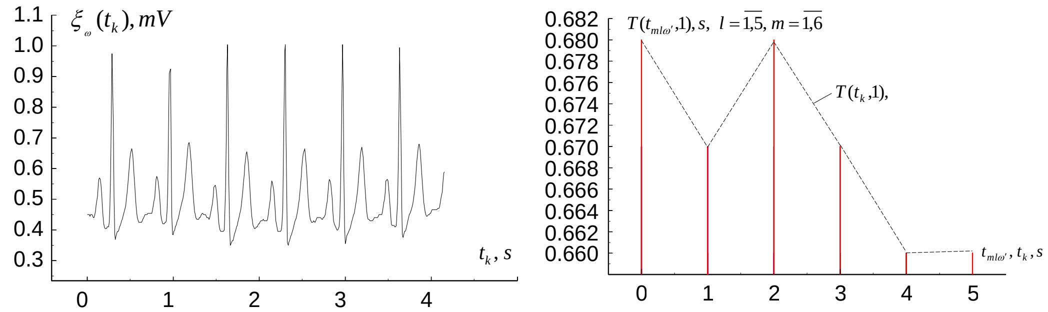
In [7], a rhythmocardio signal with increased resolution is substantiated and described using a vector of stationary and stationary-related random sequences $\Xi_L(\omega', m) = \left\{ T_l(\omega', m), \omega' \in \mathbf{\Omega}', l = \overline{1, L}, m \in \mathbf{Z} \right\}$. At the same time, its elements can be elements from a vector $\mathbf{V}_L(\omega', m)$ for the case when it is necessary to study the time distances between the same type phases of the electrocardio signal in two of its adjacent cycles. Dimensionality (number of components) of the L vector $\Xi_L(\omega', m)$ determines the resolution of the rhythmocardio signal and is equal to the number of investigated time intervals between pre-allocated phases in the electrocardio signal. By clarifying and specifying the probabilistic characteristics of the vector $\Xi_L(\omega', m)$, applied a mathematical model of the rhythmocardio signal with increased resolution in the form of a vector of stationary and stationary-related random sequences [7], which is characterized by the invariance of its family of distribution functions to time shifts by an arbitrary integer $k \in \mathbf{Z}$, namely, for the distribution function $F_{p_{T_{l_1} \dots T_{l_p}}}(x_1, \dots, x_p, m_1, \dots, m_p)$ of the order of p ($p \in \mathbf{N}$) from the family of vector distribution functions $\Xi_L(\omega', m)$ stationary and stationary-connected random sequences have the following equality:

$$F_{p_{T_{l_1} \dots T_{l_p}}}(x_1, \dots, x_p, m_1, \dots, m_p) = F_{p_{T_{l_1} \dots T_{l_p}}}(x_1, \dots, x_p, m_1 + k, \dots, m_p + k),$$

$$x_1, \dots, x_p \in \mathbf{R}, m_1, \dots, m_p \in \mathbf{Z}, l_1, \dots, l_p \in \left\{ \overline{1, L} \right\}, k \in \mathbf{Z}. \quad (1)$$

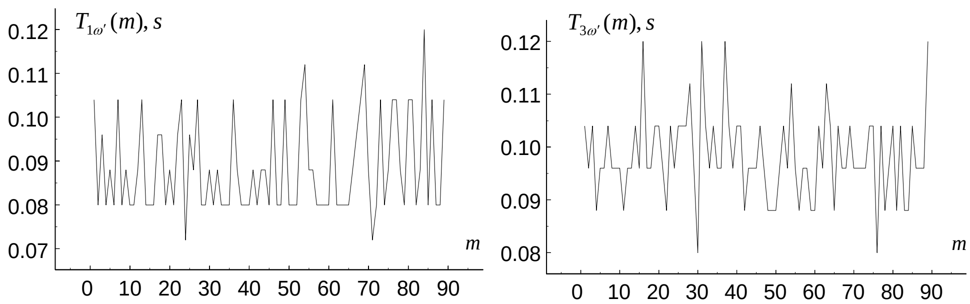
The structure of probabilistic characteristics of a high-resolution electrocardiosignal, which follow from the invariance properties of the corresponding probability characteristics of stationary and stationary-related random sequences, has been studied in works [7, 14]. These characteristics complement the known probabilistic characteristics of the electrocardiosignal based on known models [37-45].

To implement the task of modeling the ECG rhythm based on a justified mathematical model in the form of a vector of stationary-related random sequences, we consider a five-component vector $\Xi_{5\omega'}(\omega', m) = \left\{ T_{l\omega'}(m), l = \overline{1,5}, m = \overline{1,90} \right\}$ durations of the diagnostic zones of the electrocardiosignal, the model of which is a vector $\Xi_5(\omega', m) = \left\{ T_l(\omega', m), \omega' \in \mathbf{\Omega}', l = \overline{1,5}, m = \overline{1,90} \right\}$ stationary-associated random sequences obtained based on ECG processing, which is shown in Figure 1a. The method described in [14] is used to generate vector component realizations. Figure 1b shows a fragment of the discrete rhythm function obtained using the methods described in [14]. The dashed line represents the continuous rhythm function, which is an estimate of the discrete rhythm function and characterizes the rhythm of the investigated ECG. Only a few vector components, are presented in Figures 2 and 3, including the first component of the $T_1(\omega',m)$ is a random stationary sequence that describes a tooth P (diagnostic zone) in electrocardiosignal for all its 90 registered cycles. Implementation schedule $T_{1\omega'}(m)$ of this component is presented in Figure 2, a. Figure 2b shows the third component $T_3(\omega',m)$ of this vector, which is a random stationary sequence describing the duration of the diagnostic zones QRS of the complex in the electrocardiosignal. Figure 3 shows the fourth component, which in turn describes $T_4(\omega',m)$ - tooth T in the electrocardiosignal.



a) b)

Figure 1: Graphs of fragments of the investigated ECG realization and discrete rhythm function for six cycles in the ECG: a) fragment of the ECG realization (II-lead, normal ECG); b) fragment of the discrete rhythm function for six cycles of the ECG (the continuous rhythm function is indicated by a dashed line)



a) b)

Figure 2: Fragments of the implementation of the first and third components of the vector: a) implementation $T_{1\omega'}(m)$ of the first component of the vector $T_1(\omega',m)$, which describes durations P - waves in electrocardiosignals; b) implementation $T_{3\omega'}(m)$ of the third component of the vector $T_3(\omega',m)$, which describes durations of QRS - of the complex in the electrocardiosignal

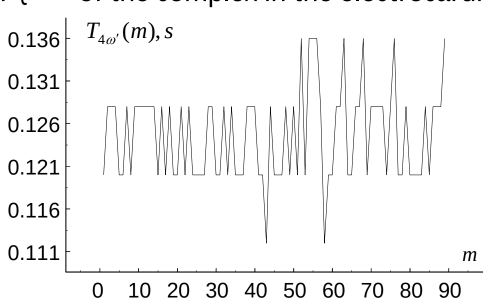


Figure 3: Implementation fragment $T_{4\omega'}(m)$ of the fourth component of the vector $T_4(\omega',m)$, which describes the duration T - teeth in the electrocardiosignal

For data components of the vector of stationary-related random sequences, estimates of correlation functions were determined according to the formula:

$$\hat{r}_{yT_{\omega'}}(u) = \hat{r}_{yT_{\omega'}}(m_1 - m_2)\frac{1}{M - M_1 + 1}\sum_{k=0}^{M-M_1}\left(T_{l_1\omega'}(k) - \hat{c}_{T_{\omega'}}(l_1)\right)\cdot\left(T_{l_2\omega'}(k+u) - \hat{c}_{T_{\omega'}}(l_2)\right), \tag{2}$$

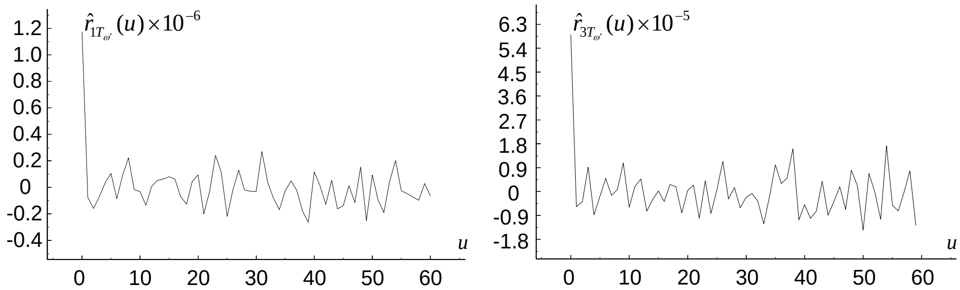
$$u = \overline{0, M_1 - 1}, m_1, m_2 \in \left\{\overline{1, M_1}\right\}, l_1, l_2 = \overline{1,5}, y = \{1,3,4\}$$

where $\hat{\mathbf{C}}_1^L = \left\{\hat{c}_{T_{\omega'}}(l), l = \overline{1,5}\right\}$ - estimates of mathematical expectations for each of the five components of the vector ($L = 5$):

$$\hat{c}_{T_{\omega'}}(l) = \frac{1}{M}\sum_{m=1}^{M} T_{l\omega'}(m),\ l = \overline{1,5},\ m = \overline{1,90}; \tag{3}$$

Where the $M = 90$ - is the number of counts corresponding to the registered cycles of the investigated EKS implementation, M_1 - is the element number in the sequence (correlation depth), y - the number of the correlation function for the corresponding component of the vector $y = \overline{1,5}$ (for this example $y = \{1,3,4\}$).

The results of the obtained statistical estimates of the correlation functions are shown in Figures 4, 5.



a) b)

Figure 4: Fragments of realizations of estimates of the correlation functions of the first and third components of the vector: a) realization of the estimation of the correlation function of the components $T_{1\omega'}(m)$ the first component of the vector $T_1(\omega', m)$, which describes durations P - teeth in the electrocardiosignal; b) realization of correlation function estimation $T_{3\omega'}(m)$ of the third component of the vector $T_3(\omega', m)$, which describes durations QRS - of the complex in the electrocardiosignal;

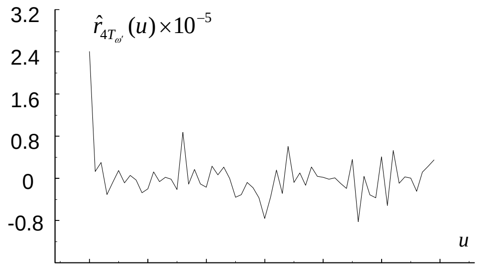
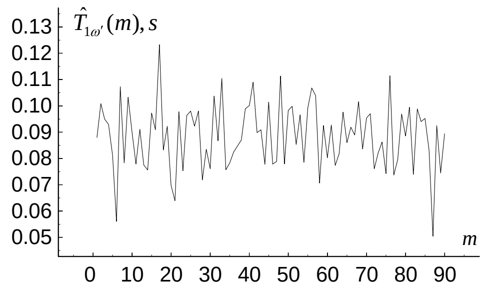
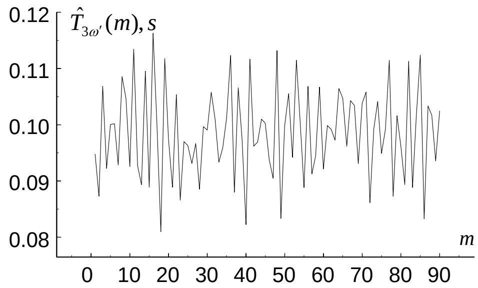


Figure 5: A fragment of the implementation of the evaluation of the correlation function $T_{4\omega'}(m)$ the fourth component of the vector $T_4(\omega', m)$, which describes durations of the T - teeth in the electrocardiosignal

Based on the computer modeling method presented in [17], modeling experiments were conducted, the results of which are the simulated realizations of vector components presented in Figures 6 and 7. During computer modeling, the obtained estimates of correlation functions presented in Figures 4 and 5 were taken into account.



a)



b)

Figure 6: Fragments of the simulated implementation of the first and third components of the vector: a) implementation of the $T_{1\omega'}(m)$ of the first component of the vector $T_1(\omega',m)$, which describes durations of *P* - teeth in the electrocardiosignal; b) implementation $T_{3\omega'}(m)$ of the third component of the vector $T_3(\omega',m)$, which describes durations of *QRS* - of the complex in the electrocardiosignal

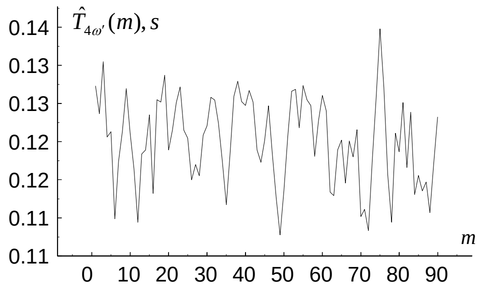
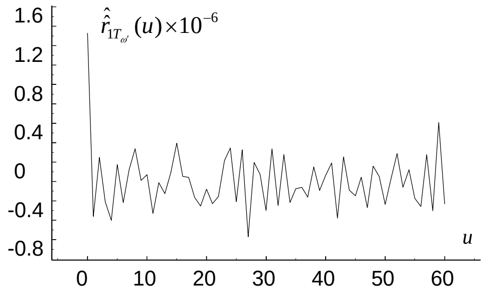
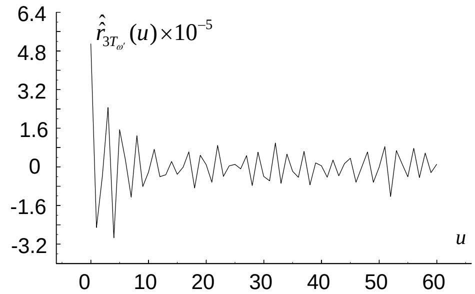


Figure 7: A fragment of the simulated implementation of $T_{4\omega'}(m)$ the fourth component of the vector $T_4(\omega',m)$, which describes durations of T - teeth in the electrocardiosignal

Let's perform a statistical evaluation of the modeled components of the vector and obtain their statistical estimates of correlation functions. The results of the statistical processing are presented in Figures 8 and 9.



a)



b)

Figure 8: Fragments of estimations of correlation functions of implementations of simulated first and third components of the vector: a) implementation of $T_{1\omega'}(m)$ the first component of the vector $T_1(\omega',m)$, which describes durations of *P* - teeth in the electrocardiosignal; b) implementation of $T_{3\omega'}(m)$ of the third component of the vector $T_3(\omega',m)$, which describes durations of *QRS*-complex in the electrocardiosignal;

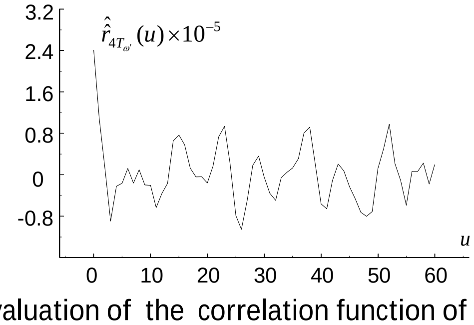


Figure 9: A fragment of the evaluation of the correlation function of the modeled implementation $T_{4\omega'}(m)$ the fourth component of the vector $T_4(\omega',m)$, which describes durations T - teeth in the electrocardiosignal

We will investigate the accuracy of the developed method of computer simulation modeling [17], and estimate the errors of computer modeling. To do this, we will determine the absolute and relative errors of the obtained statistical estimates of correlation functions for the modeled components of the vector of stationary-correlated random sequences.

The absolute and relative errors of modeling were determined as follows:

$$\Delta C_y(k) = \frac{1}{N}\sum_{j=1}^{N}\left|\hat{r}_{yT_{\omega'}}(j) - \hat{\hat{r}}_{yT_{\omega'}}(j)\right|$$

$$\delta C_y(k) = \frac{\Delta C_y(k)}{\frac{1}{N}\sum_{j=1}^{N}\left|\hat{\hat{r}}_{yT_{\omega'}}(j)\right|}, \quad k, j = \overline{1, N}, \quad y = \{1,3,4\}. \tag{4}$$

The results of the obtained absolute and relative errors of rhythm modeling are presented in Figure 10.

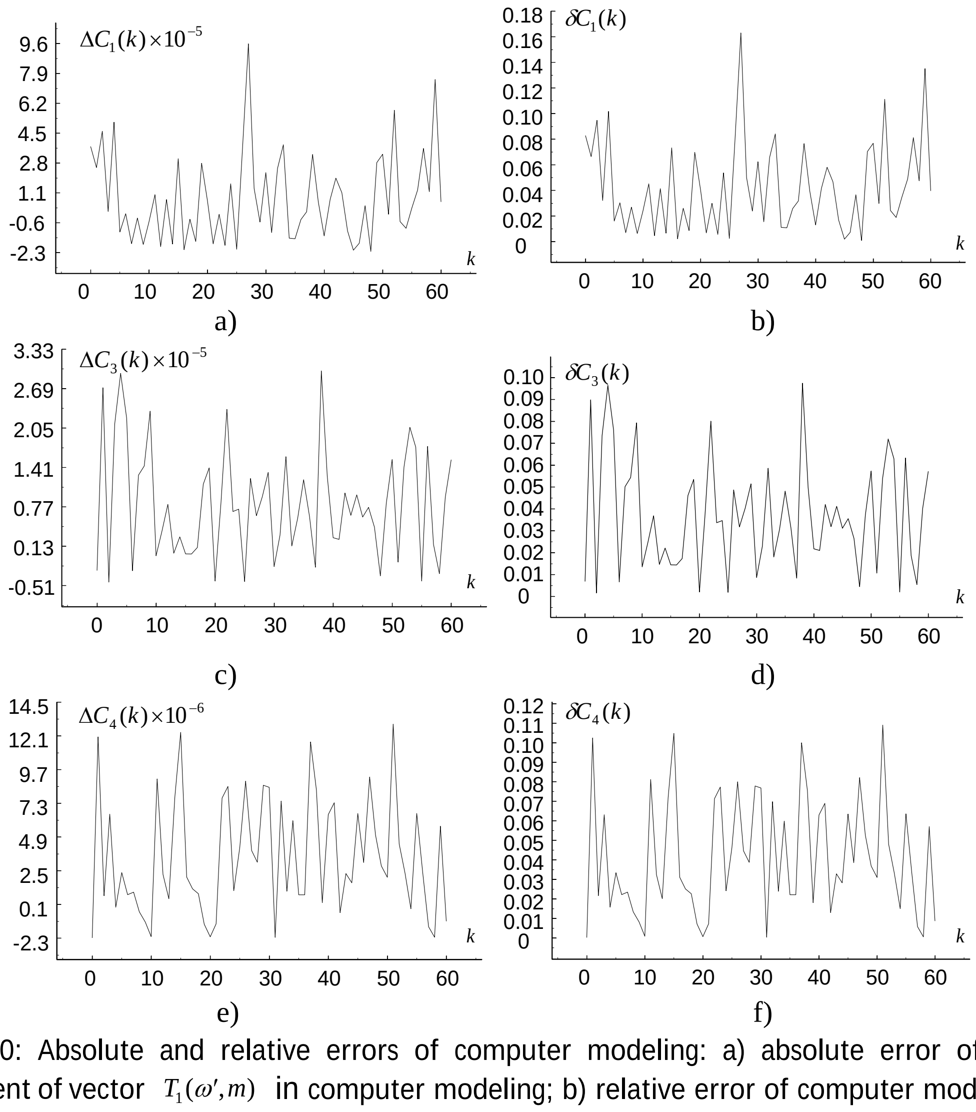


Figure 10: Absolute and relative errors of computer modeling: a) absolute error of the first component of vector $T_1(\omega', m)$ in computer modeling; b) relative error of computer modeling for estimates of the third component of vector $T_1(\omega', m)$; c) absolute error of the third component of vector $T_3(\omega', m)$ in computer modeling; d) relative error of computer modeling for estimates of the third component of vector $T_3(\omega', m)$; e) absolute error of the fourth component of vector $T_4(\omega', m)$ in computer modeling; f) relative error of computer modeling for estimates of the fourth component of vector $T_4(\omega', m)$

4. Discussion of obtained results

The obtained results suggest that for modeling the rhythm of an electrocardiosignal based on a model in the form of a vector of stationary-related random sequences, the maximum relative error of modeling statistical estimates of vector components does not exceed 17% for the studied realizations, indicating sufficient accuracy of computer modeling. In [6, 14], a structured diagram of a diagnostic complex is presented (Figure 11). We will show that this diagnostic complex includes an additional block for computer modeling of a vector cardiac signal (stationary-related random sequences) based on the obtained statistical estimates.

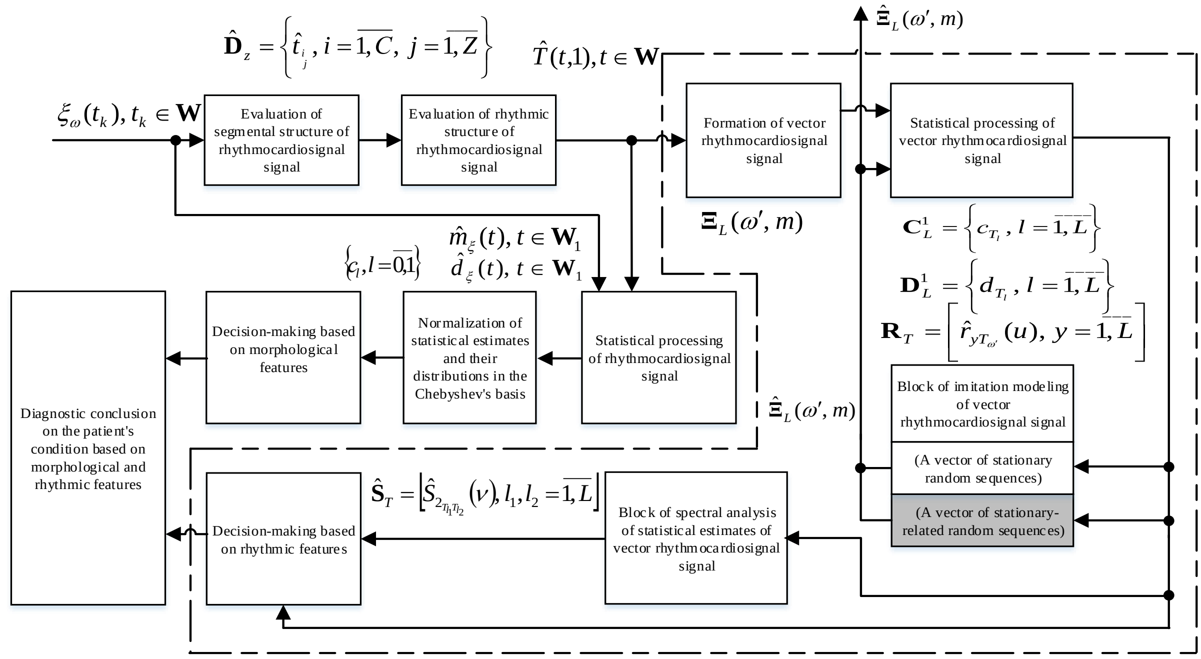


Figure 11: Structural diagram of the modernized diagnostic complex

5. Conclusions

Based on a mathematical model of vector cardiac rhythm signals, a method for computer modeling of the heart rhythm electrocardiosignal (ECG) was developed in the form of a vector of stationary-linked random sequences. Statistical processing methods were applied to the components of the vector cardiac rhythm signal based on the mathematical model in the form of a vector of stationary-linked random sequences. During the computer modeling of realizations of the vector cardiac rhythm signal components, obtained statistical estimates of the real ECG were used. An assessment of the accuracy of computer modeling of vector cardiac rhythm signal components was carried out, and it was established that the relative error of computer modeling does not exceed 17%.

In further studies, it is planned to process ECGs with various types of rhythm pathologies such as tachycardia, bradycardia, arrhythmia, and others, while establishing those marker elements of correlation function estimates of the vector components that are sensitive to heart rhythm disorders.

6. References

[1]. Lupenko S. The Ontology as the Core of Integrated Information Environment of Chinese Image Medicine / Lupenko S., Orobchuk O., Mingtang Xu. // International Conference on Computer Science,

Engineering and Education Applications. ICCSEEA 2019: Advances in Computer Science for Engineering and Education II. AISC, vol. 938, 2019. –pp. 471-481.

[2]. Arman Kilic, Artificial Intelligence and Machine Learning in Cardiovascular Health Care, The Annals of Thoracic Surgery 109 (2020) 1323-1329. doi: 10.1016/j.athoracsur.2019.09.042.

[3]. Zekai W., Stavros S., Bing Y., Hierarchical deep learning with Generative Adversarial Network for automatic cardiac diagnosis from ECG signals, Computers in Biology and Medicine, Volume 155, March 2023, 106641, https://doi.org/10.1016/j.compbiomed.2023.106641

[4]. Lupenko, S., Lytvynenko, I., Sverstiuk, A., Horkunenko, A., Shelestovskyi, B. Software for statistical processing and modeling of a set of synchronously registered cardio signals of different physical nature. CEUR Workshop Proceedings, 2021, 2864, pp. 194–205.

[5]. Lupenko, S.A., Lytvynenko, I.V., Stadnyk, N.B., Zozulia, A.M., Sverstiuk, A.S. Conditional cyclic random process of a discrete argument as a generalized mathematic model of cyclic signals with double stochasticity. Journal of Computing and Information Technology, 2020, 39, pp. 60–69.

[6]. Computer modeling of cardiac rhythm based on vector of stationary random sequences / Serhii Lupenko, Iaroslav Lytvynenko, Petro Onyskiv, Anatolii Lupenko, Oleksandr Volianyk, Olena Tsytsiura // Scientific Journal of TNTU. Tern.: TNTU, 2022. Vol 108. No 4. P. 131–143.

[7]. Lytvynenko I. V., Lupenko S. A., Onyskiv P. A., Trysniuk V. M., Zozulia A. M. Metody statystychnoho opratsiuvannia rytmokardiosyhnalu iz pidvyshchenoiu rozdilnoiu zdatnistiu na osnovi yoho modeli u vyhliadi vektora statsionarnykh vypadkovykh poslidovnostei Informatsiini tekhnolohii. Systemy upravlinnia, navihatsii ta zviazku, Natsionalnyi universytet "Poltavska politekhnika imeni Yuriia Kondratiuka". 2020, vypusk 2(60). C. 75-84. doi: 10.26906/SUNZ.2020.2.075 (in Ukraine)

[8]. W. A. Gardner, Cyclostationarity: Half a century of research, Signal Processing 86 (2006) 639–697. doi:10.1016/j.sigpro.2005.06.016.

[9]. W. A. Gardner Exploitation of cyclostationarity for identifying the Volterra kernels of non–linear systems, IEEE Transactions on Information Theory 39 (1993) 535–542. doi:10.1109/18.212283.

[10]. W. A. Gardner Fraction–of–time probability for time–series that exhibit cyclostationarity, Signal Processing 23 (1991) 273–292. doi:10.1016/0165-1684(91)90005-4.

[11]. W. A. Gardner, C. M. Spooner Higher–order cyclostationarity, in: International Symposium on Information Theory and Applications, ISITA '90, Honolulu, HI, 1990, pp. 355–358.

[12]. Fonseca, N. G.; Aleman, M. N. Cardiac arrhythmia classication based on the RMS signal and cyclostationarity. IEEE Latin Amer. Trans., vol. 19, no. 4, pp. 584-591, Apr. 2021.W.A. Gardner, C.M. Spooner The cumulant theory of cyclostationary time-series. II. Development and applications, IEEE Transactions on Signal Processing 42 (1994) 3409-3429. doi:10.1109/78.340776.

[13]. Haritopoulos, M.; Capdessus, C.; Nandi, A. K. Foetal PQRST extraction from ECG recordings using cyclostationarity-based source separation method. in Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. (EMBC), Aug. 2010, pp. 1910-1913..

[14]. I.V. Lytvynenko, S.A. Lupenko, P.A. Onyskiv, V.M. Trysniuk, A.M. Zozulia. Prohramnyi kompleks dlia avtomatyzovanoho analizu sertsevoho rytmu na osnovi vektornoho rytmokardiosyhnalu. Matematychne modeliuvannia v ekonomitsi, №1, 2020. ISSN 2409-8876 P. 27-38 (in Ukraine)

[15]. Simulation of cyclic signals (generalized approach) Lupenko, S., Lytvynenko, I., Hotovych, V. CEUR Workshop Proceedingsthis link is disabled, 2021, 3038, pp. 86–92

[16]. Modeling and Methods of Statistical Processing of a Vector Rhytmocardiosignal Lytvynenko, I., Lupenko, S., Onyskiv, P., Zozulia, A. Open Bioinformatics Journalthis link is disabled, 2021, 14(1), pp. 73–86

[17]. Lytvynenko Ya.V. Alhorytm modeliuvannia dyskretnykh statsionarnykh liniinykh vypadkovykh protsesiv. / Lytvynenko Ya., Lupenko S., Chuprin L., Shcherbak L. // Aktualni problemy avtomatyzatsii ta informatsiinykh tekhnolohii T.4. Dnipropetrovsk: Dnipropetrovskoho universytetu. 2001. S. 52-59 [In Ukraine]

[18] Mark Potse Mathematical Modeling and Simulation of Ventricular Activation Sequences: Implications for Cardiac Resynchronization Therapy J Cardiovasc Transl Res. 2012; 5(2): 146–158. Published online 2012 Jan 27. doi: 10.1007/s12265-011-9343-6

[19] Bacharova L, Mateasik A, Krause R, Prinzen F, Auricchio A, Potse M. The effect of reduced intercellular coupling on electrocardiographic signs of left ventricular hypertrophy. Journal of Electrocardiology. 2011;44:571–576.

[20] Barr RC, Pilkington TC, Boineau JP, Spach MS. Determining surface potentials from current dipoles, with application to electrocardiography. IEEE Transactions on Biomedical Engineering. 1966;13(2):88–92.

[21] Berenfeld O, Jalife J. Purkinje-muscle reentry as a mechanism of polymorphic ventricular arrhythmias in a 3-dimensional model of the ventricles. Circulation Research. 1998;82:1063–1077.

[22] Bouchard S, Jacquemet V, Vinet A. Automaticity in acute ischemia: Bifurcation analysis of a human ventricular model. Physical Review E. 2011;83:011,911.

[23] Colli Franzone P, Guerri L, Tentoni S. Mathematical modeling of the excitation process in myocardial tissue: Influence of fiber rotation on wavefront propagation and potential field. Mathematical Biosciences. 1990;101(2):155–235.

[24] Colli-Franzone P, Pavarino LF, Scacchi S. Exploring anodal and cathodal make and break cardiac excitation mechanisms in a 3D anisotropic bidomain model. Mathematical Biosciences. 2011;230:96–114.

[25] Dubé B, Gulrajani RM, Lorange M, LeBlanc AR, Nasmith J, Nadeau RA. A computer heart model incorporating anisotropic propagation: IV. Simulation of regional myocardial ischemia. Journal of Electrocardiology. 1996;29(2):91–103.

[26] Fast VG, Kléber AG. Block of impulse propagation at an abrupt tissue expansion: Evaluation of the critical strand diameter in 2- and 3-dimensional computer models. Cardiovascular Research. 1995;30:449–459

[27] . Neic, M. A. Gsell, E. Karabelas, A. J. Prassl, and G. Plank, "Automating image-based mesh generation and manipulation tasks in cardiac modeling workflows using meshtool," SoftwareX, vol. 11, p. 100454, 1 2020. doi:10.1016/j.softx.2020.100454

[28] Niederer, S. A., Lumens, J., & Trayanova, N. A. (2019). Computational models in cardiology. Nature Reviews Cardiology, 16(2), 100-111. https://doi.org/10.1038/s41569-018-0104-y

[29] Mayourian J, Savizky RM, Sobie EA, Costa KD. Modeling Electrophysiological Coupling and Fusion between Human Mesenchymal Stem Cells and Cardiomyocytes. PLoS Comput Biol. 2016 Jul 25;12(7):e1005014. doi: 10.1371/journal.pcbi.1005014.

[30] Steven A Niederer, Eric Kerfoot, Alan P Benson, Miguel O Bernabeu, Olivier Bernus, Chris Bradley, Elizabeth M Cherry, Richard Clayton, Flavio H Fenton, Alan Garny, Elvio Heidenreich, Sander Land, Mary Maleckar, Pras Pathmanathan, Gernot Plank, José F Rodríguez, Ishani Roy, Frank B Sachse, Gunnar Seemann, Ola Skavhaug, Nic P Smith Verification of cardiac tissue electrophysiology simulators using an N-version benchmark, Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences, 2011, pp 4331-4351

[31] Niederer, S.A., Lumens, J., Trayanova, N.A. (2019). Computational models in cardiology. Nature Reviews Cardiology, 16(2), 100-111.

[32] Britton, O.J., Bueno-Orovio, A., Van Ammel, K., Lu, H.R., Towart, R., Gallacher, D.J., Rodriguez, B. (2013). Experimentally calibrated population of models predicts and explains intersubject variability in cardiac cellular electrophysiology. Proceedings of the National Academy of Sciences, 110(23), E2098-E2105.

[33] Joshua Mayourian, Eric A. Sobie, and Kevin D. Costa An Introduction to Computational Modeling of Cardiac Electrophysiology and Arrhythmogenicity Methods Mol Biol. Author manuscript; available in PMC 2019 Jun 12. Methods Mol Biol. 2018; 1816: 17–35.
doi: 10.1007/978-1-4939-8597-5_2

[34] O'Hara T, Virag L, Varro A, Rudy Y (2011) Simulation of the undiseased human cardiac ventricular action potential: model formulation and experimental validation. PLoS Comput Biol 7(5):e1002061 10.1371/journal.pcbi.1002061

[35] O'Hara T, Virag L, Varro A, Rudy Y (2011) Simulation of the undiseased human cardiac ventricular action potential: model formulation and experimental validation. PLoS Comput Biol 7(5):e1002061 10.1371/journal.pcbi.1002061

[36] K Harumi , H Tsunakawa, G Nishiyama, D Wei, G Yamada, Y Okamoto, T Musha Clinical application of electrocardiographic computer model PMID: 2614315 DOI: 10.1016/s0022-0736(07)80101-4

[37] Tsunakawa H, Wei D, Mashima S, Harumi K. Study on the genesis of giant negative T wave in apical hypertrophic cardiomyopathy using a three-dimensional computer model, Jpn Heart J. 1991 Nov;32(6):799-809. doi: 10.1536/ihj.32.799. PMID: 1811088

[38] Clayton RH, Bernus O, Cherry EM, Dierckx H, Fenton FH, Mirabella L, Panfilov AV, Sachse FB, Seemann G, Zhang H. Models of cardiac tissue electrophysiology: progress, challenges and open questions. Prog Biophys Mol Biol. 2011 Oct-Nov;107(1):6-15.

[39] Y. Belhamadia et al. Towards accurate numerical method for monodomain models using a realistic heart geometry Mathematical Biosciences (2009)

[40] E.M. Cherry et al. Dynamics of human atrial cell models: restitution, memory, and intracellular calcium dynamics in single cells Progress in Biophysics & Molecular Biology (2008)

[41] Simulating patterns of excitation, repolarization and action potential duration with cardiac Bidomain and Monodomain models Mathematical Biosciences (2005)

[42] G.M. Faber et al. Action potential and contractility changes in Na+ (i) overloaded cardiac myocytes: a simulation study Biophysical Journal (2000)

[43] Damiano Fessina, Caroline M.Costa, Martin Bishop, Gernot Plank, John Whitaker, Sian E. Harding, Steven A. Niederer. Assessing the arrhythmogenic risk of engineered heart tissue patches through in silico application on infarcted ventricle models: In silico engraftment of engineered heart tissue patches 2023, Computers in Biology and Medicine, Volume 154, March 2023, 106550 https://doi.org/10.1016/j.compbiomed.2023.106550

[44] Cristina Rueda, Alejandro Rodríguez-Collado, Itziar Fernández, Christian Canedo, María Dolores Ugarte, Yolanda Larriba, A unique cardiac electrocardiographic 3D model. Toward interpretable AI diagnosis, iScience, Volume 25, Issue 12, 2022, 105617, ISSN 2589-0042,

https://doi.org/10.1016/j.isci.2022.105617.

[45] Wenge Que, Chuang Han, Xiliang Zhao, Li Shi, An ECG generative model of myocardial infarction, Computer Methods and Programs in Biomedicine, Volume 225, 2022, 107062, ISSN 0169-2607, https://doi.org/10.1016/j.cmpb.2022.107062.