Nonlinear Dynamics Method in the Impedance Signals Analysis of the Eye Blood Flow of Patients with Glaucoma

Anna A. Kiseleva[1], Petr V. Luzhnov[1], Alexander P. Nikolaev[1], Elena N. Iomdina[2] and Olga A. Kiseleva[2]

[1]*Bauman Moscow State Technical University, Moscow, Russian Federation*

[2]*Moscow Helmholtz Research Institute of Eye Diseases, Moscow, Russian Federation*

Keywords: Nonlinear Dynamics, Transpalpebral Rheophthalmography, Eye Blood Flow, Glaucoma.

Abstract: The article considers the possibility of analyzing the signals of transpalpebral reophthalmography with the help of the method of nonlinear dynamics. In analyzing the signals, it was considered a method with a reconstruction of the signal attractor. An optimal time delay was chosen for the reconstruction, which allowed us to construct an attractor in the space of selected coordinates. Next, we analyzed the mass centers of the reconstructed attractors, the position of the coordinates allowed us to formulate a decisive rule for comparing and dividing signals into groups.Verification of the results carried out on the model signals. The application of this technique was shown with the help of the examples of signal analysis in patients with primary open-angle glaucoma.

1 INTRODUCTION

In the structure of ophthalmopathology, primary open-angle glaucoma (POAG) occupies one of the first places among eye diseases that inevitably end in blindness (Quigley, H. A., Broman, A. T., 2006). Currently, the pathogenesis of the development and progression of POAG is associated with increased intraocular pressure (IOP) (Cherecheanu A.P., Garhofer G., et al., 2013). Increased IOP damages the nerve cells of the retina, from which the optic nerve is formed. It is manifested by a gradual loss of vision function. However, other factors can lead to the development of POAG. So, a lot of researches have described studies where, along with increased IOP, one of the risk factors for the development of POAG and the progressive deterioration of visual functions in this diseaseis a decreasing level of the blood filling in the brain vessels and eye vessels (Caprioli, J., Coleman, A. L., 2010; Venkataraman, S. T., Flanagan, J. G., et al., 2010; Calvo, P. et al., 2012). Studying the eye hemodynamics can provide the necessary information about the clinical course of POAG.

Electrical impedance method is a technique for obtaining an image in sections of an impedance distribution body (resistance of various organs in response to an electric current) by means of non-invasive electrical sounding (Adler A., Gaburro R., 2016). The current flowing through the body creates a volume distribution of electrical potential (voltage). The potential decreases along the current line with distance from the active (injecting current) electrode. The voltage drop per unit length (electric field strength) is proportional to the magnitude of the current and the resistance of the body in accordance with Ohm's law. By measuring the voltage drop and knowing the amount of current, it is possible to calculate the resistance value. The reconstruction algorithm allows the use of voltages measured only on the surface of the body, to calculate the spatial distribution of resistivity (or electrical conductivity) within it. This method is the basis of the method of reophthalmography (ROG) (Lazarenko V.I., Komarovskikh E.N., 2004). ROG is the method for assessing the state of the blood flow in the eye. ROG is a method for studying the pulse blood filling in the vessels of various organs and tissues, based on recording changes in the total electrical resistance of tissues. In the classical method of registration, the electrodes are mounted directly on the surface of the eye near the lens. It leads to necessity of anesthesia for conducting researches.

To solve the limitations of the classical technique, a new registration technique has been developed - the method of transpalpebral reophthalmography (TP ROG) (Luzhnov P.V., Shamaev D.M., et al., 2015;

Kiseleva, A., Luzhnov, P., Nikolaev, A., Iomdina, E. and Kiseleva, O.
Nonlinear Dynamics Method in the Impedance Signals Analysis of the Eye Blood Flow of Patients with Glaucoma.
DOI: 10.5220/0007554800750080
In *Proceedings of the 12th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2019)*, pages 75-80
ISBN: 978-989-758-353-7

Luzhnov P.V., Shamaev D.M., et al., 2017; Shamaev D. M., Luzhnov P. V., et al., 2016). In this version of the study, the electrodes are positioned on the closed eyelid.

Analysis of the received signals includes qualitative and quantitative analysis. Qualitative analysis of signals is the definition of the pulse curve form. Evaluating the type of the pulse curve, usually emit hypertonic, normotonic and hypotonic types. Unfortunately, now the method of analyzing the type of the pulse wave is not objectivized. Factors affecting vascular tone include biophysical, biomechanical and hydrodynamic factors. Together, they affect the type of the pulse curve and further determine the result of the qualitative analysis of signals.

From the point of view of modern biophysics, the combination of these factors, namely, their mutual influence on each other, can be described using the nonlinear properties of the system (Strogatz H., S., 2014). Dynamic processes play an important role in the development and manifestation of the nonlinear properties of systems, in particular dynamic chaos. Chaos is characterized, first of all, by internal self-sustaining fractal fluctuations (Betelin, V.B., Eskov, V.M., et al. 2017). This effect is found in the analysis of many biological signals - studies of the electrical activity of the heart (Elhaj, F., Salim, N., et al., 2016), neural activity of the brain (Akar S.A., Kara S., et al., 2015), respiration (Kiseleva A., Luzhnov P., et al.,2018), and blood filling of various organs. The theoretical basis for describing chaos in the work (Takens F., 1981) was proposed by F. Takens. In accordance with the Takens theorem, using phase-spatial representations of signals - attractors for analysis, it becomes possible to conduct their qualitative and quantitative comparison (Charlton P.H., Bonnici T., et al. 2017).

Thus, the main idea of this work is to evaluate the possibility of types transpalpebral reophthalmography signals comparing with the help of nonlinear dynamics methods, assessing the main comparison parameters and further verifying these parameters for analyzing signals of a transpalpebral reophthalmography in patients with primary open-angle glaucoma.

2 MATERIALS AND METHODS

2.1 Problem Statement

Due to the fact that in the qualitative analysis of pulse curves, the presence of the physiological relationship between vascular tones is taken into account, the signals are usually divided into three main types: hypotonic, hypertonic and normotonic types. As an object of study, model signals of these types were considered. An example of a pulse curve waveform is shown in Figure 1.

Currently, a contour analysis based on the method described in work (Webber C. L., Sbilut J. P., 1994), is used for the analysis of such type signals (Figure 1). In contour analysis, the most informative indicators are measured: the amplitudes of the systolic and diastolic waves, the amplitude of the rheographic wave at the incisure level, the duration of the anacrotic limb and the catacrotic limb.

This analysis underlies the classification of signals currently used in clinical practice. A significant drawback of this classification is a high probability of errors during automatic separation of the signals.

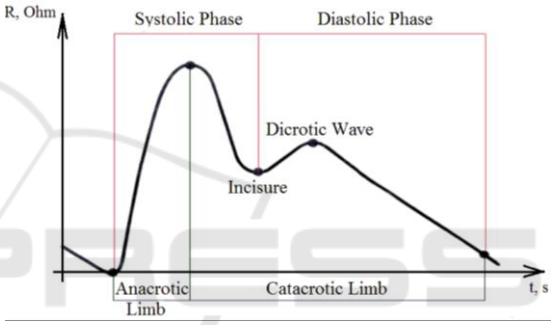

Figure 1: The shape of the pulse blood filling curve of model signals with the release of the main signal regions.

To solve this problem, it has been proposed to use the analysis of phase-spatial portraits of the pulse curve, which allows to classify signals not only by their quantitative characteristics (wave amplitude value, length of sections), but also helps to divide signals into groups with the help of analysing the shape of the pulse curve itself. As a result, the following stages of work have been formulated:

Stage 1 - The reconstruction of the pulse curve attractor;

Stage 2 - The analysis of the obtained form of the attractors;

Stage 3 - The formulation of the classification algorithm;

Stage 4 - The verification of results.

2.2 Reconstruction of the Attractor

The phase portrait (signal attractor) can be constructed in two ways. The first method (the delay method) involves constructing a pseudo-phase

portrait by displaying the observed values of x (t) on a subspace with coordinates x (t + d), where d is the time delay. The second method is based on the imaging the phase portrait on a subspace with coordinates x (t), x * (t), where x * (t) is the estimate of the first derivative of x (t) in the t point (Palit K., Mukherjee S., et al., 2013). Due to the fact that TP ROG signals are complex in their structure, we have considered the first method to simplify calculations and reduce processing time.

According to the Takens theorem (Takens F., 1981), attractor reconstruction process of a biological system consists in building on a number $\{x_i\}_{i=1,\ldots,\infty}$ a new (reconstructed) attractor with the same parameters as the original one, which have been received as a result of measurement at certain intervals of the considered signal x(t) (Palit K., Mukherjee S., 2011). For this, m-dimensional vectors are constructed $\{zj\}_{j=1,\ldots,\infty}$, where $z_{j,k}=x_{j+d(k-1)}$, where d - time delay. Then, for sufficiently large m, the parameters of the reconstructed attractor in the m-dimensional space Z coincide with the parameters of the original attractor in the n-dimensional space X (Webber C. L., Sbilut J. P., 1994). Selection and calculation of dimension m-dimensional space is described in (Luzhnov P.V., Shamaev D.M. et. al., 2018).

The key role for calculating all parameters of the obtained attractor belongs to the correct choice of time delay (Webber C. L., Sbilut J. P., 1994). Typically, the time delay is selected so that each reconstructed next vector add the most information about the attractor or less can be correlated with the previous one (Gracia J., Seppa V-P., et. al., 2017). When reconstructing biological attractors, stable results in the selection time delay gives technique proposed in (Maiorov O. Yu., Glukhov A. B., et al., 2007), which is based on the form of the original signal. To analyze the pulse curve, it is necessary to distinguish in the received portrait the beginning of the cardiac cycle, the maximum amplitude and incisure. Based on the analysis of the duration of these sections, values of 0.08 sec and 0.22 sec have been chosen in accordance with the data described in the work (Kiseleva A., Luzhnov P., et al.,2018).

Figure 2 shows an example of the resulting attractor of the signal of the pulse blood filling with the 60 seconds duration. The waveform of the signal itself (Figure 2a) and the resulting signal attractor (Figure 2b) are shown.

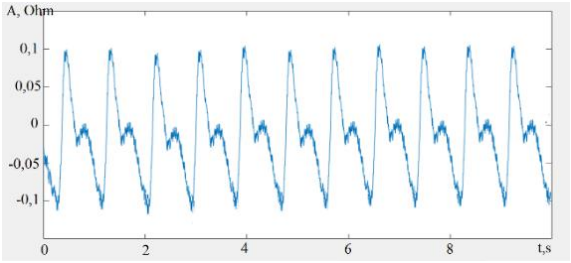

Figure 2(a): The analyzed signal of pulse blood filling (10 sec. section), X axis - time, s, Y axis - signal amplitude, Ohm.

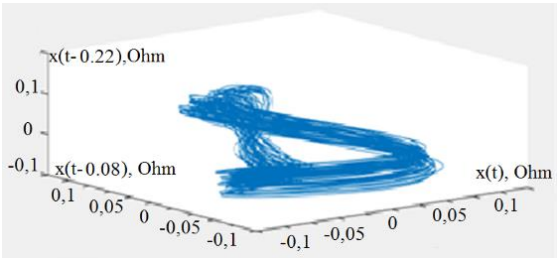

Figure 2(b): The resulting phase portrait of a signal with the 60 seconds duration, on the X axis: signal x(t), Ohm, on the Y axis: signal x(t - 0.08), Ohm, on the Z axis: signal x(t - 0.22), Ohm.

2.3 Analysis of the Shape Obtained Attractors

In (Luzhnov P. V., Shamaev D. M., et al., 2018; Kiseleva A., Luzhnov P., et al., 2018), an analysis of the obtained attractors shape based on the mass center of the obtained figures was considered. In the framework of these works, the projection of the attractors on 3 axes (XY, YZ, XZ) was considered, the resulting form of the attractor was approximated by two triangles with one common base. In the works, the ratio of heights drawn from the vertices of polynomial triangles to a common base was analyzed.

In this work, it has been proposed to modify the algorithm and consider not the attractors of the pulse curve, but analyze the attractors of the derived signal. A significant advantage of this method is the exact separation of the cardiocycle into systolic and diastolic components. Figure 3 shows the derivative of the pulse curve signal and its reconstructed attractor. Areas A and B correspond to the systolic and diastolic signal components, respectively.

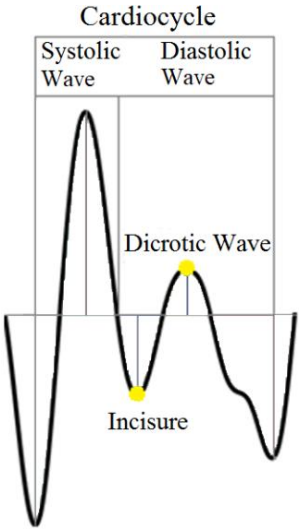

Figure 3(a): Derivative waveform pulse volume, highlighting the main areas of signal.

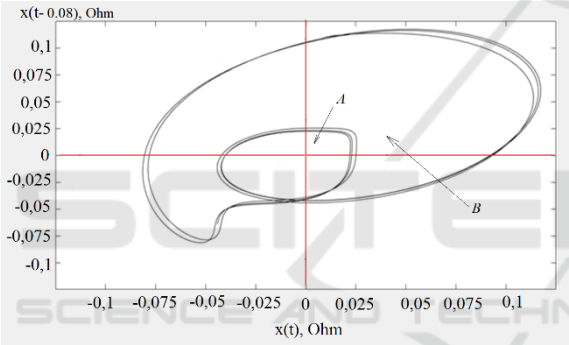

Figure 3(b): The attractor derivative signal projected on XY axis. On the X axis - the signal x (t), Ohm, on the Y axis is the signal x (t - d), Ohm, area A - the systolic part, area B - the diastolic part.

2.4 Formulation of the Classification Algorithm

Analyzing the shape of the attractor (Figure 3b), it is obvious that the resulting shape can be approximated by two geometric figures - ovals.

To analyze the obtained forms of the attractor (Figure 3b), it has been proposed to consider the distance between the mass centers of regions A and B (Figure 4). For the introduction of automatic signals separation, it was necessary to divide the mass centers of the signals according to three main types: hypotonic type, hypertonic and normotonic type.

We considered model signals of each type (normotonic, hypotonic, hypertonic), the requirements for the centers of mass location for each signal type (Figure 5) were formulated based on the

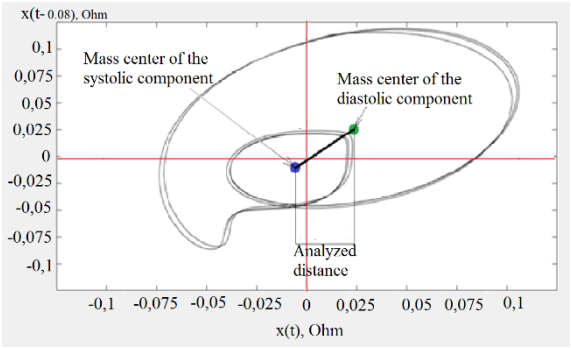

Figure 4: The attractor derivative signal with directions the mass centers of systolic and diastolic components.

analysis. Moreover, it was determined that the coordinates of the mass center of the systolic component are identical for signals of three types and had following coordinates: 0.002 (X coordinate) and 0.002 (Y coordinate). The following visual results have been obtained on the projection plane of the phase space based on the model signals with the condition of their splitting into normotonic, hypotonic and hypertonic types (Figure 5). The results with the obtained coordinates of diastolic centers are presented in Table 1. The diameter of the region around the mass center of each signal type is 0.001 and was chosen according to the average spread of the mass centers of the signal around the obtained point.

Table 1: Mass center coordinates.

Type signal	X	Y	Distance between centres
Normotonic	-0.008	-0.008	0.010
Hypotonic	0.001	0.0005	0.001
Hypertonic	-0.002	-0.002	0.004

As a result, the decision rule for signal classification have been formulated: if the mass center of the systolic component of the signal falls within the range of 0.002 (X) and 0.002 (Y), and the center of the signals diastolic component lies in the ranges presented in Table 1, the distance between centers do not exceed the values shown in Table 1 for each type of signal, then the algorithm will automatically separate the signals.

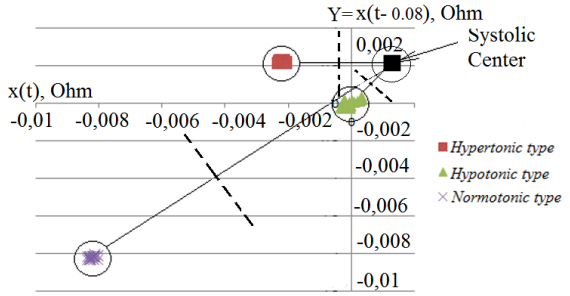

Figure 5: The mass centers of the systolic component and the diastolic component for the types of signal. The dashed line shows the boundary separation between the types of signals.

2.5 Using of the Method in Clinical Practice

The developed method can be used to classify the pulse blood filling signals. In our work, the application of this method for the signals of pulse eye blood filling was considered. The application of the considered classification method becomes possible due to the identity of the forms of the pulse curves.

To test the method on the TP ROG signals, 3 types of signals have been considered: 1) without ophthalmopathology; 2) stage II POAG; 3) stage III POAG. The study was performed in the group of 10 subjects (average age 54.2 ± 15.4 years) without ophthalmopathology and in the group of 10 patients with POAG were divided into two parts: the 1-st part - 6 patients with stage II of POAG (mean age 72.0 ± 8.2 years), the 2-nd part - 4 patients with stage III POAG (mean age 69.4 ± 6.8 years). The study has been conducted on each signals type with the 3 seconds duration. Table 2 shows the coordinates of the obtained diastolic centers. The obtained coordinates of the systolic center are 0.30 ± 0.30 (X coordinate) and 0.25 ± 0.02 (Y coordinate).

Similar to Figure 5, in Figure 6 for the case of a POAG on the plane of projections, the boundaries of the separation according to the stage of the disease are shown.

To specify the values of the mass centers, it is necessary to normalize TP ROG signals amplitudes and conduct a study on a larger sample of TP ROG signals.

Table 2: Mass center coordinates for TP ROG signals.

Type signal	X, mOhm	Y, mOhm	Distance between centers
Healthy	-1.5	-1.2	2.1
2nd stage POAG	-1.7	-1.8	2.1
3d stage POAG	-3.0	-2.1	3.8

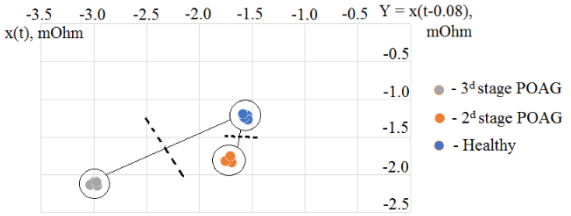

Figure 6: The centers of mass of the systolic component for ophthalmic signals. The dashed line shows the boundary separation between the types of signals.

3 RESULTS

As a result of this work, a new method for separating signals based on nonlinear dynamics has been proposed. To solve the problem, the following steps have been carried out: 1) the methods of nonlinear dynamics have been considered and the optimal method for biological systems has been selected; 2) using the selected method, phase portraits of the considered biological signals have been reconstructed; 3) a classification algorithm has been developed and a decisive rule for signal separation has been formulated; 4) verification passed.

In the future, it is planned to carry out the separation of signals in real time, as well as the possible application of this algorithm for TP ROG signals analysing for pulse blood filling in eyes researches.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest. The paper was supported by a grant from RFBR (No.18-08-01192).

REFERENCES

Adler A., Gaburro R., WRB Lionheart, "Electrical Impedance Tomography", in Handbook of Mathematical Methods in Imaging, 2nd ed O Scherzer (Ed), Springer, 2016.

Akar S.A., Kara S., Agambayev S., Bilgic V. (2015) Nonlinear analysis of EEG in major depression with fractal dimensions. 37th Annual International Conference of the IEEE on Engineering in Medicine and Biology Society: 7410–7413. DOI: 10.1109/EMBC.2015.7320104.

Betelin, V.B., Eskov, V.M., Galkin, V.A. et al. (2017) Stochastic volatility in the dynamics of complex homeostatic systemsDokl. Math. 95: 92. DOI: 10.1134/S1064562417010240.

Caprioli, J., Coleman, A. L. (2010) Blood Pressure, Perfusion Pressure, and Glaucoma. Am. J. Ophthalmol. 149, 704–712.

Calvo, P. et al. (2012) Predictive value of retrobulbar blood flow velocities in glaucoma suspects. Investig. Ophthalmol. Vis. Sci. 53, 3875–3884.

Charlton P.H., Bonnici T., Tarassenko L., et al. (2017) Extraction of respiratory signals from the electrocardiogram and photoplethysmogram: Technical and physiological determinants. Physiological Measurement 38(5): 669-690. DOI: 10.1088/1361-6579/aa670e.

Cherecheanu A.P., Garhofer G., Schmidl D., Werkmeister R., Schmetterer L. Ocular perfusion pressure and ocular blood flow in glaucoma. CurrOpinPharmacol. 2013; 13: 36-42. DOI: 10.1016/j.coph.2012. 09.003.

Elhaj, F., Salim, N., Harris, A., Swee, T. and Ahmed, T. (2016). Arrhythmia recognition and classification using combined linear and nonlinear features of ECG signals. Computer Methods and Programs in Biomedicine, 127, pp.52-63. DOI 10.1016/j.cmpb.2015.12.024.

Gracia J., Seppa V-P., Pelkonen A., Kotaniemi-Syrjanen A. et al. (2017) Nonlinear Local Projection Filter for Impedance Pneumography. European Medical andBiological Engineering Conference 65: 306-309. DOI: 10.1007/978-981-10-5122-7_77.

Kiseleva A., Luzhnov P., Dyachenko A. and Semenov Y. (2018). Rheography and Spirography Signal Analysis by Method of Nonlinear Dynamics.In Proceedings of the 11th International Joint Conference on Biomedical Engineering Systems and Technologies - Volume 1: BIODEVICES, ISBN 978-989-758-277-6, pages 136-140. DOI: 10.5220/0006579301360140.

Lazarenko V.I., Komarovskikh E.N. Results of the examination of hemodynamics of the eye and brain in patients with primary open-angle glaucoma. Vestnik Oftal'mologii 120(1), 32–36 (2004).

Luzhnov P.V., Shamaev D.M., Iomdina E.N., Markosyan G.A., Tarutta E.P., Sianosyan A.A. (2017) Using quantitative parameters of ocular blood filling with transpalpebralrheoophthalmography. In: Eskola H., Väisänen O., Viik J., Hyttinen J. (editors). EMBEC & NBC 2017. IFMBE Proceedings, vol. 65; p. 37–40, https://doi. org/10.1007/978-981-10-5122-7_10.

Luzhnov P.V., Shamaev D.M., Iomdina E.N., Tarutta E.P., Markosyan G.A., Shamkina L.A., Sianosyan A.A. (2015) Transpalpebraltetrapolarreoophtalmography in the assessment of parameters of the eye blood circulatory system. VestnikRossiiskoiakademiimeditsinskikhnauk; 70(3): 372–377, https://doi.org/10.15690/vramn.v70i3.1336.

Luzhnov P. V., Shamaev D. M., Kiseleva A. A., Iomdina E. N. (2018), Analyzing rheoophthalmic signals in glaucoma by nonlinear dynamics methods. IFMBE Proceedings 68/2: pp.827-831. DOI: 10.1007/978-981-10-9038-7_152.

Maiorov O. Yu., Glukhov A. B., Prognimak A. B., Fenchenko V. N. (2007) Realization of the method of displacement by estimating the sizes of the axes of the attractor of the dynamic brain system. - Proceedings of the Institute of Cybernetics. - K., p. 153, pp. 5–12.

Palit K., Mukherjee S., Bhattacharya D.K. (2013) A high dimensional delay selection for the reconstruction of proper phase space with cross auto-correlation.Neurocomputing 113: 49-57.https://doi.org/10.1016/j.neucom.2013.01.034.

Palit K., Mukherjee S. (2011) Generalized autocorrelation and its application in attractorreconstruction. Bull. Pure Appl. Math. 5(2): 218–230.

Quigley, H. A., Broman, A. T. (2006) Number of people with glaucoma worldwide. Br. J. Ophthalmol. 90, 262–267.

Shamaev D. M., Luzhnov P. V., Pika T. O., Iomdina E. N., Kleyman A. P., Sianosyan A. A. (2016), Applying transpalpebral rheoophthalmography to monitor effectiveness of the treatment of patients with glaucoma". International Journal of Biomedicine 6(4): pp.287–289. DOI: 10.21103/Article6(4)_OA8.

Strogatz H., S. (2014). Nonlinear Dynamics and Chaos. With Applications to Physics, Biology, Chemistry, and Engineering. 2nd ed. Boca Raton, p.532.

Takens F. Detecting strange attractors in turbulence / In Rand D.A. and Young L.S. // Dynamical Systems and Turbulence, Lecture Notes in Mathematics. 1981. V. 898. P. 366–381.

Venkataraman, S. T., Flanagan, J. G. & Hudson, C. (2010) Vascular Reactivity of Optic Nerve Head and Retinal Blood Vessels in Glaucoma- A Review. Microcirculation 17, 568–581.

Webber C. L., Sbilut J. P. Dynamic Assessment of Physiological Systems and States Using Rrecurrence Plot Strategies.// J. Appl. Physiol., 1994, 76, p.965–993.