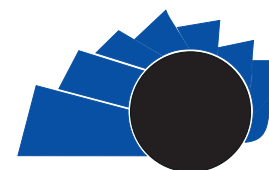


UNIVERSIDAD DISTRITAL
FRANCISCO JOSÉ DE CALDAS

Visión Electrónica

Más que un estado sólido

<https://revistas.udistrital.edu.co/index.php/visele/index>

Visión Electrónica

A RESEARCH VISION

Software for adult cardiac dynamic through dynamic systems

Software para la dinámica cardíaca adulta mediante sistemas dinámicos

Javier Oswaldo Rodríguez Velásquez¹; Jaime Alberto Páez Páez²; Sandra Catalina Correa Herrera²; Signed Esperanza Prieto Bohórquez³; Mario Fernando Castro Fernández⁴; Carlos Enrique Montenegro Marín⁵; Jairo Augusto Cortes Méndez⁶

INFORMACIÓN DEL ARTÍCULO

Historia del artículo:

Enviado: 4/12/2018

Recibido: 14/12/2018

Aceptado: 05/01/2019

Keywords:

Dynamic systems

Fractals

Probability

ABSTRACT

The normal and abnormal behavior of an adult heart dynamics and its state of evolution towards one of these two states has been characterized successfully in the context of the theory of dynamic systems and probability. The diagnostic methodology of clinical application designed under these two theories has managed to evaluate in an objective and reproducible way the cardiac dynamics from the values of the frequency of the Holter registers. The automation of this methodology through the design of a software that can be docked in any operating system for PC, and contributes as a diagnostic aid tool to generate more timely responses to the patient's clinical condition. Additionally, the values of the probability of these spaces occupied by the attractor, calculated by the Software, allow using an interface that can be consulted by the specialist to evaluate how far a cardiac dynamic is from normality, analyzing in this way the effectiveness of the treatment.

RESUMEN

A través de la teoría de la probabilidad y de los sistemas dinámicos se ha construido una metodología para evaluar la dinámica cardíaca –recientemente automatizada– mediante un software que puede ser acoplado a cualquier sistema operativo para PC. El software permite mediante una interfaz consultar la dinámica cardíaca por un especialista

**Palabras clave:**

Sistemas dinámicos

Fractales

Probabilidad

¹ BSc. In Medicine, Universidad Nacional de Colombia, Colombia. Current position: Research group Insight, Center of investigations Clínica del Country, Bogotá, Colombia. E-mail: grupointsight2025@yahoo.es ORCID: <https://orcid.org/0000-0002-4585-3010>

² BSc. In Psychology, Universidad Nacional de Colombia, Colombia. Current position: Research group Insight, Center of investigations Clínica del Country, Bogotá, Colombia. E-mail: scatalinacorrea@hotmial.com ORCID: <https://orcid.org/0000-0003-4998-1228>

³ BSc. In Physics, Universidad Nacional de Colombia, Colombia. Current position: Research group Insight, Center of investigations Clínica del Country, Bogotá, Colombia. E-mail: signed_hope@yahoo.es ORCID: <https://orcid.org/0000-0002-7896-231X>

⁴ BSc. In Biology, Universidad de los Andes, Colombia. Ph.D. In Biology, ecology and ethology, Universidad de Lyon I, Francia. Current position: Universidad Cooperativa de Colombia, Bogotá, Colombia. E-mail: mario.castro@campusucc.edu.co ORCID: <https://orcid.org/0000-0001-7239-0763>

⁵ BSc. In Systems engineering, Universidad Distrital Francisco José de Caldas, Colombia. Ph.D. In Computer systems and services for internet, Universidad de Oviedo, España. Current position: Universidad Cooperativa de Colombia, Bogotá, Colombia. E-mail: carlos.montenegrom@campusucc.edu.co ORCID: <https://orcid.org/0000-0002-3608-7158>

⁶ BSc. In Systems engineering, Universidad INCCA de Colombia, Colombia. Ph.D. In Information and knowledge society, Univesitat Oberta de Catalunya, España. Current position: Universidad Cooperativa de Colombia, Bogotá, Colombia. E-mail: jairo.cortes@campusucc.edu.co ORCID: <https://orcid.org/0000-0001-5650-4687>

del área clínica y así evaluar qué tan alejada se encuentra una dinámica cardíaca de la normalidad. En este estudio se hizo uso de dicho software para desarrollar un estudio de concordancia diagnóstica para confirmar su capacidad como herramienta de evaluación a nivel clínico. Para ello se parte de la medición de: 120 registros Holter, 100 patológicos y 20 normales, durante 21 horas; con los cuales se toman los valores de la frecuencia cardíaca y número de latidos; en base a esta información el software elabora secuencias pareadas y construye atractores con los cuales cuantifica la dimensión fractal, los espacios de ocupación en el espacio fractal de Box Counting, y los valores de la probabilidad de los espacios ocupados por el atractor. De lo anterior se encontró que este proceso permite diferenciar la normalidad de la patología aguda y su evolución, obteniendo valores de sensibilidad y especificidad del 100%. Dado este contexto, es de destacar que el proceso permite analizar de una manera objetiva y reproducible la efectividad de los tratamientos médicos.

1. Introduction

The first nonlinear dynamical systems were developed by Poincaré [1]. The geometrical representation a dynamic system is called attractor. This means that each system can be represented by an attractor through which is possible to characterize The evolution of the system across time [2]. By now, periodic, cyclic and chaotic dynamical systems exist [2]. The degree of irregularity of an attractor generated from the variables of a chaotic dynamic system can be analyzed through fractal geometry [3].

Although, in the field of cardiology some studies have analyzed the behavior of heart rate frequency in the context of nonlinear systems. Goldberger proposed these first studies; whose findings changed the classical conception of homeostasis observing that a normal cardiac dynamic is found between highly irregular and regular dynamics [4]. Even though these studies have changed the way to analyze cardiac pathologies, the application of this and other methodologies from this perspective are still on studies [5].

Within the framework of the previous remarks new diagnostic methodologies have been proposed to be clinically applicable to study the adult and neonatal cardiac dynamic, in the context of dynamical systems fractal geometry and probability [6-13]. Probability theory is a branch of mathematics that allows to evaluate the possibility of occurrence of an event whose probable results can be analyzed in a probability space [14,15]. The theories of probability and dynamical systems along fractal geometry, which are the base of these new methodologies have achieved to establish mathematical parameters that evaluate how far a normal cardiac dynamic is from abnormality, as well as the evolution towards one of these states, taking for that the values of heart

rate frequency obtained from the report of Holter registries and/or continuous electrocardiographic records [6-13].

The effectivity of these methodologies is due to their physical and mathematical principles that characterize the different behaviors of cardiac dynamic independent of the rigorous clinical studies in the context of heart rate variability (HRV) [16-18].

In the present study the scopes that the design of a software based on a methodology designed under the perspective of dynamical systems theory and probability are shown, confirming the reproducibility and clinical applicability of the software through a blind study; subsequently the results of the test performed by the software of 120 Holter or continuous electrocardiographic registries are exhibited, which were evaluated with the physical and mathematical parameters according to the previous established diagnosis [6]; then the discussion in light of the results of the scopes that the present methodology evaluates is established, in the aim of reducing the subjectivity of the clinical evaluation of the patient, established from the studies of the Holter or continuous electrocardiographic records. Finally, the conclusions of this study are established.

2. Methodology

2.1. Definitions

Phases space: geometrical space of 2 or more dimensions that through the localization of ordered pairs of a variable along time, can graphically represent the behavior of the system to the drawing of attractors.

Box-counting method: evaluates the degree of irregularity of the chaotic cardiac attractor with the following equation:

$$D = \frac{\text{Log}N_1(2^{-(k+1)}) - \text{Log}N_2(2^{-k})}{\text{Log}2^{k+1} - \text{Log}2^k} \quad (1)$$

Which can be simplified in the following way

$$D = \text{Log}_2 \left[\frac{N_1(2^{-(k+1)})}{N_2(2^{-k})} \right] \quad (2)$$

Where D: means fractal dimension, N the number of squares occupied by the object J: partition degree of the grid.

Probability of occupation of the attractor

P_{OA} : ratio between the number of squares occupied by the cardiac attractor and the totality of squares in the generalized space of box counting.

$$P_{OA} = \frac{\text{Number of occupied squares by the attractor}}{\text{Totality of squares of the space}} \quad (3)$$

2.2. Population

120 Holter or electrocardiographic records were taken in the outpatient and ICU context and belong to the database of Insight group. Samples were reported 20 as normal Holters and 100 pathological in patients older than 21 years in a period of 21 hours.

2.3. Procedure

A blind study was developed, masking the clinical evaluation, this server president to work only with the values of minimal and maximal heart rate frequency as well as the number of beats by hour of the Holter records. With this information, a series of data of heart rates within the limits defined by the associated information to each Holter and an attractor was generated in the phases space.

For each attractor generated by the software the fractal dimension (1) was calculated through the superposition of the grids called Kp (5 beats per minute) and Kg (10 beats per minute), the number of occupied squares was quantified for each attractor with the simplified method of Box-Counting (2). Later the probability of the occupied spaces by the attractors was calculated with Kp grid (3) and with this result the software established a physical mathematical diagnosis based on numeric limits defined previously for each state [16].

2.4. Statistical analysis

The clinical conventional evaluation was masked for each Holter registry considering this

evaluation as gold standard. The reproducibility and clinical applicability of the physical mathematical diagnostic methodology was confirmed with respect to the convention of clinical evaluation through estimations of sensibility and specificity.

The estimations are result of a binary classification where the following concepts are considered with respect to the values to the number of Holters or electrocardiographic records: a) true positives (TP) Are the number of hotel registries evaluated within the ranges of abnormality and contemplated in the mathematical values of the same evaluation; b) false positives (FP) are the Holter registries that mathematically behave within abnormality and its clinical evaluation belongs to normality; c) False negative (FN) are the clinical evaluations considered as abnormal but its mathematical correspondence points towards normality and d) true negatives (TN) are the normal Holter registries that both methodologies defined as normal. Con el propósito de evaluar la concordancia entre los valores físico matemático y la evaluación clínica convencional, se calculó el coeficiente Kappa.

2.5. Ethical aspects

The findings in the present investigation were obtained from noninvasive diagnostic tests prescribed with anticipation according to standard medical procedures and therefore it is considered a minimal risk in correspondence with the Resolution 8430 of 1993 from the Ministry of Health of Colombia. Likewise, the ethical principles from the Helsinki Declaration from the Word Medical Association preserving the anonymity and integrity of the participants.

3. Results

Table 1 shows, the information of 20 representative Holters or continuous electrocardiographic records from the totality of the selected registries for the study.

The fractal dimensions of the two normal Holter registries between 1.700 and 1.970 occupying 59 and 131 squares in the Kg grids (10 beats/minute) and between 201 and 476 in the Kp grid (5 beats/minute) (see Table 2). The registries with different pathologies presented a fractal dimension that varied between 1.464 and 1.980 occupying 9 and 59 squares with the Kg grid as well as 25 and 195 with Kp grid (see Table 2).

Table 1. Representative conventional evaluation of the 120 Holter registries analyzed in the present study.

No. Holter	Conventional evaluation
1	Normal
2	Normal
3	Normal
4	Normal
5	Normal
6	Normal
7	Normal
8	Normal
9	Normal
10	Normal
11	Syncope. Arrhythmia in study.
12	Tachycardia, infrequent, isolated and occasionally blocked auricular extrasystoles
13	Isolated ventricular monomorphic extrasystoles
14	Sinus tachycardia with isolated episodes of bigeminism
15	Medical history of dilated cardiopathy. Infrequent ventricular polymorphic extrasystoles and isolated short episodes of bigeminism and trigeminism
16	Auricular fibrillation with elevated ventricular response; light tendency towards sinus tachycardia
17	Auricular fibrillation, frequent ventricular monomorphic extrasystoles
18	Intermittent left bundle branch block dependent of increases of heart rate.
19	Acute myocardial infarction.
20	Acute heart failure. Auricular fibrillation with rapid ventricular response.

Source: own.

Table 2. Mathematical diagnostics of the Holter registries from Table 1. Kp: grid with small squares; Kg grid with big squares; Df fractal dimension of the attractor, P: probability of each attractor; N: normal cardiac dynamic; Ev: cardiac dynamic progressing towards disease; A: acute cardiac dynamic.

No. Holter	Kp	Kg	Df	P	Mathematical diagnosis
1	476	131	1,861	0,367	N
2	376	96	1,970	0,290	N
3	328	90	1,866	0,253	N
4	300	88	1,769	0,231	N
5	290	77	1,913	0,224	N
6	259	71	1,867	0,200	N
7	255	73	1,805	0,197	N
8	221	68	1,700	0,171	N
9	201	59	1,768	0,155	N
10	195	59	1,725	0,150	Ev
11	142	36	1,980	0,110	Ev
12	121	36	1,749	0,093	Ev
13	107	28	1,934	0,083	Ev
14	105	33	1,670	0,081	Ev
15	87	31	1,489	0,067	Ev
16	81	25	1,696	0,063	Ev
17	61	16	1,931	0,047	A
18	61	16	1,931	0,047	A
19	58	16	1,858	0,045	A
20	25	9	1,474	0,019	A

Source: own.

4. Discussion

This is the first work of investigation that achieves to confirm the reproducibility and clinical applicability of a methodology designed in the context of dynamic systems theory, fractal geometry and probability to evaluate neonatal cardiac dynamic. This confirmation was possible through the calculation of the values of sensitivity and specificity of 100% from the results generated by the software, confirming that the program is ready to be taken to any clinic in the future and that it can be used as a diagnostic tool.

In this case, previous studies developed in the same line of investigation have revealed that the occupied spaces by the normal attractor are bigger compared with the pathological attractors, the occupation values of the Kp and Kg grids differentiate in this context normality from acute disease [6,7]. Although both grids give values that allow to make comparisons the Kp grid was chosen as the one that can make more precise differences between attractors. From this point of view, a predictive measure that establishes that bigger values are diagnosed as normal while the smaller ones as abnormal from the physical mathematical diagnosis. The effects of these results are the evolution of the disease is associated with a progressive diminution of the spatial occupation of the attractor, achieving an objective measure of bigger severity

These results, compared with the conventional clinical analysis that arises from HRV, are differentiated in the way that the mathematical values that characterize the level of severity of the cardiac dynamic along the time, independent of clinical classifications, that usually involucrate another set of tests to confirm the performed evaluations within the clinical parameters bases on the clinical evidence [19-24].

In the light of these results, several advances in other fields as epidemiology in relation with the annual number of infected by malaria and dengue in Colombia, achieving the first predictions in this area [25]; likewise, some methodologies capable of predicting the number of CD4+ in patients with HIV/AIDS [26] and immunology [27] have been developed. Morphometrical characterizations of uterine cells as well as erythrocytes and arteries have been developed [28-30]. These methodologies, in a similar way to the present investigation, proportionate solutions for these fields in medicine, that take these disciplines to the predictive field of physics.

5. Conclusions

The present study produced a software based on dynamical systems and probability theories that allowed to differentiate normal from abnormal cardiac dynamics, thus being an option to be clinically applicable and detect alterations in adult patients.

Acknowledgments

This article is the result of the project INV 1950 financed by the Universidad Cooperativa de Colombia, Bogotá Office. The authors thank Doctors, Fernando Colmenares, Head of Investigation, Leonardo Galindo, National DINAI Head, Andrés Mena, Bogotá DINAI Director, Eva Prada, Bogotá Office Head and Edgar López, Engineering Faculty Dean, by their support to our investigations.

References

- [1] D. Núñez, “Poincaré, la mecánica clásica y el teorema de la recurrencia”, *Rev. Mex. Fis. E*, vol. 59, no 2, 2013, pp. 91–100.
- [2] R. Devaney, “A first course in chaotic dynamical systems: theory and experiments”, New York: Addison- Wesley, 1992.
- [3] H. Peitgen, H. Jurgens and D. Saupe, “Strange attractors, the locus of chaos”, *Chaos and Fractals*, New York: Springer-Verlag, 1992, https://doi.org/10.1007/978-1-4757-4740-9_13
- [4] A. Goldberger, L. A. Amaral, J. M. Hausdorff, P. Ivanov, C. K. Peng and H. E. Stanley, “Fractal dynamics in physiology: alterations with disease and aging”, *PNAS*, vol. 99, no. 1, 2002, pp. 2466 – 2472. <https://doi.org/10.1073/pnas.012579499>
- [5] H. V. Huikuri, T. Makikallio, C. K. Peng, A. Goldberger, U. Hintze and M. Moller, “Fractal correlation properties of R-R interval dynamics and mortality in patients with depressed left ventricular function after an acute myocardial infarction”, *Circulation*, vol. 101, no. 1, 2000, pp. 47-53, <https://doi.org/10.1161/01.CIR.101.1.47>
- [6] J. Rodríguez, et al., “Clinical application of a cardiac diagnostic method based on dynamic systems theory”, *Research Journal of Cardiology*, vol. 10, no. 1, 2017, pp. 1-7. <https://doi.org/10.3923/rjc.2017.1.7>

- [7] J. Rodríguez, et al., “Diagnóstico de la dinámica cardiaca durante 16 horas desde los sistemas dinámicos aplicable en UCI”, *Rev. Univ. Ind. Santander Salud*, vol. 49, no. 1, 2017, pp. 75-84. <https://doi.org/10.18273/revsal.v49n1-2017007>
- [8] J. Rodríguez, C. Correa and L. Ramirez, “Heart dynamics diagnosis based on entropy proportions: Application to 550 dynamics”, *Rev. Mex. Cardiol.*, vol. 28, no 1, 2017, pp. 10-20.
- [9] J. Rodríguez, et al., “Evaluación de arritmias con base en el método de ayuda diagnóstica de la dinámica cardiaca basado en la teoría de la probabilidad”, *Archivos de Medicina*, vol. 15, no. 1, 2015, pp. 33-45.
- [10] J. Rodríguez, et al., “Physical-mathematical diagnosis of cardiac dynamic on neonatal sepsis: predictions of clinical application”, *J. Med. Med. Sci.*, vol. 5, no 5, 2014, pp. 102-108. <https://doi.org/10.14303/jmms.2014.070>
- [11] J. Rodríguez, A. Bertolotto and O. Ospina, “Caracterización matemática de dinámicas cardiacas neonatales normales a partir de la teoría de la probabilidad”, *Universitas Medica*, vol. 58, no 1, 2017, pp. 1-18. <https://doi.org/10.11144/Javeriana.umed58-1.cmdc>
- [12] J. Rodríguez, et al., “Mathematical-physical prediction of cardiac dynamics using the proportional entropy of dynamic systems”, *J. Med. Med. Sci.*, vol. 4, no. 8, 2013, pp. 370-381.
- [13] J. Rodríguez, M. Sanchez, F. Barrios, N. Velásquez and J. Mora, “Exponential law of cardiac dynamics for physical-mathematical evaluation in 16 h”, *Medicina Universitaria*, vol. 19, no. 77, 2017, pp. 159-65. <https://doi.org/10.1016/j.rmu.2017.09.003>
- [14] M. R. Spiegel and L. J. Stephens, “Probabilidad y estadística”, Bogotá: Mc Graw Hill. 2003.
- [15] A.M. Mood, “Introduction to the theory of statistics”, McGraw-Hill Education, 1974.
- [16] J. Gallo, J. Farbiarz and D. L. Alvarez, “Análisis espectral de la variabilidad de la frecuencia cardíaca”, *IATREIA*, vol. 12, no. 2, 1999, pp. 61-711.
- [17] J. P. Higgins, “Nonlinear systems in medicine”, *Yale. J. Biol. Med.*, vol. 75, 2002, pp. 247-60.
- [18] M. Costa, A. L. Goldberger and C. K. Peng, “Multiscale Entropy Analysis of Complex Physiologic Time Series”, *Phys. Rev. Lett.*, vol. 89, no. 6, 2002, pp. 1021–1024. <https://doi.org/10.1103/PhysRevLett.89.068102>
- [19] G. Schmidt, et al., “Heart-rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction”, *Lancet*, vol. 353, 1999, pp. 1390–1396. [https://doi.org/10.1016/S0140-6736\(98\)08428-1](https://doi.org/10.1016/S0140-6736(98)08428-1)
- [20] A. Voss, et al., “Linear and nonlinear heart rate variability risk stratification in heart failure patients”, *Computers in Cardiology*, 2008. <https://doi.org/10.1109/CIC.2008.4749102>
- [21] R. Maestri, et al., “Nonlinear indices of heart rate variability in chronic heart failure patients: redundancy and comparative clinical value”, *J. Cardiovasc. Electrophysiol.*, vol. 18, no. 4, 2007, pp. 425–33. <https://doi.org/10.1111/j.1540-8167.2007.00728.x>
- [22] S. Ahmad, A. Tejuja, K. D. Newman, R. Zarychanski and A. J. Seely, “Clinical review: a review and analysis of heart rate variability and the diagnosis and prognosis of infection”, *Crit Care*, vol. 13, no. 6, 2009, pp. 232. <https://doi.org/10.1186/cc8132>
- [23] W. L. Chen and C. D Kuo, “Characteristics of heart rate variability can predict impending septic shock in emergency department patients with sepsis”, *Acad Emerg Med*, vol. 14, no. 5, 2007, pp. 392–397. <https://doi.org/10.1197/j.aem.2006.12.015>
- [24] V. E. Papaioannou, et al., “Relation of heart rate variability to serum levels of C-reactive protein, interleukin 6, and 10 in patients with sepsis and septic shock”, *J Crit Care*, vol. 24, no. 4, 2009, pp. 625. <https://doi.org/10.1016/j.jcrc.2008.11.010>
- [25] J. Rodríguez, “Método para la predicción de la dinámica temporal de la malaria en los municipios de Colombia”, *Rev Panam Salud Pública*, vol. 27, no. 3, 2010, pp. 211-218, <https://doi.org/10.1590/S1020-49892010000300008>

- [26] J. Rodríguez, et al., “Predictions of CD4 lymphocytes’ count in HIV patients from complete blood count”, *BMC Medical Physics*, vol. 13, no. 3, 2013. <https://doi.org/10.1186/1756-6649-13-3>
- [27] J. Rodríguez, “Teoría de unión al HLA clase II teorías de Probabilidad Combinatoria y Entropía aplicadas a secuencias peptídicas”, *Inmunología*. vol. 27, no. 4, 2008, pp. 151-166. [https://doi.org/10.1016/S0213-9626\(08\)70064-7](https://doi.org/10.1016/S0213-9626(08)70064-7)
- [28] J. Velásquez, et al., “Geometrical nuclear diagnosis and total paths of cervix cell evolution from normality to cancer”, *J Cancer Res Ther*, vol. 11, no. 1, 2015, pp. 98-104. <https://doi.org/10.4103/0973-1482.148704>
- [29] C. Correa, et al., “Geometric diagnosis of erythrocyte morphophysiology”, *J. Med. Med. Sci.*, vol. 3, no. 11, 2012, pp. 715-720.
- [30] J. Rodríguez, et al., “Theoretical generalization of normal and sick coronary arteries with fractal dimensions and the arterial intrinsic mathematical harmony”, *BMC Med Phys*, vol. 10, no. 1, 2010, pp. 1-6. <https://doi.org/10.1186/1756-6649-10-1>