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Full Length Research Paper

Mathematical law for chaotic cardiac dynamics: Predictions for clinical application

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The purpose of this study was to develop a new diagnostic methodology for cardiac dynamics. A mathematical deduction of Box-Counting equation was made, to determine the mathematical relationship between the occupancy spaces of parts and the total object, which corresponds to fractal dimension. Then, attractors of 8 dynamics were built based on a simulation, calculating its fractal dimension and the number of occupied spaces by the attractors on the box counting space, establishing a mathematical diagnostic method, which was statistically assessed for the evolution normality/disease. An exponential law that relates the parts with the fractal totality was found, differentiating normality, evolution and acute disease; it showed mathematically the severity degree of pathologies and allowed calculating all possible cardiac attractors for 21-year patients and over. Comparing to conventional diagnosis, the analysis of the evolution normality/disease with the mathematical diagnosis had a sensibility, specificity and a Kappa coefficient result of one. The law predicts that fractal dimensions could not differentiate normality and disease effectively. The chaotic cardiac behaviour obeyed to a mathematical law, which allowed differentiating in an objectively way, normality and acute disease, making it a clinical diagnosis method for preventive value, which quantitatively measures the evolution degree of cardiac disease.

Keywords: Dynamical systems, fractals, chaos, heart rate, diagnosis.

INTRODUCTION

The dynamic systems theory describes the system variables behaviour, which its state and evolution is defined. To make this possible, abstract spaces constructed with the dynamic variables of system were developed, like delay maps, to determine if the system is predictable or unpredictable. There were generated three types of attractors: pointed, cycled and chaotic (Devaney, 1992; Peitgen et al., 1992a). The punctual attractor describes a system that tends to the state which its dynamic variables take a constant value as the physical pendulum, when by friction rises its repose state. The cyclical attractor corresponds to a system which its dynamic variables periodically take the same values; that is the case of an ideal pendulum, which remains in perpetual periodic movement. Finally, the chaotic attractor describes a system which there is no tendency of a particular state, or neither a periodic behaviour regarding to a set of states. From this construct, the

chaos is conceived as a dynamic system just as the others, but fundamentally unpredictable and dependent of initial conditions (Crutchfield et al., 1990). Mathematical chaos has been differentiated in two: determinist and stochastic. Determinist chaos is characterized by: a non-linear system, impossibility of long-term prediction, exponential character on the prediction, lose of precision and knowing of the behavior and statistical properties of a trajectory, even when there are regularities of this kind (Giron, 2010). Stochastic chaos is characterized by a non-duration of statistical memory (Sanchez et al, 2008), because the probability itself could present a chaotic behavior, making impossible to determine if the underlying phenomenon is probable or not (Calabrese, 1999).

The irregularity is one of mathematical conditions of a chaotic attractor; its mathematical characteristic, from

fractal dimension, is a non-dimensional measurement proper from fractal geometry; it was developed by Benoit Mandelbrot (2000a,b). There are three types of fractals, which fractal dimensions is obtained by different methodologies: abstract ones, like Sierpinski's triangle, is characterized by equality of parts and totality; the savages, which have parts that are overlapping between them, and they are represented by nature objects (Mandelbrot, 2000b); and the statistical ones, which has hyperbolic distributions (Rodríguez, 2005). That is why fractal dimension is not a universal concept, because it is not applicable in all cases. The calculation methodology of box-counting dimension could be applied to self-similar objects; even though, is usually used to obtain fractal dimensions of non-self-similar objects (Peitgen et al., 1992b). Box-counting space allows observing the spatial occupation of an object in different scales, by different size of squares overlapped and the account of each occupied squares by the object. The fractal dimension is the incline of the straight line built by points, which Cartesian coordinates are the logarithm of the total occupied squares by the measured object, and the multiplicative inverse of the square wide. For practical effects, it could be convenient considering a $\frac{1}{2}$ proportion between the square wide and the next one's wide (Peitgen et al., 1992b).

Fractal geometry has been used in cancer studies (Luzi and Biancardi, 1999; Landini and Ripplin, 1993; Gazit et al., 1997), and also has allowed establishing differences between normality and disease in different cases, such as foetal or adult cardiac dynamics (Rodríguez, 2006; Rodríguez et al., 2008a). Based on the dynamics system theory applied to physiology, Goldberger (2002) enounced that sick systems present high periodicity or excessive randomness, whereas a healthy behaviour is related to an intermediate behaviour of those extremes. With this kind of methodologies, from R-R intervals fractals dimensions calculations of patients with Acute Myocardial Infarction (AMI) (Huikuri et al., 2000), better death predictors than the conventionally applied in clinic were achieved.

Recently Rodríguez et al. (2010a), on the basis of fractal geometry and the Intrinsic Mathematical Harmony concept, made a theoretical generalization that allows determining the total normal and disease arterial prototypes, based on a previous work on animal experimentation for restenosis phenomenon, (Rodríguez et al., 2002), that links parts and totalities of arteries to clearly differentiate normal from sick arteries through fractal dimensions; the methodology of this work consisted in a simplification of the Box Counting method, using two $\frac{1}{2}$ proportion grids, and makes a generalization with experimental and clinical applications. Through this way, this research will find a generalization of the totality of cardiac dynamics, differentiating normality from disease, based on a simplification of Box-Counting method applied to cardiac dynamic systems, and the

deduction and application of a law for the chaotic cardiac dynamics, useful as a new Holter assessment method for clinical application.

METHODS

Definitions

Box-Counting Fractal Dimension

$$D = \frac{\text{Log}N (2^{-(j+1)}) - \text{Log}N (2^{-j})}{\text{Log} 2^{j+1} - \text{Log} 2^j} = \text{Log}_2 \frac{N (2^{-(j+1)})}{N (2^{-j})} \quad (1)$$

D: Fractal Dimension.

N: Number of boxes occupied by the object.

j: Grade of division of grid.

Fractal dimension was calculated by the simplified box-counting method, using only two grids, in order to make a calculus simplification, which the squares' one side is the double of the next squares side. So, this equation could be re-written by this:

$$D = \text{Log}_2 \frac{K_p}{K_g} \quad (2)$$

Where K_p is the number of squares on the small grid, and K_g is the number of squares on the big grid, represented by $N(2^{-(j+1)})$ y $N(2^{-j})$ on the equation 1, respectively.

Then, each square-grid was placed over the images, in order to count the squares, required for the box-counting method application.

Permutations

The entire number of possible attractors (N_A) of cardiac dynamics. To calculate this, use the formula:

$$N_A = (Mx - Mn + 1) \left[\frac{3}{2} (Mx + Mn) + 1 \right] \quad (3)$$

Where,

Mx: It is the maximum number of occupied spaces for the attractors in the K_g grid of box counting space.

Mn: It is the minimum number of occupied spaces for the attractors in the K_g grid of box counting space.

For demonstration of equation, see appendix A.

METHOD

Prototypes for the clinic induction

There were studied the Holters of eight patients, three volunteers with normal exam, and five with different diseases chosen from cardiology service of the Fundación Cardio Infantil; for patients data see Table 1. Three of the pathological cases correspond to acute cases, while the other two correspond to chronic patients. The clinical examinations were assessed by a

Table 1: Conventional diagnosis and measures for the studied prototypes.

No	Conventional Diagnostic	±Kp	†Kg	*DF	Age	VE	§SVE
1	Study within the normality limits	479	131	1,8704	21		
2	Study within the normality limits	329	90	1,8700	37		
3	Study within the normality limits	200	61	1,7131	27		
4	Palpitations	161	47	1,7763	51	6	
5	Palpitations, sometimes associated with supraventricular extra systoles. Decreased variability R-R	154	52	1,5663	33	2	1266
6	AMI. RVM. Syncopate to repetition. Occasional supraventricular ectopic with formation of a triplet, occasional unifocal ventricular ectopic, slight decrease in R-R variability.	73	23	1,6662	81	20	9 with 1 Run-Supra Ventricular
7	IAM, Total minutes of ST episode 28. Maximum delta change - 1.7.	62	16	1,9541	64	2903	30
8	AMI. 2 pauses exceeding 2.5 seconds. Sinus bradycardia with a maximum 87, average of 50, breaks of up to 3.0 seconds. Ectopic atrial events not conducted without repetitive phenomena. Occasional ventricular ectopy without repetitive phenomena. It suggests sinus dysfunction.	49	16	1,6147	54		95 with 9 Run-Supra Ventricular

*Kp: number of occupied spaces in the small grid.
 †Kg: number of occupied spaces in the big grid.
 ‡DF: fractal dimension of chaotic attractors.
 §SVE: ventricular ectopy.
 ||SVE: supraventricular ectopy.

cardiology service specialist of the Clinic.

All exams were defined as basic prototypes, and were chosen because radically differentiate normality, chronic and acute disease, as AMI; its diagnoses did not have any doubts according to the conventional assessment method, and cover a wide range of ages, from 21 to 81 years, as well as a wide range of medium (51-98), minimal (32-55) and maximum (87-164) heart rate values. This allows an inductive process from these particular prototypes in the context of a finite universal phase space for all the attractors. This space has a box-counting space generalization, and allows comparing any attractor to another, containing all the attractors; in this way, it also allows to develop a generalization to deduce all the possible cardiac dynamics and make physical and mathematical comparisons in order to find clinical applications, applicable to patients whose values are contained within these numeric ranges.

Analysis of record

With the minimal and maximum cardiac frequency for each hour, for the 21 hours record in every exam, there was made a software that generates the cardiac frequencies sequence in the defined range expressed on an equiprobable algorithm, to construct the attractor of each dynamics on a delay map, which one frequency is charted against the next one on a two-dimensional space. Then, the occupied spaces by the attractor were

measured and its fractal dimension was evaluated with the Box-counting method; see definitions. The chosen grids to observe the occupied spaces by the attractor were 5 and 10 beats / minute.

Deduction of mathematical law

Starting on the Box-Counting equation (see equation 2), there were deduced the relationship between the number of occupied squares on the grids, in terms of fractal dimensions. By this method, there were changed from a logarithmical equation to an exponential one, to observe the number of occupied squares on the big and the small grids and their connection with fractal dimension.

Deduction of all the possible cardiac dynamics

Then, all the possible cardiac dynamics were determined from the maximum (Mx) and minimum (Mn) number of occupied spaces by the experimental attractors in the Box-counting space, based on the permutations calculation (Grimaldi, 1989); see equation 2.

Mathematical Analysis

After measuring the fractal dimension and the spaces occupied by the attractors with the grids, the values were

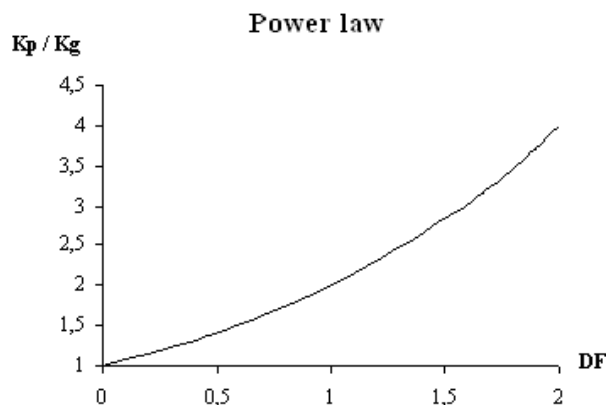


Figure 1: Exponential law of chaotic cardiac dynamics. Relation between occupied spaces proportion regard to fractal dimension.

compared, searching differences and equalities between normality and disease related to the established law, constructing a mathematical diagnosis.

Based on the equation 3, the evolution between normality and acute illness is predicted taking the minimal values of normality and maximum of acute illness from the assessed prototypes.

Statistic analysis for normality-disease evolution

The mathematical diagnosis efficacy regard to the normality-disease evolution was assessed. There were selected 100 individuals from a data base, excluding those under 21 years old. A simple random sampling was made (using a randomization table); selecting a sample of 34 patients whose Holter conclusions and clinical background were masked and established as Gold Standard. Minimum and maximum values, and total heart beats recorded on the Holter for each hour were not masked due to those are necessary to make the mathematical-physical methodology application. Then the mathematical-physical methodology fulfilled in this work was applied to the sample, and the diagnostic results of Holter were unmasked; four patients with chronic diseases included in the normal range, according to the mathematical methodology were excluded, in order to examine in a specific way the dynamics which clearly evolve from normality to acute disease. The sensitivity, specificity, false negative rate and false positive rate for the proposed diagnostic method were calculated in a contingency table. Later, the concordance between Gold Standard and the physical-mathematical diagnosis was evaluated by Kappa coefficient.

This study follows the established norms on articles 11 and 13 at 008430 of 1993 resolution of Colombia's Health Ministry, due to the physical calculations are made on results of non invasive medically prescribed exams of the clinical practice, protecting the integrity and anonymity of

participants; so, there was not necessary informed consents.

RESULTS

Theoretical results

After cleared the Box Counting equation, it has found that:

$$\frac{K_p}{K_g} = 2^{DF} \quad (4)$$

$$K_p = K_g 2^{DF} \quad (5)$$

$$K_g = \frac{K_p}{2^{DF}} \quad (6)$$

Where:

Kp: Occupied spaces by the attractor in the small grid.

Kg: Occupied spaces by the attractor in the big grid.

DF: Fractal dimension.

If the proportion values of occupancy spaces on fractal dimension is charted, it has found an exponential behaviour of variables, as it is seen at Figure 1. So, the proportion values of occupied spaces and the fractal dimension values are finite, less than four and in a range of zero and two; the exponential behaviour is finite and every attractor is included in the law.

Clinical application results execution

Prototypes analysis

The fractal dimensions for the 8 analyzed attractors ranged between 1.5663 and 1.9541. For the individuals with normal cardiac dynamics the fractal dimensions ranged between 1.7131 and 1.8704, while for the sick ones ranged between 1.5663 and 1.9541; the chronic disease Holters, corresponding to numbers 4 and 5,

Table 2: Prediction of cardiac dynamics starting from occupation spaces Kp and fractal dimensions arbitrarily chosen

	No.	*Kp	†Kg	2 ^{DF}	‡DF
Normality	1	478	130	3,6769	1,8785
	2	400	118	3,3898	1,7612
	3	300	105	2,8571	1,5145
Evolution	4	190	56	3,3928	1,7625
	5	163	88	1,8522	0,8893
	6	129	38	3,3947	1,7632
	7	100	53	1,8867	0,9159
Acute Disease	8	65	17	3,8235	1,9349
	9	51	15	3,4	1,7655
	10	34	10	3,4	1,7655

The law predicted that the fractal dimension values could not differentiate disease from normality; so, the first three calculations are associated to normal cardiac dynamics, the three last to acute disease dynamics, and the other one to evolution between them, including five with the same values in the unit and the two first decimals ciphers.

* Kp: number of occupied spaces on the small grid.

†Kg: number of occupied spaces on the big grid.

‡ DF: fractal dimension of chaotic attractors.

presented values of 1.56635 and 1.7763, while the acute disease Holters ranged between 1.6147 and 1.9541.

The number of occupied spaces on the first grid for the eight attractors, Kp ranged between 49 and 479; on the second grid, Kg resulted between 16 and 131. The occupied spaces of normal cardiac dynamics' individuals, on the first grid, Kp ranged between 200 and 479; while on the second grid, Kg ranged between 61 and 131; for sick persons the values of Kp grid ranged between 49 and 161, and for the Kg grid were between 16 and 52. The chronic Holters presented 154 and 161 occupied spaces for the Kp grid, and 52 and 47 for the Kg grid respectively, while the acute disease Holters ranged between 49 and 73 occupied spaces for the Kp grid and between 16 and 23 for the Kg grid. These measures are seen at Table 1.

Predictions of law

Kp value and fractal dimension let calculating Kg, applying the equation 6; so, knowing the empirical maximum values in the occupancy spaces of cardiac dynamics and the fractal dimension, it was possible to obtain another space combination that tends to the same fractal dimension. In this way, the law predicted that the fractal dimension value could not differentiate disease from normality. It is seen in the table 2, where 10 theoretical cardiac dynamics were constructed, and it was possible to find any fractal dimension associated to normality or disease, including five with the same values in the unit and the two first decimal ciphers on fractal

dimension. The progressive decrease in the occupancy spaces allowed a clinical evaluation of preventive nature, as well as monitoring the evolving dynamics in time.

Result for Diagnostic Aid

AMI patients presented the minimum occupancy spaces, while normal individuals presented the maximum values on the observed occupancy spaces, and the rest presented middle values. The Kp occupation parts of attractors space that represent the acute disease patients dynamics, such as AMI, showed values less than 73; those in evolution between normality and acute disease, presented values on the interval between the superior boundary of acute range and the inferior boundary of normality, it means, 73 and 200; the values corresponding to the normal attractors are higher than 200.

As predicted by the law, fractal dimensions do not effectively distinguish normality from disease. This is evidenced in a fact it is not possible to establish ranges between normality and disease on the prototypes, and the mathematical and physical diagnosis completely differentiate those states. It confirms the theoretical prediction about that the same fractal dimension equally associated to normality or disease.

Number of possible theoretical cardiac attractors

Based on the empirical ranges, there are 25,694 possible heart attractors; 20,519 normal, 476 associated to acute

Table 3: States of all possible attractors, and total possible attractors for normality and acute disease.

Conventional Diagnostic	*Max Kg	†Min Kg	Attractors
Total	131	16	25.694
Normal	131	61	20.519
Acute disease	23	16	476

*Max Kg: maximum number of empirical occupied spaces in the big grid.

†Min Kg : minimum number of empirical occupied spaces in the big grid.

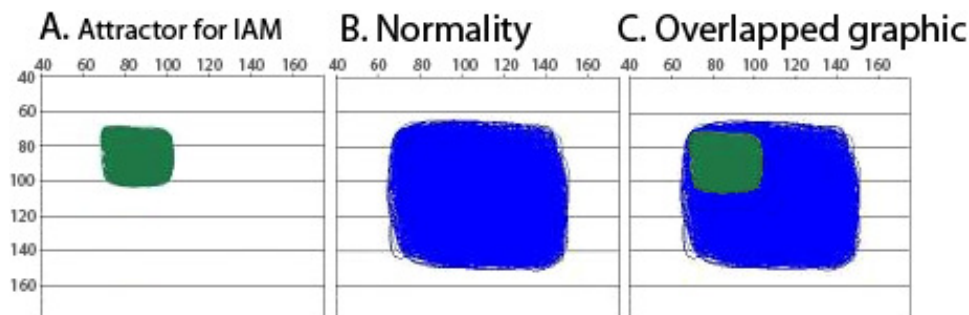


Figure 2

disease, and the remaining 4,699 in evolution between normality and acute disease (Table 3). For example, the acute disease presented a maximum of Kg of 23 and a minimum of 16; so, there are $(23-16+1) = 8$ attractors related to this interval, and when is added the combinations of possible values of Kp spaces in that defined range, using the equation 3, the all possible attractors is obtained, which are 476. The attractor's space occupation can be seen in Figure 2.

Statistical analysis for the normality-disease evolution

For the selected Holters sample, the occupying spaces Kp values ranged between 483 and 36. See Table 4. The normal Holters presents Kp values equal or higher than 258 in all cases, while those with acute disease present Kp values equal or less than 47. The corresponding Holters to normality-acute disease evolution were in the middle range, between 81 and 198, showing as a useful methodology on the characterization for each evolution.

The results show that the mathematical diagnosis sensitivity was 1; the specificity was 1, while the rate of false positives and false negatives were 0. The Kappa coefficient was 1, corresponding to the highest concordance level. As it was predicted, the fractal dimensions values are indistinguishable regarding to normality and disease.

DISCUSSION

This is the first work where an exponential law on clinical application is obtained and so as all the possible discreet chaotic cardiac attractors, achieving to differentiate normality, disease and its evolution. The difference between the minimal occupancy value of attractors with normal cardiac dynamics and the maximum of sick patients restricts a physical and mathematical space to rigorously study the normality-disease evolution. The simulations made in this work express the clinical values and are useful on the attractor's construction, so, it is not necessary to have all the frequencies information rigorously in time; the consecutive real frequencies data does not affect the result, since they are included into the simulation. The mathematical found limits allow the programs design for pacemaker, and would be important for a physical and mathematical assessment of pharmacological efficacy.

The eight prototypes constituted a simple experiment designed to develop the normality-disease differentiation, the evolution between them, and the generalization for any case in the universe; this is without taking into account the epidemiology, which is causal and studies specific populations, and here it is replaced by a general physical and acausal conception, which allows establishing a diagnosis for any cardiac functioning in patients over 21 years old. So, the mathematical diagnose possesses a preventive nature, allowing early detection of dynamic changes in health-disease evolution, regardless of symptoms or disease

Table 4: Conventional diagnosis and measures for chosen holters.

Conventional Diagnostic		*Kp	†Kg	‡DF	§VE	 SVE
1	Study within the normality limits	483	127	1,9271		
2	Study within the normality limits	315	85	1,8898		
3	Study within the normality limits	281	85	1,7250		
4	Study within the normality limits	258	67	1,9138		
5	Palpitations and chest pain	198	55	1,8479		
6	Fainting	188	51	1,8821		
7	Palpitations	182	49	1,8930		
8	Arrhythmia	175	46	1,9276		
9	Palpitations	168	43	1,9660		
10	Tachycardia	159	49	1,6981		11
11	Arrhythmia	157	47	1,7400	2	121
12	Syncope	152	49	1,6332		23
13	Cardiac Arrhythmia Blockade of Branch	155	49	1,6614		
14	Palpitations	151	41	1,8808	9670	
15	Dizziness, Palpitations	143	45	1,6680	3	94
16	Postoperative Ablation	143	36	1,9899	2	4
17	Arrhythmia	140	40	1,8073	480	509
18	Bradycardia	127	38	1,7407		
19	Syncope	125	43	1,5395		1
20	Postoperative Ablation	121	36	1,7489	2	
21	Postoperative Ablation	121	36	1,7489	2	
22	Palpitations	114	35	1,7036		
23	Complete right bundle branch block, Bradycardia, Syncope	113	36	1,6502		
24	Syncope	102	33	1,6280		
25	Palpitations	102	32	1,6724	340	2650
26	Cardio Defibrillator	81	25	1,6959	5018	
27	Control of pacemaker	47	16	1,5545	1	33
28	IAM	47	16	1,5545	349	
29	Control of pacemaker	33	9	1,8744	1	
30	Fibrillation and Ventricular Flapping	36	14	1,3625		

* Kp: number of occupied spaces in the small grid.

†Kg: number of occupied spaces in the big grid.

‡ DF: fractal dimension of chaotic attractors.

§ VE: ventricular ectopy.

|| SVE: supraventricular ectopy.

diagnosed from the traditional classification. This methodology is both clinically as mathematically reliable, and further studies can be made to determine more precisely the limits of normal, chronic and acute disease, but this does not affect the core concept of the proposed method.

Fractal geometry applications in cardiac physiology (Goldberger et al., 1990; Goldberger, 1996), usually relate a greater irregularity degree to health and a lower state for disease. However, in many cases it is found that greater or lower complexity values on fractal dimension can be presented in normal or pathological cases. For example, Rodríguez et al. (2008a) found that the fractal measurements of cardiac attractors did not differentiated normality and disease; they developed a methodology to characterize cardiac dynamics in adults, based on the

dynamical systems theory, and differentiated the normal and chronic dynamics from acute ones. In this study is evidenced, from a mathematical and physical point of view, that the association between disease and higher fractal dimension values does not have a solid mathematical fundament, which is confirmed by the resulted fractal dimensions; the empirical findings show that fractal dimensions values can be presented in any state, in the same way, it is found that chronic patients (diagnosed with arrhythmia), presented both mathematical values associated to normality and evolution. For example, cases 8, 12, 14 and 17 have values below 200, showing that their dynamics is not normal but has a clearly chronic disease.

Arrhythmias may be occasional finding without clinical significance and their commitment degree can be

assessed in a different way with the current classifications (Fernandez and Merino, 2005). Different arrhythmias may be associated with normality, evolution or acute disease, showing that the Kp values objectively quantify the dynamic evolution from disease to normality. For example, observing the Kp values of holter with arrhythmia, is notice that the case 8 does not have a normal dynamic, showing a Kp value of 175, but it has a lower severity degree than the case 12, which has a Kp value of 157; however, the case 17 presents a dynamic close to acute disease than the two previous dynamics, showing a 140 Kp value. These examples show how the measurement of Kp values can quantify the evolution degree between health and disease, which is confirmed by statistical analysis showing that the proposed diagnostic method is consistent.

Another researches developed from an acausal perspective in some medical areas, like binding phenomenon, allows the development of a predictive theory and its application for binding phenomena to HLA class II, and a binding predictive theory of malaria peptides to red blood cells (Rodríguez, 2008b; Rodríguez et al., 2010b). Also it was developed a diagnostic methodology for clinical application of foetal heart rate monitoring based on the dynamical systems theory and the Zipf-Mandelbrot law (Rodríguez, 2006). In epidemiology, there was made a prediction of the weekly dynamic of the malaria epidemic based on the entropy law (Rodríguez, 2010d). In cardiac dynamic, Rodríguez found a new diagnostic method of clinical application based on entropy proportions of the cardiac attractor, which differentiate normality from acute and chronic disease, as well as evolution on these states (Rodríguez, 2010c).

Similar to the self-similarity in abstract fractals, in this work was found that the geometric essence for the attractors is an order between parts and totality, but in this case expressed by exponential law, which explains the difficulty on establishing normal and disease ranges in other studies (Landini and Ripplin, 1993), because it is necessary to find a relationship between parts and the whole object studied, instead of variability measurements only; as studied in some works previously developed with fractals measures in reestenosed arteries (Rodríguez et al., 2002). So, fractal dimension is taken as the totality, and the occupancy spaces of attractor as the parts; having cleared the Box-Counting equation, it has revealed a law between these mathematical relations, which differentiate the clinical normality and disease behaviours. It was made a theoretical generalization based on fractal geometry that allows to determine all the artery prototypes from its application in an animal research experimental model for restenosis (Rodríguez et al., 2010a). In the same way, this work establishes all possible cardiac dynamics generalization, with clinical implications.

Also, there was found a fundamental difference related to the dynamic systems normality/disease conception (Goldberger, 2002), because there is not randomness, but the order of a law for any dynamics, and established limits to study the evolution between these behaviours, teaching a physical and mathematical self-organization to understand by laws this phenomenon.

This work shows how from particular cases and a simple experiment, laws and generalizations can be developed from physics method for all the cases in universe for medicine. In modern physics, by the statistical mechanics (Feynman et al., 1998), the quantum mechanics (Tolman, 1979) and the chaos theory (Devaney, 1992; Crutchfield et al., 1990), is showed that causality is not the way to understand the nature. In this research, the suggested law is a physical and mathematical acausal underlying order for the chaotic cardiac dynamics, applicable to any other chaotic dynamics; suggesting a law for any chaotic process and revealing clinic reproducibility, independent of initial conditions and avoiding the un-prediction problems of chaos theory. It would be possible, based on the chaotic dynamics determinist of physiological phenomena, that the physiology could be generalized from these physical laws in order to convert it as a predictive science.

LIMITATIONS

It is necessary to develop future studies for diagnostic methods constitution in patients under 21 year-old.

DEDICATION

This work is dedicated to my children.

To master Newton, since, as Einstein says, speaking about him and Kepler: "only those who understand the immense efforts, and, especially, this devotion without the innovative work would be impossible in the theoretical science, are capable of receiving the only emotion force from which such a company can arise, being as it is something so far from immediate realities of life", because this always supports me in the way.

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REFERENCES

- Calabrese JL (1999). Ampliando las fronteras del reduccionismo. Deducción y sistemas no lineales. *Psicoanálisis* 21(3):431-453.
- Crutchfield J, Farmer D, Packard N, Shaw R (1990). Caos. In: Orden y Caos. Fernández-Rañada, editor. *Sci. Am.*, Prensa Científica S.A. pp 78-90.
- Devaney R (1992). A first course in chaotic dynamical systems theory and experiments. Reading Mass. Addison- Wesley. pp 1-48.
- Fernández I, Merino JL (2006). Temas de actualidad 2005: electrofisiología y Arritmias. *Rev. Esp. Cardiol.* 59(Supl 1): 20-30
- Feynman RP, Leighton RB, Sands M (1998). Leyes de la Termodinámica. In: Física. Vol 1. Feynman RP, Leighton RB, Sands M. Física. Vol. 1. 1st ed. Wilmington: Addison-Wesley Iberoamericana, S. A. 44-1, 44-19.
- Gazit Y, Baish JW, Safabakhsh N (1997). Fractal characteristics of tumor vascular architecture during tumour growth and regression. *Microcirculation*. pp 395-402.
- Girón González Torre, Determinismo FJ (2010). caos, azar e incertidumbre, (cited 2010 December); Available from: www.rac.es/ficheros/doc/00327.pdf
- Goldberger A, Rigney D, West B (1990). Chaos and fractals in human physiolo. *Sci. Am.* 262: 42-49.
- Goldberger A (1996). Non-linear dynamics for clinicians: chaos theory, fractals, and complexity at the bedside. *Lancet.* 347:1312-1314
- Goldberger A (2002). Fractal dynamics in physiology: alterations with disease and aging. *Proc. Natl. Acad. Sci. U.S.A.* 99(suppl1):2466-72.
- Grimaldi R (1989). El sistema de los enteros. In: Matemáticas discreta y combinatoria. Wilmington: Addison-Wesley Iberoamericana S. A. 161-164.
- Huikuri H, Mäkikallio T, Peng Ch, Goldberger A, Hintze U, Møller M. (2000). Fractal correlation properties of R-R interval dynamics and mortality in patients with depressed left ventricular function after an acute myocardial infarction. *Circulation.* 101: 47-53
- Landini G, Rippon JW (1993). Fractal dimensions of epithelial-connective tissue interfaces in premalignant and malignant epithelial lesions of floor of mouth. *Anal. Quant. Cytol. Histol.* 15:144-9
- Luzi P, Bianciardi G (1999). Fractal Analysis in Human Pathology *Ann. N.Y. Acad. Sci.* 879:255-257.
- Mandelbrot B (2000a). ¿Cuánto mide la costa de Bretaña?. In: Los Objetos Fractales. Barcelona: Tusquets Eds. S.A. 27-50
- Mandelbrot B (2000b). The fractal geometry of nature. Freeman. Barcelona: Tusquets Eds S.A. 341-348.
- Peitgen H, Jurgens H, Saupe D (1992a). Chaos and Fractals: New Frontiers of Science. N.Y.: Springer-Verlag. 655-768.
- Peitgen H, Jurgens H, Saupe D (1992b). Chaos and Fractals: New Frontiers of Science. N.Y.: Springer-Verlag. 183-228
- Rodríguez J, Mariño M, Avilán N, Echeverry D (2002). Medidas fractales de arterias coronarias en un modelo experimental en restenosis. Armonía matemática intrínseca de la estructura arterial. *Rev. Colomb. Cardiol.* 10:65-72.
- Rodríguez J (2005). Comportamiento fractal del repertorio T específico contra el alérgeno Poa P9. *Rev. Fac. Med. Univ. Nac. Colomb.* 53(2):72-78.
- Rodríguez J (2006). Dynamical systems theory and ZIPF – Mandelbrot Law applied to the development of a fetal monitoring diagnostic methodology. In: Proceedings of the XVIII FIGO World Congress Of Gynecology And Obstetrics: Kuala Lumpur, Malaysia.
- Rodríguez J, Prieto S, Avilán N, Correa C, Bernal P, Ortiz L, Ayala J (2008a). Nueva metodología física y matemática de evaluación del Holter. *Rev. Colomb. Cardiol.* 15:50-54.
- Rodríguez J (2008b). Teoría de unión al HLA clase II: teoría de probabilidad, combinatoria y entropía aplicadas a secuencias peptídicas. *Inmunología.* 27(4):151-166.
- Rodríguez JO, Prieto SE, Correa C, Bernal PA, Puerta GE, Vitery S, Soracipa Y, Muñoz D (2010a). Theoretical generalization of normal and sick coronary arteries with fractal dimensions and the arterial intrinsic mathematical harmony. *BMC Med. Phys.* 10(1):1-6. Available from: <http://www.biomedcentral.com/1756-6649/10/1>
- Rodríguez J, Bernal P, Prieto S, Correa C (2010b). Teoría de péptidos de alta unión de malaria al glóbulo rojo. Predicciones teóricas de nuevos péptidos de unión y mutaciones teóricas predictivas de aminoácidos críticos. *Inmunología.* 29(1):7-19.
- Rodríguez J (2010c). Entropía proporcional de los sistemas dinámicos cardíacos. Predicciones físicas y matemáticas de la dinámica cardíaca de aplicación clínica. *Rev. Colomb. Cardiol.* 17: 115-129.
- Rodríguez J (2010d). Método para la predicción de la dinámica temporal de la malaria en los municipios de Colombia. *Rev Panam Salud Publ.* 27(3):211-8.
- Tolman R (1979). Principles of statistical mechanics. New York: Dover Publications.
- Sánchez N, Garduño MR, Ritter W, Guzmán SA (2008). “Los límites del pronóstico newtoniano y la búsqueda del orden en el caos” En *Ingeniería Investigación y Tecnología* 9(2):171-181.

APPENDIX

In order to find the expression of the equation 2, beginning from the combinatory of the maximum Mx , and minimum Mn of the spaces occupied by the attractor in the big grid, we obtain a first expression for find the whole number of possible attractors (N_A) of the cardiac dynamics:

$N_A = \sum_{Mn}^{Mx} 3j + 1$. *this is a convergent series, then we can write it so:*

$$N_A = \sum_{Mn}^{Mx} 3j + \sum_{Mn}^{Mx} 1 = 3 \sum_0^{Mx-Mn} (j + Mn) + \sum_{Mn}^{Mx} 1 \quad \text{ec. 1}$$

$$\Rightarrow \sum_{Mn}^{Mx} 1 = Mx - Mn + 1 \quad \wedge$$

$$3 \sum_0^{Mx-Mn} (j + Mn) = 3 \sum_0^{Mx-Mn} j + 3 \sum_0^{Mx-Mn} Mn = 3 \left[\frac{(Mx-Mn)(Mx-Mn+1)}{2} \right] + 3(Mn) \sum_0^{Mx-Mn} 1$$

$$- 3 \left[\frac{(Mx-Mn)(Mx-Mn+1)}{2} \right] + 3(Mn) \sum_0^{Mx-Mn} 1 = 3 \left[\frac{(Mx-Mn)(Mx-Mn+1)}{2} \right] + 3(Mn)(Mx - Mn + 1)$$

$$= 3(Mx - Mn + 1) \left[\frac{(Mx-Mn)}{2} + Mn \right] = \frac{3}{2} (Mx - Mn + 1)(Mx + Mn), \text{ if we return to the ec. 1}$$

$$\Rightarrow N_A = \frac{3}{2} (Mx - Mn + 1)(Mx + Mn) + Mx - Mn + 1 = (Mx - Mn + 1) \left[\frac{3}{2} (Mx + Mn) + 1 \right]$$

$$\Rightarrow \text{we obtained the expression of the equation 2, } N_A = (Mx - Mn + 1) \left[\frac{3}{2} (Mx + Mn) + 1 \right].$$