Exponential mathematical law applied to cardiac dynamics for 18 hours

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Abstract. An exponential law was previously developed based on dynamic systems theory to be applied to cardiac dynamics in 21 hours, so it is wanted to reduce the time of evaluation to 18 hours, to further verify its diagnostic utility differentiating normal from abnormal cardiac dynamics. To do that, 250 continuous electrocardiographic records and Holters were taken, from which 50 were normal and 200 had cardiac pathologies. Then, values of the maximum and minimum heart rates and the number of beats per hour were taken to generate a pseudo-randomized sequence in 21 and 18 hours and generate attractors. Later, occupation spaces were calculated in Kp and Kg grids as well as the fractal dimension, establishing a mathematical diagnosis Finally, the sensitivity, specificity and kappa coefficient were calculated to compare the obtained values with the Gold Standard. Normal dynamics presented occupation spaces values in the Kp grid between 233 and 401, while the abnormal ones were between 43 and 198 in 18 hours. Sensitivity and specificity values of 100% were found, with a Kappa coefficient of 1. It was possible to differentiate normal from abnormal cardiac dynamics through occupation spaces in 18 hours confirming its clinical utility.

1. Introduction
The main objective of dynamic systems theory is to study the state and evolution of systems [1,2] through the change of dynamic variables in time, allowing to evaluate its behavior. These variables are graphically represented in phase spaces, originating attractors [3]. When the trajectories are irregular, chaotic attractors are formed and they are studied with fractal geometry, which in turn studies natures’ irregular objects, or fractals [4-6].

From dynamic systems theory, it has been possible to give a new interpretation of disease and normality concepts, considering that the dynamic that presents any pathology is characterized by extremely regular or random, while normal dynamics are between those behaviors [7].

With a new diagnostic methodology based on an exponential law [8] to evaluate cardiac dynamics in 21 hours [9,10], it was possible to deduce all the possible cardiac attractors, distinguishing normal and pathologic states, as well as those in transition to disease [8]. This methodology was applied to study 115 Holter [9] and in patients with an established diagnosis of arrhythmia [10] in a successful manner,
finding elevated values of sensibility and specificity values as well as the major diagnostic correspondence against the Gold Standard.

In that order of ideas, the purpose of the present investigation is to apply the aforementioned mathematical law [8], in the context of a time reduction to evaluate the cardiac dynamic from 21 to 28 hours and confirm its diagnostic capacity.

2. Methods

2.1. Population

250 ambulatory and continuous electrocardiographic (ECG) records were taken during a minimum of 21 hours from patients older than 21 years. From those registries, 50 belonged to normality and 200 to disease according to the diagnosis of an expert cardiologist. The registries came from previous databases of Insight research group.

2.2. Procedure

The diagnostics emitted by the expert cardiologist from the taken registries for the study were hidden. Maximal and minimal values of heart rate frequencies as well as the number of beats in each hour during 18 and 21 hours were taken. With this information a semi randomized sequence was built by means of an equiprobable algorithm incorporating a previously designed and applied software. With the obtained values, a chaotic attractor from each dynamic was built plotting in the phase space a heart rate against the following value of the heart rate. Then, the fractal dimension was calculated through the Box-Counting method by overlapping Kp and Kg grids see Equation (1), with whom the space occupation were obtained for each one of the attractors. Later Equation (1) was cleared, to establish the fractal dimension in terms of the spaces occupied by the grids Kp and Kg, finding by result the Equation (2), to ultimately establish the physical mathematical diagnosis.

From Equation (3), the physical mathematical diagnosis was established from each registry, according to the previously developed exponential law [8-10], in which acute disease presents occupation spaces in the Kp grid lesser than 73, while normality states exhibit values greater than 200 and those in evolution are found between 73 and 200. Later, the obtained mathematical diagnostics from the calculations of the cardiac dynamics during 21 and 18 hours were compared with the conventional diagnostics.

2.3. Definitions

2.3.1. Phases space. Space of two or more dimensions in which the dynamic of a system is geometrically represented, through the plotting of ordered pairs of a variable consecutive value along the time.

2.3.2. Box-Counting fractal dimension. Defined by the Equation (1) [2]:

\[
D = -\frac{\log N(2^{-(K+1)}) - \log N(2^{-K})}{\log 2^{K+1} - \log 2^{-K}}
\]  

(1)

Where D corresponds to the fractal dimension; N corresponds to the number of occupied boxes by the object in the partition grid K.

2.3.3. Simplified Box-Counting equation. Obtained from Equation (1), applied to two grids, Kp and Kg, which have a proportion of on half in their dimensions, giving place to the following Equation (2).

\[
D = \log \left[\frac{Kp}{Kg}\right]
\]  

(2)
Where $K_p$ is the number of occupied squares by the attractor in the smallest grid and $K_g$ is the number of occupied squares by the attractor in the biggest grid.

### 2.3.4. Exponential law of the chaotic cardiac dynamic

Based in the clearing of Equation (2) and its mathematically expressed as the Equation (3) [8-10]:

$$K_p = 2^D K_g$$

### 2.4. Statistical analysis

Established diagnostics by the clinical expert were unmasked. For the purposes of statistical analysis, normal and acute cases were taken. The conventional diagnosis was taken as gold standard in order to realize a comparison with the physical mathematical methodology in 21 and 18 hours. False positives and negatives as well as true positives and negatives were calculated to obtain sensitivity and specificity through a binary classification. Finally, the Kappa coefficient was calculated through the Equation (4).

$$K = \frac{Co - Ca}{To - Ca}$$

Where, $Co$ represents the number of correspondences, that is, the cases equally diagnosed both by the mathematical methodology and by the conventional clinical parameters; $To$ is the total of ECG records; $Ca$ corresponds to the number of matches that can be attributed to chance and that are calculated through the Equation (5),

$$Ca = \left[ f_1 \times C_1 / To \right] + \left[ f_2 \times C_2 / To \right]$$

Where $f_1$ equals the number of ECG records with mathematical values of normality; $C_1$ represents the number of cases diagnosed as clinically normal; $f_2$ represents the number of ECG records evaluated as sick since the mathematical diagnosis; $C_2$ represents the number of ECG records evaluated as pathological since the clinical diagnosis and $To$ represents the total number of ECG records.

### 2.5. Ethical aspects

The present study is declared as a minimum risk investigation, according to the resolution 8430 of 1993 emitted by the “Ministerio de Salud de Colombia”, given that physical and mathematical calculations were performed over noninvasive diagnostic and complementary test previously requested physicians in compliance with preestablished clinical protocols, protecting the anonymity and integrity of the subjects involved. The ethical principles of the Helsinki Declaration from the World Medical Association are also followed.

### 3. Results

The clinical diagnostics of some registries are found in Table 1 as well as the calculations found in each case. In 21 hours, the fractal dimensions of normal dynamics were between 0.949 and 1.928 while the pathological ones were between 0.881 and 1.778. In 18 hours, the fractal dimensions of normal dynamics were between 0.982 y 1.957 while the pathological ones were between 0.874 y 1.778. The calculate fractal dimension values reveal that they cannot be used as measurement parameters to differentiate normal ECG records from abnormal ones. Additionally, it is confirmed the previous findings that demonstrate that fractal dimension values are not useful to distinguish normality from disease [11].

In 21 hours, values for $K_p$ grid were between 236 and 396 for normal dynamics as well as between 47 and 199 for the pathological ones. For the $K_g$ grid, values obtained for the normal dynamics were between 62 and 205 while they were between 16 and 108 for altered dynamics.

In 18 hours, the normal cardiac dynamics evaluated exhibited occupation spaces in the $K_p$ and $K_g$ grids between 233 to 401 and 60 to 203 respectively. The abnormal dynamics presented values in the
Kp and Kg grids between 43 to 198 and 15 to 108 respectively (Table 1). It was found a total coincidence in all cases between the dynamics evaluated in 18 and 21 hours.

With the obtained results it was possible to verify that the established limits for normal and pathologic dynamics in 21 hours, allow to establish reliable diagnostics evaluated in 28 hours by means of the occupation spaces of the attractor in the Kp grids, which was confirmed through the statistical analysis in 21 and 18 hours where sensitivity and specificity values of 100% and a Kappa coefficient of 1 were obtained.

Table 1. Values of spaces of occupation by the attractors evaluated in 18 and 21 hours. No: number, Kp values for the small grid, Kg values for the big grid, DF: fractal dimension, N: normal, D: dizziness, F: fainting, AF: auricular fibrillation, CH: cerebral hemorrhage, Mc: myocardopathy, A: Arrhythmia, As: arrhythmia in study, Ps: Palpitations in study and T: tachycardia.

| No | Indication | 21 hours | 18 hours |
|----|------------|----------|----------|
|    |            | Kp       | Kg       | Kp       | Kg       |
| 1  | N          | 296      | 82       | 293      | 84       | 1.851 |
| 2  | D, F, AF   | 163      | 53       | 159      | 54       | 1.620 |
| 3  | N          | 242      | 69       | 247      | 70       | 1.810 |
| 4  | CH         | 47       | 16       | 46       | 15       | 1.554 |
| 5  | Mc         | 118      | 53       | 123      | 55       | 1.154 |
| 6  | N          | 318      | 89       | 314      | 89       | 1.837 |
| 7  | N          | 275      | 99       | 274      | 101      | 1.473 |
| 8  | As         | 108      | 36       | 104      | 36       | 1.584 |
| 9  | F          | 173      | 68       | 171      | 68       | 1.347 |
| 10 | A          | 175      | 51       | 166      | 49       | 1.778 |
| 11 | N          | 382      | 109      | 381      | 109      | 1.809 |
| 12 | N          | 396      | 205      | 401      | 203      | 0.949 |
| 13 | Ps         | 119      | 51       | 119      | 52       | 1.222 |
| 14 | P          | 199      | 108      | 198      | 108      | 0.881 |
| 15 | N          | 252      | 87       | 257      | 89       | 1.534 |
| 16 | A, T       | 103      | 35       | 102      | 34       | 1.557 |
| 17 | N          | 236      | 62       | 233      | 60       | 1.928 |
| 18 | N          | 314      | 134      | 315      | 132      | 1.228 |
| 19 | N          | 347      | 96       | 343      | 93       | 1.853 |

In Figure 1, attractors for normal, in evolution to acuity and acute dynamics are shown. It can be observed that the occupation spaces from the attractor tends to diminish when the acuity of the disease is approaching.
4. Discussion
This is the first paper that reduces the time of evaluation of the cardiac dynamic from 21 to 18 hours in the context of an exponential mathematical law, achieving the establishment of accurate diagnostics in 250 electrocardiographic records, allowing to differentiate normal cardiac dynamics from the pathological ones as well as the evolution to disease. The maximal values of sensitivity and specificity were obtained, and the Kappa coefficient achieved was 1, after comparing the methodology against the conventional diagnosis taken as Gold Standard. Its diagnostic and clinical applicability was corroborated, establishing as a tool with potential application to large scale by its capacity to perform early and precise diagnostics.

In a previous paper [8] with the mentioned methodology, the totality of cardiac attractors was inferred considering the occupation of the fractal space of Box-Counting. In addition, this method allowed to differentiate normality from abnormality in function of the cardiac system self-organization.

Chaos theory and fractal analysis have made possible to develop new methods to study physiological dynamics [12-24]. New perspectives have allowed the emergence of new forms to conceive the normality and disease [7] and have given place to predictions of mortality and innovative indexes that allow to quantify the complexity level of the dynamic to study; nevertheless, more studies are necessary.

In diverse fields of medicine, fractal geometry has been applied with the purpose of achieving differentiations between normality and disease [21-24]. However, it has been demonstrated that fractal dimensions are not a reliable parameter to achieve this differentiation [11,25], which has been evidenced in studies realized with the mathematical exponential law [8,9,26]. What it has been determined to characterize and determine true differences is the occupation of the attractors in the fractal space.

Nowadays, large part of the medical decisions is based in statistical and populational analyses that establish causal relationships and are applied in a generalized manner; nonetheless, in occasions they must deal with limitations in particular cases. The present study is supported in a methodology based in the proceedings of theoretical physics, whereby it is possible to describe phenomena in a generalized manner through abstractions and inductions, taking into account parameters and clear numerical values, apart from risk factors or statistical variables that determine the behavior of populations and that are widely used in the actual clinical practice.

In different scopes, it has been possible to obtain generalizations to establish predictions of specific phenomena as in morphometry [11,25,27], infectiology [28], hematology [29], public health [30], even mortality predictions of patients in the intensive care unit (ICU) [31]. Equally, a methodology was developed to predict the peptide binding phenomena to human leukocyte antigen class II based on probability and entropy [32]. It has also been possible to apply these methodologies in the field of cardiology [33], to diagnose patients that present neonatal sepsis [34] and the ICU [35,36].

5. Conclusion
It was possible to establish differences between the patients with normal cardiac dynamics and those with abnormal ones, in the context of a reduction of the evaluation time of cardiac dynamic from 21 to 18 hours, through the occupation spaces of attractors analyzed with the exponential law.

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