A novel analysis method to characterize heartbeat dynamics through the Microcanonical Multiscale Formalism

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Abstract. Heartbeat dynamics is a complex signal whose accurate analysis is essential to detect arrhythmias and life-threatening conditions. To achieve this, advanced nonlinear processing methods are needed. In this context, recent developments in the field of reconstructible signals and multiscale information content have lead to the Microcanonical Multiscale Formalism. We show that such framework provides several signal analysis techniques that are especially adapted to the study of heartbeat dynamics. We show that the analysis of electrocardiogram signals and the electric potential measured through catheters at different points inside the human heart permits the detection of slow changing transitions. We detect different regimes of transition between atrial fibrillation and healthy cases, what could be used for early warning and in the treatment of atrial fibrillation.

Keywords: multiscale analysis, heartbeat dynamics

1 Introduction

The cardiac rhythm is the result of a complex synchronization process between pacemaker cells and, as a consequence, the heart rate exhibits small chaotic fluctuations. Typically, the amplitude of such fluctuations is much smaller than the average interbeat interval, something that makes the healthy (sinus rhythm) heartbeat appear as mainly periodic. Nevertheless, the fluctuations around this main period are not an unstructured random noise but follow a complex dynamics. Even more, the characterization of these fluctuations is vital for determining whether the heart is healthy or it is indicating signs of a transition to an arrhythmia, despite still appearing regular [10, 11, 18, 22].

The human heart is structurally complex and, as a consequence, the electrical activity in it is also complex. Cardiac action potential is leaded by polarization of pacemaker cells. These cells are not homogeneous but mainly concentrate in nodes (sinoatrial and atroventricular nodes), bundles and the Purkinje fibers
which innervate all the ventricular myocardium. The action of pacemaker cells controls the cardiac contractions (atrial and ventricular systole) and relaxation (diastole) in an organized way to ensure the optimal pumping [16]. Polarization and depolarization of the membrane potential is a collective effect and so they are affected by the conduction dynamics of the electric flow [14]. In this sense, the orientation of cardiomiyocytes [27] plays an important role and other structural particularities such as epicardial fat [2] affect also.

First studies of interbeat fluctuations found that they have a multiscale structure [15, 17] and so fractal models were proposed for it [23]. Later on, the development of more advanced analysis techniques based on multiresolution analysis and characterization of singularities, large deviations and predictability permitted a more extensive study [10], which shows that a healthy heartbeat has a multifractal structure, while a heart under congestive heart failure deviates from multifractality. In that study, multifractal analysis is based solely on the Legendre spectrum, and so it corresponds to a canonical formalism, not microcanonical, from a thermodynamic point of view.

The multiscale structure observed in heartbeat is a result of a synchronization process in a hierarchic complex network made of cardiac pacemaker cells [26]. As a consequence, the Microcanonical Multiscale Formalism (MMF) [25, 38] is especially appropriate for analyzing this dynamical structure. In particular, an analysis based on the singularity exponents [20, 19] and the optimal wavelet [24] of heartbeat time series allows directly accessing the geometric features that characterize their multiscale behavior.

The results obtained in [10] are based on a canonical analysis, meaning that the behavior of statistical averages is used to indirectly retrieve the geometric features: scaling exponents of partition functions estimate a curve that can be used to obtain the so-called singularity spectrum by means of a numerically-estimated Legendre transform). This methodology is known to give less accurate estimation on the tails of the singularity spectrum for which a microcanonical analysis has been found to be much more robust and accurate [36]. Having such estimation has a capital importance for anticipating as much as possible when heartbeat dynamics starts drifting from the healthy behavior. Given the quickness with which heart failure can be fatal or leave irreversible after-effects, the precise estimation provided by the MMF has a strong potential in helping to save lives and improve the health of people with cardiac diseases.

Multifractal models originated from the study of turbulent flows. While blood can be in turbulent regime -and notably inside the heart- it is unlikely that this turbulence is reflected to the cardiac electric flow. This electric flow, and in consequence the measured heartbeat signal, are the result of a complex synchronization process between pacemakers. As explained in [1], traffic in a complex network under certain regimes becomes multifractal. Hence, a demonstration for the observed multifractality could be derived from the analysis of that network.

The paper is structured as follows: in the next Section we introduce the empirical data to be analyzed as well as some basics of the atrial fibrillation condition that are relevant for its signal processing. In Section 3 we introduce
the basics of the Microcanonical Multiscale Formalism (MMF) and the methods to accurately retrieve the empirical singularity exponents from a signal. We also present a reconstruction method and how it can be used to separate the fast dynamics implied by the singularity exponents from a slow dynamics that indicates changes in regime. In Section 4 we apply that analysis to the heartbeat data and discuss how it can be used to identify dynamical changes, with atrial fibrillation in mind. Finally, in Section 5 we draw the conclusions of our work.

2 Atrial fibrillation and empirical data

Atrial fibrillation (AF), the most common form of cardiac arrhythmia, is responsible for significant morbidity each year in all parts of the world. It results from the chaotic operation of the top of the heart (atria). Although a priori it is not a severe condition by itself, it causes a high mortality rate by its most severe complications, either from heart failure or by stroke-related embolism. The main cause of AF is related to a change in the electrical conduction properties in some type of cardiac tissue: some areas of this tissue depolarize spontaneously or slow the spread of the pulse. Today the primary treatment for AF remains medication, but ineffective drugs or their side effects has led to the development of new forms of treatment, mainly radio-frequency ablation. This ablation technique requires the introduction of a catheter within the heart in order to burn areas become electrically deficient, and in cases of paroxysmal AF, Haïssaguerre et al. have shown [6] that for 80% of patients, the pathogenic tissue is located in one of the 4 pulmonary veins, and electrical insulation, obtained by surgical means, allows the patient to regain a normal heart rhythm [4, 28, 31, 8, 9, 7, 5]. But in more severe cases, i.e., persistent or permanent AF, locating the pathogenic areas remains difficult and is still an unsolved problem. During the ablation procedure, catheters inserted in the heart can analyze finely the electrical activity of the atria. The morphology of the signals obtained and their temporal evolution must guide the surgeon to the location of the sources to ablate. But the complexity of the acquired signal makes analysis very difficult and there is no clear identification of important information. It is in this context where nonlinear analysis techniques like the MMF can be applied to identify the changes in cardiac regime that lead to the recovery of the normal sinus rhythm.

2.1 The data

We have processed electrocardiogram signals together with endocardial potential measured through electrodes in catheters introduced in the hearts of two patients and for two regimes: sinus rhythm and atrial fibrillation. Each file contains 21 channels of data: 4 of these are from electrocardiogram electrodes measuring the potential on the skin (I, II, III and V1) and the other 17 are measured through three catheters (two from the radio-frequency catheter, a catheter of 6 electrodes and another catheter of 10 electrodes). All of the measures are electric potential differences, and all of them are bipolar except for the V1 which is unipolar. These
are sampled at a rate of 1 kHz. The ensemble of files has a total of 388,780 points (193,280 for patient P1 and 195,500 for patient P2), which when multiplied by the number of channels means a total of 8,164,380 data.

Patient P1: 50 year old man with expanded heart and persistent AF (recurrent episodes that last more than 7 days). Measurements are done in left and right atrial appendages, left superior pulmonary vein, coronary sinus and left wall of the interatrial septum. After ablation, the patient returned to sinus rhythm. About half of the measures have been done under AF and the other half at normal (sinus) rhythm.

Patient P2: 43 year old man without cardiopathy, with paroxysmal AF (recurrent episodes that self-terminate in less than 7 days) for 13 years. Measurements have been done in the left atrial appendage, ceiling of the left atrium, coronary sinus and right superior pulmonary vein. The patient returned to sinus rhythm after isolation of the right inferior pulmonary vein. Also in this case, about half of the measurements are under AF and the other half in sinus rhythm.

For illustration purposes, we show in Figure 1 how the fibrillation (desynchronized beat) is seen in the pulmonary vein and how AF is still slightly manifested in the measure from the electrode on the skin V1.

Fig. 1. Measurements done in patient P2 for illustration. At the top, we show external electrocardiogram measures, namely from V1 electrode, for the case of sinus rhythm (left) and atrial fibrillation (right). At the bottom, we show the measurements of the first pair of electrodes of the catheter on the right superior pulmonary vein. Fibrillation is clearly seen inside the heart, and can be still noticed outside.

3 The Microcanonical Multiscale Formalism

The Microcanonical Multiscale Formalism (MMF) is a theoretical and methodological framework for the analysis of multiscale signals. Its basic element of description is by means of the singularity exponents of a signal under analysis, which are the exponents describing the local regular/singular behavior of the signal around each point.

3.1 Singularity exponents

Singularity exponents have different mathematical definitions depending on the context they are used. The usual notion in complex-signal analysis is related to the Hölder or Hurst exponents, including their respective generalizations. Although different definitions are possible, the conceptual goal is always the
same: to describe how the function evolves around a given point by converging to a value (regular) or diverging (singular).

In the most general case, given a signal $s$ that is defined on $\mathbb{R}^d$ domain and images to a $\mathbb{R}^m$ space, the Hölder exponent $h(x)$ of point $x$ is the exponent satisfying the following limit, when it exists [12]:

$$\| s(x + r) - s(x) \| = \alpha(x) r^{h(x)} + o(r^{h(x)}) \quad (r \to 0) \quad (1)$$

where $r = \| r \|$. This means that in the proximity of $x$ the signal follows a power law of exponent $h(x)$. An alternative definition that analytically is slightly more restrictive is usually called the Hurst exponent [30, 13] and defined as

$$s(x + r) - s(x) = \langle \alpha(x) r \rangle r^{h(x) - 1} + o(r^{h(x)})$$

where $\alpha(x)$ is a continuous $(1, 1)$ tensor. For the purpose of this article, analysis of 1D signals of 1 component the definitions actually coincide.

The concept of singularity exponent can be interpreted also in terms of differentiability. A function that is strictly $n$-derivable at point $x$ has a singularity exponent $h(x) = n$. So that in this sense the singularity exponent can be related to non-integer differentiability. In a similar way, as we will see below, it is also related to the content of information.

Nevertheless, Hölder or Hurst exponents defined this way have very specific applicability (e.g., in the case of multiaffine functions) and cannot be directly found in real-world signals. The main reason is that the basic power-law behavior is masked by the presence of long-range correlations, noisy fluctuations, discretization and finite-size effects. All these make that the analytical limit described is not practically attainable [33, 38], and a generalized definition of singularity exponent is needed. To achieve this, the objective is to find a certain measure $\mu$ for which we could take a similar limit:

$$\mu(B_r(x)) = \alpha(x) r^{d + h(x)} + o(r^{d + h(x)}) \quad (r \to 0) \quad (2)$$

where $d$ is the dimension of the domain, i.e., $d = 1$ in the 1D case, and $B_r(x)$ is a ball centered around $x$ having a radius $r$ for a certain norm (choice to be done for multi-dimensional cases; they all coincide in 1D).

The actual definition of singularity exponent that we will be using in the present article works well in practice and is little affected by the artifacts mentioned above. For it, we will work on the gradient-modulus measure of the signal [33]. This measure is defined from its density:

$$d\mu(x) = \| \nabla s \|(x) \, dx \quad (3)$$

a definition that is absolutely continuous with respect to the Lebesgue measure. Hence, the measure of any Borelian $A$ is given by:

$$\mu(A) = \int_A dx \| \nabla s \|(x) \quad (4)$$

The gradient-modulus measure characterizes the local singularity of any point. A signal that has a Hölder exponent $h(x) + 1$ according to eq. (1) will fulfill also eq. (2), with this $+1$ shift.
Practical calculations of eq. (2) can benefit from using wavelet-projected interpolations, this way effectively avoiding some of the discretization effects [3, 21]. The wavelet projection of the measure at point $x$ and scale $r$ is expressed as

$$T_\Psi \mu(x, r) = \int_{\mathbb{R}^d} d\mu(x') r^{-d} \Psi \left( \frac{(x - x')}{r} \right)$$

with $\Psi$ being a predetermined function known as the mother wavelet. As we can see, the operator $T_\Psi$ is a map from the set $\mathcal{M}$ of $\sigma$-finite measures on $\mathbb{R}^d$ to the set of functions $\mathbb{R}^d \times \mathbb{R}^+ \rightarrow \mathbb{R}$. That is why a signal that has a singularity exponent at the point $x$ according to eq. (2) exhibits this same exponent when wavelet-projected [3, 33], i.e,

$$T_\Psi \mu(x, r) = \alpha_\Psi(x) r^{h(x)} + o(r^{h(x)}) \quad (r \to 0)$$  \hspace{1cm} (5)

It is worth mentioning that wavelet projections expressed in this way treat the wavelet function as a kernel for the measure and no additional restriction is imposed. This way, we are not limited to use only admissible wavelets (i.e., wavelets that form a basis of a function space). In particular, we can use always-positive kernels that do not have zero-crossings. High-order wavelets that exhibit several zero-crossings have a significant loss in spatial resolution [32, 36], but positive kernels minimize spatial spread and can normally reach the original resolution, that is, one pixel in the original signal.

4 Heartbeat analysis

The analysis done consists first on the validation of the multifractality hypothesis under the Microcanonical Multiscale formalism (MMF). This is pertinent because all previous studies are done under a canonical formalism, which is based on statistical averages (the scaling of structure functions or partition functions). However, the MMF is directly geometrical instead of statistical, which means that we characterize the multiscale character at each point of the signal. Once the heartbeat data has been validated to be microcanonical, i.e., it fits the singularity-exponent relation seen in eq. (5), the next step consists in analyzing the dynamical properties and characterizing transition points.

A first observation is that the measures inside the heart clearly have more abundance of most singular points. This is something that we expected is because the difference observed – more singular points – means that the internal signals are more informative and require more points to be reconstructed. Multifractal signals can be reconstructed from their component of most singular points (which therefore concentrates all the information), if such component exists [29]. In our case, the most singular component (i.e., the most informative) is also larger and more dispersed in the internal than in the external measures. We show below that the studied signals are effectively reconstructible though nevertheless, the key dynamical parameters detected in internal measures are still noticeable in the external measures.

A general theory and methods about reconstructibility of multifractal signals from the Most Singular Component (MSC) can be found in [38]. With the MMF we have access to the singularity value of each point, which is the basis
of the multiscale coordination of the components in the signal. Additionally, the methodological tools provided by this formalism are effectively adapted to work with real signals (with discretization, noise, artifacts, aliasing, correlations), and we can use this information to look at the dynamical properties of the heartbeat series.

4.1 A dynamical model for analysis

Given the points we have, we propose a dynamical model for the analysis of heartbeat signals. The first key element comes from the calculation of the singularity exponents and, in particular, their associated Most Singular Component (MSC). An interesting aspect of the MSC is that we do not need the values of the signal over its points nor the actual values of singularity exponent. In fact, most of the dynamical information of the signal is contained only in the orientation over the MSC [34] and we can use an analysis of this orientation as the starting point.

First of all, we calculate the singularity exponents of the signals to determine where their MSC is located. To achieve this, we locate where are the smallest (most singular) exponents in the series, giving a small tolerance level to account the numerical fluctuations. Then we define the oriented MSC as a function that is zero everywhere except for the most singular points, where it takes the value of the sign of the gradient.

When we apply the reconstruction formula defined in [37] to the oriented MSC, the result is a reduced signal that coincides with the original signal at short scales. At long scales, there is a slow divergence between them. This allows to model the dynamics as a combination of a fast dynamics driven by the MSC orientation and a slow-varying field that acts as a factor on it [35].

More concretely, we define the oriented MSC as $\delta_\infty(t)$ taking +1 on MSC points of positive derivative, -1 on MSC points of negative derivative and 0 on non-MSC points. This way, transitions from one point to the other can be described as a Markov chain. This way, we call $\sigma$ the Markov states. The two-point joint probability is:

$$P(\sigma_0, \sigma_\tau) = \langle P(\delta_\infty(t) = \sigma_0, \delta_\infty(t + \tau) = \sigma_\tau) \rangle$$  \hspace{1cm} (6)

and as a consequence we have the marginal probabilities:

$$P(\sigma_0) = \langle P(\delta_\infty(t) = \sigma_0) \rangle_{\!\!\sigma} = \langle P(\sigma_0, \sigma_\tau) \rangle_{\!\!\!\!\!\sigma_\tau}$$  \hspace{1cm} (7)

Under the hypothesis of distributional stationarity, we can expand the process as transitions between all the states [34]. The transition at two steps is expressed as:

$$P(\sigma_2|\sigma_0) = \sum_{\sigma} P(\sigma_2|\sigma) P(\sigma|\sigma_0)$$  \hspace{1cm} (8)
i.e., twice the one-step transition. This means that we can represent all the
dynamics through $P(\sigma_1 | \sigma_0)$. The matricial expression of this gives the so-called
transition matrix of the process. In our case, with three states:

$$
T = \begin{pmatrix}
0 & 0 & 0 \\
0 & 0 & 0 \\
-1 & -1 & -1
\end{pmatrix}
$$

(9)

At the end, applying $T$ a large number of times results in a stationary
marginal distribution. When $T$ is applied to the stationary state, the result
is the same, so the first eigenvalue of the process is 1. The other two secondary
eigenvalues give a characterization of the dynamics.

The Markov chain: To this effect, we have analyzed the Markov processes for
all the data, classified in four categories: internal channels under Atrial Fibrilla-
tion (AF) internal channels under (normal) sinus rhythm, ECG channels under
AF and ECG channels under sinus rhythm. We did not observe significant dif-
fences from one patient to the other or from one channel to the other inside
the category, so we have grouped them to enhance presentation of the results
and maximize the precision. That said, when processing one single channel the
results are already stable, so we conclude that the method is robust and little
data demanding.

As we can see in Table 1, the particular signature of AF is conserved when
the signal inside the heart is propagated to the skin. This suggests that it should
be possible to finely monitor the AF evolution and severity from external ECG
measures by means of advanced statistical measures that are stable and robust.
Even more, transitions to and from fibrillation could be immediately detected.

| .83 .09 .08 | .81 .09 .10 | .84 .09 .07 | .82 .08 .10 |
| .56 .36 .08 | .59 .34 .07 | .71 .22 .07 | .74 .21 .05 |
| .54 .09 .37 | .60 .09 .31 | .69 .07 .24 | .73 .04 .23 |
| .29 .27 | .25 .21 | .17 .13 | .17 .09 |

Table 1. Calculation of transition matrices $T$ of the oriented MSC and their respec-
tive second and third eigenvalues for (left to right): internal under AF, external under
AF, internal normal, external normal. We can observe that despite the signals differ
in appearance, dynamical parameters in internal measures are still externally observed
with minimal differences, while at the same time the AF condition significantly per-
turbs these values (both internally and externally). The estimated eigenvalues have an
uncertainty around $\pm .04$ through propagation of sampling error.

Source field: As we have mentioned above, the oriented MSC drives the fast
dynamics, meaning that the sign clustering determines a big part of the dynam-
ical structure. Nevertheless, on a longer scale the MSC alone does not precisely
reconstruct the signal because the constant factor is not really constant but slowly evolves. This leads to the definition of the source field. Given a signal $s$ and the reduced $r$ constructed from its oriented MSC, the source field $\rho$ is defined such that:

$$\nabla s(x) = \rho(x) \nabla r(x)$$  \hspace{1cm} (10)

but nevertheless this definition is not usable in practice in points outside the MSC, because the reduced signal is not well defined in them. To solve this, we make use of a more rigorous definition of source field in terms of measures [35]:

$$\mu_s(A) = \int_A d\mu_r(x) \rho(x)$$  \hspace{1cm} (11)

which implies that the source field $\rho(x)$ is the Radon-Nikodym derivative of the two measures: $\rho(x) = d\mu_s/d\mu_r$.

There exist several different strategies to numerically estimate a Radon-Nikodym derivative. Since in our case we are most interested in the detection of slow dynamical transitions, we have used an iterative algorithm that fits eq. (11) in a piecewise constant fashion. This way, we concentrate on the determination of the dynamical borders and let the MSC lead all the fast Markovianly-stable evolution. The results, shown in Figure 2 show that the source field varies infrequently though it exhibits quite sharp transitions. In consonance with the results for the MSC orientation in the subsection above, the dynamical character in the case of AF is significantly different than under sinus rhythm.

**Fig. 2.** Time evolution of the source fields and the reconstructions of the same illustration signals shown before in Figure 1 – measures from V1 electrode. At the top, source field displayed (solid) over the original signal (dashed) for the case of sinus rhythm (left) and atrial fibrillation (right). At the bottom, signal reconstruction (dashed) based on the source field and the Markov-chain modeled MSC. Signs of Atrial Fibrillation are noticed in the dynamical parameters. Reconstruction is of very good quality in all the cases, especially for the peaks.

We observe a correspondence of the transition points with the points in which the deviation between the original and the reconstructed series is more important. So these transition points correspond to transitions in the reconstructibility and in the content of information, which means that the detected transitions correspond to actual changes in the dynamical properties of the signal. The concrete mechanism that establishes the link of correspondence with some electrophysiological transition is nontrivial and complex.
5 Conclusions

In this paper, we have shown the application of a novel nonlinear signal-processing framework, the Microcanonical Multiscale Formalism (MMF) to the analysis of interbeat fluctuations in heartbeat time series. In these signals, there is a multiscale character that is reflected as a definite geometrical structure arranged around manifolds of singularity. This way, the signal can be decomposed into different components depending on their characteristic singularity exponent. The value of the singularity exponent characterizes the power-law behavior under scale changes and directly indicates the information content of the component.

As a consequence, the MMF gives a direct access to the geometry of singularity components in a way that characterizes the degree of information contained at each point of the signal. When further exploited, this geometrical structure shows that the most informative component, i.e., the Most Singular Component (MSC) reconstructs the whole signal. This means that the dynamical structure is contained in this component and the dynamics of the signal is driven by it.

A first observation is that we can reproduce under a microcanonical formalism the same type of characterizations about multifractality on heartbeat series that have been reported before in the literature under a canonical framework. Moreover, the expected observation that data from catheters inside the heart have a richer, more informative, more singular multiscale signature than those taken on the skin, does not seem to affect the Markovian MSC parameters of the signal or its reconstructibility, which means that the key dynamical features can still be detected on the skin.

We have observed that the MSC orientation is well described by means of Markov chains and the parameters of their dynamics (particularly, the eigenvalues of the transition matrix) are significantly different for the case of Atrial Fibrillation (AF) than for the normal sinus rhythm. A possible application of this would be an early detection of transitions to or from AF.

On the other hand, the signal reconstructibility is precisely what leads to the extraction of a slowly-varying source field from its dynamics. These source fields accurately describe dynamical changes of a multifractal dynamics, an effect that suggests its possible relationship with some electrophysiological transitions, such as evolution of polarization/depolarization cycles and conduction changes.

References


