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# Diagnosis of Digestive Functional Disease by the Statistics of Continuous Monitoring of Esophageal Acidity

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**Abstract.** Technological advances in the last few decennia allow the monitoring of many physiological observables in a continuous way, which in physics is called a "time series". The best studied physiological time series is that of the heart rhythm, which can be derived from an electrocardiogram (ECG). Studies have shown that a healthy heart is characterized by a complex time series and high heart rate variability (HRV). In adverse conditions, the cardiac time series degenerates towards randomness (as seen in, e.g., fibrillation) or rigidity (as seen in, e.g., ageing), both corresponding to a loss of HRV as described by, e.g., Golberger et. al [1]. Cardiac and digestive rhythms are regulated by the autonomous nervous system (ANS), that consists of two antagonistic branches, the orthosympathetic branch (ONS) that accelerates the cardiac rhythm but decelerates the digestive system, and the parasympathetic brand (PNS) that works in the opposite way. Because of this reason, one might expect that the statistics of gastro-esophageal time series, as described by Gardner et. al. [2,3], reflects the health state of the digestive system in a similar way as HRV in the cardiac case, described by Minocha et. al. In the present project, we apply statistical methods derived from HRV analysis to time series of esophageal acidity (24h pHmetry). The study is realized on data from a large patient population from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Our focus is on patients with functional disease (symptoms but no anatomical damage). We find that traditional statistical approaches (e.g. Fourier spectral analysis) are unable to distinguish between different degenerations of the digestive system, such as gastric esophageal reflux disease (GERD) or functional gastrointestinal disorder (FGID).

## INTRODUCTION

Medical diagnosis is often restricted to statistic values of physiological observables, such a heart rate in rest of >100 beats per minute (tachycardia), or <50 beats per minute (bradycardia), or sustained esophageal acidity of pH<4 (pathological reflux). Time series analysis of fluctuations in time gives additional information. One of the best studied physiological time series is that of the heart rhythm. When this time series is studied with Fourier spectral analysis, a power law results, $P(f) = 1/f^{\beta}$ , where $0 \le \beta \le 2$ is the spectral exponent [1,4,5] (see figure 1).

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Cardiac and digestive rhythms are regulated by the autonomous nervous system (ANS). In the present project, we apply statistical methods derived from HVR analysis to time series of esophageal acidity (pH continuous monitoring). Previously, degenerations of the digestive rhythm have been identified in patients with GERD [2,3].

Interestingly, the Fourier power spectrum of a typical 24h pH time series behaves according to a similar power law as observed for the heart rate time series (see figure 1). In the present contribution, we want investigate whether the spectral exponent of the power law distinguishes between different pathological conditions for 24h pH time series (see table 2). A spectral exponent β=0 in the Fourier power spectrum implies a random time series (fibrillation in the cardiological case), β=2 implies a rigid time series (aged heart in the cardiological case), β=1 implies a complex time series (healthy heart in the cardiological case) [1,4].

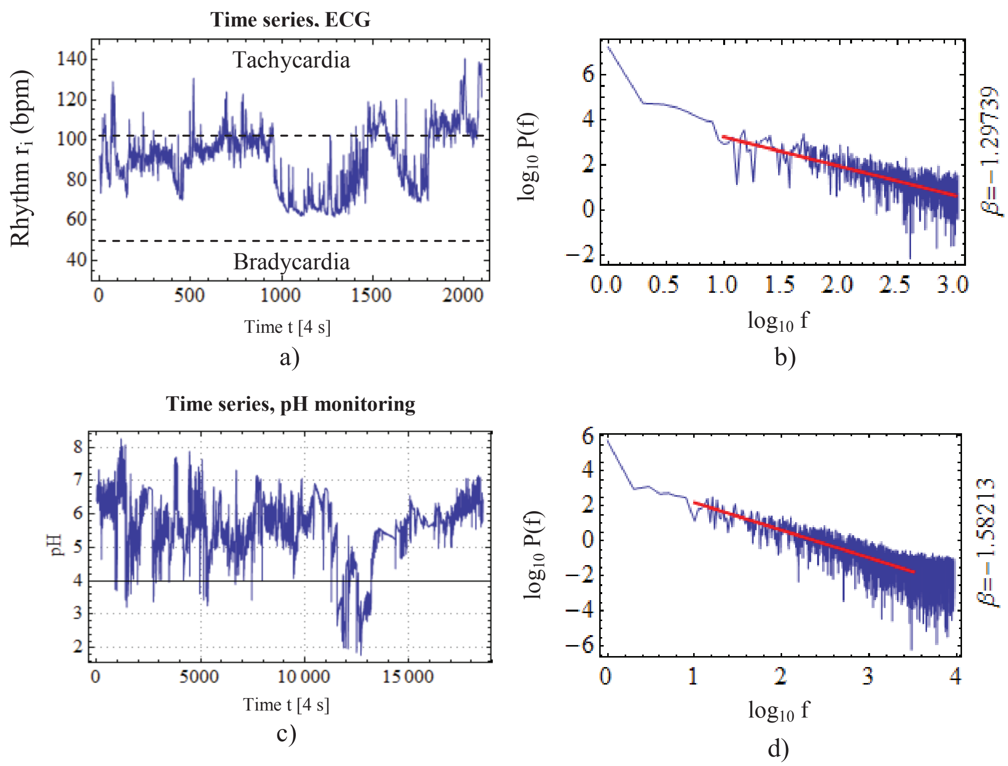



**FIGURE 1.** Example of spectral analysis from heart rate time series in beats per minute (bpm) a) and b) with an example of spectral analysis of time series from pH monitoring c) and d). The power law $1/f^{\beta}$ with β = 1.58 and β = 1.29 is indicated by the linear fit to the power spectrum in double-logarithmic scale.

## RESULTS

Studying the 24h pHmetry data base from the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, we find very diverse looking time series (see table 1). However, the observed differences between de various time series are not consistently characterized by different spectral exponents in the Fourier power spectrum. The presence of a dominant trend or nonstationarities in the time series make application of standard spectral analysis inappropriate [6]. More advanced time-series techniques, such as e.g. Singuar Spectrum Analysis (SSA) [7] have been development to take into account trends and nonstationarities in a data-adaptive way. However, the applicatin of such methods did not improve the results. Rather, we find indications that the 24h pH time series might be multifractal. Multfractality implies that a whole spectrum of scaling exponent is required to describe the dynamics correctly, which would explain why a single scaling exponent such as the Fourier Spectrum exponent β is insufficient to characterize the 24h pH time series (see e.g. [8] for a discussion on multifractal time series). We will publish our results on the multifractality of 24h pHmetry elsewere.

**TABLE 1.** Representation of mathematical noises with corresponding power spectrum, see ref [9]

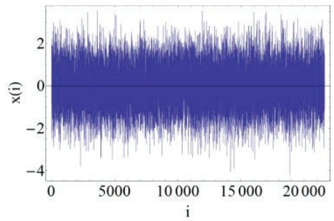
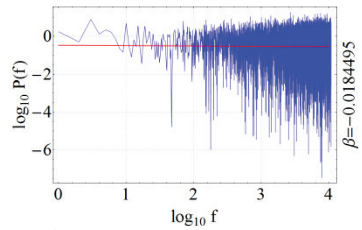
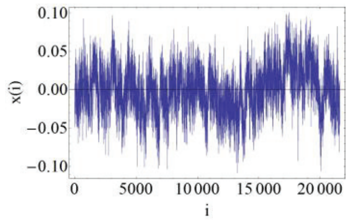
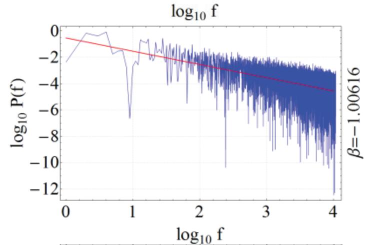
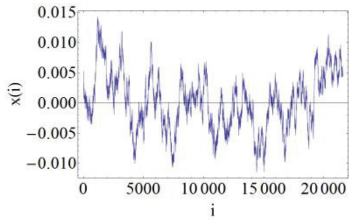
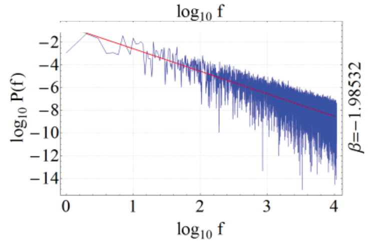
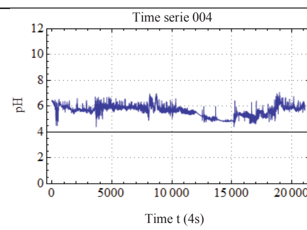
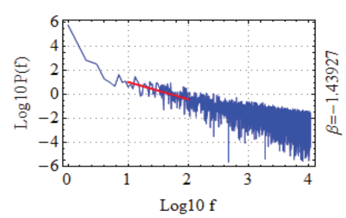
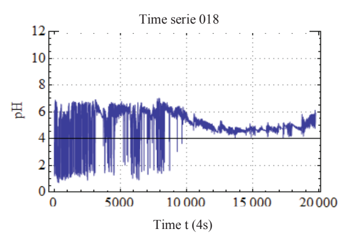
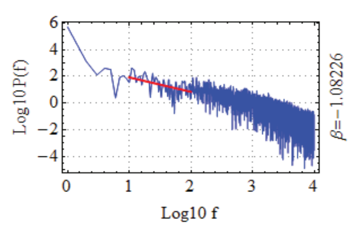
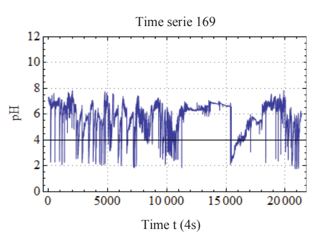
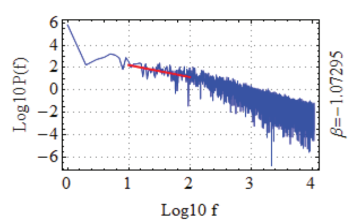
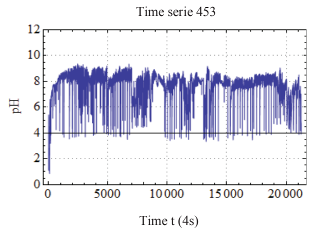
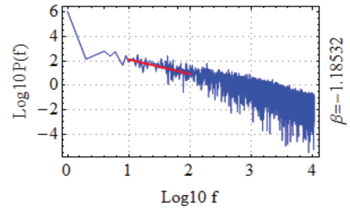
| Mathematical noise | Time series | Power spectrum |
|---|---|---|
| **White** |  |  |
| **1/f** |  |  |
| **Brownian** |  |  |

**TABLE 2.** Representative 24h pH time series and corresponding Fourier spectral analysis for various medical diagnosis, but this differences are apparently not clearly reflected in the power spectrum. Data from Dr. M. Valdovinos, Laboratorio de Motilidad del Departamento de Gastroenterología, Instituto Nacional de Nutrición Salvador Zubirán.

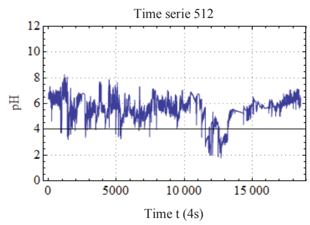
| Diagnosis | Time series | Power spectrum |
|---|---|---|
| **Patient: 004**.<br>Negative for reflux; lower esophageal sphincter hypotensive, hiatal hernia.<br>**Final Diagnosis**:<br>GERD y FGID. |  |  |
| **Patient: 018**.<br>Erythematous gastropathy. Fibromyalgia, polycystic ovary syndrome.<br>**Final Diagnosis**:<br>GERD y FGID. |  |  |
| **Patient:169**.<br>Pathological reflux, lower esophageal sphincter incompetent; gastritis. Tiroiditis autoinmune, hipotiroidismo, H pylori.<br>**Final Diagnosis**:<br>GERD. |  |  |

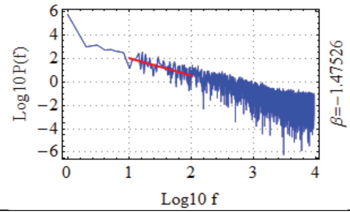
**Patient: 453**.
Hypersensitive esophagus.
Generalized anxiety disorder
**Final Diagnosis**:
FGID.




**Patient: 512**.
Hypertension, dyslipidemia.
**Final Diagnosis**:
GERD.




The line in pH = 4 indicates the limit at structural damage is caused to esophagus [10].

## CONCLUSIONS

24h pHmetry data can be studied as a time series, but standard Fourier spectral analysis does not appear to be an adequate statistical measure. The reason for this does not seem to be nonstationarity of the data. Possibly, the data are multifractal, and multifractal instead of monofractal measures might be needed to characterize pH time series.

## ACKNOWLEDGEMENTS

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