

Biological System Modeling based on Fourier Series

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Abstract: The organization, regulation, and dynamic response of biological systems are too complex to allow intuitive predictions and require the support of mathematical modeling to achieve quantitative assessments that results in reliable understanding of system functioning. In this work modeling of biological systems through Fourier series has been successfully demonstrated for biological systems with periodic-like response. We demonstrate further benefits of this approach for time series analysis, such as direct comparison of different hypotheses, inherent estimation of noise levels and parameter precision, and a flexible framework for modeling the data without pre-processing.

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1. Introduction

The central task of computational systems biology is the conversion of a biological system into a computational model. This conversion requires large amounts of data and context information, as well as a mathematical model structure along with computational methods, in order to replicate realistic environmental conditions. Useful data can come from a variety of sources. Biological systems operate within the physical world. However, due to the complexity of the processes governing these systems, in which a large amount of variables are involved, truly straightforward physics-based representations, are not often a suitable option. Instead, alternative techniques such as those based on canonical models are used. These techniques are based on some specific type of approximation that leads to a well-defined characteristic mathematical structure [1].

Biological systems modeled within such a structure are always represented by the same symbolic equations and differ exclusively in the number of variables and the values of the parameters involved in the model. The use of canonical models is particularly advantageous for inverse problems, where observations on the biological system consist of time courses of system responses. In this case, it is very difficult to determine the optimal mechanistic model, while it is comparatively easy to set up a canonical model [2].

The Fourier method to describe a signal in terms of a combination of elementary trigonometric functions had a profound effect on the way that signals are viewed, analyzed, and processed. In communication and signal processing such fundamental concepts as frequency spectrum and bandwidth result from the Fourier representation of signals [3]. The Fourier analysis method is the most extensively applied signal processing tool since it allows an easy interpretation and manipulation and leads to the concept of frequency analysis and bandwidth. Furthermore, even some biological systems, such as the human heart system, perform some form of frequency analysis of the input signals [4].

Biological different types of data are a key component of this quest of knowledge since they represent the chemical and molecular reactions and cellular processes that provide the required conditions for life. With this additional information comes the burden of making it useful. How the data is stored and analyzed is a problem of critical importance for the future of research in this area. In this paper we propose an approach based on Fourier series for effective mathematical model of a biological system [5].

2. Modeling Approaches

In contrast to physics or engineering, biological systems seldom obey simple physical laws. Biology is a part of the physical world and therefore it is in principle describable with mathematical functions of physics. However, even in

apparent simple biological systems, very many processes often act simultaneously and in concert with each other, so that the apparent behaviour is the result of a complicated mixture of physical functions and a large amount of environmental variables that is essentially impossible to de-convolute. If physical laws cannot be used for describing complex biological processes, how is it possible to find appropriate mathematical representations? The question has no answer that is generally true for all scenarios [4].

Dense time series data often contain comprehensive information, because they reflect the collective dynamics of a biological system and its pertinent individual components under the specific investigated conditions. As a result, time series data have always been very appealing to bio-mathematical modelers [6].

An arbitrary time function $f(t)$, which satisfies Dirichlet's conditions can be expanded in the trigonometric series. The Dirichlet's conditions are always satisfied for a biological system. Since equation represents only a mathematical expression for a given function, any pressure or flow pulse may be decomposed in this manner into a number of sine or cosine waves [5].

3. Parameters Estimation

The first step in building a mathematical model of a biological system is often the analysis of the temporal behavior of key variables. Mathematical relationships between the time and frequency domain, such as Fourier Transforms and wavelets, are commonly used to extract information about the underlying signal from a given time series. One primary and very important advantage of representing data as a graph is that one can apply solutions from algorithms and graph systems researchers to problems of a completely different nature. Although biological data is different, representing it as a graph allows performing certain types of analyses similar to those used in other disciplines. Fortunately, biology is organized in a hierarchical and often modular fashion, which permits the establishment of models with different degrees of granularity and coarseness. At an atomic level, existing models are able to shed light on the details of binding between a protein and a ligand.

The task of bio-mathematical modeling comprises the conversion of a biological system into a simplified analogue model that is easier to analyze, interrogate, predict, extrapolate, manipulate, and optimize than the biological system itself. Our approach to construct the corresponding mathematical model is summarized in the following steps:

- 1) Data pre-processing
- 2) Specification of assumptions and simplifications
- 3) Obtainment of the Mathematical model
- 4) Estimation of parameter values
- 5) Model refinements (number of Fourier constants)

Among the five modeling phases, the most challenging task is usually the estimation of parameter values. This estimation is not an isolated task but closely related to other phases in the modeling process.

4. Data Set and Results

Pattern recognition is central to many scientific disciplines and is often a first step in building a model that explains the behavior of the obtained data. In particular, the study of periodic phenomena and frequency detection has received much attention, leading to the well-established field of spectral analysis.

Biology is plenty of phenomena that exhibit periodic-like behavior, with sustained oscillations in the form of limit cycles playing important roles in many diverse phenomena such as glycolytic metabolism, circadian rhythms, mitotic cycles, cardiac rhythms, hormonal cycles, population dynamics, and epidemiological cycles, among others [1]. A conventional method for frequency detection is Fourier analysis. It is based on the fact that it is possible to represent any integrable function as an infinite sum of sinusoidal functions.

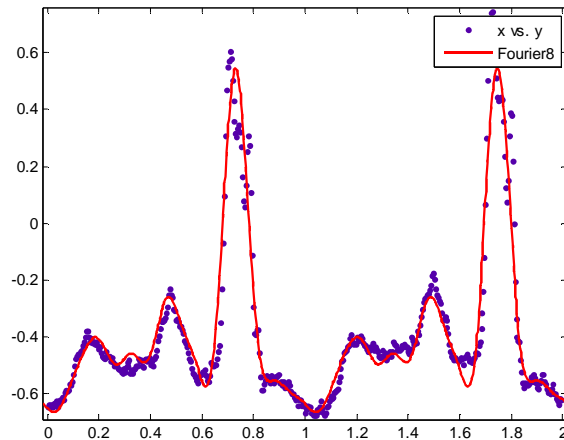


Fig. 1. Mathematical model of a biological system: cardiac system and its corresponding theoretical mathematical model.

Fig. 1 shows the experimental data of a cardiac system and its corresponding theoretical mathematical model. Blue points represent the experimental measurements of the system while the red line represents the mathematical approximation of the system obtained by using 8-constant Fourier model. In the same figure, the general expression of the obtained mathematical model as well as the corresponding values of the involved constants can be found next to the image.

General model Fourier8:

$$f(x) = -0.3899 - 0.129 \cos(x \cdot w) + b_1 \sin(x \cdot w) + a_2 \cos(2 \cdot x \cdot w) + b_2 \sin(2 \cdot x \cdot w) + a_3 \cos(3 \cdot x \cdot w) + b_3 \sin(3 \cdot x \cdot w) + a_4 \cos(4 \cdot x \cdot w) + b_4 \sin(4 \cdot x \cdot w) + a_5 \cos(5 \cdot x \cdot w) + b_5 \sin(5 \cdot x \cdot w) + a_6 \cos(6 \cdot x \cdot w) + b_6 \sin(6 \cdot x \cdot w) + a_7 \cos(7 \cdot x \cdot w) + b_7 \sin(7 \cdot x \cdot w) + a_8 \cos(8 \cdot x \cdot w) + b_8 \sin(8 \cdot x \cdot w)$$

Coefficients (with 95% confidence bounds):

$$b_1 = -0.1614; a_2 = -0.1846; b_2 = 0.06187; a_3 = 0.02465; b_3 = 0.1592; a_4 = 0.1103; b_4 = -0.1311; a_5 = -0.1017; b_5 = -0.0576; a_6 = -0.01219; b_6 = 0.0523; a_7 = 0.04375; b_7 = 0.01709; a_8 = -0.01052; b_8 = -0.02586; w = 6.183$$

5. Conclusions

The modeling of biological systems often lies on the study of time-dependent phenomena and, since a variety of biological processes exhibit periodic properties, Fourier transforms are a convenient tool for analyzing the frequency domain of time series. In this work, modeling of biological systems through Fourier series has been successfully demonstrated and, in particular, a cardiac system, with periodic-like response, was effectively modeled by using 8-constant Fourier model resulting in high similitude between the experimental data and the theoretical mathematical model.

6. References

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