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Memory effect in a self-sustained birhythmic biological system

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ABSTRACT

In this paper, birhythmicity in an enzymatic-substrate reaction described by a fractional-order extended van der Pol equation is investigated. The fractional derivatives are introduced in the system equations in order to model the memory property of the biological system. The residue harmonic balance scheme is used to study the periodic motions of the considered fractional-order van der Pol equations. It is shown that depending on system parameters and the fractional derivative order, the bistability area strongly increased. This fractional oscillator is analytically mapped, onto an ordinary bistable systems with a two stable amplitude. The obtained results clearly show an interesting collapse and revival of birhythmicity with the variation of the fractional derivative order. The amplitude and frequency of the fractional order van der Pol oscillator are derived. The analysis of amplitude equation corroborates with the results obtained by numerical simulations of the fractional-order differential equations describing the system.

1. Introduction

The fractional calculus and its applications at first glance seem to be a very difficult subject. Fractional calculus is a mathematical topic with more than 300 years of history, but the applications of fractional calculus in physics and engineering are just a recent focus of interest. Actually, the fractional-order derivation provides an excellent instrument for the description of long memory and hereditary properties of various materials,systems and processes in comparison to integer-order derivation which lacks such effects [1]. Fractional derivatives are also used in modeling of many chemical processes, mathematical biology and many other problems in physics and engineering. These findings invoked the growing interest of studies of the fractional calculus in various fields such as physics, chemistry and engineering.

Recently, more and more investigators began to study the qualitative properties and numerical solutions of FO biological models [2–4] and FO financial and economical models called FO econophysics [5]. The main reason is that FO equations are naturally related to systems with memory which exists in most biological systems. Also they are closely related to fractals which are abundant in biological systems. In Ref. [2], the FO predator-prey model and the FO rabies model were investigated; the existence and uniqueness of solutions were proved; the stability of equilibrium points were studied; numerical solutions of these models were given. In biology, it has been deduced that the membranes of cells of biological organism have FO electrical conductance [6] and then are classified in groups of non-integer order models. Enzymes are responsible for all chemical reactions that take place within a biological cell. Modeling the transient behavior of cellular processes under difficult situations like heterogeneous and in vivo conditions with classical calculus may not be realistic approach. To accurately represent such processes having inherent FO description, fractional derivative which has non-local property can be applied [7–10]. Recent investigations have shown that many complex biological systems can be represented more accurately through fractional derivative formulation. Magin [8] was the first who used fractional derivatives and fractional integrals in order to model stress-strain relationship in biomaterials. Craiem et al. [9] applied fractional calculus to model arterial viscoelasticity.

In the present work, we intend to investigate analytically and numerically the dynamics of FO forms of another self-excited model namely a biological system based on the enzymes-substrates reactions in order to show up the behavior of such system in the autonomous states. We aim to discuss the mathematical conditions of occurrence of birhythmicity based upon the residue harmonic balance scheme. Enzymes are organic catalysts produced by living organism. They are proteins made up of tens or hundreds of amino acids. Enzymes are central to every biochemical process, acting in organised sequences; they catalyse the hundreds of step-

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wise reactions that degrade nutrient molecules [11]. The study of enzymes has immense practical importance in some diseases especially inheritable genetic disorders; there may be a deficiency or even a total absence of one or more enzymes. For other disease conditions, excessive activity of an enzyme may be the cause. Measurements of activities of enzymes in blood plasma, or tissue samples are important in diagnosing certain illnesses [12]. Memory and hereditary properties may appear, for example, in hysteretic phenomena, anomalous relaxation and diffusion, peculiar lossy phenomena (such as dispersions and dissipations with unknown origins, eddy current losses, certain dielectric absorptions. . .), and self-organization in complex systems. This paper intends to give mathematically explicit relations between the frequency/amplitude of the oscillation and the order/parameter of the system.

The paper is organized as follows. The next section firstly introduce some basic facts about fractional calculus. Then the mathematical model describing the system in which the effect of memory is taken into account is derived in Section 2. The detailed analysis on the approximation to the extended FO van der Pol oscillator is given by means of the residue harmonic balance method. The relation between the frequency/amplitude and the fractional derivative order/parameter is derived analytically that provided Hopf bifurcation condition. In Section 3, The accuracy of the obtained relations is discussed by comparing them with some simulation results. It is shown that the residue harmonic balance method is effective for solving FO oscillators. Finally, Section 4 concludes the outcome of the whole study.

2. Biological model and fractional order equations of motion

In the last few decades, the theory of fractional derivatives has attracted significant attention in various areas, such as viscoelasticity [13], signal processing [14], biology [15–18]. In biology, one of its most prominent uses is in modelling diffusion processes [13,17], and the fractional model has been used to describe anomalous diffusion in complex environments [15].

2.1. Basic definitions

The idea of fractional calculus has been known since the development of the classical calculus, with the first reference probably being associated with Leibnitz and Hospital in 1695 where half-order derivative was mentioned. In this section we discussed the definitions of the fractional derivatives, three mains definitions have been established for mathematical analysis of FO systems

- Grünwald–Letnikov definition

$$ {}_aD_t^p f(t) = \lim_{h\to 0} \sum_{j=0}^{\left[\frac{t-a}{h}\right]} (-1)^j \binom{p}{j} f(t-jh). \tag{1}$$

- The Riemann–Liouville fractional derivatives is defined as follows [13,19]:
  1. The left Riemann–Liouville fractional derivatives of order p

$$ {}_aD_t^p f(t) = \frac{1}{\Gamma(n-p)} \frac{d^n}{dt^n} \int_a^t \frac{f(\tau)}{(t-\tau)^{p-n+1}} d\tau, \tag{2}$$

  2. The right Riemann–Liouville fractional derivatives of order p

$$ {}_tD_b^p f(t) = \frac{1}{\Gamma(n-p)} \frac{d^n}{dt^n} \int_t^b \frac{f(\tau)}{(t-\tau)^{p-n+1}} d\tau, \tag{3}$$

- Caputo definition [1,21,22]

$$ {}_aD_t^p f(t) = \frac{1}{\Gamma(n-p)} \int_a^t \frac{f^{(n)}(\tau)}{(t-\tau)^{p-n+1}} d\tau \tag{4}$$

where $(n-1<r<n)$, and where $\Gamma(.)$ is the Gamma function. The Caputo definition is suitable for the analysis of physical systems because it provides initial conditions, which physically can be explained [20,21]. Moreover, from an analytical point of view, it is quite simple to integrate.

2.2. Description and modeling of the system

We considered the coherent oscillations in biological system through the case of an enzymatic-substrate reaction in brain wave model [23] with ferroelectric behavior. Assuming the suggestions made by Fröhlich [24,25] as a physical base of theoretical analysis, through which a selective transport of the enzymes and particular chemical reactions become possible. The enzyme reaction model can be described by a system of nonlinear differential equations as follows (for more details on the enzyme dynamics, see [26] and the references therein)

$$\begin{cases} \dfrac{dN}{d\tau} = \upsilon NRS - \xi N \\ \dfrac{dS}{d\tau} = \gamma S - \upsilon NSR - \lambda(R-C) \\ \dfrac{dR}{d\tau} = \xi N - \upsilon NRS \end{cases} \tag{5}$$

where N is the population of enzyme molecules in the excited polar state, R is not excited population and S the number of the substrate molecules. Systems (5) can be reduced to only two equations for N and S, [26] which are the well-known Lotka–Voltera (LV) equations [27]

$$\begin{cases} \dfrac{dN}{d\tau} = \upsilon CNS - \xi N \\ \dfrac{dS}{d\tau} = \gamma S - \upsilon CNS \end{cases} \tag{6}$$

With $N(0)\geq 0$, $S(0)\geq 0$. Eq. (6) are a pair of first order non-linear differential equations frequently used to describe the dynamics of biological systems in which two species interact on each other, one is a predator with population N and the other is its prey with population S. This system and its extensions have been fully studied before by several researchers. in Ref. [28], Ahmed et al. proposed a generalization of the predator prey system (6) obtained by substituting the first-order derivatives by fractional-order ones. It is worth noticing that this is not only a mathematical generalization but the introduction of fractional-oder derivation [17] is of modeling interest in the sense that it takes into account memory effects which are inherent to almost all natural phenomena (including those modeled eventually by the LV equations). In this way, the FO LV [29,30] (or FO predator-prey model) system is described as:

$$\begin{cases} \dfrac{d^pN}{d\tau^p} = \upsilon CNS - \xi N \\ \dfrac{d^qS}{d\tau^q} = \gamma S - \upsilon CNS \end{cases} \tag{7}$$

where the fractional derivatives $\frac{d^pN}{d\tau^p}$ and $\frac{d^qS}{d\tau^q}$ are considered in the Caputo sense, p and q are parameters describing the order of the fractional time-derivatives in the Caputo sense which range are]0, 1]. From the system equations (7), we derive the two following steady states $(N_0, S_0) = (0, 0)$ and $(N_1, S_1) = (\frac{\gamma}{\upsilon C}, \frac{\xi}{\upsilon C})$. Perturbing these activated enzymes and substrate molecules around the nontrivial steady state leads to the following equations

$$\begin{cases} \dfrac{d^p\varepsilon}{d\tau^p} = \gamma\eta + \upsilon C\eta\varepsilon \\ \dfrac{d^q\eta}{d\tau^q} = -\xi\varepsilon - \upsilon C\eta\varepsilon \end{cases} \tag{8}$$

where ε and η are respectively the excess concentrations of activated enzymes and substrate molecules beyond their equilibrium