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Impulsive Goodwin oscillator with large delay: Periodic oscillations, bistability, and attractors

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ABSTRACT

The role of the time delay in the dynamics of a hybrid model of pulsatile feedback endocrine regulation is investigated. The model in hand can be seen as an impulsive and delayed version of the popular in computational biology Goodwin Oscillator, where the feedback is implemented by means of pulse modulation. The value of the time delay is related to the duration of the time interval between the firing times of the feedback impulses. Under the assumption of a cascade structure of the continuous part of the model, the hybrid dynamics of the closed-loop system are shown to be governed by a discrete mapping propagating through the firing times of the impulsive feedback. Conditions for existence and stability of periodic solutions of the model are obtained. Bifurcation analysis of the mapping reveals the phenomenon of bistability arising for larger time delay values but not observed for the smaller ones.

1. Introduction

A simple mathematical construct comprising three state variables and a nonlinear feedback was proposed by Brian C. Goodwin in [1] and further developed in [2] to portray the oscillations in a single gene that suppresses itself via the production of intermediate enzymes. Then the term Goodwin oscillator was coined finding broad application in numerous fields of biology, physiology and medicine as well as drawing significant attention in applied mathematics. In particular, the Goodwin oscillator was adopted in [3,4] to describe periodic behaviors in endocrine systems and at present is referred to in this field as the Smith model. To capture the episodic nature of pulsatile (non-basal) endocrine feedback, the model was modified in [5] by implementing the biologically motivated principles of impulsive control (see e.g. [6]). Being applied to the testosterone regulation in the human male, the impulsive model demonstrated a good agreement with experimental data in [7,8] and gave theoretical explanations to some experimentally observed phenomena, including deterministic chaos [9].

As was demonstrated in [2], the original Goodwin Oscillator needs biologically infeasible slopes of the feedback nonlinearity (i.e. Hill function order greater than eight) to possess periodic solutions. Starting from the early work of [4], a time delay was introduced into the Goodwin model to make its structure more adequate to the biological reality (see also [10–15]) and induce sustained oscillations. Similarly, in [16–18], a time delay was included into the impulsive Goodwin–Smith model, but rather in order to model the transport phenomena and the time necessary for synthesis of a hormone. In fact, the impulsive Goodwin–Smith model is known to lack equilibria [5].

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In the analysis of [16–18], the delay value is assumed to be strictly less than the least time interval between two consecutive firing times of the impulsive feedback. This assumption appears to be satisfied for the testosterone hormonal regulation (see, e.g., [10]) but not for pulsatile endocrine loops in general. For instance, in [19], where hypothalamic control of the growth hormone (GH) secretion is considered, the time delay for the stimulation by GH of the releasable store of somatostatin is estimated to 60 min. The experimental data provided by [20] demonstrate that, for adolescent females, the estimated GH interburst interval is less than an hour, while for young males it is usually greater, but can be less than an hour at certain time intervals. Hence, evidently, the results of [16,17] are not directly applicable in these cases.

The restriction on the time delay value is relaxed in [21], allowing for the delay to be greater than the least interval between two consecutive feedback firing times. In this paper, a further improvement of the time-delay value bound is provided that enables to consider delays less than a total of three consecutive intervals between the firings of the pulse-modulated feedback. This not only extends the biological applicability of the results, but also gives new mathematical insights into the dynamics of the system.

The paper is organized as follows. First the notion of finite-dimension reducible time-delay systems is briefly reviewed. Then, the impulsive Goodwin–Smith model with a delay in the continuous part is revisited under new and relaxed assumptions on the time delay value. A pointwise discrete mapping describing the propagation of the system dynamics from one firing time of the pulse-modulated feedback to another is derived and analyzed. Further, existence and stability of periodic solutions of the model in question (m-cycles) are studied. Finally, the bistability phenomenon arising for larger values of the time delay in the mapping is investigated by bifurcation analysis.

2. FD-reducible time delay systems

Consider for $t \geqslant 0$ the autonomous system with delayed state

$$\frac{dx}{dt} = A_0 x(t) + A_1 x(t-\tau), \tag{1}$$

where $x(t) \in \mathbb{R}^p$, $A_0, A_1 \in \mathbb{R}^{p\times p}$, and τ is a constant time delay, subject to the initial (vector) function $x(t) = \varphi(t)$, $-\tau \leqslant t < 0$.

The following definition was introduced in [16,17].

Definition 1. Time-delay linear system (1) is called finite-dimension reducible (*FD-reducible*) if there exists a constant matrix $D \in \mathbb{R}^{p\times p}$ such that any solution $x(t)$ of (1) defined for $t \geqslant 0$ satisfies the linear differential equation

$$\frac{dx}{dt} = Dx \tag{2}$$

for $t \geqslant \tau$.

FD-reducibility means that the solutions of time-delay system (1) are indistinguishable from those of a finite-dimensional system of order p on the time interval $[\tau, +\infty)$. The theorem below summarizes the essential properties of FD-reducible systems (see [17] for the proof).

Theorem 1. *FD-reducibility of system (1) is equivalent to any of the statements* (i), (ii)*:*

(i) *The matrix coefficients of (1) satisfy*

$$A_1 A_0^k A_1 = 0 \quad \text{for all } k = 0, 1, \ldots, p-1. \tag{3}$$

(ii) *There exists an invertible $p \times p$ matrix S such that*

$$S^{-1} A_0 S = \begin{bmatrix} U & 0 \\ W & V \end{bmatrix}, \qquad S^{-1} A_1 S = \begin{bmatrix} 0 & 0 \\ \bar{W} & 0 \end{bmatrix}, \tag{4}$$

where the blocks U, V are square and the sizes of the blocks W and $\bar{W}$ are equal.
Moreover, the matrix D in FD-reduced system (2) for a FD-reducible system (1) is uniquely given by

$$D = A_0 + A_1 e^{-A_0 \tau}. \tag{5}$$

In the special coordinate basis given by (4), system (1) can be rewritten as

$$\frac{du}{dt} = Uu, \tag{6}$$

$$\frac{dv}{dt} = Wu + Vv + \bar{W}u(t-\tau) \tag{7}$$