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# Hybrid observers for systems with intrinsic pulse-modulated feedback

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### **Abstract**

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Dynamical processes resulting from the interaction of continuous and discrete dynamics are often encountered in living organisms. Time evolutions of such processes constitute continuous variables that are subject to instant changes at discrete points of time. Usually, these discrete events cannot be observed directly and have to be reconstructed from the accessible for measurement continuous variables.

Thus, the problem of hybrid state estimation from measurements of continuous outputs is important to and naturally arises in life sciences but, so far, scarcely covered in the existing literature.

This thesis deals with a special class of hybrid systems, where the continuous linear part is controlled by an intrinsic impulsive feedback that contributes discrete dynamics. The impacting pulsatile feedback signal is not available for measurement and, therefore, has to be reconstructed. To estimate all the elements of the hybrid state vector, an observation problem is considered.

The focus of the work is on a state observation problem for an analytically tractable example of a hybrid oscillator with rich nonlinear dynamics including, e.g., monostable and bistable high-periodic and quasiperiodic solutions as well as deterministic chaos. At the same time, the three-dimensional case of the considered hybrid oscillator constitutes a mathematical model of testosterone regulation in the male validated through system identification on human endocrine data. In a pulsatile endocrine regulation loop, one of the hormones (releasing hormone) is secreted in pulses from neurons in the hypothalamus of the brain. Thus a direct measurement of the concentration of this hormone in the human is not possible for ethical reasons and it has to be estimated in some manner from the available data, for instance by applying an observer.

It is desirable for an observer to guarantee asymptotic convergence of the state estimate to that of the observable plant from all feasible initial conditions at a highest possible rate. When the state estimation error is zero, the hybrid observer is in a synchronous mode characterized by the firings of the impulses in the observer feedback and those of the plant occurring simultaneously.

Therefore, the observer design problem can be formulated as synchronization of the plant states with those of the observer. This approach does not formally demand observability of the hybrid plant solution. Further, since the dynamics of the oscillator are highly nonlinear, the state estimation problem is considered with respect to particular solutions of the observed system, whose characteristics are assumed to be known, but not the initial conditions. The observer design problem for the impulsive Goodwin's oscillator consists of the selection of the observer structure and of assigning desired properties to a discrete map that captures the observer state transitions from one impulse firing to another through manipulating the degrees of freedom of the observer.

*Keywords:* hybrid systems, impulsive systems, biomedical systems, Goodwin's oscillator, observers, time-delay

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# List of papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

- I** D. Yamalova, and A. Medvedev, and Zh. Zhusubalyiev, Bifurcation analysis for non-local design of a hybrid observer for the impulsive Goodwin's oscillator, *Nonlinear Dynamics, Springer* (submitted)
- II** D. Yamalova, and A. Medvedev, Hybrid observer with finite-memory output error correction for linear systems under intrinsic impulsive feedback, *Automatica* (submitted)
- III** D. Yamalova, and A. Medvedev, Robustification of the synchronous mode in a hybrid observer for a continuous system under an intrinsic pulse-modulated feedback, *Proc. 16th European Control Conference IEEE*, pages 107–112, Limassol, Cyprus, June 12–15 2018
- IV** D. Yamalova, and A. Medvedev, Hybrid observers for an impulsive Goodwin's oscillator subject to continuous exogenous signals, *Proc. 2017 IEEE 56th Annual Conference on Decision and Control, (CDC)*, pages 2396–2401, Melbourne, Australia, December 12–15 2017
- V** D. Yamalova, and A. Medvedev, Attractivity of the synchronous mode in hybrid observers for the impulsive Goodwin's oscillator subject to harmonic exogenous excitation, *Proc. 2019 American Control Conference 2019* (accepted)
- VI** D. Yamalova, A. Churilov, and A. Medvedev, Finite-Dimensional Hybrid Observer for Delayed Impulsive Model of Testosterone Regulation, *Mathematical Problems in Engineering*, vol. 2015, Article ID 190463, 12 pages, 2015
- VII** D. Yamalova, A. Churilov, and A. Medvedev. Hybrid state observer for time-delay systems under intrinsic impulsive feedback. In *Proc. 21st Intern. Symp. Math. Theory Networks Syst. (MTNS)*, pages 977–984, Groningen, The Netherlands, July 7 – 11 2014

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## Related Works

Additional material pertaining to the topic of this thesis but not part of it is presented in the following publications:

- Diana Yamalova, Alexander Churilov, and Alexander Medvedev. Hybrid State Observer with Modulated Correction for Periodic Systems under Intrinsic Impulsive Feedback. *IFAC-PapersOnLine*. Periodic Control Systems. Volume 46, Issue 12, 2013, Pages 119–124.
- Diana Yamalova, Alexander Churilov, and Alexander Medvedev. Design degrees of freedom in a hybrid observer for a continuous plant under an intrinsic pulse-modulated feedback. *IFAC-PapersOnLine*. Volume 48, Issue 11, 2015, Pages 1080–1085.
- Diana Yamalova, Alexander Churilov, and Alexander Medvedev. State estimation in a delayed impulsive model of testosterone regulation by a finite-dimensional hybrid observer. *Proc. 14th European Control Conference*. 15 - 17 July 2015, Linz, Austria.
- Diana Yamalova, Alexander Churilov, and Alexander Medvedev. Hybrid Observer for an Intrinsic Impulsive Feedback System. *IFAC-PapersOnLine*. Volume 50, Issue 1, 2017, Pages 4570–4575.
- Diana Yamalova and Alexander Medvedev. Design of a hybrid observer for an oscillator with an intrinsic pulse-modulated feedback. *Proc. 2017 American Control Conference (ACC)*. 24-26 May 2017. Seattle, WA, USA.
- Diana Yamalova. Poincaré mapping for a time-delay impulsive system. *Vestnik St. Petersburg University, Mathematics*. January 2017, Volume 50, Issue 1, p. 44-54
- Diana Yamalova, Alexander Medvedev, and Zhanybai T. Zhusubalyiev and Anton Proskurnikov. Nonlinear dynamics of a positive hybrid observer for the impulsive Goodwin’s oscillator: A design study. *Proc. 2019 IEEE 58th Annual Conference on Decision and Control, (CDC)* (submitted)



# Sammanfattning på svenska

Hormoner är kemiska budbärare. Den mänskliga kroppen framställer och cirkulerar uppåt 50 olika hormoner. Dessa kemiska substanser produceras av endokrina celler som till största del finns i olika körtlar. De endokrina cellerna frisätter hormoner i blodomloppet, och hormonerna cirkulerar sedan runt i kroppen för att kunna aktivera olika målceller. Det endokrina systemet och nervsystemet koordinerar tillsammans viktiga funktioner i kroppen: metabolism, tillväxt, sexuell aktivitet, muskelkontraktion, med mera.

Om någon skulle bli ombedd att lista ett antal hormoner, så skulle med stor sannolikhet testosteron nämnas. Testosteron är ett av de manliga könshormonerna, som är viktigt för sexuell och reproduktiv utveckling. Även kvinnor producerar testosteron, men i mycket mindre mängd än vad män gör. Testosteron är inblandat i utvecklingen av manliga könsorgan före födseln. Under puberteten påverkar testosteron den sekundära könskaraktistiken hos män, som till exempel djupare röst, ökad storlek på penis och testiklar, samt skäggväxt. Testosteron påverkar också sexdriften, spermaproduktionen, fettdistributionen och underhåll av muskelstyrka. Av dessa orsaker så är testosteron viktigt för hälsa och välbefinnande hos män.

För den som är orolig för låga eller höga testosteronnivåer så kan en läkare ta blodprov för att mäta koncentrationen av hormonet. Om testosteronnivån är låg så kan läkaren förordna testosteronterapi, och låta patienten få en konstgjord version av hormonet. Detta har dock flera möjliga bieffekter, även på lång sikt, eftersom det artificiella hormonet inte direkt samverkar med kroppens övriga system. I vanliga fall så koordineras kroppens olika delsystem, och nivåerna av en viss kemisk substans beror på vad nivåerna av andra kemiska substanser är. Just testosteronproduktionen påverkas framförallt av två andra hormoner: gonadotropinfrisättande hormon (GnRH), som bildas av neuron och frisätts från hypotalamus, och luteiniserande hormon (LH), som bildas i hypofysens framlob. Detta kan ses som ett system där hjärnans hypotalamus använder GnRH för att instruera hypofysen om hur mycket testosteron som ska produceras. Hypofysen skickar meddelandet vidare, med hjälp av LH, till testiklarna där testosteronet produceras. Sedan sker en återkoppling där hjärnan noterar testosteronnivån i kroppen för att avgöra hur mycket nytt GnRH som måste produceras. Därmed så frisätter hjärnan mindre GnRH om testosteronnivån i kroppen går upp, vilket i sin tur leder till att produktionen av testosteron minskar. För att få ett bättre grepp om hur denna dynamik fungerar så kan en matematisk modell tas fram.

Neurala processer i hjärnan är mycket snabbare än de kemiska processerna i resten av kroppen. Detta kompenseras genom att GnRH inte frisätts kontinuerligt. Istället så frisätts GnRH i pulser med olika amplituder och tidsintervall som bestäms av en såkallad GnRH-pulsgenerator. även för en vanlig läsare så framstår det därför som ganska naturligt att matematisk modellera den neuroendokrina regleringen med explicita pulser modulerade i frekvens och amplitud. Problemet är att en sådan matematisk modell är svår att analysera, och därför var det först 2009 denna typ av modell började användas på allvar. Modellen har också visats stämma väl överens med klinisk data.

Alltså, GnRH frisätts inte kontinuerligt, utan i korta pulser. Vidare så halveras mängden GnRH på ungefär 2–4 minuter. Eftersom GnRH därmed försvinner snabbt ifrån cirkulationen så kan det inte mätas upp via blodprov tagna utanför hjärnan. Detta innebär att det är svårt att mäta upp GnRH-pulserna kliniskt utan att göra ingrepp som riskerar att skada patients hälsa allvarligt. Därmed kan inte hela kedjan av hormoner som påverkar testosteronnivån mätas upp, vilket kan vara ett problem vid analys av till exempel låga testosteronnivåer. För att hitta en lösning på detta så kan idéer från regler-teori användas. Framförallt ger tillståndsobservatörer en möjlighet att skatta GnRH-impulserna matematiskt, och därmed kan riskerna för patienten undvikas. Syftet med en tillståndsobservatör är att ta fram en skattning av en okänd kvantitet genom att använda mätningar av andra kvantiteter och en matematisk modell av systemet. Människokroppen är dock ett invecklat dynamiskt system, vilket gör framtagandet av en tillståndsobservatör väldigt utmanande, och det är ett problem som innan denna avhandling inte har berörts särskilt mycket i den regler-teoretiska litteraturen. även om avhandlingen i första hand studerar testosteronproduktionen så kan de metoder som tagits fram även appliceras andra hormoner och regulationsmekanismer.

# List of Notation

$\mathbb{N}$	natural numbers $\{1, 2, 3, \dots\}$
$\mathbb{N}_0$	natural numbers $\mathbb{N} \cup \{0\}$
$\mathbb{R}$	real numbers
$\mathbb{R}^n$	linear space of $n$ -dimensional real vectors
$\mathbb{C}$	complex numbers
$\operatorname{Re} \lambda$	real part of $\lambda \in \mathbb{C}$
$\operatorname{Im} \lambda$	imaginary part of $\lambda \in \mathbb{C}$
$i$	imaginary unit, $\sqrt{-1}$ , unless otherwise specified
$\mathbb{C}^n$	linear space of $n$ -dimensional complex vectors
$\top$	vector or matrix transpose
$*$	complex conjugate, or for vectors and matrices, the conjugate transpose
$\ x\ $	Euclidian norm $\ x\  = \sqrt{x^*x}$ of a vector $x \in \mathbb{R}^n$ or $x \in \mathbb{C}^n$ , unless otherwise specified
$0$	denotes zero number, zero vector, or zero matrix, depending on the context
$I_n$	identity matrix (in some cases the index $n$ is omitted)
$A^{-1}$	matrix inverse to $A$
$\det A$	determinant of a matrix $A$
$\operatorname{tr} A$	trace of a matrix $A$ (the sum of its diagonal elements)
$\operatorname{adj} A$	adjunct of a matrix $A$
$\operatorname{diag}\{\lambda_1, \dots, \lambda_n\}$	diagonal matrix whose diagonal elements are $\lambda_1, \dots, \lambda_n$
$\lim_{\tau \nearrow t} f(\tau)$	left-hand-side limit of a function $f(\tau)$ of a real variable $\tau$ as $\tau$ approaches a point $t$ from below, i.e. $\lim_{\tau \nearrow t} f(\tau) = \lim_{\tau \rightarrow t-0} f(\tau)$
$\lim_{\tau \searrow t} f(\tau)$	right-hand-side limit of a function $f(\tau)$ of a real variable $\tau$ as $\tau$ approaches a point $t$ from above, i.e. $\lim_{\tau \searrow t} f(\tau) = \lim_{\tau \rightarrow t+0} f(\tau)$
$C[-\tau, 0]$	space of $\mathbb{R}^n$ -valued piecewise continuous functions on $[-\tau, 0]$
$\ f\ _\tau$	uniform norm, $\ f\ _\tau = \sup_{\theta \in [-\tau, 0]} \ f(\theta)\ $
$\operatorname{dist}(x, \mathcal{A})$	distance of a vector $x$ to a set $\mathcal{A}$ , i.e. $\operatorname{dist}(x, \mathcal{A}) = \min_{y \in \mathcal{A}} \ x - y\ $



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# 1. Introduction

Dynamical systems with impulsive action, i.e., systems whose state vector undergoes jumps at certain time instants due to impacting instantaneous pulses, appear in various areas of engineering and science, including biology and medicine [35, 25], population dynamics [3, 83], pharmacokinetics [72, 104, 103], mathematical economy [126], theoretical physics [65], chemistry [4], telecommunications [38, 125], radio engineering [15], communication security [62, 63], and mechanics [15]. Impulsive models can either describe the processes whose state changes instantly due to their principle of operation or plants that are subject to impulsive control law. These systems can be viewed as a special class of hybrid systems, where the continuous dynamics are defined by differential or integral equations specifying the system behavior in the time intervals between the jumps. The discrete dynamics are governed by functional equations that determine the instantaneous changes in the system state and the moments of impulse occurrence, i.e., the jump instants. The sequences of jump magnitudes and their timing can either be fixed and independent of the system solution or determined on-line by means of some functional relationships.

One of the prominent biomedical applications that hybrid impulsive systems currently have is mathematical modeling in the field of neuroendocrinology, where the numerous interactions between the nervous system and the endocrine system are sought to describe. In particular, a part of the brain called hypothalamus is massively involved in these interactions. The signals coming into the hypothalamus from the endocrine system activate the secretion of neurohormones from it. Spreading through the bloodstream, the hypothalamic neurohormones stimulate the secretion of pituitary hormones. The latter, reaching the corresponding endocrine glands with the blood, activate secretory functions in them. The processes of neuroendocrine regulation described above are usually closed through the nervous system, thereby forming feedback loops. However, some of the endocrine glands secrete hormones continuously, while hypothalamic neurohormones are characterized by short half-life and secreted in impulsive manner.

A simple but, at the same time, realistic model of a pulse-modulated endocrine feedback system is the impulsive Goodwin's oscillator that has been introduced in [78, 28] to portray pulsatile (non-basal) testosterone regulation in the male. It can also be straightforwardly applied to other endocrine loops, such as cortisol regulation, where the impulsive hypothalamic secretion is the

key to understanding the closed-loop dynamics of the system, [70]. In endocrine regulation, the continuous states correspond to the hormone concentrations involved in the regulatory axis, while the impulsive part is employed to reflect the amount and timing of the pulsatile hormone secretion exerted by the hypothalamus. With three continuous states, the impulsive endocrine regulation model proposed in [78, 28] can be seen as a generalization of the classical (continuous) Goodwin's oscillator [46, 45] or, as it is called in endocrinology, the Smith model [107].

It is difficult or impossible to measure the concentrations and frequency of secretion of all the hormones involved in the regulation chain without causing significant harm to the brain of a human or an animal. Therefore, unmeasured hormone concentrations in an endocrine loop have to be estimated from the measured ones by means of, e.g., an observer. This is a typical problem in biological hybrid systems, where the discrete events cannot be observed directly and have to be reconstructed from the accessible for measurement continuous variables. The problem is widely recognized in stochastic systems as event detection problem, but is seldom addressed in a deterministic setup and, so far, scarcely covered in the literature (except for [73, 76]). Mathematical modeling of neuroendocrine regulation by hybrid dynamical systems can thus provide an non-invasive tool to solve this estimation problem. Further, based on actual clinical data, deeper insights into endocrine regulation can be acquired, thus facilitating timely diagnostics of medical conditions and planning of individualized treatments.

There are several matters that complicate observer design and stability analysis. First, the dynamics of the impulsive Goodwin's oscillator do not possess equilibria [28] and exhibit monostable or bistable periodic, quasiperiodic or chaotic oscillations, [128, 77, 79]. Second, the states of the considered system undergo jumps at certain time instants (firing times) modulated by other states and, in general, the firing times produced by an observer do not coincide with those of the plant. Consequently, on the time interval defined by the mismatch in the firing times, the error between the solution to the plant and that to the observer is large and does not monotonically converge to zero as time increases, thus causing the so-called "peaking phenomenon" [14, 68, 81, 98]. In this connection, one cannot consider stability in the sense of Lyapunov. Third, an unknown initial feedback firing time (jump time) of the observed plant poses the greatest complication in the state estimation of linear continuous time-invariant systems under inaccessible for measurement pulse-modulated feedback.

The remaining of the thesis is composed in two parts: First, the necessary theoretical background and motivation are summarized. Second, reprints of the papers resulting from the research performed for this doctoral thesis are provided.

## 2. Hybrid models in life science

The research field of hybrid systems that covers interactions of discrete and continuous dynamics is gaining more attention in mathematical modeling and analysis within life science and medicine. Basically, every form of life exhibits hybrid dynamics. Hybrid behaviours commonly occur within living organisms – such as microorganisms, plants, animals, and human beings – due to their complex dynamical nature, as their evolution is subject to discontinuities. Typical examples of such discontinuities appear in threshold-triggered firing in neurons [58], on–off switching of gene expression by a transcription factor [57, 87, 102], division in cells [22, 9, 85], in disease progression, e.g., prostate cancer under intermittent hormonal therapy, where continuous tumor dynamics are switched by interruption and reinstatement of medication [49, 56, 100, 110, 111, 53, 109], in endocrine regulation, where neural processes interact with the hormone kinetics thus giving rise to hybrid models with relatively slow continuous dynamics that are controlled through impulsive action of firing neurons [60, 61, 118]. These processes admixing discrete events with continuous system evolution cannot be adequately described by linear models that are based on proportionality between two variables and/or relationships described by linear differential equations. Nonlinear modeling alone still is not able to explain all of the dynamical diversity present in a living organism.

Periodic, quasi-periodic, and chaotic modes are inherent phenomena in any living organism governed by biological rhythms and self-regulatory mechanisms. Oscillations are unavoidable in the cardiac rhythm observed in electrocardiograms [89, 40], breathing [88, 8, 90], neural system dynamics [36, 47], hormone concentrations [52, 106, 105], in enzymatic control processes [46, 45, 115], gene regulatory processes [48]. Consequently, the question of the existence of periodic and chaotic solutions is a central problem in the qualitative studies of the corresponding dynamical systems.

Looking into oscillations in cardiac rhythm, brain, or population dynamics within the framework of hybrid dynamics is also appealing. These applications have been traditionally modelled by means of systems of differential equations or by purely discrete models. In general, such a representation efficiently compares with clinical data; it has in some cases a good predictive value, but no explanatory value. Since it neither points at the actual underlying mechanisms, nor a regulatory path, it is not able to evidence control parameters of the observed behaviour and to capture all possible interactions between the continuous and discrete dynamics of such systems. A hybrid dynamics viewpoint provides useful tools to investigate the nature of the complex dynamics

in biological system and to understand the origin of the presented dynamical behaviour. Further, mathematical modeling by hybrid dynamical systems is particularly important for understanding the nonlinear dynamics of the human organism in health and in disease, in efforts to predict medical conditions, help appropriate diagnoses, and optimize treatments.

Hybrid systems can be conventionally divided into three major classes: hybrid dynamical systems, hybrid control systems, and hybrid automata. It is worth noting that, in control engineering, the concept of hybrid systems is applied mainly in controller design and optimization. In life sciences, hybrid systems are used to assist in interpreting, explaining, and predicting dynamical phenomena. However, the existing rich theoretical framework in technical applications of hybrid systems often cannot be straightforwardly applied to problems arising in biological and medical systems. This is due to the specific limitations and ethical issues arising in biomedical control and observation problems. In particular, the fact that discrete events triggered in deep parts of the brain are typically not accessible in living organisms poses a specific and seldom addressed in control theory problem of estimating discrete states of a hybrid system from only continuous measurements. Furthermore, rhythmic behaviour (i.e., repetitive but not necessarily periodic) is one of the fundamental properties of the living organism, meaning that corresponding dynamical systems exhibit sustained oscillations due to unstable equilibria or lack of point attractors, which is also not typical for most of engineering problems. Therefore, hybrid systems in biomedical applications and life science require separate consideration.

The nonlinear dynamics of hybrid dynamical systems are considerably richer and more complicated than those of smooth dynamical systems. Non-smooth dynamics even generate special classes of bifurcations [82]. Thus, studying hybrid systems is generally more challenging than purely discrete or purely continuous systems, because of the interplay between the dynamics of different nature. Due to the great diversity of such interactions, hybrid dynamical systems have not yet been formulated by a common mathematical description.

Hybrid systems may be formally described as a differential inclusion by the following model [41, 42]:

$$\begin{aligned} \dot{x} &\in \mathcal{F}(x), & x &\in \mathcal{C}, \\ x^+ &\in \mathcal{G}(x), & x &\in \mathcal{D}, \end{aligned} \tag{2.1}$$

where  $x \in \mathbb{R}^n$  is the state vector of a hybrid system,  $x^+$  is the state of a hybrid system after a jump,  $\mathcal{F}$  is a set-valued mapping (the *flow map*),  $\mathcal{C} \subset \mathbb{R}^n$  (the *flow set*),  $\mathcal{G}$  is a set-valued mapping (the *jump map*),  $\mathcal{D} \subset \mathbb{R}^n$  (the *jump set*).

A solution to the hybrid system is a piecewise absolutely continuous function satisfying  $\dot{x}(t) \in \mathcal{F}(x(t))$  almost everywhere and  $x(t) \in \mathcal{C}$  on each interval of continuity, whose right limits  $x(t^+) = \lim_{\tau \searrow t} x(\tau)$  at jump times  $t$  are determined by  $x(t) \in \mathcal{D}$  and related to  $x(t)$  through  $x(t^+) \in \mathcal{G}(x)$ , [43]. However,

this choice of the time domain does not allow for more than one jump at a given time.

A particular class of hybrid systems, namely impulsive systems, is dealt with in this thesis work and described in Section 3.

### 3. Pulse-modulated systems

Impulsive systems or systems with pulse-modulated feedback can be viewed as a special class of hybrid systems, where the continuous dynamics (the flow map and the flow set) are presented by the motion of the dynamical system in between impulsive or resetting events. The discrete dynamics (the jump map and the jump set) are defined as follows:

- *the jump map* is given by a difference equation that governs the way in which the hybrid system state is instantaneously changed when a resetting event occurs;
- *the jump set* is defined by a criterion that determines when the state of the hybrid system has to be reset.

The principal element of an impulsive system is a pulse modulator that converts a continuous-time input signal into a sequence of pulses. It can be mathematically described by a nonlinear operator [38] that maps a continuous input function  $\sigma(t)$  to a piecewise continuous output function  $f(t)$ :

$$M : \sigma(t) \mapsto f(t),$$

where the real-valued functions  $\sigma(t)$ ,  $f(t)$  are defined for  $t \geq 0$ . Any sequence of pulses is associated with an increasing sequence  $t_0 = 0 < t_1 < t_2 < \dots$ , where  $\lim_{k \rightarrow \infty} t_k = \infty$ , whose elements are called *sampling moments* or *firing times*. The time interval  $[t_n, t_{n+1})$  is called *the  $n$ -th sampling interval* and  $T_n = t_{n+1} - t_n$  is *the length of the  $n$ -th sampling interval*. If  $T_n = T = \text{const}$ ,  $n = 0, 1, 2, \dots$ , then the value  $T$  is called *a sampling period*. Thus, the function  $f(t)$  can be represented as follows

$$f(t) = f_n(t), \quad t_n \leq t < t_{n+1}, \quad n = 0, 1, \dots,$$

where the function  $f_n : [t_n, t_{n+1}) \rightarrow \mathbb{R}$  describes the shape of the  $n$ -th pulse. One-sided limits  $f_{n-1}(t_n - 0)$  and  $f_n(t_n + 0)$  exist and are finite but not necessarily equal to each other.

The simplest and most common pulse shape is a rectangular one (see Fig. 3.1), when

$$f_n(t) = \begin{cases} 0, & t_n \leq t < t'_n, \\ \lambda_n, & t'_n \leq t < t''_n, \\ 0, & t''_n \leq t < t_{n+1}. \end{cases} \quad (3.1)$$

Here  $t'_n, t''_n, \lambda_n$  are real numbers (parameters). The parameter  $\lambda_n$  is called *pulse amplitude*. The numbers  $t'_n$  and  $t''_n$  define the position of the leading and trailing

edge of a pulse, respectively. The parameter  $\vartheta_n = t'_n - t_n$  is called *pulse phase* (the displacement of the leading edge relative to the beginning of the  $n$ -th sampling interval). The parameter  $\tau_n = t''_n - t'_n$  is called *pulse width* (or *pulse duration*, *pulse length*). Note that when  $\tau_n = 0$  then the modulator is said to produce a train of impulses, i.e., instant pulses (pulses of zero duration or with point support), while the term "pulse" is used for pulses of finite duration.

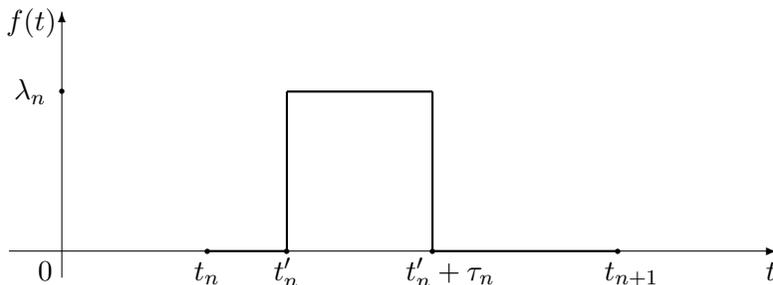


Figure 3.1. A square pulse.

Thus, (3.1) can be equivalently written as

$$f_n(t) \equiv f_n(t, p_n), \quad p_n = \{\lambda_n, \vartheta_n, \tau_n, T_n\}. \quad (3.2)$$

Some parameters of  $f(t)$  are considered fixed and known, while the others are treated as functions or functionals of  $\sigma(t)$  and called *modulated parameters*. Thereby, there are the following types of modulation (see Fig. 3.2):

- *Pulse-frequency modulation (PFM)*. The length of impulsive interval  $T_n$  depends on  $\sigma(t)$  and the other parameters are fixed.
- *Pulse-amplitude modulation (PAM)*. The value of  $\lambda_n$  depends on  $\sigma(t)$  and the other parameters are fixed.
- *Pulse-width modulation (PWM)*. The varying parameter is  $\tau_n$ .
- *Pulse-position or pulse-phase modulation (PPM)*. The value of  $t'_n$  is modulated while the other parameters are fixed.
- *Combined pulse modulation*, when several parameters depend on  $\sigma(t)$ .

In this thesis, the systems where the pulse duration is small compared with the transients time in the system will be considered. Therefore the pulse width can be neglected and, instead, pulses of zero duration (impulses) can be considered. Such systems are called impulsive systems, i.e., systems whose state vector experiences jumps at some moments of time.

There are two main types of impulsive systems. In the first case, the moments of impulse occurrence (firing times) are fixed and do not depend on the solution of the system. In the second case, which will be considered in this work, the distance  $T_n$  between the impulses is determined from some functional relationships.

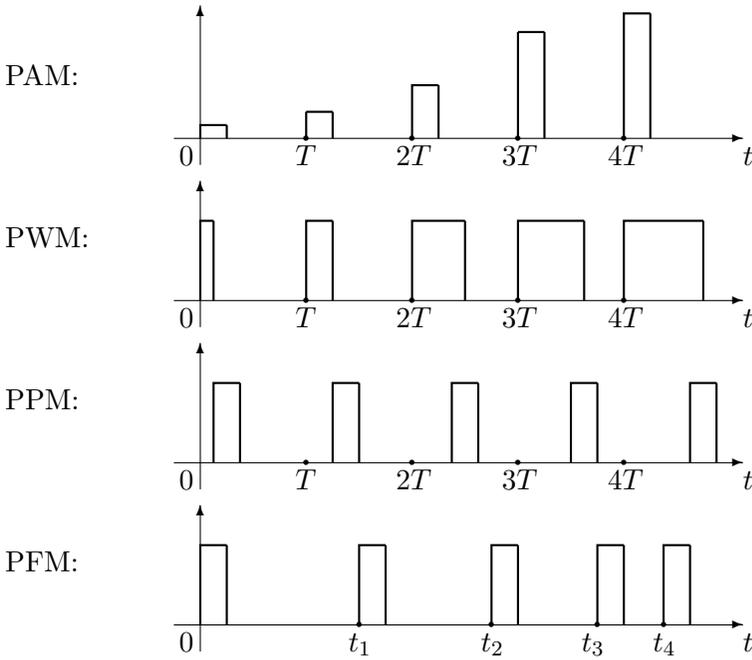


Figure 3.2. Types of pulse modulation.

In the case considered in the thesis, the position of the next pulse is calculated depending on the value of some signal (called modulating signal) at the moment of occurrence of the previous pulse. Such a principle of generation of impulse moments is sometimes called impulse modulation of the first kind (type 1 modulation) or self-triggered control. In a more complicated case, the value of  $T_n$  is defined implicitly, as a root of a functional equation depending on the modulating signal. Depending on the type of this functional, there are different types of impulse modulation: pulse modulation of the second kind (type 2 modulation), integral modulation, event-triggered control, integrate-and-fire schemes, etc.

Mathematically, an impulse (an instant pulse or a pulse of zero duration) is described with the Dirac  $\delta$ -function. When a modulator emits impulses, its output can be described by a train of impulses

$$f(t) = \sum_{n=0}^{\infty} \lambda_n \delta(t - t_n),$$

where the sampling moments  $\hat{t}_n$  and coefficients  $\lambda_n$  may be functionals of  $\sigma(t)$ .

Consider the following pulse formation model. Let  $x(t)$  be the state vector of a system at the time instant  $t$  (piecewise continuous function),  $\{t_n\}_{n=0}^{\infty}$  is an increasing sequence of impulses,  $\sigma(t)$  is the modulating signal (continuous function). Then the state jumps can be described using the following relations

$$\frac{dx}{dt} = Ax(t) + Bf(t), \quad f(t) = \sum_{n=0}^{\infty} \lambda_n \delta(t - t_n), \quad (3.3)$$

or, alternatively, as it further will be used in the thesis, the state jumps can be captured by the recursion

$$x(t_n^+) = x(t_n^-) + \lambda_n B, \quad \lambda_n = F(\sigma(t_n)). \quad (3.4)$$

Here  $x(t^+)$ ,  $x(t^-)$  are the right- and left-side limits of function  $x(\cdot)$  at the point  $t$ ,  $B$  is a given constant vector,  $F(\cdot)$  is a given continuous function. The number  $\lambda_n$  is called the amplitude (or weight) of the  $n$ -th pulse, and the function  $F(\cdot)$  is termed as amplitude characteristic of an impulse modulation law.

The firing times are determined by the following recurrence equations

$$t_{n+1} = t_n + T_n, \quad T_n = \Phi(\sigma(t_n)), \quad (3.5)$$

where  $\Phi(\cdot)$  is a given continuous function, called the frequency characteristic of an impulse modulation function.

Thus, equations (3.4), (3.5) describe the jump parameters  $\lambda_n$ ,  $T_n$  as functionals of the modulating signal  $\sigma(\cdot)$ . Such parameters are called modulated parameters, and one can say that equation (3.4) describes pulse-amplitude modulation, while equation (3.5) is the pulse-frequency modulation [38].

## 4. The impulsive Goodwin's oscillator

Periodic fluctuations in biological processes are found at all levels of life as consequence of self-organization and the periodic changes of the system in time [127, 69, 97, 13, 54]. Oscillating nonlinear dynamical systems are standard mathematical models in life science that capture periodic patterns in living organisms, from primitive bacteria to the most sophisticated life forms, where oscillating rhythms play key roles in a variety of fundamental processes, including circadian regulation, metabolism, embryo development, neuron firing, and cardiac rhythms. Biological oscillators employ biofeedback mechanisms, e.g., endogenous chemical and hormonal secretion functions, to produce oscillations. Thus, positive feedback loops, on their own or in combination with negative feedback, are a common feature of oscillating biological systems [17, 20], where the feedback mechanism is necessary for creating a self-sustained oscillation.

The equations of Goodwin's oscillator [46, 45] describe a basic mechanism of oscillation in a cascaded biochemical system of three or more variables that is based on negative feedback. Goodwin's oscillator was originally proposed to model oscillatory processes in enzymatic control, with improvements and generalizations presented later in a large number of publications [48, 116, 115, 121, 2, 86]. The prototypical Goodwin's model is a third-order linear continuous system with a static nonlinear feedback parameterized by a Hill function.

Variants of Goodwin's equations are also commonly used to model circadian and other genetic oscillators in biology [121, 93, 94, 71, 44, 21, 114, 48]. In 1980s, the Goodwin's model was adopted by R. Smith for describing biological phenomena associated with periodic behaviours in the endocrine system of testosterone regulation (referred to as the Goodwin-Smith model [106, 105]).

As was demonstrated in [48], the original Goodwin's oscillator needs biologically infeasible steep slopes of the feedback nonlinearity (i.e., Hill function order greater than eight) to possess periodic solutions. An impulsive model of non-basal endocrine regulation based on Goodwin's equations but exploiting impulsive (neurally implemented) feedback exhibits oscillation under much more reasonable conditions. The presence of nonlinear amplitude and frequency modulation functions (PAM and PFM, see Section 3) is actually sufficient to cause oscillation. System (4.1),(4.2) was considered in [28] but equivalently described there by means of Dirac  $\delta$ -functions.

The model is comprised of a continuous linear part

$$\dot{x}(t) = Ax(t), \quad z(t) = Cx(t), \quad y(t) = Lx(t), \quad (4.1)$$

and a discrete part

$$\begin{aligned} x(t_n^+) &= x(t_n^-) + \lambda_n B, & t_{n+1} &= t_n + T_n, \\ T_n &= \Phi(z(t_n)), & \lambda_n &= F(z(t_n)). \end{aligned} \quad (4.2)$$

Here  $A \in \mathbb{R}^{n_x \times n_x}$ ,  $B \in \mathbb{R}^{n_x}$ ,  $C \in \mathbb{R}^{1 \times n_x}$ ,  $L \in \mathbb{R}^{n_y \times n_x}$  are constant matrices,  $z$  is the scalar modulating signal/output,  $y$  is the vector of measurable output, and  $x$  is the state vector of (4.1).

The recursion in (4.2) gives rise to discrete dynamics in the closed-loop system and adds a discrete state variable to the hybrid system expressed by (4.1)–(4.2).

The matrix  $A$  is Hurwitz, i.e., all its eigenvalues have strictly negative real parts, the matrix pair  $(A, L)$  is observable, i.e., the matrix

$$[L \quad LA \quad LA^2 \quad \dots \quad LA^{n-1}]^T$$

is full row rank, and the relationships

$$CB = 0, \quad LB = 0 \quad (4.3)$$

apply.

The elements of the state vector  $x(t)$  experience jumps at time instants  $t_0, t_1, t_2, \dots$ , where  $t_k < t_{k+1}$  and  $t_k \rightarrow \infty$  as  $k \rightarrow \infty$  with corresponding weights  $\lambda_k$ ,  $x(t_n^-)$ ,  $x(t_n^+)$  are left-sided and right-sided limits of  $x(t)$  at  $t_n$ , respectively. However, the outputs  $y(t)$ ,  $z(t)$  are continuous due to assumption (4.3).

The amplitude and frequency modulation functions  $\Phi(\cdot)$  and  $F(\cdot)$  are continuous, strictly monotonic and bounded,

$$0 < \Phi_1 \leq \Phi(\cdot) \leq \Phi_2, \quad 0 < F_1 \leq F(\cdot) \leq F_2, \quad (4.4)$$

where  $\Phi_1$ ,  $\Phi_2$ ,  $F_1$ ,  $F_2$  are strictly positive constant numbers. Unlike modulators used in technical applications,  $\Phi(\cdot)$  is non-decreasing and  $F(\cdot)$  is non-increasing. Thus (4.2) denotes a combined (pulse-frequency and pulse-amplitude) modulation [38].

From the stability of  $A$  and the boundness of  $\Phi(\cdot)$  and  $F(\cdot)$ , it readily follows that all the solutions of (4.1)–(4.2) are bounded from below and above. In addition, system (4.1)–(4.2) does not have equilibria because all the modulation characteristics are positive. It was established that system (4.1)–(4.2) may have (orbitally) stable and unstable periodic solutions [28] and, for certain values of parameters, the system may exhibit deterministic chaos [128].

The frequency modulation law in (4.2) introduces first-order discrete dynamics in the feedback of the impulsive Goodwin's oscillator, where the first firing instant of the pulsatile feedback occurs after the initial time instant,  $t_0 \geq 0$ . Due to the hybrid dynamics, a solution of closed-loop system (4.1)–(4.2) is defined by the initial conditions  $(x(t_0^-), t_0)$ , for the continuous states and the discrete one respectively.

## 4.1 Solutions

Define  $x_n = x(t_n^-)$ . Then any solution  $x(t)$  of (4.1)–(4.2) satisfies the discrete-time equation [28]

$$x_{n+1} = P(x_n), \quad (4.5)$$

where

$$P(x) = e^{A\Phi(Cx)}(x + F(Cx)B).$$

Together with the equation  $t_{n+1} = t_n + \Phi(x_n)$ , (4.5) completely defines the dynamics of (4.1)–(4.2) at the points  $t = t_n$ ,  $n = 0, 1, \dots$

Consider periodic solutions of (4.5), and, consequently, of (4.1)–(4.2). A set of points  $S(x_0) = \{x_0, x_1, \dots\}$  with  $x_{n+1} = P(x_n)$  is usually termed as an orbit of system (4.5) through the point  $x_0$ .

A solution  $x_n$ ,  $n = 0, 1, \dots$  is called *m-periodic* (for some  $m \geq 1$ ), if  $m$  is the smallest value for which the relationships

$$\begin{aligned} x_1 &= P(x_0), \\ x_2 &= P(x_1), \\ &\vdots \\ x_m &= P(x_{m-1}), \\ x_m &= x_0 \end{aligned}$$

hold and, moreover, all the vectors  $x_0, \dots, x_{m-1}$  are different. Then the orbit of an *m*-periodic solution is  $S_m(x_0) = \{x_0, x_1, \dots, x_{m-1}\}$  with  $x_0 = P^{(m)}(x_0)$ , where

$$P^{(m)}(x_0) = \underbrace{P(P(\dots))}_m(x_0).$$

In the case of  $m = 1$ , the above relations reduce to  $x_0 = P(x_0)$ .

Let  $x_n$  be an *m*-periodic solution of (4.5). Pick a solution  $x(t)$  of (4.1)–(4.2) for  $t \geq t_0$  with some initial values  $t_0 > 0$  and  $x(t_0^-) = x_0$ . Then  $x(t)$  is periodic with the period  $T = \Phi(x_0) + \dots + \Phi(x_{m-1})$  and has exactly  $m$  impulses on the periodicity interval  $[0, T)$ . Moreover,  $t_m = t_0 + T$ . Such a solution  $x(t)$  is called an *m-cycle*.

Impulsive system (4.1), (4.2) has a continuous state  $x(t) \in \mathbb{R}^n$  and a discrete state  $t_n$ ; Therefore, the dimension of the phase space is  $n + 1$ . At the same time, the phase space of discrete system (4.5) is  $n$  – dimensional and coincides with  $\mathbb{R}^n$ . Thus, the hybrid phase space is a hyperplane in the  $(n + 1)$  – dimensional phase space of system (4.1), (4.2), and discrete transform (4.5) defines a transformation of this hyperplane into itself. In theory of hybrid systems, discrete map (4.5) is called the Poincaré map [50] (by analogy with the Poincaré map for systems in continuous time). It is easy to verify that the solutions of impulsive system (4.1) – (4.2) are not stable in the Lyapunov sense, i.e., not stable with respect to small perturbations of the initial values

[51, 101]. At the same time, one can consider the stability of (4.1) – (4.2) associated with discrete system (4.5). Unlike the impulsive system, the solutions of discrete system (4.5) can be stable in the sense of Lyapunov. From a practical point of view, the Lyapunov stability of solutions of Poincaré transform (4.5) is usually sufficient so that the system is considered to be stable. Thus, for system (4.1)–(4.2), the stability notion is understood as orbital asymptotic stability with respect to small perturbation in the initial conditions. This does not generally imply stability in Lyapunov sense, see [51, 101].

An orbit  $S(x_0)$  of discrete equation (4.5) is called *asymptotically stable* [66] if

- (i) for any neighborhood  $V \supset S$ , there exists a neighborhood  $U \supset S$  such that  $x_n \in V$  for all  $x_0 \in U$  and  $n \geq 0$ ;
- (ii) there exists a neighborhood  $U_0 \supset S$  such that the distance  $\text{dist}(x_n, S) \rightarrow 0$  for all  $x_0 \in U_0$ , as  $n \rightarrow \infty$ .

Here

$$\text{dist}(x_n, S) = \inf_{y \in S} \|x_n - y\|,$$

where  $\|\cdot\|$  – is the Euclidean vector norm.

For (4.5), an  $m$ -periodic orbit  $\{x_0, x_1, \dots, x_{m-1}\}$  is locally asymptotically stable if all the eigenvalues of the matrix product  $J_{m-1} J_1 \dots J_0$  lie inside the unit circle, where  $J_k$  is the Jacobian of  $P(x)$  evaluated at the point  $x_k$ . Thus, for (4.1)–(4.2), local stability of an  $m$ -cycle can be checked by linearizing the mapping  $P(x)$  in a neighborhood of each fixed point  $x_i = 0, \dots, m-1$ .

Since the hybrid system under consideration is of dimension  $(n+1)$  (one continuous state and one discrete), consider a  $(n+1)$ -dimensional orbit (a set of ordered pairs)  $\tilde{S}(x_0, t_0) = \{(x_n, t_n), n = 0, 1, \dots\}$ . Clearly, it is not periodic even in the case when  $S(x_0)$  is an  $m$ -periodic orbit of (4.5). Since  $t_{n+1} = t_n + \Phi(x_n)$ , for an asymptotically stable  $S$ , the orbit  $\tilde{S}$  will not be asymptotically stable. Indeed, small perturbations in  $t_0$  remain small as  $n$  increases, but do not vanish.

Thus, the solution of discrete Poincaré system (4.5) (of the order of  $n_x$ ) may have asymptotic Lyapunov stability, but for solutions of the discrete system of the order  $n_x + 1$  consisting of Poincaré system (4.5) and the equation  $t_{n+1} = t_n + \Phi(x_n)$ , one can consider only Lyapunov stability, but not asymptotic Lyapunov stability.

With respect to continuous-time impulsive system (4.1), (4.2), even the ordinary notion of Lyapunov (not asymptotic) stability (understood in the traditional sense as for ordinary differential equations) is absent for its solutions. For impulsive systems, the concept of stability requires substantial modification (see, for example, [67, 96]).

When it comes to pulsatile endocrine regulation, the state vector  $x(t)$  of (4.1)–(4.2) is composed of the concentrations of the involved hormones,  $y(t)$  represents the concentrations of the measured (in the bloodstream) hormones, and  $z(t)$  stands for the hormone concentration that modulates the pulsatile

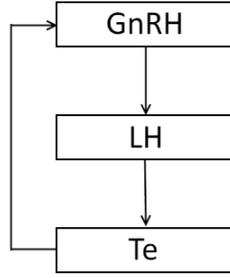


Figure 4.1. GnRH-LH-Te endocrine regulation loop

feedback. The release hormone pulses are secreted at the time instances  $t_n$ , have the weight of  $\lambda_n$ , and are immeasurable.

For biologically motivated values of parameters in endocrine regulation, autonomous system (4.1)–(4.2) normally exhibits either a stable 1-cycle, or a stable 2-cycle (i.e., periodic solutions with either one, or two impulses fired in the least period) [28], but chaotic solutions are also possible. Being extended with a time delay [128] or a continuous exogenous signal in the continuous part [77], the model may exhibit more complex nonlinear dynamics such as cycles of higher periodicity, chaos, bistability, and quasiperiodical solutions.

The purpose of the observation in hybrid system (4.1)–(4.2) is to produce the estimates  $(\hat{t}_n, \hat{\lambda}_n)$  of the impulse parameters  $(t_n, \lambda_n)$  under unknown initial conditions  $(x(0), t_0)$ . Given the sequence  $(t_n, \lambda_n), n = 0, \dots, \infty$ , estimates of the state vector  $x$  of the continuous part can be obtained by conventional state estimation techniques. The main challenge of hybrid observation is then to ensure asymptotic convergence of the sequence  $\{\hat{t}_n\}$  to  $\{t_n\}$ , i.e., to synchronize the impulses in the observer with those of the plant.

## 4.2 Mathematical model of testosterone regulation

In the endocrine system of testosterone (Te) regulation in the male, an essential role is played by three hormones, namely gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), and testosterone (Te). GnRH is released from the hypothalamus of the brain in pulsatile fashion with short latency. Reaching the pituitary gland, GnRH initiates the production of LH, which in turn stimulates production of Te in the testes. Finally, the GnRH outflow secretion is subject to feedback inhibition by Te [117], see Fig. 4.1. The action of the hypothalamic GnRH neurons can be described by a pulse element (pulse modulator) performing amplitude and frequency modulation, i.e., the Te concentration acts as a modulation signal, and the GnRH concentration as a pulse-modulated signal. That is, the frequency and amplitude of the GnRH

pulses are variable and depending on the level of Te. If there is the concentration of Te is high, then the impulses occur less frequently and with a lower amplitude; Conversely, when the concentration of Te is low, then the impulses occur more often and with a higher amplitude. As a result and due to the pulse-modulated feedback, there arises a dynamic equilibrium (homeostasis) in the system.

Thus, with  $x(t) = [x_1(t) \ x_2(t) \ x_3(t)]$ , where the elements of  $x$  correspond to the concentrations of GnRH ( $x_1$ ), LH ( $x_2$ ), and of Te ( $x_3$ ), the case of a third order system (4.1)–(4.2) with the matrices

$$A = \begin{bmatrix} -b_1 & 0 & 0 \\ g_1 & -b_2 & 0 \\ 0 & g_2 & -b_3 \end{bmatrix}, B = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix}, L = \begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, \quad (4.6)$$

$$C = [0 \ 0 \ 1],$$

can be used to model testosterone regulation in the human male [28, 27, 75]. From the biochemistry of the system, the constants  $b_i > 0$ ,  $i = 1, 2, 3$  and  $b_i \neq b_j$  for  $i \neq j$  reflect the half-life times of the involved hormones. The constants  $g_i$ ,  $i = 1, 2$  describe to what extent the production of one hormone is stimulated by another one in the model. Since hormone concentrations are non-negative, the system should be positive, which is ensured by the matrix  $A$  being Metzler. The state vector  $x(t)$  experiences jumps at the times  $t = t_n$ , portraying non-basal (episodic) release of GnRH.

To facilitate comparison with the classical version of Goodwin's oscillator, model (4.1)–(4.2) can be rewritten as below. On the continuity intervals  $t_n < t < t_{n+1}$ ,  $n = 0, 1, 2, \dots$  the dynamics are governed by

$$\begin{aligned} \dot{x}_1(t) &= -b_1 x_1(t), \\ \dot{x}_2(t) &= -b_2 x_2(t) + g_1 x_1(t), \\ \dot{x}_3(t) &= -b_3 x_3(t) + g_2 x_2(t), \end{aligned} \quad (4.7)$$

and the discrete part of the model is given then by

$$\begin{aligned} x_1(t_n^+) &= x_1(t_n^-) + \lambda_n, & x_2(t_n^+) &= x_2(t_n^-), \\ x_3(t_n^+) &= x_3(t_n^-), & t_{n+1} &= t_n + T_n, \end{aligned} \quad (4.8)$$

where

$$\lambda_n = F(x_3(t_n)), \quad T_n = \Phi(x_3(t_n)). \quad (4.9)$$

From the biology of the underlying system, the modulation functions, usually selected as Hill functions, are continuous, monotonous, strictly positive, and bounded from above and below. The function  $\Phi(\cdot)$  is monotonically increasing, while  $F(\cdot)$  is monotonically decreasing. As discussed above, this captures the experimentally observed fact that the hypothalamus responds with sparser GnRH impulses of lower amplitudes to elevated concentrations of Te.

The model structure of the impulsive Goodwin's oscillator has been demonstrated to fit well actual endocrine data [61] and be feasible for analysis of closed-loop behaviors, [74]. The model performance is illustrated by Fig. 4.2 and Fig. 4.3.

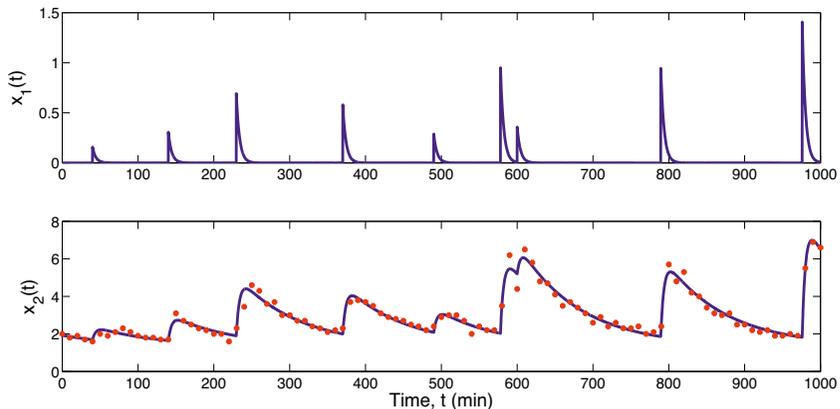


Figure 4.2. LH data measured with 10 min sampling in a healthy 27 years old man (red). Estimated GnRH and simulated LH (blue). The figure provided by Per Mattsson, per.mattsson@it.uu.se

### 4.3 The role of time-delays

The presence of a time delay in the closed loop is a significant phenomenon in many endocrine systems. Time delay exists in endocrine systems mainly due to two circumstances. First, there is a delay due to the transport of hormones in the blood stream. Second, a delay also results from the need to synthesize the hormone before secretion when releasable pools of it are lacking.

Before considering time-delay impulsive systems, some preliminary background on linear systems with time delays is provided.

#### 4.3.1 Linear time-delay systems

Consider the following linear time-delay system of retarded type:

$$\dot{x}(t) = A_0x(t) + A_1x(t - \tau), \quad (4.10)$$

where  $A_0, A_1$  are given real  $n \times n$  matrices. Let the initial conditions be given by the piecewise continuous function  $\varphi : [-\tau, 0] \rightarrow \mathbb{R}^n$  and  $x(\theta) = \varphi(\theta)$ ,  $\theta \in [-\tau, 0]$  with  $t_0 = 0$ .

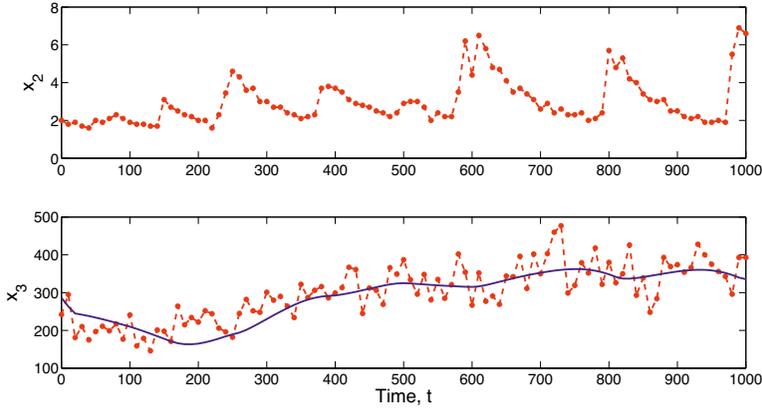


Figure 4.3. LH (upper plot) and Te (lower plot) data measured with 10 min sampling in a healthy 27 years old man (red). Estimated GnRH and simulated LH (blue), see [75].

The characteristic equation of system (4.10)

$$\rho(s) = \det [sI - A_0 - A_1 e^{-s\tau}] = 0. \quad (4.11)$$

has a quasipolynomial in the left-hand side and possesses an infinite number of roots. They have the following property: there is a finite number of the roots of (4.11) on the right hand side from any vertical line  $\text{Re } s = \text{const}$ .

Introduce a definition of exponential stability of system (4.10) that is equivalent to its asymptotic stability [64].

**Definition 1.** System (4.10) is said to be exponentially stable if there exist  $\gamma \geq 1$  and  $\sigma > 0$  such that any solution  $x(t)$  of the system satisfies the inequality

$$\|x(t)\| \leq \gamma e^{-\sigma t} \|\varphi\|_\tau, \quad t \geq 0,$$

where the norm  $\|\varphi\|_\tau = \sup_{\theta \in [-\tau, 0]} \|\varphi(\theta)\|$ .

**Definition 2.** A complex number  $s_0$  is said to be an eigenvalue of system (4.10) if it is a root of the system characteristic equation  $\rho(s) = 0$ . The set  $\Lambda = \{s \mid \rho(s) = 0\}$  is known as the spectrum of system (4.10).

**Theorem 1** ([11]). System (4.10) is exponentially stable if and only if all its eigenvalues lie in the open left half-plane of the complex plane

$$\text{Re } s_0 < 0, \quad \forall s_0 \in \Lambda.$$

### 4.3.2 Finite-dimensional reducibility

**Definition 3.** System (4.10) is said to be finite-dimensional (FD) reducible if there exists a matrix  $D$  such that any solution of (4.10) satisfies a delay-free system

$$\dot{x}(t) = \bar{A}x(t)$$

for all  $t \geq \tau$ .

The property of FD-reducibility can be characterized as follows.

**Lemma 1** ([27]). *FD-reducibility of system (4.10) is equivalent to one of the following conditions:*

1) the equalities

$$A_1 A_0^k A_1 = 0 \quad (4.12)$$

hold for all  $k = 0, 1, \dots, n-1$ ;

2) there exists a nonsingular matrix  $S \in \mathbb{R}^n$  such that

$$S^{-1} A_0 S = \begin{bmatrix} U & 0 \\ W & V \end{bmatrix}, \quad S^{-1} A_1 S = \begin{bmatrix} 0 & 0 \\ \bar{W} & 0 \end{bmatrix}, \quad (4.13)$$

where the blocks  $U, V$  are square, the blocks  $W, \bar{W}$  are of the same dimension. Further, if system (4.10) is FD-reducible, then  $\bar{A} = A_0 + A_1 e^{-A_0 \tau}$ .

For an FD-reducible system, the eigenvalue spectrum of the matrix  $A_0$  coincides with that of  $D$  and, thus, the spectrum of  $D$  is independent of  $\tau$ , i.e.

$$\det [sI - A_0 - A_1 e^{-A_0 \tau}] = \det [sI - A_0]$$

for all complex  $s$  and any  $\tau$ . Additionally, FD-reducible time-delay linear system (4.10) obviously possesses a finite spectrum, since

$$\det (sI_n - A_0 - A_1 e^{-\tau s}) = \det (sI_n - A_0),$$

for all complex  $s$ .

### 4.3.3 Impulsive model with delay

An extension of impulsive model (4.1)-(4.2) to the class of systems with delayed continuous part is as following:

$$\dot{x}(t) = A_0 x(t) + A_1 x(t - \tau), \quad z(t) = Cx(t), \quad (4.14)$$

$$\begin{aligned} x(t_n^+) &= x(t_n^-) + \lambda_n B, & t_{n+1} &= t_n + T_n, \\ T_n &= \Phi(z(t_n)), & \lambda_n &= F(z(t_n)), \end{aligned} \quad (4.15)$$

where  $A_0, A_1 \in \mathbb{R}^{p \times p}$  are square and constant matrices,  $A_1 \neq 0$ , and  $\tau > 0$  is a constant time delay. System (4.14)-(4.15) is subject to a continuous initial vector function  $x(t) = \varphi(t)$ ,  $-\tau \leq t \leq 0$ .

Since the linear part of the system represents the kinetics of the involved hormones, it has to be stable, i.e., all the roots of the characteristic equation  $\det(sI_p - A_0 - A_1 e^{-\tau s})$  have to satisfy  $\text{Re } s < 0$ . Furthermore, the continuous part of system (4.14)-(4.15) is henceforth assumed to be FD-reducible.

Besides the stability of continuous part of the model under consideration, it is also biologically feasible that all the solutions of (4.14)-(4.15) are bounded. The boundness of all the solutions for  $t \geq 0$  follows from inequality (4.4) and from the FD-reducibility.

With the time delay taken into account, the pulse-modulated model of endocrine regulation acquires an infinite-dimensional continuous part. The closed-loop dynamics are therefore both hybrid and infinite dimensional.

In [128] it was demonstrated that the delay values that strictly less than the least time interval between two consecutive firing times, i.e.,

$$\inf_z \Phi(z) > \tau \Rightarrow T_k > \tau \text{ for any } k \geq 1, \quad (4.16)$$

of the impulsive feedback in the testosterone regulation model do not cause new types of system behaviour compared to the delay-free case. Such delays can be characterized as small since they do not contribute much to the interaction of the continuous and discrete parts.

Bifurcation analysis in [30] of the pointwise mapping suggests that large values of the time delay, i.e.,

$$2 \inf_z \Phi(z) > \tau \geq \inf_z \Phi(z) \Rightarrow T_k + T_{k-1} > \tau \geq T_k \text{ for any } k \geq 1, \quad (4.17)$$

in the closed loop can lead to nonlinear (non-smooth) phenomena that are not observed in the delay-free case, e.g., bistability and quasiperiodic oscillations.

In fact, condition (4.16) is satisfied for the testosterone hormonal regulation. Only "small delays" are considered in the thesis. The delay from pituitary, where LH is secreted, to testes, where Te is produced, is the dominating one in the GnRH-LH-Te endocrine axis. The delay value  $\tau$  considered in the thesis takes into account not only the transport of LH from pituitary to testes, but also an additional time required to stimulate steroid synthesis in the testes. In [19], the following estimates of the delays are suggested: from hypothalamus to pituitary – 3 min, from pituitary to testes – 5 min, from testis to hypothalamus – 5 min, the interval between testes stimulation and testosterone release – 25 min. So, the total delay from secretion of LH to secretion of Te in the testes is  $\tau = 5 + 25 = 30$  min. The delay  $\tau$  is less than a half-period of the ultradian rhythm, with the average cycle of 1.9–2.3 h, and thus satisfies assumption (4.16).

Recall that the parameter  $g_2$  describes how the production of Te is stimulated by LH in the model. Thus, the matrices  $A_0$  and  $A_1$  with respect to

time-delay system (4.14)-(4.15) have the following structure:

$$A_0 = \begin{bmatrix} -b_1 & 0 & 0 \\ g_1 & -b_2 & 0 \\ 0 & 0 & -b_3 \end{bmatrix}, A_1 = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & g_2 & 0 \end{bmatrix}.$$

Then, in the three-dimensional case, the model reads as follows:

$$\begin{aligned} \dot{x}_1(t) &= -b_1 x_1(t), \\ \dot{x}_2(t) &= -b_2 x_2(t) + g_1 x_1(t), \\ \dot{x}_3(t) &= -b_3 x_3(t) + g_2 x_2(t - \tau), \\ x_1(t_n^+) &= x_1(t_n^-) + \lambda_n, \quad x_2(t_n^+) = x_2(t_n^-), \\ x_3(t_n^+) &= x_3(t_n^-), \quad t_{n+1} = t_n + T_n, \end{aligned}$$

where

$$\lambda_n = F(x_3(t_n)), \quad T_n = \Phi(x_3(t_n)).$$

## 4.4 The role of exogenous signals

In the context of endocrine regulation, exogenous signals represent, e.g., the influx of a hormone replacement therapy drug, the influence of circadian rhythm, and the interactions with other endocrine loops. Hormone Te therapy is recommended for men who have both low level of testosterone in the blood and show symptoms of low testosterone. Exogenous Te can be administered in several ways: injection patch, transdermal gels, implantable deposits, buccal tablets, etc [84]. The different ways of drug delivery require distinct mathematical models.

The continuous influx of exogenous Te in the closed-loop endocrine regulation system can be captured by the following model

$$\begin{aligned} \dot{x}(t) &= Ax(t) + T\beta(t), \\ x(t_k^+) &= x(t_k^-) + \lambda_k B, \end{aligned} \tag{4.18}$$

where  $\beta \in \mathbb{R}_+$  is the continuous exogenous input, while  $t_k$ , as well as  $\lambda_k$  given by (4.2),  $T = [0 \ 0 \ 1]^\top$ , the rest of the matrices are given by (4.6).

The complex dynamics arising in two important special cases of exogenous signal being constant,  $\beta = \beta_0$ ,  $\beta_0 \geq 0$ , and a positive sine wave,  $\beta = M \sin(\omega t + \theta) + N$ , where  $N \geq M > 0$ , implying that  $\beta(t) \geq 0$  for all  $t$ , were studied in detail by means of bifurcation analysis in [80]. The positivity is necessary to keep in touch with the physiological nature of the involved signals: the former case portrays a hormone replacement therapy with Te patches,

while the latter case describes the effect of circadian rhythm on  $T_e$  regulation. It was demonstrated that, for constant exogenous  $T_e$ , no new dynamical model behaviours arise, compared to the autonomous case. Entrainment of the autonomous periodic oscillations of the impulsive Goodwin's oscillator to a sine wave is observed for some combinations of the model parameters, while quasiperiodic and chaotic solutions appear often. Bistability was discovered in the forced model in contrast to the autonomous case. When in a bistable mode, the convergence of solutions to either of the coexisting attractor can be controlled by the phase of the exogenous sine wave signal. The phase of the periodic exogenous signal in the bistable mode of the forced impulsive Goodwin's oscillator can be interpreted as the local time difference in airplane travel across time zones (as well as space travel) thus relating this effect to jet lag [10]. Indeed, the coexisting periodic solutions have distinctly different mean value of  $T_e$  and can provide an explanation to the observed endocrine symptoms.

## 5. Hybrid systems: observability and synchronous mode

Observability has come to the attention of the hybrid control community only recently. Since the class of hybrid control problems is extremely broad, it is very difficult to devise general conceptions and strategy to solve them. In the existing literature on observability and observers for hybrid systems, the definitions and the testing criteria for it vary depending on the class of system under consideration and the knowledge that is assumed at the output. Autonomous switching systems were considered in [120] proposing a definition of observability based on the concept of indistinguishability of continuous initial states and discrete state evolutions from the outputs in free evolution. Incremental observability was introduced in [12] for the class of piecewise affine systems, meaning that different initial states always give different outputs independently on the applied input. In [6], the notion of generic final-state determinability proposed in [108] was extended to hybrid systems and sufficient conditions were given for linear hybrid systems. In [33], was introduced a notion of observability and detectability for the class of switching systems, based on reconstructability of the hybrid state evolution, knowing the hybrid outputs, for some suitable continuous inputs. In [5], a methodology was presented for the design of dynamic observers of hybrid systems, which reconstructs the discrete state and the continuous state from the knowledge of the continuous and discrete outputs. In [39, 34], extensions of [5] were derived. In [55], the definition of observability of [119] and the results of [5] on the design of an observer for deterministic hybrid systems were extended to the discrete-time stochastic linear autonomous hybrid systems. A rather complete discussion on different definitions of observability for some subclasses of hybrid systems can be found in [33]. Yet, this does not include the applications where the jumps (or switching) correspond to an unknown discrete state and there is a nontrivial problem of simultaneous recovery of the discrete and continuous states only from measurable continuous output. This problem is typical to biomedicine as measurements of discrete events are often not accessible in living organisms, where the continuous and discrete dynamics may not only co-exist but can also interact, and changes occur in response to discrete events and/or continuous inputs, both internally or exogenously generated. In, e.g., [5], the knowledge of the discrete state is not required, but the observer design assumes the knowledge of the hybrid plant inputs and outputs (either discrete or continuous), while the equations of the impulsive Goodwin's oscillator in (4.1)–(4.2) constitute an autonomous system.

To recapitulate, observers for hybrid systems that utilize only continuous measurements are rare and limited to specific plant types. Most of the currently existing hybrid observer design approaches either target engineered hybrid systems, typically assuming that the discrete states (or switching events) of the plant are known [1, 16, 18, 112, 37, 7], or used to achieve a special performance objective in non-hybrid plants [113, 31, 91, 92, 23, 24].

## 5.1 Hybrid state estimation in the impulsive Goodwin's oscillator

The impulsive feedback signal of the Goodwin's oscillator is intrinsic to the closed loop and essentially cannot be measured in biomedical applications, which property poses an interesting and practically meaningful problem of estimating the full hybrid state of a system from only continuous measurements. In endocrinology, the problem of reconstructing the episodic firings of a pulsatile feedback is standard and usually handled by applying deconvolution algorithms under assumptions on the signal shape of the pulse, see, e.g., [59], [32]. While deconvolution algorithms are widely used in practice due to readily available software, being applied to pulsatile endocrine regulation, they basically ignore the feedback nature of the underlying system and are not suitable for on-line implementation. The deconvolution *per se* (i.e., blind deconvolution) is not a well-posed problem and needs regularization. Therefore, it is motivated to consider output error feedback observer algorithms for the reconstruction of the impulsive feedback action along with the continuous states from a continuous output.

Since the impulsive Goodwin's oscillator only exhibits periodic and non-periodic (i.e., quasiperiodic and chaotic) oscillations, the observer design problem can be formulated as synchronization (see Section 5.2) of the plant states with those of the observer. This approach has been proposed in [29] and does not formally demand observability of the hybrid plant solution. In a certain way, the idea is similar to that of the observers for unobservable but detectable linear time-invariant systems, where the state estimates that cannot be corrected by output error feedback converge due to the stable dynamics. Similarly, the dynamics governing the observed periodical solution to the impulsive Goodwin's oscillator have to be orbitally stable for the observer to be functional. Further, since the dynamics of the oscillator are highly nonlinear, the state estimation problem is considered with respect to particular solutions of the observed system, whose characteristics are assumed to be known, but not the initial conditions. This can be compared to the situation with the Luenberger observer, where the model of the plant is available and the state estimation error due to the mismatch in the initial conditions on the plant and the observer asymptotically vanishes.

There are several features that complicate an observer design and its stability analysis. First, in the dynamics of a closed-loop system there are monostable or bistable periodic, quasiperiodic or chaotic oscillations, [128, 77, 79], and no equilibria [28]. Second, the states of the considered system undergo jumps at certain time instants (firing times) modulated by other states and, in general, the firing times produced by an observer do not coincide with those of the plant. Consequently, on the time interval defined by the mismatch in the firing times, the error between the solution to the plant and that to the observer is large and does not monotonically converge to zero as time increases, thus causing the so-called "peaking phenomenon" [14, 68, 81, 98]. In this connection, one can consider only Lyapunov stability, but not Lyapunov asymptotic stability. Third, an unknown initial feedback firing time (jump time) of the observed plant poses the greatest complication in state estimation of linear continuous time-invariant systems under inaccessible for measurement pulse-modulated feedback.

To illustrate the stability issue arising in impulsive systems, consider a nonlinear system described by an ordinary differential equation  $\dot{x}(t) = f(x(t))$ , assuming without loss of generality that  $f(0) = 0$ . Recall that the trivial solution is said to be *Lyapunov stable*, if, for every  $\varepsilon > 0$ , there exists a  $\delta > 0$  such that, if  $\|x(0)\| < \delta$ , then  $\|x(t)\| < \varepsilon$  for every  $t \geq 0$ . Now consider two solutions of the impulsive Goodwin's oscillator. Let  $(x^{[1]}(t), t_n^{[1]})$  be a stable 1-cycle, and  $(x^{[2]}(t), t_n^{[2]})$  be the same solution with the perturbed initial conditions, so that  $(x_0^{[1]}, t_0^{[1]}) \approx (x_0^{[2]}, t_0^{[2]})$ . However, the relations  $x_0^{[1]} \rightarrow x_0^{[1]}$  and  $t_0^{[1]} \rightarrow t_0^{[2]}$  do **not** imply  $\|x^{[1]}(t) - x^{[2]}(t)\| \rightarrow 0$  as  $t \rightarrow \infty$ , see Fig. 5.1 and Fig. 5.2. In other words, the inequality  $\|x^{[1]}(t) - x^{[2]}(t)\| < \varepsilon$  is not fulfilled for any  $\varepsilon$  even for sufficiently small  $\delta$ . Therefore, the convergence for pulse-modulated systems cannot be considered in Lyapunov sense within the standard analytical framework.

### 5.1.1 Observers for impulsive system

The main characteristic of the estimation problem in hand is that the firing times  $t_0, t_1, t_2, \dots$  of plant (4.1), (4.2) are not known to the observer. In particular, the initial firing time  $t_0$  is unknown. The observer design objective is then to synchronize the impulses in the observer with those of the plant by a suitable choice of observer parameters.

To estimate the state  $(x(t), t_n)$  of (4.1), (4.2), a hybrid observer was introduced in [29] as

$$\dot{\hat{x}}(t) = A\hat{x}(t) + K(y(t) - \hat{y}(t)), \quad \hat{y}(t) = L\hat{x}(t), \quad \hat{z}(t) = C\hat{x}(t), \quad (5.1)$$

$$\hat{x}(t_n^+) = \hat{x}(t_n^-) + \hat{\lambda}_n B, \quad \hat{t}_{n+1} = \hat{t}_n + \hat{T}_n, \quad \hat{\lambda}_n = F(\hat{z}(\hat{t}_n)), \quad (5.2)$$

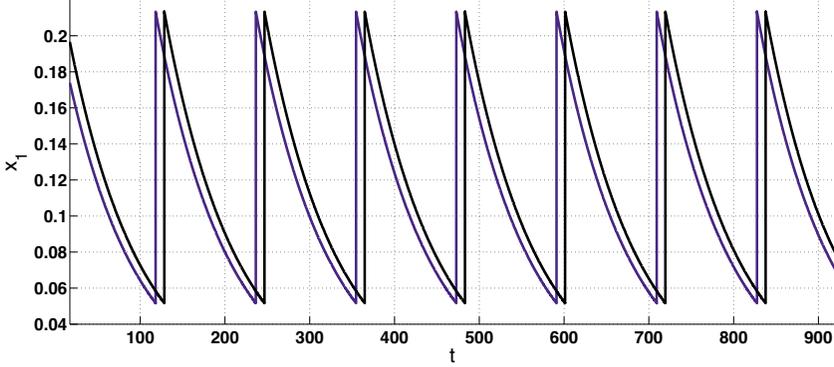


Figure 5.1. The impulsive Goodwin's oscillator. Transients in the continuous states of two 1-cycles with the initial conditions close to each other. The trajectory corresponds to the state that jumps.

where the matrix  $K$  is a constant feedback gain chosen to render  $D = A - KL$  Hurwitz. The observer modulation functions  $\Phi(\cdot), F(\cdot)$  are the same as those of the plant and

$$\hat{T}_n = \Phi(\hat{z}(\hat{t}_n)). \quad (5.3)$$

The disadvantages of observer (5.1)–(5.3) is its slow convergence rate and oscillative transients.

An improvement to the original observation scheme was proposed in [124, 122]. It increased the convergence rate by adding a second feedback loop to the discrete part of the observer. Instead of mimicking the frequency modulation in the plant, i.e., applying (5.3), it brought the output estimation error into the frequency modulation

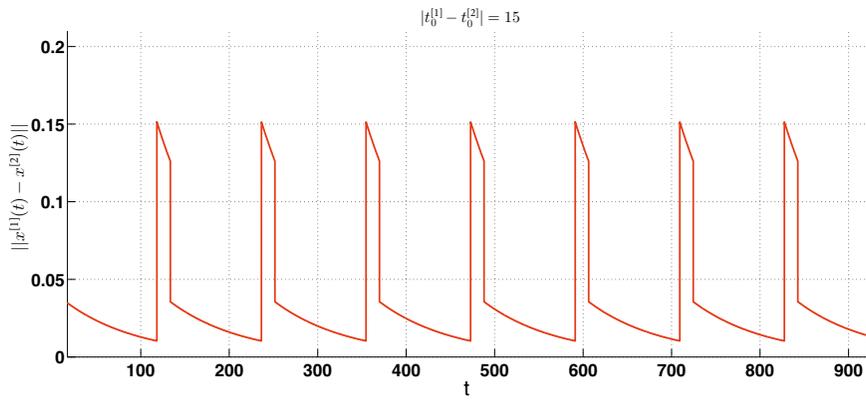
$$\hat{T}_n = \Phi(\hat{z}(\hat{t}_n) + E_d(\hat{t}_n)), \quad (5.4)$$

where  $E_d(t) = K_d(y(t) - \hat{y}(t))$ ,  $K_d \in \mathbb{R}^{1 \times n_y}$  is a constant gain matrix. For the third-order model of Te regulation given by (4.7)–(4.9), a modification of frequency modulation (5.4) was proposed in **Paper III**, allowing to enlarge the basin of attraction of the synchronous mode (see paragraph 5.2). Instead of (5.4), the frequency modulation law is given by

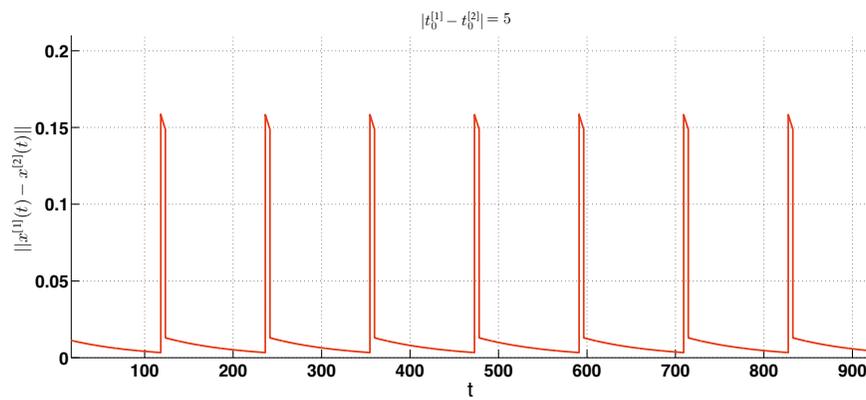
$$\hat{T}_n = \Phi(\hat{z}(\hat{t}_n) + k_f r(\hat{t}_n)), \quad (5.5)$$

where  $r(t)$  is a filtered version of the output estimation error  $e(t) = z(t) - \hat{z}(t)$  governed by  $\dot{r}(t) = -br(t) + ge(t)$ ,  $r(\hat{t}_0) = 0$ , and the parameters  $b, g > 0$ .

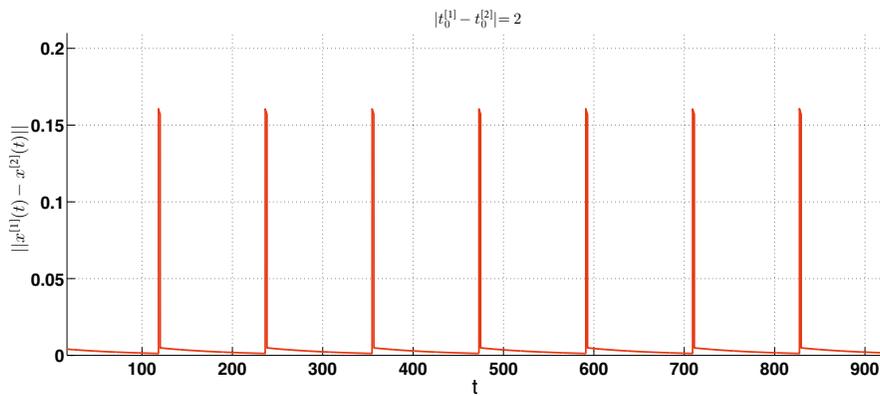
While a superior convergence of observer (5.1), (5.2), (5.4) has been demonstrated in [124, 122], it still takes into account only the momentary value of the output estimation error. Besides, the modulation functions are exact copies of those in the plant which presents a clear performance limitation. In [123]



(a)  $|t_0^{[1]} - t_0^{[2]}| = 15$



(b)  $|t_0^{[1]} - t_0^{[2]}| = 5$



(c)  $|t_0^{[1]} - t_0^{[2]}| = 2$

Figure 5.2. "Peaking phenomenon" illustration. Here  $x_0^{[1]} = x_0^{[2]}$ . The relation  $t_0^{[1]} \rightarrow t_0^{[2]}$  does not imply  $\|x^{[1]}(t) - x^{[2]}(t)\| \rightarrow 0$  as  $t \rightarrow \infty$ .

and **Paper II**, two new versions of frequency modulation in the observer were proposed. Define a convolution integral

$$R(t, f(\cdot)) = \int_{t-v}^t e^{-\varkappa(t-\tau)} f(\tau) d\tau,$$

where  $\varkappa, v$  are positive constant parameters,  $v \leq \Phi_1$ , and  $f(\cdot)$  is an integrable function. Thus the kernel of the integral transform has a compact support on  $[0, v]$ . First, consider the following feedback in the discrete part [123]:

$$\hat{T}_n = \Phi(\hat{z}(\hat{t}_n) + R(\hat{t}_n, E_d(\cdot))), \quad (5.6)$$

where  $E_d(t)$  is as defined previously. Then the next firing time in the observer depends on all the values of  $E_d$  since the previous firing. Without loss of generality, it is assumed that  $\hat{t}_0 \geq t_1$  and  $E_d(\theta) = 0$  for  $\theta \in [\hat{t}_0 - v, \hat{t}_0]$ .

Notice now that the function  $\Phi(\cdot)$  saturates for large arguments, for biological reasons. Then, for large estimation errors, the corrective role of the integral feedback in (5.6) is effectively disabled. To avoid this, instead of (5.6), consider a frequency modulation law given by [123] and **Paper II**:

$$\hat{T}_n = \Phi(\hat{z}(\hat{t}_n)) + \Psi(R(\hat{t}_n, E_d(\cdot))), \quad (5.7)$$

where the function  $\Psi(\cdot)$  is continuous, odd, strictly increasing, bounded

$$|\Psi(\cdot)| < \Phi_1, \quad (5.8)$$

and selected in the observer design. Inequality (5.8) guarantees that  $\hat{T}_n > 0$  in (5.7).

### 5.1.2 Observers for time-delay impulsive system

Consider time-delay system (4.14), (4.15) and introduce a new notion that is more restrictive than a conventional spectral observability (see, e.g., [95, 99]) and requires an FD-reducibility in addition.

**Definition 4.** *The linear part of system (4.14), (4.15) will be called spectrally FD-observable if for any given complex self-conjugate set of numbers  $\Lambda = \{\lambda_j, j = 1, \dots, n_x\}$  there exists a matrix  $K$  such that the eigenvalue spectrum of  $A_0 - KL$  coincides with  $\Lambda$ , and, moreover,*

$$A_1(A_0 - KL)^k A_1 = 0 \quad \text{for } k = 0, 1, \dots, n_x - 1. \quad (5.9)$$

In other words, (4.12) is satisfied with replacing  $A_0$  for  $A_0 - KL$ . Relationships (5.9) imply that

$$\det(sI_{n_x} - D + KL) = \det(sI_{n_x} - A_0 + KL)$$

for all complex  $s$ . Further, this property is supposed to hold with respect to the continuous part of (4.14), (4.15).

Now consider two different approaches to the observer design. The first one is based on reduction of (4.14), (4.15) to a delay-free impulsive system:

$$\begin{aligned} \frac{dx(t)}{dt} &= \bar{A}x(t), \quad z(t) = Cx(t), \quad y(t) = Lx(t), \\ t_{n+1} &= t_n + T_n, \quad x(t_n^+) = x(t_n^-) + \lambda_n \hat{B}, \\ T_n &= \Phi(z(t_n)), \quad \lambda_n = F(z(t_n)), \end{aligned} \quad (5.10)$$

where  $\bar{A} = A_0 + A_1 e^{-A_0 \tau}$ ,  $\bar{B} = e^{-\bar{A} \tau} e^{A_0 \tau} B$ . The following lemma obtained in [26] reveals the relationship between the solutions of system (4.14), (4.15) and those of system (5.10).

**Lemma 1.** *Consider solutions  $x(t)$  and  $\tilde{x}(t)$  of systems (4.14), (4.15) and (5.10), respectively. Assume that  $t_1 = \tilde{t}_1$  and  $x(t_1^-) = \tilde{x}(\tilde{t}_1^-)$ . Then it holds that  $t_n = \tilde{t}_n$ ,  $\lambda_n = \tilde{\lambda}_n$  and  $x(t_n^-) = \tilde{x}(\tilde{t}_n^-)$  for all  $n \geq 1$ . Moreover,*

$$x(t) = \tilde{x}(t), \quad \tilde{t}_n + \tau \leq t < \tilde{t}_{n+1}, \quad n = 0, 1, \dots$$

At the same time, generally, the solutions do not coincide entirely

$$x(t) \neq \tilde{x}(t), \quad \tilde{t}_n \leq t < \tilde{t}_n + \tau.$$

The result above can be exploited to design a finite-dimensional observer for the infinite-dimensional hybrid system in (4.14), (4.15). Note that the value of the time delay in the delay-free impulsive system still influences the system dynamics as  $\tau$  affects the matrix coefficients  $\bar{A}$ ,  $\bar{B}$  of (5.10). The purpose of state observation in hybrid closed-loop system (4.14), (4.15) is to produce the estimates  $(\hat{t}_n, \hat{\lambda}_n)$  of the impulse parameters  $(t_n, \lambda_n)$ . From Lemma 1, it follows that  $(\hat{t}_n, \hat{\lambda}_n)$  can be obtained by exploiting the delay-free model in (5.10). To evaluate  $(\hat{t}_n, \hat{\lambda}_n)$ , an estimate of the continuous state vector of (5.10), i.e.,  $\tilde{x}(t)$ , is calculated by the hybrid observer proposed in **Paper VI**:

$$\begin{aligned} \frac{d\hat{x}(t)}{dt} &= \bar{A}\hat{x}(t) + \mathcal{K}(t)(y(t) - \hat{y}(t)), \quad \hat{y}(t) = L\hat{x}(t), \quad \hat{z}(t) = C\hat{x}(t), \\ \hat{x}(\hat{t}_n^+) &= \hat{x}(\hat{t}_n^-) + \hat{\lambda}_n \bar{B}, \quad \hat{t}_{n+1} = \hat{t}_n + \hat{T}_n, \quad \hat{T}_n = \Phi(\hat{z}(\hat{t}_n)), \quad \hat{\lambda}_n = F(\hat{z}(\hat{t}_n)), \\ \mathcal{K}(t) &= \begin{cases} 0, & \hat{t}_n < t < \hat{t}_n + \tau, \\ K = \text{const}, & \hat{t}_n + \tau \leq t \leq \hat{t}_{n+1}. \end{cases} \end{aligned} \quad (5.11)$$

Notice that  $\hat{z}(t)$ ,  $\hat{y}(t)$  are generally discontinuous in time which property requires careful analysis. The switched feedback gain  $\mathcal{K}$  is set to zero in the time intervals where the solutions of system (4.14), (4.15) and those of system (5.10) do not coincide.

The second approach of the observer design for time-delay system (4.14), (4.15) is based on preserving the delay term in the observer equations proposed in **Paper VII**:

$$\begin{aligned} \frac{d\hat{x}(t)}{d\hat{t}} &= A_0\hat{x}(t) + A_1\hat{x}(t - \tau) + K(y(t) - \hat{y}(t)), \\ \hat{y}(t) &= L\hat{x}(t), \quad \hat{z}(t) = C\hat{x}(t), \quad \hat{x}(\hat{t}_n^+) = \hat{x}(\hat{t}_n^-) + \hat{\lambda}_n B, \\ \hat{t}_{n+1} &= \hat{t}_n + \hat{T}_n, \quad \hat{T}_n = \Phi(\hat{z}(\hat{t}_n)), \quad \hat{\lambda}_n = F(\hat{z}(\hat{t}_n)), \end{aligned} \quad (5.12)$$

where  $t \geq \hat{t}_0$ , and the initial conditions are  $\hat{t}_0$  and  $\hat{x}(t) = \hat{\phi}(t)$ ,  $\hat{t}_0 - \tau \leq t < \hat{t}_0$ . Here  $\hat{\phi}(t)$  is a vector-valued function that is continuous in the interval  $[\hat{t}_0 - \tau, \hat{t}_0]$ . Infinite-dimensional observer (5.12) has an advantage over observer (5.11) since it allows to estimate the state of system (4.14), (4.15) not only in discrete times  $t_k$  but also in continuous intervals between impulses. However, it requires a much more complex analysis, see **Paper VII**.

### 5.1.3 Observers for impulsive system with exogenous signals

Consider system (4.18) and assume that the exogenous signal  $\beta$  is a single-tone positive harmonic signal

$$\beta(t) = M \sin(\omega t + \varphi) + N, \quad (5.13)$$

where  $N \geq M > 0$ , so that  $\beta(t) \geq 0$  for all  $t$ . In terms of a state-space model, the exogenous signal  $\beta(t)$  can be represented as  $\beta(t) = Gw(t)$ , where

$$w(t) = \begin{bmatrix} M \cos(\omega t + \varphi) \\ M \sin(\omega t + \varphi) \\ N \end{bmatrix}, \quad G^T = \begin{bmatrix} 0 \\ 1 \\ 1 \end{bmatrix},$$

and  $w(t)$  is a solution to differential equation  $\dot{w}(t) = Fw(t)$ , where

$$F = \begin{bmatrix} 0 & -\omega & 0 \\ \omega & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \quad w(t_0) = \begin{bmatrix} M \cos(\omega t_0 + \varphi) \\ M \sin(\omega t_0 + \varphi) \\ N \end{bmatrix}.$$

Since  $\beta$  enters the continuous part of the impulsive Goodwin's oscillator, it can be actually incorporated into it by augmenting the continuous state vector  $x(t)$  with  $w(t)$ .

Denote  $\bar{x}(t) = [x^T(t) \quad w^T(t)]^T$  and rewrite system (4.18) as the following sixth-order model:

$$\dot{\bar{x}}(t) = \bar{A}\bar{x}(t), \quad \bar{y}(t) = \bar{L}\bar{x}(t), \quad \bar{z}(t) = \bar{C}\bar{x}(t), \quad (5.14)$$

$$\bar{x}(t_k^+) = \bar{x}(t_k^-) + \lambda_k \bar{B}, \quad t_k = t_k + \Phi(\bar{z}(t_k)), \quad \lambda_k = F(\bar{z}(t_k)), \quad (5.15)$$

$$\bar{A} = \begin{bmatrix} A & TG \\ \mathbf{0} & F \end{bmatrix}, \quad \bar{B} = \begin{bmatrix} B \\ \mathbf{0} \end{bmatrix}, \quad \bar{C} = [C \quad \mathbf{0}], \quad \bar{L} = [L \quad \mathbf{0}],$$

and  $\bar{x}(t_0) = [x^T(t_0) \quad w^T(t_0)]^T$ . Notice that the modulation variable  $\bar{z}(t)$  and the output of the forced system  $\bar{y}(t)$  are still continuous as the identities  $\bar{C}\bar{B} = 0$ ,  $\bar{L}\bar{B} = 0$  are fulfilled for the augmented system and the matrix pair  $(\bar{A}, \bar{L})$  is still observable.

A straightforward approach to the problem of estimating the hybrid state in system (4.18) subject to exogenous signal (5.13) is to apply the observer structure (5.1), (5.2), (5.4) to augmented system description (5.14), (5.15). Due to the block-triangular form of the matrix  $\bar{A}$ , the estimates of  $x(t)$  and  $w(t)$  can be written separately (see **Paper IV**):

$$\begin{aligned} \dot{\hat{x}}(t) &= A\hat{x}(t) + TG\hat{w}(t) + K_1(y(t) - \hat{y}(t)), \\ \dot{\hat{w}}(t) &= F\hat{w}(t) + K_2(y(t) - \hat{y}(t)), \\ \hat{y}(t) &= L\hat{x}(t), \quad \hat{z}(t) = C\hat{x}(t), \end{aligned} \quad (5.16)$$

$$\begin{aligned} \hat{x}(\hat{t}_k^+) &= \hat{x}(\hat{t}_k^-) + \hat{\lambda}_k \bar{B}, & \hat{w}(\hat{t}_k^+) &= \hat{w}(\hat{t}_k^-) \\ \hat{t}_k &= \hat{t}_k + \Phi(\hat{z}(\hat{t}_k) + K_d(y(\hat{t}_k) - \hat{y}(\hat{t}_k))), & \hat{\lambda}_k &= F(\hat{z}(\hat{t}_k)), \end{aligned} \quad (5.17)$$

where  $K_d \in \mathbb{R}^{1 \times 2}$  is the gain matrix in the discrete part of the observer and  $K_1, K_2 \in \mathbb{R}^{3 \times 2}$  are the gain matrices in the continuous part. In **Paper V**, a modification of (5.17) is proposed, where a separate frequency modulation was considered to prevent the occurrence of overjumps and hence to improve the observer convergence. An overjump is a situation, when the estimated firing time  $\hat{t}_n$  lies in a right neighborhood of  $t_n$ , for some  $n$ , while  $\hat{t}_{n-1}$  belonged to a left neighborhood of  $t_{n-1}$ .

The high order of observer (5.16), (5.17) can become an issue when, e.g., the signal form of  $\beta$  includes several harmonics. At the same time, some information, or even a measurement, of the exogenous signal can be available. A more economical but limiting approach to the hybrid state estimation in system (4.18) is based on the fact that any solution to (4.18) can be equivalently rewritten as  $x(t) = x_p(t) + T\zeta(t)$ , where  $x_p(t)$  satisfies

$$\dot{x}_p(t) = Ax_p(t), \quad y_p(t) = Lx_p(t), \quad z_p(t) = Cx_p(t), \quad (5.18)$$

with

$$\begin{aligned} x_p(t_k^+) &= x_p(t_k^-) + \lambda_k B, \\ t_{k+1} &= t_k + \Phi(z_p(t_k) + \zeta(t_k)), \quad \lambda_k = F(z_p(t_k) + \zeta(t_k)), \end{aligned} \quad (5.19)$$

and  $\zeta(t)$  obeys the scalar dynamics

$$\dot{\zeta}(t) = -b_3 \zeta(t) + \beta(t), \quad (5.20)$$

while signal  $\beta(t)$  is arbitrary (not restricted to model (5.13)) and  $\zeta(t)$  is assumed known. In the model of Te regulation,  $\zeta(t)$  represents a basal secretion

component of the Te concentration. A corresponding third-order observer that estimates  $x_p$  is as follows (see **Paper IV**):

$$\begin{aligned}\hat{x}_p(t) &= A\hat{x}_p(t) + K(y_p(t) - \hat{y}_p(t)), \\ \hat{y}_p(t) &= L\hat{x}_p(t), \quad \hat{z}_p(t) = C\hat{x}_p(t),\end{aligned}\tag{5.21}$$

$$\begin{aligned}\hat{x}_p(\hat{t}_k^+) &= \hat{x}_p(\hat{t}_k^-) + \hat{\lambda}_k B, \quad \hat{\lambda}_k = F(\hat{z}_p(\hat{t}_k) + \zeta(\hat{t}_k)), \\ \hat{t}_{k+1} &= \hat{t}_k + \Phi(\hat{z}_p(\hat{t}_k) + \zeta(\hat{t}_k) + K_d(y_p(\hat{t}_k) - \hat{y}_p(\hat{t}_k))).\end{aligned}\tag{5.22}$$

When the signal  $\zeta(t)$  in (5.18)–(5.20) is not available but the exogenous signal  $\beta$  is, one can use the following general form of the observer for system (4.18) (see **Paper IV**):

$$\begin{aligned}\hat{x}(t) &= A\hat{x}(t) + K(y(t) - \hat{y}(t)) + T\beta(t), \\ \hat{y}(t) &= L\hat{x}(t), \quad \hat{z}(t) = C\hat{x}(t),\end{aligned}\tag{5.23}$$

$$\begin{aligned}\hat{x}(\hat{t}_k^+) &= \hat{x}(\hat{t}_k^-) + \hat{\lambda}_k B, \quad \hat{\lambda}_k = F(\hat{z}(\hat{t}_k)), \\ \hat{t}_{k+1} &= \hat{t}_k + \Phi(\hat{z}(\hat{t}_k) + K_d(y(\hat{t}_k) - \hat{y}(\hat{t}_k))).\end{aligned}\tag{5.24}$$

## 5.2 Synchronous mode

When the state estimation error is zero, the observer is in a synchronous mode characterized by the firings of the impulses in the observer feedback and those of the plant occurring simultaneously. The synchronous mode thus corresponds to an equilibrium point of the hybrid state error dynamics. The hybrid observer design approaches considered in this thesis do not formally demand the observability of the hybrid plant solution, and are based on local asymptotic stability of the synchronous mode.

Let  $(x(t), t_n)$  be a solution of plant equations (4.1), (4.2) with the parameters  $\lambda_k$ ,  $T_k$ , and  $x_k = x(t_k^-)$ . Suppose that the plant is already running at the moment when the observer is initiated, i.e.,  $t_a \leq \hat{t}_0 < t_{a+1}$  for some  $a \geq 1$ . Consider observer (5.1), (5.2), where the frequency modulation is given by one of the introduced above laws (5.3) – (5.7). Denote  $x_k = x(t_k^-)$ ,  $\hat{x}_k = \hat{x}(\hat{t}_k^-)$ .

Assume that  $(\hat{x}(t), \hat{t}_n)$  is a solution of the observer equations subject to the initial conditions

$$\hat{t}_0 = t_a, \quad \hat{x}_0 = x_a,$$

for some integer  $a \geq 0$ . Note that the latter implies

$$\hat{T}_0 = T_a.\tag{5.25}$$

Indeed, in the case of frequency modulation (5.3),  $\hat{T}_0 = \Phi(\hat{z}(\hat{t}_0)) = \Phi(z(t_a)) = T_a$ . For modulation law (5.4), equation (5.25) holds since  $E_d(\hat{t}_0) = K_d(y(\hat{t}_0) - \hat{y}(\hat{t}_0)) = K_d(y(t_a) - \hat{y}(\hat{t}_0)) = 0$ . Similarly, for modulation (5.6)  $\hat{T}_0 = T_a$  due

to the assumption  $r(\hat{t}_0) = 0$ . In the case of integral modulation (5.7), the assumptions  $E_d(\theta) = 0$  for  $\theta \in [\hat{t}_0 - v, \hat{t}_0]$  and  $\Psi(0) = 0$  lead to  $\hat{T}_0 = \Phi(\hat{z}(\hat{t}_0)) + \Psi(0) = T_a$ . Hence, due to the uniqueness of the solution of (4.1), (4.2), for the solution  $(\hat{x}(t), \hat{t}_n)$  of observer equations subject to the initial conditions

$$\hat{t}_0 = t_a, \quad \hat{x}_0 = x_a$$

it holds

$$\hat{x}_n = x_{n+a}, \quad \hat{t}_n = t_{n+a}, \quad \hat{\lambda}_n = \lambda_{n+a}, \quad n = 0, 1, 2, \dots,$$

and  $\hat{x}(t) = x(t)$  for all  $t \geq t_a$ . Such a solution  $(\hat{x}(t), \hat{t}_n)$  is called a *synchronous mode* of the observer with respect to  $(x(t), t_n)$ , see [29]. Thus, a synchronous mode corresponds to zero dynamics of the hybrid observer.

Since the continuous plant output  $y(t)$  is the only source of information about the hybrid plant state, the following result is instrumental.

**Proposition 1** ([122] and **Paper II**). *The following conditions are equivalent*

1.  $(\hat{x}(t), \hat{t}_n)$  is the synchronous mode with respect to  $(x(t), t_n)$ ;
2.  $\hat{y}(t) \equiv y(t)$  for all  $t \geq \hat{t}_0$ .

Conditions in Proposition 1 ensure that reducing the plant output estimation error to zero brings the observer into a synchronous mode and, therefore, solves the hybrid state estimation problem.

Further, once perturbed, the observer in a synchronous mode has to rapidly return to it. To ensure practical usefulness of the observer, stability properties of the synchronous mode have to be investigated. A synchronous mode is called *locally asymptotically stable* if for any solution  $(\hat{x}(t), \hat{t}_n)$  of the observer such that the initial estimation errors  $|\hat{t}_0 - t_a|$  and  $\|\hat{x}(\hat{t}_0^-) - x(t_a^-)\|$  are sufficiently small, it follows that  $\hat{t}_n - t_{n+a} \rightarrow 0$  and  $\|\hat{x}(\hat{t}_n^-) - x(t_{n+a}^-)\| \rightarrow 0$  as  $n \rightarrow \infty$ . The latter implies  $\hat{\lambda}_n - \lambda_{n+a} \rightarrow 0$  as  $n \rightarrow \infty$ .

Note that for an impulsive system with exogenous signals, the synchronous mode is defined similarly by replacing the state  $x(t)$  with the augmented one  $\bar{x}(t)$ .

For time-delayed system (4.14), (4.15), the definition of asymptotic stability of the synchronous mode should be amended. A synchronous mode with respect to a solution  $(x(t), t_n)$  of (4.14), (4.15) is called locally asymptotically stable if for sufficiently small initial estimation errors  $|t_a - \hat{t}_0|$ ,  $\sup_{t \in \Omega} \|\varphi(t) - \hat{\varphi}(t)\|$ , where  $\Omega$  is the intersection of the intervals  $[t_a - \tau, t_a]$  and  $[\hat{t}_0 - \tau, \hat{t}_0]$ , it follows that  $\hat{t}_n - t_n \rightarrow 0$  and  $\|\hat{x}_n - x_n\| \rightarrow 0$  as  $n \rightarrow \infty$ , implying  $\hat{\lambda}_n - \lambda_n \rightarrow 0$  as  $n \rightarrow \infty$ .

For brevity sake, denote  $n_a = n + a$ . Thus, the synchronous observer mode with respect to the solution of the system  $(x(t), t_n)$  can be characterized by a vector sequence

$$\hat{q}_n^a = \begin{bmatrix} x_{n_a} \\ t_{n_a} \end{bmatrix}. \quad (5.26)$$

Since the vector  $x(t)$  can undergo jumps at certain moments of time, the closeness of  $x(t)$  and  $\hat{x}(t)$  cannot be ensured for all time moments  $t$  due to the effect of "error peaking" illustrated in Fig. 5.2. Indeed, suppose that  $\hat{t}_n$  and  $t_n$  are close enough, but not exactly the same. For definiteness, set  $t_n < \hat{t}_n$ . Then on the interval  $t_n < t < \hat{t}_n$ , the vector  $x(t)$  has already made the jump, while  $\hat{x}(t)$  has not yet, therefore  $x(t)$  and  $\hat{x}(t)$  on this interval can differ significantly. However, the proximity of the state  $x(t)$  and the estimate  $\hat{x}(t)$  may occur in the sense that there is a whole  $a \geq 0$ , depending on the initial conditions such that  $\|\hat{q}_n - \hat{q}_n^a\| \rightarrow 0$  for  $n \rightarrow +\infty$ , where

$$\hat{q}_n = \begin{bmatrix} \hat{x}_n \\ \hat{t}_n \end{bmatrix}.$$

Thus, the observer convergence is understood as the local asymptotic stability of the synchronous mode.

To investigate the stability properties of the synchronous mode, consider the pointwise mapping capturing the propagation of the continuous observer states through the discrete cumulative (plant and observer) sequence of the feedback firing instants:

$$Q : \hat{q}_n \mapsto \hat{q}_{n+1}. \quad (5.27)$$

The derivation of mapping (5.27) is a challenging mathematical problem. For each observer considered above, the precise formulas can be found in **Papers I–IV**. Under certain assumptions on the plant and observer matrices and the modulation functions  $F$  and  $\Phi$ , mapping (5.27) is smooth. Thus, the discrete observer dynamics admit linearization in the vicinity of  $(\hat{x}_n, \hat{t}_n)$ , where local stability properties of observer solutions can be analyzed. The Jacobian of  $Q$  at the point  $\hat{q}_n^a$  is calculated as

$$Q'(\hat{q}_n^a) = J_n(x_{n_a}, t_{n_a}) = \begin{bmatrix} (J_n)_{11} & (J_n)_{12} \\ (J_n)_{21} & (J_n)_{22} \end{bmatrix}. \quad (5.28)$$

By the chain rule, it follows that, for any  $m \geq 1$ , the Jacobian of the  $m$ -th iteration of the mapping is given by the expression

$$\left(Q^{(m)}\right)'(\hat{q}_n^a) = J_{n+m-1} J_{n+m-2} \dots J_{n+1} J_n.$$

Let  $(x(t), t_n)$  be an  $m$ -cycle of the plant, where  $m \geq 1$ . Then  $x_{n+m} \equiv x_n$ ,  $\lambda_{n+m} \equiv \lambda_n$ ,  $T_{n+m} \equiv T_n$ , and  $J_{n+m} \equiv J_n$ , so the sequence  $\{J_i\}_{i=0}^{\infty}$  contains no more than  $m$  distinct matrices, namely  $J_0, \dots, J_{m-1}$ . The theorem below provides a simple tool for checking local stability of the synchronous mode with respect to the  $m$ -cycle.

**Theorem 1.** *Let the matrix product  $J_{m-1} \dots J_0$  be Schur stable, i.e., all the eigenvalues of this matrix lie strictly inside the unit circle. Then the synchronous mode with respect to  $(x(t), t_n)$  is locally asymptotically stable.*

Theorem 1 formulates a stability condition guiding the choice of the observer parameters. As pointed out above, the condition is local and depends not only on the coefficients of the system, but also on the parameters of the observed periodic mode. In particular, the multiplicity of the periodical solution in the plant has to be known. The spectral radius of the Jacobian reflects the local convergence rate of the linearized observer dynamics. To optimize the observer performance, the observer gains can be chosen numerically to fulfill the conditions of Theorem 1 while minimizing the spectral radius of the Jacobian. The detailed algorithm of the observer gains synthesis is provided in **Paper I**.

As an example, consider system (4.7)–(4.9) with the following parameter values:  $b_1 = 0.018$ ,  $b_2 = 0.15$ ,  $b_3 = 0.1$ ,  $g_1 = 2.8$ ,  $g_2 = 1.5$ , and the modulation functions

$$\Phi(x_3) = 40 + 80 \frac{(x_3/2.7)^2}{1 + (x_3/2.7)^2}, \quad F(x_3) = 0.05 + \frac{5}{1 + (x_3/2.7)^2}.$$

For the selected parameter values, plant (4.7)–(4.9) has a stable 2-cycle depicted in Fig. 5.3.

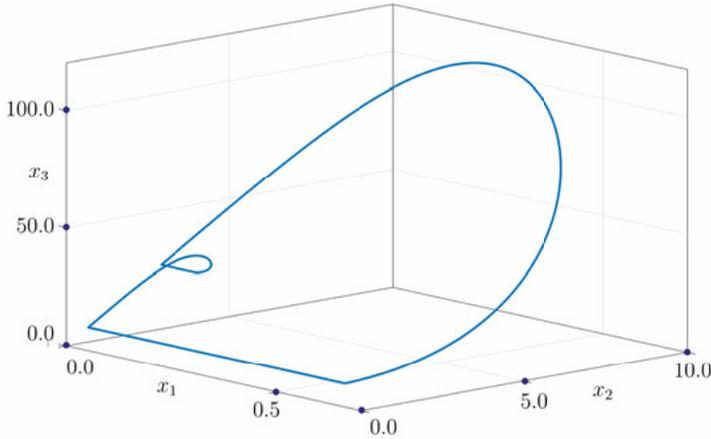


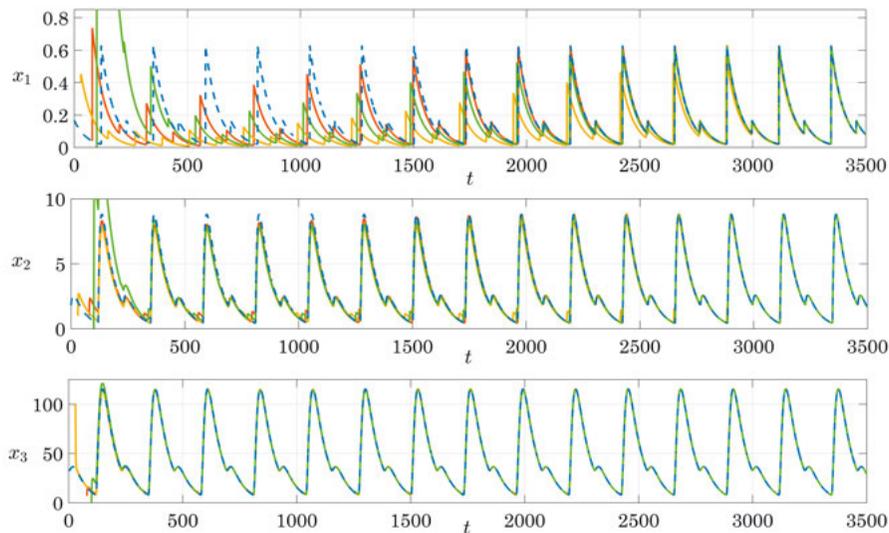
Figure 5.3. Three-dimensional phase portrait for the considered stable 2-cycle in the plant with  $t_0 = 0$ ,  $T_0 = 119.47$ ,  $T_1 = 111.05$ .

The hybrid observer dynamics are described by equations (5.1), (5.1), (5.4). Consider the gain matrix  $K$  of the following form:

$$K = \begin{bmatrix} 0 & 0 \\ 1 & 0 \\ 0 & 1 \end{bmatrix} \quad (5.29)$$

that renders the matrix  $D = A - KL$  Hurwitz stable. The motivation for restricting the structure of  $K$  and the performance consequences of it are discussed in

[122]. Here it suffices to note that, under this restriction, the observer demonstrates good performance [29, 122] with the chosen structure of the gain matrix  $K$ . The choice of the discrete gain  $K_d$  directly impacts the discrete dynamics of the observer and, therefore, is more significant. In **Paper I** it was demonstrated that  $K_d = [0, 38.2]^T$  is the most suitable discrete gain providing the convergence to the synchronous mode from admissible initial conditions at the highest rate.



*Figure 5.4.* Transients in the continuous states of the observer due to different initial conditions mismatches with respect to the corresponding plant states (blue dashed lines,  $t_0 = 0$ ). Red lines - initial conditions  $\hat{t}_0 = 80, \hat{x}_0 = [0.04, 1, 7]^T$ . Yellow lines - initial conditions  $\hat{t}_0 = 30, \hat{x}_0 = [0.4, 1, 100]^T$ . Green lines - initial conditions  $\hat{t}_0 = 100, \hat{x}_0 = [0.001, 0.01, 0.01]^T$ .

Fig. 5.4 contains time-domain illustrations of the designed observer performance starting from different initial conditions. Note that the convergence rate of the designed observer is not much dependent on the initial conditions. In fact [chaos19], the rate of convergence practically does not change depending on the components of the state  $\hat{x}_0$ , since large initial deviations are quickly compensated for by an exponential decrease in the first intervals of continuity. Therefore, the initial state of  $\hat{x}$  does not really matter. The rate of convergence is affected mostly by the discrete component  $\hat{t}_0$ , namely the distance to  $t_0$  (especially, for cycles of low periodicity, e.g., 1-cycles and 2-cycles, here the influence of  $K_d$  is preeminent) and the occurrence of a jump after the first pulse.

The detailed analysis of the performance of all proposed above hybrid observers can be found in **Papers I – VII**.

## 6. Concluding remarks

This thesis concerns a state observation problem for a special class of hybrid systems that is quite specific and new in control theory and estimation.

The novelty lies in the fact that the problem of hybrid state estimation in a continuous linear time-invariant system under an intrinsic pulse-modulated feedback, where the firing times in the feedback mechanism are treated as an unknown discrete state that, along with the continuous states, has to be reconstructed from the available continuous outputs, is not covered in the existing literature.

The problem in hand is exemplified by an endocrine system where episodically firing neurons control the production of hormones in endocrine glands. The time variation of some hormone concentrations can be obtained by taking and analyzing blood samples while the concentrations of others are inaccessible for direct measurement in the bloodstream. Thus, the immeasurable concentrations and the episodes of the pulse-modulated feedback interactions with the continuous part have to be estimated in some manner from the available data, for instance by applying an observer.

Design and analysis of hybrid observers solving this estimation problem is the focal point of the thesis. The state estimation error should tend to zero and the main observer performance criterion is its settling time. In this case, zero error does not correspond to an equilibrium point of a plant, but to a limit cycle (stable periodic solution) or to some complex attractor (including chaotic one), bistable or quasiperiodic mode.

The impulsive observers proposed in the thesis are based on synchronization of impulse sequences generated by the pulse-modulated feedback, an approach originating from [29]. For observer design, the hybrid state estimation problem is recast as a synchronization problem between the impulsive sequence in the plant and that in the observer.

Thus, the present thesis proposes and studies in detail several observer structures for hybrid systems that are able to reconstruct discrete states from only continuous measurements. The proposed observer structures cover the cases of a time-delay in the closed loop of the plant and also when the plant is forced by a continuous exogenous signal. The presence of time delays in a closed loop is inevitable in endocrine systems, where the hormones are transported in the blood by the circulatory system to target distant organs. Delays also arise due to the time necessary for an endocrine gland to produce a certain hormone quantity. With the time delay taken into account, the pulse-modulated model of endocrine regulation acquires an infinite-dimensional continuous part. The closed-loop dynamics become therefore both hybrid and

infinite-dimensional. The exogenous signal can represent, e.g., the influx of a drug used in a hormone replacement therapy, the dynamical effects due to circadian rhythm, or interactions with other endocrine loops of the organism. Being extended with an exogenous signal in the continuous part, the model may exhibit bistability and quasiperiodic solutions of a high order, which phenomenon significantly complicates observer design. Therefore, the performance of the proposed observers applied to a model of non-basal testosterone regulation in the human male is carefully assessed.

## 7. Summary of Papers

### **Paper I** Bifurcation analysis for non-local design of a hybrid observer for the impulsive Goodwin's oscillator

In Paper I, a systematic design procedure for a hybrid observer reconstructing the state variables of the impulsive Goodwin's oscillator is proposed. It is based on the numerical bifurcation analysis of a discrete mapping capturing the observer state transition from one firing of the cumulative impulsive sequence of the observer and plant feedback to another one. The design procedure produces the values of the observer continuous and discrete gains that guarantee the asymptotic convergence of the hybrid state estimation error to zero from all feasible initial conditions at a highest possible rate. The design procedure is illustrated by a simulation example that confirms efficacy of the observer.

### **Paper II** Hybrid observer with finite-memory output error correction for linear systems under intrinsic impulsive feedback

In Paper II, an improved version of the observers suggested in Paper I is considered. A Poincaré mapping capturing the propagation of the continuous observer states through the cumulative sequence of the plant and observer impulses is derived. Orbital stability of hybrid solutions to the observer equations is related to the eigenvalues of the Jacobian matrix of the mapping. A new design scheme for selecting the feedback gains of the observer for the impulsive model of testosterone regulation is derived. The design approach is enabled by the obtained results on spectral decomposition of the Jacobian by means of solving non-symmetrical algebraic Riccati equations. A downside of this concept is that only local convergence results can be obtained. The numerical example is therefore focused on low-periodicity solutions (1-cycle and 2-cycle) that are known from [29] to be most challenging. Convergence to a synchronous mode is demonstrated for a wide range of initial conditions in the observer and at a rate that is clearly superior compared to what is obtained in Paper I and [29].

### **Paper III** Robustification of the synchronous mode in a hybrid observer for a continuous system under an intrinsic pulse-modulated feedback

In Paper III, the problem of enlarging the basin of attraction of a synchronous observer mode that corresponds to a zero solution of the hybrid observer error is considered. Due to high nonlinearity of the observer error dynamics typical to impulsive systems, overestimation of firing events by the observer has more severe impact on the observer convergence than underestimation of those. The introduction of a dynamical feedback in the discrete part of the observer is proposed to alleviate the asymmetry of the basin of attraction and shown to lead to improvement of the observer convergence time.

**Paper IV** Hybrid observers for an impulsive Goodwin's oscillator subject to continuous exogenous signals

In Paper IV, the problem of hybrid state estimation in the impulsive Goodwin's oscillator subject to an exogenous signal is considered. It is primarily motivated by the well-known dependence of basal secretion in endocrine systems on the circadian rhythm. Two observer structures are considered: One assumes the dynamics of the exogenous system to be known but not the exogenous signal itself. Another one is utilized when the exogenous signal or its function is readily available. Sufficient conditions for local asymptotic stability of the synchronous mode are obtained for both structures. It is shown that an observer capable of reconstructing plant solutions that belong to two co-existing periodic attractors can be designed.

**Paper V** Attractivity of the synchronous mode in hybrid observers for the impulsive Goodwin's oscillator subject to harmonic exogenous excitation

In Paper V, a detailed analysis of the synchronous mode for the observer considered in Paper IV reveals a considerable asymmetry in the basin of attraction relative to a jump instant and susceptibility to overjumps. This may result in the observer converging to a stable stationary mode distinct from a synchronous one, for some initial conditions. To circumvent this, an improved hybrid observer with a more elaborate frequency modulation law in the output error feedback structure is proposed. Moreover, under harmonic exogenous excitation, the impulsive Goodwin's oscillator under observation exhibits bistability, which phenomenon significantly complicates observer design. The attractivity of a null solution of the hybrid state error estimation dynamics (termed as synchronous mode) has to be maximized in order to cover all possible initial state estimate deviations. Numerical analysis suggests that the new observer is able to approach the synchronous mode from all admissible initial estimates.

**Paper VI** Finite-Dimensional Hybrid Observer for Delayed Impulsive Model of Testosterone Regulation

In Paper VI, a hybrid observer for a finite-dimensional delay-free model is proposed, that can be used for a hybrid time-delay plant. This observer allows to estimate the parameters of impulses thus reconstructing both the continuous and discrete states in the hybrid time-delay plant. However, in this case, the class of observation plants is more restrictive.

**Paper VII** Hybrid state observer for time-delay systems under intrinsic impulsive feedback

Paper VII also deals with a hybrid state observer for FD-reducible impulsive time-delay system. Unlike the case treated in Paper VI, the observer proposed here explicitly involves a time delay in the description of its continuous part.

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