Preprints of the 21st IFAC World Congress (Virtual)
Berlin, Germany, July 12-17, 2020

Structural Identifiability of a Third-order Continuous System under Impulsive Feedback ⋆

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Abstract: Structural identifiablity of a third-order continuous time-invariant linear plant under an intrinsic pulse-modulated feedback is analyzed. The model represents a biomedical system, where the input signal to the continuous plant is immeasurable and the feedback modulation functions have to be identified along with the continuous dynamics. It is shown that two eigenvalues of the continuous plant system matrix (i.e. time constants), along with the times and weights of impulses occurring during a finite time interval, are identifiable from the measurement of one continuous system state over the interval in question. When an infinite time horizon is considered, all parameters are identifiable, up to gain scaling and linear block permutations.

Keywords: Structural identifiability, biomedical systems, hybrid systems, impulses

1. INTRODUCTION

Identification of hybrid systems is a challenging and intricate topic due to the nonlinear and non-smooth nature of the underlying dynamics, Paoletti et al. (2007). Therefore, it is motivated to consider specific classes of hybrid systems before facing the problem in all its complexity.

Continuous systems with impulsive feedback, see Gelig and Churilov (1998), appear in power electronics (e.g. dc-dc converters, Almer et al. (2007)), mechanics (systems with impacts, Menini and Tornambe (2001)) but are otherwise not so common in engineered systems. Yet, from a mathematical perspective, pulse-modulated impulsive control is akin to the area of event- and self-triggered control that is popular with theoreticians, e.g. Heemels et al. (2012). The scenario featuring a feedback-modulated impulsive action applied at non-commensurate time instants to control continuous dynamics arises more often in biological, medical, and environmental contexts. In natural pulse-modulated biological systems, the discrete feedback law is intrinsic to the studied plant and typically has to be identified along with the continuous dynamics.

Structural identifiability analysis concerns the uniqueness of parameter values for a given model structure and noise-free input-output data, Bellman and Åström (1970). When the goal of modeling is data prediction, one can manage without securing structural identifiability of the model. On the other hand, when the model parameter estimates serve as the basis of controller design or are used for data classification, the property in question is of paramount importance. An overview and comparison of different methods for structural identifiability analysis in systems biology is provided in Oana et al. (2011). Of these, the so-called direct method resembles the approach of the present paper the most, but applications of this method to models under intrinsic impulsive feedback are lacking in the literature.

In hybrid systems, when the input to the continuous part is not available for measurement, both the continuous dynamics and the discrete feedback law have to be identified from the output signal only. When the feedback control is due to a natural biological mechanism, the discrete variables of the hybrid system are usually not measurable and system (model) identifiability from the continuous output has to be theoretically established.

A well-studied example of a biological pulse-modulated feedback system is the testosterone regulation in the human male. It can be modeled as a third-order continuous system, where the frequency and amplitude of the driving impulses are determined by the feedback, Medvedev et al. (2006); Churilov et al. (2009). Similar models exhibiting sustained periodic and non-periodic oscillations arise in other types of endocrine systems, such as cortisol or growth hormone regulation. Since the described principle is utilized in multiple biological systems, it is appropriate to describe them in a common modeling framework, which is known as the impulsive Goodwin's oscillator, e.g. Zhusubaliyev et al. (2015). A version of this model has recently been applied to the pharmacokinetics of the anti-Parkinsonian drug levodopa, where multiple blood concentration peaks of the drug are caused by a physiological feedback acting on the pylorus, Runvik et al. (2020).

Pharmacokinetics is the study of the uptake, metabolism, and elimination of drugs in the body, Gabrielsson and Weiner (2016). A common modeling approach in this field is the use of compartments, representing different sites in the body reached by the drug.

⋆ This work is funded in part by the PhD program at the Centre for Interdisciplinary mathematics, Uppsala University, Sweden and by the Swedish Research Council, under the grant 2019-04451.

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The continuous plant in this paper describes three compartments, while the impulsive feedback is used to capture the so-called multi-peak phenomenon. The latter concept describes a situation where a single administration of a drug results in a plasma concentration profile with two or more peaks, as opposed to a single peak which is generally expected and more common. Multiple physiochemical and physiological mechanisms can cause this behavior, Davies et al. (2010). In the present case, interrupted gastric emptying is assumed to be the cause. Details about this modeling approach, applied to the pharmacokinetics of the Parkinson's medication levodopa administered orally, can be found in Runvik et al. (2020). An important difference compared to the case of endocrine regulation is that the medication comes from an external source, while the endocrine system is autonomous, which gives rise to completely different dynamical behaviors.

Previous identifiability research for this type of systems has often been aimed at endocrine systems. In Veldhuis and Johnson (1986), an algorithm is proposed for identifying and specifying pulses through identification of statistically significant increases and decreases in a data set. In Mattsson and Medvedev (2012), an observer-based approach is used to identify the impulsive input signal to a linear system, a method which is extended for state estimation in Mattsson and Medvedev (2013). A notable difference between these publications and the present work is the inclusion of the feedback model in the identifiability analysis. Notice that the classical results regarding identifiability of linear time-invariant systems under feedback (e.g. Forssell and Ljung (1999)) do not provide much insight into the problem at hand as the input to the closed-loop system is not persistenly exciting. Besides, the dynamics are highly nonlinear and non-smooth, Zhusubaliyev et al. (2015). The results of this paper dealing with the structural identifiablility conditions for a hybrid model with an intrinsic impulsive feedback are therefore novel, to the best of the authors' knowledge.

The rest of the paper is organized as follows. First, the linear plant and impulsive feedback law is presented, together with properties of the specific modulation functions that are essential to this work. Then the structural identifiability is analyzed in two steps; first with respect to the parameters that directly influence the measured output and then with respect to the remaining parameters, including those of the modulation functions. Based on this analysis, the main result is established.

2. MODEL EQUATIONS

Consider a linear system with jumps in the state vector

$$\begin{aligned} \dot{x}(t) &= Ax(t), \quad x(0) = x_0, \quad t \neq t_n, n = 0, 1, \dots \\ x(t^+) &= x(t^-) + d_n B, \qquad\quad t = t_n, \end{aligned} \tag{1}$$

where $x \in \mathbb{R}^3$, the plus and minus superscripts denote right- and left-sided limits respectively, $t_n, n = 0, 1, 2, \dots$ defines a sequence of time instants when the system undergoes instantaneous jumps, and d_n determines the amplitude of those jumps. The system matrices are

$$A = \begin{bmatrix} -b_1 & 0 & 0 \\ g_1 & -b_2 & 0 \\ 0 & g_2 & -b_3 \end{bmatrix}, B = \begin{bmatrix} \frac{1}{v} \\ 0 \\ 0 \end{bmatrix}, \tag{2}$$

where $b_1, b_2, b_3, g_1, g_2, v$ are positive parameters, and the output signal is given by

$$y = Cx, \quad C = [0\ 0\ 1]. \tag{3}$$

This hybrid system can equivalently be described using impulsive input signals as

$$\dot{x} = Ax + B\xi(t), \quad y = Cx,$$

where

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

and $\delta(\cdot)$ is the Dirac delta function.

The model above follows the structure of the one proposed for modeling testosterone regulation in Medvedev et al. (2006); Churilov et al. (2009). In Runvik et al. (2020), it is adapted to describe the pharmacokinetics of levodopa. The first two components of x represent the levodopa concentration in small intestine and blood, respectively, while the third one stands for the dopamine concentration in the brain. The jumps correspond to the instantaneous relase of the drug from the stomach to the intestine due to changes in the pylorus effective opening.

The levodopa concentration in blood is available for measurement through blood samples. In the mathematical analysis below, the discrete nature of the measurement is disregarded and the measureable system output is

$$z = Dx, \quad D = [0\ 1\ 0]. \tag{4}$$

The signal y represents the (immeasurable) dopamine level in the brain. It is hypothesised that dopamine contributes to the feedback regulation of gastric emptying and modulates the oscillative contractions of the pylorus. The feedback is impulsive and parameterized by the frequency and amplitude modulation functions

$$\begin{aligned} t_{n+1} &= t_n + \Phi(Cx(t_n)), \\ d_n &= F(Cx(t_n)). \end{aligned}$$

The model described above is known as the impulsive Goodwin's oscillator when applied to the testosterone regulation in the human male, Zhusubaliyev et al. (2015). In the original formulation of this model, the weights and times of the impulses are only determined by the output signal y, making the system completely autonomous. Later generalizations included the introduction of continuous exogenous input signals, representing basal hormonal secretion or capturing circadian rhythm, Medvedev et al. (2018). These can be incorporated in the amplitude modulation function, as demonstrated in Mattsson et al. (2016).

To represent the pharmacokinetic system, an external signal is also required, in this case to account for the availability of the drug. Therefore, the amount of levodopa in the stomach $r(t)$ is introduced. For a single oral administration of the drug, the dynamics of this state are governed by

$$r(t_n^+) = r(t_{n-1}^+) - d_n, \quad r(t_0) = d, \tag{5}$$

where d denotes the administered dose. The modulation function can then be defined to include two factors as

$$F(Cx, r) = f(r)F_0(Cx), \tag{6}$$

where $f(r)$ reflects the amount of levodopa in the stomach.

2.1 Modulation Functions

It is assumed that $\Phi(\cdot)$ is non-decreasing, $F(\cdot)$ is non-increasing, and both are bounded according to

$$0 < \Phi_1 \leq \Phi(\cdot) \leq \Phi_2, \tag{7}$$
$$0 \leq F_1 \leq F(\cdot) \leq F_2,$$

for fixed Φ_1, Φ_2, F_1, F_2. The simplest type of function satisfying these conditions (that is not constant) is a sigmoid function. In previous work on the impulsive Goodwin's oscillator, such as e.g. Churilov et al. (2009), Hill functions were used to represent the modulation functions

$$\Phi(\theta) = k_1 + k_2 \frac{(\theta/h)^p}{1 + (\theta/h)^p}, \tag{8}$$

$$F(\theta) = k_3 + k_4 \frac{1}{1 + (\theta/h)^p}, \tag{9}$$

where k_1, k_2, k_3, k_4, h and p are positive parameters.

The following property of the Hill functions will be used in the oncoming identifiability analysis.

Lemma 1. Consider the Hill functions defined by (8) and (9). Let k_1 and k_3 be known constants and the values $F(\theta_i)$, $\Phi(\theta_i)$ be available for some sequence $\{\theta_i\}$. The remaining parameters can then be uniquely determined if and only if $\{\theta_i\}$ includes at least three distinct elements.

Proof. Follows from the main result in Heidel and Maloney (1999). □

Corollary 1. Let $F(\cdot)$ and $\Phi(\cdot)$ be given by (8) and (9). If $F(0)$ and $\Phi(0)$ are fixed, all function parameters can be recovered from $F(\theta_1), F(\theta_2), F(\theta_3)$ and $\Phi(\theta_1), \Phi(\theta_2), \Phi(\theta_3)$, where $\theta_1, \theta_2, \theta_3$ are positive and distinct.

When the impulsive Goodwin's oscillator is adapted to pharmacokinetic modeling, the same class of frequency modulation functions as in the endocrine case can be used, whereas the amplitude modulation function is given by (6). The amplitude modulation function in the feedback is captured by the Hill function

$$F_0(\theta) = F_0(\theta; h_2, p_2) = \frac{1}{1 + (\theta/h_2)^{p_2}}, \tag{10}$$

again with positive parameters h_2, p_2. Since $0 \leq F_0(\cdot) \leq 1$, it is required that $0 \leq f(\theta) \leq \theta$, to stay in touch with the biophysical background. A natural choice of $f(\cdot)$ that satisfies this requirement is a smoothed saturation function. The identifiability analysis is facilitated by the following property of F_0.

Lemma 2. Let $\{\theta_i'\}$ and $\{\theta_i''\}, i \in I \subseteq \mathbb{N}$ be positive sequences and h', h'', p', p'' be positive parameters. If $F_0(\theta_i'; h', p') = F_0(\theta_i''; h'', p'')$ for all $i \in I$, then

$$\theta_i'' = \frac{h'}{h''^{\frac{p''}{p'}}} \theta_i'^{\frac{p''}{p'}},$$

for all $i \in I$.

Proof. Follows from equating $F_0(\theta_i')$ and $F_0(\theta_i'')$ and solving for θ_i''. □

2.2 Model Solutions

An important difference between modulation functions (9) and (6) is that the latter allows for impulse weights that

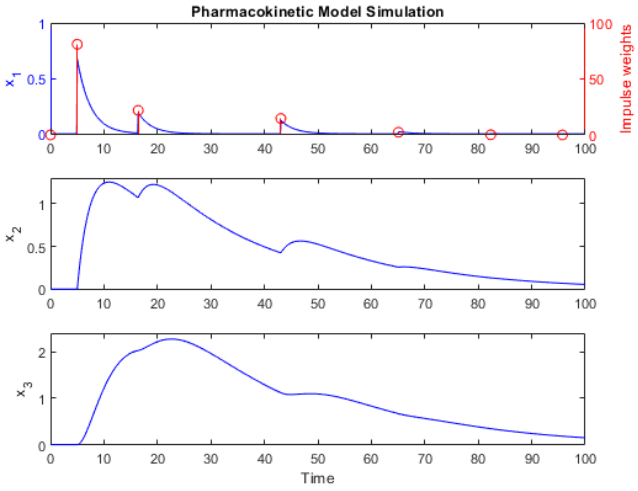

Fig. 1. Simulation of pharmacokinetic model with impulsive feedback. The upper plot also depicts the firings of the impulsive feedback (in red). The plotted sequence represents the impulse weights d_n.

are not strictly positive. The following result states that, with a modulation function in the form of (6), the model solutions asymptotically converge to zero, in contrast with the self-sustained behaviours of the impulsive Goodwin's oscillator which lacks equilibria by design.

Lemma 3. (Runvik et al. (2020)). Consider the discrete system obtained by sampling of (1), (2), (3) and (5) at the firing times of the impulsive feedback. If the frequency modulation function is bounded according to (7), the amplitude modulation function satisfies

$$0 \leq F(\cdot, \eta) \leq \eta,$$

and $F(\cdot, \eta) = 0 \iff \eta = 0$, then the unique equilibrium of the system at $x^0 = 0$, $r^0 = 0$ is asymptotically stable.

As a consequence of Lemma 3, the corresponding continuous solutions also tend to the same equilibrium. This is expected, as the solutions to a pharmacokinetic model have to die out after the drug dose has depleted. A simulation illustrating this converging behavior is shown in Fig. 1. The model parameters are selected for the solutions to resemble experimentally observed excursions of levodopa concentration. Notice also the intrinsic positivity of the system is implied by the matrix A in (2) being Metzler.

The following lemma proves that, for a typical class of $f(\cdot)$, the impulse weights decay faster than exponentially.

Lemma 4. Let $F(\cdot, \cdot)$, given by (6), determine the input impulses of (1), with $r(t)$ governed by (5). Let (10) define $F_0(\cdot)$ and $f(\theta)$ satisfy $0 \leq f(\theta) \leq \theta$ as well as $\lim_{\theta \to 0} f(\theta) = \theta$. Then, $\forall \epsilon > 0$, there exists an index $k > 0$ such that $F(Cx(t_{n+1}), r_{n+1}) \leq \epsilon F(Cx(t_n), r_n)$, $\forall n \geq k$.

Proof. See Appendix A. □

3. CONTINUOUS SUBSYSTEM

The structural identifiability analysis is divided into two distinct steps. In the first step, described in this section, the continuous subsystem defined by x_1 and x_2 in (1) is analyzed with respect to identifiability of b_1 and b_2 as well as the times and weights of the impulses. The second

step, covered in Section 4, involves the identification of b_3, together with the parameters of the modulation functions, from the identified impulses.

The identification of model parameters in exponentially decaying signals is well studied, see e.g. Landaw and DiStefano (1984). Provided that the impulse times are known, this analysis can be naturally generalized to the case when a linear system is excited with multiple impulses. With unknown impulse times, the task becomes more complicated due to the nonlinear dependence of the impulse times on the output. However, structural identifiability can still be proven according to the analysis below.

Introduce the following sequences

$$c_1^{(n)} = c_1^{(n-1)} + \frac{d_n}{b_2 - b_1} \mathrm{e}^{b_1 t_{n-1}}, \quad c_1^{(1)} = \frac{d_0 + x_1(0)}{b_2 - b_1},$$
$$c_2^{(n)} = c_2^{(n-1)} - \frac{d_n}{b_2 - b_1} \mathrm{e}^{b_2 t_{n-1}}, \quad c_2^{(1)} = -\frac{d_0 + x_2(0)}{b_2 - b_1}.$$

In between impulses, the measurement $z(t)$ is given by

$$z(t) = \frac{g_1}{v}(c_1^{(n)} \mathrm{e}^{-b_1 t} + c_2^{(n)} \mathrm{e}^{-b_2 t}), \quad t_{n-1} < t < t_n. \quad (11)$$

It follows from the structure of (11) that any scaling of the impulse weights is indistinguishable from a corresponding change in g_1 or v, which implies that the scaling of the impulses and these parameters are not identifiable *per se*. The symmetry of (11) with respect to b_1 and b_2 prevents discrimination between these parameters.

For any interval between impulses, up to the scalings and permutations mentioned above, the parameters of (11) (including the values of $c_1^{(n)}$ and $c_2^{(n)}$) are identifiable, since exponential functions with distinct half-lives (represented by b_1 and b_2) are linearly independent. When comparing between intervals of different length, the values of $c_1^{(n)}$ and $c_2^{(n)}$ always differ. The impulse times can therefore be uniquely determined as the times when the identified values of $c_1^{(n)}$ and $c_2^{(n)}$ change. Finally, (11) implies that the impulse weights also are determined (up to scaling) by the measured signal. The following result therefore holds.

Proposition 1. Assume that the system given by (1), (2) and (3) is subject to k impulses within the time interval $\tau_1 < t_1 < \ldots < t_k < \tau_2$. Then the time instants and weights of the impulses $\{d_n, t_n\}, n = 1, \ldots, k$, as well as the parameters b_1 and b_2, can be recovered from the measurement $z(\theta), \theta \in [\tau_1, \tau_2]$, where z is given by (4).

4. DISCRETE SUBSYSTEM

The structural identifiability of b_3 and the parameters of the modulation functions is now addressed, under the assumption that the impulse times and weights and the parameters b_1 and b_2 are known. A necessary condition for structural identifiability can be stated directly.

Lemma 5. Let modulation function (8) determine the times of the impulsive input to (1) with the initial condition $x_0 = 0$. If less than five impulse times are known for this system, then the parameters of the frequency modulation function cannot be uniquely determined.

Proof. With less than five known impulse times, there are no more than three intervals between impulses. Since the first interval determines k_1, there are at most two intervals left to determine the remaining three parameters. Then, Lemma 1 implies that there are multiple parametrizations of the frequency modulation function yielding the same time intervals for the same inputs. □

The rest of this section aims at finding sufficient identifiability conditions. The main difficulty in this analysis is that the input signal to the modulation function is intrinsic to the feedback loop and not measured. The function

$$f^*(x, y, z, \phi) = \frac{(z-y)\,\mathrm{e}^{-x\phi} + (x-z)\,\mathrm{e}^{-y\phi} + (y-x)\,\mathrm{e}^{-z\phi}}{(y-z)(z-x)(x-y)} \quad (12)$$

will be used to show how the value of b_3 influences the output.

Lemma 6. Let (12) define $f^*(\cdot,\cdot,\cdot,\cdot)$ and $\theta_1, \theta_2, \theta_3, \theta_4$ be distinct positive parameters such that $\theta_1 < \theta_2 < \theta_3 < \theta_4$. Then

$$\lim_{\phi \to \infty} \frac{f^*(\theta_1, \theta_2, \theta_3, \phi)}{f^*(\theta_1, \theta_2, \theta_4, \phi)} = \frac{\theta_1 - \theta_4}{\theta_1 - \theta_3},$$

and

$$\frac{f^*(\theta_1, \theta_2, \theta_3, \phi)}{f^*(\theta_1, \theta_2, \theta_4, \phi)} < \frac{\theta_1 - \theta_4}{\theta_1 - \theta_3}$$

for all $\phi \in \mathbb{R}^+$.

Proof. See Appendix B. □

Lemma 7. Let S' be given by (1) with

$$A = \begin{bmatrix} -b_1 & 0 & 0 \\ g_1 & -b_2 & 0 \\ 0 & g_2 & -b_3' \end{bmatrix}, B = \begin{bmatrix} \frac{1}{v} \\ 0 \\ 0 \end{bmatrix},$$

the output

$$y' = Cx, \quad C = [0\ 0\ 1],$$

and the input impulses according to (8) and (6), where

$$F_0(\theta) = \frac{1}{1 + (\theta/h_2')^{p_2'}},$$

and (5) determine the dynamics of $r(t)$. Define S'' in the same way, but with double primes on the corresponding parameters and variables. Assume furthermore that

- The initial conditions for S' and S'' are given by $x_0 = 0$ and d is fixed,
- $b_3'' \geq b_3' > \min(b_1, b_2)$,
- $f(\theta)$ satisfies $0 \leq f(\theta) \leq \theta$ and $f(\theta) = 0 \iff \theta = 0$ for both systems.

If the impulse times and weights are identical between S' and S'', then

$$\lim_{t \to \infty} \frac{y'(t)}{y''(t)} = \frac{\min(b_1, b_2) - b_3'}{\min(b_1, b_2) - b_3''},$$

Proof. See Appendix C. □

By combining Lemma 7 and Lemma 2, the following result is now obtained.

Lemma 8. Let the systems S' and S'' be defined as in Lemma 7. If all impulse times and weights coincide between the two systems and $f(\cdot)$ has at most one parameter to identify, then the parametrizations of the amplitude modulation functions of the two systems are identical and $b_3' = b_3''$.

Proof. See Appendix D. □

All auxiliary results are now in place to proceed with the main result of the paper.

5. HYBRID SYSTEM

Structural identifiability of the complete model, given by (1), (2), (3) and (5), under impulsive feedback defined by (6), (8) and (10), is now analyzed. In summary, it is established that the time constants of the first two system states as well as the times and weights of the impulses can be identified according to Proposition 1. The identifiability of the remaining parameters can then be analyzed by considering the consequences of assuming two distinct in parameters models producing the same measured output. For the assumed initial conditions and modulation functions, Lemma 7 can be used, which eliminates non-unique parametrizations of the amplitude modulation and non-unique b_3. This also eliminates the possibility of non-unique frequency modulation parameters.

Proposition 2. Consider the system defined by (1), (2) and (3), with impulsive feedback given by (8), (6) and (10), with $r(t)$ governed by (5). The parameters listed in Table 1 are then structurally identifiable, up to the indicated permutations and scaling, from a continuous measurement of $z(t)$, given by (4) for $t \in [0, \infty)$, under the following conditions:

- The initialization of the system is given by $x_0 = 0$ and $r(t_0) = d$ is fixed,
- $b_3 > \min(b_1, b_2)$,
- $f(\cdot)$ has at most one parameter to identify, denoted α,
- $0 \leq f(\theta) \leq \theta$ and $f(\theta) = 0 \iff \theta = 0$.

Table 1. Structurally identifiable parameters. *Identifiable up to permutation. **Identifiable up to scaling.

Parameter location	Parameter name			
Continuous plant	b_1*	b_2*	b_3	
Impulse train	t_n	d_n**		
Frequency modulation function	k_1	k_2	h	p
Amplitude modulation function	h_2	p_2	(α)	

Proof. Structural identifiability of b_1, b_2 and the sequences t_n and d_n follows from Proposition 1. Lemma 8 yields that h_2, p_2 and (if it exists) α are structurally identifiable, since the same conditions as in Lemma 8 are used. Finally Corollary 1 gives that k_1, k_2, h and p are structurally identifiable, since $y(t_0) = 0$ and there are more than four impulses in the considered time horizon. □

Notice that the initial conditions stated in Theorem 2 are consistent with a typical levodopa pharmacokinetic experimental protocol, where a Parkinson's patient with limited endogenous dopamine production receives a single dose of levodopa after an overnight washout.

6. CONCLUSION

Structural identifiability of a hybrid system with intrinsic impulsive feedback and immeasurable input has been analyzed. A necessary condition, based on the form of the frequency modulation function, is formulated in terms of the number of feedback impulses. This provides a useful lower bound on the amount of data needed for estimating the parameters for this type of model.

A sufficient condition for structural identifiability is obtained only under restrictive assumptions, indicating the difficulty of establishing general theoretical results with regard to identifiability in the considered class of models. Possible future work includes extending the analysis to other systems of similar structure, such as different versions of the impulsive Goodwin's oscillator.

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Appendix A. PROOF OF LEMMA 4

Let $x_n = x(t_n^-)$, $r_n = r(t_n^-)$ for notational simplicity. It follows from Lemma 3 that $\lim_{n\to\infty} d_n = 0$. Based on this fact and the properties of $F_0(\cdot)$ and $f(\cdot)$, it is then for all $\alpha < 1$ possible to find an index k such that $F_0(Cx_n) > \sqrt{\alpha}$, $f(r_n) > \sqrt{\alpha} r_n$, for all $n \geq k$. One then has

$$\begin{aligned}\frac{F(Cx_{n+1}, r_{n+1})}{F(Cx_n, r_n)} &= \frac{f(r_{n+1})F_0(Cx_{n+1})}{f(r_n)F_0(Cx_n)} \\ &\leq \frac{f(r_{n+1})}{f(r_n)F_0(Cx_n)} \leq \frac{r_{n+1}}{f(r_n)F_0(Cx_n)} \\ &\leq \frac{r_{n+1}}{\sqrt{\alpha}\sqrt{\alpha} r_n} = \frac{r_{n+1}}{r_n}\frac{1}{\alpha}.\end{aligned}$$

Since

$$r_{n+1} = r_n - F(Cx_n, r_n) \leq r_n - \alpha r_n,$$

it follows that

$$\frac{r_{n+1}}{r_n}\frac{1}{\alpha} \leq \frac{r_n - \alpha r_n}{r_n}\frac{1}{\alpha} = \frac{1-\alpha}{\alpha}.$$

By letting $\alpha = 1/(\epsilon+1)$ the sought inequality is obtained.

Appendix B. PROOF OF LEMMA 6

The limit can be calculated directly. To prove the inequality, notice that $f^*(\theta_1, \theta_2, \theta_3, \phi)$ is positive for $\phi > 0$ since the denominator is positive and

$$\begin{aligned}&(\theta_3 - \theta_2)e^{-\theta_1\phi} + (\theta_1 - \theta_3)e^{-\theta_2\phi} + (\theta_2 - \theta_1)e^{-\theta_3\phi} \\ &= e^{-\theta_2\phi}((\theta_3 - \theta_2)e^{(\theta_2-\theta_1)\phi} + \theta_1 - \theta_3 + (\theta_2 - \theta_1)e^{(\theta_2-\theta_3)\phi}) \\ &> e^{-\theta_2\phi}(\theta_3 - \theta_2 + \theta_1 - \theta_3 + \theta_2 - \theta_1) = 0,\end{aligned}$$

where the inequality is obtained from the relation

$$ae^{bt} + be^{-at} > a + b \tag{B.1}$$

for $a, b, t > 0$. $f^*(\theta_1, \theta_2, \theta_4, \phi)$ is then also positive. Now consider the fraction

$$\begin{aligned}&\frac{f^*(\theta_1, \theta_2, \theta_3, \phi)}{f^*(\theta_1, \theta_2, \theta_4, \phi)}\frac{\theta_1 - \theta_3}{\theta_1 - \theta_4} \\ &= \frac{(\theta_3 - \theta_2)e^{-\theta_1\phi} + (\theta_1 - \theta_3)e^{-\theta_2\phi} + (\theta_2 - \theta_1)e^{-\theta_3\phi}}{(\theta_4 - \theta_2)e^{-\theta_1\phi} + (\theta_1 - \theta_4)e^{-\theta_2\phi} + (\theta_2 - \theta_1)e^{-\theta_4\phi}} \\ &\quad \times \frac{\theta_2 - \theta_4}{\theta_2 - \theta_3} = \frac{h_n(\phi)}{h_d(\phi)}.\end{aligned}$$

The positivity of f^* implies that $h_n(\phi)$ and $h_d(\phi)$ are negative when $\phi > 0$ and zero when $\phi = 0$. The sought inequality is therefore equivalent to the condition $h_n(\phi) - h_d(\phi) > 0$ for all $\phi > 0$. This difference becomes

$$\begin{aligned}&h_n(\phi) - h_d(\phi) = (\theta_2 - \theta_1) \\ &\times ((\theta_4 - \theta_3)e^{-\theta_2\phi} + (\theta_2 - \theta_4)e^{-\theta_3\phi} + (\theta_3 - \theta_2)e^{-\theta_4\phi}) \\ &= (\theta_2 - \theta_1)e^{-\theta_3\phi} \\ &\times ((\theta_4 - \theta_3)e^{(\theta_3-\theta_2)\phi} + \theta_2 - \theta_4 + (\theta_3 - \theta_2)e^{(\theta_3-\theta_4)\phi}) \\ &> (\theta_2 - \theta_1)e^{-\theta_3\phi}(\theta_4 - \theta_3 + \theta_2 - \theta_4 + \theta_3 - \theta_2) = 0,\end{aligned}$$

where the inequality again is obtained from (B.1).

Appendix C. PROOF OF LEMMA 7

The output of S' can be written as

$$y'(t) = g_1 g_2 \left(\sum_{i=0}^{n} \frac{d_i}{v} f^*(b_1, b_2, b_3', \tau_i) \right),$$

where $\tau_i = t - t_i$ and

$$n = \arg\max_{\substack{i\in\mathbb{N} \\ t_i < t}} t_i.$$

With the very similar expression for $y''(t)$, one gets

$$\frac{y'(t)}{y''(t)} = \frac{\sum_{i=0}^{n} d_i f^*(b_1, b_2, b_3', \tau_i)}{\sum_{i=0}^{n} d_i f^*(b_1, b_2, b_3'', \tau_i)}.$$

As every numerator-denominator pair in the sums converges to the stated limit according to Lemma 6 and the impulse weights tend to zero as $n \to \infty$, the whole ratio also converges to this value.

Appendix D. PROOF OF LEMMA 8

The initial conditions and the form of $F(\cdot,\cdot)$ imply that if $f(\cdot)$ has a parameter to identify, it is fixed from the first impulse, since $F_0(0) = 1$. This requires $F_0(t_n, h_2', p_2') = F_0(t_n, h_2'', p_2'')$ for all impulse times t_n, so Lemma 2 gives

$$\frac{y''(t_n)}{y'(t_n)} = \frac{h'}{h''^{\frac{p''}{p'}}} y'(t_n)^{\frac{p''}{p'}-1}.$$

Combining this result with Lemma 7 rules out $p_2' \neq p_2''$, as $y'(t_n)/y''(t_n)$ would not be positive and bounded in that case, because $y'(t)$ tends to zero. If $p_2'' = p_2'$ then $y'(t_n)/y''(t_n) = h_2''/h_2'$. But this can only be fulfilled if $h_2'' = h_2'$, and $b_3' = b_3''$ as

$$\frac{y'(t_1)}{y''(t_1)} = \frac{f^*(b_1, b_2, b_3', \Phi(Cx(t_0)))}{f^*(b_1, b_2, b_3'', \Phi(Cx(t_0)))} < \frac{\min(b_1, b_2) - b_3'}{\min(b_1, b_2) - b_3''},$$

if $b_3' \neq b_3''$ from Lemma 6, while

$$\lim_{t\to\infty} \frac{y'(t)}{y''(t)} = \frac{\min(b_1, b_2) - b_3'}{\min(b_1, b_2) - b_3''},$$

from Lemma 7.