

On Robust Stability of Hybrid Limit Cycles in the Impulsive Goodwin's Oscillator

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Abstract—The importance of pulse modulated regulation in non-basal testosterone secretion in males has motivated research to understand properties of periodic solutions to impulsive Goodwin's oscillators (IGOs). Despite the fruitful work studying IGOs, a result certifying robustness of asymptotically stable hybrid limit cycles is not available. In this paper, the IGO with a third-order continuous part of GnRH-LH-Te axis in males is described and analyzed within a hybrid systems framework. The notion of hybrid limit cycle is introduced and results on their existence are proposed for the IGO system. A sufficient condition related to Schur stability of the Jacobian of a hybrid Poincaré map is presented for stability of hybrid limit cycles. In addition, we establish robustness properties to perturbations of stable hybrid limit cycles and validate the results numerically.

I. INTRODUCTION

The famous Goodwin's oscillator, first proposed by Goodwin in [1], [2], provides a perfect model to study the oscillatory phenomena in biochemistry and is widely regarded as a prototypical biological oscillator [3]. It allows for an analytical understanding of the oscillatory phenomena and helps one to gain insights into the mechanisms of biological rhythms. Oscillations are of a broad spectrum and understanding the periodic behaviors in biochemical oscillators is very important, such as hormone concentration self-regulation.

In biological systems, particularly in endocrine regulation, pulsatile feedback is widely used in numerous endocrine loops. To capture the episodic nature of pulsatile (non-basal) modulated feedback in the testosterone regulation, Churilov et al. [4] developed an impulsive Goodwin oscillator (IGO) model, which demonstrated a good agreement with experimental data [5] and described by the following impulsive differential equations:

$$\dot{\xi}(t) = A\xi(t) \quad t \neq t_k \quad (1a)$$

$$\xi(t_k^+) = \xi(t_k^-) + \lambda_k B \quad t = t_k \quad (1b)$$

where the nonnegative state variables $[\xi_1, \xi_2, \xi_3]^\top =: \xi$ represent the serum concentrations of the gonadotropin-releasing hormone (GnRH), the luteinizing hormone (LH), and the testosterone (Te) in the male, respectively. At time t_k ,

$k = 1, 2, \dots$, a pulse is fired,¹ that is, $\xi(t_k^+) = \xi(t_k^-) + \lambda_k B$ with $B = [1 \ 0 \ 0]^\top$. Notice that a pulse sequence does not affect the LH and Te concentrations but marks the times when GnRH pulses are fired and communicates their amplitudes, i.e., $\xi_1(t_k^+) = \xi_1(t_k^-) + \lambda_k$, $\xi_2(t_k^+) = \xi_2(t_k^-)$ and $\xi_3(t_k^+) = \xi_3(t_k^-)$. $0 < t_1 < t_2 < \dots$ is a strictly increasing sequence such that $\lim_{n \rightarrow \infty} t_k = +\infty$ and $t_{k+1} = t_k + T_k$. Here, the state trajectory $t \mapsto \xi(t)$ is considered to be left-continuous, i.e., $\xi(t_k^-) = \xi(t_k)$, $\xi(t_k^+) = \lim_{t \rightarrow t_k^+} \xi(t)$. The matrices A and L are constant, and given by

$$A = \begin{bmatrix} -a_1 & 0 & 0 \\ b_1 & -a_2 & 0 \\ 0 & b_2 & -a_3 \end{bmatrix}, \quad L = [0 \ 0 \ 1],$$

where $a_1 > 0, a_2 > 0, a_3 > 0$ are distinct constants and $b_1 > 0, b_2 > 0$ are positive gains. The output of the system (1) is $z = L\xi = \xi_3$, which means that only the Te concentration is measurable. The gains and firing periods are given by $\lambda_k = \chi(z(t_k))$ and $T_k = \Phi(z(t_k))$, $k = 1, 2, \dots$, which reflect the impulsive amplitude and impulsive frequency, respectively. Note that both the impulsive amplitude and frequency are modulated by the measured output z . The amplitude modulation scalar function χ is nonincreasing and the frequency modulation scalar function Φ is nondecreasing for $z \geq 0$. In addition, due to physiological limitations [4], both χ and Φ are continuous and satisfy²

$$0 < \chi_1 \leq \chi(z) \leq \chi_2, \quad 0 < \Phi_1 \leq \Phi(z) \leq \Phi_2 \quad \forall z \in \mathbb{R}_{\geq 0}. \quad (2)$$

Note that the condition $\Phi(\cdot) \geq \Phi_1 > 0$ renders that the impulsive events satisfy $t_{k+1} - t_k = T_k \geq \Phi_1 > 0$ for all $k = 1, 2, \dots$, and, hence, Zeno solutions cannot occur.

The IGO in (1) lacks equilibria and has been proven to admit a unique periodic solution with one firing in each period for proper parameter values [4]. The model (1) is an impulsive system, and can exhibit complex dynamic behavior, such as motions of higher periodicity and deterministic chaos [7]. In recent years, the study of limit cycles and chaotic oscillations in the IGO system has received renewed attention, mainly due to the experimentally implemented fact in increasing Te levels through the amplitude and frequency of the GnRH pulses [8]. Churilov et al. deeply address the existence and stability problems of limit cycle in the IGO system in [4]. In addition to such biological applications, the analysis of limit cycles in impulsive systems are interesting from a theoretical viewpoint, because the interaction of con-

¹The instant caused by short release hormone pulses [6].

²Possible candidates for the nonlinearities are repressor-type Hill functions.

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tinuous and discrete dynamics in the system is parsimonious.

In spite of these advances, the study of robust stability of limit cycles for such systems has not received much attention, even though important applications in circadian rhythm [3] would benefit from results guaranteeing such properties. In addition, nonrobust oscillators against small disturbances may pose risk of solutions that are not periodic. The current literature pertains to nominal IGO systems given in the form of impulsive differential equations, leaving the question of whether it is possible to guarantee robustness to generic perturbations wide open.

Motivated by the work in [4], [9], our goal in this paper is to study robust stability of limit cycles for the IGO system. Specifically, in this work, the IGO system is modeled as a hybrid dynamical system following the hybrid systems framework in [10], [11], which is a broad modeling framework guaranteeing that asymptotic stability in hybrid systems is robust to small perturbations. For this class of systems, we introduce the definition of hybrid limit cycles and the properties (including compactness, forward invariance, and transversality) of hybrid limit cycles following the notions in [12]. Then, existence and stability of a hybrid limit cycle are guaranteed under mild assumptions on the amplitude and frequency modulation functions of the IGO system. In addition, we establish robustness of asymptotically stable hybrid limit cycles of the IGO to general perturbations. Finally, we present numerical simulations to confirm the analytical finds.

Notation. The set \mathbb{R}^n denotes the n -dimensional Euclidean space, $\mathbb{R}_{\geq 0}$ denotes the set of nonnegative real numbers, i.e., $\mathbb{R}_{\geq 0} := [0, +\infty)$, and \mathbb{N} denotes the set of natural numbers including 0, i.e., $\mathbb{N} := \{0, 1, 2, \dots\}$. Given a vector $x \in \mathbb{R}^n$, $|x|$ denotes its Euclidean norm. Given a function $f : \mathbb{R}^m \rightarrow \mathbb{R}^n$, its domain is denoted by $\text{dom } f$, i.e., $\text{dom } f := \{x \in \mathbb{R}^m : f(x) \text{ is defined}\}$. Given a closed set $\mathcal{A} \subset \mathbb{R}^n$ and a point $x \in \mathbb{R}^n$, $|x|_{\mathcal{A}} := \inf_{y \in \mathcal{A}} |x - y|$. Given a set $\mathcal{A} \subset \mathbb{R}^n$, $\overline{\mathcal{A}}$ (respectively, $\overline{\text{conv}} \mathcal{A}$) denotes its closure (respectively, its closed convex hull). The set \mathbb{B} denotes a closed unit ball in Euclidean space (of appropriate dimension) centered at zero. A function $\beta : \mathbb{R}_{\geq 0} \times \mathbb{R}_{\geq 0} \rightarrow \mathbb{R}_{\geq 0}$ belongs to class- \mathcal{KL} ($\beta \in \mathcal{KL}$) if for each $t \geq 0$, $\beta(\cdot, t)$ is nondecreasing and $\lim_{s \rightarrow 0^+} \beta(s, t) = 0$ and, for each $s \geq 0$, $\beta(s, \cdot)$ is nonincreasing and $\lim_{t \rightarrow \infty} \beta(s, t) = 0$.

II. HYBRID MODEL OF IMPULSIVE GOODWIN'S OSCILLATOR

A. Well-posed Hybrid Systems

We employ the hybrid systems framework in [10], [11] to model the IGO (1a)-(1b) as hybrid equations, given by

$$\mathcal{H} \begin{cases} \dot{x} &= f(x) & x \in C, \\ x^+ &= g(x) & x \in D, \end{cases} \quad (3)$$

where the map f and the set C define the continuous dynamics (or flows), and the map g and the set D define the discrete dynamics (or jumps); see [10], [11] for more details. In particular, the function $f : \mathbb{R}^n \rightarrow \mathbb{R}^n$ (respectively, $g : \mathbb{R}^n \rightarrow \mathbb{R}^n$) is a single-valued map describing the

continuous evolution (respectively, the discrete evolution) while $C \subset \mathbb{R}^n$ (respectively, $D \subset \mathbb{R}^n$) is the set on which the flow map f is effective (respectively, from which jumps can occur).

A solution to \mathcal{H} is parameterized by ordinary time t and a counter j for jumps. It is given by a hybrid arc $\phi : \text{dom } \phi \rightarrow \mathbb{R}^n$ that satisfies the dynamics of \mathcal{H} ; see [10], [11] for more details. A solution ϕ to \mathcal{H} is said to be complete if $\text{dom } \phi$ is unbounded. It is Zeno if it is complete and the projection of $\text{dom } \phi$ onto $\mathbb{R}_{\geq 0}$ is bounded. It is discrete if $\text{dom } \phi \subset \{0\} \times \mathbb{N}$. It is said to be maximal if it is not a (proper) truncated version of another solution. The set of maximal solutions to \mathcal{H} from the set K is denoted as

$$\mathcal{S}_{\mathcal{H}}(K) := \{\phi : \phi \text{ is a maximal solution to } \mathcal{H} \text{ with } \phi(0, 0) \in K\}.$$

We define $t \mapsto \phi^f(t, x_0)$ as a solution of the flow dynamics $\dot{x} = f(x)$ $x \in C$ from $x_0 \in C$. A hybrid system \mathcal{H} is said to be well-posed if it satisfies the *hybrid basic conditions*, namely,

- (A1) The sets $C, D \subset \mathbb{R}^n$ are closed.
- (A2) The flow map $f : C \rightarrow \mathbb{R}^n$ and the jump map $g : D \rightarrow \mathbb{R}^n$ are continuous.

B. Hybrid System Modeling of the IGO

Due to the impulsive behavior of the IGO (1), we define C, f, D , and g so that $\mathcal{H} = (C, f, D, g)$ provides a model of the IGO dynamics in (1), as follows.

To trigger state resets at time instants t_k , we employ a resettable timer taking values in $[0, \Phi_2]$. Specifically, we introduce the hybrid system

$$\begin{cases} \dot{\tau} &= -1 & \tau \in [0, \Phi_2] \\ \tau^+ &= \Phi(L\xi) & \tau = 0 \end{cases} \quad (4)$$

where the timer variable τ decreases during flow (solutions to $\dot{\tau} = -1$ decrease at unit rate when $\tau \in [0, \Phi_2]$), then triggers a jump once it reaches zero, and starts to decrease again from the state-dependent reset law $\Phi(L\xi)$ until it reaches zero again, and so on. Note that after being reset, τ is equal to the amount of time for the next jump. Moreover, the value of z after jumps is controlled by the frequency modulation function $\Phi : \mathbb{R}^n \rightarrow \mathbb{R}_{> 0}$; see the discussion below (1). Therefore, the impulsive events at $t = t_k$ in (1) are described by the dynamics of τ . Note that the initial condition $\tau(0, 0)$ affects the time t_1 . However, if the initial condition is properly chosen, then it is possible to have jump times coincide with the impulse times.

In between impulsive events, ξ evolves according to (1a). Then, the controlled dynamics of \mathcal{H} are

$$\begin{bmatrix} \dot{\xi} \\ \dot{\tau} \end{bmatrix} = f(\xi, \tau) := \begin{bmatrix} A\xi \\ -1 \end{bmatrix} \quad (\xi, \tau) \in C$$

where the flow set is $C := \{(\xi, \tau) \in \mathbb{R}_{\geq 0}^4 : \tau \in [0, \Phi_2]\}$.

The impulses $\xi(t_k^+) = \xi(t_k) + \lambda_k B$ are modeled as $\xi^+ = \xi + \chi(L\xi)B$, where ξ is the value of the state variables before the impulse and χ is given in (2). Including the reset of τ

in (4), the jump map g is defined as

$$g(\xi, \tau) := \begin{bmatrix} \xi + \chi(L\xi)B \\ \Phi(L\xi) \end{bmatrix} \quad \forall (\xi, \tau) \in D$$

where the jump set is $D := \{(\xi, \tau) \in \mathbb{R}_{\geq 0}^4 : \tau = 0\}$.

A hybrid system capturing the IGO (1a)-(1b) is given by

$$\mathcal{H}_{\text{IGO}} \begin{cases} \dot{x} = f(x) = \begin{bmatrix} A\xi \\ -1 \end{bmatrix} & (\xi, \tau) \in C \\ x^+ = g(x) = \begin{bmatrix} \xi + \chi(L\xi)B \\ \Phi(L\xi) \end{bmatrix} & (\xi, \tau) \in D \end{cases} \quad (5)$$

where $x = (\xi, \tau)$ denotes the system state, $A = \begin{bmatrix} -a_1 & 0 & 0 \\ b_1 & -a_2 & 0 \\ 0 & b_2 & -a_3 \end{bmatrix}$, $B = [1 \ 0 \ 0]^\top$, and $L = [0 \ 0 \ 1]$.

Remark 2.1: From the definition of f above, which is clearly continuously differentiable, the solutions to $\dot{x} = f(x)$ continuously depend on initial conditions. By the definitions of C and D in (5), the sets are clearly closed. By (4), given a solution x to \mathcal{H}_{IGO} in (5), whenever $\tau(t, j) = 0$ for some $(t, j) \in \text{dom } x$, τ is reset to $\Phi(L\xi(t, j))$, which, by (2), satisfies $\tau(t, j + 1) = \Phi(L\xi(t, j)) \geq \Phi_1 > 0$. Therefore, we have $g(D) \cap D = \emptyset$, which, by an application of [13, Lemma 2.7], guarantees that after each jump, the solutions are mapped to the flow set, and further flowing is possible from there.

The following assumption summarizes the conditions on the system parameters and the functions χ and Φ ; see [4].

Assumption 2.2: The data of the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5) satisfies the following properties:

- 1) the parameters a_1, a_2, a_3 are distinct and positive, and b_1, b_2 are positive;
- 2) both χ and Φ are continuous and satisfy (2);
- 3) $z \mapsto \chi(z)$ is nonincreasing and $z \mapsto \Phi(z)$ is nondecreasing.

In property 1) of Assumption 2.2, the parameters are positive because they represent real biological quantities like reaction rates and substance concentrations, which cannot be negative in biological contexts [15]. The boundedness in property 2) of Assumption 2.2, arises from physiological limitations [4]. Property 3) of Assumption 2.2 arises from fundamental molecular interactions with respect to the repressor concentration, ensuring the stable operation of biological systems.

C. Basic Properties of \mathcal{H}_{IGO}

The hybrid system \mathcal{H}_{IGO} satisfies the hybrid basic conditions (A1) and (A2) in Section II-A, and consequently, it possesses the property of sequential compactness of its solution space, which is needed for robustness [10].

Lemma 2.3: Let Assumption 2.2 hold. Then, the data of the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5) satisfies the hybrid basic conditions given by (A1)-(A2).

The property in (A1) is satisfied by the construction of C and D in (5). Next, the property in (A2) follows from the definition of $f(x) := (A\xi, -1)$, which is obviously continuous on C , and the property 2) in Assumption 2.2.

Lemma 2.4: Let Assumption 2.2 hold. Then, for the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5) and each initial condition in $C \cup D (= C)$, there exists a unique nontrivial solution to \mathcal{H}_{IGO} . In particular, every maximal solution ϕ to \mathcal{H}_{IGO} from $C \cup D$ is unique, complete, $\sup_t \text{dom } \phi = \infty$, $\sup_j \text{dom } \phi = \infty$, and, hence, nonZeno.

By using Lemma 2.3, existence of nontrivial solutions follows from an application of [10, Proposition 6.10]. In addition, it can be verified that every $\phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(C \cup D)$ is complete. The uniqueness of each maximal solution to \mathcal{H}_{IGO} follows from an application of [10, Proposition 2.11]. Moreover, by using the reset of τ in (4) and condition (2), the property $\sup_j \text{dom } \phi = \infty$ holds and one can rule out the existence of Zeno solutions. Finally, the property $\sup_t \text{dom } \phi = \infty$ also holds, since every $\phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(C \cup D)$ is complete and nonZeno.

The following result shows that solutions $\phi = (\phi_\xi, \phi_\tau)$ to (5) have ϕ_ξ nonnegative; namely, they are nonnegative [4].

Lemma 2.5: Let Assumption 2.2 hold. Each nontrivial solution ϕ to \mathcal{H}_{IGO} satisfies $\phi(t, j) \geq 0$ for all $(t, j) \in \text{dom } \phi$.

For each nontrivial solution ϕ to \mathcal{H}_{IGO} satisfying $\phi(0, 0) = (\xi(0, 0), \tau(0, 0)) \geq 0$, by using the expression of \mathcal{H}_{IGO} in (5), and computing $\exp(At)$ (using the theory of divided differences and the Opitz formula), one can derive an explicit expression of ϕ , guaranteeing that, for each $j \in \mathbb{N} \setminus \{0\}$ and each $t \geq 0$ such that $(t, j) \in \text{dom } \phi$, $\phi(t, j) \geq 0$ during flows and $\phi(t, j) > 0$ after each jump.

III. HYBRID LIMIT CYCLES AND BASIC PROPERTIES

A. Definitions

In this section, we use the notion of hybrid limit cycle in [12] for the system in (5) and, in the next section, reveal its basic properties.

Definition 3.1: (flow periodic solution) A complete solution ϕ^* to \mathcal{H}_{IGO} is *flow periodic with period T^* and one jump in each period* if $T^* \in (0, \infty)$ is the smallest number such that $\phi^*(t + T^*, j + 1) = \phi^*(t, j)$ for all $(t, j) \in \text{dom } \phi^*$.

The definition of a flow periodic solution ϕ^* with period T^* and one jump implies that if $(t, j) \in \text{dom } \phi^*$, then $(t + T^*, j + 1) \in \text{dom } \phi^*$. A flow periodic solution to \mathcal{H}_{IGO} generates a hybrid limit cycle.

Definition 3.2: (hybrid limit cycle) A flow periodic solution ϕ^* with period $T^* \in (0, \infty)$ and one jump in each period defines a *hybrid limit cycle*³ $\mathcal{O} := \{x \in \mathbb{R}^n : x = \phi^*(t, j), (t, j) \in \text{dom } \phi^*\}$.

To characterize hybrid limit cycles for hybrid system \mathcal{H}_{IGO} in (5), let ξ_3^* be the solution to

$$\xi_3 = \chi(\xi_3) b_1 b_2 \sum_{i=1}^3 \frac{\alpha_i}{e^{a_i \Phi(\xi_3)} - 1},$$

³Alternatively, the hybrid limit cycle \mathcal{O} can be written as $\{x \in \mathbb{R}^n : x = \phi^*(t, j), t \in [t_s, t_s + T^*], (t, j) \in \text{dom } \phi^*\}$ for some $t_s \in \mathbb{R}_{\geq 0}$.

where $\alpha_i = \prod_{r=1, r \neq i}^3 \frac{1}{a_r - a_i}$ for each $i \in \{1, 2, 3\}$. It follows that under Assumption 2.2, \mathcal{H}_{IGO} has a unique hybrid limit cycle \mathcal{O} with period given by $T^* = \Phi(\xi_3^*)$ and one jump per period. This property will be established in Theorem 4.1.

B. Basic Properties of Hybrid Limit Cycles for the Hybrid IGO

The following result shows that a hybrid limit cycle generated by flow periodic solutions as in Definition 3.2 is closed, bounded, and forward invariant. Note that such a hybrid limit cycle for the hybrid system \mathcal{H}_{IGO} does exist, as we will show in the next section.

Lemma 3.3: For the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5), suppose that Assumption 2.2 holds and \mathcal{H}_{IGO} has a hybrid limit cycle \mathcal{O} . Then, \mathcal{O} is compact and forward invariant⁴ for \mathcal{H}_{IGO} .

The following result establishes a transversality property of any hybrid limit cycle for \mathcal{H}_{IGO} , which follows from [12, Lemma 4.7].

Lemma 3.4: For the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5), suppose that Assumption 2.2 holds and \mathcal{H}_{IGO} has a hybrid limit cycle \mathcal{O} . Then, \mathcal{O} is transversal to D , i.e., \mathcal{O} intersects D at exactly one point $\bar{x} := \mathcal{O} \cap D$.

Following [14], let us introduce the *time-to-impact function* for hybrid dynamical systems in (5). The *time-to-impact function with respect to D* is defined by $T_I : C \cup D \rightarrow \mathbb{R}_{\geq 0} \cup \{\infty\}$, where⁵

$$T_I(x) := \inf\{t \geq 0 : \phi(t, j) \in D, \phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(x)\} \quad (6)$$

for each $x \in C \cup D (= C)$.

For the hybrid IGO in (5), the function $x \mapsto T_I(x)$ is continuous on a subset of $C \cup D$, as specified next.

Lemma 3.5: Let Assumption 2.2 hold. Then, T_I is continuous at points in $\mathcal{X} := \{x \in C : 0 < T_I(x) < \infty\}$.

IV. EXISTENCE OF HYBRID LIMIT CYCLES FOR \mathcal{H}_{IGO}

In this section, we present conditions for the existence of a hybrid limit cycle for the hybrid system in (5). For this purpose, we introduce the hybrid Poincaré map $P : D \rightarrow D$, which is given by

$$P(x) := \begin{cases} \phi(T_I(g(x)), j) & \phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(g(x)), \\ (T_I(g(x)), j) & (T_I(g(x)), j) \in \text{dom } \phi \end{cases} \quad (7)$$

for all $x \in D$. From the evolution of the hybrid dynamics of (5), for each $x = (\xi, \tau) \in D$, the hybrid Poincaré map P can be analytically obtained as

$$P(x) = \left(e^{A\Phi(L\xi)}(\xi + \chi(L\xi)B), 0 \right). \quad (8)$$

The following result provides sufficient conditions on the functions χ and Φ for the existence of a hybrid limit cycle for the hybrid IGO in (5).

Theorem 4.1: Let Assumption 2.2 hold. Then, \mathcal{H}_{IGO} in (5) has a unique hybrid limit cycle \mathcal{O} with period given by $T^* = \Phi(\xi_3^*)$ and one jump per period, where ξ_3^* is the solution to

$$\xi_3 = \chi(\xi_3) b_1 b_2 \sum_{i=1}^3 \frac{\alpha_i}{e^{a_i \Phi(\xi_3)} - 1}, \quad (9)$$

where, for each $i \in \{1, 2, 3\}$, $\alpha_i = \prod_{q=1, q \neq i}^3 \frac{1}{a_q - a_i}$.

It can be shown that (9) is equivalent to $\xi_3 = V(\xi_3)$, where $V(\xi_3) := L\chi(\xi_3)(e^{-A\Phi(\xi_3)} - I)^{-1}B$. It follows from the proof of [4, Theorem 1] that a unique solution ξ_3^* to $\xi_3 = V(\xi_3)$ exists.

Next, we show that the function $x \mapsto T_I(x)$ is also continuous on a subset of \mathcal{O} . By Theorem 4.1, \mathcal{H}_{IGO} has a unique hybrid limit cycle \mathcal{O} with period given by some $T^* > 0$ and one jump per period. Therefore, the conclusion follows directly from [12, Lemma 4.9].

Lemma 4.2: Let Assumption 2.2 hold. Then, T_I is continuous on $\mathcal{O} \setminus \{\phi^*(t^*, 0)\}$, where $\mathcal{O} \subset C$ defined by a flow periodic solution ϕ^* and t^* is such that $(t^*, 0), (t^*, 1) \in \text{dom } \phi^*$, namely, $(t^*, 0)$ is a jump time of ϕ^* and $\phi^*(t^*, 0)$ is the point in D at which ϕ^* jumps.

Remark 4.3: Following [9, Proposition 2], if the amplitude and frequency modulation functions are set to be constant, that is, $\chi(L\xi) := \lambda > 0$ and $\Phi(L\xi) := T > 0$, a unique fixed point of the map (8) exists. In particular, the fixed point is given as $x^* = (\lambda(e^{-AT} - I)^{-1}B, 0)$. Then, a hybrid limit cycle with period given by T and one jump per period is uniquely defined by the fixed point. Therefore, as stated in [9], the parameters of the matrix A , λ and T can determine a hybrid limit cycle in (5). However, from [9, Proposition 2], it is unknown whether the hybrid limit cycle is stable or not. In existing low-order hormone regulation models, lack of (robustly) stable flow periodic solutions is a main shortcoming. Therefore, we will discuss the asymptotic stability of the hybrid limit cycles of the hybrid IGO in (5) next, which serves as the basis for the robustness investigations that follow.

V. STABILITY OF HYBRID LIMIT CYCLES FOR \mathcal{H}_{IGO}

In this section, we present stability properties of hybrid limit cycles for the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5). To this end, we employ the hybrid Poincaré map in (7). Let P^k denote k compositions of P with itself; namely, $P^k(x) = \underbrace{P \circ P \cdots \circ P}_k(x)$. The following stability notions involving P come from [12]. A point q is a fixed point of a hybrid Poincaré map $P : D \rightarrow D$ if $q = P(q)$.

Definition 5.1: A fixed point x^* of a hybrid Poincaré map $P : D \rightarrow D$ defined in (7) is said to be

- *stable* if for each $\varepsilon > 0$ there exists $\delta > 0$ such that for each $x \in D$, $|x - x^*| \leq \delta$ implies $|P^k(x) - x^*| \leq \varepsilon$ for all $k \in \mathbb{N}$;

⁴Every $\phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(\mathcal{O})$ is complete and satisfies $\text{rge } \phi \subset \mathcal{O}$.

⁵In particular, when there does not exist $t \geq 0$ such that $\phi^f(t, x) \in D$, we have $\{t \geq 0 : \phi^f(t, x) \in D\} = \emptyset$, which gives $T_I(x) = \infty$.

- *locally attractive* if there exists $\mu > 0$ such that, for each $x \in D$, $|x - x^*| \leq \mu$ implies $\lim_{k \rightarrow \infty} P^k(x) = x^*$;
- *locally asymptotically stable* if it is both stable and locally attractive.

Next, following the stability notion introduced in [10, Definition 3.6] for general hybrid systems, we employ the following stability notion for hybrid limit cycles.

Definition 5.2: Consider the hybrid system $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$ in (5). Then, the hybrid limit cycle \mathcal{O} is said to be

- *stable* for \mathcal{H}_{IGO} if for every $\varepsilon > 0$ there exists $\delta > 0$ such that every solution ϕ to \mathcal{H}_{IGO} with $|\phi(0, 0)|_{\mathcal{O}} \leq \delta$ satisfies $|\phi(t, j)|_{\mathcal{O}} \leq \varepsilon$ for each $(t, j) \in \text{dom } \phi$;
- *locally attractive* for \mathcal{H}_{IGO} if there exists $\mu > 0$ such that every maximal solution ϕ to \mathcal{H}_{IGO} starting from $|\phi(0, 0)|_{\mathcal{O}} \leq \mu$ is complete and satisfies $\lim_{t+j \rightarrow \infty} |\phi(t, j)|_{\mathcal{O}} = 0$;
- *locally asymptotically stable* for \mathcal{H}_{IGO} if it is both stable and locally attractive.

Given $\mathcal{H}_{\text{IGO}} = (C, f, D, g)$, for each $x \in C \cup D$, define the “distance” function $d : C \cup D \rightarrow \mathbb{R}_{\geq 0}$ as

$$d(x) := \sup_{t \in [0, T_I(x)] \cap \mathbb{R}_{\geq 0}, (t, j) \in \text{dom } \phi, \phi \in \mathcal{S}_{\mathcal{H}_{\text{IGO}}}(x)} |\phi(t, j)|_{\mathcal{O}}$$

where T_I is the time-to-impact function defined in (6). Note that d vanishes on \mathcal{O} . Then, following [12, Lemma 6.2], the following property of the function d can be established for the hybrid IGO in (5).

Lemma 5.3: Let Assumption 2.2 hold. Then, the function $d : C \rightarrow \mathbb{R}_{\geq 0}$ is well-defined and continuous on \mathcal{O} , where $\mathcal{O} \subset C$ is the unique hybrid limit cycle of \mathcal{H}_{IGO} in (5), generated by a flow periodic solution ϕ^* .

Following the elegant result on orbital asymptotic stability of 1-cycle established in [4, Theorem 2], a sufficient condition for the stability of the hybrid limit cycle of the hybrid IGO identified by Theorem 4.1 is established next.

Theorem 5.4: Suppose that Assumption 2.2 holds and that χ, Φ have continuous derivatives. Let $x^* = (\xi^*, \tau^*) \in D$ be the unique fixed point of the hybrid Poincaré map P in (8). If the Jacobian of $Q(\xi) := e^{A\Phi(L\xi)}(\xi + \chi(L\xi)B)$ at ξ^* , given by

$$\mathbb{J}_Q(\xi^*) = e^{A\Phi(\xi_3^*)} \left(I + \chi'(\xi_3^*)BL \right) + \Phi'(\xi_3^*)AQ(\xi^*)L \quad (10)$$

is Schur stable, where $\chi'(\xi_3^*) = \frac{d\chi}{d\xi_3} \Big|_{\xi_3=\xi_3^*}$, $\Phi'(\xi_3^*) = \frac{d\Phi}{d\xi_3} \Big|_{\xi_3=\xi_3^*}$, and $L\xi = [0 \ 0 \ 1]\xi = \xi_3$, then the hybrid limit cycle \mathcal{O} of \mathcal{H}_{IGO} in (5) generated by a flow periodic solution ϕ^* with period $T^* = \Phi(\xi_3^*)$ from $\phi^*(0, 0) = x^*$ is locally asymptotically stable for \mathcal{H}_{IGO} .

In fact, using (5), for solutions initialized at $x(0, 0) = (\xi^*, 0) \in D$, the unique hybrid limit cycle can be characterized as $\mathcal{O} = \{x \in C \cup D : x = e^{At}(\xi^* + \chi(\xi_3^*)B), t \in [0, \Phi(\xi_3^*)]\}$.

VI. ROBUSTNESS OF ASYMPTOTICALLY STABLE HYBRID LIMIT CYCLES

Biological regulation is an intrinsically noisy process, as it is subject to intracellular and extracellular noise perturbations and environment fluctuations [16]. To assess the effect of noise, we study the behavior of the Goodwin’s oscillator system under the influence of unmodeled dynamics and additive perturbations. In particular, when the GnRH pulses are fired and communicate their amplitudes, the pulse-modulated feedback is accomplished through measuring the Te concentration $L\xi(t) = \xi_3(t)$. In the presence of measurement noise, the impulse sequence and the GnRH amplitude will influence the state at jumps. This effect will be captured by perturbations in the jump map g .

The hybrid system \mathcal{H}_{IGO} with the perturbations mentioned above results in

$$\tilde{\mathcal{H}}_{\text{IGO}} \begin{cases} \dot{x} &= f(x) + d_1 & x \in C, \\ x^+ &= g(x + d_2) + d_3 & x \in D, \end{cases} \quad (11)$$

where $d_1 = (d_{1,\xi}, 0)$ and $d_3 = (d_{3,\xi}, 0)$ capture unmodeled dynamics or additive perturbations, and $d_2 = (d_{2,\xi}, 0)$ corresponds to state noise or measurement noise. The perturbations d_i ($i = 1, 2, 3$) might be state or hybrid time dependent, but are assumed to have Euclidean norm bounded by $\bar{M}_i \geq 0$ ($i = 1, 2, 3$), and to be admissible, namely, $\text{dom } d_i$ ($i = 1, 2, 3$) is a hybrid time domain and the function $t \mapsto d_i(t, j)$ is measurable on $\text{dom } d_i \cap (\mathbb{R}_{\geq 0} \times \{j\})$ for each $j \in \mathbb{N}$. When considering perturbations, it is important to note that the perturbations typically act on the system states that are part of the physical processes being modeled. However, since the timer variable τ is manually introduced to facilitate the analysis of the IGO system (1) within the hybrid systems framework, there is no need to consider disturbances acting on the timer variable itself.

The following result establishes that the stability of \mathcal{O} for \mathcal{H}_{IGO} is robust to the class of perturbations defined above.

Theorem 6.1: Suppose that Assumption 2.2 holds and that χ, Φ have continuous derivatives. Let $x^* = (\xi^*, \tau^*) \in D$ be the fixed point of the hybrid Poincaré map P in (8) and \mathcal{O} be the hybrid limit cycle of \mathcal{H}_{IGO} generated by a flow periodic solution ϕ^* with period $T^* = \Phi(\xi_3^*)$ from $\phi^*(0, 0) = x^*$. If the Jacobian of $Q(\xi) := e^{A\Phi(L\xi)}(\xi + \chi(L\xi)B)$ at ξ^* , given by $\mathbb{J}_Q(\xi^*) = e^{A\Phi(\xi_3^*)} \left(I + \chi'(\xi_3^*)BL \right) + \Phi'(\xi_3^*)AQ(\xi^*)L$ is Schur stable, where $\chi'(\xi_3^*) = \frac{d\chi}{d\xi_3} \Big|_{\xi_3=\xi_3^*}$, $\Phi'(\xi_3^*) = \frac{d\Phi}{d\xi_3} \Big|_{\xi_3=\xi_3^*}$, and $L\xi = [0 \ 0 \ 1]\xi = \xi_3$, then for every proper indicator ω of \mathcal{O} on the basin of attraction $\mathcal{B}_{\mathcal{O}}$ of the set \mathcal{O} , there exists $\tilde{\beta} \in \mathcal{KL}$ such that for every $\varepsilon > 0$ and every compact set $K \subset \mathcal{B}_{\mathcal{O}}$, there exist $\bar{M}_i > 0$, $i \in \{1, 2, 3\}$, such that for any admissible perturbations d_i , $i \in \{1, 2, 3\}$, with Euclidean norm bounded by \bar{M}_i , respectively, every solution $\tilde{\phi}$ to $\tilde{\mathcal{H}}_{\text{IGO}}$ with $\tilde{\phi}(0, 0) \in K$ satisfies

$$\omega(\tilde{\phi}(t, j)) \leq \tilde{\beta}(\omega(\tilde{\phi}(0, 0)), t + j) + \varepsilon \quad \forall (t, j) \in \text{dom } \tilde{\phi}.$$

VII. SIMULATION RESULTS

In this section, we validate numerically the results in previous sections. We consider the set of parameters used in

the model of GnRH-LH-Te axis in [4]. The numerical values in the matrices defining the dynamics of the IGO system (1) are as follows: $b_1 = 2.0$, $b_2 = 0.5$, $a_1 = 0.03$, $a_2 = 0.15$, and $a_3 = 0.2$. Following [4], the modulation functions Φ and χ are given by the Hill functions

$$\begin{cases} \Phi(z) &= k_1 + k_2 \frac{(z/h)^2}{1 + (z/h)^2} \\ \chi(z) &= k_3 + \frac{k_4}{1 + (z/h)^2} \end{cases} \quad (12)$$

with $h = 2.7$, $k_1 = 60$, $k_2 = 40$, $k_3 = 3$ and $k_4 = 2$.

It can be verified that Assumption 2.2 holds with the above numerical values and the functions in (12). By Theorem 4.1, the hybrid system \mathcal{H}_{IGO} in (5) has a unique hybrid limit cycle \mathcal{O} with period $T^* \approx 96.71$ min and one jump in each period. The Jacobian of $Q(\xi) := e^{A\Phi(L\xi)}(\xi + \chi(L\xi)B)$ at $\xi^* \approx (0.184, 3.066, 9.019)$,⁶ given by (10). For the chosen parameters, it evaluates to

$$\begin{aligned} \mathbb{J}_Q(\xi^*) &= e^{A\Phi(L\xi^*)} \left(I + \nabla\chi(\xi_3^*)BL \right) + \nabla\Phi(\xi_3^*)AQ(\xi^*)L \\ &\approx \begin{bmatrix} 0.0550 & 0 & -0.0055 \\ 0.9159 & 0 & -0.0923 \\ 2.6936 & 0 & -0.2713 \end{bmatrix}, \end{aligned} \quad (13)$$

which is Schur stable since its eigenvalues are $\lambda_1 = -0.2164$ and $\lambda_{2,3} = 0$. According to Theorem 5.4, the hybrid limit cycle \mathcal{O} of \mathcal{H}_{IGO} generated by the solution ϕ^* is locally asymptotically stable. The behavior of the system with the initial condition $\xi(0, 0) = (2.2, 25, 20)$ is shown in Fig. 1. One may see that the solution converges to a hybrid limit cycle \mathcal{O} .

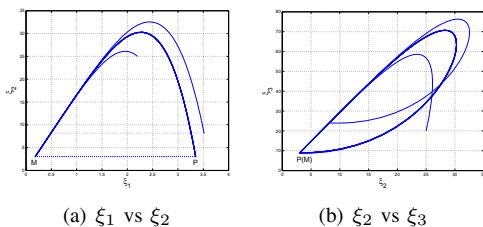


Fig. 1. Trajectories of the IGO system (1) with initial condition $(2.2, 25, 20)$, denoted by $\xi(0, 0)$.

Finally, we illustrate Theorem 6.1 for the hybrid system \mathcal{H}_{IGO} by plotting the solutions from the initial condition $(3.348, 3.066, 9.019)$, when an additive perturbation d_1 affects the jump map. We consider two cases: **Case I**: the noise is injected as an additive perturbation on the jump map as $d_3 = (\rho \sin(t), 0, 0)$; **Case II**: the noise is injected as an additive perturbation on the flow map as $d_1 = (\rho \sin(t), 0, 0)$, where a variety of values for ρ are used to verify robustness for both cases. Simulations are performed to quantify the relationship between ρ^* (the maximal value of the perturbation parameter ρ) and ε (the desired level of closeness to \mathcal{O}). Given a compact set $K := [3, 4] \times [4, 5] \times [5, 7] \times \{50\}$, and different desired region radiuses $\varepsilon \in \{0.10, 0.15, 0.20, 0.25, 0.30\}$, the simulation results for **Case I** indicate that the relationship between ρ^* and ε can

⁶The fixed point ξ^* is obtained by numerically solving $\xi = Q(\xi)$. Here, since the fixed point τ^* is 0, we consider Q instead of the map P in (8).

be approximated as $\rho^* \approx 0.044\varepsilon$. Given different desired region radiuses $\varepsilon \in \{0.05, 0.10, 0.15, 0.20\}$, the simulation results for **Case II** indicate that the relationship between ρ^* and ε can be approximated as $\rho^* \approx 0.42\varepsilon$. As it can be seen, the larger admissible convergence error ε the larger the perturbation parameter ρ^* can be. This study validates Theorem 6.1.

VIII. CONCLUSION

Robust stability of hybrid limit cycles in the IGO system was analyzed from a hybrid systems perspective. The IGO system was reformulated as a well-posed hybrid model and sufficient conditions were established for the existence and asymptotic stability of hybrid limit cycles. Comparing to previous results in the literature, we established conditions for robustness of hybrid limit cycles with respect to small perturbations, which were not available before. To illustrate our theoretical results, numerical simulations in a hybrid systems simulator were performed. Future work in this line includes extending the proposed approach to the analysis of hybrid limit cycles in the IGO with delays and pulse-coupled Goodwin oscillator networks.

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