Dynamical Properties of a Two-gene Network with Hysteresis

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Dynamical Properties of a Two-gene Network with Hysteresis

Qin Shu and Ricardo G. Sanfelice*

October 30, 2018

Abstract

A mathematical model for a two-gene regulatory network is derived and several of their properties analyzed. Due to the presence of mixed continuous/discrete dynamics and hysteresis, we employ a hybrid systems model to capture the dynamics of the system. The proposed model incorporates binary hysteresis with different thresholds capturing the interaction between the genes. We analyze properties of the solutions and asymptotic stability of equilibria in the system as a function of its parameters. Our analysis reveals the presence of limit cycles for a certain range of parameters, behavior that is associated with hysteresis. The set of points defining the limit cycle is characterized and its asymptotic stability properties are studied. Furthermore, the stability property of the limit cycle is robust to small perturbations. Numerical simulations are presented to illustrate the results.

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Contents

1 Introduction 3
  1.1 Mathematical modeling of genetic regulatory networks .................................. 3
  1.2 The role of hysteresis in genetic regulatory networks ..................................... 3
  1.3 Contributions and organization of the paper .................................................... 3

2 A Hybrid Model for Genetic Networks w/Hysteresis 4
  2.1 Introduction to Hybrid System Modeling ....................................................... 6
  2.2 Modeling of a Two-Gene Network ................................................................. 7

3 Dynamical Properties of the Two-Gene Hybrid System Model 10
  3.1 Existence of solutions ....................................................................................... 10
  3.2 Characterization of equilibria .......................................................................... 11
  3.3 Stability analysis ............................................................................................. 15
    3.3.1 Asymptotic stability of isolated equilibrium points .................................. 15
    3.3.2 Stability properties of the limit cycle ....................................................... 15
  3.4 Robustness properties ...................................................................................... 20

4 Numerical results 21
  4.1 Isolated equilibrium points in Table I ............................................................. 21
    4.1.1 Case 1 of Table I ....................................................................................... 21
    4.1.2 Case 2 of Table I ....................................................................................... 22
    4.1.3 Case 3 of Table I ....................................................................................... 23
    4.1.4 Case 4 of Table I ....................................................................................... 24
  4.2 Equilibrium set S .............................................................................................. 25

5 Conclusion 31

A
  A.1 Proof of Proposition 3.3 .................................................................................... 34
  A.2 Proof of Proposition 3.1 .................................................................................... 40
  A.3 Proof of Proposition 3.5 .................................................................................... 44
  A.4 Proof of Proposition 3.6 .................................................................................... 52
1 Introduction

1.1 Mathematical modeling of genetic regulatory networks

In recent years, the development of advanced experimental techniques in molecular biology has led to a growing interest in mathematical modeling methods for the study of genetic regulatory networks; see [1] for a literature review. A number of gene regulatory network models have been proposed to capture their main properties [2], [3], [4], [5], [6], [7], [8]. Boolean models capture the dynamics of the discrete switch in genetic networks. As introduced by Glass and Kauffman in [3], Boolean regulation functions, typically modeled as sigmoidal or step functions, can be combined with linear system models to enforce certain logic rules. The properties of such a class of piecewise linear models have been studied in the mathematical biology literature, e.g., [4], [5], [2], [6]. Snoussi presented a discrete mapping approach in [4] to study the qualitative properties of the dynamics of genetic regulatory networks. In this work, the properties of the discrete mapping were studied to determine stable isolated steady states as well as limit cycles. In [5], Gouzé and Sari employ the concept of Filippov solution to study piecewise linear models of genetic regulatory networks with discontinuities occurring on hyperplanes defined by thresholds on the variables. Chaves and coauthors [2] studied the robustness of Boolean models of gene control networks. de Jong and coauthors [6] presented a method for qualitative simulation of genetic regulatory networks based on the piecewise linear model of [3]. Genetic regulatory networks with continuous dynamics coupled with switching can be written as a hybrid system. In [7] and [8], the authors apply hybrid systems tools to model a variety of cell biology problems. More recently, hybrid models have been used in [9] for the study of molecular interactions. It is important to note that hysteresis behavior, which is typically present in genetic regulatory networks, has not been considered in the models mentioned above.

1.2 The role of hysteresis in genetic regulatory networks

Hysteresis is an important phenomenon in genetic regulatory networks. It is characterized by behavior in which, for instance, once a gene has been inhibited due to the concentration of cellular protein reaching a particularly low value, a higher value of cellular protein concentration is required to express it. In his survey paper on the impact of genetic modeling on tumorigenesis and drug discovery [10], Huang stated that “hysteresis is a feature that a synthetic model has to capture.” Through experiments, Das and coauthors [11] demonstrated the existence of hysteresis in lymphoid cells and the interaction of continuous evolution of some cellular proteins. Hysteresis was also found to be present in mammalian genetic regulatory networks; see, e.g., [12], [13]. More importantly, it has been observed that hysteresis is a key mechanism contributing to oscillatory behavior in computational biological models [14], [15]. On the other hand, it is well known that hysteresis is one of the key factors that makes a system robust to noise and parametric uncertainties [16], [17].

1.3 Contributions and organization of the paper

Our work is motivated by the following facts:

3
1. Piecewise linear models do not incorporate hysteresis, although it plays a key role in the dynamics of genetic regulatory networks. In fact, as we establish in this paper, hysteresis leads to oscillatory, robust behavior in two-gene networks.

2. The discontinuities introduced by the Boolean regulation functions yield a non-smooth dynamical system, for which classical analysis tools cannot be applied to study existence of solutions, stability, robustness, etc.

Motivated by these two limitations, we propose a hybrid system model that captures both continuous and discrete dynamics of genetic regulatory networks with hysteresis behavior. We combine the methodology of piecewise linear modeling of genetic regulatory networks with the framework of hybrid dynamical systems in [18], and construct a hybrid system model for a genetic network with two genes. Our model incorporates hysteresis explicitly, which we found leads to limit cycles. We prove existence of solutions and compute the equilibrium points in terms of parameters for the system. We analyze the stability of the isolated equilibrium points and determined conditions under which a limit cycle exists. It is found that hysteresis is the key mechanism leading to hysteresis, as without hysteresis, the limit cycle converges to an isolated equilibrium point (cf. [4]). The stability of the limit cycle is established using a novel approach consisting of measuring distance between solutions of hybrid systems (rather than the distance to the limit cycle as in classical continuous-time systems). Moreover, we show that the asymptotic stability of the limit cycle is robust to small perturbations.

The remainder of this paper is organized as follows. In Section 2, a mathematical framework of hybrid dynamical system is introduced and then applied to model a two-gene network. The analysis of existence of solutions, stability, and robustness are presented in Section 3. Section 4 presents simulations validating our results.

2 A Hybrid Systems Model for Genetic Regulatory Networks with Hysteresis

Models of genetic regulatory networks given by piecewise-linear differential equations have been proposed in [8], [19]. Such models take the form

\[ \dot{x} = f(x) - \gamma x, \quad x \geq 0, \]  

(1)

where \( x = [x_1, x_2, \ldots, x_n]^\top \) and \( x_i \) represents the concentration of the protein in the \( i \)-th cell, \( f = [f_1, f_2, \ldots, f_n]^\top \) is a function, \( \gamma = [\gamma_1, \gamma_2, \ldots, \gamma_n]^\top \) is a vector of constants, and \( 1 \leq i \leq n \). For each \( i \), \( f_i \) is a function representing the rate of synthesis, while \( \gamma_i \) represents the degradation rate constant of the protein. The function \( f_i \) is typically defined as the linear combination

\[ f_i(x) = \sum_{\ell \in L} k_{i\ell} b_{i\ell}(x) \]

where \( k_{i\ell} \) is the nonzero and nonnegative growth rate constants, \( b_{i\ell} \) is a Boolean regulation function that describes the gene regulation logic, and \( L = \{1, 2, \ldots, n\} \) is the set of indices of regulation functions.

The modeling strategy for the Boolean regulation functions \( b_{i\ell} \) is a key element that captures the behavior of a particular genetic regulatory network. A major feature of a

\footnote{The notation \( x \geq 0 \) is equivalent to \( x_i \geq 0 \) for each \( i \).}
genetic regulatory network is the presence of threshold-like relationships between the system variables, i.e., if a variable $x_i$ is above (or below) a certain level, it could cause little or no effect on another variable $x_j$, whereas if $x_i$ is below (or above) this certain value, the effect on $x_j$ would become more significant (for example, it may increase the value of $x_j$ or inhibit the growth of the value of $x_j$). Boolean regulation functions can be modeled by sigmoidal or step functions, an approach that was first proposed by Glass and Kauffman [3]. When modeling as a step function, the functions $b_{i\ell}$ are given by the combination (linear or nonlinear) of

$$s^+(x_i, \theta) = \begin{cases} 1 & \text{if } x_i \geq \theta \\ 0 & \text{if } x_i < \theta \end{cases}, \quad s^-(x_i, \theta) = 1 - s^+(x_i, \theta),$$

(2)

where $s^+(x_i, \theta)$ represents the logic for gene expression when the protein concentration exceeds a threshold $\theta$, while $s^-(x_i, \theta)$ represents the logic for gene inhibition.

To illustrate this modeling approach, let us consider the genetic regulatory network shown in Figure 1. Genes $a$ and $b$ encode proteins $A$ and $B$, respectively. When the concentration of protein $A$ is below certain threshold, it will inhibit gene $b$. Similarly, protein $B$ inhibits gene $a$ when the concentration of protein $B$ is above certain threshold. In this way, a set of piecewise-linear differential equations representing the behavior in Figure 1 is given by

$$\dot{x}_1 = k_1 s^-(x_2, \theta_2) - \gamma_1 x_1, \quad \dot{x}_2 = k_2 s^+(x_1, \theta_1) - \gamma_2 x_2,$$

(3)

where $x_1$ is representing the concentration of protein $A$, while $x_2$ is the concentration of protein $B$. The constants $\theta_1$, $\theta_2$ are the thresholds associated with concentrations of protein $A$ and $B$, respectively.

![Figure 1: A genetic regulatory network of two genes (a and b), each encoding for a protein (A and B). Lines ending in arrows represent genetic expression triggers, while lines ending in flatheads refer to genetic inhibition triggers.](image)

In this model, gene $a$ is expressed at a rate $k_1$ when $x_2$ is below the threshold $\theta_2$. Similarly, gene $b$ is expressed at a rate $k_2$ when $x_1$ is above the threshold $\theta_1$. Degradations of both proteins are assumed to be proportional to their own concentrations, a mechanism that is captured by $-\gamma_1 x_1$ and $-\gamma_2 x_2$, respectively.

Note that the model in (3) capturing the interaction between gene $a$ and gene $b$ does not incorporate binary hysteresis. Furthermore, due to the discontinuities introduced by the Boolean regulation functions, it is not straightforward to argue that solutions to (3) exist.
from every initial value of $x$. In order to overcome such limitations, we propose a hybrid system with hysteresis for this two gene genetic regulatory network, to which hybrid systems tools for analysis of existence of solutions and asymptotic stability can be applied.

2.1 Introduction to Hybrid System Modeling

Following [18] and [20], a hybrid system in this paper is defined by four objects:

- A set $C \subset \mathbb{R}^n$, called the flow set.
- A set $D \subset \mathbb{R}^n$, called the jump set.
- A single-valued mapping $F: \mathbb{R}^n \to \mathbb{R}^n$, called the flow map.
- A set-valued mapping $G: \mathbb{R}^n \rightrightarrows \mathbb{R}^n$, called the jump map.

The flow map $F$ defines the continuous dynamics on the flow set $C$, while the jump map $G$ defines the discrete dynamics or jumps on the jump set $D$. These objects are referred to as the data of the hybrid system $\mathcal{H}$. Then, defining $z \in \mathbb{R}^n$ to be the state of the system, $\mathcal{H}$ can be written in the compact form

$$\mathcal{H}: \begin{cases} \dot{z} = F(z) & z \in C \\ z^+ \in G(z) & z \in D \end{cases}$$

Solutions to hybrid systems are given by hybrid arcs which are trajectories defined on hybrid time domains.

**Definition 2.1 (hybrid time domain)** A set $E$ is a hybrid time domain if for all $(T, J) \in E, E \cap ([0, T] \times \{0, 1, \ldots, J\})$ is a compact hybrid time domain; that is, it can be written as $\bigcup_{j=0}^{J-1}([t_j, t_{j+1}], j)$ for some finite sequence of times $0 \leq t_0 \leq t_1 \leq \ldots \leq t_J$.

**Definition 2.2 (hybrid arc)** A hybrid arc $\phi$ is a function that takes values from $\mathbb{R}^n$, is defined on a hybrid time domain $\text{dom} \phi$, and is such that $t \mapsto \phi(t, j)$ is locally absolutely continuous for every $j$, $(t, j) \in \text{dom} \phi$.

Hybrid time domains impose a specific structure on the domains of solutions to hybrid systems. In simple words, solutions to $\mathcal{H}$ are defined on intervals of flow $[t_j, t_{j+1}]$ indexed by the jump time $j$ when $t_{j+1} > t_j$. Hybrid arcs specify the functions that define solutions to hybrid systems when the following conditions are satisfied. We refer the reader to [20] [18] for more details on the definition of solutions to hybrid systems.

**Definition 2.3 (solution)** A hybrid arc $\phi$ is a solution to the hybrid system $\mathcal{H}$ if $\phi(0, 0) \in C \cup D$ and

1. For all $j \in \mathbb{N} := \{0, 1, 2, \ldots\}$ and almost all $t$ such that $(t, j) \in \text{dom} \phi$,
   $$\phi(t, j) \in C, \quad \phi(t, j) = F(\phi(t, j))$$

2. For all $(t, j) \in \text{dom} \phi$ such that $(t, j + 1) \in \text{dom} \phi$,
   $$\phi(t, j) \in D, \quad \phi(t, j + 1) \in G(\phi(t, j))$$

6
Solutions to hybrid systems are classified as follows:

- A solution $\phi$ to $\mathcal{H}$ is said to be nontrivial if $\text{dom} \phi$ contains at least two points.
- A solution $\phi$ to $\mathcal{H}$ is said to be complete if $\text{dom} \phi$ is unbounded.
- A solution $\phi$ to $\mathcal{H}$ is said to be Zeno if it is complete and the projection of $\text{dom} \phi$ onto $\mathbb{R}^n_{\geq 0}$ is bounded.
- A solution $\phi$ to $\mathcal{H}$ is said to be maximal if there does not exist another solution $\varphi$ to $\mathcal{H}$ such that $\text{dom} \varphi$ is a proper subset of $\text{dom} \phi$, and $\varphi(t, j) = \phi(t, j)$ for all $(t, j) \in \text{dom} \phi$.

The reader is referred to [18] and [20] for more details on this hybrid system framework.

2.2 Modeling of a Two-Gene Network

To model the genetic network in (3) as a hybrid system $\mathcal{H}$, two discrete logic variables, $q_1$ and $q_2$, are introduced. The dynamics of these variables depend on the thresholds, $\theta_1$ and $\theta_2$, respectively. As one of our goals is to introduce binary hysteresis in the model in (3), we define hysteresis level constants $h_1$ and $h_2$ associated with gene $a$ and gene $b$, respectively. In this way, $q_i$ is governed by dynamics such that the evolution in Figure 2 holds.

![Figure 2: The update mechanism of $q_i$ as a function of $x_i$ and previous values of $q_i$.](image)

The state of the hybrid system is defined as

$$z = [x_1, x_2, q_1, q_2]^T,$$

where $z \in \mathcal{Z} := \mathbb{R}^2_{\geq 0} \times \{0, 1\}^2$; $x_1, x_2$ are (nonnegative) continuous states representing protein concentrations; and $q_1, q_2$ are discrete variables. Here, $\mathbb{R}_{\geq 0} := [0, +\infty)$. We specify constants $\theta_1$ and $\theta_2$, usually inferred from biological data, satisfying $0 < \theta_1 < \theta_1^{\text{max}}, 0 < \theta_2 < \theta_2^{\text{max}}$, where $\theta_1^{\text{max}}$ and $\theta_2^{\text{max}}$ are the maximal value of the concentration of protein $A$ and of the protein $B$, respectively.

To define the continuous dynamics of the hybrid system capturing the evolution of (3), we rewrite the piecewise-linear differential equation (3) by replacing the $s^+$ term with the
logic variables $q_i$, and the $s^-$ term with the complement of the logic variable $q_i$, i.e., $1 - q_i$. Note that the discrete logic variables $q_i$ only change at jumps, i.e., they are constants during flows. Then, $\dot{q}_i = 0$. In this way, the continuous dynamics are governed by the differential equation

$$\begin{align*}
\dot{x}_1 &= k_1(1 - q_2) - \gamma_1 x_1, \\
\dot{x}_2 &= k_2 q_1 - \gamma_2 x_2, \\
\dot{q}_1 &= \dot{q}_2 = 0,
\end{align*}$$

from where we obtain the flow map

$$F(z) = \begin{bmatrix} k_1(1 - q_2) - \gamma_1 x_1 \\ k_2 q_1 - \gamma_2 x_2 \\ 0 \\ 0 \end{bmatrix}.$$  \hfill (4)

Now, we describe the discrete update of the state vector $z$, i.e., we define $G$ and $D$. To illustrate this construction, we explain how to model the mechanism in Figure 2 for $q_1$. When

$$q_1 = 0 \quad \text{and} \quad x_1 = \theta_1 + h_1$$

the state $q_1$ is updated to 1. We write this update law as

$$q_1^+ = 1.$$  \hfill (5)

When

$$q_1 = 1 \quad \text{and} \quad x_1 = \theta_1 - h_1,$$

then the state $q_1$ is updated to 0, i.e.,

$$q_1^+ = 0.$$  \hfill (6)

It follows that the mechanism of $q_1$ in Figure 2 can be captured by triggering jumps when the components of $z$ satisfy

$$q_1 = 0, \quad x_1 = \theta_1 + h_1 \quad \text{or} \quad q_1 = 1, \quad x_1 = \theta_1 - h_1.$$  \hfill (7)

Note that the update mechanism for $q_2$ is similar to that of $q_1$ just discussed. We can define the flow and jump sets in a compact form by defining functions

$$\eta_1(x_1, q_1) := (2q_1 - 1)(-x_1 + \theta_1 + (1 - 2q_1)h_1)$$

$$\eta_2(x_2, q_2) := (2q_2 - 1)(-x_2 + \theta_2 + (1 - 2q_2)h_2).$$

In this way, the flow set is given by

$$C := \{z \in \mathcal{Z} : \eta_1(x_1, q_1) \leq 0, \eta_2(x_2, q_2) \leq 0\}$$  \hfill (5)

and the jump set is given by

$$D = \{z \in C : \eta_1(x_1, q_1) = 0\} \cup \{z \in C : \eta_2(x_2, q_2) = 0\}.$$  \hfill (6)
To define the jump map, first note that at jumps, the continuous states \( x_1 \) and \( x_2 \) do not change. Then, we conveniently define

\[
g_1(z) := \begin{bmatrix} x_1 \\ x_2 \\ 1 - q_1 \\ q_2 \end{bmatrix}, \quad g_2(z) := \begin{bmatrix} x_1 \\ x_2 \\ q_1 \\ 1 - q_2 \end{bmatrix},
\]

so that the jump map \( G \) is given by

\[
G(z) := \begin{cases} 
  g_1(z) & \text{if } \eta_1(x_1, q_1) = 0, \eta_2(x_2, q_2) < 0 \\
  g_2(z) & \text{if } \eta_1(x_1, q_1) < 0, \eta_2(x_2, q_2) = 0 \\
  \{g_1(z), g_2(z)\} & \text{if } \eta_1(x_1, q_1) = 0, \eta_2(x_2, q_2) = 0.
\end{cases}
\]  

(7)

The above definitions determine a hybrid system for (3), which is given by

\[
\mathcal{H} : z \in \mathcal{Z} \quad \begin{cases} 
  \dot{z} = F(z) = \begin{bmatrix} k_1(1 - q_2) - \gamma_1 x_1 \\ k_2 q_1 - \gamma_2 x_2 \\ 0 \\ 0 \end{bmatrix} & z \in C \\
  z^+ \in G(z) & z \in D,
\end{cases}
\]

where \( C \) is in (5), \( G \) is in (7), and \( D \) is in (3). Its parameters are given by the positive constants \( k_1, k_2, \gamma_1, \gamma_2, \theta_1, \theta_2, h_1, h_2 \), which satisfy \( \theta_1 + h_1 < \theta_1^{\max}, \theta_2 + h_2 < \theta_2^{\max}, \theta_1 - h_1 > 0, \theta_2 - h_2 > 0 \). Figure 3 depicts a hybrid automaton representation of this system when sequentially transitioning between \((q_1, q_2) = (0, 0), (1, 0), (1, 1), (0, 1)\).

**Lemma 2.4** The data \((C, F, D, G)\) satisfies the following conditions:

(A1) The sets \( C \) and \( D \) are closed.

(A2) The map \( z \mapsto F(z) \) is continuous on \( C \).

(A3) The set-valued mapping \( z \mapsto G(z) \) is outer semicontinuous relative to \( \mathbb{R}^4 \) and locally bounded, and, for all \( z \in D, G(z) \) is nonempty.

**Proof:** Properties (A1) and (A2) are obvious. Property (A3) holds since the graph of \( G \), which is given by \( \{(x, y) : y \in G(z)\} \), is closed. \( \Box \)

---

\(2\)A set-valued mapping \( G : S \rightrightarrows \mathbb{R}^n \) with \( S \subset \mathbb{R}^n \) is outer semicontinuous relative to \( S \) if for any \( z \in S \) and any sequence \( \{z_i\}_{i=1}^{\infty} \) with \( z_i \in S \), \( \lim_{i \to \infty} z_i = z \), and any sequence \( \{w_i\}_{i=1}^{\infty} \) with \( w_i \in G(z_i) \) and \( \lim_{i \to \infty} w_i = w \) we have \( w \in G(z) \).
3 Dynamical Properties of the Two-Gene Hybrid System Model

3.1 Existence of solutions

**Proposition 3.1** From every point in $C \cup D$, there exists a nontrivial solution for the hybrid system $H$ in (8). Furthermore, every maximal solution is complete and the projection of its hybrid time domain on $\mathbb{R}_{\geq 0}$ is unbounded, i.e., every solution is not Zeno.

The proof of this result uses the conditions for the existence of solutions to $H$ in [18] for general hybrid systems. More precisely, consider the hybrid system $H$ and let $z(0,0) \in C \cup D$. If $z(0,0) \in D$ or

$$(VC) \text{ there exists a neighborhood } U \text{ of } z(0,0) \text{ such that for every } z \in U \cap C,$$

$$F(z) \cap T_C(z) \neq \emptyset,$$

then there exists a nontrivial solution to $H$ from $z(0,0)$. If $(VC)$ holds for every $z(0,0) \in C \setminus D$, then there exists a nontrivial solution to $H$ from every initial point in $C \cup D$, and every maximal solution $z$ satisfies exactly one of the following conditions:

$${}^3T_C(z)$$ denotes the tangent cone of $C$ at $z$, i.e., it is the set of all $v$ for which there exists a sequence of real numbers $\alpha_i \searrow 0$ and a sequence $v_i \to v$ such that for every $i = 1, 2, ..., x + \alpha_i v_i \in C.$
1. $z$ is complete;

2. $\text{dom } z$ is bounded and the last interval is of the form $[t_J, t_{J+1})$, where $J = \sup_{(t,j) \in \text{dom } z} j$ has nonempty interior and $t \mapsto \phi(t, J)$ is a maximal solution to $\dot{z} = F(z)$, in fact $\lim_{t \to T} |z(t, J)| = \infty$, where $T = \sup_{(t,j) \in \text{dom } z} t$;

3. $z(T, J) \notin C \cup D$, where $(T, J) = \sup \text{ dom } z$.

Furthermore, if $G(D) \subset C \cup D$, then 3) above does not occur.

The proof of Proposition 3.1 uses these conditions and is given in A.2.

### 3.2 Characterization of equilibria

We compute the set of isolated equilibrium points $z^*$ as well as (nonisolated, dense) sets of equilibria for the hybrid system $\mathcal{H}$ in (8). For general hybrid systems, isolated equilibrium points are points that are an isolated equilibrium point of $\dot{z} = F(z)$, $z \in C$ or of $z^+ \in G(z), z \in D$. On the other hand, an equilibrium set (not necessarily an isolated equilibrium point) for a hybrid system $\mathcal{H}$ is defined as a set that is (strongly) forward invariant.

**Definition 3.2 (Equilibrium set)** A set $S \subset C \cup D$ is an equilibrium set of $\mathcal{H}$ if for every initial condition $z(0,0) \in S$, every solution $z$ to $\mathcal{H}$ satisfies $z(t,j) \in S$ for all $(t,j) \in S$.

The following results determine the equilibria of (8) for a range of parameters of the system.

**Proposition 3.3** The equilibria of the hybrid system $\mathcal{H}$ in (8) is given in Table 1 in terms of the positive constants $k_1, k_2, \gamma_1, \gamma_2, \theta_1, \theta_1^{\text{max}}, \theta_2, \theta_2^{\text{max}}, h_1$, and $h_2$ satisfying the conditions therein. The set $S \subset C \cup D$ in case 5 is an equilibrium set and is given by

$$S = \bigcup_{i=1}^{4} S_i,$$

where

\begin{align*}
S_1 &:= \left\{ x \in \mathbb{R}^2 : x = \begin{bmatrix} \frac{k_1}{\gamma_1} - \left( \frac{k_1}{\gamma_1} - p_0(1) \right) \exp(-\gamma_1 s) \\ p_0(2) \exp(-\gamma_2 s) \end{bmatrix}, s \in [0, t_1'] \right\} \times \{(0,0)\} \\
S_2 &:= \left\{ x \in \mathbb{R}^2 : x = \begin{bmatrix} \frac{k_1}{\gamma_1} - \left( \frac{k_1}{\gamma_1} - p_1(1) \right) \exp(-\gamma_1 s) \\ \frac{k_1}{\gamma_2} - \left( \frac{k_1}{\gamma_2} - p_1(2) \right) \exp(-\gamma_2 s) \end{bmatrix}, s \in [0, t_2'] \right\} \times \{(1,0)\} \\
S_3 &:= \left\{ x \in \mathbb{R}^2 : x = \begin{bmatrix} p_2(1) \exp(-\gamma_1 s) \\ \frac{k_2}{\gamma_2} - \left( \frac{k_2}{\gamma_2} - p_2(2) \right) \exp(-\gamma_2 s) \end{bmatrix}, s \in [0, t_3'] \right\} \times \{(1,1)\} \\
S_4 &:= \left\{ x \in \mathbb{R}^2 : x = \begin{bmatrix} p_3(1) \exp(-\gamma_1 s) \\ p_3(2) \exp(-\gamma_2 s) \end{bmatrix}, s \in [0, t_4'] \right\} \times \{(0,1)\}
\end{align*}

$p_i(j)$ is the $j$-th component of $p_i$. 
and \( p_0, p_1, p_2, p_3 \in \mathbb{R}^2 \) are the vertices of the set \( S \) (see Figure 4), where

\[
\begin{align*}
t'_1 &= \ln \left[ \frac{k_{11} - p_0(1)}{k_{11} - (\theta_1 + h_1)} \right]^{\frac{1}{\gamma_1}}, \\
t'_2 &= \ln \left[ \frac{k_{21} - p_1(2)}{k_{21} - (\theta_2 + h_2)} \right]^{\frac{1}{\gamma_2}}, \\
t'_3 &= \ln \left[ \frac{p_2(1)}{\theta_1 - h_1} \right]^{\frac{1}{\gamma_1}}, \\
t'_4 &= \ln \left[ \frac{p_3(2)}{\theta_2 - h_2} \right]^{\frac{1}{\gamma_2}},
\end{align*}
\]

and

\[
\begin{align*}
p_0 &= \begin{bmatrix} (\theta_1 - h_1) & 0 \\ 0 & (\theta_2 - h_2) \end{bmatrix}, \tag{10} \\
p_1 &= \begin{bmatrix} \theta_1 + h_1 & 0 \\ (\theta_2 - h_2) & (\frac{k_{11} - (\theta_1 + h_1)}{k_{11} - p_0(1)})^{\frac{1}{\gamma_1}} \end{bmatrix}, \tag{11} \\
p_2 &= \begin{bmatrix} \frac{k_{11} - (\theta_1 + h_1) (\frac{k_{21} - (\theta_2 + h_2)}{k_{21} - p_1(2)})^{\frac{1}{\gamma_2}}}{\theta_2 + h_2} \\ \theta_2 + h_2 \end{bmatrix}, \tag{12} \\
p_3 &= \begin{bmatrix} \frac{k_{21} - (\theta_1 - h_1) (\frac{\theta_1 - h_1}{k_{11} - (\theta_1 + h_1)})^{\frac{1}{\gamma_1}}}{\theta_1 - h_1} \\ \theta_1 - h_1 \end{bmatrix}. \tag{13}
\end{align*}
\]

Moreover, the period of the limit cycle is given by

\[
T = t'_1 + t'_2 + t'_3 + t'_4. \tag{14}
\]

The following result provides a more constructive characterization of \( S \).

**Corollary 3.4** Under the conditions of Proposition 3.3, if furthermore, \( \gamma_1 = \gamma_2 = \gamma \), then

\[
p_0(1) = \frac{-d_6 + d_8 + d_7 - d_5 - d_4 - d_3 + d_2}{d_1}, \tag{15}
\]

where

\[
\begin{align*}
d_1 &= 2h_1k_2^2\gamma + h_2k_1k_2\gamma + k_1k_2\gamma_2 - 2h_1h_2k_2^2\gamma^2 \\
&\quad - 2h_1k_2\gamma^2\theta_2, \\
d_2 &= k_1k_2\gamma_1\theta_2, \quad d_3 = h_2k_1k_2\gamma\theta_1, \quad d_4 = h_1k_1k_2\gamma\theta_2, \\
d_5 &= h_1h_2k_1k_2\gamma, \quad d_7 = h_2k_2^2k_2, \quad d_8 = h_1k_1k_2^2.
\end{align*}
\]
Table 1: Equilibria of the hybrid system (8).

| Conditions on constants | Equilibria |
|-------------------------|------------|
| 1 $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}$ | $z_1^* := \left[ \begin{array}{c} \frac{k_1}{\gamma_1} \\ \frac{k_2}{\gamma_2} \\ 1 \\ 0 \end{array} \right]^\top$ |
| 2 $0 < \frac{k_1}{\gamma_1} < \theta_2 + h_2$ | $z_2^* := \left[ \begin{array}{c} \frac{k_1}{\gamma_1} \\ 0 \\ 0 \\ 0 \end{array} \right]$ |
| 3 $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$ | $z_1^*$ or $z_2^*$ |
| 4 $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$ | $z_2^*$ |
| 5 $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}$ | equilibrium set $S$ defined in (9) |

Moreover, the sets $S_i$ are given by

$S_1 = \{x \in \mathbb{R}^2 : x_2 = m_1 x_1 - m_1 p_1(1) + p_1(2), \quad p_0(1) \leq x_1 < \theta_1 + h_1, p_1(2) \leq x_2 < \theta_2 - h_2 \} \times \{(0,0)\}$,

$S_2 = \{x \in \mathbb{R}^2 : x_2 = m_2 x_1 - m_2 p_1(1) + p_1(2), \quad \theta_1 + h_1 \leq x_1 < p_2(1), p_1(2) \leq x_2 < \theta_2 + h_2 \} \times \{(1,0)\}$,

$S_3 = \{x \in \mathbb{R}^2 : x_2 = m_3 x_1 - m_3 p_3(1) + p_3(2), \quad \theta_1 - h_1 \leq x_1 < p_2(1), \theta_2 + h_2 \leq x_2 < p_3(2) \} \times \{(1,1)\}$,

$S_4 = \{x \in \mathbb{R}^2 : x_2 = m_4 x_1 - m_4 p_3(1) + p_3(2), \quad p_0(1) < x_1 \leq \theta_1 - h_1, \theta_2 - h_2 \leq x_2 < p_3(2) \} \times \{(0,1)\}$,

where

$m_1 = \frac{p_0(2) - p_1(2)}{p_0(1) - p_1(1)}, \quad m_2 = \frac{p_2(2) - p_1(2)}{p_2(1) - p_1(1)}, \quad m_3 = \frac{p_2(2) - p_3(2)}{p_2(1) - p_3(1)}, \quad m_4 = \frac{p_0(2) - p_3(2)}{p_0(1) - p_3(1)}$ \hspace{1cm} (16)

and the points $p_0, p_1, p_2, p_3 \in \mathbb{R}^2$ are given in (10) - (13).
Figure 4: Set $S$ and its vertices corresponding to case 5 of Table 7.

**Proof:** When $\gamma_1 = \gamma_2 = \gamma$, the definitions in (10)-(13) lead to

\[
\begin{align*}
p_0(1) &= (\theta_1 - h_1) \left( \frac{\theta_2 - h_2}{p_3(2)} \right), \\
p_1(2) &= (\theta_2 - h_2) \left( \frac{k_2 \gamma - (\theta_1 + h_1)}{k_1 \gamma - p_0(1)} \right), \\
p_2(1) &= \frac{k_1}{\gamma} - \left( \frac{k_1}{\gamma} - (\theta_1 + h_1) \right) \left( \frac{k_2 \gamma - (\theta_2 + h_2)}{k_2 \gamma - p_1(2)} \right), \\
p_3(2) &= \frac{k_2}{\gamma} - \left( \frac{k_2}{\gamma} - (\theta_2 + h_2) \right) \left( \frac{\theta_1 - h_1}{p_2(1)} \right).
\end{align*}
\]

Letting $\lambda = p_0(1)$, we obtain

\[
\frac{(\theta_1 - h_1)(\theta_2 - h_2)}{\lambda} = \frac{k_2}{\gamma} - \left( \frac{k_2}{\gamma} - (\theta_2 + h_2) \right) \left( \frac{\theta_1 - h_1}{p_2(1)} \right)
\]

\[
p_2(1) = \frac{k_1}{\gamma} - \left( \frac{k_1}{\gamma} - (\theta_1 + h_1) \right) \left( \frac{k_2 \gamma - (\theta_2 + h_2)}{k_2 \gamma - (\theta_2 - h_2) \left( \frac{k_1}{\gamma} - (\theta_1 + h_1) \right) - \lambda} \right).
\]
Replacing the second equation into the first one, after elementary but tedious manipulations, we obtain that \( \lambda = p_0(1) \) as in (13).

### 3.3 Stability analysis

For convenience in the following analysis, we rewrite the flow set \( C \) as \( C = \bigcup_{i=1}^{4} C_i \) (see Figure 4), where

\[
\begin{align*}
C_1 := & \{ z \in \mathcal{Z} : q_1 = 0, q_2 = 0, x_1 \leq \theta_1 + h_1, x_2 \leq \theta_2 + h_2 \}, \\
C_2 := & \{ z \in \mathcal{Z} : q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, x_2 \leq \theta_2 + h_2 \}, \\
C_3 := & \{ z \in \mathcal{Z} : q_1 = 1, q_2 = 1, x_1 \geq \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \}, \\
C_4 := & \{ z \in \mathcal{Z} : q_1 = 0, q_2 = 1, x_1 \leq \theta_1 + h_1, x_2 \geq \theta_2 - h_2 \}.
\end{align*}
\]

#### 3.3.1 Asymptotic stability of isolated equilibrium points

The following propositions determine the stability properties of the isolated equilibrium points in Table 1. Their proofs are in Appendix A.3 and Appendix A.4.

**Proposition 3.5** For cases 1, 2, and 4 in Table 1, the corresponding equilibrium points to \( \mathcal{H} \) in (8) are globally asymptotically stable.

**Proposition 3.6** For case 3 in Table 1, if \( z(0,0) \) is in \( C_2 \), then we have that \( \lim_{t+j \to \infty} z(t,j) = z_1^* \); if \( z(0,0) \) is in \( C_1 \) or \( z(0,0) \) is in \( C_4 \), then \( \lim_{t+j \to \infty} z(t,j) = z_2^* \). If \( z(0,0) \) is in \( C_3 \), then \( \lim_{t+j \to \infty} z(t,j) = z_1^* \) or \( z_2^* \). Furthermore, \( z_1^* \) and \( z_2^* \) are stable.

#### 3.3.2 Stability properties of the limit cycle

Now, we determine conditions on the parameters under which the limit cycle \( S \) defined in (9) is asymptotically stable. As shown in Figure 5(b) the natural metric defined by the distance between the trajectories \( z \) of \( \mathcal{H} \) and the set \( S \) is not necessarily decreasing, even though Figure 5(a) shows that the trajectory converges to \( S \). In fact, as depicted in the figures, the trajectory \( x \) approaches \( S \) for some time and then gets far away from it (around the corners), until a jump to a new value of \( q \) occurs.

---

5When \( \gamma_1 = \gamma_2 = \gamma \), the sets \( S_i \) in Proposition 3.3 reduce to straight lines. In fact, define the new coordinates

\[
e := x - \begin{bmatrix} k_1(1-q_2) \\ \gamma_1 k_2 \\ \gamma_2 \end{bmatrix}.
\]

The continuous dynamics of \( e \) are given by

\[
\dot{e} = e = \begin{bmatrix} k_1(1-q_2) - \gamma_1 x_1 \\ k_2 q_1 - \gamma_2 x_2 \end{bmatrix} = -\gamma e,
\]

which implies that the trajectories on the plane are straight lines.
To overcome this issue, we augment the hybrid system $H$ with a state $\zeta \in \mathbb{R}^2$ and with continuous dynamics governed by a flow map given by a copy of the one for $x$, that is,

$$\dot{\zeta} = \begin{bmatrix} k_1(1 - q_2) - \gamma_1 \zeta_1 \\ k_2 q_1 - \gamma_2 \zeta_2 \end{bmatrix}.$$  

The discrete dynamics of $\zeta$ are chosen so that jumps occur when jumps of $H$ occur and, at such jumps, $\zeta$ is updated via the difference inclusion

$$\zeta^+ \in \tilde{G}(x, q, \zeta).$$

To define the jump map $\tilde{G}$, consider the case $\gamma_1 = \gamma_2$ and, using Corollary 3.4, we extend to $\mathbb{R}^2$ the set of points $S_i$, $i \in \{1, 2, 3, 4\}$, that is, we define the (unbounded) set

$$\tilde{S} = \bigcup_{i=1}^{4} \tilde{S}_i,$$  \hspace{1cm} (19)

where

$\tilde{S}_1 = \{ x \in \mathbb{R}^2 : x_2 = m_1 x_1 - m_1 p_1(1) + p_1(2) \} \times \{(0, 0)\},$

$\tilde{S}_2 = \{ x \in \mathbb{R}^2 : x_2 = m_2 x_1 - m_2 p_1(1) + p_1(2) \} \times \{(1, 0)\},$

$\tilde{S}_3 = \{ x \in \mathbb{R}^2 : x_2 = m_3 x_1 - m_3 p_3(1) + p_3(2) \} \times \{(1, 1)\},$

$\tilde{S}_4 = \{ x \in \mathbb{R}^2 : x_2 = m_4 x_1 - m_4 p_3(1) + p_3(2) \} \times \{(0, 1)\}.$

During flows, the set $\tilde{S}$ is forward invariant for the state component $\zeta$ (both during flows and jumps) along the dynamics of $q$ governed by $H$. This is the reason we restrict $\zeta$ to belong to $\tilde{S}$ for the current value of $q$. Then, due to the stability properties of the error system with state $\zeta - x$, the distance between $x$ and $\zeta$ strictly decreases during flows. With this useful property of the trajectories while flowing, at jumps due to $H$, which occur when
(x(t, j), q(t, j)) ∈ D and map q(t, j) to q(t, j + 1) (following the definition of G in (7)), the jump map \( \tilde{G} \) is constructed to map the state \( \zeta \) to satisfy \((\zeta(t, j + 1), q(t, j + 1)) \in \tilde{S} \) such that, if \((\zeta(t, j), q(t, j)) \in \tilde{S}_{q(t,j)} \) before the jump, then \((\zeta(t, j + 1), q(t, j + 1)) \in \tilde{S}_{q(t,j+1)} \) and with the property that

\[
\text{dist}(x(t, j + 1), \zeta(t, j + 1)) \leq \text{dist}(x(t, j), \zeta(t, j))
\]

where \text{dist} is the Euclidean distance between two points in \( \mathbb{R}^2 \). In this way, the new value of \( \zeta \) at jumps can be determined for each \( x \in \mathbb{R}^2 \) from the set

\[
\tilde{g}(x, q, \zeta) := \left\{ \zeta' : \text{dist}(x, \zeta') \leq \text{dist}(x, \zeta), (\zeta', q') \in \tilde{S}_{q'}, (x, q') \in G(x, q) \right\}
\]

(when it is not empty). Since the distance between \( x \) and \( \zeta \) decreases during flows, asymptotic stability of \( \tilde{S} \) can be established when \( \tilde{G}(x, q, \zeta) \) is nonempty since this guarantees that the distance between \( x \) and \( \zeta \) is nonincreasing. The following result imposes conditions on the parameters guaranteeing that \( \tilde{G} \) is nonempty and, furthermore, extends the attractivity property to the set \( S \).

**Theorem 3.7** For positive constants \( k_1, k_2, \gamma_1, \gamma_2, \theta_1, \theta_1^{\text{max}}, \theta_2, \theta_2^{\text{max}}, h_1, \) and \( h_2 \) such that

\[
\gamma_1 = \gamma_2 = \gamma, \quad |m_1| \leq \min\{|m_2|, |m_4|\}, \quad |m_3| \leq \min\{|m_2|, |m_4|\},
\]

(20)

where, for each \( i \in \{1, 2, 3, 4\}, m_i \) are given in (16), the following holds:

1. The set \( \tilde{S} \) is globally asymptotically stable for \( \mathcal{H} \). In particular, each maximal solution to \( \mathcal{H} \) satisfies

\[
d((x(t, j), q(t, j)), \tilde{S}) \leq \exp(-\gamma t)d((x(0, 0), q(0, 0)), \tilde{S})
\]

for all \((t, j) \in \text{dom}(x, q), \) where \( d((x, q), \tilde{S}) = \min_{(\zeta, q) \in \tilde{S}} |x - \zeta| \).

2. The set \( S \) in case 5 of Table 7 is globally attractive for \( \mathcal{H} \), i.e., every solution to \( \mathcal{H} \) converges to \( S \).
The extended version of the hybrid system \( H \) is given by the minimum distance between \( x \) and \( \tilde{S} \) for each \( x \in C \). For jumps from \( q = (0, 1) \) to \( q = (0, 0) \), in which case \( x_1 \in [0, p_0(1)] \) and \( x_2 = \theta_2 - h_2 \), the minimum distance is

\[
\frac{|m_4| |x_1 - p_0(1)|}{\sqrt{m_4^2 + 1}}
\]
Similarly, the minimum distance from \( x \) to the line defined by \( \tilde{S} \) for \( q = (0, 0) \), which is the distance between \( (x, q) \) and \( \tilde{S} \) after the jump, is given by
\[
\frac{|m_1||x_1 - p_0(1)|}{\sqrt{m_1^2 + 1}}. \tag{24}
\]
Then, imposing that (24) is no larger than (23) guarantees that, in the worst case, \( \text{dist}(x, \zeta') \leq \text{dist}(x, \zeta) \). Then, we require
\[
\frac{|m_1||x_1 - p_0(1)|}{\sqrt{m_1^2 + 1}} \leq \frac{|m_4||x_1 - p_0(1)|}{\sqrt{m_4^2 + 1}} \iff |m_1| \leq |m_4|. \tag{25}
\]
Proceeding in this way, for jumps from \( q = (0, 0) \) to \( q = (1, 0) \), from \( q = (1, 0) \) to \( q = (1, 1) \), and from \( q = (1, 1) \) to \( q = (0, 1) \) we require
\[
|m_1| \leq |m_2|, \quad |m_3| \leq |m_2|, \quad |m_3| \leq |m_4|, \tag{26}
\]
respectively. Under these conditions, which can be rewritten as in (20), \( \tilde{G} \) is nonempty.

For each \( (x, q, \zeta) \in \mathbb{R}^2 \times \{0, 1\}^2 \times \mathbb{R}^2 \), let
\[
V(x, q, \zeta) = \text{dist}(x, \zeta)^2
\]
and note that \( V \) is positive definite with respect to the closed set
\[
A := \left\{ (x, q, \zeta) : x = \zeta, (x, q) \in C \cup D, (\zeta, q) \in \tilde{S} \right\}. \tag{27}
\]
For each \( (x, q) \in C \) and \( (\zeta, q) \in \tilde{S} \), we obtain
\[
\langle \nabla V(x, q, \zeta), \bar{F}(x, q, \zeta) \rangle = -2 \left( \gamma_1 (x_1 - \zeta_1)^2 + \gamma_2 (x_2 - \zeta_2)^2 \right) = -2\gamma V(x, q, \zeta), \tag{28}
\]
where we have used the condition \( \gamma_1 = \gamma_2 = \gamma \). For each \( (x, q) \in D \) and \( (\zeta, q) \in \tilde{S} \), we have
\[
\max_{\xi \in \bar{G}(x, q, \zeta)} V(\xi) - V(x, q, \zeta) = \max_{(x, \xi_1) \in G(x, q, \zeta)} \text{dist}(x, \xi_3)^2 - \text{dist}(x, \zeta)^2 \leq 0 \tag{29}
\]
since, by definition of \( \tilde{G} \), we have that any possible value of \( \xi_3 \) obtained from \( \tilde{G} \) is such that \( \text{dist}(x, \xi_3)^2 \leq \text{dist}(x, \zeta)^2 \). Then, since every maximal solution to \( H \) (and, hence, to \( \tilde{H} \)) is complete and has a hybrid time domain unbounded in the \( t \) direction, [20, Proposition 3.29] implies that \( A \) is globally asymptotically stable. In fact, combining (28) and (29), and simple integration, we get that every solution \( (x, q, \zeta) \) to \( \tilde{H} \) satisfies
\[
\text{dist}(x(t, j), \zeta(t, j)) \leq \exp(-\gamma t)\text{dist}(x(0, 0), \zeta(0, 0)) \tag{30}
\]
for all \( (t, j) \in \text{dom}(x, q, \zeta) \).

\[\text{The same result can be obtained using the invariance principle for hybrid systems in [21].}\]
Now, we relate the asymptotic stability property above to \( \tilde{S} \). The bound (30) holds for any \( \zeta(0,0) \) such that \( (\zeta(0,0), q(0,0)) \in \tilde{S} \), in particular, when \( \zeta(0,0) \) is such that\(^7\) \( \text{dist}(x(0,0), \zeta(0,0)) = d((x(0,0), q(0,0)), \tilde{S}) \). Moreover, note that since \( (\zeta(t,j), q(t,j)) \in \tilde{S} \) for all \( (t,j) \in \text{dom}(x,q,\zeta) \), we have
\[
d((x(t,j), q(t,j)), \tilde{S}) \leq \text{dist}(x(t,j), \zeta(t,j))
\]
for all \( (t,j) \in \text{dom}(x,q,\zeta) \). Then, from (30) and the above arguments, we obtain
\[
d((x(t,j), q(t,j)), \tilde{S}) \leq \exp(-\gamma t)d((x(0,0), q(0,0)), \tilde{S})
\]
for all \( (t,j) \in \text{dom}(x,q,\zeta) \).

To show that the components \( (x,q) \) of the solutions to \( \tilde{\mathcal{H}} \) converge to \( S \), we proceed by contradiction and suppose that there exists a maximal solution to \( \tilde{\mathcal{H}} \) with components \( (x,q) \) with \( \omega \)-limit set \( \Omega(x,q) \) such that \( \Omega(x,q) \cap (\tilde{S} \setminus S) \neq \emptyset \). Let \( z^0 \in \Omega(x,q) \cap (\tilde{S} \setminus S) \neq \emptyset \). By the properties of the \( \omega \)-limit set of complete solutions to hybrid systems (see Definition 3.2 and Lemma 3.3)), there exists at least one solution starting from \( z^0 \), which is impossible since points in \( \tilde{S} \setminus S \) are not in \( C \cup D \) and \( \tilde{\mathcal{H}} \) satisfies the hybrid basic conditions. Then, \( \Omega(x,q) \) cannot contain points that are not in \( S \), which implies that \( \Omega(x,q) \subset S \). Convergence of components \( (x,q) \) of the solutions to \( \tilde{\mathcal{H}} \) to \( S \) follows by the very definition of \( \omega \)-limit set of a solution.

\[\square\]

### 3.4 Robustness properties

When the system \( \mathcal{H} \) in (8) is restricted to a compact set of the initial conditions for the state component \( x \), the asymptotic stability of the set \( \tilde{S} \) guaranteed in Theorem 3.7 is robust to small perturbations. We define this set of initial conditions as the compact box in \( \mathbb{R}^2 \geq 0 \) as
\[
K := [0, x_1^{\text{max}}] \times [0, x_2^{\text{max}}]
\]
with positive constants \( x_1^{\text{max}} \) and \( x_2^{\text{max}} \) such that \( S \subset K \times \{0,1\}^2 \). We consider perturbations on the state and on the continuous dynamics of the system. The signal \( d_1 : \mathbb{R} \geq 0 \to \delta_1 \mathbb{B} \subset \mathbb{R}^2 \) defines the perturbation on the state and the signal \( d_2 : \mathbb{R} \geq 0 \to \delta_2 \mathbb{B} \subset \mathbb{R}^2 \) defines the perturbation on the flow of \( x \), where \( \delta_1, \delta_2 > 0 \). In this way, the perturbed hybrid system is given by
\[
\mathcal{H}_\delta : \begin{cases}
\dot{z} = \begin{bmatrix}
k_1(1-q_2) - \gamma_1(x_1 + d_{11}(t)) + d_2(t) \\
k_2q_1 - \gamma_2(x_2 + d_{12}(t)) + d_2(t) \\
0 \\
0
\end{bmatrix} & (x + d_1(t), q) \in C \cap K \\
z^+ \in G(z) & (x + d_1(t), q) \in D \cap K,
\end{cases}
\]
where \( C \) is defined in (8), \( G \) in (7), and \( D \) in (6). The perturbation \( d_1 \) captures uncertainty in the values of the protein concentrations \( x \) while \( d_2 \) models the uncertainty in the dynamical

\(^7\)Note that we could also pick \( \zeta(0,0) \) such that the distance to \( S \) matches.
model governing $x_1^\beta$. In particular, the latter perturbation allows for uncertainty in the parameters $k_1, k_2$. For instance, if $k_1$ is replaced by $k_1 + k_1^\delta$ with $k_1^\delta \in \mathbb{R}$ then the continuous dynamics of $x_1$ along a solution $(x, q)$ to $\mathcal{H}$ can be rewritten as

$$
\frac{d}{dt}x_1(t, j) = (k_1 + k_1^\delta)(1 - q_2(t, j)) - \gamma_1(x_1 + d_{11}(t))
= k_1(1 - q_2(t, j)) - \gamma_1(x_1(t, j) + d_{11}(t)) + k_1^\delta(1 - q_2(t, j)),
$$

which leads to $d_{21}(t) = k_1^\delta(1 - q_2(t, j(t)))$. Note that since $q_2$ takes values from $\{0, 1\}$, then we have that $|d_{21}(t)| \leq \delta_2$ when $|k_1^\delta| \leq \frac{\varepsilon}{2} \delta_2$.

Due to $\mathcal{H}$ satisfying conditions (A1)-(A3) in Lemma 2.1, the stability property guaranteed by Theorem 3.7 is robust to small perturbations. This property follows from the results on robustness of stability for hybrid systems in [20].

**Theorem 3.8** For each positive constants $x_1^{\max}$ and $x_2^{\max}$ defining $K := [0, x_1^{\max}] \times [0, x_2^{\max}]$ such that $S \subset K \times \{0, 1\}^2$ and system constants satisfying case 5 of Table 1, there exist $\beta \in K\mathcal{L}$ such that, for each $\varepsilon > 0$ there exists $\delta > 0$ such that for each measurable functions $d_1 : \mathbb{R}_{\geq 0} \to \delta_1 \mathbb{B}$, $d_2 : \mathbb{R}_{\geq 0} \to \delta_2 \mathbb{B}$ with $\delta_1, \delta_2 \in (0, \delta]$, every solution $(x, q)$ to $\mathcal{H}_\delta$ with $(x(0, 0), q(0, 0)) \in K$ satisfies

$$
|(x(t, j), q(t, j))|_{S \cap K} \leq \beta(|(x(0, 0), q(0, 0))|_{S \cap K}, t + j) + \varepsilon \quad \forall (t, j) \in \text{dom}(x, q).
$$

4 Numerical results

In this section, we simulate the hybrid system $\mathcal{H}$ in [8] within Matlab/Simulink using the HyEQ Toolbox [22].

4.1 Isolated equilibrium points in Table I

We perform simulations with parameters satisfying the conditions in Table I for which there are isolated equilibrium points.

4.1.1 Case 1 of Table I

Figure 7 illustrates that, when $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$, the solution converges to $z^*_1 = [\frac{k_1}{\gamma_1}, \frac{k_2}{\gamma_2}, 1, 0]^T$. Initially, the concentration of protein $A$ ($x_1$) is low, which inhibits the expression of gene $b$, hence the concentration of protein $B$ ($x_2$) decreases and activates the expression of gene $a$. However, after finite time, while the concentration of protein $A$ is above the level $\theta_1 + h_1$, which can permit the expression of gene $b$, the concentration of protein $B$ increases. Finally, the concentrations of protein $A$ and $B$ come to the equilibrium $(\frac{k_1}{\gamma_1}, \frac{k_2}{\gamma_2})$. This confirms the result in Proposition 3.5.

---

8Perturbations on each of the system parameters, in particular, the thresholds $\theta_i$ and hysteresis half widths $h_i$, can be treated similarly.

9For each $t$ such that $(t, j) \in \text{dom}(x, q)$, the function $j : \mathbb{R}_{\geq 0} \to \mathbb{N}$ is given by $j(t) = j'$, where $j' = \max\{j : (t, j) \in \text{dom}(x, q)\}$.

10A function $\beta$ is of class $K\mathcal{L}$ if it is continuous, $r \mapsto \beta(r, s)$ is zero at zero and nondecreasing, and
Figure 7: The x and q components of a solution to $H$ in (8) converging to $z_1^\ast$. The initial condition is given by $q_1(0,0) = 0$, $q_2(0,0) = 0$, $x_1(0,0) = 0.4$, $x_2(0,0) = 0.4$. The parameters are as follows: $\theta_1 = 0.6$, $\theta_2 = 0.5$, $k_1 = 0.7$, $k_2 = 0.4$, $\gamma_1 = 1$, $\gamma_2 = 1$, $h_1 = 0.01$, $h_2 = 0.01$. The symbol $\ast$ denotes the initial point and $\circ$ the point that the solution converges to (i.e., $z_1^\ast$).

4.1.2 Case 2 of Table 1

Figure 8 shows a solution to the equilibrium point $z_2^\ast = \begin{bmatrix} k_1 \\ \gamma_1 \\ 0 \\ 0 \end{bmatrix}^\top$ with $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$. While both gene a and gene b are expressed at rate $k_i$, for gene a, its degradation is faster than synthesis. When the concentration of protein $A$ ($x_1$) is below some level, gene b is inhibited. This confirms the result in Proposition 3.5.

$s \mapsto \beta(r,s)$ is nonincreasing and converges to zero as $s$ goes to $\infty$. 

22
Figure 8: The x and q components of a solution to $\mathcal{H}$ in (8) converging to $z_2^*$. The initial condition is given by $q_1(0,0) = 1$, $q_2(0,0) = 0$, $x_1(0,0) = 0.7$, $x_2(0,0) = 0.3$. The parameters are as follows: $\theta_1 = 0.6$, $\theta_2 = 0.5$, $k_1 = 0.4$, $k_2 = 0.7$, $\gamma_1 = 1$, $\gamma_2 = 1$, $h_1 = 0.01$, $h_2 = 0.01$. The symbol * denotes the initial point and ◦ is the point that the solution converges to (i.e., $z_2^*$).

4.1.3 Case 3 of Table I

Figure 9 indicates that, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$ with the initial value $z(0,0) \in C_2 := \{q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, x_2 \leq \theta_2 + h_2\}$. The solution flows towards $z_1^* = [\frac{k_1}{\gamma_1}, \frac{k_2}{\gamma_2}, 1, 0]^T$. Under these conditions, gene a and gene b are expressed at rate $k_i$, $i = 1, 2$, respectively. However, for gene a, its degradation is faster than its synthesis. This confirms the result in Proposition 3.6.

Figure 10 illustrates the case when $\theta_1 - h_1 \leq \frac{k_1}{\gamma_1} \leq \theta_1 + h_1$, $\frac{k_2}{\gamma_2} \leq \theta_2 + h_2$. With the initial value $z(0,0) \notin C_2$, the solution converges to $z_2^* = [\frac{k_1}{\gamma_1}, 0, 0, 0]^T$. With these conditions, initially, gene b is expressed at $k_2$ and gene a is inhibited. After finite time, as the concen-
Figure 9: The $x$ and $q$ components of a solution to $H$ in (8) converging to $z^*_1$. The initial conditions are given by $q_1(0,0) = 1$, $q_2(0,0) = 0$, $x_1(0,0) = 0.7$, $x_2(0,0) = 0.3$. The parameters are as follows: $\theta_1 = 0.6$, $\theta_2 = 0.5$, $k_1 = 0.601$, $k_2 = 0.501$, $\gamma_1 = 1$, $\gamma_2 = 1$, $h_1 = 0.02$, $h_1 = 0.02$. The symbol $\ast$ denotes the initial point and $\circ$ is the point that the solution converges to (i.e., $z^*_1$).

Figure 11 indicates that, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{max}$ with the initial value $z(0,0) \in C_2 := \{q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, x_2 \leq \theta_2 + h_2\}$. The solution flows towards $z^*_2 = [\frac{k_1}{\gamma_1}, 0, 0, 0]^\top$. Under these conditions, gene $a$ and gene $b$ are expressed at rate $k_i$, $i = 1, 2$ initially. After some time, the concentration of protein $B$ (x2) exceeds a certain level, which triggers a jump, after which the expression of gene $a$ is inhibited. When the

4.1.4 Case 4 of Table 1

Figure 11 indicates that, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{max}$ with the initial value $z(0,0) \in C_2 := \{q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, x_2 \leq \theta_2 + h_2\}$. The solution flows towards $z^*_2 = [\frac{k_1}{\gamma_1}, 0, 0, 0]^\top$. Under these conditions, gene $a$ and gene $b$ are expressed at rate $k_i$, $i = 1, 2$ initially. After some time, the concentration of protein $B$ exceeds a certain level, which triggers a jump, after which the expression of gene $a$ is inhibited. When the
Figure 10: The \( x \) and \( q \) components of a solution to \( H \) in (8) converging to \( z^*_1 \). The initial conditions are given by \( q_1(0,0) = 1, q_2(0,0) = 1, x_1(0,0) = 0.7, x_2(0,0) = 0.7 \). The parameters are as follows: \( \theta_1 = 0.6, \theta_2 = 0.5, k_1 = 0.601, k_2 = 0.501, \gamma_1 = 1, \gamma_2 = 1, h_1 = 0.02, h_1 = 0.02 \). The symbol * is the initial point and ○ is the point that the solution converges to (i.e., \( z^*_2 \)).

concentration of protein \( A \) decreases enough, another jump occurs, after which the expression of gene \( b \) is inhibited as well. Eventually, the concentration of protein \( B \) reaches a low enough value to trigger another jump, after which the expression of gene \( a \) is activated, and the concentrations approach a steady-state value. This simulation confirms the result in Proposition 3.6.

4.2 Equilibrium set \( S \)

When the parameters are in the region \( \theta_1 + h_1 < \frac{k_1}{\gamma_1}, \theta_2 + h_2 < \frac{k_2}{\gamma_2}, \theta_1, \theta_2 \), the set of points \( S \) in (9) defines the equilibria. First, we compute this set of points for particular values of \( k_1, k_2, h_1, h_2, \gamma_1 = \gamma_2 = \gamma, \theta_1, \theta_2 \). Let \( k_1 = 1, k_2 = 1, \gamma_1 = \gamma_2 = \gamma = 1, \theta_1 = 0.6, \theta_2 = 0.5, \)
Figure 11: The $x$ and $q$ components of a solution to $H$ in (8) converging to $z_2^*$. The initial conditions are given by $q_1(0, 0) = 1$, $q_2(0, 0) = 0$, $x_1(0, 0) = 0.7$, $x_2(0, 0) = 0.3$. The parameters are as follows: $\theta_1 = 0.6$, $\theta_2 = 0.5$, $k_1 = 0.61$, $k_2 = 1$, $\gamma_1 = 1$, $\gamma_2 = 1$, $h_1 = 0.02$, $h_1 = 0.02$. The symbol $\ast$ denotes the initial point and $\circ$ is the point that the solution converges to (i.e., $z_2^*$).

\[ h_1 = 0.01, ~ h_2 = 0.01. \]  Then, using Corollary 3.4, the point $p_0$ is given by $p_0(1) = 0.4966$. Then, from (10)-(13), we obtain

\[
p_0 = \begin{bmatrix} 0.4966 \\ 0.49 \end{bmatrix}, \quad p_1 = \begin{bmatrix} 0.61 \\ 0.3796 \end{bmatrix}, \quad p_2 = \begin{bmatrix} 0.692 \\ 0.51 \end{bmatrix}, \quad p_3 = \]
With the values of $p_0, p_1, p_2, p_3$, the set $S$ in (9) is given by

$$S_1 = \{ x : x_2 = -0.973381 x_1 + 0.973381, \quad 0.4966 \leq x_1 \leq 0.61, 0.3796 \leq x_2 \leq 0.49 \} \times \{(0, 0)\},$$

$$S_2 = \{ x : x_2 = 1.590722 x_1 - 0.590722, \quad 0.61 \leq x_1 \leq 0.692, 0.3796 \leq x_2 \leq 0.51 \} \times \{(1, 0)\},$$

$$S_3 = \{ x : x_2 = -0.7081296 x_1 + 1, \quad 0.59 \leq x_1 \leq 0.692, 0.51 \leq x_2 \leq 0.5822 \} \times \{(1, 1)\},$$

$$S_4 = \{ x : x_2 = 0.9871896 x_1 - 0.000238, \quad 0.4966 \leq x_1 \leq 0.59, 0.49 \leq x_2 \leq 0.5822 \} \times \{(0, 1)\}.$$

Figure 12: Set $S$ for parameters $k_1 = 1, k_2 = 1, \gamma_1 = 1, \gamma_2 = 1, \theta_1 = 0.6, \theta_2 = 0.5, h_1 = 0.01, h_2 = 0.01$.

Figure 12(a) shows the set of points $S$ projected to $\mathbb{R}^2$ for these parameters. For the same parameter values, the period of the limit cycle obtained from Corollary 3.4 is $T = 0.8230$ sec, where $t'_1 = 0.2552$ sec, $t'_2 = 0.2359$ sec, $t'_3 = 0.1594$ sec, $t'_4 = 0.1724$ sec. Figure 12(b) confirms this result.
Figure 13: Solutions approaching the set $S$ with different initial conditions of $z$ and fixed parameters $\theta_1 = 0.6$, $\theta_2 = 0.5$, $\gamma_1 = 1$, $\gamma_2 = 1$, $k_1 = 1$, $k_2 = 1$.
Figure 13 shows simulations with several initial conditions and common parameters \( \theta_1 = 0.6, \theta_2 = 0.5, \gamma_1 = 1, \gamma_2 = 1, k_1 = 1, k_2 = 1 \), but decreasing \( h_1, h_2 \). Each solution converges to the limit cycle \( S \). The size of the limit cycle is reduced as \( h_1, h_2 \) gets smaller. From our results we know that the size of the limit cycle depends on the value of hysteresis parameters. When the magnitude of hysteresis tends to zero, the set \( S \) approaches a point, which is given by \( (\theta_1, \theta_2) \) (see similar case shown in Figure 13(d)).

Figure 14 shows simulations with several initial conditions and common parameters \( \theta_1 = 0.6, \theta_2 = 0.5, \gamma_1 = 1, \gamma_2 = 1, k_1 = 1, k_2 = 1, h_1 = 0.01, h_2 = 0.01 \), but changing \( k_1, k_2 \). Each solution converges to the limit cycle \( S \) (in cyan). The blue set of points defines the limit cycle \( S \) generated when \( k_1 = k_2 = 1 \). The variations of \( k_1 \) and \( k_2 \) can be considered to be perturbations as in Theorem 3.8. The simulations show that the smaller the perturbation on these constants, the closer the limit cycle becomes to the nominal one. Figure 15 shows simulations with several initial conditions and common parameters \( \theta_1 = 0.6, \theta_2 = 0.5, k_1 = 1, k_2 = 1, h_1 = 0.01, h_2 = 0.01 \), but now with \( \gamma_1 \) and \( \gamma_2 \) varying.

Figure 14: Solutions approaching the set \( S \) with different initial conditions of \( z \) and fixed parameters \( \theta_1 = 0.6, \theta_2 = 0.5, \gamma_1 = 1, \gamma_2 = 1, h_1 = 0.01, h_2 = 0.01 \).
Finally, Figure 16 shows the case when $\gamma_1 \neq \gamma_2$. In this case, the trajectories approach the limit cycle given in (9).
Figure 16: Solutions approaching the set $S$ with different initial conditions of $x_i$ and fixed parameters. Values of parameters: $\theta_1 = 0.6, \theta_2 = 0.5, \gamma_1 = 5, \gamma_2 = 1, k_1 = 5, k_2 = 1, h_1 = 0.01, h_1 = 0.01$. The blue line is the set $S$. The symbol $*$ denotes the initial point.

5 Conclusion

In this paper, a mathematical model of a genetic regulatory network has been developed under the formalism of hybrid dynamical systems. The model presented in this paper permits a quantitative analysis of the cellular protein dynamics under the influence of protein concentration thresholds and initial conditions. The analysis of the hybrid model with two genes determines conditions guaranteeing the existence of solutions, the equilibria of the system, stability properties of the equilibria and its robustness. In particular, we have revealed conditions on the parameters that, when hysteresis is present, the interaction between the concentrations of two proteins leads to oscillatory behavior. Such a behavior is impossible in a two-gene network without hysteresis. The obtained results are an important initial step in the analysis of genetic regulatory networks using hybrid systems theory, which we believe has great potential for the understanding of the complex mechanisms in such networks, in particular, when treated as (larger than two) interconnections of hybrid systems.

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A

A.1 Proof of Proposition 3.3

We consider the first three cases in Table 1. Since for every point in $D$, the jump map $G$ changes the value of at least one of the logic variables, we just need to consider the case when $z^* \in C$ to determine isolated equilibrium points $z^*$. The continuous state $x$ of the system satisfies

$$x = \begin{bmatrix} k_1(1 - q_2) - \gamma_1 x_1 \\ k_2 q_1 - \gamma_2 x_2 \end{bmatrix}.$$ 

To compute equilibrium points, let $F(z^*) = 0$. Then,

$$\begin{bmatrix} k_1(1 - q_2^*) - \gamma_1 x_1^* \\ k_2 q_1^* - \gamma_2 x_2^* \end{bmatrix} = 0$$

and solving for $x^*$ leads to

$$x^* = \begin{bmatrix} k_1(1 - q_2^*) \\ \frac{\gamma_1}{\gamma_2} \end{bmatrix}.$$ 

According to the possible values of $q^*$, all the possibilities of $x^*$ are listed in Table 2. These define vectors $z^a, z^b, z^c, z^d$, which are to be checked if they satisfy $z^* \in C$.

| $x^*$           | $q^*$          |
|-----------------|----------------|
| $(\frac{k_1}{\gamma_1}, 0)$ | $q_1^* = 1, q_2^* = 0$ |
| $(0, 0)$        | $q_1^* = 0, q_2^* = 1$ |
| $(\frac{k_1}{\gamma_2}, 0)$ | $q_1^* = 1, q_2^* = 1$ |

Similar to $C$, the jump set $D$ can also be written as $D = \bigcup_{i=1}^4 D_i$, where $D_1 := \{ z \in \mathbb{Z} : q_1 = 0, q_2 = 0, x_1 = \theta_1 + h_1, x_2 \leq \theta_2 + h_2 \} \cup \{ z \in \mathbb{Z} : q_1 = 1, q_2 = 0, x_1 = \theta_1 - h_1, x_2 \leq \theta_2 + h_2 \}$, $D_2 := \{ z \in \mathbb{Z} : q_1 = 1, q_2 = 1, x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \} \cup \{ z \in \mathbb{Z} : q_1 = 0, q_2 = 1, x_1 = \theta_1 + h_1, x_2 \geq \theta_2 - h_2 \}$, $D_3 := \{ z \in \mathbb{Z} : q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2 \} \cup \{ z \in \mathbb{Z} : q_1 = 1, q_2 = 1, x_1 = \theta_1 - h_1, x_2 = \theta_2 - h_2 \}$, $D_4 := \{ z \in \mathbb{Z} : q_1 = 0, q_2 = 1, x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2 \} \cup \{ z \in \mathbb{Z} : q_1 = 0, q_2 = 0, x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2 \}$. Now, we find the value of $x_1^*, x_2^*, q_1^*, q_2^*$ such that $z^* \in C$.

- Case $i$: Consider parameters such that $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_1}{\gamma_2} < \theta_2 + h_2$. Then, it can be checked that

$$z^a \in C, z^b \notin C, z^c \notin C, z^d \notin C.$$ 

Then, $z^a$ is an equilibrium point.
• Case ii: Consider parameters such that \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1, \ 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2\). Then, it can be checked that

\[ z^*_a \notin C, z^*_b \notin C, z^*_c \notin C, z^*_d \in C. \]

Then, \(z^*_d\) is an equilibrium point.

• Case iii: Consider parameters such that \(\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, \ \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}\). Then, it can be checked that

\[ z^*_a \notin C, z^*_b \notin C, z^*_c \notin C, z^*_d \notin C. \]

• Case iv: Consider parameters such that \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1, \ \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}\). Then, it can be checked that

\[ z^*_a \notin C, z^*_b \notin C, z^*_c \notin C, z^*_d \in C. \]

Then, \(z^*_d\) is an equilibrium point.

• Case v: Consider parameters such that \(\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, \ \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}\). Then, it can be checked that

\[ z^*_a \in C, z^*_b \notin C, z^*_c \notin C, z^*_d \in C \]

Then, \(z^*_a\) and \(z^*_d\) are equilibrium points.

• Case vi: Consider parameters such that \(\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, \ \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}\). Then, it can be checked that

\[ z^*_a \notin C, z^*_b \notin C, z^*_c \notin C, z^*_d \in C \]

Then, \(z^*_d\) is an equilibrium point.

From the properties above, only \(z_a^*\) and \(z_d^*\) are candidate isolate equilibrium points. We show that the first four cases in Table 1 are equilibrium points of the entire system with \(z_1^* = z_a^*\) and \(z_2^* = z_d^*\). For case 1, which is when \(\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, \ 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2\), we pick any other \(z' \neq z_1^*\). We have that if \(z' \in C\) then \(F(z') \neq 0\), so \(z_1^*\) is the isolated equilibrium point of the system. For case 2, when \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1\), we pick any other \(z' \neq z_2^*\). If \(z' \in C\), then \(F(z') \neq 0\), so \(z_2^*\) is the isolated equilibrium point of the system. For case 3, when \(\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, \ 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2\), we pick any other \(z' \neq z_i^*\) for each \(i \in \{1, 2\}\). If \(z' \in C\), then \(F(z') \neq 0\), so \(z_i^*\) or \(z_2^*\) are the equilibrium points of the entire system. For case 4, when \(\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, \ \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}\) we pick any other \(z' \neq z_2^*\). If \(z' \in C\), then \(F(z') \neq 0\), so \(z^*_a\) is the isolated equilibrium point of the system.

We now show that \(S\) in (19) is an equilibrium set for case 5 of the parameters in Table 1, namely \(\frac{k_1}{\gamma_1} \in (\theta_1 + h_1, \theta_1^{\text{max}}), \ \frac{k_2}{\gamma_2} \in (\theta_2 + h_2, \theta_2^{\text{max}})\). To this end, we establish that for parameters in such range, the logic variables evolve according to the state transition graph in Figure 18. This is due to the system not having an isolated equilibrium point in the flow set \(C\); see Case iii in the proof of Proposition 3.3. Let \(Q := \{(0,0), (0,1), (1,0), (1,1)\}\). The \(x\) component of the vector field \(F\) satisfies the following properties on the boundary of \(C\).
1. Points on the boundary of $C_1$:

- When $x \in \{x : x_1 = 0, 0 \leq x_2 \leq \theta_2 + h_2\}$, the first two components of $F$ define the vector $f_1(x) := \begin{bmatrix} k_1 \\ -\gamma_2 x_2 \end{bmatrix}$. Since $k_1 > 0$, $\gamma_2 > 0$, then $f_1(x)$ points inside of $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = 0\}$, $f_1(x) := \begin{bmatrix} k_1 - \gamma_1 x_1 \\ 0 \end{bmatrix}$. Since $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}$, then $f_1(x)$ is tangent to the boundary of $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2\}$, $f_1(x) := \begin{bmatrix} k_1 - \gamma_1 x_1 \\ -\gamma_2 (\theta_2 + h_2) \end{bmatrix}$. Since $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}$, $\gamma_2 > 0$, then $f_1(x)$ points inside of $C_1$.

- When $x \in \{x : x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) := \begin{bmatrix} k_1 - \gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. 

Figure 17: Vector fields on the boundaries of $C$ to case 5 of Table 4.
Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max}; \gamma_2 > 0 \), then \( f_1(x) \) points outside of \( C_1 \).

Then, since there is no isolated equilibrium point in \( C_1 \), trajectories starting in \( C_1 \) are such that the \( x \) component flow towards \( \{ x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2 \} \).

2. Points on the boundary of \( C_2 \):

- When \( x \in \{ x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2 \}, f_2(x) := \left[ \begin{array}{c} k_1 - \gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{array} \right] \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max}, \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max} \), then \( f_2(x) \) points inside of \( C_2 \).
- When \( x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = 0 \}, f_2(x) := \left[ \begin{array}{c} k_1 - \gamma_1 x_1 \\ k_2 \end{array} \right] \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max} \), \( \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max} \), then \( f_2(x) \) points inside of \( C_2 \).
- When \( x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2 \}, f_2(x) := \left[ \begin{array}{c} k_1 - \gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 + h_2) \end{array} \right] \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max} \), \( \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max} \), then \( f_2(x) \) points outside of \( C_2 \).

Then, since there is no isolated equilibrium point in \( C_2 \), trajectories starting in \( C_2 \) are such that the \( x \) component flow towards \( \{ x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2 \} \).

3. Points on the boundary of \( C_3 \):

- When \( x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 - h_2 \}, f_3(x) := \left[ \begin{array}{c} -\gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 - h_2) \end{array} \right] \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max} \), \( \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max} \), then \( f_3(x) \) points inside of \( C_3 \).
- When \( x \in \{ x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \}, f_3(x) := \left[ \begin{array}{c} -\gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{array} \right] \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max} \), \( \theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max} \), then \( f_3(x) \) points outside of \( C_3 \).

Then, since there is no isolated equilibrium point in \( C_3 \), the trajectories starting in \( C_3 \) have \( x \) component that flow towards \( \{ x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \} \).

4. Points on the boundary of \( C_4 \):

- When \( x \in \{ x : x_1 = \theta_1 + h_1, x_2 \geq \theta_2 - h_2 \}, f_4(x) := \left[ \begin{array}{c} -\gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{array} \right] \). Since \( \gamma_1 > 0, \gamma_2 > 0 \), then \( f_4(x) \) points inside of \( C_4 \).
- When \( x \in \{ x : x_1 = 0, x_2 \geq \theta_2 - h_2 \}, f_4(x) := \left[ \begin{array}{c} 0 \\ -\gamma_2 x_2 \end{array} \right] \). Since \( \gamma_2 > 0 \), then \( f_4(x) \) is tangent to the boundary of \( C_4 \).
- When \( x \in \{ x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 - h_2 \}, f_4(x) := \left[ \begin{array}{c} -\gamma_1 x_1 \\ -\gamma_2 (\theta_2 - h_2) \end{array} \right] \). Since \( \gamma_1 > 0, \gamma_2 > 0 \), then \( f_4(x) \) points outside of the \( C_4 \).

Then, since there is no isolated equilibrium point in \( C_4 \), the trajectories starting in \( C_4 \) have \( x \) component that flow towards \( \{ 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 - h_2 \} \).
Combining the above arguments, Figure 18 shows the transition sequence of $q \in Q$ for case 5 in Table 1.

Now, we compute the value of the trajectories as they transition according to the said sequence.

The differential equation for the $x$ components of the continuous dynamics of $H$ can be evaluated for each possible value of $q$ and written as

$$\dot{x} = K(q) - \Gamma x,$$

where $\Gamma = \begin{bmatrix} \gamma_1 & 0 \\ 0 & \gamma_2 \end{bmatrix}$ and $K: Q \rightarrow \mathbb{R}^{2 \times 1}$ is given by

$$K(q) = \begin{cases} \begin{bmatrix} k_1 \\ 0 \\ 0 \end{bmatrix} & \text{if } q = (0, 0), \\
\begin{bmatrix} 0 \\ 0 \end{bmatrix} & \text{if } q = (0, 1), \\
\begin{bmatrix} k_1 \\ k_2 \end{bmatrix} & \text{if } q = (1, 0), \\
\begin{bmatrix} 0 \\ k_2 \end{bmatrix} & \text{if } q = (1, 1). \end{cases}$$

Restricted to $C$, (34) is a linear time-invariant system. For any initial condition $z(0, 0) = [x(0, 0)^\top \ q(0, 0)^\top]^\top \in C$, the unique solution to (34) for each $t \geq 0$, up to the first jump, is given by

$$x(t, 0) = u(q(0, 0)) + \exp(-\Gamma t)(x(0, 0) - u(q(0, 0))),$$

where $u(q) = \Gamma^{-1}K(q)$ for each $q \in Q$.

Figure 18: Transition graph of $q \in Q$.

For the initial value of $q$ given by $q^0 = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$ and the initial value of $x$ given by

$$x(0, 0) = p_0 = \begin{bmatrix} p_0(1) \\ \theta_2 - h_2 \end{bmatrix},$$

the solution to (34) is given by

$$x(t, 0) = \begin{bmatrix} u_1 - (u_1 - x_1(0, 0)) \exp(-\gamma_1 t) \\ x_2(0, 0) \exp(-\gamma_2 t) \end{bmatrix}.$$
where \( u_1 = \frac{k_1}{n} \). Since \( K(0, 0) = \begin{bmatrix} k_1 \\ 0 \end{bmatrix} \) implies that \( u(q) = \begin{bmatrix} k_1 \\ 0 \end{bmatrix} \). Note that \( x_2(t, 0) \) decreases to zero in \( C_1 \) and that \( x_1(t, 0) \) is increasing in \( C_1 \), reaching the threshold value \( x_1 = \theta_1 + h_1 \) at \( t' = \ln \frac{u_1 - x_1(0, 0)}{u_1 - (\theta_1 + h_1)} \). A jump of \( q \) to \( \begin{bmatrix} 1 \\ 0 \end{bmatrix} \) occurs at \( t = t_1, j = 0 \).

After the jump, the initial value of \( x \) is \( p_1 \), where

\[
p_1 = \begin{bmatrix} \theta_1 + h_1 \\ p_0(2) \left( \frac{u_1 - (\theta_1 + h_1)}{u_1 - p_0(1)} \right) \end{bmatrix}^{\frac{2}{\gamma_1}}.
\]

Proceeding similarly as when the initial state was \( p_0 \), we obtain the following expressions for \( p_2, p_3, \) and \( p_4 \):

\[
p_2 = \begin{bmatrix} u_1 - (u_1 - p_1(1)) \left( \frac{u_2 - p_2(2)}{u_2 - p_1(2)} \right) \end{bmatrix}^{\frac{2}{\gamma_2}}, \quad \theta_2 + h_2
\]

\[
p_3 = \begin{bmatrix} u_2 - (u_2 - p_2(2)) \left( \frac{p_3(1)}{p_2(1)} \right) \end{bmatrix}^{\frac{2}{\gamma_2}}, \quad p_4 = \begin{bmatrix} p_3(1) \left( \frac{p_4(2)}{p_3(2)} \right) \end{bmatrix}^{\frac{2}{\gamma_2}}, \quad \theta_2 - h_2
\]

where \( u_2 = \frac{k_2}{\gamma_2} \). Also, similarly, we have the expression for \( t'_2, t'_3, t'_4 \):

\[
t'_2 = \ln \frac{u_2 - p_2(2)}{u_2 - (\theta_2 + h_2)}^{\frac{1}{\gamma_2}}, \quad t'_3 = \ln \frac{p_3(1)}{\gamma_1}, \quad t'_4 = \ln \frac{p_3(2)}{\gamma_2}.
\]

Then, the period of the limit cycle is given by \( T = t'_1 + t'_2 + t'_3 + t'_4 \). Note that \( t_1 = t'_1, t_2 = t'_1 + t'_2, t_3 = t'_1 + t'_2 + t'_3 \) and \( t_4 = t'_1 + t'_2 + t'_3 + t'_4 \), where \( t_1, t_2, t_3 \) and \( t_4 \) define the jump times \( (t_1, 0), (t_2, 1), (t_3, 2) \), and \( (t_4, 3) \).

Now, we define the map \( \rho : [0, \theta_1^{\max}] \rightarrow \mathbb{R} \) as

\[
\rho(r) = \rho_4 \circ \rho_3 \circ \rho_2 \circ \rho_1(r),
\]

where

\[
\rho_1(r) = (\theta_2 - h_2) \left( \frac{u_1 - (\theta_1 + h_1)}{u_1 - r} \right)^{\frac{2}{\gamma_1}},
\]

\[
\rho_2(r) = u_1 - (u_1 - (\theta_1 + h_1)) \left( \frac{u_2 - (\theta_2 + h_2)}{u_2 - r} \right)^{\frac{2}{\gamma_2}},
\]

\[
\rho_3(r) = u_2 - (u_2 - (\theta_2 + h_2)) \left( \frac{\theta_2 - h_2}{\gamma_1} \right)^{\frac{2}{\gamma_1}},
\]

\[
\rho_4(r) = (\theta_1 - h_1) \left( \frac{\theta_2 - h_2}{r} \right)^{\frac{2}{\gamma_2}}.
\]

Then, \( r \) such that \( \rho(r) = r \) defines \( p_0(1) \).

Then, combining the above expressions, we obtain \([10]-[13]\). Finally, using \([33]\), the set \( S \) is constructed by combining the \( x \) component of the \( (\text{unique}) \) solutions between these points. Since each piece of the \( x \) component corresponding to a constant value of \( q \) is a solution to a linear system, this set of points has the property that, from every point in it, the only existing solution from that point stays in the set, i.e., the set is strongly forward invariant.
A.2 Proof of Proposition 3.1

To verify the sufficient conditions for the existence of nontrivial solutions from an initial point in \( C \cup D \), it is enough to show that \( F(z) \in T_C(z) \) for every \( z \in C \setminus D \) in the boundary of \( C \) (the (VC) condition holds for every point in the interior of \( C \).)

Next, we consider each possible case.

1. Let \( z \in C_1 \setminus D_1 = \{ z : q_1 = 0, q_2 = 0, 0 \leq x_1 < \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2 \} \). Let

   \[ T^1_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0, w_2 \leq 0 \}, \]
   \[ T^2_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0 \}, \]
   \[ T^3_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0, w_2 \geq 0 \}, \]
   \[ T^4_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_2 \geq 0 \}, \]
   \[ T^5_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0, w_2 \geq 0 \}, \]
   \[ T^6_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0 \}, \]
   \[ T^7_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0, w_2 \leq 0 \}, \]
   \[ T^8_{C_1}(z) = \{ w \in \mathbb{R}^2 : w_2 \leq 0 \}. \]

Then, the tangent cone of \( C_1 \) at points \( z = (x, q) \) is given as follows:

- For \( x \in \{ x : x_1 = 0, x_2 = \theta_2 + h_2 \} \), \( T_{C_1}(z) = T^1_{C_1}(z) \),
- For \( x \in \{ x : x_1 = 0, 0 < x_2 < \theta_2 + h_2 \} \), \( T_{C_1}(z) = T^2_{C_1}(z) \).
- For \( x \in \{ x : x_1 = 0, x_2 = 0 \} \), \( T_{C_1}(z) = T^3_{C_1}(z) \).
- For \( x \in \{ 0 < x_1 < \theta_1 + h_1, x_2 = 0 \} \), \( T_{C_1}(z) = T^4_{C_1}(z) \).
- For \( x \in \{ x : x_1 = \theta_1 + h_1, x_2 = 0 \} \), \( T_{C_1}(z) = T^5_{C_1}(z) \).
- For \( x \in \{ x_1 = \theta_1 + h_1, 0 < x_2 < \theta_2 + h_2 \} \), \( T_{C_1}(z) = T^6_{C_1}(z) \).
- For \( x \in \{ x_1 = \theta_1 + h_1, x_2 = \theta_2 + h_2 \} \), \( T_{C_1}(z) = T^7_{C_1}(z) \).
- For \( x \in \{ 0 < x_1 < \theta_1 + h_1, x_2 = \theta_2 + h_2 \} \), \( T_{C_1}(z) = T^8_{C_1}(z) \).

Now, we check the vector field \( F \) on the boundary of \( C_1 \) away from \( D_1 \).

- When \( x \in \{ x : x_1 = 0, 0 \leq x_2 \leq \theta_2 + h_2 \} \), \( f_1(x) := \begin{bmatrix} k_1 \\ -\gamma_2 x_2 \end{bmatrix} \). Since \( k_1 > 0 \), \( f_1(x) \) points inside of \( C_1 \).
Figure 19: Tangent cones on the boundaries of $C_1$.

- When $x \in \{ x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = 0 \}$, $f_1(x) := \begin{bmatrix} k_1 - \gamma_1 x_1 \\ 0 \end{bmatrix}$. Then, $f_1(x)$ is tangent to the boundary of $C_1$.

Then, $F(z) \in T_{C_1}$ holds, implying that (VC) holds at each point $z \in C_1 \setminus D_1$.

2. Let $z \in C_2 \setminus D_2 = \{ z : q_1 = 1, q_2 = 0, x_1 \geq \theta_1 - h_1, 0 \leq x_2 < \theta_2 + h_2 \}$. Let

$$T^1_{C_2}(z) = \{ w \in \mathbb{R}^2 : w_2 \geq 0 \},$$
$$T^2_{C_2}(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0, w_2 \geq 0 \},$$
$$T^3_{C_2}(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0 \},$$
$$T^4_{C_2}(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0, w_2 \geq 0 \},$$
$$T^5_{C_2}(z) = \{ w \in \mathbb{R}^2 : w_2 \leq 0 \}.$$

Then, the tangent cone of $C_2$ is given by as follows:

- For $x \in \{ x : x_1 > \theta_1 - h_1, x_2 = 0 \}$, $T_{C_2}(z) = T^1_{C_2}(z)$,

- For $x \in \{ x : x_1 = \theta_1 - h_1, x_2 = 0 \}$, $T_{C_2}(z) = T^2_{C_2}(z)$.

- For $x \in \{ x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2 \}$, $T_{C_2}(z) = T^3_{C_2}(z)$.

- For $x \in \{ x_1 = \theta_1 - h_1, x_2 = \theta_2 + h_2 \}$, $T_{C_2}(z) = T^4_{C_2}(z)$.

- For $x \in \{ x : x_1 > \theta_1 - h_1, x_2 = \theta_2 + h_2 \}$, $T_{C_2}(z) = T^5_{C_2}(z)$.
Figure 20 depicts the tangent cones on the boundaries of $C_2$.

![Diagram of tangent cones on the boundaries of $C_2$.](image)

**Figure 20**: The tangent cone of $C_2$ when $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\max}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$.

Now, we check the vector field $F$ on the boundary of $C_2$ away from $D_2$.

- When $x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = 0 \}$, $f_2(x) := \begin{bmatrix} k_1 - \gamma_1 x_1 \\ k_2 \end{bmatrix}$. Since $k_2 > 0$, we have that $f_2(x)$ points inside of $C_2$.

Then, $F(z) \in T_{C_2}(z)$ holds, implying that (VC) holds at each point $z \in C_2 \setminus D_2$.

3. Let $z \in C_3 \setminus D_3 = \{ z : q_1 = 1, q_2 = 1, x_1 > \theta_1 - h_1, x_2 > \theta_2 - h_2 \}$.

Since there are no points in the boundary of $C_3$ that are not in $D_3$, (VC) holds for free.

4. Let $z \in C_4 \setminus D_4 = \{ z : q_1 = 0, q_2 = 1, 0 \leq x_1 \leq \theta_1 + h_1, x_2 > \theta_2 - h_2 \}$. Let

$$
T_{C_4}^1(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0 \},
T_{C_4}^2(z) = \{ w \in \mathbb{R}^2 : w_1 \leq 0, w_2 \geq 0 \},
T_{C_4}^3(z) = \{ w \in \mathbb{R}^2 : w_2 \geq 0 \},
T_{C_4}^4(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0, w_2 \geq 0 \},
T_{C_4}^5(z) = \{ w \in \mathbb{R}^2 : w_1 \geq 0 \}.
$$

Then, the tangent cone of $C_4$ is given by as follows:

- For $x \in \{ x : x_1 = \theta_1 + h_1, x_2 > \theta_2 - h_2 \}$, $T_{C_4}(z) = T_{C_4}^1(z)$,
- For $x \in \{ x : x_1 = \theta_1 + h_1, x_2 = \theta_2 - h_2 \}$, $T_{C_4}(z) = T_{C_4}^2(z)$.
• For \( x \in \{ x : 0 < x_1 < \theta_1 + h_1, x_2 = \theta_2 - h_2 \} \), \( T_{C_4}(z) = T_{C_4}^3(z) \).

• For \( x \in \{ x_1 = 0, x_2 = \theta_2 - h_2 \} \), \( T_{C_4}(z) = T_{C_4}^4(z) \).

• For \( x \in \{ x : x_1 = 0, x_2 > \theta_2 - h_2 \} \), \( T_{C_4}(z) = T_{C_4}^5(z) \).

\[ q_1 = 0 \quad q_2 = 1 \]

\[ \theta_2 + h_2 \quad \theta_2 - h_2 \]

\[ \theta_1 - h_1 \quad \theta_1 + h_1 \quad \theta_1^{\text{max}} \]

\[ x_2 \]

\[ x_1 \]

Figure 21: Tangent cones on the boundaries of \( C_4 \).

Now, we check the vector field \( F \) on the boundary of \( C_4 \) away from \( D_4 \).

• When \( x \in \{ x : x_1 = 0, x_2 \geq \theta_2 - h_2 \} \), \( f_4(x) := \begin{bmatrix} 0 \\ -\gamma_2 x_2 \end{bmatrix} \), and \( f_4(x) \) is tangent to the boundary of \( C_4 \). Then, \( F(z) \in T_{C_4}(z) \) holds at each point \( z \in C_4 \setminus D_4 \).

Combining the above arguments, for each case in Table 1 (VC) holds and nontrivial solutions to \( H \) in (8) exist.

Since \( f_i \) is linear, every solution to \( \dot{z} = F(z) \) subject to \( z \in C \) does not escape to infinity by flowing. Then, condition 2) below (VC) does not hold. Since \( G(D) \subset C \cup D \), then condition 3) therein does not hold either.

Finally, every solution is not Zeno, since at most after the second jump, every solution needs to flow (linearly) from the value after the jump, which is given by \( G \), for at least \( 2 \min\{h_1, h_2\} \) in the \( x_1 \) or in the \( x_2 \) direction (for certain initial conditions, e.g., \( z(0, 0) = [\theta_1 - h_1, \theta_2 - h_2, 1, 1] \), solutions jump twice consecutively, and after that, flow for the said amount).
A.3 Proof of Proposition 3.5

Note that when \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2, q_1 = 1, q_2 = 0, \)

\[
0 = \dot{x}_1 = k_1 - \gamma_1 x_1 \Rightarrow k_1 - \gamma_1 x_1 = 0 \Rightarrow x_1^* = \frac{k_1}{\gamma_1}
\]
\[
0 = \dot{x}_2 = k_2 - \gamma_2 x_2 \Rightarrow k_2 - \gamma_2 x_2 = 0 \Rightarrow x_2^* = \frac{k_2}{\gamma_2},
\]
from where we have \( z_1^* = [x_1^* \ 0]^\top \in C_2. \) Now, change to \( e \) coordinates given by

\[
e_1 = x_1 - x_1^*, \quad e_2 = x_2 - x_2^*.
\]

We have that

\[
\begin{align*}
\dot{e}_1 &= \dot{x}_1 - \dot{x}_1^* = k_1 - \gamma_1 x_1 - 0 = k_1 - \gamma_1 (e_1 + x_1^*) \\
&= k_1 - \gamma_1 e_1 - k_1 = -\gamma_1 e_1, \\
\dot{e}_2 &= \dot{x}_2 - \dot{x}_2^* = k_2 - \gamma_2 x_2 - 0 = k_2 - \gamma_2 (e_2 + x_2^*) \\
&= k_2 - \gamma_2 e_2 - k_2 = -\gamma_2 e_2.
\end{align*}
\]

Then, the \( x \) component of \( \dot{z} = F(z) \) leads to

\[
\dot{e} = \begin{bmatrix}
-\gamma_1 & 0 \\
0 & -\gamma_2
\end{bmatrix} e.
\]

Then, since \( \gamma_1 \) and \( \gamma_2 \) are positive, we have that \( z_1^* \) is (exponentially) stable – this property can be easily certified with the Lyapunov function \( V(e) = e^\top e \).

Now we check the vector fields of boundaries of \( C_2 \) (see Figure 22).

![Figure 22: The vector fields on the boundaries of \( C_2 \) when \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2 \).]
• When \( x \in \{x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2 \} \), \( f_2(x) = \begin{bmatrix} k_1 - \gamma_1(\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix} \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2 \), we have that \( f_2(x) \) points inside of \( C_2 \).

• When \( x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2 \} \), \( f_2(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ k_2 - \gamma_2(\theta_2 + h_2) \end{bmatrix} \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2 \), we have that \( f_2(x) \) points inside of \( C_2 \).

• When \( x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = 0 \} \), \( f_2(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ k_2 \end{bmatrix} \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, k_2 > 0 \), we have that \( f_2(x) \) points inside of \( C_2 \).

Then, once a trajectory enters or starts in \( C_2 \), it will stay and never leave \( C_2 \), i.e., the set \( C_2 \) is forward invariant. As a consequence, since the equilibrium point \( z_1^* \) belongs to \( C_2 \), every trajectory starting from or reaching \( C_2 \) converges to \( z_1^* \).

Global asymptotic stability follows since for every initial condition \( z(0, 0) \in (C \cup D) \setminus C_2 \), solutions reach \( C_2 \) in finite time. To establish this property, we check the vector field of the system on the boundary of each set \( C_i \), for each \( i \in \{1, 3, 4\} \).

![Figure 23: Vector fields at the boundaries of \( C_1 \), \( C_4 \), when \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2 \). (a) The vector field at the boundaries of \( C_1 \), (b) The vector field of the boundaries of \( C_4 \).](image)

- For initial points \( z(0, 0) \in C_1 \) (see Figure 23(a)), when \( x \in \{x : 0 \leq x_1 < \theta_1 + h_1, x_2 = \theta_2 + h_2 \} \), \( f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ -\gamma_2(\theta_2 + h_2) \end{bmatrix} \). Since \( \theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{\text{max}}, 0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2 \) we have that \( f_1(x) \) points inside \( C_1 \). When \( x \in \{x : x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2 \} \), \( f_1(x) = \begin{bmatrix} k_1 - \gamma_1(\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix} \). Since \( \frac{k_1}{\gamma_1} > \theta_1 + h_1 \), we have that \( f_1(x) \) points outside \( C_1 \). Thus, for every point \( z \in C_1, x_1 \) reaches \( \theta_1 + h_1 \) since there is no equilibrium point in \( C_1 \) for this range of parameters. Then, a jump occurs. After the jump, the solution belongs to \( C_2 \).
For each initial point $z(0,0) \in C_4$ (see Figure 24(b)), when $x \in \{x : 0 \leq x_1 < \theta_1 + h_1, x_2 = \theta_2 - h_2\}$, $f_4(x) = \begin{bmatrix} -\gamma_1 x_1 \\ -\gamma_2 (\theta_2 - h_2) \end{bmatrix}$. Then, we have that $f_4(x)$ points outside $C_4$ and every solution leaves $C_4$ by jumping into $C_1$ when $x_1$ reaches $\theta_1 - h_1$, from where it will enter $C_2$ in finite time. When $x \in \{x : x_1 = \theta_1 + h_1, x_2 > \theta_2 - h_2\}$, $f_4(x) = \begin{bmatrix} -\gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. Then, we have that $f_4(x)$ points inside $C_4$. Then, for every initial condition $z(0,0) \in C_4$, solutions will reach $C_2$ in finite time.

For every initial point $z(0,0) \in C_3$ (see Figure 24(a)), if $0 < \frac{k_2}{\gamma_2} < \theta_2 - h_2$, when $x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 - h_2\}$, $f_3(x) = \begin{bmatrix} -\gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 - h_2) \end{bmatrix}$. We have that $f_3(x)$ points outside of $C_3$. When $x \in \{x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2\}$, we have $f_3(x) = \begin{bmatrix} -\gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$, which points outside $C_3$. If $\theta_2 - h_2 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$ (see Figure 24(b)), when $x \in \{x : \theta_1 - h_1 < x_1 < \theta_1^{max}, x_2 = \theta_2 - h_2\}$, $f_3(x) = \begin{bmatrix} -\gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 - h_2) \end{bmatrix}$ points inside $C_3$. When $x \in \{x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2\}$, $f_3(x) = \begin{bmatrix} -\gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$ points outside $C_3$. Then, from $z(0,0) \in C_3$, solutions will leave $C_3$ and jump into $C_4$ or $C_2$. Using the arguments above, solutions will enter inside of $C_2$ in finite time.

From the arguments above, when $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{max}$, $0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$, the equilibrium point $z^*_1$ is globally asymptotically stable.

For case 2 in Table 1, it can be proven that $z^*_3$ is globally asymptotically stable.

Note that when $q_1 = 0$, $q_2 = 0$, $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$, 

Figure 24: The vector field at the boundaries of $C_3$, when $\theta_1 + h_1 < \frac{k_1}{\gamma_1} < \theta_1^{max}$, $0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$. (a) Case $\frac{k_2}{\gamma_2} < \theta_2 - h_2$, (b) Case $\theta_2 - h_2 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$
Figure 25: The vector field at the boundaries of $C_2$, when $0 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$. (a) Case $\frac{k_2}{\gamma_2} < \theta_2 + h_2$, (b) Case $\frac{k_2}{\gamma_2} > \theta_2 + h_2$.

\[
\begin{align*}
0 &= \dot{x}_1 = k_1 - \gamma_1 x_1 \quad \Rightarrow \quad k_1 - \gamma_1 x_1 = 0 \quad \Rightarrow \quad x_1^* = \frac{k_1}{\gamma_1} \\
0 &= \dot{x}_2 = \gamma_2 x_2 \quad \Rightarrow \quad -\gamma_2 x_2 = 0 \quad \Rightarrow \quad x_2^* = 0,
\end{align*}
\]

from where we have $z_2^* = [x_1^*\, 0\, 0]^T \in C_1$. Now, change to $e$ coordinates given by

\[
e_1 = x_1 - x_1^*, \quad e_2 = x_2 - x_2^*.
\]

We have that

\[
\begin{align*}
\dot{e}_1 &= \dot{x}_1 - \dot{x}_1^* = k_1 - \gamma_1 x_1 - 0 = k_1 - \gamma_1 (e_1 + x_1^*) \\
&= k_1 - \gamma_1 e_1 - k_1 = -\gamma_1 e_1, \\
\dot{e}_2 &= \dot{x}_2 = k_2 - \gamma_2 x_2 = k_2 - \gamma_2 (e_2 + x_2^*) \\
&= k_2 - \gamma_2 e_2 - k_2 = -\gamma_2 e_2.
\end{align*}
\]

Then, the $x$ component of $\dot{z} = F(z)$ becomes

\[
\dot{e} = \begin{bmatrix} -\gamma_1 & 0 \\ 0 & -\gamma_2 \end{bmatrix} e.
\]

Then, since $\gamma_1$ and $\gamma_2$ are positive, we have that $z_2^*$ is stable (this property can be certified with the Lyapunov function $V(e) = e^T e$).

Now we check the vector fields on the boundaries of $C_1$ (see Figure 26).

- When $x \in \{ x : x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2 \}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. Since $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$, we have that $f_1(x)$ points inside $C_1$. 

47
Figure 26: The vector field at the boundaries of $C_1$, when $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ -\gamma_2 (\theta_2 + h_2) \end{bmatrix}$. Since $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$, we have that $f_1(x)$ points inside $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = 0\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ 0 \end{bmatrix}$. $f_1(x)$ is tangent to the boundary of $C_1$.

- When $x \in \{x : x_1 = 0, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 \\ -\gamma_2 x_2 \end{bmatrix}$. Since $k_1 > 0$, we have that $f_1(x)$ points inside $C_1$.

Then, every trajectory that enters or starts from $C_1$ will stay or never leave $C_1$. Then, the set $C_1$ is forward invariant.

Since the equilibrium point $z^*_2$ belongs to $C_1$, every trajectory that reaches or starts from $C_1$ converges to $z^*_2$.

Global asymptotic stability follows since for every initial condition $z(0,0) \in (C \cup D) \setminus C_1$, solutions reach $C_1$ in finite time. To establish this property, we check the vector field of the system on the boundary of each set $C_i$, for each $i \in \{2,3,4\}$.

- For initial points $z(0,0) \in C_2$:
  
  - if $\frac{k_2}{\gamma_2} < \theta_2 + h_2$ (see Figure [25](a)), when $x \in \{x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_2(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$. Since $0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1$, we have that $f_2(x)$ points outside of $C_2$. When $x \in \{x : x_1 > \theta_1 - h_1, x_2 = \theta_2 + h_2\}$, $f_2(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$.
\[
\begin{bmatrix}
k_1 - \gamma_1 x_1 \\
k_2 - \gamma_2 (\theta_2 + h_2)
\end{bmatrix}.
\]
Since \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1\), we have that \(f_2(x)\) points inside of \(C_2\).

Since there is no equilibrium point in \(C_2\) for this range of parameters and the dynamics of \(x\) are linear, \(x_1\) reaches \(\theta_1 - h_1\) for every point \(z \in C_2\). Then, a jump occurs. After the jump, the solution belongs to \(C_1\).

- If \(\frac{k_2}{\gamma_2} > \theta_2 + h_2\) (see Figure 25(b)), when \(x \in \{ x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2 \}\), \(f_2(x) = \begin{bmatrix}
k_1 - \gamma_1 (\theta_1 - h_1) \\
k_2 - \gamma_2 (\theta_2 + h_2)
\end{bmatrix}\). Since \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1\), we have that \(f_2(x)\) points outside of \(C_2\). When \(x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2 \}\), \(f_1(x) = \begin{bmatrix}
k_1 - \gamma_1 x_1 \\
k_2 - \gamma_2 (\theta_2 + h_2)
\end{bmatrix}\). Since \(0 < \frac{k_1}{\gamma_1} < \theta_1 - h_1\), we have that \(f_2(x)\) points outside of \(C_2\).

Then, from \(z(0,0) \in C_2\), solutions will leave \(C_2\) and jump into \(C_1\) or \(C_3\).

- For every initial point \(z(0,0) \in C_3\):
  - if \(\frac{k_2}{\gamma_2} < \theta_2 - h_2\), when \(x \in \{ x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 - h_2 \}\) (see similar case shown in Figure 24(a)), \(f_3(x) = \begin{bmatrix}
-\gamma_1 x_1 \\
k_2 - \gamma_2 (\theta_2 - h_2)
\end{bmatrix}\). We have that \(f_3(x)\) points outside of \(C_3\). When \(x \in \{ x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \}\), we have \(f_3(x) = \begin{bmatrix}
-\gamma_1 (\theta_1 - h_1) \\
k_2 - \gamma_2 x_2
\end{bmatrix}\), which points outside of \(C_3\).
  - If \(\theta_2 - h_2 < \frac{k_2}{\gamma_2} < \theta_2 + h_2\) (see similar case shown in Figure 25(b)), when \(x \in \{ x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2 \}\), \(f_3(x) = \begin{bmatrix}
-\gamma_1 (\theta_1 - h_1) \\
k_2 - \gamma_2 x_2
\end{bmatrix}\) points outside of \(C_3\). When \(x \in \{ x : x_1 > \theta_1 - h_1, x_2 = \theta_2 - h_2 \}\), \(f_3(x) = \begin{bmatrix}
-\gamma_1 x_1 \\
k_2 - \gamma_2 (\theta_2 - h_2)
\end{bmatrix}\). We have that \(f_3(x)\) points inside of \(C_3\).

Then, from \(z(0,0) \in C_3\), solutions will leave \(C_3\) and jump into \(C_4\) or \(C_2\).

- For each initial point \(z(0,0) \in C_4\) (see similar case shown in Figure 23(b)), when \(x \in \{ x : 0 \leq x_1 < \theta_1 + h_1, x_2 = \theta_2 - h_2 \}\), \(f_4(x) = \begin{bmatrix}
-\gamma_1 x_1 \\
-\gamma_2 (\theta_2 - h_2)
\end{bmatrix}\). Then, we have that \(f_4(x)\) points outside \(C_4\) and every solution leaves \(C_4\) by jumping into \(C_1\). When \(x \in \{ x : x_1 = \theta_1 + h_1, x_2 > \theta_2 - h_2 \}\), \(f_4(x) = \begin{bmatrix}
-\gamma_1 (\theta_1 + h_1) \\
-\gamma_2 x_2
\end{bmatrix}\). Then, we have that \(f_4(x)\) points inside \(C_4\). Then, for every initial condition \(z(0,0) \in C_4\), solutions will reach \(C_1\) in finite time.

From the above analysis, we have that: 1) from \(C_2\) trajectories go to either \(C_1\) or \(C_3\); 2) from \(C_3\) trajectories go to either \(C_1\) or \(C_4\); 3) from \(C_4\) trajectories go to \(C_1\).

Then, trajectories eventually enter \(C_1\), which, using the arguments above, implies that the equilibrium point \(z_2^*\) is globally asymptotically stable.
Similarly, for case 4 in Table 1, it can be proven that $z_2^*$ is globally asymptotically stable. Since stability of $z_2^*$ was proven in the proof of case 2 in Table 1 now we check the vector fields on the boundaries of $C_1$ when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}$ (see Figure 27).

![Figure 27: The vector field at the boundaries of $C_1$, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}$.](image)

- When $x \in \{x : x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1(x_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, we have that $f_1(x)$ points inside $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ -\gamma_2 (\theta_2 + h_2) \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\text{max}}$, we have that $f_1(x)$ points inside $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = 0\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ 0 \end{bmatrix}$. $f_1(x)$ is tangent to the boundary of $C_1$.

- When $x \in \{x : x_1 = 0, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 \\ -\gamma_2 x_2 \end{bmatrix}$. Since $k_1 > 0$, we have that $f_1(x)$ points inside $C_1$.

Then, every trajectory that enters or starts from $C_1$ will stay or never leave $C_1$. Then, the set $C_1$ is forward invariant.
Figure 28: The vector field at the boundaries of $C_2$, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max}$.

Since the equilibrium point $z_2^*$ belongs to $C_1$, every trajectory that reaches or starts from $C_1$ converges to $z_2^*$.

Global asymptotic stability follows since for every initial condition $z(0, 0) \in (C \cup D) \setminus C_1$, solutions reach $C_1$ in finite time. To establish this property, we check the vector field of the system on the boundary of each set $C_i$, for each $i \in \{2, 3, 4\}$.

- For initial points $z(0, 0) \in C_2$: When $x \in \{x : x_1 = \theta_1 - h_1, 0 \leq x_2 < \theta_2 + h_2\}$ (see Figure 28), $f_2(x) = \left[ \begin{array}{c} k_1 - \gamma_1(\theta_1 - h_1) \\ k_2 - \gamma_2x_2 \end{array} \right]$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, we have that $f_2(x)$ points inside of $C_2$. When $x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2\}$, $f_2(x) = \left[ \begin{array}{c} k_1 - \gamma_1x_1 \\ k_2 - \gamma_2(\theta_2 + h_2) \end{array} \right]$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max}$, we have that $f_2(x)$ points outside of $C_2$.

Since there is no equilibrium point in $C_2$ for this range of parameters and the dynamics of $x$ are linear, $x_2$ reaches $\theta_2 + h_2$ for every point $z \in C_2$.

Then, from $z(0, 0) \in C_2$, solutions will leave $C_2$ and jump into $C_3$.

- For every initial point $z(0, 0) \in C_3$: (see Figure 29) when $x \in \{x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2\}$, since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $f_3(x) = \left[ \begin{array}{c} -\gamma_1(\theta_1 - h_1) \\ k_2 - \gamma_2x_2 \end{array} \right]$ points outside of $C_3$. When $x \in \{x : x_1 > \theta_1 - h_1, x_2 = \theta_2 - h_2\}$, $f_3(x) = \left[ \begin{array}{c} -\gamma_1x_1 \\ k_2 - \gamma_2(\theta_2 - h_2) \end{array} \right]$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, we have that $f_3(x)$ points inside of $C_3$. Then, from $z(0, 0) \in C_3$, solutions will leave $C_3$ and jump into $C_4$. 51
Figure 29: The vector field at the boundaries of $C_3$, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\theta_2 + h_2 < \frac{k_2}{\gamma_2} < \theta_2^{\max}$.

For each initial point $z(0,0) \in C_4$ (see similar case shown in Figure 23(b)) when $x \in \{x : 0 \leq x_1 < \theta_1 + h_1, x_2 = \theta_2 - h_2\}$, since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $f_4(x) = \begin{bmatrix} -\gamma_1 x_1 \\ -\gamma_2 (\theta_2 - h_2) \end{bmatrix}$. Then, we have that $f_4(x)$ points outside $C_4$ and every solution leaves $C_4$ by jumping into $C_1$. When $x \in \{x : x_1 = \theta_1 + h_1, x_2 > \theta_2 - h_2\}$, $f_4(x) = \begin{bmatrix} -\gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. Then, we have that $f_4(x)$ points inside $C_4$. Then, for every initial condition $z(0,0) \in C_4$, solutions will reach $C_1$ in finite time.

From the above analysis, we have that: 1) from $C_2$ trajectories go to $C_3$; 2) from $C_3$ trajectories go to $C_4$; 3) from $C_4$ trajectories go to $C_1$.

Then, trajectories eventually enter $C_1$, which, using the arguments above, implies that the equilibrium point $z^*_2$ is globally asymptotically stable.

A.4 Proof of Proposition 3.6

For case 3, when $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $\frac{k_2}{\gamma_2} < \theta_2 + h_2$, $z_1^*$ and $z_2^*$ are located in the region noted as $C'$ in Figure 30.

For an initial point $z(0,0) \in C_2$, we check the vector fields on the boundaries of $C_2$ (see Figure 31(a)).

- When $x \in \{x : x_1 = \theta_1 - h_1, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_2(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, $0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$, we have that $f_2(x)$ points inside of $C_2$. 

52
Then, once a trajectory enters or starts from $C$, reaching or starting from $C$, we have that $f_2(x)$ points inside of $C$.

When $x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = \theta_2 + h_2\}$, $f_2(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 + h_2) \end{bmatrix}$. Since $\theta_1 - h_1 < k_1 \gamma_1 < \theta_1 + h_1$, $0 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$, we have that $f_2(x)$ points inside of $C$.

When $x \in \{x : x_1 \geq \theta_1 - h_1, x_2 = 0\}$, $f_2(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ k_2 \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, k_2 > 0$, we have that $f_2(x)$ points inside of $C$.

Then, once a trajectory enters or starts from $C$, it will stay or never leave $C$. Then, the set $C$ is forward invariant. Since the equilibrium point $z^*_1$ belongs to $C$, every trajectory reaching or starting from $C$ converges to $z^*_1$.

For $z(0, 0) \in C_1$, we check the vector fields on the boundaries of $C_1$ (see Figure 31(b)).

- When $x \in \{x : x_1 = \theta_1 + h_1, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 + h_1) \\ -\gamma_2 x_2 \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, we have that $f_1(x)$ points inside $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 x_1 \\ -\gamma_2 (\theta_2 + h_2) \end{bmatrix}$. Since $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1$, we have that $f_1(x)$ points inside $C_1$.

- When $x \in \{x : 0 \leq x_1 \leq \theta_1 + h_1, x_2 = 0\}$, $f_1(x) = \begin{bmatrix} k_1 - \gamma_1 (\theta_1 + h_1) \\ 0 \end{bmatrix}$. $f_1(x)$ is tangent to the boundary of $C_1$.

- When $x \in \{x : x_1 = 0, 0 \leq x_2 \leq \theta_2 + h_2\}$, $f_1(x) = \begin{bmatrix} k_1 \\ -\gamma_2 x_2 \end{bmatrix}$. Since $k_1 > 0$, we have that $f_1(x)$ points inside $C_1$.  

Figure 30: Region $C'$ given by the overlap between $C_1$ and $C_2$ when projected onto the $x$ component.
Figure 31: when $\theta_1-h_1 < \frac{k_4}{\gamma_1} < \theta_1+h_1, 0 < \frac{k_2}{\gamma_2} < \theta_2-h_2$: (a) the vector field at the boundaries of $C_2$, (b) the vector field at the boundaries of $C_1$.

Then, once a trajectory enters or starts from $C_1$, it will stay or never leave $C_1$. Then, the set $C_1$ is forward invariant. Since the equilibrium point $z_2^*$ belongs to $C_1$, every trajectory reaching or starting from $C_1$ converges to $z_2^*$.

For initial points in $C_4$, the vector field of the boundary at $C_4$ is shown in Figure 23 (b). When $x \in \{x: 0 < x_1 < \theta_1+ h_1, x_2 = \theta_2-h_2\}$, $f_4(x) = \begin{bmatrix} -\gamma_1 x_1 \\ -\gamma_2(\theta_2-h_2) \end{bmatrix}$. Then, we have that $f_4(x)$ points outside $C_4$ and every solution leaves $C_4$ by jumping into $C_1$. Then, for every initial condition $z(0,0) \in C_4$, solutions will reach $C_1$ in finite time. As $z_2^* \in C_1$, so the trajectory will stay in $C_1$ and converge to $z_2^*$.

If $z(0,0) \in C_3$, the vector field at the boundary of $C_3$ is similar as that shown in Figure 24.

1. If the parameters are in the range of $\theta_1-h_1 < \frac{k_4}{\gamma_1} < \theta_1+h_1, 0 < \frac{k_2}{\gamma_2} < \theta_2-h_2$ (see similar case shown in Figure 24(a)), when $x \in \{x: \theta_1-h_1 < x_1 < \theta_1^{max}, x_2 = \theta_2-h_2\}$,

   $f_3(x) = \begin{bmatrix} -\gamma_1 x_1 \\ k_2 - \gamma_2(\theta_2-h_2) \end{bmatrix}$. We have that $f_3(x)$ points outside of $C_3$. When $x \in \{x: x_1 = \theta_1-h_1, x_2 \geq \theta_2-h_2\}$, we have $f_3(x) = \begin{bmatrix} -\gamma_1(\theta_1-h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$, which points outside $C_3$. Depending on which jump set the solution hits, two possibilities of the equilibrium points exist.

   - If the trajectory hits the set $x \in \{x: x_1 = \theta_1-h_1, x_2 > \theta_2-h_2\}$, which leads to an update of $q_1$, the solution will jump into $C_4$. For this case, the trajectory will reach $C_1$ in finite time and converge to $z_2^*$.
   - If the trajectory hits the set $x \in \{x: x_1 > \theta_1-h_1, x_2 = \theta_2-h_2\}$, $q_2$ is updated to 0 from 1, the trajectory will enter $C_2$, and converge to the equilibrium point $z_1^*$, which is inside of $C_2$. 

54
2. If the parameters are in the range of $\theta_1 - h_1 < \frac{k_1}{\gamma_1} < \theta_1 + h_1, \theta_2 - h_2 < \frac{k_2}{\gamma_2} < \theta_2 + h_2$ (see similar case shown in Figure 24(b)), when $x \in \{x : x_1 > \theta_1 + h_1, x_2 = \theta_2 - h_2\}$, $f_3(x) = \begin{bmatrix} -\gamma_1 x_1 \\ k_2 - \gamma_2 (\theta_2 - h_2) \end{bmatrix}$. We have that $f_3(x)$ points inside of $C_3$. When $x \in \{x : x_1 = \theta_1 - h_1, x_2 \geq \theta_2 - h_2\}$, we have $f_3(x) = \begin{bmatrix} -\gamma_1 (\theta_1 - h_1) \\ k_2 - \gamma_2 x_2 \end{bmatrix}$, which points outside of $C_3$. Thus, when the trajectory hits the set $\{x : x_1 = \theta_1 - h_1, x_2 > \theta_2 - h_2\}$, a jump will occur, the solution will jump into $C_4$ and finally enter $C_1$ and converge to $z_2^*$. 