J. Differential Equations 247 (2009) 1013–1042

Contents lists available at ScienceDirect

Journal of Differential Equations

www.elsevier.com/locate/jde

Multi-valued characteristics and Morse decompositions

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ARTICLE INFO

Article history:
Received 22 May 2008
Revised 16 January 2009
Available online 23 May 2009

ABSTRACT

A rapid growth of molecular and systems biology in recent years challenges mathematicians to develop robust modeling and analytical tools for this area.

We combine a theory of monotone input–output systems with a classical theory of Morse decompositions in the context of ordinary differential equations models of biochemical reactions. We show that a multi-valued input–output characteristic can be used to define non-trivial Morse decompositions which provide information about a global structure of the attractor. The previous work on input–output characteristics is shown to apply locally to individual Morse sets and is seamlessly incorporated into our global theory.

We apply our tools to a model of cell cycle maintenance. We show that changing the strength of the negative feedback loop can lead to cessation of cell cycle in two different ways: it can either lead to globally attracting equilibrium or to a pair of equilibria that attract almost all solutions.

1. Introduction

Recent advances in molecular and cell biology challenge mathematicians to develop new approaches for formulation and analysis of the appropriate mathematical models [22]. Currently available biological data often provide a good qualitative information (a product of gene A up-regulates gene B), but rarely a good quantitative information (rate constants, form of the nonlinearities). Therefore the new techniques must be able to utilize qualitative information and have robust predictions that are independent on the unknown parameters. The important role of noise in the sub-cellular

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1 This research was partially supported by NSF/NIH grant 0443863 and NSF-CRCNS grant 0515290.

0022-0396/$ – see front matter
doi:10.1016/j.jde.2009.04.019

mechanisms only underscores the need for results that would persist in the presence of perturbations in both the phase space and the parameters.

In addition to these significant constraints, biochemistry provides us with one advantage. The models used in molecular biology often arise from the mass action kinetics, often augmented by Michealis–Menten nonlinearities, and therefore are monotone in their arguments. Although they are biologically well founded exceptions to this monotonicity [15], it reflects the prevailing paradigm in the design and evaluation of biochemical experiments. The effect of knocking out a particular gene on the activity of another gene is usually characterized in binary terms as being either positive (up regulation) or negative (down regulation). Consequently, each interaction between biochemical agents can be labeled as either positive or negative, which is reflected in the choice of either a monotonically increasing, or monotonically decreasing nonlinearity in the model. This structure can be exploited by combining theory of *monotone systems* and methods from control theory using input–output characteristics.

1.1. Monotone systems and characteristics

Theory of monotone systems has its roots in both cooperative systems of ordinary differential equations [17,29] and in parabolic partial differential equations [21,29]. The monograph [29] provides a comprehensive introduction to this theory. The fundamental result [18] states that almost all solutions in a strongly monotone system converge to the set of equilibria.

Sontag and collaborators [1–4,9,10,12,31] pioneered an extension of the monotone system theory that has been particularly useful in biochemical models. Consider an arbitrary set of differential equations

$$\dot{x} = g(x), \quad x \in \mathbb{R}^n, \tag{1}$$

with monotone interactions $\frac{\partial g_i}{\partial x_j}(x) \geqslant 0$, or $\frac{\partial g_i}{\partial x_j}(x) \leqslant 0$, for all x and all $i \neq j$. We can associate a signed digraph to such system: vertices correspond to the variables and signed edges to the interactions between them. Choose a maximal *consistent subgraph* which has no negative loops, where the sign of the loop is a product of signs along the edges [2,7,11]. If we replace all edges missing from this subgraph by a set of static inputs $u \in \mathbb{R}^k$ the system is monotone for every value of u [2,7]. This yields a *parameterized monotone system*

$$\dot{x} = f(x, u), \quad u \in \mathbb{R}^k. \tag{2}$$

We recover the original system (1) via a feedback function $h : \mathbb{R}^n \to \mathbb{R}^k$ which satisfies $f(x, h(x)) = g(x)$. A study of a parameterized system (2) can be used to derive conclusions about the system (1) [1–4,9,10,12,31]. Central role in this process is played by an *input–output characteristic* of (2): for each value of u the characteristic is (assumed to be unique) equilibrium of (2). Recent extensions [8,11] allow for a *multi-valued input–output characteristic* where the value at u is the set of all equilibria of (2) at a fixed u. The power of this approach is best realized when u contains only a few variables and is preferably a single variable. The thrust of these results is the correspondence between the fixed points of the characteristic and the equilibria of the system (1) which includes their local stability [2,4,11]. The results are very robust since any change to the vector field that preserves the fixed points of the characteristic does not change the conclusions about the original system. These results are, however, local: they characterize equilibria and their local behavior, but not the global dynamics of connecting orbits between the equilibria.

1.2. Morse decompositions

Conley [6] pioneered topological methods in study of robust dynamics. An isolating neighborhood and its associated isolated invariant set are basic objects in Conley theory. A compact set N is an *isolating neighborhood* if its maximal invariant set lies in its interior. This maximal invariant set is then an *isolated invariant set.* Notice that if N is an isolating neighborhood for a flow φ^0 it is also an isolating neighborhood for all nearby flows in C^0 topology. So isolating neighborhoods are inherently robust under perturbations. Conley's key insight was that while invariant sets are not robust under perturbations, it is always possible to decompose the invariant set into a collection of isolated invariant sets, which, by their definition, are robust. This decomposition is called a *Morse decomposition.* Each Morse set can have a complicated internal structure and may contain multiple equilibria, periodic orbits, and connecting orbits between them. While this internal structure may be sensitive to changes in parameters, the relationship between different Morse sets, which is encoded in a partial order between the Morse sets, is robust. There cannot be any orbit from a lower to a higher Morse set in this order. Since every invariant set admits a trivial Morse decomposition containing exactly one Morse set, only non-trivial decompositions are informative. For the same reason a Morse decomposition does not bring a new insight into the structure of the invariant set, if the Morse sets are build from the bottom up by aggregating known invariant sets into Morse sets. The power of this concept is fully realized by methods that show the existence of a Morse decomposition *a priori*, from the top down, without a detailed knowledge of the underlying invariant set. In systems that include ordinary [14], delay-differential [20,23] and partial differential equations [24] this has been accomplished with a help of a discrete Lyapunov function. An invariant set for which the value of the discrete Lyapunov function was a particular constant i comprised ith Morse set, and the ordering followed from the fact that the Lyapunov function is non-increasing.

A concept of a Morse decomposition allows a top–down approach to study of complicated invariant sets. First we find a non-trivial Morse decomposition whose ordering defines in a broad outline the structure of the global dynamics. In the second step, and perhaps using different methods, we study the internal structure of individual Morse sets.

The difficulty with this approach is the lack of good methods to find a non-trivial Morse decomposition for a general dynamical system.

1.3. Characteristics and Morse decompositions

The main result of this paper is to show that the input–output characteristic of the parameterized system (2) can be used to construct a Morse decomposition of the original system (1) in the case when $u \in U \subset \mathbb{R}$ is scalar.

This will be done in two steps. First we use the dissipativity and the equilibria with the maximal and the minimal output values for each u in (2) to construct a closed interval $R \subset U$ which bounds the projection of the attractor of (1) to the control variable u.

With R defined, we show that a Morse decomposition of the parameterized system (2) with a particular order of Morse sets gives rise to a Morse decomposition of (1). The input–output characteristic of (2) is used to define such a decomposition. In particular, any collection of connected equilibrium branches that stretch across R corresponds to a Morse set in (1).

The last set of results concerns the internal structure of the Morse sets. Each Morse set is an isolated invariant set and has its own, perhaps finer, Morse decomposition. Our theory is fully scalable and can be applied subsequently to these finer decompositions to refine the knowledge about the Morse sets. Furthermore, we show that the majority of the constructed Morse sets (1) are non-empty. If, in addition, the Morse set corresponds to a single branch of the characteristic that spans R, this branch acts as a single-valued characteristic and convergence results [1,2,4,9–12] can be used to find conditions when this Morse set is a single equilibrium.

We apply our results to a model of a cell cycle oscillator. We analyze the effect of changing strength of the negative feedback and show how our theory implies bistability rather than oscillations for a certain range of parameters.

We finish the introduction with a brief overview of the organization of the paper. In Section 2 we review the necessary background in monotone systems theory, provide the key assumptions and formulate our main results. In Section 3 we apply the theory to a model of the cell cycle engine [25, 27,28]. We start our proofs in Section 4 where we construct the interval $R \subset U$, which we follow by the construction of a Morse decomposition in Section 5. Finally, our results about the internal structure of the Morse sets can be found in Section 6.

2. Main results

The basic framework for our results is a finite-dimensional, single-input, single-output controlled system

$$\dot{x} = f(x, u), \qquad y = h(x) \tag{3}$$

where $u(t) \in U \subseteq \mathbb{R}$ is the input, $y(t) \in Y \subseteq \mathbb{R}$ is the output, f, h are C^2, and the state space variable $x(t) \in X \subseteq \mathbb{R}^n$. We assume that U, Y, X lie in the closure of their interiors. Together with the *open loop system* (3) we will also study a *closed loop system*, where, in addition to (3), we set $u = g(y)$. The most important set of questions concerns the predictability of the closed loop dynamics

$$\dot{x} = f\big(x, g\big(h(x)\big)\big) \tag{4}$$

based on the properties of the open loop system (3). Since the function h is arbitrary, we can assume without loss of generality that $g(y) = \pm y$. The system (3) with $g(y) = y$ ($g(y) = -y$) is a closed loop system with a positive (negative) feedback.

Our main motivation is the study of gene regulatory networks [3,5], where systems of the form (3) have usually an additional structure of *monotone systems*. We now recall essential definitions in this area and refer the reader for a more thorough background to [1,29].

A *cone* is a closed, convex set with non-empty interior and with $\alpha K \subset K$ for $\alpha \in \mathbb{R}^+$ and $K \cap (-K) = \{0\}$. If a space Z is endowed with a cone K_z we will write

$$x \succcurlyeq y \quad \text{iff} \quad x - y \in K_z, \qquad x \succ y \quad \text{iff} \quad x \succcurlyeq y,\ x \neq y, \quad \text{and} \quad x \succ\succ y \quad \text{iff} \quad x - y \in \operatorname{int} K_z.$$

We assume that the input space U, the state space X and the output space Y each has a distinguished cone $K_u \subset U$, $K_x \subset X$ and $K_y \subset Y$. For $U \subset \mathbb{R}$ and $Y \subset \mathbb{R}$ this amounts to a choice of either a positive, or a negative half-line.

We say that the controlled system (3) is a *monotone system with outputs* if

$$\begin{aligned} &u_1(t) \succcurlyeq u_2(t) \quad \forall t, \quad \text{and} \quad x_1 \succcurlyeq x_2 \\ &\quad \Longrightarrow \quad \varphi(t, x_1, u_1) \succcurlyeq \varphi(t, x_2, u_2) \quad \forall t \geqslant 0, \quad \text{and} \quad h(x_1) \succcurlyeq h(x_2) \end{aligned}$$

where φ is the flow generated by (3), and the $\succcurlyeq$ is the order with respect to the appropriate cones. We say that the controlled system is *strongly monotone* if it is monotone, and

$$u_1(t) \succcurlyeq u_2(t) \quad \forall t, \quad \text{and} \quad x_1 \succ x_2 \quad \Longrightarrow \quad \varphi(t, x_1, u_1) \succ\succ \varphi(t, x_2, u_2) \quad \forall t > 0.$$

Infinitesimal characterizations of monotonicity, which are more suitable for verification, can be found in [1] and [29]. We say that two points $x, y \in Z$ are *order related* if either $x \succ y$ or $y \succ x$ with respect to cone $K_z \subset Z$. If $x \prec y$ then $[x, y] := \{z \in Z \mid x \preccurlyeq z \preccurlyeq y\}$ is the *order interval* generated by x and y. If $U, V \subset X$ are two disjoint subsets of X, we write $U \prec V$ if for all $x \in U$ and $y \in V$ we have $x \prec y$; we define $[U, V] := \{z \in Z \mid x \preccurlyeq z \preccurlyeq y,\ \forall x \in U \text{ and } \forall y \in V\}$.

Definition 2.1. We say that the controlled system (3) is endowed with an *input-state characteristic* $k_x(u) : U \to X$ if for each constant input $u(t) \equiv \bar{u}$ there exists a (necessary unique) globally asymptotically stable equilibrium $k_x(\bar{u})$ of system (3).

The system (3) is endowed with a *multi-valued input-state characteristic* $k_x(u) : U \to X$ if for each constant input $u(t) \equiv \bar{u}$ the set $k_x(\bar{u})$ is a set of equilibria of system (3), that attracts a set of initial conditions that contains an open and dense set of X.

In both cases we define the (*multi-valued*) *input–output characteristic* as

$$k(u) := g\big(h\big(k_x(u)\big)\big), \quad k: U \to U.$$

In [11] the branches of $k(u)$ are called bifurcation graphs.

Before we introduce our main results we illustrate some of these concepts on a simple example. Consider an open loop system

$$\begin{aligned} \dot{x} &= u - 8x\left(x^2 - \frac{3}{4}\right) + \frac{y}{4} =: g_1(x, y, u), \\ \dot{y} &= \epsilon\left(x - \frac{y}{2}\right) =: g_2(x, y) \end{aligned} \tag{5}$$

with an output function $h(x, y) = y$ and negative feedback $u = -y$. By the result of Kamke [19] (see [29, Proposition 3.1.1]) the strict monotonicity of g_1 and g_2 with respect to y and x respectively

$$dg_1/dy > 0 \quad \text{and} \quad dg_2/dx > 0$$

implies that (5), for a fixed u, is a strongly monotone system with respect to the positive orthant.

Furthermore for each fixed u the open loop system has either one, two, or three equilibria that are intersections of

$$y = 2x \quad \text{and} \quad u = 8x\left(x^2 - \frac{3}{4}\right) - \frac{y}{4}.$$

The value of the multi-valued input-state characteristic $k_x(u)$ at each u is this set of equilibria. To compute the input–output characteristic, we first combine these two equations to express y as an (implicit) function of u

$$u = 4y\left(\frac{y^2}{4} - \frac{3}{4}\right) - \frac{y}{4} = y\left(y^2 - \frac{13}{4}\right).$$

This represents implicitly the composition $y = h(k_x(u))$. Finally, taking the composition with the function g, which in this case represents a negative feedback $u = -y$, we obtain the multi-valued input–output characteristic $k: U \to U$ given implicitly by

$$u = -k(u)\left(\big(-k(u)\big)^2 - \frac{13}{4}\right). \tag{6}$$

This multi-valued characteristic is depicted in Fig. 1. This finishes the example and we proceed by formulating a set of *standing assumptions*. We assume that

1. the open loop system (3) is strongly monotone;
2. there is a compact set $C \subset U \subset \mathbb{R}$, such that for each $u \in C$ the system (3) with $u(t) = u$:
   (a) is dissipative, i.e. all solutions eventually enter a fixed compact set K_u;
   (b) Jacobian $\frac{\partial f}{\partial x}(x, u)$ is irreducible in K_u.

These assumptions guarantee that the open loop system (3) is a parameterized family of strongly monotone, irreducible, dissipative systems on X for all $u \in C$. By [29, Theorem 4.1.1] for each $u \in C$ there is an exceptional set $\mathcal{B}_u$ such that all solutions starting in $X \setminus \mathcal{B}_u$ converge to a unique equilibrium, and the set $X \setminus \mathcal{B}_u$ contains an open and dense set of initial data. Our first result below shows

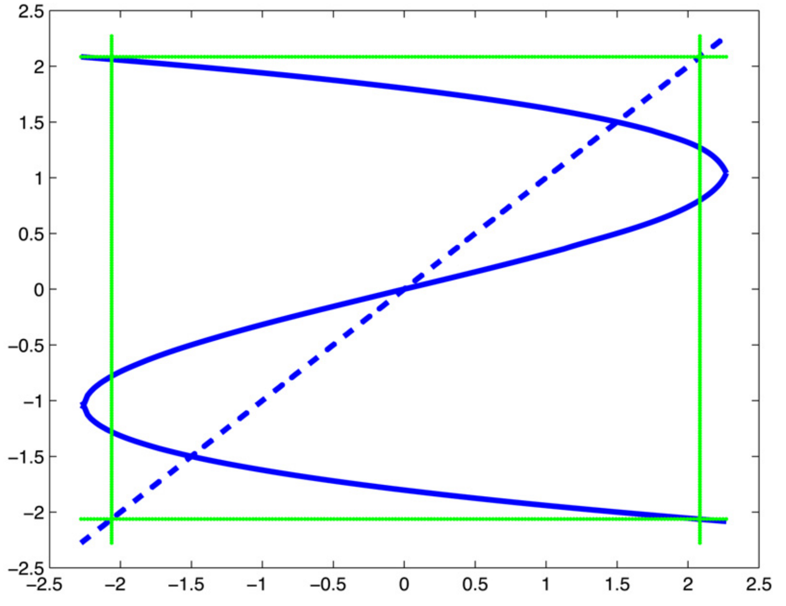

Fig. 1. I/O characteristic (solid line) given by (6).

that the open-loop SISO system, the information encoded into the input–output characteristic is sufficient to bound the attractor of the closed loop system (4). Since for each fixed u (3) is dissipative, and the set of equilibria is closed, the maximum and minimum of the set of equilibria is well defined.

Definition 2.2. Assume (3) is SISO system, i.e. $U \subset \mathbb{R}$. If k is a multi-valued input–output characteristic, we set

$$K_{\min}(u) := \min\{k(u)\} \quad \text{and} \quad K_{\max}(u) := \max\{k(u)\}. \tag{7}$$

For the function in Fig. 1 the function $K_{\min}(u)$ is continuous, except at the value of u corresponding to the left turning point, and $K_{\max}(u)$ is continuous except for u corresponding to the right turning point.

Positive and negative feedback systems differ in the general direction of their characteristic. We will not prove this fact until later, but for large $|u|$ the I/O characteristic for positive feedback is increasing and for negative feedback it is decreasing. Indeed, if we had positive feedback $u = y$ in the example (5) then the graph of the I/O characteristic satisfying $u = k(u)((k(u))^2 - \frac{9}{4})$ would be that in Fig. 1, but flipped around the y-axis.

Even though we assume in 2(a) dissipativity for each fixed input $u(t) = u$, we need a global notion of dissipativity for the entire open loop system. In order to express such a dissipativity assumption for an open loop system in the same language for both negative and positive feedbacks we define non-decreasing functions $B(u)$ (for "bottom") and $T(u)$ (for "top"). For a positive feedback system

$$B(u) := K_{\min}(u), \qquad T(u) := K_{\max}(u) \tag{8}$$

and for a negative feedback system we set

$$B(u) := K_{\min}\big(K_{\max}(u)\big), \qquad T(u) := K_{\max}\big(K_{\min}(u)\big). \tag{9}$$

We can express dissipativity in terms of functions B and T.

Definition 2.3. We say that the open loop system (3) is *dissipative* if there is a constant A such that

$$T(u) < u \quad \text{for } u \geqslant A \quad \text{and} \quad B(u) > u \quad \text{for } u \leqslant -A. \tag{10}$$

The dissipativity assumption is equivalent to a sub-linear growth of the input–output characteristic as $u \to \pm\infty$. Indeed, it is easy to check that for a negative feedback system it is equivalent to

$$K_{\max}(u) < -u \quad \text{for } u \leqslant -A, \quad \text{and} \quad K_{\min}(u) > -u \quad \text{for } u \geqslant A.$$

Our first major result is the following.

Theorem 2.4. *Assume the standing assumptions and that the open loop system* (3) *is dissipative. Define* $p_1 := \sup\{a\colon B(u) > u,\ \forall u < a\}$ *and* $p_2 := \inf\{b\colon T(u) < u,\ \forall u > b\}$. *Then for a generic set of initial conditions* $\xi \in X$ *and all* $u(t) \in U$ *for which solution* $x(t, \xi, u)$ *is bounded,*

$$p_1 \leqslant \liminf_{t\to\infty} h\big(x(t)\big) \leqslant \limsup_{t\to\infty} h\big(x(t)\big) \leqslant p_2.$$

The values p_1 and p_2 were computed for the example (5) and are represented by the dotted square in Fig. 1. As we will see in Lemmas 4.8 and 4.9 the characterization of p_1 and p_2 in terms of $B(u)$ and $T(u)$ implies that the interval $[p_1, p_2]$ is an attracting fixed point of a multi-valued map that maps intervals to intervals, and whose graph is the convex hull of the I/O characteristic. Therefore the values p_1, p_2 can be computed by iterating the functions $B(u)$ and $T(u)$.

We now introduce a concept of a Morse decomposition due to Conley [6]. As we have mentioned in the introduction, Morse decomposition represents a decomposition of the invariant set into isolated invariant sets, which, by their definition, are robust under perturbations. The robust relationship between the Morse sets is encoded in a partial order of the decomposition.

Definition 2.5. A Morse decomposition $\mathcal{M}(\mathcal{A}) = \{M_i \mid i \in (\mathcal{P}, \geqslant)\}$ of a compact invariant set $\mathcal{A}$ is a decomposition of $\mathcal{A}$ into a finite number of disjoint compact invariant subsets M_i, called *Morse sets*, indexed by a partially ordered set $(\mathcal{P}, \geqslant)$, such that if $x \in \mathcal{A}$ one of the following holds:

1. There exist $i, j \in \mathcal{P}$ such that $j \geqslant i$, $\omega(x) \in M_i$ and $\alpha(x) \in M_j$.
2. There exists $i \in \mathcal{P}$ such that $\varphi(t, x) \in M_i$ for all t, where $\varphi : \mathcal{A} \times R \to \mathcal{A}$ denotes the flow.

A power of Conley's theory is best realized in the context of continuous parameterized flow $\varphi : \mathbb{R} \times X \times U \to X \times U$, $\varphi(t, x, u) = (\varphi_u(t, x), u)$ which is the setting of the open loop system. For any interval $I \subset U$ we consider a restriction φ_I of the flow φ to $X \times I$. If S is an isolated invariant set in $X \times I$ then every $S(u) = S \cap X(u)$ is isolated in $X(u)$, where $X(u) := X \times \{u\}$ and $u \in I$ is arbitrary. We say that the family of isolated invariant sets $S(u)$ is *related by continuation over I* or it *continues over I*. Similarly, we say that a Morse decomposition *continues over I* if there is an isolated invariant set S in $X \times I$ with a Morse decomposition $\{M_i \mid i \in \mathcal{P}\}$. This implies that for each $u \in I$ there is a Morse decomposition with the partial order that is independent on u, and that the individual Morse sets are related by continuation.

We note that a Morse decomposition always exists, since the trivial Morse decomposition containing only one set comprising the entire invariant set is a valid Morse decomposition. Further, a Morse decomposition does not have to be unique. Let us denote in the example (5) by e_1, e_2, e_3 the equilibria on the bottom, middle and top branch, respectively, and by $C(e_i, e_j)$ the set of connecting orbits from e_i to e_j. Then the flow φ_I with $I = [-2, 2]$, apart from the trivial decomposition, admits decompositions $\mathcal{M}_1 := \{M_1 = \{e_1\}, M_2 = \{e_2, e_3, C(e_2, e_3)\} \mid 1 \leqslant 2\}$, $\mathcal{M}_2 := \{M_1 = \{e_1, e_2, C(e_2, e_1)\}, M_2 = \{e_3\} \mid 1 \leqslant 2\}$ and $\mathcal{M}_3 := \{M_1 = \{e_1\}, M_2 = \{e_2\}, M_3 = \{e_3\} \mid 1 \leqslant 2,\ 3 \leqslant 2\}$. Note that if we choose $I = [-2.5, 2.5]$ then there is only a trivial Morse decomposition that continues over this interval since none of the sets M_i, $i = 1, 2, 3$, are isolated over this interval. This underlines the importance of the interval of parameters over which the Morse decomposition is defined. This example also shows that we can use the multi-valued characteristic to define Morse decompositions for open loop system over arbitrary intervals in U.

We now describe our second result where we show that a Morse decomposition of the closed loop system (4) can be constructed from a Morse decomposition of the open loop system (3) over the interval $[p_1, p_2]$ from Theorem 2.4. In particular, if the open loop Morse decomposition is non-trivial over $[p_1, p_2]$ (like in the example (5)) then the closed loop Morse decomposition is non-trivial as well.

In a general dynamical system there is no link between the Morse decompositions for the open loop and closed loop systems. If u is changing on a much slower time scale then x, then such a correspondence would be in a domain of slow–fast systems theory. We do not assume such separation of time scales. The following observation is central for our next result. Assume that the basin of attraction $V_1 := V_1(u)$ of the equilibrium $e_1(u)$ did not depend on value of $u \in R$. Then if the solution of the closed loop system started in V_1 it would stay in V_1 for all $t \geqslant 0$. In other words, such a set V_1 would be positively invariant and would contain an invariant set. Under the same assumption applied to the basin $V_3 := V_3(u)$ there would be an additional, disjoint, invariant set in V_3. If the basins $V_1(u)$ and $V_3(u)$ changed with u, as they do in the example (5), we could define V_1 and V_3 as intersections of $V_1(u)$ and $V_3(u)$ over $u \in R$ drawing the same conclusion. This observation forms the basis of our general construction. However, in order to show the positive invariance of sets like V_1 and V_3 we need to characterize precisely the boundaries of these sets. In a general dynamical system this is very difficult, but in a monotone system where the Morse sets of the open loop system are ordered this is possible.

Before we introduce a definition which incorporates this assumption, we introduce a concept of a separating invariant set. Assume M_1 and M_3 are two Morse sets with open basins of attraction and such that $M_1 \prec M_3$. Since the basins of attraction of M_1 and M_3 are open, there must be a point q with $M_1 \prec q \prec M_3$ which does not belong to any of the two basins. Monotonicity now implies that the solution $\varphi(t, q, u)$ of (3) stays in the compact set $\{z \in X \mid M_1 \preccurlyeq z \preccurlyeq M_3\}$ for all $t \geqslant 0$. This implies that $\omega(q)$ lies in some invariant set S^q with $M_1 \prec S^q \prec M_3$. Let $M_2 := \bigcup_q S^q$ be the union of all such invariant sets over all q with $M_1 \prec q \prec M_3$ with $\omega(q) \not\subset \{e_1, e_3\}$. Clearly, M_2 is a compact invariant set. We say that M_2 *separates* M_1 and M_3. In many applications the set M_2 will also be an equilibrium. In the example (5) the basins of attraction of e_1 and e_3 are separated by the stable manifold of the equilibrium e_2 that lies on the middle branch. In this case $M_2 = e_2$.

Definition 2.6 *(Morse decomposition for the monotone open loop system).* We assume that there is a compact invariant set $\mathcal{A}$ under a flow $\varphi : \mathbb{R} \times X \times [p_1, p_2] \to X \times [p_1, p_2]$ of the open loop system which admits a Morse decomposition $\mathcal{M} = \{M_i \mid i = 1, \dots, 2L+1\}$ with a partial order $M_{2i} \geqslant M_{2i+1}$, $M_{2i} \geqslant M_{2i-1}$ for $i = 1, \dots, L$ that continues over $[p_1, p_2]$. We assume that $\mathcal{A}(u) := \mathcal{A} \cap X(u)$ attracts a generic set of initial conditions in $X(u)$ for each $u \in [p_1, p_2]$. Furthermore, each odd numbered Morse set $M_{2i+1}(u), i = 0, \dots, L$, has an open basin of attraction $V_{2i+1}(u)$. We assume that a generic set of initial conditions in $X(u)$ belongs to one of the sets $V_{2i+1}(u)$, $i = 1, \dots, L$. The even numbered Morse sets $M_{2i}(u)$, $i = 1, \dots, 2L$, separate $M_{2i-1}(u)$ and $M_{2i+1}(u)$. We assume that the Morse sets are ordered for each u

$$M_1(u) \prec M_2(u) \prec \cdots \prec M_{2L+1}(u). \tag{11}$$

Furthermore we assume that the Morse sets are uniformly ordered in the output

$$\bigcup_{u \in [p_1, p_2]} h\big(M_1(u)\big) \prec \bigcup_{u \in [p_1, p_2]} h\big(M_2(u)\big) \prec \bigcup_{u \in [p_1, p_2]} h\big(M_3(u)\big) \prec \cdots \prec \bigcup_{u \in [p_1, p_2]} h\big(M_{2L+1}(u)\big). \tag{12}$$

The total order of the Morse sets is a strong assumption if we insist that each Morse set is a single equilibrium, as is the case in the example (5). In such a case the assumption amounts to assuming a total ordering of all the equilibria. However, we do not require that each Morse set in the

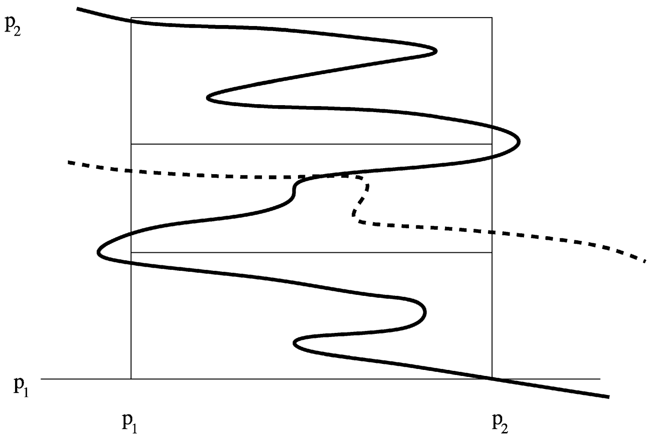

Fig. 2. A potential I/O characteristic over $[p_1, p_2]$. The Morse decomposition for the parameterized system will have three Morse sets M_1, M_2 and M_3 lying in the bottom, middle and the top strip, respectively.

decomposition in definition (2.6) is a single equilibrium. In fact, the shape of the characteristic over $[p_1, p_2]$ together with the requirements that the Morse sets be ordered and that they continue across $[p_1, p_2]$, force the definition of individual Morse sets by combining multiple branches of equilibria together. As an example, in Fig. 2 we consider a potential characteristic. The full line and the dashed line represent two connected components of the characteristic. We can define a Morse decomposition for the parameterized system that contains three sets M_1, M_2 and M_3. The set $M_1(u)$ contains all invariant sets in the bottom strip, $M_3(u)$ in the top strip and $M_2(u)$ in the middle strip. $M_2(u)$ separates $M_1(u)$ and $M_3(u)$ for each $u \in [p_1, p_2]$.

In some situations the only combination of branches that defines a Morse decomposition satisfying all the assumptions results is a trivial Morse decomposition. In such a case our methods do not provide any insight into the structure of the invariant set of the closed loop system.

Theorem 2.7. *For* (3), *assume the standing assumptions, dissipativity and that it admits a Morse decomposition described in Definition* 2.6.

Then there is an invariant set $\mathcal{A}$ of the closed loop system (4), *that attracts a generic set of solutions, and which admits a Morse decomposition $\mathcal{M}^* = \{M^*_{2i+1} \mid i = 0, \dots, L\} \cup M^*_0$, with the ordering $M^*_0 \succ M^*_{2i+1}$ for all $i = 1, \dots, L$.*

The Morse set M^*_{2i+1}, defined as the maximal invariant set in $V^*_{2i+1} := \bigcap_{u \in [p_1, p_2]} V_{2i+1}(u)$, is non-empty for all $i = 0, \dots, L$. The Morse set M^*_0 is the maximal invariant set in $X \setminus \bigcup_{i=1,\dots,L} V^*_{2i+1}$.

Our final result shows that our theory is recursive and it can be applied iteratively. If the restriction of the input–output characteristic $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is multi-valued then by applying Theorem 2.4 to this restriction we may discover that it admits a Morse decomposition over a smaller subinterval $R \subset [p_1, p_2]$. Then we can again apply Theorem 2.7 to R to complete the iterative step. In this way we may discover a finer Morse decomposition of the original invariant set $\mathcal{A}$.

If, on the other hand, the restriction of the input–output characteristic $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is single-valued, then, as we will show next, we can apply the standard theory [2,4] of single-valued characteristics. We first recall these results using our notation.

Theorem 2.8. *(See [4, Theorem 1].) Consider the open loop system* (3) *with a negative feedback $u = -y$. Suppose that X and $Y = U$ are ordered with respect to their cones K_z and $K_y = K_u$ respectively, and that they are closed under component-wise maximization and minimization. Assume that the input-state characteristic k_x is single-valued and continuous* (*thus, the I/O characteristic k is single-valued and exists, too*). *Finally, assume that all solutions of the closed-loop system* (4) *are precompact. Then the system* (4) *has a unique equilibrium*

$k_x(\bar{u})$ that attracts almost all solutions in X, provided that the following discrete dynamical system, evolving on U:

$$u^n = -k^n\big(u^0\big)$$

has a unique globally attractive equilibrium $\bar{u}$.

Theorem 2.9. *(See [2, Theorem 3].) Consider an SISO open-loop system* (3) *with a positive feedback $u = y$ and single-valued input–output characteristic k. Then the equilibria of the closed-loop system* (4) *are in* 1–1 *correspondence with the fixed points of the input–output characteristic k. Furthermore, non-degenerate stable ($k'(u) < 1$) fixed points of k correspond to stable equilibria of* (4) *and non-degenerate unstable ($k'(u) > 1$) fixed points of k correspond to unstable equilibria of* (4)*.*

We are ready for our final result. Assume that some Morse set $M_{2i+1}(u) = e_{2i+1}(u)$ consists of a single equilibrium for each $u \in [p_1, p_2]$. In such a case the branch $k_{x,2i+1} : [p_1, p_2] \to X$ of the multi-valued I/S characteristic k_x given by $k_{x,2i+1}(u) = e_{2i+1}(u)$ is well defined and single-valued. We denote by $k_{2i+1} : [p_1, p_2] \to [p_1, p_2]$ the corresponding single-valued branch of the I/O characteristic k.

Theorem 2.10. *Let i be such that $M_{2i+1}(u) = e_{2i+1}(u)$ is an equilibrium for each $u \in [p_1, p_2]$ and let $k_{x,2i+1} : [p_1, p_2] \to X$ and $k_{2i+1} : [p_1, p_2] \to [p_1, p_2]$ be the corresponding single-valued branches of the I/S and I/O characteristics. Then for a positive feedback system Theorem* 2.9 *holds with k replaced by k_{2i+1} and X replaced by V^*_{2i+1}. For a negative feedback system Theorem* 2.8 *holds with k replaced by k_{2i+1} and X replaced by V^*_{2i+1}. In particular, there is at least one fixed point e^*_{2i+1} of the I/O characteristic in M^*_{2i+1} and if for any initial condition $u \in [p_1, p_2]$ the iterations $k^n_{2i+1}(u)$ of the I/O branch converge to e^*_{2i+1}*

$$\lim_{n\to\infty} k^n_{2i+1}(u) = e^*_{2i+1} \quad \textit{for each } u \in [p_1, p_2]$$

then the Morse set M^*_{2i+1} consists of the unique equilibrium $E_{2i+1} := k_x(e^*_{2i+1})$ and all solutions starting in V^*_{2i+1} converge to E_{2i+1}.

3. A cell cycle model

We illustrate our theory on a biochemical model of the cell cycle control in *Xenopus* embryos. Over the last 15 years both the biology [26] and the modeling [25,27,28,32] of the cell cycle oscillator made great strides towards understanding of generation and control of the cell cycle oscillator. One of the most striking features of this oscillation is the abrupt change that signals entry into the M-phase of the cycle. Several experimental papers [27,28] suggest that the presence of the positive feedback loops is responsible for the switch-like behavior, and the negative feedback loop for generating the periodic oscillations. Ultimately, however, the presence of both is needed for the proper function of the cell cycle. At the center of the cell cycle engine is a heterodimer Cdc2-cyclin. Its activity is regulated by synthesis and degradation of cyclin and by phosphorylation and dephosphorylation of Cdc2. There are two major feedback loops: Cdc2-cyclin modulates kinases and phosphatases that in turn modulate their own activity in a positive feedback loop; and Cdc2-cyclin stimulates proteolytic machinery that degrades cyclin in a negative feedback loop.

The activity of Cdc2-cyclin is regulated by three phosphorylation sites: activation site Thr161, and two inhibitory phosphorylation sites Thr14 and Tyr15. Since the latter sites are always dephosphorylated simultaneously, it is sufficient to track the state of Tyr15. In *Xenopus* Thr161 is phosphorylated by CAK and dephosphorylated by PP2c; the kinase that phosphorylates Tyr15 is Wee1 and the corresponding phosphatase is Cdc25. The active form of Cdc2-cyclin is phosphorylated on Thr161, but not on Tyr15. The rapid onset of the M-phase transition is brought on by rapid conversion of the doubly phosphorylated Cdc2-cyclin to its Thr161 phosphorylated active form. There are two positive feedback loops: Cdc2-cyclin up-regulates activity of the phosphatase Cdc25 and down-regulates activity

Table 1

$k_{synth} = 0.4$	cyclin synthesis rate	$k_{dest} = 0.006$	cyclin destruction rate
$k_{wee1} = 0.05$	active Wee1 phosp. rate	$k_{wee1basal} = 0.0033$	basal Wee1 phosp. rate
$k_{cdc25} = 0.1$	active Cdc25 dephosp. rate	$k_{cdc25basal} = 0.0066$	basal Cdc25 dephosp. rate
$k_{cdc25on} = 1.75$	Cdc25 activation rate	$k_{cdc25off} = 0.2$	Cdc25 deactivation rate
$k_{wee1on} = 0.2$	Wee1 activation rate	$k_{wee1off} = 1.75$	Wee1 deactivation rate
$k_{plxon} = 1$	Plx activation rate	$k_{plxoff} = 0.15$	Plx deactivation rate
$k_{apcon} = 1$	APC activation rate	$k_{apcoff} = 0.15$	APC deactivation rate
$wee1_{tot} = 15$	total Wee1 concentration	$cdc25_{tot} = 15$	total Cdc25 concentration
$plx_{tot} = 50$	total Plx concentration	$apc_{tot} = 50$	total APC concentration
$n_{cdc25} = 4$	Cdc25 Hill coefficient	$n_{wee1} = 4$	Wee1 Hill coefficient
$n_{apc} = 3$	APC Hill coefficient	$n_{plx} = 3$	Plx Hill coefficient
$e_{cdc25} = 40$	Cdc25 half-activation	$e_{wee1} = 40$	Wee1 half-activation
$e_{apc} = 40$	APC half-activation	$e_{plx} = 40$	Plx half-activation

of the kinase Wee1. Since phosphatase Cdc25 promotes the active form of Cdc2-cyclin and the kinase promotes the inactive form of Cdc2-cyclin, both of these constitute positive feedback loops.

Cdc2-cyclin dimers are broken up by cyclin degradation, which is promoted by APC (anaphase-promoting complex). Since Cdc2-cyclin activates APC, this forms a negative feedback loop. It is very likely that the activation of the APC is done through an intermediary, since the effect is significantly delayed.

A model incorporating these ingredients was proposed and numerically analyzed by Novak and Tyson [25] and used later by Pomerening et al. [27,28]. In order to apply our theory we simplify the model to six differential equations. We will track concentrations of the total Cdc2-cyclin (y), the active Cdc2-cyclin (q), the active Cdc25 (w), active Wee1 (u), active plx (putative APC intermediary) (v) and APC (z). In contrast to the original model [27,28] we are not modeling separately cyclin concentration. Instead we assume that the dimerization of Cdc2-cyclin is very fast and so the rate of production of cyclin k_{synth} from [28] can be used as a rate of production of Cdc2-cyclin. In addition, we represent all active forms of Cdc2-cyclin by one variable.

The terms in the first equation represent the synthesis, APC mediated degradation, phosphorylation (and hence deactivation) by active and inactive Wee1, and dephosphorylation (and hence activation) by the active and inactive form of Cdc25. The third and fourth equations represent activation of Cdc25 and deactivation of Wee1, respectively, by the active Cdc2-cyclin. Finally, the last two equations represent the activation of APC by the active Cdc2-cyclin through an intermediary v:

$$\begin{aligned}
\dot{q} &= k_{synth} - k_{dest} q z - k_{wee1} u q - k_{wee1basal}(wee1_{tot} - u) q + k_{cdc25} w y + k_{cdc25basal}(cdc25_{tot} - w) y, \\
\dot{y} &= k_{synth} - k_{dest} y z, \\
\dot{w} &= k_{cdc25on} \frac{q^{n_{cdc25}}}{e_{cdc25}^{n_{cdc25}} + q^{n_{cdc25}}} (cdc25_{tot} - w) - k_{cdc25off} w, \\
\dot{u} &= -k_{wee1off} \frac{q^{n_{wee1}}}{e_{wee1}^{n_{wee1}} + q^{n_{wee1}}} u + k_{wee1on}(wee1_{tot} - u), \\
\dot{v} &= k_{plxon} \frac{q^{n_{plx}}}{e_{plx}^{n_{plx}} + q^{n_{plx}}} (plx_{tot} - v) - k_{plxoff} v, \\
\dot{z} &= k_{apcon} \frac{v^{n_{apc}}}{e_{apc}^{n_{apc}} + v^{n_{apc}}} (apc_{tot} - z) - k_{apcoff} z.
\end{aligned} \tag{13}$$

The constants and their values (taken from supplement of Pomerening et al. [28]) are given in Table 1.

The system (13) is amenable to analysis using an input–output characteristic. The only negative feedback in the system is the degradation of the Cdc2-cyclin by APC. Therefore we consider an open

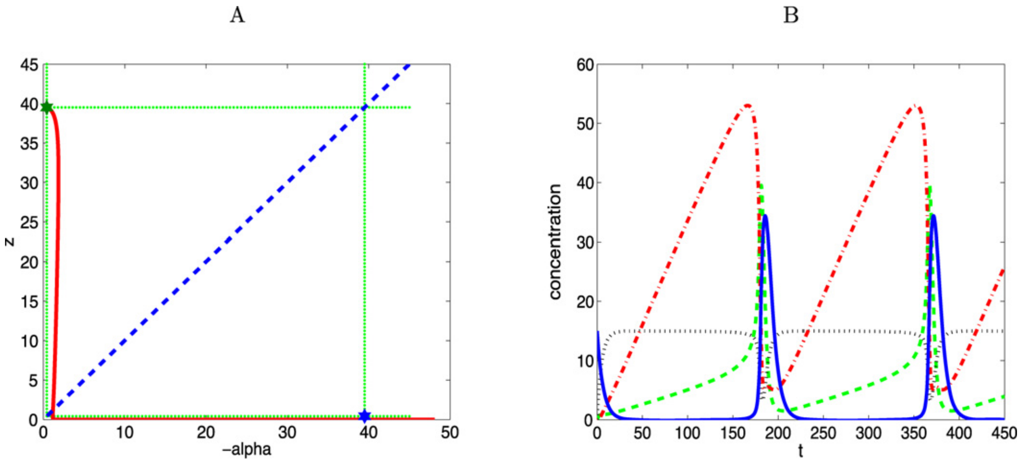

Fig. 3. (A) The input–output characteristic (solid curve) for (13) with parameters from Table 1. The attracting region $[p_1, p_2]$ is a dotted square and the dashed curve is the diagonal. (B) Dynamics of (13) with the same parameter values as in (A). Legend: solid curve $= z$, dotted curve $= u$, dashed curve $= q$, and dash–dot curve $= y - q$.

loop system, where we replace z in the first two equations by an input parameter $\alpha := -z$, with $\alpha \leqslant 0$.

The system with the input α fixed is strongly monotone, dissipative and irreducible open loop system and thus almost all solutions converge to an equilibrium [29]. The (multi-valued) input-state characteristic is the function that associates to each fixed α the corresponding set of equilibria of the system. The input–output characteristic is the value of the variable $z = h(y, q, w, u, v, z)$ on the set of equilibria. We recover the closed loop system (13) by setting $\alpha = -z$.

We investigate how the strength of the negative feedback connection from APC to Cdc2-cyclin affects the dynamics of the system. We first analyze the system for the strength of feedback provided by [28] above. To compute the I/O characteristic we set the left-hand side of the equations in (13) to zero and solve the resulting system for z as a function of α. The input–output characteristic is multi-valued (solid line in Fig. 3A) in the region approximately $\alpha \in (b_1, b_2) := (1.17, 1.85)$. Since the values of z on the upper branch are greater than 35, the characteristic is a very narrow curve. The dotted square denotes the region $[p_1, p_2] \times [p_1, p_2]$ where $p_1 \approx 0.1$ and $p_2 \approx 39.5$ are described in Theorem 2.4. The output (z) values of all solutions of the closed loop system will eventually enter $[p_1, p_2]$. Since the multi-stability region $(b_1, b_2) = (1.17, 1.85)$ is clearly a subset of the interval $[p_1, p_2]$, the only Morse decomposition that continues across this interval is a trivial decomposition that consist of only one set. In this case our theory is vacuous since it does not yield a non-trivial Morse decomposition.

This result suggests that the global attractor of the closed loop system is fundamentally different than the attractors of the open loop (monotone) system, which are collections of equilibria and their connecting orbits. Further analysis is required to determine the character of the attractor for the closed loop system. The numerical simulation of the closed loop system in Fig. 3B indicates that the attractor of the closed loop system contains a periodic orbit representing the cell cycle. It is therefore not surprising that the open loop Morse decomposition cannot predict this behavior of the closed loop system. Observe that the range of the $z(t)$ solution (solid line in Fig. 3B) matches the range of the characteristic, which suggests that the cell cycle periodic orbit may arise as a relaxation oscillator associated to the characteristic. This is theoretically justified by Gedeon and Sontag [16] in the presence of slow feedback, which is, however, not the case here. A natural question is whether the analysis using I/O charateristic can be used to prove existence of such a relaxation periodic orbit. We study this question in a forthcoming paper [13].

We now analyze different values of feedback. First, we weaken the negative feedback by decreasing the destruction rate of cyclin 100 times and set $k_{dest} = 0.00006$. The I/O characteristic shifts to the

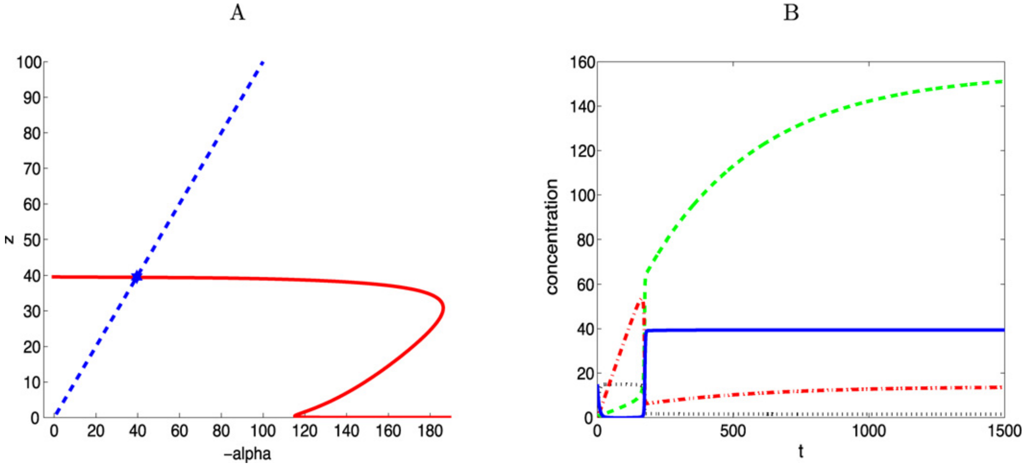

Fig. 4. (A) The input–output characteristic of (13) with $k_{dest} = 0.00006$; and (B) its dynamics. The legend is the same as in Fig. 3.

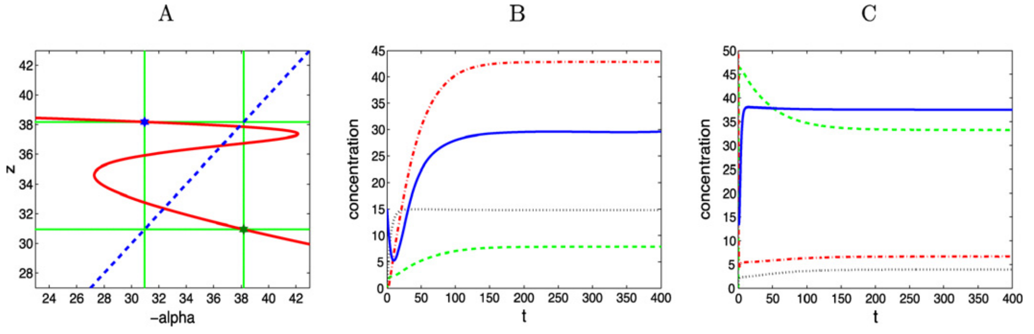

Fig. 5. (A) Input–output characteristic for the bistable system. (B) Convergence to the low equilibrium E_1 for the system (13) with the initial data $y = q = w = u = v = 0$, $z = 15$. (C) Convergence to the high equilibrium E_3 for the system (13) with the initial data $q = u = v = 0$, $y = 50$, $w = 30$, $z = 15$. The legend is the same as in Fig. 3.

right (Fig. 4A, compare the range of $-\alpha$). The diagonal (dashed line) intersects only the upper branch of the I/O characteristic. In this case $p_1 = p_2$ and Theorem 2.4 implies that the values of the output $z(t)$ for any initial condition in an open and dense set will converge to $p_1 = p_2$. The long term behavior of the closed loop system is governed by the open loop system with constant $\alpha = p_1 = p_2$. Since this system is monotone and has a unique equilibrium, almost all solutions of this system, and thus all solutions of the closed loop system, converge to this equilibrium. The numerical simulations (Fig. 4B) confirm this. Note that $z(t)$ (solid line in Fig. 4B) converges to a high value about 40 which is the value of $p_1 = p_2 = z$.

Finally we will show that by modifying few other parameters almost all solutions of the system (13) converge to one of two stable equilibria. We will increase synthesis rate from $k_{synth} = 0.4$ to $k_{synth} = 0.9$. At the same time we weaken the negative feedback by decreasing the destruction rate of cyclin 10 fold to $k_{dest} = 0.0006$; we also change cooperativity constants to $n_{apc} = 2$ and $n_{plx} = 1$ (from $n_{apc} = n_{plx} = 3$).

All remaining parameters including all rate constants remain the same. The resulting input–output characteristic is in Fig. 5A, where we again plot the region $[p_1, p_2] \times [p_1, p_2]$ as a dotted square. Both the upper and lower branches of the characteristic intersect the diagonal and the interval of multi-stability (b_1, b_2) contains $[p_1, p_2]$. Therefore there is a Morse decomposition of the open loop system that contains three ordered Morse sets $M_1(u) \prec M_2(u) \prec M_3(u)$ where $M_1(u)$, $M_2(u)$, $M_3(u)$ correspond to the equilibria on the bottom, middle and top branches, respectively. Theorem 2.7 shows the existence of the Morse decomposition with sets M_1^*, M_3^* and M_0^* with $M_0^* \prec M_3^*$, $M_0^* \prec M_1^*$ for the closed loop system. We conclude that there are two disjoint attracting Morse sets M_1^* and M_3^*.

We now probe deeper into the structure of these two Morse sets using Theorem 2.10. Let e_1^* be the intersection of the bottom branch and e_3^* the intersection of the top branch with the diagonal. Since numerical iteration of the function given by the lower branch shows that e_1^* is a stable fixed point under these iterations, and e_3^* is a stable fixed point under the iterations of the upper branch of the I/O characteristic, by Theorem 2.10 the Morse sets $M_1^* = E_1$ and $M_3^* = E_3$ are stable equilibria of the closed loop system (13). Therefore our theory shows that there are two stable equilibria for the closed loop system. We confirm this by numerical simulation where we find different initial conditions leading to solutions that converge to the equilibrium E_1 (Fig. 5B) and the equilibrium E_3 (Fig. 5C).

4. Attractor of the closed loop system

The goal of this section is to prove Theorem 2.4. Although many results in this section hold for systems with inputs of arbitrary dimension, we will assume throughout that the open loop system is a SISO system.

4.1. Multi-valued maps

The first definition generalizes monotonicity to multi-valued maps.

Definition 4.1. (See [8, Definition 2.3].) Let Z_1 and Z_2 be partially ordered Euclidean spaces and $F: Z_1 \to Z_2$ be a set-valued map. We say that F is *weakly non-increasing* (*weakly non-decreasing*) provided that the following holds for all $p, q \in Z_1$ such that $q \succcurlyeq p$ ($p \succcurlyeq q$): For each $x_p \in F(p)$ and $x_q \in F(q)$ there exist $y_p \in F(p)$ and $y_q \in F(q)$ such that $y_p \succcurlyeq x_q$ and $x_p \succcurlyeq y_q$.

We now relate the weak monotonicity of the multi-valued I/O characteristic to the regular monotonicity of functions $K_{\max}$ and $K_{\min}$.

Lemma 4.2. *The input–output characteristic k in a SISO system is weakly non-increasing* (*non-decreasing*) *if, and only if, the functions $K_{\min}$ and $K_{\max}$ defined in* (7) *are non-increasing* (*non-decreasing*).

Proof. We first observe, that in SISO system the input–output characteristic $k: \mathbb{R} \to \mathbb{R}$ and thus the order inequality $\succcurlyeq$ with respect to $\mathbb{R}^+$ is given by $\geqslant$.

Assume $q \geqslant p$. Assume first that $K_{\min}$ and $K_{\max}$ are non-increasing. Given $x_p \in k(p)$ and $x_q \in k(q)$ we set $y_p := K_{\max}(p)$ and $y_q := K_{\min}(q)$. Since $K_{\max}$ is non-increasing, our choice of y_p and y_q implies $y_p \geqslant K_{\max}(q)$ and $K_{\max}(q) \geqslant x_q$ by the definition of $K_{\max}$. Thus $y_p \geqslant x_q$. A similar argument shows that $x_p \geqslant y_q$. Therefore k is weakly non-increasing.

Now we assume that the input–output characteristic k is weakly non-increasing and $K_{\min}$ is not non-increasing, i.e. increasing. Then there are values $q_0 > p_0$ such that $K_{\min}(q_0) > K_{\min}(p_0)$. Select $x_{p_0} := K_{\min}(p_0)$. Then for all $y_{q_0} \in k(q_0)$ we have

$$y_{q_0} > K_{\min}(q_0) > K_{\min}(p_0).$$

This is a contradiction to the fact that the input–output characteristic k is weakly non-increasing.

The argument for $K_{\max}$ is analogous. $\square$

Note that the SISO assumption allows us to define the concepts of non-increasing and non-decreasing as well as to compare the values of the scalar-valued function $K_{\min}$ in the output space $\mathbb{R}$.

Lemma 4.3. *(See [8, Lemma 2.4].) An input-state characteristic k_x of a monotone open loop system is weakly non-decreasing.*

We use the previous lemma to show that the monotonicity of $K_{\max}$ and $K_{\min}$ are determined by the type of feedback. However, since we defined functions $B(u)$ and $T(u)$ differently for negative and positive feedback, they will always be non-decreasing.

Corollary 4.4.

1. *The functions $K_{\min}$ and $K_{\max}$ are non-increasing for any negative feedback system ($u = -y$) and they are non-decreasing for any positive feedback system ($u = y$).*
2. *$B(u)$ and $T(u)$ are non-decreasing functions of u for both types of feedback.*

Proof. 1. The input–output characteristic k of (3) is a composition of an input-state characteristic k_x, a non-decreasing output function h and the function $g(u) = \pm u$ where the sign depends on whether the feedback is negative or positive. Since k_x is weakly non-decreasing by Lemma 4.3 and the composition of a weakly non-decreasing function and a non-decreasing function h results in a weakly non-decreasing function, the composition $h \circ k_x$ is weakly non-decreasing. The composition with $g = \pm u$ causes k to be weakly non-decreasing for positive and weakly non-increasing for negative feedback. Lemma 4.2 now finishes the argument.

2. Recall (see (9)) that for a negative feedback system we defined $B(u) := K_{\min}(K_{\max}(u))$ and $T(u) := K_{\max}(K_{\min}(u))$; for a positive feedback system (see (8)) we set $B(u) := K_{\min}(u)$, and $T(u) := K_{\max}(u)$. The proof now follows from part 1. $\square$

Definition 4.5. We define a multi-valued map $\bar{k}(a) := [K_{\min}(a), K_{\max}(a)]$ where the value of each point is a closed interval in $\mathbb{R}$. If $a < b$ and $I = [a, b]$ is an interval, then we set

$$\bar{k}(I) = \bigcup_{u \in I} \bar{k}(u).$$

We now characterize the images of an interval under the multi-valued map $\bar{k}$. This is the key point where the SISO assumption (that is both input and output $u, y \in \mathbb{R}$) is used.

Lemma 4.6. *Consider a SISO system with a multi-valued input–output characteristic k. Then for a negative feedback system and any $a \leqslant b$, $a, b \in \mathbb{R}$,*

$$\bar{k}\big([a, b]\big) = \big[K_{\min}(b), K_{\max}(a)\big].$$

On the other hand, for a positive feedback

$$\bar{k}\big([a, b]\big) = \big[K_{\min}(a), K_{\max}(b)\big].$$

Proof. Consider first a SISO system with a negative feedback. Take $x \in \bar{k}([a, b])$. Then $x \in \bar{k}(s)$ for some s satisfying $a < s < b$. Since both $K_{\min}$ and $K_{\max}$ are non-increasing by Corollary 4.4.1, we have

$$K_{\max}(a) > K_{\max}(s) > x > K_{\min}(s) > K_{\min}(b).$$

Hence $x \in [K_{\min}(b), K_{\max}(a)]$.

Now we prove the other inclusion. Take x such that $K_{\min}(b) < x < K_{\max}(a)$. Note that both $K_{\min}(b) \in \bar{k}(b)$ and $K_{\max}(a) \in \bar{k}(a)$ and the set $\bigcup_{x \in [a,b]} \bar{k}(x)$ is connected since each $\bar{k}(x)$ is an interval. Therefore there is a $c \in [a, b]$ such that $x \in \bar{k}(c)$.

The argument for the positive feedback case is analogous. $\square$

The next lemma relates the multi-valued function $\bar{k}$ to the functions $B(u)$ and $T(u)$. Since the definition of functions B and T for the negative feedback has already built-in the composition of

$K_{\min}$ and $K_{\max}$, the formulas for $\bar{k}$ in the positive feedback case, and $\bar{k}^2$ in the negative feedback case, are identical.

Lemma 4.7. *Consider a SISO system with a multi-valued input–output characteristic k. Then for a negative feedback system*

$$\bar{k}^2(u) = \big[B(u), T(u)\big] \quad \textit{and} \quad \bar{k}^2[a,b] = \big[B(a), T(b)\big].$$

For a positive feedback system

$$\bar{k}(u) = \big[B(u), T(u)\big] \quad \textit{and} \quad \bar{k}[a,b] = \big[B(a), T(b)\big].$$

Proof. For the negative feedback system we have from Lemma 4.6

$$\bar{k}^2(u) = \bar{k}\big(\big[K_{\min}(u), K_{\max}(u)\big]\big) = \big[K_{\min}\big(K_{\max}(u)\big), K_{\max}\big(K_{\min}(u)\big)\big] = \big[B(u), T(u)\big].$$

For a positive feedback system by Definition 4.5

$$\bar{k}(u) = \big[K_{\min}(u), K_{\max}(u)\big] = \big[B(u), T(u)\big].$$

The second equality in both cases follows from the first equality and Corollary 4.4.2. □

The next lemma provides an important characterization of the points p_1 and p_2.

Lemma 4.8. *The points p_1 and p_2, defined in Theorem* 2.4, *are fixed points of $B(u)$ and $T(u)$ respectively*:

$$p_1 = \min\big\{p\colon\ p \textit{ is a fixed point of } B(u)\big\}, \qquad p_2 = \max\big\{p\colon\ p \textit{ is a fixed point of } T(u)\big\}.$$

Proof. We prove the first statement. The definition of p_1 and Lemma 4.7 imply $p_1 := \sup\{a\colon\ B(u) > u,\ \forall u < a\}$. Therefore we have

$$B(p_1) \leqslant p_1. \tag{14}$$

We now prove the opposite inequality. Since $B(u)$ is non-decreasing we have $\lim_{n\to\infty} B(x_n) \leqslant B(p_1)$ for any sequence $\{x_n\}_{n=1}^{\infty}$ with $x_n < p_1$ and $x_n \to p_1$. Therefore

$$B(p_1) \geqslant \lim_{n\to\infty} B(x_n) \geqslant \lim_{n\to\infty} x_n = p_1. \tag{15}$$

Now (14) and (15) show that p_1 is a fixed point of $B(u)$. If z satisfies $B(z) = z$ then by definition of p_1 we must have $u \geqslant p_1$. This shows that p_1 is the smallest fixed point of $B(u)$.

The second result is analogous to the first. □

The following lemma shows that for the SISO negative feedback system p_1 and p_2 form an "almost" period 2 point of the input–output characteristic.

Lemma 4.9. *For a SISO negative feedback system, the values p_1 and p_2 satisfy*

$$p_1 = K_{\min}(p_2), \qquad p_2 = K_{\max}(p_1).$$

Proof. Take $\alpha(u) := K_{\min}(u)$ and $\beta(u) := K_{\max}(u)$. For a negative feedback system, both $K_{\min}$ and $K_{\max}$ are non-increasing functions of u. By Lemma 4.8 and the definition of p_1 and p_2 we get $p_1 = B(p_1) = K_{\min}(K_{\max}(p_1))$ and $p_2 = T(p_2) = K_{\max}(K_{\min}(p_2))$. We apply $K_{\max}$ to the first equation to get $K_{\max}(p_1) = K_{\max}(K_{\min}(K_{\max}(p_1)))$. Observe that this implies that $K_{\max}(p_1)$ is a fixed point of $K_{\max} \circ K_{\min} = T$. Since by Lemma 4.8 p_2 is the largest fixed point of T, it follows that

$$K_{\max}(p_1) \leqslant p_2. \tag{16}$$

Similarly, applying $K_{\min}$ to the second equation and applying Lemma 4.8, we get

$$K_{\min}(p_2) \geqslant p_1. \tag{17}$$

Since $K_{\min}$ is non-increasing, (16) implies

$$K_{\min}(p_2) \leqslant K_{\min}\big(K_{\max}(p_1)\big) = p_1.$$

This, together with (17), implies $K_{\min}(p_2) = p_1$. A similar argument shows that $K_{\max}(p_1) = p_2$. □

In the final result of this section we will show that the iterations of the multi-valued map $\bar{k}$ will converge to the interval $[p_1, p_2]$. Since the functions $B(u)$ and $T(u)$ are constructed from the multi-valued characteristic the following lemma shows how to construct this interval.

Lemma 4.10. *Consider a SISO system with multi-valued input–output characteristic k. Then for any $u \leqslant p_1$, and both a positive and negative feedback systems we have*

$$\lim_{m\to\infty} \min \bar{k}^{2m}(u) = p_1 = \lim_{n\to\infty} B^n(u),$$

and for any $u \geqslant p_2$,

$$\lim_{m\to\infty} \max \bar{k}^{2m}(u) = p_2 = \lim_{n\to\infty} T^n(u).$$

Proof. We consider a SISO system with a positive feedback. Then by Lemma 4.7 the minimum $\min \bar{k}(u) = B(u)$. By induction we assume that for $l = n-1$ we have $\min \bar{k}^{n-1}(u) = B^{n-1}(u)$. Then

$$\begin{aligned} \min \bar{k}^n(u) &= \min \bar{k}\big(\bar{k}^{n-1}(u)\big) \\ &= \min \bar{k}\big(\min \bar{k}^{n-1}(u)\big) \\ &= \min \bar{k}\big(B^{(n-1)}(u)\big) \\ &= B^n(u). \end{aligned} \tag{18}$$

Therefore for a positive feedback system $\min \bar{k}^n(u) = B^n(u)$.

For the negative feedback system Lemma 4.7 implies that $\min \bar{k}^2(u) = B(u)$. By induction we can get as above that in this case $\min \bar{k}^{2n}(u) = B^n(u)$. In either positive or negative feedback case the first result now follows from the fact that for all $u < p_1$ we have $B(u) > u$ and thus the sequence $\{B^k(u)\}_{k=1}^{\infty}$ is monotone increasing and converges to p_1.

To prove the second result, we first observe that in analogy to (18)

$$\max \bar{k}^{2n}(u) = T^n(u) \quad \text{and} \quad \max \bar{k}^n(u) = T^n(u) \tag{19}$$

for negative and positive feedback systems, respectively. The second result now follows from the fact that for all $u \leqslant p_2$ we have $T(u) < u$ and thus the sequence $\{T^k(u)\}_{k=1}^{\infty}$ is monotone decreasing and converges to p_2. □

4.2. From open to closed loop system

In the previous section we observed a key roles the functions $B(u)$ and $T(u)$ play in open loop system. We will now show that these functions bound the projection of the trajectories of the closed loop system into the output variable y. We consider the closed loop system (4), which we write in the form

$$\dot{x} = f(x,u), \qquad y = h(x), \qquad u = \pm y, \quad x \in X,\ u \in U,\ y \in Y. \tag{20}$$

Here again $u = +y$ ($u = -y$) correspond to a positive (negative) feedback, respectively. The corresponding open loop system is

$$\dot{x} = f(x,u), \qquad y = h(x), \quad x \in X,\ u \in U,\ y \in Y. \tag{21}$$

Definition 4.11. Consider the system (20) and assume that the control function $u(t)$ is bounded. Let $u^- := \liminf_{t\to\infty} u(t)$, $u^+ := \limsup_{t\to\infty} u(t)$ and let

$$y^- := \liminf_{t\to\infty} y(t) = h\big(x(t)\big), \qquad y^+ := \limsup_{t\to\infty} y(t) = h\big(x(t)\big).$$

Lemma 4.12. *Consider a closed loop system* (20) *and assume that the corresponding open loop system* (21) *satisfies the standing assumptions.*

Then there exists a generic set $\mathcal{X} \subset X$ such that for each initial condition $\xi \in \mathcal{X}$ and each bounded input $u(t)$ with the property that the solution $\varphi(t,\xi,u(t))$ of (20) *is defined for all $t \geqslant 0$, we have*

$$B(y^-) \leqslant y^- \leqslant y^+ \leqslant T(y^+).$$

Proof. Our proof combines the argument of De Leenheer and Malisoff [8] and Angeli, De Leenheer and Sontag [4]. In a SISO system a cone $U \subset \mathbb{R}$ must be a half-line. Then by Lemma A.3 of Angeli, De Leenheer and Sontag [4] there are sequences v_n^+ and v_n^- in U such that given any compact set $K \subset U$, there exists a sufficiently large $n = n(K)$ such that $v_n^- \leqslant K \leqslant v_n^+$. It follows from standing assumptions that for each constant $u(t) = q$ there is an exceptional set $\mathcal{B}_q$ of the set of initial conditions that do not converge to an equilibrium in open loop system (21). Recall that the monotonicity assumption implies that the set $X \setminus \mathcal{B}_q$ contains an open and dense set, i.e. it is generic. Following [4] define

$$\mathcal{B} := \bigcup_{n,k\in N,\,\sigma=\pm,\,q\in U_0} \varphi\big(-n, \mathcal{B}_q, v_k^\sigma\big), \tag{22}$$

where U_0 is a countable and dense subset of U and $\varphi(t,x_0,u_0)$ is the flow generated by (20). Since flow defined maps are diffeomorphisms and $X \setminus \mathcal{B}_q$ is generic, each set $X \setminus \varphi(-n,\mathcal{B}_q,v_k^\sigma)$ is generic. Thus

$$\mathcal{X} := X \setminus \mathcal{B} = \bigcap_{n,k\in N,\,\sigma=\pm,\,q\in U_0} \big(X \setminus \varphi\big(-n,\mathcal{B}_q,v_k^\sigma\big)\big)$$

is generic, as a countable intersection of generic sets is generic.

We first prove that for $\xi \in \mathcal{X}$

$$\min k_x(u^-) \preccurlyeq \liminf_{t\to\infty} \varphi(t,\xi,u) \preccurlyeq \limsup_{t\to\infty} \varphi(t,\xi,u) \preccurlyeq \max k_x(u^+). \tag{23}$$

Take an arbitrary $\xi \in X \setminus \mathcal{B}$. By the definition of the lim inf there is an increasing sequence of integer times $n_j \to \infty$ and a sequence of constant-valued controls $u_j \in U_0$ such that $u_j \to u^-$ and $u(t) \geqslant u_j$ for all $t \geqslant n_j$. Then

$$\begin{aligned}\varphi(t,\xi,u) &= \varphi\big(t-n_j, \varphi\big(n_j,\xi,u(\cdot)\big), u(\cdot+n_j)\big)\\ &\succcurlyeq \varphi\big(t-n_j, \varphi(n_j,\xi,u), u_j\big).\end{aligned} \tag{24}$$

Since $\xi \notin \mathcal{B}$, we also have $\varphi(t-n_j, \varphi(n_j,\xi,u), u_j) \notin \mathcal{B}_{u_j}$ and therefore

$$\lim_{t\to\infty} \varphi\big(t-n_j, \varphi(n_j,\xi,u), u_j\big) = v_j,$$

where v_j is an equilibrium. Combining this with (24) yields

$$\liminf_{t\to\infty} \varphi(t,\xi,u) \succcurlyeq \liminf_{t\to\infty} \varphi\big(t-n_j, \varphi(n_j,\xi,u), u_j\big) = v_j. \tag{25}$$

We can apply (25) for every value of j thereby getting a sequence of such v_j's. There must be a subsequence of the v_j's which converges to, say, v (since there are an infinite number of them and they are bounded). We also know that along each branch, k_x is continuous and so $k_x(u_j) \to k_x(u^-)$. Therefore the subsequence of v_j must converge to some value of $k_x(u^-)$. In particular $v \succcurlyeq \min k_x(u^-)$. So we have

$$\limsup_{t\to\infty} \varphi(t,\xi,u) \succcurlyeq \liminf_{t\to\infty} \varphi(t,\xi,u) \succcurlyeq \min k_x(u^-).$$

The rest of the inequality in (23) follows by the similar argument.

Now we apply non-decreasing function h to Eq. (23) to get

$$\min h\big(k_x(u^-)\big) \leqslant \liminf_{t\to\infty} y(t) \leqslant \limsup_{t\to\infty} y(t) \leqslant \max h\big(k_x(u^+)\big). \tag{26}$$

Recall, that for the positive feedback we have $y = u$ and hence $u^- = y^-$ and $u^+ = y^+$. Therefore in this case (26) reads

$$[y^-, y^+] \subset \big[K_{\min}(y^-), K_{\max}(y^+)\big] = \big[B(y^-), T(y^+)\big]$$

which proves the lemma when $y = u$.

In the negative feedback case we have $y = -u$ and hence $u^- = y^+$ and $u^+ = y^-$ and therefore (26) reads $K_{\min}(y^+) \preccurlyeq y^- \preccurlyeq y^+ \preccurlyeq K_{\max}(y^-)$. In other words,

$$[y^-, y^+] \subset \big[K_{\min}(y^+), K_{\max}(y^-)\big]. \tag{27}$$

We now repeat the above argument starting with Eq. (23) with $u^- = K_{\min}(y^+)$ and $u^+ = K_{\max}(y^-)$. In analogy to Eq. (27) we obtain

$$\big[K_{\min}(y^+), K_{\max}(y^-)\big] \subset \big[K_{\min}\big(K_{\max}(y^-)\big), K_{\max}\big(K_{\min}(y^+)\big)\big]. \tag{28}$$

Combining Eqs. (27) and (28) with the definition (9) of $B(u)$ and $T(u)$ in the negative feedback case yields

$$[y^-, y^+] \subset \big[B(y^-), T(y^+)\big]. \qquad \square$$

Proof of Theorem 2.4. In view of Definition 4.11 it is enough to show

$$[y^-, y^+] \subset [p_1, p_2].$$

By Lemma 4.12, $[y^-, y^+] \subset [B(y^-), T(y^+)]$.

Since $u(t) = \pm y(t)$ this implies that $u(t) \subset [B(y^-), T(y^+)]$ for all t. We apply Lemma 4.12 to $u^- := B(y^-)$ and $u^+ := T(y^+)$ to get with

$$[y^-, y^+] \subset \left[B^2(y^-), T^2(y^+)\right].$$

By induction it follows that

$$[y^-, y^+] \subset \left[B^n(y^-), T^n(y^+)\right] \tag{29}$$

for all n.

Now assume that $y^- < p_1$. Since by Lemma 4.10 $\lim_{n\to\infty} B^n(y^-) = p_1$, there exists N such that for all $n \geqslant N$ we have $B^n(y^-) > y^-$. This, however, contradicts (29) and therefore we must have $y^- \geqslant p_1$. Similar argument shows that $y^+ \leqslant p_2$. This shows that $[y^-, y^+] \subset [p_1, p_2]$ and thus proves the theorem. □

5. Morse decomposition for the closed loop system

In this section we prove Theorem 2.7 that provides a construction of a Morse decomposition of a closed loop system based on a Morse decomposition of the corresponding open loop system.

Our first observation is that since $u(t) = \pm y(t)$ and by Theorem 2.4 $[y^-, y^+] \subseteq [p_1, p_2]$, we may assume without loss of generality that $u(t) \in [p_1, p_2]$ for all $t \geqslant 0$. In addition to the standing assumptions, we assume as in Theorem 2.7 that for each fixed $u(t) = u \in [p_1, p_2]$ the open loop system

$$\dot{x} = f(x, u) \tag{30}$$

admits a Morse decomposition $\mathcal{M}(u) = \{M_i(u) \mid i = 1, \dots, 2L + 1\}$ described in Definition 2.6.

Definition 5.1. Let $V_{2k+1}(u)$ be a basin of attraction of the Morse set $M_{2k+1}(u)$, $k = 1, \dots, L$, and let

$$V^*_{2k+1} := \bigcap_{u\in[p_1,p_2]} V_{2k+1}(u) \quad \text{for } k = 0, \dots, L.$$

Let $V_{2k}(u)$ be the basin of attraction of $M_{2k}(u)$.

Let $W_{2k}(u)$ be defined as

$$W_{2k}(u) := \operatorname{cl} V_{2k+1}(u) \cap \operatorname{cl} V_{2k-1}(u) \tag{31}$$

and let $\omega(\xi, u)$ be the omega limit of a trajectory starting at ξ under the flow $\varphi(t, \xi, u)$. Recall, that $\mathcal{B}_u$ is the exceptional set of initial conditions which do not converge to the set of equilibria in the open loop system with the constant input $u(t) = u$.

To show the existence of the Morse decomposition of the closed loop system, we need to show that V^*_{2k+1} is positively invariant. Since this condition is checked on the boundary, we will use the assumption that the Morse sets are ordered in the phase space and that they are uniformly ordered by the output to identify the boundary of the regions V^*_{2k+1}, $k = 0, \dots, L$.

Lemma 5.2. *For each fixed u and $k = 1, \dots, L - 1$, the set $V_{2k+1}(u)$ is bounded by $W_{2k}(u)$ and $W_{2k+2}(u)$*

$$\partial V_{2k+1}(u) = W_{2k}(u) \cup W_{2k+2}(u),$$

while for $k = 0$ and $k = L$

$$\partial V_1(u) = W_2(u), \qquad \partial V_{2L+1} = W_{2L}.$$

Furthermore,

$$W_{2k}(u) \subset V_{2k} \cup \mathcal{B}_u$$

consists of points ξ such that either $\omega(\xi, u) \subset M_{2k}(u)$ or $\xi \in \mathcal{B}_u$.

Proof. Since the value of u is fixed in this lemma, we will drop the reference to u from our notation. Recall, that $[\cdot,\cdot]$ denotes the order interval. Observe that since $M_{2k-1} \subset V_{2k-1}$ and $M_{2k+1} \subset V_{2k+1}$, both $V_{2k-1} \cap [M_{2k-1}, M_{2k+1}] \neq \emptyset$ and $V_{2k+1} \cap [M_{2k-1}, M_{2k+1}] \neq \emptyset$. Therefore $\partial V_{2k-1} \cap [M_{2k-1}, M_{2k+1}] \neq \emptyset$ and $\partial V_{2k+1} \cap [M_{2k-1}, M_{2k+1}] \neq \emptyset$ for every k.

Take $x_0 \in \partial V_{2k+1} \cap [M_{2k-1}, M_{2k+1}]$. Then for all $z \in M_{2k-1}$ and all $w \in M_{2k+1}$ we have $z \prec x_0 \prec w$. It follows from the Limit Set Dichotomy [29, Theorem 1.3.7] and strong monotonicity of (3) that

$$\omega(z) \prec \omega(x_0) \prec \omega(w). \tag{32}$$

Note that by the invariance of the Morse sets $\omega(z) \subset M_{2k-1}$ and $\omega(w) \in M_{2k+1}$. Since z, w were arbitrary, $\omega(x_0) \cap M_{2k+1} = \emptyset$ and $\omega(x_0) \cap M_{2k-1} = \emptyset$. Therefore either $\omega(x_0) \subset M_{2k}$ or $x_0 \in \mathcal{B}_u$. A similar argument shows that if $x_0 \in \partial V_{2k+1} \cap [M_{2k+1}, M_{2k+3}]$ then either $\omega(x_0) \subset M_{2k+2}$ or $x_0 \in \mathcal{B}_u$.

Now we deal with the general case. Assume $x_0 \in \partial V_{2k+1}$, but not necessarily that $x_0 \in [M_{2k-1}, M_{2k+1}]$. Since V_{2i+1}, $i = 0, \dots, L$, is a collection of disjoint open sets, $x_0 \notin V_{2i+1}$ for any $i = 0, \dots, L$, either $x_0 \in \mathcal{B}_u$ or $\omega(x_0) \subset M_{2s}$ for some $s = 1, \dots, L$. We will now show that either $s = k$ or $s = k + 1$. Since $x_0 \in \partial V_{2k+1}$ and V_{2k+1} is open, for any neighborhood N of x_0 there is an open set $V_N \subset V_{2k+1} \cap N$. Assume that $\omega(x_0) \subset M_{2s}$, for some $s < k$. Since the Morse sets are ordered by the assumption, there exists a T such that $\varphi(T, x_0, u) \in [M_{2s+1}, M_{2s-1}]$ and almost all solutions in a neighborhood $\bar{V}$ of $\varphi(T, x_0, u)$ converge to either M_{2s+1}, M_{2s-1} or M_{2s}. By the continuous dependence on initial condition there is a neighborhood $\bar{U}$ of x_0 such that $\varphi(T, \bar{U}, u) \subset \bar{V}$ and thus almost all solutions in $\bar{U}$ converge to either M_{2s+1}, M_{2s-1} or M_{2s}. This is a contradiction to the fact that there is an open set of points $V_{\bar{U}} \subset V_{2k+1} \cap \bar{U}$ that converge to M_{2k+1}. The assumption $s > k + 1$ leads to a similar contradiction. Therefore $s = k$ or $s = k + 1$ and $x_0 \in \partial V_{2k+1}(u)$ implies $\omega(x_0) \subset M_{2k}$, $\omega(x_0) \subset M_{2k+2}$ or $x_0 \in \mathcal{B}_u$. This proves the second statement of the lemma.

Our argument also shows that all points in the neighborhood of x_0 are either in $V_{2k+1}(u)$ and $V_{2k-1}(u)$, which implies $x_0 \in W_{2k}(u)$; or in $V_{2k+1}(u)$ and $V_{2k+3}(u)$ which implies $x_0 \in W_{2k+2}(u)$. This proves the first statement of the lemma. $\square$

In the next two lemmas we show that the basins of attraction for the open loop system are ordered even for different values of constant input u and v. Recall that $[p_1, p_2] \subset U$ is the interval over which the Morse decomposition $\mathcal{M}(u)$ of the open loop system is defined.

Lemma 5.3. *Assume the standing assumptions and the existence of Morse decomposition for an open loop system. Then for all $u \leqslant v$, $u, v \in [p_1, p_2]$ and all $k < s$*

$$V_k(v) \cap V_s(u) = \emptyset.$$

Proof. Assume to the contrary that there is $\zeta \in V_k(v) \cap V_s(u)$. Then by the monotonicity $\varphi(t, \zeta, u) \prec \varphi(t, \zeta, v)$ for all t and $z := \lim_{t\to\infty} \varphi(t, \zeta, u) \preccurlyeq \lim_{t\to\infty} \varphi(t, \zeta, v) =: w$. By definition $z \in M_s(u)$ and $w \in M_k(v)$. By the monotonicity of the output function h, $z \preccurlyeq w$ implies $h(z) \leqslant h(w)$ for $z \in M_s(u)$ and $w \in M_k(v)$ with $k < s$. This contradicts the assumption (12). $\square$

Lemma 5.4. *Assume the standing assumptions and the existence of open loop Morse decomposition. Then for any $u \in [p_1, p_2]$, and any fixed k*

$$\bigcup_{l \geqslant k} V_l(p_1) \subset \bigcup_{l \geqslant k} V_l(u) \cup \mathcal{B}_u, \qquad \bigcup_{l \leqslant k} V_l(p_2) \subset \bigcup_{l \leqslant k} V_l(u) \cup \mathcal{B}_u.$$

Proof. Take any $u \leqslant v$, $u, v \in [p_1, p_2]$. Since by Lemma 5.3 $V_s(u) \cap V_l(v) = \emptyset$ for all $s < l$, and

$$X = \bigcup_{s<l} V_s(v) \cup \bigcup_{s \geqslant l} V_s(v) \cup \mathcal{B}_v,$$

it follows that $V_l(u) \subset \bigcup_{s \geqslant l} V_s(v) \cup \mathcal{B}_v$. Taking union over all $l \geqslant k$ we get

$$\bigcup_{l \geqslant k} V_l(u) \subset \bigcup_{l \geqslant k} \bigcup_{s \geqslant l} V_s(v) \cup \mathcal{B}_v = \bigcup_{l \geqslant k} V_l(v) \cup \mathcal{B}_v.$$

Finally, taking $u = p_1$ and $v = u$ we obtain the first statement above.

Similarly, Lemma 5.3 and the fact that $X = \bigcup_{s \leqslant l} V_s(u) \cup \bigcup_{s > l} V_s(u) \cup \mathcal{B}_u$, imply

$$V_l(v) \subset \bigcup_{s \leqslant l} V_s(u) \cup \mathcal{B}_u. \tag{33}$$

Taking union over $l \leqslant k$ yields $\bigcup_{l \leqslant k} V_l(v) \subset \bigcup_{l \leqslant k} \bigcup_{s \leqslant l} V_s(u) \cup \mathcal{B}_u = \bigcup_{l \leqslant k} V_l(u) \cup \mathcal{B}_u$, and taking $v = p_2$ we get the second statement above. $\square$

As we will show next, the ordering of basins for the open loop systems implies that the boundaries of their intersections V^*_{2k+1} have a particularly simple form. We will use these to check the positive invariance of the sets V^*_{2k+1} in the closed loop system, which is the key step in the proof of Theorem 2.7.

Proposition 5.5. *For each $k = 0, \dots, L$, the boundary of V^*_{2k+1} satisfies*

$$\partial V^*_{2k+1} \subset W_{2k+2}(p_2) \cup W_{2k}(p_1) \cup \mathcal{B}_{p_1} \cup \mathcal{B}_{p_2}.$$

Proof. We write

$$V_{2k+1}(u) = \Bigl(\bigcup_{l \geqslant 2k+1} V_l(u)\Bigr) \cap \Bigl(\bigcup_{l \leqslant 2k+1} V_l(u)\Bigr). \tag{34}$$

From the definition of V_{2k+1} and using (34) we get

$$\begin{aligned}
V^*_{2k+1} &= \bigcap_{u \in [p_1, p_2]} V_{2k+1}(u) \\
&= \bigcap_{u \in [p_1, p_2]} \Bigl(\Bigl(\bigcup_{l \geqslant 2k+1} V_l(u)\Bigr) \cap \Bigl(\bigcup_{l \leqslant 2k+1} V_l(u)\Bigr)\Bigr) \\
&= \Bigl(\bigcap_{u \in [p_1, p_2]} \bigcup_{l \geqslant 2k+1} V_l(u)\Bigr) \cap \Bigl(\bigcap_{u \in [p_1, p_2]} \bigcup_{l \leqslant 2k+1} V_l(u)\Bigr).
\end{aligned}$$

We will show that

$$\bigcup_{l\geqslant 2k+1} V_l(p_1)=\bigcap_{u\in[p_1,p_2]}\bigcup_{l\geqslant 2k+1} V_l(u),\quad\text{and}\quad \bigcup_{l\leqslant 2k+1} V_l(p_2)=\bigcap_{u\in[p_1,p_2]}\bigcup_{l\leqslant 2k+1} V_l(u). \tag{35}$$

The one inclusion follows from Lemma 5.4

$$\bigcup_{l\geqslant 2k+1} V_l(p_1)\subset\bigcap_{u\in[p_1,p_2]}\bigcup_{l\geqslant 2k+1} V_l(u),\qquad \bigcup_{l\leqslant 2k+1} V_l(p_2)\subset\bigcap_{u\in[p_1,p_2]}\bigcup_{l\leqslant 2k+1} V_l(u). \tag{36}$$

The opposite inclusions follow from the fact that the set on the left side of each of the expressions in (36) is one of the intersected sets on the right side of these expressions. Therefore we proved (35) and thus

$$V^*_{2k+1}=\Bigl(\bigcup_{l\geqslant 2k+1} V_l(p_1)\Bigr)\cap\Bigl(\bigcup_{l\leqslant 2k+1} V_l(p_2)\Bigr). \tag{37}$$

We can write the right-hand side in (37) as

$$V_{2k+1}(p_1)\cap V_{2k+1}(p_2)\cup\bigcup_{s>r}\bigl(V_s(p_1)\cap V_r(p_2)\bigr).$$

Taking $u=p_1$ and $v=p_2$ in Lemma 5.3 we get that $V_s(p_1)\cap V_r(p_2)=\emptyset$ if $s>r$. Therefore

$$V^*_{2k+1}=V_{2k+1}(p_1)\cap V_{2k+1}(p_2).$$

We will use this expression to find the boundary of V^*_{2k+1}. Observe that

$$\begin{aligned}\partial V^*_{2k+1}&=\partial\bigl(V_{2k+1}(p_1)\cap V_{2k+1}(p_2)\bigr)\\&\subset\partial\bigl(V_{2k+1}(p_1)\bigr)\cup\partial\bigl(V_{2k+1}(p_2)\bigr)\\&=W_{2k}(p_1)\cup W_{2k+2}(p_1)\cup W_{2k}(p_2)\cup W_{2k+2}(p_2),\end{aligned} \tag{38}$$

where we used Lemma 5.2 in the last line. We wish to further simplify the right-hand side of (38). Since $W_{2k}(p_2)\subset \mathrm{cl}(V_{2k-1}(p_2))$, it follows from (33) with $v=p_2$, $u=p_1$ and $l=2k-1$ that

$$W_{2k}(p_2)\subset \mathrm{cl}\Bigl(\bigcup_{s\leqslant 2k-1} V_s(p_1)\Bigr)\cup\mathcal{B}_{p_1},$$

where we used that by [29, Theorem 4.3], $\mathcal{B}_{p_1}$ is closed. Now we select some $x\in W_{2k}(p_2)$ and consider two complementary cases: either $x\in\mathrm{int}(\bigcup_{s\leqslant 2k-1} V_s(p_1))$ or $x\in\partial(\bigcup_{s\leqslant 2k-1} V_s(p_1))$.

I. Assume first that $x\in\mathrm{int}(\bigcup_{s\leqslant 2k-1} V_s(p_1))$. Then there is a neighborhood $N(x)$ such that $N(x)\subset\bigcup_{s\leqslant 2k-1} V_s(p_1)$. Since $V_{2k+1}(p_1)\cap\bigcup_{s\leqslant 2k-1} V_s(p_1)=\emptyset$ and these sets are both open, $x\notin\partial V_{2k+1}(p_1)$.

II. Consider now the case when $x\in\partial(\bigcup_{s\leqslant 2k-1} V_s(p_1))$. Recall that

$$\bigcup_{s\leqslant 2k-1} V_s(p_1)=V_1(p_1)\cup V_2(p_1)\cup\cdots\cup V_{2k-1}(p_1).$$

Since all these sets are disjoint

$$\mathrm{cl}\Bigl(\bigcup_{s\leqslant 2k-1} V_s(p_1)\Bigr) = \mathrm{cl}\bigl(V_1(p_1)\bigr) \cup \mathrm{cl}\bigl(V_2(p_1)\bigr) \cup \cdots \cup \mathrm{cl}\bigl(V_{2k-1}(p_1)\bigr).$$

By Lemma 5.2 and (31) $\mathrm{cl}(V_{2k-1}) \cap \mathrm{cl}(V_{2k+1}) = W_{2k} \subset V_{2k} \cup \mathcal{B}_{p_1}$. Since V_{2k} is closed we have

$$\begin{aligned}\mathrm{cl}(V_{2k-1}) \cup \mathrm{cl}(V_{2k+1}) &= V_{2k-1} \cup V_{2k+1} \cup \partial V_{2k-1} \cup \partial V_{2k+1} \\ &= V_{2k-1} \cup V_{2k+1} \cup W_{2k-2} \cup W_{2k} \cup W_{2k+2} \\ &\subset V_{2k-1} \cup V_{2k+1} \cup V_{2k} \cup W_{2k-2} \cup W_{2k+2} \cup \mathcal{B}_{p_1}.\end{aligned}$$

Therefore $\mathrm{cl}(\bigcup_{s\leqslant 2k-1} V_s(p_1)) \subset (\bigcup_{s\leqslant 2k-1} V_s(p_1)) \cup W_{2k}(p_1) \cup \mathcal{B}_{p_1}$, and thus

$$\partial\Bigl(\bigcup_{s\leqslant 2k-1} V_s(p_1)\Bigr) \subset W_{2k}(p_1) \cup \mathcal{B}_{p_1}.$$

We conclude that if $x \in \partial(\bigcup_{s\leqslant 2k-1} V_s(p_1))$ then $x \in W_{2k}(p_1)$ or $x \in \mathcal{B}_{p_1}$.

We now put I and II together. We have shown that if $x \in W_{2k}(p_2) \cap \mathrm{cl}(\bigcup_{s\leqslant 2k-1} V_s(p_1))$ then either $x \notin \partial V_{2k+1}(p_1)$ or $x \in W_{2k}(p_1) \cup \mathcal{B}_{p_1}$. Therefore if $x \in W_{2k}(p_2) \cap \partial V_{2k+1}(p_1)$, then $x \in W_{2k}(p_1) \cup \mathcal{B}_{p_1}$. Therefore

$$W_{2k}(p_2) \cap \partial V_{2k+1}(p_1) \subset W_{2k}(p_1) \cup \mathcal{B}_{p_1}.$$

Similar argument shows that if $x \in W_{2k+2}(p_1) \cap \partial V_{2k+1}(p_2) \cup \mathcal{B}_{p_2}$, then $x \in W^s_{2k+2}(p_2)$ and therefore

$$W_{2k+2}(p_1) \cap \partial V_{2k+1}(p_2) \subset W_{2k+2}(p_2) \cup \bigl(\mathcal{B}_{p_2} \cap \partial V_{2k+1}(p_2)\bigr) \subset W_{2k+2}(p_2) \cup \mathcal{B}_{p_2}.$$

These two facts imply that (38) can be rewritten $\partial V^*_{2k+1} \subset W_{2k}(p_1) \cup W_{2k+2}(p_2) \cup \mathcal{B}_{p_1} \cup \mathcal{B}_{p_2}$. □

The following is the key result in this section, where we show the positive invariance of the sets V^*_{2k+1} in the closed loop system.

Theorem 5.6. *Assume the standing assumptions and the existence of a Morse decomposition for the monotone open loop system* (3)*. Then for all $k = 0, \ldots, L$ the set V^*_{2k+1} is positively invariant under the closed loop flow* (4)*.*

Proof. In the proof of this theorem we will distinguish between the flow $\phi(t, x_0)$ of the closed loop system (4) and the flow of the open loop $\varphi(t, x_0, u)$. Note that we can always represent the flow $\phi(t, x_0)$ as $\varphi(t, x_0, u)$ with $u = u(t)$ defined by $u(t) = g(h(\phi(t, x_0)))$.

We now take $x \in V^*_{2k+1}$ and assume there is a $T > 0$ such that $\phi(x, T) \in \partial V^*_{2k+1}$. By Proposition 5.5 either

$$\phi(T, x) \in W_{2k+2}(p_2) \cup \mathcal{B}_{p_2} \quad \text{or} \quad \phi(T, x) \in W_{2k}(p_1) \cup \mathcal{B}_{p_1}.$$

In order to simplify the notation we set $x(T) := \phi(T, x)$. Assume the first case and consider the flow $\phi(t, x(T))$ in the open flow form $\varphi(t, x(T), u)$. Since $u(t) \leqslant p_2$ for all t, we have

$$\varphi\bigl(t, x(T), u\bigr) \preccurlyeq \varphi\bigl(t, x(T), p_2\bigr) \quad \text{for all } t. \tag{39}$$

By Lemma 5.2 $\varphi(t, x(T), p_2)$ either converges to $M_{2k}(p_2)$ or belongs to $\mathcal{B}_{p_2}$. In either case we have $\varphi(t, x(T), p_2) \not\subset \bigcup_{l>2k+1} V_l(p_2)$. Therefore by monotonicity

$$\phi\big(t, x(T)\big) = \varphi\big(t, x(T), u\big) \in \bigcup_{l \leqslant 2k+1} V_l(p_2) \cup \mathcal{B}_{p_2} \quad \text{for all } t \geqslant 0. \tag{40}$$

On the other hand if $\phi(x(T), t) \in W_{2k}(p_1) \cup \mathcal{B}_{p_1}$ we again write $\phi(t, x(T)) = \varphi(t, x(T), u)$ for the appropriate $u = u(t)$. Since $u(t) \geqslant p_1$ for all t we have

$$\varphi\big(t, x(T), u\big) \succcurlyeq \varphi\big(t, x(T), p_1\big) \quad \text{for all } t \geqslant 0. \tag{41}$$

Again by Lemma 5.2 $\varphi(t, x(T), p_1) \not\subset \bigcup_{l<2k+1} V_l(p_1)$ and therefore

$$\varphi\big(t, x(T), u\big) \in \bigcup_{l \geqslant 2k+1} V_l(p_1) \cup \mathcal{B}_{p_1}. \tag{42}$$

Combining (40) and (42) we see that an arbitrary trajectory $\varphi(t, x, u)$ starting at $x \in V^*_{2k+1}$ has to stay in the intersection

$$\varphi(t, x, u) \subset \left(\bigcup_{l \geqslant 2k+1} V_l(p_1) \cup \mathcal{B}_{p_1}\right) \cap \left(\bigcup_{l \leqslant 2k+1} V_l(p_2) \cup \mathcal{B}_{p_2}\right).$$

The latter set (see (37)) can be written as

$$V^*_{2k+1} \cup \left(\bigcup_{l \leqslant 2k+1} V_l(p_2) \cap \mathcal{B}_{p_1}\right) \cup \left(\bigcup_{l \leqslant 2k+1} V_l(p_1) \cap \mathcal{B}_{p_2}\right) \cup (\mathcal{B}_{p_2} \cap \mathcal{B}_{p_1}). \tag{43}$$

We now note that $V^*_{2k+1} \cap (\mathcal{B}_{p_1} \cup \mathcal{B}_{p_2}) = \emptyset$. Indeed, $V^*_{2k+1} \subset V_{2k+1}(p_1)$ which is disjoint from $\mathcal{B}_{p_1}$. A similar argument applies to $\mathcal{B}_{p_2}$, proving the assertion. This implies that in $\varphi(t, x_0, u)$ is either a subset of V^*_{2k+1} for all t, or a subset of the latter three sets in (43), for all $t \geqslant 0$. Since $x_0 \in V^*_{2k+1}$ it must be that

$$\varphi(t, x, u) \in V^*_{2k+1} \quad \text{for all } t. \qquad \square$$

Proof of Theorem 2.7. Recall that each Morse set $M^*_{2i+1}, i = 1, \dots, L$, is defined as the maximal invariant set in $V^*_{2i+1} = \bigcap_{u \in [p_1, p_2]} V_{2i+1}(u)$ and M^*_0 is the maximal invariant set in $\mathcal{X} \setminus \bigcup_{i=0,\dots,L} V^*_{2i+1}$. Then by Theorem 2.4 all the ω-limit sets of arbitrary initial conditions $\xi \in \mathcal{X}$ lie in one of the set sets M^*_0 or M^*_{2i+1}, $i = 0, \dots, L$.

We now show that V^*_{2i+1} is open for all $i = 0, \dots, L$. Since the solutions of the system (3) depend continuously on the parameter u, the open sets $V_{2i+1}(u)$ vary continuously with u. Therefore for each $x \in V_{2i+1}(u)$ there is an open neighborhood $U_{2i+1}(u)$ of x such that $U_{2i+1}(u) \subset V_{2i+1}(v)$ for all $v \in N(u)$, a neighborhood of u. Since $[p_1, p_2]$ is compact it admits a finite cover by neighborhoods $N(u_1), \dots, N(u_k)$. Hence the set $\bigcap_{j=1}^k U_{2i+1}(u_j)$ is an open neighborhood of x in V^*_{2i+1}.

Since the Morse sets M^*_{2i+1}, $i = 1, \dots, L$, lie in an open positively invariant set V^*_{2i+1}, they are non-empty. At the same time there cannot be any solution with $\alpha(x) \subset M^*_{2i+1}$ and $\omega(x) \subset M^*_0$. This proves the existence of the order advertised in the theorem. $\square$

6. Convergence inside the Morse sets

In this section we show that our theory can be applied iteratively to find finer Morse decompositions and how the characteristic can be used to determine internal structure of Morse sets.

6.1. Finding a finer decomposition

If the restriction of the input–output characteristic $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is multi-valued, we can apply Theorem 2.4 to this restriction of the full characteristic to compute a perhaps smaller interval $[p_1^1, p_2^1] \subset [p_1, p_2]$ that attracts solutions of the closed loop system starting in V_{2l+1}^*. If the restriction of the characteristic defines a non-trivial Morse decomposition of $M_{2l+1}(u)$ on $[p_1^1, p_2^1]$ we apply Theorem 2.7 to find a non-trivial Morse decomposition $\bar{\mathcal{M}} = \{\{\bar{M}_j^{2l+1}\}_{j=0}^k \mid \bar{0} \preccurlyeq \bar{j} \text{ for all } j > 0\}$ of M_{2l+1}^*. Then the union of the Morse sets

$$\bigcup_{j=0}^{k} \bar{M}_j^{2l+1} \cup \bigcup_{i=0,\, i \neq l}^{L} M_{2i+1}$$

with ordering

$$0 \preccurlyeq 2i+1 \quad \text{for all } i = 1, \ldots, l-1, l+1, \ldots, L, \qquad 0 \preccurlyeq \bar{j} \quad \text{and} \quad \bar{0} \preccurlyeq \bar{j} \quad \text{for all } j = 0, \ldots, k,$$

is a Morse decomposition of the invariant set of (4). This is a *refinement* of the original Morse decomposition.

6.2. Individual Morse set

If the restriction of the input–output characteristic $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is single-valued, then we can apply the standard theory of single-valued characteristics. Note that the assumption that $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is single-valued is equivalent to the assumption that $M_{2l+1}(u) = e_{2l+1}(u)$ is a unique equilibrium for all $u \in [p_1, p_2]$. We have the following definition.

Definition 6.1. Let $k_{x,2l+1} : [p_1, p_2] \to X$ be the $(2l+1)$th branch of the I/S characteristic k_x defined by $k_{x,2l+1}(u) = e_{2l+1}(u)$. Let k_{2l+1} be the corresponding $(2l+1)$th branch of the I/O characteristic $k : [p_1, p_2] \to \mathbb{R}$ defined by $k(u) = h(e_{2l+1}(u))$. Notice that the requirement that the domain of these maps is an entire interval $[p_1, p_2]$ is essential. If $u \to M_{2l+1}(u)$ for $u \in [p_1, p_2]$ is single-valued for some l then $k_{x,2l+1}$ and k_{2l+1} are well defined. We will call them *single-valued branches* of the multi-valued characteristic and l a *single-valued index*.

Lemma 6.2. *Let l be a single-valued index and let $\xi \in V_{2l+1}^*$. Let $\varphi(t, \xi, u)$ be a solution starting at ξ with an arbitrary input $u(t)$ in the open loop system* (3)*. Let $y^- := \liminf_{t\to\infty} y(t) = h(x(t))$, $y^+ := \limsup_{t\to\infty} y(t) = h(x(t))$, $u^- := \liminf_{t\to\infty} u(t)$, and $u^+ := \limsup_{t\to\infty} u(t)$. Then*

$$[y^-, y^+] \subset \left[k_{2l+1}^2(y^-), k_{2l+1}^2(y^+)\right].$$

Proof. Observe that since V_{2l+1}^* is positively invariant by Theorem 5.6 the solution $\varphi(t, \xi, u)$ exists for all $t \geqslant 0$ and $u^-, u^+ \subset [p_1, p_2]$. Further, by the assumption on l the restriction of the input-state characteristics to the set V_{2l+1}^* is the branch $k_{x,2l+1}$

$$k_x\big([p_1, p_2]\big) \cap V_{2l+1}^* = k_{x,2l+1}.$$

The remainder of proof is completely analogous to the proof of Lemma 4.12 were we use $k_{x,2l+1}$ instead of k_x and k_{2l+1} instead of k. We will indicate the main steps in the proof.

One first shows that

$$k_{x,2l+1}(u^-) \preccurlyeq \liminf \varphi(t, \xi, u) \preccurlyeq \limsup \varphi(t, \xi, u) \preccurlyeq k_{x,2l+1}(u^+) \tag{44}$$

and then applying h we get

$$h\big(k_{x,2l+1}(u^-)\big) \leqslant \limsup y(t) \leqslant \liminf y(t) \leqslant h\big(k_{x,2l+1}(u^+)\big). \tag{45}$$

As in Lemma 4.12 this implies for the positive feedback system with $u(t) = y(t)$ that

$$k_{2l+1}(y^-) \preccurlyeq \liminf y(t) \preccurlyeq \limsup y(t) \preccurlyeq k_{2l+1}(y^+).$$

In other words,

$$[y^-, y^+] \subset \big[k_{2l+1}(y^-), k_{2l+1}(y^+)\big]. \tag{46}$$

If we apply the argument one more time starting with Eq. (23) and with $u^- = k_{2l+1}(y^-)$ and $u^+ = k_{2l+1}(y^+)$ we get

$$\big[k_{2l+1}(y^-), k_{2l+1}(y^+)\big] \subset \big[k^2_{2l+1}(y^-), k^2_{2l+1}(y^+)\big].$$

This, together with (46) proves the lemma for the positive feedback case.

For the negative feedback $u = -y$ Eq. (45) can be written as

$$[y^-, y^+] \subset \big[k_{2l+1}(y^+), k_{2l+1}(y^-)\big]. \tag{47}$$

We now repeat the above argument with $u^- = k_{2l+1}(y^+)$ and $u^+ = k_{2l+1}(y^-)$ and get

$$\big[k_{2l+1}(y^+), k_{2l+1}(y^-)\big] \subset \big[k^2_{2l+1}(y^-), k^2_{2l+1}(y^+)\big]. \tag{48}$$

Eqs. (47) and (48) imply the result for the negative feedback. □

Lemma 6.3. *The input–output characteristic k maps the interval $[p_1, p_2]$ into itself $k : [p_1, p_2] \to [p_1, p_2]$. Therefore the graph of every single-valued branch k_{2l+1} intersects the diagonal in $[p_1, p_2] \times [p_1, p_2]$.*

Proof. By Corollary 4.4 for the negative feedback system both $K_{\min}(u)$ and $K_{\max}(u)$ are non-increasing functions of u. Therefore the graph of the input–output characteristic k satisfies $K_{\min}(p_2) \leqslant k(u) \leqslant K_{\max}(p_1)$ for all $u \in [p_1, p_2]$. By Lemma 4.9 $K_{\max}(p_1) = p_2$ and $K_{\min}(p_2) = p_1$ and hence the graph satisfies $p_1 \leqslant k(u) \leqslant p_2$.

By Corollary 4.4 for the positive feedback system functions $K_{\min}(u)$ and $K_{\max}(u)$ are non-decreasing functions of u and thus the graph of k satisfies $K_{\min}(p_1) \leqslant k(u) \leqslant K_{\max}(p_2)$ for all $u \in [p_1, p_2]$. By Lemma 4.8 $K_{\min}(p_1) = B(p_1) = p_1$ and $K_{\max}(p_2) = T(p_2) = p_2$ and thus again the graph of k satisfies $p_1 \leqslant k(u) \leqslant p_2$. Therefore for both the negative and positive feedback systems $k([p_1, p_2]) \subset [p_1, p_2]$.

Observe that continuity of each single-valued branch k_{2l+1} follows from the continuity of the right-hand side of (3) and the inverse mapping theorem. Since each single-valued branch k_{2l+1} is defined for all $u \in [p_1, p_2]$ the second result follows from the continuity of k_{2l+1}. □

Lemma 6.3 implies that the following is well defined.

Definition 6.4. For each single-valued index l let e^*_{2l+1} be an intersection of the branch k_{2l+1} and the line $y = u$. Let $E_{2l+1} := k_{x,2l+1}(e^*_{2l+1})$ be the corresponding equilibrium of the closed loop system in the state space.

Proof of Theorem 2.10. The first two results follow directly from the invariance (Theorem 5.6) of the V^*_{2l+1} under the closed loop system (4) and the original papers [2,4].

The second statement is a special case of the results [2,4] which applies to both positive and negative feedback systems. Take $\xi \in V^*_{2l+1}$ and let $\varphi(t, \xi, u(t))$ be a solution starting at ξ with arbitrary $u(t)$. Let y^-, y^+, u^- and u^+ be defined as in Lemma 6.2. Then by that lemma $[y^-, y^+] \subset [k^2_{2l+1}(y^-), k^2_{2l+1}(y^+)]$.

Since $u(t) = \pm y(t)$ this implies that $u(t) \subset [k^2_{2l+1}(y^-), k^2_{2l+1}(y^+)]$ for all $t \geqslant 0$. We apply Lemma 6.2 to $u^- := k^2_{2l+1}(y^-)$ and $u^+ := k^2_{2l+1}(y^+)$ to get

$$[y^-, y^+] \subset \left[k^4_{2l+1}(y^-), k^4_{2l+1}(y^+)\right].$$

By induction it follows that

$$[y^-, y^+] \subset \left[k^{2n}_{2l+1}(y^-), k^{2n}_{2l+1}(y^+)\right] \tag{49}$$

for all n.

By assumption $k^{2n}_{2l+1}(u) \to e^*_{2l+1}$ for all $u \in [p_1, p_2]$ and since $u = \pm y$, then $k^{2n}_{2l+1}(y^-) \to e^*_{2l+1}$ and $k^{2n}_{2l+1}(y^+) \to e^*_{2l+1}$ as well. By (49) $y^- = y^+ = e^*_{2l+1}$ and thus $u^- = u^+ = e^*_{2l+1}$. Therefore $u(t)$ converges to e^*_{2l+1}. The Converging-inputs Converging-state Theorem 1 of [30] implies

$$\lim_{t\to\infty} \varphi\big(t, \xi, u(t)\big) \to E_{2l+1}. \qquad \square$$

7. Conclusions

Monotone input–output systems have proved to be very successful in analyzing complex models of biochemical regulatory networks [3,31]. The main approach is to decompose a closed loop system (1) into a parameterized system (open loop) (2) that is strongly monotone and then reconstitute the original system using either a negative or a positive feedback. If the open loop system (1) is strongly monotone its dynamics can be characterized by a (multi-valued) input–output characteristic. From this characteristic certain conclusions can be drawn about the closed loop system (2). For a single-valued characteristic and a positive feedback system, the fixed points of the characteristic are in one-to-one correspondence with the equilibria of the original closed loop system [1,2,9], including their asymptotic stability. For a negative feedback system the behavior of the closed loop system may be very different from the open loop system. In particular, a closed loop system may admit a stable periodic orbit for a sufficiently strong feedback. Therefore in the case of negative feedback the results take the form of a *small gain theorem*: if the feedback is sufficiently small, the closed loop system behaves as an open loop system and (generic) convergence to equilibria is assured [4,10].

A natural next step is to relax the requirement that the input–output characteristic is single-valued. The first steps in this direction were taken by De Leenheer and Malisoff [8] for negative feedback systems and very recently by Enciso and Sontag [11] for positive feedback systems. The goal of the first paper is to find conditions under which the small gain theorem still holds while [11] extends the local correspondence results between fixed points of the characteristic and the equilibria of the closed loop system. In the context of our results it can be shown that the assumptions imposed on the I/O characteristic in [8] imply $p_1 = p_2$ and a trivial Morse decomposition at $u = p_1 = p_2$.

The goal of our paper is more global and complementary to these efforts. The idea of a Morse decomposition of the invariant set, due to Conley [6], was developed to capture robust features of the dynamics. Each Morse set can contain multiple equilibria, periodic orbits, and the connecting orbits between them and so it can have complicated internal structure. This internal structure can vary with parameters, but the relationship between different Morse sets encoded in a partial order between the Morse sets, is robust.

We present a new method which employs an input–output characteristic to construct Morse decompositions for an arbitrary system of ordinary differential equations with monotone interactions which admits a decomposition as a monotone system with a scalar feedback. When feedback is multi-dimensional, the construction of the compact subset $R \subset U$ presents technical difficulties, as some results in Section 4 (in particular Lemma 4.6) depend on the fact that the output space is one-dimensional. We do not think, however, that the assumption of scalar feedback is essential and we believe that the technical difficulties can be resolved. We have chosen to concentrate on scalar feedback because this is the situation most often encountered in the applications. However, since any system with monotone interactions can be decomposed to a parameterized monotone system with a negative feedback [2,7] the potential extension of our result to negative feedback of arbitrary dimension is theoretically attractive, as it would allow construction of a Morse decomposition for any such system.

Other potential extensions of our results would be to develop methods that probe further into the structure of the individual Morse sets. For positive feedback systems this role is served by a recent paper [11]. For negative feedback systems the fundamental difficulty is formulation of results that would guarantee existence of a periodic orbit. Some results in this direction can be found in [16] and [13].

We have applied our theory to a model of the cell cycle. We investigate how the strength of the negative feedback loop affects the existence of the periodic orbit. Not surprisingly, if we weaken the negative feedback loop the periodic orbit disappears and we show that almost all solutions converge to a stable equilibrium. On the other hand, if we change the cooperativity constants in the negative feedback loop, we can find a bistable regime, where almost all solutions converge to one of two different stable equilibria. Our approach provides an alternative to a bifurcation analysis by Tyson and collaborators [25,32]. While our approach relies on numerically computed input–output characteristic, it can provide proofs of convergence for (almost) all initial conditions.

Acknowledgment

We would like to thank an anonymous reviewer whose careful reading and thoughtful suggestions led to great improvements in the paper.

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