ON MONOTONICITY OF SOLUTIONS OF DISCRETE-TIME NONNEGATIVE AND COMPARTMENTAL DYNAMICAL SYSTEMS

VIJAYSEKHAR CHELLABOINA, WASSIM M. HADDAD, JAMES M. BAILEY, AND JAYANTHY RAMAKRISHNAN

Received 27 October 2003

Nonnegative and compartmental dynamical system models are widespread in biological, physiological, and pharmacological sciences. Since the state variables of these systems are typically masses or concentrations of a physical process, it is of interest to determine necessary and sufficient conditions under which the system states possess monotonic solutions. In this paper, we present necessary and sufficient conditions for identifying discrete-time nonnegative and compartmental dynamical systems that only admit monotonic solutions.

1. Introduction

Nonnegative dynamical systems are of paramount importance in analyzing dynamical systems involving dynamic states whose values are nonnegative [2, 9, 16, 17]. An important subclass of nonnegative systems is compartmental systems [1, 4, 6, 8, 11, 12, 13, 14, 15, 18]. These systems involve dynamical models derived from mass and energy balance considerations of macroscopic subsystems or compartments which exchange material via intercompartmental flow laws. The range of applications of nonnegative and compartmental systems is widespread in models of biological and physiological processes such as metabolic pathways, tracer kinetics, pharmacokinetics, pharmacodynamics, and epidemic dynamics.

Since the state variables of nonnegative and compartmental dynamical systems typically represent masses and concentrations of a physical process, it is of interest to determine necessary and sufficient conditions under which the system states possess monotonic solutions. This is especially relevant in the specific field of pharmacokinetics [7, 19] wherein drug concentrations should monotonically decline after discontinuation of drug administration. In a recent paper [5], necessary and sufficient conditions were developed for identifying continuous-time nonnegative and compartmental dynamical systems that only admit nonoscillatory and monotonic solutions. In this paper, we present analogous results for discrete-time nonnegative and compartmental systems.

Copyright © 2004 Hindawi Publishing Corporation Advances in Difference Equations 2004:3 (2004) 261–271 2000 Mathematics Subject Classification: 39A11, 93C55 URL: http://dx.doi.org/10.1155/S1687183904310095

262 Monotonicity of solutions

The contents of the paper are as follows. In Section 2, we establish definitions and notation, and review some basic results on nonnegative dynamical systems. In Section 3, we introduce the notion of monotonicity of solutions of nonnegative dynamical systems. Furthermore, we provide necessary and sufficient conditions for monotonicity for linear nonnegative dynamical systems. In Section 4, we generalize the results of Section 3 to nonlinear nonnegative dynamical systems. In addition, we provide sufficient conditions that guarantee the absence of limit cycles in nonlinear compartmental systems. In Section 5, we use the results of Section 3 to characterize the class of all linear, threedimensional compartmental systems that exhibit monotonic solutions. Finally, we draw conclusions in Section 6.

2. Notation and mathematical preliminaries

In this section, we introduce notation, several definitions, and some key results concerning discrete-time, linear nonnegative dynamical systems [2, 3, 10] that are necessary for developing the main results of this paper. Specifically, for $x \in \mathbb{R}^n$, we write $x \ge 0$ (resp., $x \ge 0$) to indicate that every component of x is nonnegative (resp., positive). In this case, we say that x is *nonnegative* or *positive*, respectively. Likewise, $A \in \mathbb{R}^{n \times m}$ is *nonnegative* or *positive* if every entry of A is nonnegative or positive, respectively, which is written as $A \ge 2$ 0 or $A \gg 0$, respectively. (In this paper, it is important to distinguish between a square nonnegative (resp., positive) matrix and a nonnegative-definite (resp., positivedefinite) matrix.) Let \mathbb{R}^n_+ and \mathbb{R}^n_+ denote the nonnegative and positive orthants of \mathbb{R}^n ; that is, if $x \in \mathbb{R}^n$, then $x \in \mathbb{R}^n_+$ and $x \in \mathbb{R}^n_+$ are equivalent, respectively, to $x \ge 2$ 0 and $x \gg 0$. Finally, let \mathbb{N} denote the set of nonnegative integers. The following definition introduces the notion of a nonnegative function.

Definition 2.1. A real function $u : \mathbb{N} \to \mathbb{R}^m$ is a nonnegative (resp., positive) function if $u(k) \ge 0$ (resp., $u(k) \gg 0$), $k \in \mathbb{N}$.

In the first part of this paper, we consider discrete-time, linear nonnegative dynamical systems of the form

$$x(k+1) = Ax(k) + Bu(k), \quad x(0) = x_0, \ k \in \mathbb{N},$$
(2.1)

where $x \in \mathbb{R}^n$, $u \in \mathbb{R}^m$, $A \in \mathbb{R}^{n \times n}$, and $B \in \mathbb{R}^{n \times m}$. The following definition and proposition are needed for the main results of this paper.

Definition 2.2. The linear dynamical system given by (2.1) is *nonnegative* if for every $x(0) \in \mathbb{R}^n_+$ and $u(k) \ge 0$, $k \in \mathbb{N}$, the solution x(k), $k \in \mathbb{N}$, to (2.1) is nonnegative.

PROPOSITION 2.3 [10]. The linear dynamical system given by (2.1) is nonnegative if and only if $A \in \mathbb{R}^{n \times n}$ is nonnegative and $B \in \mathbb{R}^{n \times m}$ is nonnegative.

Next, we consider a subclass of nonnegative systems; namely, compartmental systems.

Definition 2.4. Let $A \in \mathbb{R}^{n \times n}$. A is a compartmental matrix if A is nonnegative and $\sum_{k=1}^{n} A_{(k,j)} \le 1, j = 1, 2, ..., n$.

If *A* is a compartmental matrix and $u(k) \equiv 0$, then the nonnegative system (2.1) is called an *inflow-closed compartmental system* [10, 11, 12]. Recall that an inflow-closed compartmental system possesses a dissipation property and hence is Lyapunov-stable since the total mass in the system given by the sum of all components of the state x(k), $k \in \mathbb{N}$, is nonincreasing along the forward trajectories of (2.1). In particular, with $V(x) = e^T x$, where $e = [1, 1, ..., 1]^T$, it follows that

$$\Delta V(x(k)) = e^{\mathrm{T}}(A - I)x(k) = \sum_{j=1}^{n} \left[\sum_{i=1}^{n} A_{(i,j)} - 1 \right] x_j \le 0, \quad x \in \overline{\mathbb{R}}_+^n.$$
(2.2)

Hence, all solutions of inflow-closed linear compartmental systems are bounded. Of course, if det $A \neq 0$, where det A denotes the determinant of A, then A is asymptotically stable. For details of the above facts, see [10].

3. Monotonicity of linear nonnegative dynamical systems

In this section, we present our main results for discrete-time, linear nonnegative dynamical systems. Specifically, we consider monotonicity of solutions of dynamical systems of the form given by (2.1). First, however, the following definition is needed.

Definition 3.1. Consider the discrete-time, linear nonnegative dynamical system (2.1), where $x_0 \in \mathscr{X}_0 \subseteq \overline{\mathbb{R}}_+^n$, A is nonnegative, B is nonnegative, $u(k), k \in \mathbb{N}$, is nonnegative, and \mathscr{X}_0 denotes a set of feasible initial conditions contained in $\overline{\mathbb{R}}_+^n$. Let $\hat{n} \le n$, $\{k_1, k_2, ..., k_{\hat{n}}\} \subseteq \{1, 2, ..., n\}$, and $\hat{x}(k) \triangleq [x_{k_1}(k), ..., x_{k_{\hat{n}}}(k)]^T$. The discrete-time, linear nonnegative dynamical system (2.1) is *partially monotonic with respect to* \hat{x} if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, ..., q_n], q_i = 0, i \notin \{k_1, ..., k_{\hat{n}}\}, q_i = \pm 1, i \in \{k_1, ..., k_{\hat{n}}\},$ and for every $x_0 \in \mathscr{X}_0$, $Qx(k_2) \le Qx(k_1), 0 \le k_1 \le k_2$, where $x(k), k \in \mathbb{N}$, denotes the solution to (2.1). The discrete-time, linear nonnegative dynamical system (2.1) is *monotonic* if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, ..., q_n], q_i = \pm 1, i = 1, ..., n$, and for every $x_0 \in \mathscr{X}_0, Qx(k_2) \le Qx(k_1), 0 \le k_1 \le k_2$.

Next, we present a sufficient condition for monotonicity of a discrete-time, linear nonnegative dynamical system.

THEOREM 3.2. Consider the discrete-time, linear nonnegative dynamical system given by (2.1), where $x_0 \in \mathbb{R}^n_+$, $A \in \mathbb{R}^{n \times n}$ is nonnegative, $B \in \mathbb{R}^{n \times m}$ is nonnegative, and $u(k), k \in \mathbb{N}$, is nonnegative. Let $\hat{n} \le n$, $\{k_1, k_2, \ldots, k_{\hat{n}}\} \subseteq \{1, 2, \ldots, n\}$, and $\hat{x}(k) \triangleq [x_{k_1}(k), \ldots, x_{k_{\hat{n}}}(k)]^T$. Assume there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \ldots, q_n]$, $q_i = 0$, $i \notin \{k_1, \ldots, k_{\hat{n}}\}$, $q_i = \pm 1$, $i \in \{k_1, \ldots, k_{\hat{n}}\}$, $QA \le Q$, and $QB \le 0$. Then the discrete-time, linear nonnegative dynamical system (2.1) is partially monotonic with respect to \hat{x} .

Proof. It follows from (2.1) that

$$Qx(k+1) = QAx(k) + QBu(k), \quad x(0) = x_0, \ k \in \mathbb{N},$$
(3.1)

264 Monotonicity of solutions

which implies that

$$Qx(k_2) = Qx(k_1) + \sum_{k=k_1}^{k_2-1} [Q(A-I)x(k) + QBu(k)].$$
(3.2)

Next, since *A* and *B* are nonnegative and u(k), $k \in \mathbb{N}$, is nonnegative, it follows from Proposition 2.3 that $x(k) \ge 0$, $k \in \mathbb{N}$. Hence, since -Q(A - I) and -QB are nonnegative, it follows that $Q(A - I)x(k) \le 0$ and $QBu(k) \le 0$, $k \in \mathbb{N}$, which implies that for every $x_0 \in \overline{\mathbb{R}}^n_+$, $Qx(k_2) \le Qx(k_1)$, $0 \le k_1 \le k_2$.

COROLLARY 3.3. Consider the discrete-time, linear nonnegative dynamical system given by (2.1), where $x_0 \in \mathbb{R}^n_+$, $A \in \mathbb{R}^{n \times n}$ is nonnegative, $B \in \mathbb{R}^{n \times m}$ is nonnegative, and u(k), $k \in \mathbb{N}$, is nonnegative. Assume there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \ldots, q_n]$, $q_i = \pm 1$, $i = 1, \ldots, n$, and $QA \leq \leq Q$ and $QB \leq \leq 0$ are nonnegative. Then the discrete-time, linear nonnegative dynamical system given by (2.1) is monotonic.

Proof. The proof is a direct consequence of Theorem 3.2 with $\hat{n} = n$ and $\{k_1, \dots, k_{\hat{n}}\} = \{1, \dots, n\}$.

Next, we present partial converses of Theorem 3.2 and Corollary 3.3 in the case where $u(k) \equiv 0$.

THEOREM 3.4. Consider the discrete-time, linear nonnegative dynamical system given by (2.1), where $x_0 \in \mathbb{R}^n_+$, $A \in \mathbb{R}^{n \times n}$ is nonnegative, and $u(k) \equiv 0$. Let $\hat{n} \leq n$, $\{k_1, k_2, \dots, k_{\hat{n}}\} \subseteq \{1, 2, \dots, n\}$, and $\hat{x}(k) \triangleq [x_{k_1}(k), \dots, x_{k_{\hat{n}}}(k)]^T$. The discrete-time, linear nonnegative dynamical system (2.1) is partially monotonic with respect to \hat{x} if and only if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \dots, q_n]$, $q_i = 0$, $i \notin \{k_1, \dots, k_{\hat{n}}\}$, $q_i = \pm 1$, $i \in \{k_1, \dots, k_{\hat{n}}\}$, and $QA \leq \leq Q$.

Proof. Sufficiency follows from Theorem 3.2 with $u(k) \equiv 0$. To show necessity, assume that the discrete-time, linear dynamical system given by (2.1), with $u(k) \equiv 0$, is partially monotonic with respect to \hat{x} . In this case, it follows from (2.1) that

$$Qx(k+1) = QAx(k), \quad x(0) = x_0, \ k \in \mathbb{N},$$
(3.3)

which further implies that

$$Qx(k_2) = Qx(k_1) + \sum_{k=k_1}^{k_2-1} [Q(A-I)A^k x_0].$$
(3.4)

Now, suppose, *ad absurdum*, there exist $I, J \in \{1, 2, ..., n\}$ such that $M_{(I,J)} > 0$, where $M \triangleq QA - Q$. Next, let $x_0 \in \mathbb{R}^n_+$ be such that $x_{0J} > 0$ and $x_{0i} = 0$, $i \neq J$, and define $v(k) \triangleq A^k x_0$ so that $v(0) = x_0$, $v(k) \ge 0$, $k \in \mathbb{N}$, and $v_J(0) > 0$. Thus, it follows that

$$[Qx(1)]_{J} = [Qx_{0}]_{J} + [M\nu(0)]_{J} = [Qx_{0}]_{J} + M_{(I,J)}\nu_{J}(0) > [Qx_{0}]_{J},$$
(3.5)

which is a contradiction. Hence, $QA \leq \leq Q$.

COROLLARY 3.5. Consider the discrete-time, linear nonnegative dynamical system given by (2.1), where $x_0 \in \mathbb{R}^n_+$, $A \in \mathbb{R}^{n \times n}$ is nonnegative, and $u(k) \equiv 0$. The linear nonnegative dynamical system (2.1) is monotonic if and only if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \dots, q_n], q_i = \pm 1, i = 1, 2, \dots, n, and QA \le Q$.

Proof. The proof is a direct consequence of Theorem 3.4 with $\hat{n} = n$ and $\{k_1, \dots, k_n\} = \{1, \dots, n\}$.

Finally, we present a sufficient condition for *weighted monotonicity* for a discrete-time, linear nonnegative dynamical system.

PROPOSITION 3.6. Consider the discrete-time, linear dynamical system given by (2.1), where A is nonnegative, $u(k) \equiv 0$, $x_0 \in \mathscr{X}_0 \triangleq \{x_0 \in \mathbb{R}^n : S(A - I)x_0 \le 0\}$, where $S \in \mathbb{R}^{n \times n}$ is an invertible matrix. If SAS^{-1} is nonnegative, then for every $x_0 \in \mathscr{X}_0$, $Sx(k_2) \le Sx(k_1)$, $0 \le k_1 \le k_2$.

Proof. Let $y(k) \triangleq -S(A - I)x(k)$ and note that $y(0) = -S(A - I)x_0 \in \mathbb{R}^n_+$. Hence, it follows from (2.1) that

$$y(k+1) = -S(A-I)x(k+1) = -S(A-I)Ax(k) = -SAS^{-1}S(A-I)x(k) = SAS^{-1}y(k).$$
(3.6)

Next, since SAS^{-1} is nonnegative, it follows that $y(k) \in \overline{\mathbb{R}}^n_+$, $k \in \mathbb{N}$. Now, the result follows immediately by noting that $y(k) = -S(A - I)x(k) \gg 0$, $k \in \mathbb{N}$, and hence $S(A - I)x(k) \le 0$, $k \in \mathbb{N}$, or, equivalently, $Sx(k + 1) \le Sx(k)$, $k \in \mathbb{N}$, which implies that $Sx(k_2) \le Sx(k_1)$, $0 \le k_1 \le k_2$.

4. Monotonicity of nonlinear nonnegative dynamical systems

In this section, we extend the results of Section 3 to nonlinear nonnegative dynamical systems. Specifically, we consider discrete-time, nonlinear dynamical systems \mathscr{G} of the form

$$x(k+1) = f(x(k)) + G(x(k))u(k), \quad x(0) = x_0, \ k \in \mathbb{N},$$
(4.1)

where $x(k) \in \mathfrak{D}$, \mathfrak{D} is an open subset of \mathbb{R}^n with $0 \in \mathfrak{D}$, $u(k) \in \mathbb{R}^m$, $f : \mathfrak{D} \to \mathbb{R}^n$, and $G : \mathfrak{D} \to \mathbb{R}^{n \times m}$. We assume that $f(\cdot)$ and $G(\cdot)$ are continuous in \mathfrak{D} and $f(x_e) = x_e, x_e \in \mathfrak{D}$. For the nonlinear dynamical system \mathfrak{G} given by (4.1), the definitions of monotonicity and partial monotonicity hold with (2.1) replaced by (4.1). The following definition generalizes the notion of nonnegativity to vector fields.

Definition 4.1 [10]. Let $f = [f_1, ..., f_n]^T : \mathcal{D} \to \mathbb{R}^n$, where \mathcal{D} is an open subset of \mathbb{R}^n that contains \mathbb{R}^n . Then f is *nonnegative* if $f_i(x) \ge 0$, for all i = 1, ..., n and $x \in \overline{\mathbb{R}}^n_+$.

Note that if f(x) = Ax, where $A \in \mathbb{R}^{n \times n}$, then f is nonnegative if and only if A is nonnegative. The following proposition is required for the main theorem of this section.

PROPOSITION 4.2 [10]. Consider the discrete-time, nonlinear dynamical system \mathcal{G} given by (4.1). If $f: \mathfrak{D} \to \mathbb{R}^n$ is nonnegative and $G(x) \ge 0$, $x \in \mathbb{R}^n_+$, then \mathcal{G} is nonnegative.

Next, we present a sufficient condition for monotonicity of a nonlinear nonnegative dynamical system.

THEOREM 4.3. Consider the discrete-time, nonlinear nonnegative dynamical system \mathcal{G} given by (4.1), where $x_0 \in \mathbb{R}^n_+$, $f: \mathfrak{D} \to \mathbb{R}^n$ is nonnegative, $G(x) \ge 0$, $x \in \mathbb{R}^n_+$, and u(k), $k \in \mathbb{N}$, is nonnegative. Let $\hat{n} \le n$, $\{k_1, k_2, \dots, k_{\hat{n}}\} \subseteq \{1, 2, \dots, n\}$, and $\hat{x}(k) \triangleq [x_{k_1}(k), \dots, x_{k_{\hat{n}}}(k)]^T$. Assume there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \dots, q_n]$, $q_i = 0$, $i \notin \{k_1, \dots, k_{\hat{n}}\}$, $q_i = \pm 1$, $i \in \{k_1, \dots, k_{\hat{n}}\}$, $Qf(x) \le Qx$, $x \in \mathbb{R}^n_+$, and $QG(x) \le 0$, $x \in \mathbb{R}^n_+$. Then the discrete-time, nonlinear nonnegative dynamical system \mathcal{G} is partially monotonic with respect to \hat{x} .

Proof. The proof is similar to the proof of Theorem 3.2 with Proposition 4.2 invoked in place of Proposition 2.3, and hence is omitted. \Box

COROLLARY 4.4. Consider the discrete-time, nonlinear nonnegative dynamical system G given by (4.1), where $x_0 \in \mathbb{R}^n_+$, $f : \mathfrak{D} \to \mathbb{R}^n$ is nonnegative, $G(x) \ge 0$, $x \in \mathbb{R}^n_+$, and u(k), $k \in \mathbb{N}$, is nonnegative. Assume there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \ldots, q_n]$, $q_i = \pm 1$, $i = 1, \ldots, n$, $Qf(x) \le Qx$, $x \in \mathbb{R}^n_+$, and $QG(x) \le 0$, $x \in \mathbb{R}^n_+$. Then the discretetime, nonlinear nonnegative dynamical system G is monotonic.

Proof. The proof is a direct consequence of Theorem 4.3 with $\hat{n} = n$ and $\{k_1, \dots, k_n\} = \{1, \dots, n\}$.

Next, we present necessary and sufficient conditions for partial monotonicity and monotonicity for (4.1) in the case where $u(k) \equiv 0$.

THEOREM 4.5. Consider the discrete-time, nonlinear nonnegative dynamical system \mathcal{G} given by (4.1), where $x_0 \in \mathbb{R}^n_+$, $f: \mathfrak{D} \to \mathbb{R}^n$ is nonnegative, and $u(k) \equiv 0$. Let $\hat{n} \leq n$, $\{k_1, k_2, ..., k_{\hat{n}}\} \subseteq \{1, 2, ..., n\}$, and $\hat{x}(k) \triangleq [x_{k_1}(k), ..., x_{k_{\hat{n}}}(k)]^T$. The discrete-time, nonlinear nonnegative dynamical system \mathcal{G} is partially monotonic with respect to \hat{x} if and only if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, ..., q_n]$, $q_i = 0$, $i \notin \{k_1, ..., k_{\hat{n}}\}$, $q_i = \pm 1$, $i \in \{k_1, ..., k_{\hat{n}}\}$, and $Qf(x) \leq \leq Qx$, $x \in \mathbb{R}^n_+$.

Proof. Sufficiency follows from Theorem 4.3 with $u(k) \equiv 0$. To show necessity, assume that the nonlinear dynamical system given by (4.1), with $u(k) \equiv 0$, is partially monotonic with respect to \hat{x} . In this case, it follows from (4.1) that

$$Qx(k+1) = Qf(x(k)), \quad x(0) = x_0, \ k \in \mathbb{N},$$
(4.2)

which implies that for every $k \in \mathbb{N}$,

$$Qx(k_2) = Qx(k_1) + \sum_{k=k_1}^{k_2-1} [Qf(x(k)) - Qx(k)].$$
(4.3)

Now, suppose, *ad absurdum*, there exist $J \in \{1, 2, ..., n\}$ and $x_0 \in \mathbb{R}^n_+$ such that $[Qf(x_0)]_J > [Qx_0]_J$. Hence,

$$[Qx(1)]_{J} = [Qx_{0}]_{J} + [Qf(x_{0}) - Qx_{0}]_{J} > [Qx_{0}]_{J},$$
(4.4)

which is a contradiction. Hence, $Qf(x) \leq Qx, x \in \overline{\mathbb{R}}^n_+$.

COROLLARY 4.6. Consider the discrete-time, nonlinear nonnegative dynamical system G given by (4.1), where $x_0 \in \overline{\mathbb{R}}^n_+$, $f: \mathfrak{D} \to \mathbb{R}^n$ is nonnegative, and $u(k) \equiv 0$. The discrete-time, nonlinear nonnegative dynamical system G is monotonic if and only if there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \dots, q_n]$, $q_i = \pm 1$, $i = 1, \dots, n$, and $Qf(x) \leq Qx$, $x \in \overline{\mathbb{R}}^n_+$.

Proof. The proof is a direct consequence of Theorem 4.5 with $\hat{n} = n$ and $\{k_1, \dots, k_{\hat{n}}\} = \{1, \dots, n\}$.

Corollary 4.6 provides some interesting ramifications with regard to the absence of limit cycles of inflow-closed nonlinear compartmental systems. To see this, consider the inflow-closed ($u(k) \equiv 0$) compartmental system (4.1), where $f(x) = [f_1(x), \dots, f_n(x)]$ is such that

$$f_i(x) = x_i - a_{ii}(x) + \sum_{j=1, i \neq j}^n \left[a_{ij}(x) - a_{ji}(x) \right]$$
(4.5)

and where the instantaneous rates of compartmental material losses $a_{ii}(\cdot)$, i = 1,...,n, and intercompartmental material flows $a_{ij}(\cdot)$, $i \neq j$, i, j = 1,...,n, are such that $a_{ij}(x) \ge 0$, $x \in \mathbb{R}^n_+$, i, j = 1,...,n. Since all mass flows as well as compartment sizes are nonnegative, it follows that for all i = 1,...,n, $f_i(x) \ge 0$ for all $x \in \mathbb{R}^n_+$. Hence, f is nonnegative. As in the linear case, inflow-closed nonlinear compartmental systems are Lyapunov-stable since the total mass in the system given by the sum of all components of the state $x(k), k \in \mathbb{N}$, is nonincreasing along the forward trajectories of (4.1). In particular, taking $V(x) = e^T x$ and assuming $a_{ij}(0) = 0$, i, j = 1,...,n, it follows that

$$\Delta V(x) = \sum_{i=1}^{n} \Delta x_i = -\sum_{i=1}^{n} a_{ii}(x) + \sum_{i=1}^{n} \sum_{j=1, i \neq j}^{n} \left[a_{ij}(x) - a_{ji}(x) \right] = -\sum_{i=1}^{n} a_{ii}(x) \le 0, \quad x \in \overline{\mathbb{R}}_+^n,$$
(4.6)

which shows that the zero solution $x(k) \equiv 0$ of the inflow-closed nonlinear compartmental system (4.1) is Lyapunov-stable and for every $x_0 \in \mathbb{R}^n_+$, the solution to (4.1) is bounded.

In light of the above, it is of interest to determine sufficient conditions under which masses/concentrations for nonlinear compartmental systems are Lyapunov-stable *and* convergent, guaranteeing the absence of limit-cycling behavior. The following result is

a direct consequence of Corollary 4.6 and provides sufficient conditions for the absence of limit cycles in nonlinear compartmental systems.

THEOREM 4.7. Consider the nonlinear nonnegative dynamical system \mathcal{G} given by (4.1) with $u(k) \equiv 0$ and $f(x) = [f_1(x), \dots, f_n(x)]$ such that (4.5) holds. If there exists a matrix $Q \in \mathbb{R}^{n \times n}$ such that $Q = \text{diag}[q_1, \dots, q_n]$, $q_i = \pm 1$, $i = 1, \dots, n$, and $Qf(x) \leq Qx$, $x \in \mathbb{R}^n_+$, then for every $x_0 \in \mathbb{R}^n_+$, $\lim_{k \to \infty} x(k)$ exists.

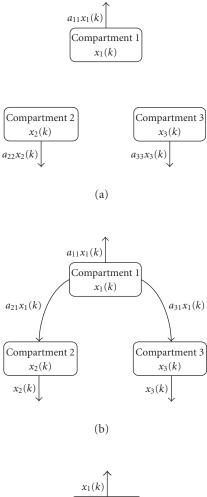
Proof. Let $V(x) = e^{T}x$, $x \in \mathbb{R}^{n}_{+}$. Now, it follows from (4.6) that $\Delta V(x(k)) \leq 0$, $k \in \mathbb{N}$, where $x(k), k \in \mathbb{N}$, denotes the solution of \mathcal{G} , which implies that $V(x(k)) \leq V(x_{0}) = e^{T}x_{0}$, $k \in \mathbb{N}$, and hence for every $x_{0} \in \mathbb{R}^{n}_{+}$, the solution $x(k), k \in \mathbb{N}$, of \mathcal{G} is bounded. Hence, for every $i \in \{1, ..., n\}$, $x_{i}(k), k \in \mathbb{N}$, is bounded. Furthermore, it follows from Corollary 4.6 that $x_{i}(k), k \in \mathbb{N}$, is monotonic. Now, since $x_{i}(\cdot), i \in \{1, ..., n\}$, is bounded and monotonic, it follows that $\lim_{k \to \infty} x_{i}(k), i = 1, ..., n$, exists. Hence, $\lim_{k \to \infty} x(k)$ exists.

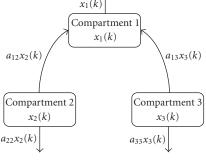
5. A Taxonomy of three-dimensional monotonic compartmental systems

In this section, we use the results of Section 3 to provide a taxonomy of linear threedimensional, inflow-closed compartmental dynamical systems that exhibit monotonic solutions. A similar classification can be obtained for nonlinear and higher-order compartmental systems, but we do not do so here for simplicity of exposition. To characterize the class of all three-dimensional monotonic compartmental systems, let $\mathfrak{Q} \triangleq \{Q \in \mathbb{R}^{3\times3} : Q = \text{diag}[q_1,q_2,q_3], q_i = \pm 1, i = 1,2,3\}$. Furthermore, let $A \in \mathbb{R}^{3\times3}$ be a compartmental matrix and let $x_1(k), x_2(k)$, and $x_3(k), k \in \mathbb{N}$, denote compartmental masses for compartments 1, 2, and 3, respectively. Note that there are exactly eight matrices in the set \mathfrak{Q} . Now, it follows from Corollary 3.5 that if $QA \leq \leq Q$, $Q \in \mathfrak{Q}$, then the corresponding compartmental dynamical system is monotonic. Hence, for every $Q \in \mathfrak{Q}$, we seek all compartmental matrices $A \in \mathbb{R}^{3\times3}$ such that $q_i A_{(i,i)} \leq q_i$, i = 1, 2, 3, and $q_i A_{(i,j)} \leq 0$, $i \neq j$, i, j = 1, 2, 3.

First, we consider the case where Q = diag[1,1,1]. In this case, $q_iA_{(i,i)} \le q_i$, i = 1,2,3, and $q_iA_{(i,j)} \le 0$, $i \ne j$, i, j = 1,2,3, if and only if $A_{(1,2)} = A_{(1,3)} = A_{(2,1)} = A_{(3,1)} = A_{(3,2)} = A_{(2,3)} = 0$. This corresponds to a trivial (decoupled) case since there are no intercompartmental flows between the three compartments (see Figure 5.1(a)). Next, let Q = diag[1, -1, -1] and note that $q_iA_{(i,i)} \le q_i$, i = 1,2,3, and $q_iA_{(i,j)} \le 0$, $i \ne j$, i, j = 1,2,3, if and only if $A_{(2,2)} = A_{(3,3)} = 1$ and $A_{(1,2)} = A_{(1,3)} = A_{(2,3)} = A_{(3,2)} = 0$. Figure 5.1(b) shows the compartmental structure for this case. Finally, let Q = diag[-1,1,1]. In this case, $q_iA_{(i,i)} \le q_i$, i = 1,2,3, and $q_iA_{(i,j)} \le 0$, $i \ne j$, i, j = 1 and $A_{(2,1)} = A_{(3,1)} = A_{(3,2)} = A_{(2,3)} = 0$. Figure 5.1(c) shows the corresponding compartmental structure.

It is important to note that in the case where Q = diag[-1, -1, -1], there does not exist a compartmental matrix satisfying $QA \le Q$ except for the identity matrix. This case would correspond to a compartmental dynamical system where all three states are monotonically increasing. Hence, the compartmental system would be unstable, contradicting the fact that all compartmental systems are Lyapunov-stable. Finally, the remaining four cases corresponding to Q = diag[-1, 1, -1], Q = diag[-1, -1, 1], Q = diag[1, -1, 1], and Q = diag[1, 1, -1] are dual to the cases where Q = diag[1, -1, -1] and Q = diag[-1, 1, 1], and hence are not presented.





(c)

Figure 5.1. Three-dimensional monotonic compartmental systems.

270 Monotonicity of solutions

6. Conclusion

Nonnegative and compartmental models are widely used to capture system dynamics involving the interchange of mass and energy between homogeneous subsystems. In this paper, necessary and sufficient conditions were given, under which linear and nonlinear discrete-time nonnegative and compartmental systems are guaranteed to possess monotonic solutions. Furthermore, sufficient conditions that guarantee the absence of limit cycles in nonlinear discrete-time compartmental systems were also provided.

Acknowledgment

This research was supported in part by the National Science Foundation under Grant ECS-0133038 and the Air Force Office of Scientific Research under Grant F49620-03-1-0178.

References

- [1] D. H. Anderson, *Compartmental Modeling and Tracer Kinetics*, Lecture Notes in Biomathematics, vol. 50, Springer-Verlag, Berlin, 1983.
- [2] A. Berman, M. Neumann, and R. J. Stern, *Nonnegative Matrices in Dynamic Systems*, Pure and Applied Mathematics, John Wiley & Sons, New York, 1989.
- [3] A. Berman and R. J. Plemmons, *Nonnegative Matrices in the Mathematical Sciences*, Academic Press, New York, 1979.
- [4] D. S. Bernstein and D. C. Hyland, Compartmental modeling and second-moment analysis of state space systems, SIAM J. Matrix Anal. Appl. 14 (1993), no. 3, 880–901.
- [5] V. Chellaboina, W. M. Haddad, J. M. Bailey, and J. Ramakrishnan, On the absence of oscillations in compartmental dynamical systems, Proc. IEEE Conference on Decision and Control (Nevada), 2002, pp. 1663–1668.
- [6] R. E. Funderlic and J. B. Mankin, Solution of homogeneous systems of linear equations arising from compartmental models, SIAM J. Sci. Statist. Comput. 2 (1981), no. 4, 375–383.
- [7] M. Gibaldi and D. Perrier, *Pharmacokinetics*, Marcel Dekker, New York, 1975.
- [8] K. Godfrey, Compartmental Models and Their Application, Academic Press, New York, 1983.
- [9] W. M. Haddad, V. Chellaboina, and E. August, Stability and dissipativity theory for nonnegative dynamical systems: a thermodynamic framework for biological and physiological systems, Proc. IEEE Conference on Decision and Control (Florida), 2001, pp. 442–458.
- [10] _____, Stability and dissipativity theory for discrete-time nonnegative and compartmental dynamical systems, Proc. IEEE Conference on Decision and Control (Florida), 2001, pp. 4236– 4241.
- [11] J. A. Jacquez, *Compartmental Analysis in Biology and Medicine*, 2nd ed., University of Michigan Press, Michigan, 1985.
- [12] J. A. Jacquez and C. P. Simon, Qualitative theory of compartmental systems, SIAM Rev. 35 (1993), no. 1, 43–79.
- [13] H. Maeda, S. Kodama, and F. Kajiya, Compartmental system analysis: realization of a class of linear systems with physical constraints, IEEE Trans. Circuits and Systems 24 (1977), no. 1, 8–14.
- [14] H. Maeda, S. Kodama, and Y. Ohta, Asymptotic behavior of nonlinear compartmental systems: nonoscillation and stability, IEEE Trans. Circuits and Systems 25 (1978), no. 6, 372–378.
- [15] R. R. Mohler, *Biological modeling with variable compartmental structure*, IEEE Trans. Automat. Control 19 (1974), no. 6, 922–926.

- [16] J. W. Nieuwenhuis, About nonnegative realizations, Systems Control Lett. 1 (1982), no. 5, 283– 287.
- [17] Y. Ohta, H. Maeda, and S. Kodama, *Reachability, observability, and realizability of continuous*time positive systems, SIAM J. Control Optim. 22 (1984), no. 2, 171–180.
- [18] W. Sandberg, On the mathematical foundations of compartmental analysis in biology, medicine, and ecology, IEEE Trans. Circuits and Systems 25 (1978), no. 5, 273–279.
- [19] J. G. Wagner, Fundamentals of Clinical Pharmacokinetics, Drug Intelligence Publications, Illinois, 1975.

VijaySekhar Chellaboina: Department of Mechanical and Aerospace Engineering, University of Missouri-Columbia, Columbia, MO 65211, USA

E-mail address: chellaboinav@missouri.edu

Wassim M. Haddad: School of Aerospace Engineering, Georgia Institute of Technology, Atlanta, GA 30332-0150, USA

E-mail address: wm.haddad@aerospace.gatech.edu

James M. Bailey: Department of Anesthesiology, Northeast Georgia Medical Center, Gainesville, GA 30503, USA

E-mail address: james.bailey@nghs.com

Jayanthy Ramakrishnan: Department of Mechanical and Aerospace Engineering, University of Missouri-Columbia, Columbia, MO 65211, USA

E-mail address: jr437@mizzou.edu