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Brief paper

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ABSTRACT

Contraction theory is a powerful tool for proving asymptotic properties of nonlinear dynamical systems including convergence to an attractor and entrainment to a periodic excitation. We consider three generalizations of contraction with respect to a norm that allow contraction to take place after small transients in time and/or amplitude. These generalized contractive systems (GCSs) are useful for several reasons. First, we show that there exist simple and checkable conditions guaranteeing that a system is a GCS, and demonstrate their usefulness using several models from systems biology. Second, allowing small transients does not destroy the important asymptotic properties of contractive systems like convergence to a unique equilibrium point, if it exists, and entrainment to a periodic excitation. Third, in some cases as we change the parameters in a contractive system it becomes a GCS just before it loses contractivity with respect to a norm. In this respect, generalized contractivity is the analogue of marginal stability in Lyapunov stability theory.

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1. Introduction

Differential analysis is based on studying the time evolution of the distance between trajectories emanating from different initial conditions. A dynamical system is called contractive if any two trajectories converge to one other at an exponential rate. This implies many desirable properties including convergence to a unique attractor (if it exists), and entrainment to periodic excitations (Aminzare & Sontag, 2014; Lohmiller & Slotine, 1998; Russo, di Bernardo, & Sontag, 2010). Contraction theory proved to be a powerful tool for analyzing nonlinear dynamical systems, with applications in control theory (Lohmiller & Slotine, 2000), observer design (Bonnabel, Astolfi, & Sepulchre, 2011), synchronization of coupled oscillators (Wang & Slotine, 2005), and

more. Recent extensions include: the notion of partial contraction (Slotine, 2003), analyzing networks of interacting agents using contraction theory (Arcak, 2011; Russo, di Bernardo, & Sontag, 2013), a Lyapunov-like characterization of incremental stability (Angeli, 2002), and a LaSalle-type principle for contractive systems (Forni & Sepulchre, 2014). There is also a growing interest in design techniques providing controllers that render control systems contractive or incrementally stable; see, e.g. Zamani, van de Wouw, and Majumdar (2013) and the references therein, and also the incremental ISS condition in Desoer and Haneda (1972).

A contractive system with added diffusion terms or random noise still satisfies certain asymptotic properties (Aminzare & Sontag, 2013; Pham, Tabareau, & Slotine, 2009). In this respect, contraction is a robust property.

In this note, we introduce three forms of generalized contractive systems (GCSs). These are motivated by requiring contraction with respect to a norm to take place only after arbitrarily small transients in time and/or amplitude. Our work was motivated by certain models from systems biology that are not contractive with respect to any (fixed) norm, yet are “almost” contractive. One example is where contraction is lost only on the boundary of the state space, but trajectories emanating from this boundary “immediately” enter the interior of the state space. Thus, we have contraction after an arbitrarily short time transient. The goal of the note is to rigorously define these forms of contraction, study its properties, and derive sufficient conditions for its existence. The contribution

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of this note is thus two-fold: the theoretical study of this type of contraction after an infinitesimal transient, and using this notion to prove important asymptotic properties in applications. Indeed, contraction is usually used to prove *asymptotic* properties, and thus allowing (arbitrarily small) transients seems reasonable. We provide several sufficient conditions for a system to be a GCS. These conditions are checkable, and we demonstrate their usefulness using several examples of systems that are *not* contractive with respect to any norm, yet are GCSs.

In some cases, as we change the parameters in a contractive system it becomes a GCS just before it loses contractivity. In this respect, a GCS is the analogue of marginal stability in Lyapunov stability theory.

We begin with a brief review of some ideas from contraction theory. See Soderlind (2006), Jouffroy (2005) and Rüffer, van de Wouw, and Mueller (2013) for more details, including the historic development of contraction theory, and the relation to other notions.

Consider the time-varying system

$$\dot{x} = f(t, x), \quad (1)$$

with the state x evolving on a positively invariant convex set $\Omega \subseteq \mathbb{R}^n$. We assume that $f(t, x)$ is differentiable with respect to x , and that both $f(t, x)$ and $J(t, x) := \frac{\partial f}{\partial x}(t, x)$ are continuous in (t, x) . Let $x(t, t_0, x_0)$ denote the solution of (1) at time $t \geq t_0$ with $x(t_0) = x_0$ (for the sake of simplicity, we assume from here on that $x(t, t_0, x_0)$ exists and is unique for all $t \geq t_0 \geq 0$ and all $x_0 \in \Omega$).

We say that (1) is *contractive* on Ω with respect to a norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ if there exists $c > 0$ such that

$$|x(t_2, t_1, a) - x(t_2, t_1, b)| \leq \exp(-(t_2 - t_1)c)|a - b| \quad (2)$$

for all $t_2 \geq t_1 \geq 0$ and all $a, b \in \Omega$. In other words, any two trajectories contract to one another at an exponential rate. This implies in particular that the initial condition is “quickly forgotten”. Note that Lohmiller and Slotine (1998) provide a more general and intrinsic definition, where contraction is with respect to a time- and state-dependent metric $M(t, x)$. Simpson-Porco and Bullo (2014) provide a general treatment of contraction on a Riemannian manifold; see also Lewis (1949). Some of the results below may be stated using this more general framework. But, for a given dynamical system finding such a metric may be difficult; see e.g. Aylward, Parrilo, and Slotine (2008) for an algorithm for finding such contraction metrics using sum-of-squares programming.

Another extension of contraction is incremental stability (Angeli, 2002). Our approach is based on the fact that there exists a simple sufficient condition guaranteeing (2), so generalizing (2) appropriately leads to *checkable* sufficient conditions for a system to be a GCS. Another advantage of our approach is that a GCS retains the important property of entrainment to periodic signals.

Recall that a vector norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ induces a matrix measure $\mu : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}$ defined by $\mu(A) := \lim_{\epsilon \downarrow 0} \frac{1}{\epsilon} (\|I + \epsilon A\| - 1)$, where $\|\cdot\| : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}_+$ is the matrix norm induced by $|\cdot|$. A standard approach for proving (2) is based on bounding some matrix measure of the Jacobian J . Indeed, it is well-known (Russo et al., 2010) that if there exist a vector norm $|\cdot|$ and $c > 0$ such that the induced matrix measure $\mu : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}$ satisfies $\mu(J(t, x)) \leq -c$, for all $t_2 \geq t_1 \geq 0$ and all $x \in \Omega$ then (2) holds. (This is in fact a particular case of using a Lyapunov–Finsler function to prove contraction Forni & Sepulchre, 2014.)

It is well-known (Vidyasagar, 1978, Ch. 3) that the matrix measure induced by the L_1 vector norm is

$$\mu_1(A) = \max\{c_1(A), \dots, c_n(A)\}, \quad (3)$$

where

$$c_j(A) := A_{jj} + \sum_{\substack{1 \leq i \leq n \\ i \neq j}} |A_{ij}|, \quad (4)$$

i.e., the sum of the entries in column j of A , with non diagonal elements replaced by their absolute values. The matrix measure induced by the L_∞ norm is $\mu_\infty(A) = \max\{d_1(A), \dots, d_n(A)\}$, where

$$d_j(A) := A_{jj} + \sum_{\substack{1 \leq i \leq n \\ i \neq j}} |A_{ji}|, \quad (5)$$

i.e., the sum of the entries in row j of A , with non diagonal elements replaced by their absolute values.

Often it is useful to work with scaled norms. Let $|\cdot|_*$ be some vector norm, and let $\mu_* : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}$ denote its induced matrix measure. If $P \in \mathbb{R}^{n \times n}$ is an invertible matrix, and $|\cdot|_{*,P} : \mathbb{R}^n \rightarrow \mathbb{R}_+$ is the vector norm defined by $|z|_{*,P} := |Pz|_*$ then the induced matrix measure is $\mu_{*,P}(A) = \mu_*(PAP^{-1})$.

One important implication of contraction is *entrainment* to a periodic excitation. Recall that $f : \mathbb{R}_+ \times \Omega \rightarrow \mathbb{R}^n$ is called *T-periodic* if $f(t, x) = f(t + T, x)$ for all $t \geq 0$ and all $x \in \Omega$. Note that for the system $\dot{x}(t) = f(u(t), x(t))$, with u an input (or excitation) function, f will be *T-periodic* if u is a *T-periodic* function. It is well-known (Lohmiller & Slotine, 1998; Russo et al., 2010) that if (1) is contractive and f is *T-periodic* then for any $t_1 \geq 0$ there exists a unique periodic solution $\alpha : [t_1, \infty) \rightarrow \Omega$ of (1), of period T , and every trajectory converges to α . Entrainment is important in various applications ranging from biological systems (Margaliot, Sontag, & Tuller, 2014; Russo et al., 2010) to the stability of a power grid (Dorfler & Bullo, 2012). Note that for the particular case where f is time-invariant, this implies that if Ω contains an equilibrium point e then it is unique and all trajectories converge to e .

The remainder of this note is organized as follows. Section 2 presents three generalizations of (2). Section 3 details sufficient conditions for their existence, and describes their implications. Due to space limitations, the proofs of all the results are placed at: <http://arxiv.org/abs/1506.06613>.

2. Definitions of contraction after small transients

We begin by defining three generalizations of (2).

Definition 1. The time-varying system (1) is said to be:

- *contractive after a small overshoot and short transient* (SOST) on Ω w.r.t. a norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ if for each $\varepsilon > 0$ and each $\tau > 0$ there exists $\ell = \ell(\tau, \varepsilon) > 0$ such that

$$\begin{aligned} |x(t_2 + \tau, t_1, a) - x(t_2 + \tau, t_1, b)| \\ \leq (1 + \varepsilon) \exp(-(t_2 - t_1)\ell)|a - b| \end{aligned}$$

for all $t_2 \geq t_1 \geq 0$ and all $a, b \in \Omega$.

- *contractive after a small overshoot* (SO) on Ω w.r.t. a norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ if for each $\varepsilon > 0$ there exists $\ell = \ell(\varepsilon) > 0$ such that

$$|x(t_2, t_1, a) - x(t_2, t_1, b)| \leq (1 + \varepsilon) \exp(-(t_2 - t_1)\ell)|a - b|$$

for all $t_2 \geq t_1 \geq 0$ and all $a, b \in \Omega$.

- *contractive after a short transient* (ST) on Ω w.r.t. a norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ if for each $\tau > 0$ there exists $\ell = \ell(\tau) > 0$ such that

$$\begin{aligned} |x(t_2 + \tau, t_1, a) - x(t_2 + \tau, t_1, b)| \\ \leq \exp(-(t_2 - t_1)\ell)|a - b| \end{aligned} \quad (6)$$

for all $t_2 \geq t_1 \geq 0$ and all $a, b \in \Omega$.

The definition of SOST is motivated by requiring contraction at an exponential rate, but only after an (arbitrarily small) time τ , and with an (arbitrarily small) overshoot $(1 + \varepsilon)$. However, as we will see below when the convergence rate ℓ may depend on ε a somewhat richer behavior may occur. The definition of SO is similar to that of SOST, yet now the convergence rate ℓ depends only on ε ,

$[0, \alpha^{-1})$ is an invariant set of the dynamics for all $r \geq 1$. Thus, (7), with $k - 1 \leq \alpha k^2$, admits a unique equilibrium point $e \in \Omega_1$ and $\lim_{t \rightarrow \infty} x(t, a) = e$, for all $a \in \mathbb{R}_+^n$. This property also follows from a more general result (Smith, 1995, Prop. 4.2.1) that is proved using the theory of irreducible cooperative dynamical systems. Yet the GCS approach leads to new insights. For example, it implies that the distance between trajectories can only decrease, and can also be used to prove entrainment to suitable generalizations of (7) that include periodically-varying inputs.

Cells often respond to external stimulus by modification of proteins. One mechanism for this is *phosphorelay* (also called phosphotransfer) in which a phosphate group is transferred through a serial chain of proteins from an initial histidine kinase (HK) down to a final response regulator (RR). The next example uses Theorem 1 to analyze a model for phosphorelay from Csikasz-Nagy, Cardelli, and Soyer (2011).

Example 3. Consider the system

$$\begin{aligned} \dot{x}_1 &= (p_1 - x_1)c - \eta_1 x_1 (p_2 - x_2), \\ \dot{x}_2 &= \eta_1 x_1 (p_2 - x_2) - \eta_2 x_2 (p_3 - x_3), \\ &\vdots \\ \dot{x}_{n-1} &= \eta_{n-2} x_{n-2} (p_{n-1} - x_{n-1}) - \eta_{n-1} x_{n-1} (p_n - x_n), \\ \dot{x}_n &= \eta_{n-1} x_{n-1} (p_n - x_n) - \eta_n x_n, \end{aligned} \tag{10}$$

where $\eta_i, p_i > 0$, and $c : [t_1, \infty) \rightarrow \mathbb{R}_+$. In the context of phosphorelay, $c(t)$ is the strength at time t of the stimulus activating the HK, $x_i(t)$ is the concentration of the phosphorylated form of the protein at the i th layer at time t , and p_i denotes the total protein concentration at that layer. Note that $\eta_n x_n$ is the flow of the phosphate group to an external receptor molecule.

In the particular case where $p_i = 1$ for all i (9) becomes the *ribosome flow model* (RFM) (Reuveni, Meilijson, Kupiec, Ruppim, & Tuller, 2011). This is the mean-field approximation of an important model from non-equilibrium statistical physics called the *totally asymmetric simple exclusion process* (TASEP) (Blythe & Evans, 2007). In the RFM, $x_i \in [0, 1]$ is the normalized occupancy at site i , where $x_i = 0$ [$x_i = 1$] means that site i is completely free [full], and η_i is the capacity of the link that connects site i to site $i + 1$. This has been used to model mRNA translation, where every site corresponds to a group of codons on the mRNA strand, $x_i(t)$ is the normalized occupancy of ribosomes at site i at time t , $c(t)$ is the initiation rate at time t , and η_i is the elongation rate from site i to site $i + 1$.

Our original motivation for generalizing (2) was to prove entrainment in the RFM (Margaliot et al., 2014). For more results on the RFM, see Margaliot and Tuller (2012a,b, 2013), Poker, Zarai, Margaliot, and Tuller (2014) and Zarai, Margaliot, and Tuller (2013).

Assume that there exists $\eta_0 > 0$ such that $c(t) \geq \eta_0$ for all $t \geq t_1$. Let $\Omega := [0, p_1] \times \dots \times [0, p_n]$ denote the state-space of (9). Eq. (9) does not satisfy (2), w.r.t. any norm, on Ω , yet it is SOST on Ω w.r.t. the L_1 norm.²

Considering Theorem 1 in the special case where all the sets Ω_ζ in Definition 2 are equal to Ω yields the following result.

Corollary 1. Suppose that (1) is contractive on Ω w.r.t. a set of norms $|\cdot|_\zeta, \zeta \in (0, 1/2]$, and that condition (c) in Definition 2 holds. Then (1) is SOST on Ω w.r.t. $|\cdot|$.

Corollary 1 may be useful in cases where some matrix measure of the Jacobian J of (1) turns out to be non positive on Ω , but

not strictly negative, suggesting that the system is “on the verge” of satisfying (2). The next result demonstrates this for the time-invariant system

$$\dot{x} = f(x), \tag{11}$$

and the particular case of the matrix measure $\mu_1 : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}$ induced by the L_1 norm. Recall that this is given by (3) with the c_j defined in (4).

Proposition 2. Consider the Jacobian $J(\cdot) : \Omega \rightarrow \mathbb{R}^{n \times n}$ of the time-invariant system (11). Suppose that Ω is compact and that the set $\{1, \dots, n\}$ can be divided into two non-empty disjoint sets S_0 and S_- such that the following properties hold for all $x \in \Omega$:

- (1) for any $k \in S_0, c_k(J(x)) \leq 0$;
- (2) for any $j \in S_-, c_j(J(x)) < 0$;
- (3) for any $i \in S_0$ there exists an index $z = z(i) \in S_-$ such that $J_{zi}(x) > 0$.

Then (11) is SOST on Ω w.r.t. the L_1 norm.

The proof of Proposition 2 is based on the following idea. By compactness of Ω , there exists $\delta > 0$ such that

$$c_j(J(x)) < -\delta, \quad \text{for all } j \in S_- \text{ and all } x \in \Omega. \tag{12}$$

The conditions stated in the proposition imply that there exists a diagonal matrix P such that $c_k(PJP^{-1}) < 0$ for all $k \in S_0$. Furthermore, there exists such a P with diagonal entries arbitrarily close to 1, so $c_j(PJP^{-1}) < -\delta/2$ for all $j \in S_-$. Thus, $\mu_1(PJ(x)P^{-1}) < 0$ for all $x \in \Omega$. Now Corollary 1 implies SOST. Note that this implies that the compactness assumption may be dropped if for example it is known that (12) holds.

Example 4. Consider the system:

$$\begin{aligned} \dot{x} &= -\delta x + k_1 y - k_2 (e_T - y)x, \\ \dot{y} &= -k_1 y + k_2 (e_T - y)x, \end{aligned} \tag{13}$$

where $\delta, k_1, k_2, e_T > 0$, and $\Omega := [0, \infty) \times [0, e_T]$. This is a basic model for a transcriptional module that is ubiquitous in both biology and synthetic biology (see, e.g., Del Vecchio, Ninfa, & Sontag, 2008, Russo et al., 2010). Here $x(t)$ is the concentration at time t of a transcriptional factor X that regulates a downstream transcriptional module by binding to a promoter with concentration $e(t)$ yielding a protein–promoter complex Y with concentration $y(t)$. The binding reaction is reversible with binding and dissociation rates k_2 and k_1 , respectively. The linear degradation rate of X is δ , and as the promoter is not subject to decay, its total concentration, e_T , is conserved, so $e(t) = e_T - y(t)$. Russo et al. (2010) have shown that (12) is contractive w.r.t. a certain weighted L_1 norm. The Jacobian of (12) is $J = \begin{bmatrix} -\delta - k_2(e_T - y) & k_1 + k_2 x \\ k_2(e_T - y) & -k_1 - k_2 x \end{bmatrix}$, and all the properties in Proposition 2 hold with $S_- = \{1\}$ and $S_0 = \{2\}$. Indeed, $J_{12} = k_1 + k_2 x > k_1 > 0$ for all $\begin{bmatrix} x & y \end{bmatrix}^T \in \Omega$. Thus, (12) is SOST on Ω w.r.t. the L_1 norm.

Arguing as in the proof of Proposition 2 for the matrix measure μ_∞ induced by the L_∞ norm (see (5)) yields the following result.

Proposition 3. Consider the Jacobian $J(\cdot) : \Omega \rightarrow \mathbb{R}^{n \times n}$ of the time-invariant system (11). Suppose that Ω is compact and that the set $\{1, \dots, n\}$ can be divided into two non-empty disjoint sets S_0 and S_- such that the following properties hold for all $x \in \Omega$:

- (1) $d_j(J(x)) \leq 0$ for all $j \in S_0$;
- (2) $d_k(J(x)) < 0$ for all $k \in S_-$;
- (3) for any $j \in S_0$ there exists an index $z = z(j) \in S_-$ such that $J_{jz}(x) \neq 0$.

Then (11) is SOST on Ω w.r.t. the L_∞ norm.

² Due to space limitations, the details of the analysis are placed at: <http://arxiv.org/abs/1506.06613>.

Contraction after a short overshoot

A natural question is under what conditions SO and SOST are equivalent. To address this issue, we introduce the following definition.

Definition 3. We say that (1) is *weakly expansive* (WE) if for each $\delta > 0$ there exists $\tau_0 > 0$ such that for all $a, b \in \Omega$ and all $t_0 \geq 0$,

$$|x(t, t_0, a) - x(t, t_0, b)| \leq (1 + \delta)|a - b|, \quad (14)$$

for all $t \in [t_0, t_0 + \tau_0]$.

Proposition 4. Suppose that (1) is WE. Then (1) is SOST if and only if it is SO.

Remark 1. Suppose that f in (1) is Lipschitz globally in Ω uniformly in t , i.e. there exists $L > 0$ such that $|f(t, x) - f(t, y)| \leq L|x - y|$, for all $x, y \in \Omega$, $t \geq 0$. Then by Gronwall's Lemma (see, e.g. Sontag, 1998, Appendix C), $|x(t, t_0, a) - x(t, t_0, b)| \leq \exp(L(t - t_0))|a - b|$, for all $t \geq t_0 \geq 0$, and this implies that (14) holds for $\tau_0 := \frac{1}{L} \ln(1 + \delta) > 0$. In particular, if Ω is compact and f is periodic in t then WE holds under rather weak continuity arguments on f .

Contraction after a short transient

For *time-invariant* systems whose state evolves on a convex and compact set it is possible to give a simple sufficient condition for ST. Let $\text{Int}(S)$ [∂S] denote the interior [boundary] of a set S . We require the following definitions.

Definition 4. We say that (1) is *non expansive* (NE) w.r.t. a norm $|\cdot|$ if for all $a, b \in \Omega$ and all $s_2 > s_1 \geq 0$

$$|x(s_2, s_1, a) - x(s_2, s_1, b)| \leq |a - b|. \quad (15)$$

We say that (1) is *weakly contractive* (WC) if (15) holds with \leq replaced by $<$.

Definition 5. The time-invariant system (11) with the state x evolving on a compact and convex set $\Omega \subset \mathbb{R}^n$, is said to be *interior contractive* (IC) w.r.t. a norm $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ if the following properties hold:

- (a) for every $x_0 \in \partial\Omega$, $x(t, x_0) \notin \partial\Omega$, for all $t > 0$;
- (b) for every $x \in \text{Int}(\Omega)$,

$$\mu(J(x)) < 0, \quad (16)$$

where $\mu : \mathbb{R}^{n \times n} \rightarrow \mathbb{R}$ is the matrix measure induced by $|\cdot|$.

In other words, the matrix measure is negative in the interior of Ω , and the boundary of Ω is “repelling”. Note that these conditions do not necessarily imply that the system satisfies (2) on Ω , as it is possible that $\mu(J(x)) = 0$ for some $x \in \partial\Omega$. Yet, (16) does imply that (11) is NE on Ω . We can now state the main result in this subsection.

Theorem 2. If the system (11) is IC w.r.t. a norm $|\cdot|$ then it is ST w.r.t. $|\cdot|$.

The proof of this result is based on showing that IC implies that for each $\tau > 0$ there exists $d = d(\tau) > 0$ such that $\text{dist}(x(t, x_0), \partial\Omega) \geq d$, for all $x_0 \in \Omega$ and all $t \geq \tau$, and then using this to conclude that for any $t \geq \tau$ all the trajectories of the system are contained in a convex and compact set $D \subset \text{Int}(\Omega)$. In this set the system is contractive with rate $c := \max_{x \in D} \mu(J(x)) < 0$. The next example, that is a variation of a system studied by Russo et al. (2010), demonstrates this reasoning.

Example 5. Consider a transcriptional factor X that regulates a downstream transcriptional module by irreversibly binding, at a rate $k_2 > 0$, to a promoter E yielding a protein–promoter complex Y . The promoter is not subject to decay, so its total

concentration, denoted by $e_T > 0$, is conserved. Assume also that X is obtained from an inactive form X_0 , for example through a phosphorylation reaction that is catalyzed by a kinase with abundance $u(t)$ satisfying $u(t) \geq u_0 > 0$ for all $t \geq 0$. The sum of the concentrations of X_0 , X , and Y is constant, denoted by z_T , with $z_T > e_T$. Letting $x_1(t)$, $x_2(t)$ denote the concentrations of X , Y at time t yields the model

$$\begin{aligned} \dot{x}_1 &= (z_T - x_1 - x_2)u - \delta x_1 - k_2(e_T - x_2)x_1, \\ \dot{x}_2 &= k_2(e_T - x_2)x_1, \end{aligned} \quad (17)$$

with the state evolving on $\Omega := [0, z_T] \times [0, e_T]$. Here $\delta \geq 0$ is the dephosphorylation rate $X \rightarrow X_0$. Let $P := \begin{bmatrix} 1 & 1 \\ 0 & 1 \end{bmatrix}$, and consider the matrix measure $\mu_{\infty, P}$. Let $\tilde{J} := PJP^{-1}$. A calculation yields $\tilde{J} = \begin{bmatrix} -u - \delta & \delta \\ k_2(e_T - x_2) & k_2(x_2 - x_1 - e_T) \end{bmatrix}$, so $d_1(\tilde{J}) = -u - \delta + |\delta| \leq -u_0 < 0$, and

$$\begin{aligned} d_2(\tilde{J}) &= k_2(x_2 - x_1 - e_T) + |k_2(e_T - x_2)| \\ &= -k_2x_1. \end{aligned}$$

Letting $S := \{0\} \times [0, e_T]$, we conclude that $\mu_{\infty, P}(x) < 0$ for all $x \in (\Omega \setminus S)$. For any $x \in S$, $\dot{x}_1 = (z_T - x_2)u \geq (z_T - e_T)u_0 > 0$, and arguing as in the proof of Theorem 2, we conclude that for any $\tau > 0$ there exists $d = d(\tau) > 0$ such that $x_1(t, a) \geq d$, for all $a \in \Omega$ and all $t \geq \tau$. In other words, after time τ all the trajectories are contained in the closed and convex set $D = D(\tau) := [d, z_T] \times [0, e_T]$. Letting $c := c(\tau) = \max_{x \in D} \mu_{\infty, P}(J(x))$ yields $c < 0$ and $|x(t + \tau, a) - x(t + \tau, b)|_{\infty, P} \leq \exp(ct)|a - b|_{\infty, P}$ for all $a, b \in \Omega$ and all $t > 0$, so (16) is ST w.r.t. $|\cdot|_{\infty, P}$.

As noted above, the introduction of GCS is motivated by the idea that contraction is used to prove asymptotic results, so allowing initial transients should increase the class of systems that can be analyzed while still allowing to prove asymptotic results. The next result demonstrates this.

Corollary 2. If (11) is IC with respect to some norm then it admits a unique equilibrium point $e \in \text{Int}(\Omega)$, and $\lim_{t \rightarrow \infty} x(t, a) = e$ for all $a \in \Omega$.

Remark 2. Consider the variational system (see, e.g., Forni & Sepulchre, 2014) associated with (11):

$$\begin{aligned} \dot{x} &= f(x), \\ \delta \dot{x} &= J(x)\delta x. \end{aligned} \quad (18)$$

Our proof of Corollary 2 is based on Theorem 2. An alternative proof is possible, using the Lyapunov–Finsler function $V(x, \delta x) := |\delta x|$, where $|\cdot| : \mathbb{R}^n \rightarrow \mathbb{R}_+$ is the vector norm corresponding to the matrix measure μ in (16), and the LaSalle invariance principle described in Forni and Sepulchre (2014).

Contraction can be characterized using a Lyapunov–Finsler function (Forni & Sepulchre, 2014). The next result describes a similar characterization for ST. For simplicity, we state this for the time-invariant system (11).

Proposition 5. The following two conditions are equivalent.

- (a) The time-invariant system (11) is ST w.r.t. a norm $|\cdot|$.
- (b) For any $\tau > 0$ there exists $\ell = \ell(\tau) > 0$ such that for any $a, b \in \Omega$ and any c on the line connecting a and b the solution of (17) with $x(0) = c$ and $\delta x(0) = b - a$ satisfies $|\delta x(t + \tau)| \leq \exp(-\ell t)|\delta x(0)|$, for all $t \geq 0$.

Note that the latter condition implies that the function $V(x, \delta x) := |\delta x|$ is a *generalized* Lyapunov–Finsler function in the following sense. For any $\tau > 0$ there exists $\ell = \ell(\tau) > 0$ such that along solutions of the variational system: $V(x(t + \tau, x(0)), \delta x(t + \tau, \delta x(0), x(0))) \leq \exp(-\ell t)V(x(0), \delta x(0))$, for all $t \geq 0$.

It is straightforward to show that each of the three generalizations of contraction in Definition 1 implies that (1) is NE. One may perhaps expect that any of the three generalizations of contraction in Definition 1 also implies WC. Indeed, ST does imply WC, because $|x(s_2, s_1, a) - x(s_2, s_1, b)| \leq \exp(-\ell(s_2 - s_1)/2) |a - b| < |a - b|$, for all $0 \leq s_1 < s_2$ if ST holds (simply apply the definition with $t_1 = s_1$, $\tau = (s_2 - s_1)/2 > 0$, and $t_2 = s_1 + \tau$ in (6)). However, the next example shows that SO does not imply WC.

Example 6. Consider the scalar system

$$\dot{x} = \begin{cases} -2x, & 0 \leq |x| < 1/2, \\ -\frac{x}{|x|}, & \frac{1}{2} \leq |x| \leq 1, \end{cases}$$

with x evolving on $\Omega := [-1, 1]$. Clearly, this system is not WC. However, it is not difficult to show that it satisfies the definition of SO with $\ell = \ell(\varepsilon) := \min\{\ln(1 + \varepsilon), 1\}$.

Fig. 1 summarizes the relations between the various contraction notions.

Acknowledgments

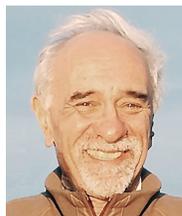
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References

- Aminzare, Z., & Sontag, E. D. (2013). Logarithmic Lipschitz norms and diffusion-induced instability. *Nonlinear Analysis. Theory, Methods & Applications*, 83, 31–49.
- Aminzare, Z., & Sontag, E. D. (2014). Contraction methods for nonlinear systems: A brief introduction and some open problems. In *Proc. 53rd IEEE conf. on decision and control, Los Angeles, CA* (pp. 3835–3847).
- Angeli, D. (2002). A Lyapunov approach to incremental stability properties. *IEEE Trans. Automat. Control*, 47, 410–421.
- Arcak, M. (2011). Certifying spatially uniform behavior in reaction–diffusion PDE and compartmental ODE systems. *Automatica*, 47(6), 1219–1229.
- Aylward, E. M., Parrilo, P. A., & Slotine, J.-J. E. (2008). Stability and robustness analysis of nonlinear systems via contraction metrics and SOS programming. *Automatica*, 44(8), 2163–2170.
- Blythe, R. A., & Evans, M. R. (2007). Nonequilibrium steady states of matrix-product form: a solver's guide. *J. Phys. A*, 40(46), R333–R441.
- Bonnabel, S., Astolfi, A., & Sepulchre, R. (2011). Contraction and observer design on cones. In *Proc. 50th IEEE conf. on decision and control and European control conference, Orlando, Florida* (pp. 7147–7151).
- Csikasz-Nagy, A., Cardelli, L., & Soyer, O. S. (2011). Response dynamics of phosphorelays suggest their potential utility in cell signaling. *J. R. Soc. Interface*, 8, 480–488.
- Del Vecchio, D., Ninfa, A. J., & Sontag, E. D. (2008). Modular cell biology: Retroactivity and insulation. *Mol. Syst. Biol.*, 4(1), 161.
- Desoer, C., & Hamed, H. (1972). The measure of a matrix as a tool to analyze computer algorithms for circuit analysis. *IEEE Transactions on Circuit Theory*, 19, 480–486.
- Dorfler, F., & Bullo, F. (2012). Synchronization and transient stability in power networks and nonuniform Kuramoto oscillators. *SIAM Journal on Control and Optimization*, 50, 1616–1642.
- Forni, F., & Sepulchre, R. (2014). A differential Lyapunov framework for contraction analysis. *IEEE Trans. Automat. Control*, 59(3), 614–628.
- Jouffroy, J. (2005). Some ancestors of contraction analysis. In *Proc. 44th IEEE conf. on decision and control, Seville, Spain* (pp. 5450–5455).
- Lewis, D. C. (1949). Metric properties of differential equations. *Amer. J. Math.*, 71(2), 294–312.
- Lohmiller, W., & Slotine, J.-J. E. (1998). On contraction analysis for non-linear systems. *Automatica*, 34, 683–696.
- Lohmiller, W., & Slotine, J.-J. E. (2000). Control system design for mechanical systems using contraction theory. *IEEE Trans. Automat. Control*, 45, 984–989.
- Margaliot, M., Sontag, E. D., & Tuller, T. (2014). Entrainment to periodic initiation and transition rates in a computational model for gene translation. *PLoS One*, 9(5), e96039.
- Margaliot, M., & Tuller, T. (2012a). On the steady-state distribution in the homogeneous ribosome flow model. *IEEE/ACM Trans. Comput. Biol. Bioinf.*, 9, 1724–1736.
- Margaliot, M., & Tuller, T. (2012b). Stability analysis of the ribosome flow model. *IEEE/ACM Trans. Comput. Biol. Bioinf.*, 9, 1545–1552.
- Margaliot, M., & Tuller, T. (2013). Ribosome flow model with positive feedback. *J. R. Soc. Interface*, 10, 20130267.
- Pham, Q.-C., Tabareau, N., & Slotine, J.-J. (2009). A contraction theory approach to stochastic incremental stability. *IEEE Trans. Automat. Control*, 54, 816–820.
- Poker, G., Zarai, Y., Margaliot, M., & Tuller, T. (2014). Maximizing protein translation rate in the nonhomogeneous ribosome flow model: A convex optimization approach. *J. R. Soc. Interface*, 11(100), 20140713.
- Reuveni, S., Meilijson, I., Kupiec, M., Ruppim, E., & Tuller, T. (2011). Genome-scale analysis of translation elongation with a ribosome flow model. *PLoS Comput. Biol.*, 7, e1002127.
- Rüffer, B. S., van de Wouw, N., & Mueller, M. (2013). Convergent systems vs. incremental stability. *Systems & Control Letters*, 62, 277–285.
- Russo, G., di Bernardo, M., & Sontag, E. D. (2010). Global entrainment of transcriptional systems to periodic inputs. *PLoS Comput. Biol.*, 6, e1000739.
- Russo, G., di Bernardo, M., & Sontag, E. D. (2013). A contraction approach to the hierarchical analysis and design of networked systems. *IEEE Trans. Automat. Control*, 58, 1328–1331.
- Simpson-Porco, J. W., & Bullo, F. (2014). Contraction theory on Riemannian manifolds. *Systems & Control Letters*, 65, 74–80.
- Slotine, J.-J. E. (2003). Modular stability tools for distributed computation and control. *Internat. J. Adapt. Control Signal Process.*, 17, 397–416.
- Smith, H. L. (1995). *Mathematical surveys and monographs: Vol. 41. Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems*. Providence, RI: Amer. Math. Soc.
- Soderlind, G. (2006). The logarithmic norm. History and modern theory. *BIT*, 46, 631–652.
- Sontag, E. D. (1998). *Texts in applied mathematics: Vol. 6. Mathematical control theory: Deterministic finite-dimensional systems* (2nd ed.). New York: Springer-Verlag.
- Sontag, E. D., Margaliot, M., & Tuller, T. (2014). On three generalizations of contraction. In *Proc. 53rd IEEE conf. on decision and control, Los Angeles, CA* (pp. 1539–1544).
- Vidyasagar, M. (1978). *Nonlinear systems analysis*. Englewood Cliffs, NJ: Prentice Hall.
- Wang, W., & Slotine, J. J. (2005). On partial contraction analysis for coupled nonlinear oscillators. *Biol. Cybernet.*, 92, 38–53.
- Zamani, M., van de Wouw, N., & Majumdar, R. (2013). Backstepping controller synthesis and characterizations of incremental stability. *Systems & Control Letters*, 62(10), 949–962.
- Zarai, Y., Margaliot, M., & Tuller, T. (2013). Explicit expression for the steady state translation rate in the infinite-dimensional homogeneous ribosome flow model. *IEEE/ACM Trans. Comput. Biol. Bioinf.*, 10, 1322–1328.



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