A contraction approach to input tracking via high gain feedback

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***Abstract*— This paper adopts a contraction approach to the analysis of the tracking properties of dynamical systems under high gain feedback when subject to inputs with bounded derivatives. It is shown that if the tracking error dynamics are contracting, then the system is input to output stable with respect to the input signal derivatives and the output tracking error. This result is then used to demonstrate that the negative feedback connection of plants composed of two strictly positive real LTI subsystems in cascade can follow external inputs with tracking errors that can be made arbitrarily small by applying a sufficiently large feedback gain. We utilize this result to design a biomolecular feedback for a synthetic genetic sensor to make it robust to variations in the availability of a cellular resource required for protein production.**

I. INTRODUCTION

High gain feedback can be an effective control strategy for achieving stabilization, disturbance rejection and tracking in applications where there is little scope for sophisticated control algorithms to be implemented and where there is knowledge of the structure, but not the exact parameters, of a plant to be regulated [15], [11], [3], [14], [16]. Motivated by design constraints in the regulation of synthetic genetic circuits, this paper presents an input to output stability approach [17], [19], [18] that derives from contraction theory [21], [26], [25], [13] to the problem of tracking inputs with bounded derivatives.

Control via high gain feedback has been extensively researched for several decades. Early works on linear time invariant systems investigated the asymptotic behavior of the root loci of multivariable systems under high feedback gains [12], [9], [10]. In [7], it was shown that high gain feedback introduces a separation of timescales in relative degree one LTI systems, dividing the state space into modes with slow eigenvalues and modes with eigenvalues that can be made arbitrarily fast by sufficiently strengthening the feedback gain. When the fast eigenvalues are stable, singular perturbation theory shows that high gain feedback stabilizes the system trajectories to a small neighborhood of the *slow manifold*, the subspace spanned by the slow eigenvectors. Reference [16] extended [7] to nonlinear systems with affine inputs. In [8] the results of [7] were also extended to LTI systems of relative degree greater than one. These methods and their applications to input tracking in singularly perturbed systems are summarized in [11], [15], [6], [1]. Following [8], [2] used a singular perturbation approach to construct a decentralized dynamic feedback controller with high observer gain for LTI systems. This controller ensures that the effect of exogenous disturbances on the output of an LTI system is attenuated below a pre-specified tolerance. Nonlinear extensions to [8] were reported in [14]. Problems of disturbance attenuation for nonlinear systems were addressed using singular perturbation techniques in [35], [33].

In contrast to the singular perturbation techniques used in the above references, in this paper we analyze the tracking properties of systems under high gain feedback using an input to output stability approach [17], [19]. In [5], Hoppensteadt's lemma [23] is used to show that for systems with slowly varying exogenous inputs, uniform asymptotic stability for all constant inputs of a system's equilibrium implies that the system is ISS with respect to input derivatives. Here, we leverage a result originally reported in [20] to show that systems that satisfy a contraction property [21] are input to state stable [22] and, under further assumptions, also input to output stable. Using this result, we show that if the feedback system's error dynamics are contracting, then it is input to output stable from the derivatives of the exogenous input to the tracking error. We then use this result to show that LTI systems composed of the cascade of two strictly positive real (SPR) subsystems under high gain feedback are able to track external inputs with a tracking error that is inversely proportional to the square root of the feedback strength and proportional to a bound on the input time derivatives. With respect to [2], we are only interested in quantifying the tracking error bounds that are achievable with a static output feedback, without access to state information. Furthermore, the approach we present here is applicable to nonlinear systems.

As discussed in [21], [25], a system can be shown to have the contraction property over a domain if there exists a common Lyapunov-type function for the system Jacobian at all points in the domain. To prove this contraction property for the cascaded SPR feedback system, we use the fact that a diagonal Lyapunov function for the interconnection of SPR systems can be constructed from the storage functions of the individual subsystems [30], [27]. By appropriately scaling the resulting composite diagonal Lyapunov function, we are able to arrive at a matrix measure that proves contraction.

The case of cascaded strictly positive real systems under feedback is of interest in design applications in synthetic biology as many chemical reactions can, at a certain level of abstraction, be dynamically modeled as processes that are SPR. For our purposes, we are interested in designing a genetic sensor, the protein output concentration of which

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tracks the concentration of an input transcription factor signal. Often, such sensors are subject to perturbations arising from changes in the availability of cellular resources [31], [32], [34], [36]. We propose to use high gain negative feedback to regulate the sensor against such perturbations. With our results, we are able to show that the effects of varying resource availability are diminshed under high gain autoregulation by a biomolecular feedback that is engineered into the gene network of interest. Because SPR is a structural property of the sensor's chemical reactions, this tracking property is preserved regardless of the exact reaction parameter values.

This paper is organized as follows. In Section II we present the main theoretical result in which we use the contraction properties of dynamical systems to establish input to output stability. Then we show how this result can be applied to determine the input to output stability of a tracking error with respect to the derivatives of input signals. In Section III, we introduce a class of LTI systems, the tracking properties of which we analyze in Section IV. We present examples in the design of a genetic sensor in Section V and summarize our results in Section VI.

II. Main result

Consider a system of the form:

$$\begin{aligned} \dot{\mathbf{e}} &= \bar{f}(t,\mathbf{e}) + \bar{B}\mathbf{v} \\ \mathbf{z} &= \bar{h}(\mathbf{e}) \end{aligned} \tag{1}$$

evolving on a convex set of states $\mathcal{E} \subseteq \mathbb{R}^n$. We assume that $\bar{f}$ is C^1 on $\mathcal{E}$, for each fixed $t \geq 0$, and denote by $D\bar{f}(t,\mathbf{e})$ the Jacobian of $\bar{f}$ with respect to $\mathbf{e}$, evaluated at $(t,\mathbf{e})$. The map $\bar{h} : \mathcal{E} \to \mathbb{R}^q$ is thought of as an output map (if we are only interested in state results, we let $\mathbf{z} = \mathbf{e}$). Inputs $\mathbf{v}(t)$ take values on a set $\mathcal{V} \subseteq \mathbb{R}^m$ and outputs $\mathbf{z}(t)$ on a set $\mathcal{Z} \subseteq \mathbb{R}^q$.

We use the same notation $|\mathbf{v}|$ and $|\mathbf{z}|$ for two arbitrary p-norms on $\mathbb{R}^m$ (for input signals $\mathbf{v}$) and $\mathbb{R}^q$ (for output signals $\mathbf{z}$). For norms on *state vectors*, we adopt the notation $|\mathbf{e}|_{p,Q}$ to denote a weighted p-norm induced by the symmetric positive matrix Q on $\mathbb{R}^n$, so that $|\mathbf{e}|^2_{2,Q} = \mathbf{e}^T Q^2 \mathbf{e}$. We define $\mu_{p,Q}(\bar{A}) := \lim_{h\searrow 0} \frac{1}{h}\left(\left\|I + hQ^{-1}\bar{A}Q\right\| - 1\right)$ as the matrix measure of $\bar{A} \in \mathbb{R}^{n\times n}$ associated to the weighted norm on states $|\cdot|_{p,Q}$. For further details on the computation of matrix measures, we refer the reader to [29], [13]. For an input $\mathbf{v} : [0,t] \to \mathcal{V}$, $\|\mathbf{v}\|_{[0,t]}$ is by definition the supremum norm $\sup_{0\leq s\leq t} |\mathbf{v}(s)|$. An "input" will be, by definition, a function which is continuous except at most in a discrete set, and one-sided limits exist at all discontinuities. Finally, we write $\left\|\bar{B}\right\|_{p,Q}$ to denote the induced operator norm of $\bar{B} : \mathbb{R}^m \to \mathbb{R}^n$, so that $\left\|\bar{B}\right\|_{p,Q} = \sup_{|\mathbf{v}|\leq 1}\left(|B\mathbf{v}|_{p,Q} / |\mathbf{v}|\right)$. The main result is as follows.

Theorem 1: Assume that $\bar{f}(t,0) = 0$ for all $t \geq 0$. Suppose that two positive constants c and d are such that:

$$\sup_{t\geq 0,\, \mathbf{e}\in\mathcal{E}} \mu_{p,Q}[D\bar{f}(t,\mathbf{e})] \leq -c \tag{2}$$

and

$$d\left|\bar{h}(\mathbf{e})\right| \leq |\mathbf{e}|_{p,Q} \quad \text{for all } \mathbf{e} \in \mathcal{E}. \tag{3}$$

Then, for every solution $\mathbf{e}(\cdot)$ corresponding to an input $\mathbf{v}(\cdot)$, and each $t \geq 0$, we have the following input to output stability estimate:

$$d|\mathbf{z}(t)| \leq \exp(-ct)|\mathbf{e}(0)|_{p,Q} + \frac{1-\exp(-ct)}{c}\left\|\bar{B}\right\|_{p,Q}\|\mathbf{v}\|_{[0,t]}\,. \tag{4}$$

In particular,

$$\limsup_{t\to\infty} |\mathbf{z}(t)| \leq \frac{1}{cd}\left\|\bar{B}\right\|_{p,Q}\|\mathbf{v}\|_{[0,\infty]}\,. \tag{5}$$

Proof: See Appendix I. ∎

We are interested in applying Theorem 1 to analyze the tracking error in the dynamical system

$$\begin{aligned} \dot{x} &= f(x,v),\ x \in \mathbb{R}^n,\ v \in \mathbb{R} \\ y &= h(x),\ y \in \mathbb{R} \end{aligned} \tag{6}$$

We define the tracking error $e := h(x) - v$. By taking $n-1$ derivatives of e we can construct a new state vector $\mathbf{e} := \begin{bmatrix} e & \dot{e} & \cdots & e^{(n-1)} \end{bmatrix}^T$.

Note that if system (6) is globally observable, we can define the map $\mathbf{e} = \tau(x, v, \cdots, v^{(n-1)})$ and express (6) in the $\mathbf{e}$ coordinates as

$$\dot{\mathbf{e}} = F(\mathbf{e}, \mathbf{v}) \tag{7}$$

where $\mathbf{v} := \phi(v, \dot{v}, \cdots, v^{(n-1)}, v^{(n)})$, with $\phi : \mathbb{R}^{n+1} \to \mathbb{R}^m$. If (7) can be expressed in the affine form (1) and if the conditions of Theorem 1 are satisfied, then it follows that system (7) is input to output stable with respect to input $\mathbf{v}$ and output $\mathbf{z}$.

In the following sections, we will analyze the tracking error in a class of LTI systems under negative output feedback of gain g. Since the systems considered are linear, the error dynamics can be written in the affine form (1). Under additional assumptions, including assumptions of observability, we will construct, in Lemma 1, a matrix weighting Q to show that condition (2) is met. Under the same assumptions, we will show, in Lemma 2 that when $\mathbf{z} = \bar{h}(\mathbf{e}) = e$ (the tracking error), condition (3) is satisfied with $d = \mathcal{O}(\sqrt{g})$. With these results we can then apply Theorem 1 to obtain the tracking error estimates (4) and (5). Subsequently, we demonstrate in Lemma 3 that the quantity $\left\|\bar{B}\right\|/c$ is independent of the feedback gain g, from which we show, in Theorem 2 that the tracking error upper bound estimate is $\mathcal{O}(1/\sqrt{g})$, meaning that, given a bound $\|\mathbf{v}\|_{[0,\infty]}$ on the input v and its derivatives, the tracking error can be made arbitrarily small by sufficiently increasing the feedback gain g.

III. Application to LTI systems

We consider the following LTI dynamical system, illustrated in Figure 1, subject to an external input v. For $i = 1, 2$ this system satisfies

$$\Sigma_i = \begin{cases} \dot{x}_i = A_i x_i + B_i u_i, & x_1 \in \mathbb{R}^{m_1}, x_2 \in \mathbb{R}^{m_2}, u_i \in \mathbb{R}, \\ y_i = C_i x_i & y_i \in \mathbb{R} \end{cases} \tag{8}$$

with the interconnection rules $u_1 = g(v - y_2),\ u_2 = y_1,\ g \in \mathbb{R}$. The combined feedback system satisfies

$$\dot{x} = Ax + gBv,\ y = Cx \tag{9}$$

where $x = \begin{bmatrix} x_1^T & x_2^T \end{bmatrix}^T$, $y = y_2$ and $A := \begin{bmatrix} A_1 & -gB_1C_2 \\ B_2C_1 & A_2 \end{bmatrix}$ $B := \begin{bmatrix} B_1 \\ 0 \end{bmatrix}$ $C := \begin{bmatrix} 0 & C_2 \end{bmatrix}$

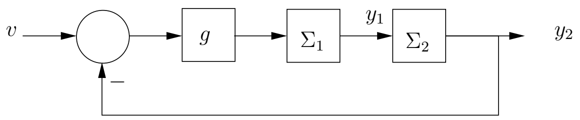

Fig. 1. Feedback interconnection of systems Σ_1, Σ_2 and feedback gain g.

We make the following assumptions on (8).

Assumption 1: System (8) is such that

- The pairs (A_i, B_i) are controllable for $i = 1, 2$.
- The pairs (A_i, C_i) are observable for $i = 1, 2$.
- Subsystems Σ_1, Σ_2 have strictly proper transfer functions $H_1(s)$ and $H_2(s)$, respectively.
- The transfer function $H_1(s)H_2(s)$ contains no pole-zero cancelations.

Assumption 2: Systems Σ_i, $i = 1, 2$, are strictly positive real [1].

As a direct result of Assumption 1, we have the following proposition.

Proposition 1: Under Assumption 1 the feedback interconnection (9) is controllable with input v and observable with output y_2.

Since (9) is observable by Assumption 1, it has an invertible observability matrix. We denote the inverse of the observability matrix by T, so that

$$T^{-1} = \begin{bmatrix} C^T \mid (CA)^T \mid \cdots \mid (CA^{n-1})^T \end{bmatrix}^T. \quad (10)$$

Proposition 2: Under Assumption 2, there exist symmetric matrices $P_i > 0$, $i = 1, 2$ and scalars $\lambda_i > 0$ such that $A_i^T P_i + P_i A_i < -\lambda_i P_i$, and $P_i B_i = C_i^T$

Proof: The result follows from the application of the KYP lemma [1] to systems Σ_1, Σ_2. ■

Proposition 3: Let $P := \begin{bmatrix} P_1 & 0 \\ 0 & gP_2 \end{bmatrix}$. Then under Assumption 2 the matrix P satisfies $A^T P + PA < -\lambda P$ where $\lambda := \min\{\lambda_1, \lambda_2\}$, with λ_1, λ_2 given in Proposition 2.

Proof: Note that

$$A^T P + PA = \left[\begin{array}{c|c} A_1^T P_1 + P_1 A_1 & S \\ \hline S^T & g(A_2^T P_2 + P_2 A_2) \end{array}\right]$$

where $S = g(P_2 B_2 C_1)^T - gP_1 B_1 C_2$. From Proposition 2, $P_i B_i = C_i^T$ for $i = 1, 2$, and therefore $g(P_2 B_2 C_1)^T - gP_1 B_1 C_2 = g(C_2^T C_1)^T - gC_1^T C_2 = 0$. It follows that

$$A^T P + PA = \begin{bmatrix} A_1^T P_1 + P_1 A_1 & 0 \\ 0 & A_2^T P_2 + P_2 A_2 \end{bmatrix} < -\lambda P$$

which concludes the proof. ■

IV. Analysis of the tracking error

For system (9), we will show that when bounds are placed on the derivatives of v, the tracking error $e := y - v = C_2 x_2 - v$ becomes small as feedback gain g grows. To this end, let $H_i(s)$, the transfer function of subsystem Σ_i, be such that $H_i = \frac{N_i(s)}{D_i(s)}$, where $N_i(s)$, $D_i(s)$ are polynomials in s, the roots of which are respectively the zeros and poles of $H_i(s)$. Denoting the Laplace transforms of y, e, v as $Y(s)$, $E(s)$, $V(s)$, respectively, the transfer function from $V(s)$ to $E(s)$ is then

$$\frac{E(s)}{V(s)} = \frac{Y(s) - V(s)}{V(s)} = \frac{D_1(s)D_2(s)}{D_1(s)D_2(s) + gN_1(s)N_2(s)}$$

Let $n := m_1 + m_2$ be the dimension of (9). Then, it follows that for constants a_i, $\bar{a}_i$, b_i, $i = 0, \cdots, n$,

$$\begin{aligned} &(s^n + a_{n-1}s^{n-1} + (a_{n-2} + g\bar{a}_{n-2})s^{n-2} \\ &\quad + \cdots + (a_1 + g\bar{a}_1)s + (a_0 + g\bar{a}_0))E(s) \\ &\quad = (b_n s^n + b_{n-1}s^{n-1} + \cdots + b_1 s + b_0)V(s). \end{aligned}$$

Defining $\mathbf{e} := \begin{bmatrix} e & \dot{e} & \ddot{e} & \cdots & e^{(n-1)} \end{bmatrix}^T$ and $\mathbf{v} := \begin{bmatrix} v & \dot{v} & \ddot{v} & \cdots & v^{(n)} \end{bmatrix}^T$ it then follows that the error vector $\mathbf{e}$ obeys the state space description

$$\dot{\mathbf{e}} = \bar{A}\mathbf{e} + \bar{B}\mathbf{v} \quad (11)$$

where

$$\bar{A} := \begin{bmatrix} 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & 1 \\ -(a_0 + g\bar{a}_0) & -(a_1 + g\bar{a}_1) & \cdots & -a_{n-1} \end{bmatrix}$$

and $\bar{B} := \begin{bmatrix} 0 & 0 & \cdots & 0 & 0 \\ 0 & 0 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & 0 & 0 \\ b_0 & b_1 & \cdots & b_{n-1} & b_n \end{bmatrix}$.

Proposition 4: The dynamics of the error system (11) are such that $\bar{A} = T^{-1}AT$, where T is the inverse of the observability matrix in (10).

Proof: This follows by taking $n - 1$ derivatives of the error $e = Cx - v$ to form an new n-dimensional basis for system (9) to take it into canonical form. ■

For any $\bar{A} \in \mathbb{R}^{n \times n}$, the matrix measure $\mu_{2,Q}(\bar{A})$ is the largest eigenvalue of the symmetric part of $Q\bar{A}Q^{-1}$, which is the largest number τ such that $\bar{A}^T Q^2 + Q^2 \bar{A} \leq 2\tau Q^2$ (see Lemma 3 in [13]). Hence, we have the following lemma:

Lemma 1: The matrix measure $\mu_{2,Q}(\bar{A})$ associated with the weighted norm induced by the symmetric positive matrix $Q := (T^T P T)^{\frac{1}{2}}$ on $\mathbb{R}^n$ satisfies $\mu_{2,Q}(\bar{A}) \leq -\frac{\lambda}{2}$ where $\lambda = \min\{\lambda_1, \lambda_2\}$.

Proof: From Proposition 3 we have the relation $A^T P + PA < -\lambda P$, from which it follows that $A^T (T^{-1})^T T^T P + PTT^{-1}A < -\frac{\lambda}{2}P$. Pre-multiplying both sides of this inequality by T^T and post-multiplying both sides by T yields

$$T^T A^T (T^{-1})^T T^T P T + T^T P T T^{-1} A T < -\lambda T^T P T$$

which gives the result using the fact that, from Proposition 4, $\bar{A} = T^{-1}AT$. ■

Lemma 2: Define the output $\mathbf{z} \in \mathbb{R}$ as $\mathbf{z} := \bar{h}(\mathbf{e}) = e$. Then, $d\left|\bar{h}(\mathbf{e})\right| \leq |\mathbf{e}|_{2,Q}$, with $Q := (T^T PT)^{\frac{1}{2}}$ and $d = \sqrt{g}/\left(C_2 P_2^{-1} C_2^T\right)^{\frac{1}{2}}$.

Proof: Define the function $W(\mathbf{e}) = \frac{1}{2}|\mathbf{e}|_{2,Q}^2 = \frac{1}{2}\mathbf{e}^T T^T PT\mathbf{e}$. To prove the result, we will show that if $W(\mathbf{e}) = K$ then $|e| \leq \frac{1}{\sqrt{g}}\left(2KC_2P_2^{-1}C_2^T\right)^{\frac{1}{2}}$. To this end, we seek to find the maximum value of $|e|$ in the set $\{\mathbf{e}|W(\mathbf{e}) \leq K\}$. We therefore seek the extrema of an objective function $\mathbf{f}(\mathbf{e}) := e = \left[\begin{array}{cc} 1 & \mathbf{0}_{n-1} \end{array}\right]\mathbf{e}$ subject to the inequality constraint $\mathbf{g}(\mathbf{e}) := K - W(\mathbf{e}) \geq 0$. Local maxima $\mathbf{e}^T$ of the objective function $\mathbf{f}(\mathbf{e})$ subject to the constraint $\mathbf{g}(\mathbf{e}) \geq 0$ can be found by defining the Lagrangian $\mathcal{L}(\mathbf{e}, \kappa) = \mathbf{f}(\mathbf{e}) + \kappa\mathbf{g}(\mathbf{e})$, where $\kappa \in \mathbb{R}$ is a Kuhn-Tucker multiplier, and solving for $\mathbf{e} = \hat{\mathbf{e}}$ and $\kappa = \hat{\kappa}$ that satisfy $\nabla\mathcal{L}(\hat{\mathbf{e}}, \hat{\kappa}) = \mathbf{0}_{n+1}$, $\kappa = \hat{\kappa} \geq 0$ and $\hat{\kappa}\mathbf{g}(\hat{\mathbf{e}}) = 0$. Therefore at the local maximum where $\mathbf{e} = \hat{\mathbf{e}}$ and $\kappa = \hat{\kappa}$ we have

$$\begin{aligned}\nabla\mathcal{L}(\hat{\mathbf{e}}, \hat{\kappa}) &= \nabla f(\hat{\mathbf{e}}) + \hat{\kappa}\nabla\mathbf{g}(\hat{\mathbf{e}}) \\ &= \left[\begin{array}{c} 1 \\ \mathbf{0}_n \end{array}\right] + \left[\begin{array}{c} \hat{\kappa}T^T PT\hat{\mathbf{e}} \\ K - \frac{1}{2}\hat{\mathbf{e}}^T T^T PT\hat{\mathbf{e}} \end{array}\right] = \mathbf{0}_{n+1}\end{aligned}$$

yielding the relations $\hat{\kappa}T^T PT\hat{\mathbf{e}} = \left[\begin{array}{cc} 1 & \mathbf{0}_{n-1}^T \end{array}\right]^T$ and $\mathbf{g}(\hat{\mathbf{e}}) = K - \frac{1}{2}\hat{\mathbf{e}}^T T^T PT\hat{\mathbf{e}} = 0$. By Assumption 1, the matrix T^{-1}, and therefore T, is full rank. By Assumption 2, $P > 0$. Therefore the matrix $T^T PT$ is positive definite and invertible. From (10), we can see that

$$(T^{-1})^T \left[\begin{array}{c} 1 \\ \mathbf{0}_{n-1} \end{array}\right] = \left[\begin{array}{c} \mathbf{0}_{m_1} \\ C_2^T. \end{array}\right]$$

This gives

$$\hat{\mathbf{e}} = \frac{1}{\hat{\kappa}}(T^T PT)^{-1}\left[\begin{array}{c} 1 \\ \mathbf{0}_{n-1} \end{array}\right] = \frac{1}{g\hat{\kappa}}T^{-1}\left[\begin{array}{c} \mathbf{0}_{m_1} \\ P_2^{-1}C_2^T \end{array}\right], \tag{12}$$

which, from the relation $\mathbf{g}(\hat{\mathbf{e}}) = 0$ and (10) yields $\frac{1}{2}\hat{\mathbf{e}}^T T^T PT\hat{\mathbf{e}} = \frac{1}{2g\hat{\kappa}^2}C_2P_2^{-1}C_2^T = K$ and $\hat{\kappa} = \pm\left(\frac{1}{2gK}C_2P_2^{-1}C_2^T\right)^{\frac{1}{2}}$. Note that $C_2P_2^{-1}C_2 > 0$ since $P_2 > 0$. To find the local maximum of $\mathbf{f}(\mathbf{e})$, the positive value of $\hat{\kappa}$ is substituted into (12) to give $\hat{\mathbf{e}} = \sqrt{\frac{2K}{g}\frac{1}{C_2P_2^{-1}C_2^T}}T^{-1}\left[\begin{array}{c} \mathbf{0}_{m_1} \\ P_2^{-1}C_2^T \end{array}\right]$, so that at this point we have the local maximum $\mathbf{f}(\hat{\mathbf{e}}) = \sqrt{\frac{2K}{g}C_2P_2^{-1}C_2^T}$. A similar analysis reveals that $\mathbf{f}(\mathbf{e})$ has local minimum value of $-\mathbf{f}(\hat{\mathbf{e}})$ at $\mathbf{e} = -\hat{\mathbf{e}}$. The ellipsoidal set $\{\mathbf{e}|W(\mathbf{e}) \leq K\}$ is compact and therefore by the extreme value theorem, $|e|$ attains its global maximum value of $\mathbf{f}(\hat{\mathbf{e}})$ in this set. Hence, if $W(\mathbf{e}) = \frac{1}{2}|\mathbf{e}|_{2,Q}^2 = K$ then $|e| \leq \frac{1}{\sqrt{g}}\sqrt{|\mathbf{e}|_{2,Q}^2 C_2P_2^{-1}C_2^T}$. ■

With the upper bound on the matrix measure $\mu_{2,Q}$ from Lemma 1 and d from Lemma 2, we can apply Theorem 1 to system (9), as in the following corollary.

Corollary 1: Suppose (9) satisfies Assumptions 1, 2 and that it is subject to an input signal v which is such that $\mathbf{v} \in \mathcal{L}_\infty$. Then the tracking error $e(t)$ satisfies

$$\limsup_{t\to\infty}|e(t)| \leq \frac{2}{\lambda\sqrt{g}}\left(C_2P_2^{-1}C_2^T\right)^{\frac{1}{2}}\left\|\bar{B}\right\|_{2,Q}\|\mathbf{v}\|_{[0,\infty]}. \tag{13}$$

where $Q := (T^T PT)^{\frac{1}{2}}$.

The following lemma shows that the quantity $\left\|\bar{B}\right\|_{2,Q}$ in (13), with $Q := (T^T PT)^{\frac{1}{2}}$, is independent of the feedback gain g. This result will be used in Theorem 2 to show that the upper bound on the tracking error given in (13) can be made arbitrarily small by sufficiently increasing g.

Lemma 3: The induced matrix norm $\left\|\bar{B}\right\|_{2,Q}$, with $Q := (T^T PT)^{\frac{1}{2}}$ is indepdendent of the feedback gain g, and therefore there exists $K > 0$ such that for all $g > 0$, $\left\|\bar{B}\right\|_{2,Q} < K$.

Proof: With $Q := (T^T PT)^{\frac{1}{2}}$, we have $\left\|\bar{B}\right\|_{2,Q} = \bar{B}^T T^T PT\bar{B}$. We will show that the elements of $\bar{B}^T T^T PT\bar{B}$ do not grow unbounded with g. We present this proof for the case where system Σ_2 is of dimension one, without loss of generality and for brevity. For a matrix M, denote by $\{M\}_{i,j}$ the matrix resulting from the deletion of the i^{th} row and j^{th} column of M. For a row vector R, denote by $\{R\}_j$ the row vector resulting from the deletion of the j^{th} element of R. We also re-write the matrix A in (9) as $A = \tilde{A} - gBC$ where $\tilde{A} := \left[\begin{array}{cc} A_1 & \mathbf{0}_{m_1\times 1} \\ B_2C_1 & A_2 \end{array}\right]$.

To show that elements of $\bar{B}^T T^T PT\bar{B}$ do not grow unbounded with g, we first make the following two claims

Claim 1: The determinants $\det(\{T^{-1}\}_{n,j})$ and $\det(T^{-1})$ are independent of g.

Proof: See Appendix II ■

Claim 2: The determinant $\det(\{T^{-1}\}_{n,n}) = 0$.

This claim follows from the fact that the first row of T^{-1} is $C = \left[\begin{array}{cc} \mathbf{0}_{m_1}^T & C_2 \end{array}\right]$ and $C_2 \in \mathbb{R}$.

Next, note that the only non-zero elements of the matrix $\bar{B}$ lie along its n^{th} row. Therefore columns of the matrix $T\bar{B}$ are scalings of the n^{th} column of T. The j^{th} element of the n^{th} column of T is given by $(-1)^{n+j}\det(\{T^{-1}\}_{n,j})/\det(T^{-1})$. From Claims 1 and 2 the n^{th} column of T can be expressed as $\left[\begin{array}{cc} \mathbf{q}^T & 0 \end{array}\right]^T$, where

$$\mathbf{q} = \frac{\left[\begin{array}{ccc} \det(\{T^{-1}\}_{n,1}) & \cdots & \det(\{T^{-1}\}_{n,n-1}) \end{array}\right]^T}{\det T^{-1}}$$

is independent of g. Hence

$$T\bar{B} = \left[\begin{array}{ccc} b_0\left[\begin{array}{c} \mathbf{q} \\ 0 \end{array}\right] & \cdots & b_n\left[\begin{array}{c} \mathbf{q} \\ 0 \end{array}\right] \end{array}\right]$$

and, from the definition of P in Proposition 3,

$$\bar{B}^T T^T PT\bar{B} = \mathbf{q}^T P_1\mathbf{q}\left[\begin{array}{cccc} b_0^2 & b_0b_1 & \cdots & b_0b_n \\ b_1b_0 & b_1^2 & \cdots & b_1b_n \\ \vdots & \vdots & \ddots & \vdots \\ b_nb_0 & & & \\ b_nb_1 & b_n^2 & \cdots & b_1b_n \end{array}\right] \tag{14}$$

the elements of which are independent of g. It therefore follows that $\|\bar{B}\|_{2,Q}$ is bounded for all g, and K is the subordinate norm of (14) on $\mathbb{R}^{n\times m}$, induced by the norms on $\mathbb{R}^m$ and $\mathbb{R}^n$. ■

Since the induced operator norm $\left\|\bar{B}\right\|_{2,Q}$ does not depend on g, it therefore follows that the upper bound estimate (13) on the tracking error can be made arbitrarily small by sufficiently increasing g. This is formalized in the following theorem.

Theorem 2: Suppose (9) satisfies Assumptions 1, 2 and that it is subject to an input signal v which is such that $\mathbf{v} \in \mathcal{L}_\infty$. Then the tracking error $e(t)$ satisfies $\limsup_{t\to\infty} |e(t)| = \mathcal{O}(1/\sqrt{g})$.

V. EXAMPLE

This example is motivated by design considerations that arise in the construction of synthetic genetic circuits in which it is desired that the total concentration of a protein p is made to track the concentration of a transcription factor v (see Table I). It is assumed that the circuit to be designed will part of a plasmid that has been transformed to *E. coli* and is forced to share the cell's resources with the chromosome. Since many translational processes simultaneously take place inside the cell, significant variations in the concentration of available ribosomes R arise, subjecting the translation of the mRNA m to the protein p to disturbances. Here, it is assumed that the rate of transcription can be amplified by the introduction of high concentrations of the RNA polymerase T7RNAP, resulting in a transcription rate g, where g is large. Furthermore, it is assumed that the mRNA degrades at a rate δ, the protein p degrades at a rate γ and the translation rate is R, the concentration of available ribosomes.

To analyze the potential of feedback regulation to mitigate the effect of disturbances on the ability of the protein to track the transcription factor concentration v, we analyze a circuit in which the protein p is an RNAase that regulates its own translation by binding with, and degrading, the mRNA m (Table II). Since the binding and unbinding reactions on relatively fast timescales, those reaction rates are scaled by a factor of $1/\epsilon$, where ϵ is small.Thus, when the amount of protein p falls, due to a shortage of ribosomes, the rate of mRNA degradation by p also falls, leading to a resurgence in the protein concentration.

R-1	$\varnothing \xrightarrow{gv} \mathrm{m}$	Transcription
R-2	$\mathrm{m} \xrightarrow{\delta} \varnothing$	Natural mRNA degradation
R-3	$\mathrm{m} \xrightarrow{R} \mathrm{p} + \mathrm{m}$	Translation
R-4	$\mathrm{p} \xrightarrow{\gamma} \varnothing$	Protein degradation

TABLE I

REACTIONS OF THE GENE EXPRESSION MODEL.

R-6	$\mathrm{p} + \mathrm{m} \underset{k_2/\epsilon}{\overset{k_1/\epsilon}{\rightleftharpoons}} \Gamma$	RNAase p binds mRNA, forms complex Γ
R-7	$\Gamma \xrightarrow{k_3} \mathrm{p}$	RNAase p degrades mRNA
R-8	$\Gamma \xrightarrow{\delta} \mathrm{p}$	Natural mRNA degradation
R-9	$\Gamma \xrightarrow{R} \mathrm{p} + \mathrm{m}$	Translation of mRNA in complex Γ
R-10	$\Gamma \xrightarrow{\gamma} \mathrm{m}$	Natural protein degradation

TABLE II

REACTIONS OF THE MRNA REGULATION MECHANISM.

From the reactions in Tables I and II, we obtain the following ODE model:

$$\begin{aligned}
\dot{\Gamma} &= -\delta\Gamma - k_3\Gamma + \frac{k_1}{\epsilon}mp - \frac{k_2}{\epsilon}\Gamma - \gamma\Gamma \\
\dot{m} &= gv - \delta m - \frac{k_1}{\epsilon}mp + \frac{k_2}{\epsilon}\Gamma + \gamma\Gamma \\
\dot{p} &= Rm + R\Gamma + k_3\Gamma - \frac{k_1}{\epsilon}mp + \frac{k_2}{\epsilon}\Gamma.
\end{aligned}$$

Define the total mRNA concentration $\hat{m} := m + \Gamma$ and total protein p concentration $\hat{p} = p + \Gamma$. Since the binding and unbinding reactions are relatively fast, we have the quasi-steady state approximation $k_1 mp \approx k_2\Gamma$, from which we obtain that $\Gamma \approx \frac{k_1 m}{k_2 + k_1 m}\hat{p}_2$. If we assume that the RNAase strongly binds the mRNA so that $k_1 \gg k_2$ we obtain $\Gamma \approx \hat{p}$. By choosing an RNAase that degrades mRNA sufficiently fast, we can also make the approximation $k_4 \approx g$. We therefore obtain the reduced order system

$$\begin{aligned}
\dot{\hat{m}} &= gv - \delta\hat{m} - g\hat{p} \\
\dot{\hat{p}} &= R\hat{m} - \gamma\hat{p}
\end{aligned} \tag{15}$$

The simplified model (15) can be decomposed into the form (8), with $\Sigma_1 = (A_1, B_1, C_1)$, $\Sigma_2 = (A_2, B_2, C_2)$, with $A_1 = -\delta = -1$, $B_1 = 1$, $C_1 = 1$, $A_2 = -\gamma = -1$, $B_2 = R$, $C_2 = 1$. Note that systems Σ_1 and Σ_2 are both strictly positive real, respectively having transfer functions $H_1 = \frac{1}{s+\delta}$ and $H_2 = \frac{R}{s+\gamma}$, each of which has strictly positive real parts. Therefore, the results of Theorem 2 can be applied to this system. Figure 2 shows a simulation of system (15), subject to an external input $v = D\sin(t/1) + 20$. At $t = 100$ the ribosome availability undergoes a step change from $R = 0.5$ to $R = 4$. At $t = 200$ the input signal's sinusoidal amplitude D undergoes a step change from $D = 10$ to $D = 20$. As can be seen, high gain feedback is able to maintain a small tracking error between the transcription factor input signal v and the protein concentration p.

Next, we will show that if there is a protease present in the cellular environment, tracking is still maintained under high gain feedback. In the presence of a protease, the system (15) is transformed into a nonlinear model of the form

$$\begin{aligned}
\dot{\hat{m}} &= gv - \delta\hat{m} - g\hat{p} \\
\dot{\hat{p}} &= R\hat{m} - \gamma\hat{p} - \frac{\hat{p}}{1+\hat{p}}
\end{aligned} \tag{16}$$

To analyze the tracking error $e := v - \hat{p}$, we first transform (16) to a coordinate system in the coordinates $\mathbf{e} = \begin{bmatrix} e & \dot{e} \end{bmatrix}^T$, as described in Section II, to obtain the time varying system

$$\dot{\mathbf{e}} = \bar{A}(t)\mathbf{e} + \bar{B}\mathbf{v}$$

where $\bar{A}(t) = \begin{bmatrix} 0 & 1 \\ -\bar{a}_1(t) & -\bar{a}_2(t) \end{bmatrix}$, $\bar{B} = \begin{bmatrix} 0 \\ 1 \end{bmatrix}$, $\bar{a}_1(t) = g + \delta$, $\bar{a}_2(t) = \gamma + \frac{1}{(1+\hat{p}(t))^2} + \delta$ and $\mathbf{v} = \delta\frac{\hat{p}(t)}{1+\hat{p}(t)} + \delta v + \left(\delta + \gamma + \frac{1}{(1+\hat{p}(t))^2}\right)\dot{v} + \ddot{v}$. Note that if $v,\ \dot{v},\ \ddot{v} \in \mathcal{L}_\infty$ then $\mathbf{v} \in \mathcal{L}_\infty$ if $\hat{p}(t) > 0, \forall t$. Without loss of generality, let $\gamma = 1$. Then, defining $Q = \begin{bmatrix} g & \frac{1}{2} \\ \frac{1}{2} & 1 \end{bmatrix}^{\frac{1}{2}}$, Theorem

1 can be applied to (16) if we can find c, d such that $\mu_{2,Q} \leq -c$ and $d|e| \leq |\mathbf{e}|_{2,Q}$. Therefore c should satisfy $M := -2cQ^2 - \bar{A}(t)^T Q^2 + Q^2 \bar{A} > 0$. Pick $c = \frac{1}{4\bar{a}_2}$. We then obtain that $M(2,2) = \left(4\bar{a}_2^2 - 2\bar{a}_2^2 - 1\right)/(2\bar{a}_2^2)$. Since $\bar{a}_2 > 1$ we have $M(2,2) > 0$. To ensure that $M > 0$ we need $\det(M) > 0$. Evaluating this determinant, we find that $\det M = g\rho_1(\bar{a}_2) - \rho_0(\bar{a}_2, \delta)$, with $\rho_1(a) = \frac{8\bar{a}_2^3 - 8\bar{a}_2^2 + 1}{4\bar{a}_2^2}$ and $\rho_0(\bar{a}_2, \delta) = \frac{\bar{a}_2^4 - 4\bar{a}_2^3\delta + 4\bar{a}_2^2\delta^2 + 4\bar{a}_2\delta - \bar{a}_2^2 + \frac{1}{4}}{4\bar{a}_2^2}$. Note that since $\bar{a}_2 > 1$ we have $\rho_1(\bar{a}_2) > 1/4\bar{a}_2^2$. Therefore, with $c = \frac{1}{4\bar{a}_2}$, we have $\det(M) > 0$ as long as $g > \bar{\rho} := \frac{\bar{a}_2^2(\bar{a}_2 - 2\delta)^2 + 4\bar{a}_2^2\delta}{4\bar{a}_2^2} > \frac{\rho_0(\bar{a}_2, \delta)}{\rho_1(\bar{a}_2)}$. To ensure condition (3), note that $|\mathbf{e}|_{2,Q}^2 > (g - \frac{1}{4})e^2$. Therefore Theorem 1 can be applied with $d = \sqrt{g - \frac{1}{4}}$, as long as $g > \max(\bar{\rho}, \frac{1}{4})$. Finally, note that as $t \to \infty$, we obtain the upper bound estimate on the tracking error

$$\limsup_{t\to\infty} |e(t)| \leq \frac{4\bar{a}_2 \left\|\bar{B}\right\|_{2,Q}}{\sqrt{g - \frac{1}{4}}} \|\mathbf{v}\|_{[0,\infty]} = \frac{4\bar{a}_2}{\sqrt{g - \frac{1}{4}}} \|\mathbf{v}\|_{[0,\infty]}$$

showing that the tracking error can be made arbitrarily small by sufficiently increasing g.

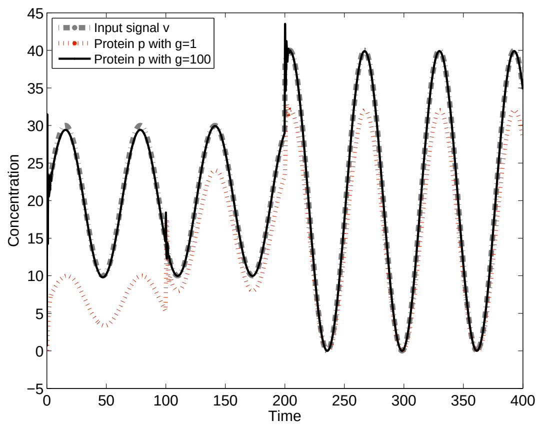

Fig. 2. Simulation of system (9) with $g = 0.1, 100$. At time $t = 100$ there is a step change in the available ribosome concentration from $R = 0.5$ to $R = 4$. At time $t = 200$ there is a change in the input amplitude from $D = 10$ to $D = 20$.

VI. Conclusions

We have shown that dynamical systems that are contracting in the sense of [21] are, under the assumptions of Theorem 1, input to output stable. This result was subsequently employed to show that if the tracking error dynamics of a system subject to an exogenous input are contracting, then the tracking error is input to output stable with respect to the derivatives of the input. In the case of LTI systems, verifying contraction in the second matrix measure is equivalent to simply finding a quadratic Lyapunov function. We have presented a method to construct this Lyuapunov function for the tracking error dynamics of a dynamical system composed of two LTI strictly positive real systems in cascade. In addition to using this result to show that the error dynamics in this case are input to output stable, we have demonstrated that the tracking error is proportional to the inverse of the square root of the feedback gain. Our results find application in the design of synthetic biomolecular networks. In this setting, most system parameters are not well characterized. Since the SPR property is a structural one, their tracking will also be robust with respect to parameter changes. Characterizing dynamical systems through their structural properties in this way therefore enables the rational design of control architectures in highly uncertain environments.

Appendix I
Proof of Theorem 1

Theorem 1 follows immediately as a special case of the more general incremental input to state stability result proved here. Henceforth we drop the notation $|\cdot|_{p,Q}$, $\mu_{p,Q}$, $\|\cdot\|_{p,Q}$ and use $|\cdot|$, $\mu(\cdot)$, $\|\cdot\|$ for shorthand.

Theorem 3: Suppose that $c > 0$ is such that

$$\sup_{t\geq 0,\, \mathbf{e}\in\mathcal{X}} \mu[D\bar{f}(t,\mathbf{e})] \leq -c\,.$$

Consider the difference between any two solutions corresponding to possibly different inputs and initial states:

$$\begin{aligned} \dot{p} &= \bar{f}(t,p) + \bar{B}\mathbf{v}_1 \\ \dot{q} &= \bar{f}(t,q) + \bar{B}\mathbf{v}_2\,. \end{aligned}$$

Denote $\mathbf{e}(t) := p(t) - q(t)$. Fix any $T \geq 0$ and let

$$r := \sup_{0\leq t\leq T} \left|\bar{B}\mathbf{v}_1(t) - \bar{B}\mathbf{v}_2(t)\right|$$

(where the norm is the norm in $\mathbb{R}^n$ being considered). Then:

$$|\mathbf{e}(T)| \;\leq\; \exp(-cT)\,|\mathbf{e}(0)| + \frac{1-\exp(-cT)}{c} r\,.$$

This theorem is the same as Theorem A in [20], which uses Coppel's inequality. The proof of that theorem is provided here with some additional details.

Proof: Observe that, for any $0 \leq t \leq T$, we have $\dot{\mathbf{e}}(t) = A(t)\mathbf{e}(t) + m(t)$, where

$$A(t) \;=\; \int_0^1 \frac{\partial \bar{f}}{\partial \mathbf{e}}(t, \lambda p(t) + (1-\lambda)q(t))\, d\lambda$$

and $m(t) := \bar{B}\mathbf{v}_1(t) - \bar{B}\mathbf{v}_2(t)$. Consider the norm of $\mathbf{e}(t)$ and its (upper) Dini derivative:

$$\begin{aligned} D^+ |\mathbf{e}(t)| &= \limsup_{h\to 0^+} \frac{1}{h}\big(|\mathbf{e}(t+h)| - |\mathbf{e}(t)|\big) \\ &= \limsup_{h\to 0^+} \frac{1}{h}\big(\,|\mathbf{e}(t) + hA(t)\mathbf{e}(t) + hm(t) + o(h)| - |\mathbf{e}(t)|\,\big) \\ &\leq \limsup_{h\to 0^+} \frac{1}{h}\big(\,|\mathbf{e}(t) + hA(t)\mathbf{e}(t)| - |\mathbf{e}(t)|\,\big) + |m(t)| \\ &\leq \limsup_{h\to 0^+} \frac{1}{h}\big(\,\|I + A(t)\| - 1)\big)\,|\mathbf{e}(t)| + r \\ &= \mu(A(t))\,|\mathbf{e}(t)| + r \leq -c\,|\mathbf{e}(t)| + r\,. \end{aligned}$$

Since the function $\psi(t) = |\mathbf{e}(t)|$ is continuous, we may apply the subdifferential version of Gronwall's inequality, as for example in Proposition 2, Appendix A, in [4], to conclude that

$$\psi(t) \;\leq\; \exp(-ct)\psi(0) + \int_0^t \exp(-c(t-s))r\, ds$$

for all t, which gives the desired conclusion. ∎

To prove Theorem 1 from Theorem 2, we compare a solution of $\dot{\mathbf{e}} = \bar{f}(t, \mathbf{e}) + \bar{B}\mathbf{v}$ with the constant solution $q \equiv 0$ corresponding to $\mathbf{v}_2 \equiv 0$. Note that $r \leq \|\bar{B}\| \, \|\mathbf{v}\|_{[0,\infty]}$.

APPENDIX II
PROOF OF CLAIM 1

Proof: We can write the k^{th} row of T^{-1} as $CA^{k-1} = C(\tilde{A} - gBC)^{k-1}$. The binomial expansion of $(\tilde{A} - gBC)^{k-1}$ results in a sum of 2^{k-1} terms composed of the matrix products $M_1 M_2 \cdots M_{k-1}$, with each M_i either $\tilde{A}$ or $-gBC$. Each term in the sum resulting from the expansion of $C(\tilde{A} - gBC)^{k-1}$ is therefore a scalar multiple of $C\tilde{A}^i$ with $i \in \{0, \cdots, k-1\}$. The vector $C(\tilde{A} - gBC)^{k-1}$ can therefore be expressed as

$$C(\tilde{A} - gBC)^{k-1} = C\tilde{A}^{k-1} + \sum_{j=1}^{k-2} \alpha_{k-1,j} C\tilde{A}^j \tag{17}$$

with $\alpha_{i,j} \in \mathbb{R}$. It follows that as $T^{-1} = D\Omega$ where Ω is the $(\tilde{A}, C)$ observability matrix and

$$D = \begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ \alpha_{1,1} & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ \alpha_{n-2,1} & \alpha_{n-2,2} & \cdots & 1 & 0 \\ \alpha_{n-1,1} & \alpha_{n-1,2} & \cdots & \alpha_{n-1,n-1} & 1 \end{bmatrix}$$

Since D is lower triangular, $\det(D) = 1$ and therefore $\det(T^{-1}) = \det(D)\det(\Omega) = \det(\Omega)$, which is independent of g.

From (17) we readily obtain that $\{C(\tilde{A} - gBC)^{k-1}\}_j = \{C\tilde{A}^{k-1}\}_j + \sum_{j=1}^{k-2} \alpha_{k-1,j} \{C\tilde{A}^j\}_j$, from which it follows that

$$\{T^{-1}\}_{n,j} = \begin{bmatrix} \{C\}_j \\ \{C(\tilde{A} - gBC)\}_j \\ \vdots \\ \{C(\tilde{A} - gBC)^{n-2}\}_j \end{bmatrix} = \{D\}_{n,n} \{\Omega\}_{n,j}$$

Therefore $\det(\{T^{-1}\}_{n,j}) = \det(\{D\}_{n,n}) \det(\{\Omega\}_{n,j}) = \det(\{\Omega\}_{n,j})$ which is independent of g.

■

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