# On the optimal control problem for a class of monotone bilinear systems

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*Abstract*—We consider a class of positive systems in which the control signal enters bilinearly with the state. Such dynamics arise naturally, for example, from modeling the evolutionary dynamics of HIV in the presence of drug therapy. For this class of system, we formulate an infinite horizon optimal control problem and show that the optimal control signal is constant over time. We further extend our results to the case of uncertain dynamics and provide a characterization of the optimal robust controller.

## I. INTRODUCTION

This work is motivated by recent developments focusing on combination drug therapy design for HIV treatment [1]– [9] and robust control for positive systems [10], [11]. These advancements provide a suitable framework for modeling the evolution of an HIV population in terms of a bilinear positive system in which drug therapy is represented by a decentralized controller.

The design of unconstrained decentralized controllers for positive systems is known to be convex [12]. However, the design of drug therapy imposes additional structural constraints on the controller which the methodology in [12], in general, cannot handle. In [5]–[7], the authors approached this problem by designing suboptimal  $\mathcal{L}_1$  and  $\mathcal{H}_{\infty}$  controllers which satisfy such structural constraints. In [8], we showed that the designing an  $\mathcal{H}_2$  optimal controller for only the symmetric component of the model provides a convex upper bound for the original problem. In [9] we built on [3], [4] and showed convexity of the structured  $\mathcal{H}_2$  and  $\mathcal{H}_{\infty}$ optimal control problems for positive systems and developed algorithms for controller design.

In [5]–[9], either a constant control signal is assumed or heuristics are used to introduce time dependance. In this work, we show that such a constant input is in fact optimal for the induced power norm over all almost-periodic control signals. Finally, we use our advancements in [10], [11] to develop methods to design controllers which account for uncertainty in the model and in the control input.

## II. PROBLEM FORMULATION

We first present the class of bilinear positive systems we study and then present the main result and a sketch of the proof. Consider the system

$$\dot{x} = (A + D(u))x + Bd, \tag{1}$$

where  $A \in \mathbb{R}^{n \times n}$  is a Metzler matrix,  $D : \mathbb{R}^m \to \mathbb{D}^{n \times n}$ is a diagonal matrix which is linear function of u, B is a nonnegative matrix, and  $Q, R \succeq 0$  are nonnegative matrices. We define the performance output of (1) as,

$$z_{ud} := \begin{bmatrix} Q^{\frac{1}{2}} \\ 0 \end{bmatrix} x + \begin{bmatrix} 0 \\ R^{\frac{1}{2}} \end{bmatrix} u,$$

given a control signal  $u \in \mathcal{B}_2^m$  and a disturbance  $d \in \mathcal{B}_2^r$ . The set  $\mathcal{B}_2^m$  is a suitable subset of power signals known as the space of Besicovitch almost periodic functions [13], which is a Hilbert space with inner product

$$\langle u, v \rangle = \lim_{T \to \infty} \frac{1}{T} \int_0^T u^T(t) v(t) dt.$$

We define our performance metric as the induced power norm of the system,

$$J_{\infty}(u) := \sup_{\|d\|_{pow}^2 \le 1} \|z_{ud}\|_{pow}^2.$$

where the power semi-norm of a signal v is given by

$$\|v\|_{\text{pow}}^2$$
, :=  $\limsup_{T \to \infty} \frac{1}{T} \int_0^T v^T(t) v(t) \, \mathrm{d}t.$  (2)

The performance metric  $J_{\infty}(u)$  measures the optimal response to the worst case persistent disturbance that can affect the system. We are now ready to formulate the optimal control problem.

Problem 1 (Optimal control problem): Find the control signal  $u(t) = \mu(x(t))$  that minimizes  $J_{\infty}(u)$ .

## III. MAIN RESULT

We can now state the main technical result of this work, namely that a constant input  $u(t) = \overline{u}$  solves Problem 1.

Theorem 1: If there exist  $\bar{u} \in \mathbb{R}^m$  such that  $(A+D(\bar{u}))$  is Hurwitz, then the power-induced norm,  $J_{\infty}(u)$ , is minimized over u by a constant function  $u(t) = \bar{u}^*$  for all  $t \ge 0$ .

*Proof:* [Sketch of the proof] The proof is divided into three main parts:

- Show that the the worst case disturbance is always constant.
- Prove that given a constant disturbance, the power norm of the output is a convex function of the control signal u(t).
- Show that given a constant disturbance, the best constant control signal  $u(t) = \bar{u}^*(t)$  is a local minimum for the power norm of the output over all  $u(t) \in \mathcal{B}_2^m$ .

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# IV. SOLUTION TO THE OPTIMAL CONTROL PROBLEM

Since Problem 1 is solved by a constant input  $u(t) = \bar{u}$ , system (1) subject to the optimal control signal is a time invariant system and the maximum power amplification coincides with the  $\mathcal{H}_{\infty}$  norm of the system. Because it is a positive system, this is given by the gain of the system with the input d(t) = v where v is the right maximum singular vector of  $Q^{\frac{1}{2}}(A + D(\bar{u}))^{-1}B$ . Since u(t) is time invariant,  $\|\bar{R}^{\frac{1}{2}}u(t)\|_{\text{pow}}^2 = \bar{u}^T R \bar{u}$ , and therefore,

$$J_{\infty}(\bar{u}) = \bar{\sigma}^2 \left( Q^{\frac{1}{2}} \left( A + D(\bar{u}) \right)^{-1} B \right) + \bar{u}^T R \bar{u}.$$

The function  $J_{\infty}$  is convex over a constant u and is continuously differentiable when the graph associated with A is strongly connected [9].

Since  $J_{\infty}(\bar{u})$  is not always differentiable, subgradient methods [14] can be used to find a solution.

Proposition 2: Let D be a linear operator and  $A_{cl} := A + D(\bar{u})$  be Hurwitz. Then,

$$\partial J_{\infty}(\bar{u}) = \left\{ 2\bar{\sigma}_{cl} \sum_{i} \alpha_{i} D^{\dagger} \left( A_{cl}^{-1} B v_{i} w_{i}^{T} C A_{cl}^{-1} \right) + 2R\bar{u} \right.$$

$$\left| w_{i}^{T} \left( C A_{cl}^{-1} B \right) v_{i} = \bar{\sigma}_{cl}, \ \alpha \in \mathcal{P}$$
(3)

where  $D^{\dagger}(u)$  is the adjoint of D(u),  $\bar{\sigma}_{cl} = \bar{\sigma}(Q^{\frac{1}{2}}A_{cl}^{-1}B)$ and  $\mathcal{P}$  is the probability simplex defined by

$$\mathcal{P} := \left\{ \alpha \mid \alpha_j \ge 0, \sum_j \alpha_j = 1 \right\}.$$

For further discussion of the algorithms, we refer the interested reader to [9, Section VI], where we discuss the use of proximal methods [15], [16] to solve optimization problems of the form of Problem 1 augmented with nonsmooth regularizers.

#### V. ROBUST CONTROL PROBLEM

In this section we tackle the robustness problem and we show that, exploiting the properties of positive systems, the robust optimal control problem is convex and no harder to solve than the standard optimal control problem. We add uncertainties  $\Delta_A$  and  $\delta_u$  to the system (1)

$$\dot{x} = ((A + \Delta_A) + D(u + \delta_u))x + Bd, \qquad (4)$$

where

$$\Delta_A = \begin{bmatrix} \delta_{11} & \cdots & \delta_{1n} \\ \vdots & \ddots & \vdots \\ \delta_{n1} & \cdots & \delta_{nn} \end{bmatrix}$$

represents the uncertainty in the A matrix and  $\delta_u$  represents the uncertainty of the control signal.

We will bound the uncertainty as  $|\delta_{ij}| < \alpha_{ij}$  for all  $(i, j) \in \{1, \ldots, n\}^2$  and  $|\delta_{u_k}| < \beta_k$  for all  $k \in \{1, \ldots, m\}$  with  $\alpha_{ij} \ge 0$  and  $\beta_k \ge 0$ . Let us define the set of admissible perturbations as

$$\mathbf{\Delta} := \{ (\Delta_A, \delta_u) \mid \|\delta_{ij}\| \le \alpha_{ij}, \ |\delta_{u_k}| < \beta_k \}$$

and

$$\tilde{A} := \begin{bmatrix} \alpha_{11} & \cdots & \alpha_{1n} \\ \vdots & \ddots & \vdots \\ \alpha_{n1} & \cdots & \alpha_{nn} \end{bmatrix}, \quad \beta = \begin{bmatrix} \beta_1 \\ \vdots \\ \beta_m \end{bmatrix}$$

For fixed  $\Delta_A$  and  $\delta_u$  and input signal u, we denote by  $J_{\infty}(u; \Delta_A, \delta_u)$  the induced gain of system (4). The robust optimal control problem is as follows.

Problem 2 (Robust optimal control problem): Find the control signal  $u(t) = \mu(x(t))$  that minimizes  $J_{\infty}(u; \Delta_A, \delta_u)$  for the worst-case uncertainty  $(\Delta_A, \delta_u) \in \mathbf{\Delta}$ ,

$$\min_{u} \max_{(\Delta_A, \delta_u) \in \mathbf{\Delta}} J_{\infty}(u; \Delta_A, \delta_u).$$

We now characterize the solution to this problem.

Theorem 3: Assume that D(u) is elementwise nonpositive when u is elementwise nonnegative. Provided there exist  $\bar{u}$ such that  $(A + \tilde{A}) + D(\bar{u} - \beta)$  is Hurwitz, the solution to the Robust Optimal Control Problem 2 is given by the solution to the Optimal Control Problem 1 applied to the system

$$\dot{x} = \left( (A + \tilde{A}) + D(u - \beta) \right) x + Bd.$$

Proof: [Sketch of the proof] We first show that the worst case uncertainty is always  $(\Delta_A, \delta_u) = (\tilde{A}, -\beta)$ . From there, the proof is immediate.

In the next section we provide and example and intuition for the main results.

## VI. COMBINATION DRUG THERAPY FOR HIV

As shown in [1], [5], the problem of designing drug dosages for treating HIV can be modeled with the following bilinear system

$$\dot{x} = \left(A - \sum_{k=1}^{m} u_k D_k\right) x + Bd.$$
 (5)

Here, the *i*th component of the state vector x represents the population of the *i*th HIV mutant. The matrix A represent the rate at which replication or mutations occur, i.e.,  $a_{ij}$  represents the rate at which mutant *i* turns into mutant *j* and  $a_{ii}$  represents the replication rate of mutant *i*. The control input  $u_k$  is the dose of drug k and the matrices  $D_k \in \mathbb{D}_+$  specify how efficiently drug k neutralizes each HIV mutant. The disturbance d represents the effect of noise and unmodeled dynamics on the system. Let us now consider the performance output

$$z := \left[ \begin{array}{c} Q^{\frac{1}{2}} \\ 0 \end{array} \right] x + \left[ \begin{array}{c} 0 \\ R^{\frac{1}{2}} \end{array} \right] u,$$

were the matrix  $Q^{\frac{1}{2}} \geq 0$  captures, for example, how deadly each virus strand is and the matrix  $R^{\frac{1}{2}} \geq 0$  captures, for example, the cost of different drugs.

Clearly, system (5) is of the form (1). Interestingly, Theorem 1 implies that the optimal treatment strategy that kills the virus population and minimizes the effect of worst case disturbance is to continuously deliver a constant dose of drugs.

## A. Uncertain model of HIV dynamics

A large challenge with HIV virus dynamics is model uncertainty. Uncertainty rises from two different aspects:

- It is difficult to estimate the mutation coefficients between viral strands.
- Once a drug dosage  $u_i$  is chosen, it is difficult to precisely deliver the correct amount of drug.

In the HIV example,  $\Delta_A$  represents the uncertainty of the replication-mutation rates of the virus and the vector  $\delta_u$ represents the uncertainty of the drug dosage. The optimal robust drug dose is obtained by solving Problem 1 for

$$\dot{x} = \left(A + \tilde{A} - \sum_{k=1}^{m} (u_k - \beta_k) D_k\right) x + Bd. \quad (6)$$

Note that when applied to the HIV example, the statement of Theorem 3 is very intuitive; the worst case perturbation is the one for which the virus replicates and mutates most aggressively and the drugs are the least effective.

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### REFERENCES

- E. Hernandez-Vargas, P. Colaneri, R. Middleton, and F. Blanchini, "Discrete-time control for switched positive systems with application to mitigating viral escape," *International Journal of Robust and Nonlinear Control*, vol. 21, no. 10, pp. 1093–1111, 2011.
- [2] E. A. Hernandez-Vargas, P. Colaneri, and R. H. Middleton, "Optimal therapy scheduling for a simplified HIV infection model," *Automatica*, vol. 49, no. 9, pp. 2874–2880, 2013.
- [3] P. Colaneri, R. H. Middleton, Z. Chen, D. Caporale, and F. Blanchini, "Convexity of the cost functional in an optimal control problem for a class of positive switched systems," *Automatica*, vol. 4, no. 50, pp. 1227–1234, 2014.

- [4] A. Rantzer and B. Bernhardsson, "Control of convex monotone systems," in *Proceedings of the 53rd IEE Conference on Decision* and Control, 2014.
- [5] V. Jonsson, A. Rantzer, and R. M. Murray, "A scalable formulation for engineering combination therapies for evolutionary dynamics of disease," *Proceedings of the 2014 American Control Conference*, 2014.
- [6] V. Jonsson, N. Matni, and R. M. Murray, "Reverse engineering combination therapies for evolutionary dynamics of disease: An  $H_{\infty}$  approach," in *Proceedings of the 52nd IEEE Conference on Decision and Control*, pp. 2060–2065, 2013.
- [7] V. Jonsson, N. Matni, and R. M. Murray, "Synthesizing combination therapies for evolutionary dynamics of disease for nonlinear pharmacodynamics," in *Proceedings of the 53rd 53rd Conference on Decision* and Control, pp. 2352–2358, IEEE, 2014.
- [8] N. K. Dhingra and M. R. Jovanović, "Convex synthesis of symmetric modifications to linear systems," in *Proceedings of the 2015 American Control Conference*, (Chicago, IL), pp. 3583–3588, 2015.
- [9] N. K. Dhingra, M. Colombino, and M. R. Jovanović, "On the convexity of a class of structured optimal control problems for positive systems," in *Proceedings of the 2016 European Control Conference*, (Aalborg, Denmark), 2016. submitted.
- [10] M. Colombino and R. Smith, "Convex characterization of robust stability analysis and control synthesis for positive linear systems," in *Proceedings of the 53rd IEEE Conference on Decision and Control*, (Los Angeles, California), 2014.
- [11] M. Colombino and R. Smith, "A Convex Characterization of Robust Stability for Positive and Positively Dominated Linear Systems," *IEEE Trans. Automat. Control.* To appear. Available online at http://arxiv.org/pdf/1508.04983v1.pdf, June 2016.
- [12] A. Rantzer, "Distributed control of positive systems," *arXiv preprint arXiv:1203.0047*, 2012.
- [13] A. S. Besicovitch, *Almost Periodic Functions*. Dover Publications, 1954.
- [14] D. P. Bertsekas, Nonlinear programming. Athena Scientific, 1999.
- [15] A. Beck and M. Teboulle, "A fast iterative shrinkage-thresholding algorithm for linear inverse problems," *SIAM Journal on Imaging Sciences*, vol. 2, no. 1, pp. 183–202, 2009.
- [16] N. Parikh and S. Boyd, "Proximal algorithms," Foundations and Trends in optimization, vol. 1, no. 3, pp. 123–231, 2013.