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Convex Reformulation of a Robust Optimal Control Problem for a Class of Positive Systems

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Abstract— **In this paper we consider the robust optimal control problem for a class of positive systems with an application to design of optimal drug dosage for HIV therapy. We consider uncertainty modeled as a Linear Fractional Transformation (LFT) and we show that, with a suitable change of variables, the structured singular value, μ, is a convex function of the control parameters. We provide graph theoretical conditions that guarantee μ to be a continuously differentiable function of the controller parameters and an expression of its gradient or subgradient. We illustrate the result with a numerical example where we compute the optimal drug dosages for HIV treatment in the presence of model uncertainty.**

I. Introduction

In recent years, significant effort has been devoted to identifying classes of convex structured control proplem. These include funnel causal and quadratically invariant systems [1], [2], positive systems [3], structured and sparse consensus and synchronization networks [4]–[7], optimal sensor/actuator selection [8], [9], and symmetric modifications to symmetric linear systems [10]. Unfortunately most of the approaches mentioned above involve variable transformations that make explicit constraints or regularizations of the control variables not tractable. Moreover there are very few approaches that consider the problem of designing optimal decentralized controllers for uncertain systems.

In [11], the authors show how the problem of designing optimal $\mathcal{H}_2$ and $\mathcal{H}_\infty$ decentralized controllers for a class of positive systems is convex with respect to the controller variables directly. It is therefore possible to solve optimization problems that involve convex constraints of the controller variable or sparsity inducing regularizations. The class of positive systems studied in [11] has applications in biology and network theory. In this work we extend these results to the decentralized optimal control for uncertain positive systems. Again we show that it is possible to solve the robust optimal control problem by convex optimization.

Positive systems have received much attention in recent years because of convenient properties that arise from their structure. A system is called positive if, for every nonnegative initial condition and input signal, its state and output remain nonnegative [12]. Such systems appear in the models of heat transfer, chemical networks, and probabilistic networks. In [13], the authors show that the KYP lemma greatly simplifies for positive systems, thereby allowing for decentralized $\mathcal{H}_\infty$ synthesis via Semidefinite Programming (SDP). In [3], it is shown that static output-feedback can be solved via Linear Programming (LP) for a class of positive systems.

Robust stability analysis for positive systems was previously studied in [14], [15], where the authors develop necessary and sufficient conditions for robust stability of positive systems with respect to induced $\mathcal{L}_1$–$\mathcal{L}_\infty$ norm-bounded perturbations and in [16], [17] where it is shown that the structured singular value is equal to its convex upper bound. Thus, assessing robust stability with respect to induced $\mathcal{L}_2$ norm-bounded perturbation is also tractable. Robust control design, however, requires a change of variables that makes constraints and regularizations intractable.

Notation

The set of real numbers is denoted by $\mathbb{R}$. $\mathbb{R}_+$ denotes the set of nonnegative reals. The set of $n \times n$ Metzler matrices (matrices with nonnegative off diagonal elements) is denoted by $\mathbb{M}^n$. The set of $n \times n$ nonnegative diagonal matrices is denoted by $\mathbb{D}^n_+$. Given a matrix A, A^T denotes its transpose. We use $\bar{\sigma}(A)$ to indicate the largest singular value of A. We write $A \geq 0$ ($A > 0$) if A has nonnegative (positive) entries and $A \succcurlyeq 0$ ($A \succ 0$) to denote that A is symmetric and positive semidefinite (definite).

II. Problem setup and motivating example

A. Combination drug therapy design for HIV treatment

Let us introduce the class of uncertain positive systems studied in this paper with a motivational example. As shown in [18], [19], a suitable model for the evolution of the HIV virus in the presence of a combination of drugs, is given by

$$\begin{aligned} \dot{x} \;&=\; \left(A \;-\; \sum_{k\,=\,1}^{m} u_k D_k \right) x \;+\; B_1 d \\ z \;&=\; C_1 x, \end{aligned} \qquad (1)$$

where A is a Metzler matrix and B_1, C_1 are nonnegative. The HIV virus is known to be present in the body in the form of different mutant strands; in the model (1), the ith component of the state vector x represents the population of the ith HIV mutant. The diagonal entries of the matrix A represent the net replication rate of each mutant, and the off diagonal entries of A, which are all nonnegative, represent

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the rate of mutation from one mutant to another. The control input u_k is the dose of drug k and the diagonal matrix D_k specifies at what rate drug k kills each HIV mutant. The signal d represents an external disturbance and z represents a performance output that we would like to keep small.

System (1) is a positive system, that is for every nonnegative initial condition x_0 and any nonnegative external disturbance d, the state and the output remain nonnegative for all time. In this paper we will deal with positive systems of the form (1) with the following key characteristics

- The system is positive, that is the matrix A is Metzler and the matrices B_1 and C_1 are nonnegative.
- The control parameter u affects linearly the diagonal elements of the system matrix.
- The control parameter u is constant in time.

The task of computing an optimal control parameter u for systems of this form has been studied in the recent literature. For example, [20] [21] explore optimal finite horizon L_1 control while [11] provide the solution to the $\mathcal{H}_2$ and $\mathcal{H}_\infty$ optimal control problems. In this work we are interested in exploring the case when the model in (1) is not known precisely.

B. Introducing uncertainty into the model

Modeling the evolution of the HIV virus is a complex task. If the model is incorrect and uncertainty is not taken into account, the efforts of designing an optimal controller (drug dosage) might be vain. In order to overcome this problem we propose the following uncertainty modeling for systems of the form (1)

$$\begin{aligned} \dot{x} &= \left(A - \sum_{k=1}^{m} u_k D_k\right) x + B_1 d + B_2 q \\ z &= C_1 x, \quad p = C_2 x, \quad q = \Delta p, \end{aligned} \tag{2}$$

where B_2 and C_2 are nonnegative matrices that specify which input-output pairs are affected by the uncertainty, which is collected in the block diagonal operator operator Δ and must satisfy the following assumption.

Assumption 1: The uncertainty operator Δ is of the form

$$\Delta = \text{diag}(\Delta_1, \dots, \Delta_N), \tag{3}$$

where each term Δ_k, $k \in \{1, ...N\}$ can represent one of the following types of uncertainty

1) An unknown real matrix in $\mathbb{R}^{m_k \times m_k}$ satisfying the norm bound $\bar{\sigma}(\Delta_k) \leq 1$.
2) An unknown stable linear system in $\mathcal{H}_\infty^{m_k \times m_k}$ satisfying the norm bound $\|\Delta_k\|_{\mathcal{H}_\infty} \leq 1$.
3) An unknown static, piecewise continuous, nonlinear function $\Delta_k : \mathbb{R}^{m_k} \to \mathbb{R}^{m_k}$ of the form $q_k = \Delta_k(p_k, t)$ satisfying the bound $\|q_k(t)\|_2 \leq \|p_k(t)\|_2$ for all time.

We further require the control parameter u to lie in a compact convex set $\mathcal{U}$. This could represent a budget constraint for the drugs or upper and lower bounds on the dosages dictated by the drugs' side effects.

Problem 1: We are interested in designing an input (drug dosage) $u \in \mathcal{U}$ which satisfies the following specifications:

- **Robust stability:** u stabilizes the system for every Δ satisfying Assumption 1.
- **Robust Performance:** u minimizes the $\mathcal{H}_\infty$ norm from d to z, for the worst case Δ satisfying Assumption 1.

III. PRELIMINARIES ON ROBUST STABILITY FOR POSITIVE LINEAR SYSTEMS

In this section we review some tools and results from the literature in order to assess robust stability and robust performance for a linear positive system

A. Robust Stability and the structured singular value

Let us now consider just the problem of assessing the robust stability of an uncertain feedback interconnection, without considering external inputs and outputs. More formally, let M be a stable linear time invariant *positive* system. We study the stability of the interconnection of the form

$$\begin{aligned} p &= Mq \\ q &= \Delta p, \end{aligned} \tag{4}$$

where Δ is an unknown operator satisfying Assumption 1.

The "μ framework" provides necessary and sufficient conditions for the interconnection in (4) to be robustly stable for all admissible uncertainties Δ in terms of the structured singular value, μ. Before defining μ, we introduce the following set of structured nonnegative matrices $\mathbb{R}_+^{m \times m}$ $\boldsymbol{\Delta} := \{\text{diag}(\Delta_1, \dots, \Delta_N) | \Delta_k \in \mathbb{R}_+^{m_k \times m_k} \forall k \in \mathbb{Z}_{[1,N]}\}$. Given the uncertainty set $\boldsymbol{\Delta}$, the structured singular value is a function $\mu_{\boldsymbol{\Delta}} : \mathbb{C}^{m \times m} \to \mathbb{R}_+$ defined as [22]

$$\mu_{\boldsymbol{\Delta}}(Q) := \frac{1}{\inf\{\bar{\sigma}(\Delta) \,|\, \Delta \in \boldsymbol{\Delta},\ \det(I - Q\Delta) = 0\}}.$$

In general, each Δ_i can be a complex matrix [22], [23], however, since M is a positive system we can restrict each Δ_i to be real and nonnegative without loss of generality [17], [24]. Furthermore, the robust stability of the interconnection (4) can be assessed with a single μ test as summarized in the following preposition.

Proposition 1 ([17], [24]): The interconnection in (4) is stable for all Δ satisfying Assumption 1 if and only if

$$\mu_{\boldsymbol{\Delta}}\left(\hat{M}(0)\right) < 1, \tag{5}$$

where $\hat{M}(j\omega)$ the Laplace transform of M evaluated along the imaginary axis.

B. Tight upper bound for μ

In general computing μ is hard, however there is a well known upper bound for the structured singular value which, in general, provides a tractable sufficient condition for robust stability, we refer the interested reader to [23] for a thorough review of the subject. It is known that for positive systems this upper bound is tight at $\omega = 0$ [17], therefore, because of Proposition 1, robust stability can be verified with convex programming.

Let us define the set of positive definite matrices that commute with all $\Delta \in \mathbf{\Delta}$:

$$\mathbf{\Theta} := \{\mathrm{diag}(\theta_1 I_{m_1}, \ldots, \theta_N I_{m_N}) | \, \theta_k > 0 \, \forall k \in \mathbb{Z}_{[1,N]}\} \quad (6)$$

Proposition 2 ([17], Theorem 10): Let M be a positive system and the sets $\mathbf{\Delta}$ and $\mathbf{\Theta}$ be as defined above. Then

$$\mu_{\mathbf{\Delta}}\left(\hat{M}(0)\right) = \inf_{\Theta \in \mathbf{\Theta}} \bar{\sigma}(\Theta^1 \hat{M}(0) \Theta^{-1}). \qquad (7)$$

Using (7) we can perform the μ test in (1) with a Linear Matrix Inequality. In particular as shown in [17] the following are equivalent

$$\begin{aligned} \mu_{\mathbf{\Delta}}\left(\hat{M}(0)\right) &< 1 \iff \\ \inf_{\Theta \in \mathbf{\Theta}} \bar{\sigma}(\Theta^1 \hat{M}(0) \Theta^{-1}) &< 1 \iff \\ \exists \Theta \in \mathbf{\Theta} \; : \; \Theta \hat{M}(0) \Theta - \Theta &\prec 0. \end{aligned} \qquad (8)$$

C. Robust performance is equivalent to robust stability for an augmented uncertainty

In the previous sections we consider the problem of assessing robust stability of a feedback interconnection without considering performance, we now consider the case where we have an external disturbance d and a performance output z as in the system in (2) and we want to guarantee robust stability and to minimize the worst case $\mathcal{H}_\infty$ norm from d to z. This setup is shown in Figure 1.

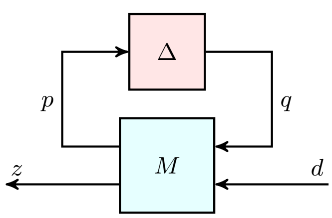

Fig. 1: The interconnection of M and Δ with an external disturbance d and a performance output z.

Let us introduce a new uncertainty block $\Delta_P \in \mathbb{R}_+^{m_d \times m_d}$, where m_d is the dimension of d and z (again one can zero pad C_1 or B_1 if the dimensions are different).

Proposition 3: The following are equivalent

1) The system (2) is stable and the $\mathcal{H}_\infty$ norm from d to z is smaller or equal to γ for all Δ satisfying assumption 1.
2) The interconnection depicted in Figure 2 is robustly stable for all Δ satisfying Assumption 1 and $\Delta_P \in \mathbb{R}_+^{m_d \times m_d}$ with $\sigma(\Delta_P) < 1$, i.e.,

$$\mu_{\mathbf{\Delta_a}}\left(\hat{M}_\gamma(0,u)\right) < 1,$$

where

$$\hat{M}_\gamma(0,u) := -\begin{bmatrix} \frac{1}{\gamma} C_1 \\ C_2 \end{bmatrix} \left(A + \sum_k D_k u_k \right)^{-1} [B_1 \;\; B_2],$$

and $\mathbf{\Delta_a} = \mathbf{\Delta} \times \mathbb{R}_+^{m_d \times m_d}$.

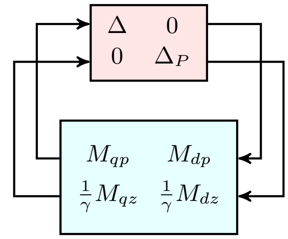

Fig. 2: Equivalent reformulation of the robust performance problem as an augmented robust stability problem.

Proposition 3 is the result of a fundamental theorem in robust control called the "Main Loop Theorem" [23] and it is important because, for a desired performance level γ, it shows that we can assess robust performance with a single μ test for an augmented uncertainty. In order to optimize for γ one can run a standard bisection algorithm.

D. A review of log-convexity

We now provide some basic definitions and preliminary results on log-convex functions. These will be useful to prove the main result of the paper.

Definition 1 ([25]): A function $f : \mathbb{R}^n \to \mathbb{R}_+$ is said to be logarithmically convex or log-convex if $g(x) := \log(f(x))$ is a convex function.

Every log-convex function is convex, the opposite is not true, for example the function $f(x) = |x|$ is convex but clearly not log-convex. We now present some properties of log-convex functions that we will be useful for developing the main result. The first result shows how log-convexity is preserved under limits

Proposition 4: Let $f_k : \mathbb{R}^n \to \mathbb{R}_+$ be a family of log-convex functions, then if $\lim_{k\to\infty} f_k$ exists, it is also a log convex function.

Proof: if $\lim_{k\to\infty} f_k$ exists,

$$\log(\lim_{k\to\infty} f_k) = \lim_{k\to\infty} \log(f_k).$$

Since, if it exists, the limit of convex functions is convex [21, Lemma 2], the proof is complete. ■

The second result show that log-convexity is preserved under conic combinations

Proposition 5 ([25]): Given two log-convex functions f_1 and f_2 mapping $\mathbb{R}^n \to \mathbb{R}_+$, and positive scalars a_1 and a_2, the conic combination

$$a_1 f_1 + a_2 f_2$$

is log-convex.

IV. Convexity of μ with a change of variables

We are now in the position to examine the problem of designing an optimal control u that robustly stabilizes the system (2). In Section III-C we show how the problem of assessing whether a system satisfies an $\mathcal{H}_\infty$ performance specification for the worst case disturbance is no harder than assessing robust stability and it can be done with a μ test. In this section we then focus on the structured singular value, μ, as a function of the control input, u. We show that, with a suitable change of variables, μ becomes a convex function of u and it can therefore be minimized efficiently.

Let us consider the uncertain interconnection

$$\begin{aligned} \dot{x} &= \left(A + \sum_k D_k u_k\right) x + Bq \\ z &= Cx \\ q &= \Delta z, \end{aligned} \tag{9}$$

with A Metzler, B, C nonnegative and Δ being uncertain and satisfying Assumption 1. We define the DC gain as a function of u as

$$\hat{M}(0,u) := -C\left(A + \sum_k D_k u_k\right)^{-1} B.$$

We know from Proposition 2 that the at DC, the structured singular value is equal to the upper bound, that is $\mu_{\mathbf{\Delta}}(M(0,u)) = \inf_{\Theta\in\mathbf{\Theta}} \bar{\sigma}\left(\Theta M(0,u)\Theta^{-1}\right)$, therefore, given a convex constraint set $\mathcal{U}$ for the input u, in order to minimize the structured singular value, we need to solve

$$\min_{u\in\mathcal{U},\Theta\in\mathbf{\Theta}} \bar{\sigma}\left(\Theta M(0,u)\Theta^{-1}\right), \tag{10}$$

where $\mathbf{\Theta}$ was defined in (6).

Remark 1: For a given u, the structured singular value, μ, can be computed by solving the LMI (8), however the LMI is not linear in the variable u and it requires a nonlinear change of variables. Thus minimizing μ while constraining u cannot be done with standard optimization tools from the literature.

We will now provide a change of variables that renders the optimization problem (10) convex and thus easy to solve.

We consider the following change of variables

$$y_i = \log(\theta_i), \quad i = 1, ..., N \tag{11}$$

The variables $y_i \in \mathbb{R}$ are well defined since $\theta_i > 0$ for all $i \in \{1, ..., N\}$.

We are now ready to prove the main result of the paper: the convexity of the structured singular value, μ, as a function of the new variables y and the control input u.

Theorem 6: The function $\bar{\sigma}\left(\Theta M(0,u)\Theta^{-1}\right)$ is jointly convex in u and the variables $y_1, ..., y_N$ defined in (11).

Proof: Let us denote with f_{ij} the ij element of the matrix $\Theta M(0,u)\Theta^{-1}$, that is $f_{ij} := \left[\Theta M(0,u)\Theta^{-1}\right]_{ij}$, and the function $\zeta_{ij}(u) := \log(m_{ij}(u))$, where $m_{ij}(u) := M_{ij}(0,u)$. We can rewrite f_{ij} in terms of the new variables as

$$f_{ij} = \theta_m \, m_{ij}(u) \, \theta_n^{-1} = \mathrm{e}^{\zeta_{ij}(u) + y_m - y_n}, \quad \text{for some } (m,n) \in \{1, ..., N\}^2.$$

If we can show that $\zeta_{ij}(u)$ is convex in u or equivalently that $m_{ij}(u)$ is *log-convex* then, since e^x is an increasing convex function, by the composition rules of convex functions [25], we know that f_{ij} is jointly convex in u and y.

To show that $\zeta_{ij}(u)$ is convex, let us consider the system

$$\begin{aligned} \dot{x} &= \left(A + \sum_i D_i u_i\right) x + Bq \\ z &= Cx. \end{aligned} \tag{12}$$

with the external disturbance $q(t) = e_j$ for all $t > 0$, where e_j is the j^{th} unit vector. We then obtain

$$m_{ij}(u) = \lim_{t\to\infty} z_i(t) = \lim_{t\to\infty} c_i^\top x(t). \tag{13}$$

Equation (13) is very intuitive as the ij element of the DC gain matrix of a linear system is the value at which output i settles when a unit disturbance is applied to the j^{th} input channel.

Now let us consider the change of variable $\xi_i(t) = \log(x_i(t))$ as in [20]. Then $\dot{\xi}_i = \frac{\dot{x}_i}{x_i}$ and

$$\dot{\xi}_i = a_{ii} + \sum_{k\neq i} a_{ik}\mathrm{e}^{\xi_k - \xi_i} + \sum_p D_{p,ii} u_p + b_{ij} e^{-\xi_i}. \tag{14}$$

The system in (14) is a convex monotone system as defined in [20] and thus every element of the trajectory $\xi(t)$ is convex in u for any initial condition. Since $\xi(t) = \log(x(t))$, every element of the original trajectory $x(t)$ is log-convex and therefore, by Proposition 4, $\lim_{t\to\infty} x(t)$ is log-convex. By Proposition 5 the conic combination of log-convex functions is log-convex, we can then conclude that $c_i^\top \lim_{t\to\infty} x(t)$ is also a log-convex function. Since

$$\zeta_{ij}(u) = \log(m_{ij}(u)) = \log\left(c_i^\top \lim_{t\to\infty} x(t)\right),$$

we conclude that $\zeta_{ij}(u)$ is a convex function of u.

Now Let us define $Y := \log(\Theta)$, we know that $Y \in \mathbf{Y}$, where

$$\mathbf{Y} := \{Y = \mathrm{diag}\left(y_1 I_{m_1}, ..., y_l I_{m_N}\right) \ : \ y_N \in \mathbb{R}\}.$$

We established that each element $e^Y M(0,u) e^Y$ is a convex function in Y and u jointly. Then, since $e^Y M(0,u) e^Y$ is a nonnegative matrix and $\bar{\sigma}(\cdot)$ is convex and nondecreasing in every entry of its argument (on $\mathbb{R}_+^{m\times m}$), from the composition rules of convex functions [25], we conclude that $\bar{\sigma}\left(\Theta M(0,u)\Theta^{-1}\right) = \bar{\sigma}\left(e^Y M(0,u) e^{-Y}\right)$, is a convex function in Y, u jointly. ■

Remark 2: The convexity of $\bar{\sigma}\left(e^Y M e^{-Y}\right)$, with respect to Y has been noted for the first time in [26]. With Theorem 6 we extend this result for positive systems and we show convexity with respect to Y and the control parameter u jointly.

Once convexity is established, In order to minimize the structured singular value we can then solve the optimization problem

$$\min_{u\in\mathcal{U},Y\in\mathbf{Y}} \bar{\sigma}\left(e^Y M(0,u) e^{-Y}\right). \tag{15}$$

This problem cannot be recast as a standard conic program amenable to commercial solvers. For this reason, in the next section we provide a description of the sub-gradient for the structured singular value so standard descent methods can be employed to solve (15).

V. Computation of the subgradient of μ

In order to simplify the notation we define the linear function $D(u) := \sum_i D_i u_i$, and we denote the convex upper bound to μ as

$$J_r(u,y) := \bar{\sigma}\left(\Theta M(0,u)\Theta^{-1}\right) = \bar{\sigma}\left(-e^Y C A_{cl}^{-1} B e^{-Y}\right),$$

where $A_{cl} := A + D(u)$ and $Y = \mathrm{diag}\left(y_1 I_{m_1}, ..., y_N I_{m_N}\right)$. As already mentioned in section III-C, for a positive system μ is equal to the upper bound at DC.

We next derive the subdifferential set of J_r both with respect to u and with respect to the variables $y_1, ..., y_N$.

Proposition 7: Let D be a linear operator and $A_{cl} := A + D(u)$ be Hurwitz. Then,

$$\partial_u J_r(u,y) = \Big\{ \sum_i \alpha_i D^\dagger \left(A_{cl}^{-1} B e^{-Y} v_i w_i^T e^Y C A_{cl}^{-1}\right) \\ \mid -w_i^T (e^Y C A^{-1} B e^{-Y}) v_i = J_r(u,y),\ \alpha_i \in \mathcal{P} \Big\} \quad (16)$$

where $D^\dagger(u)$ is the adjoint of $D(u)$, and,

$$\partial_{y_j} J_r(u,y) = \\ \Big\{ \sum_i \alpha_i w_i^T \Big(e^{y_j} \Pi_j C A_{cl}^{-1} B e^{-Y} - e^{-y_j} e^Y C A_{cl}^{-1} B \Pi_j\Big) v_i \\ \mid -w_i^T (e^Y C A^{-1} B e^{-Y}) v_i = J_r(u,y),\ \alpha_i \in \mathcal{P} \Big\} \quad (17)$$

where the matrix

$$\Pi_j := \mathrm{blkdiag}(0_{m_1}, \dots, I_{m_j}, \dots, 0_{m_N}),$$

is nonzero only at the position of the relevant uncertainty block associated with θ_j or y_j, and $\mathcal{P}$ is the simplex defined as $\mathcal{P} := \left\{\alpha \mid \alpha_j \geq 0,\ \sum_j \alpha_j = 1\right\}$.

The proof of Proposition 7 is omitted for reasons of space.

It is well known that, in general, the structured singular value, μ, is not differentiable. We next provide graph theoretic conditions on the system matrix A for μ to be continuously differentiable.

Proposition 8: Let A be Metzler, B and C be nonnegative matrices, and $K(u)$ be a diagonal linear operator such that $A_{cl} := A + K(u)$ is Hurwitz. If the graph associated with A is strongly connected, J_r is a continuously differentiable function of u.

The proof of Proposition 8 follows the same reasoning as the proof of [11, Proposition 9] and it is omitted for reason of space.

Using the expression of the (sub)gradient presented in this section one can employ standard first order methods to optimize μ as a function of the control parameter u. In the next section we illustrate our results with a numerical example.

VI. Numerical example

We now illustrate how our result can be used to compute the optimal drug dosage for HIV treatment in case of an uncertain interaction model by means of a numerical example.

A. Uncertain model

We consider a nominal model of the form (1) with five virus mutants $x_1, ..., x_5$, and an interaction matrix $A \in \{0,1\}^{n \times n}$ wwhich represents the incidence matrix of the blue graph in Figure 3 We have the choice of three drugs u_1, u_2 and u_3 acting on the dynamics through the matrices $D_1 = \mathrm{diag}(-1,\ 0,\ 0,\ 0,\ 0)$, $D_2 = \mathrm{diag}(0,\ -0.2,\ 0,\ -0.2,\ -0.2)$, and $D_3 = \mathrm{diag}(0,\ 0,\ -1,\ 0,\ 0)$. The effect of the different drugs is represented in green in Figure 3. We constrain the drugs such that $u_1 + u_2 + u_3 = 10$. We consider the matrix $B = I_5$ through which the disturbance d affects the system and the performance output is $z = C_1 x$, where $C_1 = [1\ 0\ 0\ 0\ 0]$, this is a reasonable choice, for example, if x_1 is the strand of the virus which is deadly and we care about suppressing it.

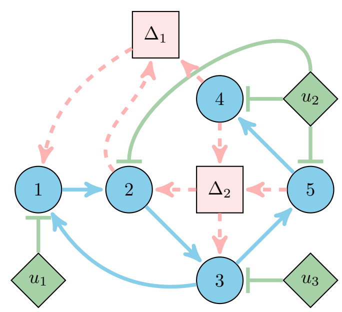

Fig. 3: The uncertain model for HIV virus dynamics. Each blue node represents a virus mutant and blue edges represent the known interactions between the mutants. The Δ blocks in red represent uncertain interactions. The green edges show the inhibitory effect of the different drugs.

We finally consider the uncertain interactions represented by the Δ blocks in Figure 3: each block in Δ represent a norm bounded unmodeled interaction which satisfies Assumption 1, i.e., it can be a static nonlinearity, a linear dynamical system or a fixed real parameter. We now show that computing an optimal controller using only the nominal model can give rise to disastrous consequences in the presence of uncertainty.

B. Robust vs nominal control

We first compute the optimal nominal $\mathcal{H}_\infty$ controller, that is the optimal controller without taking the uncertainty into account. To do so we use the proximal subgradient method proposed in [11] and we obtain $u^\star_{\text{nom}} = [5.90\ \ 1.94\ \ 2.15]$, which achieves the nominal cost $J^\star_{\text{nom}} = 0.22$.

We compute the optimal robust controller by exploiting Proposition 3 and a bisection routine.

We obtain the following drug dosage as the optimal robust controller $u^\star_{\text{rob}} = [2.38\ 5.73\ -1.90]$, which achieves the worst case cost $J^\star_{\text{rob}} = 4.45$.

The robust optimal drug dosage $u^\star_{\text{rob}}$ has a nominal cost of 0.49 which as expected, is worse than $J^\star_{\text{nom}}$, however $u^\star_{\text{rob}}$ guarantees stability for all possible uncertainties Δ satisfying Assumption 1. In Figure 4 we show some sample trajectories for the robust controller and the nominal controller. As expected the robust controller performs well for all tested values of the uncertainty while the nominal controller is often even unstable. For the sake of consistency we sampled positive Δ blocks such that closed-loop positivity is preserved. Such a restriction does not change the solution as it is shown in [16], [17] that the worst case perturbation for a positive system is always positive.

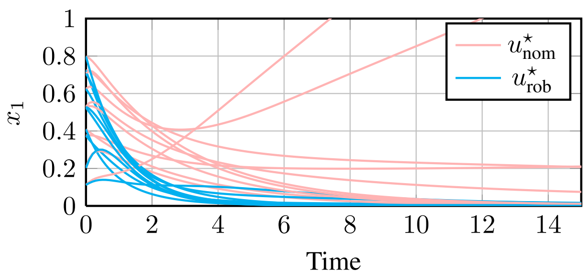

Fig. 4: Sample trajectories from random initial conditions and with random positive uncertainties Δ_1 and Δ_2 satisfying Assumption 1 using the nominal controller (red) and the robust controller (blue).

VII. Conclusion and Outlook

In this paper we complete the work from [11], [20], [21] and we show that the problem of designing an optimal robust controller for the class of positive systems of the form (1) is convex and thus tractable. We exploit this result to design the optimal drug dosage for HIV treatment when model uncertainty is considered. In our work we assume the drug dosage to be constant over time. A natural extension is to look at the possibility of time-varying drug dosage both for the nominal and uncertain case.

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