# On the convexity of a class of structured optimal control problems for positive systems


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# Positive systems

$$\begin{aligned} \dot{x} &= A\,x + B\,d \\ z &= Cx \end{aligned}$$

- Positive system, $x(0) \geq 0,\ d(t) \geq 0 \rightarrow x(t) \geq 0\ \ \forall t$
- Linear systems
  - $B, C \geq 0$
  - $A$ Metzler (off-diagonal elements nonnegative)
- E.g., Population/resource dynamics, Markov models

# Problem Formulation

$$\begin{aligned} \dot{x} &= (A + K(u))\,x + B\,d \\ z &= Cx \end{aligned}$$

- $K(u)$ diagonal – preserves positivity

**Objective:** Design optimal $u$

$\mathcal{H}_2$: minimize variance amplification

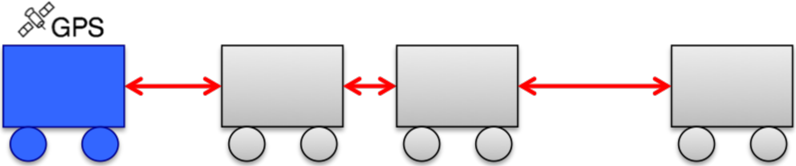
$$\lim_{t \to \infty} \mathbf{E}\left(z^T(t)\,z(t)\right)$$

$\mathcal{H}_\infty$: minimize worst-case amplification

$$\sup_{\|d\|=1} \frac{\|z\|}{\|d\|}$$

# Leader selection in directed consensus networks

$$\dot{x} \;=\; -\,(L \;+\; \text{diag}\{u\})\;x \;+\; d$$

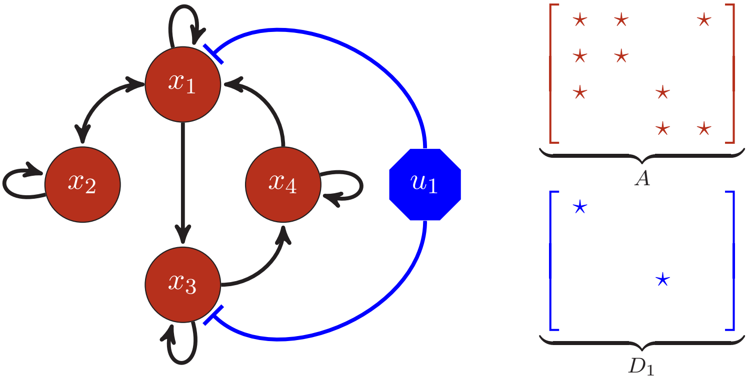



- Nodes $x_i$ determine average via *relative* information exchange
- *Some* nodes are 'leaders' with access to *absolute* measurements
- $L$ is directed graph laplacian, $u$ specifies leaders

Fitch and Leonard, CDC '13, TAC '16
Lin, Fardad, and Jovanovic, TAC '14

# Combination drug therapy

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




- Mutant $x_i$ mutates to $x_j$ at rate $A_{ji}$
- Drug $u_k$ kills $x_i$ at rate $(D_k)_{ii}$

Rantzer and Bernhardsson CDC '14
Jonsson, Rantzer, Matni, and Murray CDC '14

## Decentralized control of positive systems

**Decentralized control of positive systems**

- SDP formulation (Tanaka and Langbort, TAC '11)
- LP formulation (Rantzer '12, '15)

**Structured decentralized control**

- Combination drug therapy (Jonsson et al CDC '14)
- $\mathcal{L}_1$ control (Rantzer and Bernhardsson CDC '14)

  (Colaneri et al '14)

# Structured $\mathcal{H}_\infty$ control for positive systems

KYP Lemma

$$\begin{bmatrix} C^T C + (A + K(u))^T P + P(A + K(u)) & PB \\ B^T P & -\gamma^2 \end{bmatrix} \prec 0$$

# Structured $\mathcal{H}_\infty$ control for positive systems

KYP Lemma

$$\begin{bmatrix} C^TC + (A + K(u))^TP + P(A + K(u)) & PB \\ B^TP & -\gamma^2 \end{bmatrix} \prec 0$$

Convexity via $Y := K(u)P$

$$\begin{bmatrix} C^TC + AP + Y + PA + Y & PB \\ B^TP & -\gamma^2 \end{bmatrix} \prec 0$$

- Positive system → diagonal $P$ → sparsity structure preserved

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- Positive system $\rightarrow$ diagonal $P$ $\rightarrow$ sparsity structure preserved
- **General regularization still difficult**
    - need $YP^{-1} \in \text{Range}\{K\}$
    - box constraints on $u$ bilinear in $(P, Y)$, etc.

# Contributions

1. Convexity of the $\mathcal{H}_2$ and $\mathcal{H}_\infty$ norms over $u$ itself
   - Suitable for regularization
   - General linear function $K$

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   - Proximal gradient approach
   - Condition for continuously differentiable $\mathcal{H}_\infty$ norm

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2. Customized algorithms for optimal design
   - Proximal gradient approach
   - Condition for continuously differentiable $\mathcal{H}_\infty$ norm

3. Connections with applications
   - Leader selection in directed consensus networks
   - HIV combination drug therapy

## Convexity with respect to $u$

$$\begin{aligned} \dot{x} &= (A + K(u))\,x + B\,d \\ z &= Cx \end{aligned}$$

Output at time $t$ from initial condition $x_0$

$$z(t) = c^T e^{(A+K(u))t} x_0$$

- $z(t)$ convex in $u$ for any given $x_0$, $t$

(Colaneri et al '14)
(Rantzer and Bernhardsson '14)

## Convexity of $\mathcal{H}_2$ norm (Proposition 4)

$$\text{trace}\left(C X_c C^T\right)$$

where $A_{cl} := (A + K(u))$ and $X_c$ satisfies

$$A_{cl} X_c + X_c A_{cl}^T + B B^T = 0$$

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Use explicit expression for controllability gramian

$$= \text{trace}\left( C \int_0^\infty \mathrm{e}^{A_{cl} t} B B^T \mathrm{e}^{A_{cl}^T t} \mathrm{d}t \; C^T \right) = \int_0^\infty \| C \mathrm{e}^{A_{cl} t} B \|_F^2 \mathrm{d}t$$

$$= \int_0^\infty \sum_{ij} \left( c_i^T \, \mathrm{e}^{A_{cl} t} \, b_j \right)^2 \, \mathrm{d}t$$

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$$= \; \int_0^\infty \sum_{ij} \left( c_i^T \, \mathrm{e}^{A_{cl} t} \, b_j \right)^2 \; \mathrm{d}t$$

**Convexity over $u$**

- Linearity of $\sum$ and $\int$
- $(\cdot)^2$ nonincreasing for nonnegative argument

## Gradient of $\mathcal{H}_2$ norm (Proposition 5)

$$2K^{\dagger}(X_c X_o)$$

controllability and observablity gramians

$$\begin{aligned} 0 &= A_{cl} X_c + X_c A_{cl}^T + B B^T \\ 0 &= A_{cl}^T X_o + X_o A_{cl} + C^T C \end{aligned}$$

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- $K^\dagger$ is a weighted sum of diagonal elements of $X_c X_o$
- $X_c X_o$ used in balanced truncation
- $X_c, X_o$ nonnegative $\to$ $\mathcal{H}_2$ norm monotone in diagonal

## Convexity of $\mathcal{H}_\infty$ norm (Proposition 6)

$$\sup_{\omega} \; \bar{\sigma}\left( C \left( j\omega I - A_{cl} \right)^{-1} B \right)$$

Positive system $\rightarrow$ sup achieved at $\omega = 0$

$$= \; \bar{\sigma}\left( -C A_{cl}^{-1} B \right) \; = \; \bar{\sigma}\left( C \int_0^\infty \mathrm{e}^{A_{cl} t} \, \mathrm{d}t \; B \right)$$

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$$\sup_{\omega} \ \bar{\sigma}\left(C\left(j\omega I - A_{cl}\right)\right)^{-1} B\Big)$$

Positive system → sup achieved at $\omega = 0$

$$= \ \bar{\sigma}\left(-CA_{cl}^{-1}B\right) \ = \ \bar{\sigma}\left(C\int_0^\infty \mathrm{e}^{A_{cl}t}\,\mathrm{d}t\ B\right)$$

**Convexity over $u$**

- $\bar{\sigma}(M)$ nonincreasing in elements of argument for $M \geq 0$
- each element of $CA_{cl}^{-1}B$ nonnegative convex function of $u$

## Subgradient map of $\mathcal{H}_\infty$ norm (Proposition 7)

$$\sum_i \alpha_i \, K^\dagger \left( A_{cl}^{-1} B \, v_i w_i^T \, C A_{cl}^{-1} \right)$$

convex combination ($\alpha_i \in [0, 1]$, $\sum \alpha_i = 1$)

$$w_i^T (C A_{cl}^{-1} B) v_i \; = \; \bar{\sigma} \left( C A_{cl}^{-1} B \right)$$

$w_i, v_i$ left/right principal singular vectors

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$w_i, v_i$ left/right principal singular vectors

- monotone in diagonal
- may have nonunique principal singular vectors

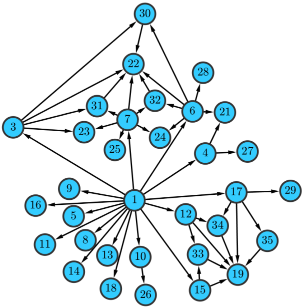
## Differentiability of $\mathcal{H}_\infty$ norm (Proposition 9)

$$\sum_i \alpha_i \, K^\dagger \left( A_{cl}^{-1} B \, v_i w_i^T \, C A_{cl}^{-1} \right)$$

- $\mathcal{H}_\infty$ norm typically nonsmooth
- $A$ strongly connected $\rightarrow$ continuous differentiability
    - $\rightarrow A^{-1}$ positive
    - $\rightarrow v_i, w_i$ unique (Perron thm)
    - subgradient is a gradient

# Example – HIV combination drug therapy

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




| | |
|---|---|
| Budget | $\sum u_k \leq T$ |
| Maximum dose | $u_k \leq T_k$ |
| $k$ requires $j$ | $u_k \leq u_j$ |
| Only $k$ or $j$ | $u_k + u_j \leq 1$ |

35 HIV mutants, 5 drugs

Model credit: Klein et al '12

# Combination drug therapy – Budget

Optimize performance subject to budget constraint

$$\begin{array}{rl} \text{minimize} & \|\cdot\|^2_{\mathcal{H}_2/\mathcal{H}_\infty} \\ \text{subject to} & \sum u_k \leq 1 \\ & u_k \geq 0 \end{array}$$

| **Antibody** | $u_{\mathcal{H}_2}$ | $u_{\mathcal{H}_\infty}$ |
|---|---|---|
| 3BC176 | 0.5952 | 0.9875 |
| PG16 | 0 | 0 |
| 45-46G54W | 0.2484 | 0.0125 |
| PGT128 | 0.1564 | 0 |
| 10-1074 | 0 | 0 |

| **Performance** | $u_{\mathcal{H}_2}$ | $u_{\mathcal{H}_\infty}$ |
|---|---|---|
| $\mathcal{H}_2$ | **0.6017** | 1.1947 |
| $\mathcal{H}_\infty$ | 0.1857 | **0.1084** |

# Combination drug therapy – Regularized

Quadratic and $\ell_1$ regularization

$$u_\lambda \;=\; \text{argmin} \quad \|\cdot\|^2_{\mathcal{H}_2/\mathcal{H}_\infty} \;+\; u^T u \;+\; \lambda \textstyle\sum_k w_k |u_k|$$

Increase $\lambda$ until desired sparsity and polish

$$\begin{array}{ll} \text{minimize} & \|\cdot\|_{\mathcal{H}_2/\mathcal{H}_\infty} \;+\; u^T u \\ \text{subject to} & \text{sp}(u) \;\in\; \text{sp}(u_\lambda) \end{array}$$

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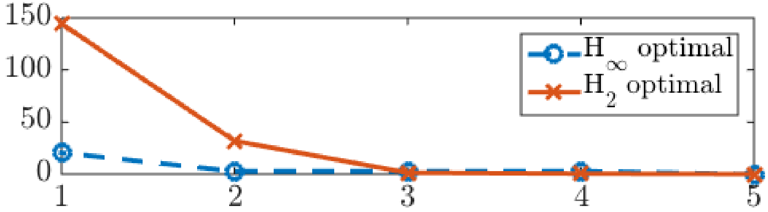


Figure: Percent $\mathcal{H}_2$ and $\mathcal{H}_\infty$ performance degradation vs number of drugs $N$

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