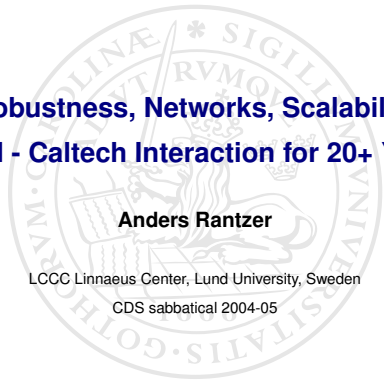


Robustness, Networks, Scalability Lund - Caltech Interaction for 20+ Years

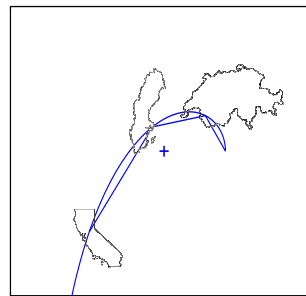
Anders Rantzer

LCCG Linnaeus Center, Lund University, Sweden

CDS sabbatical 2004-05

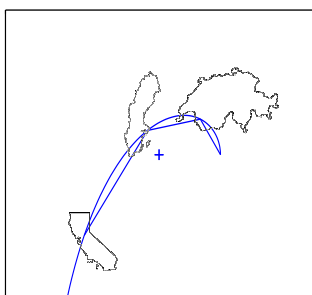


The μ -problem



Determine if $0 \notin \det(i\omega I - A - B\Delta C)$ for all $\Delta \in \mathbf{\Delta}, \omega \in \mathbb{R}$.

The Finite Argument Principle

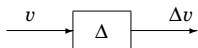


Check enough frequencies for polygons to encircle origin!

Outline

- From μ to IQCs and Beyond
- Positive and Monotone Systems
- HIV, Cancer and Beyond

Integral Quadratic Constraint

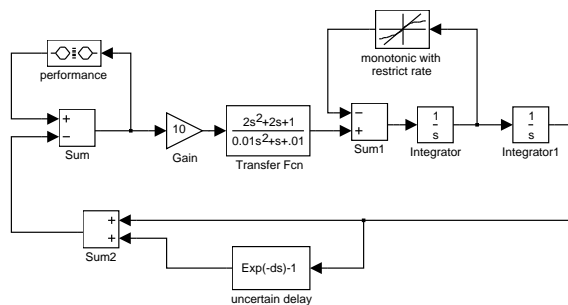


The (possibly nonlinear) operator Δ on $\mathbf{L}_2^m[0, \infty)$ is said to satisfy the IQC defined by Π if

$$\int_{-\infty}^{\infty} \begin{bmatrix} \widehat{v}(i\omega) \\ (\widehat{\Delta v})(i\omega) \end{bmatrix}^* \Pi(i\omega) \begin{bmatrix} \widehat{v}(i\omega) \\ (\widehat{\Delta v})(i\omega) \end{bmatrix} d\omega \geq 0$$

for all $v \in \mathbf{L}_2[0, \infty)$.

The IQC toolbox



S-procedure for IQC Analysis

Find $\tau_1, \dots, \tau_n \geq 0$ such that $\sigma_0(h) + \sum_k \tau_k \sigma_k(h)$ becomes negative semi-definite:

$$\begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \tau_1 \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \tau_2 \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix}$$

Positive Definite Decomposition

The sparse matrix on the left is positive semi-definite if and only if it can be written as a sum of positive semi-definite matrices with the structure on the right.

$$\begin{pmatrix} * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \end{pmatrix} = \begin{pmatrix} * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \end{pmatrix} + \begin{pmatrix} * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \end{pmatrix} + \dots + \begin{pmatrix} * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \\ * & * & * & * & * & * \end{pmatrix}$$

IQC Analysis with Decomposition

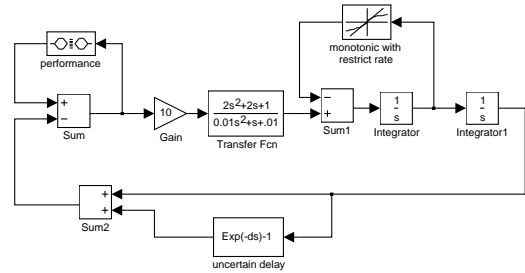
Find $\tau_1, \dots, \tau_n \geq 0$ such that $\sigma_0(h) + \sum_k \tau_k \sigma_k(h)$ has a negative semi-definite decomposition:

$$\begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \tau_1 \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \tau_2 \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} = \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix} + \begin{pmatrix} * & * & * \\ * & * & * \\ * & * & * \end{pmatrix}$$

Distributed certificates!

Scalable computations!

Distributed Verification of Large-Scale Systems



[Feron (2010)]: "The credible autocoder produces not only a target code that implements control-system specifications but also documents the target code with its properties and their proofs."

Outline

- o From μ to IQCs and Beyond
- **Positive and Monotone Systems**
- o HIV, Cancer and Beyond

Positive systems

A linear system is called *positive* if the state and output remain nonnegative as long as the initial state and the inputs are nonnegative:

$$\frac{dx}{dt} = Ax + Bu \quad y = Cx$$

Equivalently, A , B and C have nonnegative coefficients except for the diagonal of A .

Examples:

- ▶ Probabilistic models.
- ▶ Economic systems.
- ▶ Chemical reactions.
- ▶ Traffic Networks.

A Scalable Stability Test for Positive Systems



Stability of $\dot{x} = Ax$ follows from existence of $\xi_k > 0$ such that

$$\underbrace{\begin{bmatrix} a_{11} & a_{12} & 0 & a_{14} \\ a_{21} & a_{22} & a_{23} & 0 \\ 0 & a_{32} & a_{33} & a_{32} \\ a_{41} & 0 & a_{43} & a_{44} \end{bmatrix}}_A \begin{bmatrix} \xi_1 \\ \xi_2 \\ \xi_3 \\ \xi_4 \end{bmatrix} < \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

The first node verifies the inequality of the first row.

The second node verifies the inequality of the second row.

...

Verification is scalable!

A Distributed Search for Stabilizing Gains

Suppose $\begin{bmatrix} a_{11} - \ell_1 & a_{12} & 0 & a_{14} \\ a_{21} + \ell_1 & a_{22} - \ell_2 & a_{23} & 0 \\ 0 & a_{32} + \ell_2 & a_{33} & a_{32} \\ a_{41} & 0 & a_{43} & a_{44} \end{bmatrix} \geq 0$ for $\ell_1, \ell_2 \in [0, 1]$.

For stabilizing gains ℓ_1, ℓ_2 , find $0 < \mu_k < \xi_k$ such that

$$\begin{bmatrix} a_{11} & a_{12} & 0 & a_{14} \\ a_{21} & a_{22} & a_{23} & 0 \\ 0 & a_{32} & a_{33} & a_{32} \\ a_{41} & 0 & a_{43} & a_{44} \end{bmatrix} \begin{bmatrix} \xi_1 \\ \xi_2 \\ \xi_3 \\ \xi_4 \end{bmatrix} + \begin{bmatrix} -1 & 0 \\ 1 & -1 \\ 0 & 1 \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \mu_1 \\ \mu_2 \end{bmatrix} < \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

and set $\ell_1 = \mu_1/\xi_1$ and $\ell_2 = \mu_2/\xi_2$. Every row gives a local test.

Distributed synthesis by linear programming (gradient search).

Examples: Transportation Networks

- ▶ Cloud computing / server farms
- ▶ Heating and ventilation in buildings
- ▶ Traffic flow dynamics
- ▶ Production planning and logistics

Outline

- o From μ to IQCs and Beyond
- o Positive and Monotone Systems
- **HIV, Cancer and Beyond**

Combination Therapy is a Control Problem

Evolutionary dynamics:

$$\dot{x} = \left(A - \sum_i u_i D^i \right) x$$

Each state x_k is the concentration of a mutant. (There can be hundreds!) Each input u_i is a drug dosage.

A describes the mutation dynamics without drugs, while D^1, \dots, D^m are diagonal matrices modeling drug effects.

Determine $u_1, \dots, u_m \geq 0$ with $u_1 + \dots + u_m \leq 1$ such that x decays as fast as possible!

[Jonsson, Rantzer, Murray, ACC 2014]

Optimizing Decay Rate

Stability of the matrix $A - \sum_i u_i D^i + \gamma I$ is equivalent to existence of $\xi > 0$ with

$$\left(A - \sum_i u_i D^i + \gamma I \right) \xi < 0$$

For row k , this means

$$A_k \xi - \sum_i u_i D_k^i \xi_k + \gamma \xi_k < 0$$

or equivalently

$$\frac{A_k \xi}{\xi_k} - \sum_i u_i D_k^i + \gamma < 0$$

Maximizing γ is convex optimization in $(\log \xi_i, u_i, \gamma)$!

Using Measurements of Virus Concentrations

Evolutionary dynamics:

$$\dot{x}(t) = \left(A - \sum_i u_i(t) D^i \right) x(t)$$

Can we get faster decay using time-varying $u(t)$ based on measurements of $x(t)$?

Convex Monotone Systems

The system

$$\dot{x}(t) = f(x(t), u(t)), \quad x(0) = a$$

is a *monotone system* if its linearization is a positive system. It is a *convex monotone system* if every row of f is also convex.

Theorem. [Rantzer/ Bernhardsson (2014)]

For a convex monotone system $\dot{x} = f(x, u)$, each component of the trajectory $\phi_t(a, u)$ is a convex function of (a, u) .

Using Measurements of Virus Concentrations

The evolutionary dynamics can be written as a convex monotone system:

$$\frac{d}{dt} \log x_k(t) = \frac{A_k x(t)}{x_k(t)} - \sum_i u_i(t) D_k^i$$

Hence the decay of $\log x_k$ is a convex function of the input and optimal trajectories can be found even for large systems.

Example

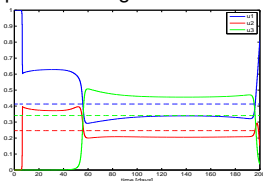
$$A = \begin{bmatrix} -\delta & \mu & \mu & 0 \\ \mu & -\delta & 0 & \mu \\ \mu & 0 & -\delta & \mu \\ 0 & \mu & \mu & -\delta \end{bmatrix}$$

clearance rate $\delta = 0.24 \text{ day}^{-1}$, mutation rate $\mu = 10^{-4} \text{ day}^{-1}$ and replication rates for viral variants and therapies as follows

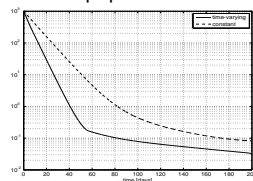
Variant	Therapy 1	Therapy 2	Therapy 3
Wild type (x_1)	$D_1^1 = 0.05$	$D_1^2 = 0.10$	$D_1^3 = 0.30$
Genotype 1 (x_2)	$D_2^1 = 0.25$	$D_2^2 = 0.05$	$D_2^3 = 0.30$
Genotype 2 (x_3)	$D_3^1 = 0.10$	$D_3^2 = 0.30$	$D_3^3 = 0.30$
HR type (x_4)	$D_4^1 = 0.30$	$D_4^2 = 0.30$	$D_4^3 = 0.15$

Example

Optimized drug doses:



Total virus population:



Thanks CDS — Open, Dynamic, Inspiring!

- ▶ Provably correct interconnected systems
- ▶ Large-scale control
- ▶ From Power Systems to HIV, Cancer and Back

