Robustness, Networks, Scalability
Lund - Caltech Interaction for 20+ Years
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The \( \mu \)-problem

Determine if
\[ 0 > \text{relation} \]
\[ \text{det}(i\omega I - A - B\Delta C) \]
for all \( \Delta \in \Delta, \omega \in \mathbb{R} \).

The Finite Argument Principle

Check enough frequencies for polygons to encircle origin!

Outline

• From \( \mu \) to IQCs and Beyond
  ○ Positive and Monotone Systems
  ○ HIV, Cancer and Beyond

Integral Quadratic Constraint

The (possibly nonlinear) operator \( \Delta \) on \( L^2_{\infty}[0, \infty) \) is said to satisfy the IQC defined by \( \Pi \) if
\[
\int_{-\infty}^{\infty} \left[ \frac{\hat{v}(i\omega)}{(\Delta v)(i\omega)} \right] \Pi(i\omega) \left[ \frac{\hat{v}(i\omega)}{(\Delta v)(i\omega)} \right] d\omega \geq 0
\]
for all \( v \in L^2_{\infty}[0, \infty) \).

S-procedure for IQC Analysis

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

The IQC toolbox

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.

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.
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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.

IQC Analysis with Decomposition

Find $r_1, \ldots, r_n \geq 0$ such that $\sigma_0(h) + \sum_k r_k \sigma_k(h)$ has a negative semi-definite decomposition:

$$
\begin{bmatrix}
  a_{00} & a_{01} & \cdots & a_{0n} \\
  a_{10} & a_{11} & \cdots & a_{1n} \\
  \vdots & \vdots & \ddots & \vdots \\
  a_{n0} & a_{n1} & \cdots & a_{nn}
\end{bmatrix}
\begin{bmatrix}
r_1 \\
r_2 \\
\vdots \\
r_n
\end{bmatrix} < 0
$$

Examples: Transportation Networks
- Cloud computing / server farms
- Heating and ventilation in buildings
- Traffic flow dynamics
- Production planning and logistics

A Scalable Stability Test for Positive Systems

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

$$
\begin{bmatrix}
a_{11} & a_{12} & 0 & a_{14} \\
a_{21} & a_{22} & a_{23} & a_{24} \\
0 & a_{32} & a_{33} & a_{34} \\
a_{41} & 0 & a_{43} & a_{44}
\end{bmatrix}
\begin{bmatrix}
\xi_1 \\
\xi_2 \\
\xi_3 \\
\xi_4
\end{bmatrix} < 0
$$

The first node verifies the inequality of the first row.
The second node verifies the inequality of the second row.

Verification is scalable!

Examples: Transportation Networks

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

Distributed Verification of Large-Scale Systems

$$\begin{array}{c}
\text{nodes} \\
\text{interconnections} \\
\text{verification}
\end{array}$$

[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.”

A Distributed Search for Stabilizing Gains

Suppose

$$
\begin{bmatrix}
a_{11} - \ell_1 & a_{12} & 0 & a_{14} \\
a_{21} + \ell_1 & a_{22} - \ell_2 & a_{23} & a_{24} \\
0 & a_{32} + \ell_2 & a_{33} & a_{34} \\
a_{41} & 0 & a_{43} & a_{44}
\end{bmatrix}
\begin{bmatrix}
\xi_1 \\
\xi_2 \\
\xi_3 \\
\xi_4
\end{bmatrix} \geq 0 \text{ for } \ell_1, \ell_2 \in [0, 1].
$$

For stabilizing gains $\ell_1, \ell_2$, find $0 < \mu_k < \xi_k$ such that

$$
\begin{bmatrix}
a_{11} & a_{12} & 0 & a_{14} \\
a_{21} & a_{22} & a_{23} & 0 \\
0 & a_{32} & a_{33} & a_{34} \\
a_{41} & 0 & a_{43} & a_{44}
\end{bmatrix}
\begin{bmatrix}
0 \\
\mu_1 \\
0 \\
\mu_2
\end{bmatrix} \leq 0
$$

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).

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**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 \((a, u)\).

**Example**

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

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

<table>
<thead>
<tr>
<th>Variant</th>
<th>Therapy 1</th>
<th>Therapy 2</th>
<th>Therapy 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild type ((x_1))</td>
<td>(D^1_1 = 0.05)</td>
<td>(D^2_1 = 0.10)</td>
<td>(D^3_1 = 0.30)</td>
</tr>
<tr>
<td>Genotype 1 ((x_2))</td>
<td>(D^1_2 = 0.25)</td>
<td>(D^2_2 = 0.05)</td>
<td>(D^3_2 = 0.30)</td>
</tr>
<tr>
<td>Genotype 2 ((x_3))</td>
<td>(D^1_3 = 0.10)</td>
<td>(D^2_3 = 0.30)</td>
<td>(D^3_3 = 0.30)</td>
</tr>
<tr>
<td>HR type ((x_4))</td>
<td>(D^1_4 = 0.30)</td>
<td>(D^2_4 = 0.30)</td>
<td>(D^3_4 = 0.15)</td>
</tr>
</tbody>
</table>

**Optimizing Decay Rate**

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

\[
(A - \sum_i u_i D^i + \gamma I)\xi < 0
\]

For row \( k \), this means

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

or equivalently

\[
A_k\xi - \sum_i u_i D_k^i + \gamma < 0
\]

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

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**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 \( x(t) \)?

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

\[ \frac{d}{dt} \log x_k(t) = \frac{A_k x(t)}{x_k(t)} - \sum_i u_i(t) D_{ki} \]

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**

Optimized drug doses:

![Optimized drug doses](image1)

Total virus population:

![Total virus population](image2)

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**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 \( D^1, \ldots, D^n \) are diagonal matrices modeling drug effects.

Determine \( u_1, \ldots, u_m \geq 0 \) with \( u_1 + \cdots + u_m \leq 1 \) such that \( x \) decays as fast as possible!

[Jonsson, Rantzer/Murray, ACC 2014]

**Example**

![Optimized drug doses](image1)

Total virus population:

![Total virus population](image2)

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**Thanks CDS — Open, Dynamic, Inspiring!**

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