Guaranteed nonlinear parameter bounding via interval analysis

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Context

- Vector $\mathbf{p}$ to be estimated from data
- Knowledge-based model $\rightarrow$ output nonlinear in $\mathbf{p}$

Classical approach

- Minimization of a cost function
- Explicit solution almost never available
- Iterative local optimization $\rightarrow$ no guarantee as to results

Need for guaranteed alternatives

Message

Interval analysis allows guaranteed results to be obtained.

$\Downarrow$

considerable advantage over usual numerical methods

Basic concepts of interval analysis

Interval

$$[x] = \{x \in \mathbb{R} \mid \underline{x} \leqslant x \leqslant \overline{x}\}$$

Width

$$w([x]) = \overline{x} - \underline{x}$$

Midpoint

$$\mathrm{mid}([x]) = \frac{\underline{x} + \overline{x}}{2}$$

Intervals have a dual nature:

- *sets* $\Rightarrow$ set-theoretic operations apply
- *pairs of real numbers* $\Rightarrow$ an arithmetic can be built

Operations on intervals

$$[x] + [y] = [\underline{x} + \underline{y}, \overline{x} + \overline{y}]$$

$$[x] - [y] = [\underline{x} - \overline{y}, \overline{x} - \underline{y}]$$

$$[x] \cdot [y] = [\min\{\underline{x}\underline{y}, \underline{x}\overline{y}, \overline{x}\underline{y}, \overline{x}\overline{y}\}, \max\{\underline{x}\underline{y}, \underline{x}\overline{y}, \overline{x}\underline{y}, \overline{x}\overline{y}\}]$$

If $0 \notin [y]$ then

$$[x]/[y] = [x] \cdot [1/\overline{y}, 1/\underline{y}]$$

(Specific formulas available for division by interval containing zero)

Interval counterpart $[f]^*$ of f from $\mathbb{R}$ to $\mathbb{R}$ satisfies

$$[f]^*([x]) = [\{f(x) \mid x \in [x]\}]$$

For any continuous function, $[f]^*([x])$ is the image set $f([x])$

Elementary interval functions expressed in terms of bounds

For instance

$$[\exp]^*([x]) = [\exp(\underline{x}), \exp(\overline{x})]$$

Specific algorithms for

- trigonometric functions
- hyperbolic functions

Interval vector (or *box*) is a Cartesian product of intervals

$$[\mathbf{x}] = [x_1] \times [x_2] \times \cdots \times [x_n] \text{ or } [\mathbf{x}] = ([x_1], [x_2], \ldots, [x_n])^{\mathrm{T}}$$

$$= \text{axis-aligned parallelepiped}$$

Lower bound

$$\underline{\mathbf{x}} = (\underline{x}_1, \underline{x}_2, \cdots, \underline{x}_n)^{\mathrm{T}}$$

Upper bound

$$\overline{\mathbf{x}} = (\overline{x}_1, \overline{x}_2, \cdots, \overline{x}_n)^{\mathrm{T}}$$

Width

$$w([\mathbf{x}]) = \max_{1 \leqslant i \leqslant n} w([x_i])$$

Midpoint

$$\mathrm{mid}([\mathbf{x}]) = (\mathrm{mid}([x_1]), \ldots, \mathrm{mid}([x_n]))^{\mathrm{T}}$$

Classical operations on vectors trivially extend to *interval vectors*

$$\alpha[\mathbf{x}] = (\alpha[x_1]) \times \cdots \times (\alpha[x_n])$$
$$[\mathbf{x}]^{\mathrm{T}} \cdot [\mathbf{y}] = [x_1] \cdot [y_1] + \cdots + [x_n] \cdot [y_n]$$
$$[\mathbf{x}] + [\mathbf{y}] = ([x_1] + [y_1]) \times \cdots \times ([x_n] + [y_n])$$

and *interval matrices*

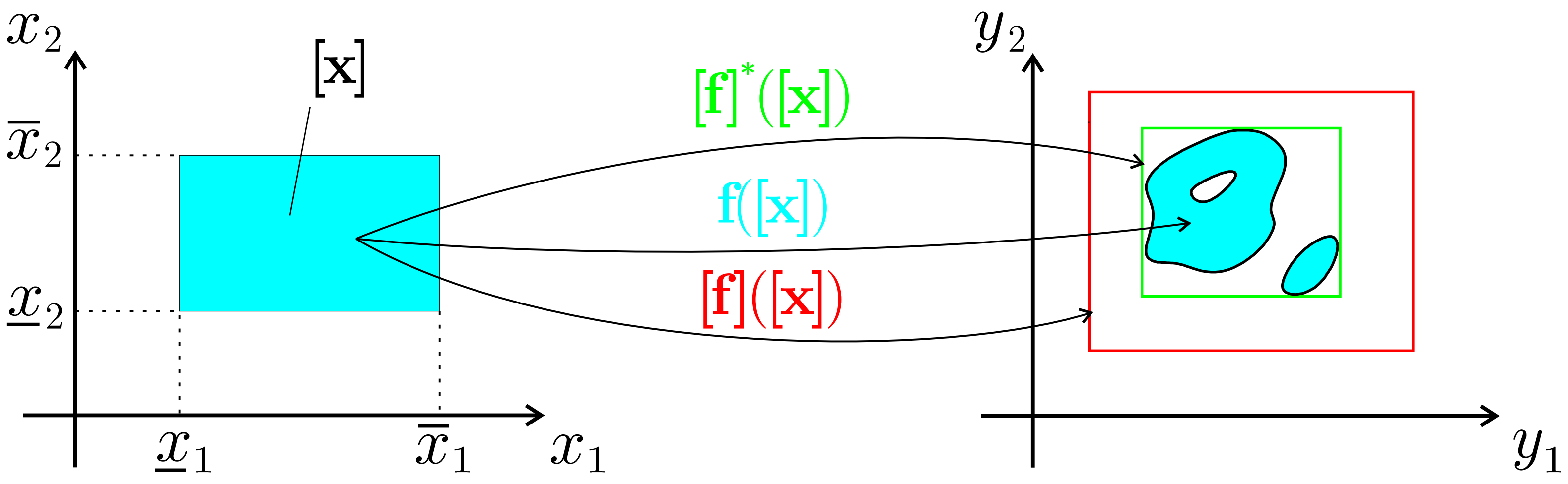
Inclusion functions

$[\mathbf{f}]$ an *inclusion function* for $\mathbf{f}$ if

$$\forall [\mathbf{x}] \in \mathbb{IR}^n, \quad \mathbf{f}([\mathbf{x}]) \subset [\mathbf{f}]([\mathbf{x}])$$

$\mathbf{f}$ may be defined by an algorithm or even by a differential equation

Infinitely many inclusion functions for the same function


x_2
$[\mathbf{x}]$
$\overline{x}_2$
$\underline{x}_2$
$\underline{x}_1$
$\overline{x}_1$
x_1
$[\mathbf{f}]^*([\mathbf{x}])$
$\mathbf{f}([\mathbf{x}])$
$[\mathbf{f}]([\mathbf{x}])$
y_2
y_1

$[\mathbf{f}]$ is

convergent if, for any sequence of boxes $[\mathbf{x}]_k$,

$$\lim_{k\to\infty} w([\mathbf{x}]_k) = 0 \Rightarrow \lim_{k\to\infty} w([\mathbf{f}]([\mathbf{x}]_k)) = 0$$

minimal if $[\mathbf{f}]\,([\mathbf{x}])$ is the smallest box that contains $\mathbf{f}\,([\mathbf{x}])$

inclusion monotonic if

$$[\mathbf{x}] \subset [\mathbf{y}] \Rightarrow [\mathbf{f}]([\mathbf{x}]) \subset [\mathbf{f}]([\mathbf{y}])$$

Construction of inclusion functions for $\mathbf{f}$

cast into that of inclusion functions for coordinate functions f_i

$\Rightarrow$ only inclusion functions for $f : \mathbb{R}^n \to \mathbb{R}$ need be considered

First idea that comes to mind = compute *infimum* and *supremum* of f over box $[\mathbf{x}]$ of interest

$\Rightarrow$ two global optimizations, usually intractable

Assume f expressed as composition of

- operators $+, -, \cdot, /$
- elementary functions $\sin, \cos, \exp$, sqrt...

$[f]$ obtained by replacing

- each x_i by $[x_i]$
- each operator or elementary function by interval counterpart

is the *natural inclusion function* of f

(convergent and inclusion monotonic)

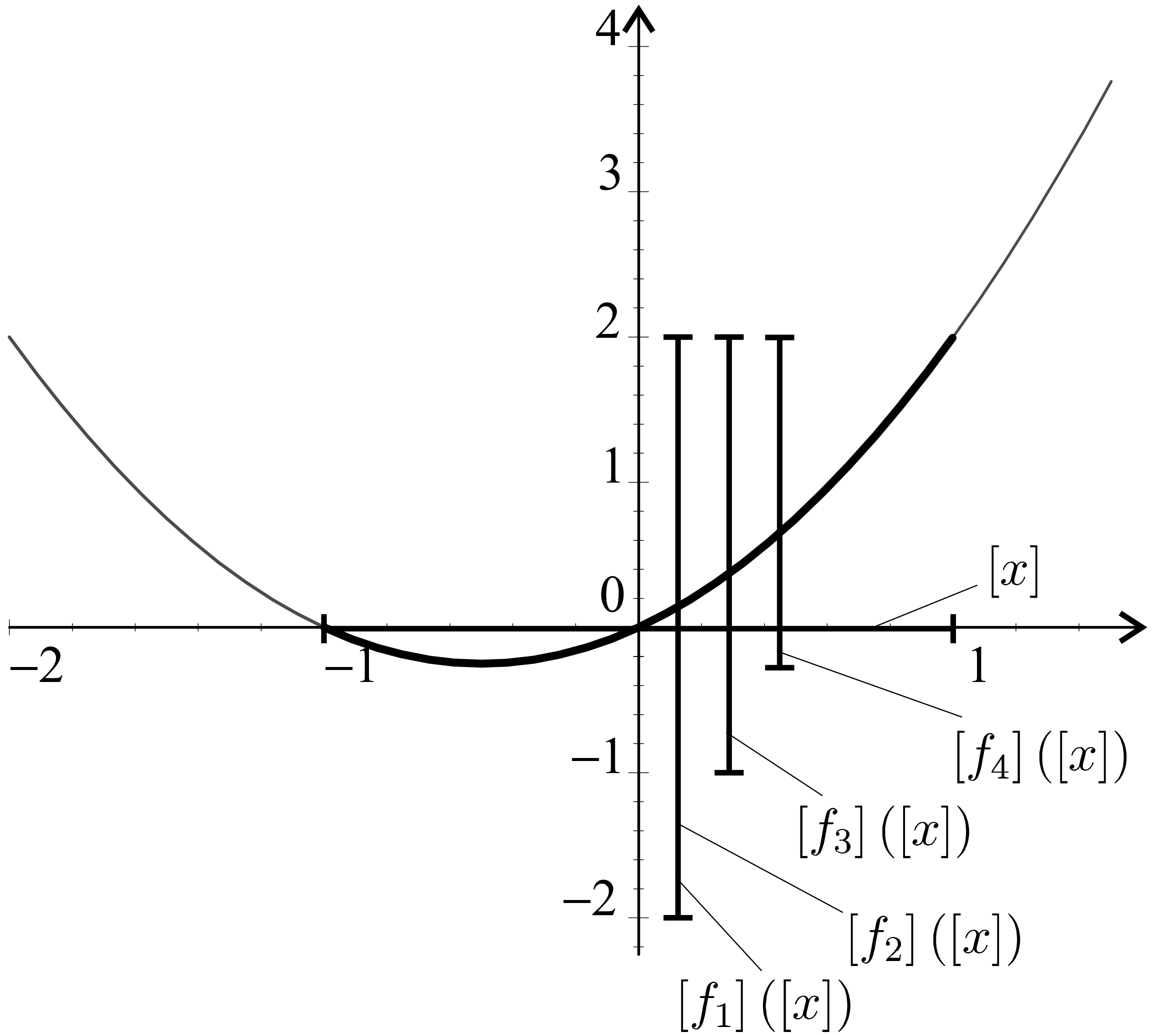
Example

Four formal expressions of the same function

$$f_1(x) = x(x+1), \qquad f_3(x) = x^2 + x,$$
$$f_2(x) = x \times x + x, \quad f_4(x) = (x + \tfrac{1}{2})^2 - \tfrac{1}{4}.$$

On $[x] = [-1, 1]$,

$$\begin{aligned}
[f_1]([x]) &= [x]([x]+1) = [-2, 2]\,, \\
[f_2]([x]) &= [x] \times [x] + [x] = [-2, 2]\,, \\
[f_3]([x]) &= [x]^2 + [x] = [-1, 2]\,, \\
[f_4]([x]) &= \left([x] + \tfrac{1}{2}\right)^2 - \tfrac{1}{4} = \left[-\tfrac{1}{4}, 2\right].
\end{aligned}$$


4
3
2
1
0
−1
−2
−2
−1
1
[x]
[f_4] ([x])
[f_3] ([x])
[f_2] ([x])
[f_1] ([x])

Why?

In $[f_1]([x]) = [x]([x]+1)$,

two occurences of $[x]$ treated as if independent.

a major source of pessimism

($[x] - [x]$ not equal to $[0, 0]$, unless $[x]$ degenerate!)

Multiplication no longer distributive with respect to addition. Instead

$$[x] \cdot ([y] + [z]) \subset [x] \cdot [y] + [x] \cdot [z]$$

known as *subdistributivity* $\Longrightarrow$ factorize as much as possible

Many other types of inclusion function

If f differentiable over $[\mathbf{x}]$, mean-value theorem implies

$$\forall \mathbf{x} \in [\mathbf{x}], \exists \mathbf{z} \in [\mathbf{x}] \text{ such that } f(\mathbf{x}) = f(\mathbf{m}) + \mathbf{g}^{\mathrm{T}}(\mathbf{z}) \cdot (\mathbf{x} - \mathbf{m})$$

with $\mathbf{g}$ the gradient of f and $\mathbf{m}$ the midpoint of $[\mathbf{x}]$

Thus,

$$\forall \mathbf{x} \in [\mathbf{x}], f(\mathbf{x}) \in f(\mathbf{m}) + [\mathbf{g}^{\mathrm{T}}]([\mathbf{x}]) \cdot (\mathbf{x} - \mathbf{m})$$

so

$$f([\mathbf{x}]) \subset f(\mathbf{m}) + [\mathbf{g}^{\mathrm{T}}]([\mathbf{x}]) \cdot ([\mathbf{x}] - \mathbf{m})$$

Yields the *centered inclusion function* for f

$$[f_{\mathrm{c}}]([\mathbf{x}]) = f(\mathbf{m}) + [\mathbf{g}^{\mathrm{T}}]([\mathbf{x}]) \cdot ([\mathbf{x}] - \mathbf{m})$$

For

$$f(x) = x^2 \exp(x) - x \exp\left(x^2\right)$$

compare

$[x]$	$f([x])$	$[f]([x])$	$[f]_c([x])$
$[0.5, 1.5]$	$[-4.148, 0]$	$[-13.82, 9.44]$	$[-25.07, 25.07]$
$[0.9, 1.1]$	$[-0.05380, 0]$	$[-1.697, 1.612]$	$[-0.5050, 0.5050]$
$[0.99, 1.01]$	$[-0.0004192, 0]$	$[-0.1636, 0.1628]$	$[-0.004656, 0.004656]$

Centered inclusion function

especially interesting when width of $[\mathbf{x}]$ is small.

Subpavings

Intervals and boxes not general enough

to describe all sets $\mathbb{S}$ of interest

$\Downarrow$

Motivates the introduction of subpavings

Subpaving of $[\mathbf{x}]$ = union of nonoverlapping subboxes of $[\mathbf{x}]$

If subpavings $\underline{\mathbb{S}}$ and $\overline{\mathbb{S}}$ such that

$$\underline{\mathbb{S}} \subset \mathbb{S} \subset \overline{\mathbb{S}}$$

then $\mathbb{S}$ bracketed between inner and outer approximations

Distance between $\underline{\mathbb{S}}$ and $\overline{\mathbb{S}}$ indicative of quality of approximation of $\mathbb{S}$

Computation on subpavings

- allows approximate computation on compact sets
- basic ingredient of estimation algorithms to be presented

Contractors

Consider a vector $\mathbf{x}$ of variables linked by relations (or constraints)

$$\mathbf{f}(\mathbf{x}) = \mathbf{0} \tag{1}$$

Assume prior domain for $\mathbf{x}$ is

$$[\mathbf{x}] = [x_1] \times \cdots \times [x_n]$$

Solving (1) for $\mathbf{x}$ in $[\mathbf{x}]$ is a *constraint satisfaction problem* (CSP)

Solution of CSP is

$$\mathbb{S} = \{\mathbf{x} \in [\mathbf{x}] \mid \mathbf{f}(\mathbf{x}) = \mathbf{0}\}$$

Inequality constraints dealt with via *slack variables*

Looking for $\mathbb{S}$ is an NP-complete problem

Contractors

- reduce size of prior domain without loosing solutions
- escape the curse of dimensionality

Interval Newton contractor:

If $\mathbf{f}$ once differentiable, mean-value theorem implies

$$\forall \mathbf{x} \in [\mathbf{x}], \exists \mathbf{z} \in [\mathbf{x}] \mid \mathbf{f}(\mathbf{x}) = \mathbf{f}(\mathbf{m}) + \mathbf{J_f}(\mathbf{z}) \cdot (\mathbf{x} - \mathbf{m}) \tag{2}$$

with $\mathbf{J_f}$ the Jacobian matrix of $\mathbf{f}$ and $\mathbf{m}$ the midpoint of $[\mathbf{x}]$.

Assume

- $\widehat{\mathbf{x}} \in [\mathbf{x}]$ a solution, so $\mathbf{f}(\widehat{\mathbf{x}}) = \mathbf{0}$
- $\mathbf{J_f}$ invertible

then (2) implies

$$\widehat{\mathbf{x}} = \mathbf{m} - \mathbf{J_f}^{-1}(\mathbf{z}) \cdot \mathbf{f}(\mathbf{m})$$

Now

$$\widehat{\mathbf{x}} = \mathbf{m} - \mathbf{J}_{\mathbf{f}}^{-1}(\mathbf{z}) \cdot \mathbf{f}(\mathbf{m})$$

implies

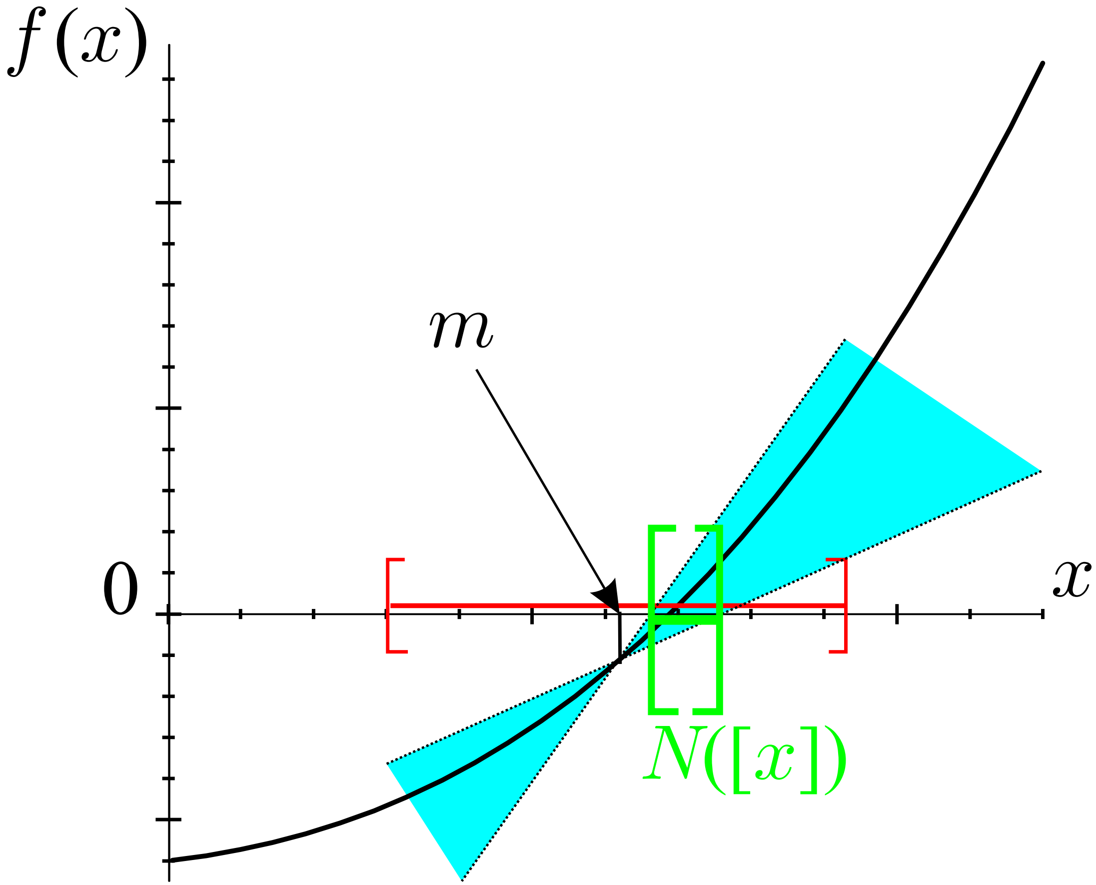
$$\widehat{\mathbf{x}} \in \mathbf{m} - \mathbf{J}_{\mathbf{f}}^{-1}([\mathbf{x}]) \cdot \mathbf{f}(\mathbf{m}) \equiv \mathbf{N}([\mathbf{x}])$$

Since $\widehat{\mathbf{x}}$ also assumed to belong to $[\mathbf{x}]$, it must belong to

$$[\mathbf{x}_{\mathrm{r}}] = [\mathbf{x}] \cap \mathbf{N}([\mathbf{x}])$$

Interval Newton contractor thus replaces $[\mathbf{x}]$ by $[\mathbf{x}_{\mathrm{r}}]$

$[\mathbf{x}_{\mathrm{r}}]$ may be much smaller (or even empty)



$\mathbf{J_f}$ is invertible

Assumption that $\mathbf{J_f}([\mathbf{x}])$ is invertible can be dropped:

Compute outer approximation of set of all solutions for $\widehat{\mathbf{x}}$ of

$$\mathbf{f}(\mathbf{m}) + \mathbf{J_f}([\mathbf{x}]) \cdot (\widehat{\mathbf{x}} - \mathbf{m}) = \mathbf{0}$$

a *linear* system of equations

Specific methods involving *preconditioning*

Basic tools for parameter bounding

- Set inversion
- Guaranteed integration

Set inversion

Let

- $\mathbf{f}$ be a possibly nonlinear function from $\mathbb{R}^{n_\mathrm{p}}$ to $\mathbb{R}^{n_\mathrm{y}}$
- $\mathbb{Y}$ be a subpaving of $\mathbb{R}^{n_\mathrm{y}}$

Set inversion is the characterization of the reciprocal image of $\mathbb{Y}$

$$\mathbb{S} = \{\mathbf{p} \in \mathbb{R}^{n_\mathrm{p}} \mid \mathbf{f}(\mathbf{p}) \in \mathbb{Y}\} = \mathbf{f}^{-1}(\mathbb{Y})$$

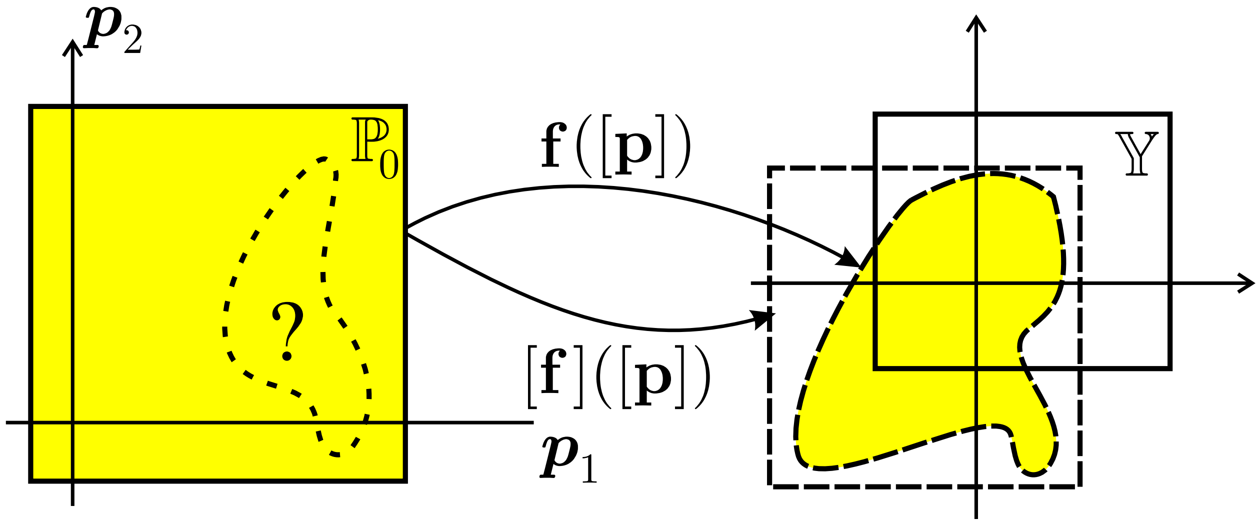
Using

- an inclusion function $[\mathbf{f}]$ for $\mathbf{f}$,
- a (possibly very large) search box $[\mathbf{p}]_0$

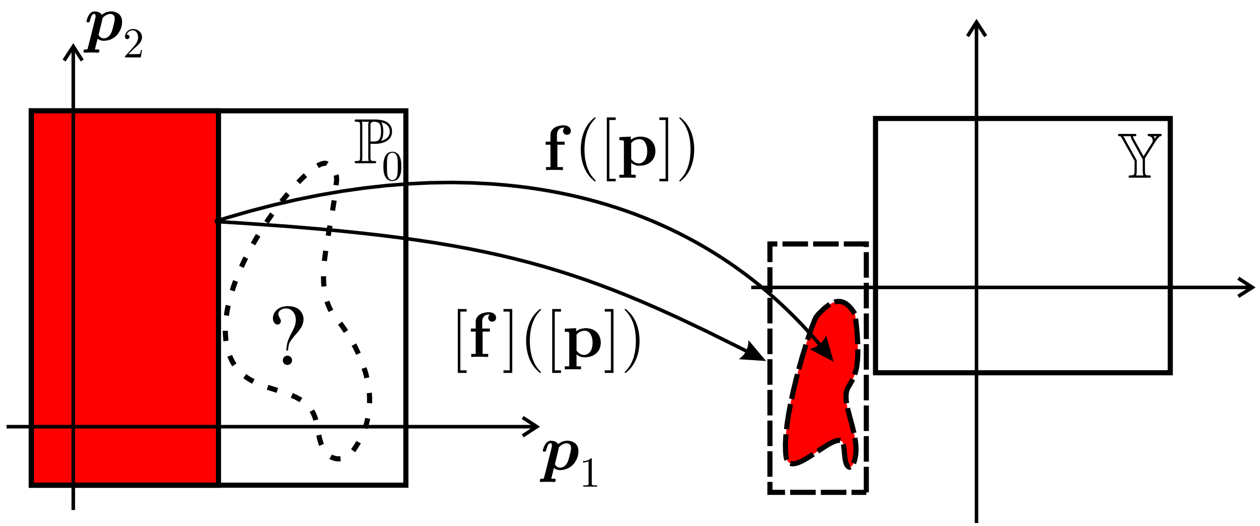
SIVIA, for *Set Inverter Via Interval Analysis*, computes subpavings $\underline{\mathbb{S}}$ and $\overline{\mathbb{S}}$ such that

$$\underline{\mathbb{S}} \subset \mathbb{S} \subset \overline{\mathbb{S}}$$

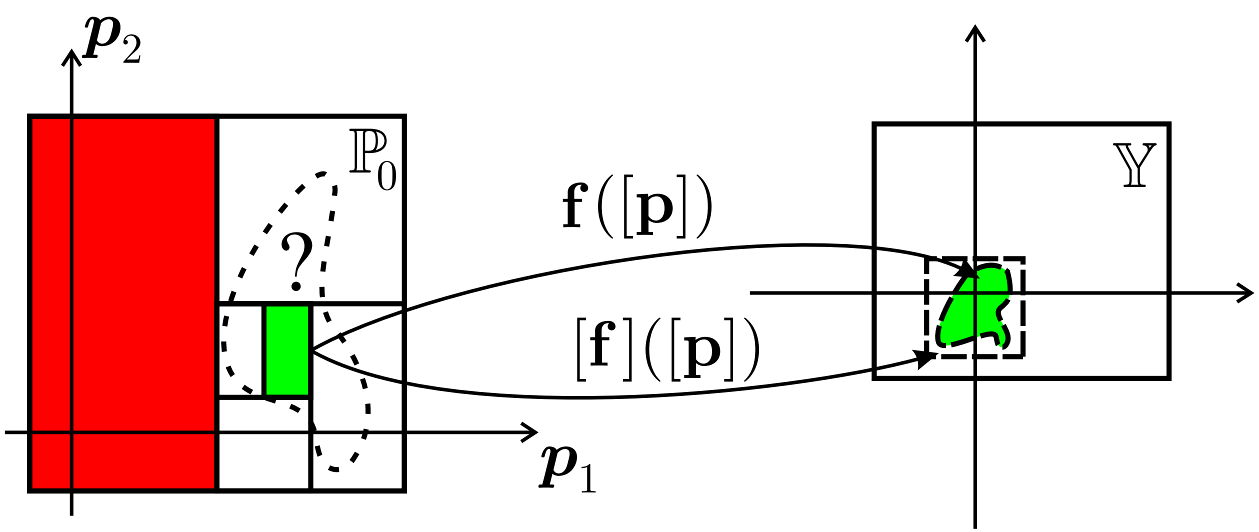
by successive bisections and selections



Yellow box is *undetermined*



Red box proven to be outside $\mathbb{S}$



Green box proven to be inside $\mathbb{S}$

Algorithm Sivia(in: $\mathbf{f}, \mathbb{Y}, [\mathbf{p}], \varepsilon$; inout: $\underline{\mathbb{S}}, \overline{\mathbb{S}}$)

```
if [f]([p]) ∩ 𝕐 = ∅ return;
if [f]([p]) ⊂ 𝕐 then
{S̲ := S̲ ∪ [p]; S̄ := S̄ ∪ [p]; return;};
if w([p]) < ε then {S̄ := S̄ ∪ [p]; return;};
Sivia(f, 𝕐, L[p], ε, S̲, S̄);
    Sivia(f, 𝕐, R[p], ε, S̲, S̄).
```

All boxes in *uncertainty layer* $\Delta\mathbb{S}$ between $\underline{\mathbb{S}}$ and $\overline{\mathbb{S}}$ have a width smaller than ε

Guaranteed numerical integration

Assume model of interest is the ODE

$$\mathbf{x}' = \mathbf{g}\left(\mathbf{x}, \mathbf{p}, t\right), \text{ with } \mathbf{x}\left(0\right) = \mathbf{x}_0\left(\mathbf{p}\right) \tag{3}$$

where $\mathbf{p}$ only known to belong to $[\mathbf{p}]$

Let $\mathbf{f}\left(\mathbf{p}, t\right)$ be the solution of (3) for a given $\mathbf{p} \in [\mathbf{p}]$

Guaranteed integrator computes a set containing $\mathbf{f}\left([\mathbf{p}], t\right)$

Guaranteed integrators based on interval analysis readily available, *e.g.*, AWA, COSY or VNODE

Well suited when $[\mathbf{p}]$ a degenerate box with zero width

For large boxes, as needed in the context of parameter estimation, enclosure for $\mathbf{f}([\mathbf{p}], t)$ may become *very* pessimistic

Solution: bound (if possible) model between *cooperative systems*

The dynamical system

$$\mathbf{x}' = \frac{\mathrm{d}\mathbf{x}}{\mathrm{d}t} = \mathbf{g}\left(\mathbf{x}, t\right)$$

where $\mathbf{x} \in \mathcal{D} \subset \mathbb{R}^n$, is *cooperative* over $\mathcal{D}$ if

$$\frac{\partial g_i\left(\mathbf{x}, t\right)}{\partial x_j} \geqslant 0 \text{ for all } i \neq j,\ t \geqslant 0 \text{ and } \mathbf{x} \in \mathcal{D}$$

If there exists a pair of cooperative systems

$$\underline{\mathbf{x}}' = \underline{\mathbf{g}}\left(\underline{\mathbf{x}}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right) \text{ and } \bar{\mathbf{x}}' = \overline{\mathbf{g}}\left(\overline{\mathbf{x}}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right)$$

satisfying

$$\underline{\mathbf{g}}\left(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right) \leqslant \mathbf{g}\left(\mathbf{x}, \mathbf{p}, t\right) \leqslant \overline{\mathbf{g}}\left(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right)$$

for all $\mathbf{p} \in \left[\underline{\mathbf{p}}, \overline{\mathbf{p}}\right]$, $t \geqslant 0$ and $\mathbf{x} \in \mathcal{D}$, and if

$$\underline{\mathbf{x}}_0\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}\right) \leqslant \mathbf{x}_0\left(\mathbf{p}\right) \leqslant \overline{\mathbf{x}}_0\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}\right)$$

for all $\mathbf{p} \in \left[\underline{\mathbf{p}}, \overline{\mathbf{p}}\right]$, then

$$\underline{\mathbf{x}}\left(t\right) \leqslant \mathbf{x}\left(t\right) \leqslant \overline{\mathbf{x}}\left(t\right), \text{ for all } t \geqslant 0$$

In theorem, $\underline{\mathbf{x}}(t)$ is the flow $\underline{\varphi}(\underline{\mathbf{p}}, \overline{\mathbf{p}}, t)$ associated with

$$\left\{\underline{\mathbf{x}}' = \underline{\mathbf{g}}\left(\underline{\mathbf{x}}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right), \underline{\mathbf{x}}(0) = \underline{\mathbf{x}}_0\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}\right)\right\}$$

and $\overline{\mathbf{x}}(t)$ the flow $\overline{\varphi}(\underline{\mathbf{p}}, \overline{\mathbf{p}}, t)$ associated with

$$\left\{\overline{\mathbf{x}}' = \overline{\mathbf{g}}\left(\overline{\mathbf{x}}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right), \overline{\mathbf{x}}(0) = \overline{\mathbf{x}}_0\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}\right)\right\}$$

Box-valued function

$$[\varphi]\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right) = \left[\underline{\varphi}\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right), \overline{\varphi}\left(\underline{\mathbf{p}}, \overline{\mathbf{p}}, t\right)\right]$$

thus an inclusion function for solution of ODE

Application to nonlinear parameter bounding

We look for the *set* of all parameter vectors that are consistent with

- experimental data
- model structure
- error bounds

Experimental datum $y(t_i)$ corresponds to a known interval $[\underline{e}_i, \overline{e}_i]$ of acceptable errors

$$\mathbf{p} \in [\mathbf{p}]_0 \text{ } \textit{acceptable} \text{ if}$$

$$\underline{e}_i \leqslant y(t_i) - y_{\mathrm{m}}(\mathbf{p}, t_i) \leqslant \overline{e}_i \text{ for all } i = 1, \ldots, n_{\mathrm{y}}$$

Parameter estimation then amounts to characterizing

$$\begin{aligned} \mathbb{S} &= \{\mathbf{p} \in [\mathbf{p}]_0 \mid \mathbf{p} \text{ is acceptable}\} \\ &= \{\mathbf{p} \in [\mathbf{p}]_0 \mid \mathbf{y}_{\mathrm{m}}(\mathbf{p}) \in [\mathbf{y}]\}, \end{aligned}$$

with

$$\begin{aligned} [\mathbf{y}] &= [y(t_1) - \overline{e}_1, y(t_1) - \underline{e}_1] \times \\ &\quad \cdots \times [y(t_{n_{\mathrm{y}}}) - \overline{e}_{n_{\mathrm{y}}}, y(t_{n_{\mathrm{y}}}) - \underline{e}_{n_{\mathrm{y}}}] \end{aligned}$$

and

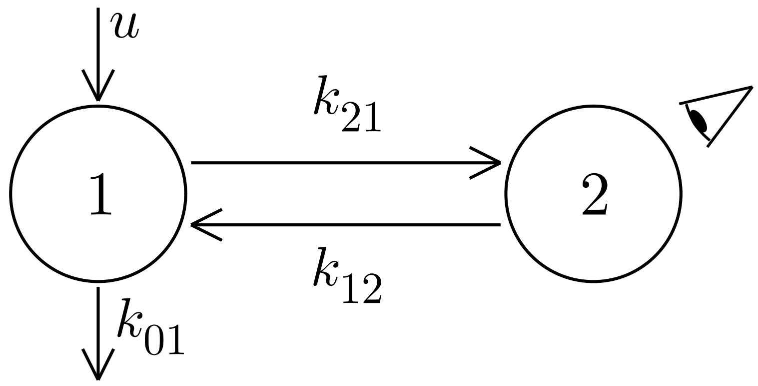
$$\mathbf{y}_{\mathrm{m}}(\mathbf{p}) = \left(y_{\mathrm{m}}(\mathbf{p}, t_1), \ldots, y_{\mathrm{m}}(\mathbf{p}, t_{n_{\mathrm{y}}})\right)^{\mathrm{T}}$$

Guaranteed enclosure of $\mathbb{S}$ obtained with SIVIA

Two approaches to be considered

- via a closed-form expression for $y_{\mathrm{m}}(\mathbf{p}, t_i)$
- via guaranteed numerical integration

illustrated on the same compartmental model



Two-compartment model

State equations readily obtained from conservation law as

$$\mathbf{x}' = \mathbf{g}\left(\mathbf{x}, \mathbf{p}, u\right)$$

where

$$\mathbf{p} = \left(k_{01}, k_{12}, k_{21}\right)^{\mathrm{T}}$$

and

$$\mathbf{g}\left(\mathbf{x}, \mathbf{p}, u\right) = \begin{pmatrix} -\left(k_{21} + k_{01}\right) x_1 + k_{12} x_2 + u \\ k_{21} x_1 - k_{12} x_2 \end{pmatrix}$$

Quantity x_2 of material in Compartment 2 is observed, so

$$y_{\mathrm{m}}(\mathbf{p}, t_i) = x_2(\mathbf{p}, t_i), \; i = 1, ..., n_{\mathrm{y}}$$

No input ($u \equiv 0$) and initial condition is $\mathbf{x}_0 = (1, 0)^{\mathrm{T}}$

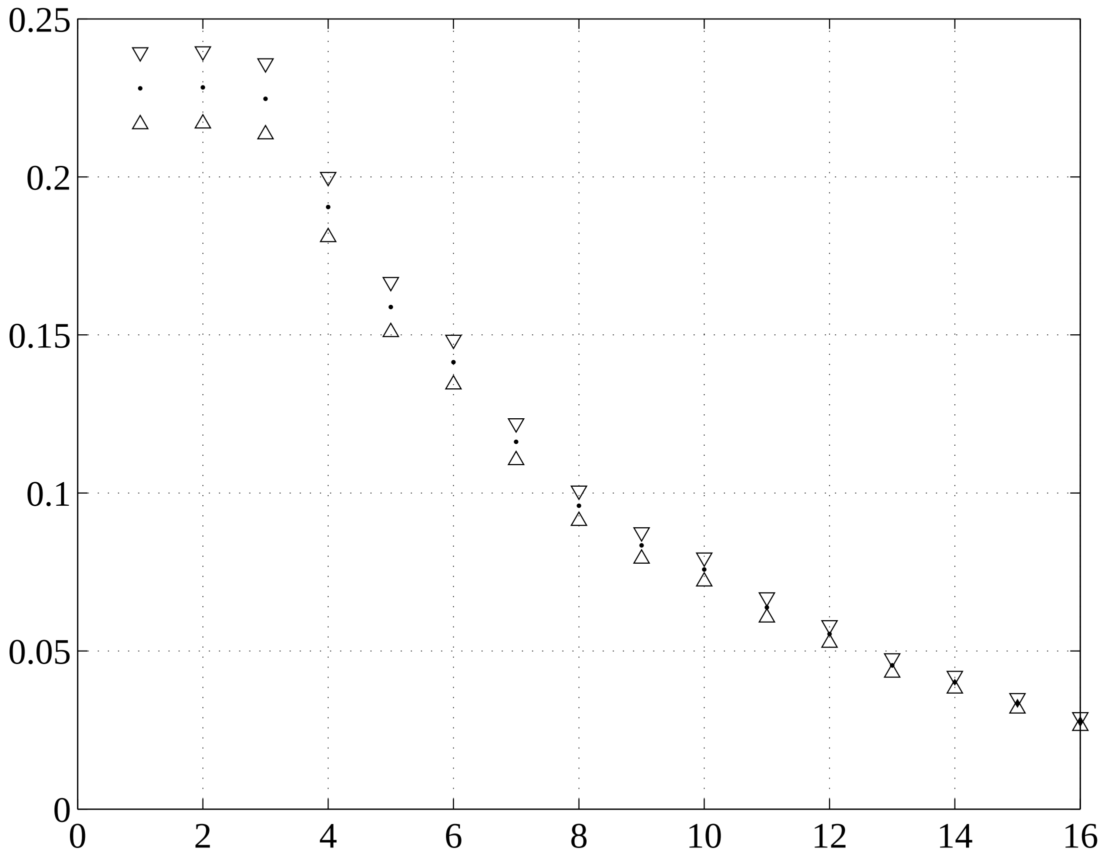
Then,

$$y_{\mathrm{m}}(\mathbf{p}, t_i) = \alpha(\mathbf{p}) \left(\mathrm{e}^{\lambda_1(\mathbf{p}) t_i} - \mathrm{e}^{\lambda_2(\mathbf{p}) t_i} \right)$$

where

$$\begin{aligned} \alpha(\mathbf{p}) &= \frac{k_{21}}{\sqrt{(k_{01} - k_{12} + k_{21})^2 + 4k_{12}k_{21}}} \\ \lambda_{1,2}(\mathbf{p}) &= -\frac{1}{2} [(k_{01} + k_{12} + k_{21}) \\ &\quad \pm ((k_{01} - k_{12} + k_{21})^2 + 4k_{12}k_{21})^{1/2}] \end{aligned}$$

Parameter bounding using a closed-form expression



Interval data (true system is linear)

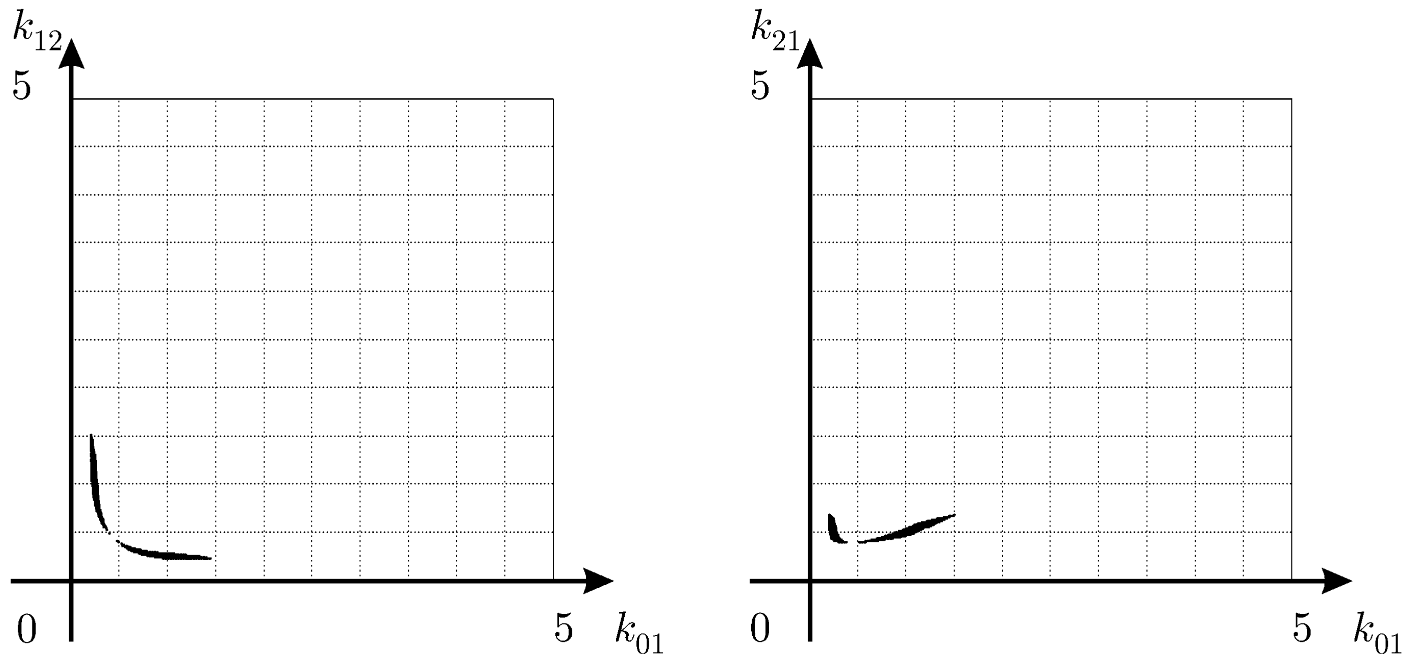
Using SIVIA in $[\mathbf{p}]_0 = [0,5]^{\times 3}$ leads to

ε	0.005	0.0025	0.00125
Comput. time (s)	9	14	24
Volume of $\overline{\mathbb{S}}$	$1.7 \cdot 10^{-3}$	$4 \cdot 10^{-4}$	$1.2 \cdot 10^{-4}$

Table 1: Results using a closed-form expression

Computations on Athlon 1800+

Projections of $\overline{\mathbb{S}}$ using a closed-form expression with $\varepsilon = 0.0025$



A consequence of lack of global identifiability

Parameter bounding using guaranteed integration

Closed-form expression for $y_{\mathrm{m}}(\mathbf{p}, t_i)$ no longer needed

For any $[\mathbf{p}] = [\underline{\mathbf{p}}, \overline{\mathbf{p}}]$ such that $\underline{\mathbf{p}} \geqslant \mathbf{0}$,

$\mathbf{g}(\mathbf{x}, \mathbf{p}, u)$ enclosed between

$$\underline{\mathbf{g}}(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, u) = \begin{pmatrix} -\left(\overline{k}_{21} + \overline{k}_{01}\right) x_1 + \underline{k}_{12} x_2 + u \\ \underline{k}_{21} x_1 - \overline{k}_{12} x_2 \end{pmatrix}$$

and

$$\overline{\mathbf{g}}(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, u) = \begin{pmatrix} -\left(\underline{k}_{21} + \underline{k}_{01}\right) x_1 + \overline{k}_{12} x_2 + u \\ \overline{k}_{21} x_1 - \underline{k}_{12} x_2 \end{pmatrix}$$

Since

$$\mathbf{x}' = \underline{\mathbf{g}}\left(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, u\right)$$

and

$$\mathbf{x}' = \overline{\mathbf{g}}\left(\mathbf{x}, \underline{\mathbf{p}}, \overline{\mathbf{p}}, u\right)$$

cooperative, easy to get an inclusion function for $y_{\mathrm{m}}\left(\mathbf{p}, t_i\right)$

Interval data are as before

SIVIA + toolbox VNODE now lead to

ε	0.01	0.005
Comput. time (s)	1300	1600
Volume of $\overline{\mathbb{S}}$	$2.5 \cdot 10^{-3}$	$6 \cdot 10^{-4}$

Table 2: Results with guaranteed integration

Shape and volume for $\varepsilon = 0.005$ similar to those obtained with closed-form solution for $\varepsilon = 0.0025$

For the same accuracy, computing time using guaranteed integration more than 100 times larger than with closed-form expression

Nonlinear system

Assume now that

$$k_{01}(x_1) = \frac{a}{1 + bx_1}$$

(Michaelis-Menten nonlinearity)

State equation becomes nonlinear

$$\mathbf{x}' = \mathbf{h}(\mathbf{x}, \mathbf{p}, u)$$

where

$$\mathbf{p} = (a, b, k_{12}, k_{21})^{\mathrm{T}}$$

and

$$\mathbf{h}(\mathbf{x}, \mathbf{p}, u) = \begin{pmatrix} -k_{21}x_1 - \dfrac{ax_1}{1 + bx_1} + k_{12}x_2 + u \\ k_{21}x_1 - k_{12}x_2 \end{pmatrix}$$

Again

- compartment 2 is observed, with input and initial conditions as before
- inclusion function based on guaranteed numerical integration can be employed

For any $\mathbf{p} \in [\underline{\mathbf{p}}, \overline{\mathbf{p}}]$ such that $\underline{\mathbf{p}} \geqslant \mathbf{0}$, possible to bound $\mathbf{h}(\mathbf{x}, \mathbf{p}, u)$ between

$$\begin{pmatrix} -\left(\overline{k}_{21} + \dfrac{\overline{a}}{1+\underline{b}x_1}\right)x_1 + \underline{k}_{12}x_2 + u \\ \underline{k}_{21}x_1 - \overline{k}_{12}x_2 \end{pmatrix}$$

and

$$\begin{pmatrix} -\left(\underline{k}_{21} + \dfrac{\underline{a}}{1+\overline{b}x_1}\right)x_1 + \overline{k}_{12}x_2 + u \\ \overline{k}_{21}x_1 - \underline{k}_{12}x_2 \end{pmatrix}$$

Resulting systems are cooperative, as $\underline{\mathbf{p}} \geqslant \mathbf{0}$

Inclusion function for $y_{\mathrm{m}}(\mathbf{p}, t_i)$ built by guaranteed numerical integration

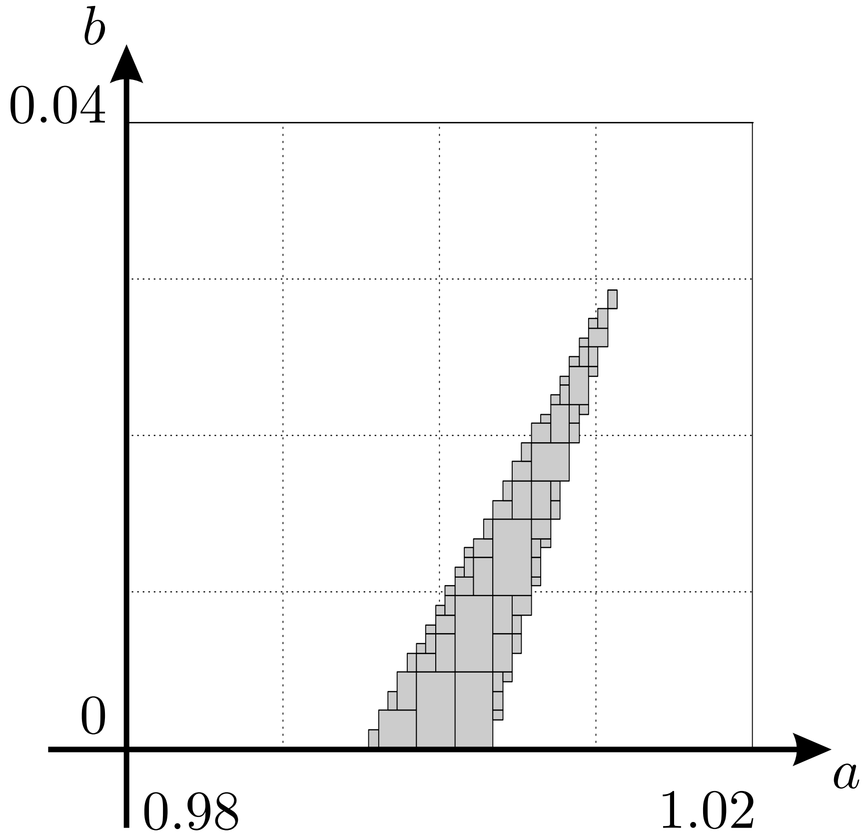
Two sets of data points considered

First data set: data generated by the same *linear* model as before

SIVIA now used with initial search box

$$[\mathbf{p}]_0 = [0, 5] \times [0, 5] \times [0.25, 0.25] \times [0.5, 0.5]$$

so k_{12} and k_{21} treated as known *a priori*



Outer approximation of solution set for (a, b) (true system is linear)

By projection of $\overline{\mathbb{S}}$, one gets

$$[a] = [0.9955, 1.0114]$$

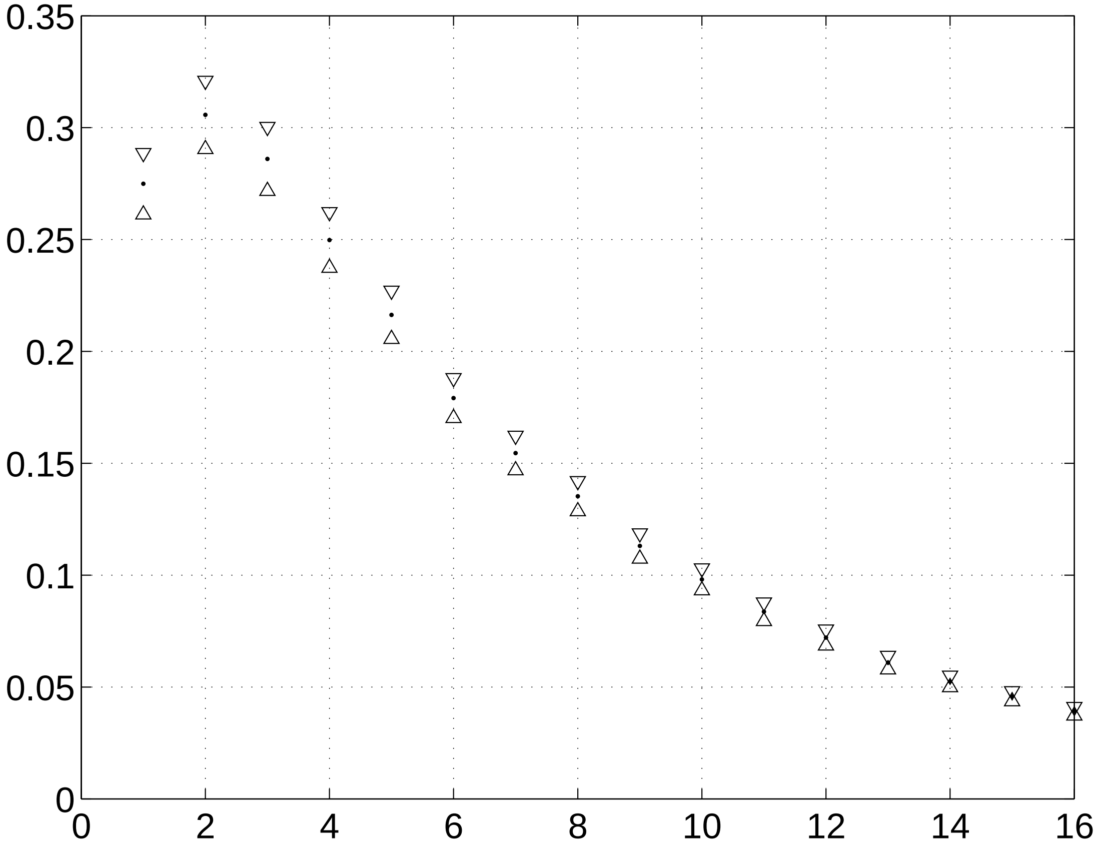
and

$$[b] = [0, 0.02930]$$

Since data generated with a linear model,

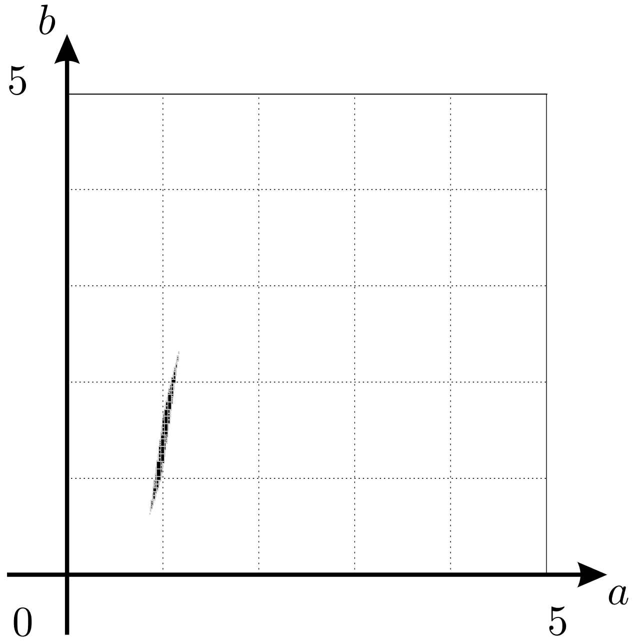
it comes as no surprise that $[b]$ includes 0

Second data set generated by a *nonlinear* system



Interval data (true system is nonlinear)

Initial search box as for first data set



Outer approximation of solution set for (a, b)
(true system is nonlinear)

As b cannot be zero, data could not have been generated by a linear model, given hypotheses

Conclusions and perspectives

Global deterministic methods based on interval analysis have definite advantages over more conventional local iterative methods, which are unable to provide guaranteed results

Structural identifiability studies can be bypassed since all solutions are provided

Examples have shown that it is possible to estimate parameters of models defined by (possibly nonlinear) ODEs

Main challenge is increasing complexity of tractable problems

Two allies in this endeavor have been briefly presented

- contractors allow boxes to be reduced and sometimes eliminated without bisection
- cooperativity allows efficient inclusion functions to be derived for ODEs

The ideas presented here in the context of parameter identification readily extend to state estimation or parameter tracking

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