Injectivity Analysis using Interval Analysis Application to Structural Identifiability ⋆

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Abstract

This paper presents a new numerical algorithm based on interval analysis able to test, in a guaranteed way, that a differentiable function $\mathbf{f} : \mathcal{A} \subset \mathbb{R}^n \to \mathbb{R}^n$ is injective. This algorithm also performs a partition of the domain $\mathcal{A}$ in subsets $\mathcal{A}_i$ where, for all $\mathbf{x} \in \mathcal{A}_i$, the cardinal of $\mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}))$ is constant.
In the context of parameter estimation, we show how this algorithm give a efficient and numerical method to study the structural identifiability of parametric models. It is able to decompose the parametric space into subsets where the number of feasible vectors of parameters is fixed. In consequence, if the decomposition leads to only one set where the feasible parameter vector is unique then the structural identifiability of the considered model is proved.

Key words: Injectivity, parametric system, structural identifiability, interval analysis.

1 Introduction

1.1 Problem Statement

Consider a differentiable function $\mathbf{f}$ defined from a set $\mathcal{A} \subset \mathbb{R}^n$ to $\mathbb{R}^n$, we define the *injectivity function of* $\mathbf{f}$ by

$$\mu : \begin{cases} \mathcal{A} \to \mathbb{N} \\ \mathbf{x} \to \left| \left\{ \tilde{\mathbf{x}} \in \mathcal{A} \mid \tilde{\mathbf{x}} = \mathbf{f}^{-1}\left(\mathbf{f}\left(\mathbf{x}\right)\right) \right\} \right| \end{cases} \quad (1)$$

where $|\cdot|$ denotes the cardinal of a set. The function μ associates to each vector $\mathbf{x}$ the number of solutions $\tilde{\mathbf{x}}$ of the equation

$$\mathbf{f}(\tilde{\mathbf{x}}) = \mathbf{f}(\mathbf{x}). \quad (2)$$

This paper proposes a new algorithm able to enclose the function μ between two functions μ^- and μ^+ such that

$$\forall \mathbf{x} \in \mathcal{A}, \mu^-(\mathbf{x}) \leq \mu(\mathbf{x}) \leq \mu^+(\mathbf{x}). \quad (3)$$

This algorithm is important for injectivity problems and identifiability analysis of parametric models as illustrated in the following. To our knowledge, it does not exist any numerical and guaranteed approaches to enclose μ. This paper presents the first attempt in that direction.
Note that Braems and al. has presented in [3] an approximated method to test whether the function μ is equal to one. Otherwise, formal approaches may turn out unsatisfactory for different reasons:

i) If Equation (2) is not polynomial, the formal calculus often fail to reach a solution.
ii) Even in the polynomial case, the degree of some of them may be too large for the existence of an analytic expression of the solutions. Then, the use of numerical methods is imposed and the formal nature of the solution is lost.
iii) The complexity of the formal manipulations (doubly exponential) is much more complicated than that allowed by computers.
iv) The number of solutions for the $\tilde{\mathbf{x}}$'s depend on the value of $\mathbf{x}$. It is then impossible to reach a structural conclusion.

The following example illustrates the points $i)$ and $iv)$. It will be treated in Section 4 with the new approach advocated in this paper.

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Example 1 *Consider the function*

$$f : \begin{cases} [-3,3] & \to \mathbb{R} \\ x & \to x\cos x \end{cases} \tag{4}$$

and let a *be the real number defined in Figure 1. One has*

$$\mu(x) = |\{\tilde{x} \in [-3,3] \mid \tilde{x}\cos\tilde{x} = x\cos x\}|, \tag{5}$$

$$= \begin{cases} 3 \text{ if } x \in]-a, a[, \\ 2 \text{ if } x = -a \text{ or } x = a, \\ 1 \text{ otherwise}. \end{cases} \tag{6}$$

Remarks that f *is injective when its injectivity function* μ *is equal to one.*

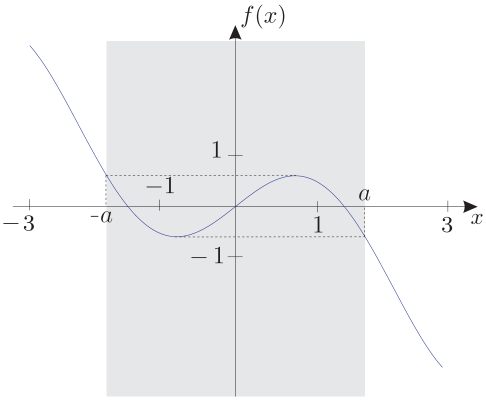

Fig. 1. The grey zone corresponds to the values of x for which the equation $f(x) = f(\tilde{x})$ has more than one solution.

1.2 Application to structural identifiability

The notion of *(structural) identifiability* is the question of whether one can hope uniquely to estimate the parameters of a model from the experimental data that can be collected. The importance of the notion has been recognized more than 50 years ago [8] and it is particularly relevant for knowledge-based models, where the parameters have a concrete meaning, and whenever decisions have to be taken on the basis of their numerical values [2].
In this paper, we show that the analysis of the structural identifiability amounts to study the injectivity function μ of a specific function build from the parametric model to be considered. If μ is equal to one, the model is globally identifiable; if μ is bounded, the model is locally identifiable and otherwise, it is unidentifiable [12].

1.3 Contents of the paper

The paper is organized as follows. Section 2 presents interval analysis and some possibilities of this tool. Section 3 defines the injectivity function restricted to a domain and points out its main properties. By a combination of interval analysis and the properties of the injectivity function, an effective algorithm is built in Section 4. It is able to enclose the injectivity function μ for any $\mathbf{x}$. In Section 5, an illustrative example shows the efficiency of the algorithm to test models for structural identifiability.
Note that a solver called IAVIA (Injectivity Analysis Via Interval Analysis) implemented in C++ is made available at `http://www.istia.univ-angers.fr/~lagrange/`.

2 Interval Arithmetic

In this section, we introduce some notations and concepts to be used in the paper. First, we present the interval arithmetic [10][11]. Then, the interval Newton method [5], usually used to prove the existence and the unicity of the zero of a function $\mathbf{f} : \mathbb{R}^n \to \mathbb{R}^n$, is generalized to functions defined from $\mathbb{R}^n \times \mathbb{R}^m$ to $\mathbb{R}^n$.

2.1 Interval Arithmetic

A vector interval or a *box* $[\mathbf{x}]$ of $\mathbb{R}^n$ is defined by

$$[\mathbf{x}] = [\underline{\mathbf{x}}, \overline{\mathbf{x}}] = \{\mathbf{x} \in \mathbb{R}^n \mid \underline{\mathbf{x}} \leq \mathbf{x} \leq \overline{\mathbf{x}}\}, \tag{7}$$

where $\underline{\mathbf{x}}$ and $\overline{\mathbf{x}}$ are two elements of $\mathbb{R}^n$ and the partial order $\leq$ is understood componentwise. The set of all bounded boxes of $\mathbb{R}^n$ is denoted by $\mathbb{IR}^n$ as in [6].
To *bisect* a box $[\mathbf{x}]$ means to cut it along a symmetry plane normal to a side of maximal length. The length of this side is the *width* of $[\mathbf{x}]$ denoted by $\omega([\mathbf{x}])$. A bisection of $[\mathbf{x}]$ generates two non overlapping boxes $[\mathbf{x}_1]$ and $[\mathbf{x}_2]$ such that $[\mathbf{x}] = [\mathbf{x}_1] \cup [\mathbf{x}_2]$ (see Figure 2).

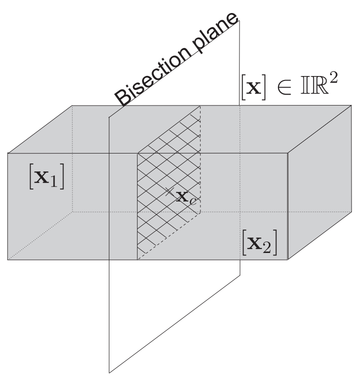

Fig. 2. Bisection of the box $[\mathbf{x}]$ into the sub-boxes $[\mathbf{x}_1]$ and $[\mathbf{x}_2]$ where $\mathbf{x}_c$ is the center of $[\mathbf{x}]$ (denoted $center([\mathbf{x}])$).

Let $\mathbf{f} : \mathbb{R}^n \to \mathbb{R}^m$ be a vector function; a set-valued function $[\mathbf{f}] : \mathbb{IR}^n \to \mathbb{IR}^m$ is a *inclusion function* of $\mathbf{f}$ if

$$\forall [\mathbf{x}] \in \mathbb{IR}^n, \mathbf{f}([\mathbf{x}]) \subset [\mathbf{f}]([\mathbf{x}]). \tag{8}$$

Note that $\mathbf{f}([\mathbf{x}])$ is usually not a box contrary to $[\mathbf{f}]([\mathbf{x}])$. Moreover, since $[\mathbf{f}([\mathbf{x}])]$ is the *hull box* [1] of $\mathbf{f}([\mathbf{x}])$, one has

$$\mathbf{f}([\mathbf{x}]) \subset [\mathbf{f}([\mathbf{x}])] \subset [\mathbf{f}]([\mathbf{x}]) \quad \text{(see Figure 3).}$$

In [11], Neumaier proves that it is always possible to find an inclusion function $[\mathbf{f}]$ when $\mathbf{f}$ is defined by an arithmetical expression.

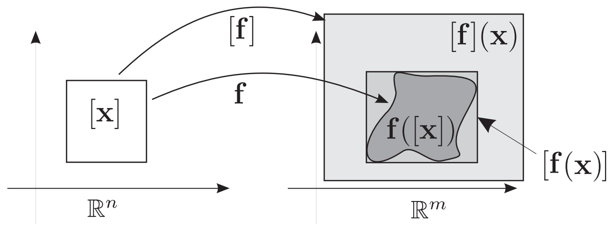

Fig. 3. Inclusion function [**f**] of the function **f**.

2.2 Interval Newton Method

The purpose of this subsection is to give a sufficient condition for verify that

$$\forall \mathbf{y} \in [\mathbf{y}], \exists! \mathbf{x} \in [\mathbf{x}] \text{ such that } \mathbf{h}(\mathbf{x}, \mathbf{y}) = \mathbf{0}, \tag{9}$$

where $\mathbf{h}$ is a differentiable function defined by

$$\mathbf{h} : \begin{cases} \mathbb{R}^n \times \mathbb{R}^m & \rightarrow \quad \mathbb{R}^n \\ (\mathbf{x}, \mathbf{y}) & \rightarrow \mathbf{h}(\mathbf{x}, \mathbf{y}) \end{cases} \tag{10}$$

and $[\mathbf{x}], [\mathbf{y}]$ are two boxes included in $\mathbb{R}^n$ and $\mathbb{R}^m$ respectively.
To perform this verification, we propose to generalize the interval Newton method by defining an extension of the unicity operators [9].
This new result will be exploited in the next section in order to show that a function $\mathbf{f} : \mathbb{R}^n \rightarrow \mathbb{R}^n$ satifies

$$\forall \mathbf{y} \in [\mathbf{y}], \exists! \mathbf{x} \in [\mathbf{x}] \text{ such that } \mathbf{f}(\mathbf{x}) = \mathbf{y}. \tag{11}$$

by setting $\mathbf{h} : \begin{cases} \mathbb{R}^n \times \mathbb{R}^n & \rightarrow \quad \mathbb{R}^n \\ (\mathbf{x}, \mathbf{y}) & \rightarrow \mathbf{f}(\mathbf{x}) - \mathbf{y} \end{cases}$.

2.2.1 Unicity operator

This paragraph recalls the definition of a (interval) unicity operator. Let us consider a function $\mathbf{f} : \mathbb{R}^n \rightarrow \mathbb{R}^n$ and a interval $[\mathbf{x}] \subset \mathbb{R}^n$.

[1] A *hull box* of a compact set $\mathcal{A} \subset \mathbb{R}^n$, denoted $[\mathcal{A}]$, is the smallest box of $\mathbb{IR}^n$ that contains $\mathcal{A}$.

Definition 1 *An operator $\mathcal{N}$ is a unicity operator of $\mathbf{f} : \mathbb{R}^n \rightarrow \mathbb{R}^n$ if*

$$\mathcal{N}(\mathbf{f}, [\mathbf{x}]) \textit{ is true } \Rightarrow \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{f}(\mathbf{x}) = \mathbf{0}.$$

Example 2 *Consider the expression*

$$\textit{center}([\mathbf{x}]) - \textbf{\textit{Inv}}([D_{\mathbf{x}}\mathbf{f}([\mathbf{x}])], \mathbf{f}(\textit{center}([\mathbf{x}]))) \tag{12}$$

*where $D_{\mathbf{x}}\mathbf{f}$ is the Jacobian matrix of $\mathbf{f}$ (according to $\mathbf{x}$) and **Inv** $([\mathbf{A}], [\mathbf{b}])$ is an interval vector that contains the set*

$$\left\{\mathbf{x} = \mathbf{A}^{-1}\mathbf{b} \mid \mathbf{A} \in [\mathbf{A}], \mathbf{b} \in [\mathbf{b}]\right\}. \tag{13}$$

(we will not explain in detail how to compute such a vector, e.g. *Gauss Interval Algorithm [1] could be used).*
The standard (interval) unicity operator is the unicity operator of Newton [5] defined by

$$\mathcal{N}(\mathbf{f}, [\mathbf{x}]) = \begin{cases} \textit{true} & \textit{if (12) is strictly included in } [\mathbf{x}] \\ \textit{false} & \textit{otherwise} \end{cases} \tag{14}$$

2.2.2 Generalized unicity operator

Now, let us extend the unicity operator defined for functions from $\mathbb{R}^n$ to $\mathbb{R}^n$ to functions defined from $\mathbb{R}^n \times \mathbb{R}^m$ to $\mathbb{R}^n$. These extended operators will be named *generalized unicity operators*.
Consider the function $\mathbf{h}$ defined by (10) and two boxes $[\mathbf{x}] \in \mathbb{IR}^n$ and $[\mathbf{y}] \in \mathbb{IR}^m$. For a fixed point $\mathbf{y} \in [\mathbf{y}]$, define

$$\mathbf{h}_{\mathbf{y}} : \begin{cases} \mathbb{R}^n & \rightarrow \mathbb{R}^n \\ \mathbf{x} & \rightarrow \mathbf{h}_{\mathbf{y}}(\mathbf{x}) = \mathbf{h}(\mathbf{x}, \mathbf{y}). \end{cases} \tag{15}$$

Now, let $\mathcal{N}(\mathbf{h}_{\mathbf{y}}, [\mathbf{x}])$ be a unicity operator of $\mathbf{h}_{\mathbf{y}}$ then, according to Definition 1, we get

$$\mathcal{N}(\mathbf{h}_{\mathbf{y}}, [\mathbf{x}]) \text{ is true } \Rightarrow \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{h}_{\mathbf{y}}(\mathbf{x}) = \mathbf{0}. \tag{16}$$

Taking

$$\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], \mathbf{y}) = \mathcal{N}(\mathbf{h}_{\mathbf{y}}, [\mathbf{x}]), \tag{17}$$

the relation (16) becomes

$$\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], \mathbf{y}) \text{ is true } \Rightarrow \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{h}(\mathbf{x}, \mathbf{y}) = \mathbf{0}. \tag{18}$$

Thus, the operator $\mathcal{N}_g$ can be view as a unicity operator of the function $\mathbf{h}$ at the point $\mathbf{y}$.
Now, according to (18) and since no assumption has been done on $\mathbf{y}$, one has

$$\forall \mathbf{y} \in [\mathbf{y}], (\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], \mathbf{y}) \text{ is true } \Rightarrow \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{h}(\mathbf{x}, \mathbf{y}) = \mathbf{0}) \tag{19}$$

and therefore

$$\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], [\mathbf{y}]) \text{ is true } \Rightarrow \forall \mathbf{y} \in [\mathbf{y}], \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{h}(\mathbf{x}, \mathbf{y}) = \mathbf{0}. \tag{20}$$

Thus, the operator $\mathcal{N}_g$ is a unicity operator of $\mathbf{h}$ for all $\mathbf{y} \in [\mathbf{y}]$, namely a *generalized unicity operator*. Concisely, the definition is the following :

Definition 2 *An operator $\mathcal{N}_g$ is a generalized unicity operator of $\mathbf{h} : \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ if*

$$\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], [\mathbf{y}]) \textit{ is true } \Rightarrow \forall \mathbf{y} \in [\mathbf{y}], \exists! \mathbf{x} \in [\mathbf{x}], \mathbf{h}(\mathbf{x}, \mathbf{y}) = \mathbf{0}.$$

Example 3 *Consider the function $\mathbf{h}$ defined in (10). According to Example 2, the unicity operator of Newton $\mathcal{N}(\mathbf{h}_\mathbf{y}, [\mathbf{x}])$ of the function $\mathbf{h}_\mathbf{y}$ (defined in (15)) is true if*

$$\textit{center}([\mathbf{x}]) - \textbf{\textit{Inv}}([D_\mathbf{x}\mathbf{h}_\mathbf{y}([\mathbf{x}])], \mathbf{h}_\mathbf{y}(\textit{center}([\mathbf{x}]))) \tag{21}$$

*is strictly included in $[\mathbf{x}]$ and false otherwise. Note that $D_\mathbf{x}\mathbf{h}_\mathbf{y}([\mathbf{x}])$ denotes the Jacobian matrix (according to $\mathbf{x}$) of $\mathbf{h}_\mathbf{y}$ and **Inv**$(\cdot,\cdot)$ is defined as in (12).*
According to (17), the corresponding generalized unicity operator of Newton $\mathcal{N}_g(\mathbf{h}, [\mathbf{x}], [\mathbf{y}])$ of $\mathbf{h}$ is true if

$$\textit{center}([\mathbf{x}]) - \textbf{\textit{Inv}}([D_\mathbf{x}\mathbf{h}([\mathbf{x}], [\mathbf{y}])], \mathbf{h}(\textit{center}([\mathbf{x}]), [\mathbf{y}])) \tag{22}$$

is strictly included in $[\mathbf{x}]$ and false otherwise.

3 Injectivity function

Consider a differentiable function $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^n \to \mathbb{R}^n$. This section presents some basic properties of the injectivity function μ of $\mathbf{f}$ defined in (1). Then, a main theorem, based on the algorithm to be presented, will be introduced. This theorem gives a sufficient condition to enclose the injectivity function.

3.1 Properties of the injectivity function

Let $[\tilde{\mathbf{x}}]$ be a box included in $[\mathbf{x}]$, we define *the injectivity function (of* $\mathbf{f}$*) restricted to* $[\tilde{\mathbf{x}}]$, denoted $\mu_{[\tilde{\mathbf{x}}]}$, by

$$\mu_{[\tilde{\mathbf{x}}]} : \begin{cases} [\mathbf{x}] \to \mathbb{N} \\ \mathbf{x} \to \left|\left\{\tilde{\mathbf{x}} \in [\tilde{\mathbf{x}}] \mid \tilde{\mathbf{x}} = \mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}))\right\}\right|. \end{cases} \tag{23}$$

$\mu_{[\tilde{\mathbf{x}}]}(\mathbf{x})$ is the number of solutions $\tilde{\mathbf{x}}$ of the equation $\mathbf{f}(\tilde{\mathbf{x}}) = \mathbf{f}(\mathbf{x})$ that belongs to $[\tilde{\mathbf{x}}]$.
Note that, since we only consider the injectivity function of $\mathbf{f}$, we omit to specify it in the following.

Example 4 *Consider the function $f(x) = x\cos x$ of Example 1. The graph of the function $\mu_{[-a,a]}$ has been depicted on Figure 4.*

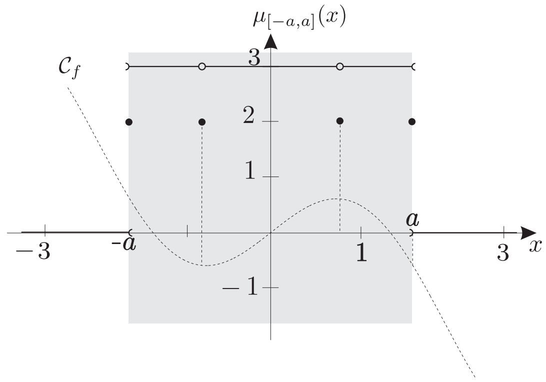

Fig. 4. Graph of the injectivity function $\mu_{[-a,a]}$ of f. The graph of f has been superposed as dotted-lines.

Now, the following proposition gives the relation between the injectivity function restricted to an union of boxes and the one restricted to each boxes.

Proposition 1 *Consider a function $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^n \to \mathbb{R}^n$ and a collection $[\tilde{\mathbf{x}}_1], \ldots, [\tilde{\mathbf{x}}_q]$ of boxes of $[\mathbf{x}]$. For $I = \{1, \ldots, q\}$, we get*

$$\mu_{\bigcup_{i\in I}[\tilde{\mathbf{x}}_i]}(\mathbf{x}) = \sum_{J\subset I} (-1)^{|I|-1} \mu_{\bigcap_{i\in J}[\tilde{\mathbf{x}}_i]}(\mathbf{x}). \tag{24}$$

Proof. By definition, one has

$$\mu_{\bigcup_i[\tilde{\mathbf{x}}_i]}(\mathbf{x}) = \left|\left\{\tilde{\mathbf{x}} \in \bigcup_i [\tilde{\mathbf{x}}_i] \mid \tilde{\mathbf{x}} = \mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}))\right\}\right|. \tag{25}$$

According to the inclusion-exclusion principle, one has

$$\left|\bigcup_{i\in I}[\tilde{\mathbf{x}}_i]\right| = \sum_{J\subset I} (-1)^{|I|-1} \left|\bigcap_{i\in J}[\tilde{\mathbf{x}}_i]\right|. \tag{26}$$

Therefore

$$\mu_{\bigcup_{i\in I}[\tilde{\mathbf{x}}_i]}(\mathbf{x}) = \sum_{J\subset I} (-1)^{|I|-1} \left|\left\{\tilde{\mathbf{x}} \in \bigcap_{i\in J}[\tilde{\mathbf{x}}_i] \mid \tilde{\mathbf{x}} = \mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}))\right\}\right|. \tag{27}$$

and according to the definition of the injectivity function, we get (24). ■

Example 5 *Consider the function $f : [x] \subset \mathbb{R} \to \mathbb{R}$ and the real number a depicted on Figure 5. Since $[x] = \bigcup_{i=1}^{i=4} [\tilde{x}_i]$ and according to Proposition 1, one has*

$$\begin{aligned} \mu_{[x]}(a) &= \sum_{i=1}^{4} \mu_{[\tilde{x}_i]}(a) \\ &= 0 + 1 + 2 + 0 = 3. \end{aligned}$$

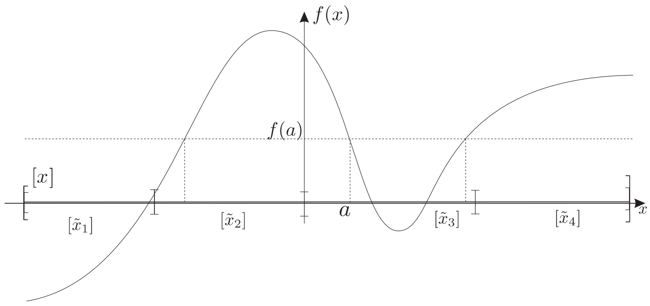

Fig. 5. Graph of the function f

Remark 1 *Consider a function* $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$ *and* $[\mathbf{x}_1] \subset [\mathbf{x}]$. *Trivially, for any box* $[\tilde{\mathbf{x}}]$ *that contains* $\mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))$ *(see Figure 6), one has*

$$\forall \mathbf{x} \in [\mathbf{x}_1], \left\{\tilde{\mathbf{x}} \in [\mathbf{x}] \setminus [\tilde{\mathbf{x}}] \mid \tilde{\mathbf{x}} = \mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}))\right\} = \emptyset. \quad (28)$$

Hence, $\mu_{[\mathbf{x}]\setminus[\tilde{\mathbf{x}}]}([\mathbf{x}_1]) = 0$.

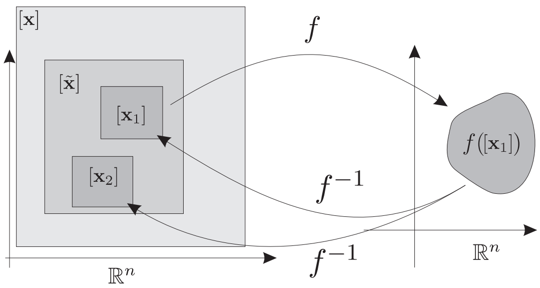

Fig. 6. Representation of the box $[\tilde{\mathbf{x}}] \supset \mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))$.

3.2 Condition to enclose the injectivity function

In this paragraph, we introduce a partial result which gives, respectively, a sufficient condition to compute and to bound the injectivity function μ of a differentiable function $\mathbf{f}$ restricted to a box $[\tilde{\mathbf{x}}_1] \subset [\mathbf{x}]$ denoted $\mu_{[\tilde{\mathbf{x}}_1]}$. Then, these results are exploited to enclose the injectivity function $\mu \equiv \mu_{[\mathbf{x}]}$.

Lemma 1 *Consider a function* $\mathbf{h}$ *defined by*

$$\mathbf{h} : \begin{cases} [\mathbf{x}] \subset \mathbb{R}^n \times \mathbb{R}^n \rightarrow & \mathbb{R}^n \\ \quad (\mathbf{x}, \mathbf{y}) & \rightarrow \mathbf{f}(\mathbf{x}) - \mathbf{y}. \end{cases} \quad (29)$$

where $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$ *is differentiable and suppose that* $\mathcal{N}_g$ *is generalized unicity operator of* $\mathbf{h}$. *Let* $[\mathbf{x}_1]$ *and* $[\tilde{\mathbf{x}}_1]$ *be two boxes included in* $[\mathbf{x}]$. *One has,*

$$\begin{aligned} &i) \;\; \mathcal{N}_g(\mathbf{h}, [\tilde{\mathbf{x}}_1], \mathbf{f}([\mathbf{x}_1])) \;\; \textit{is true} \;\Rightarrow \mu_{[\tilde{\mathbf{x}}_1]}([\mathbf{x}_1]) = 1, \\ &ii) \;\; [D\mathbf{f}_{\mathbf{x}}([\tilde{\mathbf{x}}_1])] \;\; \textit{is full rank} \;\Rightarrow \mu_{[\tilde{\mathbf{x}}_1]}([\mathbf{x}_1]) \leq 1. \end{aligned} \quad (30)$$

Proof. i) Supposed that $\mathcal{N}_g(\mathbf{h}, [\tilde{\mathbf{x}}_1], \mathbf{f}([\mathbf{x}_1]))$ is true. Since $\mathcal{N}_g$ is a generalized unicity operator of $\mathbf{h}$ (see Definition 2), then we get

$$\forall \mathbf{y} \in \mathbf{f}([\mathbf{x}_1]), \exists! \tilde{\mathbf{x}}_1 \in [\tilde{\mathbf{x}}_1], \mathbf{h}(\tilde{\mathbf{x}}_1, \mathbf{y}) = \mathbf{0}, \quad (31)$$

or equivalently,

$$\forall \mathbf{y} \in \mathbf{f}([\mathbf{x}_1]), \exists! \tilde{\mathbf{x}}_1 \in [\tilde{\mathbf{x}}_1], \mathbf{f}(\tilde{\mathbf{x}}_1) = \mathbf{y}. \quad (32)$$

Thus,

$$\forall \mathbf{x}_1 \in [\mathbf{x}_1], \exists! \tilde{\mathbf{x}}_1 \in [\tilde{\mathbf{x}}_1], \mathbf{f}(\tilde{\mathbf{x}}_1) = \mathbf{f}(\mathbf{x}_1). \quad (33)$$

Hence,

$$\forall \mathbf{x}_1 \in [\mathbf{x}_1], \left|\left\{\tilde{\mathbf{x}}_1 \in [\tilde{\mathbf{x}}_1] \mid \tilde{\mathbf{x}}_1 = \mathbf{f}^{-1}(\mathbf{f}(\mathbf{x}_1))\right\}\right| = 1, \quad (34)$$

i.e. $\mu_{[\tilde{\mathbf{x}}_1]}([\mathbf{x}_1]) = 1$.

ii) The proof is by contradiction. Supposed that

$$\mu_{[\tilde{\mathbf{x}}_1]}([\mathbf{x}_1]) \geq 2,$$

then

$$\exists \tilde{\mathbf{x}}_1, \tilde{\mathbf{x}}_2 \in [\tilde{\mathbf{x}}_1], \text{ such that } \tilde{\mathbf{x}}_1 \neq \tilde{\mathbf{x}}_2 \text{ and } \mathbf{f}(\tilde{\mathbf{x}}_1) = \mathbf{f}(\tilde{\mathbf{x}}_2). \quad (35)$$

According to the Generalized Mean value theorem [2], $\exists \tilde{\mathbf{x}}_1, \tilde{\mathbf{x}}_2 \in [\tilde{\mathbf{x}}_1]$, $\exists \mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2} \in [D\mathbf{f}([\tilde{\mathbf{x}}_1])]$, such that

$$\tilde{\mathbf{x}}_1 \neq \tilde{\mathbf{x}}_2 \text{ and } \mathbf{0} = \mathbf{f}(\tilde{\mathbf{x}}_2) - \mathbf{f}(\tilde{\mathbf{x}}_1) = \mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2} \cdot (\tilde{\mathbf{x}}_2 - \tilde{\mathbf{x}}_1). \quad (36)$$

i.e. $\exists \mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2} \in [D\mathbf{f}([\tilde{\mathbf{x}}_1])]$ such that $\mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2}$ is not full rank and thus, the (interval) matrix $[D\mathbf{f}([\tilde{\mathbf{x}}_1])]$ is not full rank. ■

Now, the following theorem uses the previous lemma to enclose the injectivity function μ. This theorem will motivate the implementation of the algorithm presented in next paragraph.

Theorem 1 *Consider a function* $\mathbf{h}$ *defined by*

$$\mathbf{h} : \begin{cases} [\mathbf{x}] \subset \mathbb{R}^n \times \mathbb{R}^n \rightarrow & \mathbb{R}^n \\ \quad (\mathbf{x}, \mathbf{y}) & \rightarrow \mathbf{f}(\mathbf{x}) - \mathbf{y}. \end{cases} \quad (37)$$

where $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$ *is differentiable and suppose that* $\mathcal{N}_g$ *is a generalized unicity operator of* $\mathbf{h}$. *Let* $[\mathbf{x}_1]$ *be*

[2] Let $\mathbf{f} : \mathcal{A} \subset \mathbb{R}^n \rightarrow \mathbb{R}^m$ be a differentiable function. If $\tilde{\mathbf{x}}_1$ and $\tilde{\mathbf{x}}_2$ belong to a convex set $\mathcal{X} \subset \mathcal{A}$. Then, $\forall \tilde{\mathbf{x}}_1, \tilde{\mathbf{x}}_2 \in \mathcal{X}$, $\exists \mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2} \in [D\mathbf{f}(\mathcal{X})]$ such that

$$\mathbf{f}(\tilde{\mathbf{x}}_2) - \mathbf{f}(\tilde{\mathbf{x}}_1) = \mathbf{J}_{\tilde{\mathbf{x}}_1,\tilde{\mathbf{x}}_2} \cdot (\tilde{\mathbf{x}}_2 - \tilde{\mathbf{x}}_1),$$

where $[D\mathbf{f}_{\mathbf{x}}(\mathcal{X})]$ denotes the hull box of the Jacobian matrix $D\mathbf{f}_{\mathbf{x}}(\mathcal{X})$. This result can be proved by applying the Mean-Value Theorem [7] on each components $f_i : \mathbb{R}^n \rightarrow \mathbb{R}$ of $\mathbf{f}$.

a set included in $[\mathbf{x}]$ *and* $\{[\tilde{\mathbf{x}}_i]\}_{i\in\{1,\dots,q\}}$ *be a partition that contains* $\mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))$ *which satisfies the two conditions*

$$\begin{aligned} &i)\ \ \forall i\in\{1,\dots,q'\}, \mathcal{N}_g(\mathbf{h},[\tilde{\mathbf{x}}_i],\mathbf{f}([\mathbf{x}_1]))\ \text{ is true},\\ &ii)\ \forall i\in\{q'+1,\dots,q\}, [D\mathbf{f}_{\mathbf{x}}([\tilde{\mathbf{x}}_i])]\ \text{ is full rank} \end{aligned} \tag{38}$$

where $q'\in\mathbb{N}$, $1\le q'\le q$. *Then, it holds*

$$q'\le\mu_{[\mathbf{x}]}([\mathbf{x}_1])\le q. \tag{39}$$

Proof. First of all, according to Proposition 1, one has

$$\mu_{[\mathbf{x}]}([\mathbf{x}_1])=\mu_{\bigcup_i[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1])+\mu_{[\mathbf{x}]\setminus\bigcup_i[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]). \tag{40}$$

Since $\bigcup_i[\tilde{\mathbf{x}}_i]\supset\mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))$ and according to Remark 1, we get

$$\mu_{[\mathbf{x}]}([\mathbf{x}_1])=\mu_{\bigcup_i[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]). \tag{41}$$

Since $\{[\tilde{\mathbf{x}}_i]\}_{i\in\{1,\dots,q\}}$ is a partition (*i.e.* $[\tilde{\mathbf{x}}_i]\cap[\tilde{\mathbf{x}}_j]=\emptyset$ $(\forall i\neq j)$) and according to Proposition 1, one has

$$\mu_{[\mathbf{x}]}([\mathbf{x}_1])=\sum_{i=1}^{q}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]). \tag{42}$$

Now, considering the condition i) and according to Lemma 1 (i), one has, $\forall i\in\{1,\dots,q'\}$,

$$\mathcal{N}_g(\mathbf{h},[\tilde{\mathbf{x}}_i],\mathbf{f}([\mathbf{x}_1]))\ \text{ is true}\Rightarrow\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1])=1. \tag{43}$$

Therefore,

$$\begin{aligned}\mu_{[\mathbf{x}]}([\mathbf{x}_1])&=\sum_{i=1}^{q'}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1])+\sum_{i=q'+1}^{q}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]) && (44)\\ &=\sum_{i=1}^{q'}1+\sum_{i=q'+1}^{q}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]) && (45)\\ &=q'+\sum_{i=q'+1}^{q}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1]). && (46)\end{aligned}$$

As a consequence, q' is a lower bound of $\mu_{[\mathbf{x}]}([\mathbf{x}_1])$, *i.e.*

$$\mu_{[\mathbf{x}]}([\mathbf{x}_1])\ge q'. \tag{47}$$

Now, according to Lemma 1 (ii), one has, $\forall i\in\{q'+1,\dots,q\}$,

$$[D\mathbf{f}_{\mathbf{x}}([\tilde{\mathbf{x}}_i])]\ \text{ is full rank }\Rightarrow\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1])\le 1. \tag{48}$$

Thus,

$$\sum_{i=q'+1}^{q}\mu_{[\tilde{\mathbf{x}}_i]}([\mathbf{x}_1])\le q-q' \tag{49}$$

and according to (46), one has

$$\mu_{[\mathbf{x}]}([\mathbf{x}_1])\le q'+q-q'=q. \tag{50}$$

As a conclusion, according to Equations (47) and (50), the Theorem 1 is proved. ■

Remark 2 *Note that, if all the boxes* $\{[\tilde{\mathbf{x}}_i]\}_{i\in\{1,\dots,q\}}$ *of the partition verify the condition i) of Theorem 1 (*i.e. $q'=q$*), then the injectivity function* μ *satisfies*

$$q\le\mu_{[\mathbf{x}]}([\mathbf{x}_1])\le q\Leftrightarrow\mu_{[\mathbf{x}]}([\mathbf{x}_1])=q.$$

4 Algorithm IAVIA

This section presents the algorithm called Injectivity Analysis Via Interval Analysis (IAVIA).
Consider a differentiable function $\mathbf{f}:[\mathbf{x}]\subset\mathbb{R}^n\to\mathbb{R}^n$, the algorithm to be presented decomposes the initial box $[\mathbf{x}]$ in a paving [3] $\{[\mathbf{x}_i]\}_i$ where injectivity function $\mu_{[\mathbf{x}]}([\mathbf{x}_i])$ is enclosed.
The principle of IAVIA can be decomposed in two distinct sub-algorithms :

- Algorithm 1 exploits the Theorem 1 in order to enclose the injectivity function over a box $[\mathbf{x}_1]\subset[\mathbf{x}]$. It returns either two positive integers (μ^-,μ^+), which correspond to the bounds of $\mu_{[\mathbf{x}]}[\mathbf{x}_1]$ or $(-1,-1)$ when no conclusion can be reached.
- Algorithm 2 divides the initial box $[\mathbf{x}]$ into a paving $\{[\mathbf{x}_i]\}_i$ such that, for all i, Algorithm 1 succeeds in obtaining an enclosure of injectivity function over the $[\mathbf{x}_i]$'boxes.

In Algorithm 1, from Step 2 to Step 12, the set inversion technique [4,6] is exploited to characterize a list $\mathcal{L}_{\tilde{\mathbf{x}}}$ of boxes $([\mathbf{x}_i])_i$ such that

$$\mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))\subset\bigcup_i[\mathbf{x}_i]. \tag{51}$$

The purpose of the condition in Step 5 is to avoid useless splitting of $[\mathbf{x}]$ *ad infinitum*.
In Step 13, all the boxes $[\mathbf{x}_i]$ of $\mathcal{L}_{\tilde{\mathbf{x}}}$ are reorganized to form a partition that still contains $\mathbf{f}^{-1}(\mathbf{f}([\mathbf{x}_1]))$ (the boxes $[\mathbf{x}_i]$ which intersect each other are collected in new boxes $([\tilde{\mathbf{x}}_i])_j$, $j\le i$ such as depicted in Figure 7).

Finally, from Step 14 to Step 24, two tests are performed according to Theorem 1 :
First, if all the boxes $[\tilde{\mathbf{x}}_i]$ of the partition verify $[D\mathbf{f}([\tilde{\mathbf{x}}_i])]$ is full rank [4] , then the number of $[\tilde{\mathbf{x}}_i]$'boxes is a upper bound of the injectivity function $\mu_{[\mathbf{x}]}([\mathbf{x}_1])$.

---

[3] A paving of $[\mathbf{x}]$ is a finite set of non-overlapping boxes $\{[\mathbf{x}_i]\}_i$ such that $[\mathbf{x}]=\bigcup_i[\mathbf{x}_i]$

[4] Several techniques could be used to test an interval matrix for full ranking. In the square case (*i.e.* $f:\mathbb{R}^2\to\mathbb{R}^2$), the simplest way consists in verifying that the determinant (which is an interval) not contains zero. Otherwise (*i.e.* $f:\mathbb{R}^n\to\mathbb{R}^p$), the Interval Gauss Algorithm could be used [11].

Algorithm 1 Injectivity_Enclosure

Input: $\mathbf{f}$ a $\mathcal{C}^1$ function, $[\mathbf{x}]$ the initial box and $[\mathbf{x}_1]$ a box included in $[\mathbf{x}]$.

Output: Two integers μ^- and μ^+ :

$$\begin{array}{lll} \mu^- \geq 1 \textit{ and } \mu^+ \geq 1 & : & \mu^- \leq \mu_{[\mathbf{x}]}([\mathbf{x}_1]) \leq \mu^+, \\ \mu^- = -1 \textit{ and } \mu^+ = -1 & : & \textit{The enclosure of the} \\ & & \textit{injectivity function failed.} \end{array}$$

1: Initialization : $\mathcal{L}_{stack} := \{[\mathbf{x}]\}$, $\mathcal{L}_{\tilde{\mathbf{x}}} := \emptyset$, $\mu^- = 0$, $\mu^+ = 0$.
2: **while** $\mathcal{L}_{stack} \neq \emptyset$ **do**
3: Pop $\mathcal{L}_{stack}$ into $[\mathbf{w}]$.
4: **if** $[\mathbf{f}]([\mathbf{w}]) \cap [\mathbf{f}]([\mathbf{x}_1]) \neq \emptyset$ **then**
5: **if** width($[\mathbf{w}]$) $>$ width($[\mathbf{x}_1]$) **then**
6: Bisect $[\mathbf{w}]$ into $[\mathbf{w}_1]$ and $[\mathbf{w}_2]$.
7: Stack $[\mathbf{w}_1]$ and $[\mathbf{w}_2]$ in $\mathcal{L}_{stack}$
8: **else**
9: Push $[\mathbf{w}]$ in $\mathcal{L}_{\tilde{\mathbf{x}}}$.
10: **end if**
11: **end if**
12: **end while**
13: Match $\mathcal{L}_{\tilde{\mathbf{x}}}$ to build a partition
14: **for** $i = 1$ to size of($\mathcal{L}_{\tilde{\mathbf{x}}}$) **do**
15: **if** $[D\mathbf{f}]([\tilde{\mathbf{x}}_i])$ is full rank **then**
16: **if** $\mathcal{N}_g(\mathbf{h}, [\tilde{\mathbf{x}}_i], [\mathbf{f}]([\mathbf{x}_1]))$ is true **then**
17: $\mu^- = \mu^- + 1$
18: **end if**
19: **else**
20: Return $(-1,-1)$ \\ "Failure"
21: **end if**
22: **end for**
23: $\mu^+ :=$ size of $(\mathcal{L}_{\tilde{\mathbf{x}}})$
24: Return (μ^-, μ^+)

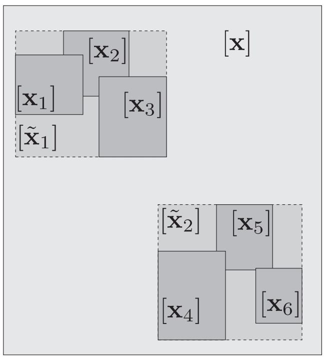

Fig. 7. Illustration of the decomposition performed in Step 13 with $\mathcal{L}_{\tilde{\mathbf{x}}} = \{[\mathbf{x}_1], \ldots, [\mathbf{x}_6]\}$. The $[\mathbf{x}_i]$'boxes of $\mathcal{L}_{\tilde{\mathbf{x}}}$ are matched in order to obtain the two disjoint (and larger) boxes $[\tilde{\mathbf{x}}_1]$ and $[\tilde{\mathbf{x}}_2]$.

Secondly, the number of boxes $[\tilde{\mathbf{x}}_i]$ of the partition such that $\mathcal{N}_g(\mathbf{h}, [\tilde{\mathbf{x}}_i], \mathbf{f}([\mathbf{x}_1])$ is true (where $\mathbf{h}$ is defined by (37)), gives a lower bound of the injectivity function $\mu_{[\mathbf{x}]}([\mathbf{x}_1])$. Otherwise, if any boxes verify one of these two conditions, then the injectivity function enclosure failed (Theorem 1 could not be used).

Remark 3 *The generalized unicity operator $\mathcal{N}_g$ of $\mathbf{h}$ used in the solver IAVIA is the generalized unicity operator of Newton defined in Equation (22). However, different generalized unicity operators could be build as Krawczyk operator or Hansen-Sengupta operator [11].*

Algorithm 2 creates a paving $([\mathbf{x}_i])_i$ of the initial box $[\mathbf{x}]$ such that, for all i, Algorithm 1 encloses the injectivity function $\mu_{[\mathbf{x}]}([\mathbf{x}_i])$. Algorithm 2 is stopped with a ε condition on the width of boxes $[\mathbf{x}_i]$ which remain to test (see Step 4). Therefore, different domains are obtained :
An indeterminate domain composed of the boxes of lower width than ε (archived in $\mathcal{U}$) for which the enclosure process failed (*i.e.* $(\mu^-, \mu^+) = (-1,-1)$).
And, domains where the injectivity function is enclosed (archived in the list $\mathcal{S}$).

Algorithm 2 IAVIA

Input: $\mathbf{f}$ a $\mathcal{C}^1$ function and $[\mathbf{x}]$ the initial box.

Output: A list $\mathcal{S}$ that contains boxes in $[\mathbf{x}]$ and their corresponding enclosure of the injectivity function.

1: Initialization : $\mathcal{L} := \{[\mathbf{x}]\}$, $\mathcal{S} = \emptyset$, $\mathcal{U} = \emptyset$.
2: **while** $\mathcal{L} \neq \emptyset$ **do**
3: Pull $[\mathbf{w}]$ in $\mathcal{L}$.
4: **if** $\omega([\mathbf{w}]) > \varepsilon$ **then**
5: $(\mu^-, \mu^+) =$Injectivity_Enclosure$(\mathbf{f}, [\mathbf{x}], [\mathbf{w}])$
6: **if** $(\mu^-, \mu^+) = (-1,-1)$ **then**
7: Bisect $[\mathbf{w}]$ into $[\mathbf{w}_1]$ and $[\mathbf{w}_2]$
8: Push $[\mathbf{w}_1]$ and $[\mathbf{w}_2]$ in $\mathcal{L}$
9: **else**
10: Push $([\mathbf{w}], (\mu^-, \mu^+))$ in $\mathcal{S}$
11: **end if**
12: **else**
13: Push $[\mathbf{w}]$ in $\mathcal{U}$
14: **end if**
15: **end while**

By combination of Algorithm 1 and Algorithm 2, a C++ solver, called IAVIA, is able to enclose the injectivity function of any function $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R}^2 \rightarrow \mathbb{R}^2$ or $\mathbf{f} : [\mathbf{x}] \subset \mathbb{R} \rightarrow \mathbb{R}$. It is made available at `http://www.istia.univ-angers.fr/~lagrange/`.

Example 6 *Consider the function*

$$f : \begin{cases} [-3,3] & \rightarrow \mathbb{R} \\ x & \rightarrow x \cos x \end{cases} \tag{52}$$

presented in Example 1 and defined in (4).
With a condition $\varepsilon = 10^{-3}$ and after 10 *seconds, the solver IAVIA returns the boundaries presented in Figure 8, where the graph of f has been superposed.*

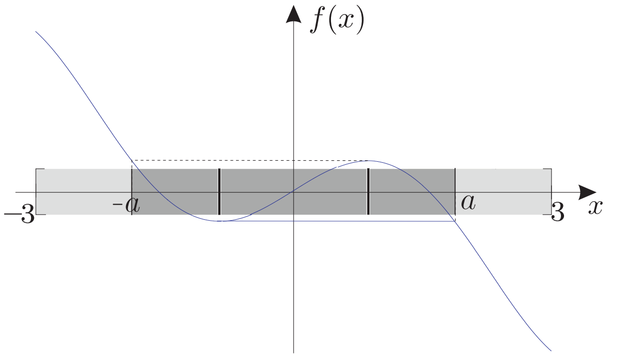

Fig. 8. Injectivity Analysis of f. Intervals from dark grey to light grey are respectively the domain where the injectivity function $\mu_{[-3,3]}$ is equal to 3 and 1 (in this example the lower bound equal the upper bound). The black intervals correspond to the undeterminate domains (where the enclosure of $\mu_{[-3,3]}$ failed). The white interval correspond to the domains where the function $\mu_{[-3,3]}$ is enclosed between 1 and 3.

5 Numerical test for structural identifiability

This section gives an illustrative example which shows the efficient of the (numerical) algorithm IAVIA to test models for structural identifiability.

5.1 Test case

Consider the parametric model $\mathcal{M}(\mathbf{p})$ defined by the following state equations :

$$\begin{cases} \frac{d}{dt}x(t) &= \left[(1-p_2)\,p_1\cos p_1 + \sin p_1 + 1\right]x(t) + u(t) \\ y(t) &= \left[p_1\left(1+\sin p_1 - p_2\sin x_1\right) + p_2\cos p_1\right]x(t) \end{cases} \tag{53}$$

where the vector of parameters $\mathbf{p} = (p_1, p_2)^T$ belongs to $[\mathbf{p}] = [5, 13] \times \left[0, \frac{1}{10}\right]$. Study the structural identifiability of parameter of (53) amounts to characterize, for all $\mathbf{p} \in [\mathbf{p}]$, the cardinal of

$$\mathbb{S}_{\mathbf{p}} = \{\tilde{\mathbf{p}} \in [\mathbf{p}] \mid \mathcal{M}(\mathbf{p}) = \mathcal{M}(\tilde{\mathbf{p}})\} \tag{54}$$

If $|\mathbb{S}_{\mathbf{p}}| = 1$, the vector of parameters $\mathbf{p}$ is structurally globally identifiable (*s.g.i*); if $|\mathbb{S}_{\mathbf{p}}|$ is finite, $\mathbf{p}$ is structurally locally identifiable (*s.l.i*). Otherwise, $\mathbf{p}$ is unidentifiable.

After the Laplace transformation of (53) and elimination of the state x, one gets the transfer function in canonical form:

$$H(s,\mathbf{p}) = \frac{y(s)}{u(s)} \tag{55}$$

$$= \frac{(1-p_2)\,p_1\cos p_1 + \sin p_1 + 1}{s - p_1\left(1+\sin p_1 - p_2\sin x_1\right) + p_2\cos p_1}. \tag{56}$$

Thus, $\mathcal{M}(\mathbf{p}) = \mathcal{M}(\tilde{\mathbf{p}})$ translates into

$$\mathbf{f}(\mathbf{p}) = \mathbf{f}(\tilde{\mathbf{p}}) \tag{57}$$

where $\mathbf{f} : \mathbb{R}^2 \to \mathbb{R}^2$ is defined by

$$\mathbf{f}(\mathbf{p}) = \begin{pmatrix} (1-p_2)\,p_1\cos p_1 + \sin p_1 + 1 \\ p_1\left(1+\sin p_1 - p_2\sin x_1\right) + p_2\cos p_1 \end{pmatrix}. \tag{58}$$

Therefore the analysis of structural identifiability of (53) amounts to count the number of solutions of Equation (57), for all $\mathbf{p} \in [\mathbf{p}]$. In other words, it consists in studying the injectivity function $\mu_{[\mathbf{p}]}(\cdot)$ of the function $\mathbf{f}$ (defined in (58)). If $\mu_{[\mathbf{p}]}(\mathbf{p}) = 1$, $\mathbf{p}$ is *s.g.i*; if $\mu_{[\mathbf{p}]}(\mathbf{p})$ is bounded, $\mathbf{p}$ is *s.l.i*. Otherwise, $\mathbf{p}$ is unidentifiable. Thus, the solver IAVIA could be used to perform the structural identifiability analysis.

5.2 Solution obtained by IAVIA

Let us enclose the injectivity function $\mu_{[\mathbf{p}]}$ of the function $\mathbf{f}$ (defined in (58) and depicted in Figure 9) with the solver IAVIA.

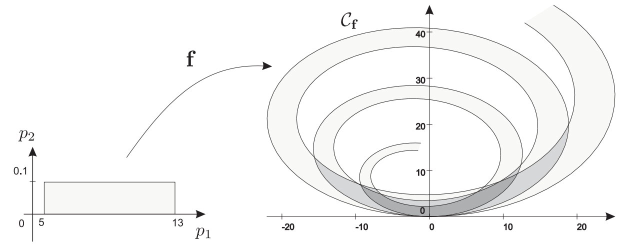

Fig. 9. The function $\mathbf{f}$ transforms the box $[5, 13] \times \left[0, \frac{1}{10}\right]$ into a ribbon which overlaps three times.

One can see that, since the graph of $\mathbf{f}$ overlaps two and three times in the dark gray domains, several vectors of parameters (respectively two and three) lead to the same input-output behaviors of the model (53).

Now, after 60 minutes, the results of the enclosure of the injectivity function obtained by IAVIA are depicted in Figure 10. As predicted, IAVIA finds out domains where the injectivity function is equal to one, two and three which correspond to the domains where one, two and three vectors of parameters are possible. As a conclusion, the structural identifiability of the model (53) is test and zones of the parametric space where several vectors of parameters are possible have been characterized.
Remark that the color of the gray domains on Figure 10 has been chosen so that they are mapped (by $\mathbf{f}$) in domains of same color on Figure 9.

6 Conclusion

Consider any differentiable function $\mathbf{f}$ defined from a box $[\mathbf{x}] \subset \mathbb{R}^n$ to $\mathbb{R}^n$. In this paper, we have proposed a new numerical and guaranteed method to enclose the injectivity function of $\mathbf{f}$ defined by

$$\mu(\mathbf{x}) = \left|\{\tilde{\mathbf{x}} \in [\mathbf{x}] \mid \mathbf{f}(\tilde{\mathbf{x}}) = \mathbf{f}(\mathbf{x})\}\right|.$$

Fig. 10. Solution of the process of enclosure of $\mu_{[\mathbf{p}]}$ obtained by IAVIA. In light gray, the value of the parameters for which the system (53) is structurally identifiable ($\mu^+ = \mu^- = 1$). The two dark gray zones correspond to the value of the parameters for which the system (53) is locally identifiable. 2 or 3 parameter vectors are possible ($\mu^+ = \mu^- = 2$ or $\mu^+ = \mu^- = 3$). In the white domains, the injectivity function is enclosed.

To our knowledge it did not exist any numerical method able to perform this enclosure. Note that, in case of functions $\mathbf{f} : \mathbb{R} \to \mathbb{R}$ and $\mathbf{f} : \mathbb{R}^2 \to \mathbb{R}^2$, the solver IAVIA developed in C++ is made available.

In the context of parameter estimation, we have shown that the proposed algorithm returns domains for which a known and fixed number of parameters is possible. Therefore, a numerical test for structural identifiability is obtained.

In order to fill out this work, note that the efficiency of the algorithm can be improved by the additional uses of constraint propagation [6]. Secondly, it will be possible to build a graph which links the domains of same image by function $\mathbf{f}$. For instance, in the context of parameter estimation, it will be interesting to take to into account this additional information. Indeed, suppose that a estimation of the parameter vector have been obtained via any numerical method (*e.g.* mean square error). Therefore, it will be possible to deduce, on the basis of their numerical values, all the equivalent vectors of parameters (linked in the graph) for which the model holds the same behavior.

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