# Applications of computer algebra in the identifiability and diagnosability studies 

Nathalie Verdière, Sébastien Orange

Normandie Univ, UNIHAVRE, LMAH, FR-CNRS-3335, ISCN, 76600 Le Havre, France ISSAC 2022


## Outline

(1) The relative identifiability

- State of the problem
- A short quiz
- A first neuron model
- Formalization of the identifiability definition
- Towards the relative identifiability with a (little) more complex example
- Conclusion
(2) Fault diagnosability
- State of the problem
- Algebraic signature
- Characterization of a single fault/Expected values of ASig
- Conclusion

Tutorial

- Relative identifiability
- Diagnosability
(4) Bibliography


## Considered model

Given a system or a process, some quantities interact:


Neuron responding to a electrical signal

- Electrical signal (I)
- Membrane potential ( $V$ )
- Perturbations
- Non measurable varying quantities
- Unknown constant values


Schematic representation of the functioning of the neuron

$$
\begin{array}{ll}
\leftrightarrow & u=I=\text { input } \\
\leftrightarrow & y=V=\text { output } \\
\leftrightarrow & b \\
\leftrightarrow & x \\
\leftrightarrow & p=\text { vector of unknown parameters. }
\end{array}
$$

## Considered model

Given a system or a process, some quantities interact:


Neuron responding to a electrical signal


Schematic representation of the functioning of the neuron

$$
\left\{\begin{array}{l}
\dot{x}(t, p)=f(x(t, p), u(t), p)  \tag{1}\\
y(t, p)=h(x(t, p), p)
\end{array}\right.
$$

$\checkmark f$, $h$ : real functions, analytic on $M$ (an open set of $\mathbb{R}^{n}$ ),
$\checkmark p \in \mathcal{U}_{\mathcal{P}}$ : vector of parameters,
$\mathcal{U}_{\mathcal{P}} \subset \mathbb{R}^{r}$ : an a priori known set of admissible parameters.

Assume that the process can be modeled by

$$
\left\{\begin{array}{l}
\dot{x}(t, p)=f(x(t, p), u(t), p), \\
y(t, p)=h(x(t, p), p) .
\end{array}\right.
$$

Two problems can be considered:
$\checkmark$ The forward problem: given $p, u$, find $x$ and $y$.
$\checkmark$ The inverse problem: given $y$ and $u$, estimate $p$.
(1) Identifiability problem

## Question

From the output(s) of the system, is it possible to estimate uniquely the parameter vector $p$ ?
If the answer is YES, then the model is said identifiable.
(2) Identification problem

Assume that the process can be modeled by

$$
\left\{\begin{array}{l}
\dot{x}(t, p)=f(x(t, p), u(t), p), \\
y(t, p)=h(x(t, p), p) .
\end{array}\right.
$$

Two problems can be considered:
$\checkmark$ The forward problem: given $p, u$, find $x$ and $y$.
$\checkmark$ The inverse problem: given $y$ and $u$, estimate $p$.
A property of lots of inverse problems: ill-posedness.

## Well-posedness is the sense of Hadamard

A problem is said well-posed in the sense of Hadamard if it satisfies the following properties:
(1) Existence: For all (suitable) data, there exists a solution of the problem (in an appropriate sense)
(2) Unicity : for all available data, the solution is unique
(3) Stability : the solution depends continuously of the data.

Example: The differentiation and integration are two inverse problems of each other.

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has .... neurons
$\checkmark$ The insects have approximatively ..... of neurons
$\checkmark$ Modern man has ........ of neurons in its best form
$\checkmark$ Every day we loose approximatively ..... neurons, which is the equivalent of ......
$\checkmark$ At 80 years old, the brain is only ..... percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively ..... of neurons
$\checkmark$ Modern man has ........ of neurons in its best form
$\checkmark$ Every day we loose approximatively ..... neurons, which is the equivalent of ......
$\checkmark$ At 80 years old, the brain is only ..... percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has ........ of neurons in its best form
$\checkmark$ Every day we loose approximatively ..... neurons, which is the equivalent of ......
$\checkmark$ At 80 years old, the brain is only ..... percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has 86 billion of neurons in its best form
$\checkmark$ Every day we loose approximatively ..... neurons, which is the equivalent of ......
$\checkmark$ At 80 years old, the brain is only ..... percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has 86 billion of neurons in its best form
$\checkmark$ Every day we loose approximatively 85.000 neurons, which is the equivalent of 31 millions by year ( $\approx 1$ by sec)
$\checkmark$ At 80 years old, the brain is only ..... percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has 86 billion of neurons in its best form
$\checkmark$ Every day we loose approximatively 85.000 neurons, which is the equivalent of 31 millions by year ( $\approx 1$ by sec)
$\checkmark$ At 80 years old, the brain is only 70 percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to ......

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has 86 billion of neurons in its best form
$\checkmark$ Every day we loose approximatively 85.000 neurons, which is the equivalent of 31 millions by year ( $\approx 1$ by sec)
$\checkmark$ At 80 years old, the brain is only 70 percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to $120 \mathrm{~m} / \mathrm{s}$, ie $430 \mathrm{~km} / \mathrm{h}$.

## What about the neuron?

$\checkmark$ Microscopic worm Caenorhabditis elegans ( $\approx 1 \mathrm{~mm}$ de long) has 302 neurons
$\checkmark$ The insects have approximatively one million of neurons
$\checkmark$ Modern man has 86 billion of neurons in its best form
$\checkmark$ Every day we loose approximatively 85.000 neurons, which is the equivalent of 31 millions by year ( $\approx 1$ by sec)
$\checkmark$ At 80 years old, the brain is only 70 percent of what it was around 20 years
$\checkmark$ Nerve information passes from neurons to neurons, up to $120 \mathrm{~m} / \mathrm{s}$, ie $430 \mathrm{~km} / \mathrm{h}$.

## Neuron

A neuron is a nerve cell, that is an electrically excitable cell that receives, processes, and transmits information through electrical and chemical signals.


## Membrane

A lipid membrane
A membrane is composed of a lipid bilayer which separates the intracellular milieu and the extracellular milieu.


The main ions in a neuron are:

- Sodium $\left(\mathrm{Na}^{+}\right)$
- Potassium ( $K^{+}$)
- Calcium ( $\mathrm{Ca}^{2+}$ )
- Chlorure $\left(\mathrm{Cl}^{-}\right)$

- Unequally distribution of ions
on both sides of the membrane
- Specific channels for each ion
- Channels can be:
$\checkmark$ open or close
$\checkmark$ active or inactive.

However there is electroneutrality!


Some mechanisms permit to regulate ionic concentrations and to maintain them constant. Two types of transport:
$\checkmark$ passive transport:

- the concentration gradient: ions go from the most concentrated milieu to the least concentrated milieu extracellular $\rightarrow$ intracellular: $\mathrm{Cl}^{-}, \mathrm{Na}^{+}, \mathrm{Ca}^{2+}$ intracellular $\rightarrow$ extracellular: $\mathrm{K}^{+}$
- electrical gradient: the membrane is electrically charged: negatively inside, positively outside extracellular $\rightarrow$ intracellular: $\mathrm{K}^{+}, \mathrm{Na}^{+}$et $\mathrm{Ca}^{2+}$ are attracted inside the neuron intracellular $\rightarrow$ extracellular: $\mathrm{Cl}^{-}$
$\checkmark$ active transport (NA/K pump) requiring energy.


Potential differences:
$\checkmark$ the potential difference of the membrane:

$$
V_{m}=\underbrace{V_{i}}_{\text {intracellular potential }}-\underbrace{V_{e}}_{\text {extracellular potential }}
$$

$\checkmark$ the potential difference due to the passage of an ion:
$V_{m}-$
$\underbrace{E_{i o n}}$
equilibrium potential of an ion
The current due to the passage of an ion in a channel:
$\underbrace{V_{m}-E_{i o n}}_{m V}=\underbrace{r}_{\text {resistance of channel }} \times \underbrace{I_{i o n}}_{\text {ionic current }(\mathrm{pA})} \Leftrightarrow I_{\text {ion }}=\underbrace{G}_{\text {conductance (siemens } S \text { ) }}\left(V_{m}-E_{i o n}\right)$.

Modeling of a simple ion channel with one activation (m):

$$
I=G(V-E) \text { where } G=g m
$$

where

- $V(m V)$ : voltage
- $g(n S)$ : maximal conductance
- $E(m V)$ : equilibrium potential
- $m$ is the probability of a canal to be open

Modeling of a simple ion channel with one activation (m):

$$
I=G(V-E) \text { where } G=g m
$$

where

- $V(m V)$ : voltage
- $g(n S)$ : maximal conductance
- $E(m V)$ : equilibrium potential
- $m$ is the probability of a canal to be open

The equation describing the activation of the gates to the answer of the potential of membrane is

$$
\frac{d m}{d t}=\frac{m_{\infty}(V)-m}{\tau(V)}
$$

where

- $m_{\infty}(V)$ : the equilibrium value of $m$,
- $\tau(V)$ : times at which the equilibrium is attained.


## Question

Is it possible to determine in a unique way $m_{\infty}, \tau, g$ from the measurement of the current?

## What can we measure?

The voltage-clamp protocol

- characterizes the activation or inactivation properties of the ionic canal
- necessitates to treat the membrane of the neuron (tetrodoxine)
- consists in holding the voltage $(=V)$ piecewise constant $\hookrightarrow$ after a while, $m_{\infty}, \tau$ can be considered as constant and we have

$$
\frac{d m}{d t}=\frac{m_{\infty}-m}{\tau}
$$

## Assumptions

$\checkmark \quad V=$ constant input
$\checkmark \quad I=$ output ( $=y$ )
$\checkmark m=$ state variable $(=x)$

A first example: The equation of one ion channel with one activation variable:

$$
\left\{\begin{array} { l l } 
{ I } & { = g m ( V - E ) } \\
{ \frac { d m } { d t } } & { = \frac { m _ { \infty } - m } { \tau } }
\end{array} \underset { \substack { \mathrm { u } : = \mathrm { V } - \mathrm { E } = c \mathrm { cst } , \\
\mathrm { y } : = 1 } } { \Longleftrightarrow } \left\{\begin{array}{ll}
y & =g m u \\
\frac{d m}{d t} & =\frac{m_{\infty}-m}{\tau}
\end{array}\right.\right.
$$

Controlled models $(u \neq 0)$ WITHOUT initial condition; $(\bar{x}, \bar{y})=$ unique set of solutions

- The model is globally identifiable if there exists an input $u$ such that, for all $p \in \mathcal{U}_{p}$, one gets

$$
\left.\begin{array}{c}
\bar{y}(t, p) \neq \emptyset  \tag{2}\\
\bar{y}(t, p) \cap \bar{y}(t, \bar{p}) \neq \emptyset, \forall t \geq 0, \bar{p} \in \mathcal{U}_{p}
\end{array}\right\} \Rightarrow p=\bar{p}
$$

- The model is locally identifiable if it is globally identifiable in an open neighborhood $v(p) \subset \mathcal{U}_{p}$ of $p$.


## Proposition

If $V$ is a constant input and $I$ is an output of the model then the model is not identifiable, in particular with respect to $\tau$ and $m_{\infty}$.

Proof.

A first example: The equation of one ion channel with one activation variable:

$$
\left\{\begin{array} { l l l } 
{ I } & { = g m ( V - E ) } \\
{ \frac { d m } { d t } } & { = \frac { m _ { \infty } - m } { \tau } }
\end{array} \underset { \substack { \mathrm { u } : = \mathrm { V } - \mathrm { E } = c s t , \\
\mathrm { y } : = 1 } } { \Longleftrightarrow } \left\{\begin{array}{rl}
y & =g m u \\
\frac{d m}{d t} & =\frac{m_{\infty}-m}{\tau}
\end{array}\right.\right.
$$

Concretely


The model can produce exactly the same output for different parameter/initial condition values!

A first example: The equation of one ion channel with one activation variable:

$$
\left\{\begin{array} { r l } 
{ l } & { = g m ( V - E ) } \\
{ \frac { d m } { d t } } & { = \frac { m _ { \infty } - m } { m ^ { 2 } } } \\
{ m ( 0 ) } & { = m _ { 0 } }
\end{array} \underset { \substack { u \\
y : = 1 \\
y : = - E = c s t } } { \Longleftrightarrow } \left\{\begin{array}{ll}
y & =g m u \\
m & =m_{\infty}+\left(m_{0}-m_{\infty}\right) e^{-\frac{t}{\tau}}
\end{array}\right.\right.
$$

Controlled model $(u \neq 0)$ WITH initial conditions; $(x, y)$ unique solution

- The model is globally identifiable if there exists an input $u$ such that, for all $p, \bar{p} \in \mathcal{U}_{p}$, there exists $t_{1}>0$ such that if for all $t \in\left[0, t_{1}\right]$, the equalities $y(t, p)=y(t, \bar{p})$ implies that $p=\bar{p}$.
- The model is locally identifiable if it is globally in an open neighborhood $v(p) \subset \mathcal{U}_{p}$ of $p$.


## Proposition

If $V$ is a constant input and $l$ is an output of the model then the model is identifiable, in particular $\tau$ and $m_{\infty}$.

Proof.

## Summary

$\checkmark$ Identifiability: based on specific relations called Input-Output (IO) polynomials.
$\checkmark$ The Rosenfeld-Groebner algorithm permits to obtain them. They take the form
$P(y, u, p)=m_{0}(y, u)+\sum_{k=1}^{q} \gamma_{k}(p) m_{k}(y, u)=0$.
$\checkmark$ If $\left(m_{k}(y, u)\right)_{k=1, \ldots, q}$ are linearly independent, the model is globally identifiable at $p$ if for all $\bar{p} \in \mathcal{U}_{p}$

$$
\begin{equation*}
\forall k=1, \ldots, q, \gamma_{k}(\bar{p})=\gamma_{k}(p) \Rightarrow p=\bar{p} \tag{3}
\end{equation*}
$$

$\checkmark$ If $\phi(p)=\left(\gamma_{k}(p)\right)_{k=1, \ldots, q}$, (3) consists in verifying that $\phi$ is injective.
$\checkmark$ Initial conditions can be introduced with algebraic relations.

A (little) more complex example....

$$
\left\{\begin{array} { l l } 
{ l = g m h ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m \infty - m } { \tau _ { m } } , } & { \multicolumn {1} { c } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , } & { x _ { 1 } = m , x _ { 2 } = h , u = v - E } \\
{ p _ { 1 } = \frac { 1 } { \tau _ { m } } , p _ { 2 } = m _ { \infty } }
\end{array} \quad \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2} \\
p_{3}=\frac{1}{\tau_{h}}, p_{4}=h_{\infty}, p_{5}=g
\end{array}\right.\right.
$$

Non identifiable mode!!

A (little) more complex example....

$$
\left\{\begin{array} { l } 
{ I = g m h ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau m } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \Longleftrightarrow \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2}, \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right), \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right)
\end{array}\right.\right.
$$

## Questions:

$x$ Key parameters permitting to obtain the identifiability of one or some non measurable parameters and eventually the identifiability of the model?
$x$ Roles of the constraints?
$x$ Natural integration of the constraints or the initial conditions in the identifiability study?

$$
\left\{\begin{array} { l } 
{ I = g m h ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau _ { m } } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \Longleftrightarrow \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2}, \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right), \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right) .
\end{array}\right.\right.
$$

Obtain from $\phi$ and a set of algebraic constraints a decision tree!

$$
\left\{\begin{array} { l } 
{ l = g m h ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau _ { m } } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \Longleftrightarrow \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2}, \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right), \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right) .
\end{array}\right.\right.
$$

First step: Redefine the identifiability: Relative identifiability For example:


- $p_{1}$ is not identifiable;
- $p_{3}$ is relatively identifiable with respect to the set $\left\{p_{1}\right\}$;
- $p_{5}$ relatively identifiable with respect to the set $\left\{p_{1}, p_{3}\right\}$;
- $p_{2}$ and $p_{4}$ are not relatively identifiable with respect to the set $\left\{p_{1}, p_{3}\right\}$.

$$
\left\{\begin{array} { l } 
{ l = \operatorname { g m h } ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau _ { m } } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \Longleftrightarrow \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2}, \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right), \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right) .
\end{array}\right.\right.
$$

Second step: definition of a semi-algebraic set from

- $\phi(p)=\left(\gamma_{k}(p)\right)_{k=1, \ldots, 9}$ the coefficient vector of the IO polynomial:

$$
\begin{equation*}
\ddot{y}^{2}+\gamma_{1} y^{2}+\gamma_{2} y \dot{y}+\gamma_{3} y \ddot{y}+\gamma_{4} y+\gamma_{5} \dot{y}^{2}+\gamma_{6} \dot{y} \ddot{y}+\gamma_{7} \dot{y}-\gamma_{8} \ddot{y}+\gamma_{9}=0 \tag{4}
\end{equation*}
$$

- $\mathcal{C}$ the semi-algebraic set defined by $C(p)$ composed of all algebraic equations and inequalities verified by the components of the parameter vector $p=\left(p_{1}, \ldots, p_{5}\right)$
to test

$$
\left\{\begin{array}{ll}
p \in \mathcal{C} & \\
\bar{p} \in \mathcal{C} & \\
p_{1} & =\bar{p}_{1}, \\
p_{3} & =\bar{p}_{3}, \\
\phi(p)=\phi(\bar{p})
\end{array} \quad \Rightarrow p_{5}=\bar{p}_{5}\right.
$$

$$
\left\{\begin{array} { l } 
{ l = \operatorname { g m h } ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau _ { m } } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \Longleftrightarrow \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2} \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right) \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right) .
\end{array}\right.\right.
$$

## Second step: definition of a semi-algebraic set from

- $\phi(p)=\left(\gamma_{k}(p)\right)_{k=1, \ldots, 9}$ the coefficient vector of the IO polynomial:

$$
\begin{equation*}
\ddot{y}^{2}+\gamma_{1} y^{2}+\gamma_{2} y \dot{y}+\gamma_{3} y \ddot{y}+\gamma_{4} y+\gamma_{5} \dot{y}^{2}+\gamma_{6} \dot{y} \ddot{y}+\gamma_{7} \dot{y}-\gamma_{8} \ddot{y}+\gamma_{9}=0 \tag{5}
\end{equation*}
$$

- $\mathcal{C}$ the semi-algebraic set defined by $C(p)$ composed of all algebraic equations and inequalities verified by the components of the parameter vector $p=\left(p_{1}, \ldots, p_{5}\right)$
to test
$S_{p_{1}, p_{3}} \cup\left\{p_{5} \neq \bar{p}_{5}\right\} \quad$ has no real solution.
where
$S_{p_{1}, p_{3}}=C(p) \cup C(\bar{p}) \cup\left\{p_{1}=\bar{p}_{1}, p_{3}=\bar{p}_{3}\right\} \cup\left\{\gamma_{k}(p)=\gamma_{k}(\bar{p}) \mid k=1, \ldots, 9\right\}$.
$\Longrightarrow$ development of a method and the algorithm IdentifiabilityTree.

$$
\left\{\begin{array} { l } 
{ l = g m h ( V - E ) , } \\
{ \frac { d m } { d t } = \frac { m _ { \infty } - m } { \tau _ { m } } , } \\
{ \frac { d h } { d t } = \frac { h _ { \infty } - h } { \tau _ { h } } , }
\end{array} \quad \begin{array} { l } 
{ x _ { 1 } = m , x _ { 2 } = h , u = v - E } \\
{ p _ { 1 } = \frac { 1 } { \tau _ { m } } , p _ { 2 } = m _ { \infty } }
\end{array} \quad \left\{\begin{array}{l}
y=u p_{5} x_{1} x_{2} \\
\dot{x}_{1}=p_{1}\left(p_{2}-x_{1}\right) \\
\dot{x}_{2}=p_{3}\left(p_{4}-x_{2}\right)
\end{array}\right.\right.
$$

## Results of the IdentifiabilityTree algorithm:

- One of the branch: $\left[D_{2}, D_{4}, p_{5}, D_{3}, p_{1}\right]$
- Two groups of parameters $\left\{p_{2}, p_{4}, p_{5}\right\}$ and $\left\{p_{1}, p_{3}\right\}$.
- Determination of the two parameters $p_{2}, p_{4}$ and the parameter $p_{3}$ ensures the identifiability of all the parameters.


## The voltage clamp experiment:

(1) Estimate the triplet $\left\{p_{2}, p_{4}, p_{5}\right\}$ from $y=u p_{5} x_{1} x_{2}$ in fixing the voltage at different values and measuring the transmembrane current trace
( $V$ constant: $\left.I=(V-E) p_{5} p_{2} p_{4}\right)$;
(2) Estimate $p_{1}$ and $p_{3}$ at a particular voltage value dependence.

## Conclusion

Identifiability study:
$\checkmark$ Ensures good properties to the mathematical model;
$\checkmark$ Extension of this definition;
$\checkmark$ Other examples: strategy to reparametrize unidentifiable ODE models into identifiable ones (Evans 2000, Meshkat 2011)....

The models

$$
\left\{\begin{array}{l}
\dot{x}(t, p, f)=g(x(t, p), u(t), f, p),  \tag{6}\\
y(t, p, f)=h(x(t, p), u(t), f, p) \\
x\left(t_{0}, p, f\right)=x_{0} \\
t_{0} \leq t \leq T
\end{array}\right.
$$

## Definitions

$\checkmark \mathbf{A}$ fault is an unpermitted deviation of at least one parameter of the system from the acceptable standard condition.
$\checkmark$ Fault diagnosability establishes which faults can be discriminated using the available sensors in a system.
$\checkmark$ Fault diagnosis consists in fault detection of the malfunction of a system and the fault isolation of the faulty component.
$f=0$ means no fault. In the case of uncontrolled models $u=0$.

Example: Mass $(m=1)$ attached to an elastic spring (force $k$ ) $u$ external force ( $\neq 0$ ), $d \geq 1$

$$
\ddot{y}+k\left(f_{1}-1\right)^{2} y-\left(d+f_{2}\right) u=0 \quad \phi(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)
$$

Example: Mass $(m=1)$ attached to an elastic spring (force $k$ ) u external force ( $\neq 0$ ), $d \geq 1$

$$
\ddot{y}+k\left(f_{1}-1\right)^{2} y-\left(d+f_{2}\right) u=0 \quad \phi(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)
$$

Algebraic signature
$\operatorname{ASig}(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)$, in particular:

$$
\begin{aligned}
& x \operatorname{ASig}\left(f_{\{1\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d\right) \text { et } \operatorname{ASig}\left(f_{\{1,2\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right) . \\
& x \operatorname{ASig}\left(f_{\{1\}}\right) \cap \operatorname{ASig}\left(f_{\{1,2\}}\right)=\emptyset \text { for all } f_{2} \in(0,2),-d \neq-d-f_{2} .
\end{aligned}
$$

Example: Mass $(m=1)$ attached to an elastic spring (force $k$ ) $u$ external force $(\not \equiv 0)$, $\bar{d} \geq 1$

$$
\ddot{y}+k\left(f_{1}-1\right)^{2} y-\left(d+f_{2}\right) u=0 \quad \phi(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)
$$

Algebraic signature
$\operatorname{ASig}(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)$, in particular:

$$
\begin{aligned}
& x \operatorname{ASig}\left(f_{\{1\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d\right) \text { et } \operatorname{ASig}\left(f_{\{1,2\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right) . \\
& x \operatorname{ASig}\left(f_{\{1\}}\right) \cap \operatorname{ASig}\left(f_{\{1,2\}}\right)=\emptyset \text { for all } f_{2} \in(0,2),-d \neq-d-f_{2}
\end{aligned}
$$

## Definitions

$x$ Two sets of faults are said algebraic discriminable if there exists an algebraic signature, such that, for all input $u$, the two signatures have an empty intersection.
$x$ If all the distinct sets of faults are algebraic discriminable, the model is said algebraically diagnosable.

Example: Mass $(m=1)$ attached to an elastic spring (force $k$ ) $u$ external force $(\not \equiv 0)$, $\bar{d} \geq 1$

$$
\ddot{y}+k\left(f_{1}-1\right)^{2} y-\left(d+f_{2}\right) u=0 \quad \phi(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)
$$

Algebraic signature
$\operatorname{ASig}(f)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)$, in particular:

$$
\begin{aligned}
& x \operatorname{ASig}\left(f_{\{1\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d\right) \text { et } \operatorname{ASig}\left(f_{\{1,2\}}\right)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right) . \\
& x \operatorname{ASig}\left(f_{\{1\}}\right) \cap \operatorname{ASig}\left(f_{\{1,2\}}\right)=\emptyset \text { for all } f_{2} \in(0,2),-d \neq-d-f_{2} .
\end{aligned}
$$

## Definitions

$x$ Two sets of faults are said algebraic discriminable if there exists an algebraic signature, such that, for all input $u$, the two signatures have an empty intersection.
$x$ If all the distinct sets of faults are algebraic discriminable, the model is said algebraically diagnosable.

## Remark

The current algebraic signature is not sufficiently discriminant!

$$
P(y, u, p, f)=m_{0}(y, u)+\sum_{k=1}^{q} \gamma_{k}(p, f) m_{k}(y, u)=0 \quad \text { and }\left\{\begin{array}{l}
\gamma_{1}(p, f)=\phi_{1} \\
\vdots \\
\gamma_{q}(p, f)=\phi_{q}
\end{array}\right.
$$

Algorithm Algebraic-Signature
$\checkmark$ Groebner basis computation;
$P(y, u, p, f)=m_{0}(y, u)+\sum_{k=1}^{a} \gamma_{k}(p, f) m_{k}(y, u)=0$ and $\left\{\begin{array}{l}\gamma_{1}(p, f)=\phi_{1}, \\ \vdots \\ \gamma_{q}(p, f)=\phi_{q},\end{array}\right.$
Algorithm Algebraic-Signature
$\checkmark$ Groebner basis computation;
Example: $\ddot{x}+k\left(f_{1}-1\right)^{2} x-\left(d+f_{2}\right) u=0, f_{1} \in[0,2), f_{2} \in[0,2)$
$\overline{\text { with } \phi(f)}=\left(\phi_{1}, \phi_{2}\right)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)$.
Algorithm Algebraic_signature: $\operatorname{ASig}(f)=\left(\phi_{1}-k, \phi_{2}+d\right)$.

## Remarks

$\checkmark$ Algebraic signature: each of its component depends only on $\phi_{k}$ and the parameters of the system;
$\checkmark$ By construction, one of the component of the algebraic signature vanishes when at least one specific (multiple) fault occurs.
$P(y, u, p, f)=m_{0}(y, u)+\sum_{k=1}^{a} \gamma_{k}(p, f) m_{k}(y, u)=0$ and $\left\{\begin{array}{l}\gamma_{1}(p, f)=\phi_{1}, \\ \vdots \\ \gamma_{q}(p, f)=\phi_{q},\end{array}\right.$
Algorithm Algebraic-Signature
$\checkmark$ Groebner basis computation;
Example: $\ddot{x}+k\left(f_{1}-1\right)^{2} x-\left(d+f_{2}\right) u=0, f_{1} \in[0,2), f_{2} \in[0,2)$
$\overline{\text { with } \phi(f)}=\left(\phi_{1}, \phi_{2}\right)=\left(k\left(f_{1}-1\right)^{2},-d-f_{2}\right)$.
Algorithm Algebraic_signature: $\operatorname{ASig}(f)=\left(\phi_{1}-k, \phi_{2}+d\right)$.

## Remarks

$\checkmark$ Algebraic signature: each of its component depends only on $\phi_{k}$ and the parameters of the system;
$\checkmark$ By construction, one of the component of the algebraic signature vanishes when at least one specific (multiple) fault occurs.

How to certify the values of ASig?

$$
\begin{array}{cccc}
\text { ASig : } & \mathbb{R}^{e} & \longrightarrow & \left(R\left[\phi_{1}, \ldots, \phi_{N}\right]\right)^{\prime} \\
f & \mapsto & \left(\operatorname{ASig}_{1}(\phi), \ldots, \operatorname{ASig}_{l}(\phi)\right)
\end{array}
$$

Notations: ( $\mathcal{N}$ subset of $\{1, \ldots, e\}$ )

- $C_{p, f}=$ set of all algebraic equations and inequalities verified by $p$ and $f$.

Example: $\ddot{x}+k\left(f_{1}-1\right)^{2} x-\left(d+f_{2}\right) u=0, \operatorname{ASig}(f)=\left(\phi_{1}-k, \phi_{2}+d\right)$.
$C_{p, f}=\left\{0<k<4,1 \leq d, 0 \leq f_{1}<2,0 \leq f_{2}<2\right\}$.

- $S_{\mathcal{N}}=\left\{\gamma_{1}(p, f)=\phi_{1}, \ldots, \gamma_{q}(p, f)=\phi_{N}\right\} \cup C_{p, f} \cup\left\{f_{i} \neq 0 \mid i \in \mathcal{N}\right\} \cup\left\{f_{i}=0 \mid i \notin \mathcal{N}\right\}$.

Example: $\ddot{x}+k\left(f_{1}-1\right)^{2} x-\left(d+f_{2}\right) u=0, \operatorname{ASig}(f)=\left(\phi_{1}-k, \phi_{2}+d\right)$.
If $\mathcal{N}=\{1\}$ then $S_{\mathcal{N}}=\left\{k\left(f_{1}-1\right)=\phi_{1},\left(d+f_{2}\right)=\phi_{2}\right\} \cup C_{p, t} \cup\left\{f_{1} \neq 0\right\} \cup\left\{f_{2}=0\right\} ;$
If $\mathcal{N}=\{1,2\}$ then $S_{\mathcal{N}}=\left\{k\left(f_{1}-1\right)=\phi_{1},\left(d+f_{2}\right)=\phi_{2}\right\} \cup C_{p, f} \cup\left\{f_{1} \neq 0\right\} \cup\left\{f_{2} \neq 0\right\}$.

$$
\begin{array}{cccc}
\text { ASig : } \quad \mathbb{R}^{e} & \longrightarrow & \left(R\left[\phi_{1}, \ldots, \phi_{N}\right]\right)^{\prime} \\
f & \mapsto & \left(\operatorname{ASig}_{1}(\phi), \ldots, \text { ASig }_{l}(\phi)\right) .
\end{array}
$$

## Criterion

Two criterion to discriminate multiple fault signatures:

- For the multiple fault $f_{\mathcal{N}}, S_{\mathcal{N}} \cup\left\{A\right.$ Sig $\left._{k}\left(f_{\mathcal{N}}\right)=0\right\}=\emptyset$ ?
- When $\operatorname{ASig}_{j}(f)=0$ is equivalent to $f_{i}=0$ ?
$\hookrightarrow$ Algorithm ExpectedValuesOfASign.
Example: $\ddot{x}+k\left(f_{1}-1\right)^{2} x-\left(d+f_{2}\right) u=0, \operatorname{ASig}(f)=\left(\phi_{1}-k, \phi_{2}+d\right)$.

$$
\begin{gathered}
C_{p, f}=\{0<k<4,1 \leq d, \\
\left.0 \leq f_{1}<2,0 \leq f_{2}<2\right\}
\end{gathered}
$$

| $f$ | ASig $_{1}(f)$ | ASig |
| :---: | :---: | :---: |
| $2(f)$ |  |  |
| $f_{\{ \}}$ | 0 | 0 |
| $f_{\{1\}}$ | $\varnothing$ | 0 |
| $f_{\{2\}}$ | 0 | $\varnothing$ |
| $f_{\{1,2\}}$ | $\varnothing$ | $\varnothing$ |

$$
C_{p, f}=\emptyset
$$

| $f$ | ASig $_{1}(f)$ | ASig $g_{2}(f)$ |
| :---: | :---: | :---: |
| $f_{\{ \}}$ | 0 | 0 |
| $f_{\{1\}}$ |  | 0 |
| $f_{\{2\}}$ | 0 | $\varnothing$ |
| $f_{\{1,2\}}$ |  | $\varnothing$ |

## Conclusion

Diagnosability study:
$\checkmark$ from the data collected on the physical system, can the chosen mathematical model permit to discriminate predefined faults that may occur on the system?
$\checkmark$ New example of the interest of computer algebra and semialgebraic approach;
$\checkmark$ Precomputations lead to efficient numerical procedures $\rightarrow$ detect and isolate (multiple) faults.

## Conclusion

Diagnosability study:
$\checkmark$ from the data collected on the physical system, can the chosen mathematical model permit to discriminate predefined faults that may occur on the system?
$\checkmark$ New example of the interest of computer algebra and semialgebraic approach;
$\checkmark$ Precomputations lead to efficient numerical procedures $\rightarrow$ detect and isolate (multiple) faults.

## Procedure RelativeIdentifiabilityTree

Objective: det. the keys param. which estimations turn the model into an ident. one. Inputs: exhaustive summary, constraints on the parameters .
Output: A set of lists def. the relative identifiability tree $\mathcal{T}$ (any prefix $b$ of $I \in \mathcal{T}$ is followed in / by an identifiable parameter wrt to $b$ if there exists one.)
Convention: $-p$ in a list I means that $p$ is not rel. identifiable wrt the param appearing before $p$ in the list $l$.


## Branch and cut tech:

- Parameters relatively ident. wrt the same set of parameters can be permuted.
- The relative identifiability wrt a list of param. does not depend on the list of parameters but on the set they define.

Procedure ASign - Computation of an algebraic signature Objective: obtaining of polynomials discriminating the faults and depending only on the parameters and the components of the exhaustive summary.
Inputs: exhaustive summary, single faults list.
Output: an algebraic signature.


## Procedure ExpectedValuesOfASign

Objective: det. the (multiple) faults which can be discriminated with the alg. signature. Inputs: Alg signature, exhaustive summary, single faults list, param constraints.
Outputs: the lists composed of a (multiple) faults and of the corresponding vector of expected values of the algebraic signature.


## Procedure SingleFaultCharacterization

Objective: Reducing the number of tests needed to determine the table of the expect. values of the algebraic signature.
Inputs: Alg. signature, exhaustive summary, single faults list, parameters contraints. Output: list of 2-uplets $\left[f_{i}\right.$, ASig $\left._{k}\right]$ such that $f_{i} \neq 0 \Leftrightarrow$ ASig $_{k} \neq 0$

$\rightarrow$ The output can be used as an optional argument in proc. ExpectedValuesOfASign.

## THANK YOU FOR YOUR ATTENTION and HAVE FUN WITH THE TUTORIAL!

- F. Boulier. Study and implementation of some algorithms in differential algebra. PhD thesis, Université des Sciences et Technologie de Lille - Lille I, June 1994.
- F. Boulier, D. Lazard, F. Ollivier, and M. Petitot. Computing representation for radicals of finitely generated differential ideals. Technical report, Université Lille I, LIFL, 59655, Villeneuve d'Ascq, 1997.
- C. Chen, J. H. Davenport, J. P. May, M. Moreno Maza, B. Xia, and R. Xiao. Triangular decomposition of semi-algebraic systems. Journal of Symbolic Computation, 49:3-26, 2013.
- D. Csercsik, K.M. Hangos, G. Szederkényi, Identifiability and parameter estimation of a single Hodgkin-Huxley type voltage dependent ion channel under voltage step measurements conditions, Neurocomputing 77, 178-188, 2012.
- L. Denis-Vidal, G. Joly-Blanchard, C. Noiret, and M. Petitot. An algorithm to test identifiability of non-linear systems. In Proceedings of 5th IFAC Symposium on Nonlinear Control Systems, volume 7, pages 174-178, St Petersburg, Russia, 2001.
- M.S. El Din. Raglib: A library for real solving polynomial systems of equations and inequalities, 2007.
- J. C. Faugère. A new efficient algorithm for computing Gröbner bases without reduction to zero (F5). In Proceedings of the 2002 International Symposium on Symbolic and Algebraic Computation, ISSAC 02, page 75-83, New York, NY, USA, 2002. Association for Computing Machinery
- F. Lemaire, C. Chen., J. H. Davenport, M. Moreno Maza, N. Phisanbut, B. Xia, R. Xiao, Y. Xie, Solving semi-algebraic systems with the RegularChains library in Maple, MACIS 2011.
- N. Verdière, C. Jauberthie, L. Travé-Massuyès, Functional diagnosability and detectability of nonlinear models based on analytical redundancy relations, Journal of Process Control, September 2014, Vol. 35, 1-10.
- N. Verdière, S. Orange, Diagnosability in the case of multi-faults in nonlinear models, Journal of Process Control, Vol 69, pp. 1-7, 2018.

