Defining and Testing Identifiability, Illustrated by a HIV model

H Le Meur, François Ollivier

To cite this version:

H Le Meur, François Ollivier. Defining and Testing Identifiability, Illustrated by a HIV model. 4th Workshop on Virus Dynamics, Oct 2019, Paris, France. hal-02415749

HAL Id: hal-02415749
https://hal.archives-ouvertes.fr/hal-02415749
Submitted on 17 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Basic mathematical definitions

In practice, a structure or parametric model is most of the time given by explicit differential equations:

\[ \dot{x}_i = f_i(x,\theta, t), \quad i = 1, \ldots, n. \]

where the \( f_i \) are rational functions, \( x \) is the time, satisfying \( x_i(t) = 0 \) if \( i \notin \mathcal{S} \) are constant parameters, so that \( f_i = 0 \), \( \theta \) are the control functions, and the \( x_i, \theta \) are the state variables.

We need to complete this differential system with initial conditions that are rarely discussed:

\[ x(0) = \xi. \]

Also we need to define outputs:

\[ y = g(x, \theta, t), \quad 1 \leq i \leq r, \]

where the \( g_i \) are also rational functions. Let \( X, Y, \mathcal{A}[\theta] \) be the unique solution defined by the control \( \theta \) and the initial condition \( c \). The differential Zariski open set \( U \) is such that the functions \( f \) and \( g \) are defined on \( U \).

Definition 1. — A function \( H \) of the parameters \( \theta \) is algebraically identifiable if there exists a Zariski open set \( U \subset \mathbb{C}^n \) such that, for every \( \epsilon > 0 \), there is a set of equations \( \mathcal{A}[\theta] \) which defines \( H \) on \( U \) for all \( \theta \) in \( U \).

Algebraically identifiable means that \( \delta_i \) is a differential rational function depending on the derivatives of the \( a \) and the outputs \( y \). Local identifiability means that it is a Zariski algebraic function, so that the value of only locally unique.

One may notice that our definition explicitly involves the local character, which is too often omitted in the literature.

Identification and identifiability

Assuming the mathematical model describes perfectly the actual behavior and the noise is zero, is identifiability the guarantee to achieve identification? And if so, what are the relations between the algebraic mathematical identifiability and the potential suffices of practical identification processes?

Consider the system corresponding to the following universal equation. Assuming that the state \( x \) is measured, it is identifiable (we will see why below).

\[ x' = \frac{h}{d}x + \cos(\nu(t)) \cos(\nu(t)), \quad n(\alpha) = \alpha. \]

where \( a, h, \nu \) and \( d > 0 \) are real numbers.

Defining and Testing Identifiability, Illustrated by a HIV model

H.V.J. Le Meur, CNRS, LAMFA, Univ. de Picardie, 80000 Amiens, France

F. Ollivier, CNRS, LIX, École polytechnique, 91288 Palaiseau Cedex, France

Using the Wronskian

We borrow the following HIV model to Wu et al. where it is assumed that only \( y_1 \) is measured:

\[ \begin{align*}
    V'(t) &= -\gamma V(t) - \beta V(t) \mathcal{I}(t) + T(t), \\
    \gamma y_1(t) &= \beta V(t) \mathcal{I}(t) - T(t), \\
    V(t) &= \mathcal{I}(t) - \mathcal{V}(t), \\
    \mathcal{V}(t) &= \mathcal{V}(t) - \mathcal{V}(t). 
\end{align*} \]

Eliminating \( T \) and \( \mathcal{V} \), one gets an equation of minimal order in \( V \):

\[ P_0(y_1) y_2'' + P_1(y_1) y_2' + P_2(y_1) y_2 = 0. \]

We see that only \( \lambda_2 + \lambda_1 \) and \( \lambda_2 \) appear in this system. So the only vector of new parameters \( \theta = \{ p, \lambda_1 = N \lambda_2, \lambda_2 \in \mathbb{R} \} \) are possibly identifiable. Their local identifiability is deduced by Wu et al. from the non-vanishing of the Jacobian determinant:

\[ \det(\mathcal{J}) = \det(\nabla V / \nabla \theta) \neq 0, \]

using the implicit function theorem. Besides the main monomial \( y_1 \), equation (4) contains the set of 12 monomials \( \{ \mathcal{I} \gamma, \mathcal{V} \gamma, y_1 \gamma, \mathcal{I}^2 \gamma, \mathcal{V}^2 \gamma, y_1^2 \gamma, \mathcal{I} \mathcal{V} \gamma, \mathcal{V} \mathcal{I} \gamma, y_1 \mathcal{I} \gamma, y_1 \mathcal{V} \gamma, y_1 y_1 \gamma, \} \). By the proof of \( \theta \) if the coefficients \( g_3(\theta) \) are not identifiable, there is a non-trivial relation between constant coefficients between these monomials: \( P_0(y_1) P_2(\theta) = P_1(y_1) \) or \( \theta \). The existence of such a relation with \( y_1 \) analytic is equivalent to the vanishing of the Wronskian determinant:

\[ \det(\mathcal{W}(\mathcal{M})) = \det(m_{ij}) = 0, \quad 0 < k < r. \]

The main idea of Sedoglavic’s algorithm is to generate Newton’s method. A key ingredient is to be able to compute the derivative of \( \mathcal{W} \) \( \partial \mathcal{W} / \partial \theta \) with respect to \( \theta \).

The free computer algebra system Maple provides efficient implementations of up to date algorithms for exact and approximate computations, including power series solutions of ODEs and ball arithmetics.

An experimental package allows to compute a linearized system in a form that allows numerical integration in Maple.

References


