

Available online at www.sciencedirect.com



automatica

Automatica 39 (2003) 619-632

www.elsevier.com/locate/automatica

Parameter identifiability of nonlinear systems: the role of initial conditions[☆]

Maria Pia Saccomani^{a,*}, Stefania Audoly^b, Leontina D'Angiò^c

^aDepartment of Information Engineering, University of Padova, Via Gradenigo 6a, 35131 Padova, Italy
 ^bDepartment of Structural Engineering, University of Cagliari, 09100 Cagliari, Italy
 ^cDepartment of Mathematics, University of Cagliari, 09100 Cagliari, Italy

Received 11 January 2002; received in revised form 12 November 2002; accepted 29 November 2002

Abstract

Identifiability is a fundamental prerequisite for model identification; it concerns uniqueness of the model parameters determined from the input—output data, under ideal conditions of noise-free observations and error-free model structure. In the late 1980s concepts of differential algebra have been introduced in control and system theory. Recently, differential algebra tools have been applied to study the identifiability of dynamic systems described by polynomial equations. These methods all exploit the characteristic set of the differential ideal generated by the polynomials defining the system. In this paper, it will be shown that the identifiability test procedures based on differential algebra may fail for systems which are started at specific initial conditions and that this problem is strictly related to the accessibility of the system from the given initial conditions. In particular, when the system is not accessible from the given initial conditions, the ideal *I* having as generators the polynomials defining the dynamic system may not correctly describe the manifold of the solution. In this case a new ideal that includes all differential polynomials vanishing at the solution of the dynamic system started from the initial conditions should be calculated. An identifiability test is proposed which works, under certain technical hypothesis, also for systems with specific initial conditions.

© 2003 Elsevier Science Ltd. All rights reserved.

Keywords: A priori global identifiability; Differential algebra; Model identification; Nonlinear system; Accessibility

1. Introduction

One could safely say that the introduction in the late 1980s of concepts of differential algebra in control and system theory, mainly due to Fliess and Glad (1993), has been an important factor for addressing nonlinear problems previously thought to be intractable. In particular, identifiability analysis requires one to solve systems of highly nonlinear algebraic equations possibly of an infinitive number and of increasing complexity with the model order. Recently differential algebra tools have been applied to study identifiability of nonlinear systems by a number of authors (see Ollivier, 1990; Ljung & Glad, 1994; Glad, 1990;

E-mail addresses: pia@dei.unipd.it (M. Pia Saccomani), audoly@unica.it (S. Audoly), ldangio@tiscali.it (L. D'Angiò).

Audoly, Bellu, D'Angiò, Saccomani, & Cobelli, 2001). These methods all exploit the characteristic set of the differential ideal associated to the dynamic equations of the system. Identifiability concerns uniqueness of the model parameters determined from input-output data, under ideal conditions of noise-free observations and error-free model structure. Identifiability is a fundamental prerequisite for model identification (see e.g. Audoly, D'Angiò, Saccomani, & Cobelli, 1998, and references therein). The idea that the characteristic set (see Section 2) of the differential ideal generated by the dynamic polynomials defining the system, provides the tool for testing global identifiability, is due to Ollivier (1990) and Ljung and Glad (1994). More recently, the authors of this paper have developed new algorithms (Audoly et al., 2001; D'Angiò, Audoly, Bellu, Saccomani, & Cobelli, 1994; Saccomani, Audoly, Bellu, D'Angiò, & Cobelli, 1997), based on differential algebra, which integrate the different strategies proposed in Ollivier (1990) and Ljung and Glad (1994) and enlarge their domain of

 $^{^{\}dot{\alpha}}$ This paper was not presented at any IFAC meeting. This paper was recommended for publication in revised form by Associate Editor Johan Schoukens under the direction of Editor Torsten Söderström.

^{*} Corresponding author.

applicability. However, it has been observed that even with the new algorithms, problems can arise in testing identifiability for systems started at given initial conditions, a situation frequently encountered in identification of biological and medical systems. As we shall see, in order to guarantee the correctness of the identifiability tests based on the characteristic set, one has to check that some structural conditions hold, which are related to the specific initial condition. In this paper, it will be shown that a natural structural condition which guarantees the validity of the identifiability test is the accessibility of the system from the given initial condition. Thus, checking accessibility from a given state appears to be a crucial step for testing identifiability from the exhaustive summary (Ollivier, 1990; Audoly et al., 2001) of the characteristic set. In particular, when the system is not accessible, a new ideal describing the solutions of the system has to be constructed. In the paper (Saccomani, Audoly, & D'Angiò, 2001) the authors propose a modified version of a previous algorithm (Audoly et al., 2001) for testing global identifiability of system which may not be accessible from specific initial states.

The layout of the paper is the following:

In Section 2, we briefly summarise the basic definitions of differential algebra and introduce the concept of characteristic set of a differential ideal.

In Section 3, after introducing the basic nonlinear dynamic structure under test, some definitions regarding parameter identifiability are recalled and the identifiability test based on the characteristic set is illustrated. In particular, the characteristic set of the ideal generated by the polynomials defining the dynamic system is introduced and the concept of *exhaustive summary* of the model is recalled. An example is presented to show that the identifiability testing procedure may lead to errors for systems started at certain "special" initial conditions.

In Section 4, in order to characterize the set of "special" initial states where the identifiability test can fail, only the state equations of the system are considered. It is shown that, if the system is accessible from the given initial conditions, the ideal *I* having as generators the polynomials defining the state equations, correctly describes the manifold of the solutions of the state equations starting at the given initial conditions. Conversely, if the system is nonaccessible from the given initial conditions, the ideal *I* does not describe exactly the manifold of the solutions. In this case, the right ideal to consider includes *I* plus the algebraic equations defining the invariant submanifold where the state evolution takes place.

In Section 5, the goal is to propose an alternative characteristic set algorithm which can be used when it is known that the system starts from "special" initial conditions. The ideal, I_{Σ} , generated by the polynomials defining the equations of the dynamic system is considered. It is shown that, when the system is accessible from given initial conditions, the identifiability test performed on the exhaustive summary provided by the characteristic set of I_{Σ} , works correctly. Conversely,

when the system is nonaccessible from the given initial conditions, it is shown that the identifiability test based on the characteristic set may lead to errors. In order to correctly set up the identifiability test, the algebraic equation defining the invariant submanifold where the state evolution takes place has to be added to the generators of I_{Σ} .

2. Background on differential algebra

2.1. Differential ideals and characteristic sets

For a formal treatment of differential algebra, the reader is referred to Ritt (1950), Kolchin (1973), Forsman (1991) and Carrà Ferro (1989). Here, we shall just recall the definitions and notions which are necessary to set the notations used in the rest of the paper.

Let $\mathbf{z} := [z_1, ..., z_n]$ be a vector of smooth functions of the variable t (time); the totality of polynomials in the variables z_i and their derivatives with coefficients in a field K, is a differential polynomial ring which will be denoted $K[\mathbf{z}]$.

Consider a set S of differential polynomials belonging to $K[\mathbf{z}]$. The differential ideal $I = I_S$, sometimes also denoted I(S), generated by S, is the smallest subset of $K[\mathbf{z}]$ containing S, which is closed with respect to addition, multiplication by arbitrary elements of $K[\mathbf{z}]$ and with respect to differentiation. The elements of S are generators of the ideal.

A differential ideal I is called *prime* if $A_iA_j \in I$ implies that $A_i \in I$ or $A_j \in I$ and *perfect* if $A \in I$ whenever A^k does (i.e. a perfect ideal coincides with its own radical).

In order to handle differential ideals, a *ranking*, i.e. a total ordering, denoted "<", among the variables and their derivatives, must be introduced (Ritt, 1950). Let $z_i^{(\mu)}$ and $z_j^{(\nu)}$ be arbitrary derivatives. Then the ranking should be such that, for arbitrary positive integer k:

$$z_i^{(v)} < z_i^{(v+k)}, \quad z_i^{(\mu)} < z_j^{(v)} \Rightarrow z_i^{(\mu+k)} < z_j^{(v+k)}.$$
 (1)

The *leader* u_j of a polynomial A_j is the highest ranking derivative of the variables appearing in that polynomial (in particular it can be a derivative of order zero).

The polynomial A_i is said to be of *lower rank* than A_j if $u_i < u_j$ or, whenever $u_i = u_j \deg_{u_i}(A_i) < \deg_{u_j}(A_j)$, where $\deg_u(A)$ denotes the algebraic degree of A, considered as a polynomial in u.

A polynomial A_i will be said to be *reduced with respect* to a polynomial A_j if A_i contains neither the leader of A_j with equal or greater algebraic degree, nor its derivatives.

If A_i is not reduced with respect to A_j it can be reduced by using the *pseudodivision algorithm* described below:

- (1) if A_i contains the kth-derivative, $u_j^{(k)}$ (possibly k = 0), of the leader of A_j , A_j is differentiated k times so its leader becomes $u_i^{(k)}$;
- (2) multiply the polynomial A_i by the coefficient of the highest power of $u_j^{(k)}$; let R be the remainder of the

division of this new polynomial by $A_j^{(k)}$ with respect to the variable $u_j^{(k)}$. Then R is reduced with respect to $A_j^{(k)}$. The polynomial R is called the *pseudoremainder* of the pseudodivision;

(3) the polynomial A_i is replaced by the pseudo-remainder R and the process is iterated using $A_j^{(k-1)}$ in place of $A_j^{(k)}$ and so on, until the pseudoremainder is reduced with respect to A_j .

A set of differential polynomials $A := \{A_1, A_2, ..., A_r\}$ that are all reduced with respect to each other, is called an *autoreduced set*.

Let π be a differential polynomial. If we apply the pseudodivision algorithm to reduce π with respect to all A_j , $j = 1, \ldots, r$, the final pseudoremainder is called the *pseudoremainder of* π *with respect to the autoreduced set* A. Such a pseudoremainder is said to be reduced with respect to A (compare with Ritt (1950), where an autoreduced set is called a *chain*).

Two autoreduced sets, $A = \{A_1, A_2, ..., A_r\}$ and $B = \{B_1, B_2, ..., B_s\}$ ordered in increasing rank so that $A_1 < A_2 < \cdots < A_r$, $B_1 < B_2 < \cdots < B_s$, are ranked according to the following principle:

- If there is an integer $k, k \le \min(s, r)$ such that rank $A_i = \operatorname{rank} B_i, i = 1, \dots, k 1$, rank $A_k < \operatorname{rank} B_k$ then A is said to be of lower rank than B.
- If r < s and rank $A_i = \text{rank } B_i$, i = 1, ..., r, then A is also said to be of lower rank than B.

Definition 1. A lowest rank autoreduced set that can be formed with the polynomials belonging to a given set *S* of differential polynomials, is called a *characteristic set* of *S*.

The concept of characteristic set of a differential ideal has been introduced by Ritt (1950) who also proposed the pseudodivision algorithm to construct it. The important property of a characteristic set is that it can be used to generate a differential ideal by means of a finite number of polynomials. In particular, the characteristic set of a prime ideal spans the whole associated ideal (Forsman, 1991).

In principle, the characteristic set is not unique. It can however be normalized in such a way as to render it unique. One such normalization has been proposed by Rabinowitsch (see Mishra, 1993).

Let K' be an extension field of K containing smooth K-valued functions of t (these functions can be differentiated, so that K' is actually a *differential field extension* of K). Let there exist in K' a set of elements $\{\mu_1, \mu_2, \ldots, \mu_n\}$ which cause every polynomial in S to vanish when μ_i is substituted for z_i . The set $\{\mu_1, \mu_2, \ldots, \mu_n\}$ will be called a zero of S. The totality of the zeros of S, for a suitably large differential extension K' of K will be called the *differential algebraic manifold of* S (Ritt, 1950, p. 21) and denoted by $\mathcal{M}(S)$. This manifold is made of all functions of time which solve the system of differential equations $\{P(\mathbf{z}) = 0: P \in S\}$.

Theorem 1. Given a differential algebraic manifold \mathcal{M} , the totality, $I(\mathcal{M})$, of differential polynomials vanishing on \mathcal{M} is a perfect polynomial ideal (in particular a prime ideal) (Ritt, 1950, p. 22).

An *algebraic set* in \mathbb{R}^n , also called a "thin" set, ¹ is defined by a finite set of nonzero polynomials according to $\{\mathbf{x} \in \mathbb{R}^n : f_1(\mathbf{x}) = 0, \dots, f_k(\mathbf{x}) = 0\}$, where $f_i : \mathbb{R}^n \to \mathbb{R}$, $i = 1, \dots, k$ are algebraic (nondifferential) polynomials.

A property is said to be *generic* if it holds for all $\mathbf{x} \in \mathbb{R}^n$ outside an algebraic set.

Intuitively, a property is generic if it holds everywhere except at a "thin" set of zeros of some polynomials.

3. Identifiability

Consider a nonlinear dynamic system depending on a vector parameter **p**, described in state space form

$$\dot{\mathbf{x}}(t) = \mathbf{f}(\mathbf{x}(t), \mathbf{p}) + \sum_{i=1}^{m} \mathbf{g}_{i}(\mathbf{x}(t), \mathbf{p})u_{i}(t),$$
(2)

$$\mathbf{y}(t) = \mathbf{h}(\mathbf{u}(t), \mathbf{x}(t), \mathbf{p}),\tag{3}$$

where the state variable $\mathbf{x}(t)$ evolves in an open set X of the n-dimensional space \mathbb{R}^n ; \mathbf{u} is the m-dimensional input ranging on some vector space of piecewise smooth (infinitely differentiable) functions 2 and \mathbf{y} is the r-dimensional output. The constant unknown p-dimensional parameter vector \mathbf{p} belongs to some open subset \mathscr{P} of the p-dimensional Euclidean space \mathbb{R}^p . Whenever initial conditions are specified, the relevant equation

$$\mathbf{x}(0) = \mathbf{x}_0 \tag{4}$$

is added to the system.

The essential assumptions here are that

- (1) there is no feedback, i.e. **u** is a free variable, in particular **u** is not allowed to depend on **x**₀;
- (2) $\mathbf{f}, \mathbf{g}_1, \dots, \mathbf{g}_m$ and \mathbf{h} are vectors of *polynomial functions* in \mathbf{x} . The dependence on \mathbf{p} may be rational.

The assumption that the system is affine in the control variables is made for mathematical simplicity and can be removed at the price of some technical complications.

Given the system-experiment model (2,3), a priori identifiability deals with theoretical uniqueness of solutions to the problem of recovering the model parameters from input—output data. A priori identifiability analysis assumes

¹ Also called an "affine variety".

² Sometimes in biological/medical applications the input functions are assumed to be impulsive. Clearly nonlinear operations on distributions are in general not defined and truly impulsive inputs cannot in general be applied to nonlinear systems. The difficulty is however purely formal, and can be circumvented by assuming that the input is a smooth function of time having support of duration negligible with respect to the smallest time constant of the system.

error-free model and noise-free data and thus is a necessary, but not a sufficient condition to ensure identification of the model from real input/output data. Several definitions have been given in the literature (Audoly et al., 1998, 2001; Ljung& Glad, 1994; Vajda, Godfrey, & Rabitz, 1989; Walter & Lecourtier, 1982). Here we essentially point out the one used in Audoly et al. (1998, 2001), by considering explicitly the dependence of identifiability from the initial conditions.

Let $\mathbf{y} = \Phi_{\mathbf{x}_0}(\mathbf{p}, \mathbf{u})$ be the input-output map³ of the system (2,3) started at the initial state \mathbf{x}_0 . The definition below describes identifiability from *input-output data*, which is the concept of interest when (as it is usually the case) the initial state is not known exactly to the experimenter.

Definition 2. System (2,3) is a priori globally (or uniquely) identifiable from input—output data if, for at least a generic set of points $\mathbf{p}^* \in \mathcal{P}$, there exists (at least) one input function \mathbf{u} such that the equation

$$\Phi_{\mathbf{x}_0}(\mathbf{p}, \mathbf{u}) = \Phi_{\mathbf{x}_0}(\mathbf{p}^*, \mathbf{u}) \tag{5}$$

has only one solution $\mathbf{p} = \mathbf{p}^*$ for all initial states $\mathbf{x}_0 \in X \subseteq \mathbb{R}^n$.

A weaker notion is that of local identifiability.

Definition 3. System (2) and (3) are *locally identifiable* at $\mathbf{p}^* \in \mathscr{P}$ if there exists (at least) one input function \mathbf{u} and an open neighbourhood $U_{\mathbf{p}^*}$ of \mathbf{p}^* , such that Eq. (5) has a unique solution $\mathbf{p} \in U_{\mathbf{p}^*}$ for all initial states $\mathbf{x}_0 \in X \subseteq \mathbb{R}^n$.

According to these definitions, for a system which is not even locally identifiable, Eq. (5) has generically an infinite number of solutions for all input functions **u**. This is commonly called *nonidentifiability* or *unidentifiability* (Audoly et al., 1998; Chappell & Godfrey, 1992; Ljung & Glad, 1994; Walter, 1982).

In cases when the initial condition is known or some a priori information on the initial condition is available, one should study *identifiability from input-state-output data*. This will be taken up later.

Remark 1 (Global). Identifiability is a *system-related* concept and should in principle hold irrespective, i.e. for all, possible initial conditions. It happens frequently in the applications that the property holds only generically, i.e. except for a "thin" set of initial conditions. In these situations the system is (incorrectly but forgivably) nevertheless declared to be (global) identifiable, excluding certain subsets of initial states. One goal of this paper will be to analyse carefully this phenomenon and characterize these "thin" sets explicitely.

3.1. Identifiability and characteristic sets

With the basic definitions at hand we can now see the role the characteristic set plays in system identifiability analysis. We return to the dynamic system (2,3) which is defined by a system, Σ , of n + r differential polynomials:

$$\dot{x}_k - f_k(\mathbf{x}, \mathbf{p}) - \sum_{i=1}^m g_{ik}(\mathbf{x}, \mathbf{p}) u_i, \quad k = 1, \dots, n,$$
 (6)

$$y_k - h_k(\mathbf{u}, \mathbf{x}, \mathbf{p}), \quad k = 1, \dots, r.$$
 (7)

We shall consider the differential polynomials (6,7) in the ring $R(\mathbf{p})[\mathbf{u}, \mathbf{y}, \mathbf{x}]$, where $R(\mathbf{p})$ is the field of rational functions of the parameter vector \mathbf{p} (Saccomani et al., 1997; Audoly et al., 2001). Hence the variables in this polynomial differential ring are the states, the inputs and the outputs and, possibly, their derivatives.

The polynomials (6) and (7) can be looked upon as the generators of a differential ideal in a differential ring. We shall denote by I the ideal in $R(\mathbf{p})[\mathbf{u}, \mathbf{x}]$, generated by the differential polynomials (6) of the "state" equations, and by I_{Σ} the ideal generated by the full system (6) and (7).

It has been proven by Diop (1992) that the state-space description structure of the system ensures that the ideal I is prime. A further theoretical result (Ritt, 1950, paragraph 27, chap. 1) ensures that also I_{Σ} , which includes polynomials in the ring $R(\mathbf{p})$ [\mathbf{u} , \mathbf{y} , \mathbf{x}], is prime. As regards to the choice of the ranking, the ranking used in the literature declares the inputs as the lowest ranked components, followed by the outputs and the highest rank is given to the state variables. Normally, we choose the following order relation:

$$\mathbf{u} < \dot{\mathbf{u}} < \ddot{\mathbf{u}} < \cdots < \mathbf{y} < \dot{\mathbf{y}} < \ddot{\mathbf{y}} < \cdots$$

$$\cdots < x_1 < x_2 < \cdots < \dot{x}_1 < \dot{x}_2 < \cdots$$
(8)

The notation reflects the fact that ordering among the components of \mathbf{u} and \mathbf{y} is immaterial (since these are known variables) whereas different ordering of the components of \mathbf{x} may lead to different characteristic sets.

Remark 2. Consider first the ideal I, if we choose the ranking:

$$\mathbf{u} < \dot{\mathbf{u}} < \dots < x_1 < x_2 < \dots < x_n < \dot{x}_1 < \dot{x}_2 < \dots$$
 (9)

it can be checked that the set of polynomials (6) is an autoreduced set and hence a *characteristic set of I* (Ollivier, 1990; Glad, 1990).

Now consider the polynomials (6) and (7). We calculate a characteristic set of I_{Σ} with respect to the ranking (8). The result is a family of differential polynomials of the following form:

$$A_1(\mathbf{u},\mathbf{y})\dots A_r(\mathbf{u},\mathbf{y})$$

$$A_{r+1}({\bf u},{\bf y},x_1)$$

³ We assume that this object exists.

$$A_{r+2}(\mathbf{u}, \mathbf{y}, x_1, x_2)$$

$$\vdots$$

$$A_{r+n}(\mathbf{u}, \mathbf{y}, x_1, \dots, x_n). \tag{10}$$

This corresponds to a finite set of n+r nonlinear differential equations which represent the totality of functions $(\mathbf{u}, \mathbf{y}, \mathbf{x})$ satisfying the equations of the original system (2) and (3).

Note that the first r differential polynomials A_i , i = 1, ..., r of (10) do not depend on \mathbf{x} . In fact, they are obtained after elimination of the state variables \mathbf{x} from the set (6) and (7). The corresponding polynomial differential equations

$$A_{1}(\mathbf{u}, \mathbf{y}) = 0$$

$$A_{2}(\mathbf{u}, \mathbf{y}) = 0$$

$$\vdots$$

$$A_{r}(\mathbf{u}, \mathbf{y}) = 0,$$
(11)

are called the *input-output relation* of the system. They describe all input-output pairs which satisfy the system Eqs. (2) and (3).

A basic advantage of the differential algebraic setting is that the input—output relation of the system can always be written, in an implicit form, as a set of r polynomial differential equations in the variables (\mathbf{u}, \mathbf{y}) . The polynomials may in theory be computed explicitly by means of the pseudodivision algorithm due to Ritt (1950), but in practice this may not always be possible, depending on the complexity of the problem. These r input—output differential equations are the basic tool used in input—output identifiability analysis.

We do not show the explicit dependence on **p** of Eq. (11) since the polynomials on the left-hand side belong to the differential ring $R(\mathbf{p})$ [\mathbf{u} , \mathbf{y}] and the dependence on \mathbf{p} is implicit in the choice of the field of coefficients.

In the following we shall assume that a suitable normalization has been introduced, for example the one proposed by Rabinowitsch (see Mishra, 1993). Also, allowing the coefficients to be rational functions of the parameters permits one to normalize the input-output relation by making the highest degree coefficient of the leader in each polynomial $A_k, k =$ $1, \ldots, r$ equal to one. Now, making each polynomial of the input-output set monic in the above sense, fixes uniquely the coefficients $c_{ij} \in R(\mathbf{p}), i = 1, \dots, r, j = 1, \dots, v_i$, (here j is an index running over the monomial indices of the polynomial A_i , the monomials being ordered, say, in a lexicographic ordering). It follows that the functions $c_{ii}(\mathbf{p})$ constitute a "canonical" set of coefficients of the input-output polynomial differential equation and are uniquely attached to the input-output relation of the system. Let $v := \sum_i v_i$ and let $\mathbf{c}:\mathscr{P}\to\mathbb{R}^{\nu}$ be the map defined by stacking the scalar components, $\{c_{ij}\}$, in some prescribed order. The map **c** is called the exhaustive summary of the model (Ollivier, 1990), since c embodies the parameter dependence of the input-output model completely.

After the exhaustive summary is found, in order to test global input-output identifiability of system (2) and (3) the injectivity of the map c from the parameter space \mathcal{P} to its range, a subset of the v-dimensional Euclidean space, has to be checked. This is the same as unique solvability of the equations

$$c_{ij}(\mathbf{p}) = c_{ij}^*, \quad i = 1, ..., r, \quad j = 1, ..., v_i$$
 (12)

for arbitrary right-hand members c_{ii}^* in the range of **c**.

In order to check *local identifiability* one has to check that $\mathbf{c}(\mathbf{p})$ is *locally injective*, which happens if system (12) has a unique solution $\mathbf{p} \in U_{\mathbf{p}^*}$ for a suitable open neighbourhood $U_{\mathbf{p}^*}$ of \mathbf{p}^* . Equality constraints (linear or nonlinear) of the form $G(\mathbf{p}) = 0$ where G is a polynomial or a rational vector function, if present, can be added to (12). The resulting system of nonlinear equations may be solved by a suitable computer algebra method, using e.g. the Buchberger algorithm (Buchberger, 1998).

Remark 3. The vector functions $\mathbf{c}_i(\mathbf{p})$ i = 1, ..., r should be uniquely determined by the input–output variables of the dynamic system (2,3). This means that the system of algebraic equations

$$a_{i1}(\mathbf{u}, \mathbf{y}) + \sum_{i=2}^{v_i} c_{ij}(\mathbf{p}) a_{ij}(\mathbf{u}, \mathbf{y}) = 0, \quad i = 1, ..., r,$$
 (13)

where $a_{ij}(\mathbf{u}, \mathbf{y})$ is the *j*th monomial term in $A_i(\mathbf{u}, \mathbf{y})$, should be uniquely solvable for the c_{ij} in terms of the input–output variables (\mathbf{u}, \mathbf{y}) .

Solvability means that a suitably large set of time instants $\{t_1, \ldots, t_N\}$ can be found, such that the system of rN equations obtained by evaluating (13) at t_1, \ldots, t_N , has a solution in the unknowns c_{ij} .

This solvability condition is the natural analogue of the "persistence of excitation of the input" in linear system identification (Söderström & Stoica, 1987).

The differential algebraic approach allows one to distinguish between global and local identifiability. This is particularly useful in biological and biomedical modelling. The distinction is not possible by using traditional local identifiability tests based on computing the rank of a matrix (e.g the Fisher information matrix) at a point (Jacquez & Greif, 1985).

3.2. Identifiability with a priori information on initial conditions

In biological/medical applications identification experiments are often performed on systems at rest, or started from known (equilibrium) initial conditions. Furthermore, one or more components of the initial condition vector or some relations among them may be known. In these fortunate circumstances, the data of the identifiability problem involve also the known initial state components, i.e. the problem at hand is *identifiability from input-state-output data*. We

(14)

 $A_{r+1}(\mathbf{u}, \mathbf{y}, x_1) = 0$

 $A_{r+2}(\mathbf{u}, \mathbf{y}, x_1, x_2) = 0$

shall not propose formal definitions to analyse this case, but just show that the characteristic set plays a fundamental role also in this circumstance. The idea recalled below has been used previously in Audoly et al. (2001).

We shall need to recall the concept of Algebraic Observability, of system (2) and (3).

If the derivatives of the state components do not appear in the last n equations of the characteristic set (10), dynamical system (2) and (3) is called algebraically observable (Glad, 1990). In this case, one can in principle solve for x_1, \ldots, x_n the triangular set of algebraic equations

$$\vdots$$

$$A_{r+n}(\mathbf{u}, \mathbf{v}, x_1, \dots, x_n) = 0, \tag{14}$$

recovering the state as an (instantaneous) function of the input-output variables and their derivatives. It has been shown by Glad (1990), that the sum of the orders of the leaders of a characteristic set of an algebraically observable state-space system is equal to the order n of the system.

Assume that the system is algebraically observable. An identifiability test with known initial conditions can be based on the exhaustive summary, equations (12), plus a set of n algebraic relations obtained by evaluating Eqs. (14) at time t=0. The left-hand members of these equations, evaluated at t = 0 become known polynomial (or rational) functions of the unknown parameter vector **p** with coefficients which are monomials in the known data $(\mathbf{x}_0, \mathbf{u}(0), \dot{\mathbf{u}}(0), \ddot{\mathbf{u}}(0), \dots, \mathbf{y}(0), \dot{\mathbf{y}}(0), \ddot{\mathbf{y}}(0), \dots)$. Under this hypothesis, the input-state-output identifiability test consists of checking the (global or local) injectivity of an overall exhaustive summary, i.e. the exhaustive summary constituted by Eqs. (12) and the *n* functions on \mathbf{p} above obtained from the knowledge of the initial conditions.

In this case we may also allow the initial state to be a (rational) function of the parameter **p**, say $\mathbf{x}(0) = \mathbf{x}_0(\mathbf{p})$, as it is sometimes assumed in the literature. This dependence may arise for example from a reparametrization of the system resulting from the substitution of input functions of impulsive character with suitable initial conditions (Chappell & Godfrey, 1992).

This notion of identifiability has received less attention than the input-output one. It is of use when the system has to be identified by running ad hoc input-output experiments (Audoly et al., 2001).

3.3. Input-output identifiability from "special" initial conditions

As we have seen, the construction of the characteristic set ignores the initial conditions (4). It is sometimes stated in the literature that, the input-output relation (11) describes

the input-output pairs of the system for "generic" initial conditions (Ollivier, 1990; Ljung & Glad, 1994). Often, however, physical systems have to be started at specific initial conditions. Thus, the question arises if the general identifiability testing procedure described in the previous section works also in this situation.

Indeed, we will prove by means of an example that the input-output identifiability test described above, can lead to errors for systems which are started at some "special" initial conditions (the meaning of the term "special" will be made precise later on). The example considered will be linear, since identifiability of linear systems can be checked by standard transfer function methods thereby allowing comparison with the nonlinear setting.

Example 1. The system will be a three-compartment model (Walter, 1982) describing e.g. the dynamics of a substance in a tissue. Let

$$\dot{x}_1 = p_{13}x_3 + p_{12}x_2 - p_{21}x_1 + u, \quad x_1(0) = x_{10},
\dot{x}_2 = -p_{12}x_2 + p_{21}x_1, \quad x_2(0) = x_{20},
\dot{x}_3 = -p_{13}x_3, \quad x_3(0) = 0,
v = x_2,$$
(15)

where $\mathbf{x} = [x_1, x_2, x_3]$ is the state variable vector, specifically, x_1, x_2, x_3 are the masses of substance in compartments 1, 2 and 3, respectively; u is the substance input; y is the measured output; $\mathbf{p} = [p_{12}, p_{21}, p_{13}] \in \mathbb{R}^3_+ \setminus \{\mathbf{0}\}$ is the (constant) rate parameter vector, in particular p_{ij} is the fractional transfer rate from compartment j to compartment i. Below we shall just assume that the third compartment is empty but we have no information on the initial state of compartments 1 and 2. The question is: assume $x_3(0) = 0$, are all the unknown parameters p_{12} , p_{21} , p_{13} globally identifiable from the input-output experiment?

The main steps of the algorithm are:

- (1) Choice of the ranking of the input, output and state variables; the standard ranking of Eq. (8) is chosen.
- (2) At this stage the reduction procedure starts and the normalized characteristic set is calculated:

$$A_{1} \equiv \ddot{y} + \ddot{y}(p_{12} + p_{21} + p_{13}) + \dot{y}(p_{12}p_{13} + p_{21}p_{13}) + \dot{u}p_{21} + up_{21}p_{13},$$

$$A_{2} \equiv \dot{y} + yp_{12} - x_{1}p_{21},$$

$$A_{3} \equiv y - x_{2},$$

$$A_{4} \equiv \ddot{y} + \dot{y}(p_{12} + p_{21}) + up_{21} - x_{3}p_{13}p_{21}.$$
 (16)

Note that only the differential polynomial A_1 contains information on model identifiability, in fact it does not contain as variables either x or its derivatives. This polynomial represents the input-output relation of the model.

(3) By extracting the coefficients of the input-output relation (which is already monic), and setting them equal to known symbolic values, the following exhaustive summary equations, see Section 3, are obtained:

$$p_{21} = c_1,$$

 $p_{12} + p_{21} + p_{13} = c_2,$
 $p_{12}p_{13} + p_{21}p_{13} = c_3,$
 $p_{21}p_{13} = c_4.$ (17)

(4) The injectivity of this map it is easy to check, so that all three parameters p_{12} , p_{21} and p_{13} appear to be globally identifiable.

However, as we can check from the model equations, starting from $x_3(0) = 0$, p_{13} does not influence the output y and hence p_{13} cannot be identifiable from input—output data. This also agrees with the transfer function test (Walter, 1982). So unfortunately the conclusion of the test is wrong. What goes wrong? Three observations are in order.

- (1) The computation of the characteristic set does not require knowledge of the initial conditions. The construction seems to work for *arbitrary* initial states.
- (2) The system is not reachable from \mathbf{x}_0 (and hence non-minimal). In fact, all states reachable from the initial state $\mathbf{x}(0) = [x_1, x_2, 0]$ keep the third component $x_3 = 0$ for all times. Hence the state evolves on the invariant subspace $\{\mathbf{x}: x_3 = 0\}$ for all times, regardless of which input function is applied. The dynamics visible from the output terminal are the dynamics restricted to this subspace.
- (3) Eqs. (17) coincide with those provided by the transfer function method (Audoly et al., 1998; Walter, 1982), without performing the cancellations on the transfer function due to nonminimality. The parameter p_{13} only enters in the nonreachable subsystem.

To gain some more insight to be used in the non-linear situation, let us introduce the constraint that the system evolves on the invariant manifold $x_3 = 0$, in the characteristic set. Adding $x_3 = 0$ we get one more equation involving only the input—output variables

$$H(u, y) := \ddot{y} + \dot{y}(p_{12} + p_{21}) + u p_{21} = 0.$$
 (18)

Note that the first equation (input-output relation) can be rewritten as

$$A_1 \equiv \dot{H} + p_{13}H = 0. \tag{19}$$

In other words, A_1 and H are differentially algebraically dependent and the lower rank polynomial H should be substituted in place of A_1 to get a characteristic set, which now consists of

$$\hat{A}_1 \equiv \ddot{y} + \dot{y}(p_{12} + p_{21}) + up_{21},$$

 $A_2 \equiv \dot{y} + yp_{12} - x_1p_{21},$

$$A_3 \equiv y - x_2,$$

 $A_4 \equiv -x_3 p_{13} p_{21}.$ (20)

Applying the test to the new $\hat{A}_1 \equiv H$, only p_{12} and p_{21} are uniquely identifiable while p_{13} has disappeared from the input–output relation.

This is in agreement with the transfer function method. Since $\hat{A}_1 \notin I$, we are sure that the new characteristic set is *different* from the characteristic set computed from the polynomials defining the dynamic system (2) and (3) without taking into account initial conditions. Hence we have discovered that if the system is started at any initial state for which $x_3(0) = 0$, a different input—output relation results. In other words

the characteristic set may *change* if the system is started at "special" initial conditions.

What is special about the initial conditions having $x_3(0)=0$, is that they all belong to an *invariant set* of the state space, in fact to the invariant (reachable) subspace $\{x: x_3 = 0\}$. The example shows that reachability plays a crucial role in identifiability analysis and gives a hint on why the method may fail. In particular it shows that lack of reachability from the initial state may be the cause of trouble.

In the next sections we shall consider the following questions:

- When does the input-output identifiability test based on the characteristic set give the right answer?
- Can we characterize the set of "special" initial states where the test may fail?
- Is there an alternative characteristic set algorithm which can be used when it is known that we start from a "special" set of initial states?

4. The role of accessibility

In this section, we will use some concepts of geometric nonlinear control theory. For the basic definitions we will refer the reader to Hermann and Krener (1977), Isidori (1995), Lobry (1970) and Sontag (1998). In particular we shall often refer to a nonlinear counterpart of the concept of reachability (from an arbitrary initial state) which will be called *accessibility*. The following definition is essentially taken from Sontag (1998, p. 157).

Definition 4. System (2) is accessible from \mathbf{x}_0 if the set of states reachable from \mathbf{x}_0 (at any finite time) has a nonempty interior, i.e. contains an open ball in \mathbb{R}^n .

See also Hermann and Krener (1977) where this notion is called *weak local controllability*.

Let $[\mathbf{f}, \mathbf{g}]$ denote the *Lie Bracket* of the vector fields \mathbf{f}, \mathbf{g} , defined as

$$[\mathbf{f}, \mathbf{g}] := \left(\frac{\partial}{\partial \mathbf{x}} \mathbf{g}\right) \mathbf{f} - \left(\frac{\partial}{\partial \mathbf{x}} \mathbf{f}\right) \mathbf{g}$$

where $(\partial/\partial \mathbf{x})$ denotes the Jacobian matrix. To study accessibility one looks at the *Control Lie Algebra*, i.e. the smallest Lie algebra \mathscr{C} containing the vector fields $\mathbf{f}, \mathbf{g}_1, \dots, \mathbf{g}_m$ of (2) and invariant under Lie bracketing with $\mathbf{f}, \mathbf{g}_1, \dots, \mathbf{g}_m$.

To the Lie algebra \mathscr{C} we associate the distribution $\Delta_{\mathscr{C}}$ mapping each $\mathbf{x} \in \mathbb{R}^n$ into the vector space

$$\Delta_{\mathscr{C}}(\mathbf{x}) = \operatorname{span}\{\tau(\mathbf{x}): \tau \in \mathscr{C}\}.$$

We recall from the literature the following result.

Theorem 2. (Hermann & Krener, 1977; Isidori, 1995; Sontag, 1998). For analytic, in particular polynomial, systems, a necessary and sufficient condition for accessibility from \mathbf{x}_0 is that

$$\dim \Delta_{\mathscr{C}}(\mathbf{x}_0) = n. \tag{21}$$

This condition is called the *accessibility rank condition*.

Since our system is polynomial (and hence analytic), there exists a unique maximal submanifold $M_{\mathbf{x}_0}$ of \mathbb{R}^n through \mathbf{x}_0 which carries all the trajectories of the control system (2) started at \mathbf{x}_0 . In particular, if the dimension of $\Delta_{\mathscr{C}}(\mathbf{x}_0)$ is n then $\dim(M_{\mathbf{x}_0})=n$ (Hermann & Krener, 1977). Note that $\Delta_{\mathscr{C}}$ may be singular 4 , in which case the dimensions of different maximal integral submanifolds of $\Delta_{\mathscr{C}}$ may be different. Thus, it may happen that when starting at two different initial states \mathbf{x}_0^1 and \mathbf{x}_0^2 , the state trajectories of (2) may fill manifolds $M_{\mathbf{x}_0^1}$ and $M_{\mathbf{x}_0^2}$ of a different dimension.

We shall call a manifold $M \subset \mathbb{R}^n$ algebraic, if it can be described as the set of zeros of algebraic (i.e. non-differential) polynomials in $\mathbb{R}[\mathbf{x}]$, nonalgebraic if it does not admit such a representation.

We now return to the nonlinear system (2) and (3). Given that accessibility does not depend on the output equation, in this section we shall consider only state equation (2). Let $\mathcal{M}(I)$ be the set of all solutions of the state differential equations of system (2) corresponding to all admissible control functions

Following Ritt (1950), a differential algebraic submanifold \mathscr{V} , of $\mathscr{M}(I)$, is a subset of $\mathscr{M}(I)$ which can be described as the zeros of a family of differential polynomials in $R(\mathbf{p})[\mathbf{u}, \mathbf{x}]$. Let $I(\mathscr{V})$ be the totality of differential polynomials vanishing on \mathscr{V} . It is clear that $I(\mathscr{V})$ is an ideal and since $\mathscr{V} \subseteq \mathscr{M}(I)$, it is obvious that $I(\mathscr{V}) \supseteq I$.

Consider the set $\mathcal{X}_0 = \{\mathbf{x} : \mathbf{x} \in \mathcal{M}(I), \ \mathbf{x}(0) = \mathbf{x}_0\}$ of trajectories of system (2) passing through \mathbf{x}_0 at time t = 0. We shall say that \mathcal{V}_0 is a *differential algebraic manifold through* \mathbf{x}_0 if \mathcal{V}_0 is differential algebraic and contains \mathcal{X}_0 .

Trivially, one such differential algebraic manifold is $\mathcal{M}(I)$ and hence the set of such \mathcal{V}_0 's is nonempty.

Definition 5. The *smallest differential algebraic manifold* through \mathbf{x}_0 , $\hat{\mathcal{Y}}_0$, is the intersection of all differential algebraic manifolds through \mathbf{x}_0 , i.e.

$$\hat{\mathscr{V}}_0 := \bigcap_{\mathscr{V}_0 \supseteq \mathscr{X}_0} \mathscr{V}_0.$$

Below we shall argue that the question whether the characteristic set of Σ changes when the system is started at the initial condition \mathbf{x}_0 is essentially the same question as to whether $I(\hat{\mathcal{V}}_0) \equiv I$. The reason why this equivalence is of interest for identifiability will be clarified in the next section.

Theorem 3. For all \mathbf{x}_0 from which system (2) is accessible, $\hat{\mathcal{V}}_0 \equiv \mathcal{M}(I)$, $I(\hat{\mathcal{V}}_0) \equiv I$ and the characteristic set does not change.

The proof will be through a series of intermediate results.

Lemma 1. If (2) is accessible from the initial state \mathbf{x}_0 , there are no nontrivial (i.e. of dimension smaller than n) invariant submanifolds of \mathbb{R}^n , through \mathbf{x}_0 .

Proof. If (2) is accessible from \mathbf{x}_0 , we can reach an n-dimensional open ball in \mathbb{R}^n from the initial state \mathbf{x}_0 , so the evolution of (2) starting from \mathbf{x}_0 cannot take place on an invariant submanifold of dimension smaller than n. \square

Lemma 2. The pseudoremainder $\rho(\mathbf{u}, \mathbf{x})$ of any differential polynomial $\pi(\mathbf{u}, \mathbf{x})$ with respect to a characteristic set of I is either 0 or a nondifferential polynomial algebraic in \mathbf{x} .

Proof. Since $\rho(\mathbf{u}, \mathbf{x})$ is reduced with respect to a characteristic set of I, it must be of lower rank than all polynomials belonging to that characteristic set (Ritt, 1950). Since the characteristic sets of I have order one in \mathbf{x} , $\rho(\mathbf{u}, \mathbf{x})$ must either be zero or of order zero. \square

Proposition 1. The following statements are equivalent

- (i) there exists a nontrivial proper invariant algebraic manifold $M_{\mathbf{x}_0} \subset \mathbb{R}^n$ containing all solutions to (2) with initial condition \mathbf{x}_0 ,
- (ii) there exists a nontrivial proper differential algebraic submanifold \hat{V}_0 of $\mathcal{M}(I)$ through \mathbf{x}_0 ,
- (iii) the ideal $I(\hat{V}_0)$ contains I properly.

Proof. It is obvious that (ii) and (iii) are equivalent. Now we prove that (iii) implies (i). Assume that $I \subset I(\hat{\mathcal{V}}_0)$ properly. Hence the ideal $I(\hat{\mathcal{V}}_0)$ must contain all the polynomials of the original ideal I plus at least one more nonzero polynomial vanishing on $\hat{\mathcal{V}}_0$. In particular, assume that

⁴ I.e. the dimension of $\Delta_{\mathscr{C}}(\mathbf{x})$ is not constant with \mathbf{x} .

there is a differential polynomial $\varphi(\mathbf{u}, \mathbf{x}) \in R[\mathbf{u}, \mathbf{x}]$ such that $\varphi(\mathbf{u}, \mathbf{x}) \in I(\hat{\mathcal{V}}_0)$ and $\varphi \notin I$.

Now, let us construct a characteristic set of the ideal $I(\hat{\mathcal{V}}_0)$. Without loss of generality this characteristic set may be constructed by choosing the polynomials (6) (i.e. a characteristic set of I), plus some polynomials $\{\varphi_k(\mathbf{u}, \mathbf{x})\}$ of the type described above, in such a way that, together with (6), they generate $I(\hat{\mathcal{V}}_0)$. In general, the family consisting of the polynomials (6) and the $\varphi_k(\mathbf{u}, \mathbf{x})$'s will not be a characteristic set and will have to be autoreduced. However, once the reduction of $\varphi_k(\mathbf{u}, \mathbf{x})$ with respect to the polynomials (6) is performed, we see, on the strength of Lemma 2, that the final pseudoremainder has to be either 0 or a non differential algebraic polynomial in \mathbf{x} . When different from 0, this remainder, $\rho(\mathbf{u}, \mathbf{x})$, can always be written as an algebraic polynomial in \mathbf{x} with coefficients depending on the variables $\mathbf{u}, \mathbf{u}, \dots, \mathbf{u}^{(\mu)}, \dots$ i.e.

$$\rho(\mathbf{u}, \mathbf{x}) = \sum_{k=1}^{q} \psi_k(\mathbf{u}) \phi_k(\mathbf{x}),$$

where $\{\psi_k(\mathbf{u}); k = 1,...,q\}$ is a list of monomials in the variables $\mathbf{u}, \dot{\mathbf{u}}, ..., \dot{\mathbf{u}}^{(\mu)}, ...$ for example lexicographically ordered according to the chosen ranking of the variables. Since $\rho(\mathbf{u}, \mathbf{x}) \equiv 0$ for all inputs \mathbf{u} and for all state evolutions started at the initial condition (4), one has

$$\sum_{k=1}^{q} \psi_k(\mathbf{u}) \phi_k(\mathbf{x}) \equiv 0$$

which can be true only if

$$\phi_k(\mathbf{x}) = 0, \quad k = 1, \dots, q, \tag{22}$$

identically. Thus the state trajectories $t \to \mathbf{x}(t)$ started at \mathbf{x}_0 belong to a nontrivial algebraic manifold of \mathbb{R}^n , say $M_{\mathbf{x}_0}$, of dimension strictly smaller than n.

Conversely, if we assume (i) then there exists a family (22) of differential polynomials vanishing at the solution of system (2) when started at \mathbf{x}_0 it follows that these polynomials must belong to $I(\hat{\mathcal{Y}}_0)$. Therefore $I(\hat{\mathcal{Y}}_0) \supset I$.

Proof of Theorem 3. By Proposition 1 there exists a nontrivial proper differential algebraic submanifold of $\mathcal{M}(I)$ if and only if there is a nontrivial proper invariant algebraic submanifold $M_{\mathbf{x}_0} \subset \mathbb{R}^n$ through \mathbf{x}_0 . But this cannot be true since the system is accessible from \mathbf{x}_0 . Therefore $\hat{\mathcal{V}}_0 \equiv \mathcal{M}(I)$ and $I(\hat{\mathcal{V}}_0) \equiv I$. \square

A special case of some interest in applications is when the system is started from an initial condition belonging to a "thin" set where accessibility does not hold.

Theorem 4. Assume that system (2) is accessible except from an algebraic set $T \subset \mathbb{R}^n$, i.e. the system is generically accessible, and suppose that the initial condition \mathbf{x}_0 belongs to T

Then \mathcal{X}_0 is differential algebraic (in fact, $\hat{\mathcal{V}}_0 = \mathcal{X}_0$), $I(\hat{\mathcal{V}}_0) \supset I$ and the characteristic set changes.

Proof. Let $\mathbf{x}_0 \in T$, then the trajectory started at \mathbf{x}_0 (corresponding to any admissible control function) cannot leave the set T; for if at some time t > 0 the state $\mathbf{x}(t)$ belongs to $\mathbb{R}^n - T$, then by accessibility, starting from the initial state $\mathbf{x}(t)$, we could reach an open ball in \mathbb{R}^n at some positive time t_1 . But then by transitivity of the accessibility relation, we could reach the same open ball in \mathbb{R}^n starting from \mathbf{x}_0 in $t + t_1$ time units and therefore the system would be accessible from \mathbf{x}_0 .

Hence T is an invariant set made of points \mathbf{x} where the accessibility rank condition fails to hold. In fact T is an algebraic subset of \mathbb{R}^n described by imposing that all the minors of maximum rank of a matrix representation $D_{\mathscr{C}}$ of $\Delta_{\mathscr{C}}$ are zero in a neighbourhood of \mathbf{x}_0 . Hence \mathbf{x}_0 must satisfy a set of algebraic equations which define the invariant submanifold T (note that \mathbf{x}_0 could well be an isolated uncontrollable equilibrium point of the system). Let $\{\varphi_k(\mathbf{x})=0;\ k=1,\ldots,q\}$ be the set of algebraic equations defining the invariant manifold T. Clearly the algebraic polynomials $\varphi_k(\mathbf{x})$ vanish at the solution of (2) started at \mathbf{x}_0 but do not belong to I. Hence $I(\hat{\mathscr{V}}_0)=(I\cup\{\varphi_k(\mathbf{x});\ k=1,\ldots,q\})$, i.e. $I(\hat{\mathscr{V}}_0)\supset I$ and the characteristic set changes. \square

Since the state equation (2) is polynomial, only two cases may arise:

- (1) system (2) is generically accessible, i.e. accessible except perhaps from a set of measure zero, in particular accessible from all \mathbf{x}_0 ;
- (2) system (2) is never accessible, i.e. is not accessible from any $\mathbf{x}_0 \in \mathbb{R}^n$. In this case dim $\Delta_{\mathscr{C}}(\mathbf{x}) < n$ for all $\mathbf{x} \in \mathbb{R}^n$ and there is a d > 0 such that dim $\Delta_{\mathscr{C}}(\mathbf{x}) = n d$ for a generic subset of \mathbb{R}^n .

In the second circumstance, Theorem 1.8.9 of Isidori (1995) can be applied. It follows that every region of the state space where dim $\Delta_{\mathscr{C}}(\mathbf{x}) = n - d$ can be partitioned into (n - d)-dimensional invariant submanifolds.

Theorem 5. Assume that system (2) is not accessible (from any point in \mathbb{R}^n), and let the system be started at the initial condition \mathbf{x}_0 . If the invariant submanifold through \mathbf{x}_0 , $M_{\mathbf{x}_0}$, is algebraic, then $I(\hat{V}_0) \supset I$ properly and the characteristic set changes.

Proof. By analyticity, the tangent space to $M_{\mathbf{x}_0}$ has constant dimension, say n-d, at every point $\mathbf{x} \in M_{\mathbf{x}_0}$. In other words

$$\dim \{\Delta_{\mathscr{C}}(\mathbf{x})\} = n - d \quad \text{for all } \mathbf{x} \in M_{\mathbf{x}_0}$$
 (23)

identically. Hence there exist d independent polynomial covector fields

$$\{\mu_1(\mathbf{x}),\ldots,\mu_d(\mathbf{x})\}\$$

in the left kernel of $D_{\mathscr{C}}$, i.e.

$$\mu_k(\mathbf{x})D_{\mathscr{C}}(\mathbf{x}) = 0, \quad \mathbf{x} \in M_{\mathbf{x}_0}, \quad k = 1, \dots, d.$$
 (24)

Since $\Delta_{\mathscr{C}}$ is involutive, by the Frobenius Theorem the codistribution spanned by the covector fields $\{\mu_k(\mathbf{x}); k = 1, \ldots, d\}$ is integrable. Hence there are d smooth functions ϕ_1, \ldots, ϕ_d vanishing at \mathbf{x}_0 , such that all solutions of the system started at \mathbf{x}_0 evolve in the submanifold

$$M_{\mathbf{x}_0} = \{ \mathbf{x} : \phi_1(\mathbf{x}) = 0, \dots, \phi_d(\mathbf{x}) = 0 \}.$$
 (25)

Assume that ϕ_1, \ldots, ϕ_d are (algebraic) polynomials, i.e. that $M_{\mathbf{x}_0}$ is algebraic. These polynomials vanish at the solutions of the system starting at \mathbf{x}_0 and do not belong to I because, being algebraic, they are reduced with respect to the characteristic sets of I (Ritt, 1950). Thus the ideal $I(\hat{V}_0)$ is

$$I(\hat{\mathcal{V}}_0) = (I \cup \{\phi_k; \ k = 1, \dots, d\})$$
 (26)

and hence contains I properly. \square

Remark 4. Note that if some of the ϕ_k are not polynomials but there are algebraic polynomials ψ_k vanishing at their solutions, (for example, consider $\phi(\mathbf{x}) = \tanh \psi(\mathbf{x})$ where $\psi(\mathbf{x})$ is a polynomial function. Since $\tanh \psi(\mathbf{x}) = 0 \Leftrightarrow \psi(\mathbf{x}) = 0$ then $\{\mathbf{x}: \phi(\mathbf{x}) = 0\} = \{\mathbf{x}: \psi(\mathbf{x}) = 0\}$ i.e. the solution set is the same) the polynomials ψ_k also vanish at the solution of the system starting at \mathbf{x}_0 and do not belong to I. Hence we would have an algebraic submanifold and

$$I(\hat{\mathcal{V}}_0) = (I \cup \{\psi_k; \quad k = 1, ..., d\}) \supset I.$$
 (27)

Remark 5. Note that there is no guarantee that the functions $\{\phi_k\}$ which define the invariant manifold $M_{\mathbf{x}_0}$, whose existence is guaranteed by the Frobenius Theorem, are algebraic. In some of our examples we are able to find polynomial functions, $\phi_k, k=1,\ldots,d$. However, in general some of the ϕ_k 's need not be polynomials and there may be no algebraic polynomials vanishing at their solutions. In this case $M_{\mathbf{x}_0}$ is not algebraic (as it does not admit algebraic polynomial descriptions). Hence in this case $\hat{V}_0 \supseteq \mathcal{X}_0$, so that \hat{V}_0 does not describe exactly the solutions of the system passing through \mathbf{x}_0 at time zero.

Example 2. Consider the system

$$\dot{x}_1 = p_1 x_2 - p_2 x_3 - u, \quad x_1(0) = x_{10},
\dot{x}_2 = p_3 x_1^2, \quad x_2(0) = x_{20},
\dot{x}_3 = p_4 x_1^2 x_3, \quad x_3(0) = x_{30},$$
(28)

for which $\dot{x}_3/\dot{x}_2 = (p_4/p_3)x_3$. By integrating this relation it is easily seen that, no matter which input is chosen, the system evolves in the cylindrical surface in \mathbb{R}^3 described by

$$x_3 - x_{30} \exp\left[\frac{p_4}{p_3}(x_2 - x_{20})\right] = 0$$
 (29)

and we have a system which is not accessible from any point in \mathbb{R}^3 . To check this formally, one computes the matrix made with the vector fields f,g and the Lie brackets $[f,g],[f,[f,g]],[f,[f,g]],\ldots$. Now it may be seen that the last two rows of this matrix are always proportional

and all covectors μ orthogonal to the distribution $\Delta_{\mathscr{C}}$ must be of the form:

$$\mu = \alpha(\mathbf{x})[0, -p_4x_3, p_3],$$

where $\alpha(\mathbf{x})$ is an arbitrary nonzero smooth function. Therefore dim $\Delta_{\mathscr{C}} < 3$ for all $\mathbf{x} \in \mathbb{R}^3$.

By applying the Frobenius Theorem in a relatively open neighbourhood of any \mathbf{x}_0 for which dim $\Delta_{\mathscr{C}}(\mathbf{x}_0) = 2$, it must follow that, for some suitable α , the covector μ generates a closed differential form. In fact, using as integrating factor the function $\alpha(\mathbf{x}) = \exp[-(p_4/p_3)(x_2 - x_{20})]$ it is easy to check that

$$\phi(\mathbf{x}) = x_3 \exp \left[-\frac{p_4}{p_3} (x_2 - x_{20}) \right] - x_{30}$$

has a differential which is proportional to μ , namely $d\phi = \alpha[-p_4x_3 dx_2 + p_3dx_3]$. This of course checks with the observation made at the beginning, that the solution of system (28) evolves in the invariant submanifold described by the transcendental equation (29).

In this case there is no algebraic polynomial vanishing at the solutions of the system started at any \mathbf{x}_0 . Even if $I(\hat{\mathcal{Y}}_0) = I$ the ideal $I(\hat{\mathcal{Y}}_0)$ does not describe the solutions of (28) through \mathbf{x}_0 .

Remark 6. When dim $\Delta_{\mathscr{C}} = n - d$ for a generic subset of \mathbb{R}^n , it may nevertheless happen that \mathbf{x}_0 belongs to a "thin" set T where dim $\Delta_{\mathscr{C}}(\mathbf{x}) < n - d$. In this case Theorem 4 can be applied to the (generically accessible) system obtained by restricting (2) to the (n-d)-dimensional invariant manifold through \mathbf{x}_0 . See Example 5.2.

5. Reducing the characteristic set

Our goal in this section is to propose an alternative characteristic set algorithm which can be used when it is known that the system starts from initial conditions from which it may not be accessible.

Recall that the ideal $I_{\Sigma} \subset R(\mathbf{p})[\mathbf{u}, \mathbf{y}, \mathbf{x}]$, generated by the polynomials (6) and (7) is prime. Suppose the system is started at the initial condition \mathbf{x}_0 , and define $I_{\Sigma}(\hat{\mathcal{V}}_0)$ to be the ideal generated by the polynomials of (the characteristic set of) $I(\hat{\mathcal{V}}_0)$ plus the "output" polynomials (7). $I_{\Sigma}(\hat{\mathcal{V}}_0)$ may not be prime; this happens for example when some of the polynomials ϕ_k 's in (25) are factorizable. In this general case, the reasoning below has to be applied to each component of the factorisation (Ljung & Glad, 1994).

Roughly speaking, the question of whether the general identifiability algorithm based on the characteristic set of the ideal generated by the polynomials of the system gives the right answer when the system is started at the initial state \mathbf{x}_0 , can be reduced to checking whether the characteristic set of $I_{\Sigma}(\hat{\mathscr{V}}_0)$ is equal to or different from that of the original I_{Σ} . In more abstract language, it can be reduced to just checking if $I_{\Sigma}(\hat{\mathscr{V}}_0) \equiv I_{\Sigma}$ or not.

More precise statements can be given if we distinguish among several possible situations.

Theorem 6. If system (2) is accessible from all initial states \mathbf{x}_0 from which it may have been started, then $I_{\Sigma} \equiv I_{\Sigma}(\hat{V}_0)$ and the characteristic set of I_{Σ} provides the correct identifiability test.

Proof. Since there is no nontrivial differential algebraic submanifold through \mathbf{x}_0 , $I(\hat{\mathcal{V}}_0) \equiv I$ and therefore, also $I_{\Sigma}(\hat{\mathcal{V}}_0) := (I(\hat{\mathcal{V}}_0), \{y_k - h_k(\mathbf{u}, \mathbf{x}, \mathbf{p}); k = 1, \dots, r\})$, is equal to I_{Σ} . \square

Theorem 7. If system is accessible except from a set of zero measure T and $\mathbf{x}_0 \in T$, let $\{\phi_k(\mathbf{x}) = 0; k = 1, ..., d\}$ be a set of algebraic equations defining the smallest invariant manifold T containing \mathbf{x}_0 . Then the identifiability test applied to the characteristic set of the ideal $I_{\Sigma}(\hat{V}_0) := (I, \{\phi_k; k = 1, ..., d\}, \{y_k - h_k; k = 1, ..., r\})$ provides a correct identifiability test.

Proof. Follows from Theorem 4 and from the general discussion presented at the beginning of the present section. \Box

Example 3. The following system:

$$\dot{x}_1 = -p_0 u - p_2 x_1 - p_3 x_2, \quad x_1(0) = x_{10},
\dot{x}_2 = p_3 x_1 x_2 - p_1 x_1, \quad x_2(0) = x_{20},$$
(30)

where $\mathscr{P} = \mathbb{R}^3_+ \setminus \{\mathbf{0}\}$, is generically accessible, i.e. dim $\Delta_{\mathscr{C}} = 2$ for all \mathbf{x} not in the invariant set T defined by $\phi(\mathbf{x}) = p_3 x_2 - p_1 = 0$. Assume the output equation is

$$y = x_1. (31)$$

The characteristic set, starting from an initial condition not belonging to T, is (the calculations are reported in Appendix A)

$$A_1 \equiv -\dot{u}p_0 - \ddot{y} + \dot{y}yp_3 - \dot{y}p_2 + uyp_0p_3 + y^2p_2p_3 + yp_1p_3,$$

$$A_2 \equiv y - x_1$$
,

$$A_3 \equiv \dot{y} + u \, p_0 + y \, p_2 + x_2 \, p_3. \tag{32}$$

The coefficients of the input-output relation, A_1 , provide the following exhaustive summary

$$c_1(\mathbf{p}) = p_0,$$

$$c_2(\mathbf{p}) = p_3,$$

$$c_3(\mathbf{p})=p_2,$$

$$c_4(\mathbf{p})=p_0\,p_3,$$

$$c_5(\mathbf{p}) = p_2 p_3,$$

$$c_6(\mathbf{p}) = p_1 p_3, \tag{33}$$

from which it is evident that all parameters p_0 , p_1 , p_2 , p_3 have one and only one solution. Thus the system is globally identifiable from "generic" initial conditions.

Consider the case of initial condition $\mathbf{x}_0 = [x_{10}, p_1/p_3]^T$. The system is not accessible and the solution evolves in the slice $\phi(\mathbf{x}) = 0$. In this case, we know that $I(\hat{\mathcal{V}}_0) = (I \cup \{\phi(\mathbf{x})\})$, i.e. $I_{\Sigma}(\hat{\mathcal{V}}_0) \supset I_{\Sigma}$. Now we will show that the exhaustive summary provided by the coefficients of the characteristic set of $I_{\Sigma}(\hat{\mathcal{V}}_0)$ is different from that provided by the characteristic set of I_{Σ} . Following Theorem 4 the characteristic set of the ideal $I(\hat{\mathcal{V}}_0)$ generated by the polynomials defining the dynamic system plus the algebraic polynomial defining T has to be calculated. This characteristic set is

$$\hat{A}_{1} \equiv \dot{y} + u p_{0} + y p_{2} + p_{1},$$

$$\hat{A}_{2} \equiv y - x_{1},$$

$$\hat{A}_{3} \equiv x_{2} p_{3} - p_{1},$$
(34)

it is easy to see that p_0 , p_1 , p_2 are uniquely determined while p_3 can be arbitrary and hence the system started in T is nonidentifiable.

Theorem 8. Assume that system (2) and (3) is not accessible (from any point in \mathbb{R}^n), and let the system be started at the initial condition \mathbf{x}_0 . If the invariant manifold through \mathbf{x}_0 , $M_{\mathbf{x}_0}$, is algebraic, let $\{\phi_k(\mathbf{x}) = 0; k = 1, ..., d\}$ be the set of algebraic equations defining the invariant manifold containing \mathbf{x}_0 . Then the identifiability test applied to the characteristic set of the ideal $I_{\Sigma}(\hat{V}_0) := (I, \{\phi_k; k = 1, ..., d\}, \{y_k - h_k; k = 1, ..., r\})$ provides the correct identifiability test.

Proof. Follows from Theorem 5 and from the general discussion presented at the beginning of the present section. \Box

Note that if the system is never accessible, the functions $\{\phi_k(\mathbf{x})\}$ describing the invariant submanifold are calculated by integration (see Section 4) and hence depend on the initial state \mathbf{x}_0 . Assume the ϕ 's are algebraic and are added to the characteristic set of I_{Σ} . After the reduction procedure, the input—output relation turns out to depend not only on \mathbf{u} and \mathbf{y} but in general also on the initial condition \mathbf{x}_0 . Hence the identifiability test is applied to $A_{\mathbf{x}_0}(\mathbf{y},\mathbf{u})=0$ where \mathbf{x}_0 ranges over the new state space $M_{\mathbf{x}_0}$.

Remark 7. Note that observability (or algebraic observability (Glad, 1990) does not play a role in the identifiability criteria given in this section. This may seem in contrast with various requirements of (local) minimality (or *local reducedness* (Chappell & Godfrey, 1992) which are found in the literature. The reason is that, with the chosen ranking in which the output variables are "smaller" than the state, in the computation of the input—output relation, the unobservable subsystem (see Isidori, 1995, pp. 50–51) is automatically "factored out". This can easily be checked by applying

the Ritt algorithm to a polynomial system described in the canonical form 1.3.8 of Isidori (1995).

Example 4. Consider the system:

$$\dot{x}_1 = p_1 u x_3, \quad x_1(0) = x_{10},$$
 $\dot{x}_2 = p_2 x_1, \quad x_2(0) = x_{20},$
 $\dot{x}_3 = p_3 x_1 x_2, \quad x_3(0) = x_{30},$
(35)

where $\mathscr{P} = \mathbb{R}^3_+ \setminus \{\mathbf{0}\}$ and with output equations

$$y_1 = x_1,$$

 $y_2 = x_2.$ (36)

The polynomials defining system (35) already form a characteristic set of the ideal I.

System (35) is never accessible, since dim $\Delta_{\mathscr{C}} < 3$, for all $\mathbf{x} \in \mathbb{R}^3$. In fact, generically in \mathbb{R}^3 , dim $\Delta_{\mathscr{C}} = 2$. Note that dim $\Delta_{\mathscr{C}} = 2$ for all $\mathbf{x} \in \{\mathbb{R}^3 - T\}$ where T is the "thin" set of equilibrium points

$$T := \{ \mathbf{x} : x_1 = 0, \ x_2 = x_{20}, \ x_3 = 0 \},$$
 (37)

where dim $\Delta_{\mathscr{C}} = 0$.

Since all Lie brackets in the sequence [f,g],[f,[f,g]], [f,[f,[f,g]]],... are zero after the fifth, the distribution is involutive

All covectors μ orthogonal to $\varDelta_{\mathscr{C}}$ are easily found to be of the form

$$\mu = \alpha(\mathbf{x})[0, -p_3x_2, p_2],$$

where $\alpha(\mathbf{x})$ is an arbitrary nonzero smooth function.

By the Frobenius Theorem it must follow that for some suitable α , the covector μ generates a closed differential form. In fact, it is easy to check that

$$\phi(\mathbf{x}) = -p_3 x_2^2 / 2 + p_2 x_3 + p_3 x_{20}^2 / 2 - p_2 x_{30}$$

has a differential which is proportional to μ , namely $d\phi = [-p_3x_2 dx_2 + p_2 dx_3]$.

The solution of system (35) starting from any \mathbf{x}_0 for which dim $\Delta_{\mathscr{C}} = 2$ evolves in the slice described by $\phi(\mathbf{x}) = 0$.

In order to see what the restricted dynamics may look like, choose the equation $\phi(\mathbf{x}) = 0$ corresponding to the initial condition $\mathbf{x}_0 = (x_{10}, 0, 0)$, where dim $\Delta_{\mathscr{C}}(\mathbf{x}_0) = 2$, and compute the new characteristic set. By applying the pseudodivision algorithm one obtains

$$-p_3x_2^2 + 2p_2x_3,$$

$$2p_2\dot{x}_1 - p_1p_3ux_2^2,$$

$$\dot{x}_2 - p_2 x_1.$$
 (38)

The first equation $x_3 = p_3 x_2^2/(2 p_2)$ is redundant since it does not affect the input–output relation. The other two together with the output equations (36) represent a state-space system of order two describing the accessible portion of system (35).

To test the identifiability of (35) and (36), consider first the dynamic system regardless of the initial conditions. In this case an easy computation provides the characteristic set of I_{Σ}

$$A_{1} \equiv -\ddot{u}\dot{y}_{1}uy_{1} + 2\dot{u}^{2}\dot{y}_{1}y_{1} - 2u\dot{u}y_{1}\ddot{y}_{1} + \dot{u}\dot{y}_{1}^{2}u + \ddot{y}_{1}u^{2}y_{1} - \ddot{y}_{1}\dot{y}_{1}u^{2} - u^{3}y_{1}^{3}p_{1}p_{2}p_{3},$$

$$A_{2} \equiv -\dot{u}\dot{y}_{1} + \ddot{y}_{1}u - p_{1}p_{3}u^{2}y_{1}y_{2},$$

$$A_{3} \equiv y_{1} - x_{1},$$

$$A_{4} \equiv -\dot{u}\dot{y}_{1} + \ddot{y}_{1}u - p_{1}p_{3}u^{2}y_{1}x_{2},$$

$$A_{5} \equiv \dot{y}_{1} - p_{1}ux_{3}$$
(39)

with the exhaustive summary

$$c_1(\mathbf{p}) = p_1 p_2 p_3,$$

 $c_2(\mathbf{p}) = p_1 p_3,$
(40)

from which it is evident that only p_2 is uniquely determined, while for p_1 and p_3 there is an infinite number of solutions. Thus system (35) is nonidentifiable.

Now assume that the system is started from an unknown initial condition $\mathbf{x}_0 = [x_{10}, x_{20}, x_{30}]^T$ with all the components different from zero so that dim $\Delta_{\mathscr{C}}(\mathbf{x}_0) = 2$.

In this case the equation $\phi(\mathbf{x}) = 0$ has to be added to system equations (35) and (36) in order to compute the characteristic set of $I_{\Sigma}(\hat{\mathcal{V}}_0)$, which turns out to be

$$\hat{A}_{1} \equiv \dot{y}_{1}\dot{u}(-\dot{u}\dot{y}_{1} + 2u\ddot{y}_{1}) + 2p_{2}p_{1}p_{3}\dot{y}_{1}u^{3}y_{1}^{2}
+ u^{4}y_{1}^{2}p_{1}^{2}p_{3}(-2p_{2}x_{30} + p_{3}x_{20}^{2}) - \ddot{y}_{1}^{2}u^{2},
\hat{A}_{2} \equiv \dot{u}\dot{y}_{1} - \ddot{y}_{1}u + u^{2}y_{1}y_{2}p_{1}p_{3},
\hat{A}_{3} \equiv y_{1} - x_{1},
\hat{A}_{4} \equiv -\dot{u}\dot{y}_{1} + \ddot{y}_{1}u - u^{2}y_{1}x_{2}p_{1}p_{3},
\hat{A}_{5} \equiv \dot{y}_{1} - ux_{3}p_{1}.$$
(41)

The exhaustive summary extracted from the input-output relation is formally

$$c_{1}(\mathbf{p}) = p_{1} p_{2} p_{3},$$

$$c_{2}(\mathbf{p}) = p_{1} p_{3},$$

$$c_{3}(\mathbf{p}) = p_{1}^{2} p_{3}(-2 p_{2} x_{30} + p_{3} x_{20}^{2}),$$

$$(42)$$

however, since \mathbf{x}_0 is not known, $c_3(\mathbf{p})$ cannot be used to test identifiability. Therefore the results show that only p_2 is uniquely determined, while for p_1 and p_3 there is an infinite number of solutions. Thus the identifiability test in this case gives the same results obtained regardless of initial conditions. ⁵

⁵ Note that if the initial condition is known, the system is globally identifiable.

Finally, consider initial conditions starting in T, in this case Theorem 4 can be applied to calculate $I_{\Sigma}(\hat{\mathscr{V}}_0)$ which becomes:

$$I(\hat{\mathcal{V}}_0) = (I \cup \{e_1, e_3\}),$$

where

$$e_1(\mathbf{x}) := x_1, \quad e_3(\mathbf{x}) := x_3.$$

In this case $I_{\Sigma}(\hat{\mathscr{V}}_0) \supset I_{\Sigma}$.

It is easy to see that the input-output relation reduces to the pair of equations

$$y_1 = 0,$$

 $\dot{y}_2 = 0$ (43)

which does not contain parameters. In this case trivially $\mathbf{p} = [p_1, p_2, p_3]$ can be chosen arbitrary. Note that this result is different from the corresponding one obtained without adding the equation $\phi(\mathbf{x}) = 0$ to Eqs. (35) and (36).

If some of the $\{\phi_k, k=1,...,d\}$ are not polynomial and there are no algebraic polynomials vanishing at their solutions, $M_{\mathbf{x}_0}$ is not algebraic, see Remark 5 in the previous section. In this case, it does not make sense to add all of the $\{\phi_k\}$ to the original system Σ to compute a new characteristic set. Testing identifiability in this situation is an open problem which requires further study. Note that this may happen only when the original *n*-dimensional state space of the system turns out to be unnecessarily large, i.e. model (2) and (3) is nonminimal and provides a "redundant" description of the underlying physical/biological dynamics. Nonalgebraic invariant manifolds can occur only in this circumstance. In fact, one may argue that if this is the case, then the original system can in principle be transformed, by a suitable coordinate transformation, to a "reduced" dynamical system of dimension smaller than n, which is necessarily nonalgebraic, i.e. is not describable by polynomial differential equations.

6. Conclusions

In this paper, it has been observed that, when methods based on differential algebra are used, problems can arise in testing the identifiability of systems started at some special initial conditions. We have analysed the difficulty and shown that it has to do with possible lack of accessibility of the system from the initial state. We have described a method to compute the new ideal describing the system evolving from the given state, which can be used to set up a correct identifiability test even when accessibility does not hold.

Naturally the development of a reliable and general computer-algebra algorithm to test the identifiability of a nonlinear dynamic system under the conditions described in this paper is a priority for our future work. Although some preliminary work in this direction has been done already (see Saccomani, Audoly, & D'Angiò, 2001), a description of the ongoing research regarding the development of this

code does not fall within the scope of this paper and will appear elsewhere.

Appendix A. Calculation of the characteristic set (Example 5.1)

Consider the system of example (30)

$$\dot{x}_1 = -p_0 u - p_2 x_1 - p_3 x_2, \quad x_1(0) = x_{10},
\dot{x}_2 = p_3 x_1 x_2 - p_1 x_1, \quad x_2(0) = x_{20},
y = x_1.$$
(A.44)

With the standard ranking (8) of the input, output and state variables

$$u < \dot{u} < \ddot{u} < v < \dot{v} < \ddot{v} < x_1 < x_2 < \dot{x}_1 < \dot{x}_2$$
 (A.45)

the set of polynomials defining system of Eqs. (30) and (31) are ordered by following the increasing ranking

$$A_{1} \equiv y - x_{1},$$

$$A_{2} \equiv \dot{x}_{1} + p_{0}u + p_{2}x_{1} + p_{3}x_{2},$$

$$A_{3} \equiv \dot{x}_{2} - p_{3}x_{1}x_{2} + p_{1}x_{1},$$
(A.46)

where \mathbf{x}_1 is leader of A_1 , $\dot{\mathbf{x}}_1$ is leader of A_2 and $\dot{\mathbf{x}}_2$ is leader of A_3 . At this stage the reduction procedure starts to calculate the characteristic set. Polynomial A_2 is reduced with respect to polynomial A_1

$$A_{1} \equiv y - x_{1},$$

$$A_{2} \equiv \dot{y} + p_{0}u + p_{2}y + p_{3}x_{2},$$

$$A_{3} \equiv \dot{x}_{2} - p_{3}yx_{2} + p_{1}y,$$
(A.47)

where now A_2 has \mathbf{x}_2 as leader.

where now A_3 has \mathbf{x}_2 as leader.

Now polynomial A_3 is reduced with respect to the derivative of A_2

$$A_{1} \equiv y - x_{1},$$

$$A_{2} \equiv \dot{y} + p_{0}u + p_{2}y + p_{3}x_{2},$$

$$A_{3} \equiv \ddot{y} + p_{0}\dot{u} + p_{2}\dot{y} + p_{3}(p_{3}yx_{2} + p_{1}y),$$
(A.48)

Polynomial A_3 is reduced with respect to A_2

$$A_{1} \equiv y - x_{1},$$

$$A_{2} \equiv \dot{y} + p_{0}u + p_{2}y + p_{3}x_{2},$$

$$A_{3} \equiv -\ddot{y} - p_{0}\dot{u} - p_{2}\dot{y} + \dot{y}yp_{3} + p_{0}p_{3}uy + p_{2}p_{3}v^{2} + yp_{1}p_{3},$$
(A.49)

where now A_3 has \ddot{y} as leader.

The set (A.49) is ordered and the characteristic set, starting from an initial condition not belonging to T, is

$$A_1 \equiv -\dot{u}p_0 - \ddot{y} + \dot{y}yp_3 - \dot{y}p_2 + uyp_0p_3 + y^2p_2p_3 + yp_1p_3,$$

 $A_2 \equiv y - x_1,$ $A_3 \equiv \dot{y} + u p_0 + y p_2 + x_2 p_3.$ (A.50)

References

- Audoly, S., Bellu, G., D'Angiò, L., Saccomani, M. P., & Cobelli, C. (2001). Global identifiability of nonlinear models of biological systems. IEEE Transactions on Biomedical Engineering, 48(1), 55–65.
- Audoly, S., D'Angiò, L., Saccomani, M. P., & Cobelli, C. (1998). Global identifiability of linear compartmental models. *IEEE Transactions on Biomedical Engineering*, 45, 36–47.
- Buchberger, B. (1998). An algorithmical criterion for the solvability of algebraic system of equation. *Aequationes Mathematicae*, 4(3), 45–50.
- Carrà Ferro, G. (1989). Gröbner bases and differential algebra. Lecture Notes in Computer Science, 356, 129–140.
- Chappell, M. J., & Godfrey, K. R. (1992). Structural identifiability of the parameters of a nonlinear batch reactor model. *Mathematical Biosciences*, 108, 245–251.
- D'Angiò, L., Audoly, S., Bellu, G., Saccomani, M.P., & Cobelli, C. (1994). Structural identifiability of nonlinear systems: Algorithms based on differential ideals. In *Proceedings of the SYSID*'94 10th IFAC Symposium on System Identification, Vol. 3, Copenhagen, Denmark (pp. 13–18).
- Diop, S. (1992). Differential algebraic decision methods and some applications to system theory. *Theoretical Computer Science*, 98, 137–161.
- Fliess, M., & Glad, S.T. (1993). An algebraic approach to linear and nonlinear control. In *Essays on control: Perspectives in the theory and its applications*, H.L. Treutelman, J.C. Willeuis, Eds. Birkhäuser, Boston (pp. 223–267).
- Forsman, K. (1991). Constructive commutative algebra in nonlinear control theory. Linköping studies in science and technology. Dissertation No. 261, Linköping University, Sweden.
- Glad, S.T. (1990). Differential algebraic modelling of nonlinear systems. In *Realization and modelling in system theory*, *Proceedings of the MTNS*'89, Vol. 1 (pp. 97–105). Basel: Birkhäuser.
- Hermann, R., & Krener, A. J. (1977). Nonlinear controllability and observability. *IEEE Transactions on Automatic Control*, AC-22(5), 728–740.
- Isidori, A. (1995). Nonlinear control systems (3rd ed.). London: Springer. Jacquez, J. A., & Greif, P. (1985). Numerical parameter identifiability and estimability: Integrating identifiability, estimability, and optimal sampling design. Mathematical Biosciences, 77, 201–227.
- Kolchin, E. (1973). Differential algebra and algebraic groups. New York: Academic Press.
- Ljung, L., & Glad, S. T. (1994). On global identifiability for arbitrary model parameterizations. *Automatica*, 30(2), 265–276.
- Lobry, C. (1970). Controlabilité des systèmes nonlineaires. SIAM Journal on Control, 8(4), 573–605.
- Mishra, B. (1993). Algorithmic algebra. Springer-Verlag texts and monographs in computer science. Berlin: Springer.
- Ollivier, F. (1990). Le problème de l'identifiabilité structurelle globale: étude théorique, méthodes effectives et bornes de complexité. Thèse de Doctorat en Science, École Polytéchnique, Paris, France.
- Ritt, J. F. (1950). Differential algebra. Providence, RI: American Mathematical Society.
- Saccomani, M. P., Audoly, S., Bellu, G., D'Angiò, L., & Cobelli, C. (1997). Global identifiability of nonlinear model parameters.

- In Proceedings of the SYSID '97 11th IFAC Symposium on System Identification, Vol. 3 (pp. 219–224).
- Saccomani, M. P., Audoly, S., & D'Angiò, L. (2001). A new differential algebra algorithm to test identifiability of nonlinear systems with given initial conditions. In *Proceedings of the 40th IEEE Conference on Decision and Control*, Orlando, Florida, USA (pp. 3108–3113).
- Söderström, T., & Stoica, P. (1987). System identification. Englewood Cliffs, NJ: Prentice Hall.
- Sontag, E. D. (1998). Mathematical control theory (2nd ed.). Berlin: Springer.
- Vajda, S., Godfrey, K., & Rabitz, H. (1989). Similarity transformation approach to identifiability analysis of nonlinear compartmental models. *Mathematical Biosciences*, 93, 217–248.
- Walter, E. (1982). Identifiability of state space models. Berlin: Springer.Walter, E., & Lecourtier, Y. (1982). Global approaches to identifiability testing for linear and nonlinear state space models. Math and Comput in Simula, 24, 472–482.



Maria Pia Saccomani was born in Venice, Italy, on February 10, 1961. She received the Doctoral degree (Laurea) in Mathematics in 1985 from the University of Padova, Padova, Italy and the Ph.D. degree in Biomedical Engineering in 1990 from the Polytechnic of Milan, Milan, Italy. In 1991 she became Assing at the Department of Electronics and Informatics, University of Padova, Padova, Italy. She has published around 20 papers in internationally refereed journals.

Her main research activity is in the field of mathematical modeling of biological and physiological systems, parameter identifiability, and system identification.



Stefania Audoly was born in Milan, Italy, on May 21, 1937. She received the Doctoral degree (Laurea) in Mathematics in 1961 from the University of Cagliari, Cagliari, Italy. In 1985 she became Associate Professor of Numerical Analysis at the Department of Structural Engineering, University of Cagliari, Cagliari, Italy. Her main research activity is on parameter identifiability of linear and nonlinear dynamic systems and symbolic manipulation languages.



Leontina d'Angio' was born in Cagliari, Italy, on October 26, 1931. She received the Doctoral degree (Laurea) in Mathematics in 1953 from the University of Cagliari, Cagliari, Italy. In 1985 she become Associate Professor of Mathematics at the Department of Mathematics, University of Cagliari, Cagliari, Italy. Her main research activity is on parameter identifiability of linear and nonlinear dynamic systems, differential and computer algebra.