Computing all identifiable functions for ODE models

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Abstract

Parameter identifiability is a structural property of an ODE model for recovering the values of parameters from the data (i.e., from the input and output variables). This property is a prerequisite for meaningful parameter identification in practice. In the presence of nonidentifiability, it is important to find all functions of the parameters that are identifiable. The existing algorithms check whether a given function of parameters is identifiable or, under the solvability condition, find all identifiable functions. Our first main result is an algorithm that computes all identifiable functions without any additional assumptions. Our second main result concerns the identifiability from multiple experiments. For this problem, we show that the set of functions identifiable from multiple experiments is what would actually be computed by input-output equation-based algorithms if the solvability condition is not fulfilled. We give an algorithm that not only finds these functions but also provides an upper bound for the number of experiments to be performed to identify these functions. We provide an implementation of the presented algorithms.

Keywords: parameter identifiability, multiple experiments, input-output equations, differential algebra, characteristic sets

1. Introduction

In this paper, we study structural parameter identifiability of rational ODE systems. Roughly speaking, a parameter is structurally identifiable if its value can be recovered from the observations assuming continuous noise-free measurements and sufficiently exciting inputs (also referred to as the persistence of excitation, see [16, 37]). If not all of the parameters of a model are identifiable, the next question usually is what functions \( h(\bar{\mu}) \in \mathbb{C}(\bar{\mu}) \) of the parameters \( \bar{\mu} \) are identifiable. The knowledge of identifiable functions can be used in these ways:

- If the functions of interest to the modeler are identifiable, then the lack of identifiability of some parameters is not an issue (sometimes, this is even an advantage [33]).

- Identifiable functions can be used to find an identifiable reparametrization of the model [1, 18, 19].

- Knowledge of identifiable functions can be used to discover parameter transformations that preserve the input-output behavior (see Section 5.2).

To the best of our knowledge, all existing approaches to computing identifiable functions extract them from the coefficients of input-output equations (going back to [24]; for a concise summary, we refer to [26, Introduction and Algorithm 3.1]). To conclude that the coefficients of an input-output equation are identifiable, one can, for example,

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verify if the solvability condition [30, Remark 3] holds for the equation. The condition can be checked by an algorithm
(see [6, Section 4.1] and [23, Section 3.4]) and holds for some classes of models [26]. If the condition does not hold,
then this approach of finding identifiable functions of parameters is not applicable. For a simple example of a system
for which this condition does not hold, see [12, Example 2.14] (see also Section 5.2). Therefore, we are not aware of
any prior algorithm that can compute all identifiable functions (e.g., by computing generators of the field of identifiable
functions). Note that the existing software allows, for any fixed rational function of parameters, to check whether it is
identifiable [26, Remark 4.8].

This motivates the following questions we study in this paper

(Q1) How to find the identifiable functions of a model even if the solvability condition does not hold?

(Q2) If the condition does not hold, what is the meaning of the coefficients of the input-output equations?

Our main results are the following answers to these questions:

• We answer (Q1) by providing Algorithm 1 for computing generators of the field of identifiable functions. The
algorithm is based on the theory established in Theorem 11.

• We show in Theorem 21 that the coefficients of the input-output equations are generators of the field of func-
tions identifiable from multiple experiments (with generically different inputs and initial conditions), thus an-
swering (Q2). Furthermore, we use this to derive an upper bound for the number of experiments.

A theoretical basis for this work is differential algebra. Our results are informed by model theory in the sense of
mathematical logic, though this does not appear explicitly in our presentation. We will return to this connection in
a follow-up work. Additional related results on identifiability using input-output equations and differential algebra
include [2, 10, 13, 20–22, 29–31].

The rest of the paper is organized as follows. Section 2 contains definitions and notation that we use. In Section 3,
we give our algorithm for computing the generators of the field of identifiable functions. Section 4 is on multi-
experimental identifiability. We illustrate our methods with examples in Section 5.

We have implemented Algorithm 1 and an algorithm for computing the bound from Theorem 21 (as in Remark 22)
in Maple. This proof-of-concept implementation together with the examples from Section 5 is available at https:
//github.com/pogudingleb/AllIdentifiableFunctions.

2. Basic notions and notation

In this section, we will present the basic notions and notation from differential algebra and parameter identifiability
that are essential for our main results.

2.1. Background and notation from differential algebra

Differential algebra has been a standard theory behind identifiability, and we will simply fix the basic notation.
General references include [15, 28]. For other presentations of these concepts in the context of control theory, see [7,
14, 16, 30].

Notation 1 (Differential rings and ideals).

(a) A differential ring \((R, \cdot')\) is a commutative ring with a derivation \(\cdot': R \to R\), that is, a map such that, for all
\(a, b \in R\), \((a + b)' = a' + b'\) and \((ab)' = a'b + ab'\). A differential field is a differential ring that is a field. For \(i > 0\),
a\(d^i\) denotes the \(i\)-th order derivative of \(a \in R\). \(\text{Const}(K)\) denotes the field of constants of a differential field \(K\).

(b) The ring of differential polynomials in the variables \(z_1, \ldots, z_n\) over a differential field \((K, \cdot')\) is the ring
\[K[z_j^{(i)} | i \geq 0, 1 \leq j \leq n]\]
with a derivation defined on the ring by \((z_j^{(i)})' := z_j^{(i+1)}\). This differential ring is denoted by \(K[z_1, \ldots, z_n]\).
(c) For differential fields $F \subset L$ and $a_1, \ldots, a_n \in L$, the smallest differential subfield of $L$ that contains $F$ and $a_1, \ldots, a_n$ is denoted by $F(a_1, \ldots, a_n)$.

(d) For a commutative ring $R$ and a subset $F \subset R$, the smallest ideal containing $F$ is denoted by $(F)$.

(e) An ideal $I$ of a differential ring $(R, \cdot)$ is called a differential ideal if, for all $a \in I, a' \in I$. For $F \subset R$, the smallest differential ideal containing $F$ is denoted by $(F)$.

(f) For an ideal $I$ and element $a$ in a ring $R$, we denote $I: a^\infty = \{ r \in R \mid \exists n: a^n r \in I \}$. This set is also an ideal in $R$. This will be useful for dealing with ODE systems in which (non-polynomial) rational functions appear.

(g) For $a_1, \ldots, a_n$ in a differential ring $R$, we denote the $n \times n$ matrix with $(i, j)$-entry $a_j^{(i-1)}$ by $\text{Wr}(a_1, \ldots, a_n)$ and call it the Wronskian of $a_1, \ldots, a_n$. For example,

$$\text{Wr}(a_1, a_2) = \begin{pmatrix} a_1 & a'_2 \\ a'_1 & a_2 \end{pmatrix}. $$

The rest of the definitions in this section generalize Gaussian elimination to systems of non-linear ODEs. Differential rankings are analogous to ordering of variables in Gaussian elimination; characteristic sets and presentations are analogous to row echelon form and reduced row echelon forms, respectively.

**Definition 2.** A differential ranking is a total order $>$ on $Z := \{ z_j^0 \mid i \geq 0, 1 \leq j \leq n \}$ satisfying:

$$\forall x \in Z \ x' > x \quad \text{and} \quad \forall x, y \in Z \ (x > y \implies x' > y').$$

**Notation 3.** For $f \in K[z_1, \ldots, z_n] \setminus K$ and a differential ranking,

- lead$(f)$ is the element of $\{ z_j^0 \mid i \geq 0, 1 \leq j \leq n \}$ of the highest rank appearing in $f$. This is partly analogous to the leading variable in Gaussian elimination.

- The leading coefficient of $f$ viewed as a polynomial in lead$(f)$ is called the initial of $f$. This is similar to the leading coefficient in Gaussian elimination.

- The separant of $f$ is $\frac{\partial f}{\partial \text{lead}(f)}$. One can show that it is equal to the leading coefficient of any derivative of $f$.

- The rank of $f$ is $\text{rank}(f) = \text{lead}(f)^{\deg_{\text{lead}(f)} f}$. The ranks are compared first by lead, and in the case of equality, by deg. This is analogous to the leading variable in Gaussian elimination/leading term in Gröbner bases.

- For $S \subset K[z_1, \ldots, z_n] \setminus K$, the product of initials and separants of $S$ is denoted by $H_S$. This is used in handling division with remainder algebraically.

**Definition 4 (Characteristic sets).**

- For $f, g \in K[z_1, \ldots, z_n] \setminus K$, $f$ is said to be reduced w.r.t. $g$ if no proper derivative of lead$(g)$ appears in $f$ and $\deg_{\text{lead}(g)} f < \deg_{\text{lead}(g)} g$.

- A subset $\mathcal{A} \subset K[z_1, \ldots, z_n] \setminus K$ is called autoreduced if, for all $p \in \mathcal{A}$, $p$ is reduced w.r.t. every element of $\mathcal{A} \setminus \{ p \}$. Every autoreduced set is finite [15, Section I.9].

- Let $\mathcal{A} = A_1 < \ldots < A_r$ and $\mathcal{B} = B_1 < \ldots < B_s$ be autoreduced sets ordered by their ranks (see Notation 3). We say that $\mathcal{A} \subset \mathcal{B}$ if

  - $r > s$ and rank$(A_i) = \text{rank}(B_i)$, $1 \leq i \leq s$, or

  - there exists $q$ such that rank$(A_q) < \text{rank}(B_q)$ and, for all $i, 1 \leq i < q$, rank$(A_i) = \text{rank}(B_i)$.

- An autoreduced subset of the smallest rank of a differential ideal $I \subset K[z_1, \ldots, z_n]$ is called a characteristic set of $I$. One can show that every non-zero differential ideal in $K[z_1, \ldots, z_n]$ has a characteristic set.
**Definition 5 (Characteristic presentation).** (cf. [4, Definition 3]) A polynomial is said to be monic if at least one of its coefficients is 1. This is how monic is typically used in identifiability analysis and not how it is used in [4]. A set of polynomials is said to be monic if each polynomial in the set is monic.

Let $C$ be a characteristic set of a prime differential ideal $P \subset K[z_1, \ldots, z_n]$. Let $N(C)$ denote the set of non-leading variables of $C$. Then $C$ is called a characteristic presentation of $P$ if all initials of $C$ belong to $K[N(C)]$ and none of the elements of $C$ has a factor in $K[N(C)]$.

2.2. Parameter identifiability for ODE models

Consider an ODE system of the form

$$
\Sigma = \begin{cases} 
\dot{x} = f(x, \mu, \bar{u}), \\
\dot{y} = g(x, \mu, \bar{u}),
\end{cases}
$$

where $\bar{x}$: a vector of state variables, $\bar{y}$: a vector of output variables, $\bar{\mu}$: a vector of time-independent parameters, $\bar{u}$: a vector of input variables, and $\bar{f}$ and $\bar{g}$: tuples of elements of $C(\bar{x}, \bar{\mu}, \bar{u})$.

Bringing $\bar{f}$ and $\bar{g}$ to the common denominator, write $\bar{f} = F/\bar{Q}$ and $\bar{g} = G/\bar{Q}$, for $F_1, \ldots, F_n, G_1, \ldots, G_m, \bar{Q} \in C[\bar{x}, \bar{\mu}, \bar{u}]$. Consider the (prime, see [12, Lemma 3.2]) differential ideal

$$
I_{C} := \{Q\bar{x}_i - F_i, Q\bar{y}_j - G_j, 1 \leq i \leq n, 1 \leq j \leq m\} : \bar{Q}^\infty.
$$

Note that every solution of (1) is a zero of every element of $I_{C}$.

**Definition 6 (Generic solution, cf. [8, 9]).** The image of $(\bar{x}, \bar{y}, \bar{u})$ under the canonical homomorphism

$$
C(\bar{\mu})(\bar{x}, \bar{y}, \bar{u}) \rightarrow C(\bar{\mu})(\bar{x}, \bar{y}, \bar{u})/I_{C}
$$

is called the generic solution of (1).

Rigorously written definitions of identifiability in analytic terms can be found in [26, Definition 2.3] and [12, Definition 2.5]. [12, Proposition 3.4] implies that the following is an equivalent definition of identifiability, which we will use.

**Definition 7 (Identifiability).** A function $h \in C(\bar{\mu})$ is said to be (single-experiment, or SE-) identifiable for (1) if, for every generic solution $(x^*, \bar{y}^*, \bar{u}^*)$ of (1), we have $h \in C(\bar{y}^*, \bar{u}^*)$.

**Definition 8 (Input-output equations).** For a fixed differential ranking $>$ on $(\bar{y}, \bar{u})$, the set of input-output equations (IO-equations) of the system $\Sigma$ from (1) is the characteristic presentation of $I_{C} \cap C[\bar{y}, \bar{u}]$.

It can be computed by computing the characteristic presentation of $I_{C}$ with respect to the differential ranking that is compatible with $>$ and in which any derivative from $\bar{x}$ is greater than any derivative from $(\bar{y}, \bar{u})$, and returning $C \cap C[\bar{y}, \bar{u}]$ (e.g., by the Rosenfeld-Gröbner algorithm [5]).

3. Single-experiment identifiability

In this section, we give an algorithm to compute all functions of the parameters that are identifiable from a single experiment for system (1). We begin with a construction in Section 3.1, which is a refinement of considering Wronskians of monomials (cf. [6, 8, 23, 26]). Using this, we give an algebraic characterization, Theorem 11, of the identifiable functions, which we turn into Algorithm 1.

3.1. Preparation for Theorem 11

To find the identifiable functions, we will begin with a new construction. Let $K$ be a differential field and $k$ a constant subfield such that $\bar{C} \subset k$ and let $\bar{\alpha} = (\alpha_1, \ldots, \alpha_n) \in K^n$. For $p \in k[\bar{\alpha}]$, where $\bar{\alpha} = (\alpha_1, \ldots, \alpha_n)$, such that $p(\bar{\alpha}) = 0$, we construct a subfield $F(p) \subset K$ as follows:

1. Let $W_p$ denote the Wronskian (see Notation 1(g)) of the monomials of $p$ evaluated at $\bar{\alpha}$.

2. Define $F(p)$ to be the field generated over $\bar{C}$ by (the nonleading) entries in the reduced row echelon form of $W_p$. 

$$
4
$$
Example 9. Let \( K = \mathbb{C}(x), n = 2, \tilde{a} = (x+1, 2/(x+1)) \), and \( p = z_1' + 2z_1z_2 + 3 \). Then the monomials of \( p \) are \( z_1', z_1z_2 \), and 1, their Wronskian and its evaluation at \( \tilde{a} \) are

\[
\begin{pmatrix}
z_1'
z_1z_2
\end{pmatrix}
\begin{pmatrix}
z_1'z_2
\end{pmatrix}'
0
1
\]

and

\[
W_p = \begin{pmatrix} 1 & 2 & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix},
\]

which is already in reduced row echelon form, and so \( F(p) = \mathbb{C}(1, 2, 1) = \mathbb{C} \). For examples in which \( F(p) \) is strictly greater than \( \mathbb{C} \), see Example 16 and Section 5.2. There, evaluation of the Wronskian at a point is by differential ideal calculations.

For a tuple \( \hat{p} \subset k[\mathcal{L}] \) of differential polynomials,

\[
F(\hat{p}) := \mathbb{C}(F(p) \mid p \in \hat{p}).
\]

Lemma 10. For every \( p \in k[\mathcal{L}] \) such that \( p(\tilde{a}) = 0 \), we have \( F(p) \subset \mathbb{C}(\tilde{a}) \).

Proof. Follows from all entries of \( W_p \) being from \( \mathbb{C}(\tilde{a}) \).

3.2. Main result

We will now show that the problem of finding the field of identifiable functions is reduced to computing the intersection of fields of constants defined by their generators. This is a key step in Algorithm 1 to find the field of all identifiable functions.

Theorem 11 (Single-experiment identifiability). For system (1), the field of identifiable functions is equal to

\[
\mathbb{C}(\tilde{a}) \cap F(\hat{p}),
\]

where \( \hat{p} \) is a set of input-output equations of (1) (Definition 8).

Remark 12 (\( F(p) \) is generated by first integrals). Lemma 13 implies that \( F(\hat{p}) \) consists of constants (that is, first integrals). [26, Lemma 5.1] implies that \( F(\hat{p}) \subset \mathbb{C}(\tilde{a}, \tilde{b}) \).

Lemma 13. In the setup of Section 3.1, \( F(p) \subset \text{Const}(K) \).

Proof. We will show that the space of linear relations between columns of \( W_p \) is defined over \( \text{Const}(K) \). This will imply that all the entries in the reduced row echelon form of \( W_p \) are constants. Let \( X \) be a maximal set of linearly independent columns of \( W_p \), and let \( Y \) denote the rest of the columns. The monomials corresponding to \( X \) are linearly independent over \( \text{Const}(K) \) because any such dependence would yield a dependence of \( X \). For each \( v \in Y \), there exists a column dependence of \( X \cup \{v\} \), unique up to scaling. These dependencies span the space of column dependencies of \( W_p \). [15, Chapter II, Section 1, Theorem 1] implies that the monomials corresponding to \( X \cup \{v\} \) are dependent over \( \text{Const}(K) \). Therefore, the corresponding column dependence can be chosen to be over \( \text{Const}(K) \) as well.

Proof of Theorem 11. To prove the theorem, we will show that, for all differential fields \( k \subset K \) with \( \mathbb{C} \subset k \subset \text{Const}(K) \) and \( k \) being algebraically closed in \( K \), every \( n \), and every tuple \( \tilde{a} \in K^n \),

\[
k \cap F(\hat{p}) = k \cap \mathbb{C}(\tilde{a}),
\]

where \( \hat{p} := \{p_1, \ldots, p_m \} \subset k[y_1, \ldots, z_n] \) is a characteristic set of the prime ideal of all differential polynomials vanishing at \( \tilde{a} \). This is then applied to \( k = \mathbb{C}(\tilde{a}) \) and the differential field \( K \) generated over \( k \) by the \((\tilde{y}, \tilde{a})\)-components (denoted by \( \tilde{a} \)) of a generic solution of (1).

Lemma 10 implies that \( k \cap F(\hat{p}) \subset k \cap \mathbb{C}(\tilde{a}) \). Assume that

\[
k \cap \mathbb{C}(\tilde{a}) \supseteq k \cap F(\hat{p})
\]

and let \( b \in k \cap \mathbb{C}(\tilde{a}) \setminus k \cap F(\hat{p}) \).

Recall (see [17, Section 2]) that a differential field \( K \) is differentially closed if: for all \( m \) and finite \( G \subset K[w_1, \ldots, w_m] \), if there exists \( L \supset K \) such that \( G = 0 \) has a solution in \( L \), then \( G = 0 \) has a solution in \( K \). Let
$K^{\text{diff}}$ be a differential closure of $K$, that is, a differentially closed field containing $K$ that embeds into any other differentially closed field containing $K$.

We have $K^{\text{diff}} \supsetneq K^{\text{ac}}$, the algebraic closure of $k$, and $K^{\text{ac}} \cap K = k$. Since $b \notin F(p)$, there exists an automorphism $\alpha : \text{Const}(K^{\text{diff}}) \to \text{Const}(K^{\text{diff}})$ such that $\alpha|_{F(p)} = \id$ and $\alpha(b) \neq b$. We pick such an $\alpha$ and extend it to a differential automorphism of $K^{\text{diff}}$ and denote the extension by $\alpha$ as well.

For a vector $K$-subspace $V$ of $K^n$ with $\mathbb{C} \subseteq K$, we denote the field of definition of the subspace over $\mathbb{C}$ by $F(D(V))$.

Recall that $V$ has a $K$-basis $e_1, \ldots, e_f$ of $V$ such that $e_1, \ldots, e_f \in F(D(V))$.

Fix $1 \leq i \leq m$. Let $V_{p_i}$ denote the right kernel of $W_{p_i}$. Note that $V_{p_i}$ is defined over $\text{Const}(K)$. Since $p_i(\bar{a}) = 0$, the vector of coefficients of $p_i$ belongs to $V_{p_i}$. Note that $F(V_{p_i}) = F(p_i)$. By the preceding paragraph, there exist $r_{i,1}, \ldots, r_{i,n_i} \in F(V_{p_i})$ such that

- for every $1 \leq j \leq N$, the vector of the coefficients of $r_{i,j}$ belongs to $V_{p_i}$ (in particular, $r_{i,j}(\bar{a}) = 0$);
- $p_i$ is a $K$-linear combination of $r_{i,1}, \ldots, r_{i,n_i}$.

Since $b \in \mathbb{C}(\bar{a})$, there exist differential polynomials $R_1, R_2 \in \mathbb{C}[\bar{a}]$ such that $b = \frac{R_2(\bar{a})}{R_1(\bar{a})}$. We write $H = S_1 \cdot \ldots \cdot S_m \cdot I_1 \cdot \ldots \cdot I_m$, where $I_i$ and $S_i$ are the initial and separant of $p_i$. Since $b \in k$, $bR_2 - R_1 \in (\bar{a})$. Since additionally $bR_2(\bar{a}) - R_1(\bar{a}) = 0$,

$$H(bR_2 - R_1) \in \sqrt{[b]}.$$  

Since, for every $1 \leq i \leq \ell$, $p_i \in [r_{i,1}, \ldots, r_{i,n_i}]$, we have

$$H(bR_2 - R_1) \in \sqrt{[r_{i,1}, \ldots, r_{i,n_i}]}.$$  

(2)

We apply $\alpha$ to (2) and use that $r_{i,j}$'s are invariant under $\alpha$:

$$\alpha(H)(\alpha(b)R_2 - R_1) \in \sqrt{[r_{i,1}, \ldots, r_{i,n_i}]}.$$  

(3)

We multiply (2) by $\alpha(H)$ and (3) by $H$, and subtract. We obtain

$$H\alpha(H)R_2(\alpha(b) - b) \in \sqrt{[r_{i,1}, \ldots, r_{i,n_i}]}.$$  

Every element of $\sqrt{[r_{i,1}, \ldots, r_{i,n_i}]}$ vanishes at $\bar{a}$ since every $r_{i,j}$ vanishes at $\bar{a}$. Since $H(\bar{a}) \neq 0$ and $R_2(\bar{a})(\alpha(b) - b) \neq 0$, it is sufficient to show that $\alpha(H)(\bar{a}) \neq 0$ to arrive at contradiction.

Assume there are $1 \leq i \leq m$ and $h \in \{S_i, I_i\}$ such that $\alpha(h(\bar{a})) = 0$. Consider the sets $M_0$ and $M_1$ of monomials of $h(\bar{a})$ (or, equivalently, of $h(\bar{a})$) and $p_i(\bar{a})$, respectively. Observe that there is a monomial $A$ in $\bar{a}$ with $A M_0 \subset M_1$ because

- if $h = S_i$, take $A$ to be lead $p_i(\bar{a})$;
- if $h = I_i$, take $A$ to be the appropriate power of lead $p_i(\bar{a})$.

As $A M_0 \subset M_1$, we have $F(A M_0) \subset F(p_i)$. Kernels of Wronskians are defined over the constants due to Lemma 13, so the kernel of the Wronskian of a tuple does not change if the tuple is multiplied by a nonzero element. Hence, $F(A M_0) = F(M_0) = F(\bar{a}(h))$, and so $F(\alpha(h)) \subset F(p_i)$. Since $\alpha(h(\bar{a})) = 0$, there are $r_1, \ldots, r_s \in F(\alpha(h)[\bar{a}]) = F(h)[\bar{a}] \subset K[\bar{a}]$ and $A_1, \ldots, A_s \in K$ such that

$$\alpha(h) = A_1 r_1 + \ldots + A_s r_s \quad \text{and} \quad r_1(\bar{a}) = \ldots = r_s(\bar{a}) = 0.$$  

Applying $\alpha^{-1}$, we get

$$h = \alpha^{-1}(A_1) r_1 + \ldots + \alpha^{-1}(A_s) r_s,$$

so $h(\bar{a}) = 0$, which is impossible, hence the contradiction. \qed

**Remark 14.** Similarly to Theorem 21, the statement of Theorem 11 remains true if, in the calculation of $F(\bar{a})$, for each $p_i$, one replaces the Wronskian of the monomials evaluated at $\bar{a}$ by the Wronskian of any $q_1, \ldots, q_n \in \mathbb{C}[\bar{a}]$ evaluated at $\bar{a}$ such that $p = \sum_{i=1}^n c_i q_i$, for some $c_1, \ldots, c_n \in k$. 


3.3. An algorithm for computing all identifiable functions

In this section, we present an algorithm that computes generators of the field of all identifiable functions of system (1). We also give an example following the algorithm step by step.

**Algorithm 1** Computing all identifiable functions

**Input** System $\Sigma$ as in (1)

**Output** Generators of the field of identifiable functions of $\Sigma$

(Step 1) Compute a set $\bar{p}$ of input-output equations of $\Sigma$ (see Definition 8).

(Step 2) For each $p \in \bar{p}$, let $W_p$ be the Wronskian of the monomials of $p$ taken modulo the equations of $\Sigma$ (see [12, proof of Lemma 3.2]).

(Step 3) For each $p \in \bar{p}$, calculate the reduced row echelon form of the matrix $W_p$ and let $F(\bar{p})$ be the field generated over $\mathbb{C}$ by all non-leading coefficients of all matrices $W_p$. By [12, Lemma 3.1] and Remark 12, the generators of $F(\bar{p})$ belong to $\mathbb{C}(\bar{\mu}, \bar{x})$.

(Step 4) Apply Algorithm 2 to find generators of $\mathbb{C}(\bar{\mu}) \cap F(\bar{p})$. Return these generators.

**Remark 15.** In practice, the runtime of the algorithm depends on the chosen ranking, and it would be interesting to have a way to choose the ranking based on the problem.

**Example 16 (Computing identifiable functions).** To illustrate, we will follow Algorithm 1 for the system:

$$
\begin{align*}
\Sigma = \begin{cases} 
    x_1' = 0, \\
    x_2' = x_1 x_2 + ax_1 u + bu, \\
    y = x_2
\end{cases}
\end{align*}
$$

where $\bar{x} = (x_1, x_2), \bar{y} = (y), \bar{\mu} = (a, b), \bar{u} = (u)$. This system is a variant of the example from [25, Section 5].

(Step 1) For the elimination differential ranking with $x_1 > x_2 > y > u$, a calculation shows that

$$
\begin{align*}
x_1 y - ax_1 u - y' - bu,
    x_2 - y, 
    yy'' - auy'' - y'^2 + au'y' - bu'y + bu'y
\end{align*}
$$

is a monic characteristic presentation for $I_\Sigma$. Therefore, $\bar{p} = (p)$, where $p = yy'' - auy'' - y'^2 + au'y' - bu'y + bu'y$.

(Step 2) The Wronskian $\text{Wr}(u'y, uy', u'y', y'^2, au'y', yy'')$ is computed and reduced modulo $\Sigma$ (too large to be displayed here).

(Step 3) A calculation shows that the corresponding reduced row echelon form is:

$$
\begin{pmatrix}
1 & 0 & 0 & 0 & -x_1 & -ax_1 - b \\
0 & 1 & 0 & 0 & x_1 & ax_1 + b \\
0 & 0 & 1 & 0 & 1 & 0 \\
0 & 0 & 0 & 1 & 0 & 1 \\
0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix}
$$

Therefore, $F(\bar{p}) = \mathbb{C}(ax_1 + b, x_1)$.

(Step 4) By Theorem 11, the field of identifiable functions is

$$
\mathbb{C}(a, b) \cap \mathbb{C}(ax_1 + b, x_1).
$$

Applying Algorithm 2, we find that

$$
\mathbb{C}(a, b) \cap \mathbb{C}(ax_1 + b, x_1) = \mathbb{C},
$$
so there are no nontrivial identifiable functions in this model.

4. Multi-experiment identifiability

In this section, we show that the coefficients input-output equations generate the field of multi-experiment identifiable function and derive a generally tight upper bound for the number of independent experiments for system (1) sufficient to recover the field of multi-experiment identifiable functions of parameters. These results are stated and proven in Section 4.1. We apply them to specific examples from the literature in Section 5. The tightness of the bound from the mathematical point of view is discussed in the appendix.

4.1. Main result

Definition 17 (Input-output identifiable functions). A function of parameters $h \in \mathbb{C}(\bar{\mu})$ in system (1) is said to be input-output (IO) identifiable if $h$ can be expressed as a rational function of the coefficients of the IO-equations of system (1) (see Definition 8), see also [26, Definition 2.4 and Corollary 4.12].

As shown in [26, Sections 4.4-4.5], every identifiable function is input-output identifiable but not every input-output identifiable function is necessarily identifiable.

Definition 18 (Multi-experiment identifiability). (cf. [26, Proposition A.3]) A function of parameters $h \in \mathbb{C}(\bar{\mu})$ in system (1) is said to be multi-experiment identifiable (ME-identifiable) if there exists $N \geq 1$ such that $h$ is identifiable in the following "$N$-experiment" system

$$\Sigma_N := \begin{cases} \dot{x}_i = f(x_i, \bar{\mu}, u_i), \\ y_{i1} = g(x_i, \bar{\mu}, u_i), \end{cases} \quad 1 \leq i \leq N. \quad (5)$$

We also say that $h$ is $N$-experiment identifiable in this case.

Example 19 (Illustrating the definition). Consider the system (an intentionally simple example to illustrate the definition)

$$\begin{cases} x'_1 = 0 \\ y_1 = x_1 \\ y_2 = \mu_1 x_1 + \mu_2. \end{cases}$$

As in [12, Example 2.14], neither $\mu_1$, nor $\mu_2$ are identifiable. Consider now the corresponding 2-experiment system

$$\begin{cases} x'_{1,1} = x'_{2,1} = 0 \\ y_{1,1} = x_{1,1} \\ y_{1,2} = \mu_1 x_{1,1} + \mu_2 \\ y_{2,1} = x_{2,1} \\ y_{2,2} = \mu_1 x_{2,1} + \mu_2; \end{cases}$$

now $\mu_1 = \frac{y_{2,2} - y_{1,2}}{y_{2,1} - y_{1,1}}$ and $\mu_2 = \frac{y_{1,1} y_{2,2} - y_{1,2}}{y_{2,1} y_{2,1} - y_{1,1}}$, so are identifiable.

Remark 20. SIAN [11] (see also [27, Remark 2.3]) is software that can check (SE-) global and local identifiability of any given function $h \in \mathbb{C}(\bar{\mu})$ of parameters of an ODE model $\Sigma$. If $h$ is globally ME-identifiable, then, running SIAN on models of the form $\Sigma_N$ (see (5)) for $N = 1, 2, \ldots$, one will in principle eventually find this out. However, if $h$ is not globally ME-identifiable, one will not be able to conclude this from assessing SE-identifiability of $\Sigma_N$ without a bound on the number of experiments (provided by Theorem 21).

On the other hand, one could use SIAN to find the sufficient number of experiments given a set of generators of the field of ME-identifiable functions. Indeed, for each of these generators, there is an $N$ such that the generator is SE-identifiable in $\Sigma_N$, so the sufficient number of experiments can be taken as the maximum of these $N$s. However, this approach works only if generators of the field of ME-identifiable functions are known in advance. Theorem 21 and an algorithm to compute IO-equations (Definition 8) yield an algorithm to find such generators.
Theorem 21 (Multi-experiment identifiability). A function of parameters $h \in \mathbb{C}(\bar{\mu})$ in system (1) is multi-experiment identifiable if and only if it is input-output identifiable in system (1).

Moreover, if $h$ is multi-experiment identifiable, then, for all

$$N \geq \max_{1 \leq i \leq m} (s_i - r_i + 1),$$

$h$ is identifiable in the $N$-experiment system, where $s_i$ and $r_i$ are defined by the following:

- $\bar{p} = p_1, \ldots, p_m$ is a set of input-output equations of system (1), and for all $i, 1 \leq i \leq m$,
  - we write $p_i = f_{i,1} + \sum_{j=1}^{s_i} c_{i,j} f_{i,j}$, where $f_{i,j} \in \mathbb{C}[\bar{y}, \bar{u}]$ and linearly independent over $\mathbb{C}$ (so, $s_i$ is the length of such a presentation of $p_i$ minus 1),
  - $r_i := \text{rank} \text{Wr}(f_{i,1}(\bar{y}, \bar{u}), \ldots, f_{i,s_i}(\bar{y}, \bar{u})) \bmod I_{\Sigma}$.

Remark 22 (Computing the bound). The rank of the Wronskian matrix from Theorem 21 can be found by:

1. Calculating the Wronskian matrix in $\bar{y}, \bar{u}$,
2. For each matrix entry, computing its differential remainder [15, Section I.9] with respect to the characteristic set defined by $\Sigma$, and
3. Applying a (symbolic) algorithm for rank computation.

The correctness follows from [12, Lemma 3.1]. Before computing the rank, one can evaluate the Wronskian at a point. Since the rank cannot increase after an evaluation, the resulting bound will always be correct although might be larger than the bound from Theorem 21.

Remark 23. The bound for $N$ from Theorem 21 can be improved if some of the output variables are constant as discussed in Section 5.3. Constant outputs arise, e.g., to encode the case of constant inputs, which is common in some application domains [36]. The general idea of the refinement is first to treat the constant outputs as parameters, apply Theorem 21 to the rest of the outputs, and then use simultaneous rational interpolation to extract the coefficients with respect to the constant outputs.

Example 24 (Degenerate Wronskian). The goal of this intentionally simple example is to demonstrate that the Wronskians in the theorem can indeed be singular. Consider the system

$$\Sigma = \begin{cases} 
    x_1' = 0, \\
    y_1 = x_1, \\
    y_2 = \theta x_1 + \theta^2,
\end{cases}$$

(6)

in which $\theta$ is the unknown parameter. A calculation shows that

$$\bar{p} = \left\{ y_1', y_2 - \theta y_1 - \theta^2 \right\}$$

is a set of IO-equations for (6). Then $m = 2$, $s_1 = 0$, and $s_2 = 2$. We have

$$\text{Wr}(y_1, 1) = \begin{pmatrix} y_1 & 1 \\ y_1' & 0 \end{pmatrix} \bmod I_{\Sigma} = \begin{pmatrix} x_1 & 1 \\ 0 & 0 \end{pmatrix},$$

and so $r_2 = 1$. From [12, Example 2.14], $\theta$ is not (globally) identifiable (so, we cannot take $N = 1$). By Theorem 21, for all

$$N \geq 2 - 1 + 1 = 2,$$

the field of ME-identifiable functions $\mathbb{C}(\theta, \theta^2) = \mathbb{C}(\theta)$ is $N$-experiment identifiable.

Proof of Theorem 21. For simplicity of notation, we denote the tuple of variables $\bar{y}, \bar{u}$ by $\bar{w}$. Note that, for every $N \geq 1$, the set

$$\bar{p}(\bar{w}_1), \ldots, \bar{p}(\bar{w}_N) \subset k[\bar{w}_1, \ldots, \bar{w}_N]$$
is a set of IO-equations of \( N \). The coefficients of \( \bar{p}(\bar{w}_1), \ldots, \bar{p}(\bar{w}_N) \) are also \( c_{1,1}, \ldots, c_{m,n} \). Hence, as in \cite[Corollary 5.8 and Theorem 4.2]{27}, the field of \( N \)-experiment identifiable functions is contained in \( C(c_{1,1}, \ldots, c_{m,n}) \).

For the reverse inclusion, let \( p \in \bar{p} \),

\[
p = \sum_{i=1}^{s} b_i f_i + f_{s+1},
\]

where, for each \( i, f_i \in C[\bar{w}] \) and \( f_1, \ldots, f_s \) are linearly independent over \( C \). By dividing \( p \) by an element of \( k \), we may assume that \( \deg f_{s+1} = \deg p \). Let

\[
A := \left( \begin{array}{c}
f_1(\bar{a}_1) & \ldots & f_1(\bar{a}_i) \\
n_{\ell} & \ldots & n_{\ell} \\
\vdots & \ddots & \vdots \\
f_i(\bar{a}_1) & \ldots & f_i(\bar{a}_i)
\end{array} \right),
\]

where, for each \( i, \bar{a}_i \) is the image of \( \bar{w}_i \) modulo \( I_{\bar{w}_i} \). We will first show that \( \det A \neq 0 \). For this, let \( M \) be a minimal (by size) zero minor of \( A \). Let, \( f_j(\bar{a}_i) \) appear in \( M \) and \( q \in k[\bar{w}] \) be the differential polynomial obtained from \( M \) by replacing \( f_j(\bar{a}_i) \) with \( f_j(\bar{w}_j) \), \( 1 \leq j \leq s \). By the minimality of \( M \) and linear independence of \( f_1, \ldots, f_s \), \( q(\bar{w}) \neq 0 \). Since \( q(\bar{a}_i) = 0 \), there exist \( q_i, j \in k[\bar{w}_j] \) such that

\[
\forall i, q_{i,1}(\bar{w}) \in I_{\bar{w}_i} \text{ or } \ldots \text{ or } q_{i,s}(\bar{w}) \in I_{\bar{w}_i} \quad \text{and} \quad q = \sum_{i=1}^{s} q_{i,1}(\bar{w}), \ldots, q_{i,s}(\bar{w}).
\]

Hence, there exist \( \alpha \), and \( q_1, \ldots, q_{\alpha}, b_1, \ldots, b_{\alpha} \in k(\bar{a}_1, \ldots, \bar{a}_{\ell-1}, \bar{a}_{\ell+1}, \ldots, \bar{a}_m) \) such that \( q = \sum_{i=1}^{\alpha} b_i q_i \) and, for each \( i \), every monomial that appears in \( q_i \) also appears in \( q \) (and, therefore, in \( p \)). Let \( \bar{q} \) be the primitive part of \( q \). Since \( M \) is prime, \( \bar{q} \notin I_{\bar{w}_i} \). Since \( \bar{p} \) is autoreduced and \( \bar{q} \) divides a linear combination of the monomials of \( p \), the characteristic set \( \bar{p} \) of \( p \setminus \{ \bar{q} \} \) satisfies \( \operatorname{rank} \bar{p} \leq \operatorname{rank} \bar{p} \). Hence, \( \bar{p} \) is a characteristic set of \( J \), and so

\[
\bar{p} = \bar{p} \setminus \{ \bar{q} \} \cup \{ \bar{q} \}.
\]

Thus, \( \bar{p} \) is a characteristic presentation of \( I_{\bar{w}_i} \). If \( \bar{q} \neq \bar{q} \), then \( \deg \bar{q} < \deg \bar{q} \). If \( \bar{q} = \bar{q} \), then \( \bar{q} \) has fewer monomials than \( p \) does. Thus, in either case, \( p/\bar{q} \notin k \). However, \cite[Theorem 3]{4} implies that \( p/\bar{q} \in k \), which is a contradiction. This shows that \( \det A \neq 0 \). Thus, the rows of \( A \) are linearly independent.

Let \( r = \operatorname{rank} \operatorname{Wr}(f_1(\bar{a}_i), \ldots, f_s(\bar{a}_i)) \) and the rows \( i_1 = 0, i_2, \ldots, i_r \) of the Wronskian be linearly independent. Since the rows of \( A \) form a basis of \( C(\bar{a}_1, \ldots, \bar{a}_m)^s \), there exist rows \( j_1, \ldots, j_r \) of \( A \) such that they together with the rows \( i_1, \ldots, i_r \) of the Wronskian form a basis of \( C(\bar{a}_1, \ldots, \bar{a}_m)^s \) as well. Hence,

\[
B := \left( \begin{array}{c}
f_1(\bar{a}_1) & \ldots & f_1(\bar{a}_i) \\
f_i^1(\bar{a}_1) & \ldots & f_i^1(\bar{a}_i) \\
\vdots & \ddots & \vdots \\
f_1(\bar{a}_i) & \ldots & f_1(\bar{a}_{i_r}) \\
\vdots & \ddots & \vdots \\
f_i(\bar{a}_i) & \ldots & f_i(\bar{a}_{i_r})
\end{array} \right)
\]

is invertible. Replacing \( \bar{a}_1, \bar{a}_j, \ldots, \bar{a}_{j_{r+1}} \) in \( \operatorname{det} B \) by the indeterminates \( \bar{w}_1, \ldots, \bar{w}_{j_{r+1}} \), we obtain a differential polynomial with coefficients in \( C \) that does not belong to the vanishing ideal of \( \bar{a}_1, \bar{a}_j, \ldots, \bar{a}_{j_r} \). Since this ideal is the same
as the vanishing ideal of \( \tilde{a}_1, \tilde{a}_2, \ldots, \tilde{a}_{s+r+1} \), we conclude that the matrix

\[
C := \begin{pmatrix}
    f_1(\tilde{a}_1) & \cdots & f_i(\tilde{a}_1) \\
    f_1(\tilde{a}_1) & \cdots & f_i(\tilde{a}_1) \\
    \vdots & \ddots & \vdots \\
    f_i(\tilde{a}_2) & \cdots & f_i(\tilde{a}_2) \\
    \vdots & \ddots & \vdots \\
    f_i(\tilde{a}_{s+r+1}) & \cdots & f_i(\tilde{a}_{s+r+1}) 
\end{pmatrix}
\]

is invertible. Thus,

\[
\begin{pmatrix}
    b_1 \\
    \vdots \\
    b_s 
\end{pmatrix} = C^{-1} \begin{pmatrix}
    f_{r+1}(\tilde{a}_1) \\
    \vdots \\
    f_{r+1}(\tilde{a}_s) \\
    f_{r+1}(\tilde{a}_s) 
\end{pmatrix},
\]

which is in \( \mathbb{C}(\tilde{a}_1, \ldots, \tilde{a}_{s+r+1})^s \) and so is \( (s - r + 1) \)-experiment identifiable. Thus, the field of IO-identifiable functions is \( N \)-experiment identifiable. 

\[ \square \]

5. Examples

We illustrate our results with 3 examples. In Section 5.1, Lotka-Volterra model with control, we show that the SE-identifiable and ME-identifiable functions coincide, so one can find the generators of the field of identifiable functions from the coefficients of the IO-equations. The second example (Section 5.2) is a chemical reaction exhibiting the slow-fast ambiguity [35]. Here, the bound from Theorem 21 is exact, and yields that all parameters are identifiable from 2 experiments. In Section 5.3, we show another Lotka-Volterra model, for which some of the parameters become identifiable only after 2 experiments. For other models with more ME-identifiable functions than SE-identifiable ones, we refer to [36, Section III]. Finally, in Section 5.4, we apply our results to the SEIR epidemiological model studied in [34].

All the computations for the examples in this section can be performed automatically using our implementation. The corresponding files can be found in the examples folder in the repository https://github.com/pogudingleb/AllIdentifiableFunctions.

5.1. Lotka-Volterra model with control

Consider the following system

\[
\Sigma = \begin{cases}
    \dot{x}_1' = ax_1 - bx_1x_2, \\
    \dot{x}_2' = -cx_2 + dx_1x_2 + eu, \\
    y = x_1, 
\end{cases}
\]

in which \( a, b, c, d, e \) are the unknown parameters and \( u \) is the input (control). With Theorem 21, we show that, for this model, the fields of SE-identifiable and of ME-identifiable functions coincide. A computation shows that the IO-equation is:

\[
\tilde{p} = (yy' - y^2 - dy^2y' + cyy' + ady^2 - beuy^2 - acy^2),
\]

so, in the notation of Theorem 21, \( m = 1 \) and, for \( f_1 = y^2y' \), \( f_2 = yy', f_3 = y^3, f_4 = uy^2, f_5 = y^2 \), and \( f_6 = yy'' - y'^2 \), we have \( s_1 = 5 \). A computation shows that

\[
r_1 := \text{rank}(\text{Wr}(f_1, f_2, f_3, f_4, f_5)) \mod I_2 = 5.
\]
By Theorem 21, for any
\[ N \geq 5 - 5 + 1 = 1 \]
the ME-identifiable functions are identifiable from \( N \) experiments (cf. [26, Theorems 1 and 2]). In particular, 1 experiment is sufficient. Hence, by Theorem 21, the field of SE-identifiable functions is \( \mathbb{C}(d, c, ad, be, ac) = \mathbb{C}(a, be, c, d) \).

### 5.2. Slow-fast ambiguity in chemical reactions

In this example, we consider the system [11, Section A.1, equation (3)]. This system originates from the following chemical reaction network [35, equation (1.1)]:

\[ A \xrightarrow{k_1} B \xrightarrow{k_2} C. \]

Then the quantities \( x_A, x_B, \) and \( x_C \) of species satisfy the system:

\[
\begin{align*}
    x'_A &= -k_1 x_A, \\
    x'_B &= k_1 x_A - k_2 x_B, \\
    x'_C &= k_2 x_B.
\end{align*}
\]

The observed quantities will be

- \( y_1 = x_C \), the concentration of \( C \);
- \( y_2 = \varepsilon_A x_A + \varepsilon_B x_B + \varepsilon_C x_C \), which may represent a property of the mixture, e.g. absorbance or conductivity [35, p. 701].

As explained in [35, p. 701], in practice, \( x_B \) might be hard to isolate, so \( \varepsilon_B \) is also an unknown parameter, while the values \( \varepsilon_A \) and \( \varepsilon_C \) can be assumed to be known but could depend on \( A, C \), and the details of the experimental setup. The assumption that \( \varepsilon_A \) and \( \varepsilon_C \) are known can be encoded into the ODE system by making them state variables with zero derivatives and adding outputs to make them observable. This will yield the following final ODE model (the same as [11, Section A.1, equation (3)):

\[
\Sigma = \begin{cases}
    x'_A = -k_1 x_A, \\
    x'_B = k_1 x_A - k_2 x_B, \\
    x'_C = k_2 x_B, \\
    \varepsilon'_A = \varepsilon'_C = 0, \\
    y_1 = x_C, \\
    y_2 = \varepsilon_A x_A + \varepsilon_B x_B + \varepsilon_C x_C, \\
    y_3 = \varepsilon_A, \\
    y_4 = \varepsilon_C,
\end{cases}
\]

where \( \bar{x} = (x_A, x_B, x_C, \varepsilon_A, \varepsilon_C) \), \( \bar{y} = (y_1, y_2, y_3, y_4) \), and \( \bar{\mu} = (k_1, k_2, \varepsilon_B) \). As noted in [35] (see also [11, Section A.1]), this model has slow-fast ambiguity: it is possible to recover a pair of numbers \( \{k_1, k_2\} \) from the observations but impossible to know which one is \( k_1 \) and which one is \( k_2 \). A similar phenomenon occurs in epidemiological models, see [34, Proposition 2].

We start with assessing the SE-identifiability of the model (8) using Algorithm 1 to find the field of identifiable functions. For (Step 1), a calculation in Maple shows that the following set \( \tilde{p} = \{ p_1, p_2, p_3, p_4 \} \) is a set of IO-equations of (8):

\[
p_1 = k_1 k_2 (y_2 - y_1 y_4) - \varepsilon_B k_1 y'_1 y_3 - k_2 y'_1 y_3 - y''_1 y_3, \quad p_2 = y''_1 + (k_1 + k_2) y'_1 + k_1 k_2 y'_1, \quad p_3 = y'_3, \quad p_4 = y'_4.
\]

In (Step 2) and (Step 3), we compute the reduced row echelon forms of \( W_{p_1} = W(y_2, y_1 y_4, y'_1 y_3, y''_1 y_3) \) and \( W_{p_2} = \)
Finally, in experiments with the same respectively. identifiable functions is generated by the coe
the ambiguity can be resolved by one extra experiment. The first part of Theorem 21 implies that the field of ME-
Before going to (Step 4), we show that this intermediate result of computation can provide additional insights, for example, recover the parameter transformation corresponding to the slow-fast ambiguity [35, equation (1.3)]. From the proof of Theorem 11, we have 
\begin{align*}
F(p) &= \mathbb{C}(k_1 + k_2, k_1 k_2, e_A, e_A k_2 + e_B k_1).
\end{align*}
Therefore, 
\begin{align*}
\exists \alpha \in F(p), \text{ with } \alpha(k_1) = k_1, \alpha(k_2) = k_2 \text{ and } \alpha(0) = 0, \text{ the Wronskian does not always have full rank in practical examples either.}
\end{align*}
Finally, in (Step 4), we compute 
\begin{align*}
\mathbb{C}(k_1, k_2, \bar{e}_b) \cap F(p) &= \mathbb{C}(k_1, k_2, k_1 + k_2).
\end{align*}
Now we will consider model (8) in the multi-experiment setup in which one is allowed to perform several experiments with the same \(k_1, k_2, \bar{e}_b\) but different initial concentrations and \(e_A, e_C\). We will show that, in this setup, the ambiguity can be resolved by one extra experiment. The first part of Theorem 21 implies that the field of ME-identifiable functions is generated by the coefficients of \(\bar{p}\) so it equals 
\begin{align*}
\mathbb{C}(k_1, k_2, e_b, k_1, k_2, k_1 + k_2) = \mathbb{C}(k_1, k_2, e_b).
\end{align*}
Therefore, all the parameters can be identified from several experiments. Now we use the bound from Theorem 21 to find the number of experiments sufficient to make all the parameter identifiable. In the notation of the theorem, for \(i = 1\) we take 
\begin{align*}
f_{1,1} &= y_2 - y_1 y_4, \quad f_{1,2} = y'_1, \quad f_{1,3} = y'_1 y_3, \quad f_{1,4} = y''_1 y_3,
\end{align*}
and so \(s_1 = 3\). A calculation in MAPLE shows that 
\begin{align*}
r_1 &= \text{rank } \text{Wr}(f_{1,1}, f_{1,2}, f_{1,3}) \mod I_2 = 2.
\end{align*}
so the Wronskian does not always have full rank in practical examples either. For \(i = 2\), \(f_{2,1} = y''_1, f_{2,2} = y'_1\), so \(s_2 = 2\), and 
\begin{align*}
r_2 &= \text{rank } \text{Wr}(f_{2,1}, f_{2,2}) \mod I_2 = 2.
\end{align*}
Finally, \(f_{3,1} = y'_2\) and \(f_{4,1} = y'_2\), and so \(s_3 = s_4 = 0\). Thus, all parameters are \(N\)-identifiable for all 
\begin{align*}
N &\geq \max(3 - 2 + 1, 2 - 2 + 1, 0 - 0 + 1, 0 - 0 + 1) = 2.
\end{align*}
This bound is tight because, as we demonstrated earlier, neither of the parameter is identifiable from a single experiment.
5.3. Lotka-Volterra model with “mixed” output

In this example, we will illustrate the refinement of the bound on the number of experiments mentioned in Remark 23 on the following variant of the Lotka-Volterra model:

\[
\begin{align*}
\Sigma &= \begin{cases} 
    x'_1 &= ax_1 - x_1 x_2, \\
    x'_2 &= -c x_2 + d x_1, \\
    y &= e x_1 + f x_2,
\end{cases}
\end{align*}
\]

where we assume that \(a, b, c, d, e\) are unknown parameters and \(f\) is a known parameter that takes different values if multiple experiments are conducted. In the context of our differential algebra setup, this can be encoded as follows:

\[
\begin{align*}
\Sigma &= \begin{cases} 
    x'_1 &= ax_1 - bx_1 x_2, \\
    x'_2 &= -c x_2 + d x_1, \\
    f' &= 0, \\
    y_1 &= e x_1 + f x_2, \\
    y_2 &= f
\end{cases}
\end{align*}
\]

Our implementation shows that the field of ME-identifiable functions is

\[
\mathbb{C}(a, b, c, d/e).
\]

In particular, \(a, b, c\) are ME-identifiable, \(d\) and \(e\) are not but their ratio is.

We now discuss the number of experiments for globally identifying the functions (11). A straightforward application of Theorem 21 yields a bound 35 (Wronskian of dimension 51 and rank 17). 35 could be viewed as a rather high number of experiments and is far from the actual number (2, as shown below).

We can get a better bound equal to 4 using the same Theorem 21 as follows. Observe that, since \(y_2\) is constant, then there will be the following input-output equations for the model: \(y'_2 = 0\) and \(p = 0\), where \(p\) is a differential polynomial \(y_1\) and \(y_2\) over \(\mathbb{C}(\mu)\) of zero order in \(y_2\). We observe that, if one replaces \(y_2\) in \(p = 0\) with \(f\), the resulting equations will be the input-output equations for the following simplified model, in which \(f\) is considered as a scalar parameter:

\[
\begin{align*}
\Sigma &= \begin{cases} 
    x'_1 &= ax_1 - bx_1 x_2, \\
    x'_2 &= -c x_2 + d x_1, \\
    y &= e x_1 + f x_2,
\end{cases}
\end{align*}
\]

Our implementation shows that the bound for this model is one, so SE-identifiable and ME-identifiable functions for this model are the same. In particular the coefficients of the monic input-output equation of (12) are identifiable from a single experiment. These coefficients are rational function in \(f\) over \(\mathbb{C}(a, b, c, d, e)\). We write them as \(C_1/C, \ldots, C_s/C\), where \(C, C_1, \ldots, C_s\) are polynomials in \(f\) over \(\mathbb{C}(a, b, c, d, e)\), and \(C\) is monic. We denote the number coefficients not belonging to \(C\) in \(C_1, \ldots, C_s\) by \(n, n_1, \ldots, n_s\), respectively. Then these coefficients can be determined uniquely from evaluations for different values of \(f\). To show this, assume that \(n_1 = \min n_i\). Then \(n + n_1\) evaluations are sufficient to reconstruct coefficients of \(C_1/C\) as a rational function in \(f\). Then, once the coefficients of \(C\) are known, evaluations of \(C_2/C, \ldots, C_s/C\) can be used to find the coefficients of \(C_2, \ldots, C_s\) via polynomial interpolation. In this example, \(n = 2\), \(\min n_i = 2\), and \(\max n_i = 4\), so four evaluations (that is, four experiments with different known values of \(f\) will be enough).

The obtained bound 4 is close to the exact bound 2, which can be obtained using Theorem 21 and SIAN as follows. Using SIAN, we obtain that \(a, b, c, d/e\) are only locally identifiable (from one experiment), so \(N > 1\). Running SIAN for 2 experiments shows that the functions (11) are 2-experiment globally identifiable. Since from Theorem 21 we know that these functions generate all ME-identifiable functions, we conclude that \(N = 2\). Replication of the system makes it substantially more challenging for SIAN, so this approach might be impractical if \(N\) is large, while computing
the bound above may be feasible.

5.4. SEIR epidemiological model

Structural identifiability of the following epidemiological model has been considered in [34, Equation 2.2]

\[
\begin{align*}
S' &= -\beta \frac{SI}{N}, \\
E' &= \beta \frac{SI}{N} - \eta E, \\
I' &= \eta E - \alpha I, \\
R' &= \alpha I,
\end{align*}
\]

(13)

where \( N \) is the total population which is constant and known. The following two setups are considered in [34]:

- **Prevalence observation.** In this case, these is an output \( y_1 = I \). We also add \( y_2 = N \) to account for the fact that \( N \) is known. Our implementation shows that the bound from Theorem 21 is equal to one, so the fields of ME-identifiable and SE-identifiable functions coincide. It also finds that these fields are equal to \( C(\alpha, \beta, \eta, \alpha + \beta, N) \).

- **Cumulative incidence observation.** In this case, the observed quantity is \( \int \eta E \, dt \). This can be encoded by introducing a new state variable \( C \) with \( C' = \eta E \) and the outputs \( y_1 = C \) and \( y_2 = N \). Our algorithm again shows that the fields of ME-identifiable and SE-identifiable functions coincide and that they equal \( C(\alpha, \beta, \eta, N) \), so all of the parameters are globally identifiable.

These results confirm the findings of [34] obtained from analysis of input-output equations (that is, for ME-identifiability) and show that they are valid for SE-identifiability as well.

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References


Appendix A: intersection for rational function fields

In this subsection, we will describe how [3, Algorithm 2.38] can be used to compute the intersection $L_1 \cap L_2$, where $L_1 = C(\mu)$ and $L_2 = F(\bar{\mu})$ as required by Algorithm 1.

Algorithm 2 below is a version of [3, Algorithm 2.38]. It has been shown [3, p. 37-38] that the output of the algorithm is correct it the algorithm terminates. Termination was proved only for the case when both input fields are algebraically closed in the ambient rational function field. For our applications, we relax this condition to requiring only one of the fields to be algebraically closed ($C(\mu)$ in $C(\mu, \bar{x})$ in Proposition 25.

Therefore, being algebraically closed in the prime components $P$.

Since $0$ is a subfield. For $d$ and $K$ as in Proposition 2.37 implies that $I_i$ is algebraically closed in $K$.

We will assume that $K(f)$ is algebraically closed in $K(\bar{x})$. Therefore, since $I_i$ is algebraically closed in $K(\bar{x})$.

The proof for the case of $K(\bar{g})$ implies that $P_i$ is algebraically closed in $K(\bar{x})$ is analogous. Assume that the algorithm does not terminate. By the construction, $I_j \supset J_j$ for every $j \geq 1$. The ideals $I_0$ and $\bar{x}$ are radical (the latter is due to [3, Definition 2.16 and Proposition 2.21]) and since the intersection of a radical ideal with a subring is radical and the extension of a radical ideal is radical). It follows then that all $I_j$’s and $J_j$’s are radical. For every $i \geq 1$, we define $d_i$ to be the minimum of the dimensions of the prime components $P_j$ of $J_i$, such that $P_j \supset I_i$. We will show that the sequence $d_i$ is strictly increasing thus arriving at a contradiction.

Fix $i \geq 1$. Let $P_1, \ldots, P_m$ be the prime components of $J_i$ so that $P_1, \ldots, P_r$ are the components of the dimension $< d_i$ and $P_{r+1}, \ldots, P_m$ are the components of the dimension $\geq d_i$. By the construction, $J_i$ is defined over $K(f)$. [3, Proposition 2.37] implies that $P_1, \ldots, P_m$ are also defined over $K(f)$.

Since $I_j \supset J_j$, and $P_1, \ldots, P_r$ contain $I_j$, $P_1, \ldots, P_r$ are exactly the prime components of $I_j$ of dimension $< d_i$, so $Q := P_1 \cap \cdots \cap P_r$ is the intersection of the equidimensional components of $I_j$ of dimensions $< d_i$. Therefore, since $I_j$ is defined over $K(\bar{g})$, $Q$ is defined over $K(\bar{g})$.

Hence, $Q = \langle Q \cap K(\bar{g}) \rangle \supset I_{r+1}$.

Consider $C := \{ C \mid C$ is a prime component of $\langle P_j \cap K(\bar{g}) \rangle$ for $j > r \}$
Example 27 (Ranking dependency of \( F(p) \) in Theorem 11). We show that the field \( F(p) \) from Theorem 11 can depend on the ranking although \( \mathbb{C}(\mu) \cap F(p) \) cannot. Consider the following input-output equations

\[
p_1 := y_1^2 + y_2^2 + y_3, \quad p_2 := y_2' - 1, \quad p_3 := y_3' - 1.
\]

For the elimination differential ranking \( y_1 > y_2 > y_3, p_1, p_2, p_3 \) is the characteristic presentation of the prime differential ideal \( P := \sqrt{[p_1, p_2, p_3]} \). A calculation in Maple shows that \( F(p_1) = F(p_2) = F(p_3) = \mathbb{C} \), and so \( F(p) = \mathbb{C} \). However, a calculation in Maple shows that \( \bar{q} := [q_1, q_2, q_3] \),

\[
q_1 := 2y_2 + 2y_1y_1' + 1, \quad q_2 := 4y_1^2y_1'^2 + 4y_1y_1' + 4y_1^2 + 4y_3 + 1, \quad q_3 := y_3' - 1,
\]

is the characteristic presentation of \( P \) with respect to the elimination differential ranking \( y_2 > y_1 > y_3 \) and that \( F(q_2) = \mathbb{C}(y_1y_1' + y_3) \) and \( F(q_1) = F(q_3) = \mathbb{C} \), and so \( F(\bar{q}) \supseteq F(p) \).

Example 28 (Achieving the bound in Theorem 21). A natural mathematical question about a bound is whether it is tight in the sense that the equality can be reached for all the values of the parameters appearing in the bound. We will give an indication of the tightness of the bound from Theorem 21 by providing, for every positive integers \( h \leq n \), a model with \( n+1 \) monomials in the IO-equations and the corresponding Wronskian having rank \( h \) so that every element of the field of IO-identifiable functions is \((n - h + 1)\)-identifiable but not necessarily \((n - h)\)-identifiable. Fix \( h \leq n \) and consider the system

\[
\Sigma = \begin{cases}
    x'_i = c_1 + \sum_{i=2}^{n} c_i x_i, & \quad 2 \leq i \leq h \\
    x'^{(h)}_i = 0, & \quad 2 \leq i \leq h \\
    x'_i = 0, & \quad h + 1 \leq i \leq n \\
    y_i = x_i, & \quad 1 \leq i \leq n
\end{cases}
\]

(15)

with unknown parameters \( \{c_i, 1 \leq i \leq n\} \). By a calculation,

\[
\bar{p} = \left\{ y_i' - c_1 - \sum_{i=2}^{n} c_i y_i, x'^{(h)}_i, 2 \leq i \leq h, y_i', h + 1 \leq i \leq n \right\}
\]

\[\text{dim } C \geq d_i \text{ for all } C \in \mathcal{I}_i.\]

For every \( C \subseteq \mathcal{I}_i \), denote \( \tilde{C}_i := \langle C \cap \mathcal{I}_i \rangle \). \[32\] implies that, for every \( j > r \), all prime components of \( \langle P_j \cap \mathcal{J}(\bar{t}) \rangle \) are of the same dimension, so, for all \( C \in \mathcal{I}_i \), \( \text{dim } C \geq d_i \). For every \( C \subseteq \mathcal{I}_i \), denote \( \tilde{C}_i := \langle C \cap \mathcal{I}_i \rangle \). \[3, Proposition 2.37\] implies that \( \tilde{C}_i \) is prime. If \( C \neq \tilde{C}_i \), then \( \text{dim } C > d_i \). Otherwise, \( C = \mathcal{I}_i \). Therefore, due to Lemma 26, we have:

\[
J_{i+1} = \langle I_{i+1} \cap \mathcal{K}(\bar{t}) \rangle = \langle \langle Q \cap \mathcal{K}(\bar{t}) \rangle \cap \bigcap_{C \in \mathcal{I}_i \cap \mathcal{C}} C' \rangle \cap \bigcap_{C \in \mathcal{I}_i \cap \mathcal{C}} C'
\]

Since \( \langle Q \cap \mathcal{K}(\bar{t}) \rangle \supset I_{i+1} \) (see (14)), we have \( A \supset I_{i+1} \). Since every component of \( B \) has dimension at least \( d_i + 1 \), we deduce that \( d_{i+1} > d_i \).
is a set of IO-equations of (15). We have modulo \( I_2 \):

\[
\text{Wr}(y_2, \ldots, y_n, 1) = \begin{pmatrix}
y_2 & \cdots & y_h & y_{h+1} & \cdots & y_n & 1 \\
y_2' & \cdots & y_h' & 0 & \cdots & 0 & 0 \\
\vdots & \ddots & \vdots & \vdots & \ddots & \vdots & \vdots \\
y_2^{(h-1)} & \cdots & y_n^{(h-1)} & 0 & \cdots & 0 & 0 \\
0 & \cdots & 0 & 0 & \cdots & 0 & 0 \\
\vdots & \ddots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & \cdots & 0 & 0 & \cdots & 0 & 0
\end{pmatrix}
\]

whose rank is \( r \). On the one hand \( r_1 \leq h \) because the matrix has only \( h \) non-zero rows. On the other hand, \( \det \text{Wr}(y_2, \ldots, y_h, 1) \neq I_2 \) since \( \text{Wr}(y_2, \ldots, y_h, 1) \) is not reducible (to zero) by \( \bar{p} \). Thus, \( r_1 = h \). Also, \( s_1 = n \) and, for all \( i \geq 2, s_i = 0 \). So, by Theorem 21, for all

\[
N \geq s_1 - r_1 + 1 = n - h + 1,
\]

the field of IO-identifiable functions \( \mathbb{C}(c_1, \ldots, c_n) \) is \( N \)-experiment identifiable. We will show that it is not \((n - h)\)-experiment identifiable, thus showing the desired tightness of the bound in Theorem 21. For this, consider the following set of IO-equations for the \((n - h)\)-experiment system \( \Sigma_{n-h} \):

\[
\bigcup_{j=1}^{n-h} \left\{ y_{i,j} - c_1 - \sum_{i=2}^{n} c_i y_{i,j}, \quad y_{i,j}^{(h)}, \quad 2 \leq i \leq h, \quad y_{i,j}^{(h)}, \quad h + 1 \leq i \leq n \right\}
\]

Let \( a_{ji} \) denote the image of \( y_{ij} \) modulo \( I_{n-h} \). Since, for all \( i \) and \( j, h + 1 \leq i \leq n, 1 \leq j \leq n - h, a_{ji} \) is constant, we can define a differential field automorphism \( \varphi \) of \( \mathbb{C}(\bar{a}_1, \ldots, \bar{a}_{n-h})(c_1, \ldots, c_n) \) over \( \mathbb{C}(\bar{a}_1, \ldots, \bar{a}_{n-h}) \) by

\[
\varphi(c_1, c_2, \ldots, c_h, c_{h+1}, \ldots, c_n) := (c_1 + b_{n-h+1}, c_2, \ldots, c_h, c_{h+1} + b_1, \ldots, c_n + b_{n-h}),
\]

where \( (b_1, \ldots, b_{n-h+1}) \in \mathbb{C}(a_{ji} \mid 1 \leq j \leq n - h, h + 1 \leq i \leq n) \) is a non-zero linear dependence among the columns of the \((n - h) \times (n - h + 1)\) matrix

\[
\begin{pmatrix}
a_{1,h+1} & \cdots & a_{1,n} & 1 \\
\vdots & \ddots & \vdots & \vdots \\
\vdots & \ddots & \vdots & \vdots \\
a_{n-h,h+1} & \cdots & a_{n-h,n} & 1
\end{pmatrix}
\]

Thus, there exists \( i \in \{1, h + 1, \ldots, n\} \) such that \( c_i \notin \mathbb{C}(\bar{a}_1, \ldots, \bar{a}_{n-h}) \), and so the IO-identifiable parameter \( c_i \) is not \((n - h)\)-experiment identifiable.

19