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.

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 [14, 34]). If not all of the parameters of a model are identifiable, the next question usually is what functions \( h(\hat{\mu}) \in \mathbb{C}(\hat{\mu}) \) of the parameters \( \hat{\mu} \) are identifiable. The knowledge of identifiable functions can be used in following 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 [30]).
- Identifiable functions can be used to find an identifiable reparametrization of the model [1, 16, 17].
- 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 [22]; for a concise summary, we refer to [23, Introduction and Algorithm 3.1]). To conclude that the coefficients of an input-output equation are identifiable, one can, for example,
verify if the solvability condition [27, Remark 3] holds for the equation. The condition can be checked by an algorithm (see [7, Section 4.1] and [21, Section 3.4]) and holds for some classes of models [23]. 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 [11, 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 [24, Remark 2.3].

This motivates the following two 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 10.

• We show in Theorem 18 that the coefficients of the input-output equations are generators of the field of functions identifiable from multiple experiments (with generically different inputs and initial conditions), thus answering (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 equation and differential algebra include [2, 9, 12, 18–20, 26, 28, 29].

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 devoted to multi-experimental identifiability. We illustrate our methods on two examples in Section 5.

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 [13, 25].

Notation 1 (Differential rings and ideals).

(a) A differential ring \((R, \delta)\) is a commutative ring with a derivation \(\delta : R \to R\), that is, a map such that, for all \(a, b \in R\), \(\delta(a + b) = \delta(a) + \delta(b)\) and \(\delta(ab) = \delta(a)b + a\delta(b)\).

(b) The ring of differential polynomials in the variables \(z_1, \ldots, z_n\) over a differential field \((K, \delta)\) is the ring \(K[\delta^iz_j \mid i \geq 0, 1 \leq j \leq n]\) with a derivation defined on the ring by \(\delta(\delta^iz_j) := \delta^{i+1}z_j\). 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 differential field \(K\), its field of constants is denoted by \(\text{Const}(K)\).

(e) For a commutative ring \(R\) and a subset \(F \subset R\), the smallest ideal containing \(F\) is denoted by \(\langle F \rangle\).
(f) An ideal \( I \) of a differential ring \( (R, \delta) \) is called a differential ideal if, for all \( a \in I \), \( \delta(a) \in I \). For \( F \subset R \), the smallest differential ideal containing \( F \) is denoted by \([F]\).

(g) For an ideal \( I \) and element \( a \) in a ring \( R \), we denote \( I: a^\infty = \{ r \in R \mid \exists n: a^nr \in I \} \). This set is also an ideal in \( R \).

(h) For a \( a_1, \ldots, a_n \) in a differential ring \( R \), we denote the \( n \times n \) matrix with \((i, j)\)-entry \( a_j^{(i-1)} \) by \( Wr(a_1, \ldots, a_n) \). For example, 

\[
Wr(a_1, a_2) = \begin{pmatrix}
  a_1 & a_2 \\
  a_1' & a_2'
\end{pmatrix}.
\]

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

- for all \( x \in Z \), \( \delta(x) > x \) and
- for all \( x, y \in Z \), if \( x > y \), then \( \delta(x) > \delta(y) \).

**Notation 3.** For \( f \in K[z_1, \ldots, z_n]\setminus K \) and differential ranking \( > \),

- \( \text{lead}(f) \) is the element of \( \{ \delta^i z_j \mid i \geq 0, 1 \leq j \leq n \} \) of the highest rank appearing in \( f \).
- The leading coefficient of \( f \) considered as a polynomial in \( \text{lead}(f) \) is denoted by \( \text{in}(f) \) and called the initial of \( f \).
- The separant of \( f \) is \( \frac{\partial f}{\partial \text{lead}(f)} \).
- The rank of \( f \) is \( \text{rank}(f) = \text{lead}(f)^{\deg_{\text{lead}(f)} f} \). The ranks are compared first with respect to lead, and in the case of equality with respect to deg.
- For \( S \subset K[z_1, \ldots, z_n]\setminus K \), the product of initials and separants of \( S \) is denoted by \( H_S \).

**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 \( \text{lead}(g) \) 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 \( \mathcal{A} \setminus \{ p \} \). One can show that every autoreduced set is finite [13, 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 \( \mathcal{A} < \mathcal{B} \) if
  - \( r > s \) and \( \text{rank}(A_i) = \text{rank}(B_i), 1 \leq i \leq s \), or
  - there exists \( q \) such that \( \text{rank}(A_q) < \text{rank}(B_q) \) and, for all \( i, 1 \leq i < q, \text{rank}(A_i) = \text{rank}(B_i) \).
- 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. [5, Definition 3]) A polynomial is said to be monic if at least one of its coefficients is 1. Note that this is how monic is typically used in identifiability analysis and not how it is used in [5]. 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 systems of the form

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

(1)

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

By bringing $\dot{f}$ and $\dot{g}$ to the common denominator, we can write $\dot{f} = F/Q$ and $\dot{g} = G/Q$, where $F_1, \ldots, F_n, G_1, \ldots, G_m, Q \in \mathbb{C}[\bar{x}, \bar{\mu}, \bar{u}]$. We introduce the (prime, see [11, Lemma 3.2]) differential ideal

$$I_2 := [Qx'_1 - F_1, \ldots, Qx'_n - F_n, Qy_1 - G_1, \ldots, Qy_m - G_m] : Q^\omega.$$

**Definition 6 (Generic solution).** Let $L$ be a differential field containing $\mathbb{C}(\bar{u})$. A tuple $(\bar{x}^*, \bar{y}^*, \bar{u}^*)$ with entries in $L$ is called a generic solution of (1) in $L$ if there exists a differential field homomorphism

$$\varphi : \text{Frac}(\mathbb{C}(\bar{u})[\bar{x}, \bar{y}, \bar{u}] / I_2) \to L, \quad \varphi(\bar{x}, \bar{y}, \bar{u}) := (\bar{x}^*, \bar{y}^*, \bar{u}^*).$$

Rigorously written definitions of identifiability in analytic terms can be found in [23, Definition 2.2] and [11, Definition 2.5]. It follows from [11, Proposition 3.4] that the following is an equivalent definition of identifiability, which we will use.

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

**Definition 8 (Input-output equations).** For a fixed differential ranking $>$ on $(\bar{y}, \bar{u})$, the set of input-output equations of the system $\Sigma$ from (1) is the characteristic presentation of $I_2 \cap \mathbb{C}[\bar{y}, \bar{u}]$.

It can be computed by computing the characteristic presentation $C$ of $I_2$ 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 $C \cap \mathbb{C}[\bar{y}, \bar{u}]$.

3. Single-experiment identifiability

In this section, we give an algorithm to compute all functions of the parameters that can be identified from a single experiment for system (1). We begin with a construction for this in Section 3.1, which is a refinement of considering Wronskians of solutions as in [7, 21, 23]. Using this, we give an algebraic characterization, Theorem 10, of the identifiable functions, which we then turn into Algorithm 1 in Section 3.4. One of the ingredients of our algorithm is [4, Algorithm 2.38], which calculates generators of the intersection of two finitely-generated fields, whose termination in our situation was unknown but we establish it in Section 3.3.

3.1. Preparation for Theorem 10

To modify the approach of finding the identifiable functions from input-output equations, we will begin with a new construction. Let $K$ be a differential field and $k$ a subfield such that $\mathbb{C} \subset k$.

Let $\bar{a} = (a_1, \ldots, a_n) \in K^n$. For a polynomial $p \in k[\bar{z}]$, where $\bar{z} = (z_1, \ldots, z_n)$, such that $p(\bar{a}) = 0$, we construct a subfield $F(p) \subset \text{Const}(K)$ as follows:

1. Consider the Wronskian $W_p$ of the monomials of $p$ evaluated at $\bar{a}$.
2. Define $F(p)$ to be the field generated over $Q$ by (the nonleading) entries in the reduced row echelon form of $W_p$.

For a tuple $\bar{p} \subset k[\bar{z}]$ of differential polynomials,

$$F(\bar{p}) := \mathbb{C}(F(p) \mid p \in \bar{p}).$$

**Lemma 9.** For every $p \in k[\bar{z}]$ such that $p(\bar{a}) = 0$, we have $F(p) \subset \mathbb{C}(\bar{a})$.

**Proof.** Follows from the fact that all the entries of $W_p$ are from $\mathbb{C}(\bar{a})$. \qed

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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 producing our Algorithm 1 to find the field of all identifiable functions.

**Theorem 10** (Single-experiment identifiability). For system (1), the field of identifiable functions is equal to

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

where \( \bar{p} \) is any set of input-output equations of (1) (see Definition 8).

**Proof.** 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 \( \bar{a} \in K^n \),

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

where \( \bar{p} := \{ p_1, \ldots, p_m \} \subset k[z_1, \ldots, z_n] \) is a characteristic set of the prime ideal of all differential polynomials vanishing at \( \bar{a} \). This is then applied to \( k = \mathbb{C}(\bar{a}) \) and the differential field \( K \) generated over \( k \) by the \((\bar{y}, \bar{u})\)-components (denoted by \( \bar{a} \)) of a generic solution of (1).

Lemma 9 implies that

\[ k \cap F(\bar{p}) \subset k \cap \mathbb{C}(\bar{a}). \]

Assume that

\[ k \cap \mathbb{C}(\bar{a}) \supseteq k \cap F(\bar{p}), \]

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

Recall (see, e.g., \[15, Section 2\]) that a differential field \( K \) is said to be 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 \( K_{\text{diff}} \supset k_{\text{al}} \), the algebraic closure of \( k \), and \( k_{\text{al}} \cap K = k \). Since \( b \notin F(\bar{p}) \), there exists an automorphism \( \alpha: \text{Const}(K_{\text{diff}}) \to \text{Const}(K_{\text{diff}}) \) such that \( \alpha|_{F(\bar{p})} = \text{id} \) 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 \( K^n \), we denote the field of definition by \( \text{FD}(V) \). Recall that \( V \) has a \( K \)-basis \( e_1, \ldots, e_\ell \) of \( V \) such that \( e_1, \ldots, e_\ell \in \text{FD}(V)^0 \).

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 \( \text{FD}(V_{p_i}) = \text{FD}(p_i) \). By the preceding paragraph, there exist \( r_{i,1}, \ldots, r_{i,N_i} \in \text{FD}(V_{p_i})(z_1, \ldots., z_n) \) such that

- for every \( 1 \leq j \leq N_i \), 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 \( R_1, R_2 \in \mathbb{C}[z] \) such that \( b = R_2(\bar{a}) \). 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 \( b \in k \), \( bR_2 - R_1 \in k[z] \). Since additionally \( bR_2(\bar{a}) - R_1(\bar{a}) = 0 \), we conclude that

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

Since, for every \( 1 \leq i \leq \ell \), \( p_i \in \{r_{i,1}, \ldots, r_{i,N_i}\} \), we have

\[ H(bR_2 - R_1) \in \sqrt{[r_{i,1}, \ldots, r_{m,N_m}]} \quad (2) \]
We apply $\alpha$ to (2) and use the fact that $r_{i,j}$’s are invariant under $\alpha$:
\[
\alpha(H)(\alpha(b)R_2 - R_1) \in \sqrt{[r_{1,1}, \ldots, r_{m,N_0}]}.
\]
We multiply (2) by $\alpha(H)$ and (3) by $H$, and subtract. We obtain
\[
H\alpha(H)R_2(\alpha(b) - b) \in \sqrt{[r_{1,1}, \ldots, r_{m,N_0}]}.
\]
Since every $r_{i,j}$ vanishes at $\bar{a}$, every element of $\sqrt{[r_{1,1}, \ldots, r_{m,N_0}]}$ 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 that there exists $1 \leq i \leq m$ and $\bar{h} \in [S_i, I_i]$ such that $\alpha(h)(\bar{a}) = 0$. Consider the sets $M_0$ and $M_1$ of monomials of $\alpha(h)(\bar{a})$ (or, equivalently, of $h(\bar{a})$) and $p_i(\bar{a})$, respectively. Observe that there exists a monomial $A$ in $\bar{a}$ such that $AM_0 \subset M_1$ because
- if $h = S_i$, then $A$ can be taken to be lead $p_i(\bar{a})$;
- if $h = I_i$, then $A$ can be taken to be the appropriate power of lead $p_i(\bar{a})$.

Since $AM_0 \subset M_1$, we have $F(AM_0) \subset F(p_i)$. Kernels of Wronskians are defined over the constants, so the kernel of the Wronskian of a tuple does not change if the tuple is multiplied by a nonzero elements. Therefore, $F(AM_0) = F(M_0) = F(\alpha(h))$, and so we have $F(\alpha(h)) \subset F(p_i)$. Since $\alpha(h)(\bar{a}) = 0$, there exist $r_1, \ldots, r_s \in F(\alpha(h))[\bar{z}] = F(h)[\bar{z}] \subset K[\bar{z}]$ and $\lambda_1, \ldots, \lambda_s \in K$ such that
\[
\alpha(h) = \lambda_1 r_1 + \ldots + \lambda_s r_s \quad \text{and} \quad r_i(\bar{a}) = \ldots = r_s(\bar{a}) = 0.
\]
Applying $\alpha^{-1}$, we get
\[
h = \alpha^{-1}(\lambda_1)r_1 + \ldots + \alpha^{-1}(\lambda_s) r_s.
\]
Thus, $h(\bar{a}) = 0$ which is impossible and leads to the desired contradiction. \qed

We now show, in Example 11, that $F(\bar{p})$ from Theorem 10 can depend on the choice of ranking.

**Example 11 (Ranking dependency).** This example shows that the field $F(\bar{p})$ can depend on the ranking although $\mathbb{C}(\bar{p}) \cap F(\bar{p})$ cannot. Therefore, one could speed up the computation by choosing an appropriate ranking, as, for instance, the size of the computed generators could vary. Consider the following input-output equations
\[
p_1 := y_1^2 + y_2^2 + y_3^2, \quad p_2 := y_2^2 - 1, \quad p_3 := y_3^2 - 1.
\]
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 $F(p_1) = F(p_2) = F(p_3) = \mathbb{Q}$, and so $F(\bar{p}) = \mathbb{C}$. However, a calculation in Maple shows that $\bar{q} := [q_1, q_2, q_3]$, where
\[
q_1 := 2y_2 + 2y_1 y_1', \quad q_2 := 4y_1^2 y_1'' + 4y_1 y_1' + 4y_1^2 + 4y_3 + 1, \quad q_3 := y_3' - 1,
\]
is the characteristic presentation of $P$ with respect to the elimination differential ranking $y_2 > y_1 > y_3$ and that $F(q_2) = \mathbb{Q}(y_1 y_1' + y_3)$ and $F(q_3) = F(q_1) = \mathbb{Q}$, and so $F(\bar{q}) \supsetneq F(\bar{p})$.

**3.3. How to compute intersections of fields**

In this subsection, we will describe how [4, Algorithm 2.38] can be used to compute the intersection $L_1 \cap L_2$, where $L_1 = \mathbb{C}(\bar{u})$ and $L_2 = F(\bar{p})$, which are finitely generated, inside the field $L := \mathbb{C}(\bar{x}, \bar{u}, \bar{u}', \ldots, \bar{u}^{(s)})$, where $s$ is so that $L_2 \subset L$ (in the notation of the algorithm, $K(x_1, \ldots, x_s) = L$). We then apply this in our new Algorithm 1 (cf. [23, Algorithm 3.1]), whose correctness is guaranteed in special cases, as shown in [23]).

It is shown in [4] that the algorithm is correct as long as it terminates, and the termination is proven there for $L_1$ and $L_2$ that are both algebraically closed in $L$. In our setup, we are only guaranteed that $L_1$ is algebraically closed in $L$, so there is more to do.
Lemma 12 (Termination). For the termination of [4, Algorithm 2.38], it is sufficient to have one of $L_1$, $L_2$ algebraically closed in $L$.

Proof. Let $L_1$ be algebraically closed in $L$. In what follows, we will use the notation from the algorithm. We will also use that, since scalar extension for polynomial rings is flat, the extension of the intersection of ideals is equal to the extension of the intersection. For $i \geq 1$, let $d_i$ be the smallest of the dimensions of the components of $J_i$ that are not components of $I_i$.

By [4, Proposition 2.42], the ideal $J_1$ is prime, and also $d_1 = \dim J_1$. If $I_2 \neq J_1$, then the algorithm terminates. If $I_2 \subseteq J_1$, By [8, Theorem 2.5] (see also [35, Theorem 6.2.10] and [6, Theorem 1]), all prime components of $I_2$ have the same parametric sets (transcendence bases) and so the same dimension. Hence, we have:

- for every prime component $P$ of $I_2$, $\dim P > \dim J_1$, and so, for every prime component $Q$ of $J_2$, $\dim Q > \dim J_1$, and so $d_2 > d_1$, or

- for every prime component $P$ of $\dim I_2$, $\dim P = \dim J_1$. Then either $J_2 = I_2$, and so the algorithm will terminate, or $I_2 \supseteq J_2$. Applying [4, Proposition 2.37] to each prime component $P$ of $I_2$, we obtain that the image of $P$ under the restriction/extension is a prime ideal contained in $P$. As a result, for every prime component $Q$ of $J_2$ that is not a component of $I_2$, we have $\dim Q > \dim J_1$, thus $d_2 > d_1$.

In any case, we obtain that, either the algorithm has terminated, or $d_2 > d_1$.

Let $m \geq 1$, and assume that the algorithm has reached $J_{m+1}$ and has not terminated. Let $P$ be any prime component of $J_m$. As in the case $m = 1$, the restriction/extension while calculating $J_{m+1}$ applied to $P$ will result in an equi-dimensional (radical) ideal $Q'$. Passing to $J_{m+1}$, either $Q'$ does not change or one of the components transforms into a smaller prime ideal. Therefore, $d_{m+1} > d_m$. Thus, the algorithm will terminate either before or by reaching $J_n$. \hfill $\square$

3.4. An algorithm for computing all identifiable functions

In this section, we will present an algorithm that computes generators of the field of all identifiable functions of system (1). We will 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 [11, proof of Lemma 3.2]). Thus, by [11, Lemma 3.1], the matrix $W_p$ has entries in $\mathbb{C}(\bar{\mu}, \bar{e}(\bar{a}))$.

(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 $W_p$.

(Step 4) Apply [4, Algorithm 2.38] to find generators of $\mathbb{C}(\bar{\mu}) \cap F(\bar{p})$ (see Section 3.3). Return the computed generators.

Remark 13. Similarly to Theorem 18, the statement of Theorem 10 remains true if, in the calculation of $F(\bar{p})$, for each $p$, replaces the Wronskian of the monomials evaluated at $\bar{a}$ by the Wronskian of any $q_1, \ldots, q_n \in \mathbb{C}[z]$ evaluated at $\bar{a}$ such that $p = \sum_{i=1}^{n} c_i q_i$ for some $c_1, \ldots, c_n \in k$.

Example 14 (Computing identifiable functions). We will follow the steps of Algorithm 1 for this system:

\[
\Sigma = \begin{cases} 
  x' = 0, \\
  y_1 = ax + b, \\
  y_2 = x,
\end{cases}
\]
where \( \tilde{x} = (x), \tilde{y} = (y_1, y_2), \) and \( \tilde{\mu} = (a, b). \)

**(Step 1)** For the elimination differential ranking with \( x > y_1 > y_2, \)

\[ x', y_1 - ay_2 - b, y_2' \]

is a monic characteristic presentation for \( I_{\xi}. \) Therefore, \( \tilde{\rho} = (p_1, p_2), \) where \( p_1 = y_1 - ay_2 - b \) and \( p_2 = y_2'. \)

**(Step 2)** We have

\[
W_{p_1} = \begin{pmatrix} 1 & y_1 & y_2 \\ 0 & y_1' & y_2' \\ 0 & 0 & 0 \end{pmatrix} \mod I_{\xi} = \begin{pmatrix} 1 & ax + b & x \\ 0 & 0 & 0 \end{pmatrix}
\]

\[
W_{p_2} = \begin{pmatrix} y_2' \end{pmatrix} \mod I_{\xi} = (0).
\]

**(Step 3)** The corresponding reduced row echelon forms are the same. Therefore, \( F(\tilde{\rho}) = \mathbb{C}(ax + b, x). \)

**(Step 4)** Hence, by Theorem 10, the field of identifiable functions is

\( \mathbb{C}(a, b) \cap \mathbb{C}(ax + b, x). \)

Applying [4, Algorithm 2.38], we find that

\( \mathbb{C}(a, b) \cap \mathbb{C}(ax + b, x) = \mathbb{C}, \)

so there are no nontrivial identifiable functions in this model. For the sake of completeness, we show how to apply [4, Algorithm 2.38] in this case. In the notation of [4, Algorithm 2.38], we have

\[
L_1 = \mathbb{C}(a, b), \quad L_2 = \mathbb{C}(ax + b, x), \quad K = \mathbb{C}
\]

\[
K(x_1, \ldots, x_n) = \mathbb{C}(a, b, ax + b, x) = \mathbb{C}(a, b, x)
\]

\( n = 3, \ x_1 = a, \ x_2 = b, \ x_3 = x. \)

And so \( I_1 = (1) \) and \( J_1 \) is the extension of

\[
(Z_1 - a, Z_2 - b, Z_3 - x) \cap \mathbb{C}(a, b)[Z_1, Z_2, Z_3] = (Z_1 - a, Z_2 - b),
\]

to \( \mathbb{C}(a, b, x)[Z_1, Z_2, Z_3], \) which is also \( (Z_1 - a, Z_2 - b). \) Using [3], we now compute \( J_1 \cap \mathbb{C}(ax + b, x)[Z_1, Z_2, Z_3]. \) For this, we first find

\[
J := (A - a, B - b, X - x) \cap \mathbb{C}(ax + b, x)[A, B, X] = (AX + B - ax - b, X - x),
\]

and we now consider the ideal (which is prime)

\[
I := (Z_1 - A, Z_2 - B, AX + B - ax - b, X - x)
\]

in \( \mathbb{C}(ax + b, x)[Z_1, Z_2, Z_3, A, B, X], \) whose intersection with \( \mathbb{C}(ax + b, x)[A, B, X] \) is \( (X - x, AX - ax + B - b) \subset J, \) and so, by [3, Remark, page 377], we compute the elimination ideal

\[
I_2 := I \cap \mathbb{C}(ax + b, x)[Z_1, Z_2, Z_3] = (Z_1 x + Z_2 - ax - b).
\]

We now compute \( J_2 := I_2 \cap \mathbb{C}(a, b)[Z_1, Z_2, Z_3]. \) For this, we first consider

\[
J' := (A - a, B - b, X - x) \cap \mathbb{C}(a, b)[A, B, X] = (A - a, B - b),
\]

and then consider the ideal, which is prime,

\[
I' := (Z_1 X + Z_2 - AX - B, A - a, B - b)
\]

in \( \mathbb{C}(a, b)[Z_1, Z_2, Z_3, A, B, X], \) whose intersection with \( \mathbb{C}(a, b)[A, B, X] \) is \( (A - a, B - b) \subset J', \) and so, by [3, Remark, page 377], we compute the elimination ideal

\[
J_2 := I' \cap \mathbb{C}(a, b)[Z_1, Z_2, Z_3] = (0),
\]

which implies that \( I_3 = J_3 = (0), \) and so [4, Algorithm 2.38] terminates here, and we conclude that the field of identifiable functions is

\( \mathbb{C}(a, b) \cap \mathbb{C}(ax + b, x) = \mathbb{C}. \)
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 15 (Input-output identifiable functions). A function of parameters $h \in \mathbb{C}(\bar{\mu})$ in system (1) is said to be input-output identifiable if $h$ can be expressed as a rational function of the coefficients of the input-output equations of system (1) (see Definition 8), see also [23, Definition 2.4 and 2.5] and [24, Corollary 5.8].

As shown in [24, Section 4.1], every identifiable function is input-output identifiable but not every input-output identifiable function is necessarily identifiable.

Definition 16 (Multi-experiment identifiability). A function of parameters $h \in \mathbb{C}(\bar{\mu})$ in system (1) is said to be multi-experiment identifiable if there exists $N \geq 1$ such that $h$ is identifiable in the following "$N$-experiment" system

$$\Sigma_N := \begin{cases} \bar{x}_i = f(\bar{x}_i, \bar{\mu}, \bar{u}_i), \\ y_i = g(\bar{x}_i, \bar{\mu}, \bar{u}_i), \end{cases} \quad 1 \leq i \leq N.$$  

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

Example 17 (Illustrating the definition). To give an intentionally simple example just to illustrate the definition, consider the system

$$\begin{align*}
\dot{x}_1 &= 0 \\
y_1 &= x_1 \\
y_2 &= \mu_1 x_1 + \mu_2.
\end{align*}$$

As in [11, Example 2.14], neither $\mu_1$, nor $\mu_2$ are identifiable. Consider now the corresponding 2-experiment system

$$\begin{align*}
\dot{x}_{1,1} &= 0 \\
\dot{x}_{2,1} &= 0 \\
y_{1,1} &= x_{1,1} \\
y_{1,2} &= \mu_1 x_{1,1} + \mu_2 \\
y_{2,1} &= x_{2,1} \\
y_{2,2} &= \mu_1 x_{2,1} + \mu_2,
\end{align*}$$

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

Theorem 18 (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 $\bar{p} = p_1, \ldots, p_m$ is a set of input-output equations of system (1), and for all $i$, $1 \leq i \leq m,$
that the Wronskians in the theorem can indeed be singular. Consider the system

\[ \Sigma = \begin{cases} x'_1 = 0, \\ y_1 = x_1, \\ y_2 = \theta x_1 + \theta^2, \end{cases} \quad (4) \]

in which \( \theta \) is the only unknown parameter. A calculation shows that

\[ p = \begin{bmatrix} y'_1 \\ y_2 - \theta y_1 - \theta^2 \end{bmatrix} \]

is a set of input-output equations for (4). Then \( m = 2, s_1 = 0, \) and \( s_2 = 2 \). We have

\[ \text{Wr}(y_1, 1) = \begin{bmatrix} y_1 & 1 \\ 0 & 0 \end{bmatrix} \mod I_{\mathbb{C}}, \]

and so \( r_2 = 1 \). As noted in [11, Example 2.14], \( \theta \) is not (globally) identifiable (so, we cannot take \( N = 1 \)). By Theorem 18, for all

\[ N \geq 2 - 1 + 1 = 2, \]

the field of multi-experiment identifiable functions

\[ \mathbb{C}(\theta, \theta^2) = \mathbb{C}(\theta) \]

is \( N \)-experiment identifiable.

**Proof.** For simplicity of notation, we will denote the tuple of variables \( \tilde{y}, \tilde{u} \) by \( \tilde{w} \). Note that, for every \( N \geq 1 \), the set

\[ \tilde{p}(\tilde{w}_1), \ldots, \tilde{p}(\tilde{w}_N) \subset k[\tilde{w}_1, \ldots, \tilde{w}_N] \]

is a set of input-output equations of \( \Sigma_{\tilde{w}} \). The coefficients of \( \tilde{p}(\tilde{w}_1), \ldots, \tilde{p}(\tilde{w}_N) \) are also \( c_{1,1}, \ldots, c_{m,s_2} \). Hence, as in [24, Theorem 4.2 and Corollary 5.8], the field of \( N \)-experiment identifiable functions is contained in \( \mathbb{C}(c_{1,1}, \ldots, c_{m,s_2}) \).

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

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

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

\[ A := \begin{bmatrix} f_1(\tilde{a}_1) & \cdots & f_s(\tilde{a}_1) \\ \vdots & \ddots & \vdots \\ f_1(\tilde{a}_s) & \cdots & f_s(\tilde{a}_s) \end{bmatrix}, \]

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

\[ \forall i, q_{i,1}(\tilde{w}) \in I_{\mathbb{C}} \quad \text{or} \quad \forall i, q_{i,\ell}(\tilde{w}) \in I_{\mathbb{C}} \quad \text{and} \quad q = \sum_{i} \prod_{\ell=1}^s q_{i,\ell}(\tilde{a}_i). \]
Hence, there exist \( \alpha \) and \( q_1, \ldots, q_\alpha \in \mathbb{I}_q \) and \( b_1, \ldots, b_\alpha \in \mathbb{k}(\bar{\alpha}_1, \ldots, \bar{\alpha}_{r-1}, \bar{\alpha}_{r+1}, \ldots, \bar{\alpha}_s) \) such that \( q = \sum_{\alpha=1}^{\alpha} b_\alpha q_\alpha \) and, for each \( \alpha \), every monomial that appears in \( q_\alpha \) also appears in \( q \) (and, therefore, in \( p \)). Let \( \bar{\alpha} \) be the primitive part of \( q_1 \) considered as a polynomial in its leader. Since \( \mathbb{I}_q \) is prime, \( \bar{\alpha} \in \mathbb{I}_q \). Since \( \bar{\beta} \) is autoreduced and \( \bar{\alpha} \) divides a linear combination of the monomials of \( p \), the characteristic set \( \bar{\beta} \) of \( \bar{\beta} \setminus \{ p \} \cup \{ \bar{\alpha} \} \) satisfies \( \text{rank } \bar{\beta} \leq \text{rank } \bar{\beta} \). Therefore, \( \bar{\beta} \) is a characteristic set of \( J \), and so

\[
\bar{\beta} = \bar{\beta} \setminus \{ p \} \cup \{ \bar{\alpha} \}.
\]

Thus, \( \bar{\beta} \) is a characteristic presentation of \( \mathbb{I}_q \). If \( \bar{\alpha} \neq q \), then \( \deg \bar{\alpha} < \deg q \). If \( \bar{\alpha} = q \), then \( \bar{\alpha} \) has fewer monomials than \( p \) does. Thus, in either case, \( p/q \notin k \). However, [5, Theorem 3] implies that \( p/q \in k \), which is a contradiction. This shows that \( \text{det } A \neq 0 \). Thus, the rows of \( A \) are linearly independent.

Let \( r = \text{rank Wr}(f_1(\bar{\alpha}), \ldots, f_s(\bar{\alpha})) \) and the rows \( \bar{i}_1 = 0, \bar{i}_2, \ldots, \bar{i}_r \) of the Wronskian be linearly independent. Since the rows of \( A \) form a basis of \( \mathbb{C}(\bar{\alpha}_1, \ldots, \bar{\alpha}_s) \), there exist rows \( j_1, \ldots, j_{\bar{s}-r} \) of \( A \) such that they together with the rows \( \bar{i}_1, \ldots, \bar{i}_r \) of the Wronskian form a basis of \( \mathbb{C}(\bar{\alpha}_1, \ldots, \bar{\alpha}_s) \) as well. Therefore, the matrix

\[
B := \begin{pmatrix}
 f_1(\bar{\alpha}_1) & \cdots & f_s(\bar{\alpha}_1) \\
 f_1^{(2)}(\bar{\alpha}_1) & \cdots & f_s^{(2)}(\bar{\alpha}_1) \\
 \vdots & \ddots & \vdots \\
 f_1^{(i)}(\bar{\alpha}_1) & \cdots & f_s^{(i)}(\bar{\alpha}_1) \\
 f_1(\bar{\alpha}_{j_1}) & \cdots & f_s(\bar{\alpha}_{j_1}) \\
 \vdots & \ddots & \vdots \\
 f_1(\bar{\alpha}_{j_{\bar{s}-r+1}}) & \cdots & f_s(\bar{\alpha}_{j_{\bar{s}-r+1}})
\end{pmatrix}
\]

is invertible. Replacing \( \bar{\alpha}_1, \bar{\alpha}_{j_1}, \ldots, \bar{\alpha}_{j_{\bar{s}-r+1}} \) in \( \text{det } B \) by the indeterminates \( \bar{w}_1, \ldots, \bar{w}_{s-r+1} \), we obtain a differential polynomial with coefficients in \( \mathbb{C} \) that does not belong to the vanishing ideal of \( \bar{\alpha}_1, \bar{\alpha}_{j_1}, \ldots, \bar{\alpha}_{j_{\bar{s}-r+1}} \). Since this ideal is the same as the vanishing ideal of \( \bar{\alpha}_1, \bar{\alpha}_{j_1}, \ldots, \bar{\alpha}_{j_{\bar{s}-r+1}} \), we conclude that the matrix

\[
C := \begin{pmatrix}
 f_1(\bar{\alpha}_1) & \cdots & f_s(\bar{\alpha}_1) \\
 f_1^{(2)}(\bar{\alpha}_1) & \cdots & f_s^{(2)}(\bar{\alpha}_1) \\
 \vdots & \ddots & \vdots \\
 f_1^{(i)}(\bar{\alpha}_1) & \cdots & f_s^{(i)}(\bar{\alpha}_1) \\
 f_1(\bar{\alpha}_{j_1}) & \cdots & f_s(\bar{\alpha}_{j_1}) \\
 \vdots & \ddots & \vdots \\
 f_1(\bar{\alpha}_{j_{\bar{s}-r+1}}) & \cdots & f_s(\bar{\alpha}_{j_{\bar{s}-r+1}})
\end{pmatrix}
\]

is invertible. Thus,

\[
\begin{pmatrix}
 b_1 \\
 \vdots \\
 b_s
\end{pmatrix} = C^{-1} \begin{pmatrix}
 f_{i_1}(\bar{\alpha}_1) \\
 f_{i_1}^{(2)}(\bar{\alpha}_1) \\
 \vdots \\
 f_{i_1}^{(i)}(\bar{\alpha}_1) \\
 f_{i_1}(\bar{\alpha}_{j_1}) \\
 \vdots \\
 f_{i_1}(\bar{\alpha}_{j_{\bar{s}-r+1}})
\end{pmatrix},
\]

which is in \( \mathbb{C}(\bar{\alpha}_1, \ldots, \bar{\alpha}_{s-r+1}) \) and so is \((s-r+1)\)-experiment identifiable. Thus, the field of input-output identifiable functions is \( N \)-experiment identifiable.

\textbf{Remark 20.} Note that [23, Theorems 1 and 2] provide sufficient conditions for classes of systems to have a non-degenerate Wronskian constructed as in the statement of Theorem 18, so \( r_1 = s_1 \), therefore, Theorem 18 holds for all \( N \geq 1 = s_1 - s_1 + 1 \) for such systems.
Remark 21. The rank of the Wronskian matrix from the statement of Theorem 18 can be found by:

1. Calculating the Wronskian matrix in \( \bar{y}, \bar{u} \),
2. For each matrix entry, computing its differential remainder [13, Section I.9] with respect to the characteristic set defined by \( \Sigma \), and
3. Applying any particular (symbolic) algorithm performing rank computation.

The correctness follows from [11, Lemma 3.1].

5. Examples

In this section, we illustrate our results on two examples. For the first example (Section 5.1), two compartment model, we show that the single-experiment and multi-experiment functions coincide, so one can find the generators of the field of identifiable functions from coefficients of the input-output equations. The second example (Section 5.2) is a chemical reaction exhibiting the slow-fast ambiguity [32]. In this example, the bound from Theorem 18 is exact, and yields that all the parameters are identifiable from two experiments. For other models in which there are more multi-experiment identifiable functions than single-experiment ones, we refer to [33, Section III].

5.1. A two-compartment model

Consider the following system

\[
\begin{align*}
\dot{x}_1 &= -(a_{01} + a_{21})x_1 + a_{12}x_2, \\
\dot{x}_2 &= a_{21}x_1 - a_{12}x_2, \\
y &= x_2,
\end{align*}
\]

in which \( a_{01}, a_{21}, a_{12} \) are the unknown parameters. Using Theorem 18, we will show that, for this model, the functions identifiable from a single experiment and the functions identifiable from multiple experiments coincide. A computation shows that the input-output equation is:

\[
\bar{p} = \{y'' + (a_{01} + a_{12} + a_{21})y' + a_{01}a_{12}y\},
\]

so, in the notation of Theorem 18, \( m = 1 \) and, for \( f_1 = y' \) and \( f_2 = y \), we have \( s_1 = 2 \). We have

\[
\text{Wr}(\bar{y}', \bar{y}) = \left( \begin{array}{c} y' \\ y'' \\ \bar{y} \end{array} \right) = \left( \begin{array}{c} y' \\ -(a_{01} + a_{12} + a_{21})y' - a_{01}a_{12}y \\ \bar{y} \end{array} \right) \mod I_\Sigma,
\]

which has a non-zero determinant because \( I_\Sigma \) does not contain first-order differential equations over \( k \) (as \( \text{ord} p = 2 \)). Therefore, \( r_1 = 2 \). By Theorem 18, for any

\[
N \geq 2 - 2 + 1 = 1
\]

the multi-experiment functions are identifiable from \( N \) experiments (cf. [23, Theorems 1 and 2]). In particular, one experiment is sufficient. Therefore, we can use Theorem 18 to compute the field of functions identifiable from a single experiment, and it is:

\[\mathbb{C}(a_{01} + a_{12} + a_{21}, a_{01}a_{12})\].
5.2. Slow-fast ambiguity in chemical reactions

In this example, we consider the system [10, Section A.1, equation (3)]. This system originates from the following chemical reaction network with three species [32, equation (1.1)]:

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

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

\[
\begin{aligned}
\dot{x}_A &= -k_1 x_A, \\
\dot{x}_B &= k_1 x_A - k_2 x_B, \\
\dot{x}_C &= k_2 x_B.
\end{aligned}
\] (7)

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 some property of the mixture, e.g. absorbance or conductivity, see [32, p. 701].

As explained in [32, 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 [10, Section A.1, equation (3)]):

\[
\begin{aligned}
\dot{x}_A &= -k_1 x_A, \\
\dot{x}_B &= k_1 x_A - k_2 x_B, \\
\dot{x}_C &= k_2 x_B, \\
\dot{\varepsilon}_A &= 0, \\
\dot{\varepsilon}_C &= 0, \\
y_1 &= x_C, \\
y_2 &= \varepsilon_A x_A + \varepsilon_B x_B + \varepsilon_C x_C, \\
y_3 &= \varepsilon_A, \\
y_4 &= \varepsilon_C,
\end{aligned}
\] (8)

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 has been noted in [32] (see also [10, Section A.1]), this model exhibits slow-fast ambiguity, that is, 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 [31, Proposition 2].

We start with assessing the single-experimental 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 \( \bar{\mu} = \{p_1, p_2, p_3, p_4\} \) is a set of input-output equations of (8):

\[
\begin{align*}
p_1 &= k_1 k_2 (y_2 - y_1 y_4) - \varepsilon_B k_1 y'_1 - k_2 y'_3 y_3 - y''_4 y_3, \\
p_2 &= y''_1 + (k_1 + k_2) y''_4 + k_1 k_2 y'_4, \\
p_3 &= y''_3, \\
p_4 &= y'_4.
\end{align*}
\]

In (Step 2) and (Step 3), we compute the reduced row echelon forms of \( W_{p_1} = \text{Wr}(y_2, y_1 y_4, y'_1, y'_3 y_3, y''_4 y_3) \) and \( W_{p_2} = \text{Wr}(y''_1, y''_4) \) modulo the equations \( \Sigma \) and obtain the matrices

\[
\begin{pmatrix}
1 & 0 & 0 & 0 & k_1 k_2 \\
0 & 1 & 0 & 0 & -k_1 k_2 \\
0 & 0 & 1 & \varepsilon_A & -(\varepsilon_A k_2 + \varepsilon_B k_1) \\
0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0
\end{pmatrix}
\quad \text{and} \quad
\begin{pmatrix}
1 & 0 & -k_1 k_2 \\
0 & 1 & -k_1 k_2 \\
0 & 0 & 0 \\
0 & 0 & 0
\end{pmatrix}.
\]
respectively. $W_{p_1}$ and $W_{p_2}$ are $1 \times 1$ matrices with the reduced row echelon form (1). Therefore, $F(\bar{p}) = \mathbb{C}(k_1 + k_2, k_1 k_2, e_{A}, e_A k_2 + e_B k_1)$.

Before going to (Step 4), we will show that this intermediate result of computation can also provide additional insights, for example, recover the parameter transformation corresponding to the slow-fast ambiguity [32, equation (1.3)]. From the proof of Theorem 10, we know that $F(\bar{p})$ consists of identifiable constants. Therefore, any parameter transformation will induce an automorphism $\alpha$ of the constants over $F(\bar{p})$. Since, $k_1 + k_2$ and $k_1 k_2$ are identifiable, $\alpha(k_1) = k_1$ and $\alpha(k_2) = k_2$ or $\alpha(k_1) = k_2$ and $\alpha(k_2) = k_1$. Consider the latter case. Since $e_A \in F(\bar{p})$, we have $\alpha(e_A) = e_A$. Therefore,

$$e_A k_2 + e_B k_1 = \alpha(e_A) k_2 + \alpha(e_B) k_1 = e_A k_1 + k_2 \alpha(e_B),$$

so we have $\alpha(e_B) = e_A + \frac{k_1 (e_B - e_A)}{k_2}$. This gives us the transformation [32, equation (1.3)]:

$$k_1 \rightarrow k_2, k_2 \rightarrow k_1, e_A \rightarrow e_A, e_B \rightarrow e_A + \frac{k_1 (e_B - e_A)}{k_2}. \quad (9)$$

Finally, in (Step 4), we compute

$$\mathbb{C}(k_1, k_2, e_B) \cap F(\bar{p}) = \mathbb{C}(k_1 k_2, k_1 + k_2).$$

This computation could be performed without human intervention using the algorithm from Section 3.3. Alternatively, one can observe that $F(\bar{p}) \subset \mathbb{C}(k_1, k_2, e_A, e_B)$ is a degree-two field extension, so $F(\bar{p})$ are exactly the functions fixed by the transformation (9). Hence, the intersection $\mathbb{C}(k_1, k_2, e_B) \cap F(\bar{p})$ will consist of the functions in $\mathbb{C}(k_1, k_2, e_B)$ invariant under this transformation. Since the image of $e_B$ depends on $e_A$, the intersection belongs to $\mathbb{C}(k_1, k_2)$. Therefore, it consists of all symmetric functions in $f_1, k_2$, that is, $\mathbb{C}(k_1 k_2, k_1 + k_2)$. Thus, we conclude that the field of single-experiment identifiable functions is generated by $k_1 k_2$ and $k_1 + k_2$. This confirms that an unordered pair of numbers $\{k_1, k_2\}$ can be identified while the values $k_1$ and $k_2$ cannot.

Now we will consider model (8) in the context of multi-experiment setup in which one is allowed to perform several experiments with the same $k_1, k_2, e_B$ 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 18 implies that the field of multi-experiment identifiable functions is generated by the coefficients of $\bar{p}$, so it is equal to

$$\mathbb{C}(k_1, k_2, e_B k_1, k_2, k_1 + k_2) = \mathbb{C}(k_1, k_2, e_B).$$

Therefore, all the parameters can be identified from several experiments. Now we will use the bound from Theorem 18 to find the number of experiments sufficient to make all the parameter identifiable. In the notation of the theorem, for $i = 1$, we can take

$$f_{1.1} = y_2 - y_1 y_4, \quad f_{1.2} = y'_1, \quad f_{1.3} = y'_3 y_3, \quad f_{1.4} = y''_1 y_3,$$

and so $s_1 = 3$. A calculation in Maple shows that

$$n_1 = \text{rank } \text{Wr}(f_{1.1}, f_{1.2}, f_{1.3}) \mod I_2$$

$$= \text{rank } \begin{pmatrix} y_2 - y_1 y_4 & y'_1 & y'_3 \\ y''_2 - (y_1 y_4)' & y''_1 & (y'_1 y_3)' \\ y''_2 - (y_1 y_4)'' & y''_1 & (y''_1 y_3)'' \end{pmatrix} \mod I_2$$

$$= \text{rank } \begin{pmatrix} y_2 - y_1 y_4 & y'_1 & y'_3 \\ y''_2 - y'_1 y_4 & y''_1 & y''_3 \\ y''_2 - y''_1 y_4 & y''_1 & y''_3 \end{pmatrix} \mod I_2$$

$$= \text{rank } \begin{pmatrix} y_2 - y_1 y_4 & y'_1 & 0 \\ y''_2 - y'_1 y_4 & y''_1 & 0 \\ y''_2 - y''_1 y_4 & y''_1 & 0 \end{pmatrix} \mod I_2 = 2,$$
so the Wronskian does not always have full rank in practical examples either. For $i = 2$,

$$f_{2,1} = y_1^{(r)}, \quad f_{2,2} = y_1'$$

so $s_2 = 2$, and we have

$$r_2 = \text{rank} \, \text{Wr}(f_{2,1}, f_{2,2}) \mod I_2$$

$$= \text{rank} \begin{pmatrix} y_1^{(r)} \\ y_1^{(r-1)} \end{pmatrix} \mod I_2$$

$$= \text{rank} \begin{pmatrix} y_1^{(r)} \\ -(k_1 + k_2)y_1^{(r-1)} - k_1k_2y_1' \end{pmatrix} \mod I_2,$$

which is equal to 2. Finally, $f_{3,1} = y_3'$ and $f_{4,1} = y_4'$, and so $s_3 = s_4 = 0$. Summarizing, the all the parameters are $N$-identifiable for all

$$N \geq \max(3 - 2 + 1, 2 - 2 + 1, 0 - 0 + 1, 0 - 0 + 1) = 2.$$

This bound turns out to be tight because, as we demonstrated earlier, neither of the parameter is identifiable from a single experiment.

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References

Appendix: Mathematical discussion of the bound from Theorem 18

A natural mathematical question about a bound is whether it is tight or not 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 18 by providing, for every positive integers $h \leq n$, a model with $n + 1$ monomials in the input-output equations and the corresponding Wronskian having rank $h$ so that every element of the field of input-output identifiable functions is $(n - h + 1)$-identifiable but not necessarily $(n - h)$-identifiable.

Fix $h \leq n$ and consider the system

$$
\Sigma = \begin{cases}
x'_1 = c_1 + \sum_{i=2}^{n} c_ix_i, \\
x_i^{(h)} = 0, & 2 \leq i \leq h \\
x'_i = 0, & h + 1 \leq i \leq n \\
y_i = x_i, & 1 \leq i \leq n
\end{cases}
$$

(10)
with unknown parameters \( \{c_i, 1 \leq i \leq n\} \). A calculation shows that

\[
\bar{p} = \left[ y'_1 - c_1 - \sum_{i=2}^{n} c_i y_i, \ y^{(h)}_j, \ 2 \leq i \leq h, \ y'_j, \ h + 1 \leq i \leq n \right]
\]

is a set of input-output equations of (10). We have modulo \( I_c \):

\[
\begin{pmatrix}
y_2 & \ldots & y_h & y_{h+1} & \ldots & y_n & 1 \\
y'_2 & \ldots & y'_h & 0 & \ldots & 0 & 0 \\
\vdots & \ddots & \vdots & \vdots & \ddots & \vdots & \vdots \\
y^{(h-1)}_2 & \ldots & y^{(h-1)}_h & 0 & \ldots & 0 & 0 \\
0 & \ldots & 0 & 0 & \ldots & 0 & 0 \\
\vdots & \ddots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & \ldots & 0 & 0 & \ldots & 0 & 0
\end{pmatrix}
\]

whose rank is \( r_1 \). On the one hand \( r_1 \leq h \) because the matrix has only \( h \) non-zero rows. On the other hand, \( \text{det} \mathbf{W}(y_2, \ldots, y_n, 1) \notin I_c \) since \( \mathbf{W}(y_2, \ldots, y_n, 1) \) 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 18, for all

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

the field of input-output 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 18. For this, consider the following set of input-output equations for the \( (n - h) \)-experiment system \( \Sigma_{n-h} \):

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

Let \( a_{i,j} \) denote the image of \( y_{i,j} \) modulo \( I_{n-h} \). Since, for all \( i \) and \( j \), \( h + 1 \leq i \leq n, \ 1 \leq j \leq n - h \), \( a_{i,j} \) 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 \( (b_1, \ldots, b_{n-h+1}) \in \mathbb{C}(a_{i,j} \mid 1 \leq j \leq n-h, \ h+1 \leq i \leq n) \) is a non-zero linear dependence among the columns of the \((n-h) \times (n-h+1)\) matrix

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

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 input-output identifiable parameter \( c_i \) is not \( (n - h) \)-experiment identifiable.