Parameter identifiability and input-output equations

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Abstract

Structural parameter identifiability is a property of a differential model with parameters that allows for the parameters to be determined from the model equations in the absence of noise. One of the standard approaches to assessing this problem is via input-output equations and, in particular, characteristic sets of differential ideals. The precise relation between identifiability and input-output identifiability is subtle. The goal of this note is to clarify this relation. The main results are:

- identifiability implies input-output identifiability;
- these notions coincide if the model does not have rational first integrals;
- the field of input-output identifiable functions is generated by the coefficients of a "minimal" characteristic set of the corresponding differential ideal.

We expect that some of these facts may be known to the experts in the area, but we are not aware of any articles in which these facts are stated precisely and rigorously proved.

1 Introduction

Structural identifiability is a property of an ODE model with parameters that allows for the parameters to be uniquely determined from the model equations in the absence of noise. Performing identifiablity analysis is an important first step in evaluating and, if needed, adjusting the model before a reliable practical parameter identification (determining the numerical values of the parameters) is performed. Details on different approaches to assessing identifiability can be found, for example, in [5, 11, 35], which also contain additional references showing practical relevance of studying structural identifiabilty in biological models, from animal sciences to oncology.

In more detail but still roughly speaking, a function of parameters in an ODE model is identifiable if, generically, two different values of the function result in two different values of the output of the model. A preciese formulation of this concept is given in Definition 2.2. These functions of parameters could be just the parameters themselves, in which case we consider the more standard notion of identifiability of individual parameters. However, it could happen that all of the parameters are not identifiable but some non-trivial functions of the parameters are. Since identifiability is a desirable property to have, finding identifiable functions of non-identifiable parameters could be helpful in reparametrizing the model so that the new model has fewer non-identifiable parameters (see an intentionally simple Example 2.6 to illustrate this issue).

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Input-output equations have been used to assess structural identifiability for three decades already going back to [25], and several prominent software packages are based on this approach [1, 31, 20, 8, 2, 3, 30, 32, 19, 13, 21]. However, it has been known that input-output identifiability is not always the same as identifiability ([11, Example 2.16], [26, Section 5.2 and 5.3]). The goal of this note is to state and prove basic facts about these relations, some of which seem to be implicitly assumed in the current literature. The main results are

- identifiability implies input-output identifiability (Theorem 4.2);

- these notions coincide if the model does not have rational first integrals (Theorem 4.7);

- the field of input-output identifiable functions is generated by the coefficients of a "minimal" characteristic set of the corresponding differential ideal (Corollary 5.7).

The paper is organized as follows. We begin by stating an analytic definition of identifiabily and algebraic definition of input-output identifiability and show a few simple examples comparing these two not equivalent notions in Section 2. In Section 3, we prove a technical result, an algebraic criterion for identifiability of functions in terms of field extensions, which is typically much easier to use than the analytic Definition 2.2. In Section 4, we establish theoretical connections between identifiability and input-output identifiability. We finish with Section 5, in which we prove that input-output identifiability can be computed with characteristic sets from differential algebra, introducing the corresponding mathematical background and notation there.

2 General definition of identifiability

2.1 Identifiability

Fix positive integers λ, n, m, and κ for the remainder of the paper. Let $\boldsymbol{\mu} = (\mu_1, \ldots, \mu_\lambda)$, $\mathbf{x} = (x_1, \ldots, x_n)$, $\mathbf{y} = (y_1, \ldots, y_m)$, and $\mathbf{u} = (u_1, \ldots, u_\kappa)$. These are called the parameters, the state variables, the outputs, and the inputs, respectively. Consider a system of ODEs

$$\Sigma = \begin{cases} \mathbf{x}' = \dfrac{\mathbf{f}(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u})}{Q(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u})}, \\ \mathbf{y} = \dfrac{\mathbf{g}(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u})}{Q(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u})}, \\ \mathbf{x}(0) = \mathbf{x}^*, \end{cases} \tag{1}$$

where $\mathbf{f} = (f_1, \ldots, f_n)$ and $\mathbf{g} = (g_1, \ldots, g_m)$ are tuples of elements of $\mathbb{C}[\boldsymbol{\mu}, \mathbf{x}, \mathbf{u}]$ and $Q \in \mathbb{C}[\boldsymbol{\mu}, \mathbf{x}, \mathbf{u}] \setminus \{0\}$.

Notation 2.1 (Auxiliary analytic notation)**.**

(a) Let $\mathbb{C}^\infty(0)$ denote the set of all functions that are complex analytic in some neighborhood of $t = 0$.

(b) A subset $U \subset \mathbb{C}^\infty(0)$ is called *Zariski open* if there exist $h \in \mathbb{Z}_{\geqslant 0}$ and a non-zero polynomial $P(u_0, u_1, \ldots, u_h) \in \mathbb{C}[u_0, \ldots, u_h]$ such that

$$U = \left\{ \hat{u} \in \mathbb{C}^\infty(0) \mid P\big(\hat{u}, \hat{u}^{(1)}, \ldots, \hat{u}^{(h)}\big)\big|_{t=0} \neq 0 \right\}.$$

(c) Let $\tau(\mathbb{C}^s)$ denote the set of all Zariski open non-empty subsets of $\mathbb{C}^s$ and $\tau(\mathbb{C}^\infty(0))$ denote the set of all Zariski open non-empty subsets of $\mathbb{C}^\infty(0)$.

(d) Let $\Omega = \{(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in \mathbb{C}^n \times \mathbb{C}^\lambda \times (\mathbb{C}^\infty(0))^\kappa \mid Q(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}(0)) \neq 0\}$ and

$$\Omega_h = \Omega \cap (\{(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}) \in \mathbb{C}^{n+\lambda} \mid h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}) \text{ well-defined}\} \times (\mathbb{C}^\infty(0))^\kappa)$$

for every given $h \in \mathbb{C}(\mathbf{x}^*, \boldsymbol{\mu})$.

(e) For $(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in \Omega$, let $X(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})$ and $Y(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})$ denote the unique solution over $\mathbb{C}^\infty(0)$ of the instance of Σ with $\mathbf{x}^* = \hat{\mathbf{x}}^*$, $\boldsymbol{\mu} = \hat{\boldsymbol{\mu}}$, and $\mathbf{u} = \hat{\mathbf{u}}$ (see [9, Theorem 2.2.2]).

Definition 2.2 given below, being a generalization from individual parameters to functions of parameters, is a precise (and unambiguous) way of expressing the following widely used analytic understanding of the identifiability concept: a parameter in (1) is identifiable if generically two different parameter values result in two different values of the output [7, 36, 37, 33, 34, 16, 38, 39, 17, 3, 31, 23]. A discussion on the comparison can be found in [11, Remark 2.6]. The complexity of the presentation of Definition 2.2 is the price to pay for being precise.

Definition 2.2 (Identifiability, see [11, Definition 2.5]). We say that $h(\mathbf{x}^*, \boldsymbol{\mu}) \in \mathbb{C}(\mathbf{x}^*, \boldsymbol{\mu})$ is *identifiable* if

$$\exists \Theta \in \tau(\mathbb{C}^n \times \mathbb{C}^\lambda) \; \exists U \in \tau((\mathbb{C}^\infty(0))^\kappa)$$
$$\forall (\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in (\Theta \times U) \cap \Omega_h \quad |S_h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})| = 1,$$

where
$$S_h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) := \{h(\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}) \mid (\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in \Omega_h \text{ and } Y(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) = Y(\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}})\}.$$

In this paper, we are interested in comparing identifiability and IO-identifiability (Definition 2.5), and the latter is defined for functions in $\boldsymbol{\mu}$, not in $\boldsymbol{\mu}$ and $\mathbf{x}^*$. Thus, just for the purpose of comparison, we will restrict ourselves to the field

$$\{h \in \mathbb{C}(\boldsymbol{\mu}) \mid h \text{ is identifiable}\},$$

which we will call *the field of identifiable functions*.

Remark 2.3. The above definition can be extended to functions $h(\mathbf{x}^*, \boldsymbol{\mu}) \in \mathbb{C}(\mathbf{x}^*, \boldsymbol{\mu})$ (see Definition 2.2). There are software tools that can assess identifiability of initial conditions (e.g., SIAN [10]). Any such tool can be used to assess identifiability of a given function $h(\mathbf{x}^*, \boldsymbol{\mu}) \in \mathbb{C}(\mathbf{x}^*, \boldsymbol{\mu})$ by means of the transformation described in (2) in the proof of Proposition 3.1.

2.2 IO-identifiability

Notation 2.4 (Differential algebra). (a) A *differential ring* (R, δ) is a commutative ring with a derivation $': R \to R$, that is, a map such that, for all $a, b \in R$, $(a+b)' = a' + b'$ and $(ab)' = a'b + ab'$.

(b) The *ring of differential polynomials* in the variables $x_1, \ldots, x_n$ over a field K is the ring $K[x_j^{(i)} \mid i \geqslant 0, 1 \leqslant j \leqslant n]$ with a derivation defined on the ring by $(x_j^{(i)})' := x_j^{(i+1)}$. This differential ring is denoted by $K\{x_1, \ldots, x_n\}$.

(c) An ideal I of a differential ring (R, δ) is called a *differential ideal* if, for all $a \in I$, $\delta(a) \in I$. For $F \subset R$, the smallest differential ideal containing set F is denoted by $[F]$.

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

(e) Given Σ as in (1), we define the differential ideal of Σ as $I_\Sigma = [Q\mathbf{x}' - \mathbf{f}, Q\mathbf{y} - \mathbf{g}] : Q^\infty \subset \mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}$.

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The following definition of IO-identifiability captures the most probable, in our opinion, actual intent of prior attempts of defining and computing it via a characteristic set of the prime differential ideal of I_Σ [19, 3, 32, 30].

For a subclass of models, called linear compartment models, for each output variable, an explicit linear algebra-based formula was proposed in [20] to find IO-equations to determine IO-identifiability. In general, using these equations instead of the just mentioned characteristic set-based approach would give incorrect results (see [8, Remark 3.11]). However, [28, Theorem 3] shows that such an approach is valid for a large class of linear compartment models.

We will see in Corollary 5.7 that characteristic sets (more precisely, characteristic presentations) provide a tool of computing IO-identifiability. However, for the purposes of mathematical elegance and a more explicit connection with other branches of mathematics, e.g., with model theory (which was recently discovered to be useful for identifiability [27]), we present a definition that is short and avoids notationally heavy definitions leading to characteristic sets:

Definition 2.5 (IO-identifiability)**.** The smallest field k such that $\mathbb{C} \subset k \subset \mathbb{C}(\boldsymbol{\mu})$ and $I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$ is generated (as an ideal or as a differential ideal) by $I_\Sigma \cap k\{\mathbf{y}, \mathbf{u}\}$ is called *the field of IO-identifiable functions*. We call $h \in \mathbb{C}(\boldsymbol{\mu})$ *IO-identifiable* if $h \in k$.

We will now briefly compare Definitions 2.2 and 2.5 by considering intentionally simple examples.

Example 2.6. Consider the system
$$\Sigma = \begin{cases} x' = (a+b)x \\ y = x. \end{cases}$$

So, $\lambda = 2$, $n = m = 1$, and $\kappa = 0$. Let us check the identifiability of $h_1(x_1^*, a, b) = a$. As there are no denominators, $Q = 1$, and so $\Omega_h = \mathbb{C}^3$. Let $\Theta \in \tau(\mathbb{C}^3)$ and $(\hat{x}_1^*, \hat{a}, \hat{b}) \in \Theta$. Then
$$Y(\hat{x}_1^*, \hat{a}, \hat{b}) = \hat{x}_1^* e^{(\hat{a}+\hat{b})t}.$$

Hence,
$$\begin{aligned} S_{h_1}(\hat{x}_1^*, \hat{a}, \hat{b}) &= \left\{ h_1(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \mid (\tilde{x}_1^*, \tilde{a}, \tilde{b}) \in \mathbb{C}^3 \text{ and } Y(\hat{x}_1^*, \hat{a}, \hat{b}) = Y(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \right\} \\ &= \left\{ \tilde{a} \in \mathbb{C} \mid \exists (\tilde{x}_1^*, \tilde{b}) \in \mathbb{C}^2 \text{ such that } Y(\hat{x}_1^*, \hat{a}, \hat{b}) = Y(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \right\} \\ &\supset \left\{ \tilde{a} \in \mathbb{C} \mid \exists (\tilde{x}_1^*, \tilde{b}) \in \mathbb{C}^2 \text{ such that } \hat{x}_1^* = \tilde{x}_1^* \text{ and } \hat{a} + \hat{b} = \tilde{a} + \tilde{b} \right\} \\ &= \left\{ \tilde{a} \in \mathbb{C} \mid \exists \tilde{b} \in \mathbb{C} \text{ such that } \hat{a} + \hat{b} - \tilde{a} = \tilde{b} \right\} = \mathbb{C}, \end{aligned}$$

therefore, by Definition 2.2, $h_1 = a$ is not identifiable. We will now check the identifiability of $h_2(x_1^*, a, b) = a + b$. Let
$$\Theta = \left\{ (x_1^*, a, b) \in \mathbb{C}^3 \mid x_1^* \neq 0 \right\} \in \tau(\mathbb{C}^3)$$
and consider any $(\hat{x}_1^*, \hat{a}, \hat{b}) \in \Theta$. We have
$$\begin{aligned} S_{h_2}(\hat{x}_1^*, \hat{a}, \hat{b}) &= \left\{ h_2(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \mid (\tilde{x}_1^*, \tilde{a}, \tilde{b}) \in \mathbb{C}^3 \text{ and } Y(\hat{x}_1^*, \hat{a}, \hat{b}) = Y(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \right\} \\ &= \left\{ \tilde{a} + \tilde{b} \mid (\tilde{a}, \tilde{b}) \in \mathbb{C}^2 \text{ such that } \exists \tilde{x}_1^* \in \mathbb{C} \text{ such that } Y(\hat{x}_1^*, \hat{a}, \hat{b}) = Y(\tilde{x}_1^*, \tilde{a}, \tilde{b}) \right\} \\ &= \left\{ \tilde{a} + \tilde{b} \mid (\tilde{a}, \tilde{b}) \in \mathbb{C}^2 \text{ such that } \exists \tilde{x}_1^* \in \mathbb{C} \text{ such that } \hat{x}_1^* = \tilde{x}_1^* \text{ and } \hat{a} + \hat{b} = \tilde{a} + \tilde{b} \right\} \\ &= \left\{ \hat{a} + \hat{b} \right\}. \end{aligned}$$

Therefore, by Definition 2.2, $h_2 = a + b$ is identifiable. With this conclusion, it is now natural to consider the following reparametrization of Σ:
$$\begin{cases} x' = cx \\ y = x, \end{cases}$$

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in which the only parameter c is identifiable. This shows how considering identifiable functions of parameters rather than just the parameters could be helpful for improving the model.

We will now investigate the IO-identifiability of Σ. We have

$$I_\Sigma = [x' - (a+b)x, y-x] = [y' - (a+b)y, x-y] \subset \mathbb{C}(a,b)\{x,y\}.$$

Hence $I_\Sigma \cap \mathbb{C}(a+b)\{y\}$ generates $I_\Sigma \cap \mathbb{C}(a,b)\{y\} = [y' - (a+b)y]$. So $k \subset \mathbb{C}(a+b)$. On the other hand, $I_\Sigma \cap \mathbb{C}(a,b)[y,y']$ is the principal ideal generated by $f := y' - (a+b)y$ because, for instance, the non-zero solution of Σ being an exponential function, is not algebraic over the constants. Hence, since f has one of the coefficients equal 1, k must contain $a+b$, so $k = \mathbb{C}(a+b)$. We will later see in Corollary 5.7 how one can avoid considering actual solutions to find input-output identifiable functions.

We will now consider an example in which the identifiability and IO-identifiability do not coincide.

Example 2.7. Consider an example of a twisted harmonic oscillator:

$$\begin{cases} x_1' = (\omega + \alpha)x_2 \\ x_2' = -\omega x_1 \\ y = x_2 \end{cases}$$

in which α can be measured separately, so is assumed to be known. This can be reflected as follows:

$$\Sigma = \begin{cases} x_1' = (\omega + x_3)x_2 \\ x_2' = -\omega x_1 \\ x_3' = 0 \\ y_1 = x_2 \\ y_2 = x_3. \end{cases}$$

So, $\lambda = 1$, $n = 3$, $m = 2$, and $\kappa = 0$. Let $h(x_1^*, x_2^*, x_3^*, \omega) = \omega$, so we are checking the identifiability of ω. As there are no denominators, $Q = 1$, and so $\Omega_h = \mathbb{C}^4$. Let $\Theta \in \tau(\mathbb{C}^4)$ and $(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) \in \Theta$ be such that $\hat{\omega}(\hat{x}_3^* + \hat{\omega}) \neq 0$ and $\hat{x}_3^* \neq -2\hat{\omega}$. Then, denoting the frequency by $\hat{\varphi} := \sqrt{\hat{\omega}(\hat{x}_3^* + \hat{\omega})}$, we have

$$Y(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) = \begin{pmatrix} -\hat{x}_1^* \frac{\hat{\omega}}{\hat{\varphi}} \sin(t\hat{\varphi}) + \hat{x}_2^* \cos(t\hat{\varphi}) \\ \hat{x}_3^* \end{pmatrix}.$$

Note that $Y(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega})(0) = \begin{pmatrix} \hat{x}_2^* \\ \hat{x}_3^* \end{pmatrix}$. Therefore,

$$\begin{aligned}
&S_h(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) \\
&= \left\{ h(\tilde{x}_1^*, \tilde{x}_2^*, \tilde{x}_3^*, \tilde{\omega}) \mid (\tilde{x}_1^*, \tilde{x}_2^*, \tilde{x}_3^*, \tilde{\omega}) \in \mathbb{C}^4 \text{ and } Y(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) = Y(\tilde{x}_1^*, \tilde{x}_2^*, \tilde{x}_3^*, \tilde{\omega}) \right\} \\
&= \left\{ \tilde{\omega} \in \mathbb{C} \mid \exists (\tilde{x}_1^*, x_2^*, x_3^*) \in \mathbb{C}^3 \text{ such that } Y(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) = Y(\tilde{x}_1^*, \tilde{x}_2^*, \tilde{x}_3^*, \tilde{\omega}) \right\} \\
&= \left\{ \tilde{\omega} \in \mathbb{C} \mid \exists \tilde{x}_1^* \in \mathbb{C} \text{ such that } Y(\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \hat{\omega}) = Y(\tilde{x}_1^*, \hat{x}_2^*, \hat{x}_3^*, \tilde{\omega}) \right\} \\
&\supset \left\{ \tilde{\omega} \in \mathbb{C} \mid \exists \tilde{x}_1^* \in \mathbb{C} \text{ s.t. } \hat{x}_1^* \hat{\omega} = \tilde{x}_1^* \tilde{\omega} \text{ and } \hat{\omega}(\hat{x}_3^* + \hat{\omega}) = \tilde{\omega}(\hat{x}_3^* + \tilde{\omega}) \right\},
\end{aligned}$$

which has cardinality 2 because the second conjunct has distinct solutions $\tilde{\omega} \in \{\hat{\omega}, -(\hat{x}_3^* + \hat{\omega})\}$ and by the first conjunct $\tilde{x}_1^*$ is uniquely determined by the choice of $\tilde{\omega}$. Therefore, by Definition 2.2, ω is not identifiable.

On the other hand,

$$I_\Sigma = [x_1' - (\omega + x_3)x_2, x_2' + \omega x_1, x_3', y_1 - x_2, y_2 - x_3] \subset \mathbb{C}(\omega)\{x_1, x_2, x_3, y_1, y_2\}.$$

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One can verify that $I_\Sigma \cap \mathbb{C}(\omega)[y_1, y_1', y_2] = \{0\}$. Indeed, if there were a polynomial $p(\omega, y_1, y_1', y_2) \neq 0$ in this intersection, then, for every solution of Σ, the evaluation at $t = 0$ would imply that $p(\widehat{\omega}, \hat{x}_2^*, -\widehat{\omega}\hat{x}_1^*, \hat{x}_3^*) = 0$ yielding that $\hat{x}_1^*, \hat{x}_2^*, \hat{x}_3^*$, and $\widehat{\omega}$ always satisfy such a polynomial relation. But this is not the case because they can be chosen to be any complex numbers. Therefore, $I_\Sigma \cap \mathbb{C}(\omega)[y_1, y_1', y_1'', y_2]$ is a principal ideal generated by $f := y_1'' + \omega^2 y_1 + \omega y_1 y_2$. Since f has one of its coefficients equal to 1, the field k from Definition 2.5 must contain ω, so $k = \mathbb{C}(\omega)$. In particular, ω is input-output identifiable (but is not identifiable). A more systematic way of computing this field using characteristic sets, as described in Corollary 5.7 and shown in Example 5.8.

3 Technical result: algebraic criterion for identifiability

Proposition 3.1 extends the algebraic criterion for identifiability [11, Proposition 3.4] to identifiability of functions of parameters rather than identifiability of just specific parameters themselves.

Proposition 3.1. *For every $h \in \mathbb{C}(\mathbf{x}^*, \boldsymbol{\mu})$, the following are equivalent:*

- *h is identifiable;*

- *the image of h in $Frac(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$ lies in the field generated by the image of $\mathbb{C}\{\mathbf{y}, \mathbf{u}\}$ in $Frac(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$.*

Example 3.2. For Σ from Example 2.6, we have $I_\Sigma = [x' - (a+b)x, y - x]$, and see that

$$\begin{aligned} L := \mathrm{Frac}(\mathbb{C}(a,b)\{x,y\}/I_\Sigma) &= \mathrm{Frac}(\mathbb{C}(a,b)\{x,y\}/[x' - (a+b)x, y - x] \\ &= \mathrm{Frac}(\mathbb{C}(a,b)\{x,y\}/[y' - (a+b)y, y - x]. \end{aligned}$$

Hence, the field of fractions of the image of $\mathbb{C}(a,b)\{y\}$ in L is

$$M := \mathrm{Frac}\left(\mathbb{C}(a,b)\{y\}/[y' - (a+b)y]\right).$$

Since $a + b = y'/y$, we have $h_2 = a + b \in M$, and so h_2 is identifiable by Proposition 3.1.

Proof. Write $h = h_1/h_2$, where $h_1, h_2 \in \mathbb{C}[\mathbf{x}^*, \boldsymbol{\mu}]$. Let $\mathcal{F} = \mathrm{Frac}(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$ and $\mathcal{E}$ the subfield generated by the image of $\mathbb{C}\{\mathbf{y}, \mathbf{u}\}$ in $\mathcal{F}$. Let Σ_1 be the system of equations obtained by adding

$$\begin{aligned} x_{n+1}' &= \sum_{i=1}^{n} f_i \frac{\partial h}{\partial x_i}, \\ y_{m+1} &= x_{n+1} - h, \\ x_{n+1}(0) &= x_{n+1}^* \end{aligned} \tag{2}$$

to Σ, where x_{n+1} is a new state variable and y_{m+1} is a new output. Note that $x_{n+1}' = h'$ and $y_{m+1}' = 0$. We define

$$\mathcal{F}_1 = \mathrm{Frac}(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, x_{n+1}, \mathbf{y}, y_{m+1}, \mathbf{u}\}/I_{\Sigma_1}),$$

and let $\mathcal{E}_1$ be the subfield generated by the image of $\mathbb{C}\{\mathbf{y}, y_{m+1}, \mathbf{u}\}$ in $\mathcal{F}_1$. We will talk about Σ-identifiability of h and Σ_1-identifiability of x_{n+1}^*. The proof will proceed in the following three steps.

Step 1. *h is Σ-identifiable $\iff$ x_{n+1}^* is Σ_1-identifiable.* Assume that h is Σ-identifiable. Let Θ and U be the corresponding open subsets from Definition 2.2. We set

$$\Theta_1 := \{(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}) \mid (\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}) \in \Theta \,\&\, h_2(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}) \neq 0\}.$$

We will show that x_{n+1}^* is identifiable with the open sets from Definition 2.2 being Θ_1 and U. Let Ω_1 be the set Ω for the model Σ_1, and consider $(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in (\Theta_1 \times U) \cap \Omega_1$. Since, for a fixed known value of y_{m+1}, the values of x_{n+1}^* and $h(\mathbf{x}^*, \boldsymbol{\mu})$ uniquely determine each other, we have

$$|S_{x_{n+1}^*}(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})| = |S_h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})| = 1.$$

Thus, x_{n+1}^* is Σ_1-identifiable.

For the other direction, assume that x_{n+1}^* is Σ_1-identifiable, and Θ_1 and U_1 are the corresponding open sets from Definition 2.2. Let Θ be the projection of Θ_1 onto all of the coordinates except for x_{n+1}^*. We will show that h is Σ-identifiable with the open sets being Θ and U_1. Consider $(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in (\Theta \times U_1) \cap \Omega_h$. Let $\hat{x}_{n+1}^* \in \mathbb{C}$ be such that $(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}) \in \Theta_1$. Then, using the fact that y_{m+1} is constant so is equal to its initial condition, we have

$$
\begin{aligned}
1 &= |S_{x_{n+1}^*}(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})| \\
&= |\{\tilde{x}_{n+1}^* \mid (\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in \Omega_h, \; \tilde{x}_{n+1}^* \in \mathbb{C} \text{ and } Y_1(\hat{\mathbf{x}}^*, \hat{x}_{n+1}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) = Y_1(\tilde{\mathbf{x}}^*, \tilde{x}_{n+1}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}})\}| \\
&= \left| \left\{ h(\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}) \mid (\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}}) \in \Omega_h, \tilde{x}_{n+1}^* \in \mathbb{C} \text{ and } \begin{cases} Y(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}}) = Y(\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}, \hat{\mathbf{u}}), \\ \hat{x}_{n+1}^* - h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}) = \tilde{x}_{n+1}^* - h(\tilde{\mathbf{x}}^*, \tilde{\boldsymbol{\mu}}) \end{cases} \right\} \right| \\
&= |S_h(\hat{\mathbf{x}}^*, \hat{\boldsymbol{\mu}}, \hat{\mathbf{u}})|.
\end{aligned}
$$

Step 2. $h \in \mathcal{E} \iff x_{n+1} \in \mathcal{E}_1$. Observe that we have natural embeddings $\mathcal{F} \hookrightarrow \mathcal{F}_1$ and $\mathcal{E} \hookrightarrow \mathcal{E}_1$. If $h \in \mathcal{E}$, then $x_{n+1} = y_{m+1} + h \in \mathcal{E}_1$.

Assume that $x_{n+1} \in \mathcal{E}_1$. Then $h = x_{n+1} - y_{m+1} \in \mathcal{E}_1$. Observe that $\mathcal{F}_1 = \mathcal{F}(x_{n+1})$, and x_{n+1} is transcendental over $\mathcal{F}$. Since none of the right-hand sides of the equations for the state variables involves x_{n+1}, there is a differential automorphism $\alpha \colon \mathcal{F}_1 \to \mathcal{F}_1$ such that $\alpha(x_{n+1}) = x_{n+1} + 1$ and $\alpha|_{\mathcal{F}} = \mathrm{id}$. Since $\alpha(y_{m+1}) = y_{m+1} + 1$, we have $\alpha(\mathcal{E}_1) \subset \mathcal{E}_1$. Since $\mathcal{E}_1 = \mathcal{E}(y_{m+1})$ and $\alpha(y_{m+1}) = y_{m+1} + 1$, every α-invariant element of $\mathcal{E}_1$ belongs to $\mathcal{E}$. Since $\alpha(h) = h$, we have $h \in \mathcal{E}$.

Step 3. From **Step 1.**, h is identifiable if and only if x_{n+1}^* is Σ_1-identifiable. By [11, Proposition 3.4 (a) $\iff$ (c); Remark 2.2], x_{n+1}^* is Σ_1-identifiable if and only if $x_{n+1} \in \mathcal{E}_1$. Finally, **Step 2.** implies that $x_{n+1} \in \mathcal{E}_1$ if and only if $h \in \mathcal{E}$.

$\square$

4 Identifiability and IO-identifiability

4.1 Identifiability $\implies$ IO-identifiability but not the other way around

Remark 4.1. We have already seen an ODE model in which all parameters are IO-identifiable but are not identifiable (Example 2.7). Real-life examples of "slow-fast ambiguity" in chemical reactions and of a Lotka-Volterra model with the same conclusion can be found in [26, Sections 5.2 and 5.3].

Theorem 4.2. *For all Σ and $h \in \mathbb{C}(\boldsymbol{\mu})$,*

$$h \text{ is identifiable} \implies h \text{ is IO-identifiable}$$

Proof. Let $h \in \mathbb{C}(\boldsymbol{\mu})$ be identifiable. By Proposition 3.1, there exist $g \in \mathbb{C}\{\mathbf{y}, \mathbf{u}\} \setminus I_\Sigma$ and $w \in \mathbb{C}\{\mathbf{y}, \mathbf{u}\}$ such that $gh + w \in I_\Sigma$. Therefore, there exist $m_1, \ldots, m_r \in \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$ and $p_1, \ldots, p_r \in I_\Sigma \cap k\{\mathbf{y}, \mathbf{u}\}$ such that

$$gh + w = m_1 p_1 + \ldots + m_r p_r. \tag{3}$$

Suppose $h \notin k$. By [24, Theorem 9.29, p. 117], there exists an automorphism σ on $\overline{\mathbb{C}(\boldsymbol{\mu})}$ that fixes k pointwise and such that $\sigma(h) \neq h$. Let $R_1 := \overline{\mathbb{C}(\boldsymbol{\mu})}\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}$. We extend σ to R_1 by letting σ fix $\mathbf{x}$, $\mathbf{y}$, and $\mathbf{u}$. Applying σ to (3) and subtracting the two equations yields

$$g(h - \sigma(h)) = (m_1 - \sigma(m_1))p_1 + \ldots + (m_r - \sigma(m_r))p_r \tag{4}$$

in R_1. Let P denote the differential ideal generated by Σ in R_1. Since P is a prime differential ideal and the right-hand side of (4) belongs to P, it follows that either $g \in P$ or $h - \sigma(h) \in P$. But since $h - \sigma(h)$ is a non-zero element of $\overline{\mathbb{C}(\boldsymbol{\mu})}$ and P is a proper ideal, it cannot be that $h - \sigma(h) \in P$. Therefore, $g \in P$. Hence, $g \in P \cap R = I_{\Sigma}$, contradicting our assumption on g. □

4.2 Sufficient condition for "identifiable $\Longleftrightarrow$ IO-identifiable"

The aim of this section is Theorem 4.7, which gives a sufficient condition for the fields of identifiable and IO-identifiable functions to coincide.

Notation 4.3.

- For a differential ring (R, δ), its ring of *constants* is $C(R) := \{r \in R \mid \delta(r) = 0\}$.

- For elements $a_1, \ldots, a_N$ of a differential ring, let $\mathrm{Wr}_M(a_1, \ldots, a_N)$ denote the $M \times N$ Wronskian matrix of $a_1, \ldots, a_N$, that is,

$$\mathrm{Wr}_M(a_1, \ldots, a_N)_{i,j} = a_j^{(i-1)}, \quad 1 \leqslant j \leqslant N, \ 1 \leqslant i \leqslant M.$$

Definition 4.4 (Field of definition). Let $L \subseteq K$ be fields and let X be a (possibly infinite) set of variables. Let I be an ideal of $K[X]$. We say the *field of definition of I over L* is the smallest (with respect to inclusion) field k, $L \subseteq k \subseteq K$, such that I is generated by $I \cap k[X]$.

Remark 4.5. For a given X and I, the field of definition of K over $\mathbb{Q}$ is what is called the field of definition of K (with no reference to a subfield) in [18, Definition and Theorem 3.4, p. 55]. By [18, Theorem 3.4], for every K and I, there is a smallest field $k_0 \subseteq K$ such that I is generated by $I \cap k_0[X]$. The smallest intermediate field k, $L \subseteq k \subseteq K$, such that I is generated by $I \cap k[X]$ is equal to the smallest subfield of K containing L and k_0. Therefore, for every L, K, and I, the field of definition of I over L is well defined.

Lemma 4.6 (cf. [6, Section 4.1], [22, Section 3.4], and [40, Section V.]). *Let $g \in I_{\Sigma}$ be such that we can write $g = \sum_{i=1}^N a_i z_i$, where $N \geqslant 2$, $a_i \in \mathbb{C}(\boldsymbol{\mu}) \setminus \{0\}$, $a_1 = 1$, and $z_1, \ldots, z_N$ are distinct monomials in $\mathbb{C}\{\mathbf{y}, \mathbf{u}\}$. If for some $Z \subsetneq \{z_1, \ldots, z_N\}$ of size $N-1$ it holds that $\det \mathrm{Wr}_{N-1}(Z) \notin I_{\Sigma}$, then a_i is identifiable for all $i = 1, \ldots, N$.*

Proof. Suppose $\det \mathrm{Wr}_{N-1}(z_1, \ldots, z_{t-1}, z_{t+1}, \ldots, z_N) \notin I_{\Sigma}$. Modulo I_{Σ}, we have

$$\sum_{i \neq t} \frac{a_i}{a_t} z_i = -z_t \tag{5}$$

Since I_{Σ} is a differential ideal, the derivatives of (5) are also true. Differentiating (5) $N-2$ times, we obtain the following linear system:

$$M \left(\frac{a_1}{a_t}, \ldots, \frac{a_{t-1}}{a_t}, \frac{a_{t+1}}{a_t}, \ldots, \frac{a_N}{a_t} \right)^T = -(z_t, \ldots, z_t^{(N-2)})^T,$$

where $M = \mathrm{Wr}_{N-1}(z_1, \ldots, z_{t-1}, z_{t+1}, \ldots, z_N)$. Since M is nonsingular modulo I_{Σ}, in $\mathrm{Frac}(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}\}/I_{\Sigma})$, we have

$$\left(\frac{a_1}{a_t}, \ldots, \frac{a_{t-1}}{a_t}, \frac{a_{t+1}}{a_t}, \ldots, \frac{a_N}{a_t} \right) = (-z_t, \ldots, z_t^{(N-2)})(M^{-1})^T.$$

Since the entries of the right-hand side belong to the subfield generated by $\mathbb{C}\{\mathbf{y}, \mathbf{u}\}$, the entries of the left-hand side are identifiable by Proposition 3.1. Since $a_1 = 1$, a_t is identifiable and it follows that $a_2, \ldots, a_N$ are identifiable. $\qquad \square$

Theorem 4.7. *Assume that model Σ does not have rational first integrals (i.e., first integrals that are rational functions in the parameters and state variables), that is, the constants of $Frac(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$ coincide with $\mathbb{C}(\boldsymbol{\mu})$. Then, for every $h \in \mathbb{C}(\boldsymbol{\mu})$,*

$$h \text{ is identifiable} \iff h \text{ is IO-identifiable}.$$

Proof. Proposition 4.2 implies that the field of all identifiable functions is contained in the field of all IO-identifiable functions.

Let $J := I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$. We fix an indexing of differential monomials in $\mathbf{y}$ and $\mathbf{u}$ by $\mathbb{N}$, it defines an $\mathbb{N}$-indexed basis $\mathcal{B}$ of $\mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$. Consider an infinite matrix with each row being an element of a $\mathbb{C}(\boldsymbol{\mu})$-basis of J written as a vector in basis $\mathcal{B}$. Let M be the reduced row echelon form of the matrix. Notice that, since the original matrix has only finitely many nonzero entries in each row, M also has only finitely many nonzero entries in each row. The field of definition of J over $\mathbb{C}$ is contained in the field generated by the entries of M. Therefore, it is sufficient to prove that the entries of M are identifiable. Consider any row of M. It corresponds to a differential polynomial $p \in J$. Assume that a proper subset of monomials of p is linearly dependent modulo J over $\mathbb{C}(\boldsymbol{\mu})$. This dependence yields a polynomial $q \in J$. The representation of q in basis $\mathcal{B}$ must be reducible to zero by the rows of M. However, the reduction of q with respect to p is not zero (as they are not proportional), and the result of this reduction is not reducible by any other row of M by the definition of reduced row echelon form. Thus, there is no such q. Hence, the image of every proper subset of monomials of p in $Frac(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$ is linearly independent over the constants of $Frac(\mathbb{C}(\boldsymbol{\mu})\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}/I_\Sigma)$. Thus, [14, Theorem 3.7, p. 21] implies that the Wronskian of every proper subset of monomials of p does not belong to I_Σ. Lemma 4.6 implies that the coefficients of p are identifiable. $\quad \square$

Example 4.8. System Σ from Example 2.7 has x_3 as a rational first integral, and, in this example, function $h = \omega$ is IO-identifiable and is not identifiable.

5 IO-identifiability via characterstic sets

5.1 Differential algebra preliminaries

We will use the following notation and definitions standard in differential algebra (see, e.g., [15, Chapter I], [29, Chapter I], and [4, Section 2]):

Definition 5.1. A *differential ranking* on $K\{x_1, \ldots, x_n\}$ is a total order $>$ on $X := \{\delta^i x_j \mid i \geqslant 0, 1 \leqslant j \leqslant n\}$ satisfying:

- for all $x \in X$, $\delta(x) > x$ and

- for all $x, y \in X$, if $x > y$, then $\delta(x) > \delta(y)$.

It can be shown that a differential ranking on $K\{x_1, \ldots, x_n\}$ is always a well order.

Notation 5.2. For $f \in K\{x_1, \ldots, x_n\} \backslash K$ and differential ranking $>$,

- $\text{lead}(f)$ is the element of $\{\delta^i x_j \mid i \geqslant 0, 1 \leqslant j \leqslant n\}$ appearing in f that is maximal with respect to $>$.

- 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 $\frac{\partial f}{\partial \operatorname{lead}(f)}$, the partial derivative of f with respect to $\operatorname{lead}(f)$.

- The rank of f is $\operatorname{rank}(f) = \operatorname{lead}(f)^{\deg_{\operatorname{lead}(f)} f}$.

- For $S \subset K\{x_1, \ldots, x_n\} \backslash K$, the set of initials and separants of S is denoted by H_S.

- for $g \in K\{x_1, \ldots, x_n\} \backslash K$, say that $f < g$ if $\operatorname{lead}(f) < \operatorname{lead}(g)$ or $\operatorname{lead}(f) = \operatorname{lead}(g)$ and $\deg_{\operatorname{lead}(f)} f < \deg_{\operatorname{lead}(g)} g$.

Definition 5.3 (Characteristic sets). • For $f, g \in K\{x_1, \ldots, x_n\} \backslash K$, f is said to be reduced w.r.t. g if no proper derivative of $\operatorname{lead}(g)$ appears in f and $\deg_{\operatorname{lead}(g)} f < \deg_{\operatorname{lead}(g)} g$.

- A subset $\mathcal{A} \subset K\{x_1, \ldots, x_n\} \backslash K$ is called *autoreduced* if, for all $p \in \mathcal{A}$, p is reduced w.r.t. every element of $\mathcal{A} \backslash \{p\}$. One can show that every autoreduced set has at most n elements (like a triangular set but unlike a Gröbner basis in a polynomial ring).

- Let $\mathcal{A} = \{A_1, \ldots, A_r\}$ and $\mathcal{B} = \{B_1, \ldots, B_s\}$ be autoreduced sets such that $A_1 < \ldots < A_r$ and $B_1 < \ldots < B_s$. We say that $\mathcal{A} < \mathcal{B}$ if

  - $r > s$ and $\operatorname{rank}(A_i) = \operatorname{rank}(B_i)$, $1 \leqslant i \leqslant s$, or
  - there exists q such that $\operatorname{rank}(A_q) < \operatorname{rank}(B_q)$ and, for all i, $1 \leqslant i < q$, $\operatorname{rank}(A_i) = \operatorname{rank}(B_i)$.

- An autoreduced subset of the smallest rank of a differential ideal $I \subset K\{x_1, \ldots, x_n\}$ is called a *characteristic set* of I. One can show that every non-zero differential ideal in $K\{x_1, \ldots, x_n\}$ has a characteristic set. Note that a characteristic set does not necessarily generate the ideal.

Definition 5.4 (Characteristic presentation). • 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 [4]. A set of polynomials is said to be monic if each polynomial in the set is monic.

- Let $\mathcal{C}$ be a characteristic set of a prime differential ideal $P \subset K\{z_1, \ldots, z_n\}$. Let $N(\mathcal{C})$ denote the set of non-leading variables of $\mathcal{C}$. Then $\mathcal{C}$ is called a *characteristic presentation* of P if all initials of $\mathcal{C}$ belong to $K[N(\mathcal{C})]$ and none of the elements of $\mathcal{C}$ has a factor in $K[N(\mathcal{C})] \backslash K$. It follows from [4] that P has a characteristic presentation.

Definition 5.5 (Monomial). Let K be a differential field and let X be a set of variables. An element of the differential polynomial ring $K\{X\}$ is said to be a *monomial* if it belongs to the smallest multiplicatively closed set containing 1, X, and the derivatives of X. An element of the polynomial ring $K[X]$ is said to be a *monomial* if it belongs to the smallest multiplicatively closed set containing 1 and X.

5.2 IO-identifiable functions via characteristic presentations

Corollary 5.7 shows how the field of IO-identifiable functions can be computed via input-output equations.

Proposition 5.6. *Let $L \subseteq K$ be differential fields and let X be a finite set of variables. Let P be a prime non-zero differential ideal of $K\{X\}$ such that the ideal generated by P in $\overline{K}\{X\}$ is prime. If $\mathcal{C}$ is a monic characteristic presentation of P, then the field of definition of P over L is the field extension of L generated by the coefficients of $\mathcal{C}$.*

Proof. Let A be the set of coefficients of $\mathcal{C}$ and let k be the field of definition of P over L.

Suppose $A \not\subset k$. Let P_1 be the ideal generated by the image of P in $\overline{K}\{X\}$. We show that $\mathcal{C}$ is a monic characteristic presentation for P_1. We have that $\mathcal{C}$ is a characteristic set for P_1. Since the initials of $\mathcal{C}$ lie

in $K[N(\mathcal{C})]$, they also lie in $\overline{K}[N(\mathcal{C})]$. The property of not having a factor in the nonleading variables does not depend on the coefficient field as well. By [12, Definition 2.6] and the paragraph thereafter, we have that $P = [\mathcal{C}] : H_\mathcal{C}^\infty$ in $K\{X\}$, and therefore $[\mathcal{C}] : H_\mathcal{C}^\infty \subset P_1$, where the differential ideal operation is taken over $\overline{K}\{X\}$. Since $\mathcal{C}$ is a characteristic set of P_1, the paragraph following [12, Definition 2.4] implies that P_1 is contained in $[\mathcal{C}] : H_\mathcal{C}^\infty$, so $P_1 = [\mathcal{C}] : H_\mathcal{C}^\infty$. Hence, [4, Corollary 1, p. 42], we conclude that $\mathcal{C}$ is a monic characteristic presentation for P_1.

By [24, Theorem 9.29, p. 117], there is an automorphism α of $\overline{K}$ that fixes k but moves some element of A. Extend α to a differential ring automorphism on $\overline{K}\{X\}$ that fixes X. We show that $\alpha(\mathcal{C})$ is a monic characteristic presentation of P_1. Since the initials of $\mathcal{C}$ lie in $K[N(\mathcal{C})]$ and no element of $\mathcal{C}$ has a factor in $K[N(\mathcal{C})]\backslash K$, it follows that the initials of $\alpha(\mathcal{C})$ lie in $\overline{K}[N(\alpha(\mathcal{C}))]$ and no element of $\alpha(\mathcal{C})$ has a factor in $\overline{K}[N(\alpha(\mathcal{C}))]\backslash \overline{K}$. Since the rank of $\alpha(\mathcal{C})$ is the same as that of $\mathcal{C}$, it remains to show that $\alpha(\mathcal{C}) \subset P_1$. Let $f \in \mathcal{C}$. Since P is defined over k, it follows that P_1 is defined over k. Therefore, there exist $a_i \in k\{X\} \cap P_1$ and $b_i \in \overline{K}\{X\}$ such that $f = \sum_i a_i b_i$. Thus,

$$\alpha(f) = \sum_i a_i \alpha(b_i) \in P_1.$$

We conclude that $\alpha(\mathcal{C}) \subset P_1$ and thus is a characteristic set of P_1.

We have shown that $\mathcal{C}$ and $\alpha(\mathcal{C})$ are monic characteristic presentations of P_1. By [4, Theorem 3, p. 42], $\alpha(\mathcal{C}) = \mathcal{C}$. However, since α moves some coefficient appearing in $\mathcal{C}$, we have a contradiction. We conclude that our assumption that $A \not\subset k$ is false.

It remains to show that $k \subseteq L(A)$. Let $\{h_i\}_{i \in B}$ be a monic generating set of P_1 as an ideal such that, for all $i \in B$ and for all $g \in P_1 \backslash \{h_i\}$, the support of $h_i - g$ is not a proper subset of the support of h_i. We argue that such a generating set exists. We describe a map $\phi \colon P_1 \to \mathcal{P}(P_1)$, where $\mathcal{P}(P_1)$ denotes the power set of P_1, such that $\forall b \in P_1$

- b belongs to the ideal generated by $\phi(b)$ and

- $\forall a \in \phi(b) \; \forall d \in P_1 \backslash \{0\}$ the support of d is not a proper subset of the support of a.

Let $b \in P_1$. Construct $\phi(b)$ recursively as follows. If there is no element of $P_1 \backslash \{0\}$ whose support is a proper subset of the support of b, let $\phi(b) = \{b\}$. If there is an $a \in P_1 \backslash \{0\}$ whose support is a proper subset of the support of b, let $\phi(b) = \phi(a) \cup \phi(b - ca)$, where $c \in \mathbb{C}$ is such that $b - ca$ has smaller support than b. This completes the construction of ϕ. Note that the procedure terminates since for each non-terminal step, the support of each element of the output is smaller than the support of the input. Let $\{b_i\}_{i \in B_0}$ be a generating set for P_1 as an ideal. Now $\bigcup_{i \in B_0} \phi(b_i)$, after normalization so that each element is monic, has the desired properties.

Fix i and suppose that some coefficient of h_i does not belong to $L(A)$. Then by [24, Theorem 9.29, p. 117], there is an automorphism α of $\overline{K}$ such that α fixes $L(A)$ and $\alpha(h_i) \neq h_i$. Since h_i is monic, we have that $h_i - \alpha(h_i)$ has smaller support than h_i. Now we show that $h_i - \alpha(h_i) \in P_1$. Since $h_i \in P_1$, we have that $h_i \in [\mathcal{C}] : H_\mathcal{C}^\infty$. Therefore, since α fixes the coefficients of $\mathcal{C}$, we have

$$\alpha(h_i) \in [\mathcal{C}] : H_\mathcal{C}^\infty.$$

Hence,

$$h_i - \alpha(h_i) \in [\mathcal{C}] : H_\mathcal{C}^\infty = P_1.$$

This contradicts the definition of $\{h_i\}_{i \in B}$. Since the coefficients of h_i belong to $L(A)$, $\{h_i\}_{i \in B}$ is also a generating set for P. Therefore, P is generated by $P \cap L(A)\{X\}$. By the definition of k, it follows that $k \subseteq L(A)$. $\qquad\square$

The following result reduces the problem of finding the field of IO-identifiable functions of (1) to the problem of finding a monic characteristic presentation of the corresponding prime differential ideal. The latter problem has been solved (see e.g., [4]), and there is an implementation of the corresponding algorithm, Rosenfeld-Gröbner, in MAPLE.

Corollary 5.7. *If C is a monic characteristic presentation of $I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$, then the field of IO-identifiable functions (as in Definition 2.5) is generated over $\mathbb{C}$ by the coefficients of the elements of C.*

Proof. The proof of [11, Lemma 3.2] shows that both I_Σ and the ideal generated by the image of I_Σ in $\overline{\mathbb{C}(\boldsymbol{\mu})}\{\mathbf{x}, \mathbf{y}, \mathbf{u}\}$ are prime, since the argument does not depend on the coefficient field. Therefore $I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$ and the ideal generated by $I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$ in $\overline{\mathbb{C}(\boldsymbol{\mu})}\{\mathbf{y}, \mathbf{u}\}$ are prime. By Proposition 5.6 with $L = \mathbb{C}$, $K = \mathbb{C}(\boldsymbol{\mu})$, and $P = I_\Sigma \cap \mathbb{C}(\boldsymbol{\mu})\{\mathbf{y}, \mathbf{u}\}$, we have that the field of definition of P over $\mathbb{C}$ is equal to the field extension of $\mathbb{C}$ generated by the coefficients of C. This is exactly the field of IO-identifiable functions. $\square$

Example 5.8. Consider the following ODE model

$$\Sigma = \begin{cases} x_1' = 0 \\ x_2' = x_1 x_2 + \mu_1 x_1 + \mu_2 \\ y = x_2 \end{cases}$$

As shown in [27, Lemma 5.1], neither μ_1 nor μ_2 are identifiable (which can be seen by observing that adding 1 to μ_1 and subtracting x_1 from μ_2 at the same time changes the parameters but does not change the output) and, moreover, the field of identifiable functions is just $\mathbb{C}$.

On the other hand, let us use Corollary 5.7 to compute the field of IO-identifiable functions. We enter these equations in MAPLE and set the elimination differential ranking on the differential variables with $x_1 > x_2 > y$. Within a second, we receive the following characteristic presentation of I_Σ:

$$C = \{yx_1 + \mu_1 x_1 - y' + \mu_2, \ x_2 - y, \ yy'' + \mu_1 y'' - y'^2 + \mu_2 y'\}.$$

Hence,

$$\mathcal{C} = C \cap \mathbb{C}(\mu_1, \mu_2)\{y\} = \{yy'' + \mu_1 y'' - y'^2 + \mu_2 y'\}.$$

By Corollary 5.7, the field of IO-identifiable functions is $\mathbb{C}(\mu_1, \mu_2)$, which is also not equal to the field of identifiable functions.

Acknowledgments

References

[1] J. Baaijens and J. Draisma. On the existence of identifiable reparametrizations for linear compartment models. *SIAM Journal on Applied Mathematics*, 76(4), 2016. URL https://doi.org/10.1137/15M1038013.

[2] D. Bearup, N. Evans, and M. Chappell. The input-output relationship approach to structural identifiability analysis. *Computer Methods and Programs in Biomedicine*, 109(2):171–181, 2013. URL https://doi.org/10.1016/j.cmpb.2012.10.012.

[3] G. Bellu, M. P. Saccomani, S. Audoly, and L. D'Angió. DAISY: A new software tool to test global identifiability of biological and physiological systems. *Computer Methods and Programs in Biomedicine*, 88(1):52–61, 2007. URL https://doi.org/10.1016/j.cmpb.2007.07.002.

[4] F. Boulier and F. Lemaire. Computing canonical representatives of regular differential ideals. In *Proceedings of the 2000 International Symposium on Symbolic and Algebraic Computation (ISSAC)*, pages 38–47. ACM, 2000. URL https://doi.org/10.1145/345542.345571.

[5] O.-T. Chis, J. R. Banga, and E. Balsa-Canto. Structural identifiability of systems biology models: A critical comparison of methods. *PLoS ONE*, 6(11):1–16, 11 2011. URL https://doi.org/10.1371/journal.pone.0027755.

[6] L. Denis-Vidal, G. Joly-Blanchard, C. Noiret, and M. Petitot. An algorithm to test identifiability of non-linear systems. *IFAC Proceedings Volumes*, 34(6):197–201, 2001. URL https://doi.org/10.1016/S1474-6670(17)35173-X.

[7] J. DiStefano and C. Cobelli. On parameter and structural identifiability: Nonunique observability/reconstructibility for identifiable systems, other ambiguities, and new definitions. *IEEE Transactions on Automatic Control*, 25(4):830–833, 1980. URL http://dx.doi.org/10.1109/TAC.1980.1102439.

[8] E. Gross, H. A. Harrington, N. Meshkat, and A. Shiu. Linear compartmental models: input-output equations and operations that preserve identifiability. *SIAM Journal on Applied Mathematics*, 79(4):1423–1447, 2019. URL https://doi.org/10.1137/18M1204826.

[9] E. Hille. *Ordinary Differential Equations in the Complex Domain*. Dover, 1997.

[10] H. Hong, A. Ovchinnikov, G. Pogudin, and C. Yap. SIAN: software for structural identifiability analysis of ODE models. *Bioinformatics*, 35(16):2873–2874, 2019. URL https://doi.org/10.1093/bioinformatics/bty1069.

[11] H. Hong, A. Ovchinnikov, G. Pogudin, and C. Yap. Global identifiability of differential models. *Communications on Pure and Applied Mathematics*, 73(9):1831–1879, 2020. URL https://doi.org/10.1002/cpa.21921.

[12] E. Hubert. Factorization-free decomposition algorithms in differential algebra. *Journal of Symbolic Computation*, 29(4):641–662, 2000. URL https://doi.org/10.1006/jsco.1999.0344.

[13] A. Kalami Yazdi, M. Nadjafikhah, and J. DiStefano. COMBOS2: an algorithm to the input–output equations of dynamic biosystems via Gaussian elimination. *Journal of Taibah University for Science*, 14(1):896–907, 2020. URL https://doi.org/10.1080/16583655.2020.1776466.

[14] I. Kaplansky. *An Introduction to Differential Algebra*. Hermann, Paris, 1957.

[15] E. Kolchin. *Differential Algebra and Algebraic Groups*. Academic Press, New York, 1973.

[16] L. Ljung and T. Glad. On global identifiability for arbitrary model parametrizations. *Automatica*, 30(2):265–276, 1994. URL https://doi.org/10.1016/0005-1098(94)90029-9.

[17] G. Margaria, E. Riccomagno, M. Chappell, and H. Wynn. Differential algebra methods for the study of the structural identifiability of rational function state-space models in the biosciences. *Mathematical Biosciences*, 174(1):1–26, 2001. URL http://dx.doi.org/10.1016/S0025-5564(01)00079-7.

[18] D. Marker. *Model Theory of Differential Fields*, volume 5 of *Lecture Notes in Logic*, pages 38–113. Springer-Verlag, Berlin, 1996. URL https://doi.org/10.1017/9781316716991.003.

[19] N. Meshkat, C. Kuo, and J. DiStefano. On finding and using identifiable parameter combinations in nonlinear dynamic systems biology models and COMBOS: A novel web implementation. *PLoS ONE*, 9(10):e110261, 2014. URL https://doi.org/10.1371/journal.pone.0110261.

[20] N. Meshkat, S. Sullivant, and M. Eisenberg. Identifiability results for several classes of linear compartment models. *Bulletin of Mathematical Biology*, 77:1620–1651, 10 2014. URL https://doi.org/10.1007/s11538-015-0098-0.

[21] N. Meshkat, Z. Rosen, and S. Sullivant. Algebraic tools for the analysis of state space models. In T. Hibi, editor, *The 50th Anniversary of Gröbner Bases, July 1–10, 2015, Osaka, Japan*, volume 77 of *Advances in Pure Mathematics*, pages 171–205, Tokyo, Japan, 2018. Mathematical Society of Japan. URL https://doi.org/10.2969/aspm/07710171.

[22] H. Miao, X. Xia, A. S. Perelson, and H. Wu. On identifiability of nonlinear ODE models and applications in viral dynamics. *SIAM Review*, 53(1):3–39, 2011. URL https://doi.org/10.1137/090757009.

[23] H. Miao, X. Xia, A. S. Perelson, and H. Wu. On identifiability of nonlinear ODE models and applications in viral dynamics. *SIAM Review*, 53(1):3–39, 2011. URL https://doi.org/10.1137/090757009.

[24] J. S. Milne. Fields and Galois theory (v4.60), 2018. URL https://www.jmilne.org/math/CourseNotes/ft.html.

[25] F. Ollivier. *Le problème de l'identifiabilité structurelle globale: approche théorique, méthodes effectives et bornes de complexité*. PhD thesis, École polytechnique, 1990.

[26] A. Ovchinnikov, A. Pillay, G. Pogudin, and T. Scanlon. Computing all identifiable functions for ODE models, 2020. URL https://arxiv.org/abs/2004.07774.

[27] A. Ovchinnikov, A. Pillay, G. Pogudin, and T. Scanlon. Multi-experiment parameter identifiability of ODEs and model theory. 2020. URL https://arxiv.org/abs/2011.10868.

[28] A. Ovchinnikov, G. Pogudin, and P. Thompson. Input-output equations and identifiability of linear ODE models. 2020. URL https://arxiv.org/abs/1910.03960.

[29] J. F. Ritt. *Differential Algebra*. Colloquium Publications. American Mathematical Society, 1950.

[30] M. Saccomani and L. D'Angió. Examples of testing global identifiability with the DAISY software. *IFAC Proceedings Volumes*, 42(10):48–53, 2009. URL https://doi.org/10.3182/20090706-3-FR-2004.00007.

[31] M. Saccomani, S. Audoly, and L. D'Angiò. Parameter identifiability of nonlinear systems: the role of initial conditions. *Automatica*, 39:619–632, 2003. URL http://dx.doi.org/10.1016/S0005-1098(02)00302-3.

[32] M. P. Saccomani and G. Bellu. DAISY: An efficient tool to test global identifiability. Some case studies. In *2008 16th Mediterranean Conference on Control and Automation*, pages 1723–1728, 2008. URL https://doi.org/10.1109/MED.2008.4602152.

[33] S. Vajda. Structural identifiability of dynamical systems. *International Journal of Systems Science*, 14(11):1229–1247, 1983. URL http://dx.doi.org/10.1080/00207728308926526.

[34] S. Vajda. Structural identifiability of linear, bilinear, polynomial and rational systems. *IFAC Pro-*

ceedings Volumes, 17(2):717–722, 1984. URL http://dx.doi.org/10.1016/S1474-6670(17)61056-5.

[35] A. F. Villaverde. Observability and structural identifiability of nonlinear biological systems. *Complexity*, 2019:1–12, Jan. 2019. URL https://doi.org/10.1155/2019/8497093.

[36] E. Walter and Y. Lecourtier. Unidentifiable compartmental models: what to do? *Mathematical Biosciences*, 56(1-2):1–25, 1981. URL https://doi.org/10.1016/0025-5564(81)90025-0.

[37] E. Walter and Y. Lecourtier. Global approaches to identifiability testing for linear and nonlinear state space models. *Mathematics and Computers in Simulation*, 24(6):472–482, 1982. URL http://dx.doi.org/10.1016/0378-4754(82)90645-0.

[38] E. Walter and L. Pronzato. On the identifiability and distinguishability of nonlinear parametric models. *Mathematics and Computers in Simulation*, 42(2–3):125–134, 1996. URL http://dx.doi.org/10.1016/0378-4754(95)00123-9.

[39] E. Walter and L. Pronzato. *Identification of Parametric Models from Experimental Data*. Springer, 1997.

[40] X. Xia and C. Moog. Identifiability of nonlinear systems with application to HIV/AIDS models. *IEEE Transactions on Automatic Control*, 48(2):330–336, Feb. 2003. URL https://doi.org/10.1109/tac.2002.808494.