

Identifiability of Linear and Linear-in-Parameters Dynamical Systems from a Single Trajectory*

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Abstract. Certain experiments are nonrepeatable because they result in the destruction or alteration of the system under study, and thus provide data consisting of at most a single trajectory in state space. Before proceeding with parameter estimation for models of such systems, it is important to know whether the model parameters can be uniquely determined, or identified, from idealized (error-free) single trajectory data. In the case of a linear model, we provide precise definitions of several forms of identifiability, and we derive some novel, interrelated conditions that are necessary and sufficient for these forms of identifiability to arise. We also show that the results have a direct extension to a class of nonlinear systems that are linear in parameters. One of our results provides information about identifiability based solely on the geometric structure of an observed trajectory, while other results relate to whether or not there exists an initial condition that yields identifiability of a fixed but unknown coefficient matrix and depend on its Jordan structure or other properties. Lastly, we extend the relation between identifiability and Jordan structure to the case of discrete data, and we show that the sensitivity of parameter estimation with discrete data depends on a condition number related to the data's spatial confinement.

Key words. parameter estimation, identifiability, linear systems, Krylov subspace, condition number, inverse problem

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1. Introduction. Mathematical models of physical systems often include parameters for which numerical values are not known a priori and cannot be directly measured. Parameter estimation relies on the comparison of experimental observations of the modeled system with corresponding model output to obtain values for these parameters. There are many computational techniques for parameter estimation that can be employed, most of which rely on minimization of the difference between model output and observed data. However, before numerical estimates of parameter values are pursued, it is important to address the question of whether the parameters of the model are identifiable; that is, does the parameter estimation problem have a unique solution, given access to some amount of error-free data? If the model's parameters are not identifiable from such idealized data, then numerical estimates of parameters from data may be misleading. Clearly, the answer to this question depends on the structure of the underlying model, the amount and type of the data given, and the precise definition of uniqueness.

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Identifiability analysis of dynamical systems has been an area of intense study [2, 4, 7, 28, 30, 38] and it is usually employed to aid model development, which ideally proceeds in the following order: first, a model of a system of interest is designed; second, the identifiability of model parameters is analyzed and the model is appropriately adjusted; third, a sufficient amount of data about the physical system is collected using experimental studies; and, finally, values of model parameters are estimated from the data. In many biological studies, however, the order is often reversed, and modelers use data that were collected before any thought was given to the modeling of the system. The modeler then faces the challenging task of designing a model that represents and explains the existing data for a system that is no longer available or for which measurements cannot be repeated under the original conditions. In some cases, repeated collection of data from a single subject is impossible because it has been destroyed during the process of data collection. This happens frequently in studies of disease models in clinical settings, in which either the disease itself or the manipulations performed to assay the subject's state may be fatal to the subject (laboratory animal). In immunological studies on mice, for example, each data point is an aggregate of data obtained from several different animals which are sacrificed during the process [34, 20]. In disease studies on larger mammals or humans, longitudinal data may be obtained for a single subject, but the experiment is not reproducible because the subject's immune system has been altered by the disease [15, 27]. In this paper we take this problem to the extreme and address the question of *identifiability of parameters of dynamical systems from a single observed trajectory*.

Linear models are a natural starting point for our study because they have a simple structure, but the identifiability question in this setting is nonetheless nontrivial because the solution to such a system depends nonlinearly on its parameters. This setting is also convenient because there is existing theory to build on, and one can exploit invertible operators for numerical techniques for handling linear systems. Parameter identifiability for linear dynamical systems has been studied extensively in control theory and related areas [2, 13, 14, 22, 30, 31, 37, 38]. A time-invariant linear control model typically has the form

$$(1.1) \quad \begin{aligned} \dot{x}(t) &= Ax(t) + Bu(t), \\ y(t) &= Cx(t), \end{aligned}$$

where A, B, C are parameter matrices, $x(t)$ is a vector function that defines the state of the system at time t , $u(t)$ is the vector of input (control), and $y(t)$ is the vector output. Zero initial conditions are typically chosen, but delta-function controls can be used to represent any desired initial condition. The impulse response function $Y(s) = C(sI - A)^{-1}B$ fully describes the (Laplace transformed) solutions of the system. In this context the matrix parameters A, B, C are said to be identifiable if they can be determined from the set of output observations y obtained by varying the control u . It is known that even with all control functions available, the matrices A, B, C are not all simultaneously identifiable, since the impulse response function is invariant under the transformation $(A, B, C) \rightarrow (T^{-1}AT, T^{-1}B, CT)$, where T is an invertible matrix [2]. Kalman [22] devised a nomenclature in which the system (1.1) is transformed into a new set of variables that can be divided into four classes: (a) controllable but unobservable, (b) controllable and observable, (c) uncontrollable and unobservable, and (d) uncontrollable but observable. Bellman and Åström showed that if C is square and has full rank (i.e., all states x are observable) and the matrix $[B \mid AB \mid \cdots \mid A^{n-1}B]$ has full rank (i.e., the system

is controllable), then both A and B are identifiable from the impulse response of the system when a full set of controls is available [2]. In special situations in which the matrices A, B, C depend on a parameter, that parameter may be identifiable even when C does not have full rank. It is not clear whether enough information can be obtained to identify the parameters from a smaller set of controls, perhaps even a single trajectory (i.e., single control), however, which is all that may be available in our motivating applications. Sontag has shown that when the model is identifiable, the parameters can be estimated even from information about a single variable extracted from a single trajectory, provided that enough data points have been measured: no more than $2r + 1$ data points are required to identify r parameters in the case in which the dynamical system is real analytic [32]. Since the classical results discussed above imply that C must be full rank for identifiability to be possible, we predominantly focus here on the case in which C is full rank in (1.1), in which case, without loss of generality, we can in fact assume that $C = I$. However, we also briefly consider the issue of partial identifiability when C is of lower rank.

As the next step, we examine nonlinear dynamical systems that depend linearly on parameters. Such systems can be written in the form

$$(1.2) \quad \dot{x}(t) = Af(x(t)) + u(t) - \mu(t)x(t),$$

where A is a parameter matrix, f is a known, locally Lipschitz continuous map (to ensure existence and uniqueness of solutions), $u(t)$ is a time-dependent input, and $\mu(t)$ is a decay control. Such systems commonly arise in differential equation models of chemical reaction networks that are derived from mass-action kinetics; in those cases, A is the stoichiometric matrix, f is the vector of reaction rate functions (each of which is a product of a reaction rate constant and a monomial in the components of x), u is the inflow into the reaction chamber, and μ is the outflow [18, 10, 11]. Among models of type (1.2) one can also include the generalized Lotka–Volterra models that are commonly used in ecology or population dynamics [8, 29, 19], in which case A is usually a sparse matrix. The problem of identifying the model (1.2) consists of two separate tasks: (i) identification of the parameter matrix A and (ii) identification of the reaction rate functions $f(x)$. Each of these problems has been studied extensively [16, 36, 23]. Several conditions for identifiability have also been derived. For example, Chen and Bastin [3] found necessary and sufficient conditions for identifiability of A in the case when full response of the system to the controls u and μ is available. Farina et al. [9] addressed the problem of identifying the reaction rate constants in $f(x)$ by expanding the system and linearizing about an equilibrium state and found that the Jacobian must be full rank and that knowledge of dynamical data for any time-dependent input to the system is essential. Craciun and Pantea [5] related the identifiability of chemical reaction network systems to the topology of the reaction network. Here we assume that the functions $f(x)$ are known and focus on task (i).

We begin in section 2 by presenting several definitions of identifiability and reviewing established theorems on identifiability for linear dynamical systems. In section 3, we expand on these results to provide a complete rigorous characterization of identifiability from a single trajectory for linear dynamical systems. More specifically, we discuss several equivalent characterizations of the identifiability criterion, which ultimately yield an identifiability condition solely based on geometric properties of the known trajectory, namely whether or not

the trajectory is confined to a proper subspace of the relevant phase space. This criterion provides practical utility, since it can be applied using what is known about the trajectory, without knowledge of the structure of the parameter matrix. Subsequently, we investigate the existence of a trajectory for which the parameter matrix is identifiable, obtaining a necessary and sufficient requirement for existence based on the properties of the coefficient matrix associated with the model. Several examples illustrate identifiability for various systems and initial conditions. In section 4, we briefly discuss some implications of our confinement result for partial identifiability and for identifiability when not all model variables are observable. In section 5, we extend our results to a broader class of dynamics by deriving necessary and sufficient conditions for identifiability of a nonlinear system that is linear in parameters. The sufficient condition again has geometrical character and refers to the confinement of an image of the trajectory in the space of reaction rates. In section 6, we discuss the problem of finding parameter values explicitly using discrete data and show that some linear models are identifiable from a complete trajectory but not from a finite set of data, and that the accuracy of parameter estimation is related to how significantly the available data deviate from confinement. The paper concludes with a brief summary of results and possible future directions in section 7.

2. Definitions and preliminaries. We consider a model defined as a linear dynamical system in which data for all of the state variables are available (i.e., $C = I$) and the set of inputs (controls) consists of the set of initial conditions

$$(2.1) \quad \begin{aligned} \dot{x}(t) &= Ax(t), \\ x(0) &= b. \end{aligned}$$

In (2.1), $x(t) \in \mathbb{R}^n$ is the state of the system at time t , the system parameters are the entries of the coefficient matrix $A \in \mathbb{R}^{n \times n}$, and $b \in \mathbb{R}^n$ is the initial condition. For clarity of exposition we will refer to the entire matrix A as the (matrix) parameter A . Analysis of linear systems of the form (2.1) is greatly simplified, since we have an explicit formula for their solutions, which we generally refer to as trajectories:

$$(2.2) \quad x(t; A, b) = e^{At}b = \sum_{j=0}^{\infty} \frac{A^j t^j}{j!} b.$$

In the context of this paper the term *model identifiability* is meant to represent the identifiability of the parameters of the model. In other words, we fix the model structure and ask whether the matrix parameter A can be uniquely determined from error-free data consisting of a trajectory or some subset thereof. This question is strongly related to whether, independently of the data, two distinct parameters can lead to identical solutions. The term *parameter distinguishability* has been used in this context in the literature [4, 14]. It is clear that these characteristics depend not only on the properties of the system, but also on the set of possible parameters being considered for comparison. The identifiability problem should therefore be reformulated as determining whether, on a particular subset of $\mathbb{R}^{n \times n}$, the map from parameter space to solution space is injective. The extreme cases are to allow parameters from the full parameter space $\mathbb{R}^{n \times n}$ and to restrict to a single point in the parameter space.

In the latter case, identifiability is trivial since there are no other competing parameters to consider.

The initial condition b determines the trajectory (2.2) of the system (2.1) uniquely for any given A . It needs to be taken into consideration, since we may or may not know or be able to select the initial values of the states represented in a model before running an experiment, and hence we may wish to consider identifiability from a given initial condition or from a larger set of initial conditions. We will discuss here three progressively more constrained definitions of identifiability. In the first definition, we allow for an initial condition to be chosen to aid identifiability.¹

Definition 2.1. *Model (2.1) is identifiable in $\Omega \subseteq \mathbb{R}^{n \times n}$ if and only if for all $A, B \in \Omega$, $A \neq B$, there exists $b \in \mathbb{R}^n$ such that $x(\cdot; A, b) \neq x(\cdot; B, b)$.*²

For identifiability in the sense of Definition 2.1, we immediately have the following result.

Theorem 2.2. *Model (2.1) is identifiable in $\mathbb{R}^{n \times n}$.*

Proof. Consider the negation of the statement: model (2.1) is not identifiable in Ω if there exist $A, B \in \Omega$, $A \neq B$, such that for all $b \in \mathbb{R}^n$, for all $t \in \mathbb{R}$, $x(t; A, b) = x(t; B, b)$. This negation cannot hold on a set Ω containing distinct elements A and B , since if $x(t; A, b) = x(t; B, b)$ for all $b \in \mathbb{R}^n$, for all $t \in \mathbb{R}$, then differentiation of (2.2) and evaluation at $t = 0$ give $Ab = Bb$ for all b . Applying this result to n linearly independent choices of b gives $AW = BW$ for the invertible matrix W , with the selected b vectors as its columns, and hence $A = B$. As a consequence, we see that for any two distinct linear systems (2.1), there is an initial condition $b \in \mathbb{R}^n$ that will distinguish the solutions. ■

Theorem 2.2 implies that if we are free to choose the initial condition, then any two linear models with distinct parameter matrices in $\mathbb{R}^{n \times n}$ can be distinguished because we can choose the initial condition b such that the corresponding trajectories will be distinct. In practice, however, control over the initial condition may not be available, and more restrictive definitions of identifiability are needed.

Identifiability from a single trajectory is addressed by the following definition.

Definition 2.3. *Model (2.1) is identifiable in Ω from $b \in \mathbb{R}^n$ if and only if for all $A, B \in \Omega$ with $A \neq B$, it holds that $x(\cdot; A, b) \neq x(\cdot; B, b)$.*

Since in most practical applications with biological data, the initial condition is fixed and cannot be chosen at will, most of our results in section 3 relate to identifiability in the sense of Definition 2.3. It is also of interest, however, to consider the problem of identifiability from any initial condition.

Definition 2.4. *Model (2.1) is unconditionally identifiable in Ω if and only if for all $A, B \in \Omega$, $A \neq B$ implies that for each nonzero $b \in \mathbb{R}^n$, $x(\cdot; A, b) \neq x(\cdot; B, b)$.*

Sufficient conditions for unconditional identifiability will be revealed at the end of section 3.

We will now show that necessary and sufficient conditions for identifiability of model (2.1) in the sense of Definition 2.3 follow from published results of Thowsen [33] and Bellman and

¹The definitions above employ the term *identifiability* in the same sense in which *global identifiability* has been used in some literature (e.g., [33]) to distinguish this concept from that of *local identifiability*, which focuses on a small neighborhood of a given parameter. However, since Ω may be just a proper subset of the full parameter space, the use of the word *global* in this context could be misleading, and thus we omit it.

²The notation $x(\cdot; A, b) \neq x(\cdot; B, b)$ indicates that there exists at least one $t > 0$ such that $x(t; A, b) \neq x(t; B, b)$. Analogously, $x(\cdot; A, b) = x(\cdot; B, b)$ indicates that $x(t; A, b) = x(t; B, b)$ for all t .

Åström [2]. First, suppose that Ω is an open set, in which case we have the following.

Theorem 2.5. For $\Omega \subset \mathbb{R}^{n \times n}$ open and a fixed $b \in \mathbb{R}^n$, model (2.1) is identifiable in Ω from b if and only if $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent for all $A \in \Omega$.

Remark. An alternative, but equivalent, formulation would replace the condition of linear independence with the condition that the matrix $[b|Ab|\dots|A^{n-1}b]$ has full rank, which would bring the wording closer to that of Bellman and Åström.

We will obtain Theorem 2.5 from the following theorem, presented by Thowsen [33] (and simplified later by Gargash and Mital [12]), which we state without proof.

Theorem 2.6. Let $\Omega \subset \mathbb{R}^{n \times n}$ be a set of matrices such that $\Omega = \{\sum_{j=1}^p A_j \alpha_j | \alpha \in \Theta\}$, where $A_j \in \mathbb{R}^{n \times n}$ for all j and Θ is an open subset of \mathbb{R}^p . Fix $b \in \mathbb{R}^n$ and let

$$G(A) = \begin{bmatrix} A_1 b & \dots & A_p b \\ A_1 A b & \dots & A_p A b \\ \vdots & \ddots & \vdots \\ A_1 A^{n-1} b & \dots & A_p A^{n-1} b \end{bmatrix}_{n^2 \times p}.$$

Model (2.1) is identifiable in Ω from b if and only if $\text{rank } G(A) = p$ for all $A \in \Omega$.

Proof of Theorem 2.5. Consider the decomposition of A into elementary matrices, $A = \sum_{i,j=1}^n E_{ij} a_{ij}$, where $\{E_{ij}\}$ is the standard basis for $n \times n$ matrices, and the set Θ is equal to \mathbb{R}^{n^2} . Under this decomposition, the matrix $G(A)$ in Theorem 2.6 takes the special form

$$G(A) = \begin{bmatrix} \overline{E_{11}b} & \overline{E_{12}b} & \dots & \overline{E_{nn}b} \\ \overline{E_{11}Ab} & \overline{E_{12}Ab} & \dots & \overline{E_{nn}Ab} \\ \vdots & \vdots & \ddots & \vdots \\ \overline{E_{11}A^{n-1}b} & \overline{E_{12}A^{n-1}b} & \dots & \overline{E_{nn}A^{n-1}b} \end{bmatrix} = \begin{bmatrix} b^T & 0 & \dots & 0 \\ 0 & b^T & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & b^T \\ \overline{(Ab)^T} & 0 & \dots & 0 \\ 0 & (Ab)^T & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ \overline{(A^{n-1}b)^T} & \overline{(A^{n-1}b)^T} & \dots & \overline{(A^{n-1}b)^T} \\ 0 & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \dots & \overline{(A^{n-1}b)^T} \end{bmatrix}_{n^2 \times n^2}.$$

Let

$$\tilde{G}(A) = \begin{bmatrix} b^T \\ (Ab)^T \\ \vdots \\ (A^{n-1}b)^T \end{bmatrix}_{n \times n}.$$

With this definition, $\text{rank } G(A) = n \cdot \text{rank } \tilde{G}(A)$. Hence, $\text{rank } G(A) = n^2$ if and only if $\text{rank } \tilde{G}(A) = n$, which holds if and only if $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent. ■

Next, we note that the sufficiency of the condition of linear independence of $\{b, Ab, \dots, A^{n-1}b\}$ is not tied to the requirement that Ω be an open set. This observation

becomes obvious from a reformulation of a result of Bellman and Åström obtained for the control system (1.1) [2].

Theorem 2.7. *For $\Omega \subset \mathbb{R}^{n \times n}$ and a fixed $b \in \mathbb{R}^n$, if $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent for all $A \in \Omega$, then model (2.1) is identifiable in Ω from b .*

Let us define, for a fixed $b \in \mathbb{R}^n$, the set $\Omega_b = \{A \in \mathbb{R}^{n \times n} : \{b, Ab, \dots, A^{n-1}b\} \text{ are linearly independent}\}$. This set has a special significance for the identifiability of the model from b in view of the following corollary of Theorem 2.5.

Corollary 2.8. *Let $b \in \mathbb{R}^n$ be fixed. The set Ω_b is the largest open set in which model (2.1) is identifiable from b .*

Proof. Clearly, by Theorem 2.5, any open set $\Omega \subseteq \mathbb{R}^{n \times n}$ in which the model (2.1) is identifiable from b satisfies $\Omega \subseteq \Omega_b$. That Ω_b is an open set follows from Corollary 3.9, which is stated at the end of the next section. ■

In view of Theorem 2.5, the set Ω_b can be employed to characterize sets in which the model (2.1) is unconditionally identifiable.

Corollary 2.9. *Let $\Omega \subseteq \mathbb{R}^{n \times n}$ be open. Model (2.1) is unconditionally identifiable in Ω if and only if $\Omega \subseteq \bigcap_{b \in \mathbb{R}^n \setminus \{0\}} \Omega_b$.*

Although the conditions stated in Theorems 2.5 and 2.7 and Corollary 2.9 reveal the properties of sets in which the model is identifiable, their practical applicability is limited because we cannot test whether the system obeys the condition $A \in \Omega_b$ unless we know the matrix parameter A . In the next section, we derive a more practical condition based on the properties of a model trajectory. That is, let $\gamma(A, b) = \{x(t; A, b) : t \in \mathbb{R}\} \subset \mathbb{R}^n$ denote the orbit of the model (2.1) corresponding to the trajectory with initial condition b . The condition that we obtain specifies, for any given trajectory, whether or not we can identify the model from that trajectory. Specifically, we show that the model (2.1) is identifiable from a trajectory if and only if the orbit corresponding to that trajectory is not confined to a proper subspace of \mathbb{R}^n .

3. Identifiability conditions based on trajectory behavior or coefficient matrix properties.

3.1. Analysis. Now that we have established that the identifiability of the model from a fixed initial condition b is characterized by the linear independence of the set $\{b, Ab, \dots, A^{n-1}b\}$, we will discuss certain equivalent characterizations of that property that reveal its implications for the geometrical behavior of the corresponding orbit.

We will denote the space formed by linear combinations of the vectors $\{b, Ab, \dots, A^{n-1}b\}$ as $K_n(A, b) = \text{span}\{b, Ab, \dots, A^{n-1}b\}$. This space is the Krylov subspace generated by A and b [39], which is also called the A -cyclic subspace generated by b [17] and is the range of the controllability matrix $[b \mid Ab \mid \dots \mid A^{n-1}b]$.

Lemma 3.1. *$\{b, Ab, \dots, A^{n-1}b\}$ are linearly dependent or, equivalently, $\dim(K_n(A, b)) < n$, if and only if b is contained in an A -invariant proper subspace of \mathbb{R}^n .*

Proof. Recall that a space V is called A -invariant if for all $v \in V$, $Av \in V$. For the forward direction, assume that $\dim(K_n) < n$. Certainly, $b \in K_n$. The result thus follows from showing that K_n is invariant under A . To establish this invariance, let $x \in K_n$. Then, $x = c_0b + c_1Ab + \dots + c_{n-1}A^{n-1}b$ and $Ax = c_0Ab + c_1A^2b + \dots + c_{n-1}A^n b$. By the Cayley–Hamilton theorem, A^n can be written as a linear combination of $I, A, A^2, \dots, A^{n-1}$. Hence,

$Ax = d_0b + d_1Ab + \dots + d_{n-1}A^{n-1}b \in K_n$, as desired.

The reverse direction follows immediately, as $b \in V$ for an A -invariant set V with $\dim(V) < n$ implies that, since $K_n \subseteq V$, $\dim(K_n) \leq \dim(V) < n$ as well. ■

Lemma 3.2. *Orbit $\gamma(A, b)$ is confined to a proper subspace of \mathbb{R}^n if and only if b is contained in an A -invariant proper subspace of \mathbb{R}^n .*

Proof. For the backward direction, let $V \subset \mathbb{R}^n$ be an A -invariant proper subspace of \mathbb{R}^n . If $b \in V$, then $A^j b \in V$ for all $j = 0, 1, \dots$. Hence,

$$x(t; A, b) = e^{At}b = \sum_{j=0}^{\infty} \frac{t^j A^j b}{j!} \in V$$

for all $t \in \mathbb{R}$. So, $\gamma(A, b) \subseteq V$.

For the forward direction, assume that $\gamma(A, b)$ is confined to a proper subspace of \mathbb{R}^n . Then there exists $v \neq 0 \in \mathbb{R}^n$ such that $v^T x(t; A, b) = 0$ for all $t \in \mathbb{R}$. Since $x(t; A, b) = e^{At}b$, we have $v^T e^{At}b = 0$ for all $t \in \mathbb{R}$ as well. Furthermore, differentiation gives $v^T A e^{At}b = 0, \dots, v^T A^j e^{At}b = 0$ for all $t \in \mathbb{R}$, for $j = 0, 1, \dots, n-1$. In particular, for $t = 0$, $v^T A^j b = 0$ for $j = 0, 1, \dots, n-1$. Hence, $v^T [b \ Ab \ \dots \ A^{n-1}b] = 0$. Since $v \neq 0$, $[b \ Ab \ \dots \ A^{n-1}b]$ cannot have full rank, and thus Lemma 3.1 gives the desired result. ■

In light of Theorem 2.5, Lemmas 3.1 and 3.2 yield the following corollary.

Corollary 3.3. *For $\Omega \subset \mathbb{R}^{n \times n}$ open, model (2.1) is identifiable in Ω from b if and only if for all $A \in \Omega$, $\gamma(A, b)$ is not confined to a proper subspace of \mathbb{R}^n .*

Combining the above results, we obtain one of the main results of this paper, which is a concise relation between the uniqueness of the parameters of the model (2.1) and the geometric structure of its orbits.

Theorem 3.4. *For the model (2.1) there exists no $B \in \mathbb{R}^{n \times n}$ with $A \neq B$ such that $x(\cdot; A, b) = x(\cdot; B, b)$ if and only if the orbit $\gamma(A, b)$ is not confined to a proper subspace of \mathbb{R}^n .*

Proof. Suppose that the orbit $\gamma(A, b)$ of model (2.1) is not confined to a proper subspace of \mathbb{R}^n , i.e., the parameter matrix A that supplied the orbit obeys $A \in \Omega_b$. If $B \in \Omega_b$ with $A \neq B$, then the trajectories $x(t; A, b)$ and $x(t; B, b)$ are distinct as a result of the identifiability of the model (2.1) in Ω_b from b . If, on the other hand, $B \notin \Omega_b$, then the set of vectors $\{b, Bb, \dots, B^{n-1}b\}$ is linearly dependent, and hence Lemmas 3.1 and 3.2 imply that the orbit $\gamma(B, b)$ is confined to a proper subspace of \mathbb{R}^n . Therefore $x(t; B, b)$ is not equal to $x(t; A, b)$. Conversely, if $\gamma(A, b)$ is confined to a proper subspace S of \mathbb{R}^n , then $b \in S$ and S is an A -invariant subspace. Let $B \neq A$ be an $n \times n$ matrix such that the restrictions of A and B to S are identical; then $x(\cdot; A, b) = x(\cdot; B, b)$. ■

Theorem 3.4 implies that the parameter matrix of model (2.1) is uniquely defined by any trajectory that has an orbit that is not confined to a proper subspace. It is a practical result that provides immediate information about the possibility of model identification from a single trajectory while relying solely on the geometrical description of the trajectory. Note that the full trajectory is needed to identify the matrix A since the orbit provides no information about the transit time.

With this relation of identifiability to trajectory behavior, we can also observe that identifiability is invariant under similarity transformation.

Corollary 3.5. *Model (2.1) is identifiable in $\Omega \in \mathbb{R}^{n \times n}$ from $b \in \mathbb{R}^n$ if and only if model (2.1) is identifiable in $\tilde{\Omega}_S = \{C = SAS^{-1} : A \in \Omega\}$ from Sb for all $S \in \mathbb{R}^{n \times n}$ invertible.*

Proof. For the forward direction, assume that model (2.1) is identifiable in Ω from b and let $A \in \Omega$. Let S be an invertible $n \times n$ matrix and define $C = SAS^{-1}$. Assume C and D yield the same trajectory for the initial condition Sb . Since C and D yield the same trajectory, $e^{Ct}Sb = e^{Dt}Sb$, and hence $e^{S^{-1}CSt}b = e^{S^{-1}DSt}b$ and $e^{At}b = e^{S^{-1}DSt}b$, for all $t \in \mathbb{R}$. Since A is identifiable from b , $A = S^{-1}DS$. So, $SAS^{-1} = D$, which yields $C = D$. Hence, model (2.1) is identifiable in Ω from Sb for all $S \in \mathbb{R}^{n \times n}$ invertible. The reverse direction follows similarly. ■

Having related identifiability on Ω to the linear independence of $\{b, Ab, \dots, A^{n-1}b\}$ for $A \in \Omega$, it is natural to ask whether for every parameter matrix A the set Ω_b is nonempty, i.e., whether for every A there is an initial condition b such that $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent. We will now show that such a b need not necessarily exist, and hence there are models (2.1) that cannot be identified from any single trajectory.

The following result determines under what conditions on the structure of A the set Ω_b is nonempty.

Theorem 3.6. *There exists b such that $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent if and only if A has only one Jordan block for each of its eigenvalues.*

Proof. The result follows from the cyclic decomposition theorem for square matrices. In particular, a vector b such that $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent is called a cyclic vector for A . A corollary of the cyclic decomposition theorem [17, p. 237] states that A has a cyclic vector if and only if the characteristic and minimal polynomials for A are identical, which holds if and only if the matrix A has only one Jordan block for each of its eigenvalues.

This condition results from the fact that a nilpotent matrix $(J - \lambda I)$, where J is a $k \times k$ elementary Jordan matrix with eigenvalue λ , has a minimal polynomial of the form x^k , and furthermore the minimal polynomial of A is of order $m = \sum_{i=0}^s k_i$, where k_i is the size of the largest Jordan block corresponding to the eigenvalue λ_i of A , with the sum being taken over all distinct eigenvalues of A . Now, the property that A has only one Jordan block for each of its eigenvalues holds if and only if $m = \sum_{i=0}^s k_i = n$, which is equivalent to the characteristic and minimal polynomials for A being identical. ■

An additional proposition elucidates a certain structure for b that is useful for attaining identifiability.

Proposition 3.7. *For a $k \times k$ elementary Jordan matrix J with eigenvalue λ and vector $b \in \mathbb{R}^k$ with $b_k \neq 0$, $(J - \lambda I)^m b = 0$ if and only if $m \geq k$.*

Proof. The backward direction is immediate since for $m \geq k$, $(J - \lambda I)^m = 0$. The forward direction follows because for $p < k$, $(J - \lambda I)^p b = [b_{p+1}, \dots, b_k, 0, \dots, 0]^T \neq 0$ whenever $b_k \neq 0$. ■

Theorem 3.6 establishes the existence of b from which model (2.1) is identifiable under the linear independence condition and Proposition 3.7 specifies a structure for such b . In particular, for such b , the component corresponding to each $k_i \times k_i$ Jordan block J_i of A must not be annihilated by $(J_i - \lambda_i I)^{k_i-1}$. For diagonalizable A , this result reduces to the requirement that such b has a nonzero component in each eigenspace of A (see Lee [25]). This

property, sometimes referred to in control theory as persistent excitability for systems, has been discussed in [1, 26]. A result closely related to Theorem 3.6 can be found in [24]. More interesting examples arise for matrices that do not have distinct real eigenvalues, and these examples are discussed below.

Another helpful characterization of the linear independence of $\{b, Ab, \dots, A^{n-1}b\}$ can be stated in terms of left eigenvectors of A , using the well-known PBH (Popov–Belevitch–Hautus) controllability test for linear systems [21].

Theorem 3.8. *The vectors $\{b, Ab, \dots, A^{n-1}b\}$ are linearly independent if and only if there is no left eigenvector of A orthogonal to b .*

In our case we employ this theorem for the following result.

Corollary 3.9. *For $\Omega \subset \mathbb{R}^{n \times n}$ open, model (2.1) is identifiable in Ω from b if and only if there is no left eigenvector of A orthogonal to b for any $A \in \Omega$.*

Corollary 3.9 provides a new criterion for identifiability of the model (2.1) and can be used to characterize the set Ω_b from section 2: $\Omega_b = \{A \in \mathbb{R}^{n \times n} : w^T A = \lambda w \Rightarrow w^T b \neq 0\}$ defines the largest open set in which the model is identifiable from b . Likewise,

$$\bigcap_{b \in \mathbb{R}^n \setminus \{0\}} \Omega_b = \{A \in \mathbb{R}^{n \times n} : w^T A = \lambda w \Rightarrow w^T b \neq 0 \text{ for all } b \in \mathbb{R}^n \setminus \{0\}\}$$

defines the largest set Ω in which the model is unconditionally identifiable.

For matrices of even dimensions we can use this representation to define sets Ω in which model (2.1) is unconditionally identifiable. For example, let $\Omega_c = \{A \in \mathbb{R}^{2 \times 2} : A \text{ has a complex pair of eigenvalues}\}$. Any left eigenvector w of a matrix A in this set has nonzero imaginary part, and hence w is not orthogonal to any vector $b \in \mathbb{R}^2$. By Corollary 3.9, $\{b, Ab\}$ are linearly independent (over \mathbb{R}), and hence the model is unconditionally identifiable in Ω_c by Corollary 2.9.

Interestingly, matrices with odd dimensions always have a real-valued left eigenvector w , and our results imply that there is no set $\Omega \subseteq \mathbb{R}^{(2n+1) \times (2n+1)}$ in which model (2.1) is unconditionally identifiable, since in that case one can find $b \in \mathbb{R}^{2n+1}$ such that $w^T b = 0$.

3.2. Examples. We will now discuss several examples of identifiability in Ω from b for various sets Ω in parameter space and initial conditions b . We start by discussing certain special choices of Ω selected based on the properties we have established as important for identifiability. Subsequently, we consider how the behaviors of trajectories of (2.1) for some particular matrices relate to our results.

As we have discussed, $\Omega_b = \{A \in \mathbb{R}^{n \times n} : \{b, Ab, \dots, A^{n-1}b\} \text{ are linearly independent}\} = \{A \in \mathbb{R}^{n \times n} : w^T A = \lambda w \Rightarrow w^T b \neq 0\}$ is the largest open set in which the model is identifiable from b . Thus, identifiability from b holds in any subset of Ω_b , regardless of whether that set is open. Also, we can define a larger (nonopen) set Ω in which we have identifiability from b by extending Ω_b in trivial ways, such as by combining Ω_b with a single matrix $A_0 \in \Omega_b^c$. For $\Omega = \Omega_b \cup \{A_0\}$, the model will be identifiable in Ω from b because the orbit $\gamma(A_0, b)$ is confined to a proper subspace of \mathbb{R}^n and will not coincide with any orbit for a matrix in Ω_b (which cannot be so confined). This type of trivial extension could be continued with a sequence of matrices that have confined trajectories for the initial condition b , but with no two solutions that are the same. On the other hand, define $\Omega = \mathbb{R}^{n \times n} \setminus \Omega_b$, which is not open, such that Theorem 2.5 and Corollary 3.3 do not apply. It is clear that any two distinct matrices A, B

with the same eigenvalues that share b as an eigenvector for the same eigenvalue will yield the same solution, $x(t; A, b) = x(t; B, b)$ for all $t \in \mathbb{R}$, and such matrices can be found in Ω . Hence, by Definition 2.3, model (2.1) is not identifiable in Ω from b . This argument shows that we do not have identifiability from b on the complement of Ω_b .

Next, define $\Omega_J = \{A \in \mathbb{R}^{n \times n} : A \text{ has more than one Jordan block for some eigenvalue}\}$. From Theorem 3.6 we know that for any $A \in \Omega_J$, $\{b, Ab, \dots, A^{n-1}b\}$ are linearly dependent for any $b \in \mathbb{R}^n$. Ω_J is a set of measure zero and is not open in $\mathbb{R}^{n \times n}$, however, so Theorem 2.5 does not apply to the identifiability of Ω_J . We can again appeal directly to Definition 2.3 to show that the model is not identifiable in Ω_J from b for any choice of $b \in \mathbb{R}^n$. For example, in $\mathbb{R}^{3 \times 3}$, fix $b = [1, 1, 1]^T$. Let

$$A = \begin{bmatrix} -2 & 0 & 0 \\ 0 & -2 & 0 \\ 2 & -1 & -3 \end{bmatrix} \quad \text{and} \quad B = \begin{bmatrix} -2 & 0 & 0 \\ 1 & -2.5 & -0.5 \\ 1 & -0.5 & -2.5 \end{bmatrix}.$$

A and B both have the Jordan matrix

$$D = \begin{bmatrix} -2 & 0 & 0 \\ 0 & -2 & 0 \\ 0 & 0 & -3 \end{bmatrix},$$

which has two Jordan blocks for $\lambda = -2$, so $A, B \in \Omega_J$. A and B also share b as an eigenvector for $\lambda = -2$. So, $x(t; A, b) = x(t; B, b)$ for all $t \in \mathbb{R}$, but $A \neq B$; hence by Definition 2.3, model (2.1) is not identifiable in Ω_J from b . An analogous pair of matrices that violate identifiability can be obtained for any $b \in \mathbb{R}^n$ by simply choosing two matrices with the same Jordan form, having more than one Jordan block for some eigenvalue and sharing b as an eigenvector for that eigenvalue. In fact, $\Omega_J \cap \Omega_b = \emptyset$. So it is straightforward to construct sets $\Omega \subseteq \mathbb{R}^{n \times n}$ on which the model is not identifiable from b , using elements of Ω_J .

To illustrate the application of Theorem 3.4, we will now discuss several examples of 2×2 and 3×3 matrices. For each, we consider under what conditions they have confined trajectories and correspondingly, for what initial conditions b we have $A \in \Omega_b$.

Figure 1 shows the phase plane for each of four matrices with trajectories plotted for a few different initial conditions. Matrix

$$A_a = \begin{bmatrix} -2 & 1 \\ 1 & -2 \end{bmatrix}$$

has distinct eigenvalues. For any initial condition b lying on an eigenvector, the corresponding orbit will be confined to a proper subspace of \mathbb{R}^2 . These are the only initial conditions that lead to confined trajectories, so $A_a \in \Omega_b$ for all b not on an eigenvector. This observation is consistent with the requirements on the structure of b for identifiability, as given in Proposition 3.7 and the associated discussion. That is, if we were to consider A_a and b written in the basis in which A_a is in Jordan form (diagonalized), then b would have a zero component if and only if it were an eigenvector.

Matrix

$$A_b = \begin{bmatrix} -5/2 & 1/2 \\ -1/2 & -3/2 \end{bmatrix}$$

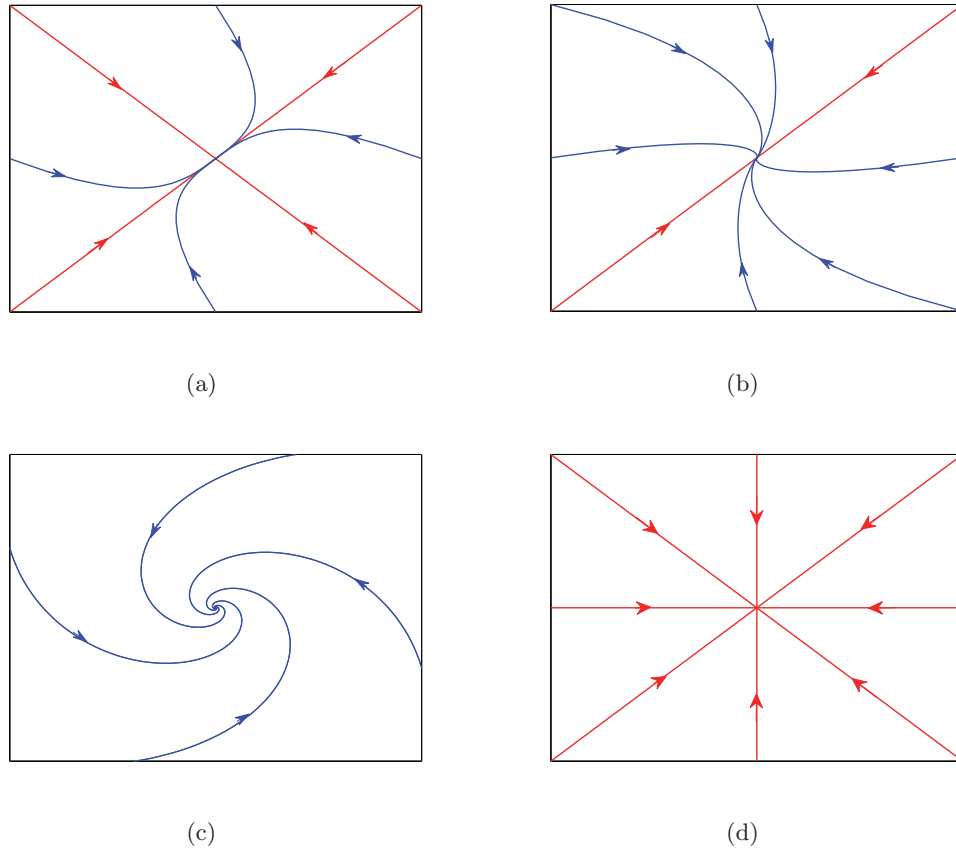


Figure 1. Phase portraits for system (2.1) generated by four matrices with different eigenvalue structures. In this and subsequent figures, red curves are trajectories from which the corresponding model is not identifiable, while blue curves are trajectories that yield identifiability. Matrices A_a, A_b, A_c, A_d , as given in the text, were used to generate panels (a), (b), (c), and (d), respectively.

has a repeated eigenvalue of -2 and is not diagonalizable. Since it has only one Jordan block, the requirement on b for the orbit to not be confined is that in the basis in which A_b is given in Jordan form, b must have a nonzero component in the last entry. Equivalently, this requirement means that b cannot lie on the genuine eigenvector $[1, 1]^T$. From the phase plane it is easy to see that the orbit arising from any initial condition lying on this eigenvector will be confined to a proper subspace of \mathbb{R}^2 . So, $A_b \in \Omega_b$ for all b not on the genuine eigenvector.

Matrix

$$A_c = \begin{bmatrix} -2 & -3 \\ 3 & -2 \end{bmatrix}$$

has a complex conjugate pair of eigenvalues. In this circumstance, \mathbb{R}^2 has no nontrivial A_c -invariant proper subspaces. Therefore, the orbit from any nonzero initial condition is not confined to a proper subspace of \mathbb{R}^2 . This conclusion is clear from the phase plane. Hence, $A_c \in \Omega_b$ for all $b \in \mathbb{R}^2 \setminus \{0\}$.

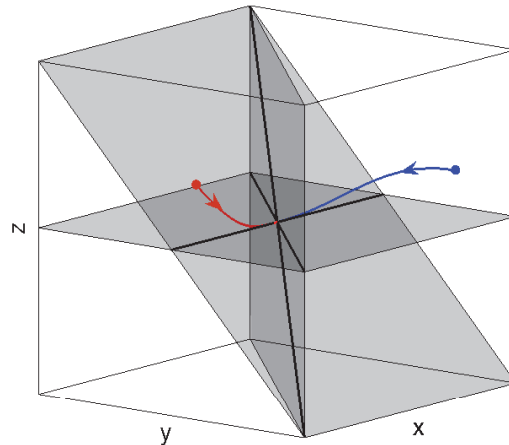


Figure 2. Phase space structures for matrix A_e .

Finally, matrix

$$A_d = \begin{bmatrix} -2 & 0 \\ 0 & -2 \end{bmatrix}$$

represents the case of a repeated Jordan block for $\lambda = -2$. This is a star-shaped system in which every initial condition lies on an eigenvector, and hence every orbit is confined to a proper subspace. Thus, in this case, there exists no b such that $A_d \in \Omega_b$.

Figure 2 corresponds to the matrix

$$A_e = \begin{bmatrix} -1 & -3 & 2 \\ 0 & -4 & 2 \\ 0 & 0 & -2 \end{bmatrix},$$

which has three distinct real eigenvalues. The corresponding eigenvectors are plotted in black and the planes represent the two-dimensional invariant subspaces spanned by pairs of eigenvectors. Any initial condition lying in one of these planes will have a zero component (in the basis in which A is diagonalized) and the corresponding orbit will be confined to that plane. Any initial condition outside of these planes will have an orbit that is not confined to a proper subspace. Hence, $A_e \in \Omega_b$ for all b not lying in one of the planes. This example is the three-dimensional analogue of A_a but is more interesting because for A_e to be in Ω_b , not only must b not lie on an eigenvector of A_e , but also it may not land on any two-dimensional plane spanned by two eigenvectors of A_e .

Figure 3 was generated from

$$A_f = \begin{bmatrix} -0.2 & -1 & 0 \\ 1 & -0.2 & 0 \\ 0 & 0 & -0.3 \end{bmatrix},$$

which has a complex conjugate pair of eigenvalues and one real eigenvalue: $\lambda_{1,2} = -0.2 \pm i$ and $\lambda_3 = -0.3$. Any orbit with an initial condition on the xy plane will stay confined to that

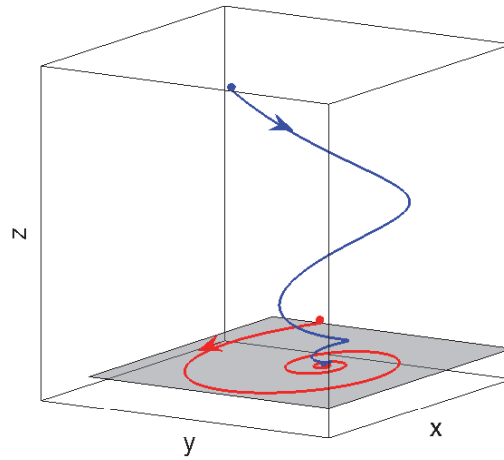


Figure 3. Phase space structures for matrix A_f .

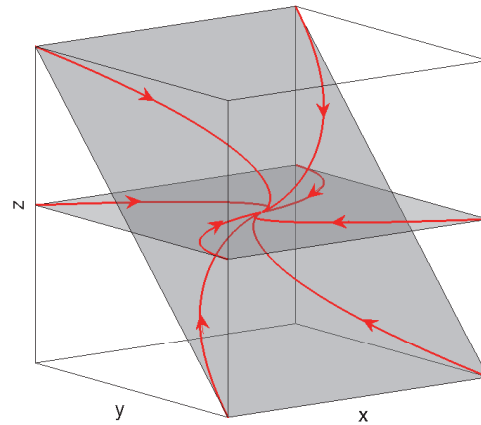


Figure 4. Phase space structures for matrix A_g .

plane. This is the only proper A_f -invariant subspace of \mathbb{R}^3 . It is clear from the phase plane that any orbit from an initial condition outside of this plane will not be confined to a proper subspace. Hence, $A_f \in \Omega_b$ for all b not lying in the xy plane.

Figure 4 corresponds to

$$A_g = \begin{bmatrix} -1 & 1 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & -1 \end{bmatrix},$$

which has two Jordan blocks for the eigenvalue $\lambda = -1$. Because of the repeated block, the orbit from any initial condition is confined to a proper subspace of \mathbb{R}^3 . Hence, there is no $b \in \mathbb{R}^3$ such that $A_g \in \Omega_b$. This conclusion can also be verified from Theorem 3.8. The left eigenvectors of A_g are $x_1 = [0, 1, 0]$, $x_2 = [0, 0, 1]$. For an arbitrary $b = [b_1, b_2, b_3]^T$,

there exists a left eigenvector, namely, $x = [0, -b_3, b_2]$, such that $xb = 0$. Thus, Theorem 3.8 implies that $\{b, A_g b, A_g^2 b\}$ are linearly dependent for all $b \in \mathbb{R}^3$.

4. Partial identifiability from a confined trajectory.

4.1. Analysis. The examples presented in the last section bring up the following question: if the model (2.1) is not identifiable from a single trajectory, how much information about A can be obtained from such a trajectory? The answer is provided by a natural generalization of the results leading to Theorem 3.4.

Theorem 4.1. *Suppose V is a proper linear subspace of \mathbb{R}^n invariant under A with $k = \dim V$. Let $A|_V$ denote the linear operator on V that is obtained as a restriction of A to the subspace V . The following statements are equivalent:*

- (i) V is the minimal A -invariant subspace such that $b \in V$.
- (ii) $\{b, Ab, \dots, A^{k-1}b\}$ are linearly independent in V .
- (iii) The orbit $\gamma(A, b)$ is in V and is not confined to a proper subspace of V .
- (iv) There exists no $B \in \mathbb{R}^{n \times n}$ such that $B|_V \neq A|_V$ and $x(\cdot; B, b) = x(\cdot; A, b)$.

Proof. The proof of the theorem can be constructed by a generalization of the proofs discussed above. In particular, proof of the equivalence of (i) and (ii) is analogous to the proof of Lemma 3.1, proof of the equivalence of (i) and (iii) is analogous to the proof of Lemma 3.2, and proof of the equivalence of (iii) and (iv) is analogous to the proof of Theorem 3.4. ■

It may be of concern that the subspace V depends on the matrix to be identified and hence is not known in advance. However, in view of statement (iii) of Theorem 4.1, the subspace V is clearly defined by the orbit $\gamma(A, b)$ as the smallest linear subspace of \mathbb{R}^n containing $\gamma(A, b)$. Therefore, given the trajectory $x(t; A, b)$ one can identify both the invariant subspace V and the restriction $A|_V$ but no more information about the model (2.1).

The restriction operator $A|_V$ is identical to a submatrix of A if the subspace V is a span of vectors from the standard basis $\{e_1, e_2, \dots, e_n\}$ of \mathbb{R}^n . In general, $A|_V$ can be decomposed using a basis $\{v_1, v_2, \dots, v_k\}$ of V as follows:

$$(4.1) \quad A|_V = \sum_{i=1}^k \sum_{j=1}^k \alpha_{ij} A_{ij},$$

where A_{ij} are rank-1 matrices such that $A_{ij}v_j = v_i$, $A_{ij}v_m = 0$ for $m \neq j$, and α_{ij} with $i, j = 1, \dots, k$ are determined by the trajectory $x(t; A, b)$. By completing $\{v_1, v_2, \dots, v_k\}$ to a basis $\{v_1, v_2, \dots, v_n\}$ of \mathbb{R}^n one can write the unidentified part of the parameter matrix, $A - A|_V$, as

$$(4.2) \quad A - A|_V = \sum_{i=1}^n \sum_{j=k+1}^n \alpha_{ij} A_{ij} + \sum_{i=k+1}^n \sum_{j=1}^k \alpha_{ij} A_{ij},$$

where the remaining coefficients α_{ij} are free parameters.³

³The matrix $[A]_{\mathcal{B}} = [\alpha_{ij}]$ is comprised of the coefficients of A in the basis $\mathcal{B} = \{v_1, v_2, \dots, v_n\}$.

The full parameter matrix A can be reconstructed from several confined trajectories of the system. The minimum number of such trajectories needed to fully identify A depends on the number and relative positions of the subspaces to which those trajectories are confined.

As a final comment in this section let us note that the results above can also be used to characterize the case in which the model variables are not fully observable, i.e., the case

$$(4.3) \quad \begin{aligned} \dot{x}(t) &= Ax(t), & x(0) &= b, \\ y(t) &= Cx(t), \end{aligned}$$

in which the known matrix C is not of rank n . Suppose that the orbit $\gamma(A, b)$ of the trajectory $x(t; A, b)$ of the system is confined to a subspace V . Suppose, in addition, that $\dim V \leq \text{rank } C$ and that $V \cap \text{null } C = 0$. Then one can construct an invertible map \tilde{C} that takes V into range C and determine $x(t; A, b)$ from the observed image of the trajectory $y(t; A, b, C)$ as $x(t; A, b) = \tilde{C}^{-1}y(t; A, b, C)$. Using the procedure above, one can then identify $A|_V$ from the trajectory $x(t; A, b)$. Unfortunately, the information on whether $x(t; A, b)$ is confined and to which subspace cannot be directly ascertained by observing $y(t; A, b, C)$.

4.2. Example. The matrix A_e defined in the last section has a two-dimensional invariant subspace $V = \text{span}\{v_1, v_2\}$ where $v_1 = [1, 1, 0]^T$, $v_2 = [0, 0, 1]^T$. Trajectory $x(t; A_e, b)$ starting at $b = [-1, -1, 1]^T$ is confined to V but not to any lower-dimensional subspace of V . In accordance with Theorem 4.1, we can use the trajectory $x(t; A_e, b)$ to identify $A_e|_V$. Specifically, we transform A_e into the coordinate system with the basis $\mathcal{B} = \{v_1, v_2, v_3\}$, where $v_3 = [0, 1, 0]^T$, as

$$[A_e]_{\mathcal{B}} = \begin{bmatrix} -4 & 2 & -3 \\ 0 & -2 & 0 \\ 0 & 0 & -1 \end{bmatrix}.$$

The expansion in the basis $\{v_1, v_2\}$ of the restriction $A_e|_V$ is given by the upper left 2×2 submatrix of $[A_e]_{\mathcal{B}}$.

Now, for any matrix B with invariant subspace V and such that $B|_V = A_e|_V$, the trajectory $x(t; B, b)$ is identical to $x(t; A_e, b)$. Each such matrix, in the coordinates of V , must agree with the upper left 2×2 block of $[A_e]_{\mathcal{B}}$ and take the form

$$[B]_{\mathcal{B}} = \begin{bmatrix} -4 & 2 & \beta_{13} \\ 0 & -2 & \beta_{23} \\ 0 & 0 & \beta_{33} \end{bmatrix}$$

for some $\beta_{13}, \beta_{23}, \beta_{33} \in \mathbb{R}$. Transforming $[B]_{\mathcal{B}}$ into the standard coordinate system yields

$$B = \begin{bmatrix} -\beta_{13} - 4 & \beta_{13} & 2 \\ \beta_{13} - \beta_{33} - 4 & \beta_{13} + \beta_{33} & 2 \\ -\beta_{23} & \beta_{23} & -2 \end{bmatrix}.$$

Note that in this particular case, the third column of matrix A is identifiable from the confined trajectory $x(t; A_e, b)$.

5. Systems that are linear in parameters.

5.1. Analysis. Consider now a nonlinear dynamical system that depends linearly on parameters and has only its initial condition as a control:

$$(5.1) \quad \begin{aligned} \dot{x}(t) &= Af(x(t)), \\ x(0) &= b. \end{aligned}$$

In (5.1), $x(t) \in \mathbb{R}^n$ is the state of the system at time t , the system parameters are the entries of the coefficient matrix $A \in \mathbb{R}^{n \times m}$, $b \in \mathbb{R}^n$ is the initial condition, and $f = (f_1, \dots, f_m) : \mathbb{R}^n \rightarrow \mathbb{R}^m$, where f_j are functions that are locally Lipschitz continuous in x . The initial condition b determines the trajectory $x(t; A, b)$ of the system (5.1) for any given A . A definition of identifiability, analogous to Definition 2.1, can be stated as follows.

Definition 5.1. *Model (5.1) is identifiable in $\Omega \subseteq \mathbb{R}^{n \times m}$ if and only if for all $A, B \in \Omega$, $A \neq B$, there exists $b \in \mathbb{R}^n$ such that $x(\cdot; A, b) \neq x(\cdot; B, b)$.*

Recall that for the linear model (2.1), Theorem 2.2 implies identifiability in $\mathbb{R}^{n \times n}$. Such general identifiability, however, does not hold for systems that are linear in parameters. Instead, we can obtain a necessary condition for identifiability of the model (5.1) using the properties of the map f . We first introduce \mathcal{F} , the largest linear subspace of \mathbb{R}^m that contains the range of f , as $\mathcal{F} = \text{span}\{f(x) | x \in \mathbb{R}^n\} \subseteq \mathbb{R}^m$. The dimension of \mathcal{F} determines the identifiability of the model (5.1) as follows.

Theorem 5.2. *If $\dim \mathcal{F} < m$, then model (5.1) is not identifiable in $\mathbb{R}^{n \times m}$.*

Proof. Assume $\dim \mathcal{F} = r < m$. Let $\{v_1, \dots, v_r\}$ be a basis for \mathcal{F} . Complete $\{v_1, \dots, v_r\}$ to a basis $\{v_1, \dots, v_r, v_{r+1}, \dots, v_m\}$ of \mathbb{R}^m and let $V = [v_1 | \dots | v_m]$. For fixed $A \in \mathbb{R}^{n \times m}$, choose $C \in \mathbb{R}^{n \times (m-r)}$ such that $C \neq [Av_{r+1} | \dots | Av_m]$ and let $D = [Av_1 | \dots | Av_r | C]$. Finally, let $B = DV^{-1}$. This procedure yields $B \in \mathbb{R}^{n \times m}$ such that (i) $Av_j = Bv_j$, $j = 1, \dots, r$, and (ii) $Av_j \neq Bv_j$ for some $j \in \{r+1, \dots, m\}$. Since (i) implies that $Af(x) = Bf(x)$ for all $x \in \mathbb{R}^n$, the trajectories $x(t; A, b)$ and $x(t; B, b)$ of the model (5.1) are identical for any initial condition $b \in \mathbb{R}^n$, yet (ii) implies that $B \neq A$. Hence, the model (5.1) is not identifiable in $\mathbb{R}^{n \times m}$. ■

One of the main results for linear systems described in section 3 was Theorem 3.4, which provides a connection between the uniqueness of the parameters of model (2.1) and the confinement of the orbit of that model. Interestingly, a similar result can be shown for model (5.1), but here, parameter uniqueness is instead linked to the geometric structure of the image of the orbit of the model in the flux space. Let $\phi(A, b) = \{f(x(t; A, b)) | t \in \mathbb{R}\}$ be a curve in \mathbb{R}^m that represents the image under the map f of the orbit $\gamma(A, b)$ of the model (5.1).

Theorem 5.3. *There exists no $B \in \mathbb{R}^{n \times m}$ with $A \neq B$ such that $x(\cdot; A, b) = x(\cdot; B, b)$ if and only if $\phi(A, b)$ is not confined to a proper subspace of \mathbb{R}^m .*

Proof. To prove the reverse implication, suppose that $\phi(A, b)$ is not confined to a proper subspace of \mathbb{R}^m . Then one can find the matrix A uniquely as follows: since $\phi(A, b)$ is not confined, one can choose m distinct time points t_1, \dots, t_m , such that the matrix $F = [f(x(t_1)) | \dots | f(x(t_m))]$ is invertible. From knowledge of the trajectory, one knows $\dot{x}(t_1), \dots, \dot{x}(t_m)$. Appending this information into a matrix yields the linear equation $[\dot{x}(t_1) | \dots | \dot{x}(t_m)] = A[f(x(t_1)) | \dots | f(x(t_m))] = AF$, which has a unique solution $A = [\dot{x}(t_1) | \dots | \dot{x}(t_m)]F^{-1}$. Therefore, there is no other matrix B that would produce a trajectory identical to A . The forward direction is proven by contrapositive utilizing an argument

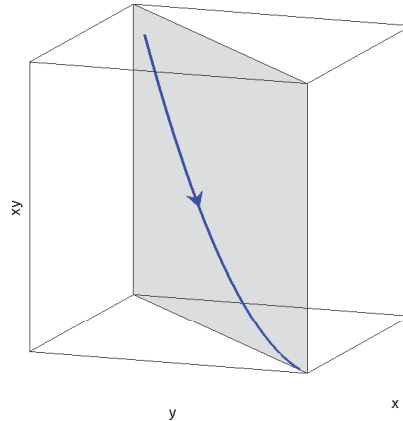


Figure 5. Confinement of $\phi(A, b)$ in the flux space.

similar to the one used in the proof of Theorem 5.2. Assume that $\phi(A, b)$ is confined to a proper subspace of \mathbb{R}^m and define $\mathcal{F}_\gamma = \text{span}\{f(x(t, A, b)), t \in [0, \infty)\}$. By the confinement of $\phi(A, b)$, $\dim \mathcal{F}_\gamma = r < m$. Let $V = \{v_1, \dots, v_r\}$ be a basis for \mathcal{F}_γ . Complete V to a basis of \mathbb{R}^m , $\hat{V} = \{v_1, \dots, v_r, v_{r+1}, \dots, v_m\}$. Construct $B \in \mathbb{R}^{n \times m}$ such that $Av_j = Bv_j$, $j = 1, \dots, r$, but $Av_j \neq Bv_j$ for some $j \in \{r+1, \dots, m\}$ (as in the previous proof). With this construction, $A \neq B$, but $Af(x) = Bf(x)$ for all $x \in \mathbb{R}^n$, and hence $x(t; A, b) = x(t; B, b)$. ■

As in the linear case, this theorem is a statement about identifiability of the model from a single trajectory. In fact, since the linear model (2.1) is a special case of the nonlinear model (5.1) with f being the identity map, Theorem 3.4 is a special case of Theorem 5.3. In that case, the confinement of the orbit image $\phi(A, b)$ in the flux space is equivalent to the confinement of the orbit $\gamma(A, b)$ of the trajectory.

5.2. Examples. As an illustrative example, consider the system

$$(5.2) \quad \begin{aligned} \dot{x} &= a_{11}x + a_{12}xy + a_{13}y, \\ \dot{y} &= a_{21}x + a_{22}xy + a_{23}y. \end{aligned}$$

System (5.2) is linear in parameters and can be represented in the form of model (5.1) with

$$A = \begin{bmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \end{bmatrix}$$

and $f(x, y) = [x, xy, y]^T$. For the matrix

$$A = \begin{bmatrix} -2 & 1 & -2 \\ -1 & 1 & -3 \end{bmatrix}$$

and initial condition $b = [1, 1]^T$, $\phi(A, b)$ is confined to a proper subspace of \mathbb{R}^3 , as shown in Figure 5. Theorem 5.3 implies that there exists a matrix $B \in \mathbb{R}^{2 \times 3}$ with $A \neq B$ such that $x(t; A, b) = x(t; B, b)$. One can construct B using the procedure described in the proof of the

theorem. Since $x(t) = y(t)$ for the solution of the IVP, we have $\mathcal{F}_\gamma = \text{span}\{(x, x^2, x)^T | x \in \mathbb{R}\}$. Thus $\{(1, 0, 1)^T, (0, 1, 0)^T\}$ is a basis for \mathcal{F}_γ . Complete this basis to $\{v_1, v_2, v_3\} = \{(1, 0, 1)^T, (0, 1, 0)^T, (1, 0, -1)^T\}$, a basis of \mathbb{R}^3 . Let

$$D = [Av_1 | Av_2 | w] = \left[\begin{array}{cc|c} -4 & 1 & w \\ -4 & 1 & w \end{array} \right]$$

such that $w \neq Av_3 = [0, 2]^T$. For example, let

$$D = \left[\begin{array}{ccc} -4 & 1 & -2 \\ -4 & 1 & -6 \end{array} \right].$$

Then

$$B = D[v_1 | v_2 | v_3]^{-1} = \left[\begin{array}{ccc} -3 & 1 & -1 \\ -5 & 1 & 1 \end{array} \right]$$

is one such example.

Another example is provided by the Lotka-Volterra model of competing species [8, 29],

$$(5.3) \quad \begin{aligned} \dot{x} &= x(1 - ax - cy) \\ \dot{y} &= y(1 - ay - cx). \end{aligned}$$

Model (5.3) is linear in parameters with

$$A = \left[\begin{array}{ccccc} 1 & -a & -c & 0 & 0 \\ 0 & 0 & -c & 1 & -a \end{array} \right]$$

and $f(x, y) = [x, x^2, xy, y, y^2]^T$.

For any initial condition of the form $b = [x_0, x_0]^T$, the trajectory of the system obeys $x(t) = y(t)$ and depends on the sum $a+c$ but not on the individual values of the parameters a, c . This is consistent with Theorem 5.3, which concludes that since $f(x, x) = [x, x^2, x^2, x, x^2]^T$ and $\phi(A, b)$ is confined to a proper subspace of \mathbb{R}^5 , the parameter matrix which yields this trajectory is not unique, and therefore model (5.3) is not identifiable in $\mathbb{R}^{2 \times 5}$.

6. Discrete data. In practical applications, one does not typically have knowledge of a full trajectory of the system, but rather a sample of discrete data points that lie on a trajectory, possibly perturbed by measurement noise. Suppose for now that we have m accurate data points x_1, x_2, \dots, x_m in \mathbb{R}^n that lie on the trajectory of the model (2.1), defined as $x_k = x(t_k; A, b)$, $k = 1, 2, \dots, m$, where t_1, t_2, \dots, t_m are distinct time points. Nonconfinement of the orbit $\gamma(A, b) = \{x(t; A, b) : t \in \mathbb{R}\}$ is obviously determined by the dimension of the span of the vectors x_1, x_2, \dots, x_m .

Lemma 6.1. *Orbit $\gamma(A, b)$ is not confined to a proper subspace of \mathbb{R}^n if and only if there exist t_1, t_2, \dots, t_n such that x_1, x_2, \dots, x_n are linearly independent.*

Note that the confinement of an orbit cannot be established from a fixed, finite data set in an obvious manner. For example, in a two-dimensional system, the available data may lie in a straight line, but the underlying solution may be a spiral, which is not a confined orbit. Model (2.1) is identifiable from the full trajectory in this example, since the corresponding orbit is not confined to a proper subspace.

It now remains to show how the parameter matrix A is determined from the data. The parameter matrix A can be computed explicitly without the need for optimization from $n + 1$ data points x_1, \dots, x_{n+1} such that $x_k = x(t_k)$ for each $k = 1, \dots, n + 1$, $t_{k+1} - t_k = \Delta t$ for all $k = 1, \dots, n$, and $\dim(\text{span}\{x_1, x_2, \dots, x_n\}) = n$. Let $\Phi(\Delta t)$ denote the principal matrix solution of model (2.1), and let X_k denote the matrix $[x_k \mid x_{k+1} \mid \dots \mid x_{k+n-1}]$. Then X_1 is invertible, and from the property that $\Phi(\Delta t)x_k = x_{k+1}$, we have

$$(6.1) \quad \Phi(\Delta t) = X_2(X_1)^{-1}.$$

In theory, the matrix A can be computed by taking the matrix logarithm of $\Phi(\Delta t)$, since $\Phi(\Delta t) = e^{A\Delta t}$. It is important to note, however, that the logarithm of a matrix does not always exist, and if it does, it is not necessarily unique. Requirements for the existence of a real matrix logarithm are given in the following theorem [6].

Theorem 6.2. *Let C be a real square matrix. Then there exists a real solution Y to the equation $C = e^Y$ if and only if C is nonsingular and each Jordan block of C belonging to a negative eigenvalue occurs an even number of times.*

In our case, $C = X_2(X_1)^{-1}$ is nonsingular due to the invertibility of matrices X_1 and X_2 . The second condition of Theorem 6.2 is satisfied trivially if x_1, x_2, \dots, x_n are indeed discrete points on a trajectory of the linear model (2.1). More importantly, uniqueness of the matrix logarithm, which is directly related to the identifiability of the model (2.1), is addressed in the following theorem [6].

Theorem 6.3. *Let C be a real square matrix. Then there exists a unique real solution Y to the equation $C = e^Y$ if and only if all the eigenvalues of C are positive real and no Jordan block of C belonging to any eigenvalue appears more than once.*

Given the data x_1, x_2, \dots, x_{n+1} , the matrix logarithm yields a unique corresponding parameter matrix A if and only if $\Phi(\Delta t)$, defined using (6.1), satisfies the hypotheses of Theorem 6.3. We have established earlier (in Theorem 3.6) that model (2.1) can be identified from $\gamma(A, b)$ if and only if A has only one Jordan block for each of its eigenvalues. If A satisfies this requirement and has real eigenvalues, then $\Phi(\Delta t)$ has positive eigenvalues and has one Jordan block for each of them and hence satisfies the hypotheses of Theorem 6.3. We can then conclude that model (2.1) is identifiable from the data x_1, x_2, \dots, x_{n+1} . If, however, A has a complex eigenvalue pair, then $\Phi(\Delta t)$ has a complex eigenvalue pair, or a negative eigenvalue with a pair of Jordan blocks associated to it. For example,

$$A = \begin{bmatrix} 0 & \pi \\ -\pi & 0 \end{bmatrix}$$

has eigenvalues $\pm\pi i$ and gives

$$e^A = \begin{bmatrix} -1 & 0 \\ 0 & -1 \end{bmatrix}$$

with a repeated Jordan block and negative eigenvalues. In such a case, Theorem 6.3 implies that one can find a matrix $B \neq A$ such that $e^{B\Delta t} = \Phi(\Delta t) = e^{A\Delta t}$. Although the trajectories $x(t; A, x_1)$ and $x(t; B, x_1)$ must necessarily differ (since the model with matrix A is identifiable from the full trajectory $x(t; A, x_1)$), the data obtained from these trajectories for the same set

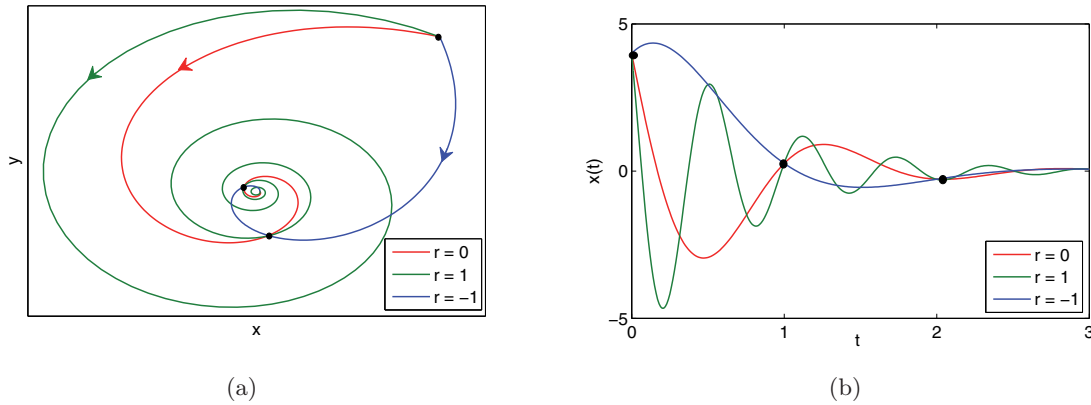


Figure 6. (a) Plot of the orbits for A_r with $r = 0, 1, -1$. (b) Plot of the x component of the trajectory. Each of the three distinct systems satisfies the data.

of time points $\{t_1, t_2, \dots, t_{n+1}\}$ are identical. Thus, we have the following observation.

Corollary 6.4. *The model (2.1) with matrix A that has a pair of complex eigenvalues is not identifiable from any set of data x_1, x_2, \dots, x_{n+1} that are uniformly spaced in t .*

Figure 6 illustrates the nonidentifiability that arises with complex eigenvalues in the case of discrete data for 2×2 linear systems. In this example, the solution to the system with parameter matrix

$$A_r = \begin{bmatrix} -3/2 & -4 \\ 4 & -3/2 \end{bmatrix} + 2\pi r \begin{bmatrix} 0 & -1 \\ 1 & 0 \end{bmatrix}$$

will satisfy the data for any integer value of r . The solutions shown in Figure 6 are for the cases $r = 0, 1$, and -1 .

The extension of the above computation to the model (5.1) is simple, provided one can measure not only the values x_1, x_2, \dots, x_m of the variables at t_1, t_2, \dots, t_m , but also their rates of change y_1, y_2, \dots, y_m , where $y_k = dx(t; A, b)/dt|_{t=t_k}$. Just as in the proof of Theorem 5.3, if $f(x_1), f(x_2), \dots, f(x_n)$ are linearly independent (and hence $\phi(A, b)$ is not confined to a proper subspace), then the unique parameter matrix that yields this data is given by

$$(6.2) \quad A = YF^{-1},$$

where $Y = [y_1 | \dots | y_m]$ and $F = [f(x_1) | \dots | f(x_m)]$.

The computations outlined above are valuable not only because they offer direct methods for computing the parameter matrix A that do not rely on minimization of an error function, but also because they can be used to provide insight into the sensitivity of A to the data. Since both computations are based on linear algebraic operations, one can use the tools of numerical analysis to determine the conditioning of the problem (see, e.g., [35]). In the case of the linear model (2.1), equation (6.1) implies that the problem of computing $\Phi(\Delta t)$ has condition number $\kappa(X_1) = \|X_1\| \|(X_1)^{-1}\|$, and indeed one can compute that any perturbations of the data (δX_1 of X_1 and δX_2 of X_2) induce a perturbation $\delta\Phi(\Delta t)$ of $\Phi(\Delta t)$ that obeys

$$(6.3) \quad \frac{\|\delta\Phi(\Delta t)\|}{\|\Phi(\Delta t)\|} \leq \kappa(X_1) \left(\frac{\|\delta X_1\|}{\|X_1\|} + \frac{\|\delta X_2\|}{\|X_2\|} \right),$$

where $\|\cdot\|$ is any norm of choice. Note that if $\|\cdot\|$ is the Euclidean norm $\|\cdot\|_2$, then $\kappa(X_1)$ equals the ratio of the largest to the smallest singular values of X_1 . It follows that the closer the data vectors x_1, x_2, \dots, x_n (i.e., the columns of X_1 and X_2) are to being linearly dependent, the more ill-conditioned is the inverse problem.

Likewise, in the case of the model (5.1), equation (6.2) implies that the problem of computing A has the condition number $\kappa(F) = \|F\| \|F^{-1}\|$, and hence any perturbations δF and δY induce a perturbation δA that obeys

$$(6.4) \quad \frac{\|\delta A\|}{\|A\|} \leq \kappa(F) \left(\frac{\|\delta F\|}{\|F\|} + \frac{\|\delta Y\|}{\|Y\|} \right).$$

Again, the closer the vectors $f(x_1), f(x_2), \dots, f(x_m)$ (i.e., the columns of F) are to being linearly dependent, the more ill-conditioned is the inverse problem.

The observations made at the end of this section indicate that the highest accuracy in the inverse problem (and hence the lowest sensitivity to measurement errors) can be achieved by selecting data so as to minimize the condition number of the data matrix. This result has an important practical implication: although the results in sections 3 and 5 indicate that for an identifiable model any infinitesimally small portion of a trajectory is sufficient to identify the parameter matrix, in any practical situation a small segment of trajectory will have a nearly linear orbit, and hence any selection of data from that segment will yield a data matrix with high condition number. Thus, in order to minimize the condition number, one must have a sufficiently large portion of the trajectory that explores all dimensions of the underlying space.

7. Conclusions. In this paper, for both linear and nonlinear dynamical systems, we have derived necessary and sufficient conditions for identifiability of parameters from a single trajectory based solely on the geometry of the trajectory or the geometry of an image of the trajectory. Furthermore, we have shown that an improved accuracy of parameter estimation can result when the trajectory deviates farther from being confined. These results have a practical utility since the criterion can be applied using only what is known about the trajectory, without any knowledge of the model parameters. Additional results for linear systems include a link between identifiability from a single trajectory with initial condition b and the linear independence of $\{b, Ab, \dots, A^{n-1}b\}$, several characterizations of the linear independence of $\{b, Ab, \dots, A^{n-1}b\}$ including a condition on the Jordan form of A , and the result that unconditional identifiability cannot occur outside of $\mathbb{R}^{2n \times 2n}$. Finally, we addressed the question of explicitly computing model parameter values from a discrete collection of data points.

There are several directions for possible extension of the results in this paper. First, our results imply that discrete data contained within a lower-dimensional subspace of the full state space will not yield identifiability of an underlying system. Such data may arise, however, from particular samplings of a trajectory that is not confined in this way. The derivation of more general identifiability conditions from discrete data remains for future exploration. Second, the condition $C = I$ is highly restrictive because in real scenarios not all variables of the system may be observable. We have shown that when C is not of full rank, confinement of an orbit to an invariant subspace of dimension not greater than the rank of C can yield partial identifiability of the parameter matrix. A natural extension of the present study would be to investigate whether there are ways to enhance the practical

applicability of this result or to obtain more general identifiability results in this case. A third direction for future study would be the consideration of general nonlinear systems. We have shown that identifiability conditions based on confinement can be derived for systems that feature linearity in parameters, regardless of whether the dynamics is linear or nonlinear. For nonlinear dynamical systems lacking this form of parameter dependence, the assessment of identifiability will likely require new ideas. The prospects for addressing this problem using linearization about trajectories appear to be limited, based on our observations about sensitivity associated with parameter estimation from small segments of trajectories. A final direction to consider is the identifiability of systems that are linear or linear in parameters with time-dependent parameter matrices. Our methods would likely be useful for systems with rather trivial time-dependence, such as piecewise constant parameter matrices, where switching times between different constant values are known and full solution trajectories are available, but handling more general time-dependence appears to be a difficult problem. These and other related topics represent important directions for follow-up studies.

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REFERENCES

- [1] K. J. ÅSTRÖM AND P. EYKHOFF, *System identification—a survey*, Automatica J. IFAC, 7 (1971), pp. 123–162.
- [2] R. BELLMAN AND K. J. ÅSTRÖM, *On structural identifiability*, Math. Biosci., 7 (1970), pp. 329–339.
- [3] L. CHEN AND G. BASTIN, *Structural identifiability of the yield coefficients in bioprocess models when the reaction rates are unknown*, Math. Biosci., 132 (1996), pp. 35–67.
- [4] C. COBELLI AND J. J. DiSTEFANO, *Parameter and structural identifiability concepts and ambiguities: A critical review and analysis*, Am. J. Physiol., 239 (1980), pp. R7–R24.
- [5] G. CRACIUN AND C. PANTEA, *Identifiability of chemical reaction networks*, J. Math. Chem., 44 (2008), pp. 244–259.
- [6] W. J. CULVER, *On the existence and uniqueness of the real logarithm of a matrix*, Proc. Amer. Math. Soc., 17 (1966), pp. 1146–1151.
- [7] J. DiSTEFANO III AND C. COBELLI, *On parameter and structural identifiability: Nonunique observability/reconstructibility for identifiable systems, other ambiguities, and new definitions*, IEEE Trans. Automat. Control, 25 (1980), pp. 830–833.
- [8] L. EDELSTEIN-KESHET, *Mathematical Models in Biology*, Classics Appl. Math. 46, SIAM, Philadelphia, 2005. Unabridged republication of the work first published by Random House, New York, 1988.
- [9] M. FARINA, R. FINDEISEN, E. BULLINGER, S. BITTANTI, F. ALLGOWER, AND P. WELLSTEAD, *Results towards identifiability properties of biochemical reaction networks*, in Proceedings of the 45th IEEE Conference on Decision and Control, IEEE Press, Piscataway, NJ, 2006, pp. 2104–2109.
- [10] M. FEINBERG, *Chemical reaction network structure and the stability of complex isothermal reactors—I. The deficiency zero and deficiency one theorems*, Chem. Engrg. Sci., 42 (1987), pp. 2229–2268.
- [11] M. FEINBERG, *The existence and uniqueness of steady states for a class of chemical reaction networks*, Arch. Ration. Mech. Anal., 132 (1995), pp. 311–370.
- [12] B. C. GARGASH AND D. P. MITAL, *A necessary and sufficient condition of global structural identifiability of compartmental models*, Comput. Biol. Med., 10 (1980), pp. 237–242.
- [13] K. GLOVER AND J. WILLEMS, *Parametrizations of linear dynamical systems: Canonical forms and identifiability*, IEEE Trans. Automat. Control, 19 (1974), pp. 640–646.
- [14] M. GREWAL AND K. GLOVER, *Identifiability of linear and nonlinear dynamical systems*, IEEE Trans. Automat. Control, 21 (1976), pp. 833–837.

- [15] F. G. HAYDEN, J. J. TREANOR, R. F. BETTS, M. LOBO, J. D. ESINHART, AND E. K. HUSSEY, *Safety and efficacy of the neuraminidase inhibitor GG167 in experimental human influenza*, JAMA, 275 (1996), pp. 295–299.
- [16] D. M. HIMMELBLAU, C. R. JONES, AND K. B. BISCHOFF, *Determination of rate constants for complex kinetics models*, Indust. Engrg. Chem. Fund., 6 (1967), pp. 539–543.
- [17] K. HOFFMAN AND R. KUNZE, *Linear Algebra*, Prentice–Hall, Englewood Cliffs, NJ, 1971.
- [18] F. HORN AND R. JACKSON, *General mass action kinetics*, Arch. Ration. Mech. Anal., 47 (1972), pp. 81–116.
- [19] B. P. INGALLS, *Mathematical Modeling in Systems Biology: An Introduction*, MIT Press, Cambridge, MA, 2013.
- [20] A. KADIOGLU, N. A. GINGLES, K. GRATAN, A. KERR, T. J. MITCHELL, AND P. W. ANDREW, *Host cellular immune response to pneumococcal lung infection in mice*, Infect. Immun., 68 (2000), pp. 492–501.
- [21] T. KAILATH, *Linear Systems*, Prentice–Hall, Englewood Cliffs, NJ, 1980.
- [22] R. E. KALMAN, *Mathematical description of linear dynamical systems*, J. Soc. Indust. Appl. Math. Ser. A Control, 1 (1963), pp. 152–192.
- [23] A. V. KARNAUKHOV, E. V. KARNAUKHOVA, AND J. R. WILLIAMSON, *Numerical matrices method for nonlinear system identification and description of dynamics of biochemical reaction networks*, Biophys. J., 92 (2007), pp. 3459–3473.
- [24] B. KISAČANIN AND G. C. AGARWAL, *Linear Control Systems: With Solved Problems and MATLAB Examples*, Kluwer Academic/Plenum Publishers, New York, 2001.
- [25] R. C. K. LEE, *Optimal Estimation, Identification, and Control*, Research Monographs 196, MIT Press, Cambridge, MA, 1964.
- [26] L. LJUNG AND T. GLAD, *On global identifiability for arbitrary model parametrizations*, Automatica J. IFAC, 30 (1994), pp. 265–276.
- [27] J. A. MCCULLERS, J. L. MCAULEY, S. BROWALL, A. R. IVERSON, K. L. BOYD, AND B. HENRIQUES-NORMARK, *Influenza enhances susceptibility to natural acquisition of and disease due to Streptococcus pneumoniae in ferrets*, J. Infect. Dis., 202 (2010), pp. 1287–1295.
- [28] H. MIAO, X. XIA, A. S. PERELSON, AND H. WU, *On identifiability of nonlinear ODE models and applications in viral dynamics*, SIAM Rev., 53 (2011), pp. 3–39.
- [29] J. D. MURRAY, *Mathematical Biology I: An Introduction*, Interdiscip. Appl. Math. 17, Springer, New York, 2002.
- [30] V. V. NGUYEN AND E. F. WOOD, *Review and unification of linear identifiability concepts*, SIAM Rev., 24 (1982), pp. 34–51.
- [31] H. H. ROSENBROCK, *Structural properties of linear dynamical systems*, Int. J. Control, 20 (1974), pp. 191–202.
- [32] E. D. SONTAG, *For differential equations with r parameters, $2r + 1$ experiments are enough for identification*, J. Nonlinear Sci., 12 (2002), pp. 553–583.
- [33] A. THOWSEN, *Identifiability of dynamic systems*, Int. J. Systems Sci., 9 (1978), pp. 813–825.
- [34] F. R. TOAPANTA AND T. M. ROSS, *Impaired immune responses in the lungs of aged mice following influenza infection*, Respir. Res., 10 (2009), pp. 112–131.
- [35] L. N. TREFETHEN AND D. BAU III, *Numerical Linear Algebra*, SIAM, Philadelphia, 1997.
- [36] S. VAJDA, P. VALKO, AND A. YERMAKOVA, *A direct-indirect procedure for estimation of kinetic parameters*, Comput. Chem. Engrg., 10 (1986), pp. 49–58.
- [37] E. WALTER, Y. LECOURTIER, AND J. HAPPEL, *On the structural output distinguishability of parametric models, and its relations with structural identifiability*, IEEE Trans. Automat. Control, 29 (1984), pp. 56–57.
- [38] E. WALTER AND L. PRONZATO, *Identification of Parametric Models from Experimental Data*, translated from the 1994 French original and revised by the authors, with the help of John Norton, Comm. Control Engrg. Ser., Springer-Verlag, Berlin, Masson, Paris, 1997.
- [39] S. YOUSEF, *Iterative Methods for Sparse Linear Systems*, 2nd ed., SIAM, Philadelphia, 2003.