# Parameter Identifiability in Ordinary Differential Equations

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## Introduction

In modeling real-world phenomena, a system of ordinary differential equations is a ubiquitous tool. The quality of such model for a practitioner matters strongly and can be improved by ensuring identifiability of parameters in the ODE system.

In the following, we will use the ODE system in the form as below

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

where $\mathbf{x} = (x_1, \ldots, x_n)$ is a time-dependent state vector-function (variable) with initial condition $\mathbf{x}^*, \mathbf{y} = (y_1, \ldots, y_n)$ is a vector-function of model outputs. The vector $\boldsymbol{\mu} = (\mu_1, \ldots, \mu_\lambda)$ represents the parameters of the system and $\mathbf{u} = (u_1, \ldots, u_s)$ is a vector of input variables. The functions $\mathbf{f} = (f_1, \ldots, f_n)$ and $\mathbf{g} = (g_1, \ldots, g_n)$ where $f_i = f_i(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u}),\ g_i = g_i(\mathbf{x}, \boldsymbol{\mu}, \mathbf{u})$ are assumed to be rational functions of $\mathbb{C}$.

## What is structural identifiaibility?

Structural identifiability is a theoretical property that helps one assess whether a parameter or the whole system are identifiable. That is, whether, given experimental data, one is able to obtain the parameter quantity from the measurements. Note that this property does not tell us how to obtain such value and is only *theoretical*. It can be further split into two categories:

- *local structural identifiability*: a parameter can be identified up to finitely many values,
- *global structural identifiability*: a parameter can be identified uniquely.

Here we imply a generic experiment when talking about identifiability properties. For a given system, one can create an example with a trivial solution (zero initial conditions, zero inputs, zero parameters) and nothing will be identifiable.

## Examples

Let us consider some examples of identifiability problems for ODE systems.

### Example (1)

$$\begin{cases} x' = Ax, \\ y = x,\ x(0) = x_0. \end{cases} \tag{2}$$

We are interested in identifiability of parameters $A$ and $x_0$. Clearly, the solution to 2 is $x = x_0 e^{At}$. Therefore, we know $y = x_0 e^{At}$, hence we can globally identify

$$x_0 = y(0)$$

from the output function $y$. To answer about $A$, consider that we uniquely know $y' = Ay$, therefore

$$A = \frac{y'(0)}{y(0)}.$$

### Example (2)

$$\begin{cases} x' = \theta^2, \\ y = x,\ x(0) = x_0. \end{cases} \tag{3}$$

Here, the solution is $x = \theta^2 t$ and we can identify $x_0 = y(0)$ as before. Note that $y(1) = \theta^2$, however, this implies $\theta = \pm\sqrt{y(1)}$, hence identifiable locally.

### Example (3)

$$\begin{cases} x' = 0, \\ y_1 = x, y_2 = ax + b,\ x(0) = x_0. \end{cases} \tag{4}$$

This is an example where the initial condition is identifiable from $y_1 = x$. Note that for $a,\ b$ parameters we cannot find values since the system of algebraic equations is underdetermined:

$$y_2 = ay_1 + b.$$

## Existing Algorithms

There is a variety solutions to identifiability problems that can be separated into groups by the underlying methods. Some of the solutions deal with local and global identifiability, others seek answer to finding identifiable combinations or functions of parameters.

1. **Series Based:** an example of a program that relies on series solution is GenSSI [1].
2. **Differential Algebraic approaches:** DAISY [7, 6], COMBOS [5, 4], SIAN[2, 3].
3. **Other Approaches:** StrikeGOLDD [9].

## Local Identifiability: Sedoglavic's Algorithm

An example of a differential-algebraic approach to local identifiability problem is an algorith developed by Alexandre Sedoglavic in 2002 [8]. The underlying idea of the algorithm is straightforward: we check the rank of the Jacobian of the output functions $Y$ with respect to states and parameters and conclude the identifiability based on the rank value (see [8, Corollary 2.1]).

It can be expensive to compute everything directly, so instead the following numerical probabilistic procedure is used:

1. Create random (integer) power series for input functions, parameters, and initial conditions, initialize a max degree $\nu$ and starting degree $d = 1$,
2. Find power series solution up to degree $d$ to the numerators of the original ODE system,
3. Construct a power series solution to the variational system (definition here is omitted)
4. Set $d := 2d$. Steps 2, 3 are repeated until the order of power series is at most $\nu$.
5. Calculate the Jacobian of outputs with respect to new power series solution, calculate rank.

## Global Identifiability: SIAN

## Julia-Based Solutions

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## Work-in-Progress

## References

[1] O. Chis et al. "GenSSI: a software toolbox for structural identifiability analysis of biological models". In: *Bioinformatics* 27.18 (2011), pp. 2610–2611.

[2] H. Hong et al. "SIAN: a tool for assessing structural identifiability of parametric ODEs". In: *ACM Communications in Computer Algebra* 53.2 (2019), pp. 37–40.

[3] H. Hong et al. "Global identifiability of differential models". In: *Communications on Pure and Applied Mathematics* 73.9 (2020), pp. 1831–1879.

[4] A. Kalami Yazdi et al. "COMBOS2: an algorithm to the input–output equations of dynamic biosystems via Gaussian elimination". In: *Journal of Taibah University for Science* 14.1 (2020), pp. 896–907.

[5] N. Meshkat et al. "On finding and using identifiable parameter combinations in nonlinear dynamic systems biology models and COMBOS: a novel web implementation". In: *PLoS One* 9.10 (2014), e110261.

[6] M. P. Saccomani et al. "A new version of DAISY to test structural identifiability of biological models". In: *International conference on computational methods in systems biology*. Springer. 2019, pp. 329–334.

[7] M. Saccomani and G. Bellu. "DAISY: An efficient tool to test global identifiability. Some case studies". In: *2008 16th Mediterranean Conference on Control and Automation*. IEEE. 2008, pp. 1723–1728.

[8] A. Sedoglavic. "A probabilistic algorithm to test local algebraic observability in polynomial time". In: *Journal of Symbolic Computation* 33.5 (2002), pp. 735–755.

[9] A. F. Villaverde et al. "Structural Identifiability of Dynamic Systems Biology Models". In: *PLOS Computational Biology* 12.10 (Oct. 2016), pp. 1–22.



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