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On the different flavours of practical identifiability

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Identifiability is fundamental to any parameter estimation process and plays a role in a wide range of scientific research disciplines. Structural identifiability is a well-defined and purely model-based property that can be analysed in the absence of experimentally measured data with various methods. In contrast, practical identifiability lacks a concise technical definition that is agreed upon, leading to conflicting assessments. We focus on the practical identifiability analysis of ordinary differential equation models in systems biology and point out the differences between definitions and their implications. We differentiate between classifications based on sensitivity and classifications based on confidence intervals. We advocate for precise wording in discussions of practical identifiability analysis results so that the employed method is clear from the terminology.

We propose that model parameters should be termed a priori or a posteriori sensitive if sensitivity-based methods are used and finitely identified if the assessment is based on confidence intervals.

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Introduction

Advancements in computational power have significantly enhanced the role of mathematical modelling in systems biology and medicine. Mathematical models can be used to determine reaction rates, make predictions for the concentrations of reactants that cannot be experimentally observed directly, and develop an understanding of the specific mechanisms that drive a system's behaviour. Furthermore, they are used in the development of clinical decision tools. Particularly for mechanistic models, identifiability is a crucial property that must be fulfilled in order for the mechanistic interpretation to be valid and the model predictions to be trustworthy. A structurally and practically identifiable model should exhibit finite confidence intervals for all estimated parameters and provide unique predictions. In contrast, structurally nonidentifiable models can yield identical predictions for different parameter configurations and are at high risk of producing unreliable out-of-sample predictions. In short, identifiability analysis is of high importance to achieve reliable and reproducible results and thereby support research performed in a wet laboratory and in clinical applications.

As mathematical models have grown in size and complexity, more advanced identifiability analysis methods are needed. Several methods [1–13] have been developed to address the question of structural identifiability, a property that solely depends on the model structure itself, not on measured data. If, depending on the model structure, the right method is chosen, nearly any model can be analysed within minutes, making a priori structural identifiability analysis accessible for routine modelling workflows [14,15].

Beyond a priori structural identifiability, an a posteriori practical identifiability analysis is also needed to confirm the robustness of the modelling results. In this context, a priori means before the model is calibrated or applied to real experimental data, and a posteriori means after the model has been calibrated with the available data. If the data are insufficient, the signal-to-noise level is too low, or the time-points at which measurements were taken are not in the regions of informative dynamics, an a priori structurally identifiable model can still be a posteriori practically nonidentifiable with respect to the available data. This aspect has been less explored, with fewer powerful methods available for its assessment [16–18].

We review the differences between various definitions of practical identifiability and illustrate their implications with the help of toy models. The goal is to highlight the different flavours of practical identifiability analyses, establish clear wording, and also to provide guidance in choosing a suitable method for a given problem.

Defining practical identifiability

In general, structural identifiability is a prerequisite for practical identifiability. Moreover, it is easy to misinterpret results of practical identifiability analyses if a structurally nonidentifiable model is not recognised as such.

Both structural and practical identifiability can be assessed for any differentiable nonlinear model. In particular, for (partially observed) dynamical systems, represented by a system of ordinary differential equations (ODEs)

$$\dot{\mathbf{x}}(t) = f(\mathbf{x}(t), \boldsymbol{\theta}, \mathbf{u}(t)), \tag{1}$$

with n model states $\mathbf{x}(t)$, a set of p unknown parameters $\boldsymbol{\theta}$ that have to be estimated from experimental data, and external possibly unknown stimuli $\mathbf{u}(t)$. The model predictions y are generated from the model states via the observation function g

$$\mathbf{y}(t, \boldsymbol{\theta}) = g(\mathbf{x}(t), \boldsymbol{\theta}, t) \tag{2}$$

and can be mapped to the discrete, time-resolved experimental data (t^{D}, y^{D}), which are typically noisy. For systems biological models, it is typical for only about 50 %–80 % of states $\mathbf{x}(t)$ to be experimentally observed [19].

A parameter component i is said to be globally structurally identifiable if for all parameter configurations $\boldsymbol{\theta}$, $\boldsymbol{\theta}'$

$$\mathbf{y}(\boldsymbol{\theta}) = \mathbf{y}(\boldsymbol{\theta}') \implies \theta_i = \theta_i' \tag{3}$$

holds, where $\mathbf{y}(\boldsymbol{\theta}) \equiv \mathbf{y}(\bullet, \boldsymbol{\theta})$ denotes the entire prediction trajectory graph [20,21]. Similarly, a parameter component i is locally structurally identifiable at a point $\boldsymbol{\theta}$ if there exists a local neighbourhood $\eta(\boldsymbol{\theta})$ around it such that condition (3) holds for all $\boldsymbol{\theta}' \in \eta(\boldsymbol{\theta})$. Thus, a parameter θ_i is structurally nonidentifiable if its value can be changed without any influence on the trajectories $\mathbf{y}$ because the changes can be fully compensated by changing the values of the remaining parameters.

In contrast to structural identifiability, practical identifiability does not have a single universally agreed upon definition. Usually, the question of practical identifiability arises either during the design of new experiments or after new experimental data have been recorded. The broad idea on which researchers seem to agree is that practical identifiability analysis should answer the question of whether and how precisely the parameter values of a model can be estimated given a specific experiment [22–31].

One tool commonly used to analyse whether changes in the value of a parameter are influential for the model outputs is sensitivity analysis. The sensitivity of a parameter θ_i given by $\mathbf{s}_i = \partial\mathbf{y}/\partial\theta_i$ can be used to assess the influence of a parameter, and based on some definitions, a parameter that scores below a certain threshold is then termed practically nonidentifiable [22]. If the uncertainty associated with a measurement is known, it can be used to scale the parameter sensitivity $\partial\mathbf{y}/\partial\theta_i$ of the associated prediction, yielding the residual sensitivity $\partial\mathbf{r}/\partial\theta_i = \sigma^{-1}\partial\mathbf{y}/\partial\theta_i$. Combining these sensitivities for all model predictions with respect to all parameters yields the sensitivity matrix

$$\mathcal{S} = \begin{pmatrix} \frac{\partial y_1(\widehat{\boldsymbol{\theta}}, t_1)}{\partial\theta_1} & \cdots & \frac{\partial y_1(\widehat{\boldsymbol{\theta}}, t_1)}{\partial\theta_n} \\ \vdots & \vdots & \vdots \\ \frac{\partial y_m(\widehat{\boldsymbol{\theta}}, t_1)}{\partial\theta_1} & \cdots & \frac{\partial y_m(\widehat{\boldsymbol{\theta}}, t_1)}{\partial\theta_n} \\ \vdots & \vdots & \vdots \\ \frac{\partial y_1(\widehat{\boldsymbol{\theta}}, t_N)}{\partial\theta_1} & \cdots & \frac{\partial y_1(\widehat{\boldsymbol{\theta}}, t_N)}{\partial\theta_n} \\ \vdots & \vdots & \vdots \\ \frac{\partial y_m(\widehat{\boldsymbol{\theta}}, t_N)}{\partial\theta_1} & \cdots & \frac{\partial y_m(\widehat{\boldsymbol{\theta}}, t_N)}{\partial\theta_n} \end{pmatrix} \tag{4}$$

evaluated at a fixed $\widehat{\boldsymbol{\theta}}$ and time-points $t_1, \ldots, t_N$. Using the sensitivity matrix, collinearity of parameter directions in the prediction space can be analysed with principal component analysis or singular value decomposition [13,22–25]. This not only tests the sensitivity of the model predictions with respect to changes in the value of a single parameter at a time, but also detects linear combinations of multiple parameters, which can together compensate for changes in any single one of the parameters in this group. For all of these methods, usually some kind of heuristic threshold value must be chosen, below which a model or a parameter is called nonidentifiable. What unites these methods is that they are usually performed on simulated data that are designed to resemble the real experimental conditions, but were not actually measured experimentally. Additionally, the sensitivity analysis presented here is a local property calculated around a particular parameter configuration $\widehat{\boldsymbol{\theta}}$, but can be expanded by repeating the analysis for different parameter configurations.

Before the practical identifiability analysis, the model may have been fitted to actual measurement data to achieve a local analysis in the relevant region of the parameter space. However, sensitivity-based methods do not incorporate the goodness of fit of a model to data, which means that they can only provide a ranking of the model parameters from most sensitive to least sensitive

given an experimental design. If the actual measurement data are not used to calibrate the model before the analysis, these methods can and should be applied a priori to use the results for experimental design. To clarify, we will refer to the results and assessments produced by the various forms of sensitivity matrix analysis as parameter sensitivity. If the model was calibrated to actual measurement data before the analysis, it is an a posteriori parameter sensitivity analysis, and if the analysis is performed before any calibration, an a priori parameter sensitivity analysis. In the following, the terminology used for describing the outcome of such an analysis will be that a parameter θ_i is a priori/a posteriori (in)sensitive given the (planned) experimental design.

Another major branch of practical identifiability focuses on a posteriori analyses using the profile likelihood or its local approximation through the Fisher information matrix, and defines a parameter as practically identifiable at a given confidence level, if the associated profile likelihood based confidence interval is finite [25–27,31–37]. The profile of a parameter θ_i is calculated by fixing θ_i to values around its optimum and reoptimising the remaining parameters. Then, the likelihood after reoptimisation is plotted against the different values for θ_i and if the likelihood is not influenced by changing the parameter, this parameter is nonidentifiable. The boundary of the confidence interval is determined by the parameter values at which the profile likelihood for the parameter crosses a certain critical value, which depends on the desired confidence level. However, in contrast to sensitivity-based approaches, the critical value to be crossed by the profile likelihood is not based on a heuristic choice but is instead determined by the asymptotic distribution of the likelihood ratio test statistic. If the profile likelihood flattens out and does not cross the necessary critical value for arbitrarily small or large parameter values (or both), the confidence interval is not bounded in this direction, which means that the parameter value is not constrained to a finite range by the available data, at the specified confidence level. As illustrated, for instance, in Ref. [16], the Fisher information matrix cannot be used to construct reliable confidence intervals or decide a posteriori practical identifiability for nonlinear models in the finite identification sense, due to the fact that it only encodes a local quadratic approximation of the likelihood landscape at the point estimate. Analyses using the profile likelihood depend on measured data and thus can only be applied a posteriori. The terminology for describing the outcome of such a profile-based practical identifiability analysis will be that a parameter θ_i is finitely identified to the confidence level α, given the experimental data, if the profile crosses the critical value. Conversely, a parameter is not finitely identified if the profile does not cross the critical value on at least one side. Moreover, a model is finitely identified to the confidence level α as a whole, if all its parameters are finitely identified.

On a higher level, both the sensitivity-based and confidence-interval-based methods can be applied in the scope of Monte Carlo simulations, where the respective criteria are evaluated for many different randomly sampled parameter configurations and/or many simulated data realisations [23,38–40]. However, in both cases the analysis is predicated on the fact that either some heuristic threshold value must be chosen for the sensitivity-based criteria, or realistic values for the parameters must already be known, so that realistic data realisations can be simulated from them.

It should be stressed that it is not only possible but common for a parameter that was found to be sensitive according to either an a priori or a posteriori sensitivity analyses, not to be finitely identified by specific measurement data realisations up to the desired confidence level. This is why precise and coherent wording regarding practical identifiability analyses is crucial to avoid miscommunication or misinterpretation of results.

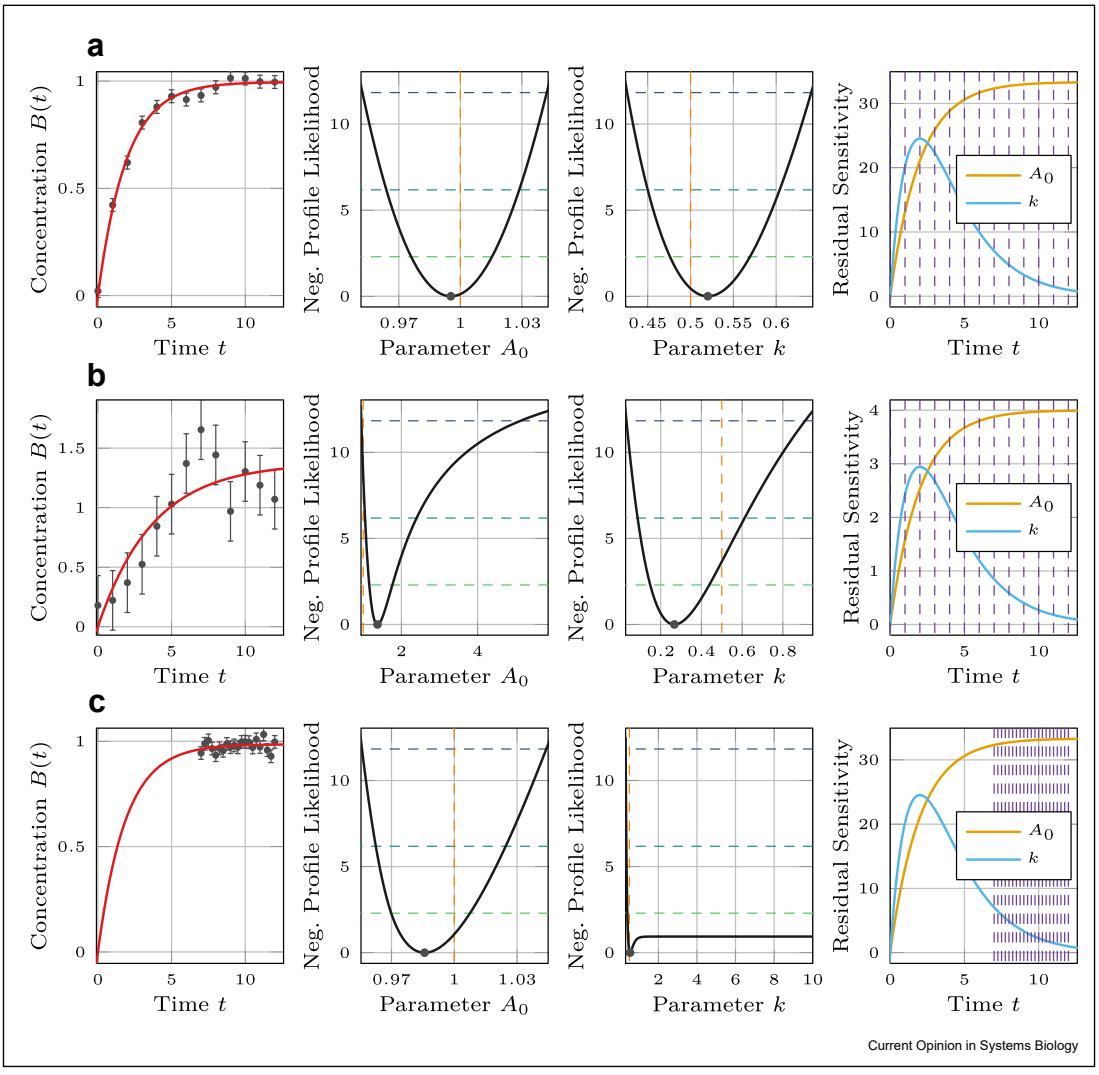
Typical causes for practical non-identifiability

In order to better understand practical identifiability, the differences between sensitive and finitely identified parameters, and to disentangle the possibilities and limitations of different analysis methods, it is important to understand possible causes of parameter insensitivity and nonfinitely identified parameters, respectively. Here, we focus on two of the most common causes. For the following discussion, we assume a structurally identifiable model whose predictions provide a good fit to the observed data.

Imprecise or unsuitable data

The most prominent and common causes for practical identifiability problems can be summarised under imprecise or unsuitable data. Two cases can be distinguished: imprecisely informative data due to large noise, and uninformative, unsuitable data due to unsuitable experimental design. Even for a globally structurally identifiable model with well-fitted data, it is possible to find that, due to high uncertainty in the data, the values of some or all of the parameters are not strongly constrained by the data, rendering them insensitive. In such cases, an a priori sensitivity analysis could be used to determine the maximal data uncertainty, such that the model sensitivity is above some threshold. Similarly, an a posteriori analysis can be used to determine an appropriate heuristic threshold from the data. In a profile likelihood analysis, increasing the data uncertainty generally results in larger confidence intervals. The scenario of insufficient data is shown in row B of Figure 1 in comparison to sufficient data in row A.

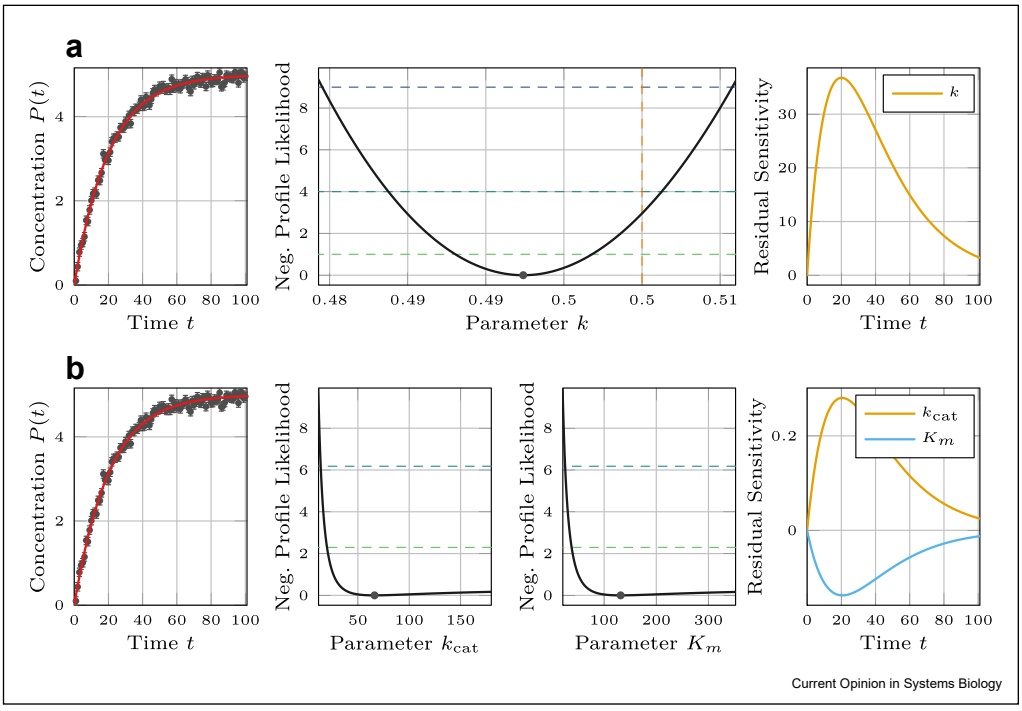
Figure 1



Example of effects of uninformative data on identifiability, illustrated using a simple two-state ODE system $A \xrightarrow{k \cdot A} B$, where $A(0) = A_0$ and the reaction rate k are estimated, $B(0) = 0$ is fixed and only the second component $B(t)$ is observed. The true parameter values were taken as $(A_0, k)_{\text{true}} = (1, 0.5)$. **Row A**: Ideal case of data with sufficiently high signal-to-noise ratio ($\sigma_B = 0.03$) coupled with observations in informative time ranges. The first panel shows the simulated data and a fit to the data. The combination of the model with the data leads to finite identification of both parameters up to a confidence level of $3\sigma \approx 99.7\%$ and beyond, as shown in the second and third columns. The fourth panel shows the a posteriori sensitivities of the prediction trajectories with respect to the true parameter values, divided by the respective observation uncertainties. It can be seen that measurements cover the respective regions of high sensitivity for both parameters. **Row B**: Case of low signal-to-noise ratio ($\sigma_B = 0.25$) in the data. This leads to much wider but still finite confidence intervals for both parameters and thus the parameters are still finitely identified. The sensitivity analysis in the fourth panel shows the same dynamics as in row A, except for a shift on the vertical axis due to the lower signal-to-noise ratio. **Row C**: Case of high signal-to-noise ratio ($\sigma_B = 0.03$) in terms of the noise magnitude but insufficient observations in informative time ranges, wherefore the reaction rate k is not finitely identified by the given observations. At a confidence level of $1\sigma \approx 68.3\%$, the confidence interval of k is only bounded from below, but arbitrarily fast reaction speeds $k \to \infty$ are still consistent with the data. The fourth panel shows that the taken time points only cover the region of low sensitivity for k.

The second point of an unsuitable experimental design is of greater interest. One example of this is a very fast reaction, where the relevant dynamic part of the reaction is not captured by data and only late observations are given, where the system is already in saturation, resulting in nearly constant data for that observable. For that reaction parameter, an upper bound cannot be found using these kinds of data, as it only restricts the parameter to a lower bound. This can be discovered using the profile likelihood and is illustrated in row C of Figure 1. Here, the results of a sensitivity analysis are less clear. An a priori sensitivity analysis, where information about the most likely parameter values and measured time points is not yet available, cannot reliably

Figure 2



Effects of mismatched model complexity for given data, illustrated on data generated via a mass-action mechanism and fitted by both a mass-action and Michaelis–Menten mechanism. The data, showing concentration over time, were generated via mass-action law $S \xrightarrow{k\,E\,S} P$ with $\mathrm{d}E/\mathrm{d}t = 0$, where $(S_0, E_0, P_0) = (5, 0.1, 0)$ are the initial concentrations of the substrate S, enzyme E, and product P, respectively, with simulated observation noise $\sigma_P = 0.1$ at true parameter value $k_{\mathrm{true}} = 0.5$. **Row A**: Fit of single-parameter mass-action $S \xrightarrow{k\,E\,S} P$ from which the data were generated. Unsurprisingly, the single parameter k is *finitely identified* by the simulated data, as we see by the parabolic profile in the second panel. **Row B**: Two-parameter Michaelis–Menten mechanism $S \xrightarrow{k_{\mathrm{cat}}\,E\,S/(K_m+S)} P$ fitted to mass-action data. As one can see from the profiles (columns 2 and 3), due to the over-parametrised model, neither parameter is finitely identified by the data, although the model is locally structurally identifiable at the MLE. Overall, the ratio of the parameters k_{cat}/K_m in the Michaelis–Menten model is similar to the value of k of the underlying process. However, the associated profiles illustrate that even at a constant ratio k_{cat}/K_m, the quality of the model fit is worse if both parameters are small, leading to a lower bound on both parameter values. Instead, if both values are increased to arbitrarily large values, the resulting model fit is still compatible with the given data up to a confidence level of $1\sigma \approx 68.3$ %, leading neither parameter being finitely identified. The sensitivity analysis in the last column illustrates that although data points are given in the region where the model parameters are most *sensitive*, the parameters are nevertheless *not finitely identified* by the data.

detect this problem. This is because the time window where the informative dynamics take place depends on the reaction rate. Therefore, it cannot be guaranteed that an experimental design will cover the relevant time points without knowledge about the likely parameter values. In comparison, an a posteriori sensitivity analysis, based on parameter values that were already calibrated on measured data and reusing the same time points in the simulation as those given in the measurements, will detect parameters which are insensitive at the given most likely parameter values. This example of an a posteriori sensitivity analysis also highlights how an a priori sensitivity analysis can be of use here: If the parameter values are unknown, sensitivity analysis can be used for a range of possible parameters to determine the experimental time points needed to sufficiently calibrate the model to data for any parameter value in the possible range.

Model complexity mismatches the data

Usually, when a new model is developed with the aim of explaining given experimental data, it is not clear from the outset which of the many conceivable reaction mechanisms are essential for describing the system's behaviour and which can be neglected. In this case, identifiability analysis can be used to find the smallest model that describes the data sufficiently well. An illustrative example is the relation between a Michaelis–Menten type kinetic of the form $\mathrm{d}[P]/\mathrm{d}t = k_{\mathrm{cat}}\,[S]/(K_m + [S])$, describing the steady-state approximation of enzyme kinetics and mass-action kinetics following the equation $\mathrm{d}[P]_{\mathrm{m.a.}}/\mathrm{d}t \propto [S]$. A direct comparison between their respective equations shows that mass-action kinetics are recovered as a limiting case from the Michaelis–Menten mechanism for $K_m \gg [S]$. If a Michaelis–Menten model is fitted to mass-action data, the Michaelis–Menten mechanism is able to fit

the mass-action data perfectly. Nevertheless, if one calculates profile likelihoods for the parameters, the K_m-value is only bounded from below by the data, but not from above. Thus, a profile likelihood-based identifiability analysis would reveal the K_m-parameter as practically nonidentifiable, thereby assisting in the data-driven reduction of superfluous mechanisms from the model [41]. This case is illustrated in Figure 2, where a Michaelis–Menten kinetic is fitted to mass-action data, resulting in the parameters k_{cat} and K_m not being finitely identified.

The case of an over-parametrised model cannot be detected using sensitivity analysis methods. Usually, parameters such as the K_m are a priori less sensitive than other parameters, but it is still possible for its values to be finitely determined, given suitable data. As sensitivity methods perform the analysis based on simulated data, using the given model as the basis for the simulations, the case of an over-parametrised model cannot be detected. In the last column of Figure 2 it can be seen that the data were simulated in regions of high sensitivity for this model. Nevertheless, the overall sensitivities of the parameters k_{cat} and K_m are lower compared to the simpler mass-action model with parameter k.

Conclusion

Even though practical identifiability analysis has been accepted as a useful tool for model analysis and development, the technical definition of practical identifiability itself remains vague and differs between authors. Furthermore, it is common for models to be practically identifiable with respect to some definitions but practically nonidentifiable with respect to others. To limit miscommunication among practitioners, we advocate for the use of clear and distinctive wording when discussing the results of practical identifiability analyses, such that it is unambiguously clear from the terminology which class of methods was employed in the analysis and thus which of the possible definitions of practical identifiability is implied by this.

A priori practical identifiability analyses using a purely model-based method, i.e. without referring to recorded measurements of any kind, such as sensitivity analysis, result in statements about the sensitivity of the model with respect to its parameters. This flavour of practical identifiability analysis can be performed a priori to determine the necessary signal-to-noise ratio or to aid in developing an experimental design by scanning the expected parameter range and possible combinations of observables for insensitive parameters. On the other hand, a posteriori analyses via purely model-based methods, without referring to measurements, also use information about the experimental design, and, if available, fitted parameter values, and can determine insensitive parameters that occur, for example, due to an unsuitable experimental protocol.

A posteriori practical identifiability analyses using data-based methods, such as the profile likelihood, assess the confidence intervals of parameters given a confidence level and typically require more computational resources. Such analyses ultimately make statements about whether a parameter is finitely identified at a certain critical value, given the model and the data.

Nevertheless, both major categories of practical identifiability analysis have valid applications, which we attempted to highlight with two small examples, presenting their respective benefits and limitations. We hope that the aspects highlighted in this review aid newcomers to the field and provide an overview of practical identifiability for researchers in the life sciences, who usually come from a wide range of backgrounds.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Sedoglavic A: **A probabilistic algorithm to test local algebraic observability in polynomial time**. In *Proceedings of the 2001 international symposium on symbolic and algebraic computation, ISSAC01*. ACM; 2001:309–317, https://doi.org/10.1145/384101.384143.

2. Karlsson J, Anguelova M, Jirstrand M: **An efficient method for structural identifiability analysis of large dynamic systems**. *IFAC Proc Vol* 2012, **45**:941–946, https://doi.org/10.3182/20120711-3-be-2027.00381. ISSN 1474-6670.

3. Villaverde AF, Tsiantis N, Banga Julio R: **Full observability and estimation of unknown inputs, states and parameters of nonlinear biological models**. *J R Soc Interface* 2019, **16**,

20190043, https://doi.org/10.1098/rsif.2019.0043. ISSN 1742-5662.

4. Díaz-Seoane S, Rey Barreiro X, Villaverde AF: **STRIKE-GOLDD 4.0: user-friendly, efficient analysis of structural identifiability and observability**. *Bioinformatics* 2022, **39**, https://doi.org/10.1093/bioinformatics/btac748. ISSN 1367-4811.

5. Rey Rostro D, Villaverde AF: *StrikePy*: *nonlinear observability analysis of inputs, states, and parameters in Python*. Servizo de Publicacións da UDC; 2022:430–435, https://doi.org/10.17979/spudc.9788497498418.0430.

6. Shi X, Chatzis MN: **An efficient algorithm to test the observability of rational nonlinear systems with unmeasured inputs**. *Mech Syst Signal Process* 2022, **165**, 108345, https://doi.org/10.1016/j.ymssp.2021.108345. ISSN 0888-3270.

7. Ligon TS, Fröhlich F, Chiş OT, Banga JR, Balsa-Canto E, Hasenauer J: **GenSSI 2.0: multi-experiment structural identifiability analysis of SBML models**. *Bioinformatics* 2017, **34**: 1421–1423, https://doi.org/10.1093/bioinformatics/btx735. ISSN 1367-4811.

8. Hong H, Ovchinnikov A, Pogudin G, Yap C: **SIAN: software for structural identifiability analysis of ODE models**. *Bioinformatics* 2019, **35**:2873–2874, https://doi.org/10.1093/bioinformatics/bty1069. ISSN 1367-4811.

9. Ilmer I, Ovchinnikov A, Pogudin G: *Web-based structural identifiability analyzer*. Springer International Publishing; 2021: 254–265, https://doi.org/10.1007/978-3-030-85633-5_17. ISBN 9783030856335.

10. Bellu G, Saccomani MP, Audoly S, D'Angiò Daisy L: **A new software tool to test global identifiability of biological and physiological systems**. *Comput Methods Progr Biomed* 2007, **88**:52–61, https://doi.org/10.1016/j.cmpb.2007.07.002. ISSN 0169-2607.

11. Meshkat N, Kuo CE, DiStefano J: **On finding and using identifiable parameter combinations in nonlinear dynamic systems biology models and COMBOS: a novel web implementation**. *PLoS One* 2014, **9**, e110261, https://doi.org/10.1371/journal.pone.0110261. ISSN 1932-6203.

12. Dong R, Goodbrake C, Harrington HA, Pogudin G: **Differential elimination for dynamical models via projections with applications to structural identifiability**. *SIAM Journal on Applied Algebra and Geometry* 2023, **7**:194–235, https://doi.org/10.1137/22m1469067. ISSN 2470-6566.

13. Stigter JD, Molenaar J: **A fast algorithm to assess local structural identifiability**. *Automatica* 2015, **58**:118–124, https://doi.org/10.1016/j.automatica.2015.05.004. ISSN 0005-1098.

14. Rey Barreiro X, Villaverde AF: **Benchmarking tools for a priori identifiability analysis**. *Bioinformatics* 2023, **39**, https://doi.org/10.1093/bioinformatics/btad065. ISSN 1367-4811.

15. Heinrich M, Rosenblatt M, Wieland F-G, Stigter H, Timmer J: **On structural and practical identifiability: current status and update of results**. *Curr Opin Syst Biol* 2025, **41**, 100546, https://doi.org/10.1016/j.coisb.2025.100546. ISSN 2452-3100.

16. Wieland F-G, Hauber AL, Rosenblatt M, Tönsing C, Timmer J: **On structural and practical identifiability**. *Curr Opin Syst Biol* 2021, **25**:60–69, https://doi.org/10.1016/j.coisb.2021.03.005. ISSN 2452-3100.

17. ** Muñoz-Tamayo R, Tedeschi LO: **ASAS-NANP symposium: mathematical modeling in animal nutrition: the power of identifiability analysis for dynamic modeling in animal science: a practitioner approach**. *J Anim Sci* 2023, **101**, https://doi.org/10.1093/jas/skad320. ISSN 1525-3163.
This work emphasises the importance of identifiability analysis in dynamic modeling in animal nutrition. It advocates integrating identifiability assessments into the modeling process to enhance the reliability and applicability of models in animal science. It gives an important overview and is well written for readers of different backgrounds and levels.

18. * Lam NN, Docherty PD, Murray R: **Practical identifiability of parametrised models: a review of benefits and limitations of various approaches**. *Math Comput Simulat* 2022, **199**: 202–216, https://doi.org/10.1016/j.matcom.2022.03.020.
This review discusses different approaches to studying practical identifiability and illustrates them with simple examples.

19. Hass H, Loos C, Raimúndez-Álvarez E, Timmer J, Hasenauer J, Kreutz C: **Benchmark problems for dynamic modeling of intracellular processes**. *Bioinformatics* 2019, **35**:3073–3082, https://doi.org/10.1093/bioinformatics/btz020. ISSN 1367-4803.

20. Walter E, Pronzato L. *Identification of parametric models from experimental data*, vol. 44. Springer; 1997, https://doi.org/10.1109/TAC.1999.811220.

21. Anstett-Collin F, Denis-Vidal L, Millérioux G: **A priori identifiability: an overview on definitions and approaches**. *Annu Rev Control* 2020, **50**:139–149, https://doi.org/10.1016/j.arcontrol.2020.10.006. ISSN 1367-5788.

22. Gábor A, Villaverde AF, Banga JR: **Parameter identifiability analysis and visualization in large-scale kinetic models of biosystems**. *BMC Syst Biol* 2017, **11**, https://doi.org/10.1186/s12918-017-0428-y. ISSN 1752-0509.

23. Miao H, Xia X, Perelson AS, Wu H: **On identifiability of nonlinear ODE models and applications in viral dynamics**. *SIAM Rev* 2011, **53**:3–39, https://doi.org/10.1137/090757009. ISSN 0036-1445.

24. Saccomani MP, Thomaseth K: **The union between structural and practical identifiability makes strength in reducing oncological model complexity: a case study**. *Complexity* 2018:2018, https://doi.org/10.1155/2018/2380650. ISSN 1076-2787.

25. Pironet A, Docherty PD, Dauby PC, Chase JG, Desaive T: **Practical identifiability analysis of a minimal cardiovascular system model**. *Comput Methods Progr Biomed* 2019, **171**: 53–65, https://doi.org/10.1016/j.cmpb.2017.01.005. ISSN 0169-2607.

26. Eisenberg MC, Jain HV: **A confidence building exercise in data and identifiability: modeling cancer chemotherapy as a case study**. *J Theor Biol* 2017, **431**:63–78, https://doi.org/10.1016/j.jtbi.2017.07.018. ISSN 0022-5193.

27. ** Aoki Y, Sugiyama Y: **Cluster gauss-Newton method for a quick approximation of profile likelihood: with application to physiologically-based pharmacokinetic models**. *CPT Pharmacometrics Syst Pharmacol* 2023, https://doi.org/10.1002/psp4.13055.
The authors present the Cluster-Gauss-Newton method as an alternative to the profile likelihood. The method is applied to three models and shows promising results. This seems to be an interesting candidate for fast practical identifiability analysis.

28. * Villaverde AF: **Employing observability rank conditions for taking into account experimental information a priori**. *Bull Math Biol* 2025, **87**, https://doi.org/10.1007/s11538-025-01415-3. ISSN 1522-9602.
The authors uses the observability rank condition to analyse experimental information, such as the influence of noise, inputs, and sampling constraints a priori.

29. Wanika L, Egan JR, Swaminathan N, Duran-Villalobos CA, Branke J, Goldrick S, Chappell M: **Structural and practical identifiability analysis in bioengineering: a beginner's guide**. *J Biol Eng* 2024, **18**, https://doi.org/10.1186/s13036-024-00410-x. ISSN 1754-1611.

30. Saucedo O, Laubmeier A, Tang T, Levy B, Asik L, Pollington T, Feldman OP: **Comparative analysis of practical identifiability methods for an SEIR model**. *AIMS Mathematics* 2024, **9**: 24722–24761, https://doi.org/10.3934/math.20241204. ISSN 2473-6988.

31. Raue A, Kreutz C, Maiwald T, Bachmann J, Schilling M, Klingmüller U, Timmer J: **Structural and practical identifiability analysis of partially observed dynamical models by exploiting the profile likelihood**. *Bioinformatics* 2009, **25**:1923–1929, https://doi.org/10.1093/bioinformatics/btp358.

32. Conte M, Woodall RT, Gutova M, Chen BT, Shiroishi MS, Brown CE, Munson JM, Rockne RC: **Structural and practical identifiability of contrast transport models for DCE-MRI**. *PLoS Comput Biol* 2024, **20**, e1012106, https://doi.org/10.1371/journal.pcbi.1012106. ISSN 1553-7358.

33. Liu Y, Suh K, Maini PK, Cohen DJ, Baker RE: **Parameter identifiability and model selection for partial differential equation models of cell invasion**. *J R Soc Interface* 2024, **21**, https://doi.org/10.1098/rsif.2023.0607. ISSN 1742-5662.
* This study employs a profile-likelihood approach to assess practical parameter identifiability in four extensions of the Fisher–Kolmogorov–Petrovsky–Piskunov (Fisher–KPP) model. It discusses practical identifiability in the context of partial differential equation models.

34. Chen J-S, Jennrich RI: **Simple accurate approximation of likelihood profiles**. *J Comput Graph Stat* 2002, **11**:714–732, https://doi.org/10.1198/106186002493. ISSN 1537-2715.

35. Simpson MJ, Browning AP, Warne DJ, Maclaren OJ, Baker RE: **Parameter identifiability and model selection for sigmoid population growth models**. *J Theor Biol* 2022, **535**, 110998, https://doi.org/10.1016/j.jtbi.2021.110998. ISSN 0022-5193.

36. Murphy RJ, Maclaren OJ, Calabrese AR, Thomas PB, Warne DJ, Williams ED, Simpson MJ: **Computationally efficient framework for diagnosing, understanding and predicting biphasic population growth**. *J R Soc Interface* 2022, **19**, https://doi.org/10.1098/rsif.2022.0560. ISSN 1742-5662.

37. Simpson MJ, Walker SA, Studerus EN, McCue SW, Murphy RJ, Maclaren OJ: **Profile likelihood-based parameter and predictive interval analysis guides model choice for ecological population dynamics**. *Math Biosci* 2023, **355**, 108950, https://doi.org/10.1016/j.mbs.2022.108950. ISSN 0025-5564.

38. Necibe T, Trang TL: **Structural and practical identifiability analysis of outbreak models**. *Math Biosci* 2018, **299**:1–18, https://doi.org/10.1016/j.mbs.2018.02.004. ISSN 0025-5564.

39. Pieschner S, Hasenauer J, Fuchs C: **Identifiability analysis for models of the translation kinetics after mRNA transfection**. *J Math Biol* 2022, **84**, https://doi.org/10.1007/s00285-022-01739-x. ISSN 1432-1416.

40. Wu H, Zhao Y, Zhang C, Wu J, Lou J: **Structural and practical identifiability analyses on the transmission dynamics of Covid-19 in the United States**. *J Appl Anal Comput* 2022, **12**:1475–1495, https://doi.org/10.11948/20210300. ISSN 2156-907X.

41. Maiwald T, Hass H, Steiert B, Vanlier J, Engesser R, Raue A, Kipkeew F, Bock HH, Kaschek D, Kreutz C, Timmer J: **Driving the model to its limit: profile likelihood based model reduction**. *PLoS One* 2016, **11**, e0162366, https://doi.org/10.1371/journal.pone.0162366.