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A Note on the Accurate Computation of Structural Properties for Dynamic Control Systems

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Abstract: In analysing the observability, identifiability, and controllability of smooth (possibly non-linear) dynamic control systems, the authors identified numerous ways to improve both the accuracy and efficiency of their computations. We summarize a few techniques that help to pinpoint exactly what kind of linear dependencies exist between parametric output sensitivities. These relations, in turn, can be traced back with the help of computer algebra software to an exact re-parametrizations of the original model. The suggested techniques to increase the accuracy of results will be presented on the basis of a few examples.

Keywords: Non-linear system identification, Identification and model reduction, identifiability, controllability, observability

1. INTRODUCTION

With the ever-growing size of dynamic systems models in, for example, biology or the environmental or medical sciences, it is important to question the necessity of such complex models in the context of their intended purpose. A very relevant question that is often omitted is whether a model can/should not be reduced in size when its generated simulations of the system outputs, once compared with expert knowledge and measured data, are not unique. In the case of parameter identifiability, for example, it is known that two different sets of parameter values for a given model may yield *exactly* the same output trajectories obtained for a model simulation. If, in the inverse problem, the parameter values in these two sets must then be reconstructed from a given data record, it is mathematically *impossible* to find a unique answer for the parameter estimation problem that one tries to solve. One of the primary reasons for not completely addressing the question of observability (or its dual problem controllability) for a general dynamic control system model in the literature is that the problem is often very difficult to solve using computer algebra systems. Indeed, the observability problem suffers from the curse of dimensionality, meaning that its complexity tends to grow *exponentially* with an increase in model size (the number of state variables and/or parameters). The result is that extremely long computation times are required to actually solve the problem, (Chis et al., 2011; Chappell et al., 1990).

1.1 Motivating Example

As a demonstration example (arguably not large, but it serves well for explaining the issues we wish to highlight) that provides context to this paper, we first introduce a typical environmental model. It describes the dynamics of a population of micro-organisms that grows on two substrates. The case has been covered in the well-known paper Brun et al. (2001), where the issue of *practical* identifiability is put forward as an important topic in the environmental sciences (see also Guillaume et al. (2019)). In Stigter et al. (2017) the case is further analysed and theoretical identifiability of the model is investigated in detail.

Let $S_t(t)$ and $S_b(t)$ denote two different substrates on which a biomass $X(t)$ grows with the following dynamics:

$$\frac{dS_t}{dt} = -\frac{k_t\, S_t\, X}{K_{st} + S_t + S_b\, z_b} \tag{1}$$

$$\frac{dS_b}{dt} = -\frac{k_b\, S_b\, X}{K_{sb} + S_b + S_t\, z_t} \tag{2}$$

$$\frac{dX}{dt} = -b\, X + \frac{k_b\, S_b\, X\, Y_b}{K_{sb} + S_b + S_t\, z_t} + \frac{k_t\, S_t\, X\, Y_t}{K_{st} + S_t + S_b\, z_b} \tag{3}$$

$$S_t(0) = S_{t0} \tag{4}$$

$$S_b(0) = S_{b0} \tag{5}$$

$$X(0) = X_0 \tag{6}$$

The two terms $S_t\, z_t$ and $S_b\, z_b$ denote inhibition due to the presence of benzene and toluene in the reactor. The model comprises 9 system parameters b, k_b, K_{sb}, K_{st}, k_t, Y_b, Y_t, z_b, z_t and 3 initial conditions S_{t0}, S_{b0} and X_0, totalling to 12 parameters that determine the output behaviour of this system. We are interested in finding unique values for all parameters, including initial conditions, *from substrate measurements only.*

1.2 A Sensitivity Based Algorithm

In Stigter and Molenaar (2015) an algorithm is presented that utilizes parametric output sensitivities as a pre-processor for assessing the identifiability of model parameters from given input-output data. This numerical part

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precedes the symbolic computations that are performed in a classical observability test with Lie-derivatives. The algorithm has been extended to account for controllability and observability of state variables as well (Stigter et al., 2018; van Willigenburg et al., 2021). Given a general state space model

$$\frac{\mathrm{d}x(t)}{\mathrm{d}t} = f(x(t), u(t), \theta) \tag{7}$$

$$y(t) = h(x(t), u(t), \theta) \tag{8}$$

with $x(t)$ the vector of state variables, $u(t)$ the vector of input variables, and θ the vector of all system parameters in the model description f. The vector function h summarizes the output variables that are measured directly. We can now compute the so-called forward parametric output sensitivities in a straightforward manner as

$$\frac{\mathrm{d}}{\mathrm{d}t}\frac{\mathrm{d}x(t,\theta)}{\mathrm{d}\theta} = \frac{\partial f}{\partial x}\frac{\mathrm{d}x}{\mathrm{d}\theta} + \frac{\partial f}{\partial \theta} \tag{9}$$

$$\frac{\mathrm{d}y(t,\theta)}{\mathrm{d}\theta} = \frac{\partial h}{\partial x}\frac{\mathrm{d}x}{\mathrm{d}\theta} + \frac{\partial h}{\partial \theta} \tag{10}$$

Note that $\frac{\mathrm{d}x(t,\theta)}{\mathrm{d}\theta}$ is a $(n \times p)$ matrix, whose columns contain the sensitivity of each state-vector element $x_i(t), i = 1, \ldots, n$, to one specific parameter θ_j, $j = 1, \ldots, p$ in the parameter vector θ. To guarantee accuracy of our results, all Jacobi matrices $\frac{\partial f}{\partial x}$, $\frac{\partial f}{\partial \theta}$, $\frac{\partial h}{\partial x}$, and $\frac{\partial h}{\partial \theta}$ are calculated up to machine precision with so-called complex derivatives (Martins et al., 2001). Once the combined equations (7)–(10) have been solved numerically for a specific (also referred to as nominal) vector $\bar{\theta}$, and the solution is known on a time grid $[t_0, \ldots, t_f]$, we build the sensitivity matrix $S(t_0, \ldots, t_f, \bar{\theta})$:

$$S(t_0, \ldots, t_f, \bar{\theta}) = \begin{pmatrix} \frac{\mathrm{d}y_1(t_0)}{\mathrm{d}\theta_1} & \cdots & \frac{\mathrm{d}y_1(t_0)}{\mathrm{d}\theta_p} \\ \vdots & & \vdots \\ \frac{\mathrm{d}y_m(t_0)}{\mathrm{d}\theta_1} & \cdots & \frac{\mathrm{d}y_m(t_0)}{\mathrm{d}\theta_p} \\ \vdots & & \vdots \\ \frac{\mathrm{d}y_1(t_f)}{\mathrm{d}\theta_1} & \cdots & \frac{\mathrm{d}y_1(t_f)}{\mathrm{d}\theta_p} \\ \vdots & & \vdots \\ \frac{\mathrm{d}y_m(t_f)}{\mathrm{d}\theta_1} & \cdots & \frac{\mathrm{d}y_m(t_f)}{\mathrm{d}\theta_p} \end{pmatrix} \tag{11}$$

If we now perform a singular value decomposition of $S(t_0, \ldots, t_f, \bar{\theta})$, then zero singular values may indicate a rank deficiency of the sensitivity matrix. This can now be symbolically verified as extensively described in e.g. Stigter and Molenaar (2015); Joubert et al. (2020).

We further note that our approach to the identifiability problem has close connections with the analysis of nonlinear systems structure on the basis of empirical (cross) gramians as worked out in, e.g., Streif et al. (2006); Himpe and Ohlberger (2014); Sun and Hahn (2006). An important difference with the approach taken here is that we do not use an *empirical* gramian as a basis for the model reduction but, rather, a *precise* solution of the forward sensitivity equations that constitute the matrix (11). Checking for exact linear dependencies between the columns

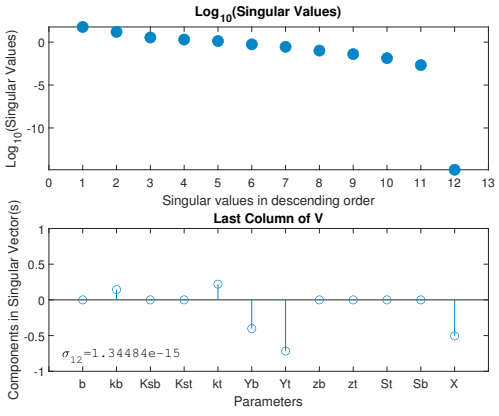

Fig. 1. Identifiability signature of the microbial degradation model with singular values (top panel) and singular vector (bottom pannel) for the only zero singular value in this case.

of this matrix and, subsequently, corroborating these dependencies with a symbolic computation, then yields a better insight in the exact state/parameter transformation that causes the lack of uniqueness in the input/output mapping. In fact, we do not even compute a gramian in this paper but, rather, analyse its pre-cursor, i.e., the matrix (11).

1.3 Accuracy of the Rank Computation

We now discuss the accuracy of the numerical SVD results for the above output sensitivity matrix and, more precisely, we seek for an accurate *rank* computation of this matrix. In our microbial degradation example an SVD of the matrix $S(t_0, \ldots, t_f, \bar{\theta})$ can be graphically represented as shown in figure 1[1]. We refer to this graph as the 'identification signature' of the given local structural identifiability problem. It shows (i) if there is a distinct gap observable in the singular values that points to a rank deficient output sensitivity matrix (top panel of the figure) and (ii) which parameters are exactly involved in a total correlation that hampers accurate parameter estimation (bottom panel of the figure). If we only measure substrate, then clearly the parameters k_b, k_t, Y_b, Y_t, and the state $X(t)$ are correlated since these show up as non-zero entries in the last singular vector of the SVD. This non-trivial nullspace that was found in the SVD analysis alludes to a possible lack of identifiability that must now be verified through a symbolic computation. The numerical issue that needs attention is that in an SVD analysis the rank deficiency of the parametric output sensitivity matrix may not be very well visible as demonstrated in figure 2. This is exactly the same case study as for the previous figure but now evaluated on a shorter integration interval. Here, the spectrum of singular values does not show a distinct gap, although the correlated parameters are still visible in the bottom panel (the zero singular vector for this particular case). 'How do we handle such cases where an SVD of the output sensitivity matrix does not give a definitive answer?' is the question that needs further investigation.

[1] All results in this paper have been computed with the StrucID App (in Matlab) that was introduced in Stigter and Joubert (2021).

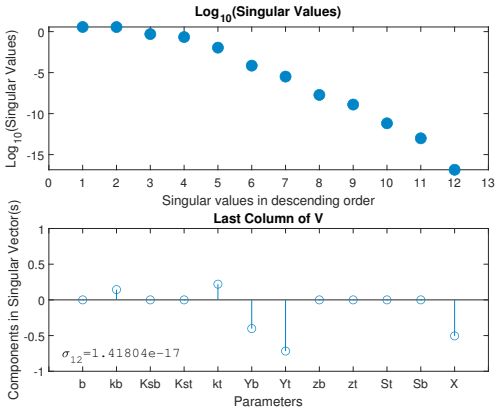

Fig. 2. Inaccurate identifiability signature of the microbial degradation model.

As it turns out several options are available to improve upon the SVD results. These include

(1) Increasing the integration time for a numerical solution of (7)-(8) to a larger final time t_f to ensure that all time scales of the problem are included in the dynamics
(2) Concatenating several sensitivity matrices, each generated by varying certain parameters in the model. Stacking of these sensitivity matrices for each individual simulation with $\{\theta_i, i = 1, \ldots, N\}$ yields one large matrix (N is the number of simulations or experiments we conduct)
(3) Adding sensors as to better expose the lack of identifiability, effectively measuring close to problematic states and/or parameters in the model

We will further elaborate on these options in the following.

2. REMEDIES

2.1 Integration Time

The first option is probably the easiest route to a better accuracy of the SVD rank test. The parametric state sensitivities (11) constitute *a linear time-varying system*, whose time scales can be checked via the eigenvalues of the Jacobi matrix $\frac{\partial f}{\partial x}$. For the microbial degradation example problem in section 1.1 these time scales were not covered completely in the identifiability signature graph of figure 2, for which the combined dynamics f and state sensitivities $\frac{\mathrm{d}x(t,\bar{\theta})}{\mathrm{d}\theta}$ were computed on the interval $[t_0, t_f] = [0, 0.5]$, whilst the results in figure 1 were computed on the interval $[t_0, t_f] = [0, 10]$. Of course, longer integration time intervals yield a richer sensitivity output (in terms of changes) and this helps in the rank determination. As a rule-of-thumb we suggest to integrate the combined dynamics (7)-(10) up to and including 3 times the *slowest* time-scale, if possible.

Yet, another option is available in this context. In case the chosen values for the parameters θ constitute *a regular point* in the parameter space (and this is often the case!), we know by definition (Kwatny and Blankenship, 2000) that the rank of the sensitivity matrix $S(t_0, \ldots, t_f, \bar{\theta})$ does *not* change on an open neighbourhood of the chosen realisation $\bar{\theta}$. But since the timescales of the problem depend on exactly these parameter values, we are allowed to tune the parameters in the model in such a way that the timescales that are computed from the Jacobi matrix are of a comparable magnitude. If such a normalisation can be performed (using e.g. a simple optimization routine), then an integration length of one time unit suffices, so that $[t_0, t_f] = [0, 1]$.

Making the integration time too long will result in loss of accuracy, in general. Hence, if no knowledge is available on the timescales of the problem, as a rule-of-thumb one should start with a relatively small integration time of one time unit, for example, and double this value several times to see if a change in the rank occurs. Since numerical integration and SVD computations can be computed rapidly, this is easy to perform. Our experience with many case studies, however, has shown that extending the final integration time does *sometimes* improve results but in practice, especially when realistic values for the nominal parameters set $\bar{\theta}$ are used, this is *not* the case. Only in few cases an extension of the integration time or, alternatively, tuning the parameters in the vicinity of a regular point as to normalize time-scales of the dynamics, will result in better results.

2.2 Concatenation

For an alternative remedy to improve upon the accuracy of our rank computation of $S(t_0, \ldots, t_f, \bar{\theta})$ we need to look better at the symbolic computations for the observability matrix at *one* specific time t_0. This is demonstrated best using our microbial degradation model (1)-(6). Since we only measure substrate concentrations in this example, the observability matrix evaluated at time $t_0 = 0$ is generated by taking successive Lie-derivatives of the two substrate outputs $y(t) = \begin{pmatrix} S_t(t) \\ S_b(t) \end{pmatrix}$ and, subsequently, compute the Jacobi matrix $\frac{\mathrm{d}G}{\mathrm{d}\theta}$ of these Lie-derivatives with respect to the correlated parameters $k_b, k_t, Y_b, Y_t, X(0)$ that have been found from the initial SVD analysis (see identifiability signature in figure 1), (Tunali and Tarn, 1987; Stigter and Molenaar, 2015):

$$\begin{pmatrix} 0 & 0 & 0 & \ldots \\ 0 & 0 & 0 & \ldots \\ 0 & -\frac{S_t(0)X(0)}{Ksb + S_b(0) + S_t(0)z_b} & 0 & \ldots \\ -\frac{S_b(0)X(0)}{Ksb + S_b(0) + S_t(0)z_t} & 0 & 0 & \ldots \\ \vdots & \vdots & & \end{pmatrix}$$

$$\begin{pmatrix} 0 & 0 \\ 0 & 0 \\ 0 & -\frac{k_t S_t(0)}{K_{st} + S_t(0) + S_b(0)z_b} \\ 0 & -\frac{k_b S_b(0)}{Ksb + S_b(0) + S_t(0)z_t} \\ \vdots & \vdots \end{pmatrix}$$

The expressions for the Lie derivatives quickly become very complicated whilst generating more rows in the above observability matrix. However, since we know from our SVD analysis that only *five* parameters are involved in a correlation, the depth of taking successive Lie derivatives can be reduced substantially. Since two measured quantities are available in this case, each new Lie derivative will generate two more rows in the observability matrix. After

three iterations we already have enough rows to compute the nullspace of the above matrix with a computer algebra package (e.g. Kwatny's ProPac in Mathematica (Kwatny and Blankenship, 2000)) as

$$\mathcal{N}(\frac{\mathrm{d}G}{\mathrm{d}\theta}) = \left(-\frac{k_b}{X(0)} \; -\frac{k_t}{X(0)} \; \frac{Y_b}{X(0)} \; \frac{Y_t}{X(0)} \; 1 \right) \qquad (12)$$

Computing more Lie derivatives does not destroy this nullspace and, hence, we have verified the lack of identifiability symbolically. Having this result, the explicit nullspace characterization (12) now reveals how exactly the output of our model is invariant (Anguelova et al., 2012):

$$-\frac{k_b}{X(0)}\frac{\partial y(0)}{\partial k_b} - \frac{k_t}{X(0)}\frac{\partial y(0)}{\partial k_t} + \frac{Y_b}{X(0)}\frac{\partial y(0)}{\partial Y_b} + \ldots \\ \frac{Y_t}{X(0)}\frac{\partial y(0)}{\partial Y_t} + \frac{\partial y(0)}{\partial X(0)} = 0 \qquad (13)$$

In fact, the above equation shows that at time $t_0 = 0$ a linear combination of the *output sensitivities* of $y(0)$ with respect to the correlated parameters $k_b, k_t, Y_b, Y_t, X(0)$ is zero. Since *all* parameters in the correlated set are *time-invariant* by definition, it is not surprising to see that the linear dependence between sensitivities will hold at *any* time t on a smooth output trajectory $y(t)$, starting at $x(0)$. Of course, these time dependent parametric output sensitivities can be computed easily via (9)-(10)!

For our microbial degradation model with substrate measurements only, we now have for any time t that:

$$-\frac{k_b}{X(0)}\frac{\partial y(t)}{\partial k_b} - \frac{k_t}{X(0)}\frac{\partial y(t)}{\partial k_t} + \frac{Y_b}{X(0)}\frac{\partial y(t)}{\partial Y_b} + \ldots \\ \frac{Y_t}{X(0)}\frac{\partial y(t)}{\partial Y_t} + \frac{\partial y(t)}{\partial X(0)} = 0 \qquad (14)$$

A verification of the linear dependency between parametric output sensitivities is depicted in figure 3. Here, parametric output sensitivities of the signal $S_t(t)$ with respect to the correlated parameters are shown, together with the linear combination as represented in (14). Indeed, we see a confirmation of the exact linear dependencies between parameteric output sensitivities. This result opens up another possibility of improving the accuracy of our rank determination of $S(t_0, \ldots, t_f, \bar{\theta})$: Since parametric output sensitivities depend, in general, on *all* parameters in the model, we can *fix* the values of those parameters that are present in the coefficients of (14), while the remaining parameters are varied. This will generate N different output trajectories $\{y_i(t), i = 1, \ldots, N\}$ and their corresponding sensitivity matrices. Each of these matrices now exhibits exactly the same dependencies between its columns. If we now stack the matrices $\{S(t_0, \ldots, t_f, \theta_i), i = 1, \ldots, N\}$ vertically, the equivalent dependency between sensitivities (read columns of the sensitivity matrix) persists. The different values of the sensitivities $y_{\theta_i}(t)$, however, cause a more pronounced/accurate finding for the zero singular value(s) that underlie(s) the lack of identifiability. This is clearly shown for our leading example in figures 4 and 5. The last figure was generated by using information obtained from 3 curves, each with different parameter values. The resulting 3 sensitivity matrices were concatenated (vertically) after which an SVD was performed. Note the clear gap in the singular values in figure 5. This clearly suggests rank deficiency. Although the above concatenation method works very well, the alert reader will notice that, in fact, we get caught in a circular argument in our exposition of the method: To improve our numerical results using concatenation, we need to know in advance which parameters are present in the coefficients of the nullspace equation (14). Yet, we can only compute these coefficients efficiently (using computer algebra software) once we know in advance which parameters are involved in such a correlation. But when using only one simulated curve of the output signal this is not always directly clear... Yet, knowing about the potential advantage of concatenating sensitivity matrices for an increased accuracy of the rank result for $S(t_0, \ldots, t_f, \theta)$ may still help a great deal in practice. For example: In our microbial degradation model we know that substrate measurements (direct state measurements) will identify the initial conditions $S_b(0)$ and $S_t(0)$ for sure and these two parameters may therefore be ruled out of the identification problem. Using these parameters as 'free' variables to generate curves that start from different values

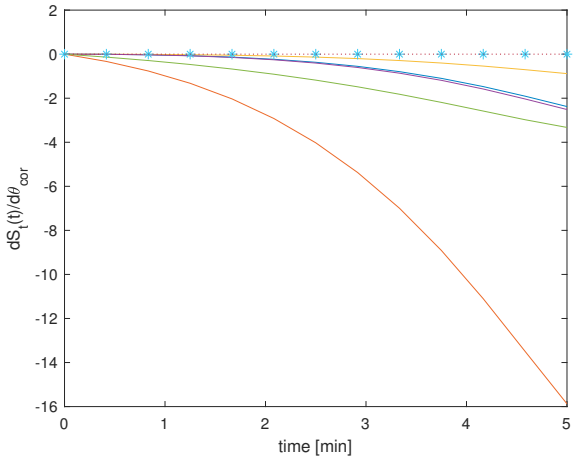

Fig. 3. A graph of the dynamic sensitivities for the sensor $S_t(t)$ with respect to the correlated parameters $k_b, k_t, Y_t, Y_b, X(0)$. The dotted line with $*$-marks is relation (14) on the interval $[t_0, t_f]$. Its zero value is clearly confirmed.

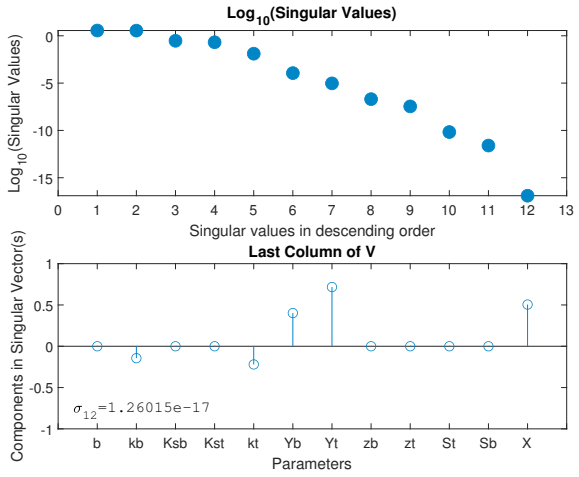

Fig. 4. Identifiability signature of the microbial degradation model with singular values (top panel) and singular vector (bottom pannel) for one sensitivity matrix $S(t_0, \ldots, t_f, \bar{\theta})$ (no concatenation).

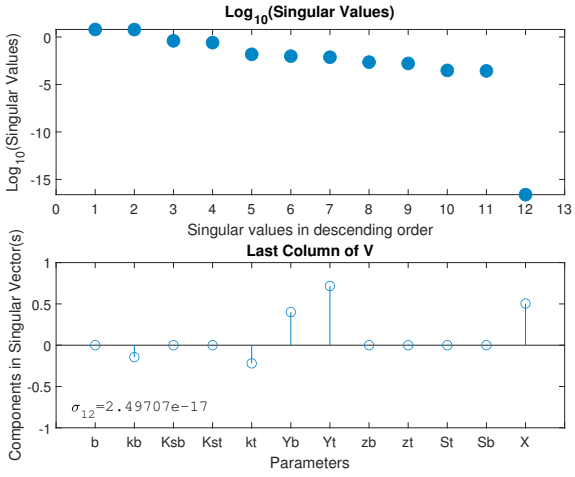

Fig. 5. Identifiability signature of the microbial degradation model with singular values (top panel) and singular vector (bottom pannel) for concatenation with three sensitivity matrices $\{S(t_0,\ldots,t_f,\theta_i), i = 1,2,3\}$ where the values of the correlated parameters $X(0), k_b, k_t, Y_t, Y_b$ have been fixed for each simulation.

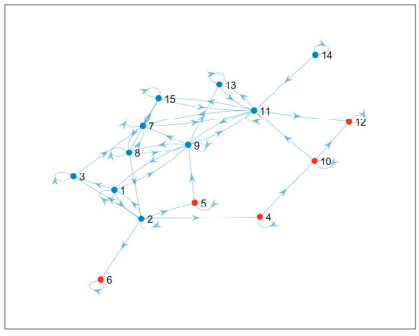

Fig. 6. Directed graph of the well-known NFκB model with the red nodes indicating the minimal sensor set. These sensors must be included for all parameters to be identifiable from the measurements.

for these initial states enable concatenation and this will already yield a better rank computation.

2.3 Smart Choice of Sensors

Another remedy for a better rank computation of the matrix $S(t_0,\ldots,t_f,\bar{\theta})$ is best demonstrated with a high-dimensional non-linear example. The NFκB model is well-known in Systems Biology and it comprises 15 states. The information flow between these 15 states is depicted in the directed graph in figure 6.

Lack of identifiability has been shown to hold by Anguelova if one of the five red-coloured sensors in this directed graph is omitted (Anguelova et al., 2012). This implies that identifiability is guaranteed if only these 5 sensors are used (also known as a minimal sensor set). If for example node 5 in the minimal sensor set is omitted, then a typical result of the SVD based algorithm is depicted in figure 7. Increasing the final integration time would already yield better results as suggested in an earlier section. Yet, if we look at the gap

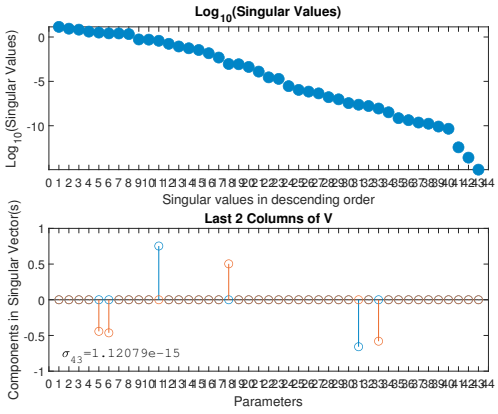

Fig. 7. Identifiability signature if node 5 is omitted from the minimal sensor set

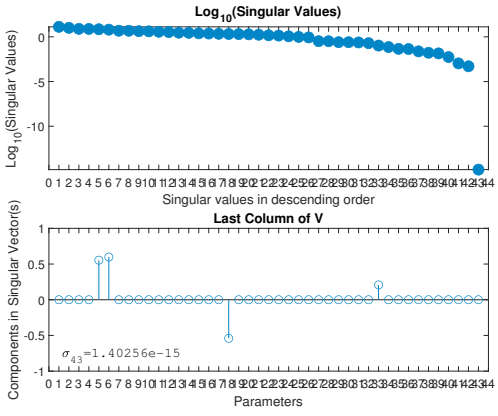

Fig. 8. Identifiability signature if all nodes in the NFκB network, *except node 5*, are measured.

size in this figure (and also the nullspace vector) we observe no distinct gap in the singular values. This is because the four remaining sensors (nodes 4, 6, 10, and 12) are too far away from the problematic node 5 in the network (figure 6). Interestingly enough there is a remedy to this problem: If, instead of measuring with a small number of sensors, we invert the configuration by measuring *all but one* of the nodes (sensor 5, for example) a clear gap in singular values emerges. This can be seen in figure 8 where the increased accuracy for the rank computation is evident.

The increase in accuracy of the correct rank for the sensitivity matrix $S(t_0,\ldots,t_f,\bar{\theta})$ is clearly seen. This is simply because the redundant number of sensors tremendously contribute to a richer measurement signal and, hence, an accurate rank computation. We further investigated this case study by systematically omitting one of the 15 state measurements and computing identifiability signatures for all cases (Joubert et al., 2018). A minimal output sensor set was immediately visible from these results and computations for the 15 sub-analyses took only 0.05 seconds on a normal desktop computer.

3. CONCLUDING REMARKS

In this paper we have suggested a few techniques to enhance the accuracy of a numerical evaluation of observability/identifiability properties of a general dynamic system.

Finding accurate zero singular values that demonstrate the rank deficiency of the parametric output sensitivity matrix is shown to be feasible. It should be further noted that the examples we have discussed in this paper have been made challenging for obvious reasons, i.e. we designed the cases in such a way that zero singular values are hard to find. Our experience has shown that these 'tricks' can be very useful for large models and their associated complex networks in particular. In general, though, for normal sized networks the tuning of, e.g. an integration time or concatenation of sensitivity matrices, is often not necessary. Rather, what happens in practice is that a good indication of a correlated set of parameters is found after 1 run of the SVD algorithm. The techniques as summarized in this paper can subsequently be used to zoom-in on a specific correlation.

A big advantage of applying the SVD algorithm is its computational speed and this pays off substantially whilst investigating a given network and sensor collection for identifiability problems. Using the StrucID App (Stigter and Joubert, 2021) quickly reveals any issues that, after the numerical part has been completed, can further be corroborated on the basis of a symbolic (*reduced*) computation with a classical observability test employing Lie-derivatives.

Appendix A. INPUT CODE STRUCID V3.5 FOR MICROBIAL DEGRADATION EXAMPLE

```
Algebraic Rules!
v1 = kt*St*X/(Kst+St+Sb*zb)
v2 = kb*Sb*X/(Ksb+Sb+St*zt)

ODEs (define the individual ODE equations - 1 per line)!
dSt/dt = -v1  % t-substrate
dSb/dt = -v2  % b-substrate
dX/dt  = -b*X + v1*Yt + v2*Yb  % biomass growth

Input variables!

Measured Outputs (define the measured sensors - 1 per line)!
y1 = St % t-substrate measurement
y2 = Sb % b-substrate measurement

Parameter names (OPTIONAL - define known parameter values)!
b = 0.0367 % decay rate biomass
kb = 0.229 % maximum degradation rate for benzene
Ksb = 0.477 % saturation constant b-substrate
Kst = 0.863 % saturation constant t-substrate
kt = 0.35 % maximum degradation rate for toluene
Yb = 0.639 % yield t-substrate
Yt = 1.14 % yield b-substrate
zb = 0.01 % benzene inhibition coefficient
zt = 1.18 % toluene inhibition coefficient

State variable names (OPTIONAL - define known initial values)!
St = 5.11
Sb = 4.72
X = 0.803

Analyse. If empty all parameters and ICs are analysed!
```

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