

Parameter Identifiability in Parallel Reaction Networks with Application to Single-Walled Carbon Nanotubes

Kejia Chen, Masako Kishida, Nitish Nair, Michael S. Strano, and Richard D. Braatz, *IEEE Fellow*

Abstract— The class of parameter estimation problems is characterized for which only the ratio of the model parameters can be identified. A mathematical signature is provided for identifying such systems, which include fed-batch reactors commonly operated in the chemical and biotechnology industries, in which reaction networks operate under quasi-steady-state conditions due to limiting addition of a reagent. The theoretical results are demonstrated through application to a single-walled carbon nanotube (SWNT) reaction network relevant to the design of nanobiosensors. Sensitivity analysis implies that such a quasi-steady-state operation of a fed-batch reactor results in the loss of information, in which none of the model parameters can be estimated.

I. INTRODUCTION

Parallel reaction networks are common in chemical and biological processes, including in polymerization [1], membrane reactors [2], isomerization in porous catalysts [3], hydrodesulfurization to remove sulfur from petroleum [4], Diels-Alder reactions to produce organic compounds with cyclohexene rings [5], hydrotreating for disposal of toxic wastes [6], multispecies reactive transport in porous media [7], carbon nanotube reaction networks [8], protein signaling networks [9], biological neural networks [10], immune systems [11], fermentations [12], and anaerobic digestion [13]. Most of these reactions are commonly carried out in the laboratory or at the production scale in fed-batch operations, in which fresh feed is added continuously or periodically. Some applications of fed-batch operations include catalytic degradation of organic molecules in wastewater [14], organic and heavy metal removal from landfill leachate by coagulation and flocculation using CaO or FeCl₃ [15], microbially-derived plastics [16,17], the fermentation of ethanol and butanol from biomass [18,19], and microbial production of proteins, amino acids, growth factors, antibodies, and antibiotics [20-23]. A large number of papers have considered the estimation of kinetic parameters in reaction networks from experimental data collected during fed-batch operations [24-27].

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K. Chen and M. Kishida are with University of Illinois at Urbana-Champaign, 600 South Mathews Avenue, Box C-3, Urbana, IL 61801 USA.

N. Nair and M. S. Strano are with Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139 USA.

R. D. Braatz is with Massachusetts Institute of Technology, Room 66-372, 77 Massachusetts Avenue, Cambridge, MA 02139 USA (phone: 617-253-3112; fax: 617-258-0546; email: braatz@mit.edu).

The accuracy of the kinetic parameters in reaction networks and in fed-batch operations depends strongly on the operating conditions of the experiment [28,29]. While some papers propose to rapidly vary the flow rate of fresh feed to excite the process dynamics [28,29], other papers propose to design fed-batch operations so that the system operates at steady-state, quasi-steady-state, or nearly quasi-steady-state conditions [26,30-32]. This paper considers a potential consequence of the latter operations on the identifiability of the estimated kinetic parameters, namely, that for some reaction networks such operations can lead to an inability to estimate *any* of the kinetic parameters from the experimental data. More specifically, a mathematical signature is derived that identifies parameter estimation problems for which only the ratios of model parameters can be identified. Identifying such experimental designs before completing the experiments would save time and effort, as well as reduce the chance of encountering this phenomenon as a surprise during the data analysis.

The theoretical results are applied to an experimental design in which 4-hydroxybenzene diazonium reacts with single-walled carbon nanotubes (SWNTs) of varying chirality [8,32,33]. This chirality, which is uniquely characterized by a pair of integers (n,m) , defines the geometric structure of the nanotube and specifies electronic structure and hence reactivity. The interest in SWNTs is motivated by their commercial potential as nanoscale wires, nanotube field effect transistors [34], and sensors [35,36]. The determination of the rate constants for SWNT parallel reaction networks is needed for the design of chirality distributions to enhance performance in SWNT-based devices [32].

II. STRUCTURAL IDENTIFIABILITY

The next result characterizes a class of systems for which values for none of the parameters can be identified from the measured variables.

Theorem 1: For a system with measured variables $y \in \mathcal{R}^r$, assume that y is a continuously differentiable function of the vector of parameters $k \in \mathcal{R}^s$ and there are no constraints or prior information regarding the parameters. If the vector of parameters k is in the null space of the sensitivity matrix $\nabla_k y \in \mathcal{R}^{r \times s}$ then no parameter k_i can be uniquely estimated.

It is not surprising that some loss in parameter identifiability occurs when k is in the null space of $\nabla_k y$; Theorem 1 is interesting in that it shows that identifiability is lost for *all* of

the model parameters for a class of systems in which $\nabla_k y$ is nearly full column rank. The proof of Theorem 1 indicates that, if the vector of model parameters is in the null space of the sensitivity matrix, then a scaling of the model parameters by a constant does not affect the measured variables and no model parameter can be identified. Theorem 1 provides a necessary condition for *any* of a system's parameters to be *structurally identifiable* [37], that is, for it to be possible to uniquely estimate any parameter from the measured variables y (as is common in the control systems literature, e.g., [37], for brevity the dependency on the measured variables on the experimental design inputs is suppressed). In most applications the sensitivity matrix $\nabla_k y$ is a function of the vector of parameters k . Since the value of k is unknown before the experiments have been carried out, in applications where Theorem 1 is applied, k is typically in the null space of $\nabla_k y$ for all k (see Section III).

Theorem 1 is complemented by the following result, which relates the structural identifiability of ratios of parameters to the above null-space condition.

Theorem 2: For a system with measured variables $y \in \mathfrak{R}^r$, assume that y is a continuously differentiable function of the vector of parameters $k \in \mathfrak{R}^s$, the parameters k_i are nonzero, and there are no constraints or other prior information regarding the parameters. If y is a function only of ratios of parameters, then the vector of parameters k is in the null space of the sensitivity matrix $\nabla_k y \in \mathfrak{R}^{r \times s}$.

For dynamical systems it is much more common to have available an explicit analytical expression for dy/dt in terms of the model parameters than to have such an expression for y . For this reason, the following corollary to Theorem 2 is typically more useful in applications to dynamical systems.

Corollary 1: For a system with measured variables $y \in \mathfrak{R}^r$, assume that y is a continuously differentiable function of the vector of parameters $k \in \mathfrak{R}^s$, the parameters k_i are nonzero, there are no constraints or other prior information regarding the parameters, and the initial value of y is independent of the parameters k_i . If dy/dt is a function only of ratios of parameters, then the vector of parameters k is in the null space of the sensitivity matrix $\nabla_k y \in \mathfrak{R}^{r \times s}$.

The above results are complemented by the following result, which is a test for whether all of the ratios of the model parameters are structurally identifiable.

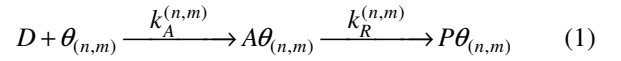
Theorem 3: For a system with measured variables $y \in \mathfrak{R}^r$, assume that (i) y is a continuously differentiable function of the parameters $k \in \mathfrak{R}^s$, (ii) the parameters k_i are nonzero and k is in the null space of the sensitivity matrix $\nabla_k y \in \mathfrak{R}^{r \times s}$, and (iii) there are no other constraints or prior information

regarding the parameters. Then *all* of the ratios of the model parameters are structurally identifiable if and only if the rank of the sensitivity matrix is $s-1$.

Theorem 3 characterizes systems with experimental designs in which the relative values of parameters can be determined. To simplify notation, the vector of experimental design variables in the above results is implicit in the definition of the vector of measurements y . A different experimental design can change the experimental design variables as well as the dependency of y on k . In either case, the above results can be applied for each y to compare different experimental designs in terms of their ability to identify the vector of parameters k . The next section demonstrates the application of the theoretical results for a parallel reaction network of carbon nanotubes.

III. APPLICATION TO THE DIAZONIUM-SWNT SYSTEM

The reaction of SWNTs with diazonium follows a two-step process [38]: an (n,m) -selective adsorption step followed by a covalent reaction step, with the adsorption step being rate limiting. The rate constants are different for SWNTs of different chirality due to the differences in electronic structures. The reaction network consists of a large number of parallel reactions, in which each path in the network is associated with SWNTs of one chirality. For each (n,m) nanotube:



where D denotes the 4-hydroxybenzene diazonium molecule, $k_A^{(n,m)} > 0$ is an adsorption rate constant, $k_R^{(n,m)} > 0$ is a reaction rate constant, and $\theta_{(n,m)}$, $A\theta_{(n,m)}$, and $P\theta_{(n,m)}$ refer to the vacant sites on the nanotube, sites occupied by the adsorption intermediate, and sites occupied by the reaction product, respectively.

Consider a fed-batch reactor in which diazonium is introduced at a known molar flow rate F_{D_0} . The conservation equations for 4-hydroxybenzene diazonium (N_D) and for vacant sites on each nanotube ($N_{\theta_{(n,m)}}$) are

$$N_D = F_{D_0} t - N_T + \sum_{(n,m)} N_{\theta_{(n,m)}}, \quad (2)$$

$$\frac{dN_{\theta_{(n,m)}}}{dt} = -k_A^{(n,m)} \frac{N_D}{V_R} N_{\theta_{(n,m)}}, \quad (3)$$

where N_T is the total moles of sites on all the nanotubes in solution and V_R is the volume of reactants, which are both known during an experiment. The value of N_D is too low to be directly measured during an experiment, and the terms on the right-hand side of (2) are not measured within sufficient accuracy for (2) to be used as a way of indirectly measuring N_D (the right-hand side of (2) involves the difference between two large numbers of very similar magnitude, N_T

and $\sum_{(n,m)} N_{\theta_{(n,m)}}$; even very accurate measurement of these

values results in order-of-magnitude errors in N_D if an attempt is made to estimate N_D from the right-hand side of (2)). Taking ratios in (3) relates the coverages of nanotubes of different chiralities to each other:

$$\frac{dN_{\theta_{(n,m)}}}{dN_{\theta_{(n',m')}}} = \frac{k_A^{(n,m)} N_{\theta_{(n,m)}}}{k_A^{(n',m')} N_{\theta_{(n',m')}}} \Rightarrow N_{\theta_{(n,m)}} = N_{\theta_{0(n,m)}} \left(\frac{N_{\theta_{(n',m')}}}{N_{\theta_{0(n',m')}}} \right)^{k_A^{(n,m)}/k_A^{(n',m')}}. \quad (4)$$

Inserting (2) and (4) into (3) results in decoupled differential equations [8]:

$$\frac{dN_{\theta_{(n',m')}}}{dt} = \frac{k_A^{(n',m')} N_{\theta_{(n',m')}}}{V_R} \left(F_{D_0} t - N_T + \sum_{(n,m)} N_{\theta_{0(n,m)}} \left(\frac{N_{\theta_{(n',m')}}}{N_{\theta_{0(n',m')}}} \right)^{k_A^{(n,m)}/k_A^{(n',m')}} \right). \quad (5)$$

The values of $N_{\theta_{(\tilde{n},\tilde{m})}}$ at each time in the experiment can be measured by deconvolution of the absorption spectrum of the SWNT solution [39], which is a very large quantity of highly informative data for estimating the adsorption rate constants $k_A^{(\tilde{n},\tilde{m})}$, in that the states are measured for all time during a dynamic experiment and all of the parameters enter the decoupled state equations (5) in a simple algebraic manner. It can be shown, however, that the *structural identifiability of all of the rate constants is lost when the experiment is operated in a quasi-steady-state manner*. Specifically, assume that the fresh feed is added slowly so that the diazonium concentration is not allowed to accumulate¹ [32]:

$$\frac{dN_D}{dt} = F_{D_0} - \frac{N_D}{V_R} \sum_{(n,m)} k_A^{(n,m)} N_{\theta_{(n,m)}} \doteq 0$$

¹ This is the quasi-steady-state approximation, as described in any chemical reaction engineering textbook, e.g., [40]. The convention used in such textbooks (e.g., see page 343 of [40]) is to use equality signs in (6) and (7) to indicate that the left- and right-hand sides are so close to being equal as to be indistinguishable in experiments, usually with less than 0.1% error except for very short times. This paper uses the rigorous notation \doteq . For a detailed singular perturbation analysis of the accuracy of such the quasi-steady-state approximation for a particular reaction network, see pages 104-108 of [41]. There is no value in analyzing the higher order terms in a singular perturbation expansion when considering structural identifiability for this example because such higher order terms are not measurable in the experiment.

$$\Rightarrow N_D \doteq \frac{F_{D_0} V_R}{\sum_{(n,m)} k_A^{(n,m)} N_{\theta_{(n,m)}}} \quad (6)$$

so that the operations are always at quasi-steady-state. Substituting (4) and (6) into (3) results in

$$\frac{dN_{\theta_{(n',m')}}}{dt} \doteq - \frac{F_{D_0} N_{\theta_{(n',m')}}}{\sum_{(n,m)} \frac{k_A^{(n,m)}}{k_A^{(n',m')}} N_{\theta_{0(n,m)}} \left(\frac{N_{\theta_{(n',m')}}}{N_{\theta_{0(n',m')}}} \right)^{k_A^{(n,m)}/k_A^{(n',m')}}} \quad (7)$$

which indicates that the derivative of the number of vacant sites on a nanotube has only the *ratios* of rate constants as parameters (as well as the flow rate F_{D_0} and the initial conditions). Application of Corollary 1 to (7) implies that $(\nabla_k y)k \doteq 0$, where $k \in \mathfrak{R}^s$ is the vector of rate constants $k_A^{(n,m)}$ stacked in any order and $y \in \mathfrak{R}^r$ is the vector of open-site coverages $N_{\theta_{(n,m)}}$ stacked up for all (n,m) and all measurement times t . This result and Theorem 1 imply that *no rate constant $k_A^{(n,m)}$ can be uniquely estimated from experimental data collected from the quasi-steady-state operations*.

To assess what information on the model parameters can be determined from experimental data, first consider experiments in which 4-hydroxybenzene diazonium D is added to the reactor at any rate. To apply Theorem 3, it is useful to arbitrarily select SWNTs of chirality (n',m') as a reference to which the coverages of nanotubes of other chiralities will be related, and apply the chain rule to (4) to determine the elements of the sensitivity matrix $\nabla_k y$ as (without loss in generality, it is assumed that $k_A^{(n',m')} \neq 0$):

$$\frac{\partial N_{\theta_{(n,m)}}}{\partial k_A^{(n,m)}} = \frac{k_A^{(n,m)} N_{\theta_{(n,m)}}}{k_A^{(n',m')} N_{\theta_{(n',m')}}} \frac{\partial N_{\theta_{(n',m')}}}{\partial k_A^{(n,m)}} + \frac{N_{\theta_{(n,m)}}}{k_A^{(n',m')}} \ln \frac{N_{\theta_{(n',m')}}}{N_{\theta_{0(n',m')}}}, \quad (n,m) \neq (n',m'). \quad (8)$$

$$\frac{\partial N_{\theta_{(n,m)}}}{\partial k_A^{(\tilde{n},\tilde{m})}} = \frac{k_A^{(n,m)} N_{\theta_{(n,m)}}}{k_A^{(n',m')} N_{\theta_{(n',m')}}} \frac{\partial N_{\theta_{(n',m')}}}{\partial k_A^{(\tilde{n},\tilde{m})}}, \quad (n,m) \neq (\tilde{n},\tilde{m}) \neq (n',m'), \quad (9)$$

$$\frac{\partial N_{\theta(n,m)}}{\partial k_A^{(n',m')}} = \frac{k_A^{(n,m)} N_{\theta(n,m)}}{k_A^{(n',m')} N_{\theta(n',m')}} \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n',m')}} - \frac{k_A^{(n,m)} N_{\theta(n,m)}}{(k_A^{(n',m')})^2} \ln \frac{N_{\theta(n',m')}}{N_{\theta_0(n',m')}} \quad (14)$$

$$\sum_{(n,m)} k_A^{(n,m)} \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n,m)}} \doteq 0 \quad (14)$$

$$(n,m) \neq (n',m'). \quad (10)$$

Pre- and post-multiplication of the sensitivity matrix by two full-rank matrices results in

$$\begin{pmatrix} I_{s-1} & \begin{bmatrix} \vdots \\ \frac{k_A^{(n,m)} N_{\theta(n,m)}}{k_A^{(n',m')} N_{\theta(n',m')}} \\ \vdots \\ 1 \end{bmatrix} \\ \mathbf{0}_{1 \times s-1} & 1 \end{pmatrix} \nabla_k y \begin{pmatrix} I_{s-1} & \begin{bmatrix} \vdots \\ \frac{k_A^{(n,m)}}{k_A^{(n',m')}} \\ \vdots \\ 1 \end{bmatrix} \\ \mathbf{0}_{1 \times s-1} & 1 \end{pmatrix} \\ = \begin{pmatrix} \text{diag} \left\{ \frac{N_{\theta(n,m)}}{k_A^{(n',m')}} \ln \frac{N_{\theta(n',m')}}{N_{\theta_0(n',m')}} \right\} & \mathbf{0}_{s-1 \times 1} \\ \left[\dots \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n,m)}} \dots \right] & \sum_{(n,m)} \frac{k_A^{(n,m)}}{k_A^{(n',m')}} \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n,m)}} \end{pmatrix}, \quad (11)$$

where this $y \in \mathfrak{R}^s$ has been defined for a single time instance and its elements $N_{\theta(n,m)}$ ordered to correspond to the same order of the rate constants $k_A^{(n,m)}$ in k . The nonzero value for the (s,s) principal minor in (11) implies that the sensitivity matrix $\nabla_k y$ is full rank and all of the parameters are structurally identifiable if and only if

$$\sum_{(n,m)} k_A^{(n,m)} \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n,m)}} \neq 0. \quad (12)$$

Equations (8)-(10) imply that

$$(\nabla_k y)k = \begin{pmatrix} \vdots \\ \frac{k_A^{(n,m)} N_{\theta(n,m)}}{k_A^{(n',m')} N_{\theta(n',m')}} \\ \vdots \\ 1 \end{pmatrix} \sum_{(n,m)} k_A^{(n,m)} \frac{\partial N_{\theta(n',m')}}{\partial k_A^{(n,m)}}. \quad (13)$$

Comparison of the last element of (13) with the above result that $(\nabla_k y)k \doteq 0$ for the quasi-steady-state operations implies that

for such experiments, which is consistent with condition (12) being necessary and sufficient for all of the parameters to be structurally identifiable. The nonzero value for the (s,s) principal minor in (11) implies that the sensitivity matrix has rank $s-1$ when (14) holds, which implies from Theorem 3 that *all of the ratios* of the rate constants are structurally identifiable under quasi-steady-state operations, from experimental data collected at a single time instant. The ratios can be estimated by fitting (7) to experimental data, with the accuracy of the ratios improved by including data from multiple time points.

IV. CONCLUSIONS

The behavior characterized in Theorems 1-3 and Corollary 1 is likely to occur in reaction networks with parallel intermediate reactions with quasi-steady-state operation in the initial or subsequent reactions. Such behavior may not be obvious from inspection in a highly integrated complex reaction network. The theoretical results provide signatures that can be used to identify such behavior. While analytical expressions for the sensitivity matrix can be derived for some systems, such as the diazonium-SWNT reaction network, usually the sensitivity matrix for complex reaction networks is computed numerically by applying finite differences to a simulation model. In this case, the null space and rank conditions in Theorems 1 and 3 can be evaluated for the numerically obtained sensitivity matrix without requiring any algebraic manipulations. When $(\nabla_k y)k = 0$ then none of the model parameters can be uniquely estimated and if also rank $\{\nabla_k y\} = \dim\{k\} - 1$ then all of the ratios of model parameters are structurally identifiable. When $(\nabla_k y)k = 0$ is observed and the value for each model parameter is desired then the experimental apparatus or process operations should be redesigned to better excite the process dynamics, such as by D-optimal design (e.g., see [37,43-45] and citations therein).

APPENDIX

Proof of Theorem 1: Given $(\nabla_k y)k = 0$, the measurement vector y is not affected by multiplication of the parameter vector k by any scalar:

$$\delta y = (\nabla_k y)\delta k = (\nabla_k y)\gamma k = \gamma(\nabla_k y)k = 0. \quad (A1)$$

Since scaling all of the parameters by a constant has no effect on the measurement vector y , no parameter can be uniquely estimated (identified) from y . QED.

Proof of Theorem 2: Under the assumptions, all ratios of parameters can be written in terms of the elements of $k' = [k_1/k_s \dots k_{s-1}/k_s]^T$ and the i th measurement is a

continuously differentiable function of these ratios, $y_i = f_i(k')$. Then

$$(\nabla_k y_i)k = \left[\frac{\partial f_i}{\partial(k_1/k_s)} \frac{1}{k_s} \quad \dots \quad \frac{\partial f_i}{\partial(k_{s-1}/k_s)} \frac{1}{k_s} \right. \\ \left. \frac{\partial f_i}{\partial(k_1/k_s)} \left(-\frac{k_1}{k_s^2} \right) + \dots + \frac{\partial f_i}{\partial(k_{s-1}/k_s)} \left(-\frac{k_{s-1}}{k_s^2} \right) \right] k = 0. \quad (\text{A2})$$

QED.

Proof of Corollary 1: Under the assumptions, following similar steps as in the proof of Theorem 2,

$$\left(\nabla_k \frac{dy_i}{dt} \right) k = 0, \quad (\text{A3})$$

where k is the vector of adsorption rate constants. Swapping the order of differentiation gives

$$\left(\nabla_k \frac{dy_i}{dt} \right) k = \frac{d}{dt} (\nabla_k y_i) k = \frac{d}{dt} ((\nabla_k y_i) k) = 0. \quad (\text{A4})$$

The independence of the initial value of y with respect to k implies that

$$(\nabla_k y_i) k \Big|_{t=0} = 0. \quad (\text{A5})$$

Together (A4) and (A5) imply that $(\nabla_k y_i) k = 0$ and $(\nabla_k y) k = 0$ for all time $t > 0$. QED.

Proof of Theorem 3: For the vector of parameters $k = [k_1 \dots k_s]^T$, define the vector of parameter ratios as $k' = [k_1/k_s \dots k_{s-1}/k_s]^T$, which is identifiable if and only if all parameter ratios are identifiable. Given $(\nabla_k y) k = 0$ and all $k_i \neq 0$, the differential in the ratio of the parameters satisfies

$$\delta k'_i = \delta(k_i/k_s) = \delta k_i/k_s - k_i \delta k_s/k_s^2 \text{ for } i = 1, \dots, s-1 \\ \delta k = \begin{pmatrix} k_s \delta k' \\ 0 \end{pmatrix} + \frac{\delta k_s}{k_s} k \\ \delta y = (\nabla_k y) \delta k = \nabla_k y \left(\begin{pmatrix} k_s \delta k' \\ 0 \end{pmatrix} + \frac{\delta k_s}{k_s} k \right) = k_s \nabla_k y \begin{pmatrix} \delta k' \\ 0 \end{pmatrix} \quad (\text{A6}) \\ = k_s [(\nabla_k y)_{1:s-1} \quad (\nabla_k y)_s] \begin{pmatrix} \delta k' \\ 0 \end{pmatrix} = k_s (\nabla_k y)_{1:s-1} \delta k'$$

Applying equation (6.1.57) from Beck and Arnold [42] to this system results in the equivalent conditions

$$k' \text{ is structurally identifiable} \Leftrightarrow k_s^2 (\nabla_k y)_{1:s-1}^T (\nabla_k y)_{1:s-1} > 0 \\ \Leftrightarrow \text{rank} (\nabla_k y)_{1:s-1} = s-1, \quad (\text{A7})$$

which are used to prove Theorem 3 in the forward direction:

- (i) k' is structurally identifiable $\Rightarrow \text{rank} (\nabla_k y)_{1:s-1} = s-1$
 $\Rightarrow \text{rank} (\nabla_k y) \geq s-1$
- (ii) \exists at least 1 nonzero vector in the null space of $\nabla_k y$ (A8)
 $\Rightarrow \text{rank} (\nabla_k y) \leq s-1$
- (i) and (ii) $\Rightarrow \text{rank} (\nabla_k y) = s-1$.

The reverse direction of Theorem 3 is shown by proof by contrapositive. Denote the columns of the sensitivity matrix by $\nabla_k y = [c_1 \ c_2 \ \dots \ c_s]$. If all of the ratios of the parameters are not structurally identifiable, then (A7) implies that

$$\text{rank} (\nabla_k y)_{1:s-1} < s-1 \\ \Rightarrow \text{the vectors } \{c_1, c_2, \dots, c_{s-1}\} \text{ are linearly dependent} \quad (\text{A9}) \\ \Rightarrow \exists \text{ a non-zero vector } \beta \text{ such that } \sum_{i=1}^{s-1} \beta_i c_i = 0.$$

Then

$$\sum_{i=1}^{s-1} \beta_i c_i + 0c_s = 0 \\ \Rightarrow [\beta_1 \ \beta_2 \ \dots \ \beta_{s-1} \ 0]^T \text{ is in the null space of } \nabla_k y \\ \Rightarrow \exists \text{ at least two linearly independent vectors in the null} \\ \text{space of } \nabla_k y \text{ (i.e., } [\beta_1 \ \beta_2 \ \dots \ \beta_{s-1} \ 0]^T \text{ and } k \text{ where } k_s \neq 0) \\ \Rightarrow \text{rank} (\nabla_k y) \neq s-1.$$

QED.

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