REMARKS ON BELLMAN'S STRUCTURAL IDENTIFIABILITY

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Abstract. This paper remarks on unidentifiable compartmental systems. Emphasis is placed on detecting properties of the system directly from the compartmental diagram without resort to complicated analysis. New concepts are introduced. One is separability, a condition in which two or more parameters enter the identification equations only as a certain combination thereby preventing their identification. Concepts from linear algebra such as span, basis, and dimension are adopted to "parameter spaces". A necessary and sufficient condition for interval identification is presented.

1. Introduction. This paper is dedicated in memory of Richard Bellman. Although only a small portion of Bellman's work deals directly with compartmental systems, his contributions to this discipline are well-known, fundamental in nature, and enormously inspirational. When asked to define compartmental analysis in a few words, Bellman's reply was simply this, "it is so determined what is occurring in one compartment by sampling another." Bellman formalized this notion in his celebrated paper with Astrom [1] in which the term "structural identifiability" was coined. This paper focused attention on an important question. Given an experimental configuration and a proposed model describing the flow from input compartments to output (observed) compartments, is it at all possible to identify the model parameters from observed data? The paper pointed out that even under the best of circumstances, in so far as the quality of data and computer methodology, at best only the impulse response function could be identified. Consequently, only those parameters which could be determined from the impulse response function, or equivalently, from the transfer function, could be identified. These are the structural identifiable parameters. The paper illustrated this concept by the following simple example.

Example (Bellman and Astrom). Consider the system in Figure 1 with input/output from compartment 1.

Figure 1 Bellman-Astrom example

The transfer function for this system is

$$T(s) = (s + c_1)/(s^2 + c_2s + c_3),$$

where

$$c_1 = a_{02} + a_{12},$$

$$c_2 = a_{01} + a_{21} + a_{02} + a_{12},$$

$$c_3 = (a_{01} + a_{21})(a_{02} + a_{12}) - a_{12}a_{21},$$

are the (structurally) identifiable parameters. The above three equations constitute the "identification equations" for the four unknown parameters $a_{01}, a_{21}, a_{02}, a_{12}$. The number of unknowns exceeds the number of equations and there exists an infinite number of solutions. It is not possible to determine from the values of c_1, c_2 , and c_3 the proper solution. The system is unidentifiable.

Following publication of the Ballman-Astrom paper a rigorous effort has been pursued to determine algorithms or tests for identifiability (e.g., [2-20]). In this paper some further remarks will be contributed to the theory of structural identifiability all of which are motivated by the above example.

The first remark deals with a predicament which is characteristic of unidentifiable systems. For instance, in reference to Figure 1, if the outflow coefficients $a_{11} = -(a_{01} + a_{21})$, $a_{22} = -(a_{02} + a_{12})$ are used in place of the excretion coefficients a_{01}, a_{02} , then the identification equations are written as

$$c_1 = -a_{22}, c_2 = -a_{11} - a_{22}, c_3 = a_{11}a_{22} - (a_{12}a_{21}),$$

where $a_{11}, a_{22}, a_{12}, a_{21}$ are now to be regarded as the four unknowns.

Observe that a_{12} and a_{21} appear only as the product $(a_{12}a_{21})$ and since there are no relations between the four unknown parameters, it is clear that a_{12} and a_{21} are not identifiable; only their product $\gamma = a_{12}a_{21}$ is identifiable. The source of the system unidentifiability is the "inseparability" of a_{12} and a_{21} . Section 3 shows that inseparability

may be detected from the flow diagram without resort to the identification equations and complicated analysis.

Interest in the identifiability question should not end with the discovery that the system is not identifiable. Distefano [17] posed an interesting question which may be phrased as follows. Given that a parameter is not identifiable then what is the extent of its unidentifiability? If the parameter p can be confined to an interval $|p - \bar{p}| < \epsilon$ then ϵ provides a measure of unidentifiability. If ϵ is relatively small then $\bar{p}$ provides a practical estimate of the parameter's value. Naturally one seeks to determine the smallest interval constraining p but this problem makes no sense unless it is ascertained first that p is at least "interval identifiable", i.e., it contained in a finite interval. It is shown in Section 4 that interval identifiability is apparent from the flow diagram; see Proposition 4.1.

The example in Figure 1 is not identifiable but certain physiologically important parameters are identifiable. For instance, the residence time in compartment 1 for particles initiating in compartment 1 is given by $t_{11} = -a_{22}/(a_{11}a_{22} - a_{12}a_{21})$ [19]. Since $t_{11} = c_1/c_3$ it is identifiable. In large systems it may be difficult to determine whether or not a particular parameter is identifiable. The problem is reminiscent of linear spaces. If one thinks of the set of all identifiable parameters as a "subspace" of the "space" of all parameters then the first step would be to find a suitable "basis" for this subspace. Having accomplished this, the next step would be to determine whether the parameter in question is spanned by the basis. These notions from linear vector spaces would be very useful for structural identifiability; however, the set of identifiable parameters is not a linear space, in fact its structure is typically

highly nonlinear. Yet an analogy between parameter sets and linear spaces is possible. This point is taken up in Section 5.

The next section discusses the meaning of structural identifiability which has been subject to confusion and misunderstanding [3].

2. The meaning of structural identifiability. The definition of structural identifiability originally presented by Bellman and Astrom left some ambiguities which have been clarified by Cobelli and Distefano [2]. The latter definition, which is used here, may be summarized for the casual reader as follows.

In each problem there is a set of unknown parameters $U = \{u_1, u_2, \dots, u_v\}$. In a series of experiments on different subjects the values of these parameters will vary from subject to subject. In each experiment, and for a given subject, one anticipates a set of data. As pointed out by Bellman and Astrom, the data can at best determine the impulse response function. The latter is typically represented as a sum of exponentials, but it can be represented in other ways such as by its Laplace transform, i.e., the transfer function, or by a series expansion, i.e., by the Markov parameters. Each representation of the impulse response function furnishes a set of parameters, $O_R = \{r_1, r_2, \dots, r_\mu\}$, e.g., an exponential sum representation furnishes the exponential time constants and their associated coefficients. These parameters are considered identifiable. The term "identifiable" in this context means that the input/output model configuration does not, by itself, prevent the identification of the parameter. Of course, other factors, such as the quality of the data or the computer "fitting" algorithm may cause identification errors, but structural identification addresses the issue only from the standpoint of the validity of input/output configuration. Each impulse-response parameter is composed of the unknown parameters; let $r_i = f_i(u_1, u_2, \dots, u_v)$ express these relations. These μ relations comprise the identification equations for the v unknown parameters u_j . The identification equations necessarily have at least one solution; the structural identification question concerns

the uniqueness of solutions.

The unknown parameters vary from subject to subject but are restricted to a physiological realistic domain, say Ω . In each experiment and for a particular subject one will determine a nominal point $u^* = (u_1^*, u_2^*, \dots, u_v^*)$ in Ω . If u^* is the only solution of the identification equations in Ω then the system is said to be identifiable, meaning that the input/output configuration is acceptable but even if there are other solutions the system may still be considered acceptable. For instance, suppose that u^{**} is another solution along with u^* . If the two solutions are sufficiently far apart, then because a "ball-park" estimate of the true solution may be available, one may be able to distinguish the valid solution from the extraneous solution. For this reason the input/output configuration is considered acceptable (locally identifiable) if each solution is unique in some neighborhood of the point; i.e., if it is locally unique. Suppose that solutions are not all locally unique but the instance of non-local uniqueness is rare then the input/output configuration is still considered acceptable provided that the "bad points" are scarce enough to be within a set of zero measure. Roughly speaking, a set has zero measure if lumping its points together produces a set which has "zero(n-dimensional)volume," such as a lower dimensional hyperplane. A property which holds everywhere except on a set of zero measure is said to occur almost everywhere (a.e.). If solutions are locally unique (a.e.) then the input/output configuration is given the stamp of approval by saying that it is structurally identifiable, or identifiable, for short.

Structural identifiability theory has generated a number of tests which have been formalized and computerized. These tests serve to avoid the situation illustrated by the Bellman-Astrom example, where the identification

equations do not determine locally unique parameter values (a.e.) but rather only certain combinations of parameters are unique. The tests are particularly advantageous in that actual data is not involved; the tests can be applied during the planning stage prior to the experiment.

3. Inseparability. Unidentifiability is typically the result of two or more parameters entering the identification equations only as combinations and therefore these parameters are inseparable, a property already noted in Section 1 in regard to the Bellman-Astrom example. In general, let U denote the set of unknown parameters. The parameters in U are assumed to be independent in the sense of having no a priori relations between them. A subset S of U is said to be inseparable if the parameters in S enter the identification equations only as a certain combination. The main purpose of this section is to show how inseparability might be apparent directly from the flow diagram.

A (linear, time-invariant) compartmental system is defined by three matrices: the $n \times n$ compartmental matrix A , the $p \times n$ input matrix B , and the $n \times q$ output matrix C . A subset U of the elements of these matrices, denoted respectively, a_{ij} , b_{lm} , c_{rs} , are the unknown parameters to be identified. It is assumed throughout this paper that the parameters in U are not a priori related.

The impulse response function (matrix) is

$$R(t) = C \exp(tA)B.$$

Identifiable parameters are obtained by representing $R(t)$ in a convenient form. Popular forms for representing $R(t)$ include the exponential sum, the transfer function, the Jordan canonical form, and the Markov parameter form. All these forms are equivalent in the sense that they each generate the same set of identifiable parameters, θ . It is convenient for the purpose of this section to exploit the Markov parameter (or power series) form,

$$R(t) = M_0 + M_1 t + \dots + M_k t^k / k! + \dots, \quad t > 0,$$

where

$$M_k = CA^k B,$$

are called the Markov matrices; their elements are the Markov parameters [13]. The set of all Markov parameters, which depend on u , is denoted by O_R . A parameter is identifiable if and only if it can be constructed from parameters in O_R . (O_R can be thought of as a "basis" for O as discussed in Section 5).

Before proceeding further additional notation is required. A compartment, say (compartment) j , is said to be an input compartment if $b_{jk} \neq 0$ for at least one index k ; it is said to be an output compartment if $c_{ij} \neq 0$ for at least one index i .

The (directed) graph of the matrix A consist of vertices and directed arcs connecting the vertices. Each vertex corresponds to a compartment. It is common practice to refer to a vertex as a compartment when no confusion should arise as to the intended meaning. A directed arc $j \rightarrow i$ exists in the graph of A if and only if $a_{ij} \neq 0$. The graph of A has the same structure as the compartmental diagram with two exceptions. (i) The compartmental diagram presents the excretion elements a_{0j} from compartments j to the environment 0 but these arcs are absent from the graph of A (unless the environment is considered as a compartment). (ii) The graph of the matrix A contains arcs $j \rightarrow j$ when $a_{jj} \neq 0$, these special arcs are called loops, but loops are absent in the compartmental diagram. Loops are not necessary in the compartmental diagram because of the relations

$$a_{jj} = -\sum_{i \neq j} a_{ij}, \quad (3.1)$$

where the index i takes on all values from 0 to n except j . Since $a_{ij} \geq 0$ for all $i \neq j$, $a_{jj} = 0$ if and only if $a_{ij} = 0$ for all $i \neq j$, in which case j is absorbing. Thus the graph of A is obtained from the compartmental diagram by eliminating the arcs to the environment and placing a loop at j when there is at least one arc emanating from j to

another compartment or to the environment (compare figures 1 and 2).

Figure 2. The graph of the compartmental matrix associated with Figure 1.

It is useful to review some concepts from graph theory. A sequence (of directed arcs (in the graph of A)) is an ordered set of arcs $j \rightarrow r$, $r \rightarrow q, \dots, k \rightarrow i$, where each successor emanates away from the compartment that its precursor directs toward. The length of a sequence is the number of arcs in the sequence. A sequence may intersect one compartment more than once. A sequence which traverses each compartment along its route only once and such that the last arc does not join the first is called a path. Thus, a path involving m compartments is of length $m - 1$. A sequence which traverses each compartment along its route only once such that the last arc joins the first is called a cycle. Thus a cycle involving m compartments is of length m and a loop is a cycle of unit length. The weight of an arc $j \rightarrow i$ is a_{ij} . The weight of a sequence is the product of the weights of the arcs along the sequence. This definition applies as well to the weight of a path or to the weight of a cycle as these are special sequences.

Returning to consideration of the Markov parameters, let $m(s, t; k)$ denote the element of M^k in the (s, t) position. It follows from matrix multiplication that $m(s, t; k)$ is the sum of those terms which can be expressed as $c_{s1} a(i, j; k) b_{jt}$ where $a(i, j; k)$ denotes the element of A^k in the (i, j) position ($k \geq 1$). Let $\Gamma(i, j; k)$ denote the set of sequences from j to i of length k ($k \geq 1$) and let $w(\sigma)$ denote the weight of a sequence σ . It follows from matrix multiplication [15] that

$$a(i,j;k) = \sum_{\sigma \in \Gamma} w(\sigma) \quad (k \geq 1), \quad (3.2)$$

where $\Gamma = \Gamma(i,j;k)$. From this representation of the Markov parameters one obtains the following observations.

Remark 3.1. $a(i,j;k)$ is nonzero only if: 1) there is at least one input compartment j such that $b_{jt} \neq 0$ 2) there is at least one output compartment i such that $c_{si} \neq 0$ and 3) there is at least one sequence σ from j to i of length k ($k \geq 1$).

Remark 3.2. If an arc $u \rightarrow v$ is not contained in a sequence from an input compartment to an output compartment then the associated matrix element a_{vu} does not appear explicitly in the representation of Markov parameters and therefore it does not appear explicitly in the identification equations. A compartment is said to be input/output reachable if the compartment is traversed by at least one sequence from an input compartment to an output compartment. If a compartment, say j , is not input/output reachable then the matrix elements a_{ij} , associated with transfers away from j , do not appear explicitly in the identification equations.

Remark 3.3. Suppose that $S = \{u_i \rightarrow v_i: i=1,2,\dots,m\}$, $m > 1$ is a subset of arcs such that every sequence from an input compartment to an output compartment that contains one member of S also contains the others. Then every sequence σ which contains S must traverse each member of S the same number of times, say p , in which case $w(\sigma)$ can be factored as $w(\sigma) = r\pi^p$, where π is the product of the weights of the arcs in S and r is independent of these weights. The matrix elements associated with the arcs in S are inseparable; at most their product π is expressed in the identification equations.

Remark 3.4. (the excretory condition). Although a parameter a_{1j} may be inseparable from other parameters it may still be identifiable if the other parameters occurring in relation (3.1) are identifiable. But this special situation is possible only when $a_{0j} = 0$ because a_{0j} does not occur explicitly in the identification equations (obtained from the Markov parameter representation of the impulse response function). If a_{1j} is inseparable from other parameters and if compartment j is excretory (i.e., $a_{0j} \neq 0$) then a_{1j} is not identifiable from the identification relations and neither is a_{0j} .

Remark 3.5. (exclusion of loops). The set S in Remark 3.3 cannot contain a loop. In fact if σ is a sequence, of length > 1 , from an input compartment to an output compartment which contains a loop δ then when δ is deleted the resulting sequence still connects the input compartment to the output compartment.

Remark 3.6. (compartmental diagram). Since neither loops nor excretion coefficients are involved in the inseparability condition discussed in Remark 3.3 it makes no difference whether one appeals to the graph of the compartmental matrix or the compartmental diagram to detect the inseparability. Some of the salient points covered in the above remarks are illustrated in Figure 3

Figure 3. D and E are subsets of compartments connected by a sequence (x,y) from D to E and by a single arc z from E to D. Inputs and outputs occur only in $D \cup E$. Let a, b , and c denote the weights (transfer coefficients) of x, y , and z , respectively. a and b are inseparable (at most ab is

identifiable.) and the excretion coefficients from compartments u and v are not identifiable. Moreover, if all inputs and outputs occur in either D or E (but not both) then a, b , and c are inseparable (at most abc is identifiable) and the excretion coefficient from compartment w , along with those from u and v , are not identifiable.

For ease of reference and for emphasis the main point covered in the above remarks is formalized in Proposition 2.1.

Proposition 2.1. Let a_{ij} and a_{qp} be transfer coefficients such that:

- (i) every sequence from an input compartment to an output compartment which contains either one of the arcs $j \rightarrow i$ or $p \rightarrow q$ contains the other and
- (ii) compartments i and p are excretory.

Then a_{ij} , a_{qp} , a_{0j} and a_{0p} are unidentifiable parameters.

Example 3.1. (catenary systems). Consider the catenary system, Figure 4, with an arbitrary number, say n , of compartments, and with both input and output occurring at compartment n . All n compartments are excretory.

Figure 4: n compartmental catenary system.

The sequences from n to n are composed the cycles of length one and two associated with parameters $a_{ii} = -a_i - b_{i-1} - c_i$, $i=1,2,\dots,n$ ($a_n = b_0 = 0$) and $\gamma_j = a_j b_j$, $j=1,2,\dots,n-1$, respectively. Since every sequence from n to n which contains the arc associated with a_i also contains the arc associated with b_i , a_i and b_i are inseparable, $i=1,2,\dots,n-1$. None of the parameters a_i , b_j or c_k are identifiable; at most the combinations a_{ii} and γ_j are identifiable. It is easily

shown from the method used by Bellman and Astrom that the $2n-1$ parameters a_{ii} and γ_j are indeed identifiable.

Example 3.2. (mammillary systems). Consider the mammillary system, Figure 5, with an arbitrary number, say n , of compartments, and with both input and output occurring in compartment 1. All n compartments are excretory.

Figure 5. Mammillary systems.

As in the above example, the sequences from 1 to 1 are composed of cycles of length one and two with associated weights $e_i = a_{ii}$, $i=1,2,\dots,n$ and $\gamma_j = a_j b_j$, $j=1,2,\dots,n-1$, respectively. Moreover, as in the above example, the sets $\{a_i, b_i\}$ are inseparable, $i=1,2,\dots,n-1$, and none of the parameters a_i , b_j , or c_k are identifiable. At most the combinations e_i and γ_j are identifiable. Following the method used by Bellman and Astrom it will be shown that these $2n-1$ parameters are indeed identifiable. This result was recently obtained [20] by a different method.

Let $d_n(s)$ denote the characteristic polynomial of the submatrix of A associated with compartments $1,2,\dots,k$. Then $d_1(s) = s - e_1$, $d_2(s) = (s - e_2)d_1(s) - \gamma_1$ and

$$d_{k+1}(s) = (s - e_{k+1})d_k(s) - \gamma_k p_k(s), \quad (3.3)$$

where $p_k(s) = (s - e_2)(s - e_3)\dots(s - e_k)$, $k=2,3,\dots,n-1$. The transfer function is $T(s) = q(s)/d_n(s)$, where $q(s) = (s - e_2)(s - e_3)\dots(s - e_n)$, so $q(s)$ and $d_n(s)$ are considered identifiable polynomials. In particular, the roots $e_2, e_3, \dots, e_n$ are identifiable and so the $p_k(s)$ are identifiable polynomials, $k=2,3,\dots,n-1$. The parameter e_1 is also identifiable since

it is the Markov parameter M_1 . To see that the γ_k are identifiable one divides $d_n(s)$ by $(s-e_n)$. Setting $k = n-1$ in (3.3) one sees that the quotient of this division is $d_{n-1}(s)$ and the remainder is $-\gamma_{n-1}p_{n-1}(s)$. By the Euclidean algorithm and the fact that $d_n(s)$ and $(s-e_n)$ are identifiable it follows that $d_{n-1}(s)$ and $\gamma_{n-1}p_{n-1}(s)$ are identifiable polynomials. Since γ_{n-1} is the leading coefficient of $\gamma_{n-1}p_{n-1}(s)$, this parameter is identifiable. Repeating this argument recursively for $k = n-2, n-3, \dots, 1$, each time dividing $d_{k+1}(s)$ by $s - e_{k+1}$, one obtains in succession that $d_k(s)$ and γ_k are identifiable.

4. Interval identifiability. A parameter p is said to be interval identifiable if its values are confined to an interval, $a \leq p \leq b$, where a and b are either a priori known constants or identifiable parameters (If $a = b$ then p is identifiable). Naturally, one seeks to obtain the smallest interval bounding a parameter but this problem is meaningless unless the parameter is known to be interval identifiable in the first place.

Consider a parameter

$$p = a_{ij}, i \neq j \text{ or } p = -a_{jj}, i = 0, 1, \dots, n, j = 1, 2, \dots, n, \quad (4.1)$$

which is either a transfer, excretion or outflow coefficient. Since $p > 0$ the problem of interval identifiability concerns only the upper bound. Assuming that there are no a priori constants bounding the parameters (4.1) an upper bound can only be obtained from the identification equations or the relation (3.1). It is clear from Remark 3.2 that an upper bound is possible only if compartment j is input/output reachable. Moreover, it is clear from relation (3.1) that a_{jj} is interval identifiable if and only if a_{ij} is interval identifiable for all $i \neq j$.

Let $T(s) = P(s)/d(s)$ denote the transfer function (in general $P(s)$ is a polynomial with matrix coefficients). Let $T(s)$ be expressed in irreducible form (a.e.) then $d(s)$ is the characteristic polynomial of the input/output reachable subsystem, provided that this subsystem has no traps (i.e., each of its compartments reaches the environment). This follows because $T(s)$ is irreducible if and only if the system is completely controllable and completely observable [13] and a system without traps is completely controllable and completely observable (a.e.) if and only if all compartments are input/output reachable [12]. Thus, the next to the leading coefficient of $d(s)$ is identifiable. This coefficient is $d_1 = -\sum a_{jj}$, where the summation ranges over all input/

output reachable compartments j . Since all the terms in the sum are non-positive one obtains the inequalities

$$0 \leq a_{ij} \leq -a_{jj} \leq d_1,$$

for all $i \neq j$ and j input/output reachable. These observations are formalized in Proposition 4.1.

Proposition 4.1. Given a compartmental system without traps, then a priori unknown transfer coefficient a_{ij} is interval identifiable if and only if compartment j is input/output reachable.

The assumption regarding traps is not essential but this condition avoids technicalities (see Theorem 2.2 in [12]).

Other or related interval identifiability conditions may be found in [21].

5. The concept of a basis for a parameter space. Bellman and Astrom raised an important question, "Is the system identifiable?" but the identification question does not end with the discovery that the system is not identifiable. Besides obtaining interval bounds on unidentifiable parameters, one would like to know which parameters are identifiable. Since every combination of identifiable parameters is also identifiable, the set of identifiable parameters, call it O , is infinite and non-denumerable. In order to describe such a set one requires a concept similar to the notion of "basis" which is used to specify a linear space. But a set of parameters does not form a linear space and the key algebraic operation by which parameters are related to one another is not addition but rather it is nonlinear composition. However, it is possible to establish certain properties of what will be defined as a "parameter space" in analogy with linear space theory.

The development is motivated by Examples 3.1 and 3.2. In each example the set of parameters associated with the cycles (of lengths one or two) are identifiable and moreover, an arbitrary parameter is identifiable if and only if it is composable from these "basic" parameters. That is to say, an identifiable parameter p must be given by $p = f(b_1, b_2, \dots, b_r)$, where $b_1, b_2, \dots, b_r$ are the basic parameters and f is the function giving the composition of p . The function f can be chosen so that its partial derivatives are nonzero (a.e.). Since functions having the above property will occur more than once in this discussion, it is convenient to denote by F_k , the set of smooth (continuously differentiable) real-valued functions of k real variables with nonzero partial derivatives (a.e.), $k = 1, 2, \dots$.

Recall from Section 2 the set of unknown parameters $U = \{u_1, u_2, \dots, u_v\}$. Each unknown parameter takes values in an interval $a_k < u_k < b_k$ and

each point in the domain $\Omega = [a_1, b_1] \times [a_2, b_2] \times \dots \times [a_v, b_v]$ is a feasible value of the parameter vector $u = (u_1, u_2, \dots, u_v)$. In light of local identifiability, attention is focused on an arbitrarily small neighborhood Ω_0 of a nominal point u^* in Ω .

Other parameters occurring in the system are constructs of the unknown parameters, i.e., p is a parameter if there is a subset, say $\{v_1, v_2, \dots, v_k\}$ of parameters in U and a function $f \in F_k$ such that $p = f(v_1, v_2, \dots, v_k)$. The set of all parameters is denoted by P . Note that the condition on f of nonzero partial derivatives prohibits a priori known constants from P . Observe also that if $p \in P$ then $-p \in P$ but $p + (-p) = 0 \notin P$, thus P is not closed under addition. Moreover, P is not closed under scalar multiplication so that P is not a linear space in the ordinary sense.

Given a set V of parameters, the span of V , SpV , is the set of parameters p which can be expressed as $p = f(q_1, q_2, \dots, q_k)$ where $q_1, q_2, \dots, q_k$ are parameters in V and $f \in F_k$. For instance, $P = SpU$ and $0 = SpO_R$ (O_R is defined in Section 2). The system is identifiable if and only if $P = Sp(O_R)$. Note that $Sp(SpV) = SpV$ for any set of parameters V .

A set of parameters S is said to form a parameter space if $S = SpS$. From the last relation it is clear that a set of parameters S forms a parameter space if and only if $S = SpV$ for some set of parameters V . In particular, P and 0 are parameter spaces.

A set of parameters V is said to be dependent if there is a set of parameters Q having fewer parameters than V such that $V \subset SpQ$. Since every set of parameters $V \subset P = SpU$ it is clear that every set of parameters which contains more than v parameters is dependent (recall

that v is the number of parameters in U). A set of parameters is said to be independent if it is not dependent. For instance, U is independent.

A set of parameters V is said to be a basis for a parameter space S if $S = \text{Sp}V$ and V is independent. For instance, U is a basis for P . Suppose that V and Q are both bases for S , then the fact that both V and Q are independent, along with the relations $Q \subset \text{Sp}V$ and $V \subset \text{Sp}Q$, imply that V and Q have the same number, say d , of parameters. This number d is called the dimension of S .

There is an enormous wealth of results comprising the theory of linear spaces. It is of practical value ~~as well as academic~~ ^{to explore} to explore the extension of such results to parameter spaces. This will be the topic of future work. For the present, attention is focused on the problem of determining when a set of parameters is independent. One approach is furnished by the following results.

Proposition 5.1. Let V be a set of parameters and let J be the Jacobian matrix of the map from U to V , then V is independent if the rank of J equals the number of parameters in V .

Proof. Suppose, in the contrapositive, that V is dependent. Then $V \subset \text{Sp}Q$ where Q has fewer members than V . Let G and H be the Jacobian matrices of the map from U to Q and from Q to V , respectively. Then $J = HG$. But then the rank of J cannot be greater than the rank of G , which in turn, does not exceed the number of parameters in Q . Thus, V dependent implies that the rank of J is less than the number of parameters in V .

Proposition 5.2. Let $V = \{v_1, v_2, \dots, v_k\}$ be a set of parameters. Suppose that for each j there is a parameter in U , say u_j , such that $\partial v_j / \partial u_j \neq 0$ (a.e.) and $\partial v_i / \partial u_j = 0$ for $i \neq j$. Then V is independent.

Proof. Let J be the Jacobian matrix of the map from U to V and let Q be the $k \times k$ submatrix composed of the first k columns of J . Then Q is a diagonal matrix with nonzero elements along the diagonal. Clearly, the determinant of Q is nonzero and so the rank of J is k . The result follows from Proposition 5.1.

Example 5.1. (catenary systems). Consider the catenary systems, Figure 4. Recall from Example 3.1 that the parameters in the set $V = \{a_{11}, a_{22}, \dots, a_{nn}, a_{12}a_{21}, a_{23}a_{32}, \dots, a_{n-1n}a_{nn-1}\}$ are identifiable and that all identifiable parameters are constructs of these parameters, i.e., $O = SpV$. To show that V is independent let its parameters be numbered $v_1 = a_{11}, v_2 = a_{22}, \dots, v_n = a_{nn}, v_{n+1} = a_{12}a_{21}, v_{n+2} = a_{23}a_{32}, \dots, v_{2n-1} = a_{n-1n}a_{nn-1}$. Let the parameters in U be numbered $u_1 = a_{11}, u_2 = a_{22}, \dots, u_n = a_{nn}, u_{n+1} = a_{12}, u_{n+2} = a_{23}, \dots, u_{2n-1} = a_{n-1n}, u_{2n} = a_{21}, u_{2n+1} = a_{32}, \dots, u_{2n-2} = a_{nn-1}$. Direct application of Proposition 5.2 shows that V is independent and hence is a basis for the space of identifiable parameters, O . The dimension of O is $2n-1$.

Example 5.1 illustrates the derivation of Proposition 5.3 (below) which is immediate from Proposition 5.2. If each v_j corresponds to a set of arcs A_j and if these sets are disjoint, then one satisfies the conditions of Proposition 5.2 by choosing u_j to be the weight of some arc in A_j .

Proposition 5.3. Let V be a set of parameters such that each parameter

in V is associated with a set of arcs (in the graph of the compartmental matrix). That is, for each v in V there corresponds a set of arcs

$A_v = \{a_1, a_2, \dots, a_{k(v)}\}$ and a function $f \in F_{k(v)}$ such that

$v = F(w_1, w_2, \dots, w_{k(v)})$, where w_j is the weight of a_j , $j = 1, 2, \dots, k(v)$.

If the sets A_v are disjoint and the w_j are unknown parameters then V is independent.

An advantage of Proposition 3.3 is that the hypothesis is observable directly from the compartmental diagram. For instance, the set of parameters associated with the cycles of length one and two occurring in the mammillary systems (Example 3.2) are independent. Since these parameters span the space of identifiable parameters they serve as a basis for the space.

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