THE ROLE OF NONREAL EIGENVALUES IN THE IDENTIFICATION OF CYCLES IN A COMPARTMENTAL SYSTEM

by

J. Eisenfeld[1,2], W. F. Beltz[2] and S. M. Grundy[2]

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[1]Department of Mathematics, University of Texas at Arlington, Arlington, Texas 76019

[2]Center for Human Nutrition, University of Texas Health Science Center at Dallas, Dallas, Texas 75235

ABSTRACT

The paper concerns the relationship between the cycles in the graph of a compartmental system and the modes of the impulse response function associated with an input-output experiment. Suppose that there is at least one oscillatory mode, $e^{\mu t}\cos(\nu t-\alpha)$. Let $e^{\rho t}$ be the slowest mode. The main result is that the system contains a cycle of length three or longer and that the length of the longest cycle is at least $\pi/\tan^{-1}(|\nu|/(\rho-\mu))$. The paper also deals with the problem of estimating cycle length from discrete data.

1. INTRODUCTION

Compartmental analysis [1] concerns the identification of parameters in a compartmental system. Often the parameters to be identified are the fractional transfer coefficients k_{ij} (into compartment i from compartment j) but sometimes even the graph (flow diagram) of the system may not be known a priori. For instance, the number of compartments, n, and the connections between compartments may not be known.

In order to identify the system, an experiment is performed in which q inputs excite the compartments. The q inputs are regarded as a column vector $\underline{u}(t) = (u_1(t), u_2(t), \ldots, u_q(t))^T$. (Here T means transpose.) The paths by which the q inputs enter the n compartments is represented be a $n \times q$ matrix B. When the state (concentration, mass, etc.), $x_i(t)$ of compartment i at time $t > 0$ is a response to the input $u(t)$ and only to $u(t)$, then $\underline{x}(t) = (x_1(t), x_2(t), \ldots, x_n(t))^T$ is determined by the system of differential equations

$$\dot{\underline{x}}(t) = K\underline{x}(t) + B\underline{u}(t), \quad t \geq 0, \quad x(0) = 0, \tag{1.1}$$

where K is the $n \times n$ matrix of fractional transfer coefficients, k_{ij}.

It may not be possible to observe each individual state by itself; however, there are observations $\underline{y}(t) = (y_1(t), y_2(t), \ldots, y_p(t))^T$ which are related to the states through a system of linear equations

$$\underline{y}(t) = C\underline{x}(t), \quad t \geq 0, \tag{1.2}$$

where C is a $p \times n$ matrix representing the paths from compartments to recording devices. The observations $y_i(t)$ are called outputs.

Each input and each output is sampled at discrete time yielding a collection of data, by means of which, one estimates the impulse-response matrix [2]

$$\phi(t) = Ce^{tK}B \ . \tag{1.3}$$

he entry $\phi_{ij}(t)$ of $\phi(t)$ is the response $y_j(t)$ resulting from a delta unction (bolus) input $u_j(t)$. More precisely,

$$\phi_{ij}(t) = \underline{c}_i^T e^{tK} \underline{b}_j \ , \tag{1.4}$$

here $\underline{b}_j$ is the $j^{\underline{th}}$ input (the $j^{\underline{th}}$ column vector of B) and $\underline{c}_i$ is the $\underline{th}$ output (the $i^{\underline{th}}$ row vector of C). Let $\underline{b}$ and $\underline{c}$ denote particular nput and output vector, then the associated entry of the impulse-response atrix may be written in the more explicit form [2]

$$\phi(t) \equiv \underline{c}^T e^{tK} \underline{b} = \sum_{k=1}^{r} \sum_{i=1}^{r_k} d_{ki} t^{i-1} e^{\mu_k t} \cos(\nu_k(t-\alpha_k)) \tag{1.5}$$

n which the eigenvalues $\mu_k = (\mu_k,0)$ are real numbers.

As a matter of terminology, a (complex) number λ with real part μ and maginary part ν, is written as an ordered pair $\lambda = (\mu,\nu)$. A number is real f its imaginary part is zero; a real number is written either as $(\mu,0)$ or, ore concisely, as μ.

The numbers $\lambda_k = (\mu_k,\nu_k)$, which *appear* (i.e., at least one of the oefficients d_{ki} $(1 \le i \le r_k)$ are nonzero) in equation (1.5), are eigenvalues f the matrix K, although not all the eigenvalues of K need be present n the representation of a particular impulse response. If $r_k > 1$ then the igenvalue λ_k admits a Jordan chain of length > 1; in this case the mode ssociated with λ_k is said to be resonant. If the eigenvalue λ_k is not eal then the mode is oscilatory. In the absense of either resonant or oscilatory modes the impulse response has the more simple multi-exponential form

$$\phi(t) = d_1 e^{\mu_1 t} + d_2 e^{\mu_2 t} + \ldots + d_r e^{\mu_r t} . \tag{1.6}$$

A set of compartments $\{j_1, j_2, \ldots, j_m\}$ is said to form a *(simple) cycle* (in the graph of the matrix K) if the fractional transfer coefficient from compartment j_ν to compartment $j_{\nu+1}$, $\nu = 1,2,\ldots,m-1$, and from compartment j_m to j_1 are nonzero (i.e., if substance can cycle around the m compartments). The integer m denotes the length of the cycle. Obviously, the number, n, of compartments in the system must be at least as large as the length of the longest cycle. The *main purpose* of this paper is to obtain the following relationships between the impulse response and the length of the longest cycle. All matrices are assumed to be real.

Theorem 1. Let $\phi(t) = \underline{c}^T e^{tK} \underline{b}$ be an impulse response with input vector $\underline{b}$, output vector $\underline{c}$, and suppose that the matrix K has nonnegative offdiagonal entries.

Suppose further that the expansion (1.5) for $\phi(t)$ contains at least one oscillatory mode (i.e., at least one nonreal eigenvalue is expressed). Let m denote the length of the longest cycle in the graph of K. Then $m \geq 3$. Furthermore, if $\underline{b}$ and $\underline{c}$ are nonnegative (componentwise) then the expansion (1.5) contains an eigenvalue ρ such that (i) ρ is a real number and (ii) ρ is greater then the real part of any other eigenvalue which occurs in expansion (1.5). Let (μ,ν) be any nonreal eigenvalue which occurs in the expansion (1.5), then

$$m \geq \pi/\tan^{-1}((\rho-\mu)/|\nu|) \tag{1.7}$$

$(0 < \tan^{-1}((\rho-\mu)/|\nu|) < \pi/2)$.

Remark 1.1. A matrix K which arises in compartmental systems is characterized by the properties: (a) the offdiagonal entries of K are nonnegative,

(b) the column sums are nonpositive. A matrix with these properties is called a *compartmental matrix*. Note that the hypothesis of Theorem 1 requires only the first property. Thus theorem 1 applies to a class of systems that includes compartmental systems. The states of the system will be referred to as compartments even though a more general class of system is being considered.

Remark 1.2. In regards to the second part of the theorem ($\underline{b} \geq 0$, $\underline{c} \geq 0$), $\phi(t) \sim d_{1r_1} t^{r_1-1} e^{\rho t}$ as $t \to \infty$ (the eigenvalues are numbered so that $\rho = \lambda_1$) with $d_{1r_1} > 0$. Thus ρ is given by the formula

$$\rho = \lim_{t\to\infty} t^{-1} \log \phi(t). \tag{1.8}$$

The number ρ is called the *asymptotic decay rate* of $\phi(t)$.

Remark 1.3. A well-known result by Hearon [3] states that if a compartmental matrix K is sign symmetric ($k_{ij} > 0$ implies $k_{ji} > 0$) and its graph does not contain cycles of length ≥ 3 then the eigenvalues of K are real. Theorem 1 shows that the sign-symmetry condition is not needed. Theorem 1 also extends a result by Maeda et al [4] which is stated only for 3×3 matrices (see Section 4).

Remark 1.4. The problem of identifying nonreal eigenvalues from discrete data is discussed in Sections 4 and 6.

Remark 1.5. Recently there appeared an article concerning cycles in ecosystems [5] but from a different point of view. This paper does not consider the problem of identifying the existence of cycles from impulse-response data. The article contains several interesting examples of cycles arising in large compartmental systems.

2. PROOF OF THEOREM 1.

Theorem 1 will be proved with aid of the following lemmas which are of independent interest. The first is a result of Kellogg and Stephans [6].

Lemma 1. Let A be a nonnegative matrix of order n with Perron eigenvalue r and associated directed graph G. Let m be the length of the longest cycle of G. If $m \leq 2$ all the eigenvalues of A are real. If $2 < m \leq n$ and (σ,ν) is a nonreal eigenvalue of A, then $\sigma + |\nu| \tan(\pi/m) \leq r$.

Remark 2.1. Lemma 2 is a slight modification of the result in [6] as the latter does not discuss the case $m = 1$. However, if $m = 1$ then the compartments can be permuted so that $i > j$ implies $a_{ji} = 0$. Therefore A is similar to a real lower-triangle matrix which implies that the eigenvalues of A are real.

A matrix K is said to have a *leading eigenvalue* ρ if (i) ρ is a real eigenvalue of K and (ii) ρ is greater than the real part of any other eigenvalue of K.

Lemma 2. Let K be a matrix with nonnegative offdiagonal entries. Let m be the length of the longest cycle in the graph of K. If $m \leq 2$, all the eigenvalues of K are real. If $m > 2$ and (μ,ν) is a nonreal eigenvalue of K, then $\mu + |\nu| \tan(\pi/m) \leq \rho$.

Proof. Let $-q$ be the least diagonal entry of K. Then $A = K + qI$ is nonnegative, where here and elsewhere I denotes the identity matrix. Moreover, λ is an eigenvalue of K if and only if $\lambda + q$ is an eigenvalue of A. Let r be the Perron eigenvalue of A, then r is also the leading eigenvalue of A and $\rho = r - q$ is the leading eigenvalue of K. Let m be the length of the longest cycle in the graph of A. Since K and A have identical off-diagonal entries they have the same graph. Since $(\mu + q, \nu)$ is a nonreal eigenvalue of A, it follows from Lemma 1 that $m \geq 3$ and $\mu + q + |\nu| \tan(\pi/m) \leq r = p + q$. This completes the proof.

Remark 2.2. Note that the first part of Theorem 1 follows from Lemma 2.2 because if $\phi(t) = \underline{c}^T e^{tK} \underline{b}$ has an oscillatory mode then K must have a non-real eigenvalue which implies that K has a cycle of length ≥ 3. The second part of Theorem 1 would also follow from Lemma 2.2 if it were always true that the leading eigenvalue of K appears in the expansion (1.5). However, it is not difficult to construct a counter example. For instance, consider the matrix

$$K = \begin{bmatrix} -2 & 0 & 0 & 0 & 0 & 0 \\ 1 & -2 & 0 & 0 & 1 & 0 \\ 0 & 1 & -2 & 0 & 0 & 0 \\ 0 & 0 & 1 & -2 & 0 & 0 \\ 0 & 0 & 0 & 1 & -2 & 0 \\ 0 & 1 & 1 & 1 & 1 & 0 \end{bmatrix} \qquad (2.1)$$

The eigenvalues of K are 0 (the leading eigenvalue), -1, -2, -3 and the nonreal eigenvalues $(2,\pm1)$. However, the impulse response for input in compartment 1 and output from compartment 4 is

$$\phi(t) = (1/2)e^{-t} - (1/\sqrt{2})e^{-2t}\cos(t-\pi/4), \qquad (2.2)$$

which does not contain the leading eigenvalue. In fact, the asymptotic decay rate of $\phi(t)$ is -1. However, it is clear from the graph of K, Fig.1, that there is no path from compartment 6 to compartment 4, i.e., compartment 6 is not output reachable. Consequently, compartment 6 is not involved in the impulse response. Consider the subsystem formed by compartments 1, 2, 3, 4 and 5, all of which are both reached by compartment 1 and reach compartment 4. This is the subsystem of input-output reachable compartments. The matrix for the susbsystem is

$$\tilde{K} = \begin{bmatrix} -2 & 0 & 0 & 0 & 0 \\ 1 & -2 & 0 & 0 & 1 \\ 1 & 1 & -2 & 0 & 0 \\ 0 & 0 & 1 & -2 & 0 \\ 0 & 0 & 0 & 1 & -2 \end{bmatrix} . \tag{2.3}$$

The leading eigenvalue of $\tilde{K}$ is -1. The impulse response corresponding to input into compartment 1 and output from compartment 4 of the subsystem is again the expression (2.2). The example illustrates that although the asymptotic decay rate may not be equal to the leading eigenvalue of a certain system which realizes the impulse response it is equal to the leading eigenvalue of the subsystem of input-output reachable compartments (see the definition given below). This fact will be proved after the following definitions.

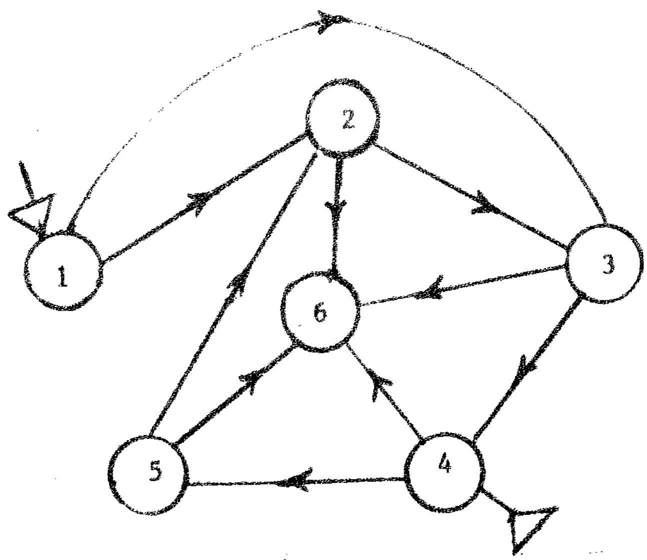

Figure 1. Graph of the compartmental system with matrix (2.1). The input is into compartment 1 and observations are from compartment 4.

Let K be an $n \times n$ matrix with graph G. Let $\underline{b} = (b_1, b_2, \ldots, b_n)^T$, $\underline{c} = (c_1, c_2, \ldots, c_n)$ be input and output vectors, respectively. Compartment i is said to be an *input (resp. output) compartment* if $b_i \neq 0$ (resp. $c_i \neq 0$). Compartment j is said to be *input (resp. output) reachable* if there is a path in G from an input compartment to compartment j (resp. from compartment j to an output compartment). A compartment is said to be *input-output reachable* is it is both input and output reachable.

<u>Lemma 3</u>. Let K be a matrix and let $\underline{b}$ and $\underline{c}$ be input and output vectors, respectively. Let $\tilde{K}$, $\tilde{\underline{b}}$, and $\tilde{\underline{c}}$ be formed from K, $\underline{b}$, and $\underline{c}$, respectively, by deleting the compartments which are not input-output reachable. Then the impulse response $\underline{c}^T e^{tK} \underline{b}$ of the system $(K, \underline{b}, \underline{c})$ is the same as the inpulse response, $\tilde{\underline{c}}^T e^{t\tilde{K}} \tilde{\underline{b}}$, of the *input-output subsystem* $(\tilde{K}, \tilde{\underline{b}}, \tilde{\underline{c}})$.

<u>Proof</u>. Partition the compartments into 4 sets:

S_1 is the set of compartments which are input reachable but not output reachable.

S_2 is the set of compartments which are both input and output reachable.

S_3 is the set of compartments which are output reachable but not input reachable.

S_4 is the set of compartments which are niether input nor output reachable.

Let K_{ij} be the submatrix of K whose entries are the fractional transfer rates from compartments in S_j to compartments in S_i. The matrix K is partitioned as

$$K = \begin{bmatrix} K_{11} & K_{12} & K_{13} & K_{14} \\ K_{21} & K_{22} & K_{23} & K_{24} \\ K_{31} & K_{32} & K_{33} & K_{34} \\ K_{41} & K_{42} & K_{43} & K_{44} \end{bmatrix}.$$

Let $\underline{b} = [\underline{b}_1^T, \underline{b}_2^T, \underline{b}_3^T, \underline{b}_4^T]^T$, $\underline{c} = [\underline{c}_1, \underline{c}_2, \underline{c}_3, \underline{c}_4]$ be the corresponding partitioning of the input and ouput vectors, respectively. Let $L(s) = \underline{c}^T(sI-K)^{-1}\underline{b}$ be the transfer function, i.e., the Laplace transform of the impulse response. Then $L(s) = \underline{c}_1^T\underline{x}_1(s) + \underline{c}_2^T\underline{x}_2(s) + \underline{c}_3^T\underline{x}_3(s) + \underline{c}_4^T\underline{x}_4(s)$, where $\underline{x}(s) = [\underline{x}_1(s)^T, \underline{x}_2(s)^T, \underline{x}_3(s)^T, \underline{x}_4(s)^T]^T$ is the solution of $s\underline{x}(s) - K\underline{x}(s) = \underline{b}$. Since the compartments in either S_1 or S_4 are not output reachable, $\underline{c}_1$ and $\underline{c}_4$ are zero vectors and so, $L(s) = \underline{c}_2^T\underline{x}_2(s) + \underline{c}_3^T\underline{x}_3(s)$. It is easy to see from the definition of the sets S_i that K_{21}, K_{24}, K_{31}, K_{32}, K_{34} and $\underline{b}_3$ all have zero entries. Thus $s\underline{x}_3(s) - K_{33}\underline{x}_3(s) = \underline{0}$. This implies that $\underline{x}_3(s) = \underline{0}$ for all s in the domain of L. Consequently, $L(s) = c_2^T\underline{x}_2(s)$. Since K_{21} and K_{24} are zero matrices and $\underline{x}_3(s) = \underline{0}$ one sees that $s\underline{x}_2(s) - K_{22}\underline{x}_2(s) = \underline{b}_2$ which gives $L(s) = \underline{c}_2^T\underline{x}_2(s) = \underline{c}_2^T(sI-K_{22})^{-1}\underline{b}_2$. Therefore the transfer function for the system is the same as the transfer function for the input-output reachable subsystem, $(K_{22}, \underline{b}_2, \underline{c}_2)$ and the proof is complete.

Lemma 4. Let K be an $n \times n$ matrix with nonnegative offdiagonal entries. Let $\underline{b}$ and $\underline{c}$ be nonnegative input and output vectors, respectively. Suppose all compartments are input-output reachable with respect to the system $(K, \underline{b}, \underline{c})$. Let $\phi(t) = \underline{c}^T e^{tK}\underline{b}$ be the impulse response. Then the asymptotic decay rate of $\phi(t)$ is the leading eigenvalue of K.

Proof. Let $\underline{x}(t)$ be the solution of $\dot{\underline{x}} = K\underline{x}$, $\underline{x}(0) = \underline{b}$. Then

$$\phi(t) = c_1x_1(t) + c_2x_2(t) + \ldots + c_nx_n(t). \tag{2.4}$$

It is to be shown that equation (1.8) is satisfied. Since each compartment is input reachable and since the offdiagonal entries of K are nonnegative it is easy to show (e.g., see [7]) that each component $x_i(t) > 0$ for $t > 0$. Moreover, the nonnegativity of the offdiagonal entries imply that each entry $X_{uv}(t)$

of e^{tK} is nonnegative. Furthermore, it is well known that there is at least one entry, $\chi_{ij}(t)$, of order $t^q e^{\rho t}$ as $t \to \infty$, where ρ is the leading eigenvalue of K and q + 1 is the length of the longest Jordan chain of K. Choose $\tau > 0$, then $\underset{\sim}{x}(t+\tau) = e^{tK}\underset{\sim}{x}(\tau)$. Thus

$x_i(t+\tau) = \chi_{i1}(t+\tau)x_1(\tau) + \ldots + \chi_{ij}(t+\tau)x_j(\tau) + \ldots + \chi_{in}(t+\tau)x_n(\tau) \geq \chi_{ij}(t+\tau)x_j(\tau)$.

Because $x_j(\tau) > 0$ and $\chi_{ij}(t+\tau)$ is of order $t^q e^{\rho t}$ it follows that

$$LN^-(x_j(t)) \equiv \underline{\lim}_{t\to\infty} t^{-1} \log x_i(t) = \rho. \tag{2.5}$$

Since compartment i is output reachable, there is an output compartment d (i.e., $c_d \neq 0$) such that compartment i reaches compartment d. If it can be shown that

$$LN^-(x_d(t)) \geq \rho \tag{2.6}$$

then it would follow from (2.4) that $LN^-(\phi(t)) \geq \rho$. However, it is clear from the representation (1.5) and from the fact that ρ is the leading eigenvalue, that $LN^+(\phi(t)) \equiv \overline{\lim}_{t\to\infty} t^{-1}\log \phi(t) \leq \rho$. Consequently, the limit superior and the limit inferior of $t^{-1} \log \phi(t)$ both equal ρ, which means that the limit of $t^{-1} \log \phi(t)$ exists and that its value is ρ.

To complete the proof it is sufficient to show the validity of (2.6) but this conclusion follows from the next Lemma.

<u>Lemma 5</u>. Let K be an $n \times n$ matrix with nonnegative offdiagonal entries and let $x(t) = (x_1(t), x_2(t), \ldots, x_n(t))^T$ be the solution of $\dot{\underset{\sim}{x}} = K\underset{\sim}{x}$ with $x_i(0) \geq 0$, $1 \leq i \leq n$. Let $LN^-(x_i(t))$ be defined as (2.5). If compartment j reaches compartment i in the graph of K then $LN^-(x_i(t)) \geq LN^-(x_j(t))$.

<u>Proof</u>. By induction on the length of the path from j to i it suffices to verify the result in the case that the length of the path is unity, i.e., $k_{ij} > 0$.

Let $b = LN^{-}(x_j(t))$. Then for each $\varepsilon > 0$ there is a $t_0 > 0$ such that $x_j(t) \geq e^{(b-\varepsilon)t}$, $t \geq t_0$. Because of the nonnegativity of the components of $x(t)$ and of the offdiagonal entries of K, $\dot{x}_i(t) \geq k_{ii}x_i(t) + k_{ij}x_j(t) \geq k_{ii}x_i(t) + k_{ij}e^{(b-\varepsilon)t}$, $t \geq t_0$. In particular, $\dot{x}_i(t) \geq k_{ii}x_i(t)$ which gives $x_i(t+t_0) \geq x(t_0)e^{k_{ii}t}$. Thus $LN(x_i(t)) \geq k_{ii}$. If $k_{ii} \geq b$ the desired result is obtained. For the case $k_{ii} < b$, apply the variation of constants formula to obtain $x_i(t+t_0) \geq x(t_0)e^{k_{ii}t} + [e^{(b-\varepsilon)t} - e^{k_{ii}t}]/[b-\varepsilon-k_{ii}]$, where ε is now restricted to the interval $(0, b-k_{ii})$. It is not difficult to see that $LN^{-}(x(t)) \geq b - \varepsilon$. Letting $\varepsilon \to 0$ yields the result.

Proof of Theorem 1. The first part of the theorem, $m \geq 3$, follows from Lemma 2 as discussed in Remark 2.2. To obtain the second part apply Lemma 3 to obtain $\phi(t) = \tilde{\underline{c}}^T e^{t\tilde{K}}\tilde{\underline{b}}$, where $(\tilde{K}, \tilde{\underline{b}}, \tilde{\underline{c}})$ denotes the input-output-reachable subsystem. Thus the eigenvalues appearing in the expansion (1.5) of $\phi(t)$ are eigenvalues of $\tilde{K}$. Lemma 4, applied to the system $(\tilde{K}, \tilde{\underline{b}}, \tilde{\underline{c}})$, yields that the leading eignevalue of $\tilde{K}$ is the asymptotic decay rate, ρ, of $\phi(t)$. Applying Lemma 2 to $\tilde{K}$ one obtains $\mu + |\nu| \tan(\pi/\tilde{m}) \leq \rho$, where $\tilde{m}$ is the length of the longest cycle in the graph $\tilde{G}$ of $\tilde{K}$. Since $\tilde{G}$ is contained in G, $m \geq \tilde{m} \geq \pi/\tan^{-1}((\rho-\mu)/|\nu|)$. This completes the proof.

3. THE NUMBER OF COMPARTMENTS

It was noted earlier that Theorem 1 gives a lower bound on the number n of compartments since $n \geq m \geq \pi/\tan^{-1}((\rho-\mu)/|\nu|)$. One can say more if the term on the right takes an integer value.

Observe that the graph of the matrix

$$\begin{bmatrix} \alpha_1 & \beta_1 & 0 & \cdot & \cdot & \cdot & 0 & 0 \\ 0 & \alpha_2 & \beta_2 & \cdot & \cdot & \cdot & 0 & 0 \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ 0 & 0 & 0 & \cdot & \cdot & \cdot & \alpha_{n-1} & \beta_{n-1} \\ \beta_n & 0 & 0 & \cdot & \cdot & \cdot & 0 & \alpha_n \end{bmatrix} \tag{3.1}$$

consists of a single cycle of order n. A system is said to be a *simple cycle of order* n if the compartments can be permuted so that the matrix of the system has the form (3.1) with the $\beta_i > 0$.

<u>Theorem 2</u>. Let the hypothesis of Theorem 1 be satisfied with $\underline{b}, \underline{c} \geq \underline{0}$. Let n be the number of compartments and define

$$n_0 = \pi/\tan^{-1}((\rho-\mu)/|\nu|).$$

Then $n \geq n_0$. If $n = n_0$ then the system is a simple cycle of order n.

<u>Proof</u>. The fact that $n \geq n_0$ is immediate from Theorem 1. Consider the case $n = n_0$. Then Theorem 1 gives $n \geq m \geq n_0$ and so the system has a cycle of length n which contains all the compartments. In particular, the graph is strongly connected, i.e. K is irreducible. Moreover, all compartments are input-output reachable. It follows from Lemmas 3 and 4 that ρ is the leading eigenvalue of K. Note that replacing K by $K - cI$, where c is a positive constant, does not alter the hypothesis or the conclusion since ρ and μ would be replaced by $\rho + c$ and $\mu + c$, respectively. Since the offdiagonal entries of K are nonnegative $cI - K$ is an invertible M-matrix for c sufficiently large. Thus it may be assumed without loss of generality that $M = -K$ is an invertible M-matrix. Moreover, $(-\mu,-\nu)$ is a nonreal eigenvalue of M, $-\rho$ is the minimal eigenvalue of M and $-\mu - |\nu| \tan(\pi/n) = -\rho$. It follows from Theorem 1 in [8]

that the system is a simple cycle of order n. This completes the argument.

Remark 3.1. An impulse response associated with a simple cycle has a special form (see Section 4). If a simple cycle can be ruled out then the conclusion of Theorem 2 is $n > \pi/\tan^{-1}((\rho-\mu)/|\nu|)$.

4. AN EXAMPLE

Consider the system in Figure 1. The input-output reachable subsystem has 5 compartments and a cycle of length 4. Are these facts derivable from discrete data? The question will be considered in two parts. In the first part the analytic form of the impulse response, $\phi(t) = (1/2)e^{-t} - (1/\sqrt{2})e^{-2t}\cos(t-\pi/4)$, is assumed to be known a priori. The second part deals with the problem of obtaining the analytic form of $\phi(t)$ from discrete data.

Assume the analytic form of the impulse response as given above with $\underline{b}, \underline{c} \geq \underline{0}$. Then $n_0 = \pi/\tan^{-1}((-1)-(-2))/1) = 4$. So Theorem 1 implied that the length of the longest cycle, $m \geq 4$. In particular, the number of compartments, $n \geq 4$. Suppose $n = 4$, then Theorem 2 implies that the system is a simple cycle of length 4. Let the compartments be numbered so that compartment 1 is an input compartment and compartment $i + 1$ is the successor of compartment i along the cycle, $i = 1,2,3$. Then $b_1 \neq 0$ and K has the form given in (3.1) with $\beta_i > 0$, $i = 1,2,3,4$. Since $\underline{c}^T\underline{b} = \phi(0) = 0$, $\underline{c}^TK\underline{b} = \phi'(0) = 0$ and $\underline{c}^TK^2\underline{b} = \phi''(0) = 1$ it follows that the shortest path between an input compartment and output compartment has length 2. Thus $c_1 = c_2 = 0$. Since $b_3 \neq 0$ implies $c_3 = c_4 = 0$ this possibility can be ruled out. Suppose that there is only one input compartment and only one output compartment. Then $\underline{b} = [b_1,0,0,0]$, $\underline{c}^T = [0,0,c_3,0]$. One can see by calculating the transfer function, $\underline{c}^T(sI-K)^{-1}\underline{b}$, that the simple-cycle system is irreducible, i.e. 4 eigenvalues are present. But the given impulse

impulse response has only 3 eigenvalues. This shows that a single cycle s stem of length 4 with a single input compartment and a single output compartme t is not compatible with the given impulse response. Thus $n \geq 5$. Since the n n-input-output reachable compartments are inconsequential (Lemma 3) it is co cluded that the input-output reachable subsystem has at least 5 compartments and hat the system has a cycle of length 4 or more. The result is sharp because t e system $(\tilde{K},\underline{b},\underline{c})$ where $\tilde{K}$ is defined in (2.3), $\underline{b} = (1,0,0,0,0)^T$ and $\underline{c} =$),0,0,1,0) is a realization of the given impulse response which has exactly 5 compart ents and only one cycle of length 4.

This example was considered by Maeda et al [4] but these investigator con-cluded only that the number of compartments is at least 4.

Next consider the problem of reconstructing the analytic form of the npulse response from discrete data. Several methods are available. The method o least squares optimization will be illustrated using the above example. Another ıethod, the method of moments, will be discussed briefly in Section 5.

The least-squares method requires two phases. In the first phase one den-tifies the parametrized form of the impulse response and estimates the init al values of the parameters. Consider data points (t_k, y_k). The first step of phase 1 is to estimate the leading mode. This may be accomplished by using the peeling method [1], i.e., one fits a line, $y = mt + b$, through the tail p rtion of the "log plot": $(t_k, \log y_k)$. Then, if $de^{\rho t}$ denotes the leading mode, the estimates $\hat{\rho}$, $\hat{d}$ are given by $\hat{\rho} = m$, $\hat{d} = e^b$. For instance, if one simula es data:

$$y_k = (1/2)e^{-t_k} - (1/\sqrt{2})e^{-2t_k}\cos(t_k-\pi/4), \quad t_k = 0.2k, \ k = 0,1,\ldots,25. \tag{4.1}$$

and peels on the interval [2.5,5] then the estimated values are $\hat{\rho} = -1.028$ $\hat{d} = 0.5896$.

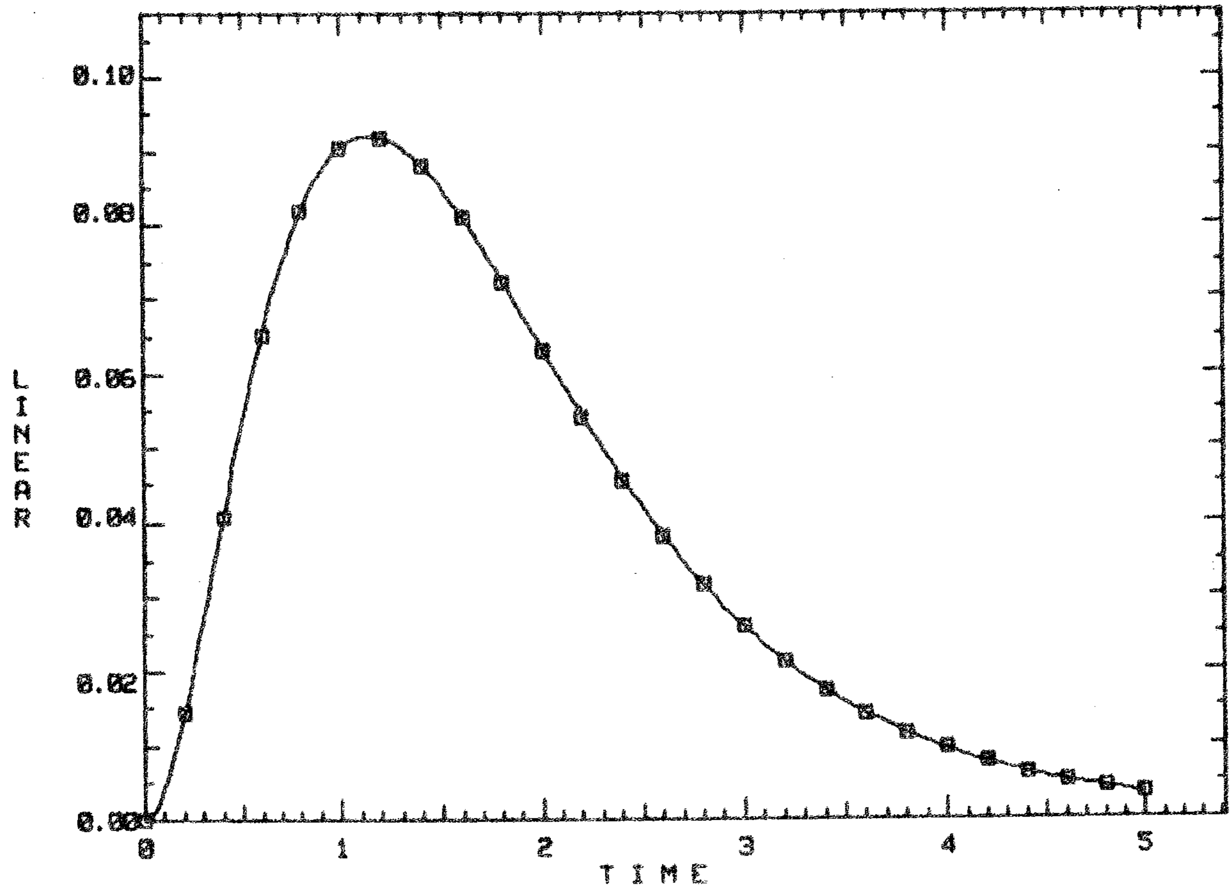

Figure 2. Fit of data (4.1) by means of a combined peeling and least-squares method.

The next step is to subtract the estimated leading mode giving the "residual plot", $r_k = y_k - \hat{d}e^{\hat{\rho}t_k}$. If the residual appears to be an oscilatory mode, $ae^{\mu t}\cos(\nu t-\alpha)$, then one can estimate the parameters a, μ, ν, α by measuring the peaks. For the example at hand, the following rough estimates were obtained: $\hat{a} = 0.004$, $\hat{\mu} = -0.9$, $\hat{\nu} = 1.6$, $\hat{\alpha} = 2.5$. In the event that peeling off the leading mode does not exhibit an oscilatory mode then the peeling process would be continued until an oscillatory mode is exposed (if one exists) or all nonoscillatory modes are identifie

Now consider the second phase of the least-squares method. Although the initial estimates of the parameters in the parametrized model, $de^{\rho t} + ae^{\mu t}\cos(\nu t-\alpha)$, found from the peeling method, were poor, the SAAM 27 computer program [9] gave good final estimates: $\hat{d} = 0.4985$, $\hat{\rho} = -0.9996$, $\hat{a} = -0.7038$, $\hat{\mu} = -1.9992$, $\hat{\nu} = 1.0029$, $\hat{\alpha} = 0.7840$. The fit is shown in Figure 2.

5. CONNECTION WITH AN AGE-DEPENDENT MODEL

An example of an age-dependent compartmental model, Figure 3, is discussed by Matis and Wehrly [10]. Each species i $(i = 1,2)$ is separated into n_i age compartments.

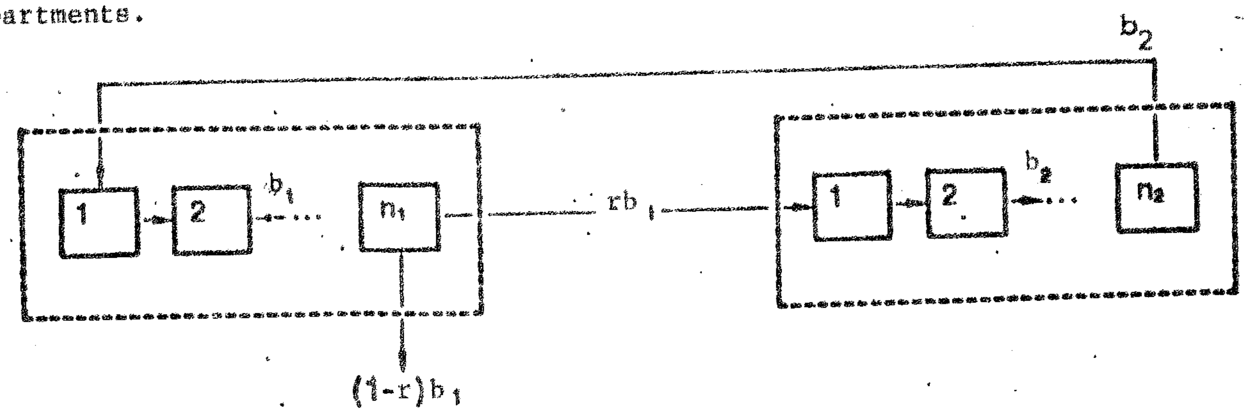

Figure 3. An age-dependent compartmental model.

The system has a cycle of order $n = n_1 + n_2$. Nonreal eigenvalues exist for $n \geq 3$ except under the following conditions [10]: (i) $n_1 = n_2 = 2$ with $r \leq (b-1)^4/16b^2$, (ii) $n_1 = 2$, $n_1 = 1$ with $r \leq 4(1-b)^3/27b^2$, (iii) $n_1 = 1$, $n_2 = 2$ with

$r \leq 4(1-b)^3/27b$, where $b = b_1/b_2$.

It is interesting to conjecture that there is at least one nonreal eigenvalue such that

$$n - 1 < \pi/\tan^{-1}(|\nu|/(\rho-\mu)) < n$$

for this is true for the cases: $n_2 = 1$, $b = n_1$, $r = 1/2$, $2 \leq n_1 \leq 7$.

6. DISCUSSION

Although the theoretical results, Theorems 1 and 2, are interesting, their application to data analysis hinges on the construction of the analytic form of the impulse response from data. This problem is difficult because real data tends to be noisy and sparse. "Nice data" were used in the example in Section 4 in order to illustrate an approach to the problem and to demonstrate that a good approximation of the impulse-response parameters can be obtained under ideal conditions. Several additional numerical experiments were performed with simulated real data. A detailed report of the results will be presented in a forthcoming paper; however, a few pertinant remarks can be made at this time.

Remark 6.1. In general, the least-squares procedure is not successful unless the leading modes are peeled off first as illustrated in the example. The reason is that the oscillatory modes tend to be overshadowed by the leading modes.

Remark 6.2. The least-squares procedure by itself can not be relied upon to expose an oscillatory mode. For instance, $\chi(t) = 1.29 \exp(-1.21t) - 7.29 \exp(-2.05t) + 6.00 \exp(-2.24t)$ might be considered an acceptable fit to the data y_k (Fig. 4) although it does not contain an oscillatory mode. However, a plot of the residuals $(y_k - \chi(t_k))$ exhibits oscillatory shape, Figure 5. This property was observed consistently when performing numerical experiments.

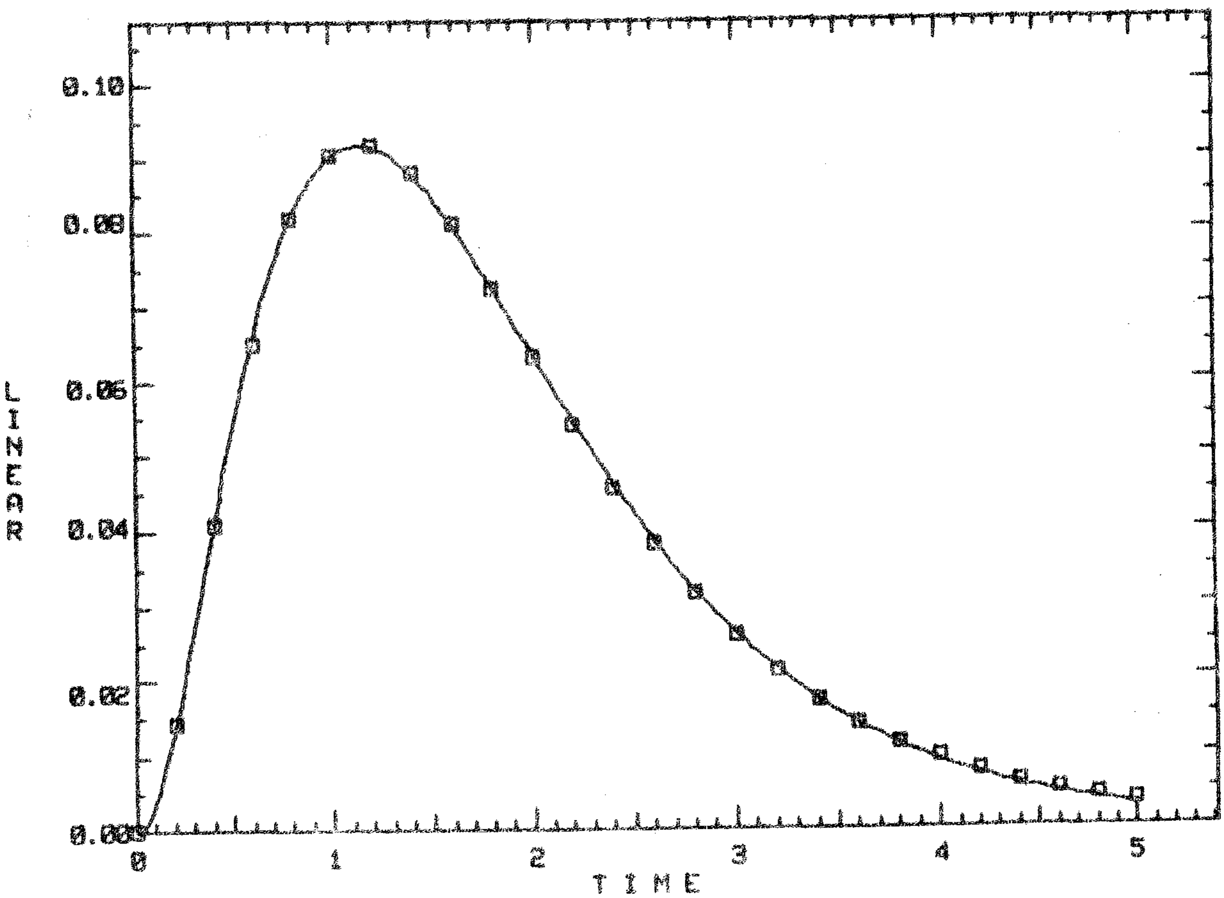

Figure 4. Fit of data (4.1) by a tri-exponential.

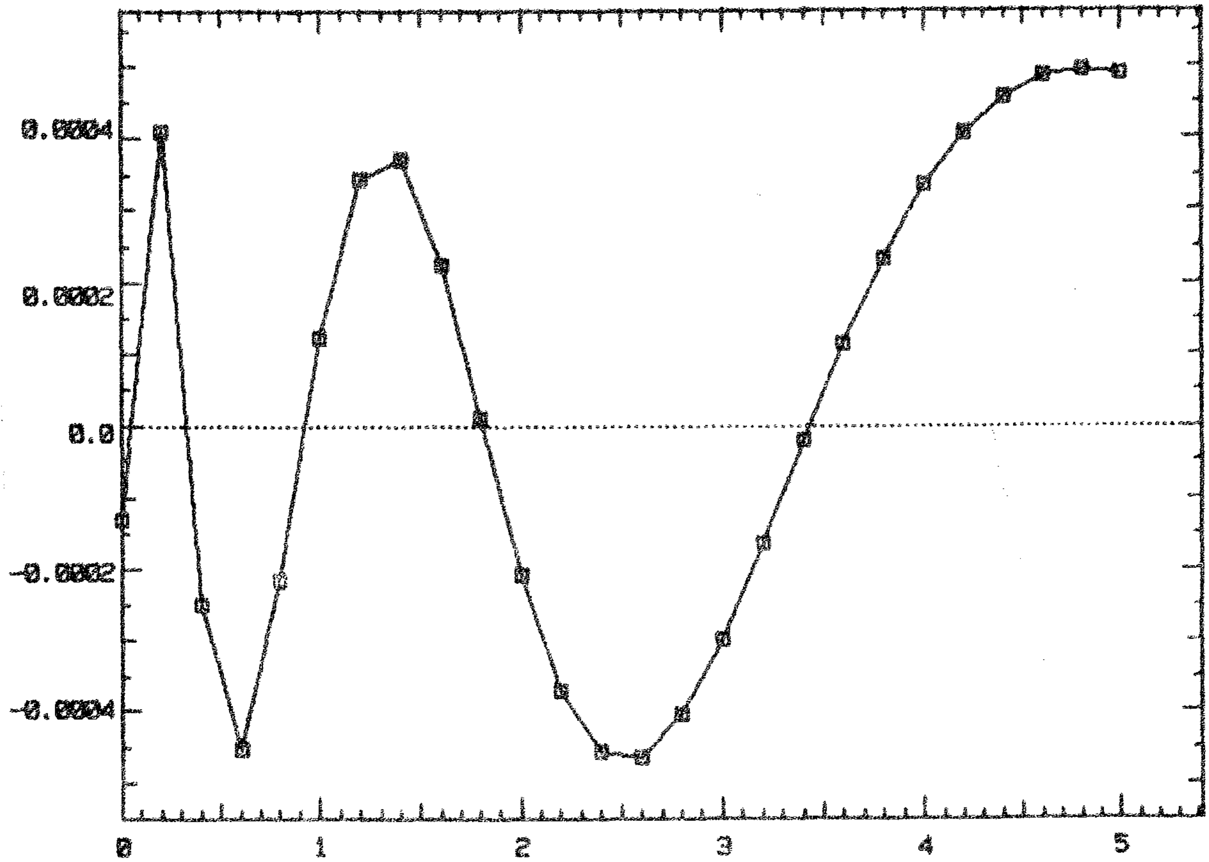

Figure 5. Residual plot associated with an attempt to fit "Oscillatory data" by a multi-exponential.

It seems that a pure exponential sum tends to fit the leading modes sufficiently well so that the residual plot exhibits the oscillatory mode. The property could be used as a method for detecting an oscillatory mode.

Remark 6.3. As an alternative to the least squares procedure one can use the method of moments [11,12]. The advantage of this method is that the characteristic polynomial, i.e., the monic polynomial whose roots are the eigenvalues, can be estimated directly from the data without an iterative procedure. Therefore initial estimates are not needed. Moreover, the number of parameters that are determined at a time is reduced by a factor of two. However, the method requires estimation of certain integrals. Therefore, the data points should be sufficiently close so that good integral approximations are obtainable when applying the method of moments.

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