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# AN EFFICIENT ALGORITHM FOR DISCRETE MODELLING OF TRACER KINETICS

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**Abstract**—Effective study of certain health care problems and biomedical systems requires development and utilization of duly validated models for characterization of tracer kinetics in compartmental systems. This report presents an efficient algorithm for evaluation of discrete-time models in this context, starting from real patient data. The procedure evolved is systematic and involves parameter identification, model order determination and ascertaining the validity of the model: mathematical techniques proposed for this three-tier approach are robust as well as simple. A method for deriving state-space representations for multicompartmental systems directly from observations vector is also outlined. An illustrative example is given which demonstrates the effectiveness of the algorithm when applied to tracer analysis of the hepatobiliary system. The methodology proposed is recursive in nature such that it can be implemented very conveniently utilizing a microcomputer or even a programmable pocket calculator.

## 1. INTRODUCTION

Classical compartmental analysis has provided useful and conceptually simpler mathematical representations for studying the kinetics of distribution of a substance or a tracer in a biomedical system [1]. Some recent investigations have demonstrated that the methodology can provide efficient models for studying the system physiology, the primary objective in most cases being optimization of drug administration. Search for optimal compartmental models utilizing real life data has consequently become increasingly important in biosciences. In a recent paper, Brown [2] has presented a state-of-the-art survey, whereas an excellent study of the mathematical foundations has been made by Sandberg [3]. Conventionally, the output

of the tracer process observed from an accessible compartment is generally assumed to be represented by a sum of exponential functions with distinct decay constants [4].

Structural identification of compartmental systems essentially presents two fundamental problems: (i) the estimation of the number of compartments and (ii) the estimation of the corresponding kinetic parameters. Many algorithms have been developed for the second part of the problem which utilize the ordinary or generalized least-squares method, or the maximum liklihood method, for estimating the parameters of the compartmental model of a known order [5–27). The estimation of the number of exponential functions and the pertinent parameters in the output of a radioactive tracer kinetic process applying the Akaike information theoretical criterion has been discussed by Kajiya *et al.* [28]; although this appears to present a very powerful practical approach to the problem of model structure identification, it has been utilized so far only in relation to purely stochastic systems and is defined specifically in relation to maximum likelihood estimation.

Derivation of conceptually simple compartmental models with explicit algorithms for practical implementation constitutes an important avenue of concern currently. The biomedical scientist often requires a simple yet roboust procedure which is of a more general nature and emerges naturally during analysis. The present paper is an attempt to fill this gap. An efficient algorithm willl be presented for estimating the order as well as the parameters of a compartmental model from the observed output samples of a tracer experiment. This algorithm is recursive in nature and can be implemented even on a programmable pocket calculator.

The method for estimation of the parameters of a linear discrete-time model of known order using the output sampled data is outlined first. This is followed by a discussion of the procedure for determination of order of a model in the presence of noisy observations. Tests to be performed for validation of the models are described next. An example demonstrates that the algorithm is very efficient in developing a discrete-time model for studying the hepatobiliary system.

## 2. PARAMETER IDENTIFICATION: MODEL OF KNOWN ORDER

Assuming that the compartmental system is linear, the output of a tracer process may be considered as the impulse response of the linear system. The equally-spaced samples of its output may thus be utilized to obtain the discrete-time transfer function of a known order. Let this transfer function of order $n$ be

$$G(z) = \frac{a_0 + a_1 z^{-1} + a_2 z^{-2} + \cdots + a_n z^{-n}}{1 + b_1 z^{-1} + b_2 z^{-2} + \cdots + b_n z^{-n}}, \tag{1}$$

where $z = e^{sT}$ is the unit advance operator, and $T$ is the sampling interval.

The objective is to determine the $(2n + 1)$ parameters $a_0, a_1 \ldots a_n, b_1, b_2 \ldots b_n$ from the samples of the impulse response $w_0, w_1, w_2 \ldots w_N$, where $N$ is much larger than $2n$, and

$$w_i = w(iT) \tag{2}$$

From Eqs. (1) and (2),

$$G(z) = \sum_{i=0}^{\infty} w_i z^{-i} \tag{3}$$

Since Eqs. (1) and (3) represent the same transfer function, one can multiply both by the

denominator of Eq. (1) to obtain

$$a_0 + a_1 z^{-1} + a_2 z^{-2} + \cdots + a_n z^{-n} = w_0 + (w_1 + b_1 w_0) z^{-1} + \cdots + \left( w_n + \sum_{i=1}^{n} b_i w_{n-i} \right) z^{-n} + \cdots$$

$$+ \left( w_m + \sum_{i=1}^{n} b_i w_{m-1} \right) z^{-m} + \cdots + \left( w_N + \sum_{i=1}^{n} b_i w_{N-1} \right) z^{-N} \tag{4}$$

where $m > n$. Thus the coefficients of like powers of $z$ in Eq. (4) yield $(n+1)$ equations for the numerator coefficients, which can be arranged in the following form:

$$\begin{bmatrix} a_0 \\ a_1 \\ a_2 \\ \vdots \\ a_n \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 \\ b_1 & 1 & 0 \ldots & 0 & 0 \\ b_2 & b_1 & 1 \ldots & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ b_n & b_{n-1} & b_{n-2} \cdots & b_1 & 1 \end{bmatrix} \begin{bmatrix} w_0 \\ w_1 \\ w_2 \\ \vdots \\ w_n \end{bmatrix} \tag{5}$$

Due to the lower triangular nature of the matrix in Eq. (5), it is evident that the calculation of the numerator coefficients does not require any matrix inversion, provided that the denominator coefficients, $b_i$ are known.

To determine $b_i$, we consider the terms containing $z^{-(n+1)}$ to $z^{-N}$. Since there are no such terms on the left-hand side of Eq. (4), these equations do not contain $a_i$, and can be rearranged in the following form:

$$\begin{bmatrix} w_1 & w_2 \ldots & w_n \\ w_2 & w_3 \ldots & w_{n+1} \\ \vdots & \vdots & \vdots \\ w_{N-n} & W_{N-n+1} \cdots & w_{N-1} \end{bmatrix} \begin{bmatrix} b_n \\ b_{n-1} \\ \vdots \\ b_1 \end{bmatrix} = \begin{bmatrix} -w_{n+1} \\ -w_{n+2} \\ \vdots \\ -w_N \end{bmatrix} \tag{6}$$

It may be noted that we have $(N-n)$ equations and $n$ unknowns. Since $N$ should be much greater than $2n$, we have many more equations than unknowns. Hence, we can obtain a least-squares solution for the denominator coefficients through the matrix pseudoinverse [29]. Matrix inversion may be completely avoided by using the recursive pseudoinverse algorithm given below. Define

$$\phi_i = [W_i, w_{i+1} \ldots w_{i+n-1}]^T, \tag{7}$$

$$\theta = [b_1, b_2 \ldots b_n]^T. \tag{8}$$

Then, starting with $\hat{\theta}_0 = 0$, $Q_0 = I$, $P_0 = 0$, where $Q_i$ and $P_i$ are $n \times n$ matrices and $\hat{\theta}_i$ is the $i$th estimate of $\theta$, we have for $i \leq n$,

$$\hat{\theta}_{i+1} = \hat{\theta}_i + \frac{Q_i \phi_i (w_{i+n} - \phi_i^T \hat{\theta}_i)}{\phi_i^T Q_i \phi_i} \tag{9}$$

$$Q_{i+1} = Q_i - \frac{(Q_i \phi_i)(Q_i \phi_i)^T}{\phi_i^T Q_i \phi_i} \tag{10}$$

$$P_{i+1} = Q_i - \frac{(P_i \phi_i)(Q_i \phi_i)^T + (Q_i \phi_i)(P_i \phi_i)^T}{\phi_i^T Q_i \phi_i} + \frac{(Q_i \phi_i)(Q_i \phi_i)^T \cdot (1 + \phi_i^T P_i \phi_i)}{(\phi_i^T Q_i \phi_i)^2}. \tag{11}$$

For $i > n$,

$$\hat{\theta}_{i+1} = \hat{\theta}_i + \frac{P_i\phi_i(w_{i+n} - \phi_i^T\phi_i)}{1 + \phi_i^T P_i \phi_i} \tag{12}$$

$$P_{i+1} = P_i - \frac{(P_i\phi_i)(P_i\phi_i)^T}{1 + \phi_i^T P_i \phi_i} \tag{13}$$

Details of the derivation are given in [29]. It may be added that if the impulse–response sequence is contaminated with uncorrelated zero-mean noise, the least-square estimate of the parameters $b_i$ obtained using the above algorithm will be unbiased. From these estimates of the denominator parameter, the numerator parameters using Eq. (5) may now be obtained.

## 3. ORDER ESTIMATION

If the observations are noise-free, it is well known that the order can be determined from the rank of the Hankel matrix $H(l, k)$, defined as

$$H(l,k) \triangleq \begin{bmatrix} w_k & w_{k+1} & w_{k+2} \cdots w_{k+l-1} \\ w_{k+1} & w_{k+2} & w_{k+3} \cdots w_{k+l} \\ \vdots & \vdots & \vdots \quad \vdots \\ w_{k+l-1} & w_{k+l} & w_{k+l+1} \cdots w_{k+2l-2} \end{bmatrix} \tag{14}$$

It is well known that if the order of the system is $n$, then the rank of $H(l, k)$ is equal to $n$, provided that $l$ is greater than or equal to $n$.

Thus, one can determine $n$ by evaluating the deteminant of $H(l, k)$ for different values of $l$ since the determinant will vanish for all $k$ when $l$ is greater than $n$. In practice, the rank determinants will not vanish identically because of the noise contained in the data. There are several techniques available to circumvent this problem.

One approach is to use the determinant ratio test: average the value of the determinant $H(l, k)$ for each $l$, and plot the ratio $D_l$ against $l$, where

$$D_l \triangleq \frac{\text{Average value of the determinant of } H(l,k)}{\text{Average value of the determinant of } H(l+1,k)}. \tag{15}$$

From this plot, the order $n$ is obtained as that value of $l$ for which $D_l$ is a maximum. Another approach is to first obtain an estimate of the autocorrelation sequence from the impulse response data using the relationship

$$\phi_i = \frac{1}{N-i+1} \sum_{k=0}^{N-i} w_k w_{k+i} \tag{16}$$

and then determine the rank of the Hankel matrix, the elements of which are estimated autocorrelation coefficients, defined as

$$\rho_i = \frac{\phi_i}{\phi_0}, \qquad i = 0, 1, 2 \ldots \tag{17}$$

Again, the determinant may not exactly vanish, and one may use the determinant ratio test as before.

Another method of order determination is the information criterion (AIC) proposed by Akaike [30]. It is defined specifically in relation to maximum likelihood estimation, and the AIC is

$$\text{AIC} = (-2)\log_e(\text{maximum likelihood}) \tag{18}$$

$$+ 2(\text{number of independently adjustable model parameters})$$

This criterion is very powerful and practical in the sense that it also emphasizes the parsimony of the model. However, the computation is rather cumbersome, as one must first estimate the parameters of models of different orders using the maximum likelihood method before the AIC can be calculated for each case. On the other hand, the determinant ratio tests are fairly easy to perform, and give very good results when the noise level is low. Since this happens to be the situation with most of the experiments on tracer kinetics, it is not necessary to use the AIC.

## 4. MODEL VALIDATION

The simplest diagnostic test for validating the model is to calculate the sequence of residuals, defined as the error between the actual response and the response calculated using the model. If the model is good, the residual sequence should be a zero-mean white-noise sequence. If there are several models for which the residual sequence satisfies the above condition, then among these, the model for which the variance of the sequence is minimum, will be regarded as the best model. This diagnostic validation therefore depends basically on testing the residual sequence for whiteness.

We now outline two tests which may be used for determining whether a given sequence is white [31]. As is well known, a white noise sequence has the property that all of its correlation ordinates, with lag one or more, must be zero. This, however, requires that the correlation ordinates be calculated from an infinite sequence. In practice, however, we always have a finite amount of data, say $N$ samples. Hence, one can only approximate the correlation ordinates, as in Eq. (16) and the calculate the correlation coefficients by dividing each of these by the estimated variance (which is the correlation ordinate for lag zero). These will seldom be zero. However, if each of the first twenty correlation ordinates is less than $1.85/\sqrt{N}$, we can be certain, within 95% confidence limits, that the sequence under test is white.

Another test is the so-called Portmanteau Test. Following Stoica [31], a sequence of $N$ samples is white within 95% confidence limits, if its correlation coefficients, $\rho_i$, satisfy the following inequality

$$N \sum_{i=1}^{k} \rho_i^2 < k + 1.65\sqrt{2k} \tag{19}$$

where $k \geq 20$. In general, it is desirable to apply both of these tests. If the residual sequence satisfies both the tests, we can be certain that it is white and that the model is satisfactory.

## 5. EXAMPLE

An illustrative example indicating the strength of the proposed methodology is described in this section. The data considered for this analysis is that related to the radioactive rose bengal which is considered to be an excellent tracer in studying the hepatobiliary system. The uptake of the radioactive tracer by the liver and its decay in blood are observed following an intravenous injection which is considered to be an impulse function. Therefore, the two

observed outputs $y_1$ and $y_2$ in this case are considered to be impulse responses. Values recorded both from the blood and the liver at 2.5 min intervals for two hours are given in Table 1. Curves showing the uptake and decay are displayed in Fig. 1.

The discrete model evaluation involves three steps: order determination, parameter estimation, and validation of the model. The ratio test using the impulse response data in constructing the Hankel matrix as well as the test that employs the autocorrelation sequence

Table 1. Observed outputs over the blood and the liver regions*

| Time (min) | Blood ($y_1$) | Liver ($y_2$) |
|---|---|---|
| 0.0000000 | 1.0000000 | 0.0000000 |
| 2.5000000 | 0.8000000 | 0.1900000 |
| 5.0000000 | 0.5500000 | 0.3300000 |
| 7.5000000 | 0.5400000 | 0.4400000 |
| 10.0000000 | 0.4600000 | 0.5100000 |
| 12.5000000 | 0.3900000 | 0.5700000 |
| 15.0000000 | 0.3500000 | 0.6200000 |
| 17.5000000 | 0.3100000 | 0.6400000 |
| 20.0000000 | 0.2800000 | 0.6500000 |
| 22.5000000 | 0.2600000 | 0.6700000 |
| 25.0000000 | 0.2400000 | 0.6700000 |
| 27.5000000 | 0.2300000 | 0.6700000 |
| 30.0000000 | 0.2200000 | 0.6600000 |
| 32.5000000 | 0.2100000 | 0.6600000 |
| 35.0000000 | 0.2000000 | 0.6500000 |
| 37.5000000 | 0.1900000 | 0.6400000 |
| 40.0000000 | 0.1900000 | 0.6300000 |
| 42.5000000 | 0.1800000 | 0.6200000 |
| 45.0000000 | 0.1800000 | 0.6100000 |
| 47.5000000 | 0.1800000 | 0.6000000 |
| 50.0000000 | 0.1700000 | 0.5900000 |
| 52.5000000 | 0.1700000 | 0.5800000 |
| 55.0000000 | 0.1600000 | 0.5800000 |
| 57.5000000 | 0.1600000 | 0.5700000 |
| 60.0000000 | 0.1600000 | 0.5600000 |
| 62.5000000 | 0.1500000 | 0.5500000 |
| 65.0000000 | 0.1500000 | 0.5300000 |
| 67.5000000 | 0.1500000 | 0.5200000 |
| 70.0000000 | 0.1500000 | 0.5100000 |
| 72.5000000 | 0.1400000 | 0.5000000 |
| 75.0000000 | 0.1400000 | 0.4900000 |
| 77.5000000 | 0.1400000 | 0.4800000 |
| 80.0000000 | 0.1300000 | 0.4700000 |
| 82.5000000 | 0.1300000 | 0.4700000 |
| 85.0000000 | 0.1300000 | 0.4600000 |
| 87.5000000 | 0.1300000 | 0.4500000 |
| 90.0000000 | 0.1200000 | 0.4400000 |
| 92.5000000 | 0.1200000 | 0.4400000 |
| 95.0000000 | 0.1200000 | 0.4300000 |
| 97.5000000 | 0.1200000 | 0.4200000 |
| 100.0000000 | 0.1200000 | 0.4100000 |
| 102.5000000 | 0.1100000 | 0.4100000 |
| 105.0000000 | 0.1100000 | 0.3900000 |
| 107.5000000 | 0.1100000 | 0.3800000 |
| 110.0000000 | 0.1100000 | 0.3800000 |
| 112.5000000 | 0.1000000 | 0.3700000 |
| 115.0000000 | 0.1000000 | 0.3600000 |
| 117.5000000 | 0.1000000 | 0.3600000 |
| 120.0000000 | 0.1000000 | 0.3500000 |

*Values of $y_1$ and $y_2$ are percentages of an initial injected dose.

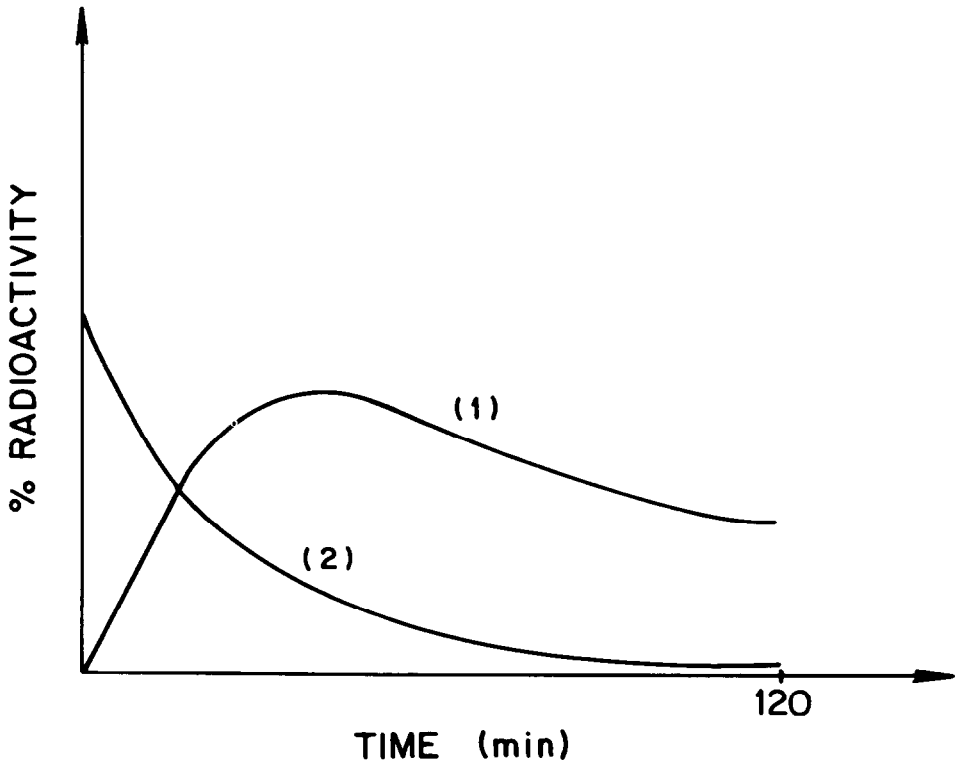


Fig. 1. Radioactive tracer kinetics: (1) its uptake by the liver and (2) its decay in the blood. Both are shown as percentages of the dose injected initially.

of the impulse response data reveal that system order is either 2 or 3 in both the blood and liver compartments. Therefore, the results for a second order as well as a third order model are recorded, and final decision follows after model validation. The computed results are shown in Tables 2 and 3, together with the values of the residuals mean and variance in each case.

The residuals in all models satisfy the whiteness test according to the first criterion discussed earlier in Sec. 4, within 95% confidence limit except in one case. This case was the second order model regarding the blood. In this case, one of the correlation coefficients slightly exceeded the 95% confidence limit. However, from Tables 2 and 3, it is clear that the variance of the residuals is smaller in the case of a third order model than that of a second order, both in the blood as well as the liver. This indicates that the third order models are

Table 2. Second-order models obtained for both the activity in the blood as well as the liver

| Identified Model | Blood $\dfrac{-0.842054z^{-1}-0.0081457z^{-2}}{1-1.64205z^{-1}+0.655498z^{-2}}$ | Liver $\dfrac{0.19z^{-1}+0.00162315z^{-2}}{1-1.7283z^{-1}+0.732812z^{-2}}$ |
|---|---|---|
| Residuals Mean | 0.0063725 | 0.0000756421 |
| Residuals Variance | 0.00173434 | 0.00250406 |

Table 3. Third-order models obtained for both the activity in the blood as well as the liver

| Identified Model | Blood $\frac{-0.288923z^{-1}-0.551215z^{-2}-0.00128784z^{-3}}{1-1.08892z^{-1}-0.330077z^{-2}+0.430574z^{-3}}$ | Liver $\frac{0.19z^{-1}+0.100155z^{-2}+0.00968121z^{-3}}{1-1.20971z^{-1}-0.163764z^{-2}+0.379728z^{-3}}$ |
|---|---|---|
| Residuals Mean | 0.000285606 | −0.000295917 |
| Residuals Variance | 0.00112519 | 0.00177536 |

more appropriate; they also satisfy the whiteness test. It should be noted here that twenty correlation coefficients for the residuals data have been calculated for the whiteness test discussed earlier in the context of model validation.

## 6. CONCLUSIONS AND REMARKS

An efficient algorithm for discrete modeling of tracer kinetics utilizing actual patient data is proposed in this paper. Determination of the model order is explained, and a straightforward recursive technique to identify the model parameters is presented. Having obtained the parameters of model, two ways to ascertain the validity of the model are demonstrated.

The recursive algorithm proposed in this paper eliminates the need for matrix inversion and hence is very suitable for implementation on a microcomputer or even a programmable pocket calculator. Moreover, unlike most of the techniques proposed in the literature which usually formulate the problem as a nonlinear programming problem, the new technique of this paper offers a systematic and efficient alternative which is both robust, fast and simple.

It is well known that nonlinear formulations normally result in convergence questions or lead to a local minimum, unless the initial conditions provided are very close to the solution: the proposed methodology avoids such mathematically intractable situations.

Keeping in view the relevance of state-space formulations corresponding to multicompartmental models of biosystems, it may be remarked that in such cases the response sequences of the output vectors can be utilized directly for evaluation of the model parameters. The procedure is outlined briefly in Appendix I.

In case one requires a continuous-time model which has the same impulse response as $G(z)$, this can also be achieved readily. A suggested procedure is given in Appendix II.

It is envisaged that the methodology proposed would find applications not only in modelling of numerous biomedical systems but would also prove to be of interest to researchers from other disciplines.

## APPENDIX I. STATE-SPACE MODELS FOR MULTICOMPARTMENTAL SYSTEMS

In many cases, multicompartmental models in the state-space form are more desirable. Such models are not unique, since a linear transfer of the state does not change the transfer function matrix. Hence, one often uses the state equations in some canonical form. An efficient algorithm for obtaining the state equation in a canonical form from the transfer function matrix is described in [32, 33].

However, in practice, it is always better to determine state equations directly from the impulse response sequence when the observations are contaminated with noise. This is

because the different elements of the estimated transfer function matrix may not exhibit common eigenvalues with the result that the corresponding state equations may turn out to be of higher order than necessary. A method for obtaining the least-squares estimate of the parameters of the state-space model directly from the impulse response sequence is given below. Consider the state equations

$$\begin{aligned} \dot{x} &= Ax + Bu \\ y &= Cx + Du, \end{aligned} \tag{1.1}$$

where $x$ is the $n$-dimensional state vector, $u$ is the $m$-dimensional input vector, and $A$, $B$, $C$, and $D$ are constant matrices of appropriate dimensions. Since compartmental models usually have one input and several outputs, let $m = 1$, that is, let $u$ be a scalar.

For the case when the initial state $x(0) = 0$, and the input $u(t) = \delta(t)$, the unit impulse, Eqs. (1.1) can be solved to obtain

$$\begin{aligned} x(t) &= \mathrm{e}^{At}B \\ y(t) &= c\ \mathrm{e}^{At}B + D\delta(t). \end{aligned} \tag{1.2}$$

The output vectors at the sampling instants are given by

$$y_k = y(kT) \triangleq CF^kB, \tag{1.3}$$

where

$$F = \mathrm{e}^{At}. \tag{1.4}$$

First, we note that the order $n$ of the model can be determined from the rank of the block Hankel matrix, defined as

$$S = \begin{bmatrix} y_0 & y_1 & y_2 & y_k \\ y_1 & y_2 & y_3 & y_{k+1} \\ y_2 & y_3 & y_4 & y_{k+2} \\ y & y_{l+1} & y_{l+2} & y_{k+l} \end{bmatrix} \tag{1.5}$$

provided that $k$ and $l$ are sufficiently large. In practice, the order can be determined using the determinant ratio test.

For the estimation of $F$, $B$, and $C$, it is most convenient to use the output identifiable canonical form. In this form the rows of $C$ are the first $p$ unit row vectors of dimension $n$, whereas $B$ is obtained as the top $n$ elements of the first column of $S$. The elements of the matrix $F$ are then obtained to provide a least-squares solution to Eq. (1.3).

The continuous-time state-space model can also be obtained after the matrix $F$ has been estimated. From Eq. (1.4), it follows that the eigenvectors of $F$ and $AT$ are identical, whereas the eigenvalues of $F$ are related to the eigenvalues $AT$. The prodedure for determining $A$ from $F$, therefore, consists of the following steps:

(i) Determine the eigenvalues of $F$. Let these be $\lambda_1, \lambda_2 \ldots \lambda_n$.

(ii) The eigenvalues of $A$ are then

$$\frac{1}{T}\ln\lambda_1, \frac{1}{T}\ln\lambda_2 \ldots \frac{1}{T}\ln\lambda_n.$$

(iii) Let the eigenvectors of $F$ be given by $v_1$, $v_2$, and form the modal matrix

$$P = [v_1, v_2 \ldots v_n]. \tag{1.6}$$

(iv) Then $A$ is determined from the relationship

$$A = \frac{1}{T} P \operatorname{diag}[l_n\lambda_1, l_n\lambda_2 \ldots l_n\lambda_n] P^{-1}. \tag{1.7}$$

## APPENDIX II. CONTINUOUS-TIME MODEL

The problem of determining the continuous-time transfer function, $G(s)$, which has the same impulse response as $G(z)$ at the sampling instants is considered here. A unique solution is obtained if it is assumed that $G(s)$ is of the same order as $G(z)$. The procedure for determining $G(s)$ consists of the following steps:

(i) Determine the poles of $G(z)$.

(ii) Corresponding to each pole of $G(z)$, determine a pole of $G(s)$ according to the equation

$$s = \frac{1}{T} \ln(z),$$

where $T$ is the sampling interval. It may be noted that for complex conjugate poles of $G(z)$, one gets correspondingly complex conjugate poles of $G(s)$.

(iii) Evaluate the residues of $(1/z)G(z)$ at its poles.

(iv) Using the same residues at the corresponding poles of $G(s)$, the transfer function $G(s)$ is obtained.

It may be noted that although the impulse response of $G(s)$ is equal to that of $G(z)$ at the sampling instants, there is no guarantee that the responses of $G(s)$ and $G(z)$ to other inputs will be equal at the sampling instants; the response of $G(s)$ is determined largely by how the input varies between sampling instants.

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