of the elements of the matrix A. They are identical to the critical constraints [13] obtained from the polynomial in (1). Obtaining the stability within the unit circle directly simplifies considerably the use of the bilinear transformation on the A matrix.

Finally, it may be mentioned that Theorem 1 represents an alternate form of the stability criteria within the unit circle than those earlier obtained. It represents the discrete version of the classical results of Routh obtained for the continuous case.

The computational aspects of the various theorems presented will be an interesting topic for future research.

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On the Factorization of Discrete-Time Rational Spectral Density Matrices

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***Abstract*—For a discrete-time rational spectral density matrix $\Phi(z)$, the relationship between the factorizations $\Phi(z)=Z(z)+Z^T(z^{-1})$ and $\Phi(z)=W(z)QW^T(z)$, in terms of minimal state space realizations of $Z(z)$ and $W(z)$, are derived in a straightforward way, without resorting to the use of the bilinear transformation. The obvious application of this result to performing a spectral factorization of $\Phi(z)$ is discussed.**

I. Introduction

The problem considered here is the following. Given a factorization of a discrete-time spectral density matrix $\Phi(z)$ into the form

$$\Phi(z)=Z(z)+Z^T(z^{-1}) \tag{1}$$

where $Z(z)$ has poles only in the region $|z|<1$, determine the relationship between a minimal realization of $Z(z)$ and that of $W(z)$ in the factorization

$$\Phi(z)=W(z)QW^T(z^{-1}). \tag{2}$$

These relationships have been obtained elsewhere [1], in the study of discrete positive real matrices. In [1], use was made of the bilinear transformation and corresponding relationships in continuous time [2]. For the problem in hand, however, our main result obtains this relationship directly. The obvious use of such a relationship is in obtaining a spectral factorization of $\Phi(z)$ given by (2). An algorithm for performing this, analogous to that described by Anderson for the continuous-time case, is discussed.

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II. Main Result

The following lemmas will be useful in proving the main theorem.

Lemma 1: For an $n\times n$ matrix A

$$z(zI-A)^{-1}=A(zI-A)^{-1}+I=(zI-A)^{-1}z=(zI-A)^{-1}A+I.$$

Lemma 2: For a nonsingular $n\times n$ matrix A, denote $(A^T)^{-1}$ by A^*. Then

$$(z^{-1}I-A^T)^{-1}=-A^*[I+(zI-A^*)^{-1}A^*]. \tag{3}$$

Proof: Multiplying on the left by $(z^{-1}I-A^T)$, and using the result of Lemma 1, the right-hand side of (3) becomes

$$\begin{aligned}-(z^{-1}I-A^T)A^*[I+(zI-A^*)^{-1}A^*]&=(-z^{-1}A^*+I)[z(zI-A^*)^{-1}]\\&=-A^*(zI-A^*)^{-1}+z(z(zI-A^*)^{-1}\\&=I.\end{aligned}$$

The next lemma concerns a minimal realization of $W(z)$ in the spectral factorization (2). We make the assumption that $W(z)$ is a factor of least degree, i.e., given $\Phi(z)$, there exists no factorization $\Phi(z)=\hat{W}(z)Q\hat{W}^T(z^{-1})$ such that degree $\hat{W}(z)<$ degree $W(z)$, where the degree of a rational function matrix is defined in the usual sense of a McMillan degree [3]. It is well known [3] that the order of a minimal realization of $G(z)$ is equal to the degree of $G(z)$.

Lemma 3: Let $W(z)$ be a factor of $\Phi(z)$ such that $W(z)$ is of least degree n, and has a minimal realization $\{A,B,C,D\}$. Then the $n\times n$ matrix A is nonsingular.

Proof: Assume that A has rank $r<n$. This implies that the characteristic polynomial of A

$$\psi(z)=\det(zI-A)$$

has $(n-r)$ zeros at $z=0$. It then follows that $W(z)$ can be written

$$W(z)=\frac{1}{z^{n-r}p(z)}N(z)$$

where $N(z)$ is a polynomial matrix. Thus, from (2)

$$\begin{aligned}\Phi(z)&=\frac{1}{z^{n-r}p(z)}N(z)Q\frac{1}{z^{-(n-r)}p(z^{-1})}N^T(z^{-1})\\&=G(z)QG^T(z^{-1})\end{aligned}$$

where $G(z)=(N(z)/p(z))$ has degree less than m, contradicting our assumption of least degree of $W(z)$.

We can now state and prove our main theorem.

Theorem 1: Given a real, rational spectral density matrix $\Phi(z)$ and factorizations of $\Phi(z)$ as follows, where $W(z)$ is assumed to be of least degree:

$$\Phi(z)=Z(z)+Z^T(z^{-1}) \tag{4}$$

$$\Phi(z)=W(z)QW^T(z^{-1}),\qquad Q>0 \tag{5}$$

then, if $\{F,G,H,J\}$ is a minimal realization of $Z(z)$, there exists matrices B and $P>0$ such that

$$P=FPF^T+BQB^T \tag{6}$$

$$BQ=G-FPH^T \tag{7}$$

$$Q=J+J^T-HPH^T \tag{8}$$

and $\{F,B,H,I\}$ is a minimal realization of $W(z)$.

Proof: From (4) it follows that we can write

$$\begin{aligned}\Phi(z)&=[H(zI-F)^{-1}G+J]+[H(z^{-1}I-F)^{-1}G+J]^T\\&=[H\ \ G^T]\begin{bmatrix}(zI-F)^{-1} & 0\\ 0 & (z^{-1}I-F)^{-1}\end{bmatrix}\begin{bmatrix}G\\ H^T\end{bmatrix}+J+J^T.\end{aligned}$$

We assume that F is nonsingular. Lemma 3 ensures that this involves no restriction on the result. Then using the result of Lemma 2, $\Phi(z)$ can be rewritten as

$$\Phi(z)=[H \quad -G^TF^*]\begin{bmatrix} zI-F & 0 \\ 0 & zI-F^* \end{bmatrix}^{-1}\begin{bmatrix} G \\ F^*H \end{bmatrix}+J+J^T-GF^*H^T. \tag{9}$$

where F^* denotes $(F^T)^{-1}$.

Now let $\{A,B,C,I\}$ be a minimal realization of $W(z)$, where again we assume A is nonsingular. Then, from (5) and using the result of Lemma 2 as before,

$$\Phi(z)=[C-QB^TA^*]\begin{bmatrix} zI-A & BQB^TA^* \\ 0 & zI-A^* \end{bmatrix}^{-1}\begin{bmatrix} BQ(I-B^TA^*C^T) \\ A^*C^T \end{bmatrix} + Q - QB^TA^*C^T$$

where A^* denotes $(A^T)^{-1}$. Now let P be the symmetric, positive definite solution to

$$P=APA^T+BQB^T$$

and define $T=\begin{bmatrix} I & P \\ 0 & I \end{bmatrix}$. Then

$$T\begin{bmatrix} zI-A & BQB^TA^* \\ 0 & zI-A^* \end{bmatrix}T^{-1}=\begin{bmatrix} zI-A & 0 \\ 0 & zI-A^* \end{bmatrix}$$

and

$$[C \quad -QB^TA^*]T^{-1}=[C \quad -CP-QB^TA^*].$$

Thus

$$\Phi(z)=[C \quad -CP-QB^TA^*]\begin{bmatrix} zI-A & 0 \\ 0 & zI-A^* \end{bmatrix}^{-1} \cdot T\begin{bmatrix} BQ(I-B^TA^*C^T) \\ A^*C^T \end{bmatrix}+Q-QB^TA^*C^T. \tag{10}$$

Equating the two expressions (9) and (10) for $\Phi(z)$, setting $C=H$ and $A=F$ in (10), then yields (6)–(8). The existence of a solution to (6)–(8) is guaranteed by the existence of the factorizations (4) and (5) of $\Phi(z)$.

III. Application to Spectral Factorization of $\Phi(z)$

The application of equations (6)–(8) to performing a spectral factorization of $\Phi(z)$ are obvious. The form of such a procedure is analogous to that for the continuous time case [2], i.e.,

1) Obtain a factorization of $\Phi(z)$ of the form (4).
2) Perform a minimal realization of $Z(z)$ to obtain $\{F,G,H,J\}$.
3) Solve (6)–(8) to obtain B and Q, and hence a minimal realization $\{F,B,H,I\}$ of $W(z)$ in (5).

The technique is particularly suitable for the case when $\Phi(z)$ is given in the form

$$\Phi(z)=\sum_{j=-\infty}^{\infty} M_j z^{-j}$$

in which case we can immediately write

$$Z(z)=1/2M_0+\sum_{j=1}^{\infty} M_j z^{-j}.$$

The minimal realization of step (2) can then be most efficiently carried out by one of the well known methods using a Hankel matrix formed from $M_1, M_2, \cdots$, etc., e.g., [4]. It is desirable that the realization is in a canonical form, the uniqueness of which, in the equivalence class of realizations of spectral factors of $\Phi(z)$, will be useful in ensuring a unique solution to (6)–(8). The following theorem demonstrates this uniqueness property.

Theorem 2: Let $W(z)$ be any factor of $\Phi(z)$ which together with its left inverse is real, rational, regular, and stable, such that

$$\Phi(z)=W(z)QW^T(z^{-1}) \tag{11}$$

for $Q=Q^T, Q>0$. Then a minimal realization $\{A,B,C,I\}$ of $W(z)$, in a canonical form for the equivalence class of minimal realizations of $W(z)$, together with Q, are uniquely determined by $\Phi(z)$.

Proof: Since $Q>0$ and symmetric, we can write $Q=DD^T, |D|\neq 0$. Then

$$\Phi(z)=Y(z)Y^T(z^{-1})$$

where

$$Y(z)=W(z)D$$
$$=C(zI-A)^{-1}BD+D.$$

Let $\overline{W}(z)$ be any other factorization of $\Phi(z)$, such that

$$\Phi(z)=\overline{W}(z)\overline{Q}\overline{W}^T(z^{-1})=\overline{Y}(z)\overline{Y}^T(z^{-1})\overline{Y}(z)$$

and $\overline{W}(z)$ has a minimal realization $\{\overline{A},\overline{B},\overline{C},I\}$ in the same canonical form as that assumed for $\{A,B,C,I\}$. Hence

$$\overline{Y}(z)=\overline{C}(zI-\overline{A})^{-1}\overline{B}\overline{D}+\overline{D}$$

where $\overline{D}\overline{D}^T=\overline{Q}$. Assume $\overline{W}(z)$ satisfies the same conditions as for $W(z)$, i.e., regularity, stable inverse, etc.

Then, it has been proved [5] that

$$Y(z)=\overline{Y}(z)U$$

for some orthogonal matrix U, i.e., $UU^T=I$. Hence

$$C(zI-A)^{-1}B+D=\overline{C}(zI-\overline{A})^{-1}\overline{B}\overline{D}U+\overline{D}U$$

and by uniqueness of the canonical form, it follows that $C=\overline{C}$, $A=\overline{A}$, $BD=\overline{B}\overline{D}U$, $D=\overline{D}U$. Thus,

$$Q=DD^T=\overline{D}UU^T\overline{D}^T=\overline{D}\overline{D}^T=\overline{Q}$$

and

$$B=\overline{B}\overline{D}UD^{-1}=\overline{B}$$

proving uniqueness of the minimal realization A,B,C,I and the matrix Q.

Considering now (6), given that F, B, and Q are fixed uniquely by $\Phi(z)$, it is then straightforward to see that P also is unique. Consider two solutions P_1 and P_2. Then clearly

$$P_1-P_2=FP_1F^T-BQB^T-FP_2F^T+BQB^T$$
$$=F(P_1-P_2)F^T.$$

Writing $\overline{P}$ for P_1-P_2 and F^* for $(F^T)^{-1}$ as before, then

$$\overline{P}F^*=F\overline{P}.$$

Since F^* and F have no common eigenvalues, the only solution to this equation is $\overline{P}=0$, or $P_1=P_2$ proving uniqueness.

The solution to (6)–(8) can be reformulated as the steady-state solution P of the Riccati-type equation

$$P_{i+1}=FP_iF^T+(G-FP_iH^T)(R-HP_iH^T)^{-1}(G-FP_iH^T)$$

where $R \triangleq J+J^T$. Then, from (7)

$$B=(G-FPH^T)(R-HPH^T)^{-1}.$$

The existence of the solution is guaranteed by the existence of a factorization (11), proved elsewhere [5].

IV. Conclusion

A direct proof, not involving use of the bilinear transformation, of the relationships (6)–(8) has been given. The application of this result to the discrete spectral factorization problem has been described, and existence and uniqueness of the solution to the resulting Riccati-type equation has been established.

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Optimal Control of Multiplicative Control Systems Arising from Cancer Therapy

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Abstract—**This study deals with ways of curtailing the rapid growth of cancer cell populations. The performance functional that measures the size of the population at the terminal time as well as the control effort is devised. With use of the discrete maximum principle, the Hamiltonian for this problem is determined and the condition for optimal solutions are developed. The optimal strategy is shown to be a bang-bang control. It is shown that the optimal control for this problem must be on the vertices of an N-dimensional cube contained in the N-dimensional Euclidean space. An algorithm for obtaining a local minimum of the performance function in an orderly fashion is developed. Application of the algorithm to the design of antitumor drug and X-irradiation schedule is discussed.**

I. Introduction

Extensive research has been done on experimental cell cycle kinetics and chemotherapy and radiotherapy (see [2], [5], [17], [20]). Theoretical models for some aspects of the cell cycle kinetics of cell population systems have been developed [8], [9], [21]. The dynamics of cell population systems consisting of proliferating and nonproliferating cells has been represented by state-space models in which the cell age vector is the state vector, and the cell size and DNA vectors are the output vectors [8].

In this paper, attention is focused on solving the optimal control problem that arises when one attempts to study the effectiveness of a given drug regimen on reducing the size of a tumor cell population. The difference matrix equation describing the state is bilinear. The performance functional selected is not convex. These factors lead to the formulation of an interesting optimization problem. The peculiar structure of the Hamiltonian and the dynamics of the system for this problem is used to develop an algorithm for determining optimum drug regimens.

II. Problem Formulation

The dynamics of cellular proliferation in a cancer cell population system under the effect of antitumor drugs can be represented by the following state equation which is discussed in Appendix A.

$$\tilde{x}(k+1)=(\tilde{\phi}+\tilde{\psi}u(k))\tilde{x}(k),\ \tilde{x}(0)=\tilde{x}_0 \tag{2.1}$$

and

$$u(k)\in\Re,\ u(K)\in[0,1]k=0,1,2,\cdots,N-1,$$

where $x(k)$ is the age state vector, $u(k)$ is the control function, $\tilde{\phi}$ and $\tilde{\psi}$ form the state transition matrices. Since the control function $u(k)$ is multiplied by the state vector, the state equation is bilinear. The objective of administering an antitumor drug is to minimize the size of the tumor population at the terminal time. An excessive amount of the drug causes harmful side effects to the patient due to the toxicity of the drug [7]. Therefore, it is important to constrain the amount of drug in the treatment.

The performance functional J is selected to include the size of the final population as well as to penalize the excessive use of the drug.

$$J=\alpha^T(N)x(N)+\sum_{k=0}^{N-1}\beta_k u(k). \tag{2.2}$$

In (2.2) $\alpha(N)$ is a weighing vector with constant positive entries, N is the final stage in the system, and $\beta_k\geqslant 0$ for $k=0,1,2,\cdots N-1$ weighs the control effort $u(k)$ used to take the system from k to $k+1$. The purpose of an optimal drug regimen is to minimize J. This corresponds to achieving a low-total final population while keeping the amount of drug used small. There is a tradeoff between the final population and the amount of drug used. The tradeoff is governed by the relative values of $\alpha^T(N)$ and β_k's, and has to be based upon physical considerations.

In the expression for J in (2.2), N may be thought of as a fixed time (fixed terminal time problem) or as a variable time (variable terminal time problem). Only the case of fixed terminal time is considered here.

The problem, then, is to minimize the performance functional J expressed by (2.2), subject to the dynamics of the system given by (2.1), and with the constraint the $u(k)\in[0.1]$. The necessary conditions that the optimal solution must satisfy are given by the discrete maximum principle (6), as follows:

$$H_k=\beta_k u(k)+p^T(k+1)(\tilde{\phi}+\tilde{\psi}u)\tilde{x} \tag{2.3}$$

$$\tilde{x}(k+1)=\frac{\partial H_k}{\partial p(k+1)}=(\tilde{\phi}+\tilde{\psi}u)\tilde{x} \tag{2.4}$$

$$p(k)=\frac{\partial H_k}{\partial \tilde{x}(k)};\ \text{or}\ p(K)=(\tilde{\phi}+\tilde{\psi}u)p(k+1) \tag{2.5}$$

$$p(N)=\alpha(N) \tag{2.6}$$

$$\tilde{x}(0)=\tilde{x}_0 \tag{2.7}$$

and for $k=0,\ 1,\ 2,\cdots N-1$ control $u(k)$ is selected such that

$$H_k=\min_{u(k)} H_k(u(k),\tilde{x}(k),k). \tag{2.8}$$

These conditions indicate that in an optimal drug regimen or X-irradiation schedule, the full allowable dosage should be used whenever the treatment is administered. The optimal administration follows a bang-bang policy. The conditions for the optimal solution are those of solving a two point boundary problem, where the initial condition on $\tilde{x}$ is given ($\tilde{x}(0)=\tilde{x}_0$) and the final condition on p is given ($p(N)=\alpha(N)$). Extensive amount of computation is required to solve the resulting two point boundary value problem by successive approximation techniques.

III. Algorithm: Control Vector Iteration

In this section the authors develop the algorithm for the case when matrices $\tilde{\phi}$ and $\tilde{\psi}$ of (2.1) are independent of $\tilde{x}(k)$. The algorithm is based on control vector iteration. The discrete maximum principle requires that H_k be minimized for $u(k)\epsilon[0,1]$ for all $k=0,1,\cdots N-1$. This is equivalent to minimizing

$$\beta_k u(k)+p^T(k+1)\tilde{\psi}\tilde{x}(k)u(k);\ u(k)\epsilon[0,1]. \tag{3.1}$$

Note that

$$H_{ku(k)}=\beta_k+p^T(k+1)\tilde{\psi}\tilde{x}(k). \tag{3.2}$$

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