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Controllability of Positive Systems<sup>+</sup>

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## 1. Introduction

Positive systems, in which the state is constrained to lie in the positive orthant  $\mathbb{R}^n_+$ , are common in economic, social science, biological, and chemical applications. The state variables may represent populations, quantities of goods, or masses of chemical species. In the past, the underlying positivity of these systems has often been ignored or accommodated in an ad hoc fashion in order to take advantage of the well developed theory of linear systems which assumes that the states are drawn from a vector space. Recently, there have been a number of attempts to address systems issues directly in the context of positive systems. Ohta, Maeda and Kodama ([6],[8]) and Nieuwenhuis [7] have reported progress on the positive realization problem. Boothby [3] initiated a study of positive orthant controllability for bilinear systems, and Bacciotti [1] extended that work. These research efforts have answered some questions and have raised many new questions. They have revealed important qualitative differences from the corresponding theories for unconstrained systems.

In this paper we examine the issue of controllability for positive linear systems. In particular, we look at the connections between reachability, reachability from zero, and the rank criterion for controllability as they relate to systems in which both the state and inputs are constrained to lie in the positive orthant. Several examples which are representative of a large class of industrial applications are used to point out some fundamental differences from the control problem for systems without the positivity constraint.

### 1.1 Notation and Definitions

The discrete autonomous linear control system,

$$x(k+1) = Ax(k) + Bu(k) \quad x_0 = x(0) \text{ in } \mathbb{R}^n, \quad u(k) \text{ in } \mathbb{R}^m, \quad (1-1)$$

is denoted by the matrix pair  $(A,B)$ . We will say that  $(A,B)$  has positive dynamics if the unforced solution  $x(k) = A^k x_0$  lies in  $\mathbb{R}^n_+$  for each choice of  $x_0$  in  $\mathbb{R}^n_+$  and for all  $k \geq 0$ . Vectors  $x$  in  $\mathbb{R}^n_+$  are nonnegative vectors, denoted  $x \geq 0$  ( $x > 0$  if  $x$  is not equal to 0,  $x \gg 0$  if every entry is strictly positive). Similarly, a nonnegative matrix,  $M \geq 0$ , is one which has all of its entries in  $\mathbb{R}_+$ . We will use established results on nonnegative matrices, as given in the first two chapters of [2]. We write  $(A,B) \geq 0$  to indicate that  $A \geq 0$  and  $B \geq 0$ . The notion of a positive system is defined below.

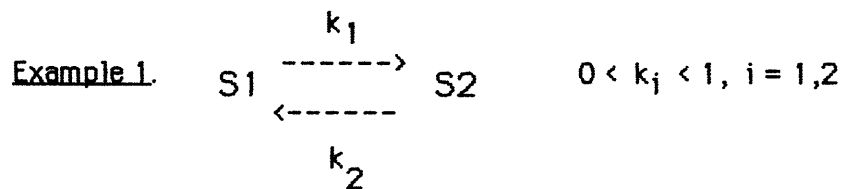
**Definition:** The discrete system  $(A,B)$  in (1-1) is a positive system if, whenever  $x_0 \geq 0$  and  $u(k) \geq 0$  for each  $k \geq 0$ , then  $x(k) \geq 0$  for  $k \geq 0$ . //

Given this definition, note that  $(A,B)$  is a positive system if and only if  $(A,B) \geq 0$ .

Finally, we will have occasion to refer to the class of matrices which are nonnegative and have nonnegative inverses. It is well known (e.g. [2]) that all such matrices can be expressed as the product of a nonnegative nonsingular diagonal matrix and a permutation matrix. The product of a nonsingular diagonal matrix (not necessarily nonnegative) and a permutation matrix is called a monomial.

### 1.2. Examples

The examples which follow will be useful throughout our development to motivate concepts and illustrate the results. The first system represents a two species reversible chemical reaction. The state of this system is the species composition vector specifying the distribution of mass between the two chemical compounds involved in the reaction.

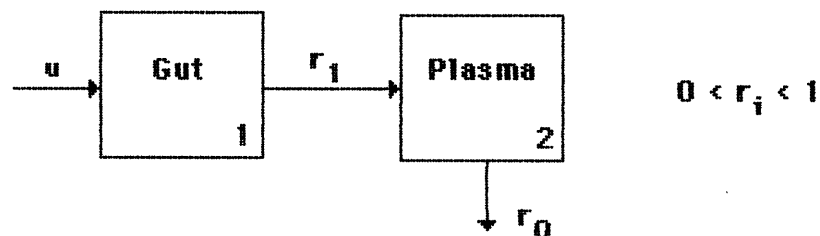


$$x(k) = \begin{pmatrix} \text{mass of } S_1 \\ \text{mass of } S_2 \end{pmatrix}; \quad x(k+1) = \begin{pmatrix} 1 - k_1 & k_2 \\ k_1 & 1 - k_2 \end{pmatrix} x(k) + \begin{pmatrix} p \\ 1 - p \end{pmatrix} u(k)$$

Here  $p$  gives the proportion of  $S_1$  in the feedstock  $u$ . //

The second and third examples are pharmacokinetic models of drug distribution in the human body.

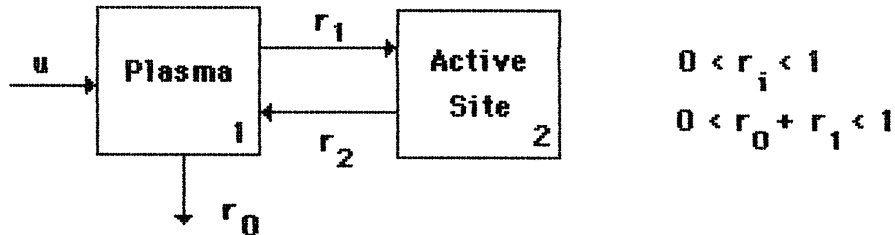
Example 2. Gut absorption model.



A dose  $u$  of the modeled drug is introduced into the gut and is subsequently absorbed into the plasma in the proportion  $r_1$ . The amount of drug in compartment  $i$  is the  $i$ th component of the state  $x$ . The drug is eliminated from the plasma in the proportion  $r_0$ . The discrete dynamic equation is:

$$x(k+1) = \begin{pmatrix} 1-r_1 & 0 \\ r_1 & 1-r_0 \end{pmatrix} x(k) + \begin{pmatrix} 1 \\ 0 \end{pmatrix} u(k)$$

**Example 3.** Active site model.



Here the dose  $u$  is introduced directly into the plasma, where an exchange takes place with the active site. The corresponding dynamic equation is:

$$x(k+1) = \begin{pmatrix} 1-r_1-r_0 & r_2 \\ r_1 & 1-r_2 \end{pmatrix} x(k) + \begin{pmatrix} 1 \\ 0 \end{pmatrix} u(k)$$

(Note: The most common pharmacokinetic model used for clinical applications is a three compartment model combining features of examples 2 and 3.)

## 2. Controllability of Unconstrained Linear Systems

The system  $(A,B)$  in (1-1) is said to be completely controllable if any desired state  $x_f$  in  $\mathbb{R}^n$  can be reached from any given initial state  $x_0$  in some finite time  $k_f$  in  $\mathbb{Z}^+$ , for appropriate choice of  $u(0), u(1), \dots, u(k_f-1)$ . It is well known that the following conditions on  $(A,B)$  are equivalent:

1. Complete controllability of  $(A,B)$ .
2. Reachability from 0: Any prescribed final state  $x_f$  can be reached from the zero state  $x(0) = 0$  in finite time.
3. Reachability from 0 in fixed time: Any prescribed final state  $x_f$  can be reached from the zero state in at most  $n$  steps (i.e.  $k_f \leq n$ ).
4. The matrix  $C_k$ , defined by  $C_k = [B \mid AB \mid A^2B \mid \dots \mid A^{k-1}B]$ , has full rank ( $= n$ ), for some  $k$ .
5. Rank  $C_n = n$ .

The equivalence of conditions 1 to 5 follows directly from consideration of the solution of (1-1):

$$x(k) = A^k x_0 + A^{k-1} B u(0) + A^{k-2} B u(1) + \dots + B u(k-1) = A^k x_0 + C_k \cdot u. \quad (2-1)$$

$x(k) = x_f$  has a solution  $u(0), \dots, u(k-1)$  if and only if  $x_f - A^k x_0$  lies in the column span of  $C_k$ . Since  $x_f$  and  $x_0$  can be selected arbitrarily from  $\mathbb{R}^n$ , every vector in  $\mathbb{R}^n$  must be in the range of some  $C_k$ . The requirement is not weakened if  $x_0$  is taken to be 0. Statements 5 and 3 are consequences of the Cayley Hamilton theorem which guarantees that  $A$  satisfies a polynomial of degree  $n$ .

Applied to the examples in section 1.2, the criterion of complete controllability provides sensible if fairly obvious necessary conditions. For the pharmacokinetic model of example 1, the controllability matrix  $C_n$  is given by

$$C_2 = \begin{pmatrix} 1 & 1 - r_1 - r_0 \\ 0 & r_1 \end{pmatrix}$$

The (unconstrained) system is completely controllable if and only if there is a non-zero transfer of drug from the plasma to the active site. The two species chemical reaction of example 2 is completely controllable, ignoring positivity, if and only if the feedstock composition  $(p, 1-p)^T$  is not the equilibrium composition  $(k_2/(k_1+k_2), k_1/(k_1+k_2))^T$  for the reaction.

Among industrial chemical engineers, the sufficiency of the above criterion is regarded with skepticism. A widely accepted rule of thumb says that if you have  $N$  variables to control, you need  $N$  controls and they should directly affect the variable to be controlled. This suggests that a requirement for  $B$  to be monomial is necessary for complete control. On the other hand, the standard compartmental pharmacokinetic model incorporates an assumption that the distribution of the drug among compartments can be controlled by inputs to one compartment alone. In the next section we look at the implications of positivity on our ability to move the positive system from one state to another. We examine conditions 1 through 5, and address questions motivated by the apparently contradictory messages from chemical engineering and pharmacokinetics sources.

### 3. Controllability of Positive Systems by Positive Inputs

The five equivalent conditions for complete controllability of unconstrained linear

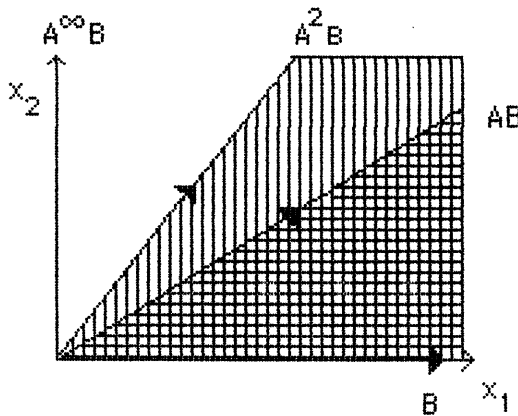
systems will be seen to represent distinct properties when the state is constrained to lie in the positive orthant. It is important to note here that there are two constraints involved: a positivity constraint on the state and a corresponding constraint on the inputs  $u$ . In our examples, the inputs are constrained by practical considerations to be positive (removal of a drug is difficult and rare). In this paper, we restrict our attention to positive input control.

We consider conditions 1 to 5 of section 2 for  $(A,B) \geq 0$  with the added requirements that  $x_0 \geq 0$ ,  $x_f \geq 0$ , and  $u(i) \geq 0$ , referring to the constrained conditions as 1P, 2P, 3P, 4P, and 5P.

A nonnegative state  $x_f$  is reachable from 0 in  $k$  steps if  $x_f$  is in the  $k$ -reachable cone.

$$R_k(A,B) = \{ x_f \text{ in } \mathbf{R}^n_+ \mid x_f = \sum_{i=0}^{k-1} A^i B u(k-1-i), u(j) \text{ in } \mathbf{R}^m_+ \}$$

Thus  $R_k(A,B)$  is the cone generated by the columns of  $C_k$ , and  $R_k$  is contained in  $R_{k+1}$  for every  $k$ .  $R_\infty(A,B)$  denotes the convex cone of states which are reachable in finite time. The reachable cone  $R(A,B)$  is the closure of  $R_\infty(A,B)$ . The  $k$ -reachable cones for the gut absorption and active site pharmacokinetic models of examples 2 and 3 are illustrated below.

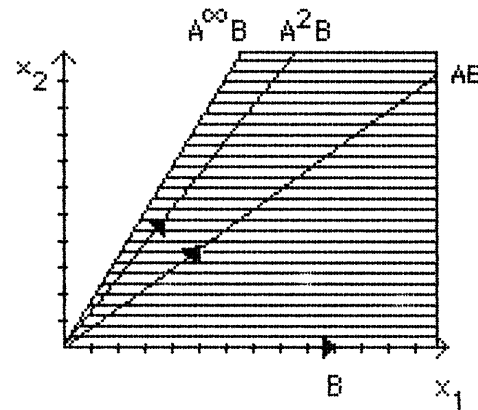


$$C_2 = \begin{pmatrix} 1 & 1-r_1 \\ 0 & r_1 \end{pmatrix} \quad R_2(A,B) = \text{grid}$$

$$R_3(A,B) = \text{grid} \cup \text{vertical strip}$$

$$R(A,B) = \mathbf{R}^2_+$$

a) Gut Absorption Model



With  $r_0 = 0.1, r_1 = 0.4, r_2 = 0.3$

$$C_k = \begin{pmatrix} 1 & 0.5 & 0.37 & \dots \\ 0 & 0.4 & 0.48 & \dots \end{pmatrix}$$

$$R(A,B) = \text{horizontal strip}$$

b) Active Site Model

In the gut absorption model,  $R_{k+1}(A,B)$  is not equal to  $R_k(A,B)$  for any  $k$ ; 4P is satisfied, but 3P is violated. A large set of positive states cannot be reached in 2 steps. Furthermore, for any  $k$ , there are states  $x_f$  in  $R^2_+$  which cannot be reached in  $k$  or fewer steps. Condition 2P is essentially satisfied -- i.e. all states  $x_f \geq 0$ , except possibly those on the boundary of  $R^n_+$ , are reachable in finite time. We will call this property 2PE. 2PE is clearly equivalent to  $R = R^n_+$ . 2P requires  $R_\infty(A,B) = R^n_+$ .

For the active site model,  $R(A,B)$  is not equal to  $R^2_+$ , so that even 2PE fails. Thus 4P does not imply 1P, 2P, 2PE, or 3P. It is in fact known (and easy to see) that 4P is equivalent to the requirement that the interior of  $R(A,B)$  in  $R^n$  be non-empty.

One conclusion from the observations above is that time plays a role which is at least more transparent than in the unconstrained control problem. When we consider reachability from non-zero initial states, timing is a critical factor. The set of states which are reachable from  $x_0$  in exactly  $k$  steps is given by the cone  $A^k x_0 + R_k(A,B)$ . The dynamic element,  $A^k x_0$ , drags the reachable cones around in the positive orthant. States which can be achieved in two steps may be inaccessible in three. Complete positive orthant controllability by positive inputs (property 1P) is possible only in very restricted circumstances, as indicated below.

Proposition 1P.  $(A,B) \geq 0$  is completely positive orthant controllable if and only if  $R_\infty(A,B) = R^n_+$  and  $A$  is nilpotent.

Proof: (a) Assume i)  $R_\infty(A,B) = R^n_+$  and ii)  $A$  is nilpotent.

For any given  $x_0 \geq 0$  and  $x_f \geq 0$ , nilpotence of  $A$  ensures that  $A^n x_0 = 0$ . Then, by assumption i),  $x_f$  can be reached in a finite number of additional steps.

(b) Assume that for every  $x_0 \geq 0$  and  $x_f \geq 0$  there is a finite sequence of inputs  $u(j) \geq 0, j = 0, 1, \dots, k-1$ , so that  $x_f$  can be reached from  $x_0$ . Let  $u = [u(k-1)^T, u(k-2)^T, \dots, u(0)^T]^T$ . Taking  $x_0 = 0$ , it follows that  $R_\infty(A,B) = R^n_+$ . If  $x_f = 0$ , then  $-A^k x_0 = C_k \cdot u \geq 0$ . Thus  $A^k x_0 = 0$ , the spectral radius of  $A$  is 0, and  $A$  is nilpotent. //

None of our examples are completely positive orthant controllable, but if we weaken the requirements so that the boundary of the positive orthant does not have to be reachable, then the class of controllable systems is considerably enlarged. The positive system  $(A,B)$  will be said to

be essentially completely positive orthant controllable if for every  $x_0 \geq 0$  and  $x_f \gg 0$  there exist inputs  $u(0), u(1), \dots, u(k-1)$  for some  $k < \infty$  such that  $x(k) = x_f$ . The next theorem shows that both of the necessary conditions of proposition 1 can be relaxed for essential controllability, property 1PE.

Proposition 1PE.  $(A,B) \geq 0$  is essentially completely positive orthant controllable if and only if  $R(A,B) = R^n_+$  and  $A$  is stable (spectral radius  $r < 1$ ).

Proof: (a) Assume i)  $R(A,B) = R^n_+$  and ii)  $A$  is stable.

Given  $x_0 \geq 0$  and  $x_f \gg 0$ , assumption i) implies that for some  $j$ ,  $x_f$  is in  $\text{int}(R_j(A,B))$  and this interior is open in  $R^n$ . Since  $A$  is stable,  $x_f - A^k x_0$  is in  $\text{int}(R_j(A,B))$  for all  $k$  sufficiently large. Choose  $k > j$ , sufficiently large. Then

$$x_f - A^k x_0 = C_j \cdot w, \quad \text{where } w = [w_{j-1}^T, w_{j-2}^T, \dots, w_0^T]^T,$$

and

$$x_f - A^k x_0 = C_k \cdot u, \quad \text{where } u = [w^T, 0, 0, \dots, 0]^T.$$

Thus  $x_0$  can be steered to  $x_f$  in finite time.

(b) Assume that for any  $x_0 \geq 0$  and  $x_f \gg 0$ ,  $x_f = A^k x_0 + C_k \cdot u$  for some  $k$  and for some  $u$  in  $R^{km}_+$ .

Taking  $x_0 = 0$ , it follows that  $x_f$  is in  $R_\infty(A,B)$  and therefore,  $R(A,B) = R^n_+$ .

Let  $v \geq 0$  be the eigenvector associated with the spectral radius ( $r$ ) of  $A$ . Choose  $x_f \gg 0$  so that  $x_f - v \leq 0$ , and let  $v$  be the initial state. The assumption guarantees that  $x_f = A^k v + C_k \cdot u$ , so  $x_f - A^k v \geq 0$ . But  $x_f - A^k v = x_f - r^k v$  which is  $\leq 0$  unless  $r < 1$ .

Thus  $A$  must be stable. //

Next, we turn to the question of reachability from 0. In addition to any intrinsic interest that reachability might have, the controllability characterizations given above incorporate reachability from 0 as a necessary condition. Thus any insights into properties 2P and 2PE will help clarify 1P and 1PE as well. Proposition 2P and conjecture 2PE below are first attempts in this direction.

Proposition 2P. For  $(A,B) \geq 0$ ,  $R_\infty(A,B) = R^n_+$  if and only if for some  $k$ ,  $C_k$  has an  $n \times n$  monomial submatrix.

Proof: (a) If  $C_k$  has an  $n \times n$  monomial submatrix, then it follows trivially that



$$R_{\infty}(A,B) = R^n_+.$$

(b) If  $R_{\infty}(A,B) = R^n_+$ , then the canonical unit vector  $e_i$  is in the cone spanned by the columns of  $C_k$  for some  $k$ , i.e.  $e_i = C_k \cdot u$ ,  $u = (u_1, u_2, \dots, u_{km})^T \geq 0$ . Since  $e_i$  is extremal in  $R^n_+$ , this is only possible if  $C_k$  has a column(s) which is a positive multiple of  $e_i$ . //

Since  $A \gg 0$  implies  $A^k B \gg 0$  for all  $k$ , we have the following corollary to Proposition 2P:

Corollary 2P. If  $A \gg 0$ , then  $R_{\infty}(A,B) = R^n_+$  if and only if  $B$  is a monomial.

Essential reachability (2PE) depends more explicitly on the eigenstructure of  $A$ . We believe that the following conjecture does represent a characterization of property 2PE.

Conjecture 2PE. For  $(A,B) \geq 0$ ,  $R(A,B) = R^n_+$  if and only if for some  $k$  and  $r$ :

(i)  $C_k$  has an  $n \times r$  monomial submatrix  $M_r$  (define  $M_0 = 0$ ),

(ii) the  $n-r$  nonzero columns,  $e_{j(1)}, e_{j(2)}, \dots, e_{j(n-r)}$ , of  $I - M_r M_r^+$  (where  $M_r^+$  denotes the Moore Penrose inverse) are each a linear combination of eigenvectors of  $A$  associated with eigenvalues of equal modulus.

and (iii) each  $e_{j(i)} = \lim_{k \rightarrow \infty} (a_i / c_{kk}) A^{kk} b$  for some  $a_i > 0$  and a column  $b$  of  $B$ ,

where  $c_{kk} = (A^{kk} b)_{j(i)}$  and  $kk = k_0, 2k_0, 3k_0, \dots$  //

Sufficiency of conditions i), ii), and iii) is clear. If the conjecture is correct, the necessity of (ii) implies that properties 2P and 2PE are equivalent for strictly positive  $A$ . Thus corollary 2P would hold with  $R(A,B)$  in place of  $R_{\infty}(A,B)$ . We state this latter result below and include a proof which is independent of the conjecture.

Corollary 2PE. If  $(A,B) \geq 0$  and  $A$  is strictly positive, then  $R(A,B) = R^n_+$  if and only if  $B$  is an  $n \times n$  monomial matrix.

Proof: (a) Sufficiency of  $B$  monomial is obvious.

(b) To show necessity, we rely on the following lemma:

lemma If  $A$  is irreducible with a Jordan basis of eigenvectors and generalized eigenvectors  $\{v_i\}$ ,  $i = 1, \dots, n$ , and  $0 \ll v_1 =$  the Perron vector, then the expansion in this basis of any nonzero vector  $x$  in  $R^n_+$  has a positive component (say  $a_1 v_1$ ) in the

direction of  $v_1$ . //

Proof of the lemma: The left Perron vector  $w \gg 0$  is orthogonal to all eigenvectors and generalized eigenvectors of  $A$  (except  $v_1$ ). Thus  $w \cdot x = a_1 w \cdot v_1$ . The left hand side is positive and  $w \cdot v_1$  is positive, so it follows that  $a_1 > 0$ . //

As a consequence of the lemma,  $(1/(r^i a_1))A^i x \rightarrow v_1$  for all  $x \gg 0$ , where  $r$  is the dominant eigenvalue. In particular, the columns  $A^i b$  of  $C_k$  tend toward the direction of  $v_1$ , as  $i \rightarrow \infty$ . If  $R(A,B) = R^n_+$ , there must be  $k$  such that  $R_k(A,B) = R^n_+$ . Then  $A \gg 0$  forces the conclusion that  $B$  is monomial. //

Corollaries 2P and 2PE cannot be extended to the class of primitive matrices  $A$  (that is,  $A$  such that for some  $k$ ,  $A^k \gg 0$ ), as evidenced by the following example.

$$A = \begin{pmatrix} 1 & 4 \\ 3 & 0 \end{pmatrix} \quad B = \begin{pmatrix} 0 \\ 1 \end{pmatrix} \quad \implies \quad C_2 = \begin{pmatrix} 0 & 4 \\ 1 & 0 \end{pmatrix}$$

$A^2 \gg 0$  and  $R(A,B) = R^2_+$ , but  $B$  is not a full monomial matrix. However, it is also easy to construct examples of system matrices which are not strictly positive and yet require  $B$  to be monomial for reachability (e.g.  $A = nxn$  identity matrix).

For the sake of completeness, we include propositions 3P and 4P.

**Proposition 3P.** For  $(A,B) \geq 0$ ,  $R_n(A,B) = R^n_+$  if and only if  $C_k$  has an  $nxn$  monomial submatrix.

**Proposition 4P.** Rank  $C_k = n$  for some  $k$ , if and only if  $\text{int}(R(A,B))$  is nonempty in  $R^n$ .

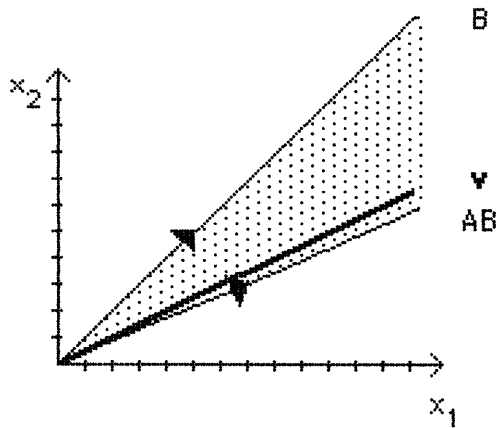
Properties 4 and 5 were not affected by the constraints we imposed, so they remain equivalent. Other implications between the P-properties are summarized below.

$$\begin{aligned} 1P &\implies 2P \implies 4; & 3P &\implies 2P; & 1PE &\implies 2PE \implies 4, \\ 1P &\not\leq 2P \not\leq 4; & 3P &\not\leq 2PE; & 1PE &\not\leq 2PE \not\leq 4. \end{aligned}$$

In the next section, we return to the chemical reaction and pharmacokinetic examples introduced in section 1.

#### 4. Implications of Positive Controllability

The chemical reaction system of example 1 with  $k_1 = 0.4$ ,  $k_2 = 0.8$ , and  $p = 0.5$ , is considered below.



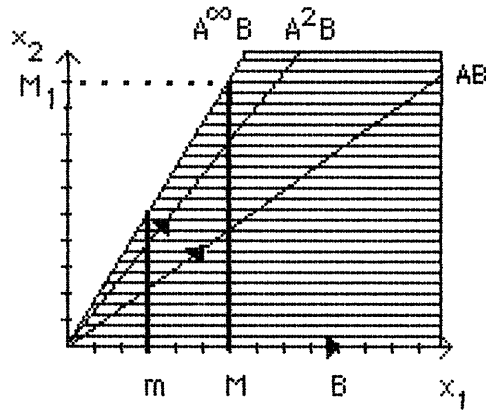
Chemical Reaction System

$$C_k = \begin{pmatrix} 0.5 & 0.7 & 0.66 & \dots \\ 0.5 & 0.3 & 0.33 & \dots \end{pmatrix}$$

$$R(A,B) = \begin{matrix} \boxed{\dots} \end{matrix}$$

Since  $A \gg 0$ , corollary 2PE applies and the reachable cone  $R(A,B)$  cannot be the entire positive orthant for any choice of  $k_i$  and  $p$  unless  $B$  is monomial. In other words, control of such a system requires  $n$  inputs, each one acting directly on one state component. Corollary 2PE provides a dramatic contrast to the situation for unconstrained control, where the number of single component inputs required is (heuristically) inversely related to the density of the system matrix. If the unconstrained system matrix is diagonal, then  $n$  inputs are necessary, but if all states are connected, it may be possible to control the system with an input to one state component alone. In the proof of the corollary, we see that it is the "pull" of the dominant eigenvector  $v$  which keeps the columns of  $C_k$  from spreading out to fill up the positive orthant.

For the pharmacokinetic systems, the situation is quite different. As in the chemical reaction model, the system matrix for the two compartment active site model is strictly positive. Still this system is controlled with a single input. The stated control objective in pharmacokinetics is to achieve and maintain plasma levels which are above some level ( $m$ ), the minimum level for therapeutic effect, and below a maximum safe level ( $M$ ). The implicit objective is to similarly constrain the drug levels at the active site. The justification given for focusing on plasma levels is the clinical observation that "identical plasma levels produce reasonably predictable effects" (in contrast to identical doses which can produce very different responses in different subjects) [5]. The effect of constraining plasma levels is illustrated below for the active site model.



Active Site Model

$$m < x_1 < M$$

We observe first that the maximum plasma level  $M$  imposes a corresponding maximum level  $M_1$  on the active site levels. This occurs precisely because the reachable cone is not all of  $\mathbb{R}^2_+$ . Note also that if negative doses were feasible, one could not conclude that the active site level was safe on the basis of a plasma reading. At the minimum level, the restricted reachability cone does not in itself guarantee a minimum active site level. Instead, the system dynamics play a role. The upper extremal of the cone is the dominant eigenvector, to which the state is attracted over time. Thus the state tends toward the subset of the reachable cone which represents safe and therapeutic levels at the active site. This same factor explains how it is possible to keep the plasma level below  $M$  with only positive  $u$ . Complete "point" controllability, as studied in section 3, is clearly not the relevant issue for pharmacokinetic systems. More appropriate measures of controllability for such systems will be considered elsewhere.

## References

1. A Bacciotti, On the positive orthant controllability of two dimensional bilinear systems, *Systems and Control Letters*, vol. 3, no. 1, June 1983, 53-55.
2. A. Berman and R.J. Plemmons, Nonnegative Matrices in the Mathematical Sciences, Academic Press, New York, 1979.
3. W. Boothby, Some comments on positive orthant controllability of bilinear systems, *SIAM J. Control Optim.*, vol. 20, no. 5, Sept. 1982, 634-644.
4. F.R. Gantmacher, The Theory of Matrices, Vol. 1 and 2, Chelsea, New York, 1964.
5. A. Goldstein, W. Aronow, and S. Kalman, Principles of Drug Action: The Basis of Pharmacology, 2nd ed., John Wiley & Sons, New York, 1974.

6. H. Maeda and S. Kodama, Positive realization of difference equations, IEEE Trans. Circuits and Systems, CAS-28, no. 1, Jan. 1981, 39-47.
7. J. W. Nieuwenhuis, About nonnegative realizations, Systems and Control Letters, vol. 1, no. 5, March 1982, 283-287.
8. Y. Ohta, H. Maeda, and S. Kodama, Reachability, observability and realizability of continuous-time positive systems, SIAM J. Control Optim., vol. 22, no. 2, March 1984, 171-180.