Applications of Pick-Nevanlinna Interpolation Theory to Retention-Solubility Studies in the Lungs

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ABSTRACT

Computational procedures for retention-solubility studies are given which determine data feasibility and some extreme properties of lung models compatible with given data. The procedures are analytic and are based on the interpolation theory of Pick and Nevanlinna.

1. INTRODUCTION

Under steady state conditions in a subject receiving an inert test gas in dissolved form by constant intravenous drip, the fraction of the gas retained in the blood after a pass through the lungs is called the retention of the gas, and the dependence of this retention on test gas solubility is called the retention-solubility relation. A widely used model for this relation is the parallel ventilation and perfusion model [7–9], in which a set number of compartments are assumed to be ventilated and perfused in parallel, with test gas at equilibrium (no diffusion impairment) in each compartment and with fluctuations due to cyclical breathing and blood flow averaged out. In [6] it is shown that such a parallel system may be regarded as an equivalent “diagonalized” version of more general compartmental models.

In this paper the classical interpolation theory for analytic functions of Pick and Nevanlinna [2, 5, 14] is shown to yield computational techniques of considerable utility in analyzing retention-solubility studies in terms of the above parallel models.

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We begin with a derivation of the retention-solubility relation for parallel lung models in Section 2. This leads to the definition of "retention functions" in Section 3. In Section 4 the inverse problem is outlined and the main results of this paper are indicated.

In Sections 5, 6, 7, and 8 the main results are presented: computational procedures for determining data feasibility and some properties of lung models compatible with given data. The remaining sections, 9 through 24, are devoted to the development of basic tools, the classification of data points, and proofs. Readers uninterested in the details of the proofs should skip sections 9 through 24.

2. THE RETENTION-SOLUBILITY RELATION FOR PARALLEL VENTILATION AND PERFUSION LUNG MODELS

A parallel ventilation and perfusion model of the lungs as given by Farhi and others [7–9] consists of \( n \) perfused compartments and one unperfused compartment called dead space.

Let \( \dot{Q}_1, \ldots, \dot{Q}_n > 0 \) be the perfusions in blood volume per unit time to the \( n \) compartments, and let \( \dot{V}_1, \ldots, \dot{V}_n \) be the corresponding ventilations. Let \( \lambda \) be the blood-gas partition coefficient of an inert test gas which has partial pressure \( \bar{P}_v \) in the venous blood coming into the lungs.

If

\[
\dot{Q}_T \overset{\text{def}}{=} \dot{Q}_1 + \cdots + \dot{Q}_n
\]  

(2.1)

is the total perfusion, then the amount of test gas per unit time delivered to the lungs is \( \lambda \bar{P}_v \dot{Q}_T \). The partial pressure in the \( k \)th compartment \( P_k \) must satisfy

\[
\lambda \dot{Q}_k P_k + \dot{V}_k P_k = \lambda \dot{Q}_k \bar{P}_v
\]

under the equilibrium hypothesis, so that

\[
P_k = \frac{\lambda \bar{P}_v}{\lambda + \dot{V}_k / \dot{Q}_k}.
\]

The amount of test gas retained from the \( k \)th compartment in blood is

\[
\lambda \dot{Q}_k P_k, \quad \text{which is} \quad \lambda \dot{Q}_k \left( \frac{\lambda \bar{P}_v}{\lambda + \dot{V}_k / \dot{Q}_k} \right).
\]

If we set \( x_k = \dot{V}_k / \dot{Q}_k \), the \( k \)th ventilation-perfusion ratio, we obtain the
retention by summing the amount retained from each compartment and dividing by $\lambda P_c \dot{Q}_T$. Thus the retention $R(\lambda)$ satisfies

$$R(\lambda) = \frac{1}{\dot{Q}_T} T(\lambda)$$

(2.2)

where

$$T(\lambda) = \sum_{k=1}^{n} \frac{\lambda \dot{Q}_k}{\lambda + x_k}.$$  

(2.3)

Let $\dot{V}_T$ be the total ventilation, set

$$\dot{V}_D \overset{\text{def}}{=} \dot{V}_T - \sum_{i=1}^{n} \dot{V}_i,$$

and take $\dot{V}_D$ as the ventilation to the unperfused compartment (dead space). Of course we must have $\dot{V}_D \geq 0$.

Let us say that a model is given in fully reduced form if all compartments with like ventilation-perfusion ratio have been lumped together so that $x_j \neq x_k$ whenever $j \neq k$ for $1 \leq j, k \leq n$. In this case we will generally take $0 < x_1 < x_2 < \cdots < x_n$. In the sequel all models are assumed to be given in fully reduced form.

3. RETENTION FUNCTIONS

DEFINITION: We say that a rational function $T(\lambda)$ is a retention function if

$$T(\lambda) = \sum_{j=1}^{n} \frac{\lambda \dot{Q}_j}{\lambda + x_j}$$

(3.1)

for some $n \geq 0$ and for some $0 < x_1 < \cdots < x_n < \infty$ and $\dot{Q}_1, \ldots, \dot{Q}_n > 0$.

The singular part of $T(\lambda)/\lambda$ at $-x_j$ is $\dot{Q}_j/(\lambda + x_j)$, so that clearly $n$, $\dot{Q}_1, \ldots, \dot{Q}_n$, and $x_1, \ldots, x_n$ are unique for a given $T$. We call (3.1) the canonical form of $T(\lambda)$.

We note that

$$T(\infty) \overset{\text{def}}{=} \lim_{\lambda \to \infty} T(\lambda) = \sum_{j=1}^{n} \dot{Q}_j$$

(3.2)

and that

$$T'(\infty) \overset{\text{def}}{=} \lim_{\lambda \to \infty} \lambda (T(\lambda) - T(\infty)) = - \sum_{i=1}^{n} \dot{Q}_i x_i = - \sum_{i=1}^{n} \dot{V}_j$$

(3.3)
where

$$\dot{V}_j \equiv \dot{Q}_j x_j \quad \text{for } 1 \leq j \leq n.$$  

From (3.1) we see that there is a retention function associated with every lung model in fully reduced form and that, with the exception of dead space ventilation $\dot{V}_D$, a complete description of the fully reduced form of the model can be obtained from the retention function. If the model has total perfusion $\dot{Q}_T$, then $\dot{Q}_T = T(\infty)$. The total ventilation $\dot{V}_T$ and the dead space ventilation $\dot{V}_D$ satisfy $\dot{V}_D = \dot{V}_T + T'(\infty)$.

We are thus led to define a lung model as a pair $(T, \dot{V}_D)$ where $T$ is a retention function and $\dot{V}_D$ is a real number which gives the ventilation to the dead space.

4. DATA: THE INVERSE PROBLEM

We assume that the blood-gas partition coefficients $0 < \lambda_1 < \cdots < \lambda_m$ are fixed. For each $0 \leq k \leq m$ we denote the entries of a point $d \in \mathbb{R}^2 \times \mathbb{R}^k$ as $(d_q, d_v, d_1, \ldots, d_k)$, with the interpretation that such a $d$ is possibly a vector of data where

- $d_q$ is the total perfusion,
- $d_v$ is the total ventilation, and
- $d_j/d_q$ is the retention value of a test gas with partition coefficient $\lambda_j$ for $1 \leq j \leq k$.

The basic “inverse problem” may be stated as: given $d \in \mathbb{R}^2 \times \mathbb{R}^k$, find and characterize the retention functions $T(\lambda)$ which satisfy the requirements

$$T(\infty) = d_q - T'(\infty) \leq d_v \quad \text{and} \quad T(\lambda_j) = d_j \quad \text{for } j = 1, \ldots, k.$$  

Any retention function meeting these requirements is said to be compatible with $d$. Note that for many $d \in \mathbb{R}^2 \times \mathbb{R}^k$ no retention function exists meeting the requirements; such a $d$ is called infeasible. A feasible $d$ is one for which some retention function exists which is compatible with $d$. Given a lung model $(T, \dot{V}_D)$ and a point $d \in \mathbb{R}^2 \times \mathbb{R}^k$ such that $T$ is compatible with $d$ and $\dot{V}_D = d_v + T'(\infty)$, we say that $d$ is the output of $(T, \dot{V}_D)$.

Of course, if $T$ is compatible with $d$, then $(T, d_v + T'(\infty))$ is a lung model with output $d$. We say that the retention function $T$ itself has output $d$ if the model consisting of $T$ with zero dead space has output $d$ [i.e. if $T'(\infty) = -d_v$].
The main results of this paper are methods for determining

1. the feasibility of a data point \( d \in R^2 \times R^k \),
2. the maximum (minimum) possible retention value at any blood-gas partition coefficient \( \lambda > 0 \) for a retention function compatible with a data point \( d \in R^2 \times R^k \),
3. the maximum possible perfusion at any given ventilation-perfusion ratio \( x \) for a retention function compatible with a data point \( d \in R^2 \times R^k \).

Also, in the process of doing (1) and (2) we actually give a method for constructing a retention function compatible with a given feasible \( d \in R^2 \times R^k \). This receives no emphasis, because the form of the constructed function seems inconvenient for practical use.

These procedures are of considerable practical value in a program of investigation presented in an earlier paper [7] in which Monte Carlo methods are used to analyze retention-solubility test results.

We first present these results without elaboration or proof. In the second part of the paper we give proofs. These use a classification of retention functions, lung models, and data points by “rank” and are based on a procedure which simultaneously transforms a retention function and a data point to one of lower rank.

5. FEASIBILITY DETERMINED BY RECURSION

The following is an elementary method of determining the feasibility of a point \( d^k \in R^2 \times R^k \) for \( k \geq 0 \):

If \( k = 0 \), then \( d^k \) is feasible if and only if \( d^k_q, d^k_e \geq 0 \).

Otherwise (when \( k > 0 \)): If any entry of \( d^k \) is negative, then \( d^k \) is not feasible. If all entries of \( d^k \) are nonnegative, we consider two cases:

Case i. If \( d^k_k = 0 \), then \( d^k \) is feasible if and only if

\[
\begin{align*}
&d^k_q - d^k_e = \ldots = d^k_k = 0 \quad \text{and} \quad d^k_e \geq 0.
\end{align*}
\]

Case ii. If \( d^k_k > 0 \), then set

\[
\begin{align*}
d^{k-1} &= \text{det} \left( \begin{array}{ccc}
d^k_q - 1 & d^k_e - \lambda_k \frac{d^k_q}{d^k_k} & d^k_k - 1 \\
d^k_k - \lambda_k \frac{d^k_q}{d^k_k} & d^k_k - \lambda_k & 0 \\
\lambda_k (d^k_k - d^k_k) & \ldots & \lambda_{k-1} (d^k_k - d^k_k) \\
\lambda_1 d^k_k & \ldots & \lambda_{k-1} d^k_k - \lambda_k d^k_k \\
\end{array} \right),
\end{align*}
\]

and \( d^k \) is feasible if and only if \( d^{k-1} \) is feasible. We may now continue recursively and determine the feasibility of \( d^k \).
6. FEASIBILITY DETERMINED USING THE PICK MATRIX

The following is an alternative to the method in Section 5. Set \( z_j = 1/\sqrt{\lambda_j} \) for \( j = 1, \ldots, m \). Given \( d \in \mathbb{R}^2 \times \mathbb{R}^k \), let \( M(d) \), the Pick matrix of \( d \), be defined as

\[
\begin{bmatrix}
  d_0 & 0 & d_1 & \cdots & d_k \\
  0 & d_0 - d_1 & z_1 & \cdots & z_k d_1 + z_k d_2 \\
  d_1 & z_1 d_1 + z_2 d_2 & z_2 d_2 + z_3 d_3 & \cdots & z_k d_k + z_{k-1} d_{k-1} \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  d_k & z_k d_k + z_{k-1} d_{k-1} & \cdots & \cdots & z_{k-1} d_{k-1} + z_k d_k \\
\end{bmatrix}
\]

Then \( d \) is feasible if and only if \( M(d) \) is positive semidefinite (i.e. has only nonnegative eigenvalues; cf. [10]).

7. EXTREME RETENTIONS CONSTRUCTED BY RECURSION

From a data point \( d^k \in \mathbb{R}^2 \times \mathbb{R}^k \) which we collect using gases with fixed partition coefficients \( \lambda_1, \ldots, \lambda_k \), it is possible to predict (approximately) the retention value we would obtain using a gas with a different partition coefficient \( \lambda > 0 \). To be more precise: The set

\[ \{ T(\lambda) : T \text{ is compatible with } d^k \} \]

turns out to be an interval whose endpoints are determined by the following elementary method:

Determine the feasibility of \( d^k \) by recursion. If \( d^k \) is not feasible, there are no compatible retention functions. Otherwise we consider two cases:

Case i. If the feasibility search terminates at \( d' \) for \( 0 \leq l \leq k \) with \( d'_{l-1} = d'_{l-2} = \cdots = d'_0 = 0 \), then define two rational functions \( T^{(l,0)} \) and \( T^{(l,1)} \) of \( \lambda \) by setting

\[ T^{(l,0)}(\lambda) \overset{\text{def}}{=} T^{(l,1)}(\lambda) \overset{\text{def}}{=} 0 \quad \text{for all } \lambda. \]
Now proceed as in case ii after $T^{(l,0)}$ and $T^{(l,1)}$ are defined.

**Case ii.** In this case the feasibility search has produced $d^k, d^{k-1}, \ldots, d^0$ with $d^0_q > 0$. Define $T^{(0,0)}$ and $T^{(0,1)}$, rational functions of $\lambda$, as follows:

$$
T^{(0,0)}(\lambda) \overset{\text{def}}{=} d^0_q, \quad (7.1)
$$

$$
T^{(0,1)}(\lambda) \overset{\text{def}}{=} \frac{\lambda d^0_q}{\lambda + d^0_q/d^0_q}, \quad (7.2)
$$

and assuming that $T^{(l,0)}$ and $T^{(l,1)}$ have been defined for $0 \leq l < k$, define

$$
T^{(l+1,j)}(\lambda) = d_{l+1}^j \frac{\lambda [T^{(l,j)}(\lambda) + 1]}{\lambda_{l+1} T^{(l,j)}(\lambda) + \lambda} \quad (7.3)
$$

for $j = 1, 2$.

If $d^k$ is feasible, the above procedure yields $T^{(k,0)}(\lambda)$ and $T^{(k,1)}(\lambda)$ which are retention functions compatible with $d^k$ and are such that

$$
T^{(k,1-j)}(\lambda) \leq T(\lambda) \leq T^{(k,j)}(\lambda)
$$

for any $T(\lambda)$ compatible with $d^k$. Here

$$
\hat{j} = \begin{cases} 
1 & \text{for } \lambda \geq \lambda_k, \\
0 & \text{for } \lambda_{k-1} \leq \lambda \leq \lambda_k, \\
1 & \text{for } \lambda_{k-2} \leq \lambda \leq \lambda_{k-1}, \\
\vdots & 
\end{cases}
$$

Note that in case i above, or when $d^0_v = 0$ in case ii above, we have $T^{(k,0)}(\lambda) \equiv T^{(k,1)}(\lambda)$ and there is a unique retention function compatible with $d^k$.

8. EXTREME VALUES OF PERFUSION

Given a feasible $d^k \in R^2 \times R^k$ and a ventilation perfusion ratio $x \geq 0$, we find the maximum possible perfusion at $x$ in a retention function compatible with $d^k$. Namely, we find the maximum $\hat{Q}$ such that some retention function compatible with $d$ has the form

$$
\frac{\lambda \hat{Q}_1}{\lambda + x_1} + \cdots + \frac{\lambda \hat{Q}}{\lambda + x} + \cdots + \frac{\lambda \hat{Q}_n}{\lambda + x_n}.
$$
If the preceding determination of extreme retention has shown that there is a unique retention function compatible with $d^k$, then the canonical form of this retention function gives the only possible perfusion values at the uniquely determined ventilation-perfusion ratios.

Otherwise the Pick matrix $M(d^k)$ is nonsingular. Set

$$a \equiv u^T M(d^k)^{-1} u,$$

$$b \equiv w^T M(d^k)^{-1} w,$$

$$c \equiv w^T M(d^k)^{-1} u^T,$$

where

$$u^x \equiv \left(1, 0, \frac{1}{xz_1^2 + 1}, \ldots, \frac{1}{xz_k^2 + 1} \right)$$

and

$$w^x \equiv \sqrt{x} \left(0, 1, \frac{z_1}{xz_1^2 - 1}, \ldots, \frac{z_k}{xz_k^2 + 1} \right).$$

Then the desired maximum perfusion at $x$ is

$$\frac{2}{a + b + \sqrt{(a - b)^2 + 4c}}.$$

The methods of the proofs are in the spirit of the original ones of Pick and Nevanlinna. However, they literally follow the ones of [14] pretty closely. Those were done on the unit disk rather than right half plane. However, we have performed the appropriate modification. For cultural interest we remark that "retention functions" arise directly in electric circuit theory. In particular, the impedance as a function of operating frequency for a circuit consisting of resistors and capacitors only (with no series inductance at the input) has the same mathematical form as a retention function, and all retention functions can be gotten as the impedance function of some such circuit. Some tricks from circuit theory proved useful here. In particular, the Cauer transform is used in Sections 6, 11 and influenced the derivation of other formulas in this paper. A good reference is [11, Chapter 6].
9. SOME REMARKS

We now proceed with the development of some basic mathematical tools. After preliminary remarks we define the “rank” of a retention function and of a lung model. We then demonstrate the existence of a rank increasing and of a rank decreasing map of retention functions. These maps give rise in a natural way to maps from $R^2 \times R^k$ to $R^2 \times R^{k+1}$ and back which are maps between feasible data points in the two spaces. Data points through their association with compatible retention functions inherit a “rank.” The set of feasible data points in $R^2 \times R^k$ is conveniently described as the union of subsets of differing rank. With this classification of feasible data points completed, we give the proofs of the main results.

10. MATHEMATICAL PRELIMINARIES; FRACTIONAL LINEAR TRANSFORMATIONS

For complex numbers $a, b, c, d$ let $f(z) = (az + b)/(cz + d)$. Observe that $f(A) = B$ where $A$ and $B$ are $2 \times 2$ matrices with complex entries and $AB$ is the usual matrix product. Observe also that if $a, b, c, d$ are all real with $ad \neq bc$, then $f$ takes the extended real line $\tilde{R} = R \cup \{\infty\}$, viewed as a subset of the Riemann sphere, onto itself. To avoid exceptional cases we consider all fractional linear transformations from now on as maps from $\tilde{R}$ to $\tilde{R}$ considered as a subset of the Riemann sphere [1].

11. RANK OF A RETENTION FUNCTION

For $T(\lambda) = \sum_{i=1}^n \lambda \hat{Q}_i/\lambda + x_i$ with $0 \leq x_1 < \ldots < x_n$ and $\hat{Q}_1, \ldots, \hat{Q}_n > 0$, we define $\rho(T)$, the rank of $T$, to be

$$\rho(T) = \begin{cases} 2n & \text{if } x_1 > 0, \\ 2n - 1 & \text{if } x_1 = 0. \end{cases}$$

Thus each perfused compartment of $T$ with nonzero ventilation-perfusion ratio contributes 2 to the rank, while the “shunt” compartment with no ventilation contributes 1 to the rank if present. We note that if $T(\lambda) = 0$ then $\rho(T) = 0$.

The rank of a lung model $(T, \hat{V}_D)$, denoted by $\rho(T, \hat{V}_D)$ is defined as $\rho(T) + \rho(\hat{V}_D)$, where

$$\rho(\hat{V}_D) = \begin{cases} 1 & \text{if } \hat{V}_D > 0, \\ 0 & \text{if } \hat{V}_D = 0. \end{cases}$$
12. THE INCREMENTAL MAP $\mathcal{I}$

Given a rational function $S$ and a real number $a$ such that $S(a) \neq -1$, let $\mathcal{I}(a, S)$ be that rational function whose value at $\lambda$ is $\frac{\lambda}{a} S(\lambda)$. We call $\mathcal{I}(a, S)$ the increment of $S$ with value $1$ at $a$. For $b \neq 0$ the rational function $b\mathcal{I}(a, S)$ is called the increment of $S$ with value $b$ at $a$. The map $\mathcal{I}$ is called the incremental map. We have the following theorem about $\mathcal{I}$.

**THEOREM 1**

If $S$ is a retention function and $a, b > 0$, then $b\mathcal{I}(a, S)$ is a retention function with rank equal to $\rho(S) + 1$, whose value at $a$ is $b$.

The domain of definition of the incremental map $\mathcal{I}$ may be extended to include complete lung models by defining the increment of a lung model $(S, \hat{V}_D)$ with value $b$ at $a$ to be the lung model with retention function $b\mathcal{I}(a, S)$ and with dead space $b\hat{V}_D$, i.e. $b\mathcal{I}(a, (S, \hat{V}_D)) = (b\mathcal{I}(a, S), b\hat{V}_D)$. Theorem 1 then implies that $\mathcal{I}$ is a rank increasing map of lung models.

13. THE DECREMENTAL MAP $\mathcal{D}$

Given a rational function $T$ and a real number $a$ such that $T(a) \neq 0$, let $\mathcal{D}(a, T)$ be that rational function whose value at $\lambda$ is

$$\mathcal{D}\left(\begin{bmatrix} \lambda & -\lambda T(a) \\ -a & \lambda T(a) \end{bmatrix}; T(\lambda) \right).$$

We call $\mathcal{D}(a, T)$ the decrement of $T$ at $a$, and we call the map $\mathcal{D}$ the decremental map. We have the following theorem about $\mathcal{D}$.

**THEOREM 2**

If $T$ is a retention function with $\rho(T) > 0$ and $a > 0$, then $\mathcal{D}(a, T)$ is a retention function with rank equal to $\rho(T) - 1$.

The domain of definition of the decremental map $\mathcal{D}$ may be extended to include complete lung models by defining the decrement of a lung $(T, \hat{V}_D)$ at $a$, where $\rho(T) > 0$, to be the lung model with retention function $\mathcal{D}(a, T)$ and with dead space $\hat{V}_D/T(a)$, i.e.

$$\mathcal{D}(a, (T, \hat{V}_D)) = (\mathcal{D}(a, T), \hat{V}_D/T(a)).$$

Theorem 2 then implies that $\mathcal{D}$ is a rank decreasing map of lung models with nonzero retention functions.

Before proving the theorems we note some properties of $\mathcal{I}$ and $\mathcal{D}$. 

14. RELATIONS BETWEEN $\mathcal{F}$ AND $\mathcal{G}$

The following relations between $\mathcal{F}$ and $\mathcal{G}$ hold for $a$ and $b$ real with $b \neq 0$ and for $S$ and $T$ rational functions:

\[ \mathcal{G}(a, b \mathcal{F}(a, S)) = S \quad (14.1) \]

and

\[ T(a) \mathcal{F}(a, \mathcal{G}(a, T)) = T. \quad (14.2) \]

To prove the first equality we observe that if $T(a) \neq 0$, then $\mathcal{G}(a, bT)$ is independent of $b \neq 0$ and thus

\[ \mathcal{G}(a, b \mathcal{F}(a, S)) = \mathcal{G}(a, \mathcal{F}(a, S)) \mathcal{G}(a, L) \]

\[ = \mathcal{F}\left( \begin{bmatrix} \lambda & -\lambda \\ -a & \lambda \end{bmatrix}; \mathcal{F}(a, S)(L) \right) \]

\[ = \mathcal{F}\left( \begin{bmatrix} \lambda & -\lambda \\ -a & \lambda \end{bmatrix}; \mathcal{F}\left( \begin{bmatrix} \lambda & \lambda \\ a & \lambda \end{bmatrix}; S(L) \right) \right) \]

\[ = \mathcal{F}\left( \begin{bmatrix} \lambda^2 - a \lambda & 0 \\ 0 & \lambda^2 - a \lambda \end{bmatrix}; S(L) \right) = S(L). \]

Here we have used the fact that $\mathcal{F}(a, S)(a) = 1$ for all rational $S$ where $\mathcal{F}$ is defined.

The second equality holds because

\[ T(a) \mathcal{F}(a, \mathcal{G}(a, T)) = T(a) \mathcal{F}\left( \begin{bmatrix} \lambda & \lambda \\ a & \lambda \end{bmatrix}; \mathcal{F}\left( \begin{bmatrix} \lambda & -\lambda T(a) \\ -a & \lambda T(a) \end{bmatrix}; T(L) \right) \right) \]

\[ = \mathcal{F}\left( \begin{bmatrix} \lambda T(a) & \lambda T(a) \\ a & \lambda \end{bmatrix}; T(L) \right) \mathcal{F}\left( \begin{bmatrix} \lambda & -\lambda T(a) \\ -a & \lambda T(a) \end{bmatrix}; T(L) \right) \]

\[ = \mathcal{F}\left( \begin{bmatrix} (\lambda^2 - a \lambda) T(a) & 0 \\ 0 & (\lambda^2 - a \lambda) T(a) \end{bmatrix}; T(L) \right) \]

\[ = T(L). \]

Here we have used the fact that

\[ b \mathcal{F}\left( \begin{bmatrix} \lambda & \lambda \\ a & \lambda \end{bmatrix}; \cdot \right) = \mathcal{F}\left( \begin{bmatrix} b \lambda & b \lambda \\ a & \lambda \end{bmatrix}; \cdot \right) \]

with $b = T(a)$. 
15. PROOF OF THEOREM 1

Let \( S \) be given in canonical form by

\[
S(\lambda) = \sum_{j=1}^{n} \frac{\lambda \hat{Q}_j}{\lambda + \bar{x}_j},
\]

and let \( T = b \mathcal{G}(a, S) \) for \( a, b > 0 \).

Case 1: \( \bar{x}_1 > 0 \). Note that \( S \) may be expressed as \( \frac{p}{q} \) where \( p \) and \( q \) are polynomials of degree \( n \), and \( T(\lambda)/\lambda \) then has the form \( b(p + q)/(ap + \lambda q) \), an expression whose denominator (numerator) is a polynomial of degree \( n + 1 \) (degree \( n \)). We thus achieve the partial fraction representation [1] of \( T(\lambda)/\lambda \) if we locate \( n + 1 \) distinct singular parts of the equivalent expression

\[
\frac{b[S(\lambda)+1]}{\lambda \left( \frac{S(\lambda)}{\lambda} + 1 \right)}.
\]

The denominator here vanishes at \( x_1 \equiv 0 \) and for any \( \lambda \) such that \( S(\lambda)/\lambda = -1/a \). Because of the behavior of \( S(\lambda)/\lambda \) near \( \lambda = -x_j \) for \( j = 1, \ldots, n \) and as \( \lambda \) tends to \(-\infty\), we see that there are \( x_2 < \cdots < x_{n+1} \) interdigitating \( \bar{x}_1, \ldots, \bar{x}_n, \infty \) such that \( S(-x_j)/(-x_j) = -1/a \) for \( j = 2, \ldots, n + 1 \). The values \( -x_1, \ldots, -x_{n+1} \) are the \( n + 1 \) desired singular points of \( T(\lambda)/\lambda \), and the partial fraction representation is then, by our earlier remarks,

\[
\frac{T(\lambda)}{\lambda} = \sum_{j=1}^{n+1} \frac{b[S(-x_j)+1]}{(aS'(-x_j)+1)(\lambda + x_j)}.
\]

This is a complete representation because

\[
S(-x_j)+1 = \frac{x_j}{a} + 1 > 0 \quad \text{for } j = 1, \ldots, n+1,
\]

and because

\[
S'(\lambda) = \sum \frac{\hat{Q}_j \bar{x}_j}{(\lambda - \bar{x}_j)^2}
\]

is greater than zero wherever it is defined. Thus, if we set

\[
\hat{Q}_j - \frac{b(x_j/a + 1)}{aS'(-x_j)+1} \quad \text{for } j = 1, \ldots, n + 1,
\]
we have that

\[ T(\lambda) = \sum_{j=1}^{n+1} \frac{\lambda \hat{Q}_j}{\lambda + x_j} \]

in canonical form, and \( \rho(T) = 2n + 1 \). Since \( \rho(S) = 2n \), the proof is complete.

Case 2: \( \bar{x}_1 = 0 \). Here \( S \) may be expressed as \( \hat{Q}_1 + p/q \) where \( p \) and \( q \) are polynomials of degree \( n - 1 \). The function \( T(\lambda)/\lambda \) then has the form

\[ b \left[ \left( \hat{Q}_1 + 1 \right) q + p \right] / \left[ (a\hat{Q}_1 + 1) q + ap \right], \]

an expression where the denominator (numerator) is a polynomial of degree \( n \) (degree \( n - 1 \)). The \( n \) required singular points of \( T(\lambda)/\lambda \) here are the negatives of \( x_1, \ldots, x_n \), where \( S(-x_j) = x_j/a \) for \( 1 \leq j \leq n \) and \( 0 = \bar{x}_1 < x_1 < x_2 < \cdots < \bar{x}_n < x_n < \infty \). Again we set \( Q_j = b(x_j/a + 1)/(aS'(-x_j) + 1) \) and have \( T(\lambda) = \sum_{j=1}^{n} \lambda \hat{Q}_j / (\lambda + x_j) \) in canonical form. Here \( \rho(T) = 2n \) and \( \rho(S) = 2n - 1 \), and we are done.

16. PROOF OF THEOREM 2

Let \( T \) be given in canonical form by

\[ T(\lambda) = \sum_{j=1}^{n} \frac{\lambda \hat{Q}_j}{\lambda + x_j}. \]

Case 1: \( x_1 = 0 \). \( T(\lambda) \) may be expressed as \( \hat{Q}_1 + p/q \) where \( p \) and \( q \) are polynomials in \( \lambda \) of degree \( n - 1 \). Then \( S(\lambda)/\lambda \) has the form \( (b - \hat{Q}_1) q - p) / (a\hat{Q}_1 - b\lambda) q + ap \). Both the numerator and denominator of this last expression have \( \lambda - a \) as a factor, since \( T(a) = \hat{Q}_1 + p(a)/q(a) = b \). We achieve the partial fraction decomposition of \( S(\lambda)/\lambda \) as defined if we locate \( n - 1 \) distinct singular parts of the equivalent expression \( [b - T(\lambda)]/\lambda [aT(\lambda)/\lambda - b] \). Because of the behavior of \( T(\lambda)/\lambda \) at \( -x_1, \ldots, -x_n \) there must be \( x_1 < \bar{x}_1 < x_2 < \cdots < \bar{x}_n - 1 < x_n \) such that \( aT(-\bar{x}_k)/(\bar{x}_k) = b \) for \( 1 \leq k \leq n - 1 \). If we set

\[ \hat{Q}_k = \frac{b(1 + \bar{x}_k/a)}{aT'(-x_k) + bx_k} \]

and note the \( T' \) is positive when defined, we have that the partial fraction
decomposition of \( S(\lambda) / \lambda \) is given by

\[
\sum_{k=1}^{n-1} \frac{\tilde{Q}_k \lambda}{\lambda + \bar{x}_k},
\]

and the proof is complete.

Case 2: \( x_1 > 0 \). Here we may write \( T \) as \( p/q \), where \( p \) and \( q \) are polynomials in \( \lambda \) of degree \( n \). Then \( S(\lambda) / \lambda \) may be written as \( (bq - p)/(ap - b\lambda q) \) when \( (\lambda - a) \) is a factor in both the numerator and the denominator. There are \( n \) distinct singularities of the equivalent expression \( (b - T)/\lambda(aT/\lambda - b) \) occurring at \(- \bar{x}_k \) for \( 1 \leq k \leq n \) where \( 0 = \bar{x}_1 < x_1 < \bar{x}_2 < \cdots < \bar{x}_n < x_n \). We set

\[
\tilde{Q}_k = \frac{b(1 - \bar{x}_k/a)}{aT'(-x_k) + bx_k} > 0 \quad \text{for} \quad k = 1, \ldots, n
\]

and have that the partial fraction decomposition of \( S(\lambda) / \lambda \) is given by \( \sum_{k=1}^{n} \tilde{Q}_k \lambda / (\lambda + \bar{x}_k) \) to complete the proof.

17. FURTHER PROPERTIES OF THE INCREMENTAL AND DECREMENTAL MAPS

For \( T = b \Re(a, S) \) we have

\[
T(\infty) = b[S(\infty) + 1]
\]  

(17.1)

and

\[
T'(\infty) = b[S'(\infty) - a[S(\infty) + 1]S(\infty)].
\]  

(17.2)

For \( S = \Re(a, T) \) we have

\[
S(\infty) = \frac{T(\infty) - b}{b}
\]  

(17.3)

and

\[
S'(\infty) = \frac{T'(\infty)}{b} + \frac{a[T(\infty) - b]T(\infty)}{b^2}
\]

\[
= \frac{T'(\infty)}{b} + a[S(\infty) + 1]S(\infty).
\]  

(17.4)

These relations follow directly from the definition of \( T(\infty), S(\infty), T'(\infty), \) and \( S'(\infty) \).
18. INCREMENTING AND DECREMENTING DATA

If a retention function $S$ has output $d \in R^2 \times R^k$, then for $T = b^\delta(\lambda_{k+1}, S)$, the increment of $S$ with value $b$ at $\lambda_{k+1}$, we have that $T$ has output $(T(\infty), -T'(\infty), T(\lambda_1), \ldots, T(\lambda_{k+1})) = b(E_k(d), 1) \in R^2 \times \bar{R}^{k+1}$, where

$$E_k(d) \overset{\text{def}}{=} \left(d_q + 1, d_v + \lambda_{k+1} d_q (d_q + 1), \left\langle \begin{bmatrix} \lambda_1 & \lambda_1 \\ \lambda_{k+1} & \lambda_1 \end{bmatrix}; d_1 \right\rangle, \ldots, \left\langle \begin{bmatrix} \lambda_k & \lambda_k \\ \lambda_{k+1} & \lambda_k \end{bmatrix}; d_k \right\rangle \right).$$

This is immediate from the definition of $\delta$.

The map $E_k : R^2 \times R^k \to R^2 \times \bar{R}^k$ has an inverse $E_k^{-1}$ given by

$$E_k^{-1}(e) = \left(e_q - 1, e_v - \lambda_{k+1} e_q (e_q - 1), \left\langle \begin{bmatrix} \lambda_1 & -\lambda_1 \\ -\lambda_{k+1} & \lambda_1 \end{bmatrix}; e_1 \right\rangle, \ldots, \left\langle \begin{bmatrix} \lambda_k & -\lambda_k \\ -\lambda_{k+1} & \lambda_k \end{bmatrix}; e_k \right\rangle \right).$$

Both $E_k$ and $E_k^{-1}$ are everywhere infinitely differentable with nonvanishing Jacobian on $R^2 \times \bar{R}^k$.

Conversely, if $T$ is a retention function of nonzero rank, its output in $R^2 \times \bar{R}^{k+1}$ may be written as $b(e, 1)$ for $e \in R^2 \times R^k$ and $b > 0$, and then for $S = \gamma^\delta(\lambda_{k+1}, T)$, the decrement of $T$ at $\lambda_{k+1}$, we have that $S$ has an output in $R^2 \times \bar{R}^k$ equal to $E_k^{-1}(e)$. This is immediate from the definition of $\gamma$.

Closre examination shows that a lung model $(S, \dot{V}_D)$ has output $d \in R^2 \times \bar{R}^k$ if and only if the incremental lung model $b^\delta(\lambda_{k+1}, (S, \dot{V}_D))$ has output $b(E_k(d), 1)$.

We now define the incremental data map

$$I_k : R^2 \times \bar{R}^k \times (0, \infty) \to R^2 \times \bar{R}^k \times (0, \infty) \subset R^2 \times \bar{R}^{k+1}$$

by

$$I_k(d, b) \overset{\text{def}}{=} b(E_k(d), 1).$$

and the decremental data map

$$D_k : R^2 \times \bar{R}^k \times (0, \infty) \to R^2 \times \bar{R}^k$$
by
\[
D_k(d) \overset{\text{def}}{=} F_k^{-1}\left( \frac{1}{d_{k+1}} (d_q, d_v, \ldots, d_k) \right). \tag{18.4}
\]

19. RANKS OF DATA POINTS; GLOBAL CONSIDERATIONS

The notion of rank is valuable in classifying data points. For \( d \in \mathbb{R}^2 \times \mathbb{R}^k \) we define \( \rho(d) \), the rank of \( d \), as the infimum of \( \rho(T, \hat{V}_D) \) where \((T, \hat{V}_D)\) has output \( d \). Thus, \( \rho(d) = -\infty \) if there is no \( T \) compatible with \( d \).

We set
\[
F^{(k,l)} = \{ d \in \mathbb{R}^2 \times \mathbb{R}^k : \rho(d) = l \}
\]
and
\[
F^k = \bigcup_{0 \leq l \leq \infty} F^{(k,l)},
\]
so that \( F^k \) is the set of feasible \( d \in \mathbb{R}^2 \times \mathbb{R}^k \).

We begin by noting that \( F^0 \) consists of those points \( d = (d_q, d_v) \in \mathbb{R}^2 \) which are feasible. Clearly this is true if and only if \( d_q, d_v \geq 0 \). We see at once that for \( d = (d_q, d_v) \) we have
\[
\rho(d) = \begin{cases} 
0 & \text{if } d_q = 0 \text{ and } d_v = 0, \\
1 & \text{if } d_q = 0, \ d_v > 0 \text{ or if } d_q > 0 \text{ and } d_v = 0, \\
2 & \text{if } d_q, d_v > 0, \\
-\infty & \text{if } d_q < 0 \text{ or } d_v < 0.
\end{cases}
\]

Thus \( F^0 = F^{(0,0)} \cup F^{(0,1)} \cup F^{(0,2)} \). Moreover, if \( d \in F^{(0,2)} \), then there are two lung models of rank 2 compatible with \( d \). One model is \( T(\lambda) = d_q \) with \( \hat{V}_D = d_v \), and the second is \( T(\lambda) = d_q \lambda / (\lambda + d_v / d_q) \) with \( \hat{V}_D = 0 \).

We now show that
\[
F^k = F^{(k,0)} \cup \ldots \cup F^{(k,k+2)}
\]
for \( 0 \leq k \leq m \) and that \( F^{(k,l)} \) can be constructed from \( F^{(k-1,l-1)} \) for \( 1 \leq l \leq k+1 \) by using the incremental data map defined in the previous section. We have the following theorem.

**THEOREM 3**

(i) The set \( F^k \) for \( 0 \leq k \leq m \) is a closed convex cone in \( \mathbb{R}^2 \times \mathbb{R}^k \subset \mathbb{R}^2 \times \mathbb{R}^k \) with interior \( F^{(k,k+2)} \) and with boundary \( F^{(k,0)} \cup \ldots \cup F^{(k,k+1)} \).

(ii) For each \( d \in F^{(k,l)} \) with \( 0 \leq l \leq k+1 \) there is a unique lung model \((T, \hat{V}_D)\) with output \( d \).
(iii) For each \( d \in F^{(k,k+2)} \) there are exactly two lung models with rank \( k + 2 \) which have output \( d \), and any other lung models which have output \( d \) have rank \( > k + 2 \).

(iv) In terms of the Pick matrix \( M(d) \), the interior of \( F^k \) is

\[
\{ d : \text{the lowest eigenvalue of } M(d) \text{ is } > 0 \},
\]

and the boundary of \( F^k \) is

\[
\{ d : \text{the lowest eigenvalue of } M(d) \text{ equals } 0 \}.
\]

20. PROOF OF THEOREM 3

We have seen that the statement is true for \( k = 0 \). Suppose now that the statement is true for \( k - 1 \) where \( 0 < k \leq m \). Let \( d \in F^k \) be the output of \((T, \tilde{V}_D)\). If \( \rho(T) = 0 \), then either \( d = (0,\ldots,0) \in F^{(k,0)} \) or \( d = (0, d_v, 0, \ldots, 0) \in F^{(k,1)} \). In either case there is a unique lung model with output \( d \). If \( \rho(T) > 0 \), then \( d_k > 0 \) and \( D_k(d) \) is defined. By the induction hypothesis \( D_k(d) \) is in one of \( F^{(k-1,0)}, \ldots, F^{(k-1,k)}, F^{(k-1,k+1)} \). If \( D_k(d) \in F^{(k-1,l)} \) for \( 0 \leq l \leq k \), then there is a unique \( S \) compatible with this data point. In this case \( d_k \frac{\partial}{\partial \lambda_k}(\lambda_k, S) \) is necessarily the unique retention function compatible with \( d \), for if \( T \) is a retention function compatible with \( d \), then \( \frac{\partial}{\partial \lambda_k}(\lambda_k, T) \) is compatible with \( D_k(d) \) and therefore is equal to \( S \), but then \( T = d_k \frac{\partial}{\partial \lambda_k}(\lambda_k, S) \) from Section 14, since \( T(\lambda_k) = d_k \).

If \( D_k(d) \in F^{(k-1,k+1)} \), then for each \( S \) compatible with \( d \) we see that \( d_k \frac{\partial}{\partial \lambda_k}(\lambda_k, S) \) is compatible with \( d \) and that the unique lung model with retention function \( S \) and output \( D_k(d) \) has nonzero dead space if and only if the unique lung model with retention function \( d_k \frac{\partial}{\partial \lambda_k}(\lambda_k, S) \) and output \( d \) has nonzero dead space. So \( d \in F^{(k,k+2)} \), and the assertions of (iii) of the theorem follow immediately.

Thus \( F^k = F^{(k,0)} \cup \cdots \cup F^{(k,k+2)} \) as claimed, and the assertions for uniqueness for compatible retention functions hold.

That \( F^k \) considered as a subset of \( R^2 \times R^k \) is a convex one is obvious, since if \( T \) is compatible with \( d \) and \( T' \) is compatible with \( d' \), then \( (1-t)T + tT' \) is compatible with \( (1-t)d + td' \) for \( 0 \leq t \leq 1 \), and since \( tT \) is compatible with \( td \) if \( T \) is compatible with \( d \) for \( t \geq 0 \).

The above proof shows that

\[ F^{(k,l)} = I_{k-1}(F^{(k-1,l-1)} \times (0,\infty)) \]

for \( l = 1, \ldots, k + 2 \). We now show that \( F^k \) is closed.

Let \( \{d^p\}_{p=1}^{\infty} \) be a convergent sequence in \( F^k \), and let \( d = \lim_{p \to \infty} d^p \). If \( d_k > 0 \), then without loss of generality we may assume \( d_x^p > 0 \) for \( 1 \leq p \), and we then have that \( D_k(d^p) \to D_k(d) \). But \( F^{k-1} \) is closed by the induction hypothesis, and so \( D_k(d) \in F^{k-1} \), and thus \( d = d_k(E_{k-1}(D_k(d)), 1) \) is in \( F^k \).
Otherwise we have \( d_k = 0 \). Since necessarily \( d_i^p \leq \cdots \leq d_k^p \), this implies \( d_i = \cdots = d_k = 0 \). For any retention function \( T(\lambda) = \Sigma Q_i \lambda / (\lambda + x_i) \) compatible with \( d^p \), we have \( \Sigma Q_i x_i \leq d_p^p \). Now

\[
\Sigma Q_i = \Sigma_{x_i < 1/\sqrt{d_k^p}} Q_i + \Sigma_{x_i > 1/\sqrt{d_k^p}} Q_i.
\]

However,

\[
\Sigma_{x_i > 1/\sqrt{d_k^p}} Q_i = \Sigma_{x_i > 1/\sqrt{d_k^p}} \frac{Q_i x_i}{x_i} \leq d_p^p \sqrt{d_k^p},
\]

while

\[
\Sigma_{x_i < 1/\sqrt{d_k^p}} Q_i = \Sigma_{x_i < 1/\sqrt{d_k^p}} \frac{Q_i (\lambda_k + x_i)}{(\lambda_k + x_i)} \leq \frac{\lambda_k + \frac{1}{\sqrt{d_k^p}}}{\lambda_k} \sum \frac{Q_i \lambda_k}{\lambda_k + x_i} = \frac{\lambda_k + \frac{1}{\sqrt{d_k^p}}}{\lambda_k} d_k^p,
\]

so

\[
\Sigma Q_i \leq \left( d_p^p + \frac{1}{\lambda_k^p} \right) \sqrt{d_k^p} + d_k^p.
\]

Consequently if \( d_p^p \) remains bounded while \( d_k^p \to 0 \), we have that \( d_q^p \to 0 \). Thus \( d \in F^k \). In either case we see that \( F^k \) is closed.

Finally, if \( d \in F^{(k,k+2)} \), a neighborhood of \( d \) contained in \( F^{(k,k+2)} \) is easily constructed using the \( I_{k-1} \) data map. If \( d \in F^{(k,l)} \) for \( 2 \leq l \leq k+1 \), then points not in \( F^k \) which are arbitrarily close to \( d \) are again easily constructed using \( I_{k-1} \). For \( d \in F^{(k,0)} \) or \( F^{(k,1)} \), clearly points not in \( F^k \) are arbitrarily close to \( d \), and so statement (i) of the theorem holds.

To prove (iv) one simply uses the result presented in Section 6. If \( M(d) > 0 \), then any small change \( d_{\epsilon} \) of \( d \) produces a matrix \( M(d_{\epsilon}) > 0 \); that is, \( M(d) > 0 \) implies \( d \in \text{interior } F^k \). If the lowest eigenvalue of \( M(d) \) equals 0, then since \( d \) enters the formula for \( M(d) \) linearly, there is a small perturbation \( d_{\epsilon} \) of \( d \) which makes the lowest eigenvalue of \( M(d_{\epsilon}) \) negative.
Thus a \( d \) producing an \( M(d) \) whose lowest eigenvalue is 0 lies on the boundary of \( F^k \). Since by Section 6 \( d \) lies in \( F^k \) if and only if the lowest eigenvalue of \( M(d) \) is \(\geq 0 \), we have proved (iv).

We now give a development with proofs of the main results stated earlier.

21. PROOF OF CORRECTNESS FOR THE RECURSIVE PROCEDURE TO DETERMINE FEASIBILITY

All the statements given in Section 5 are obvious except those in case ii. In case ii with \( d_k^k > 0 \) we see that \( d_k^{-1} \) as defined is just \( D_k(d_k) \), the decrement of \( d_k \), and thus \( d_k \) is feasible if and only if \( d_k^{-1} \) is feasible, as claimed.

22. THE PICK MATRIX

Data point feasibility can be reformulated in terms of the positive semidefiniteness (see [10]) of a certain matrix, the Pick matrix associated with the data point. This is developed here.

For a retention function

\[
T(\lambda) = \sum_{j=1}^{n} \frac{\hat{Q}_j}{\lambda + x_j}
\]

let

\[
f(z) \overset{\text{def}}{=} zT\left(1/z^2\right) = \sum_{j=1}^{n} \frac{z\hat{Q}_j}{1 + z^2x_j}.
\]  

(22.1)

Observe that if \( x_j = 0 \), then

\[
z\hat{Q}_j = z\hat{Q}_j
\]

while for \( x_j > 0 \) we have

\[
\frac{z\hat{Q}_j}{1 + z^2x_j} = \frac{\hat{Q}_j}{2\sqrt{x_j}} \left( \frac{1}{\sqrt{x_j}z - i} + \frac{1}{\sqrt{x_j}z + i} \right),
\]

where \( i \) is the imaginary unit satisfying \( i^2 = -1 \). Thus each term in the sum (22.1) maps the right half of the complex plane into itself, and since \( f \) is a sum of such terms, so does \( f \).
Observe also that if $0 = x_1 < \cdots < x_n$, then $f(z)$ has singularities at $\infty$ and at $\pm \sqrt{x_j}i$ for $2 \leq j \leq n$, while if $0 < x_1 < \cdots < x_2$, then $f(z)$ has singularities at $\pm 2\sqrt{x_j}$ for $1 < j < n$, so that the number of singularities of $f$ is equal to the rank of $T$. We have in addition that

$$f(0) = 0,$$
$$f'(0) = \sum \hat{Q}_j = \hat{Q}_T,$$
$$f''(0) = 0,$$
$$f'''(0) = -6 \sum \hat{Q}_j x_j,$$

where we must have $\sum \hat{Q}_j x_j \leq \hat{V}_T$.

Now suppose that we have a data point

$$d = (d_q, d_v, d_1, \ldots, d_k) \in \mathbb{R}^2 \times \mathbb{R}^k.$$

Following the transformation $f(z) = z T(1/z^2)$, we set $z_j = 1/\sqrt{x_j}$ and $d'_j = z_j d_j$ for $1 \leq j \leq k$, and set

$$d' = (d_q, d_v, d'_1, \ldots, d'_k).$$

We now have the following theorem.

**THEOREM 4**

The point $d \in \mathbb{R}^2 \times \mathbb{R}^k$ is a feasible data point if and only if the matrix

$$M(d) = \begin{bmatrix}
  d_q & 0 & d'_1 & \cdots & d'_k \\
  0 & d_v & d'_1 & \cdots & d'_k \\
  d'_1 & d_q & d'_1 & \cdots & d'_k \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  d'_k & d_q & d'_k & \cdots & d'_k \\
  z_1 & z_1 & z_1^2 & \cdots & z_1^k \\
  z_1 & z_1 & z_1^2 & \cdots & z_1^k \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  z_k & z_k & z_k^2 & \cdots & z_k^k \\
  z_k & z_k & z_k^2 & \cdots & z_k^k
\end{bmatrix}$$

is positive semidefinite. The definition agrees with that of Section 6 because of the definition of $d'_j$ for $1 \leq j \leq k$.

There are two possible proofs. One is an appeal to the literature. What is known for this general type of interpolation problem is: If $M(d') > 0$, then
there is a function compatible with \( d \). If \( d \) is feasible then \( M(d) \geq 0 \). Here 
\( > 0 \) means strictly positive definite, and \( \geq 0 \) means positive semidefinite.
(See [5], [4].) Actually our interpolation problem has special structure which allows us to conclude Theorem 4. To see this recall from Theorem 3 that \( F^k \)
is closed, and observe that

1. \( \{ d : M(d) \geq 0 \} \) is closed,
2. \( F^k \cap \{ d : M(d) \geq 0 \} \) is dense in \( \{ d : M(d) \geq 0 \} \).

These are easily proved facts about matrices. Now (1) and (2) together imply 
\( F^k = \{ d : M(d) \geq 0 \} \), which is Theorem 4. The loophole in this argument is 
that to a particular interpolation problem one can assign many equivalent Pick matrices. The form one finds in articles may well be different than the
one listed here.

The other proof uses the methods derived here directly. It is in the spirit of 
some classical proofs, but one won’t find this particular case worked out in 
detail in classical approaches such as [5]. The proof is by induction on \( k \). For
\( k = 0 \) the theorem asserts that \( d = (d_q, d_s) \) is feasible if and only \( d_q, d_s \geq 0 \).
This is obviously true. Also if \( d_q = d_1 = \cdots = d_k = 0 \) the theorem is true. As
a special case note that if \( T(\lambda) \) is a nonzero retention function, then \( T(\lambda)/\lambda \)
is strictly decreasing in \( \lambda > 0 \). Thus \( \lambda_r > \lambda_s \) implies that \( T(\lambda_r)/\lambda_r < 
T(\lambda_s)/\lambda_s \), and thus if \( d'_r z_r = d'_s z_s \neq 0 \), there is no retention function \( T(\lambda) \)
such that \( d'_j = z_j T(1/z_j^2) \) for \( j = r, s \). At the same time, if \( d'_j z_r = d'_j z_s = \alpha \),
then

\[
\frac{d'_j}{z_j} = \frac{\alpha}{z_j^2} \quad \text{for } j = r, s \quad \text{and} \quad \frac{d'_r + d'_s}{z_r + z_s} = \frac{\alpha}{z_r z_s},
\]

so that

\[
M' \quad \text{def} \quad \begin{bmatrix}
\frac{d_q}{z + 2} & \frac{t}{z^2} & \frac{\alpha}{z^2_s} \\
\frac{t}{z + 2} & \frac{\alpha}{z^2_r} & \frac{\alpha}{z_r z_s} \\
\frac{\alpha}{z^2_s} & \frac{\alpha}{z_r z_s} & \frac{\alpha}{z^2_s}
\end{bmatrix}
\]
is a principal submatrix of \( M \). Now if

\[
v(t) \quad \text{def} \quad (t, z_r, -z_s)^T \quad \text{and} \quad h(t) \quad \text{def} \quad v(t)^T M' v(t),
\]

it can be confirmed that \( h(0) = 0 \) and \( h'(0) = 2(1/z, -1/z_s) \neq 0 \), so that
\( h(t) < 0 \) for some \( t \). But then \( M' \) and \( M \) are not positive semidefinite. Thus in the above cases the theorem is true.

Suppose now that neither \( d_q' = d_1' = \cdots = d_s' = 0 \) or \( d'_z z_r = d'_z z_s \), for any \( 1 \leq r, s \leq k \), and that the theorem is true for \( k - 1 \). Let \( d' = D(\lambda_k, d) \), and let \( N \) be the Pick matrix of \( d' \). Clearly \( d' \) is feasible if and only if \( d \) is feasible, but it can be verified by direct computation that

\[
\begin{bmatrix}
N \\
\vdots \\
0 \\
0 \\
f_k \\
z_k
\end{bmatrix}
= C^T B^T A^T M A B C,
\]

where

\[
A = I - \begin{bmatrix}
0 \\
\vdots \\
0 \\
z_k \\
d_k' \\
\end{bmatrix}
\begin{bmatrix}
d_q, 0, d_1', \ldots, d_k'-1, 0 \\
0, z_1 \\
0, z_k \\
\end{bmatrix}
\begin{bmatrix}
d_k' \\
0 \\
\end{bmatrix}
\]

and

\[
B = I - \begin{bmatrix}
1 \\
0 \\
0 \\
0
\end{bmatrix}
\begin{bmatrix}
d_q \\
0 \\
\end{bmatrix}
\begin{bmatrix}
d_k' - \frac{d_k}{z_k} \\
0, \ldots, 0 \\
\end{bmatrix}
\]

and since \( A, B, \) and \( C \) are nonsingular and \( d'_k/z_k > 0 \), we have that \( M \) is positive semidefinite if and only if \( N \) is positive semidefinite, as desired. This completes the proof. Note that it also follows from the inductive proof that \( M(d) \) is positive definite if and only if \( d \in F(k, k+2) \) and that the rank of \( d \in R^2 \times R^k \) is equal to the matrix rank of \( M(d) \).

23. EXTREME RETENTION: PROOF OF RESULTS

We can now recognize that the procedure of Section 7 for finding the extreme values of retention compatible with a given \( d^k \) can be rephrased:
Apply the decremental data map repeatedly to produce \( d^k, d^{k-1}, \ldots \) until either there is a \( d^l \) with \( d_q^l = 0 \), or \( d^0 \) with \( d_q^0 > 0 \) is obtained. If \( d^k \) is in the boundary of \( F^k \), there is a unique retention function compatible with \( d^k \) which is constructed by repeated use of the incremental map as given in the procedure. If \( d^k \) is in the interior of \( F^k \), then \( d^0 \) is in the interior of \( F^0 \), and we begin by defining \( T^{(0,0)}(\lambda) \) and \( T^{(1,0)}(\lambda) \) as before and proceed, using the incremental map, to define \( T^{(l+1,j)}(\lambda_{l+1}, T^{(l,j)}(\lambda)) \) for \( j = 0, 1 \).

That \( T^{(k,0)}(\lambda) \) and \( T^{(k,1)}(\lambda) \) have the desired properties follows at once from the following theorem.

**Theorem 5**

The maximum (minimum) value of a retention function \( T(\lambda) \) compatible with \( d^l \) is \( T^{(l+1,j)}(\lambda_{l+1}, T^{(l,j)}(\lambda)) \), where \( j = 1 \) (0) if there are an even (odd) number of values from the set \( \{ \lambda_1, \ldots, \lambda_l \} \) greater than \( \lambda > 0 \).

**Proof.** The proof is by induction on \( l \). The statement holds for \( l = 0 \) since for a retention function

\[
\frac{\lambda}{\lambda + \frac{d_q}{d_q}} \leq \frac{\sum_{i=1}^{n} \lambda_i x_i}{\lambda + \frac{\sum_{i=1}^{n} \lambda_i}{d_q}} \leq \sum_{i=1}^{n} Q_i
\]

provided \( \sum_{i=1}^{n} \hat{Q}_i x_i \leq d_q \) and \( \sum_{i=1}^{n} \hat{Q}_i = d_q \). Here we have used the fact that as a function of \( x \) the expression \( f(x) \equiv \lambda/(\lambda = x) \) has a positive second deviation for \( x \geq 0 \) and thus by Jensen’s inequality [12] satisfies

\[
f \sum_{i=1}^{n} \frac{\hat{Q}_i}{d_q} x_i \leq \sum_{i=1}^{n} \frac{\hat{Q}_i}{d_q} f(x_i).
\]

Suppose now that the statement holds for \( 0 \leq l \leq k \). Note that for \( \lambda \geq a \) the value of \( \hat{f}(a, S)(\lambda) \) is monotone nondecreasing as a function of the value of \( S(\lambda) \), while for \( 0 \leq \lambda \leq a \) it is monotone nonincreasing. Thus, to obtain a maximum (minimum) of \( T(\lambda) \) where \( T(\lambda) \) is compatible with the \( (l+1) \)st data set and \( \lambda \geq \lambda_{l+1} \), we substitute the maximum (minimum) of \( S(\lambda) \) in the right hand side of (3) for \( S \) compatible with the \( l \)th data set, where \( a, b \) are set equal to \( \lambda_{l+1}, d^l_{l+1} \). To obtain a maximum (minimum) when \( \lambda \leq \lambda_{l+1} \), we substitute in the reverse order the minimum (maximum) \( S(\lambda) \) for such an \( S \). The choice of \( j \) given in the proposition is exactly the result of these substitutions.

24. MAXIMUM PERFUSIONS: PROOF

Given a feasible \( d^k \in R^2 \times R^k \) and given \( x \geq 0 \), we are to find the maximum perfusion at \( x \) in a retention function compatible with \( d^k \).
If $d^k \notin F^{(k,k+2)}$, there is a unique compatible retention function as stated.

Suppose that $d \in F^{(k,k+2)}$. If $T(\lambda)$ is compatible with $d$, and $T$ has perfusion $\geq y$ at $x$, then $T(\lambda) - \frac{\lambda y}{(\lambda + x)}$ is a retention function compatible with $d - yd^x$, where

$$d^x \defeq \left(1, x, \frac{\lambda_1}{\lambda_1 + x}, \frac{\lambda_2}{\lambda_2 + x}, \ldots, \frac{\lambda_k}{\lambda_k + x}\right)^T.$$ 

Thus $d - yd^x$ is feasible. Conversely, if $d - yd^x$ is feasible, a retention function with perfusion $\geq y$ compatible with $d$ is easily constructed. The maximum perfusion at $x$ in a retention function compatible with $d$ is thus

$$\max\{ y \geq 0 : d - yd^x \in F^{k}\}$$

which is

$$\max\{ y \geq 0 : M(d - yd^x) \text{ is positive semidefinite} \}.$$ 

Now $M(d - yd^x) = M(d) - yM(d^x)$, and it can be verified that $M(d^x) = u^x(u^x)^T + w^x(w^x)^T$, where

$$u^x \defeq \left(1, 0, \frac{1}{xz_1^2 + 1}, \ldots, \frac{1}{xz_k^2 + 1}\right)^T$$

and

$$w^x \defeq \sqrt{x} \left(0, 1, \frac{z_1}{xz_1^2 + 1}, \ldots, \frac{z_k}{xz_k^2 + 1}\right)^T.$$ 

Since $M(d)$ is positive definite, there is an $L$ such that $M(d) = LL^T$. Moreover, $M(d - yd^x)$ is positive semidefinite if and only if $L^{-1}M(d - yd^x)(L^T)^{-1}$ is.

The last term is equal to

$$I - y \left[ (L^{-1}u^x)(L^{-1}u^x)^T + (L^{-1}w^x)(L^{-1}w^x)^T \right],$$

where $I$ is the identity matrix.

The desired maximum is thus the reciprocal of the largest eigenvalue of the matrix $u'u'^T + w'w'^T$, where

$$u' \defeq L^{-1}u \quad \text{and} \quad w' \defeq L^{-1}w.$$ 

By examining the action of this symmetric matrix on vectors of the form
for \( a, b \) real, we see that the nonzero eigenvalues of this matrix are eigenvalues of the 2 by 2 matrix

\[
\begin{bmatrix}
    u^T u' & u^T w' \\
    w^T u' & w^T w'
\end{bmatrix}.
\]

We note that \( u^T u' = u^T (L^T)^{-1} L^{-1} u^x = u^T M^{-1} u^x \), with a similar result for the other entries of the matrix. As stated before, we set \( a \overset{\text{def}}{=} u^T M^{-1} u^x \),

\[
b \overset{\text{def}}{=} w^T M^{-1} w^x,
\]

and \( c \overset{\text{def}}{=} w^T M^{-1} u^x \), and seek the largest eigenvalue of

\[
\begin{bmatrix}
a & c \\
c & b
\end{bmatrix}.
\]

This is the value given in the procedure. It is a root \( \mu \) of

\[
(a - \mu)(b - \mu) - c^2 = 0
\]

or

\[
\mu^2 - (a + b) \mu + (ab - c^2) = 0,
\]

so

\[
\mu = \frac{a + b + \sqrt{(a - b)^2 + 4c^2}}{2},
\]

so that

\[
q = \frac{2}{u^T M^{-1} u^x + w^T M^{-1} w^x + \sqrt{(u^T M^{-1} u^x - w^T M^{-1} w^x)^2 + 4(w^T M^{-1} u^x)^2}}
\]

gives the desired maximum perfusion at \( x \).

25. INTERPOLATION THEORY: NUMERICS AND EXTENSIONS

Our key mathematical tool has been an adaptation of the highly developed subject of interpolation theory to the particular circumstance at hand. Section 3 of [13] is a survey of modern interpolation theory, so we will not undertake a full description of the literature here. We shall however mention recent numerical work. J. Evans has successfully introduced several of the algorithms described herein into numerical simulations of retention-solubility
phenomena in the lungs. A numerical solution of a problem *mathematically equivalent* to the inverse problem for a given $d \in R^2 \times R^k$ has been developed by A. C. Allison and Nicholas Young [3]. They use the Pick matrix to test feasibility as in Section 6 and then use an eigenvalue of the Pick matrix to construct a "retention type" function. The numerics of another *mathematically equivalent* problem has been studied Trefethen [15]. Warning: though the problems are mathematically equivalent, a practitioner would find a great gulf between these algorithms and exactly what one needs for a retention-solubility study.

We note that there is an algorithm based on the Pick matrix for computing the upper and lower bounds on retention values which we obtained in Section 7 by other means. We have not worked it out in detail; however, general theory assures one that such an algorithm exists.

In conclusion, one feature of this article which is mathematically new and of interest is the fact that the set $F^k$ of feasible $d$ in $R^2 \times R^k$ is closed, or equivalently that $M(d) \geq 0$ is necessary and sufficient for $d$ to be feasible. Also, we have never seen the results of Section 7 for the class of functions here. Analogous bounds were obtained before for a larger class of functions, but restricting to the class of retention functions changes the problems significantly.

REFERENCES