FUNDAMENTAL CONCEPTS AND METHODS
FOR SYSTEMS MODELING:
A Mathematical Foundation for the Description of
Physical, Chemical, and Biological Processes

Outline of Lecture Unit 5
APPLICATIONS OF LINEAR OPERATOR METHODS
TO FINITE DIMENSIONAL CHEMICAL/BIOCHEMICAL SYSTEMS

prepared by
Panos G. Georgopoulos
Computational Chemodynamics Laboratory
Department of Environmental and Community Medicine, UMDNJ-RWJMS
Departments of Chemical and Biochemical Engineering and Environmental Sciences, Rutgers

EOHSI, the Environmental and Occupational Health Sciences Institute
a joint institute of UMDNJ-R.W. Johnson Medical School and Rutgers, The State University of NJ
170 Frelinghuysen Road, Piscatway, NJ 08854
APPLICATIONS OF LINEAR OPERATOR METHODS TO FINITE DIMENSIONAL CHEMICAL/BIOCHEMICAL SYSTEMS: Closed Linear Reversible Systems

1 INTRODUCTION

1.1 Motivation for Study

Spectral properties and spectral representations (i.e. expressions in terms of eigenvalues and eigenvectors) of linear operators are useful in a wide variety of applications, including this lecture unit’s focus on continuous-time dynamic process systems that are:

- finite-dimensional (i.e. lumped),
- linear (or pseudolinear),
- kinetic (or pseudokinetic),
- closed (homogeneous),
- time invariant.

Linear operator methods allow elucidation and understanding of system dynamics (and linear vector space methods offer a geometric analog and visualization for systems of few dimensions), so that:

- the mathematical representation of the system assumes its simplest and most “physical” forms,
- individual “modes” of the system are revealed,
- constraints and bounds in the behavior of the system are identified,
- asymptotic behavior is revealed,
- methods for optimal design of experiments for system analysis are determined,
- methods for “rational” parameter estimation are determined.
1.2 Recall the Following Concepts and Facts from the Spectral Properties of Linear Operators

- A self-adjoint ("hermitian") operator has real eigenvalues.
- The eigenvalues $\lambda_i$ of a self-adjoint operator $A$ can be calculated from its eigenvectors $v_i$, each as the inner product of the corresponding eigenvector with the transformation of this eigenvector by the operator: $\lambda_i = (Av_i \cdot v_i)$.
- The eigenvectors $v_i$ of a self-adjoint operator $A$ corresponding to distinct eigenvalues $\lambda_i$ are orthogonal.

2 A "MODEL PROBLEM": DYNAMICS OF LINEAR KINETIC SYSTEMS

2.1 Problem Definition

Consider the general $n$-component process system

$$A_i \overset{k_{ij}}{\leftrightarrow} A_j, \quad i, j = 1, 2, \ldots, n, \quad i \neq j$$

where $A_i$ are appropriate "extensive" entities such as chemical species (or compartments or phases or . . .), each associated with a state variable $x_i$ (coordinate in the $n$-dimensional linear vector state space $V$), the dynamics of which are governed by the coupled linear (or pseudolinear) "kinetic" (or pseudokinetic) set of ordinary differential equations:

$$\frac{dx_i}{dt} = k_{i,1}x_1 + k_{i,2}x_2 + \ldots + k_{i,i-1}x_{i-1} - \sum_{j=1, i}^{n} k_{j,i}x_i + k_{i,i+1}x_{i+1} + \ldots + k_{i,n}x_n, \quad i = 1, 2, \ldots, n$$

Notice (and pay attention to) the following two conventions in the notation:

- $k_{i,j} = k_{j,i}$, $k_{j,i} = k_{i,j}$
- $\sum_{j=1, i}^{n}$ denotes summation over all values of $j$ from 1 to $n$ with the exception of $j = i$

2.2 Objectives

- understand qualitatively the system in its general form,
- determine/design appropriate experiments for quantifying the system,
- devise strategies for parameter estimation.

2.3 Linear Vector Space Formulation of the Problem and Spectral Properties

In vector/tensor notation one has

$$\frac{dx}{dt} = Kx$$
where

\[
K = \begin{bmatrix}
-n \sum_{j=2}^{n} k_{j,1} & k_{1,2} & k_{1,3} & \ldots & k_{1,n} \\
-k_{2,1} & -n \sum_{j=1}^{n} k_{j,2} & k_{2,3} & \ldots & k_{2,n} \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
k_{n,1} & k_{n,2} & k_{n,3} & \ldots & -n \sum_{j=1}^{n} k_{j,n}
\end{bmatrix}
\]

or

\[
K = [k_1 \ k_2 \ k_3 \ldots k_n]
\]

with the rate constant vectors \( k_j \) defined by

\[
k_j = [k_{1,j}, k_{2,j}, \ldots, k_{n,j}], \quad k_{j,j} \equiv -n \sum_{i=1 \{j\}}^{n} k_{i,j}
\]

\( K \) is a nonsymmetric singular matrix (\( k_j \)'s are not linearly independent). Assuming a unique equilibrium solution for the system, \( \mathbf{x} = \mathbf{a} \) one has

\[
K\mathbf{a} = 0
\]

and \( \dim(K) = n - 1 \). Let \( x_i \) be a normalized intensive state variable, i.e., a mole fraction in the case of kinetic systems. Then

\[
\sum_{j=1}^{n} x_j = 1
\]

and at equilibrium (principle of detailed balancing or microscopic reversibility)

\[
k_{j,i} a_i = k_{i,j} a_j \Rightarrow \frac{1}{a_j} k_{j,i} = \frac{1}{a_i} k_{i,j}
\]

To Simplify your View of the System Define the Space in an Appropriate Manner: Let us define the following inner product on \( \mathcal{V} \):

\[
(\mathbf{x} \cdot \mathbf{y}) \equiv \sum_{i=1}^{n} \frac{1}{a_i} x_i y_i
\]

with corresponding norm

\[
\| \mathbf{x} \| = \sqrt{\sum_{i=1}^{n} \frac{1}{a_i} x_i^2}
\]

Then, the operator \( K \) represented by the matrix \( K \)

\[
\mathbf{y} = K\mathbf{x} : \quad y_i = \sum_{j=1}^{n} k_{i,j} x_j
\]

is self-adjoint:

\[
(K\mathbf{x} \cdot \mathbf{y}) = (\mathbf{x} \cdot K\mathbf{y}) \quad \forall \mathbf{x}, \mathbf{y} \in \{\mathcal{V}, (\circ \circ)\}
\]
2.3.1 Spectral Properties of the Transformation

Since $K$ is self-adjoint, it has $n$ real eigenvalues one of which is $\lambda_0 = 0$, and it is not repeated since $\text{rank}(K) = n - 1$, and orthogonal eigenvectors. Let us assume that the nonzero eigenvalues $\lambda_1, \lambda_2, \ldots, \lambda_{n-1}$ are not repeated. Then all the eigenspaces

$$\mathcal{N}_j \equiv \mathcal{N}(K - \lambda_j I), \quad j = 1, 2, \ldots, n - 1$$

of $K$, as well as its null space

$$\mathcal{N}_0 \equiv \mathcal{N}(K)$$

are orthogonal subspaces of $\mathcal{V}$ with dimension 1. For an arbitrary “batch experiment” he equilibrium mole fraction $a$ is the eigenvector $v_0$ corresponding to the eigenvalue $\lambda_0 = 0$. The eigenvectors $v_0, v_1, v_2, \ldots, v_{n-1}$ of $K$ can be normalized to form an orthonormal basis for $\mathcal{V}$; every $x \in \mathcal{V}$ can then be expressed as

$$x = \sum_{i=0}^{n-1} (x \cdot v_i) v_i$$

**Sign of the Eigenvalues**  A most important property of the operator $K$ is that it is *nonpositive*; i.e. all its nonzero eigenvalues $\lambda_1, \lambda_2, \ldots, \lambda_{n-1}$ are negative. Indeed, for self-adjoint operators (such as $K$) one has

$$\lambda_i = (Kv_i \cdot v_i)$$

However, for any $x \in \mathcal{V}$, one can show that

$$(Kx \cdot x) \leq 0$$

Indeed,

$$(Kx \cdot x) = \sum_{i=1}^{n} \frac{1}{a_i} x_i \sum_{i=1}^{n} k_{i,j} x_j$$

$$= \sum_{i \neq j} \sum_{i} \frac{k_{i,j} x_i x_j}{a_i} - \sum_{i \neq j} \sum_{i} \frac{k_{j,i} x_i^2}{a_i}$$

$$= \sum_{i \neq j} \left[ \sqrt{\frac{k_{j,i}}{a_i}} x_i \sqrt{\frac{k_{i,j}}{a_j}} x_j - \left( \sqrt{\frac{k_{j,i}}{a_i}} x_i \right)^2 \right]$$

Similarly

$$(Kx \cdot x) = \sum_{i \neq j} \left[ \sqrt{\frac{k_{i,j}}{a_j}} x_j \sqrt{\frac{k_{i,j}}{a_i}} x_i - \left( \sqrt{\frac{k_{i,j}}{a_j}} x_j \right)^2 \right]$$

and therefore

$$Kx \cdot x = -\frac{1}{2} \sum_{i \neq j} \left( \sqrt{\frac{k_{i,j}}{a_j}} x_j - \sqrt{\frac{k_{i,j}}{a_i}} x_i \right)^2 \leq 0$$

The following ordering of the eigenvalues is assumed (convention): $0 > \lambda_1 > \lambda_2 > \ldots > \lambda_{n-1}$. 
2.3.2 Rates in Terms of Spectral Properties

K, representing a linear operator on \( V \), can be transformed to be expressed in the \( \{ v_i \} \) basis; so, the rate constant vectors can be expressed in terms of the eigenvectors as

\[
  k_j = \sum_{i=0}^{n-1} (k_j \cdot v_i) v_i
\]

(Notice that the rank of \( K \) is less than the dimension \( n \) of the space \( V \) on which it operates and therefore \( k_j \)'s are not linearly independent.) Using the definition of the inner product and the principle of microscopic reversibility one has

\[
  (k_j \cdot v_i) = \sum_{l=1}^{n} \frac{1}{a_l} k_{l,j} v_{l,i} = \frac{1}{a_j} \sum_{l=1}^{n} k_{j,l} v_{l,i}
\]

The second subscript denotes the eigenvector; the first the component of the eigenvector:

\[
  v_i = [v_{1,i}, v_{2,i}, \ldots, v_{n,i}]
\]

Using

\[
  Kv_i = \lambda_i v_i
\]

one has

\[
  (k_j \cdot v_i) = \frac{1}{a_j} \lambda_i v_{j,i} \Rightarrow k_j = \frac{1}{a_j} \sum_{i=1}^{n-1} \lambda_i v_{j,i} v_{i} \Rightarrow k_{m,j} = \frac{1}{a_j} \sum_{l=1}^{n} \lambda_l v_{j,i} v_{m,i}
\]

2.3.3 Reaction Subspaces

Consider the subspaces

\[
  H = \{ x = a + z; z \in \mathcal{N}(K)^\perp \}
\]

\[
  H_j = \{ x = a + z; z \in \mathcal{N}_j \}
\]

\[
  H^+ = \{ x = a + z; z \in \mathcal{N}(K)^\perp, \ x_i \geq 0, i = 1, 2, \ldots, n \}
\]

\[
  H_j^+ = \{ x = a + z; z \in \mathcal{N}_j, \ x_i \geq 0, i = 1, 2, \ldots, n \}
\]

Clearly \( H_j \subset H, H_j^+ \subset H^+ \), and all mole fraction vectors lie in \( H^+ \).

2.3.4 Reaction Paths and their Properties

A (batch) reaction path in \( V \) is a parametrically defined curve \( x = x(t) \equiv x(t; x_0) \), where \( x(t) \) is the solution of

\[
  \frac{dx}{dt} = Kx, \ x(0) = x_0 \in H^+
\]

Every batch reaction path lies entirely in \( H^+ \) (obvious).\(^1\)

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\(^1\)The term reaction path is used in a general sense since we may consider a general closed (pseudo)linear (pseudo)kinetic process system; in essence it is the state trajectory of the system.
**For Special Initial Conditions there are Straight-Line Reaction Paths:**

If

\[ x_0 \in \mathcal{H}_j^+ \Rightarrow x(t) \in \mathcal{H}_j^+ \ \forall t \]

that is, \( x(t) \) is in this case a straight-line reaction path. Indeed, for \( x_0 = a + \alpha v_j \) the inner product of the governing vector differential equation with \( v_k \) gives

\[
\frac{d}{dt}(x \cdot v_k) = (Kx \cdot v_k) = \lambda_k (x \cdot v_k)
\]

the solution of which is

\[
(x \cdot v_k) = (x_0 \cdot v_k) e^{\lambda_k t} = (a + \alpha v_j \cdot v_k) e^{\lambda_k t} = \alpha e^{\lambda_j t} \delta_{jk}
\]

Since \( x = a + z; z \in N(K) \) it follows that

\[
(x \cdot v_k) = (z \cdot v_k) = \alpha e^{\lambda_j t} \delta_{jk}
\]

because this is true for all \( x \), therefore for \( x = z \). So

\[
z = \alpha e^{\lambda_j t} v_j \Rightarrow x = a + \alpha e^{\lambda_j t} v_j \Rightarrow x(t) \in \mathcal{H}_j^+ \ \forall t
\]

- **Significance:** If, somehow, one can obtain an initial composition \( x_0 \in \mathcal{H}_j^+ \) the reaction path will be a straight line

\[
\frac{x_i(t) - a_i}{\alpha z_i, j} = e^{\lambda_j t}
\]

(independent of \( i \)) and a plot of \( \ln(x_i - a_i) \) versus \( t \) will produce a straight line with the eigenvalue \( \lambda_j \) as the slope.

**All Reaction Paths Lead to Equilibrium:** In a closed linear system every reaction path leads to equilibrium. Indeed,

\[
\frac{d}{dt}(x \cdot a) = (Kx \cdot a) = (x \cdot Ka) = 0
\]

and therefore

\[
(x \cdot a) = (x_0 \cdot a) = \sum_{i=1}^{n} \frac{1}{a_i} x_i a_i = \sum_{i=1}^{n} x_i = 1
\]

Also

\[
(x \cdot v_j) = (x_0 \cdot v_j) \exp(\lambda_j t)
\]

So, since \( \{a, v_1, v_2, \ldots, v_{n-1}\} \) are an orthonormal basis for \( V \), it follows that

\[
x(t) = a + \sum_{j=1}^{n-1} (x_0 \cdot v_j) e^{\lambda_j t} v_j \Rightarrow \lim_{t \to \infty} x(t) = a
\]

because \( \lambda_j < 0, \ j = 1, 2, \ldots, n - 1. \)
All Reaction Paths are Asymptotically Straight Close to Equilibrium: Let us define a hyperplane that represents a translation of the algebraic sum of some (or all) the eigenspaces of \( K \):

\[
\mathcal{H}(j) = \{ x = a + z; z \in \mathcal{N}_j + \mathcal{N}_{j+1} + \ldots + \mathcal{N}_{n-1} \}
\]

and \( \mathcal{H}^+_j \) for \( x_i \geq 0 \). Clearly, \( \mathcal{H} = \mathcal{H}(1) \) and \( \mathcal{H}^+ = \mathcal{H}^+_1 \).

Also, let \( P_j \) be the orthogonal projection operator from \((\mathcal{on}\) \( V \) to \( \mathcal{N}_j \). Then \( x(t; a + P_j x_0) \) is called the projection of the reaction path \( x(t; x_0) \) on \( \mathcal{H}_j \). Clearly, such projections of reaction paths are also reaction paths. Let \( x(t; x_0) \) be a reaction path with \( x_0 \in \mathcal{H}^+_1 \). Since

\[
x(t; a + P_j x_0) = a + (P_j x_0 \cdot v_j) e^{\lambda_j t} v_j = (x_0 \cdot v_j) e^{\lambda_j t} v_j
\]

(since the other component of \( x_0 \) is orthogonal to \( v_j \)). Therefore,

\[
x(t; x_0) - x(t; a + P_j x_0) = \sum_{k=j+1}^{n-1} (x_0 \cdot v_k) e^{\lambda_k t} v_k
\]

\[
\Rightarrow e^{-\lambda_j t} [x(t; x_0) - x(t; a + P_j x_0)] = \sum_{k=j+1}^{n-1} (x_0 \cdot v_k) e^{(\lambda_k - \lambda_j) t} v_k
\]

Then, since \( (\lambda_k - \lambda_j) < 0, k = j + 1, j + 2, \ldots, n, \)

\[
\lim_{t \to \infty} \| x(t; x_0) - x(t; a + P_j x_0) \| = 0
\]

Clearly, \( x(t; a + P_j x_0) \) is a straight-line reaction path, therefore all reaction paths are asymptotically straight. In other words, the reaction path \( x(t; x_0) \) starting in \( \mathcal{H}^+_j \), asymptotically approaches its projection on a hyperplane (eigenspace \( \mathcal{H}_j \)) which corresponds to the maximum of the eigenvalues represented in \( \mathcal{H}^+_j \). The straight-line region of \( x(t; x_0) \) with \( x_0 \in \mathcal{H}^+_1 \) will depend on the relative magnitude ("spread") of the eigenvalues \( \lambda_j, \ldots, \lambda_{n-1} \). A larger value of \( (\lambda_j - \lambda_{j+1}) \) will produce a more pronounced straight-line region. The straight line portion is approximated by

\[
x(t) \simeq a + (x_0 \cdot v_j) e^{\lambda_j t} v_j
\]

\[
\Rightarrow \frac{x_i - a_i}{x_k - a_k} \simeq \frac{v_{i,j}}{v_{k,j}} \equiv b_{(i,k)j}
\]

So, a plot of \( x_i \) versus \( x_k \) will yield a straight line of slope \( b_{(i,k)j} \) for each \( i \).

2.4 Experimental Determination of the Eigenvectors

\( z_0 \) is \( a \), the mole fraction at equilibrium; its determination is straightforward. The other eigenvectors can be calculated from the asymptotic straight-line portions of the reaction paths through

\[
\frac{v_{i,j}}{v_{k,j}} \simeq b_{(i,k)j} \frac{x_i - a_i}{x_k - a_k}
\]

The \( j \)-th eigenvector \( v_j \) is estimated as

\[
v_j = \frac{1}{\| b_{(k)j} \|} b_{(k)j}
\]
where
\[ b_{(k)j} = [b_{(1,k)j}, b_{(2,k)j}, \ldots, b_{(n,k)j}] \]

The actual design of experiments for characterization of complex linear and pseudolinear chemical kinetic systems uses extensively the notions covered in this outline but is beyond the scope of the present lecture unit.  

3 EXTENSIONS OF THE MODEL PROBLEM

These include

- irreversible linear systems,
- pseudolinear systems,
- various systems of stage-wise and compartmental operations.

4 PROBLEMS FOR THE MATERIAL OF LECTURE UNIT 5

A problem set covering material of this lecture (as well as material from lecture units 3 and 4) is given with this outline.

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