ANALYSIS BY MIGRATION IN THE PRESENCE OF CHEMICAL REACTION

Norman Shapiro

June 1962
ANALYSIS BY MIGRATION IN THE PRESENCE OF

CHEMICAL REACTION

Norman Shapiro*

The RAND Corporation, Santa Monica, California

INTRODUCTION

In many quantitative analytical techniques (such as electrophoresis, ultracentrifugation, countercurrent distribution, column or paper chromatography, various distillation techniques etc.) a mixture of several species of molecules is analyzed by subjecting it to conditions under which the several species migrate at different rates. In situations where chemical reactions may occur among the several species and where the extents of the reactions are non-negligible these techniques fail in the sense that the usual methods for numerically determining

*Any views expressed in this paper are those of the author. They should not be interpreted as reflecting the views of The RAND Corporation or the official opinion or policy of any of its governmental or private research sponsors. Papers are reproduced by The RAND Corporation as a courtesy to members of its staff.
the quantities of the various species are not applicable. In such situations the analytical system is ordinarily modified so that no non-negligible reactions occur. However, in some cases a modification of this kind may be either impossible or inconvenient. This paper will present a mathematical framework which under certain circumstances will allow a quantitative analysis, even in the presence of non-negligible chemical reactions amongst the species. This framework will be applicable under the following circumstances:

1) The non-negligible chemical reactions which can occur are known.

2) The reactions which can occur to a non-negligible extent are all sufficiently rapid relative to the rates at which the migratory processes occur, that they may be considered to be instantaneous equilibrium reactions. For this purpose, a one way reaction which is so rapid that it always instantaneously exhausts the supply of at least one of its reactants, may be considered a special case of an equilibrium reaction.

3) A moderately powerful digital computer is available.

The methods described here may well be applicable to systems other than those of analytical chemistry. For example, they may well apply to the analysis of certain systems, in vivo. However, they were developed with chemical analysis in mind.
The material presented here has been given elsewhere, in a more general form, and with a more mathematical orientation [1].

The Mathematical Framework

Consider $N$ species, $A_1, \ldots, A_i, \ldots, A_N$, of molecules, in solution (either gaseous or liquid) and subject to any number of migratory effects and to chemical reaction. The following assumptions will be made:

**Assumption 1:** The processes take place in a long "tube" such that the concentration of each $A_i$ is constant in every cross section of the tube perpendicular to the tubes longitudinal axis. That is, the concentration of $A_i$ is a function, $c_i(x,t)$, of only the longitudinal coordinate, $x$, along the tube, and time, $t$, where $-\infty < x < \infty$ and $0 \leq t < \infty$.

The cross sectional area of the tube will be allowed to depend on both $x$ and $t$. Let $Q(x,t)$ be the area of the cross section of the tube at $x$, at time, $t$.

Assumption 1 embodies a description of the geometry in which the processes are to occur. Actually the methods presented here, are applicable to a much wider class of situations than is indicated by assumption 1 (with rather trivial modifications in the development). For example,
instead of a single dimension, \( x \), in which the processes take place, I could, as easily, have chosen several (as would be necessary for certain kinds of paper chromatography) or instead of allowing \( x \) to take continuous values, I could have restricted \( x \) to discrete values, (as would be necessary for counter-current distribution). In [1] a more general geometry is used.

**Assumption 2:** All the chemical reactions amongst the \( A_i \) are either infinitely fast or infinitely slow, relative to the migratory processes. That is, the chemical reactions to which the \( A_i \) are subject, fall into two distinct classes:

a) Those whose reaction rates are so large (relative to the migratory rates) that they may be considered to attain equilibrium instantaneously. It will also be assumed that these reactions obey the mass action law. These reactions will be called "fast" reactions.

b) Those whose reaction rates are so small, relative to the migratory rates, that their effects may be neglected.

Assumption 2, unlike assumption 1, is crucial to the developments of this paper. If it is not valid, the methods of this paper will not directly apply.

**Assumption 3:** The laws under which the various migratory effects take place can be expressed in terms of:
To state assumption 3 more precisely, let $S_1(x,t)$ be the time rate of the number of molecules of $A_1$ which cross $x$ (in the positive direction) at time $t$, as a result of the totality of migratory effects. (In the literature, the quantity analogous to my $S$ is written as $\frac{\partial S}{\partial t}$, presumably because $S$ is a rate.)

Then, the assumption is, that for appropriate functions $s_i$:

\( s_1(x,t) = s_1(x,t,c_1(x,t),\ldots,c_N(x,t),\frac{\partial c_1(x,t)}{\partial x},\ldots,\frac{\partial c_N(x,t)}{\partial x}) \)

I believe that this assumption is general enough to embrace almost any situation of interest. (Of course, if assumption 1, is modified, then a corresponding modification of assumption 3 will be necessary. The crucial fact about assumption 3 is that it does not allow $S_1(x,t)$ to depend on time derivatives of the $c_i$'s). For example, if the migration is due to a combination of diffusion and translation it allows the coefficients of diffusion mobility for any of the $c_i$ to depend on all of the other $c_i$'s and their spatial derivatives. It allows the force
field causing the translation to vary with position and
time.

Consider a reaction to which the $A_i$ are subject.
Associate with this reaction an $N$ dimensional vector,
r = $(r_1, \ldots, r_N)$ such that the reaction may be written:

$$ (2) \sum_{i} r_i A_i = \sum_{i} (-r_i) A_i $$

$r_i > 0$ \hspace{1cm} $r_i < 0$

(those unfamiliar with vector analysis should regard a vector as, simply an ordered sequence of numbers).

That is, if $A_i$ does not occur in the reaction, let

$r_i = 0$, if $A_i$ appears on the left side of the reaction
equation, let $r_i$ be the coefficient of $A_i$, if $A_i$ appears
on the right hand side of the reaction equation, then

let $r_i$ be the negative of the coefficient of $A_i$. Note,
that given the vector associated with a reaction we can
immediately form the equation governing that reaction.

Note also, that if a vector $r$ is associated with a re-
action, then the vector $-r$ is associated with the re-
action obtained by reversing the left and right hand
sides of (2).

I will call a vector, $r$; a reaction vector if it is
associated with a "fast" reaction.

Note that, for any reaction vector, $r$, we have the
mass balance equation:

\[
\prod_{1}^{n} c_i(x,t) r_i^n = k_r
\]

Where \( k_r \) is the mass balance constant of the reaction with which \( r \) is associated.

Let \( R \) be the set of all reaction vectors.

Theorem 1: \( R \) is a linear subspace of the set of all \( n \) dimensional vectors (that is if \( r \) and \( r^* \) are members of \( R \), then so is \( r + r^* \); and if \( r \) is a member of \( R \) then so is \( br \), for any scalar \( b \)).

Proof: Let \( r \) be associated with the fast reaction \( \rho \) and \( r^* \) with the fast reaction \( \rho^* \). Then, the reaction whose equation is obtained by adding the equations for \( \rho \) and \( \rho^* \) will be a fast reaction and will be associated with \( r + r^* \). Similarly the reaction obtained by multiplying both sides of the reaction equation for \( \rho \) by \( b \) will be a fast reaction and will be associated with \( br \). Q.E.D.

Theorem 2: Consider a small volume \( dV \), such that the concentration of each of the \( A_i \) may be considered spatially constant within \( dV \). Suppose that concentrations \( c_1, \ldots, c_N \) (not necessarily in equilibrium ratios) of the \( A_i \) are suddenly placed in \( dV \) and that all the fast reactions instantaneously occur producing equilibrium concentrations
\[ c_1 + \Delta c_1, \ldots, c_N + \Delta c_N. \]

Let \( f \) be a vector which is perpendicular to every reaction vector, (two vectors are perpendicular if their dot or scalar product is zero).

Then:

\[ (4) \sum_i f_i \cdot \Delta c_i = 0 \]

**Proof:** For any reaction vector, \( r \), let \( \Delta r, i \) denote the change in \( c_i \) due to the fast reaction associated with \( r \).

We have:

\[ (5) \Delta r, i = e_r r_i, \] where \( e_r \) is a measure of the extent to which the reaction occurred in reaching equilibrium.

Hence:

\[ (5) \sum_i f_i \Delta r, i = \sum_i f_i e_r r_i = e_r \sum_i f_i r_i = 0 \]

Since each \( \Delta c_i \) is the sum over all reaction vectors, \( r \), of the \( \Delta r, i \), equation (4) can be obtained by adding equation (5) for all reaction vectors.

**Theorem 3:** Let \( f \) be a vector which is perpendicular to every reaction vector. Then, the following partial differential equation holds:

\[ (6) \sum_i f_i \frac{\partial}{\partial x} \left( c_i(x,t) Q(x,t) \right) = -\sum_i f_i \frac{\partial S_i(x,t)}{\partial x} \]

**Proof:** Let \( dV \) be the volume between \( x \) and \( x + dx \). Note, that the volume of \( dV \) is \( dxQ(x,t) \). The net number of molecules of \( A_i \) which migrate into \( dV \) between \( t \) and
Imagine that at time \( t \) the concentrations within \( dV \) are at equilibrium, and that during the interval between \( t \) and \( t + dt \) migrations are allowed to occur but that no chemical reactions occur until \( t + dt \), when equilibrium is instantaneously reattained. The number of molecules of \( A_i \) in \( dV \) at time \( t + dt \) just before instantaneous reactions occur is then:

\[
c_i(x, t) Q(x, t) \, dx - \frac{\partial S_i(x, t)}{\partial x} \, dx \, dt
\]

and the concentrations \( c_i \) are:

\[
(7) \quad c_i = \frac{c_i(x, t) Q(x, t) \, dx - \frac{\partial S_i(x, t)}{\partial x} \, dx \, dt}{Q(x, t + dt) \, dx}
\]

After the reaction takes place, the concentration \( c_i + \Delta c_i \) may be expressed in the form:

\[
(8) \quad c_i + \Delta c_i = c_i(x, t) + \frac{\partial c_i(x, t)}{\partial t} \, dt
\]

subtracting (7) from (8)

\[
\Delta c_i = \frac{c_i(x, t)}{Q(x, t + dt)} (Q(x, t + dt) - Q(x, t)) \frac{\partial S_i(x, t)}{\partial x} \, dt + \frac{\partial c_i(x, t)}{\partial t} \, dt
\]

or (ignoring higher order terms)

\[
(9) \quad \frac{\Delta c_i}{\partial t} Q(x, t) = \frac{\partial}{\partial x} \left( c_i(x, t) Q(x, t) \right) + \frac{\partial S_i(x, t)}{\partial x}
\]

Now apply Theorem 3 to the \( \Delta c_i \), multiply (6) of
Theorem (3) by $\frac{Q(x,t)}{dt}$ and then use (9) to arrive at (6).

Q.E.D.

Returning to the mass balance equation, (3), which holds for every reaction vector, $r$, note that we can write down an infinite number of equations of this form, since there are an infinite number of possible reaction vectors. (For example, if $r$ is a reaction vector then, by Theorem 1, so is $br$, for all scalars, $b$). However, it turns out that all of these equations are not independent. In fact:

**Theorem 4:** Let $r$, and $r^*$ be reaction vectors, then the mass balance equation for the reaction associated with $r + r^*$ is obtained by multiplying corresponding sides of the mass balance equations for the reactions associated with $r$ and $r^*$.

In particular:

$$k_r r^* = k_{r^*} r$$

(10)

Furthermore the mass balance equation for the reaction associated with $br$ is obtainable by taking the $b$'th power of both sides of the mass balance equation of the reaction associated with $r$.

In particular:

$$k_{br} = (k_r)^b$$

(11)

**Proof:** Theorem 4 follows from the way in which vectors
are added and multiplied by scalars, and from the form of equation (3).

Let \( \text{dim } R \) be the dimension of \( R \) (the dimension of a linear sub-space is the maximum number of linear independent vectors in the space). Then by Theorem 4, there are exactly \( \text{dim } R \) independent mass balance equations relating the concentrations \( c_i(x,t) \).

Similarly, Theorem 3 seems to indicate that there are an infinite number of partial differential equations of the form, (6), relating the \( c_i(x,t) \), since there are an infinite number of vectors perpendicular to every reaction vector. However, any linear relation between \( f' \)'s, will reflect itself as a linear relation amongst the equations of the form (6) induced by those \( f' \)'s. Let \( R_1 \) denote the set of all vectors, \( f \), which are perpendicular to every reaction vector. We know from vector analysis that \( R_1 \) is also a linear subspace. Let \( \text{dim } R_1 \) be the dimension of \( R_1 \). There are thus only \( \text{dim } R_1 \) independent partial differential equations of the form, (6). It is a theorem from vector analysis that:

\[
(12) \quad \text{dim } R + \text{dim } R_1 = N
\]

We thus have a total of \( N \) independent simultaneous relations amongst the \( c_i(x,t) \). - \( \text{dim } R \) independent mass
balance equations of the form, (3), and dim R₁ independent partial differential equations, (6).

The dim R equations (3) can be used to express dim R of the \( c_i(x,t)'s \) in terms of the remaining \( (N - \dim R = \dim R_1) \), \( c_i(x,t)'s \). Note that, in general there is no guarantee that we can eliminate any particular dim R of the \( c_i(x,t)'s \): we only know that we can eliminate some set of \( (\dim R) \) of the \( c_i(x,t)'s \). For example if \( N = 4 \), \( \dim R = 2 \) and the mass balance equations are: (omitting for convenience the arguments \( x,t \))

\[
\begin{align*}
c_1^{-1} c_2^{-1} c_3^2 c_4 &= k \\
c_1^{-1} c_2^{-1} c_3 c_4^2 &= k^*
\end{align*}
\]

Then the mass balance equations can not be used to eliminate \( c_1 \) and \( c_2 \) (that is to solve for \( c_1 \) and \( c_2 \) in terms of \( c_3 \) and \( c_4 \)). Although they can be used to eliminate any other pair of the \( c's \).

It can also be shown that the question of which \( \dim R \) of the \( c_i(x,t)'s \) can be eliminated does not depend on which of the \( \dim R \) independent mass balance equations are chosen.

I can assume (if necessary by rearranging the order of the \( c_i(x,t)'s \)) that the last \( \dim R \) of the \( c_i(x,t) \) can be eliminated. That is, that \( c_{\dim R_1 + 1}(x,t), \ldots, c_N(x,t) \)
can be expressed in terms of $c_1(x,t), \ldots, c_{\dim R}(x,t)$. The last $R$ of the $c_i(x,t)$ can then be eliminated from the $R$ independent simultaneous partial differential equations, of the form (6).

I have thus far shown that the process involved can, in effect, be expressed in terms of $R$ independent simultaneous partial differential equations in the quantities $c_1(x,t), \ldots, c_{\dim R}(x,t)$. With this system of partial differential equations we could address ourselves to various problems.

For example:

**Problem 1:** Given the functions $Q(x,t)$ and $s_i$ (see equation (1) in assumption (3) and given the initial concentrations $c_1(x,0), \ldots, c_{\dim R}(x,0)$; to determine the $c_i(x,t)$, that is, to solve the system of partial differential equations with the $c_i(x,0)$ as boundary values.

**Problem 2:** Given the functions $Q(x,t)$ and $s_i$ and certain information about the $c_i(x,t)$ to determine the $c_i(x,0)$. That is, to solve the system of partial differential equations given more complex boundary values. This is, in fact, the problem which occurs in quantitative analysis.

**Problem 3:** Given $Q(x,t)$ and certain information about the $c_i(x,t)$'s to determine the functions $s_i$, that is, to determine the laws under which the migration occurs.
The most straightforward of these problems is problem 1.

All three problems are of practical importance, various numerical techniques are available for all 3 problems. In this exposition, only problem 1 will be considered. The numerical techniques used in problem 1 will be applicable to more complex problems. In our exposition we shall barely indicate one possible numerical attack.

Solution to problem:

Let \( P = \dim R_L \)

Let \( f^{(1)}, \ldots, f^{(j)}, \ldots, f^{(p)} \), be a set of \( P \) independent members of \( R_L \). Then, the system of \( P \) partial differential equations takes the form: (see (6))

\[
(13) \sum_i f_i^{(j)} \frac{\partial c_i(x,t)}{\partial t} (c_i(x,t) q(x,t)) = \\
- \sum_i f_i^{(j)} \frac{\partial^2 s_i(x,t)}{\partial x^2} \text{ for } 1 \leq j \leq P
\]

If we carry out the differentiation on the left of (13), we obtain:

\[
(14) \sum_i f_i^{(j)} \frac{\partial c_i(x,t)}{\partial t} = - \frac{\partial q(x,t)}{\partial x} \sum_i f_i^{(j)} c_i(x,t) \\
- \frac{1}{q(x,t)} \sum_i f_i^{(j)} \frac{\partial s_i(x,t)}{\partial x} \text{ for } 1 \leq j \leq P
\]
We also have, as a result of solving the mass balance equations for the first \( P \) of the \( c_i(x,t) \)'s:

\[
(15) \quad c_i(x,t) = \beta_1 \left( c_1(x,t), \ldots, c_P(x,t) \right) \quad \text{for} \quad P + 1 \leq i \leq N
\]

By the partial differentiation of the equations (14)

we can express

\[
\frac{\partial c_1(x,t)}{\partial t} \quad \text{for} \quad P + 1 \leq i \leq N \quad \text{in terms of} \quad c_1(x,t) \quad \text{and} \quad \frac{\partial c_1(x,t)}{\partial t} \quad \text{for} \quad 1 \leq i \leq P.
\]

If this is done, note that the result is linear in the

\[
\frac{\partial c_i(x,t)}{\partial t}, \quad 1 \leq i \leq P.
\]

If we then use (1) to express the \( S_i(x,t) \) in terms of \( x,t \), the \( c_i(x,t) \) and \( \frac{\partial c_i(x,t)}{\partial x} \) carry out the indicated differentiation of the \( S_i(x,t) \) (in practice this indicated differentiation would, perhaps, only be done numerically - but, the exposition is simplified if it is assumed that the indicated differentiation is actually carried out)

and eliminate:

\[
c_i(x,t), \quad \frac{\partial c_1(x,t)}{\partial x}, \quad \frac{\partial^2 c_i(x,t)}{\partial x^2} \quad \text{for} \quad P + 1 \leq i \leq N,
\]

the system (14) becomes:

\[
(16) \quad \sum_{i=1}^{P} \alpha_{j,i} \frac{\partial c_i(x,t)}{\partial t} = \beta_j \quad \text{for} \quad 1 \leq j \leq P
\]

where the \( \alpha_{j,i} \) for \( 1 \leq i, \; j \leq P \) are known functions of the \( c_i(x,t) \),
and for a fixed time $t$, $C''$ and $C'''$ can be computed by numerically determining all the elements in the system, \( \sum_{i=1}^{P} \gamma_{j,i}(C) \frac{\partial c_i(x,t)}{\partial t} = \beta_j(C',C'',C''') \) for $1 \leq j \leq P$

where $C$ denotes $c_1(x,t),\ldots,c_P(x,t)$, 

$C'$ denotes $\frac{\partial c_1(x,t)}{\partial x},\ldots,\frac{\partial c_P(x,t)}{\partial x}$ and 

$C''$ denotes $\frac{\partial^2 c_1(x,t)}{\partial x^2},\ldots,\frac{\partial^2 c_P(x,t)}{\partial x^2}$;

and where the $\gamma_{j,i}$ and $\beta_j$ are known functions.

The basic computational procedure to be used in the numerical solution of (16) involves extending the knowledge of the $c_i(x,t_0)$ for a fixed $t_0$, to a knowledge of the $c_i(x,t_0+\Delta t), c_i(x,2\Delta t), c_i(x,3\Delta t),\ldots$ etc. $\Delta t$ chosen small enough so that the $c_i(x,t)$ for $t$ a multiple of $\Delta t$ will adequately describe the $c_i(x,t)$.

Thus, assume that the $c_i(x,t_0)$ are known for all $x$ and for a fixed $t_0$. The $C$, $C'$ and $C''$ can be computed by numerical differentiation with respect to $x$, and $\gamma_{j,i}(C)$ and $\beta_j(C',C'',C''')$ can be numerically evaluated, thus, numerically determining all the elements in the system, (16), except the $\frac{\partial c_i(x,t)}{\partial t}$. But (16) is now a system of linear algebraic equations in the unknown $\frac{\partial c_i(x,t_0)}{\partial t}$ which can be numerically solved by standard methods.
We then have:
\[ c_i(x, t_0 + \Delta t) = c_i(x, t_0) + \Delta t \frac{\partial c_i(x, t_0)}{\partial t} \]

The above computational process, even in the simplest situations, is such that it could only be undertaken by means of a high speed digital computer.

The process that has been described is also somewhat simpler than one which will actually be employed. The exposition has been designed only to indicate the basic ideas involved.
REFERENCES