

CHROM. 8010

THEORY OF ISOTACHOPHORESIS

DEVELOPMENT OF CONCENTRATION BOUNDARIES

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(Received July 24th, 1974)

SUMMARY

Three-dimensional partial differential equations describing the migration of ions through a stationary medium under the influence of an electric field are developed and then applied to the analysis of steady-state and unsteady-state properties of isotachophoresis in one dimension. The shape of the front region between two ion species in the steady state is discussed, and the time development of the system from an arbitrary initial distribution of ions to the steady state is analyzed and illustrated by a numerical example.

INTRODUCTION

Isotachophoresis^{1,2} is a type of electrophoresis wherein different ion species of the same sign become spatially separated from one another under the influence of an electric field as they migrate parallel to the field. The boundaries (fronts) between the different ion species all move with the same velocity. The ions of higher mobility move ahead of those with lower mobility. A common counter-ion species migrating in the opposite direction maintains charge neutrality.

In this paper we present a theoretical analysis of the process of isotachophoresis. Partial differential equations describing the migration of ions through a stationary medium under the influence of an electric field are developed and then applied to the analysis of steady-state and unsteady-state properties of isotachophoresis in one dimension. The original equations are three dimensional, contain terms describing ion diffusion, and also allow the possibility of arbitrary temperature and mobility distributions. It is shown that charge imbalance can be neglected to an excellent approximation, and that the electric field is determined in terms of the ion distributions by an equation similar to Poisson's equation. The solution of this equation is trivial for one-dimensional systems. Analysis of a one-dimensional system with constant temperature and mobilities shows that the transition region between the two ion species in the steady state has a finite thickness (typically 10^{-3} cm) determined by the effect of diffusion. The exact shape of the transition region is discussed. The steady state

with an arbitrary number of ions present can be determined completely by solving one ordinary first-order differential equation. The unsteady state is analyzed using a model in which the diffusion constants approach zero. The approach to the steady state from an arbitrary initial state is particularly simple if only a leader ion and a terminator ion are present. This is described using the method of characteristics. The non-linear partial differential equation being solved is not by itself sufficient to determine the evolution of the system after the shock front (boundary between leader and terminator) becomes sharp, but must be supplemented by the relation between the instantaneous speed of the front and the discontinuity in ion density. A computer-generated numerical example is presented which shows the time development of such an isotachophoretic system from an arbitrary initial state, the formation of the shock front and the eventual approach to the steady-state configuration.

FUNDAMENTAL EQUATIONS OF ISOTACHOPHORESIS*

Suppose that several species of ions are present in an isotachophoresis apparatus, where they migrate through a tube under the influence of an applied electric field \mathbf{E} . We restrict our treatment here to the case where the ions are contained in a *stationary* medium. Let the j th species of ion have charge q_j , charge density ρ_j , mass m_j and velocity \mathbf{v}_j . The dynamical equation describing the balance of forces acting on this ion species is of the usual hydrodynamic type:

$$(m_j \rho_j / q_j)(d\mathbf{v}_j / dt) = \mathbf{F}_j - \nabla P_j \quad (1)$$

where $m_j \rho_j / q_j$ is the mass density of this ion species, $d\mathbf{v}_j / dt$ is the acceleration (material derivative of the velocity field) (t is the time), \mathbf{F}_j is the force per unit volume, and P_j is the ion pressure. In practical situations ions adjust their velocity very rapidly to adapt to changes in the applied force, so that the effect of ion inertia is negligible. Therefore, we take

$$\mathbf{F}_j - \nabla P_j = 0 \quad (2)$$

Two kinds of force acting on individual ions contribute to \mathbf{F}_j . One of these is the electric force $q_j \mathbf{E}$. The other is the viscous force $-\eta_j \mathbf{v}_j$, which opposes motion of the ion through the medium. This force is proportional to the velocity. The coefficient of proportionality η_j in general depends on the temperature T , but is otherwise constant if the density of ions is low. To get \mathbf{F}_j we multiply the force per ion, $q_j \mathbf{E} - \eta_j \mathbf{v}_j$, by the number of ions per unit volume ρ_j / q_j . Thus

$$\mathbf{F}_j = \rho_j (\mathbf{E} - \mathbf{v}_j / \mu_j) \quad (3)$$

where $\mu_j = q_j / \eta_j$ defines the ionic mobility. Note that for a given ion species ρ_j and μ_j are either both positive or both negative. Since we are assuming that the density of ions is low, the ion pressure is given adequately by the ideal-gas law

$$P_j = (\rho_j / q_j) kT \quad (4)$$

where k is Boltzmann's constant.

* Boldface symbols represent vector terms only. The same symbols not in boldface represent the analyses of systems with one-dimensional geometry.

Inserting eqns. 3 and 4 into eqn. 2, we obtain

$$\rho_j(\mathbf{E} - \mathbf{v}_j/\mu_j) - \nabla[(kT/q_j)\rho_j] = 0 \quad (5)$$

Thus, the current density of the j th ion species \mathbf{J}_j is given by

$$\mathbf{J}_j = \rho_j \mathbf{v}_j = \mu_j \rho_j \mathbf{E} - \mu_j \nabla[(kT/q_j)\rho_j] \quad (6)$$

Conservation of the number of ions of the j th species is expressed mathematically by the continuity equation

$$\partial \rho_j / \partial t = -\nabla \cdot \mathbf{J}_j = -\nabla \cdot (\mu_j \rho_j \mathbf{E}) + \nabla \cdot \{ \mu_j \nabla [(kT/q_j)\rho_j] \} \quad (7)$$

Note that, if μ_j and T are independent of position, the last term in eqn. 7 can be written as $D_j \nabla^2 \rho_j$, where D_j , which is a diffusion constant, is given by the Einstein relation

$$D_j = \mu_j kT/q_j \quad (8)$$

To get some idea of the meaning of eqn. 7, suppose for the moment that we can choose μ_j , T and \mathbf{E} all to be constant. (In reality we are not free to choose \mathbf{E} arbitrarily). Then eqn. 7 becomes

$$\partial \rho_j / \partial t = -\mu_j \mathbf{E} \cdot \nabla \rho_j + D_j \nabla^2 \rho_j \quad (9)$$

which is an easily soluble equation. One can show that the time evolution of solutions to eqn. 9 consists of a gradual diffusive spreading of ρ_j imposed on a uniform propagation with velocity $\mu_j \mathbf{E}$. In other words, in a coordinate system moving with velocity $\mu_j \mathbf{E}$, only a diffusive spreading would be observed. This fictitious example illustrates the concepts of ion drift and diffusion. However, the formation of sharp boundaries (shock fronts) between different ion species, which is the principal distinguishing characteristic of isotachophoresis, occurs precisely because \mathbf{E} in reality is not constant, but depends on the charge densities present. Thus, eqn. 7 describes *non-linear* wave propagation. Ordinarily the effect of diffusion is very small, with one important exception. Diffusion gives the shock fronts a finite thickness and determines the properties of the transition regions between different ion species.

In order to show how \mathbf{E} is related to the charge densities, we begin by considering the Maxwell equation

$$\nabla \times \mathbf{H} = \mathbf{J} + \epsilon \partial \mathbf{E} / \partial t \quad (10)$$

where \mathbf{H} is the magnetic field, $\mathbf{J} = \sum_j \mathbf{J}_j$ is the total current density, and ϵ is the dielectric constant of the medium. Using eqn. 6, we can write eqn. 10 in the following form:

$$\partial \mathbf{E} / \partial t + (\sum_j \mu_j \rho_j / \epsilon) \mathbf{E} = (1/\epsilon) \{ \nabla \times \mathbf{H} + \sum_j \mu_j \nabla [(kT/q_j)\rho_j] \} \quad (11)$$

If we pretend for a moment that \mathbf{E} is the only quantity in eqn. 11 which depends on t , then the solution of eqn. 11 is seen to consist of the sum of two terms, a "static" term

$$\mathbf{E} = \{ \nabla \times \mathbf{H} + \sum_j \mu_j \nabla [(kT/q_j)\rho_j] \} / \sum_j \mu_j \rho_j \quad (12)$$

and an exponential decay with a decay rate $\gamma = \Sigma \mu_j \rho_j / \epsilon$. We can estimate the size of γ by using values of mobility and charge density which are typical of isotachopheresis experiments. Assuming a mobility of $5 \times 10^{-4} \text{ cm}^2/\text{V} \cdot \text{sec}$, a charge density of 2 C/cm^3 , and $\epsilon = \epsilon_0 = 8.854 \times 10^{-14} \text{ C/V} \cdot \text{cm}$, we see that γ has the order of magnitude

$$\gamma \approx 10^{10} \text{ sec}^{-1} \quad (13)$$

This is much faster than any rates which occur in isotachopheresis. Even in the vicinity of the shock fronts, field and charge density variations occur at a rate many orders of magnitude slower than γ , as we shall show later. Therefore, the electric field is well able to follow variations in γ and variations in the right-hand side of eqn. 11, and \mathbf{E} is given to an excellent approximation by eqn. 12. Clearly this approximation is equivalent to neglecting the displacement current terms proportional to $\partial \mathbf{E} / \partial t$ in eqns. 10 and 11, so that eqn. 10 now becomes

$$\nabla \times \mathbf{H} = \mathbf{J} \quad (14)$$

Combining eqn. 14 with the law of conservation of charge, we obtain

$$\partial \rho / \partial t = -\nabla \cdot \mathbf{J} = -\nabla \cdot (\nabla \times \mathbf{H}) = 0 \quad (15)$$

so that the net charge density $\rho = \Sigma \rho_j$ is independent of time. In fact, it is entirely consistent with our approximation to set $\rho = 0$. We do so henceforth. Note that this approximation can be regarded as the zeroth order of an expansion of the exact solution in powers of ϵ . In particular, the net charge density is given to first order by Gauss's law ($\rho = \epsilon \nabla \cdot \mathbf{E}$), where \mathbf{E} is the zeroth order solution for the electric field.

Magnetically-induced electric fields (Faraday's law) are negligible in isotachopheresis, so that $\nabla \times \mathbf{E} = 0$, and we can derive \mathbf{E} from a scalar potential:

$$\mathbf{E} = -\nabla \varphi \quad (16)$$

Summing eqn. 7 over j and using eqn. 16 and the condition $\rho = 0$, we obtain

$$\nabla \cdot (\Sigma \mu_j \rho_j \nabla \varphi) = -\nabla \cdot \{ \Sigma \mu_j \nabla [(kT/q_j) \rho_j] \} \quad (17)$$

This is the fundamental equation determining φ at any given time once ρ_j , μ_j and T are specified as functions of position at that time. Eqn. 17 is similar in structure to Poisson's equation. In essentially the same way as for Poisson's equation one can prove that the solution of eqn. 17 is unique, once boundary conditions have been specified. The proof depends only on the fact that the conductivity $\Sigma \mu_j \rho_j > 0$ everywhere. In general, mixed boundary conditions must be used. The potential φ is specified on the electrodes by the externally applied voltage, and the normal component of $\mathbf{E} = -\nabla \varphi$ must be zero on the walls of the vessel. The latter condition may be obtained by multiplying eqn. 6 by q_j / μ_j , summing over j , and using the facts that $\rho = 0$ and that the normal component of each ion current density \mathbf{J}_j is zero on the walls of the vessel. Once eqn. 17 has been solved for \mathbf{E} and the result substituted into eqn. 7, one can in principle integrate eqn. 7 to find the complete solutions for the charge densities

as functions of space and time. These solutions are subject to the boundary conditions that the normal component of $\nabla[(kT/q_j)\rho_j]$ be zero on the walls of the vessel.

As a practical matter eqn. 17 can be solved easily only for the simplest geometries. For the remainder of this paper we consider the very important case of one-dimensional ion migration, where all quantities are assumed to depend only on the x -coordinate and on time. This case therefore describes isotachophoresis inside straight cylindrical tubes. The stability of the one-dimensional solutions with respect to small three-dimensional perturbations is an open theoretical question which is not treated in this paper, but which is under investigation. However, nearly one-dimensional ion migration is observed experimentally under a wide range of conditions, though not under all conditions.

We restrict our treatment to the case where T and μ_j are simply constants. This is often not close to being true experimentally, since Ohmic heating (at a power density $\mathbf{E} \cdot \mathbf{J}$) is occurring in the medium. However, this case is much easier to analyze mathematically. The effects of temperature gradients have been considered by Coxon and Binder³ and previously by Hinckley⁴. The solution of eqn. 17 for one-dimensional ion migration is trivial:

$$E(x,t) = [J(t) + \sum D_j \partial \rho_j / \partial x] / \sum \mu_j \rho_j \quad (18)$$

The current density J may depend on t but not on x . For simplicity we assume henceforth that J is simply a constant, *i.e.*, we are operating the apparatus with a constant-current power supply. Eqn. 18 is the one-dimensional equivalent of eqn. 12. Inserting eqn. 18 into eqn. 7, we obtain

$$\frac{\partial \rho_j}{\partial t} = - \frac{\partial}{\partial x} \left\{ \frac{\mu_j \rho_j}{\sum_k \mu_k \rho_k} \left[J + \sum_l D_l \frac{\partial \rho_l}{\partial x} \right] \right\} + D_j \frac{\partial^2 \rho_j}{\partial x^2} \quad (19)$$

If we multiply eqn. 19 by $1/\mu_j$, sum over j and use the condition $\rho = 0$, we obtain the useful relation

$$\frac{\partial}{\partial t} \sum_j \frac{1}{\mu_j} \rho_j = \frac{\partial^2}{\partial x^2} \sum_j \frac{D_j}{\mu_j} \rho_j \quad (20)$$

At this point we restrict our consideration to the following example of an isotachophoresis system. This example can be generalized in a straightforward manner. Suppose \mathbf{E} and \mathbf{J} point to the right (direction of increasing x coordinate). A single negative counter-ion ρ_0 occupies the whole tube and migrates to the left. A leader ion ρ_1 of high mobility occupies the right end of the tube. ρ_1 is asymptotically constant as $x \rightarrow \infty$. A terminator ion ρ_n of low mobility occupies the left end of the tube. ρ_n is asymptotically constant as $x \rightarrow -\infty$. The middle of the tube contains positive ions $\rho_1, \rho_2, \dots, \rho_n$ which may be mixed together. We suppose that $\mu_1 > \mu_2 > \dots > \mu_n$. By using the condition of charge neutrality we can eliminate the negative ion ρ_0 from the dynamical equations. In particular, eqn. 20 may be written:

$$\frac{\partial}{\partial t} \sum_{j=1}^n \frac{\mu_j - \mu_0}{\mu_j} \rho_j = \frac{\partial^2}{\partial x^2} \sum_{j=1}^n \left(D_0 - \frac{\mu_0 D_j}{\mu_j} \right) \rho_j \quad (21)$$

THE STEADY STATE

As the system just described evolves in time, it approaches a steady-state configuration in which the ion species are separated from each other into zones with ρ_1 leading ρ_2 , ρ_2 leading ρ_3 , etc., and ρ_n following behind. All the positive ions migrate with a constant speed c to the right. The different ion species are separated by rather sharp boundaries, but away from the boundaries the charge densities and the electric field are essentially constant. In this section we analyze the steady-state configuration. In the following section we show for a simple example how a general initial state evolves toward the steady state.

In the steady state we can assume that all dynamical variables are functions only of the variable $\xi = x - ct$. Then, for instance, the equation

$$\partial \rho_j / \partial t = -(\partial / \partial x)(\mu_j E \rho_j) + D_j \partial^2 \rho_j / \partial x^2 \quad (22)$$

becomes

$$-c \rho_j' = -\mu_j (E \rho_j)' + D_j \rho_j'' \quad (23)$$

where ' indicates differentiation with respect to ξ . For $j = 1, \dots, n$ eqn. 23 can be integrated immediately to give

$$(-c + \mu_j E) \rho_j = D_j \rho_j' \quad (24)$$

The integration constant must be 0, since ρ_j does not fill the whole tube. This is not true for ρ_0 . In fact, one can show that

$$(-c + \mu_0 E) \rho_0 = D_0 \rho_0' + J \quad (25)$$

This can be proven by summing eqn. 24 over the positive ions, adding eqn. 25 and comparing the result with eqn. 18. The steady-state equivalent of eqn. 21 can also be integrated immediately to give

$$\sum_{j=1}^n \frac{\mu_j - \mu_0}{\mu_j} \rho_j = \omega - \frac{1}{c} \sum_{j=1}^n \left(D_0 - \frac{\mu_0 D_j}{\mu_j} \right) \rho_j' \quad (26)$$

where ω is an integration constant which can be thought of as an overall measure of ionic concentration.

We can obtain the Kohlrausch relations⁵, which relate the electric field and charge densities in the different constant regions away from the fronts, by using eqns. 24 and 26. In the region containing the j th species of positive ion the field E_j and charge density ρ_j are given by

$$E_j = c / \mu_j \quad (27)$$

and

$$\rho_j = \mu_j \omega / (\mu_j - \mu_0) \quad (28)$$

Furthermore, if we multiply eqn. 27 and eqn. 28, we obtain $E_j = c \omega [(\mu_j - \mu_0) \rho_j]$,

whereas eqn. 18 gives $E_j = J/[(\mu_j - \mu_0)\varrho_j]$. Hence, we see that the wave speed is given by

$$c = J/\omega \quad (29)$$

The relative magnitude of the charge densities everywhere in the tube, including the vicinities of the fronts, can be calculated from eqn. 24. This was first discovered by Konstantinov and Oshurkova⁶ and was discussed by them for the case $n = 2$. If we solve eqn. 24 for E , we obtain

$$E = (c/\mu_j) + (D_j/\mu_j)(\varrho_j'/\varrho_j) \quad \text{for } j = 1, \dots, n \quad (30)$$

Since the right-hand side is directly integrable and the left-hand side is independent of j , one can easily show that all of the charge densities can be expressed in terms of a single function $\sigma(\xi)$ according to

$$\exp [(D_j/\mu_j) \ln \varrho_j] = \{\exp[-c(\xi - \xi_j)/\mu_j]\} \sigma(\xi) \quad (31)$$

where the numbers ξ_j are integration constants. Thus, for any two charge densities ϱ_j and ϱ_k , we have

$$\varrho_j = \{\exp [(D_k\mu_j/D_j\mu_k) \ln \varrho_k]\} \{\exp[-c(\xi - \xi_j)/D_j + c(\xi - \xi_k)\mu_j/\mu_k D_j]\} \quad (32)$$

One can see from eqn. 32 that, if ϱ_j and ϱ_k do overlap, the thickness of the overlap region is of the order $(D_j/c)(\mu_k/|\mu_k - \mu_j|)$. Thus, the thickness of the fronts is of the order of a diffusion constant divided by c , except that it may be appreciably greater if the mobilities of the adjoining ion species are nearly equal. To obtain a numerical estimate of D_j/c , assume that q_j is equal to the absolute value of the electron charge and that $\mu_j = 5 \times 10^{-4} \text{ cm}^2/\text{V}\cdot\text{sec}$. At room temperature $kT/q_j \approx 1/40 \text{ V}$, so that we find from eqn. 8 that $D_j \approx 10^{-5} \text{ cm}^2/\text{sec}$. Assuming that $c = 10^{-2} \text{ cm/sec}$, which is a typical value, the front thickness is of the order $D_j/c \approx 10^{-3} \text{ cm}$. The time required for the front to pass by a given fixed point is $D_j/c^2 \approx 10^{-1} \text{ sec}$. Since this time is much longer than the time $1/\gamma \approx 10^{-10} \text{ sec}$, we have established that the neglect of displacement current and charge imbalance (eqn. 14) is an excellent approximation even in the vicinity of the fronts.

By substituting eqn. 31 into eqn. 26, one obtains a single first-order differential equation for $\sigma(\xi)$:

$$\begin{aligned} & \sum_{j=1}^n \frac{\mu_j - \mu_0}{\mu_j} \{\exp[-c(\xi - \xi_j)/D_j]\} \{\exp[(\mu_j/D_j) \ln \sigma]\} \\ & = \omega - \frac{1}{c} \left[\sum_{j=1}^n \left(D_0 - \frac{\mu_0 D_j}{\mu_j} \right) \{\exp[-c(\xi - \xi_j)/D_j]\} \{\exp[(\mu_j/D_j) \ln \sigma]\} \right] \quad (33) \end{aligned}$$

If all of the positive ions carry the same charge q , then eqn. 33 is a linear differential equation in the variable $\sigma^{q/kT}$. We have succeeded in reducing the analysis of isotachophoresis in the steady state to the solution of eqn. 33. However, this equa-

tion in general cannot be solved except by numerical techniques. For the sake of simplicity we restrict our discussion to an elementary example which illustrates the qualitative features of the general case. Suppose that all the positive ions have the same charge. Also suppose that the counter-ion is fixed in the medium, so that $\mu_0 = 0$ and $D_0 = 0$. Then eqn. 33 has the solution

$$\sigma^{q/kT} = \omega / \sum_{j=1}^n \exp [-c(\xi - \xi_j)/D_j] \quad (34)$$

and the charge densities are given by inserting eqn. 34 into eqn. 31:

$$\rho_j = \omega \cdot \exp [-c(\xi - \xi_j)/D_j] / \sum_{k=1}^n \exp [-c(\xi - \xi_k)/D_k] \quad (35)$$

Clearly in this case $\omega = -\rho_0$. We now show that eqn. 35 describes a situation in which the different ion species are separated from each other in the order of their mobilities. To do this we write eqn. 35 in the form

$$\rho_j = \omega / \sum_{k=1}^n \exp [-c(\xi - \xi_k)/D_k + c(\xi - \xi_j)/D_j] \quad (36)$$

The term in the sum for which $k = j$ is equal to one. All of the other terms are either very big or very small, except in the neighborhoods of the fronts, which we assume for now to be very narrow and omit from the present discussion. In order for the magnitude of ρ_j to be appreciable, none of these other terms can be very big. Thus, ρ_j is essentially equal to ω at position ξ if $(\xi - \xi_k)/D_k$ is minimized when $k = j$. Otherwise ρ_j is essentially equal to zero. The ion species are separated, with one and only one species present at each position. Consider two species ρ_j and ρ_k for which $D_j < D_k$ and suppose that ρ_j is present at position $\xi^{(j)}$ and ρ_k is at position $\xi^{(k)}$. Then

$$(\xi^{(j)} - \xi_j)/D_j < (\xi^{(j)} - \xi_k)/D_k \quad (37)$$

and

$$(\xi^{(k)} - \xi_k)/D_k < (\xi^{(k)} - \xi_j)/D_j$$

From these two inequalities one can easily show that

$$\xi^{(j)} < \xi_{jk} < \xi^{(k)} \quad (38)$$

where

$$\xi_{jk} = \xi_{kj} = (D_j \xi_k - D_k \xi_j)/(D_j - D_k) \quad (39)$$

Thus, the ρ_j of lower mobility is located to the left of the ρ_k of higher mobility. The ions are separated in the order of their mobilities. The position of the boundary between adjacent species ($j = k + 1$) is $\xi_{k, k+1}$. One can invert eqn. 39 to give the constants ξ_j in terms of the positions of the fronts. Since the charge densities are unaf-

ected by transformations of the type $\xi_j \rightarrow \xi_j + \alpha D_j$, we can choose $\xi_1 = 0$ without loss of generality. The other constants ξ_j are then given by

$$\xi_j = \sum_{k=2}^j \frac{D_j}{D_k} \cdot \frac{D_{k-1} - D_k}{D_{k-1}} \cdot \xi_{k-1,k} \quad (40)$$

The situation just described becomes more complicated if some of the ionic mobilities are nearly equal or if c is very small. Then some of the fronts are broad, so that the ion species are not all well-separated from each other. The ionic concentrations vary smoothly as a function of position and are given by eqn. 35.

THE UNSTEADY STATE

We now return to the partial differential equations (eqn. 19) and discuss how an arbitrary initial distribution of ions evolves toward the steady state. We shall suppose that the fronts which form are all very sharp. The diffusion terms in eqn. 19 are very small except in the neighborhoods of the fronts, where the derivatives of the charge densities are large. In this case it is a good approximation to idealize the exact equations by taking the limit in which the diffusion constants approach zero and the fronts become infinitely sharp. Thus, in this limit the charge densities develop discontinuities at the fronts, and it is necessary to relate the instantaneous speed of the fronts to these discontinuities.

In the limit in which diffusion is neglected, eqn. 21 can be integrated to give

$$\sum_{j=1}^n \frac{\mu_j - \mu_0}{\mu_j} \varrho_j = \omega(x) \quad (41)$$

Recall that in the steady state we found the expression on the left side of eqn. 41 to be simply a constant, except in the neighborhoods of the fronts (see eqn. 26). However, we see now that it is more generally a function of position determined by the initial conditions. As a simple illustration of how this situation can arise in practice, suppose that a tube is prepared containing leader and terminator ions initially separated by a thin partition at $x = 0$, but that the concentrations ϱ_1 and ϱ_2 do *not* satisfy the Kohlrausch relation $\varrho_1/\varrho_2 = [\mu_1(\mu_2 - \mu_0)]/[\mu_2(\mu_1 - \mu_0)]$. This means that ω has different values on the two sides of the partition. At $t = 0$ the partition is removed, the current switched on, and the ions migrate to the right. However, the discontinuity in ω remains fixed at $x = 0$. In other words, ϱ_2 is equal to its initial value for $x < 0$, but is given by the Kohlrausch relation for $0 < x < ct$. This is exactly what is observed experimentally. Eventually, however, the discontinuity in ϱ_2 at $x = 0$ becomes smeared out because of diffusion.

For simplicity we henceforth restrict our discussion to the case where ω is constant. This is no real loss of generality, since the case where $\omega(x)$ is an arbitrary positive function of x can always be reduced to the case mathematically equivalent to $\omega = 1$ by writing the dynamical equations in terms of new dependent variables $\hat{\varrho}_j = \varrho_j/\omega(x)$ and a new spatial coordinate $\hat{x} = \int^x \omega(x') dx'$.

In the absence of diffusion eqn. 19 becomes

$$\partial \varrho_j / \partial t = -J(\partial / \partial x) [\mu_j \varrho_j / \sum_{k=1}^n (\mu_k - \mu_0) \varrho_k] \quad (42)$$

We can make a minor simplification in this set of equations by defining new variables

$$s_j = [(\mu_j - \mu_0)/\mu_j]\varrho_j \quad (43)$$

Then eqn. 42 becomes

$$\partial s_j / \partial t = -J(\partial / \partial x) [\mu_j s_j / \sum_{k=1}^n \mu_k s_k] \quad (44)$$

while eqn. 41 becomes

$$\sum_{j=1}^n s_j = \omega \quad (45)$$

Note that all explicit reference to the counter-ion has been removed by this transformation.

Eqn. 44 is an example of a system of quasilinear equations. The theory of equations of this type has been developed in an article by Gel'fand⁷. As a practical matter the solution of eqn. 44 is much simpler if only one dependent variable is involved. On account of eqn. 45, this corresponds to the case $n = 2$. Aside from some remarks in an appendix, we shall confine our discussion to this case. We shall suppose for definiteness that $n = 2$ means that only a leader ion and a terminator ion are present in the tube. However, the same theory applies if other ion species with mobilities greater than or less than those of the two species under consideration are present respectively ahead of or behind ϱ_1 and ϱ_2 and are separated from them by fronts. These fronts necessarily move at the steady-state speed. A region of pure ϱ_2 immediately begins to form ahead of the trailing front and a region of pure ϱ_1 immediately begins to form behind the leading front. This situation has been analyzed for the case of uniform mixtures of ions by Brouwer and Postema⁸.

For the case $n = 2$ we can reduce eqn. 44 to the following equation:

$$\partial \psi / \partial t = (\partial / \partial x)(1/\psi) \quad (46)$$

where

$$\psi = (J\mu_1\mu_2\omega)^{-\frac{1}{2}} (\mu_1 s_1 + \mu_2 s_2) \quad (47)$$

The variable ψ is proportional to the conductivity, which means it is inversely proportional to the electric field:

$$\psi = (J/\mu_1\mu_2\omega)^{\frac{1}{2}}/E \quad (48)$$

Since $s_1(\infty) = \omega$, $s_1(-\infty) = 0$, $s_2(\infty) = 0$, and $s_2(-\infty) = \omega$, we find that at \pm infinity, ψ has the asymptotic values:

$$\psi(\infty) = (\mu_1\omega/\mu_2J)^{\frac{1}{2}}$$

and

$$\psi(-\infty) = (\mu_2\omega/\mu_1J)^{\frac{1}{2}} \quad (49)$$

An alternative form of eqn. 46 which is slightly easier to understand may be obtained by using the variable $u = 1/\psi^2$, so that eqn. 46 becomes

$$\partial u/\partial t + u\partial u/\partial x = 0 \quad (50)$$

The left-hand side of eqn. 50 has the form of a hydrodynamic derivative, and u has the units of velocity. The general solution of the non-linear wave equation (eqn. 50) is

$$u = f(x - ut) \quad (51)$$

where $f(x)$ is the initial value $u(x,0)$ of the function $u(x,t)$. Eqn. 51 has a simple interpretation. It says that if the wave amplitude at a point x_0 is u_0 , then the speed of this part of the wave is also u_0 . Thus, the higher amplitude parts of the wave travel faster than the lower amplitude parts. Since $u(-\infty,0) = J\mu_1/\mu_2\omega$ is greater than $u(\infty,0) = J\mu_2/\mu_1\omega$, the fast part of the wave to the left in time overtakes the slow part of the wave to the right, and a discontinuity or shock front is formed. The time evolution of the solution can be exhibited in detail by using the characteristic curves of eqn. 50. These are straight lines

$$x = x_0 + u_0 t \quad (52)$$

along which the value of u is constant:

$$u_0 = u(x,0) = u(x_0 + u_0 t, t) \quad (53)$$

By using the initial data $u(x,0)$ to determine the characteristics and drawing the characteristics on a graph as illustrated in Fig. 1, the solution $u(x,t)$ at later times can be determined. However, this method by itself is not adequate past the time τ when a front forms, because the characteristics then begin to intersect. After this time the solution becomes discontinuous.

We can calculate τ as follows: Suppose that the characteristics through the points $(x_0,0)$ and $(x_1,0)$ intersect at (x,t) . From eqn. 52, we have

$$-1/t = [u(x_1,0) - u(x_0,0)]/(x_1 - x_0) \quad (54)$$

The right-hand side of eqn. 54 is the slope of the chord joining the points $(x_0, u(x_0,0))$ and $(x_1, u(x_1,0))$. Clearly t is minimized when this slope becomes the most negative, which is when x_0 and x_1 both approach the point where $u(x,0)$ has the steepest slope. Thus,

$$\begin{aligned} 1/\tau &= \max.[-\partial u(x,0)/\partial x] \\ &= (\mu_1\mu_2\omega/J) \max.[-\partial E^2(x,0)/\partial x] \end{aligned} \quad (55)$$

For large t the solution for u or ψ has the form of a step which propagates to the right with velocity $c = J/\omega$:

$$\begin{aligned} \psi(x,t) &= (\mu_2\omega/\mu_1J)^{\frac{1}{2}} \text{ for } x < x_0 + ct \\ \psi(x,t) &= (\mu_1\omega/\mu_2J)^{\frac{1}{2}} \text{ for } x > x_0 + ct \end{aligned} \quad (56)$$

Observe that the front speed is given in terms of the discontinuity in ψ by

$$c = 1/\psi^{(-)}\psi^{(+)} = (u^{(-)}u^{(+)})^{\frac{1}{2}} \quad (57)$$

where, for instance, $\psi^{(-)}$ and $\psi^{(+)}$ are respectively the values of ψ immediately to the left and right of the discontinuity. It is possible to obtain eqn. 57 in a different way. We can "smooth out" the discontinuity in ψ by putting a diffusive term back into eqn. 46:

$$\partial\psi/\partial t = (\partial/\partial x)(1/\psi) + D\partial^2\psi/\partial x^2 \quad (58)$$

If we insert the steady-state solution $\psi(\xi)$ into eqn. 58, we can integrate once to obtain

$$-c\psi = 1/\psi + D\psi' + K \quad (59)$$

where K is a constant. However, since $\psi' \rightarrow 0$ as $x \rightarrow \pm\infty$, we find

$$c\psi(-\infty) + 1/\psi(-\infty) = c\psi(\infty) + 1/\psi(\infty) \quad (60)$$

or

$$c = 1/\psi(-\infty)\psi(\infty) \quad (61)$$

In the limit $D \rightarrow 0$ the front becomes sharp, and eqns. 61 and 57 become equivalent. Note, however, that one does not obtain the correct front speed by adding a diffusive term to eqn. 50:

$$\partial u/\partial t + u\partial u/\partial x = D\partial^2 u/\partial x^2 \quad (62)$$

Eqn. 62, which is known as Burgers' equation, instead has the front speed $\frac{1}{2}[\mu(-\infty) + u(\infty)]$. Thus, limiting solutions of eqns. 58 and 62 when $D \rightarrow 0$ are related according to $u = 1/\psi^2$ as long as these limiting solutions are continuous, but are different after the time when discontinuities develop.

Between the time τ when discontinuities develop and the time when the establishment of the steady state is essentially complete, the front speed is still given by eqn. 57 but $c(t)$ in general will depend on time, since $\psi^{(-)}$ and $\psi^{(+)}$ will continually change as new characteristics impinge on both sides of the front (viewed as a curve in the (x,t) -plane). It is also possible that more than one front will form. This can happen, for instance, if the system is prepared in an initial state consisting of a region containing a mixture of terminator and leader ions sandwiched between regions containing pure terminator and pure leader. However, if multiple fronts form they move at different speeds and eventually collide and merge to form the single front which persists in the steady state and moves at constant speed $c(\infty) = [u(-\infty)u(+\infty)]^{\frac{1}{2}}$.

This phenomenon has previously been predicted by the theory of Brouwer and Postema⁸, and the dissolution of mixed steps has been documented by Longworth⁹. (See also ref. 10.)

In Figs. 1-5 a numerical example is plotted to show the time development of $u(x,t)$ from an initial continuous function $u(x,0)$ to a function which has nearly reached

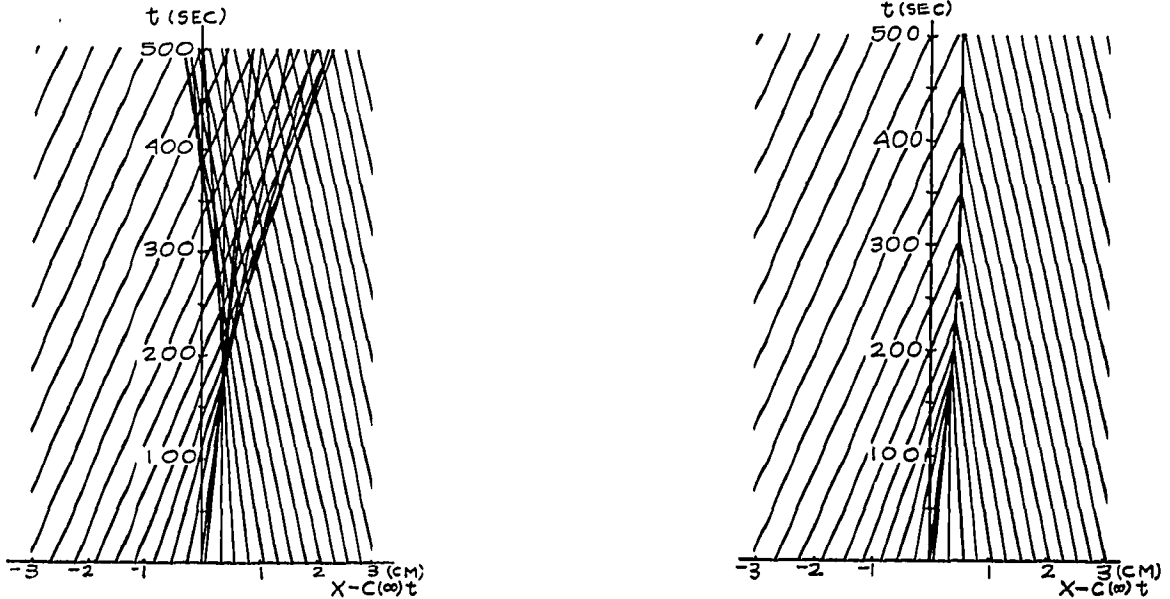


Fig. 1. In this figure, as well as in Figs. 2-5, we use a numerical example to illustrate the isotachophoretic separation of two ion species. These results are computed assuming that ω is a constant and that the initial distribution of ions is described by $u(x,0) = [0.01 \text{ cm/sec}][1 - 0.6 \tanh(x/\text{cm})]$. This distribution implies that $\mu_1/\mu_2 = 2$ and $c(\infty) = 0.008 \text{ cm/sec}$. The characteristics (lines of constant u) of eqn. 50 are plotted (without regard to the formation of the shock front), using a space-time coordinate system moving with the speed $c(\infty)$. After the time $\tau = 166.67$ sec the characteristics begin to intersect, and it is impossible to determine $u(x,t)$ from this graph at times later than τ .

Fig. 2. This graph shows both the characteristics and the shock front. The front develops from the characteristic through the origin, where $u(x,0)$ has the steepest slope. The trajectory of the shock front is determined by numerical integration of eqn. 57. Since the characteristics terminate at the shock front, $u(x,t)$ is well-defined at all times.

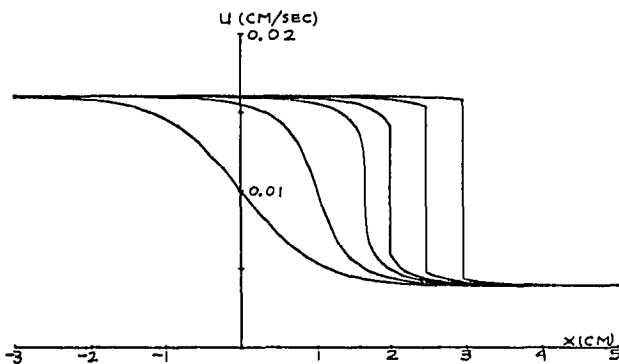


Fig. 3. This graph shows the progressive steepening of $u(x,t)$ and the development of the shock front as viewed in a stationary coordinate system. The curves are shown for time values $t = 0, 100, 166.67, 200.84, 254.12, \text{ and } 310.70$ sec.

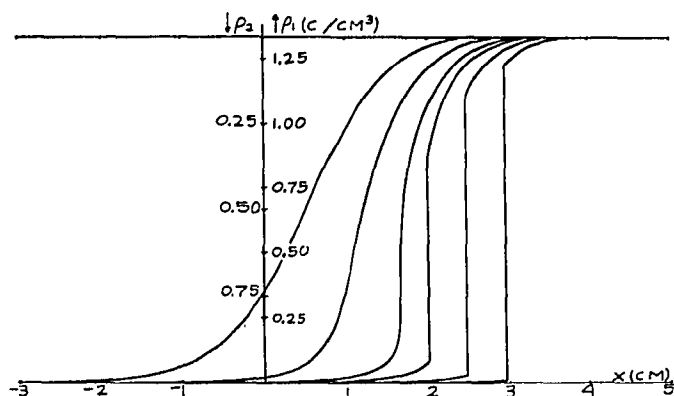


Fig. 4. The leader and terminator charge densities are shown as functions of x for the same values of t as in Fig. 3. We have assumed here that $\mu_1/2 = \mu_2 = -\mu_0 = 4 \times 10^{-4} \text{ cm}^2/\text{V} \cdot \text{sec}$ and $J = 1.6 \times 10^{-2} \text{ A/cm}^2$. The values of ρ_1 and ρ_2 are read on the scales which increase upward and downward, respectively.

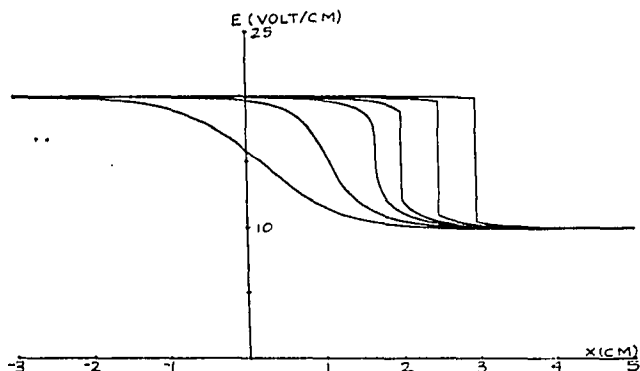


Fig. 5. The electric field is shown as a function of x for the same values of t as in Figs. 3 and 4.

the steady state. Fig. 1 shows the characteristics, determined from the initial data, plotted in the $(x - c(\infty)t, t)$ plane without regard to the formation of the shock front. After the time when the characteristics begin to intersect it is impossible to determine $u(x, t)$ from this graph. Fig. 2 shows both the characteristics and the shock front. The front velocity is determined from eqn. 57. Here the characteristics do not cross each other but terminate at the front. Fig. 3 shows $u(x, t)$ plotted as a function of x for several values of time, beginning with $t = 0$. Figs. 4 and 5 show the corresponding curves for $\rho_1(x, t)$, $\rho_2(x, t)$ and $E(x, t)$, assuming typical numerical values for μ_0 , μ_1 , μ_2 , and J . These computer-generated curves show quite clearly the ion separation and boundary sharpening which are the principal characteristics of isotachophoresis.

ACKNOWLEDGEMENTS

I would like to thank M. Bier, M. Binder, M. Coxon, J. O. N. Hinckley, J. Kessler, T. W. Nee, M. O. Scully, and H. Shih for helpful discussion. I would par-

ticularly like to thank J. K. Chao for his help with the computer calculations. This work was supported by U.S. National Aeronautics and Space Administration Contract NAS8-29566.

APPENDIX

A simplified form of the unsteady-state equations

The solution of the unsteady-state problem in isotachophoresis is more complicated if $n > 2$. In this case one has a system of $n - 1$ quasilinear equations to be solved for $n - 1$ linearly independent functions of x and t . Analysis of this system of equations is still in its preliminary states. The main result reported in this appendix is a linear transformation by which it is possible to reduce the n eqn. 44 to $n - 1$ equations in a simple and symmetric way. The mathematical structure of the equations is simplified in terms of the new variables, although the boundary conditions become more complicated. We define the transformation as follows:

$$\begin{aligned} \omega &= \sum_{j=1}^n s_j \\ p &= \sum_{j=1}^n \mu_j s_j \\ q_k &= \sum_{j=1}^n \mu_j \gamma_{nkj} s_j \text{ for } k = 1, \dots, n - 2 \end{aligned} \quad (\text{A1})$$

Here γ_{nkj} is defined as the sum of all different products of combinations of different mobilities, excluding μ_j , and taken k at a time. For example, if $n = 4$, then

$$q_1 = \mu_1(\mu_2 + \mu_3 + \mu_4)s_1 + \mu_2(\mu_1 + \mu_3 + \mu_4)s_2 + \mu_3(\mu_1 + \mu_2 + \mu_4)s_3 + \mu_4(\mu_1 + \mu_2 + \mu_3)s_4 \quad (\text{A2})$$

and

$$q_2 = \mu_1(\mu_2\mu_3 + \mu_2\mu_4 + \mu_3\mu_4)s_1 + \mu_2(\mu_1\mu_3 + \mu_1\mu_4 + \mu_3\mu_4)s_2 + \mu_3(\mu_1\mu_2 + \mu_1\mu_4 + \mu_2\mu_4)s_3 + \mu_4(\mu_1\mu_2 + \mu_1\mu_3 + \mu_2\mu_3)s_4 \quad (\text{A3})$$

The variable p is simply the conductivity. The index k on the variables q_k generates independent variables only for $k \leq n - 2$, since q_{n-1} is just a constant a , where $a = (\mu_1\mu_2 \dots \mu_n)\omega$. By using eqn. 44 the system of quasi-linear equations obeyed by the variables p and q_k is easily shown to be

$$\begin{aligned} \partial p / \partial t &= J(\partial / \partial x)(q_1 / p) \\ \partial q_1 / \partial t &= J(\partial / \partial x)(q_2 / p) \\ &\vdots \quad \quad \quad \vdots \\ &\vdots \quad \quad \quad \vdots \\ &\vdots \quad \quad \quad \vdots \\ \partial q_{n-2} / \partial t &= J a (\partial / \partial x)(1 / p) \end{aligned} \quad (\text{A4})$$

The first equation in A4 is equivalent for $n = 2$ to eqn. 46. The determinant of the transformation A1 is equal to the product of the $n(n - 1)/2$ mobility differences

$\mu_i - \mu_m, i \neq m$. Thus, the inverse of the transformation A1 exists provided that no two ion species have the same mobility. It is not surprising that the transformation is singular if two ion species of equal mobility are present, since there is obviously no way that isotachophoretic separation of such ions can occur. Notice that, aside from the parameters α , the ionic mobilities do not occur explicitly in eqns. A4. Even the parameters J and α could be removed by a scaling transformation. However, the mobilities appear in the boundary conditions; the asymptotic values of p and q_k are functions of the mobilities and of ω .

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