

Approximate Solutions of Chemical Separation Equations with Diffusion

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Many problems in the analysis of biochemical separation techniques require the solution of a Fickian equation of the form

$$\frac{\partial c}{\partial \tau} = \epsilon \frac{\partial}{\partial x} \left(f(x) \frac{\partial c}{\partial x} \right) - \frac{\partial}{\partial x} (g(x)c)$$

where ϵ is proportional to the diffusion constant. This paper presents an approximate solution to this equation valid for small ϵ . For many separation systems ϵ is 10^{-3} or less, while $f(x)$ and $g(x)$ are of the order of 1. Applications are given to velocity centrifugation experiments, with pressure dependent sedimentation, and to pore gradient electrophoresis.

Many problems related to biochemical separation systems require solution to a transport equation of the form

$$\frac{\partial c}{\partial \tau} = \epsilon \frac{\partial}{\partial x} \left(f(x) \frac{\partial c}{\partial x} \right) - \frac{\partial}{\partial x} (g(x)c) \quad (1)$$

in which c is solute concentration, $g(x)$ is the transport term, and $\epsilon f(x)$ is the diffusion term. Some examples of systems which fall into this category are:

- (1) Pressure dependent systems in velocity sedimentation (1, 2, 3, 4).
- (2) Gel pore electrophoresis (5, 6).
- (3) Analytical gradient chromatography (7, 8).

Undoubtedly other examples can be found. In the study of the systems cited above, a common property is that the (dimensionless) parameter ϵ is very small compared with the (dimensionless) terms $f(x)$ and $g(x)$ which can be chosen to be of the order of 1. In all of the examples cited ϵ is 2.5×10^{-2} or less. In this paper we summarize a singular perturbation technique for the solution of Equation 1, which is to be solved subject to an initial condition $c(x,0)$, and on the assumption that boundary effects (in x) can be ignored.

To see why it is impossible to obtain a solution to Equation 1 by ordinary perturbation theory, consider the simple system

$$\frac{\partial c}{\partial \tau} = \epsilon \frac{\partial^2 c}{\partial x^2} \quad (2)$$

subject to an initial condition $c(x,0) = \delta(x)$, a delta function. If we set $\epsilon = 0$, then the solution is $c(x,\tau) = \delta(x)$. On the other hand, the solution to Equation 2 is known to be:

$$c(x, \tau) = \frac{1}{\sqrt{4\pi\epsilon\tau}} \exp\left(-\frac{x^2}{4\epsilon\tau}\right) \quad (3)$$

that is, spreading occurs because of diffusion. The solution (Equation 3) cannot be found by expanding the variables in Equation 2 in a power series in ϵ . In particular if we consider a point $x \neq 0$, the concentration is identically equal to 0 when $\epsilon = 0$, but it can be much greater than 0 for any nonzero ϵ .

To derive an approximate solution we start by transforming the space variable x to one that moves by the convective transport mechanism—*i.e.*, a coordinate that remains fixed with the solute motion when diffusion can be neglected. This coordinate will be denoted by ξ and is

$$\xi = \int_0^x \frac{du}{g(u)} - \tau \quad (4)$$

If we define a function $H(z)$ to be the solution to

$$\int_0^{H(z)} \frac{du}{g(u)} = z \quad (5)$$

then a molecule initially at position ξ_0 (or $x_0 = H(\xi_0)$) will be transported to position $\xi_0 + \tau$ at time τ in the absence of diffusion. If we also define a new dependent variable $\psi(x,\tau)$ by

$$\psi(x, \tau) = g(x)c(x, \tau) \quad (6)$$

then Equation 1 can be transformed to

$$\frac{\partial \psi}{\partial \tau} = \epsilon \frac{\partial}{\partial \xi} \left[\frac{F(\xi + \tau)}{G(\xi + \tau)} \frac{\partial}{\partial \xi} \left(\frac{\psi}{G(\xi + \tau)} \right) \right] \quad (7)$$

where

$$F(u) = f(H(u)), \quad G(u) = g(H(u)) \quad (8)$$

Equation 7 is exact, no approximation having been made.

At this point we can introduce the perturbation procedure based on the fact that ϵ is small. Let us assume that the initial condition is $c(x, 0) = c_0 \delta(x)$, where $\delta(x)$ is a delta function (—i.e., an initial pulse injection). The principal consequence of a small ϵ is the fact that the bandwidth of the diffusion broadened peak is narrow, going to zero as ϵ vanishes. Thus, we make the approximation that only the region near $\xi = 0$ in the terms $F(\xi + \tau)$ and $G(\xi + \tau)$ is of interest. The resulting value, denoted by $\psi_0(\xi, \tau)$, therefore satisfies the equation

$$\frac{\partial \psi_0}{\partial \tau} = \epsilon \frac{F(\tau)}{G^2(\tau)} \frac{\partial^2 \psi_0}{\partial \xi^2} \quad (9)$$

subject to the initial condition $\psi_0(x, 0) = c_0 g(x) \delta(x)$. This is a diffusion equation with a time-dependent diffusion constant. It can be reduced to a more familiar form by introducing a new dimensionless time $\Delta(\tau)$ by

$$\Delta(\tau) = \int_0^\tau \frac{F(u)}{G^2(u)} du \quad (10)$$

in which case Equation 9 becomes

$$\frac{\partial \psi_0}{\partial \Delta} = \epsilon \frac{\partial^2 \psi_0}{\partial \xi^2} \quad (11)$$

The solution to this equation is straightforward and can be written

$$\psi_0(\xi, \Delta) = \frac{C_0}{\sqrt{4\pi\epsilon\Delta(\tau)}} \exp\left(-\frac{\xi^2}{4\epsilon\Delta(\tau)}\right) \quad (12)$$

If we can assume that $g(0) = 1$ (this can always be done without loss of generality), then the final expression for $c(x, \tau)$ becomes

$$c(x, \tau) = \frac{C_0}{g(x)\sqrt{4\pi\epsilon\Delta(\tau)}} \exp\left(-\frac{\xi^2}{4\epsilon\Delta(\tau)}\right) \quad (13)$$

where ξ is given in Equation 4. Notice that $c(x, \tau)$ is not generally symmetric in x because ξ is equal to a function of x that is not necessarily symmetric. The maximum peak concentration is very closely given by

$$\frac{c_{\max}}{c_0} = \frac{1}{g(H(\tau))\sqrt{4\pi\epsilon\Delta(\tau)}} \quad (14)$$

This relation enables one to determine ϵ (or equivalently, the diffusion constant) experimentally.

To put the preceding analysis into a more applied framework, let us consider the peak broadening in pore gradient electrophoresis (5, 6, 9). For this problem, let D and D_0 represent the diffusion coefficient in the gel and in the absence of a gel, and M and M_0 the respective mobilities. For many gels these variables experimentally satisfy Equation 5:

$$D/D_0 = M/M_0 = \exp(-x/L) \quad (15)$$

for a linear gel gradient, where x is distance and L is an experimentally measured parameter. Let V be the voltage gradient. Then the dimensionless parameters τ and ϵ that characterize the Fick equation are

$$\tau = M_0 V t / L, \quad \epsilon = D_0 / (M_0 V L) \quad (16)$$

In addition we will let $z = x/L$ be a dimensionless distance. The transport equation for this system is

$$\frac{\partial c}{\partial \tau} = \epsilon \frac{\partial}{\partial z} \left(e^{-z} \frac{\partial c}{\partial z} \right) - \frac{\partial}{\partial z} (e^{-z} c) \quad (17)$$

An exact solution to this equation subject to an initial pulse of amount c_0 can be found (9), and the following expression can be found from it:

$$\begin{aligned} \frac{c(x, \tau)}{c_0} &= \frac{1}{L\tau(2\pi\epsilon)^{1/2}} (1 + \lambda^2)^{-1/4} \left(\frac{\lambda}{\sqrt{1 + \lambda^2} - 1} \right)^{1+1/\epsilon} \\ &\times \exp \left[\frac{1}{\epsilon} \left(\sqrt{1 + \lambda^2} + \frac{z}{2} - \frac{1 + e^z}{2} \right) \right] \end{aligned} \quad (18)$$

in which $\lambda = (z/\tau) \exp(z/2)$. Although this expression is very close to being exact, it is difficult to work with. Since ϵ is small, we can use the theory developed in earlier paragraphs. The functions required are easily found to be

$$\begin{aligned} \xi &= e^z - 1 - \tau \\ H(y) &= \ln(1 + y) \\ \Delta(\tau) &= \tau(1 + \tau/2) \end{aligned} \quad (19)$$

A comparison of the results of the exact calculation and the approximate one is shown in Figure 1 for the values $\epsilon = 5 \times 10^{-3}$, $\tau = 5$. The error is fairly small, and the relative error is generally less than 5%. There is no great advantage to using the perturbation theory for the example just discussed because an exact solution is available. However, a gel for which the diffusion coefficients and mobilities are

$$D/D_0 = \exp(-\alpha x/L), M/M_0 = \exp(-x/L) \quad (20)$$

for example, requires an approximate theory because an exact one is not available.

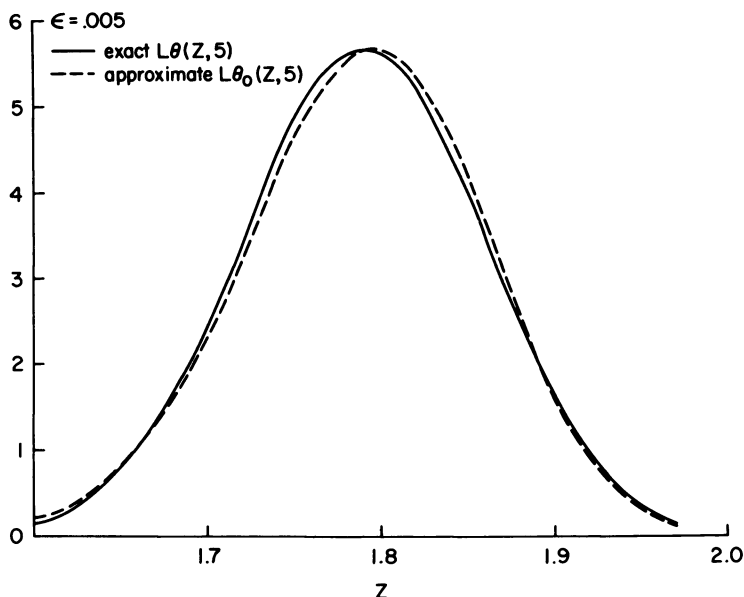


Figure 1. A comparison of the exact and approximate concentration profiles ($\theta \equiv c/c_0$) (Equations 13 and 18) for pore gradient electrophoresis, for $\epsilon = 5 \times 10^{-3}$, $\tau = 5$

Extensive application of the theory has been made in treating pressure effects on velocity centrifugation. If ω denotes angular speed, s_p the sedimentation coefficient at pressure p , r_a the radius of the meniscus, $x = (r/r_a)^2$, the usual representation of pressure effects leads to the relation (10),

$$s_p/s_0 = 1 + m(x - 1) \quad (21)$$

where m is a parameter to be determined experimentally, that contains the solvent compressibility. The parameters ϵ and τ for this model are

$$\epsilon = 2D/(s_0\omega^2 r_a^2), \tau = 2\omega^2 s_0 t \quad (22)$$

and the Lamm equation is

$$\frac{\partial c}{\partial \tau} = \epsilon \frac{\partial}{\partial x} \left(x \frac{\partial c}{\partial x} \right) - \frac{\partial}{\partial x} [x(1 + mx - m)c] \quad (23)$$

This equation is to be solved subject to the initial condition

$$c(x, 0) = c_0 H_0(x - 1) \text{ where } \begin{matrix} H_0(y) = 1 & y > 0 \\ H_0(y) = 0 & y < 0 \end{matrix} \quad (24)$$

The approximate solution for the concentration for the model of Equation 23 is (11),

$$\frac{c(x, \tau)}{c_0} = e^{-(1+m)\tau} \left(\frac{1+m}{1+m-mx+mx e^{-(1+m)\tau}} \right)^2 \phi \left(\frac{\xi}{\sqrt{2\epsilon\Delta(\tau)}} \right) \quad (25)$$

in which

$$\begin{aligned} \xi &= \frac{1}{1+m} \ln \frac{x}{1+m-mx} - \tau \\ \phi(x) &= (2\pi)^{-1/2} \int_{-\infty}^x \exp(-u^2/2) du \\ \Delta(\tau) &= \frac{1}{(1+m)^4} \left[1 - e^{-(1+m)\tau} + 3m(1+m)\tau \right. \\ &\quad \left. + 3m^2(e^{(1+m)\tau} - 1) + \frac{m^3}{2}(e^{2(1+m)\tau} - 1) \right] \end{aligned} \quad (26)$$

The relative error in using Equation 25 is less than 0.005 over most of the concentration profile (11) for parameters that are characteristic of several polymer systems (12) while the error in the concentration gradient is generally less than 0.02 for these same parameters.

An iterative method for developing higher order approximations to the solution to Equation 1 can be devised by using some of the ideas of singular perturbation theory (15). To display the systematics of the procedure let us rewrite Equation 7 as

$$\frac{\partial \psi}{\partial \tau} = \epsilon A(\xi + \tau) \frac{\partial^2 \psi}{\partial \xi^2} + \epsilon B(\xi + \tau) \frac{\partial \psi}{\partial \xi} + \epsilon C(\xi + \tau) \psi \quad (27)$$

in which

$$A(u) = F(u)/G^2(u)$$

$$B(u) = F'(u)/G^2(u) - 2F(u)G'(u)/G^3(u) \quad (28)$$

$$C(u) = 3F(u)G'(u)/G^4(u) - F(u)G''(u)/G^3(u) - F'(u)G'(u)/G^3(u)$$

where the prime denotes differentiation with respect to u . In Equation 27 we now define a new space variable $\rho = \xi/\sqrt{\epsilon}$ and introduce an expansion for ψ in powers of $\sqrt{\epsilon}$

$$\psi = \psi_0 + \epsilon^{1/2}\psi_1 + \epsilon\psi_2 + \epsilon^{3/2}\psi_3 + \dots \quad (29)$$

in which we will assume that $\psi_n(\rho, 0) = 0$ for $n \neq 0$ —that is, the initial value for ψ_0 is the same as that for ψ . When we make the indicated substitutions and collect the terms, multiplying successive powers of $\epsilon^{1/2}$, we find:

$$\begin{aligned} \epsilon^0 : \quad & \frac{\partial \psi_0}{\partial \tau} = A(\tau) \frac{\partial^2 \psi_0}{\partial \rho^2} \\ \epsilon^{1/2} : \quad & \frac{\partial \psi_1}{\partial \tau} - A(\tau) \frac{\partial^2 \psi_1}{\partial \rho^2} = \rho A'(\tau) \frac{\partial^2 \psi_0}{\partial \rho^2} + B(\tau) \frac{\partial \psi_0}{\partial \rho} \\ \epsilon : \quad & \frac{\partial \psi_2}{\partial \tau} - A(\tau) \frac{\partial^2 \psi_2}{\partial \rho^2} = \frac{1}{2} \rho^2 A''(\tau) \frac{\partial^2 \psi_0}{\partial \rho^2} + \rho B'(\tau) \frac{\partial \psi_0}{\partial \rho} \\ & + c(\tau) \psi_0 + \rho A'(\tau) \frac{\partial^2 \psi_1}{\partial \rho^2} + B(\tau) \frac{\partial \psi_1}{\partial \rho} \end{aligned} \quad (30)$$

and so forth.

The successive equations in Equation 30 can be represented in the general form

$$\begin{aligned} \frac{\partial \psi_0}{\partial \tau} &= A(\tau) \frac{\partial^2 \psi_0}{\partial \rho^2} \\ \frac{\partial \psi_n}{\partial \tau} - A(\tau) \frac{\partial^2 \psi_n}{\partial \rho^2} &= U_n(\rho, \tau) \end{aligned} \quad (31)$$

where the function $U_n(\rho, \tau)$ is calculated in terms of $\psi_0, \psi_1, \dots, \psi_{n-1}$, and can be considered known at any stage of the calculation. Equation 31 can be solved by means of a Fourier transformation, the final result being

$$\begin{aligned} \psi_n(\rho, \tau) &= \frac{1}{\sqrt{4\pi}} \int_0^\tau \frac{d\tau'}{\sqrt{\Delta(\tau) - \Delta(\tau')}} \int_{-\infty}^\infty U_n(\rho', \tau') \times \\ &\quad \exp \left\{ -\frac{(\rho - \rho')^2}{4 [\Delta(\tau) - \Delta(\tau')]} \right\} d\rho' \end{aligned} \quad (32)$$

For an initial pulse distribution we have, from Equation 12 the result

$$\psi_0(\rho_1\tau) = \frac{1}{\sqrt{4\pi\epsilon\Delta(\tau)}} \exp\left(-\frac{\rho^2}{4\Delta(\tau)}\right) \quad (33)$$

If we insert this into the equation for ψ_1 that appears in Equation 30, we find, after some lengthy calculation, that

$$\begin{aligned} \epsilon^{1/2}\psi_1 = & \exp\left(-\frac{\rho^2}{4\Delta(\tau)}\right) \left\{ \frac{3\rho}{(16\pi)^{1/2}\Delta^{5/2}(\tau)} \int_0^\tau A'(\tau')[\Delta(\tau) - \Delta(\tau')]^2 d\tau' \right. \\ & + \frac{\rho^3}{(64\pi)^{1/2}\Delta^{7/2}(\tau)} \int_0^\tau A'(\tau')\Delta(\tau') d\tau' - \frac{\rho}{(16\pi)^{1/2}\Delta^{3/2}(\tau)} \times \\ & \left. \times \int_0^\tau [A'(\tau') + B(\tau')] d\tau' \right\} \quad (34) \end{aligned}$$

showing no correction at the peak maximum, but there is some shift in the tails of the concentration profile. Detailed calculations can also be made for the initial condition $c(x,0) = H(x-1)$ where $H(u) = 0$, $u < 0$, $H(u) = 1$, $u > 0$. This case is appropriate to the problem of ultracentrifugation and leads to a result different from that given in Equation 34. Further details of this correction procedure will be given in a forthcoming publication, but for most applications at the present stage of separation technology the simple approximation given by ψ_0 should suffice for whatever information is required.

It would be of considerable interest to extend the technique just presented to problems involving nonlinear equations because there are many situations in ultracentrifugation where nonideality is a dominant feature. Furthermore, it is known (4, 14) that even for two-component systems with nonideality the theory for estimating the sedimentation constant based on a diffusion-free ($\epsilon = 0$) approximation can lead to systematic error. Therefore, the development of an approximate procedure for nonlinear equations would be useful for further progress in analytical separation methods.

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