2-0

Chapter 3

MACROSCOPIC DIFFUSION PROCESSES

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3.1 Introduction

3.1.1 Background

Diffusion is an important transport process in physical, chemical, and biological systems. Two theoretical models of diffusion capture complementary aspects of the phenomenon. The microscopic model describes the probabilistic behavior of a population of individual solute particles which execute statistically independent, but otherwise identical, random walks. Software dealing with such a microscopic model of diffusion is described in Chapter 2. The software described in this chapter involves macroscopic diffusion which describes the aggregate behavior of large populations of solute molecules.

3.1.2 Macroscopic Model of Diffusion

In 1855, Adolph Fick proposed a macroscopic model for passive diffusion [Fick, 1855]. By analogy to Fourier's law of heat conduction and Ohm's law for electrical conduction, Fick proposed that the flux of solute particles at a point in space is proportional to the concentration gradient at that point. Mathematically, this relation is expressed by *Fick's First Law,* which, in its one-dimensional form, is as follows:

$$\phi = -D\frac{\partial c}{\partial x},\tag{3.1}$$

where $c(x, t)$ is the solute concentration and $\phi(x, t)$ is the solute flux. The constant of proportionality, D, is known as the *diffusion coefficient.* Conservation of solute particles (in the absence of sources or sinks or of chemical reactions that create or destroy particles) results in a second relation between concentration and flux, the *Continuity Equation*:

$$\frac{\partial \phi}{\partial x} = -\frac{\partial c}{\partial t}.\tag{3.2}$$

Differentiating both sides of Equation 3.1 with respect to x and using the Continuity Equation yields Fick's Second Law, or the *One-Dimensional Diffusion Equation*:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2}\tag{3.3}$$

In principle, any one-dimensional diffusion process can be modelled by solving this equation subject to the appropriate initial conditions and boundary conditions.

We next consider the same problem but with a body force acting uniformly on the solute particles so that they are convected and a chemical reaction occurring between the solute particles and the solvent. The solute flux, $\phi(x, t)$, is now the sum of the diffusive flux, given by Fick's law, and the *convective* flux due to the body force. Thus, in this case,

$$\phi = -D\frac{\partial c}{\partial x} + vc,\tag{3.4}$$

where v is the *convection velocity* of the solute particles; i.e., the velocity at which the particles would move in response to the body force but no diffusion. If r is the reaction rate between solute and solvent, then the Continuity Equation becomes

$$\frac{\partial \phi}{\partial x} = -\frac{\partial c}{\partial t} - rc. \tag{3.5}$$

Combining these expressions yields a modified diffusion equation:

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} - v\frac{\partial c}{\partial x} - rc. \tag{3.6}$$

Thus, solute convection and a chemical reaction rate between solute and solvent appear as additional terms in the Diffusion Equation.

   If the initial concentration, $c(x,0)$ is known in some region of space and if the relation between the concentration and flux is known at each boundary of this region, then a unique solution exists for $t > 0$. This agrees with intuition: given an initial concentration profile, $c(x,0)$, Fick's laws govern the unique evolution of the concentration profile for all later times.

3.1.3   Overview of Software

While macroscopic diffusion has been successfully modelled by Fick's equations, studying the equations alone provides only limited insight into the behavior of diffusion processes. The goal of this software is to help students gain intuition about diffusion in one dimension. The solutions to the diffusion equation are functions of two variables: one spatial variable, x, and time, t. These solutions can be plotted either as a function of time at a particular point in space or as a function of the spatial variable at a particular instant in time. Such isolated "snapshots", however, do not fully convey the dynamic behavior of diffusion processes. With this software, the user can view a "movie" of the solute concentration or flux profile, as a function of position, as it evolves in time. Thus, the software enables the student learning about diffusion theory to gain intuition about the dynamic behavior of macroscopic diffusion processes.

   Furthermore, the software provides an opportunity for students to experiment with the macroscopic model. For example, the user can explore how changing the diffusion coefficient affects the time-course of the simulation. The user can also specify transparent or reflecting boundaries and can explore how a body force acting on the solute particles or a chemical reaction between solute and solvent influence the diffusion process. Thus, the software can be used as a tool for investigating how various parameters and boundary conditions influence diffusion.

   Five classes of initial concentration profiles, corresponding to five characteristic one-dimensional diffusion problems, are implemented in the software (Figure 3.1). Four of these problems involve diffusion from a specified initial concentration profile contained within a single compartment (which may be infinite), while the fifth involves diffusion between two compartments, through a membrane.
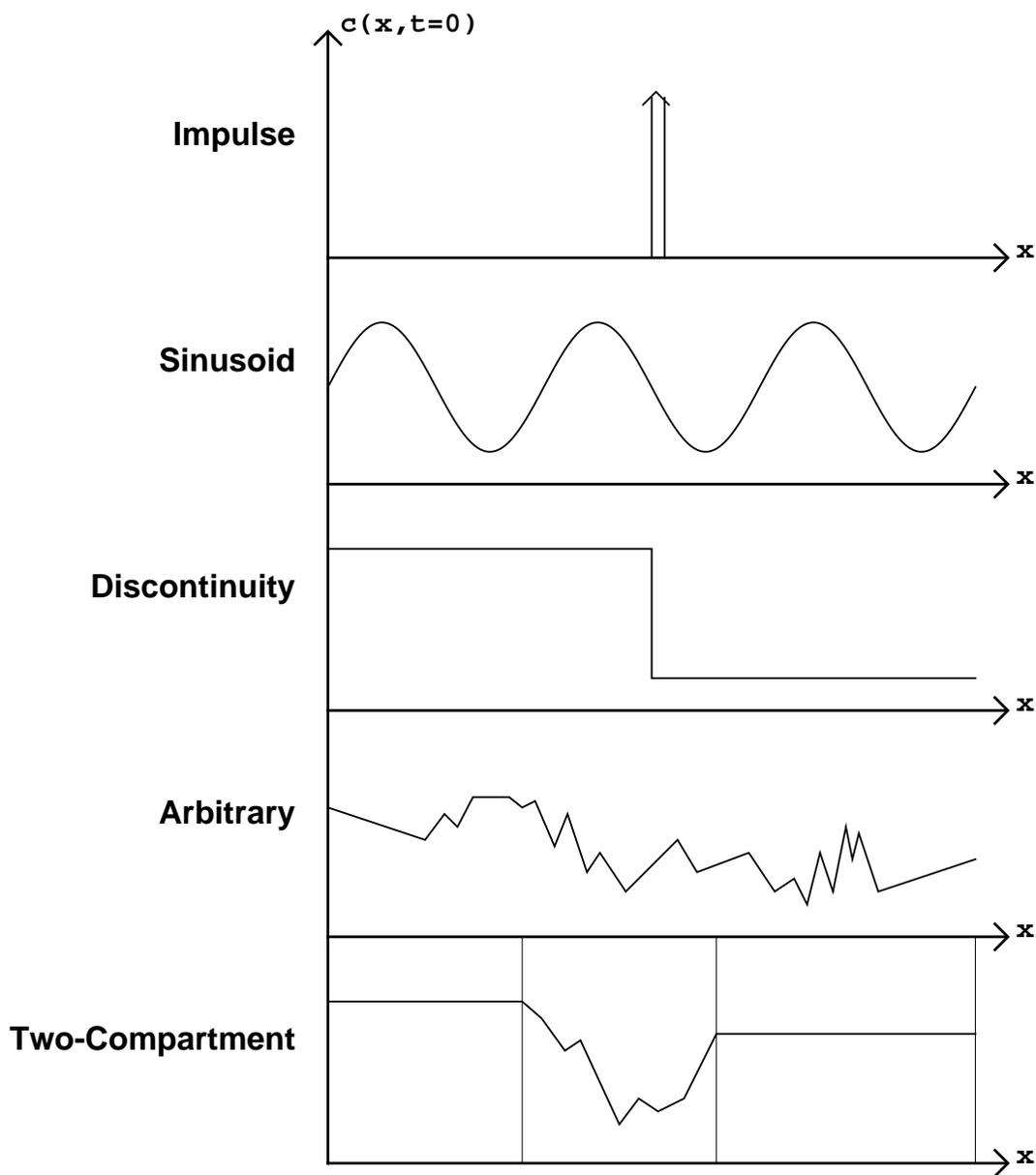
Figure 3.1: Schematic representation of the five classes of initial concentration profiles for one-dimensional problems simulated by the software.

One-Compartment Diffusion

In one-compartment diffusion problems, the initial concentration can be chosen to be one of four types: impulses, sinusoids, piece-wise constant, and arbitrary distributions. An impulse of solute concentration is a mathematical idealization corresponding to a finite amount of solute initially concentrated at a single point in space. The user can specify the magnitude and position of up to four impulses. This case illustrates diffusion from point sources. Initially sinusoidal concentration profile illustrate the spatial frequency response of a system governed by the Diffusion Equation, specifically, the low-pass spatial filtering effect of diffusion. By superimposing up to four sinusoids, the student can observe the dependence of the space-time evolution of a concentration distribution on its spatial frequency content. An initial concentration profile may be piecewise-constant but contain jump discontinuities (as, for example, if a thin, impermeable membrane separating two baths with unequal solute concentrations is suddenly removed). The user can specify the magnitude and location of up to four such discontinuities. The user can also explore the response for more complicated initial conditions which can be specified by drawing on the workstation screen with a mouse.

For these different initial distributions, the user can specify the boundary type (transparent or reflecting), the value of the convection velocity, and the chemical reaction rate between the solute particles and the solvent.

Two-Compartment Diffusion through a Membrane

The user can also investigate diffusion between two well-stirred compartments, or baths, through a membrane which is permeable to the solute. Two-compartment diffusion through a membrane is an important transport process in biological systems. It can model, for example, diffusion between the cytoplasm of a cell and the extracellular fluid, across the plasma membrane. The baths are assumed to be well-stirred, so that the concentration within each bath varies with time only. The total amount of solute in the system is assumed to be finite. The user can specify the width of each bath and of the membrane, the initial concentration of each bath, and an arbitrary initial concentration profile in the membrane.

3.2   Methods of Solution

For several of the diffusion problems implemented in the software, exact solutions of the modified diffusion equation (Equation 3.6) are available in a form that makes computation efficient. Such solutions have been used wherever possible. The remainder of the solutions were obtained by numerical methods. The methods are described in some detail elsewhere [Berkenblit, 1990]; only a brief summary of the methods is given here.

The method used to obtain solutions depends upon the type of boundary condition. Two types of boundary conditions for the diffusion problems can be selected by the user: *transparent* or *reflecting* boundary conditions. If transparent boundaries are specified, then the region over which diffusion occurs is infinite; the "boundaries" are merely the endpoints

of the region viewed by the user. At a reflecting boundary, on the other hand, the solute flux is constrained to be zero, since no solute particles can cross such a boundary.

3.2.1 Exact Solutions

Exact solutions were used to compute the response for all one-compartment diffusion problems with transparent boundaries. These are described in this section.

Impulse response — Green's function

No convection, no chemical reaction. First we shall find the spatial and temporal evolution of the solute concentration profile, $c(x, t)$, in the absence of convection and in the absence of a chemical reaction when the initial profile consists of a unit impulse in concentration, located at position $x = \xi$ and delivered at time $t = 0$. That is we need to find a solution to Equation 3.3 subject to the initial condition

$$c(x, 0) = \delta(x - \xi). \tag{3.7}$$

The solution, called the *Green's function* $G(x, t; \xi, 0)$, can be shown by a variety of methods to be

$$c(x, t) = G(x, t; \xi, 0) = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-\xi)^2/4Dt}. \tag{3.8}$$

Thus, the concentration profile is a *Gaussian* function of the spatial variable. The standard deviation of the curve, $\sqrt{2Dt}$, increases with increasing time, but the total area under the concentration curve remains constant, corresponding to conservation of particles.

Convection but no chemical reaction. We next consider the same problem but with a non-zero convection term. In this case, the concentration satisfies the modified diffusion equation, Equation 3.6, with $r = 0$:

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} - v \frac{\partial c}{\partial x}, \tag{3.9}$$

with the initial condition

$$c(x, 0) = \delta(x - \xi). \tag{3.10}$$

The solution can be shown to be

$$c(x, t) = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-\xi-vt)^2/4Dt} = G(x - vt, t; \xi, 0). \tag{3.11}$$

Thus, the response in this case is a Gaussian function, as before, but the entire profile "drifts" in the positive x-direction with velocity v.

Convection and chemical reaction. With a non-zero chemical rate, r, and convection velocity, v, we need to solve Equation 3.6 which has a solution

$$c(x,t) = e^{-rt}G(x - vt, t; \xi, 0). \tag{3.12}$$

In general, if $c'(x,t)$ is the solution to Equation 3.3, with a specified initial concentration profile and transparent boundaries, then the solution to the modified equation, 3.6, satisfying the same intitial conditions, is given by

$$c(x,t) = e^{-rt}c'(x - vt, t). \tag{3.13}$$

Sinusoid

First we consider the solution to Equation 3.3 with the initial condition

$$c(x,0) = A\left\{1 + \sin(\omega x + \theta)\right\} \tag{3.14}$$

for some arbitrary constant amplitude, A, spatial radian frequency, ω, and phase, θ. The solution for $t > 0$ is given by

$$c(x,t) = A\left\{1 + e^{-D\omega^2 t}\sin(\omega x + \theta)\right\}, \tag{3.15}$$

which can be verified by substituting this expression into Equation 3.3. Thus, an initially sinusoidal concentration profile remains sinusoidal for all later time, but the amplitude decreases exponentially with time. The rate of attenuation is proportional to the square of the spatial frequency.

With convection and a chemical reaction between solute and solvent, the solution is

$$c(x,t) = Ae^{-rt}\left\{1 + e^{-D\omega^2 t}\sin\left(\omega(x - vt) + \theta\right)\right\}, \tag{3.16}$$

where v is the convection velocity and r is the reaction rate.

Discontinuous Initial Profile

We next consider the case of an initial profile that is piecewise-constant but contains a jump discontinuity at $x = \xi$. The initial condition is that

$$c(x,0) = \begin{cases} c_L, & x < \xi \\ c_R, & x > \xi \end{cases}, \tag{3.17}$$

which can also be written as

$$c(x,0) = c_L + (c_R - c_L)\int_\xi^\infty \delta(x - x')\,dx'. \tag{3.18}$$

For $t > 0$, we can integrate the Green's function defined by Equation 3.8 to obtain the solution:

$$
\begin{aligned}
c(x,t) &= c_L + (c_R - c_L) \int_\xi^\infty G(x,t;x',0)\,dx' \\
&= c_L + (c_R - c_L) \int_\xi^\infty \frac{1}{\sqrt{4\pi Dt}} e^{-(x-x')^2/4Dt}\,dx' \\
&= c_L + (c_R - c_L) \left\{ 1 - \frac{1}{2}\mathrm{erfc}\left(\frac{x-\xi}{2\sqrt{Dt}}\right) \right\},
\end{aligned}
\tag{3.19}
$$

where the *complementary error function*, $\mathrm{erfc}(x)$, is defined by the integral

$$
\mathrm{erfc}(x) = \frac{2}{\sqrt{\pi}} \int_x^\infty e^{-t^2}\,dt.
\tag{3.20}
$$

With a convection velocity, v, and reaction rate, r, the solution is

$$
c(x,t) = c_L e^{-rt} + (c_R - c_L)e^{-rt} \left\{ 1 - \frac{1}{2}\mathrm{erfc}\left(\frac{x - vt - \xi}{2\sqrt{Dt}}\right) \right\}.
\tag{3.21}
$$

Arbitrary Initial Profile

Suppose $c(x,0)$ is an arbitrary *periodic* function of x, with period L. Then $c(x,0)$ can be expanded in a Fourier series,

$$
c(x,0) = \sum_{n=0}^{\infty} A_n e^{jn\pi x/L},
\tag{3.22}
$$

where $\{A_n\}$ is the sequence of complex Fourier coefficients, defined by

$$
A_n = \frac{2}{L} \int_0^L c(x,0) e^{-jn\pi x/L}\,dx.
\tag{3.23}
$$

By an extension of the solution for a sinusoidal initial profile, 3.15, the solution for $t > 0$ is

$$
c(x,t) = \sum_{n=0}^{\infty} A_n e^{-D\left(\frac{n\pi}{L}\right)^2 t} e^{jn\pi x/L}.
\tag{3.24}
$$

Thus, the complex Fourier coefficients of $c(x,t)$ can be obtained from the Fourier coefficients of the initial profile, $c(x,0)$, by multiplying each term by the appropriate attenuation factor. For simulation purposes, an arbitrary initial profile is represented as a discrete sequence of samples. If N is the number of samples per period, then the waveform is completely specified by its N Fourier coefficients, obtained by taking the spatial *Discrete Fourier Transform* of the initial profile. If N is a power of two, then the transform can be computed efficiently via any of several *Fast Fourier Transform* (FFT) algorithms [Oppenheim and Schafer, 1975]. Applying this result, the evolution of a concentration profile from an arbitrary periodic initial profile can be determined as follows:

1. Compute the FFT of $c(x,0)$ and store the result.

2. At any later time, t, multiply each Fourier coefficient of $c(x,0)$ by the appropriate attenuation factor, $\exp\left\{-D\left(\frac{n\pi}{L}\right)^2 t\right\}$.

3. Perform an inverse FFT to obtain $c(x,t)$.

3.2.2   Numerical Solutions

One-compartment problems with reflecting boundaries and the two-compartment problem are solved using numerical methods. To solve a diffusion problem numerically over some specified spatial region and some specified time interval, the position and time variables are discretized. Denoting the time increment by Δt and the position increment by Δx, we define

$$u_i^j = c(x_i, t_j), \tag{3.25}$$

where

$$\begin{aligned} x_i &= x_0 + i\Delta x, \quad i = 1, \dots, N \\ t_j &= t_0 + j\Delta t, \quad j = 1, \dots, M. \end{aligned} \tag{3.26}$$

A general approach to solving partial differential equations numerically is to replace the partial derivatives by finite-difference approximations. The finite-difference expressions involve the u_i^j terms defined above and result in sets of algebraic equations that can be solved by numerical methods for solving matrix equations. In the software, the equation with no convective term is solved by the implicit *Crank-Nicolson* algorithm, while for problems with a non-zero convective term, this algorithm is combined with the explicit *Two-Step Lax-Wendroff* method [Press et al., 1988, Gerald and Wheatley, 1989] by a technique known as *operator splitting*. When a non-zero chemical reaction rate, r, is specified, the computed concentration is multiplied by the attenuation factor, e^{-rt}. The Crank-Nicolson and Lax-Wendroff formulas involve the parameters $\alpha = D\Delta x/(\Delta x)^2$ and $\beta = v\Delta t/\Delta x$ for the one-compartment case and $\gamma_1 = D\Delta x/L_1\Delta t$ and $\gamma_2 = D\Delta x/L_2\Delta t$ for the two-compartment case, where L_1 and L_2 are the widths of the baths of the two compartments. The numerical methods give stable solutions provided $\alpha < 0.5$, $|\beta| \leq 1$, and $\gamma <$.

3.2.3   Summary

A variety of techniques are used to find exact solutions to one-compartment diffusion problems with transparent boundaries. The specific methods used in the software to solve one-compartment problems depend on the initial conditions and are summarized in Table 3.1. With two reflecting boundaries and in the absence of convection, the exact solutions consist of infinite series. Thus it is cumbersome to compute these exact solutions. With two reflecting boundaries and with convection, exact solutions are in general not available. Therefore, we have chosen to solve these problems numerically using the Crank-Nicolson

Option	Boundary Type	Computational Method
Impulse	Transparent	Exact solution (Gaussian)
	Reflecting	Crank-Nicolson
Sinusoid	Transparent	Exact solution (sinusoid)
Discontinuity	Transparent	Exact solution (erfc)
	Reflecting	Crank-Nicolson
Arbitrary	Transparent	FFT
	Reflecting	Crank-Nicolson
Two-Compartment		Crank-Nicolson

Table 3.1: Summary of computational methods.

and Lax-Wendroff methods. The latter methods are also used to compute the solutions to the two-compartment problem.

3.3   User's Guide to the Software

3.3.1   Options and environments

The four one-compartment diffusion problems and the two-compartment problem are implemented in the software as five *options*: Impulse, Sinusoid, Discontinuity, Arbitrary, and Two-Compartment. At all times, one of these options is the *current option*. Each option has a corresponding set of parameters specific to that option.

Impulse Parameters

- The magnitude and position of four impulses. The user can set the position of each impulse only if the magnitude is non-zero.

- The boundary type (transparent or reflecting), and, if the boundaries are reflecting, the positions of the two boundaries.

- Diffusion coefficient, convection velocity, and chemical reaction rate.

Sinusoid Parameters

- The amplitude, frequency, and phase of four sinusoids. The user can set the frequency and phase of a sinusoid only if its amplitude is non-zero.

- Diffusion coefficient, convection velocity, and chemical reaction rate.

Discontinuity Parameters

- A constant concentration offset.

- The magnitude and position of four jump discontinuities. The user can set the position only if the magnitude is non-zero.

- Boundary type and position (for reflecting boundaries).

- Diffusion coefficient, convection velocity, and chemical reaction rate.

Arbitrary Profile Parameters

- Boundary type and position (for reflecting boundaries).

- Spatial period of the profile (for transparent boundaries).

- The initial profile. The user draws the initial profile on the workstation screen by moving the mouse. The details are described in Section 3.3.2.

- Diffusion coefficient, convection velocity, and chemical reaction rate.

Two-Compartment Parameters

- Bath widths and the initial concentration in each bath.

- Membrane width and the initial membrane concentration profile, drawn with the mouse (as described in Section 3.3.2).

- Diffusion coefficient, convection velocity, and chemical reaction rate.

The software is always in one of five *environments*. When the program is in the *Parameters* environment, the user can modify the values of the option-specific parameters, change the graph parameters, and run a simulation. The other environments (*Simulate*, *Paused*, *Continue*, and *Done*), indicate the state of a simulation run. These environments are described in more detail in Section 3.3.3.

When the software is initiated, the Impulse option is initially selected and the program is in the Parameters environment. A typical session with the software consists of selecting one of the five options, modifying the values of the option-specific parameters and possibly the graph parameters, and then executing a simulation using the current parameter values. The results can be saved in a file or printed.
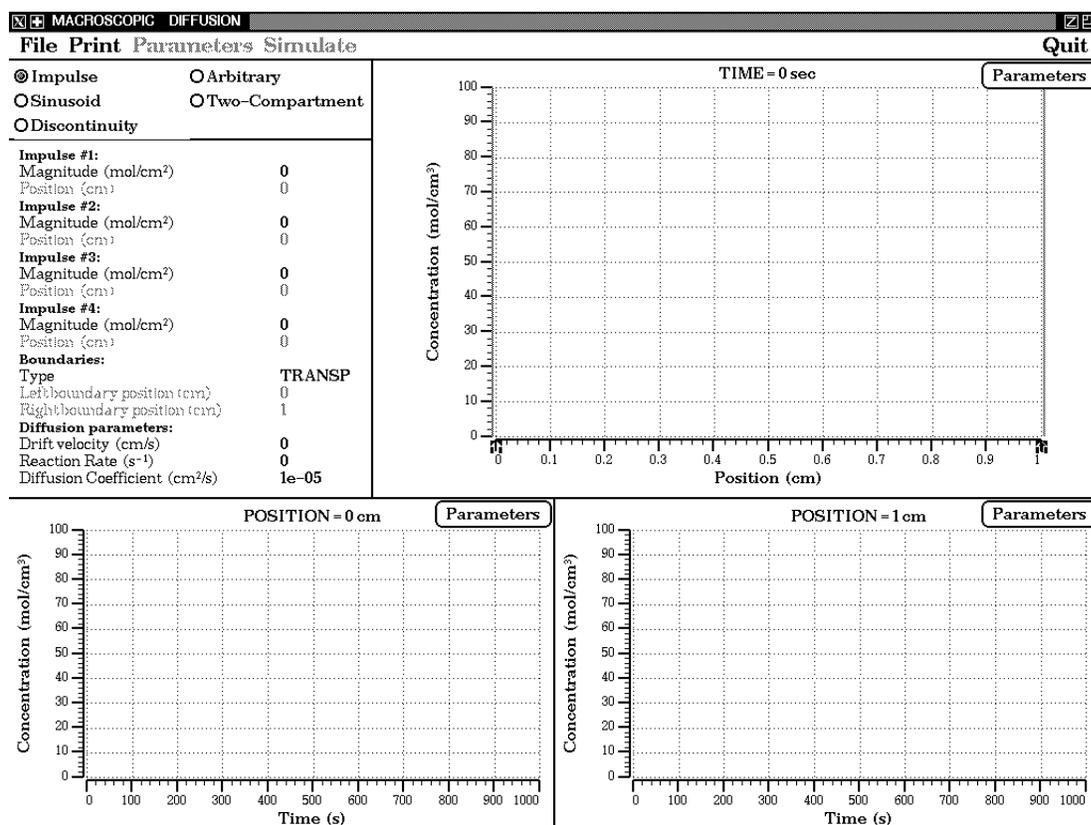
Figure 3.2: Appearance of the workstation screen after the software has been initiated.

3.3.2   Screen Layout

Figure 3.2 shows the appearance of the workstation screen after the software has been initiated. The screen is divided into a number of rectangular regions.

Menubar

The title bar at the top of the screen is generated by the window manager program. Just below this title bar is a *menubar*, containing entries labelled *File*, *Print*, *Parameters*, *Simulate*, and *Quit*. Pointing to one of these labels and clicking a mouse button causes the software to take an action that depends on which menubar entry was selected:

File: Causes the file-handling menu to be posted. File handling is discussed in Section 3.3.4.

Print: Causes the printer menu to be posted so that a printed version of the screen contents may be obtained. Printing is discussed in Section 3.3.4.

Parameters: Returns the software to the Parameters environment when a simulation run has been completed or paused. When the software is already in the Parameters environment, this item is *inactive* and is displayed in gray (as in Figure 3.2).

Simulate: When the software is in the Parameters environment, clicking on this entry causes the Simulation Parameters menu to be posted. The parameters in this menu are discussed below, in the section on running a simulation (3.3.3). A simulation can only be run if a non-trivial initial concentration profile has been specified. In Figure 3.2, no non-zero impulses have been specified, so the initial concentration is identically zero. Thus, the Simulate menubar entry is currently inactive and is printed in gray. When a simulation is running, clicking on this menubar entry *pauses* the simulation, and clicking on it while a simulation is paused causes the paused simulation to *resume* running.

Quit: Exits from the software. To prevent the user from exiting accidentally, a dialogue box is posted asking the user to confirm that he or she "really wants to quit."

Graphs

Three graphs occupy large regions of the screen. The largest one is called the *time graph*, since it displays a plot of concentration, flux, or position versus any other one of these variables at each successive point in time during a simulation. The current *simulation time* is displayed in the title of the graph. In Figure 3.2, since no simulation is running, the simulation time is zero. Since no initial profile has been specified, no points are plotted.

Clicking on the "Parameters" button in the upper right-hand corner of the time graph window causes a *graph parameter menu* to be posted in the graph window. The graph parameters (i.e., which variable is plotted on each axis, and the minimum and maximum axis bounds) can then be modified by selecting the appropriate menu entry. Axis bounds are modified by clicking on the menu entry and then typing in the modified value, followed by a carriage return or another button press on the same entry. The horizontal and vertical variables are implemented as *toggle* variables; clicking on one of these parameters causes it to toggle between two different values. There are *three* possible values for each variable (concentration, flux, and position), but the menu entry will only toggle between the *two* variables that are not displayed on the other axis. Thus, trivial plots of one variable versus itself are avoided. To save time when changes are made to the parameters, the graph is not redrawn until the user exits from the menu (by clicking on the "DONE" entry or clicking outside the menu). The user can force the graph to be redrawn at any time by clicking on the "REDRAW GRAPH" menu entry.

The two smaller graphs at the bottom of the screen are the *position graphs*; each displays a plot of concentration, flux, or time versus any other one of those variables at a fixed position. The parameters for each graph are modified by clicking on the "Parameters" button in the upper right-hand corner, as described for the time graph.

The position corresponding to each position graph is indicated both in the graph title and by the two arrows just below the position axis of the time graph. By default, the positions are initially 0 and 1, as in Figure 3.2. To modify the position for one of the position graphs, the user clicks on the title region of the graph. A *dialog box* is then displayed in the graph window. The dialog box contains a button labelled "DONE" and a *twiddle box* which allows the user to make incremental changes to a variable. To change the value of

the position, the user can either click on the old value and type in a new one or use the twiddle box knobs to increment or decrement the value by a fixed amount. As the value is varied, the arrow on the position axis of the time graph moves to indicate the current value. No changes are permanent, however, until the user clicks on the DONE button. Clicking elsewhere aborts the procedure, and the position retains its previous value.

Option Buttons

In the upper left-hand corner of the screen, just below the menubar, five *radio buttons*, corresponding to the five options, are displayed. In figure 3.2, the Impulse button is highlighted, indicating that this option is currently selected. To change the current option, the user simply clicks on the name of the new option.

Option-Specific Parameters

Just below the option buttons, the option-specific parameters for the selected option are displayed. Often, a change in a parameter value requires that the time graph be redrawn to correctly portray the initial concentration profile. In order to speed up the parameter selection process, the graph is not redrawn every time such a change occurs. Instead, a button labelled "Redraw Graph" is posted in the center of the time graph whenever the graph is not up to date. Clicking on that button causes the graph to be redrawn. Thus, the time graph only needs to be redrawn once after changes to several parameters have been made.

There are several types of parameters for each option. For most parameters, the name, units, and value are displayed. To modify the value of the parameter, the user clicks on the parameter and then types in the new value, followed either by a carriage return or another button press on the same parameter. Clicking a mouse button when the pointer is *not* on the parameter aborts the procedure and cause the parameter to retain its previous value. For parameters that represent positions (i.e., the positions of reflecting boundaries, impulses, or discontinuities), the value may also be modified by using the mouse, in the following manner:

- The user clicks on the parameter and then clicks in the time graph window.

- The cursor changes to a pointing hand when the pointer moves outside the boundaries of the time graph. When the pointer is within the graph boundaries, the cursor vanishes and a vertical line (or a horizontal line, in the unlikely case that position is plotted on the vertical axis) indicating the pointer position appears on the graph and moves with the pointer.

- Clicking any mouse button within the time graph window sets the parameter value to the current pointer position. Clicking outside the time graph window, on the other hand, aborts the procedure, and the parameter retains its previous value.

This method can only be used if position is one of the variables plotted on the time graph and if the time graph is up to date (i.e., if the "Redraw Graph" button is not posted).

The boundary type is indicated by a toggle parameter whose value toggles between "TRANSPARENT" and "REFLECTING." For the Arbitrary and Two-Compartment options, the user can draw an initial profile by clicking on the "DRAW INITIAL PROFILE" parameter and can erase an existing profile by selecting the "ERASE INITIAL PROFILE" parameter. The ERASE parameter does not become active until a profile has been drawn, and it becomes inactive after a profile has been erased. The implementation of the user-drawn profile feature is described in the next section.

User-Drawn Concentration Profile

Representation of an Arbitrary Profile   An arbitrary concentration profile is represented by the software as a sequence of concentration values at an arbitrarily spaced, monotonically increasing sequence of position coordinates. The position and concentration coordinates corresponding to the Arbitrary and Two-Compartment options are stored in *span structures*. A span structure has three members: the array of position coordinates, the corresponding array of concentration values, and a member indicating the number of points in the span.

For computation purposes, the software must determine the initial concentration values at a specified number of *equally* spaced sample points. Such an array is generated from the span data as follows:

- For the Arbitrary option with transparent boundaries, the profile is assumed to be periodic; the period, specified by the user, may be longer than the length of the profile stored in the span structure. The period is divided into 256 equal subintervals. At each position, the initial concentration is determined by *linear interpolation* between the two surrounding points of the span. At points lying beyond the end of the span, the initial concentration is taken to be zero. For example, if the user has drawn a profile of length 1 cm and specified a period of 2 cm, the concentration will be identically zero for half of each period.

- For the Arbitrary option with reflecting boundaries, the distance between the boundaries is divided into a specified number of equally spaced points. The number of points is set by the user, using the Simulate menu, as discussed in Section 3.3.3. At positions that lie within the span, the initial concentration is determined by linear interpolation between the two surrounding points of the span, while at points lying outside the span, the initial concentration is taken to be zero. For the Two-Compartment option, the initial membrane concentration profile is computed in the same manner.

Drawing a Profile   The user can draw an initial profile only if the time graph has concentration plotted on its vertical axis and position on its horizontal axis. When the user clicks on the "DRAW INITIAL PROFILE" parameter (in the Arbitrary or Two-compartment option): the cursor changes to a pencil whenever the pointer is outside the time graph window;

when the pointer is within the time graph window, the cursor vanishes and the pointer position is indicated by vertical and horizontal cross-hairs.

Drawing a profile consists of generating a list of concentration values at a corresponding array of positions. The user selects these points by moving the mouse and clicking any mouse button. As the pointer moves within the window, a "rubber-band" line joins the last point which was selected to the current pointer position. There are two modes of action that the user can use to draw the profile:

- Clicking a mouse button within the time graph window adds a position and concentration value to the coordinate lists and draws a line segment from the previous point to the current point. In this manner, the user can construct a profile made up of line segments.

- Moving the mouse while a mouse button is held down causes a series of points to be added to the coordinate lists. In this manner, the user can construct more complicated curves.

The two methods can be combined in drawing a single profile. As soon as a complete profile has been drawn, the drawing routine terminates and stores the profile data in the appropriate span structure.

When a button is pressed, the position and concentration that are added to the coordinate arrays depend on the pointer location:

- A button press at a position that does not lie to the right of the previous point is ignored, in order to ensure that the user-drawn concentration profile is a single-valued function of position.

- If a button is pressed within the boundaries of the time graph, then the coordinates of the pointer location are added to the list.

- If a button is pressed outside the boundaries of the graph (but still within the graph window), then the point that is added to the list is the point of intersection between the graph boundary and a line from the previous point to the current position. Thus, while a profile is being drawn, it is constrained to lie entirely within the boundaries of the graph.

- By default, the concentration at the left-hand point of the profile is zero. The user can change the first value, however, by making the first button press at the desired vertical location but to the left of the concentration axis.

Clicking outside the time graph window at any time aborts the drawing procedure.

3.3.3   Running a Simulation

Once a non-trivial initial concentration profile exists for the current option, the user can run a simulation. The following criteria are used to determine whether a non-trivial initial profile has been specified:

⊠⊞ MACROSCOPIC DIFFUSION ▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦▦ ⊡⊡
File Print Parameters **Simulate**   **Quit**

◉ Impulse   ○ Arbitrary
○ Sinusoid   ○ Two-Compartment
○ Discontinuity

Impulse #1:	
Magnitude (mol/cm²)	80
Position (cm)	0.3
Impulse #2:	
Magnitude (mol/cm²)	50
Position (cm)	0.6
Impulse #3:	
Magnitude (mol/cm²)	0
Position (cm)	0
Impulse #4:	
Magnitude (mol/cm²)	0
Position (cm)	0
Boundaries:	
Type	TRANSP
Left boundary position (cm)	0
Right boundary position (cm)	1
Diffusion parameters:	
Drift velocity (cm/s)	0
Reaction Rate (s⁻¹)	0
Diffusion Coefficient (cm²/s)	1e−05

TIME = 0 sec   [Parameters]
(Concentration (mol/cm³) vs Position (cm) graph, with impulse arrows labeled (80.000) and (50.000))

POSITION = 0.43 cm   [Parameters]
(Concentration (mol/cm³) vs Time (s) graph)

POSITION = 0.8 cm   [Parameters]
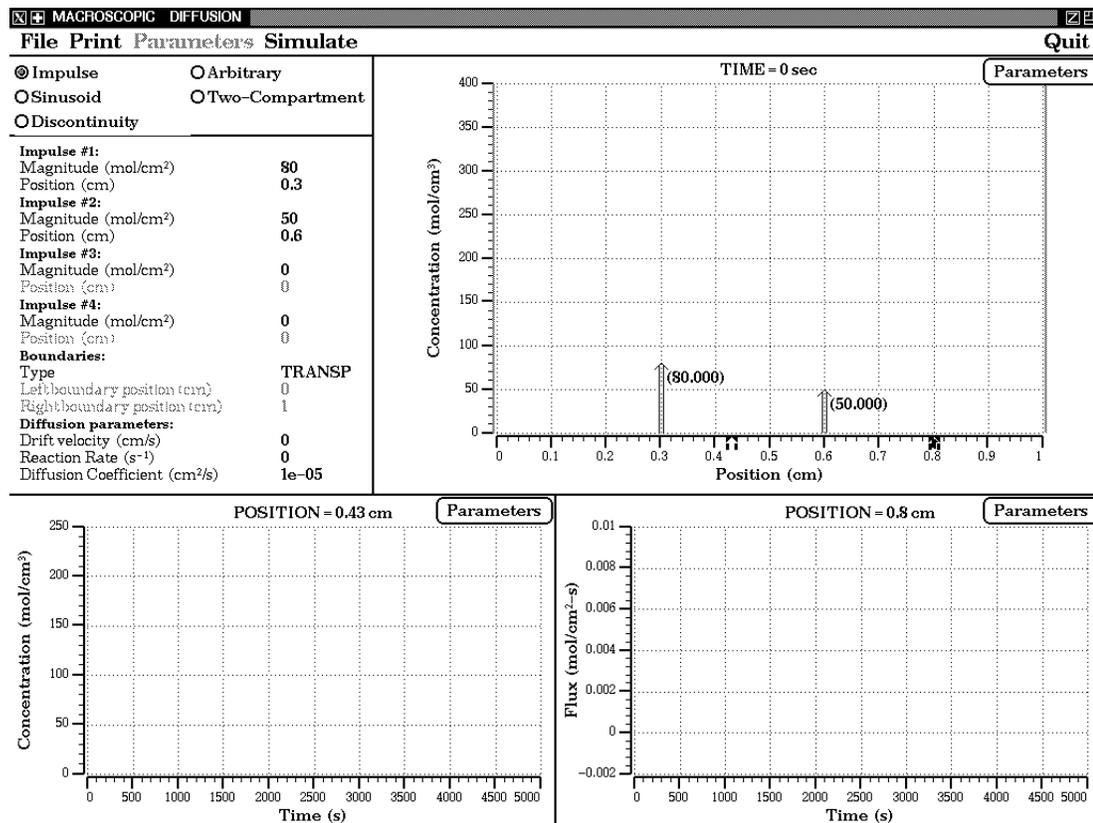(Flux (mol/cm²·s) vs Time (s) graph)

Figure 3.3: Appearance of the workstation screen after an initial concentration profile, consisting of two impulses, has been specified but the simulation has not yet been run.

- For the Impulse, Sinusoid, and Discontinuity options, a non-trivial profile exists if there is at least one impulse, sinusoid, or discontinuity of non-zero magnitude.

- For the Arbitrary and Two-Compartment options, a profile exists if the user has drawn a complete profile (and not erased it).

The "Simulate" menubar entry is active only when an initial profile exists for the current option. Figure 3.3 shows the appearance of the workstation screen when a typical initial profile has been specified but the simulation has not yet been run. In this case, the profile consists of two impulses, which are indicated schematically by tall vertical arrows on the time graph with the magnitude of each impulse displayed in parentheses next to each arrow. The positions corresponding to each position graph have been changed from their default values, and the variables and axis bounds of the position graphs have been modified.

During a simulation run, the concentration and/or flux are computed at successive points in time until the specified final time. At each step, the time is incremented by a specified amount. The final time and the time increment are set by clicking on the "Simulate" entry in the menubar at the top of the screen. The menu which is then posted contains the following entries:

Final time: The time (in seconds) at which the simulation will end. This is the simulation time, *not* actual elapsed time.

Time increment: Amount (in seconds) by which the simulation time is incremented at each step. This increment is different from the integration time increment used in the numerical computation methods.

Number of sample points: For computations involving the Crank-Nicolson algorithm, the number of spatial sample points. This parameter is inactive if another computation method is used. The default value is 128, but it can be set as high as 256 for greater accuracy or as low as 32 for greater speed. The value does not have to be a power of two, but since the region of the workstation screen in which the time graph is plotted is 512 pixels wide, setting this number to be power of two ensures that the sample points will be evenly spaced.

START SIMULATION: Starts the simulation run.

EXIT FROM MENU: Exits from the menu without starting a simulation run. Clicking a mouse button anywhere outside the menu window has the same effect.

When a simulation run is started, the program enters the *Simulate* environment. The graph parameter buttons disappear, the initial concentration profile is replotted if necessary, and all the menubar entries are inactivated except the Simulate entry, whose name changes to "Pause." At each step of the simulation, the following sequence of actions occurs:

- The simulation time is incremented by the specified amount, and the new simulation time is displayed in the title of the time graph.

- The specified time graph parameters (concentration and/or flux) are computed as functions of position at the current time, and the time graph is replotted.

- The specified position graph parameters for each graph are computed at the current time and the specified positions, and a new point is added to each position graph.

Pausing and Resuming a Simulation

Clicking on the Pause entry of the menubar while a simulation is running suspends the simulation. The program enters the *Paused* environment, in which the Print, Parameters, Help, and Quit menubar entries are activated. The name of the Pause entry changes to "Resume"; clicking on this entry causes the paused simulation to resume running. Clicking on the Parameters entry, however, returns the software to the Parameters environment and resets the simulation time to zero. When a simulation is paused, the graph parameter buttons reappear, so that the graph parameters may be modified. The positions corresponding to each position graph, however, can only be modified from the Parameters environment.
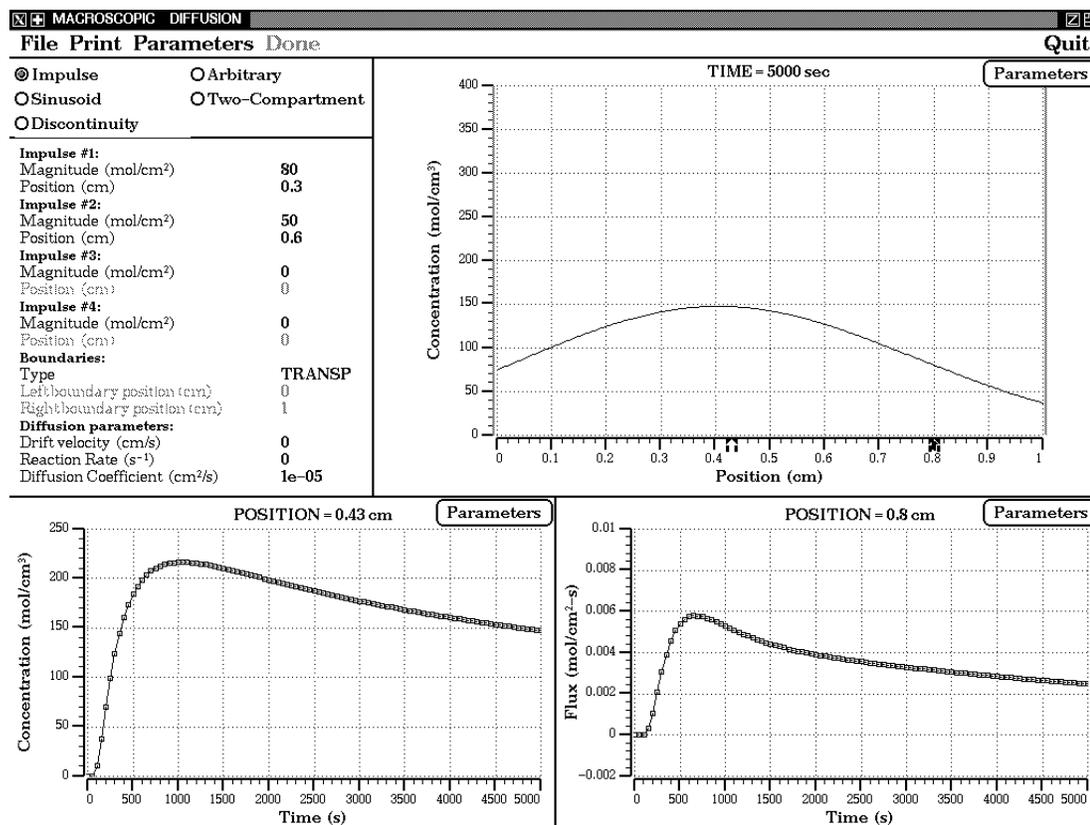
Figure 3.4: Appearance of the workstation screen after a simulation has been continued four times. The software is now in the Done environment; the "Done" menubar entry is inactive since the simulation cannot be continued further.

Continuing a Simulation

When the simulation time has reached the specified final time, the simulation halts. The isolated points plotted on the position graphs are joined by lines, and the software enters the *Continue* environment. In this environment, all the menubar entries are active, and the name of the Simulate entry is changed to "Continue." Clicking on this entry causes a menu similar to the Simulate menu to be posted. By selecting the appropriate entries from this menu, the user can modify the time increment and the new final time; clicking on the "CONTINUE SIMULATION" entry causes the simulation to continue running, from the current time until the specified final time.

A simulation run may be continued up to four times. After the fourth continuation, the software enters the *Done* environment. This environment resembles the Continue environment, except that the name of the Continue menubar entry is changed to "Done" and this entry is inactive, since the simulation cannot be continued further. The user can return to the Parameters environment (by clicking on the appropriate menubar entry) to run a new simulation. Figure 3.4 shows the workstation screen after a simulation has been continued four times.

Summary of a Simulation Run

After setting the option-specific parameters for the current option, the user can set the simulation parameters and *start* a simulation. While a simulation is running, it can be *paused* by clicking on the Pause menubar entry; a paused simulation can be made to *resume* by clicking on the Resume menubar entry. When a simulation run has finished, it may be *continued* up to four times by clicking on the Continue menubar entry and selecting the appropriate entry from the menu. After four continuations, the simulation is *done* and may not be continued again. Clicking on the Parameters menubar entry returns the software to the Parameters environment.

3.3.4   Saving Results

Simulation parameters and results may be preserved in two ways: by obtaining a hardcopy printout of the screen image and by saving the simulation state in a data file, which can be read in by the simulation at a later time.

Printing

To obtain a printed copy of the screen contents, the user simply clicks on the "Print" menubar entry, which is active in all environments except the Simulate environment (i.e., while a simulation is running). Clicking on this entry causes a menu to appear which contains a list of all available printers. The screen contents are sent to the printer selected by the user; alternatively, the user can select the "Default Printer" entry, in which case the user's default printer is used.

File Handling

Clicking on the "File" menubar entry, which is active in the Parameters, Continue, and Done environments, causes the file-handling menu to be posted. Selecting the appropriate entry from this menu allows the user to *read* from a data file, *write* the current state of the software to a data file, or *delete* a file. Selecting any one of these entries cause a *file dialog box* to be posted in the center of the screen. For the diffusion software, all data files have the extension "`.D`". Currently, only one file may be selected at a time.

The following data are written to the file:

- The application name and version ("diffuse, version 1.0"), file name, date and time.

- The current option, followed by the values of all option-specific parameters that have values that the user can modify.

- For the Arbitrary and Two-Compartment options, information about the user-drawn profile (as stored in the appropriate span structure).

- The position graph locations.

- The axis bounds.

- Time graph parameters.

- Simulation parameters (including the simulation time, number of iterations, and number of continuations) and the current environment.

- For cases in which the Crank-Nicolson method is used, the current concentration profile.

- Time graph plotting data.

- Position graph parameters and plotting data.

Thus, the current state of the simulation is written to the data file. A file may be written when the software is in the Parameters, Continue, or Done environment. An error message is posted if the software is unable to write to the specified file. Reading a file into the software results in reading the above items from the specified file and resetting all the parameters. An error message is posted if the specified file could not be opened for reading, if the file is of the wrong format, or if the user tries to read a file when the software is not in the Parameters environment.

3.3.5   Numerical issues

Computations of concentration and flux are performed at each point in time at 256 points equally spaced between the position axis bounds. These results are used to plot the time and space graphs. As indicated in Table 3.1, for the Impulse, Sinusoid, and Discontinuity options with transparent boundaries, the exact solution described in Section 3.2 are implemented directly. For the Arbitrary option with transparent boundaries, the profile is assumed to be periodic in space. The spatial period is one of the option-specific parameters for the Arbitrary option; thus, its value is chosen by the user. However, the period must be chosen to be at least as long as the length of the span of the user-drawn profile. The initial concentration profile is constructed from the span structure as described in Section 3.3.2. The FFT methods is used to compute the concentration at any later time.

For all one-compartment problems with reflecting boundaries, as well as the Two-Compartment option, numerical methods are used to approximate the solutions. The value of Δt used in the numerical methods must be chosen small enough so that the methods are stable. The software determines such values of Δt automatically. However, for a particular choice of parameters, the maximum value of Δt that can be used will often be smaller, and sometimes considerably smaller, than the time increment specified for the simulation run. Note — the increments at which the solution is computed is not the same as the time increment between displayed solutions. Thus, at each step of the simulation, many iterations of the numerical methods must be performed. When the user starts a simulation, the software determines the number of iterations, N, that must be performed at each step. Depending on the value of this number, one of several actions then occurs:

- If $N < 500$, the simulation run proceeds normally.

- If $500 \leq N < 5000$, a message is posted warning the user that the simulation will be "somewhat slow," due to the large number of computations to be performed. The user must click in the message window to continue.

- If $5000 \leq N < 50000$, a more emphatic message is posted, warning the user that the simulation "will be slow." The user can abort the simulation run by clicking on the "Pause" entry in the menubar and then returning to the Parameters environment.

- Finally, if $N \geq 50000$, the software posts a message warning the user that the simulation could not be run because of the huge number of computations required.

3.4 Problems

Problem 3.1 In this problem you will investigate the space-time evolution of solute diffusion from a point source. For all parts of this problem use a single impulse and transparent boundaries. Set the impulse strength to 100 moles/cm^2, place the impulse at position 0.5 cm, and set the drift velocity and the reaction rate to zero. Set the position for the position graphs to 0.55 and 0.6 cm unless indicated otherwise. Set the diffusion coefficient to 10^{-5} cm^2/s and run the simulation for 1000 seconds (simulation time). Obtain a print of the solution on appropriate ordinate scales. The time graph should contain the spatial distribution of concentration at 1000 seconds and position graphs should contain the concentration versus time at the two position. Also obtain a print of the flux versus position and time for the same parameters. Repeat these two steps for a diffusion coefficient of 4×10^{-5} cm^2/s.

a) Describe qualitatively the effect of the change in diffusion coefficient on the spatial distribution of concentration. Be brief.

b) Using the time graph, determine for both values of the diffusion coefficient the maximum amplitude of the concentration versus position and the width of the spatial distribution of concentration at an amplitude that is e^{-1} of its peak value. Explain the numerical values of all four measurements. Be brief and precise; state your assumptions explicitly.

c) For the diffusion coefficient at 10^{-5} cm^2/s, examine the concentration versus time at the two positions 0.55 and 0.6 cm. Describe qualitatively the differences in concentration versus time at the two positions. Be brief.

d) For the diffusion coefficient at 10^{-5} cm^2/s, measure the maximum concentration as a function of time at the two positions and the time of occurrence of this maximum. Explain the values of all four measurements. Be brief and precise; state your assumptions explicitly.

e) Explain the shape of the spatial distribution of flux for a diffusion coefficient of 10^{-5} cm^2/s.

f) Explain the relation between the flux and concentration versus time at location 0.55 cm for a diffusion coefficient of 10^{-5} cm^2/s.

g) Rerun the simulation for a diffusion coefficient of 10^{-5} cm^2/s at positions 0.45 and 0.55 cm. Explain the differences in the flux as a function of time for these two locations.

Problem 3.2 This problem deals with the solution from a point source in the presence of convection. Set the impulse strength to 100 moles/cm^2; place the impulse at position 0.5 cm; set the diffusion coefficient to 10^{-5} cm^2/s, and the reaction rate to zero. Set the position for the position graphs to 0.75 and 0.9 cm unless indicated otherwise.

a) Set the boundary conditions to TRANSPARENT and the drift velocity to zero and run the simulation for 1000 s. Now set the drift velocity to 10^{-4} cm/s and run the simulation again for 1000 s. Describe the effect of the convection on the spatial distribution of concentration. Account quantitatively for the position of the peak of the spatial distribution at 1000 s.

b) Set the boundary conditions to REFLECTING and the drift velocity to zero. Run the simulation until the spatial distribution is no longer a function of time. This is the equilibrium distribution. What is the spatial distribution at equilibrium? Explain your answer.

c) Set the boundary conditions to REFLECTING, the drift velocity to 10^{-4} cm/s, and run the simulation. Describe the effect of convection on the spatial distribution of concentration. Illustrate your description with printed copies of the distribution at characteristic times.

d) With the boundary conditions still set to REFLECTING and the drift velocity 10^{-4} cm/s, determine the equilibrium spatial distribution of concentration. Account quantitatively for this distribution.

e) It is known that the density of air decreases exponentially with distance above the earth's surface. Explain this phenomenon.

Problem 3.3 Two-compartment diffusion was examined in Chapter 3 of the Notes beginning with 4 assumptions:

1. The two compartments are well-mixed so that the concentrations of solute n are uniform and have values at time t of $c_n^1(t)$ and $c_n^2(t)$.

2. Solute particles are conserved, e.g., there is no chemical reaction present that either creates or destroys particles.

3. The membrane is sufficiently thin and the number of solute particles contained in the membrane at any time is negligibly small.

4. The membrane is sufficiently thin that at each instant in time the concentration profile in the membrane is in steady state.

This problem concerns the conditions for the validity of assumptions 3 and 4. Specifically, you will explore the effect of bath dimensions on two-compartment diffusion without making these two assumptions.

   In all parts of the problem, use the *Two-compartment* mode of the software. Set the membrane **Width** to 0.01 cm, and the concentration of **Bath #1** to 70 and **Bath #2** to 10 mol/cm^3. Leave the **Drift velocity** and **Reaction rate** at 0 and the **Diffusion Coefficient** at 10^{-5} cm^2/s. Set the parameters of the plot of concentration versus position so that the membrane and a little of each bath are visible on the screen — e.g., display a portion of the bath that is 0.0005 cm to the left and right of the membrane. Note that the left edge of the membrane is at a position of 0 cm. Using DRAW INITIAL PROFILE, draw the initial concentration in the membrane. It is a bit tricky, but after a few trials you should get it. Make sure all ordinate scales on all plots are 0 to 100 mol/cm^3. Keep these parameters fixed throughout this problem. Initially set the simulation parameters to be a **Final time** of 5 s, a **Time increment** of 0.2 s, and the **Number of sample points** at 128. You may wish to adjust these parameters to observe different aspects of the diffusion processes.

   For each of the pairs of bath widths — Bath #1 = 1 cm, Bath #2 = 1 cm; Bath #1 = 0.1 cm, Bath #2 = 0.1 cm; Bath #1 = 0.01 cm, Bath #2 = 0.01 cm; Bath #1 = 0.01 cm, Bath #2 = 0.05 cm; Bath #1 = 0.001 cm, Bath #2 = 0.001 cm; — answer the following questions.

   a) Assess the validity of assumption 4.

        i) Make rough estimates of both the steady-state (τ_{ss}) and equilibrium (τ_{eq}) time constants from the computations.

        ii) Estimate the same two time constants from the developments in Chapter 3 of the Notes.

        iii) What is your conclusion based on your computations and your estimates of time constants?

   b) Assess the validity of assumption 3.

        i) Before you do the computation, make an estimate of the final concentration in each bath. Then do the computation, and check your initial estimates against the computed values

        ii) If they differ, explain the basis of the difference.

        iii) How good is the assumption that the quantity of solute in the membrane is negligible? If you decide that the quantity of solute in the membrane is not negligible, design a simulation experiment to test your conclusion.

   e) Are the bath concentrations exponential functions of time? Explain.

Problem 3.4 Some problems in diffusion with a reflecting boundary can be solved by using the solution for a transparent boundary and the method of images to match the reflecting boundary condition. This problem explores the successes and pitfalls of this method. In all parts of this problem, set the drift velocity to zero, the reaction rate to zero, and the diffusion coefficient to 10^{-5} cm^2/s unless state otherwise.

a) Use REFLECTING boundaries, and an initial impulse of concentration of strength 100 moles/cm^2 located at 0.2 cm. Run the simulation for 1000 s and obtain a print of the spatial distribution of concentration at time 1000 s and the concentration versus time at locations 0 and 0.3 cm.

b) At a reflecting boundary, the flux must be zero. Change the boundary condition to TRANSPARENT and determine the parameters of two impulses: one to match the left boundary condition and another to independently match the right boundary condition. Run the simulation again and compare with the results in part a). Does this "method of images" work exactly? Explain.

Problem 3.5 Diffusion from an initial sinusoidal concentration distribution gives important insights into the space-time evolution of diffusion processes. In all parts of this problem, use a drift velocity of zero, a reaction rate of zero, and a diffusion coefficient of 10^{-5} cm^2/s unless state otherwise.

a) Use an initial sinusoidal concentration distribution with amplitude 50 moles/cm^2 and a spatial frequency of 1 cycle/cm. Run the simulation for 1000 s and print the spatial distribution of concentration at 1000 s and the concentration versus time at 0.25 and 0.75 cm. Repeat this procedure for sinusoids with the same amplitudes but the following spatial frequencies: 3, 5, and 7 cycles/cm. Summarize your results both qualitatively (in words) and then quantitatively (with suitable calculations).

b) Construct a periodic waveform from four sinusoids with the following amplitudes (moles/cm^2) and spatial frequencies (cycles/cm): 105, 1; 35, 3; 21, 5; 15, 7. Run the simulation and observe the spatial distribution of concentration. Summarize your results and relate them to results of part a).

c) Switch to the Arbitrary initial distribution option and set the boundary conditions to reflecting. Using the mouse draw an arbitrary, preferably jagged, initial profile. Run the simulation and watch the spatial distribution of concentration change. Summarize your results. What is the effect of diffusion on the spatial distribution?

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