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A Computational Study of Facilitated Diffusion Using The Boundary Element Method

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Abstract

The steady-state equations of carrier-mediated transport are solved numerically by means of the boundary element method and the limiting cases of fast reaction, fast diffusion and excess of carrier are studied critically. It is confirmed that the facilitation factor, defined as the ratio between the total flux of solute to that in the case of absence of carrier, shows a maximum for an optimal value of the equilibrium constant K of the solute-carrier reaction. Also, there appears to be a broad range of K values where neither the fast reaction assumption (which is valid when the reaction proceeds much faster than the diffusion) nor the fast diffusion assumption (valid in the opposite case) constitute good approximations.

1. Introduction

Facilitated diffusion [1] is a carrier-mediated transport process in which a solute (S) diffuses through a membrane and reacts homogeneously with a ligand (L) contained in the membrane to form a complex (LS)

$$L + S \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} LS. \tag{1}$$

This phenomenon has become a current topic in several fields because it represents a step further to a classical passive transport system. In membrane biophysics the transport of oxygen is known to occur with the mediation of hemoglobin or myoglobin [2–5]. In chemical engineering, carrier-mediated diffusion is a promising separation technique which combines high selectivity (because of the specific carrier-solute reactions) with important facilitation factors [6–9]. And finally, in applied mathematics facilitated diffusion also constitutes an attractive subject because of the nonlinear character of the reaction-diffusion equations ruling the problem [10, 11]. For instance,

the flux of solute has a nonlinear dependence on the concentration difference across the membrane, opposing to the case of passive diffusion.

The boundary element method (BEM) deals with the problem of solving a system of nonlinear differential equations within a given domain by transforming it into an equivalent integral equation system at the boundary of the domain. It was originally developed by Banerjee and Butterfield [12] and Brebbia and coworkers [13–15] for heat transfer and electrostatics problems [16–20], but it has recently found applications to mass transport phenomena [21–23]. Our aim here is to show that BEM computational techniques can also be of interest for the solution of the reaction-diffusion equations of facilitated diffusion. In particular, the present work will make use of the BEM in a problem of considerable practical importance: the range of validity of the assumptions of fast reaction, fast diffusion and excess of carrier [1–7].

Equations of facilitated diffusion

The process of facilitated diffusion [1] through a liquid membrane of thickness d is schematically depicted in Figure 1. Transport is considered to occur along the positive x direction. A concentration c_T of carrier is dissolved in the membrane phase, and confined there because of its negligible solubility in the external aqueous solutions. The concentration of solute in the source and receiving solutions is c_{Ss} and c_{Sr}, respectively. Inside the liquid membrane, the solute concentration is lower than in the external solution because of the reduced solubility of the solute in the organic phase. In particular, the interfacial concentrations of solute $c_S(0)$ and $c_S(d)$ are lower than c_{Ss} and c_{Sr}, respectively, and determined by the partition coefficient [1] of the solute. Since we are interested here in the carrier-mediated transport through the membrane, we consider that $c_S(0)$ and $c_S(d)$ are known.

During diffusion through the membrane phase, the solute S reacts with the ligand L according to reaction (1) and forms a complex LS which also diffuses in the positive x direction. The concentration of solute bound to the ligand can be much higher than the free solute concentration due to the larger solubility of the complex in the membrane phase. This additional transport mechanism (i.e., the carrier-mediated diffusion) increases the solute flux and can lead to important facilitation factors, defined as the ratio between the total flux of solute (i.e., free plus bound solute) to that in the case of absence of carrier [24]

$$F = \frac{\left(-D_S \frac{dc_S}{dx} - D_{LS} \frac{dc_{LS}}{dx} \right)_{c_T \neq 0}}{\left(-D_S \frac{dc_S}{dx} \right)_{c_T = 0}}. \tag{2}$$

In order to compare the diffusion and reaction rates, the Damköhler number [24] is introduced as $Da = k_{-1} d^2/D$, where D is a typical diffusion coefficient of the solute and k_{-1} is the reverse rate constant of the solute-carrier reaction (1). (This dimensionless number can also be defined in terms of the forward rate constant k_1 but this is not

interesting in our case.) Thus, the limits of fast diffusion and fast reaction correspond to low and high Damköhler numbers, respectively [1, 7, 24]. In the first case, the transport through the membrance occurs as if no carrier were present, and therefore the facilitation factor reduces to one. In the second case, the concentration of the different species are related everywhere by

$$K = \frac{c_{LS}}{c_L c_S} \tag{3}$$

where $K \equiv k_1/k_{-1}$ is the equilibrium constant of reaction (1). However, there are still some differences with respect to the case of heterogeneous solute-carrier reaction.

The study of facilitated diffusion involves the solution of a boundary value problem. In particular, the three continuity equations for the steady-state transport through the membrane [1]

$$D_S \frac{d^2 c_S}{dx^2} = k_1 c_S c_L - k_{-1} c_{LS} \tag{4a}$$

$$D_L \frac{d^2 c_L}{dx^2} = k_1 c_S c_L - k_{-1} c_{LS} \tag{4b}$$

$$D_{LS} \frac{d^2 c_{LS}}{dx^2} = -(k_1 c_S c_L - k_{-1} c_{LS}) \tag{4c}$$

must be solved under the boundary conditions

$$c_S = c_S(0), \quad p_L = p_{LS} = 0 \quad \text{at } x = 0, \tag{5a}$$

$$c_S = c_S(d), \quad p_L = p_{LS} = 0 \quad \text{at } x = d, \tag{5b}$$

and

$$\int_0^d (c_L + c_{LS}) dx = c_T d. \tag{6}$$

Here D_j, c_j and $p_j \equiv dc_j/dx$ denote the diffusion coefficient, concentration and concentration gradient of species j ($j = S$, L, and LS), respectively. The boundary conditions indicate that the carrier is confined to the membrane phase, and equation (6) holds indeed because the total carrier flux (i.e., free and bound carrier) is constant and therefore the specification of the carrier fluxes as zero at $x = 0$, already implies that they are also zero at $x = d$ (i.e., only three of the four boundary conditions related to the carrier are independent, cp. Fig. 1).

In most of the situations of practical interest, the carrier and its complex are of about the same size, and then the assumption $D_L \approx D_{LS}$ can be used with negligible error. In

this case, equation (6) simplifies to the local condition

$$c_L(x) + c_{LS}(x) = c_T, \quad 0 < x < d, \tag{7}$$

which allows to work with concentrations c_S and c_L only and reduce in one the number of differential equations. Still, no exact analytical solution to the above equation system exists, and thus the three approximated solutions based on the limiting cases of fast reaction ($Da \gg 1$), fast diffusion ($Da \ll 1$), and excess of carrier ($c_L \gg c_{LS}, c_S$) have become very popular [1, 7].

Though these limiting cases constitute fairly good approximations in many practical applications [1], the need of numerical solution often arises. Numerical solutions can serve not only to deal with situations where these cases do not apply [25] but also to predict theoretical optimal regimes of facilitated transport [24] and explore the consequences of the coupling between the reaction-diffusion phenomena with a convective flow [26, 27]. The computational techniques employed in these studies are the method of orthogonal collocation on finite elements [25] and a combined finite element and boundary element method [26]. More recently, lattice Boltzmann computations for general reaction-diffusion equations have also been attempted [28]. However, as far as we know, this work is the first implementation of the BEM to the problem of facilitated diffusion.

Boundary element method

Lately, Ramachandran [21, 22] has presented a BEM procedure for a single ordinary differential equation of the form

$$\frac{d^2c}{dx^2} = f(x, c, p) \tag{8a}$$

where c is a concentration, $p \equiv dc/dx$ is the concentration gradient, and f is an arbitrary function of x, c and p. The numerical method employed here can be considered as a generalization of this procedure to a system of reaction-diffusion equations

$$\frac{d^2c_j}{dx^2} = f_j(x, c_S, c_L, p_S, p_L), \quad j = S, L. \tag{8b}$$

First, we choose a set of n nodal points $x_1 = 0, x_2, \ldots, x_n = d$, defining a nonuniform grid, and take two convenient weighting functions $w_1(x)$ and $w_2(x)$ satisfying the condition [22]

$$\frac{d^2w_k(x)}{dx^2} = 0, \quad k = 1, 2. \tag{9}$$

Multiplication of equation (8b) by w_k ($k = 1, 2$), and integration between two consecutive nodal points, x_i and x_{i+1}, yields

$$\int_{x_i}^{x_{i+1}} w_k \frac{d^2 c_j}{dx^2} dx = -w_k(x_i)p_j(x_i) + w_k' c_j(x_i) + w_k(x_{i+1})p_j(x_{i+1}) - w_k' c_j(x_{i+1})$$

$$= \int_{x_i}^{x_{i+1}} w_k f_j dx \quad i = 1, \ldots, n-1; \quad j = L, S; \quad k = 1, 2 \tag{10}$$

where the left hand side has been integrated twice by parts, and $w_k' \equiv dw_k/dx$.

In a general formulation, the boundary conditions for this problem can be written as four linear relationships between c_j and p_j ($j = L, S$) at both ends of the membrane

$$L_{1j}c_j(x_1) + L_{2j}p_j(x_1) + L_{3j} = 0, \quad j = L, S \tag{11a}$$

$$R_{1j}c_j(x_n) + R_{2j}p_j(x_n) + R_{3j} = 0, \quad j = L, S \tag{11b}$$

where L_{1j}, L_{2j}, L_{3j}, R_{1j}, R_{2j}, and R_{3j} are constants. Thus, equations (10) and (11) constitute a system of $2*2(n-1)+4 = 4n$ relationships between the $4n$ independent variables ($c_j(x_i)$ and $p_j(x_i)$ for $j = L$, S and $i = 1, \ldots, n$). The solution of this system requires an initial guess for the $4n$ independent variables. Then, Newton-Raphson method is applied to obtain the corrections to the values of $c_j(x_i)$ and $p_j(x_i)$ [22]. Whenever necessary, the integrals in equations (10) are calculated via gaussian quadratures by using polynomial approximations for $c_j(x)$ and $p_j(x)$ in every subinterval $x_i \leq x \leq x_{i+1}$ [22, 23]. The process is iterated until the corrections are smaller than some previously determined tolerance.

It is interesting to note that some methods need an initial guess relatively close to the exact solution to converge. On the contrary, the BEM can reach the right solution even with poor starting guesses.

Results and discussion

As stated in the Introduction, the results here presented, and hence the values considered for the system parameters, are intended to show the conditions of validity of the assumptions of fast reaction, fast diffusion, and excess of carrier rather than simulate a particular experimental situation. In particular and unless otherwise stated, we have chosen $c_S(0) = c_T = 10^{-5}$ mol cm^{-3}, $c_S(d) = 0$, $D_S = D_L = D_{LS} = 10^{-5}$ cm^2 s^{-1}, $d = 10^{-2}$ cm, and $k_{-1} = 10^5$ s^{-1}.

Figure 2 shows the facilitation factor F as a function of the equilibrium constant K of reaction (1). It can be seen that there is a broad range of values ($10^4 < K$ (cm^3 mol^{-1}) $< 10^7$) where neither the fast reaction nor the fast diffusion constitute good approximations. The computed values for F in the above limits agree with the analytical expressions given in the literature (see equations (15.3–13) and (15.3–19) in reference [1]). Also, F takes its maximum value for an optimal value of K

tion between two consecu-

$x_{i+1}) - w'_k c_j(x_{i+1})$

; $k = 1, 2$ (10)

, and $w'_k \equiv dw_k/dx$.

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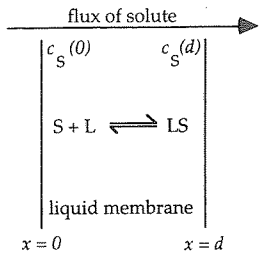

Fig. 1: Schematic representation of carrier-mediated transport (facilitated diffusion) through a liquid membrane.

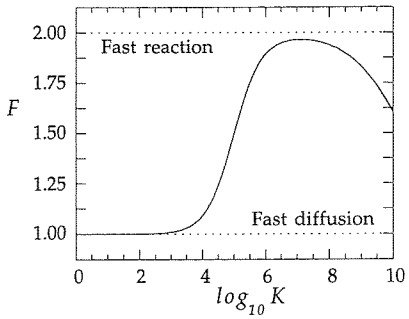

Fig. 2: Facilitation factor vs. the reaction equilibrium constant.

($K \approx 10^7\,\mathrm{cm^3\,mol^{-1}}$ in Fig. 2). This fact has been discussed previously [24], and can be easily understood from the definition $K \equiv k_1/k_{-1}$. For low values of K, the amount of complex is so small that the diffusion is not facilitated at all. However, very high values of K also inhibit facilitation, since in this case the complex is very stable, and does not dissociate to release the solute (see Figs. 1 and 2). The maximum value of F increases with concentration c_T.

The concentration profiles corresponding to fast reaction appear in Figure 3. At both sides of the center of the membrane, the profiles are linear which means that the reaction equilibrium has been achieved there. At the membrane center, carrier-solute association predominates over dissociation but still equation (3) constitutes a good approximation. Thus, the solute diffuses to the membrane center and reacts there with the carrier to form a complex species which diffuses then from the center towards the receiving solution. At the interface with this solution, the reaction is reversed. The carrier liberated diffuses back to the membrance center, where it reacts to form the complex, and so on. In the case of fast diffusion, the solute behaves as if no carrier where present and, therefore, its concentration profile is simply linear, while all the carrier is in free form. Note that the reaction front is located at $x = d/2$ because $c_S(0) = c_T$. When $c_S(0) > c_T (c_S(0) < c_T)$ the reaction front moves to the left (right).

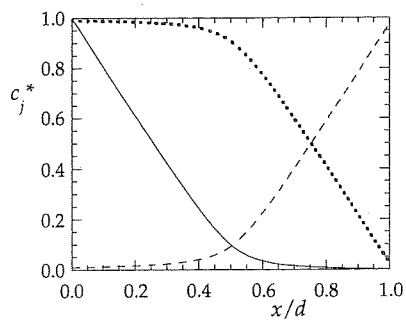

Fig. 3: Concentration profiles through the membrane for $K = 10^7\,\mathrm{cm^3\,mol^{-1}}$ (fast reaction limit) and $k_1 = 10^{12}\,\mathrm{cm^3\,mol^{-1}\,s^{-1}}$. Here, $c_S^* = c_S/c_S(0)$(—), $c_L^* \equiv c_L/c_T$(– –), and $c_{LS}^* \equiv c_{LS}/c_T$(· · · · ·).

Figure 4 gives F as a function of the total carrier concentration c_T under conditions of excess of carrier. We see that diffusion can increase considerably with c_T ($F \approx 10$–10^2) and that this increase starts earlier for the higher values of K. Again, the computed values agree with the analytical expression for F derived under the condition of excess of carrier (equations (15.3–26) in ref. [1]). However, this agreement gets poorer for higher values of K since the chemical reaction proceeds then so fast that the carrier can no longer be in excess. Indeed, the differences between the values derived from equations (15.3–26) in reference [1] and those in Figure 4 are of about 10% for $\log_{10}(c_T/c_S(0)) = 3$ and $K = 10^4\,\mathrm{cm^3\,mol^{-1}}$.

Figure 5 shows the concentration profiles for the case of excess of carrier. Note that c_L is almost constant and larger than c_S and c_{LS} through most of the membrane. Since $Da = 10^6$ here, and the reaction layer thickness is approximately given by $d/(Da)^{1/2}$, the grid must include many points close to the membrane/solution interfaces, as usual in those transport phenomena where two different spatial zones coexist [29–31]. In

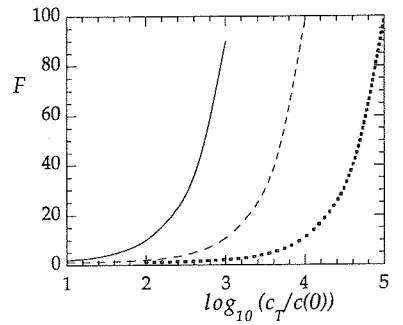

Fig. 4: Facilitation factor vs. total carrier concentration for different values of the equilibrium constant $K = 10^4$ (——), 10^3 (– – –) and $10^2\,\mathrm{cm^3\,mol^{-1}}$ (· · · · ·).

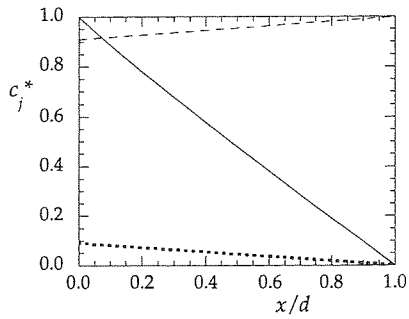

Fig. 5: Concentration profiles through the membrane for $K = 10^4\ \mathrm{cm^3\ mol^{-1}}$ and $c_T/c_S(0) = 10^2$ (excess of carrier). Here, $c_S^* = c_S/c_S(0)$(—), $c_L^* \equiv c_L/c_T$(– –), and $c_{LS}^* \equiv c_{LS}/c_T$(· · · · ·).

particular, we have used here the following grid on $n = 41$ points:

$$x_i/d = \begin{cases} 2(i-1)\,10^{-7}, & 1 \le i \le 6 \\ (1+1.8(i-6))10^{-6}, & 7 \le i \le 11 \\ (1+1.8(i-11))10^{-5}, & 12 \le i \le 16 \\ 0.1(i-16), & 17 \le i \le 21 \\ 1 - x_{n+1-i}/d, & 22 \le i \le 41 \end{cases} \tag{12}$$

Though the c_S profile seems to be linear in Figure 5, this is not strictly true because there is a reaction layer near to the membrane interface. This fact is shown in Figure 6, where some nodal points in the neighborhood of the left interface are depicted in a suitable scale: there are 16 nodal points between $x = 0$ and $x/d = 10^{-4}$, although the first ones are too close to distinguish them. Several runs using different grids showed that the critical factor to achieve convergence is to take the distance between consecutive nodal points to be of the same order of magnitude as the reaction layer thickness. If

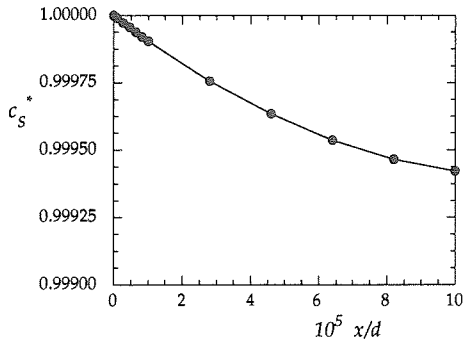

Fig. 6: Concentration profile c_S^* in the vicinity of left interface for the same case as in Figure 5.

this condition is satisfied, convergence is achieved virtually in all realistic cases, and the results are independent of the number and distribution of the additional nodal points.

To test further the validity of our numerical results, a comparison between the values obtained here for the facilitation factor and those reported by Kemena *et al.* [24] using a standard numerical procedure was made. A good agreement (better than 8% for all the cases studied) between our results and those in Figure 1 of reference [24] was found.

The BEM algorithm was written in C programming language, and run on a HP 9000/330 computer. Convergence in the Newton-Raphson procedure was attained after some 8–15 iterations in all cases. The computer code, which is available on request, can also be used on a PC working under DOS.

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