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REACTION RATE PROFILES IN MEMBRANE SYSTEMS

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SUMMARY

Some of the simplifying assumptions involved in obtaining an expression for chemical reaction rate profiles in membrane, presented in a recent interesting paper by BLUMENTHAL AND KATCHALSKY[1], are delineated, such that one may include coupling between fluxes of different species. It is shown that under the approximation of neglect of nonlinear terms, inclusion of coupling of fluxes does not alter the general structure of differential equation for reaction rate. A perturbation procedure is suggested to incorporate the variation of mobilities as function of position variable.

INTRODUCTION

In a recent interesting paper, BLUMENTHAL AND KATCHALSKY[1] have considered a model for facilitated diffusion in which a nonelectrolyte component diffuses through a membrane and simultaneously undergoes an association–dissociation reaction with a carrier to form a complex. Essentially their analysis involves consideration of equations of continuity for the three species participating in a chemical reaction of the type

$$\alpha + \beta \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \gamma \tag{1.1}$$

taking place in the membrane region and derivation of a differential equation valid for stationary states, for the rate of reaction, J_r, *viz.*,

$$\mathrm{d}^2 J_r/\mathrm{d}x^2 = \lambda^{-2} J_r \tag{1.2a}$$

$$\lambda^{-2} = \frac{k_1\overline{C}_\alpha + k_2}{D} + \frac{k_1\overline{C}_\beta}{D_\alpha} \tag{1.2b}$$

$$J_r(x) = k_1 C_\alpha(x) C_\beta(x) - k_2 C_\gamma(x) \tag{1.2c}$$

$$D = D_\beta = D_\gamma \tag{1.2d}$$

k_1 and k_2 are the rate constants for association and dissociation reactions respectively. $C_\alpha(x)$, $C_\beta(x)$ and $C_\gamma(x)$ are the concentrations at location x inside the membrane of the species α, β and γ respectively, while $\overline{C}_\alpha$, $\overline{C}_\beta$ and $\overline{C}_\gamma$ are the concentrations corresponding to the equilibrium of the reaction satisfying the relation

$$J_r = 0 = k_1\overline{C}_\alpha\overline{C}_\beta - k_2\overline{C}_\gamma \tag{1.3}$$

The parameter λ is identified as relaxation distance, independent of the position variable x. The ratio of λ to the thickness of diffusion barrier enters as a parameter in BLUMENTHAL AND KATCHALSKY's solution of Eqn. 1.2a.

In obtaining their fundamental differential Eqn. 1.2a for J_r, BLUMENTHAL AND KATCHALSKY have assumed that the flows of components obey Fick's law locally and that coupling between flows of different species may be neglected. It is also assumed that the diffusion coefficients of free (D_β) and associated carrier (D_γ) have the same value D, and that they are independent of the position variable x. One additional approximation involved in the derivation of Eqn. 1.2a is that one may write

$$J_r = k_1\overline{C}_\alpha\delta C_\beta + k_1\overline{C}_\beta\delta C_\alpha - k_2\delta C_\gamma$$

$$\delta C_\alpha(x) = C_\alpha(x) - \overline{C}_\alpha \tag{1.4}$$

where a term $k_1\delta C_\alpha\delta C_\beta$ is neglected. One obtains by elementary operations from Eqn. 1.2c that

$$\frac{\mathrm{d}^2J_r}{\mathrm{d}x^2} = k_1\{C_\alpha(x)C_\beta'' + C_\beta(x)C_\alpha'' + 2C_\alpha'C_\beta'\} - k_2C_\gamma'' \tag{1.5}$$

$$C_\alpha' = \frac{\mathrm{d}C_\alpha}{\mathrm{d}x} = \frac{\mathrm{d}(\delta C_\alpha)}{\mathrm{d}x} \qquad C_\alpha'' = \frac{\mathrm{d}^2C_\alpha}{\mathrm{d}x^2} \tag{1.6}$$

Eqn. 1.5 is correct subject only to the validity of Eqn. 1.2c and Eqn. 1.2a is an approximation derivable by invoking the assumptions mentioned above.

Our objective in this communication is to derive the differential equation for J_r, when coupling between flows are included. We shall also analyse the problem when mobilities are functions of position. Interest in this work arose, since the derivation of Eqn. 1.2a and its solution is of general interest for membrane transport and not necessarily restricted to the specific model considered in detail by BLUMENTHAL AND KATCHALSKY for carrier transport. In addition one may note that Eqn. 1.2b was derived by utilising Eqn. 16 of BLUMENTHAL AND KATCHALSKY's paper, namely that the second derivatives of concentrations of the three species are proportional to each other. Our method presented in the next section, involves similar technique. Impositions of the assumptions mentioned above in our final results lead to the Eqns. 1.2a and 1.2b. Summarising the results of our method, it follows that so long as one may neglect the term $k_1\delta C_\alpha\delta C_\beta$, retention of the off-diagonal elements of diffusion coefficient matrix, leads to a differential equation of the form

$$\frac{\mathrm{d}^2J_r}{\mathrm{d}x^2} = \theta J_r \tag{1.7}$$

provided that the flows of species other than those participitating in the reaction are neglected. θ is a parameter independent of the position variable x. An explicit expression for θ is presented in the next section. θ becomes a function of x, if one utilises Eqn. 1.5, or, when one regards mobilities as functions of position. Under the conditions when Eqn. 1.7 is valid, and when θ is a constant, the solutions of BLUMENTHAL AND KATCHALSKY of the differential equation (Eqn. 1.2a) can be utilized by replacement of λ^{-2} by θ.

The problem of relaxing the assumption that cross-diffusional coefficients are independent of position variable x is considered under PERTURBATION THEORY. There are insufficient number of equations at our disposal when one retains Eqn. 2.2. Since the variation of elements of diffusion matrix with position arises due to variation of concentrations with position, we adopt the partial frictional coefficient formalism and resort to a perturbation procedure.

CONSTANT DIFFUSION COEFFICIENTS

Under conditions of stationary flows across a diffusional barrier (membrane), the diffusional fluxes and reaction rates are related by equations of continuity:

$$J_r(x) = -\mathrm{d}J_\alpha/\mathrm{d}x = -\mathrm{d}J_\beta/\mathrm{d}x = \mathrm{d}J_\gamma/\mathrm{d}x \qquad (2.1)$$

where J_α, J_β and J_γ are the fluxes of the three components participating in the reaction presented in Eqn. 1.1. By a generalisation of Fick's law, one may assume the validity of the expression locally,

$$J_\alpha(x) = -\sum_{j=1}^{n} D_{\alpha j}\frac{\mathrm{d}C_j}{\mathrm{d}x} \qquad (2.2)$$

If the system has n components, one has n such equations. In matrix notation, one may write these n equations as

$$-\vec{J} = D\vec{C'} \qquad (2.3)$$

The diffusion matrix D has elements D_{ij} $(i,j = 1, \ldots n)$. $\vec{J}$ and $\vec{C'}$ are n-component vectors. The elements of the former are the matter fluxes of the various species and those of the latter are derivatives of concentrations. If the species present are the ones that react chemically (α,β,γ), the reaction rate at steady state can be written as

$$J_r\vec{U} = D\vec{C''} + D'\vec{C'} \qquad (2.4)$$

where

$$\vec{U} = \begin{vmatrix} 1 \\ 1 \\ -1 \end{vmatrix} \qquad \vec{C''} = \begin{vmatrix} C_\alpha'' \\ C_\beta'' \\ C_\gamma'' \end{vmatrix} \qquad D = \begin{vmatrix} D_{\alpha\alpha} & D_{\alpha\beta} & D_{\alpha\gamma} \\ D_{\beta\alpha} & D_{\beta\beta} & D_{\beta\gamma} \\ D_{\gamma\alpha} & D_{\gamma\beta} & D_{\gamma\gamma} \end{vmatrix} \qquad (2.5)$$

In Eqn. 2.4 D' is a matrix whose elements are the derivatives (with respect to x) of the elements of D. We assume in this section the constancy of elements of D, so that all elements of D' are identically zero. Defining

$$C_\beta'' = C_\alpha''Q \qquad C_\gamma'' = C_\alpha''P \qquad (2.6)$$

the first of Eqns. 2.4 can be written as

$$J_r = \{D_{\alpha\alpha} + D_{\alpha\beta}Q + D_{\alpha\gamma}P\}C_\alpha'' \qquad (2.7)$$

On combining the linearised form of Eqn. 1.5 with Eqn. 2.6 one obtains

$$\frac{\mathrm{d}^2J_r}{\mathrm{d}x^2} = \{k_1(\overline{C_\beta} + Q\overline{C_\alpha}) - k_2P\}C_\alpha'' \qquad (2.8)$$

Eqns. 2.7 and 2.8 considered together lead to Eqn. 1.7 where

$$\theta = [k_1(\overline{C_\beta} + Q\overline{C_\alpha}) - k_2P]\,\{D_{\alpha\alpha} + D_{\alpha\beta}Q + D_{\alpha\gamma}P\}^{-1} \qquad (2.9)$$

It only remains to write down the explicit forms of P and Q defined in Eqn. 2.6. As may be easily verified from Eqns. 2.4, we have

$$\begin{aligned} P &= [(D_{\alpha\alpha} - D_{\beta\alpha})(D_{\gamma\beta} + D_{\alpha\beta}) + (D_{\beta\beta} - D_{\alpha\beta})(D_{\alpha\alpha} + D_{\gamma\alpha})]/F \\ Q &= [(D_{\alpha\gamma} - D_{\beta\gamma})(D_{\alpha\alpha} + D_{\gamma\alpha}) - (D_{\alpha\alpha} - D_{\beta\alpha})(D_{\gamma\gamma} + D_{\alpha\gamma})]/F \\ F &= -(D_{\beta\beta}D_{\gamma\gamma} + D_{\beta\beta}D_{\alpha\gamma} + D_{\alpha\gamma}D_{\gamma\beta} + D_{\alpha\gamma}D_{\alpha\beta}) + D_{\alpha\beta}D_{\gamma\gamma} + D_{\beta\gamma}D_{\gamma\beta} \\ &\quad + D_{\beta\gamma}D_{\alpha\beta} + D_{\alpha\beta}D_{\alpha\gamma} \end{aligned} \tag{2.10}$$

The constancy of θ is an immediate consequence of the assumption that the elements of D are independent of x. (Professor KATCHALSKY has drawn our attention that similar results are contained in a forthcoming publication of OSTER AND KATCHALSKY[5]). Thus when one includes coupling of fluxes of the three species participating in the chemical reaction, one obtains Eqn. 1.7 which is similar to Eqn. 1.2a. If the off-diagonal elements of D were zero (one neglects coupling between fluxes), one has

$$P = \frac{D_{\alpha\alpha}}{D_{\beta\beta}} \qquad Q = -\frac{D_{\alpha\alpha}}{D_{\gamma\gamma}}$$

and

$$\theta = \frac{k_1\bar{C}_\beta}{D_{\alpha\alpha}} + \frac{k_1\bar{C}_\alpha}{D_{\beta\beta}} + \frac{k_2}{D_{\gamma\gamma}} \tag{2.11}$$

If the diffusion coefficients of carrier and associated complex are set equal (*i.e.*, $D_{\beta\beta} = D_{\gamma\gamma} = D$) one obtains $\theta = \lambda^{-2} = (k_1\bar{C}_\beta/D_{\alpha\alpha}) + (k_1\bar{C}_\alpha + k_2)/D$, which is in agreement with the expression of BLUMENTHAL AND KATCHALSKY, *viz.*, Eqn. 1.2b.

PERTURBATION THEORY

Let us suppose that the elements of the diffusion matrix D are functions of concentrations. In the spirit of BLUMENTHAL AND KATCHALSKY's approximation, we neglect terms bilinear in concentration derivatives.
Thus, Eqn. 2.4 reduces to

$$J_r\vec{U} = D\vec{C}'' \tag{3.1}$$

Equivalently

$$J_r = \frac{1}{3}(\vec{U}, D\vec{C}'') \tag{3.2}$$

where the notation $(\vec{a},\vec{b})$ means the scalar product of two vectors a and b. On neglecting the term bilinear in concentration derivatives, Eqn. 1.5 yields

$$C_\alpha'' = J_r''[k_1(C_\beta + QC_\alpha) - k_2P]^{-1} \tag{3.3}$$

where P and Q are defined in Eqn. 2.6. The first of Eqns. 3.1 taken together with Eqn. 3.3 results in a differential equation for J_r in the desired form:

$$\begin{aligned} J_r'' &= AJ_r \\ A &= [k_1(C_\beta + QC_\alpha) - k_2P]\{D_{\alpha\alpha} + D_{\alpha\beta}Q + D_{\alpha\gamma}P\}^{-1} \end{aligned} \tag{3.4}$$

This differential equation has the same formal structure as Eqns. 1.2a and 1.7 with the difference that the coefficient of J_r in the right hand side is now a function of x. With the objective of solving Eqn. 3.4, let us write

$$\Lambda(x) = \theta + \Lambda^*(x) \tag{3.5}$$

where $\theta^{-1/2}$ is the position-independent part of relaxation distance. A formal solution of Eqn. 3.4 may hence be written as

$$J_r = J_r^\circ + \int \mathrm{d}x' G(x,x')\Lambda^*(x')J_r(x') \tag{3.6}$$

where the Green's function G satisfies the equation

$$\left[\frac{\mathrm{d}^2}{\mathrm{d}x^2} - \theta\right] G(x,x') = \delta(x - x') \tag{3.7}$$

$\delta(x - x')$ being the Dirac delta function. Given the boundary conditions of the problem, the Green's function can be determined. In addition

$$\left[\frac{\mathrm{d}^2}{\mathrm{d}x^2} - \theta\right] J_r^\circ = 0 \tag{3.8}$$

Thus, it is evident that an iterative procedure can be employed in Eqn. 3.6 to solve for J_r, when the elements of the diffusion matrix are position dependent. Let us consider a situation which lends itself to easy treatment.

Suppose that

$$\begin{aligned} D_{\varepsilon\eta} &= D_{\varepsilon\varepsilon}\delta_{\varepsilon\eta} \qquad (\varepsilon,\eta = \alpha,\beta,\gamma) \\ D_{\varepsilon\varepsilon} &= D_{\varepsilon\varepsilon}^\circ + \omega f_\varepsilon(C_\alpha,C_\beta,C_\gamma) \\ \delta_{\varepsilon\eta} &= 1 \text{ when } \varepsilon = \eta \\ \delta_{\varepsilon\eta} &= 0 \text{ when } \varepsilon \neq \eta \end{aligned} \tag{3.9}$$

$D_{\varepsilon\varepsilon}^\circ$ is a constant independent of x and ω is regarded as a small perturbation parameter. If ω were zero, one knows the exact solution of Eqn. 3.4. One can find Λ^*, to first order in ω, by a perturbation expansion using Eqn. 3.9. Substituting this result in Eqn. 3.6 one obtains to first order in ω,

$$\begin{aligned} J_r &= J_r^\circ - \omega \int \mathrm{d}x' G(x,x') J^\circ{}_r(x') \\ &\left\{\frac{k_1\overline{C}_\beta f_\alpha}{(D_{\alpha\alpha}^\circ)^2} + \frac{k_1\overline{C}_\alpha f_\beta}{(D_{\beta\beta}^\circ)^2} + \frac{k_2 f_\gamma}{(D_{\gamma\gamma}^\circ)^2} + \frac{k_1(C_\beta^\circ - \overline{C}_\beta)}{D_{\alpha\alpha}^\circ} + \frac{k_1(C_\alpha^\circ - \overline{C}_\alpha)}{D_{\beta\beta}^\circ}\right\} \end{aligned} \tag{3.10}$$

It may be noted that the arguments of the f's in Eqn. 3.10 are the C°'s, the known concentration profiles corresponding to a constant diagonal diffusion matrix. Equations similar to Eqn. 3.10 can be obtained when coupling of fluxes is included (*i.e.*, when off-diagonal elements of diffusion matrix are nonvanishing). Similarly one may incorporate terms which are nonlinear in concentration derivatives. Since the resulting expressions are messy and add nothing new to the philosophy of thought, we do not present them.

However, it is essential to note that position dependence of elements of diffusion matrix arises essentially due to concentration profiles affecting the values of local partial frictional coefficients. A better approximation is to regard the partial frictional coefficients as constant and consider the explicit influence of concentration profiles on the diffusion coefficient of species as presented in Eqn. 4.2.

MOLECULAR APPROACH

A reasonable starting point for molecular approach of the problem is the equation for the nonequilibrium mean frictional force acting on a molecule of kind α at x, in the system given by the expression, valid under isothermal and isobaric stationary state conditions,

$$F_\alpha(x) = \sum_\eta C_\eta \xi_{\alpha\eta}(u_\eta - u_\alpha) \tag{4.1}$$

Eqn. 4.1 has been obtained by BEARMAN AND KIRKWOOD[3] from statistical mechanics. $\xi_{\alpha\eta}$ is the partial frictional coefficient of a molecule of kind α located at x, due to interactions of all molecules of kind η present in the system. The diffusion coefficient D_α and the frictional coefficient ξ_α are related to the partial frictional coefficients by the relations

$$\begin{aligned} D_\alpha &= \frac{\mathbf{k}T}{\xi_\alpha} \\ \xi_\alpha &= \sum_\eta C_\eta(x)\xi_{\alpha\eta}(x) \end{aligned} \tag{4.2}$$

k is the Boltzmann constant and T is the absolute temperature. Eqn. 4.1 is obtained in the absence of chemical reaction for a multicomponent fluid mixture. For the present, we shall assume its validity for the system under consideration. For a three-component system, in vector notation, Eqns. 4.1 read as

$$-\vec{\mu}' = A\vec{J} \tag{4.3}$$

where

$$\vec{\mu}' = \left|\begin{matrix} \mu_\alpha' \\ \mu_\beta' \\ \mu_\gamma' \end{matrix}\right| \qquad A_{\alpha\alpha} = \sum_{\eta \neq \alpha}^{n} (C_\eta/C_\alpha)\xi_{\alpha\eta} \qquad A_{\alpha\beta} = \xi_{\alpha\beta}$$

The matrix A is singular. The frictional force is identified as negative of the gradient of chemical potential. Differentiating Eqn. 4.3 one obtains

$$-\vec{\mu}'' = A\vec{J}' + A'\vec{J} = -A\vec{U}J_r + \vec{A}'J \tag{4.4}$$

Utilizing the well-known[4] prescription that the reaction rate is proportional to the affinity, let us write*

$$J_r = L(\mu_\alpha + \mu_\beta - \mu_\gamma) \tag{4.5}$$

L being a phenomenological coefficient. On taking the scalar product of the vectors $\vec{U}$ and $\vec{\mu}''$, Eqn. 4.4 yields

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* Even if one assumes that J_r is some function of $\mu_\alpha + \mu_\beta - \mu_\gamma$, the subsequent development is valid; the resulting equation for J_r would be more complicated.

$$(\vec{U},\vec{\mu}'') = \mu_\alpha'' + \mu_\beta'' - \mu_\gamma''$$

$$= (\vec{U},A\vec{U})J_r - (\vec{U},A'\vec{J}) \qquad (4.6)$$

Combining Eqns. 4.5 and 4.6, one obtains

$$L^{-1}J_r'' = (\vec{U},A\vec{U})J_r - (\vec{U},A'\vec{J}) \qquad (4.7)$$

In obtaining Eqn. 4.7, it is assumed that L is a constant. If L were dependent on x, the equation for J_r has a more complicated structure; nevertheless the procedure outlined is still applicable. Further taking into consideration Eqn. 2.1, we can cast Eqn. 4.7 in the form

$$L^{-1}J_r'' = (\vec{U},A\vec{U})J_r + \{(\vec{U},A'\vec{U}) \int J_r \mathrm{d}x + (\vec{U},A'\vec{q})\} \qquad (4.8)$$

where $\vec{q}$ is a vector whose components are independent of x:

$$\vec{q} = \left| \begin{matrix} q_1 \\ q_2 \\ q_3 \end{matrix} \right|$$

Eqn. 4.8 is an integro-differential equation for J_r. If the terms within the curly brackets of Eqn. 4.8 are neglected, the resulting equation has the same structure as Eqn. 3.4. With the objective of solving this simplified form of Eqn. 4.8 let us make the following assumptions: (a) the partial frictional coefficients are independent of position; (b) the coefficients of partial frictional coefficients in Eqn. 4.8 are also constants. (The coefficients of partial frictional coefficient $\xi_{\alpha\eta}$ are of the form $(r_{\alpha\eta} + r_{\eta\alpha} \pm 2)$ where $r_{\alpha\eta}$ equals (C_α/C_η). It is easily verified that assumption (b) implies, in the present approximation, the constancy of the ratio of second derivatives of concentrations, and this is assumed in the work of BLUMENTHAL AND KATCHALSKY.) Both these assumptions together imply a constant matrix A. Thus, on neglecting the terms within curly brackets, Eqn. 4.8 has the solution

$$J_r^\circ = M \exp (x\theta^{1/2}) + N \exp (-x\theta^{1/2}) \qquad (4.9)$$

where M and N are constants to be determined from boundary conditions and

$$\theta = L(\vec{U},A^\circ\vec{U}) \qquad (4.10)$$

A° is a constant matrix. If one writes that

$$A = A^\circ + A^*(x) \qquad (4.11)$$

one has, by precisely the same kind of arguments presented before

$$J_r = J_r^\circ + L \int \mathrm{d}x' G(x,x') \, (\vec{U},A^*(x')\vec{U}) J_r(x') \qquad (4.12)$$

Eqn. 4.12 can be solved by an iterative procedure, outlined before.

DISCUSSION

Using a simplified model for the effect of carrier association–dissociation reaction rates on the flux of a permeant nonelectrolyte, BLUMENTHAL AND KATCHALSKY[1] have obtained an analytical expression for the chemical reaction rate profile in the membrane system. Their result is remarkable, since the expressions for $J_r(x)$ involve the concentration profiles of the three species participating in the reaction and profiles of fluxes of all species present in the system in general. Inspired by their success, we have ventured to demonstrate that if one can evaluate J_r and the fluxes by assuming constant phenomenological coefficients (a situation where the problem is soluble subject to the approximation of neglect of nonlinear terms), one can refine the solutions so obtained by a kind of an iterative scheme, allowing for concentration dependence of the coefficients. One expects, on physical grounds, this procedure to be meaningful either when the phenomenological coefficients vary rapidly with concentrations or the concentrations vary rapidly with position. Although the results of this communication are essentially formal, nevertheless, given some information about the coefficients and their concentration dependence, the perturbation corrections can be computed. We have shown that inclusion of coupling of fluxes of different species does not alter the nature of the problem significantly in agreement with the conclusions of OSTER AND KATCHALSKY[5].

ADDENDUM (Received March 23rd, 1970)

The effect of slowly varying phenomenological coefficients on reaction rates

In the above paper, we showed that apart from terms nonlinear in concentration derivatives, the reaction rate $J_r(x)$ satisfies the following integral equation:

$$J_r(x) = J_r^0(x) + L \int_0^d \mathrm{d}x' G(x,x') \, (\vec{U}, A^*(x')\vec{U}) J_r(x') \tag{1}$$

d being the membrane thickness. The reaction rate $J_r^0(x)$ corresponding to constant phenomenological coefficients is given by

$$J_r^0(x) = M \exp(\theta x) + N \exp(-\theta x) \tag{2a}$$

$$\theta^2 = L(\vec{U}, A^0\vec{U}) \tag{2b}$$

If one assumes that the partial friction coefficients are constants and that the phenomenological coefficients vary slowly with x, as one moves across the membrane, A^0 and $A^*(x)$ have the following forms:

$$A_{\mu\mu}{}^0 = \sum_{\eta \neq \mu} (C_\eta/C_\mu)_0 \zeta_{\eta\mu} \qquad A_{\mu w}{}^0 = \zeta_{\mu w} \tag{3a}$$

$$A^* = a^* x \qquad a_{\mu w}{}^* = \delta_{\mu w} \sum_{\eta \neq \mu} (C_\eta/C_\mu)_0{}' \zeta_{\eta w} \tag{3b}$$

$\delta_{\mu w}$ being the Kronecker delta. Eqns. 3 follow on Taylor expanding $A = A^0 + A^*(x)$ about one edge of the membrane ($x = 0$). The suffix "0" in Eqns. 3 means that the object in parenthesis is evaluated at $x = 0$.

The Green's function $G(x,x')$ for the differential operator $(\mathrm{d}^2/\mathrm{d}x^2 - \theta^2)$ has the following form[6]:

$$G(x,x') = \left\{\frac{\sinh \theta(x - x')}{\theta}\right\} \varepsilon(x - x')$$

$$\varepsilon(x - x') = \begin{cases} 1 & x < x' \\ 0 & x > x' \end{cases} \tag{4}$$

Iterating Eqn. 1 once, we obtain

$$J_r(x) = J_r^0(x) + L \int_0^d \mathrm{d}x' G(x,x') \, (\vec{U},A^*(x')\vec{U}) J_r^0(x') + \ldots\ldots \tag{5}$$

Substituting the explicit forms of G and A^*, the integration in Eqn. 5 is easily carried out:

$$J_r(x) \simeq J_r^0(x) + \frac{L(\vec{U},A^*\vec{U})}{4\theta} \left[(M\mathrm{e}^{\theta x} - N\mathrm{e}^{-\theta x})x^2 + \frac{M\mathrm{e}^{-\theta x}}{2} f(2x) \, \frac{N\mathrm{e}^{\theta x}}{2} f(-2x) \right] \tag{6a}$$

where

$$f(u) = \frac{\mathrm{e}^{\lambda u} - 1}{\lambda^2} - \frac{u}{\lambda} \mathrm{e}^{\lambda u}$$

Higher order corrections to $J_r^0(x)$ arise due to (a) higher order terms in the Taylor expansion of A and (b) the terms not explicitly written out in Eqn. 5. We avoid reference to them in view of their complexity. (In some special situations results can be obtained in closed form; R. Caplan and B. Bunow, personal communication.) The species that do not participate in the chemical reaction are formally characterized by zero stoichiometric coefficients. Hence the scalar product $(\vec{U}, A\ \vec{U})$ does not have an explicit dependence, on the concentrations of such species. Only when A has a position dependence, do the concentrations and fluxes of these species appear explicitly in the problem.

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