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Kinetic model for membrane transport. III. Solute transport through an asymmetrical membrane

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Abstract

We have modified our previous solute tranport through a membrane model (Makino et al. Biophys. Chem. 35 (1990) 85; 38 (1990) 231) by taking into account a possible asymmetry of the membrane, that is, the situation in which the rate constants relating to the solute transport between the donor and membrane phases may be different from the rate constants for the solute transoport between the receiver and membrane phases. We discuss the effects of membrane asymmetry on the solute transport process.

Keywords: Membrane Transport; Asymmetrical membrane

1. Introduction

In previous papers [1,2], we presented a kinetic model for the complete time course of solute transport from a donor solution to a receiver solution through a homogeneous membrane. The model involves two kinetic parameters, k_1 and k_2, which are, respectively, the rate constant relating to the solute transport from the solution phase into the membrane phase and that for the reverse process. In that model we assumed that the transport process from the donor phase to the membrane phase and that from the receiver phase to the membrane phase are governed by the same rate constants, k_1 and k_2. In other words, the membrane was considered to be symmetrical, or both sides of the membrane to be equivalent. In the present paper, we shall deal with an asymmetrical membrane, by introducing two additional parameters, ε_1 and ε_2. That is, we consider the situation in which the rate constants relating to the solute transport from the donor phase to the membrane phase and to the reverse process are given by $\varepsilon_1 k_1$ and $\varepsilon_1 k_2$; and the corresponding rate constants for the transport from the receiver into membrane phase and for the reverse process are $\varepsilon_2 k_1$ and $\varepsilon_2 k_2$. Usually, the membrane is functionally asymmetrical and the

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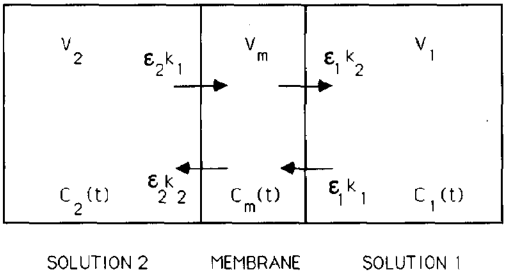

Fig. 1. A membrane of volume V_m separating two solutions, 1 and 2, whose volumes are V_1 and V_2, respectively. ϕ and ϕ_m, respectively, are the volume fractions of solution 2 and membrane, whilst $\varepsilon_1 k_1$, $\varepsilon_1 k_2$, $\varepsilon_2 k_1$ and $\varepsilon_2 k_2$, are the rate constants. $C_1(t)$, $C_2(t)$, and $C_m(t)$, are the solute concentrations of the respective phases.

biological membrane can function normally only when the conditions of the internal and external surface are different [3,4]. In the asymmetrical membrane, the solute moves through the membrane with different permeabilities according to the direction. In plant cells, the inward hydraulic conductivity is found to be larger than the outward one, which is considered to be caused by the structural asymmetry of the plasma membrane [5,6]. The structural asymmetry of the biomembrane is generally known, and is indicated by the difference in the thickness between the inner and outer leaflet of the membrane and the difference in the densitites of their protein particles [7]. Analyses of experimental data based on our treatment in the present paper will provide us with novel information on the permeation process across asymmetric membranes.

2. Theory

Consider the transport of solute through a planar membrane of volume V_m separating two solutions (solution 1 and 2), the volumes of which are V_1 and V_2, respectively (Fig. 1). Let the concentrations of solute in solutions 1 and 2 at time t be $C_1(t)$ and $C_2(t)$, respectively, with the average concentration in the membrane phase being $C_m(t)$. The time course of variations in solute concentration may be described as follows.

$$V_1 \frac{dC_1(t)}{dt} = \varepsilon_1 k_2 C_m(t) - \varepsilon_1 k_1 C_1(t) \tag{1}$$

$$V_2 \frac{dC_2(t)}{dt} = \varepsilon_2 k_2 C_m(t) - \varepsilon_2 k_1 C_2(t) \tag{2}$$

$$V_m \frac{dC_m(t)}{dt} = k_1(\varepsilon_1 C_1(t) + \varepsilon_2 C_2(t)) - k_2 C_m(t)(\varepsilon_1 + \varepsilon_2) \tag{3}$$

where k_1 denotes the rate constant relating to solute transport from solution 1 or 2 to the membrane phase, k_2 corresponding to that from the membrane phase to solution 1 or 2. The coefficient relating to the solute partitioning rate between the membrane phase and solution 1 is ε_1 and ε_2 is that between the membrane phase and solution 2. Therefore, $\varepsilon_1 k_1$ and $\varepsilon_1 k_2$ denote the rate constants relating to solute transport from solution 1 to the membrane phase and that from the membrane phase to solution 1, respectively. Also, $\varepsilon_2 k_1$ and $\varepsilon_2 k_2$ are that from solution 2 to the membrane phase and that from the membrane phase to solution 2, respectively.

The solutions to eqs. (1)–(3), subject to the initial conditions ($t = 0$)

$$C_1(0) = C_0 \tag{4}$$

$$C_2(0) = 0 \tag{5}$$

$$C_m(0) = 0 \tag{6}$$

are expressed as

$$\frac{C_1(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m} + \frac{\gamma\varepsilon_1}{1-\phi-\phi_m}\left[\frac{L-N}{L(L-M)}e^{-Lt} - \frac{M-N}{M(L-M)}e^{-Mt}\right] \tag{7}$$

$$\frac{C_2(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m} + \frac{\gamma^2\varepsilon_1\varepsilon_2}{K\phi\phi_m}\left[\frac{1}{L(L-M)}e^{-Lt} - \frac{1}{M(L-M)}e^{-Mt}\right], \tag{8}$$

$$\frac{C_m(t)}{C_0} = \frac{K(1-\phi-\phi_m)}{1+K\phi_m-\phi_m} - \frac{\gamma\varepsilon_1}{\phi_m}\left[\frac{L-Q}{L(L-M)}e^{-Lt} - \frac{M-Q}{M(L-M)}e^{-Mt}\right] \tag{9}$$

with

$$\gamma = k_1/(V_1+V_2+V_m) \tag{10}$$

$$\phi = V_2/(V_1+V_2+V_m) \tag{11}$$

$$\phi_m = \frac{V_m}{V_1+V_2+V_m} \tag{12}$$

$$K = k_1/k_2 \tag{13}$$

$$L = \frac{\gamma}{2}\left[\frac{\varepsilon_1+\varepsilon_2}{K\phi_m} + \frac{\varepsilon_2}{\phi} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right] + \frac{\gamma}{2}\sqrt{\left[\frac{\varepsilon_1+\varepsilon_2}{K\phi_m} + \frac{\varepsilon_2}{\phi} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right]^2 - \frac{4\varepsilon_1\varepsilon_2(1+K\phi_m-\phi_m)}{K\phi\phi_m(1-\phi-\phi_m)}} \tag{14}$$

$$M = \frac{\gamma}{2}\left[\frac{\varepsilon_1+\varepsilon_2}{K\phi_m} + \frac{\varepsilon_2}{\phi} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right] - \frac{\gamma}{2}\sqrt{\left[\frac{\varepsilon_1+\varepsilon_2}{K\phi_m} + \frac{\varepsilon_2}{\phi} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right]^2 - \frac{4\varepsilon_1\varepsilon_2(1+K\phi_m-\phi_m)}{K\phi\phi_m(1-\phi-\phi_m)}} \tag{15}$$

$$N = \frac{\gamma\varepsilon_2(K\phi_m+\phi)}{K\phi\phi_m} \tag{16}$$

$$Q = \gamma\varepsilon_2/\phi \tag{17}$$

where ϕ and ϕ_m denote the volume fractions of solution 2 and the membrane, respectively, and K is the solute partition coefficient between the membrane and solution phases. At equilibrium since ($t \to \infty$), eqs. (7)–(9) yield:

$$C_m(\infty) = KC_1(\infty) = KC_2(\infty) \tag{18}$$

Equations (1)–(3) satisfy the condition

$$V_1C_1(t) + V_2C_2(t) + V_mC_m(t) = V_1C_0 \tag{19}$$

which means that the total amount of solute remains constant throughout (conservation of mass).

3. Results and discussion

We have derived a system of equations describing the time course for variations in solute concentrations in solutions 1 and 2 and within the membrane, which take into account membrane asymmetry by introducing ε_1 and ε_2. These equations involve two different exponential functions of time t, $\exp(-Lt)$ and $\exp(-Mt)$, both of which are related to the relaxation time for reaching equilibrium. The former corresponds to the faster relaxation, while $\exp(-Mt)$ refers to the slower one, since $0 < M < L$. We use a scaled time γt, since γt does not depend on ϕ, ϕ_m, ε_1 or ε_2. When the structure of a membrane is asymmetrical, the time courses of variations in solute concentrations in solutions 1 and 2 and in the membrane are considered to be dependent on the direction of solute transport. The time courses of solute transport through the asymmetrical membrane from solution 1 to solution 2 ($C_1(0) = C_0$ and $C_2(0) = 0$) is different from that from solution 2 to solution 1 ($C_2(0) = C_0$ and $C_1(0) = 0$). The effects of membrane asymmetry can be given by interchanging the values of ε_1 and ε_2 in this model.

Figure 2 shows the effects of membrane asymmetry upon $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$. If ε_1 is large, $C_1(t)/C_0$ decreases quickly with time in the initial stage of transport, as shown in Fig. 2(a). If ε_1 is large and ε_2 is small, $C_m(t)/C_0$ is large in the initial stage, as shown in Fig. 2(a), because the solute tends to remain in the membrane. From a comparison of Fig. 2(a) with Fig. 2(b), it is clearly that in the initial stage of transport, $C_2(t)/C_0$ is not affected by membrane asymmetry, although $C_1(t)/C_0$ and $C_m(t)/C_0$ are affected by the interchange of ε_1 and ε_2, as mentioned above. This is because the smaller value of ε_1 or ε_2 dominates $C_2(t)/C_0$. The values of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ at equilibrium are independent of ε_1 and ε_2 because the values of $C_1(\infty)/C_0$, $C_2(\infty)/C_0$ and $C_m(\infty)/C_0$ do not include

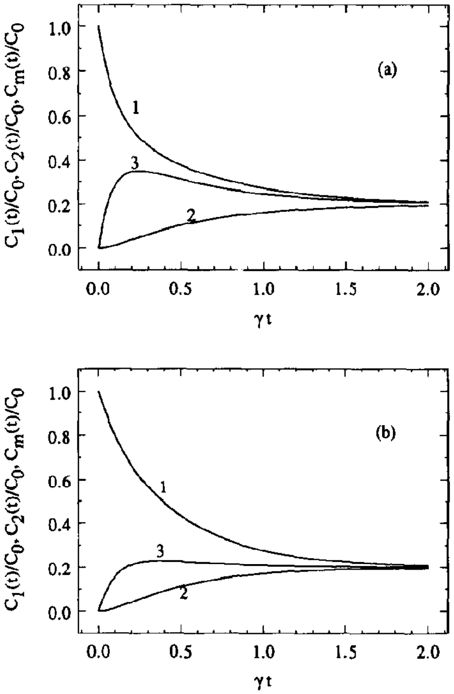

Fig. 2. Effects of the asymmetry of the membrane on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, and $K = 1$. (a) $\varepsilon_1 = 1$ and $\varepsilon_2 = 0.5$, and (b) $\varepsilon_1 = 0.5$ and $\varepsilon_2 = 1$.

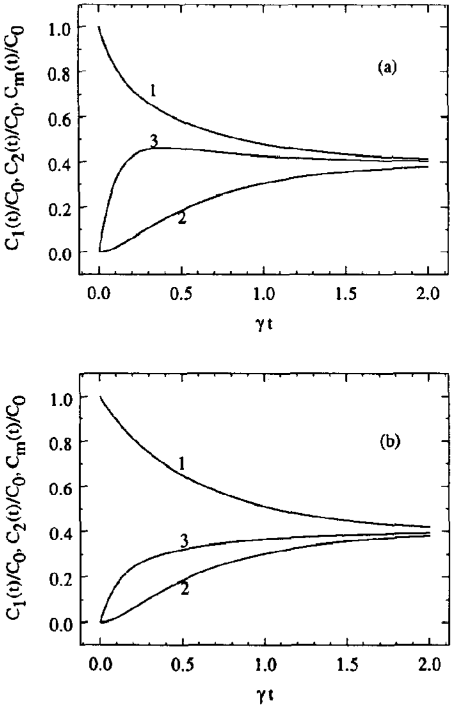

Fig. 3. Effects of the asymmetry of the membrane on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.4$, $\phi_m = 0.2$, and $K = 1$. (a) $\varepsilon_1 = 1$ and $\varepsilon_2 = 0.5$, and (b) $\varepsilon_1 = 0.5$ and $\varepsilon_1 = 1$.

ε_1 and ε_2. These effects of membrane asymmetry on $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ are not necessarily caused by the volume difference between solutions 1 and 2, because these effects are observed even in the case when $V_1 = V_2$, as shown in Fig. 3. It should be emphasized that the membrane asymmetry hardly affects $C_1(t)/C_0$ and $C_2(t)/C_0$ if K is very small, as shown in Fig. 4. In order to determine the general features of eqs. (7)–(9), we will now consider the effects of K, ϕ, ϕ_m, ε_1 and ε_2 on $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ for several limiting cases.

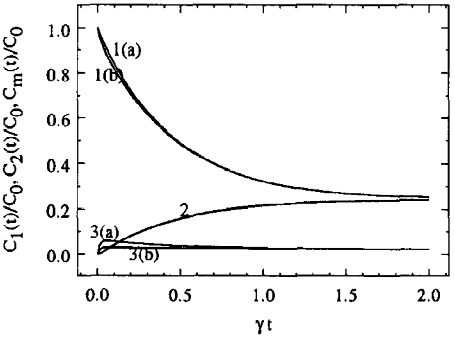

Fig. 4. Effects of the asymmetry of the membrane on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, and $K = 0.1$. (a) $\varepsilon_1 = 1$ and $\varepsilon_2 = 0.5$, and (b) $\varepsilon_1 = 0.5$ and $\varepsilon_2 = 1$.

3.1 Case 1: $K \to 0$

In the limiting case of $K \to 0$, we have

$$L = \gamma(\varepsilon_1 + \varepsilon_2)/K\phi_m \tag{20}$$

$$M = \frac{\gamma\varepsilon_1\varepsilon_2(1-\phi_m)}{\phi(1-\phi-\phi_m)(\varepsilon_1+\varepsilon_2)} \tag{21}$$

$$N = \gamma\varepsilon_2/K\phi_m \tag{22}$$

$$Q = \gamma\varepsilon_2/\phi \tag{23}$$

$$\frac{C_1(t)}{C_0} = \frac{1-\phi-\phi_m}{1-\phi_m} + \frac{K\phi_m\varepsilon_1^2}{(1-\phi-\phi_m)(\varepsilon_1+\varepsilon_2)^2}\exp\left(-\frac{\varepsilon_1+\varepsilon_2}{K\phi_m}\gamma t\right) + \frac{\phi}{1-\phi_m}\exp\left(-\frac{\varepsilon_1\varepsilon_2(1-\phi_m)}{\phi(1-\phi-\phi_m)(\varepsilon_1+\varepsilon_2)}\gamma t\right) \tag{24}$$

$$\frac{C_2(t)}{C_0} = \frac{1-\phi-\phi_m}{1-\phi_m} + \frac{K\phi_m\varepsilon_1\varepsilon_2}{\phi(\varepsilon_1+\varepsilon_2)^2}\exp\left(-\frac{\varepsilon_1+\varepsilon_2}{K\phi_m}\gamma t\right) - \frac{1-\phi-\phi_m}{1-\phi_m}\exp\left(-\frac{\varepsilon_1\varepsilon_2(1-\phi_m)}{\phi(1-\phi-\phi_m)(\varepsilon_1+\varepsilon_2)}\gamma t\right) \tag{25}$$

$$\frac{C_m(t)}{C_0} = \frac{K(1-\phi-\phi_m)}{1-\phi_m} - \frac{\varepsilon_1 K}{\varepsilon_1+\varepsilon_2}\exp\left(-\frac{\varepsilon_1+\varepsilon_2}{K\phi_m}\gamma t\right) + \frac{\{\varepsilon_1(1-\phi_m)-(\varepsilon_1+\varepsilon_2)(1-\phi-\phi_m)\}K}{(1-\phi_m)(\varepsilon_1+\varepsilon_2)} \times\exp\left(-\frac{\varepsilon_1\varepsilon_2(1-\phi_m)}{\phi(1-\phi-\phi_m)(\varepsilon_1+\varepsilon_2)}\gamma t\right) \tag{26}$$

As is clear from eqs. (24)-(26), if K is very small, $C_1(t)/C_0$ and $C_2(t)/C_0$ are not affected when interchanging ε_1 and ε_2, because the first exponential term in eq. (24) is negligibly small (Fig. 4).

If $K = 1$, in the later stage of solute transport the decreasing rate of $C_1(t)/C_0$ and that of $C_m(t)/C_0$ become almost the same, as shown in Fig. 5. This phenomenon is observed if $K = 1$ and ε_1 is very large or if $K = 1$ and ε_2 is very small, as will be described later. Conversely, if $K = 1$ and ε_1 is very small, or if $K = 1$ and ε_2 is very large, then $C_2(t)/C_0$ becomes equal to $C_m(t)/C_0$, as shown in Fig. 6.

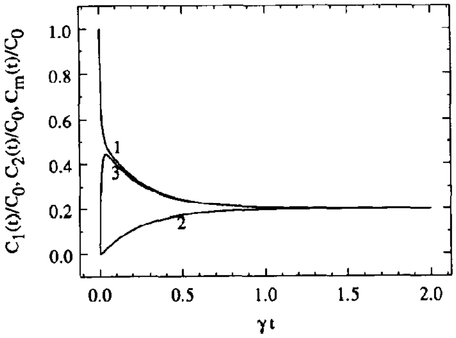

Fig. 5. Effects of K and ε_1 or ε_2 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, and $K = 1$, $\varepsilon_1 = 10$, and $\varepsilon_2 = 1$

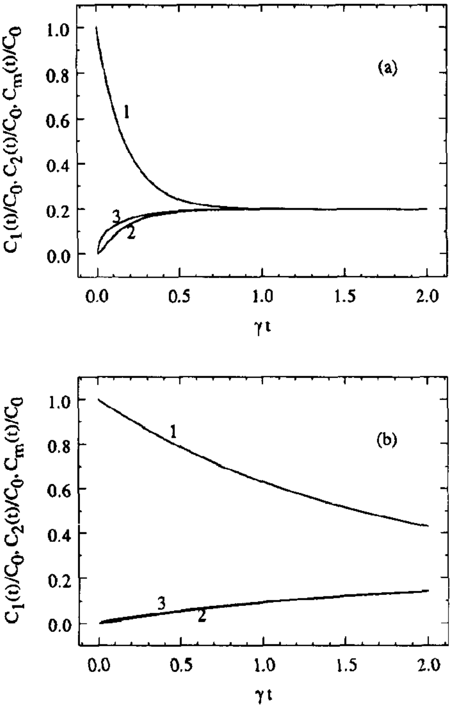

Fig. 6. Effects of K and ε_1 or ε_2 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, and $K = 1$, (a) $\varepsilon_1 = 1$ and $\varepsilon_2 = 10$, (b) $\varepsilon_1 = 0.1$ and $\varepsilon_2 = 10$.

3.2 Case 2: $K \to \infty$

If $K \to \infty$, we have

$$L = \gamma\left[\frac{\varepsilon_2}{\phi} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right] \tag{27}$$

$$M = \frac{\gamma\varepsilon_1\varepsilon_2}{\varepsilon_2(1-\phi-\phi_m)+\varepsilon_1\phi} \tag{28}$$

$$N = \gamma\varepsilon_2/\phi \tag{29}$$

$$Q = \gamma\varepsilon_2/\phi \tag{30}$$

$$\begin{aligned}\frac{C_1(t)}{C_0} = {} & \frac{\varepsilon_1^2\phi^2}{\varepsilon_1^2\phi^2+\varepsilon_1\varepsilon_2\phi(1-\phi-\phi_m)+\varepsilon_2^2(1-\phi-\phi_m)^2}\exp\left(-\left(\frac{\varepsilon_2}{\phi}+\frac{\varepsilon_1}{1-\phi-\phi_m}\right)\gamma t\right)\\ & +\frac{\varepsilon_2(1-\phi-\phi_m)\{\varepsilon_2(1-\phi-\phi_m)+\varepsilon_1\phi\}}{\varepsilon_1^2\phi^2+\varepsilon_1\varepsilon_2\phi(1-\phi-\phi_m)+\varepsilon_2^2(1-\phi-\phi_m)^2}\exp\left(-\frac{\varepsilon_1\varepsilon_2}{\varepsilon_2(1-\phi-\phi_m)+\varepsilon_1\phi}\gamma t\right)\end{aligned} \tag{31}$$

$$C_2(t)/C_0 = 0 \tag{32}$$

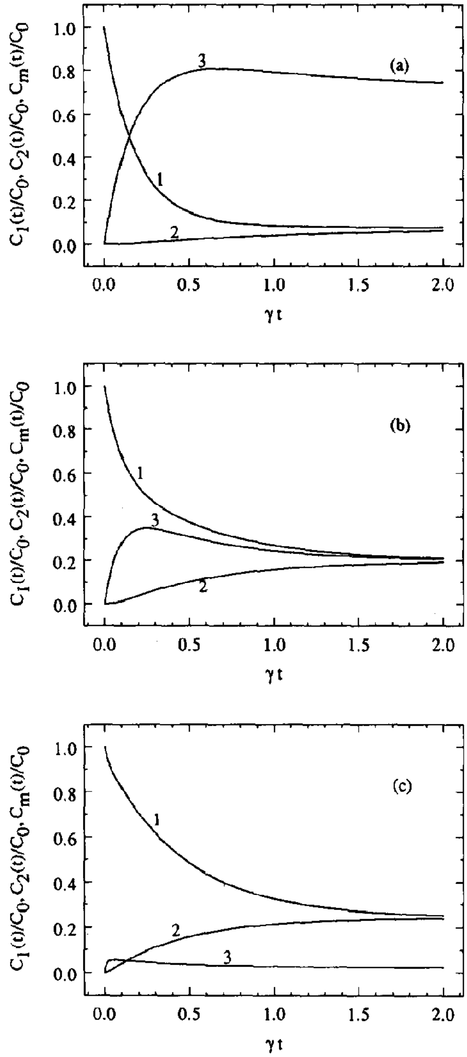

Fig. 7. Effects of K on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 1$, $\varepsilon_2 = 0.5$, and $K = 10$ (a), 1 (b), and 0.1 (c).

$$\frac{C_m(t)}{C_0} = \frac{1-\phi-\phi_m}{\phi_m} - \frac{\varepsilon_1^2\phi^2(1-\phi-\phi_m)}{\phi_m\left(\varepsilon_1^2\phi^2+\varepsilon_1\varepsilon_2\phi(1-\phi-\phi_m)+\varepsilon_2^2(1-\phi-\phi_m)^2\right)}$$
$$\times\exp\left(-\left(\frac{\varepsilon_2}{\phi}+\frac{\varepsilon_1}{1-\phi-\phi_m}\right)\gamma t\right)$$
$$-\frac{\varepsilon_2(1-\phi-\phi_m)^2\{\varepsilon_2(1-\phi-\phi_m)+\varepsilon_1\phi\}}{\phi_m\left(\varepsilon_1^2\phi^2+\varepsilon_1\varepsilon_2\phi(1-\phi-\phi_m)+\varepsilon_2^2(1-\phi-\phi_m)^2\right)}\exp\left(-\frac{\varepsilon_1\varepsilon_2}{\varepsilon_2(1-\phi-\phi_m)+\varepsilon_1\phi}\gamma t\right) \quad (33)$$

Figure 7 shows the effects of K on $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$. In the initial stage of solute transport, as K increases, $C_1(t)/C_0$ decreases rapidly with time, although $C_2(t)/C_0$ increases slowly.

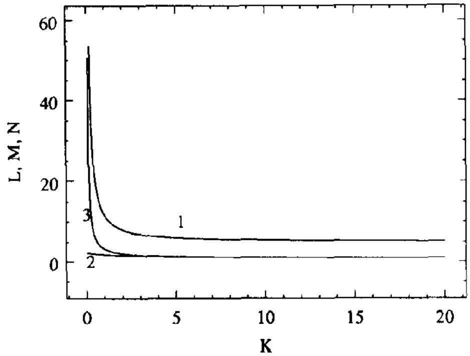

Fig. 8. Effects of K on L (curve 1), M (curve 2) and N (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 1$ and $\varepsilon_2 = 0.5$.

Overshoot seen with variations in solute concentration in the membrane phase occurs earlier for small K than for large K. The time instant t_o, at which overshoot occurs, becomes smaller and $C_m(t_o)/C_0$ becomes lower as K decreases. The relaxation times, $1/L$ and $1/M$ [1], become larger as K increases. Figure 8 shows the effects of K on L, M and N. The value of Q is independent of K. As K increases, L and M decrease, demonstrating that both relaxation times grow longer. Therefore, we cannot explain the dependence on K of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ in the earlier stage of solute transport, which we mentioned above with two relaxation times. We consider the initial stage of membrane transport,

$$\frac{C_1(t)}{C_0} = 1 - \frac{\gamma\varepsilon_1}{1-\phi-\phi_m}t + \frac{\gamma^2\varepsilon_1^2(1-\phi-\phi_m+K\phi_m)}{2K\phi_m(1-\phi-\phi_m)^2}t^2 \tag{34}$$

$$\frac{C_2(t)}{C_0} = \frac{\gamma^2\varepsilon_1\varepsilon_2}{2K\phi\phi_m}t^2 \tag{35}$$

$$\frac{C_m(t)}{C_0} = \frac{\gamma\varepsilon_1}{\phi_m}t - \frac{\gamma^2\varepsilon_1}{2\phi_m}\left(\frac{\varepsilon_1+\varepsilon_2}{K\phi_m} + \frac{\varepsilon_1}{1-\phi-\phi_m}\right)t^2 \tag{36}$$

If t is very small, as K increases, $\mathrm{d}C_1(t)/\mathrm{d}t$ becomes more negative, demonstrating that $C_1(t)/C_0$ decreases more rapidly. Also, as K decreases, $\mathrm{d}C_2(t)/\mathrm{d}t$ becomes more positive and $C_2(t)/C_0$ increases more rapidly. In the time course of $C_m(t)/C_0$, t_o increases as K increases, as shown in Fig. 9.

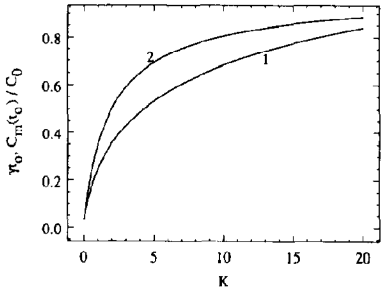

Fig. 9. Effects of K on γt_0 (curve 1) and $C_m(t_0)/C_0$ (curve 2) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 1$ and $\varepsilon_2 = 0.5$.

3.3 Case 3: $\phi_m \to 0$

If $\phi_{\mathrm{m}} \to 0$, we have

$$L = \gamma(\varepsilon_1\varepsilon_2)/K\phi_{\mathrm{m}} \tag{37}$$

$$M = \frac{\gamma\varepsilon_1\varepsilon_2}{\phi(1-\phi)(\varepsilon_1+\varepsilon_2)} \tag{38}$$

$$N = \gamma\varepsilon_2/K\phi_{\mathrm{m}} \tag{39}$$

$$Q = \gamma\varepsilon_2/\phi \tag{40}$$

$$\frac{C_1(t)}{C_0} = (1-\phi) + \phi\,\exp\left(-\frac{\varepsilon_1\varepsilon_2}{\phi(1-\phi)(\varepsilon_1+\varepsilon_2)}\gamma t\right) \tag{41}$$

$$\frac{C_2(t)}{C_0} = (1-\phi)\left(1-\exp\left(-\frac{\varepsilon_1\varepsilon_2}{\phi(1-\phi)(\varepsilon_1+\varepsilon_2)}\gamma t\right)\right) \tag{42}$$

$$\frac{C_{\mathrm{m}}(t)}{C_0} = K(1-\phi) - \frac{K\varepsilon_1}{\varepsilon_1+\varepsilon_2}\exp\left(-\frac{\varepsilon_1+\varepsilon_2}{K\phi_{\mathrm{m}}}\gamma t\right) + \frac{K\{\varepsilon_1\phi-\varepsilon_2(1-\phi)\}}{\varepsilon_1+\varepsilon_2}\exp\left(-\frac{\varepsilon_1\varepsilon_2}{\phi(1-\phi)(\varepsilon_1+\varepsilon_2)}\gamma t\right) \tag{43}$$

It is clear that if ϕ_{m} is very small, $C_1(t)/C_0$ and $C_2(t)/C_0$ are not affected by K, and this is shown in Fig. 10.

As is seen in eq. (26), if $K \ll 1$, $C_{\mathrm{m}}(t)/C_0$ is negligibly small and is not affected by ϕ_{m}.

If both ϕ_{m} and K is very small and $\varepsilon_1 = \varepsilon_2 = 1$, we have

$$\frac{C_1(t)}{C_0} = (1-\phi) + \phi\,\exp\left(-\frac{1}{2\phi(1-\phi)}\gamma t\right) \tag{44}$$

$$\frac{C_1(t)}{C_0} = (1-\phi)\left(1-\exp\left(-\frac{1}{2\phi(1-\phi)}\gamma t\right)\right) \tag{45}$$

$$C_{\mathrm{m}}(t)/C_0 = 0 \tag{46}$$

which correspond to the usual model [8,9] which does not take into account the membrane volume.

3.4 Case 4: $\phi \to 0$

If $\phi \to 0$, we have

$$L = \gamma\varepsilon_2/\phi \tag{47}$$

$$M = \frac{\gamma\varepsilon_1(1+K\phi_{\mathrm{m}}-\phi_{\mathrm{m}})}{K\phi_{\mathrm{m}}(1-\phi_{\mathrm{m}})} \tag{48}$$

$$N = \gamma\varepsilon_2/\phi \tag{49}$$

$$Q = \gamma\varepsilon_2/\phi \tag{50}$$

$$\frac{C_1(t)}{C_0} = \frac{1-\phi_{\mathrm{m}}}{1+K\phi_{\mathrm{m}}-\phi_{\mathrm{m}}} + \frac{K\phi_{\mathrm{m}}}{1+K\phi_{\mathrm{m}}-\phi_{\mathrm{m}}}\exp\left(-\frac{\varepsilon_1(1+K\phi_{\mathrm{m}}-\phi_{\mathrm{m}})}{K\phi_{\mathrm{m}}(1-\phi_{\mathrm{m}})}\gamma t\right) \tag{51}$$

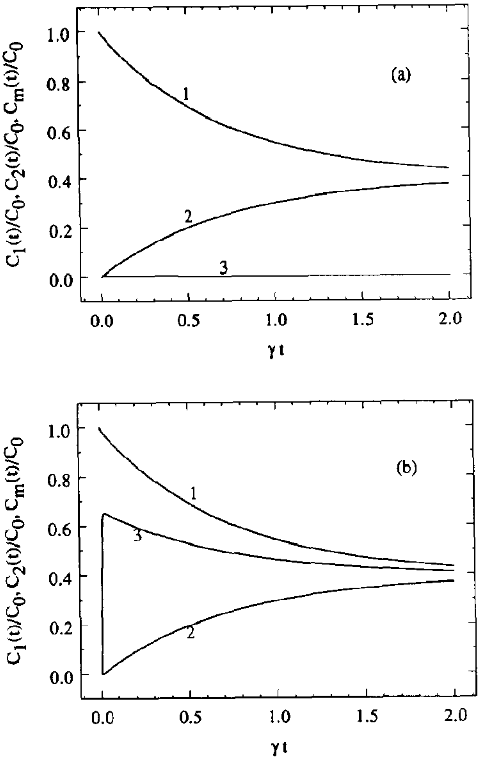

Fig. 10. Effects of K on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi=0.6$, $\phi_m=0.005$, $\varepsilon_1=1$, $\varepsilon_2=0.5$ and $K=0.005$ (a), and 1 (b).

$$\frac{C_2(t)}{C_0}=\frac{1-\phi_m}{1+K\phi_m-\phi_m}\left(1-\exp\left(-\frac{\varepsilon_1(1+K\phi_m-\phi_m)}{K\phi_m(1-\phi_m)}\gamma t\right)\right) \tag{52}$$

$$\frac{C_m(t)}{C_0}=\frac{K(1-\phi_m)}{1+K\phi_m-\phi_m}\left(1-\exp\left(-\frac{\varepsilon_1(1+K\phi_m-\phi_m)}{K\phi_m(1-\phi_m)}\gamma t\right)\right) \tag{53}$$

If ϕ is very small, $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ are not affected by ε_2, as shown in Fig. 11, which reflects the situation where eqs. (51)–(53) do not include ε_2.

3.5 Case 5: $\varepsilon_1 \to 0$

If ε_1 is very small, we have

$$L=\gamma\varepsilon_2(K\phi_m+\phi)/K\phi\phi_m \tag{54}$$

$$M=\frac{\gamma\varepsilon_1(1+K\phi_m-\phi_m)}{(1-\phi-\phi_m)(K\phi_m+\phi)} \tag{55}$$

$$N=\gamma\varepsilon_2(K\phi_m+\phi)/K\phi\phi_m \tag{56}$$

$$Q=\gamma\varepsilon_2/\phi \tag{57}$$

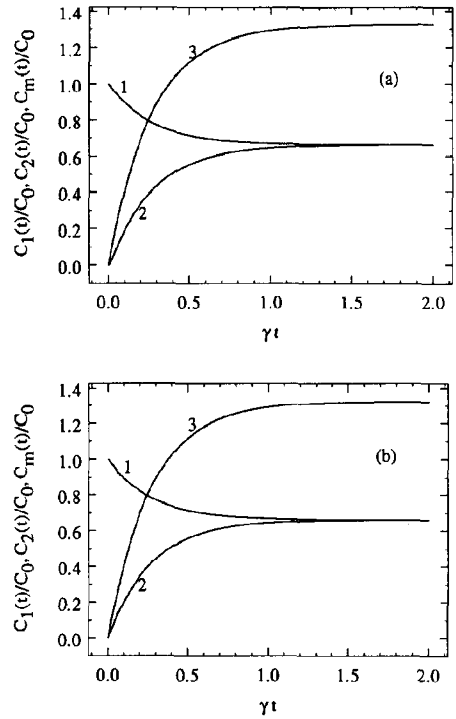

Fig. 11. Effects of ε_2 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.005$, $\phi_m = 0.2$, $\varepsilon_1 = 1$, $K = 2$ and $\varepsilon_2 = 0.5$ (a), and 10 (b).

$$\frac{C_1(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m} + \frac{K\phi_m+\phi}{1+K\phi_m-\phi_m}\exp\left(-\frac{\varepsilon_1(1+K\phi_m-\phi_m)}{(1-\phi-\phi_m)(K\phi_m+\phi)}\gamma t\right) \tag{58}$$

$$\frac{C_2(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m}\left(1-\exp\left(-\frac{\varepsilon_1(1+K\phi_m-\phi_m)}{(1-\phi-\phi_m)(K\phi_m+\phi)}\gamma t\right)\right) \tag{59}$$

$$\frac{C_m(t)}{C_0} = \frac{K(1-\phi-\phi_m)}{1+K\phi_m-\phi_m}\left(1-\exp\left(-\frac{\varepsilon_1(1+K\phi_m-\phi_m)}{(1-\phi-\phi_m)(K\phi_m+\phi)}\gamma t\right)\right) \tag{60}$$

It is clear, that if ε_1 is very small $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ are independent of ε_2. It is considered that the smaller value of ε_1 and ε_2 plays a dominant role. Figure 12 shows the effects of ε_2 on $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ if ε_1 is 0.005.

Figure 13 shows the effects of ε_1 on $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$. As ε_1 decreases the relaxation of each of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ becomes slower. This is because L and M increase as ε_1 increases, as shown in Fig. 14. N and Q are independent of ε_1. Also, as seen in this figure, Q is greater than M when

$$\varepsilon_1 < \varepsilon_2(1-\phi-\phi_m)/\phi$$

while M becomes greater than Q when ε_1 has greater values than this.

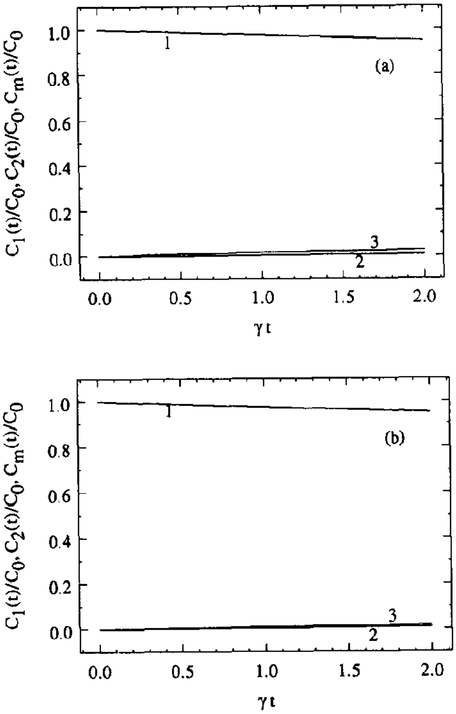

Fig. 12. Effects of ε_2 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 0.005$, $K = 2$ and $\varepsilon_2 = 0.5$ (a), and 10 (b).

3.6 Case 6: $\varepsilon_2 \to 0$

If ε_2 is very small, we have

$$L = \frac{\gamma\varepsilon_1(1-\phi-\phi_m+K\phi_m)}{K\phi_m(1-\phi-\phi_m)} \tag{61}$$

$$M = \frac{\gamma\varepsilon_2(1+K\phi_m-\phi_m)}{\phi(1-\phi-\phi_m+K\phi_m)} \tag{62}$$

$$N = \gamma\varepsilon_2(K\phi_m+\phi)/K\phi\phi_m \tag{63}$$

$$Q = \gamma\varepsilon_2/\phi \tag{64}$$

$$\frac{C_1(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m} + \frac{K\phi_m}{1-\phi-\phi_m+K\phi_m}\exp\left(-\frac{\varepsilon_1(1-\phi-\phi_m+K\phi_m)}{K\phi_m(1-\phi-\phi_m)}\gamma t\right)$$
$$+\frac{\phi(1-\phi-\phi_m)}{(1+K\phi_m-\phi_m)(1-\phi-\phi_m+K\phi_m)}\exp\left(-\frac{\varepsilon_2(1+K\phi_m+\phi_m)}{\phi(1-\phi-\phi_m+K\phi_m)}\gamma t\right) \tag{65}$$

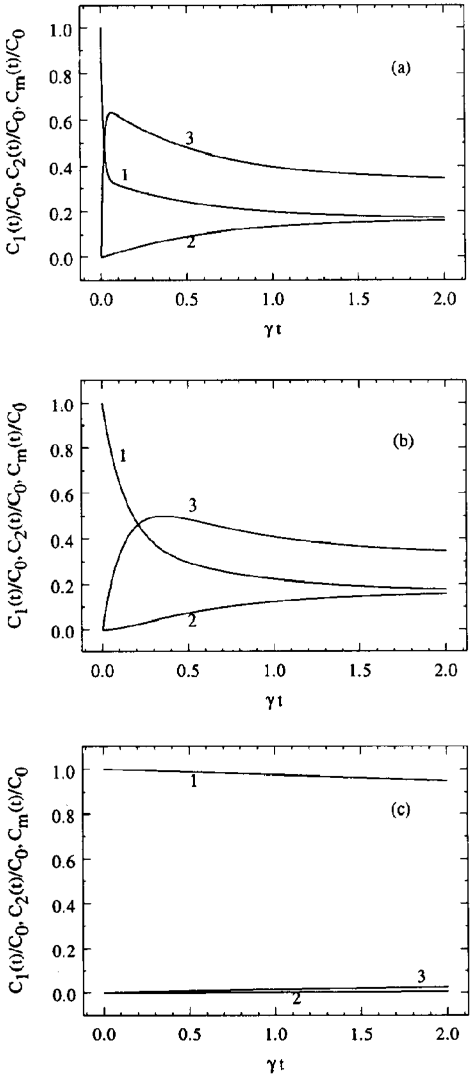

Fig. 13. Effects of ε_1 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_2 = 0.5$, $K = 2$, and $\varepsilon_1 = 10$ (a), 1 (b), and 0.005 (c).

$$\frac{C_2(t)}{C_0} = \frac{1-\phi-\phi_m}{1+K\phi_m-\phi_m}\left(1-\exp\left(-\frac{\varepsilon_2(1+K\phi_m-\phi_m)}{\phi(1-\phi-\phi_m+K\phi_m)}\gamma t\right)\right) \tag{66}$$

$$\begin{aligned}\frac{C_m(t)}{C_0} = {} & \frac{K(1-\phi-\phi_m)}{1+K\phi_m-\phi_m} - \frac{K(1-\phi-\phi_m)}{1-\phi-\phi_m+K\phi_m}\exp\left(-\frac{\varepsilon_1(1-\phi-\phi_m+K\phi_m)}{K\phi_m(1-\phi-\phi_m)}\gamma t\right) \\ & + \frac{K\phi(1-\phi-\phi_m)}{(1+K\phi_m-\phi_m)(1-\phi-\phi_m+K\phi_m)}\exp\left(-\frac{\varepsilon_2(1+K\phi_m-\phi_m)}{\phi(1-\phi-\phi_m+K\phi_m)}\gamma t\right)\end{aligned} \tag{67}$$

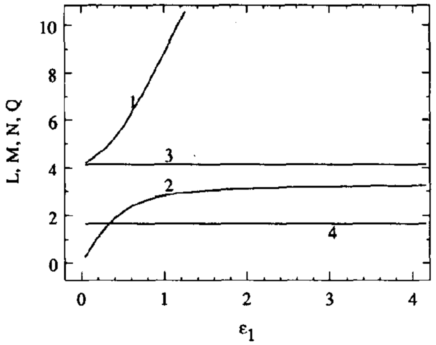

Fig. 14. Effects of ε_1 on L (curve 1), M (curve 2), N (curve 3) and Q (curve 4) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_2 = 0.5$ and $K = 2$.

If ε_2 is very small, $C_2(t)/C_0$ does not depend on ε_1, as shown in Fig. 15. Figure 16 shows that as ε_2 decreases, the relaxation times of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$ become longer. This is explained by the dependence of ε_2 on L and M. Figure 17 shows the effects of ε_2 on L, M, N, and Q.

If ε_2 is very large ($\varepsilon_2 \to \infty$), we have the same form of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$, respectively, as those (eqs. 58–60) obtained in the limiting case with very small ε_1 ($\varepsilon_1 \to 0$). Also, if ε_1 is very large ($\varepsilon_1 \to \infty$), we have the same form of $C_1(t)/C_0$, $C_2(t)/C_0$ and $C_m(t)/C_0$, respectively, as those (eqs. 65–67) in the limiting case with very small ε_2 ($\varepsilon_2 \to 0$). This phenomenon is explained by the asymmetry of the membrane.

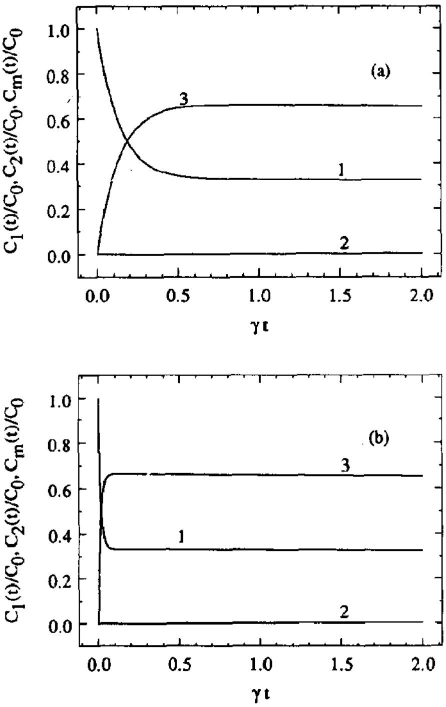

Fig. 15. Effects of ε_1 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_2 = 0.005$ and $K = 2$, $\varepsilon_1 = 1$ (a), and 10 (b).

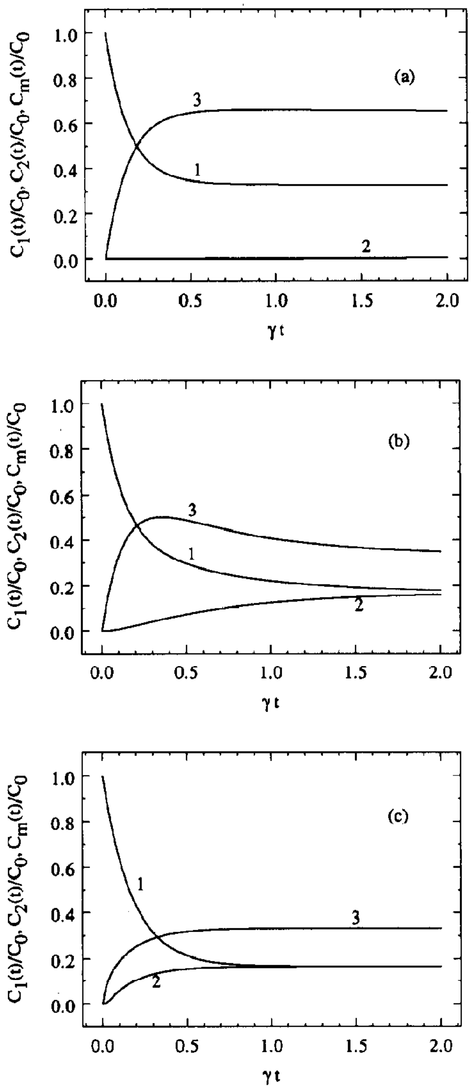

Fig. 16. Effects of ε_2 on $C_1(t)/C_0$ (curve 1), $C_2(t)/C_0$ (curve 2) and $C_m(t)/C_0$ (curve 3), when $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 1$ and $K = 2$ $\varepsilon_2 = 0.005$ (a), 0.5 (b), and 10 (c).

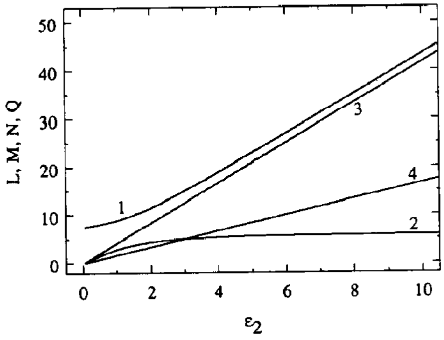

Fig. 17. Effects of ε_2 on L (curve 1), M (curve 2), N (curve 3) and Q (curve 4) for $\phi = 0.6$, $\phi_m = 0.2$, $\varepsilon_1 = 1$ and $K = 2$.

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[1] In Ref. 1, on p. 87, in the legend to Fig. 2(b), $e^{-f\alpha}$ (curve 3) and $e^{-g\alpha}$ (curve 4) should read $e^{-f\alpha t}$ (curve 3) and $e^{-g\alpha t}$ (curve 4), respectively. On p. 90, in eq. (45), $C_m(t)$ should read $C_m(t)/C_0$. On p. 94, the legend to Fig. 8 should include the final part of the last sentence: if $\phi = 0.6$, $\phi_m = 0.2$ and $K = 1$.

[2] In Ref. 2, on p. 232 in eq. (3) the minus sign should be omitted, i.e. $-k_1(C_1(t) + C_2(t))$ should read $+k_1(C_1(t) + C_2(t))$.