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THE RELATION BETWEEN OSMOTIC FLOW AND TRACER SOLVENT DIFFUSION FOR SINGLE-FILE TRANSPORT

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It is demonstrated that a reasonably general model for single-file passage of solvent through an ultra-narrow pore implies the equality of tracer diffusion and osmotic flow. This result is not trivial, but follows from the exactly compensating effects of solvent–solvent interaction on the partitioning of bulk solvent into the pore and on the diffusion rate within the pore. A previous calculation of Longuet-Higgins and Austin is seen to be valid only in the absence of interactions among solvent molecules in the pore.

1. Introduction

The concept of single-file transport through a membrane was first introduced by Hodgkin and Keynes [1] in connection with their ionic transport data for the giant squid axon. The idea is that transport occurs through a pore so narrow as to be able to accommodate only one molecule in its width. Sometimes [2], the model is specialized to the case for which the pore is completely filled along its length by the transported molecules, sometimes [3] to that for which the pore contains only one molecule at any instant; such definite specification of the linear density will not be necessary in this article, which treats the relation between the transport of a tracer solvent species induced by a difference in tracer concentration on either side of the membrane (tracer solvent diffusion) and the solvent transport induced by a difference in concentration of a solute species too large to enter the pore (osmotic flow).

Indeed, one may define three coefficients of solvent flow, corresponding to three distinct experimental situations:

$$j_{S*} = -K^*(c^B_{S*} - c^A_{S*}) \qquad \text{(tracer flow)}, \qquad (1)$$

$$j_S = -K_s(c^A_s - c^B_s) \qquad \text{(osmotic flow)}, \qquad (2)$$

$$j_S = -K_P(P_B - P_A) \qquad \text{(pressure flow)}. \qquad (3)$$

The measurement described by eq. (1) is tracer diffusion. The only species present in addition to solvent species S is a tracer species S* of the solvent. The membrane separates two compartments A and B, the respective tracer concentrations are c^A_{S*} and c^B_{S*}, and, by convention, the tracer flux j_{S*} is positive if it is directed from compartment A to compartment B. Eq. (2) describes osmotic flow of solvent. Compartments A and B are filled with solutions of a solute s which is impermeable to the membrane. The pressures in compartments A and B are equal. The solvent flux j_S is directed into the compartment of larger solute concentration c_s, and, again, by convention, is positive in sign if $c^B_s > c^A_s$. In the situation specified by eq. (3), only solvent is present and its flux j_S through the membrane is driven by unequal pressures in the two compartments. The sign convention for the flux is identical to the preceding two cases, since the flux is directed into the compartment with the lower pressure.

The coefficients K_s and K_P are directly related by a priori phenomenological considerations independent of the nature of the membrane [4,5]. Both eqs. (2) and (3) are, in fact, included in a general relation of linear irreversible thermodynamics

$$j_S = -L\,\Delta\mu_S = -L(\mu^B_S - \mu^A_S), \qquad (4)$$

where μ_S is the chemical potential per mole of the solvent and L is a positive phenomenological coefficient. For ideal dilute solutions with solute s, then, with v_S^0 the molar volume of pure solvent,

$$j_S = -L v_S^0(\Delta P - RT\Delta c_s), \qquad (5)$$

whereupon comparison with eqs. (2) and (3) yields

$$K_s = RTK_P. \qquad (6)$$

More important than the quantitative relation expressed by eq. (6) is the implication of eq. (4) that osmotic flow and pressure-driven flow are mechanistically equivalent. Contrary to common belief among physical chemists, for example, osmotic flow is, in general, not a diffusion process [6–8].

There is no similar relation between K^* and K_s (or K_P). It has been experimentally determined [4] that K_s is orders of magnitude greater than K^* for membranes with high solvent content, a result consistent with the expectation that, for such membranes, pressure-driven flow will be highly cooperative (the idealized model being Poisseuille laminar flow). Even for membranes with quite narrow pores [2], K_s may be four or five times greater than K^*, although for membranes with no pores at all [9], into which water must dissolve in order to traverse the barrier, K_s is, as expected for this case, equal to K^*.

No definitive measurements have been done for transport across ultra-narrow, single-file, pores, for the simple reason that for no system has it been demonstrated that such pores exist. A theoretical relation between K_s and K^* for the model of single-file transport is therefore of interest for the purpose of interpreting data on transport across pores of molecular dimension which conceivably could be sufficiently narrow to allow only single-file passage [10]. For example, Dick [2] has presented a formula which predicts that K_s is greater than K^* for single-file transport when the pore is filled with solvent along its entire length. The relation contains as a parameter the total number of pore sites for solvent molecules, and by comparison with measured values of K_s/K^* Dick calculates this number for a variety of cell membranes. The formula for K_s/K^* given by Dick is, however, incorrect, being based on an erroneous mechanism for osmotic flow [11].

The problem has also been treated by Longuet-Higgins and Austin [5], whose conclusion implies that $K_s = K^*$. However, as will be seen below, their argument is valid only for the special case of negligible interactions among solvent molecules inside the pore.

The relation between K_s and K^* for single-file transport appears, therefore, to be an unresolved problem, both experimentally and theoretically. It must be stated immediately that there can exist no relation between K_s and K^* of the same generality as the equivalence expressed by eq. (6) between K_s and K_P. The latter depends only on the first and second laws of thermodynamics, the applicability of these laws within the domain of linear irreversible thermodynamics, and the dilute-solution form of the solvent chemical potential, which, although nonthermodynamic in origin, is a consequence of the most general foundations of statistical mechanics [12,13]. It is proposed in this paper to prove that a consistent and plausible model of single-file transport has as consequence the relation $K_s = K^*$.

2. Specification of the model

The solvent in the pore will be regarded as constituting a macroscopic one-dimensional phase. If compartments A and B contain pure solvent at the same pressure P_0, the linear concentration of solvent in the pore will be uniform (if end effects are neglected) and will be designated by ρ_0. That is, if the pore is of length l and contains N_0 solvent molecules,

$$\rho_0 \equiv N_0/L \qquad (7)$$

Corresponding to the three experimental flow conditions described by the macroscopic eqs. (1)–(3), we adopt the following microscopic flow equations:

$$j_{S^*} = -k^*(\rho_B^* - \rho_A^*) \quad \text{(tracer flow)}, \qquad (8)$$

$$j_S = -k_s(\rho_B - \rho_A) \quad \text{(osmotic flow)}, \qquad (9)$$

$$j_S = -k_P(\rho_B - \rho_A) \quad \text{(pressure flow)}. \qquad (10)$$

These equations are motivated by the consideration that only a "diffusion" mechanism can operate in the pore interior. The flow in each case is therefore driven by a solvent, or tracer solvent, concentration gradient; the linear solvent concentration ρ_B at the interface with compartment B must be different from its value ρ_A at the interface with compartment A. It is obvious that

$$k_s = k_P, \qquad (11)$$

since the response to identical linear concentration differences $\rho_B - \rho_A$ must be identical, regardless of the physical reason for the existence of this difference (i.e., whether induced by a pressure difference between the two compartments or a difference in impermeable solute concentrations). Eq. (11) will also be obtained below by an independent argument. It will also be seen that k^* (the tracer diffusion coefficient in the pore divided by pore length) is different from k_s and k_p; nonetheless, K^* in eq. (1) turns out to be equal to K_s, a result which is both non-trivial and surprising for the general case in which solvent–solvent interactions inside the pore are taken fully into account.

A central position is held by the linear solvent chemical potential λ_S in the interior of the pore:

$$\lambda_S[T, \rho(x)] = \bar{\lambda}_S(T) + RT \ln \rho(x) + \lambda_S^{ex}[T, \rho(x)] \,. \quad (12)$$

Pressure is not a meaningful variable in the interior of an ultra-narrow pore, so λ_S is considered as a function of the temperature T of the entire isothermal system and of $\rho(x)$, the linear solvent concentration at position x in the pore. If the pressure is P_0 in both compartments A and B, and if these compartments contain pure solvent, then $\rho(x) \equiv \rho_0$ and λ_S is uniform throughout the pore. The term $\bar{\lambda}_S$ accounts for the translational degrees of freedom of a single solvent molecule in the pore and for the interactions of the solvent molecule with the constituent molecules of the pore. The term $RT \ln \rho$ is the usual concentration term appearing in the "ideal dilute" form of a solute chemical potential. The sum of the first two terms is in fact the dilute-solution form of a solute chemical potential, the solvent molecules in the pore playing the role of "solute", while the "solvent" is the pore material. The final term λ_S^{ex}, crucial for a proper understanding of the derivation to follow, is the "excess' part of the chemical potential; it accounts for the effect of interactions among solvent particles in the pore. The reader may wish to think of this term as equal to RT times the natural logarithm of an activity coefficient, but regardless of the notation employed, the important point is that λ_S^{ex} represents the effect of solvent–solvent forces in the pore. Moreover, if ρ is appreciable, λ_S^{ex} may be large compared to RT, and, in any event, should not be regarded as a small activity coefficient correction. Incidentally, the interaction forces are averages and are strongly influenced by the close proximity of the pore material; they cannot be assumed similar to solvent interactions in bulk solvent.

3. Tracer diffusion

For this experiment, the total linear concentration, solvent plus tracer solvent, is equal to ρ_0 at all points in the pore. We have

$$\rho_B^* = \rho_0 v_S^0 c_{S*}^B, \quad \rho_A^* = \rho_0 v_S^0 c_{S*}^A,$$

that is, the ratio of tracer solvent to total solvent must be the same at each side of a pore–compartment interface. Substitution into eq. (8) yields,

$$j_{S*} = -k^* \rho_0 v_S^0 (c_{S*}^B - c_{S*}^A). \quad (13)$$

Comparison with eq. (1) provides the connection between the phenomenological coefficient K^* and the "microscopic" quantities k^* and ρ_0:

$$K^* = v_S^0 \rho_0 k^*. \quad (14)$$

4. Pressure flow

To transform eq. (10) into the form of eq. (3) requires calculation of the relation between $\rho_B - \rho_A$ and $P_B - P_A$. To this end, assume local equilibrium at the pore–compartment interfaces,

$$\lambda_S(\rho) = \mu_S^0(P). \quad (15)$$

This equation states that the chemical potential of the linear pore solvent at the interface equals the chemical potential of pure bulk solvent and provides an implicit relation between ρ and P. Taking differentials of both sides and integrating, we get

$$\int_{\rho_0}^{\rho_A} (d\lambda_S/d\rho) d\rho = v_S^0 (P_A - P_0). \quad (16)$$

With use of eq. (12),

$$RT \ln(\rho_A/\rho_0) + \int_{\rho_0}^{\rho_A} (d\lambda_S^{ex}/d\rho) d\rho = v_S^0 (P_A - P_0). \quad (17)$$

Eq. (17) shows that ρ is not generally related to P in a linear manner; however, if $P_A - P_0$ is sufficiently small, the left side may be linearized in $\rho_A - \rho_0$,

$$(RT/\rho_0)(\rho_A-\rho_0)+(\mathrm{d}\lambda_S^{ex}/\mathrm{d}\rho_0)(\rho_A-\rho_0) = v_S^0(P_A-P_0) \qquad (18)$$

or

$$\rho_A-\rho_0=(v_S^0\rho_0/RT)[1+\mathrm{d}(\lambda_S^{ex}/RT)/\mathrm{d}\ln\rho_0]^{-1}(P_A-P_0). \qquad (19)$$

An analogous relation may be written at the interface with compartment B, so that

$$\rho_B-\rho_A=(v_S^0\rho_0/RT) \times [1+\mathrm{d}(\lambda_S^{ex}/RT)/\mathrm{d}\ln\rho_0]^{-1}(P_B-P_A). \qquad (20)$$

Substitution of eq. (20) into eq. (10) and comparison with eq. (3) shows

$$K_P=(k_P v_S^0\rho_0/RT)[1+\mathrm{d}(\lambda_S^{ex}/RT)/\mathrm{d}\ln\rho_0]^{-1}. \qquad (21)$$

Thus the relation between K_P and k_P is not simple, depending strongly on solvent–solvent interaction in the pore.

There is, however, a relation between k_P and k^* which greatly simplifies eq. (21). The flux j_S caused by a gradient $\mathrm{d}\rho/\mathrm{d}x$, where x is position in the pore, may be written as the superposition of two terms,

$$j_S=-D^*(\mathrm{d}\rho/\mathrm{d}x)-(\rho/\zeta^*)(\mathrm{d}\lambda_S^{ex}/\mathrm{d}x). \qquad (22)$$

The first term is due to the purely random motion of the solvent in the pore, and D^* is the self-diffusion constant in the pore. The second term describes the drift velocity of a pore solvent molecule directed by the net force $-(\mathrm{d}\lambda^{ex}/\mathrm{d}x)$ which does not average to zero because there are more solvent molecules on one side of any given solvent molecule than on the other. This force is absent in a tracer diffusion experiment because the environment about a solvent molecule in the interior of the pore is then symmetric. The contribution to the flux is obtained by multiplying the force by the concentration ρ and dividing by the friction coefficient ζ^*. Using the Einstein relation $D^*\zeta^* = RT$, noting that $\mathrm{d}\lambda_S^{ex}/\mathrm{d}x=(\mathrm{d}\lambda_S^{ex}/\mathrm{d}\rho)(\mathrm{d}\rho/\mathrm{d}x)$, and integrating along the length l of the pore, we may reduce eq. (22) to the form,

$$j_S=-l^{-1}D^*[1+\mathrm{d}(\lambda_S^{ex}/RT)/\mathrm{d}\ln\rho_0](\rho_B-\rho_A). \qquad (23)$$

Since $k^*=D^*l^{-1}$, eq. (23) implies that

$$k_P=k^*[1+\mathrm{d}(\lambda_S^{ex}/RT)/\mathrm{d}\ln\rho_0], \qquad (24)$$

a formula exactly analogous to the well-known general relation between the tracer diffusion coefficient of a solute in bulk solution and the binary diffusion constant (i.e. that which governs solute diffusion in a macroscopic solute gradient) when account is taken of solute–solute interaction by means of an activity coefficient correction [14]. In this case, however, since the solvent molecules in the pore may be closely packed, the "activity coefficient correction", that is, the second term of the bracketed factor in eq. (24), is possibly very large.

With eq. (24), eq. (21) becomes

$$K_P=v_S^0\rho_0k^*/RT, \qquad (25)$$

or, with eq. (14),

$$K_P=K^*/RT. \qquad (26)$$

Eq. (26) is the central result of this paper. Together with eq. (6) it also affirms that

$$K_s=K^*, \qquad (27)$$

the equality of the osmotic permeability and the tracer diffusion permeability for single-file solvent transport. Although the result may be said to be trivially obvious in the absence of interactions among solvent molecules in the pore (consider the limiting case of a pore whose molecular nature is such that ρ is very small), in the presence of such interactions (large ρ), it is quite surprising. Indeed, it then is a consequence of the exact compensation of two opposing effects of the interaction: if the interaction is such as to decrease the equilibrium partitioning of solvent into the pore, as described by eq. (19), it nevertheless increases the diffusion rate within the pore, as described by eq. (24).

5. Osmotic flow

In this section we rederive eq. (27) by direct consideration of an osmotic flow experiment. The pressures in compartments A and B are both equal to P_0, but there is a concentration difference $c_s^B-c_s^A$ of impermeable solute. At a pore–compartment interface,

$$\mu_S=\lambda_S \qquad (28)$$

or

$$\mu_S^0 - RTv_S^0 c_s = \bar{\lambda}_S + RT \ln \rho + \lambda_S^{ex}(\rho), \tag{29}$$

where the ideal dilute-solution form of the bulk solvent chemical potential μ_S has been used (i.e. osmotic coefficient equals unity). But

$$\mu_S^0 = \bar{\lambda}_S + RT \ln \rho_0 + \lambda_S^{ex}(\rho_0), \tag{30}$$

that is, the chemical potentials are equal in the absence of solute also. Combination of eqs. (29) and (30) yields

$$RT \ln(\rho/\rho_0) + [\lambda_S^{ex}(\rho) - \lambda_S^{ex}(\rho_0)] = -RTv_S^0 c_s. \tag{31}$$

Linearizing,

$$(RT/\rho_0)(\rho - \rho_0) + (d\lambda_S^{ex}/d\rho_0)(\rho - \rho_0) = -RTv_S^0 c_s \tag{32}$$

or

$$\rho - \rho_0 = -v_S^0 \rho_0 [1 + d(\lambda_S^{ex}/RT)/d \ln \rho_0]^{-1} c_s. \tag{33}$$

This relation holds both when $\rho = \rho_A$, $c_s = c_s^A$ and when $\rho = \rho_B$, $c_s = c_s^B$. Hence,

$$\rho_B - \rho_A = v_S^0 \rho_0 [1 + d(\lambda_S^{ex}/RT)/d \ln \rho_0]^{-1} (c_s^A - c_s^B). \tag{34}$$

Substitution into eq. (9) and comparison with eq. (2) gives

$$K_s = k_s v_S^0 \rho_0 [1 + d(\lambda_S^{ex}/RT)/d \ln \rho_0]^{-1}. \tag{35}$$

Eqs. (6), (21), and (35) imply that $k_s = k_P$, an independent verification of a result already stated in eq. (11). Hence, eq. (24) remains valid if k_P is replaced by k_s, and its substitution into eq. (35) yields the desired result,

$$K_s = k^* v_S^0 \rho_0 = K^*, \tag{36}$$

where reference is made to eq. (14).

6. Comparison with calculations of Dick and of Longuet-Higgins and Austin

We have concluded here that, in spite of interactions among solvent molecules in the pore, the osmotic permeability equals the tracer diffusion permeability. As mentioned in the introduction, Dick's result [2] is that the former is greater than the latter. Although his calculation fails because it is not rooted in sound kinetic theory and hence is internally inconsistent, it does have the virtue of emphasizing that the presence of solvent–solvent interactions (in Dick's model, these are pure repulsions among "billiard balls"), means that separate calculations must be given for each of the two experimental situations and that the result of the calculations is not obvious in advance.

The calculation of Longuet-Higgins and Austin [5], on the other hand, yields the same result obtained in this paper, $K_s = K^*$. Although their argument proceeds from the auto-correlation formalism of irreversible statistical mechanics and therefore gives the impression of great generality, close inspection of their paper indicates that it oversimplifies the fluctuating solvent flux at equilibrium and neglects entirely the effect of solvent–solvent interaction inside the pore. The flux is incompletely described because a solvent molecule, initially inside the pore, and which proceeds to the end of the pore, is counted as having traversed the pore–compartment interface, i.e., passed from the pore into the solution; the boundary process, the partitioning effect, is neglected. Further, their eq. (43), expressing the lack of correlation between velocities of any two different solvent molecules in the pore, is an unambiguous statement of the neglect of solvent–solvent interactions within the pore. The effect of these omissions, translated into the notation employed here, is to conclude incorrectly that $k_s = k^*$ [see eqs. (11) and (24)], and also to conclude, equally incorrectly, that $K_s = v_S^0 \rho_0 k_s$ [see eq. (35)], whence the correct result, $K_s = K^*$, is obtained, but only due to cancellation of errors, from eq. (14).

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