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TRACERS, TRANSFER THROUGH MEMBRANES, AND COEFFICIENTS OF TRANSFER*

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Abstract. The rate of flow of a tagged species of a material substance through a permeable membrane is proportional to the rate of flow of the substance itself when, and only when, the species mol fraction of the substance is the same on both sides of the barrier. The ratio of the osmotic transfer coefficient of a substance in a particular barrier to the exchange coefficient, determinable with a tracer, is greater than one.

The relation between the rate of flow of a substance, $\dot{n}_s$, and the rate of flow of a tagged species of the substance, $\dot{n}_{s^*}$, across a plane of observation located within the barrier of the linear transfer system, phase α , membrane, phase β , has been derived (1). A more general but less awkward derivation of the same equation is given below (2).

The general equation for the rate of flow of s across a plane of observation may be written,

$$-\dot{n}_s = \sum_k M_{sk} \frac{d\mu_k}{dx} \quad (1)$$

in which the M_{sk} 's are the generalized admittance coefficients of a barrier and $d\mu_k/dx$ is the algebraic representation of the chemical potential gradient of a neutral molecule, or the electrochemical potential gradient of an ion in the barrier of a linear transfer system. The summation is to include all the kinetic species present at the plane of observation (3). An outline of the derivation of equation 1 from Newton's first and second laws of motion applied to steady state transfer systems, and a demonstration of the validity of the Onsager reciprocal relations, $M_{sk} = M_{ks}$, based upon Newton's third law of motion, have also been presented (4).

Suppose the transfer system to be closed to s . Imagine that the substance s is composed of two subspecies, s' and s'' , whose kinetic properties are identical. Let s' and s'' have some property by which they can be distinguished but which has no effect on their motions. The species mol fraction of the two subspecies and other relations among them can be written as follows:

$$n_s = N_1 n_s, \quad , \text{ also } N_1 + N_2 = 1 \quad (2)$$

$$\dot{n}_s = N_1 \dot{n}_s + n_s \dot{N}_1 \quad dN_1 = -dN_2$$

The equations for the flow rates of the two subspecies across the plane of observation may be obtained by writing equation 1 in greater detail. They are

$$\begin{aligned} -\dot{n}_s &= M_{11} \frac{d\mu_1}{dx} + M_{12} \frac{d\mu_2}{dx} + \sum_{k=3}^s M_{1k} \frac{d\mu_k}{dx} \\ -\dot{n}_{s''} &= M_{21} \frac{d\mu_1}{dx} + M_{22} \frac{d\mu_2}{dx} + \sum_{k=3}^s M_{2k} \frac{d\mu_k}{dx} \end{aligned} \quad (3)$$

The flow rate of the substance s is the sum of the flow rates of the two subspecies, or

$$-\dot{n}_s = (M_{11} + M_{12}) \frac{d\mu_1}{dx} + (M_{12} + M_{22}) \frac{d\mu_2}{dx} + \sum_{k=3}^s (M_{1k} + M_{2k}) \frac{d\mu_k}{dx} \quad (4)$$

when use is made of the Onsager reciprocal relations. Let $d\mu_1/dx$ and $d\mu_2/dx$ in equations 3 and 4 be zero. The following equations then hold:

$$-\dot{n}_1 = \quad (5)$$

since the $(d\mu_k/dx)$'s cannot produce a $\dot{n}_1$ or a $\dot{n}_2$ because of the presumed identical kinetic properties of s' and s'' . Equations 5, therefore, require that

$$M_{1k} = N_1 M_{2k} \quad \text{also} \quad \frac{M_{1k}}{M_{2k}} = \frac{N_1}{N_2} \quad (6)$$

The relations of the chemical potential gradients of the two subspecies to the chemical potential gradient of the species s and the gradient of mol fraction are known (1). These may be written

$$\begin{aligned}\frac{d\mu_1}{dx} &= \frac{d\mu_s}{dx} + RT \frac{d \ln N_1}{dx} = \frac{d\mu_s}{dx} + \frac{RT}{N_1} \frac{dN_1}{dx} \\ \frac{d\mu_2}{dx} &= \frac{d\mu_s}{dx} + RT \frac{d \ln N_2}{dx} = \frac{d\mu_s}{dx} - \frac{RT}{N_2} \frac{dN_2}{dx}\end{aligned}\quad (7)$$

Replacing the chemical potential gradients in equation 4 by their equivalents as given by equation 7 yields

$$-\dot{n}_s = (M_{11} + 2M_{12} + M_{22}) \frac{d\mu_s}{dx} + \left[M_{11} + M_{12} - \frac{N_1}{N_s} (M_{12} + M_{22}) \right] \frac{RT}{dx} \frac{d \ln N_1}{dx} + \sum_{k=3}^s M_{sk} \frac{d\mu_k}{dx} \quad (8)$$

Now the gradient, $d \ln N_1 / dx$, cannot affect $\dot{n}_s$ since n_s , and $n_{s,0}$ are presumed to have identical kinetic properties. Thus in order for equation 8 to be exact, the following relation must hold.

$$M_{11} + M_{12} = \frac{N_1}{N_s} (M_{12} + M_{22}) \quad (9)$$

and $\dot{n}_s$ is given by

$$-\dot{n}_s = (M_{11} + 2M_{12} + M_{22}) \frac{d\mu_s}{dx} + \sum_{k=3}^s M_{sk} \frac{d\mu_k}{dx} \quad (10)$$

By substituting the relations given in equations 7 back into the first member of equations 3, and using the relations given by equations 6 and 9, $\dot{n}_s$ may now be written as

$$-\dot{n}_s = N_s \left[(M_{11} + 2M_{12} + M_{22}) \frac{d\mu_s}{dx} + \sum_{k=3}^s M_{sk} \frac{d\mu_k}{dx} \right] + \left(\frac{M_{11}M_{22} - M_{12}^2}{M_{12} + M_{22}} \right) \frac{RT}{dx} \frac{d \ln N_1}{dx} \quad (11)$$

On comparison of this equation with equation 10 it is seen that

$$-j_s = -N_1 \dot{n}_s + M_{ex} \frac{RT d \ln N_1}{dx} \quad (12)$$

in which M_{ex} , designated as an exchange coefficient, is taken equal to

$$(M_{11}M_{22} - M_{12}^2)/(M_{12} + M_{22}).$$

Equation 12 is the basic equation for the relation of the rate of flow of a tagged species across a plane of observation to the rate of flow of the species itself, and may be applied to an actual experiment if the tagged subspecies does not differ materially in molecular mass or density from the second subspecies. In the majority of biological experiments, the errors introduced by assuming identical kinetic properties for two subspecies containing isotopes of the same chemical element are usually much smaller than the experimental errors, therefore, neglecting isotope effects is entirely proper. As equation 12 implies, the flow of the tagged material is proportional to the flow of the substance itself when, and only when, the mol fraction of the species is the same in the two phases adjacent to the barrier.

In the usual tracer experiments, the tracer is added to one phase or the other in "weightless" amounts when radioactive isotopes are used as tags, or in small amounts when stable isotopes are employed. This means that N_1 , the species mol fraction of the tracer at the plane of observation approaches zero, and that the observed flow of the tracer bears little relation to the flow of the substance concerned. Such was the case, for example, in the experiments performed by Ussing (5) and Durbin, Frank and Solomon (6). In the experiments of Prescott and Zeuthen (7) N_1 was appreciable, and then the flow of the substance concerned did have a measurable effect on the flow of tracer. The majority of tracer experiments allow one to determine only the magnitude of M_{ex} for a particular substance in a particular membrane.

If separate experiments of the proper kind are done on a particular membrane the ratio of M_{os}/M_{ex} , where M_{os} is defined as equal to $M_{11} + 2M_{12} + M_{22}$ (See equation 10), should be greater than one, for

$$\frac{M_{os}}{M_{ex}} = \frac{(M_{11} + 2M_{12} + M_{22})(M_{11} + M_{22})}{M_{11}M_{22} - M_{12}^2} > 1 \quad (13)$$

since $M_{11}M_{22} - M_{12}^2$ is positive. The experiments of Hevesy, Hofer, and Krogh(8) done on the frog's skin yielded "unexplained" ratios of three to five, and the ratios obtained for certain artificial membranes by Mauro (9) were several hundredfold.

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References and Notes

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