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The Gibbs paradox and unidirectional fluxes

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Abstract. The Gibbs paradox is introduced by means of a particular example: the interdiffusion of two molecular species through a membrane. In the limit when passing from the interdiffusion of two distinct species to that of identical species, the equation for dissipation (or, equivalently, entropy production) fails catastrophically. In the case of an equilibrium system, one finds the paradoxical situation of a zero net flux in conjunction with nonzero dissipation. A general analysis of the problem is given in terms of a metrical theory of irreversible thermodynamics. Its mathematical structure provides a criterion for *identity* sufficient to resolve the paradox. Metrical aspects of the Principle of Superposition are examined. The paper ends with a discussion of the conceptual and physical difficulties that the Gibbs paradox poses for the idea of unidirectional fluxes. In particular, it is demonstrated that the commonly held notion that net flux is a superposition of an inward and an outward flux violates the Second Law.

Key words: Gibbs paradox, membrane transport theory, unidirectional fluxes

1. Introduction

It might well be claimed that biology is the science of the Second Law, whereas physics is the science of the First Law. Not that physicists do not have a keen appreciation of the majesty of the Second Law. Eddington (1929) boldly asserts that "the law that entropy always increases – the second law of thermodynamics – holds, I think, the supreme position among the laws of Nature ... if your theory is found to be against the second law of thermodynamics I can give you no hope; there is nothing for it but to collapse in deepest humiliation." Quite true, but essentially beside the point since physics has its foundations in mechanics, quantum mechanics, and field theory – all based in the realm of the Hamiltonian, where entropy makes no appearance. In fact, it remains a mystery to the physicist how macroscopic irreversibility springs from a primary microscopic world of perfect reversibility: Prigogine (1980).

On the other hand, the theories of the biologist are almost always at risk, being, as they are, much concerned with the directionality of spontaneous processes. The biochemist is well aware that a proposed reaction scheme must proceed with a diminution of Gibbs free energy. The biophysicist watches carefully to see if a supposedly passive transport system does indeed have positive dissipation. In biology, this focus upon positive entropy production is central and essential – but one can have too much of a good thing. One of the basic concepts in the analysis of transport through biological membranes, unidirectional fluxes, leads immediately to an *over*-evaluation of entropy production. In the extreme, this concept leads to the scandal of positive entropy production in equilibrium systems: the Gibbs paradox.

In this paper we shall *(1)* review the equations describing the interdiffusion of two distinct molecular species, *(2)* show that one is led to the Gibbs paradox upon assuming the two species are identical, *(3)* resolve the paradox using a metrical theory of irreversible thermodynamics, and *(4)* discuss the implications for the concept of unidirectional fluxes. A metrical theory of transport has a powerful mathematical structure which allows a precise analysis of superposition and identity – crucial elements in the resolution of the paradox.

2. Interdiffusion

Consider the interdiffusion of two molecular species labeled with the indices 1 and 2. Suppose the usual experiment situation where a membrane separates two well-stirred reservoirs labeled I and II (Fig. 1a). As-

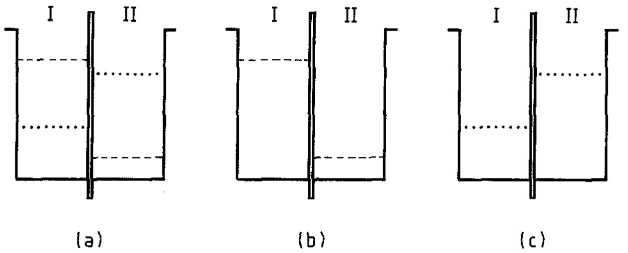

Fig. 1. In the three transport systems above a membrane separates reservoirs I and II. Concentrations of molecular species 1 are indicated by *dashed lines*, those of species 2 by *dotted lines*

sume that there is no volume flow and that there is no coupling between the two species. For a large class of membranes separating moderate concentration differences the steady-state fluxes are given simply by

$$J_1 = P_1 \Delta C_1 \qquad \text{and} \qquad J_2 = P_2 \Delta C_2 , \tag{1}$$

where $\Delta C_i = C_i^{\mathrm{I}} - C_i^{\mathrm{II}}$ $(i=1, 2)$ is the concentration difference and P_i is the membrane permeability. These fluxes, dropping through a potential difference $\Delta\mu_i = RT \ln (C_i^{\mathrm{I}}/C_i^{\mathrm{II}})$, dissipate energy in the membrane at the rate[1]

$$\delta = J_1 \Delta\mu_1 + J_2 \Delta\mu_2 = RTP_1 \Delta C_1 \ln \frac{C_1^{\mathrm{I}}}{C_1^{\mathrm{II}}} + RTP_2 \Delta C_2 \ln \frac{C_2^{\mathrm{I}}}{C_2^{\mathrm{II}}} . \tag{2}$$

Note that each term above is positive, thus assuring that the Second Law is not violated: i.e. $\delta \geq 0$. In terms of the entropy source term for irreversible processes, σ_s, the dissipation function is $\delta \equiv T\sigma_s$.

Now let us consider a special case, and then a very special (and perplexing) case. First, we impose a bit of symmetry on the experiment depicted in Fig. 1 by setting $C_1^{\mathrm{I}} = C_2^{\mathrm{II}} \neq 0$ and $C_1^{\mathrm{II}} = C_2^{\mathrm{I}} \neq 0$. Thus, $\Delta C_1 = -\Delta C_2$. By (1) and (2)

$$J_1 = P_1 \Delta C_1 \qquad \text{and} \qquad J_2 = -P_2 \Delta C_1 \tag{3}$$

and

$$\delta = RT (P_1 + P_2) \Delta C_1 \ln \frac{C_1^{\mathrm{I}}}{C_1^{\mathrm{II}}} . \tag{4}$$

For the very special case, assume that molecular species 1 and 2 are identical. This implies that $P_1 = P_2$. Here we find from (3) that

$$J_1 = P_1 \Delta C_1 \qquad \text{and} \qquad J_2 = -P_1 \Delta C_1 . \tag{5}$$

But since the species are identical, J_2 is a flux of species 1. Therefore, we must combine the two fluxes above to give the *net* flux

$$J = J_1 + J_2 = 0 . \tag{6}$$

This is to be expected since the *net* concentration difference is really

$$\Delta C = \Delta C_1 + \Delta C_2 = 0 . \tag{7}$$

The dissipation function for this system is given by (4) as

$$\delta = 2RTP_1 \Delta C_1 \ln \frac{C_1^{\mathrm{I}}}{C_1^{\mathrm{II}}} , \tag{8}$$

which is not equal to zero. This is profoundly disturbing because the system is obviously at equilibrium. We have just encountered a variant of the famous Gibbs paradox. The crux is that an analysis that gives the proper evaluation of the entropy change (or, equivalently, the dissipation) associated with a process involving distinct interdiffusing species fails catastrophically in the limit as the species become identical. The above analysis will not precipitate a crisis in thermal physics. The problem does not lie in physics, but rather in our assumption that two systems involving identical species can be superimposed in a naive manner. Linear systems superimpose, and if we had stopped our analysis at (6) and (7), all would appear to be well. However, in going one step further, we see that in each of the two systems to be superimposed the fluxes, though they "cancel" each other, give rise to positive dissipations which do not "cancel" in the superposition. As we shall see, superposition is possible but involves a bilinear (not linear) form.

No other problem in classical physics seems to have the staying power of the Gibbs paradox; it has exercised the minds of theoreticians for over a century. With the certitude of the discrete structure of atoms came the assertion that the paradox, in fact, does not occur because of the physical impossibility of two distinct atomic species becoming identical in the limit of a continuous process. The appealing simplicity of this explanation has made it a favorite for elementary textbooks. One of the objections to this resolution to the paradox is that it raises a more perplexing and profound question: is a certain granularity of the material world all that prevents the Second Law from being violated with impunity? More serious analyses focus upon whether identity is absolute or operationally relative: Van Kampen (1984). When reservoir I in Fig. 1a

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[1] If we follow Kedem and Katchalsky (1958) and set $\ln (C_i^{\mathrm{I}}/C_i^{\mathrm{II}}) = \Delta C_i/\bar{C}_i$, we obtain the dissipation function (2) as a quadratic form, namely:

$$\delta = RT\frac{P_1}{\bar{C}_1}(\Delta C_1)^2 + RT\frac{P_2}{\bar{C}_2}(\Delta C_2)^2 , \tag{2a}$$

with $\bar{C}_i \cong (C_i^{\mathrm{I}} + C_i^{\mathrm{II}})/2$. In this manner the singularity in (2) for zero concentrations can be avoided.

contains a solution of two distinct species, the decomposition into the subsystem of Fig. 1 b and c is unique. However, when reservoir I contains only a single species, there is no conceivable procedure to make a unique partition into subsystems. Thus, from an operational viewpoint, (1) and (2) are sufficient but the passage to the limit of identical species is not allowed. We shall follow the dictum of modern physics that what is not expressly prohibited must be allowed. Since there can be no unique partition, all possible partitions must be allowed in our analysis. Therefore, the conceptual prohibition against the limit process is lifted. This necessitates the conclusion that (1) and (2) are not sufficient. In their re-evaluation of Von Neumann's quantum mechanical analysis, Dieks and Van Dijk (1988) conclude that certain conceptual difficulties in applying the concept of mixing entropy make it doubtful that his calculation, though mathematically correct, does indeed resolve the paradox for quantum systems – and hence it does not alleviate the classical Gibbs paradox. A shift in viewpoint from equilibrium to nonequilibrium thermodynamics allows us to calculate directly the entropy production from irreversible processes and thereby gain some fresh insights into the Gibbs paradox – insights which are particularly relevant to an examination of the concept of unidirectional fluxes.

3. Irreversible thermodynamics

Any resolution of the Gibbs paradox must proceed from a precise mathematical characterization of *identity*. In the preceding discussion we assumed that being identical implied $P_1 = P_2$. This is true, but as we shall see, not the whole story. Furthermore, we shall see that identity is central to the applicability of superposition. But first we must present the analytical tools to be used in the following discussion: namely, techniques from a metrical theory of irreversible thermodynamics we have developed in a series of papers.

It suffices here to present in a formal manner the basic metrical structure of irreversible thermodynamics. We shall proceed by analogy to the structure of a simple n-dimensional vector space with skew-rectilinear *coordinates* e^i $(i = 1, \dots n)$. In the dual space the covariant coordinates are denoted e_i. As regards representation, a vector $\boldsymbol{R}$ is invariant: i.e.

$$\boldsymbol{R} = e^i x_i = e_j x^j\,, \tag{9}$$

where x_i and x^i are scalar *components*. The Einstein summation convention is used here and in the following. Indices are raised (or lowered) by means of the fundamental metric tensor $g^{ij} \equiv e^i \cdot e^j$ $(g_{ij} \equiv e_i \cdot e_j)$. This can be summarized graphically in a duality-invariance-diagram (DID) as

$$\begin{tikzcd} x_i \arrow[rr, "g^{ij}"] \arrow[dr, dash] & & x^j \arrow[dl, dash] \\ & e^i x_i = \boldsymbol{R} = e_j x^j & \\ e^i \arrow[ur, dash] & & e_j \arrow[ll, "g^{ij}"'] \arrow[ul, dash] \end{tikzcd} \tag{10}$$

The metric structure is established by the norm

$$\|\boldsymbol{R}\|^2 = \boldsymbol{R} \cdot \boldsymbol{R} = e^i x_i \cdot e^j x_j = g^{ij} x_i x_j\,. \tag{11}$$

In our metrical theory of irreversible thermodynamics, Richardson et al. (1982), the central concept is the *response tensor* (dyadic) $\underset{\sim}{\mathbf{R}} = \boldsymbol{a}^i \boldsymbol{F}_i$, where the vector $\boldsymbol{F}_i$ is the force imposed upon molecular species i, and $\boldsymbol{a}^i$ is a conjugate constitutive parameter. A given transport system is characterized by a fixed set of constitutive parameters, $\{\boldsymbol{a}^i\}$. The forces, being under the experimenter's control, are freely ranging variables. The space spanned by $\underset{\sim}{\mathbf{R}}$ is called description space (D-space). It is postulated that an equivalent description of system response can be given in terms of the associated fluxes, $\boldsymbol{J}^j$, and a set of constitutive parameters, $\{\boldsymbol{a}_j\}$. Thus, $\underset{\sim}{\mathbf{R}}$ is invariant in D-space: i.e.

$$\underset{\sim}{\mathbf{R}} = \boldsymbol{a}^i \boldsymbol{F}_i = \boldsymbol{a}_j \boldsymbol{J}^j\,. \tag{12}$$

In D-space, the $\boldsymbol{a}^i$ and $\boldsymbol{a}_j$ "behave" as coordinates, and the $\boldsymbol{F}_i$ and $\boldsymbol{J}^j$ "behave" as components.[2] Indices are raised by the metric tensor $L^{ij} \equiv \boldsymbol{a}^i \cdot \boldsymbol{a}^j$ (e.g. $\boldsymbol{a}^i = L^{ij} \boldsymbol{a}_j$), giving the following DID:

$$\begin{tikzcd} \boldsymbol{F}_i \arrow[rr, "L^{ij}"] \arrow[dr, dash] & & \boldsymbol{J}^j \arrow[dl, dash] \\ & \boldsymbol{a}^i \boldsymbol{F}_i = \underset{\sim}{\mathbf{R}} = \boldsymbol{a}_j \boldsymbol{J}^j & \\ \boldsymbol{a}^i \arrow[ur, dash] & & \boldsymbol{a}_j \arrow[ll, "L^{ij}"'] \arrow[ul, dash] \end{tikzcd} \tag{13}$$

The norm in D-space is given by the double-dot product

$$\begin{aligned} \|\underset{\sim}{\mathbf{R}}\|^2 &= \underset{\sim}{\mathbf{R}} : \underset{\sim}{\mathbf{R}} = (\boldsymbol{a}^i \boldsymbol{F}_i) : (\boldsymbol{a}^j \boldsymbol{F}_j) \geq 0 \\ &= (\boldsymbol{a}^i \cdot \boldsymbol{a}^j)(\boldsymbol{F}_i \cdot \boldsymbol{F}_j) = L^{ij} \boldsymbol{F}_i \cdot \boldsymbol{F}_j\,. \end{aligned} \tag{14}$$

The expression on the right-hand side is the well-known quadratic formula for the dissipation function, δ. Therefore, we are led to conclude $\|\underset{\sim}{\mathbf{R}}\|^2 \equiv \delta$. Thus, the metrical structure inherent in D-space corresponds to the mathematical form of irreversible thermodynamics. Onsager reciprocity is provided by the symmetry of the dot product via $L^{ij} = (\boldsymbol{a}^i \cdot \boldsymbol{a}^j) = (\boldsymbol{a}^j \cdot \boldsymbol{a}^i) = L^{ji}$. A note of caution is in order. The analogy between the DID's (10) and (13) must not be taken beyond what is presented above. For example, the $\{\boldsymbol{a}^i\}$

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[2] Note that the use of the Einstein summation convention introduces *variance* and that $\boldsymbol{J}^j$ lies in the space dual to $\boldsymbol{F}_i$. In terms of the notation of Sect. 2, $\boldsymbol{J}^2$ is just J_2 (and not flux squared)

are not actually a basis for D-space, and the matrix $[L^{ij}]$ does not necessarily have a unique inverse. For a precise mathematical derivation of the properties of this intriguing metric space, the reader should consult Richardson et al. (1982) and Louie and Richardson (1986).

4. Identity and the Gibbs paradox

Now we are prepared to re-examine the membrane transport system depicted in Fig. 1 a. It is essential to start with flux equations which explicitly include coupling: i.e. by (13)

$$J^i = L^{ij} F_j \qquad i, j = 1, 2\,, \tag{15}$$

where

$$L^{11} = \boldsymbol{a}^1 \cdot \boldsymbol{a}^1\,, \qquad L^{22} = \boldsymbol{a}^2 \cdot \boldsymbol{a}^2\,, \qquad L^{12} = L^{21} = \boldsymbol{a}^1 \cdot \boldsymbol{a}^2\,, \tag{16}$$

and the dissipation function δ is given by (14).[3] We shall reconsider each of the assumptions made in the earlier analysis of the interdiffusion of two molecular species.

It is physically reasonable to assume that there may be no coupling between two distinct molecular species. In that case, it is certainly true that $L^{12} = L^{21} = 0$, and (14) and (15), like (1) and (2), pose no problems for distinct species. At this point, we can use the mathematical structure of our metrical theory of irreversible thermodynamics to probe a bit deeper into the implications of assuming zero coupling. By (16), zero coupling implies $\boldsymbol{a}^1 \cdot \boldsymbol{a}^2 = 0$, which means that $\boldsymbol{a}^1$ and $\boldsymbol{a}^2$ are orthogonal. This is depicted graphically in Fig. 2 a. The *angle of coupling*, ϑ, can be calculated via (16) as

$$\vartheta = \cos^{-1}(L^{12}/\sqrt{L^{11} L^{22}})\,. \tag{17}$$

Note that for the condition of zero coupling, the lengths of the constitutive vectors are immaterial. Even if $\|\boldsymbol{a}^1\| = \|\boldsymbol{a}^2\|$ (and thus $L^{11} = L^{22}$), one still has $L^{12} = 0$ for $\vartheta = \pi/2$. Non-zero coupling is depicted in Fig. 2 b.

The special case $F_1 = -F_2$ poses no problems. Let us now examine the very special case where it is assumed that species 1 and 2 are identical. It was physically reasonable to assume that $P_1 = P_2$ for identical species since these permeabilities are, to a great extent, independent of concentrations. This is not true for the L^{ij}'s (nor for the $\boldsymbol{a}^i$'s) because they are highly dependent upon concentrations. However, we can state that

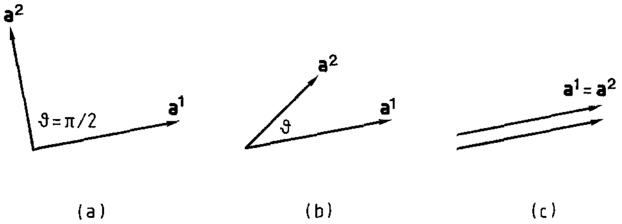

Fig. 2. The coupling coefficient $L^{12} = \boldsymbol{a}^1 \cdot \boldsymbol{a}^2$ is determined by the lengths of the constitutive parameters $\boldsymbol{a}^1$ and $\boldsymbol{a}^2$ and the angle of coupling ϑ

$L^{11} = L^{22}$ for identical species in identical physical circumstances. In particular, this is valid for our very special case, where Fig. 1 c becomes the mirror image of Fig. 1 b. Furthermore, in this symmetric system $\boldsymbol{a}^1 = \boldsymbol{a}^2$, as depicted in Fig. 2 c. As will be seen below, this criterion for identity is crucial – it mandates an essential coupling. The flux equation (15) for species 1, with $F_1 = -F_2$ and identical species, is

$$J^1 = L^{11} F_1 - L^{12} F_1 = L^{11} F_1 - L^{11} F_1 = 0\,, \tag{18}$$

since $L^{12} = \boldsymbol{a}^1 \cdot \boldsymbol{a}^2 = \boldsymbol{a}^1 \cdot \boldsymbol{a}^1 = L^{11}$. Similarly, $J^2 = 0$. Thus, the net flux (6) is trivially zero. The question is: will we find $\delta \neq 0$, as in (8)? By (14) the dissipation function for this very special case is

$$\begin{aligned}\delta &= L^{11}(F_1 \cdot F_1) + L^{12}(F_1 \cdot F_2) + L^{22}(F_2 \cdot F_2) + L^{21}(F_2 \cdot F_1)\\ &= L^{11}(F_1)^2 - L^{11}(F_1)^2 + L^{11}(F_1)^2 - L^{11}(F_1)^2 = 0\,.\end{aligned} \tag{19}$$

Therefore, in this analysis the Second Law is not violated. We do not have the scandal of positive dissipation by an equilibrium system. By establishing identity at the level of $\boldsymbol{a}^1 = \boldsymbol{a}^2$ rather than at the level of $P_1 = P_2$ or $L^{11} = L^{22}$, the Gibbs paradox is resolved. With a deeper criterion for identity, the paradox simply does not occur. The epistemiological problem of the identity of subsystems comprising a complex system is developed at length in Richardson and Louie (in review). A closely related problem is that of recognition: see Louie et al. (1982). Anyone wishing to pursue this topic should start with Morrison's article (1964) on the thermodynamics of self-reproducing systems. In the replication of a complex system one does not demand an atom-for-atom identical copy; but it must be "almost" identical. The requirement for a test of replication leads Morrison to a discussion of the recognition and discrimination properties of semipermeable membranes (and to the Gibbs paradox). He proposes a quantitative test for replication which, by incorporating a measure for complexity, provides a continuous scale from non-living to living self-reproducing systems. When compared with our papers, his paper gives an instructive contrast between the methods of equilibrium and nonequilibrium thermodynamics.

The interrelated concepts of coupling, recognition, and identity emerge naturally in the thermodynamic

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[3] We have used vectors, and not scalars as in (15), because this analysis is general and not restricted to one-dimensional fluxes through a membrane (discrete systems). It applies equally well to free diffusion (continuous systems)

analysis of bioenergetics. Assuming scalar forces and fluxes (so that division is allowed), (15) can be simply manipulated to show that the dimensionless number $q = L^{12}/\sqrt{L^{11}\,L^{22}}$ is a normalized force ratio. This ratio determines uniquely the maximum efficiency of energy conversion in fuel cells: Osterle (1964) and Kedem and Caplan (1965). This *degree of coupling*, q, can be interpreted in terms of the geometry of the space of constitutive parameters, $\boldsymbol{a}_i$, by means of (17). The degree of coupling has been applied to energetic processes in biological systems, and this work is thoroughly reviewed in the monograph by Caplan and Essig (1983).

5. Superposition

At the core of the Gibbs paradox lies a principle of fundamental importance in the analysis of complex systems: namely, superposition. Physical intuition makes one feel strongly that the composite transport system in Fig. 1 a is a superposition of the two subsystems in Fig. 1 b and c. Indeed the conviction is so strong that the failure of superposition in the limit of identical species is called a paradox. It is not, however, that superposition fails for dissipative systems. It is simply that the proper quantities must be superimposed. In (3) and (4) the fluxes and the dissipation of the two subsystems were superimposed, and that did not work in the limit.

For dissipative systems, the quantity to be superimposed is the response tensor

$$\underset{\sim}{\mathbf{R}} = \boldsymbol{a}^1 F_1 + \boldsymbol{a}^2 F_2 + \ldots + \boldsymbol{a}^m F_m = \underset{\sim}{\mathbf{R}}_1 + \underset{\sim}{\mathbf{R}}_2 + \ldots + \underset{\sim}{\mathbf{R}}_m\,, \tag{20}$$

where $\underset{\sim}{\mathbf{R}}_1, \underset{\sim}{\mathbf{R}}_2, \ldots \underset{\sim}{\mathbf{R}}_m$ are the responses of the separate subsystems.

The dissipation function is the squared norm of $\underset{\sim}{\mathbf{R}}$. For two species (subsystems) we have

$$\delta \equiv \|\underset{\sim}{\mathbf{R}}\|^2 = \|\underset{\sim}{\mathbf{R}}_1 + \underset{\sim}{\mathbf{R}}_2\|^2\,. \tag{21}$$

As in any normed space one has, in general,

$$\delta \equiv \|\underset{\sim}{\mathbf{R}}_1 + \underset{\sim}{\mathbf{R}}_2\|^2 \neq \|\underset{\sim}{\mathbf{R}}_1\|^2 + \|\underset{\sim}{\mathbf{R}}_2\|^2 \equiv \delta_1 + \delta_2\,, \tag{22}$$

thereby demonstrating that one must not assume that dissipation superimposes. For our very special case, the response tensor (20) collapses to the zero tensor. Since $\delta \equiv \|\underset{\sim}{\mathbf{R}}\|^2 = \|\underset{\sim}{\mathbf{0}}\|^2 = 0$, there is no entropy production, and the paradox does not arise.

Equations (20) and (21) bear a remarkable similarity to two basic tenets of quantum mechanics: (1) amplitudes superimpose and (2) probabilities of composite events are given by the absolute values (norms) of the combined amplitudes. This superposition at the level of amplitudes, and not of probabilities, gives rise, for example, to the phenomenon of interference (classically illustrated by Young's experiment with photons passing through two slits). There are strong homologies between the mathematical structures of quantum mechanics and the metric theory of irreversible thermodynamics: Richardson and Louie (1983) and (1986).

The foregoing discussions of superposition and the resolution of the Gibbs paradox do not depend upon a strict imposition of linearity in the force-flux equations. In a metrical theory of irreversible thermodynamics, one can have Riemannian D-spaces: that is, the constitutive parameters, $\{\boldsymbol{a}^i\}$, can be functions of the forces. Thus, the force-flux equations are locally linear, but globally nonlinear.

6. Unidirectional fluxes

The Gibbs paradox is more than a mere academic curiosity. It lies unheeded in one of the basic concepts of experimental membrane physiology: the idea of unidirectional fluxes. The paradox immediately becomes apparent if in our very special case we adopt standard notation and let J^1 denote the "inward" flux, J^{in}, and J^2 denote the "outward" flux, J^{out}. In considering this situation of the interdiffusion of identical species in an equilibrium system, the membrane physiologist would qualify (6) by stating that there was a large inward flux and a large outward flux, and, being of the same magnitude, they cancelled, giving a zero net flux. In contrast, by (18) it is seen that $J^{\text{in}} = J^{\text{out}} = 0$ because of the (maximal) coupling condition for identical species: $L^{12} = L^{11} = L^{22}$. It should, by the way, be obvious that the Gibbs paradox (i.e. spurious entropy production because of improper superposition) occurs even when there is a non-zero net flux. The zero flux of the equilibrium case is simply more dramatic.

An apparently universal acceptance of a reification of simple unidirectional fluxes and their superposition makes it beside the point to cite any particular instances. However, it is instructive to consult a variety of books on membrane transport in the biology library and see at what point the Gibbs paradox enters, unnoticed, into the discussions on unidirectional fluxes. In a typical manner, one author opens his development of membrane transport theory with the proposition that a flux "is determined by the *net* movement of permeant molecules across the membrane, that is, by the excess of, say, inward movement over outward movement," and later asserts that "the unidirectional flux $J_{\text{I}\rightarrow\text{II}}$ of a penetrating species [uncharged] should be strictly proportional to the concentration C_{I} of the permeant on the side I from which penetration is occurring": Stein (1967).

There are legitimate unidirectional fluxes: namely, fluxes measured in the usual tracer experiments. The tracer placed outside the cell provides an inward tracer flux, and the tracer placed inside the cell provides an outward tracer flux. These are two distinct experiments under two distinct system conditions, and much information about transport parameters can be reduced from the tracer data. For example, the Ussing (1949) flux-ratio provides a valid test for passive transport because it is empirically determined from tracer fluxes which are unidirectional by experimental design.

One must not assume that tracers actually *trace*. The inward tracer flux does not trace an associated unidirectional flux of the cold species, nor does the outward tracer flux trace an oppositely directed unidirectional flux of the cold species. In carefully conceived experiments, superposition of such fictitious fluxes may well give the correct net flux, but the concomitant occurrence of the Gibbs paradox shows that physically they do not exist.

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