A field and circuit thermodynamics for integrative physiology. II. Power and communicational spectroscopy in biology

A. S. Iberall, H. Soodak and F. Hassler

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IBERALL, A. S., H. SOODAK, AND F. HASSLER. *A field and circuit thermodynamics for integrative physiology. II. Power and communicational spectroscopy in biology*. Am. J. Physiol. 234(1): R3–R19, 1978 or Am. J. Physiol.: Regulatory Integrative Comp. Physiol. 3(1): R3–R19, 1978.—This paper continues the development begun in Part I (15), to show in what way it is meaningful to reduce biological phenomena to physical theory at any level of organization. The appropriate level-independent physics is comprised of thermostatics, thermodynamics of irreversible processes, statistical mechanics, and nonlinear mechanics. Generalized, these approaches lead to a spectroscopic description of the constellation of periodic processes that constitute the living states. The spectroscopic description is here applied also to the inputs received by living systems, from lethal, high-energy, nuclear particles and radiation to low-energy communicational signals that make up languages understandable at the various levels in an hierarchical system. The concept of language is then itself generalized, showing how the empirical relation discovered by Zipf can be derived from a thermodynamic basis. It is demonstrated that certain linguistic and statistical-mechanical distribution functions can be related. Applications of the field thermodynamic approach to two problems in transport phenomena are given in APPENDIX I; applications of field thermodynamics to language and communication are given in APPENDIX II.

homeokinesis; membrane transport; networks; models; languages; nonholonomic constraints; holonomic constraints; hydrodynamics; radiation effects; compartmental models; Zipf-Mandelbrodt relation; biophysics; information theory; communications; population dynamics; noise

PART I OF THIS SERIES presented selected themes from physics that in combination provide the basis for a level-independent, scientific explanation of systems of all kinds (15). The development of the general notions began with a discussion of the field concept, and the idea of a challenge. It was also pointed out that autonomous systems, such as living systems, operate as thermodynamic engines, with cyclic transformations of energy occurring externally or internally. Implicit in the above notions is the appropriateness of a spectroscopic description of systems.

In physics, spectroscopy is well understood to offer a useful description, but in biology this approach has not been well developed. The aim of the present article is to show how a spectroscopic description can present even familiar facts in a new light, and generate new insights. In addition, through two appendixes, prepared in collaboration with H. Soodak and F. Hassler, I shall show three specific applications of field thermodynamics to problems in biological science. The first two applications concern transport phenomena (APPENDIX I), and the last (APPENDIX II) deals with communication.

Throughout the discussion that follows the reader will note that there is a recurring theme. The thesis is that thermodynamic systems, at all their various levels, organize and operate with informational fluxes as well as with power fluxes. Both these fluxes are manifestations of thermodynamic processes, and regardless of the physical nature of the symbols used, the information fluxes comprise languages, and languages themselves have a thermodynamic basis and character (APPENDIX II).

Spectroscopic Analysis

In very broad terms, we can say that a spectroscopic analysis gives the relationship between the important repetitive business going on within a system, and the time domains in which it occurs. In common engineering practice, a conventional spectral plot presents "power" or amplitude on the ordinate, against frequency on the abscissa, but the precise terms power (energy or work rate) and frequency (reciprocal of the period of periodic or near-periodic processes) can be broadened so that the ordinate is thought of as some expression of the magnitude of activity, response, or behavior, and the abscissa is thought of as discrete time domains in which the activities occur. In this view we assume that biological spectra will be discontinuous rather than continuous; i.e., that the constellations of near-periodic thermodynamic engines underlying life processes will manifest their intrinsic frequencies (time domains) of operation, and that because the number of such oscillators is finite, the predominant frequencies will not slur the underlying discrete spectrum so that it looks continuous. One convenient way to develop a standard spectroscopic description is to classify the responses to challenges into zero frequency, low frequency, medium frequency, high frequency, and very high frequency, as is often done in engineering practice. Elsewhere such an approach to biospectroscopy has been presented (1).

In the present discussion I wish to take a slightly different view of a spectroscopic analysis. Instead of considering the power spectrum of the internal processes of a biological system, I shall examine the spectrum of the possible inputs to the system, to continue the idea that much can be learned about the physics of a system, by challenging it with an energetic particle, and interpreting its subsequent behavior according to field concepts (15). Table 1 shows the spectral decomposition, according to energy levels of challenges, that I shall follow here. Superficially it may appear that Table 1 is organized primarily by morphological level (ranging from photons to ecological systems). Indeed, there is a morphological hierarchy in Table 1, but the organizing principle is energy level. It is, in fact, a nontrivial aspect of thermodynamic analysis that there will be a relationship between the energetics of a challenge and the hierarchial level at which the challenge arises and is dealt with.

TABLE 1. *Spectral analysis of energy levels of challenges or inputs*

Relative (Terrestrial) Energy Level of Inputs, in Decreasing Order	Example of Challenges or Inputs
1 (Extremely high energy)	High-energy nuclear particles or photons
2	Ionizing radiation (we will take R (roentgens), and rads as being essentially equivalent), at various levels (R)
3	Chemical inputs, simple molecules, complex molecules, substrates, nutrients, drugs, antigens
4	Information – language
5	Stress inputs as language
6	Languages of intercellular communication – cell to cell; ensembles
7 (Extremely low energy)	Higher level languages; messages of social organizations. Intraspecific communication

Before examining the spectrum of inputs to living systems, I would like to contrast the engineering approach to modeling and explanation with the physical or scientific basis for modeling provided by field thermodynamics, so that the reader will be better able to appreciate the necessity for considering physical details that may seem unfamiliar and strange.

Contrast Between Engineering and Thermodynamic Approaches to Model Building

In the jargon of engineering, the terms hard-wired, and hard-geared are used informally to describe a system that has information and power fluxes channeled very exactly along highly conducting, preferred routes, almost without slippage or loss. The preferred routes are describable by holonomic constraints that provide well-defined, integrable couplings between stages or elements. In sharp contrast are biological systems: these are not hard-wired, nor are they hard-geared. Their field boundary constraints are of the nonholonomic type. We also note that living systems are not "hard-molded" either; i.e., they are not produced by an assembly line process with geometric precision. Instead their form is guaranteed by multistage processing through competing force systems under nonholonomic constraints. It is the purpose of the three articles of this series to explore the physics of autonomous systems, operating, as biological systems do, under nonholonomic constraints. A general systems theory has to explain such systems, as well as the easier cases that arise in engineering practice.

Scientific models of any system must satisfy the physical requirements of field thermodynamics, implicitly, if not explicitly. There is a strategy of modeling that assures satisfaction of these requirements, and I shall present it in detail elsewhere. For the present it is enough to point out that biochemical networks and processes must confront the thermodynamic issues described in Part I of this series (see Table 3 (15)). These are issues of equations of state, mass balance, energy balance and entropy production, field boundary conditions in the form of nonholonomic restraints, potentials, and transports. Currently the study of reaction-diffusion systems is becoming very fashionable, and these systems demand a thermodynamic treatment to explain the conditions that permit inhomogeneities and fluctuations to be captured as structure and persistent function.

Applications of the engineering notions of feedback in the modeling of biological systems have been popular with physiologists, but the resulting models have many shortcomings, as we have pointed out previously (17). The most common process that the physiologist is confronted with is chemical transformation: a complex A, of concentration c_a, is transformed to B with concentration c_b. Often the process arises not from chemical thermodynamics, but from system thermodynamics, in which cells as systems receive A as input and—as a system process—transduce information (through chemical transformations) into the form of new molecules, B. To describe the transformations, the engineer might suggest that the biologist use feedback network concepts, but the biologist would do better to accept the more primitive physical language of transformation, transduction, and transponding. Transformation is the change of one physical quantity into a like physical quantity; transduction is the change of one physical quantity into a different quantity. Transponding means providing a common response to many different forms of transduction; e.g., mast cells respond to a variety of stimuli with histamine release. Another term, transmutation, strictly refers to change in form, but more loosely it refers to changes that are difficult, exotic, or almost forbidden.

Many physical processes, including some of those occurring within living systems, involve long delays that are describable in terms of field transport processes and their bulk viscosity coefficients (H. Soodak and A. Iberall. *Physical Basis for Complex Systems—Some Propositions Relating Levels of Organization;* to be published). This characteristic arises from the properties of complex flow fields and is the basis for the emergence of hierarchies, and homeokinetic operation (15). Whereas the engineer is accustomed to deal with only one, or a few, atomistic entities (e.g., electrons), the biologist must confront a large list of elements in flux—electrons, small ions, information-carrying macromolecules, etc.; fluxes are coupled; the elements can be transduced and transformed. The physical issues to be dealt with do not appear primarily as chemistry, but rather as pattern recognition involving information flow. All these circumstances taken together vitiate the feedback engineering approach to modeling living systems and require that these systems be viewed as hydrodynamic fields, even at relatively high levels of organization (26).

The practicing engineer has begun to learn about the complexity of dealing with the coupled fluxes in hierarchical systems. (After all the manufacturing plant he is associated with has a finance and sales department; it has a command-control system; and it has to deal with a worldwide market of individuals, corporate entities, states.) But he has no techniques for probing hierarchical systems that are any sharper than the biologist's perceptions and intuitions, except perhaps the ability to symbolize his abstractions of reality in a compact fashion.

The image that best suits the circumstances encountered in living systems is that of a giant pinball machine with many local, unit-process elements (15). That view can only feebly be described by a block diagram. The difficulty is that a multilevel game is in progress: different levels of organization impose their patterns on the play on the pinball field; chemical trigger begets chemical signal, begets cellular response, begets organ response, begets organism response. Activities at each level of response have to be treated independently. Field thermodynamics offers a means to assure that each of these levels can be treated independently, and that the various results then can be coupled to describe the overall behavior in a consistent fashion.

I turn now to the spectral analysis of inputs of energy to living systems, as shown in Table 1.

Input Level 1: High-Energy Nuclear Particles

Solar and cosmic (11, 51) radiation both must have had a strong influence on the evolution of living systems. One may surmise that living systems are well adapted to the low background radiation levels that have been striking the earth during the past few billions of years. It has been argued with great force, with considerable support from biophysicists, that the ultraviolet radiation background from our sun was an essential ingredient in the formation of life (34). But, living systems cannot tolerate challenges by high-energy missiles, whether these missiles are matter, or photons. All high-energy challenges by nuclear particles are destructive. Only in a rather shielded environment can life continue. This limitation can be expressed in terms of kinetic energy: normal chemical processes in the body involve temperatures under 100°C, energy levels under 10 eV per molecular process, or chemical bondings of less than a few 10 thousands of kcal/mol.

Input Level 2: Ionizing Radiation Less Than 100 Electron Volts

Biological tissue is an absorber for weak ionizing radiation, at the fraction-of-100-eV level. A field of living material (e.g., tissue, cell colonies, whole organisms), when exposed to beams of energetic particles, will show characteristic energy absorptions in certain energy ranges. These absorptions will be associated with specific metabolic processes and usually cause a general or a selective deterioration in particularly sensitive tissues, cell colonies, or organ systems. This damage may show up as immediate or delayed changes that can be viewed as lethal effects, debilitation effects, or genetic effects. At certain levels, probably very low, radiation may cause improvement of performance, but this point has not been satisfactorily proved and is doubted by many.

A physicist would be inclined to examine radiation effects as resulting from volume absorption, or selective scattering processes. The biologist could follow a similar line of analysis by first obtaining some idea, experimentally, of what the gross spectrum of effects is, and then proceeding to analyze processes according to a carefully selected, network thermodynamic model. To be stressed is the notion that the analysis must concentrate on what characteristic "chemical bonding" process is involved. In a study in which the challenge of ionizing radiation was addressed to mammals, it was possible to decompose responses to radiation by spectroscopic methods (14).

Consequences of absorption of several different levels of radiation need to be considered: 10^6 R, 40,000 R acutely, 30,000 to 3,000 R acutely, 600 to 500 R as an impulse, 600 to 500 R over 1 mo, and finally, doses under 300 R. The effects on living systems are very much a function of dose. At 10^6 R protein is denatured by absorption of these levels of whole-body radiation, and nucleic acid polymers are broken. The absorbed radiation splits bonds. Various tissues show differential sensitivity to destruction, as would be expected from the diversity of structures.

The permanent nuclear moieties (protons, proton-neutron combinations, electrons) are assembled from very strong bonds. If these bonds were completely symmetrical, there would be no possibility of any other kinds of bonds. But they are not symmetrical, and so they create local inhomogeneous fields. Out of this property a weaker secondary bonding can take place, e.g., ionization among atomic and molecular bonds, or multipolar bonds. When secondary bonds are almost saturated, as when complex molecules form, even weaker bonds are left over for succeeding levels of organization, yielding increasing complexity, increasing diversity, and increasing inhomogeneity. When such diverse structures are challenged by an energetic input, a great variety of end points of response can be noted, and selective absorption will be seen. Because these end points are the resultants of complex nonlinear processes, there is no linear superposition of results. A more relevant description would be in the form of Markov chains of associated phenomena.

The original study (14) was concerned with the details of only one end point – lethality following exposure to ionizing radiation; but it was intended to be a generalizable method of analysis.

Whole-body radiation dosages of about 40,000 R, given acutely in less than 5 h, will quickly kill an entire mammalian population. Somewhat lower doses (30,000 to 3,000 R) will also cause death, but the cause of death will be different and the demise is delayed. For each pattern of dose and time of exposure, a particular pattern of failure of the mammalian subsystems may be seen, and at lower doses, over long times, the pattern may be that of accelerated aging without a precise source of deterioration of specific organ systems having been implicated. The subsequent mortality experience simply resembles that of an aging process in an unexposed population.

The point to be made by this brief description of the variety of ways in which mammals exposed to radiation can fail and die is that the results require consideration of the general notions of thermodynamic field effects previously set forth (15). Otherwise there is no explanation, only description.

Input Level 3: Simple Chemical Inputs

At a next lower energy level of challenge, we confront the most common input-output processing problem facing the living system, that of the input of organized molecular entities convected into the system. These molecules are broken down, recombined, stored, or delayed in transit and ultimately rejected. This form of transient challenges has been highlighted in the specialized subject of pharmacokinetics (see, for example, papers by Bischoff, Jusko, Tozer, and Dedrick in (19) or Levy in (49)). Physiologists are ordinarily concerned with physical-chemical actions at the low operational input levels. In contrast, pharmacologists examining dose-response curves attempt to identify plausible physical-chemical actions over a wider range of responses, from highly visible to imperceptible. Both views take note of a large degree of system nonlinearity (48) that precludes use of what would otherwise be straightforward linear (or near-linear) network analysis that the electrical engineer or control engineer commonly employs.

Both physiologist and pharmacologist visualize thresholds, nonlinear amplifications, binding, alternate pathways, parasitic effects, and, above all, selectivities and regional instabilities. Yet at present the most common modeling of this schema has been as equivalent 1st- and 2nd-order chemical reaction processes, essentially of linear form, combined with compartmental descriptions in which the law of mass balance is applied to some lumped compartments. Compartments provide storage, and a time delay is imagined to arise from storages and linear (resistive) transports or transformations.

I would now like to show how approximate compartmental models, often arrived at by intuition rather than physical reasoning, in fact do have in them the issues addressed by field thermodynamics, as set forth in Table 3 of (15). To make this comparison it is convenient to describe compartmental models, even those representing biochemical processes, in hydraulic analogue form. Sometimes the biologists have presented biochemical systems in this form, and the model shown in (50) serves as a useful example in the discussion that follows.

The biologist can imagine his transports and transformations as laminar flow processes occurring through capillary tubes. For instance, imagine a serial array of containers holding liquid which are connected by linear flow-resistance elements (e.g., capillary tubes obeying the Poiseuille flow law). When flow is initiated, by opening a valve, a large reservoir begins to fill the first vessel through the first resistance. Flow into the second vessel takes place from a horizontal capillary discharging from the floor of the first vessel. If the driving potential is considered to be the (linear) gravity field, then the linear head of liquid in the first vessel drives fluid into the second vessel. That process, in cascade, from vessel to vessel, is a prototype for the nth order, resistive-capacitive time delay of compartmental models.

What is the relation between such (hydraulic) compartmental models and field thermodynamics? Compartmental models, crude as they are, when properly done address several of the important thermodynamic issues. Mass balance is taken care of very obviously in these models – many of the equations are explicitly of this type. Less obviously, compartment models address momentum balance by incorporating it into the "resistance" laws of the transports. Energy balance and energy degradation (entropy production) are implicit in the proportionality assumed between energy and the volume head (in the hydraulic analogues such as used in

(50)) and how that energy is absorbed. Isothermal flow fields for one mass-species are (implicitly) assumed in such a model. Thus, some chief issues appropriate to irreversible thermodynamics are in fact latent in (proper) compartmental models. What about those of reversible thermodynamics?

Concerns of the thermodynamics of reversible processes, such as the equation of state, and potentials, appear in proper compartmental models (again taken in their hydraulic analogue form) through the isothermal, constant-density assumption for the water, and the representation of processes using potentials such as the force of gravity.

Field boundary conditions in the form of holonomic constraints are acknowledged in hydraulic analogues of compartmental models, through the assumptions that: the flow in capillaries is laminar; the velocity at the wall is zero; the dissipation of energy occurs through interaction of atomistic entities (the water molecules), represented in the resistance term as a viscosity transport coefficient; and these effects are exactly balanced through the shearing force.

At this point the reader may wonder why the more physically detailed descriptions of network thermodynamics need to be involved, when the simpler compartmental model seemed to suffice. The answer is twofold. The simpler compartmental model had to come to terms with the underlying thermodynamics, as shown above, and it is merely a fortunate, but limited, circumstance that biologists using simple Ohm's law or Poiseuille's law concepts often satisfactorily accommodate the thermodynamic requirements without explicitly recognizing them. If biological systems were linear, and simply coupled, there would be no quarrel with this kind of modeling, but they are not. In the more interesting real cases, we may find such complexities as those listed below (again given in terms of hydraulic analogues for compartmental models).

a) A nonlinear resistor may be found.

b) The resistance might come from an erratic blockage in a passageway (e.g., tube collapse, rouleaux formation).

c) The resistance might be set by some erratic deus ex machina with its own purposes (e.g., by the whimsical actions of an investigator that impose boundary conditions far removed from the proper operating conditions).

d) The transport might not be isothermal. In fact, portions might be vaporized or precipitated (phase transformations may occur).

e) The containers might be inertially compliant.

f) Container size might be governed by a deus ex machine (investigator) with other purposes.

g) If the capillary is extremely fine (in the Angstrom range), the wall constraint of zero velocity is not valid.

Input Level 4: Information and Language

I now wish to consider a generalized idea of information and language. The coding strategies addressed by the Shannon "information" theory are not the main concern here; instead I shall regard information as a set of discrete, impulsive inputs that can change the state of a system. Some of these inputs arise internally, e.g., in the form of peptides (2) or hormones (12), and some arise externally. Elsewhere my colleagues and I have expressed our views on the nature and origin of information at several different levels of biological systems (1, 18, 20, 26), but many important inputs are probably still unrecognized, partly because living systems may operate with very long delays (as in memory processes) between input and output.

A language is built out of low-energy amplitude or frequency variations (signals), with encoding and decoding rules to protect against corruption by noise, and with grammatical rules to define or enhance meaning and reduce ambiguity. What I wish to emphasize here is the idea that each level of an hierarchical system has one or more languages appropriate to that level, and that languages have thermodynamic characteristics. Thermodynamics addresses communicational fluxes as well as power fluxes, and the coupling between them.

To illustrate the thermodynamic aspects of language, F. Hassler and I have prepared APPENDIX II of this paper, in which a thermodynamic approach to language is developed, based upon the classical earlier work of Zipf and its extensions (5, 10, 18, 53). The starting point is the Zipf-Mandelbrot relation

$$p(r + r_0)^n \approx p_0(1 + r_0)^n \tag{1}$$

where p = probability (or frequency) of occurrence of a particular symbol in the language; r = rank order (1 to n) in the frequency of usage of the symbol; r_0, n = constants; and p_0 = highest probability (that of the first ranked symbol).

In an elementary Zipfian language, $r_0 \approx 0$ and $n \approx 1$, which says that there is an inverse relationship between frequency of usage and numerical rank order. A biological example of such a language has been given by Moulenaar et al. (31) in their analysis of membrane noise ($1/f$ type) and locomotion in a paramecium. APPENDIX II of this paper explains Zipfian languages, by deriving such logarithmically divergent distributions within a statistical mechanical framework. For a simple system, e.g., near-ideal gas molecules, or molecules in a dilute solution, the distribution of energy will be Maxwellian-Gaussian. The analogous prototype of a thermodynamic language of such systems involves low-energy signals of Zipfian form. In such complex, autonomous systems, languages have a catalytic character: information flows are low-energy processes that become amplified for implementation. Theories of language, including what we present here (APPENDIX II), deal with frequency distributions. They are not capable of explaining syntax.

The important points are that languages are inputs at low-energy levels, that they are thermodynamic physical entities made up from the bits and pieces of internal and external materials and energies available; that they are level dependent in an hierarchical system; and that they can produce amplified effects, sometimes substantially delayed. All these characteristics need serious analysis from the viewpoint of physics.

Input Level 5: Stress Inputs – More Languages

In physics stress is a force per unit area exerted by one part of a medium upon another. The result is a strain, or strain rate. At first glance it appears that biologists use the term stress in a very different way, to specify psychological states, as well as pathophysiological conditions. Can the two views of stress be related? I believe so.

A living system is embedded in an environmental niche, or system, that is time varying – usually slowly changing. The environment can be viewed as having a mean state, with fluctuations around the mean. The fluctuations affect the living systems in the niche, and the effects may be either beneficial (rain ends a drought) or damaging (rain causes flooding and destroys the shelter). The organism, if mobile, or capable of design, can seek other regions, or modify the one it is in, but it cannot toally control its surroundings. Thus, impulsive inputs beyond the usual and expected range may occur, and these are stresses. The strains appear in the many internal degrees of freedom of the living system. Manifestations of the stress-response relation in physics include first- or second-order phase transitions. In biology they may appear as changes in stability, so that local steady-state operations are displaced from or toward periodic processing, for example.

At this level of many challenging stresses, we are no longer dealing with inputs representing small molecular complexes, but with patterns that are part of an information process. Stresses form a language, but the science of psychology has not adequately characterized the language. Perhaps the science of animal behavior, ethology, will provide the necessary descriptions to relate various internal states, the switching signals that express the messages, and the language being used. Ions, peptides, neurotransmitters, hormones, and paracrines presumably are some equivalent of lexical units in these languages (2, 12, 27, 28, 36, 39). Both phonetics (the study of the external signals) and phonemics (the study of their internalized meaning), the "etics" and "emics" of culture, in anthropological terms, are aspects of stress inputs viewed as part of a language. Although this view may at first seem somewhat forced, I believe it is the one that will serve best to encourage a reduction of animal behavior to physical principles. It is not merely metaphorical to look at the inputs and switch states of biological systems through a linguistic frame of reference. Again I call attention to APPENDIX II of this paper, in which the attempt is made to generalize the distributional properties of symbols in languages, with the aim of exposing their underlying thermodynamic character.

Input Level 6: Cell-to-Cell Languages; Communication in Groups

Organisms operate with ancient themes. Their modern languages arise out of cellular properties that appeared early in the course of biological evolution, and presumably these themes can be glimpsed in the process of growth and development of higher animals. Although not strictly true, the notion that ontogeny recapitulates phylogeny still calls attention to a fundamental strategy: old processes and parts are the basis of the new. I have considered these ideas elsewhere, and in collaboration with R. Llinas (16, 26), to try to find a physical basis for languages used by organisms.

The first step in a thermodynamic analysis of cellular or organismic languages requires specification of the distribution function that represents the frequency of occurrence of the many, various, discriminable states in the phase space of cellular or organismic life and activity. All the activities necessary for survival must be considered. From the point of view of the living system these activities include the basic functions of sensing, movement, ingestion, command-control switching, and reproduction. In addition, multicellular animal organisms (regardless of level of organization) exhibit certain vegetative functions, e.g., growth stemming from ingestion, energy and materials metabolism, breathing, heartbeat, interior circulation. These are primitive engine functions that are a basic part of its homeokinetic regulation. These are primitive modes that are almost never switched off. Beyond these, other more elaborate switch modes are orchestrated as patterns of states of internal subsystems. To accomplish this patterning, a command-control center is required, with a rich enough algorithm to use a matrix of switch modes as a reliable and clear language. I believe that the language will be uniformly logarithmic or Zipfian, although further exploration of deep language structures in the organism may uncover more of an information theoretic for thermodynamic systems than that which I am prepared to offer now (see (18) and APPENDIX II). Clearly in the cell, the control algorithm starts from the genetic code, and DNA.

Input Level 7: Higher Level Languages. The Strategy of Analysis

At the level of species and societies we find languages again, and processes of organism-substrate binding (7) in which the distribution of sizes of communities may be looked at as an expression of a social language ((18) and APPENDIX II). Populations are distributed in an inhomogeneous manner. It is a process akin to condensation and evaporation. This is a conspicuous fact that, on reflection, suggests once again that it may be a valuable strategy of analysis to start with the inhomogeneity, define a distribution function, and then to interpret the spread of the distribution function both as a manifestation of a language, and as a manifestation of a thermodynamic field. The final step is to comprehend that language itself is a manifestation of the thermodynamic field processes. It seems to me that any serious reduction of biology to physics must face these issues, and follow this, or a related strategy. It is the aim of this article to call attention to the need for, and form of, this reduction.

Specific Applications of Network Thermodynamics in Biology

This subject will gain emphasis from some examples to illustrate its power. Three are appended here. Two examples elaborate the ideas of Part I (15) of this series. They concern the thermodynamics of membrane transport, and bridge the gap between direct and indirect transport mechanisms, and relate them to thermodynamics. A final example concerns communicational properties within complex systems. It bridges the gap between basic thermodynamic processes (motive power, reproduction) and internal communications. The specific example is social, but its application can be generalized to the actions of all communal ensembles (e.g., cell complexes).

The examples are given in APPENDIXES I and II.

APPENDIX I

Links Among Phenomena of Membrane Transport, Irreversible Thermodynamics, Navier-Stokes Hydrodynamics, and Onsager Linear Reciprocity[1]

Investigators seem to be vague in explaining rigorously how to couple hydrodynamic flow processes to irreversible thermodynamics (8, 22, 35, 40). They do not provide assurance that for mobile, atomistic entities irreversible thermodynamics is hydrodynamics. A case in point is the standard Onsager approach, adopted from Kedem and Katchalsky (22, 23), for one- or two-component flow in membrane transport.

In this approach one writes equations for the fluxes J_i for i types

$$J_1 = L_{11}\,\Delta V_1 + L_{12}\Delta V_2 \tag{A1.1}$$

$$J_2 = L_{21}\,\Delta V_1 + L_{22}\Delta V_2 \tag{A1.2}$$

$$L_{12} = L_{21} \text{ (the Onsager condition)}$$

where ΔV_i is a potential difference, L_{ii}, L_{ij} are conductances, due respectively to direct effects (e.g., temperature difference, ΔT, causing heat flow) and to indirect effects (e.g., concentration difference, Δc, causing heat flow). Onsager indicated that, for near-thermodynamic equilibrium, such linear, phenomenological laws could always be written. As with similar reciprocity laws in many other fields (e.g., acoustics, elastic deflection), a symmetry exists between the off-diagonal "influence" or transconductance coefficients.

The subtle difficulty in using these equations is that direct coupled conductances can pose the same theoretical difficulties as do the indirect coupled conductances. There seems to be doubt about how to combine kinetics and near-continuum hydrodynamics (4). We shall try to clarify the issues by an example, below.

Suppose, as in the case of a semipermeable membrane, there is only one component of flow. The problem is how to compute the hydraulic conductance L_{11}, and to show whether an indirect transconductance L_{12} exists. DeGroot (8) and Iberall and Schindler (21) state that no indirect L_{12} exists for a macroscopic field, but that one exists for a microscopic hydrodynamic field. However they do not perform any specific and transparent hydrodynamic exercise to demonstrate these results.

For want of any other theoretical apparatus, biophysical authors write a Poiseuillian flow law for L_{11}, but this law is not valid for small pores below 400 Å with waterlike plasma because molecular graininess begins to manifest itself (21). In the proper approach it is recognized that Navier-Stokes hydrodynamic theory, Onsager reciprocity, and DeGroot-Kedem-Katchalsky irreversible thermodynamic relations all are coextensive in their linear range of applicability, and that these second-order fluctuation theories can be used for a near-continuum flow theory good for the pore size range 15–400 Å in waterlike media. (The first-order theories provide the distribution functions of thermostatics, of quasi-static reversible thermodynamics; the second-order theory provides the nondispersive coefficients for linear transport processes.) Near-continuum flow is part and parcel of near-equilibrium irreversible thermodynamics.

For flow in a long line in the continuum range (e.g., for parallel plates with separation greater than 400 Å) we can write the Navier-Stokes law of flow, which, for parallel plates, is given by

$$\frac{dp}{dx} = -g = \mu\frac{d^2u}{dy^2} \tag{A1.3}$$

$$u = -\frac{g}{2\mu}y^2 + C_1y + C_2 \tag{A1.4}$$

A continuum boundary condition of velocity vanishing at the two symmetrically placed walls gives

$$u = \frac{g}{2\mu}(h^2 - y^2) \tag{A1.5}$$

which specifies Poiseuille flow. Here p = pressure; g = uniform long-line pressure gradient in the x direction; h = half-separation of plates, placed at $y = \pm h$; u = channel velocity in the x direction; μ = coefficient of viscosity; and C_1, C_2 = constants of integration. In (21) we showed that this continuum boundary assumption *leads to no coupled indirect effects* in macroscopic fields.

To show an indirect effect, one must change the boundary condition, and it must be selected to be equipollent with the field equations. The field is written as a first-order expansion in terms of mean free path; so must the boundary condition be written. Viscosity, as an integrative form of delayed momentum transfer due to mean free path time delays, in the field equations represents effects of sustained collisional motions. There is a similar, first-order delay process of molecules rebounding from walls. This is known, in gas flow theory, as Knudsen slip. We have provided a corresponding theory of boundary roll for liquids (21).

Where do such boundary effects originate? They originate from kinetic theory. We shall offer an illustration, using a theory that is old, that was formerly well known, and is now apparently nearly forgotten.

For a near-continuum flow between the walls at $y = \pm$ h (24, 47), there is a velocity discontinuity at the wall

$$u = -\frac{\mu}{\beta}\frac{du}{dy} + \frac{3}{4}\frac{\mu}{\rho T}\frac{dT}{dx} \tag{A1.6}$$

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[1] This section was developed in collaboration with Dr. Harry Soodak.

and a discontinuity in temperature T

$$T = T_w + \frac{\lambda}{k}\frac{dT}{dy} \qquad (A1.7)$$

β = coefficient of sliding friction; k = coefficient of temperature discontinuity; λ = coefficient of thermal conductivity; and T_w = wall temperature.

These two discontinuity parameters are related to the mean free path, l, by

$$\frac{\mu}{\beta} = 0.998\left[\frac{2-f}{f}\right] l \approx l \qquad (A1.8)$$

$$\frac{1}{k} = 1.995\left[\frac{2-\alpha}{\alpha}\right]\frac{\gamma}{\gamma+1}\frac{l}{\mu C_p} \approx \frac{6}{\gamma+1}\frac{l}{\mu C_v} \qquad (A1.9)$$

γ = ratio of specific heats C_p, C_v and C_p, C_v = specific heat at constant pressure or constant volume.

Maxwell's reflection coefficient f (the loss of tangential momentum) is essentially 1.0 for very smooth surfaces. The Smoluchowski-Knudsen accommodation coefficient α (the fraction by which normally bounding molecules accommodate their energy to the wall temperature) is of the order of 0.25–1, e.g., ≈0.5. Also

$$\mu = 0.499\rho Cl \approx 0.5\rho Cl \qquad (A1.10)$$

$$\lambda = \frac{9\gamma - 5}{4}\mu C_v \qquad (A1.11)$$

C = velocity of sound and ρ = gas density.

Thus

$$u = -l\frac{du}{dy} + \frac{3}{4}\frac{\mu}{\rho T}\frac{dT}{dx} \qquad (A1.12)$$

$$T = T_w + \frac{3(9\gamma-5)}{2(\gamma+1)}l\frac{dT}{dy} \qquad (A1.13)$$

Applying the first boundary condition to our Navier-Stokes result, we find that the constant of integration C_2 is not h^2, but rather

$$C_2 = h^2 + 2hl + \frac{3}{2}\frac{\mu^2}{\rho g T}\frac{dT}{dx} \qquad (A1.14)$$

$$u = \frac{g}{2\mu}\left[h^2 + 2hl + \frac{3}{2}\frac{\mu^2}{\rho g T}\frac{dT}{dx} - y^2\right] \qquad (A1.15)$$

Let us apply this one flux result to derive the Soret effect (thermal transpiration; also called thermoosmosis). We ask, Can a pressure difference arise between two reservoirs of different temperature connected by a very fine capillary slit?

At mechanical equilibrium there is no net mean flux $\bar{u}$

$$\bar{u} = \frac{1}{h}\int_0^h u\,dy = 0 \qquad (A1.16)$$

Neglecting small temperature jumps, the temperature near the wall in the channel is nearly the same as the wall temperature. Because the temperature equation in the field at equilibrium is the Laplacian law

$$\nabla^2 T = 0 \qquad (A1.17)$$

the axial temperature is a constant gradient of temperature along the wall. To be more precise, we can imagine the connecting capillary to be adiabatically shielded. Therefore, for a long line, dT/dx is a constant. Thus integrating u, we find

$$h^2 + 2hl + \frac{3}{2}\frac{\mu^2}{\rho g T}\frac{dT}{dx} - \frac{h^2}{3} = 0 \qquad (A1.18)$$

$$\frac{\Delta p}{\Delta T} = \frac{g}{dT/dx} = \frac{-\frac{9}{4}\frac{\mu^2}{\rho h^2 T}}{1 + 3l/h} = \frac{-\frac{9}{4}\left(\frac{l}{2h}\right)^2}{1 + 6l/2h}\frac{p}{T} \qquad (A1.19)$$

If the mean free path vanishes, then the thermoosmotic pressure vanishes (continuum flow). We have shown that the near-continuum limit holds up to $l/2h \approx 0.1$. At that limit the thermoosmotic coefficient approaches

$$\frac{\Delta p}{\Delta T} \approx -0.014\frac{p}{T} \qquad (A1.20)$$

or about 0.33 Torr/10°C at normal temperature and pressure (p) for a diatomic gas, using a 0.5-μm slit. (No great precision is intended for the numerical coefficient.) However one should note that even if this result is stretched beyond its valid range of convergence (i.e., into the range $l/2h \approx 0.33$, thereby requiring a second-order expansion in the square of the mean free path in the distribution function – a range where only the Burnett results and the Stokes-Einstein theory hold), the numerical answer is not bad. Even if stretched beyond any of the ranges of convergence, e.g., to $l/2h \approx 1$, beyond which only the kinetics of free molecular flow hold, the numerical values still are not bad. At $l/2h = 1$, we get

$$\frac{\Delta p}{\Delta T} \approx -\frac{1}{3}\frac{p}{T} \qquad (A1.21)$$

For a small, thin orifice, the coefficient is −0.5. This result simply demonstrates that the transition from near continuum to free molecular flow is generally smooth.

The point to the above demonstration is that indirect effects are coupled by near-continuum hydrodynamics to a first-order kinetic theory for the boundary conditions. In contrast, if Poiseuille flow is assumed, there is no consistent theory for indirect coupled effects. The assumption of slip at the wall provides the condition through which the thermoosmosis can take place, and there is a reverse circulation occurring within a mean free path of the wall, so that net flow can vanish at equilibrium.

For a second illustration we will treat an example closer to biological interest, the partitioned fluxes of solvent and solute due to mechanical pressure and chemical potential (e.g., concentration) differences through fine resistances (e.g., membranes with pores or slits). The current writings (examples, (3, 6, 25, 29, 37, 38)) which highlight the engineering phenomenological equations (43) face the reader with a confusing complex discussion that poses great difficulty in untangling the logic and physics of the subject. We will not detail a complete field hydrodynamic exposition for these problems, but we will illustrate in primitive field form what its principal elements consist of—which seems never to have been done—and how it answers the kinds of transport questions that are raised, i.e., how the hydraulic conductance is computed, what is the essence of a theory of a so-called reflection coefficient, some basic commentary on local and global Onsager linear reciprocity, *and* a determination of the character of solvent counterflow to solute diffusion. The fundamental connection between so-called osmotic processes and the chemical potential will be touched on. Global application of the second law and the convection-dissipation field form will be explained. Also, we will clearly and simply indicate how hydrodynamic-thermodynamic issues are separated from but compatible with kinetic theory issues.

For simplicity, we confine ourselves to the near-isothermal liquid transport of a two-component nonelectrolyte (solute 2, solvent 1) steady-state, near-rest equilibrium (creeping) partitioned flow under pressure and concentration difference drives. The field system will be a single one-dimensional flow in the x direction through a single long slit, with walls at $y = \pm a$ and axial length l, between two large fluid reservoirs. The fluxes are characterized by velocity vectors v_1 and v_2

Conservation of mass

$$\nabla \cdot v_1 = 0 \qquad (A1.22)$$

$$\nabla \cdot v_2 = 0 \qquad (A1.23)$$

For simple exposition, we will use this "incompressible" condition for both components.

Momentum balance. Two stress tensors and two momentum balances must be constructed, one for each component. The force per unit area on each component of density ρ_1, ρ_2 in a region consists of an effective partial hydrostatic pressure, *and* shearing momentum forces from both the velocity gradient of its own motional distribution and the coupled velocity gradient of the motional distribution of the other component. A second tensor component from the dilational process vanishes because of the incompressible assumptions. The accelerational forces are negligible because of the small amplitude creeping assumptions. Thus

$$\nabla \mathrm{p}_1 = \mu_1 \nabla^2 v_1 + \mu_{12} \nabla^2 v_2 + k_{12}(v_2 - v_1) \qquad (A1.24)$$

$$\nabla \mathrm{p}_2 = \mu_2 \nabla^2 v_2 + \mu_{21} \nabla^2 v_1 + k_{21}(v_1 - v_2) \qquad (A1.25)$$

To characterize the stresses on each component, independent pressure components, p_1, p_2, a full complement of possible isotropic viscosity coefficients μ_1, μ_2, μ_{12}, μ_{21}, and the relative drag coefficients k_{12} and k_{21} are all assumed. Summing the two equations

$$\nabla(\mathrm{p}_1 + \mathrm{p}_2) = (\mu_1 + \mu_{21})\ \nabla^2 v_1 + (\mu_2 + \mu_{12}) \nabla^2 v_2 \qquad (A1.26)$$

$$\nabla \mathrm{p} = \mu_{\mathrm{m}} \nabla^2 v_{\mathrm{m}} \qquad (A1.27)$$

a Navier-Stokes creeping flow law.

The driving forces $\nabla \mathrm{p}_1$ and $\nabla \mathrm{p}_2$ are thermodynamically defined, such that

$$\nabla \mathrm{p}_1 + \nabla \mathrm{p}_2 = \nabla \mathrm{p} \qquad (A1.28)$$

provides a definition of total pressure where p is the hydrostatic pressure.

$$(\mu_1 + \mu_{21}) v_1 + (\mu_2 + \mu_{12}) v_2 = \mu_{\mathrm{m}} v_{\mathrm{m}} \qquad (A1.29)$$

provides a definition of an effective mean Navier-Stokes velocity v_{m} but μ_{m} will have to be defined by a kinetic theory.

Also

$$k_{12} = k_{21}$$

the drags forces, which are coupled body forces, are equal and opposite.

Since it is only a matter of definition, at this stage, we will select for the definition of μ_{m}

$$\mu_{\mathrm{m}} = \mu_1 + \mu_{21} + \mu_2 + \mu_{12} \qquad (A1.31)$$

It follows that

$$v_{\mathrm{m}} = \frac{\mu_1 + \mu_{21}}{\mu_{\mathrm{m}}} v_1 + \frac{\mu_2 + \mu_{12}}{\mu_{\mathrm{m}}} v_2 \qquad (A1.32)$$

The additivity of drives and flows exhibited by these field equations is expected for small departures from thermodynamic rest equilibrium. Although it is no surprise that the hydrostatic pressure gradient drives a mean effective Navier-Stokes velocity, which in the one-dimensional case is Poiseuillian, the form of the flow as a viscosity weighted average is novel.

If one species (say 2) were fixed, i.e., an obstacle to flow, we would have a

$$\nabla \mathrm{p}_1 = \mu_1 \nabla^2 v_1 \qquad (A1.33)$$

flow law, in which the obstacles furnished boundary conditions. With dual mobility, their relative drag on each other assures a common velocity flow field, and their differential interpenetrability (in every macroscopically infinitesimal space) assures the existence of field friction due to relative motion. The complexity of the moving boundary conditions is buried in the theory for the friction coefficient k_{12} and the viscosity coefficients.

Thermodynamics of the driving forces. The form of the driving forces $\nabla \mathrm{p}_1$ and $\nabla \mathrm{p}_2$ is dictated by thermodynamics. Under isothermal conditions, constituent i is driven by the gradient (negative) of its chemical potential ν_i. In a single constituent material, the chemical potential varies with pressure p according to the Gibbs formula

$$\rho\, \mathrm{d}\nu = \mathrm{dp} \quad \text{for} \quad \mathrm{dT} = 0 \qquad (A1.34)$$

where ρ is the volume molal density (moles per unit volume). Thus, the "mechanical equivalent" pressure differential is defined by the above equation. In a multicomponent solution, the variation of chemical potentials with pressure satisfies the Gibbs-Duhem equation which, if isothermal, is

$$\Sigma\rho_i \, \mathrm{d}\nu_i = \mathrm{dp} \tag{A1.35}$$

where ρ_i is the volume molal concentration (moles of constituent i per unit volume of solution). It is thus consistent and expected that the "mechanical equivalent" pressure differential dp_i driving constituent i is given by

$$\mathrm{dp}_i = \rho_i \, \mathrm{d}\nu_i \tag{A1.36}$$

The same mechanical equivalence is also consistent with irreversible thermodynamics. The rate of entropy production per unit volume s, due to transport of chemicals across chemical potential gradients is given by

$$\mathrm{T}\dot{\mathrm{s}} = -\Sigma\rho_i v_i \nabla\nu_i \tag{A1.37}$$

This net dissipation can be resolved into a sum of mechanical viscous dissipation and a diffusive dissipation by resolving the velocities into mean and diffusive components

$$v_i = v_\mathrm{m} + (v_i - v_\mathrm{m}) \tag{A1.38}$$

Then

$$\mathrm{T}\dot{\mathrm{s}} = -v_\mathrm{m}\Sigma\rho_i\nabla\nu_i - \Sigma\rho_i(v_i - v_\mathrm{m})\nabla\nu_i \tag{A1.39}$$

where the second term on the right is the diffusive dissipation (see (13)). The identification of $\rho_i \, \mathrm{d}\nu_i$ with dp_i leads to

$$\mathrm{T}\dot{\mathrm{s}} = -v_\mathrm{m}\nabla\mathrm{p} - \Sigma(v_i - v_\mathrm{m})\nabla\mathrm{p}_i \tag{A1.40}$$

where it is clear that the diffusive dissipation is also described in terms of the power dissipated by the mechanical equivalent pressure gradients acting on the diffusive velocities.

This sort of derivation exhibits the essential characteristic of near-equilibrium irreversible thermodynamics as it is formulated in field form. Beyond this level of derivation, it is dubious that there is any thermodynamics (although there is a field kinetics). On one hand, field thermodynamics is characterized as being locally near equilibrium. On the other hand, the global field would be judged to be quite far from equilibrium as a result of the various transports. It is the identification of the positive definite form of the transport terms contributing to dissipation that "proves" their thermodynamic character (13, 41), and the "proper" choice of descriptive variables.

That dissipation must include the loss due to the body force coupled friction factor k_{12} (and globally as a system, friction loss at the walls).

Kinetic considerations; the transport parameters. We shall base a cursory kinetic theory examination of the transport coefficients, generally under the small solute concentration assumption, within the long line system in which all pressure gradients are constant. The velocities v_1 and v_2 can be resolved into

$$v_1 = v_\mathrm{m} - \frac{\mu_{12} + \mu_2}{\mu_\mathrm{m}} v_\mathrm{d} \tag{A1.41}$$

$$v_2 = v_\mathrm{m} + \frac{\mu_1 + \mu_{21}}{\mu_\mathrm{m}} v_\mathrm{d} \tag{A1.42}$$

where v_m is the viscosity weighted mean velocity introduced earlier and v_d is the difference velocity

$$v_\mathrm{d} = v_2 - v_1 \tag{A1.43}$$

Eliminating v_m from the field equations by using

$$\nabla^2 v_\mathrm{m} = \frac{1}{\mu_\mathrm{m}} \nabla\mathrm{p} \tag{A1.44}$$

leads to the equation for the difference velocity

$$\nabla\mathrm{p}_\mathrm{d} = \mu_\mathrm{d}\nabla^2 v_\mathrm{d} - k_{12} v_\mathrm{d} \tag{A1.45}$$

where

$$\nabla\mathrm{p}_\mathrm{d} = \nabla\mathrm{p}_2 - \frac{\mu_{21} + \mu_2}{\mu_\mathrm{m}} \nabla\mathrm{p} \tag{A1.46}$$

and

$$\mu_\mathrm{d} = \frac{\mu_2\mu_1 - \mu_{12}\mu_{21}}{\mu_\mathrm{m}} \tag{A1.47}$$

In a fully macroscopic theory, the solution satisfying zero velocities, and thus zero for v_d, at the wall is

$$v_\mathrm{d} = \frac{-\nabla\mathrm{p}_\mathrm{d}}{k_{12}} \left(1 - \frac{\cosh y/a_0}{\cosh a/a_0}\right) \tag{A1.48}$$

where a_0, a scale parameter, is given by

$$a_0 = \left[\frac{\mu_\mathrm{d}}{k_{12}}\right]^{1/2} \tag{A1.49}$$

and generally satisfies

$$\frac{a_0}{a} \ll 1 \tag{A1.50}$$

The resulting value of v_d is a trapezoidal flat top, a uniform diffusion field with a sharp break at distance a_0 from the wall. The flat value is

$$v_\mathrm{d} \approx -\frac{\nabla\mathrm{p}_\mathrm{d}}{k_{12}} \tag{A1.51}$$

In a dilute solution with uniform hydrostatic pressure ($\nabla\mathrm{p} = 0$).

$$\nabla\mathrm{p}_\mathrm{d} = \nabla\mathrm{p}_2 \tag{A1.52}$$

and

$$\nabla\mathrm{p}_2 = \nabla\Pi \tag{A1.53}$$

where Π is the osmotic pressure

$$\Pi = \rho_2 R\mathrm{T} \tag{A1.54}$$

More generally (9)

$$\Pi = \phi\rho_2 R\mathrm{T} \tag{A1.55}$$

where ϕ, a molal osmotic coefficient, is either an empirical constant slightly greater than unity for nonelectrolytes in water, or is estimable theoretically from the interchange energy (30) as

$$\phi \approx 1 + f_2\left(0.5\,\beta - \sqrt{\beta}\,\frac{\Delta u^0}{kT}\right) \qquad (A1.56)$$

where f_2 is the volume fraction of solute in solution, β is the ratio of solute molecule volume to solvent, and Δu^0 is the interchange energy per molecule (for sucrose in water, $\Delta u^0/kT = -7$).

For the dilute case, the relative velocity is related to the diffusion coefficient D_{12} through the equation for the mass flux j_d

$$j_d = \rho_2 v_d = -D_{12}\nabla\rho_2 \qquad (A1.57)$$

But

$$\nabla\rho_2 = \frac{1}{RT}\nabla\Pi \qquad (A1.58)$$

Thus

$$v_d = -\frac{D_{12}}{\rho_2 RT}\nabla\Pi = -\frac{D_{12}}{\rho_2 RT}\nabla p_d \qquad (A1.59)$$

and

$$k_{12} = \frac{\rho_2 RT}{D_{12}} \qquad (A1.60)$$

By use of the Stokes-Einstein relation

$$D_{12} = \frac{kT}{6\pi\mu b_2} \qquad (A1.61)$$

where b_2 is the radius of a solute molecule and μ is the solvent viscosity, and k is again Boltzmann's constant, we arrive at

$$k_{12} = 6\pi\mu b_2 N_A \rho_2 \qquad (A1.62)$$

where N_A is Avogadro's number and $N_A\rho_2$ is the number of solute molecules in unit volume of solution.

Turning now to the viscosities, we note that a fully macroscopic theory with zero velocity boundary condition at the walls gives the Poiseuillian form for the mean velocity, $\bar{v}_m$

$$\bar{v}_m = -\frac{1}{3}\frac{\nabla p}{\mu_m} \qquad (A1.63)$$

We thus expect that μ_m is the viscosity of the mixture, i.e., as given by the Einstein or Simha (42) theories.

Is it also to be expected that the difference velocity vanishes in a sufficiently large viscometer with uniform concentration? This will be the case only when cross-coupling between mean flow and difference flow is negligible. Such cross-coupling may arise from the effects of graininess at the wall boundaries and also within the volume. Boundary effects are expected to distinguish between solvent and solute molecules when these are of different size, leading to cross-coupling effects including that due to the difference in stearic hindrances of the constituents. Because these effects are proportional to wall surface area, they become negligible in comparison with the volume flow in large viscometers as the surface-to-volume ratio goes to zero.

Cross-coupling within the volume arises from differential viscosity effects on the constituents, which in turn depend partly on molecular size differences. Differential viscosity effects cause a difference velocity to arise in response to a pressure gradient in a uniform solution. For a given pressure gradient, the difference velocity is essentially independent of the viscometer size because it is basically a local phenomenon. The mean velocity, on the other hand, is proportional to the square of the linear extent of the viscometer cross section. Thus, the ratio of the difference velocity to mean velocity becomes negligible for large enough viscometers.

Phenomenological coefficients. These notions are now illustrated by a number of approximate calculations. We assume solute molecules ($i = 2$) larger than the solvent molecule ($i = 1$) and neglect the effects of the finite size of the solvent molecules.

The driving force ∇p_d for the difference flow may be expressed in the form

$$\nabla p_d = \frac{\mu_1 + \mu_{12}}{\mu_m}\nabla p_2 - \frac{\mu_2 + \mu_{21}}{\mu_m}\nabla p_1 \qquad (A1.64)$$

Explicitly expressing the constituent driving forces by

$$\nabla p_i = f_i \nabla p + \frac{RT}{V}\nabla x_i \qquad (A1.65)$$

where f_i is the volume fraction of constituent i, x_i is the mole fraction and x_i/V is the moles of i per unit volume of solution, leads to

$$\nabla p_d = \nabla\Pi - \epsilon\nabla p \qquad (A1.66)$$

where $\Pi = RTx_2/V$ is the osmotic pressure, and ϵ is

$$\frac{\mu_1 + \mu_{12}}{\mu_m} = f_1 - \epsilon \qquad (A1.67)$$

$$\frac{\mu_2 + \mu_{21}}{\mu_m} = f_2 + \epsilon \qquad (A1.68)$$

The value of ϵ determines the cross-coupling between pressure gradient and difference flow within the volume. Another manifestation is exhibited as the difference between the viscosity weighted mean flow v_m of *Eq. A1.32* and the volume weighted mean flow v_v defined by

$$v_v = f_1 v_1 + f_2 v_2 \qquad (A1.69)$$

The difference is given by

$$v_m = v_v + \epsilon' v_d \qquad (A1.70)$$

where ϵ' is defined through the viscosity weighting coefficients of *Eq. A1.32*, as

$$\frac{\mu_1 + \mu_{21}}{\mu_m} = f_1 - \epsilon' \qquad (A1.71)$$

$$\frac{\mu_2 + \mu_{12}}{\mu_m} = f_2 + \epsilon' \qquad (A1.72)$$

Both manifestations of volume cross-coupling, *Eqs. A1.66* and *A1.70* are equivalent when the reciprocity relation

$$\mu_{12} = \mu_{21} \tag{A1.73}$$

holds. In the following, we assume the validity of this relation. In this case, cross-coupling effects within the volume arise from the nonvanishing of the single parameter

$$\epsilon = \epsilon' \tag{A1.74}$$

which we write as

$$\epsilon = \gamma f_2 \tag{A1.75}$$

We apply these results to a uniform solution, $\nabla\Pi = 0$, driven through a channel by a pressure gradient ∇p. The channel cross section has total area A, consisting of a core zone and a wall zone from which solute molecule centers are excluded. The core zone has area A_c. For a parallel plate channel

$$A_c/A = 1 - \alpha \tag{A1.76}$$

where α is the ratio of solute molecule radius b_2 to the half width of the channel a.

Strictly speaking, the field equations do not apply to the wall zone, and the problem should be tackled as a two-zone problem with a separate equation needed to describe the flow of solvent in the wall zone.

For simplicity, however, we approximate as follows: we resolve the velocities into a Poiseuillian component v_m valid across the entire channel with zero wall value, and a difference component v_d which is flat across the core zone. Solute and solvent flow in the core zone with the appropriate superposition of these modal velocities. In the wall zone, solvent flows with the velocity v_m.

We then have, relative to center channel value $v_m{}^0$

$$v_m = v_m{}^0(1 - y^2/a^2) \tag{A1.77}$$

$$v_m{}^0 = -\frac{a^2}{2\mu_m}\nabla p \tag{A1.78}$$

$$v_d = -\frac{\nabla p_d}{k_{12}} = \frac{\epsilon}{k_{12}}\nabla p \tag{A1.79}$$

The friction coefficient k_{12} can be written as

$$k_{12} = 6\pi\mu_m b_2 n_2 \tag{A1.80}$$

where n_2 is the number of solute molecules per unit volume of solution. The quantity n_2 can be eliminated by using

$$f_2 = \frac{4}{3}\pi b_2{}^3 n_2 \tag{A1.81}$$

The difference velocity then takes the form

$$v_d = \frac{2}{9}\gamma b_2{}^2\frac{\nabla p}{\mu_m} \tag{A1.82}$$

or

$$v_d = -\frac{4}{9}\gamma\alpha^2 v_m{}^0 \tag{A1.83}$$

where γ was defined previously.

To calculate the volume flow (to which the hydraulic conductance is proportional), we write the volume weighted velocities—in the core zone $v_v{}^c$, in the wall zone $v_v{}^w$. They are

$$v_v{}^c = v_m - \frac{4}{9}\alpha^2\gamma^2 f_2 v_m{}^0 \tag{A1.84}$$

$$v_v{}^w = f_1 v_m = (1 - f_2)v_m \tag{A1.85}$$

The average values of v_m over the core zone and wall zone (barred values) are

$$\overline{v_m{}^c} = v_m{}^0\left[1 - \frac{1}{3}(1 - \alpha)^2\right] \tag{A1.86}$$

$$\overline{v_m{}^w} = v_m{}^0\left[\alpha - \frac{\alpha^2}{3}\right] \tag{A1.87}$$

The total volume flow rate is then

$$\overline{v_v{}^c}A_c + \overline{v_v{}^w}A_w = [(1 - \alpha)\overline{v_v{}^c} + \alpha\overline{v_v{}^w}]A \tag{A1.88}$$

The ratio of this flow rate to the flow rate $^2/_3\, v_m{}^0 A$, obtained by setting $\alpha = 0$, gives us the effect of graininess on the hydraulic conductance L_p. The result is, for the ratio of such conductances

$$\frac{L_p(\alpha)}{L_p(0)} = 1 - \left(\frac{3}{2} + \frac{2}{3}\gamma^2\right)\alpha^2 f_2 + \left(\frac{1}{2} + \frac{2}{3}\gamma^2\right)\alpha^3 f_2 \tag{A1.89}$$

which correctly reduces to unity in the $\alpha = 0$ limit of no graininess, and in the $f_2 = 0$ limit of infinite dilution. We will remark on the numerical value of γ in connection with an estimation of the reflection coefficient σ.

The reflection coefficient may be defined by the relation

$$1 - \sigma = \frac{n_2\overline{v_2{}^c}A_c}{n_2\overline{v_v}A} \tag{A1.90}$$

The numerator in the ratio is the solute flow rate (molecules per second) due only to a pressure gradient (when $\nabla\Pi = 0$). The denominator is the product of the associated volume flow rate and the solute molecular density. Writing the volume flow rate $v_v A$ in the form

$$\overline{v_v}A = \frac{2}{3}v_m{}^0 A\frac{L_p(\alpha)}{L_p(0)} \tag{A1.91}$$

leads to

$$1 - \sigma = \frac{3}{2}(1 - \alpha)\frac{\overline{v_2{}^c}}{v_m{}^0}\frac{L_p(\alpha)}{L_p(0)} \tag{A1.92}$$

The solute velocity v_2 takes the form

$$v_2 = v_m + [1 - (1 - \gamma)f_2]v_d \tag{A1.93}$$

with v_m and v_d as before.

The result for $1 - \sigma$ is

$$1 - \sigma = \frac{3}{2}(1 - \alpha) \cdot \left\{ 1 - \frac{1}{3}(1 - \alpha)^2 - [1 - (1 - \gamma)f_2]\frac{4}{9}\,\alpha^2 \right\} \cdot \frac{L_p(\alpha)}{L_p(0)} \qquad (A1.94)$$

This reduces, in the dilute limit $f_2 \rightarrow 0$, to

$$\sigma = \left(\frac{3}{2} + \frac{2}{3}\gamma\right)\alpha^2 - \left(\frac{1}{2} + \frac{2}{3}\gamma\right)\alpha^3 \qquad (A1.95)$$

We note that this result for σ is not very sensitive to values of γ in the range from 0 to 1. A numerical value for γ may be obtained in a hydrodynamic limit by regarding solute molecules as balls suspended in the solvent. Such a calculation relates the value of γ to the coefficient of α^2 in the expression for the friction function G (see Curry (6)).

A similar approximational calculational scheme can be used to estimate the comparable grainy correction for the diffusive conductance ratio $L_d(\alpha)/L_d(0)$.

We expect our local field equations to satisfy local Onsager reciprocity. Global Onsager reciprocity need not be obeyed, however, and will not be obeyed in cases where the solute concentration differs by significant fractional amounts at the two ends of the channel.

Interesting field systems interact with their own graininess.

APPENDIX II

The Communicational Language of Internally Complex Thermodynamic Systems is Logarithmically Uniform[2]

Communication becomes very necessary when systems have great complexity. A language is needed to control the cycling through all of the internal modes that express the time-delayed, internal degrees of freedom. Language is a weak but persistent catalytic process that urges a complex system through various low-force barriers that separate equienergetic, singular states (complexions) of the system toward its evolutionary goal.

Zipf, and later Mandelbrot, attempted to provide a theoretical construct for languages (see Brillouin (5), for an introduction to the themes).

The following development, we believe, presents the primitive, statistical mechanical basis for the distribution characteristics of thermodynamic languages. It is not a theory of syntax.

If a homeokinetic system required only one switch state, then a one word vocabulary would be sufficient (e.g., "move"—to get out of a normal state of rest). But as internal modal complexity increases, more switch-state signals, "words," are needed. Almost by definition, the power available for communication is small; otherwise it would be treated as a major thermodynamic variable. Thus, communication is catalytic; the small signals used are amplified to control modal switch states. After long-term development and evolution, as communication processes approach an equilibrium status, they take on thermodynamiclike, near-noise, distributional characteristics.

A case in point would be the "evaporation" and "condensation" of human populations within an ecosystem. In the absence of strong political bonding, as with pre-Neolithic societies, the size distribution of human colonies is Boltzmannian. To account for this fact, consider the three cases that follow.

Case 1. The Maxwell-Boltzmann distribution. We first review a derivation of the Maxwell-Boltzmann distribution. The derivation requires the Boltzmann assumption—that interactions (collisions) are independent, and that Newtonian mechanics applies, with three conservations

$$mnu^0,\quad mnu^1,\quad mnu^2 \qquad (A2.1)$$

m = mass (individual), n = number of particles, u = velocity

Σmn = total mass which is conserved
Σmnu = momentum, which is conserved
Σmnu^2 = vis viva (the modern value, times 0.5, gives kinetic energy) which is conserved.

Conservation (i.e., specification) of these three (statistical) moments provided by Newton's laws gives the Maxwell-Boltzmann distribution.

The statistical independence lends support for assuming that the logarithm of the distribution function is made up of the linearly independent associations of these integral moments

$$\ln p = A\,mn + B_1 mnu + B_2 mnv + B_3 mnw + C_1 mnu^2 + C_6 mnv^2 + C_7 mnw^2 \qquad (A2.2)$$

velocity here is a vector with three components, u, v, w; p is the associated probability (or number); the coefficients A, B, C are as yet undetermined.

If the ensemble is isolated, mn is a constant, u^2 can be arranged in the form $(u - u_0)^2$, by substitution, because isotropic ensemble characteristics make $B_1 = B_2 = B_3$, and $C_1 = C_2 = C_3$. Three constants, now denoted as A, C, u_0, remain

$$\ln p = \ln A + C[(u - u_0)^2 + (v - v_0)^2 + (w - w_0)^2] \qquad (A2.3)$$

The first moment is fixed by choice of axes, and the condition of isolation, to

$$u_0 = v_0 = w_0 = 0$$

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[2] This thesis and this section were developed in collaboration with Dr. Frank Hassler.

Thus

$$p = Ae^{C(u^2+v^2+w^2)} \qquad (A2.4)$$

Contact with an ideal gas thermometer (i.e., assuming the validity of equipartitioning) provides the metric for C.

$$p = A \exp - \left(\frac{u^2 + v^2 + w^2}{k\mathrm{T}}\right) \qquad (A2.5)$$

Case 2. The Boltzmannian distribution. We now offer the following parallel derivation, in terms of social phenomena, for an ensemble of isolated or at least poorly interacting primitive human societies. There exists a population p of each isolated, active group (atomism); a total mass, Mp, of the group, where M is the average mass of the species member (e.g., adult); a total daily energy consumption, Hp, of the group, where H is the daily energy requirement (power) of the average species member. These are the invariants. The daily power is partitioned among the various behavioral modes of the individual, approximately 20 for human beings (1). The independence of these modes leads to an associated probability (measured as group number N) of these invariants with undetermined multipliers A, B, C, N_0.

$$\ln N = \ln N_0 + A\mathrm{p} + B\mathrm{Mp} + C\mathrm{Hp} \qquad (A2.6)$$

$$N = N_0 e^{(A + BM + CH)\mathrm{p}} = N_0 e^{-a\mathrm{p}} \qquad (A2.7)$$

The number of groups of various sized populations diminishes exponentially with the constant measure a. (It is thermodynamically impossible that a monotonic increasing probability be associated with infinite population. Thus the exponent is negative.) While N_0 is the asymptotic value of the number of groups with zero population, there obviously is a finite size cutoff. We have referred to this as the Boltzmannian distribution (18).

Another derivation (a little closer to the field thermodynamic form we offer for physiology) is the following.

Consider a ground territory marked by N nucleating centers of population. These centers may have populations 1, 2, . . . k. Thus let there be n_1 . . . n_k centers, where n_i is the number of centers with population i. Let p_i denote the total population of all centers with population i

$$N = \sum_1^k n_i \qquad (A2.8)$$

gives the number of population centers N

$$\mathrm{P} = \sum_1^k i n_i \qquad (A2.9)$$

gives the total population P. The total number of complexions, W, with which the centers can be filled is

$$\mathrm{W} = \frac{N!}{\prod_1^k n_i!} \qquad (A2.10)$$

A statistical mechanical construct requires that ln W be an extremum for the most probable complexion. (Recall that according to the Boltzmann construct, S (entropy) = k ln W, where k is the Boltzmann constant)

$$\ln \mathrm{W} = \ln N! - \sum_1^k \ln n_i! \qquad (A2.11)$$

Now

$$\ln x! = (x + 0.5) \ln\left(\frac{x + 0.5}{e}\right) + 1.5 \ln \frac{e}{1.5} \qquad (A2.12)$$

is a very good approximation for ln x! even for small integral values of x. Maximizing ln W, while conserving N and P, is achieved by the use of Lagrangian multipliers, A and B, applied to the variations

$$\delta \ln \mathrm{W} + A\delta \mathrm{N} + B\delta \mathrm{P} = 0 \qquad (A2.13)$$

$$n_i + 0.5 = Ce^{-b\mathrm{p}_i} \qquad (A2.14)$$

which, outside of the minor increase in accuracy in the term 0.5, is the Boltzmannian. Note again, no significant interactions were provided for. Basically the statistics of their size and number of groups of settlements remained fixed.

Experimental data from the Ethnographic Atlas (32) on independent isolated cultures confirm this law. The criteria the Atlas gives for isolation is separation by 200 miles, or 1,000 years. Its catalog purports to exhaust the set of all such well-documented cultures.

Case 3. The Zipfian distribution. Now we turn, finally, to population centers that are politically bound; they are sociopolitically and economically interactive. Essentially the only constraint is total population P. The sociopolitical relations modify the fixed spatial order established by primitive societies. Using measures n_i, p_i, and i, as before

$$\mathrm{P} = \sum_1^k \mathrm{p}_i = \sum_1^k i n_i \qquad (A2.15)$$

While the total number of settlements N still is defined by

$$N = \sum n_i \qquad (A2.16)$$

it is no longer constrained. The number of complexions, W, is

$$\mathrm{W} = \frac{\mathrm{P}!}{\prod_1^k \mathrm{p}_i!} \qquad (A2.17)$$

Extremizing this, when only population intervals are constrained, gives

$$\delta \ln W + A\delta P = 0 \qquad (A2.18)$$

$$p_i = i n_i = \text{constant} \qquad (A2.19)$$

This is Zipf's law.

This law does not conserve the numbers of settlements N, only the population P. Its significant implication is not the $1/r$ rank-ordering relation, but the fact that in any logarithmic interval, e.g., among all centers of a certain size, as with populations between 2,500–5,000, 5,000–10,000, 10,000–20,000, etc., the cumulative population is constant. (Suppose we classify harmonic fractions, $1/n$, into equal octave intervals, $1 - 1/2$, $1/2 - 1/4$, $1/4 - 1/8$, etc., the sum of fractions in each interval quickly converges to a constant, i.e., 1, $1/2 + 1/3 = 0.83$, $1/4 + 1/5 + 1/6 + 1/7 = 0.76, \ldots, 0.67$. Thus the sum converges very quickly to the same constancy as the logarithm integral.) Zipf's law really states that any individual has no more reason to be attracted to one interval size than another. Thus it is a very weak, essentially nonphysical (i.e., communicational) constraint. Physical constraints, as we have shown, attract and condense population by a higher physically constrained moment equation, e.g., in mechanical motion as a result of the second moment kinetic energy constraint.

Note that in the first two examples (gas and noninteracting populations) the variables were full thermodynamic variables, number and energy. Thus very strong distribution constraints resulted – the Maxwell-Boltzmann law and the Boltzmannian. In the third case, individuals were free to move within and between cities (as least compared to movement in primitive cultures). Therefore the total population number is still a conserved full thermodynamic variable, but results in a much weaker distribution constraint, the unbound condensation population (city size). However, the long-range socio-political order between members of the ensemble removes the fixed local spatial order, and the total number of settlements is free to be determined by its Zipfian distribution, parameterized by the size of the largest city in population.

We note that strong physical constraints result in tightly bound forms of short-range scale and short-term duration. Weak physical constraints result in spatiotemporal order over long scale.

We refer to the Zipfian (or uniform log) distribution as a "near-noiselike" thermodynamic language. If we ignore the differences among individuals, the values they derive or offer to the cities in which they live, and consider only the "conservation of total individuals," we obtain the Zipfian, a distribution representing random probability of finding an individual in any particular city, while meeting the overall conservation constraints. In that sense the distribution is "random." Changes in the complexion of the system are "random" and communication (or language) is purely random "noise."

If, however, the different complexions are subtly different, some more viable than others, with significant alternative future systems evolution being possible, then the distribution in fact is "near noise," one with the true value (or signal), from the systems point of view, "lost" in the noise – but present nonetheless.

Therefore, from a mechanistic view, if there was a system evolving in a large context, composed of a fixed number of subsystems, it can be treated as a thermodynamically constrained system with an internal modal language of many complexions, where the system has constructed the near noiselike language out of materials or energies at hand in a "natural" process that fits the system. The $1/f$ noise associated with membranes, complex speech, and even music patterns, and more recently exhibited with regard to the total pattern of cellular mobility (31), exhibits that character of filling each frequency octave with ongoing signal, presumably communicational, and not noise, yet near noise.

While the demonstration provided here applied to "population," it seems clear that it can also be applied to probability, and thus to actual interval period or frequency, i.e., to any equally tempered series.

Zipf also extended his claim to space, i.e., to influence reciprocal to distance. The measure that provides the bridge is "cost," or "effort," to intercommunicate or intertransport between centers. That notion of cost or effort has been adopted in information theory (5). In the simplest form, the time interval itself ("cost" of using a telegraphic channel) is considered to be the cost. But in any case, one should note that population, probability, frequency, or distance are all potential measures for these logarithmically uniform distributions.

This statistical mechanical derivation of Zipf's law is an improvement over the notions offered by Zipf (as the principle of least effort (53)), Stewart (a social physics; see, for example (44–46)) and others (see (33)) who have based their studies on a so-called "gravity" theory (or inverse square law theory) for population. These authors, generally taking off from Zipf's seminal work, have attempted to offer, as a full physically applicable theory, the notion of $1/d^2$ force attraction (where d is an interaction distance), and therefore a $1/d$ potential law for all kinds of weakly associated social phenomena (Zipf offered both the spatial process of $1/d$ attraction, and the temporal process of $1/n$ probability). Yet very often there seems to be an underlying confusion as to whether they mean a potential law or a force law.

Clearly there is no physical basis for a literal $1/d^2$ law, and there is no physical basis for a potential law (the character of a force system F that only depends on position and for which a single-valued potential function V can be defined by $F = -\nabla V$).

On the other hand, there is a physics for spatiotemporal influence that can be invoked for distinct a priori equal probability complexions achieved by interaction which provides a measure of the statistics and thus the changes in entropy. There *are* real physical forces at work, but they are "internalized," homeokinetic. They result in switching states of the organism. It is interesting to note that we derive the forms associated with a weak logarithm divergence, and that we could get both spatial, temporal, or simply frequency forms (e.g., language probabilities) out of one physical process, a quantization of complexions.

A prior application of such interactive influence has been to the interpersonal force between people (20), or to cell-environment interaction (26), and to value-in-trade (18). The appeal was made to exchange force. The current physical generalization which is being invoked is gauge theory (52), whose generality this kind of work attempts to extend to interacting populations of homeokinetic systems.

Interesting field systems evolve through their own graininess.

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A. S. Iberall
General Technical Services, Inc., Upper Darby, Pennsylvania 19082
H. Soodak
Physics Department, City College of New York, New York City
F. Hassler
Systems' Research Office, Transportation Systems Center (DOT), Cambridge, Massachusetts