AUTONOMIC ENERGY CONVERSION

I. THE INPUT RELATION: PHENOMENOLOGICAL AND MECHANISTIC CONSIDERATIONS

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ABSTRACT The differences between completely and incompletely coupled linear energy converters are discussed using suitable electrochemical cells as examples. The output relation for the canonically simplest class of *self-regulated* incompletely coupled linear energy converters has been shown to be identical to the Hill force-velocity characteristic for muscle. The corresponding input relation (the "inverse" Hill equation) is now derived by two independent methods. The first method is a direct transformation of the output relation through the phenomenological equations of the converter; Onsager symmetry has no influence on the result. The second method makes use of a model system, a hydroelectric device with a regulator mechanism which depends only on the operational limits of the converter (an electro-osmosis cell operated in reverse) and on the load. The inverse Hill equation is shown to be the simplest solution of the regulator equation. An interesting and testable series of relations between input and output parameters arises from the two forms of the Hill equation. For optimal regulation the input should not be greatly different in the two limiting stationary states (level flow and static head). The output power will then be nearly maximal over a considerable range of load resistance, peak output being obtained at close to peak efficiency.

INTRODUCTION

The problem of self-regulation, or self-adaptive control, of a linear energy converter of the type shown in Fig. 1 has been treated in a previous publication (1).[1] It was shown that the resistive load, $R_L = -X_1/J_1$, for *maximal efficiency* is independent of input restrictions (i.e. restrictions on X_2 or J_2 or both). For *maximal output,*

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[1] Since the output of an energy converter is usually more accessible than the input in biological systems, the output process is regarded as proximal to the observer and denoted by 1, while the input is denoted by 2. A linear energy converter is described by the linear phenomenological relations

$$J_1 = L_{11}X_1 + L_{12}X_2, \qquad J_2 = L_{21}X_1 + L_{22}X_2.$$

The efficiency, η, is defined by (2)

$$\eta = \text{output/input} = -J_1X_1/J_2X_2.$$

however, the input restriction must be considered. Frequently it is imposed by maintaining a constant driving force (X_2) or a constant driving flow (J_2). In electrical terms these restrictions correspond, respectively, to constant voltage or constant current operation. In the two modes of operation the power output of a reasonably tightly coupled converter is maximized by very different values of the load R_L. The former mode favors low loads, the latter high. However, if high output power is required over a wide range of loads, as is the case in some biological energy converters such as the muscle, operation in one of the above modes is not profitable. Instead, it pays to equip the converter with a device which *regulates* the input in response to the load. Regulatory mechanisms are well-known both in engineering and biology.

An analysis of autonomic modes of energy conversion made it clear that the behavior of linear converters which are not completely coupled (and hence have two degrees of freedom), operate between specified limits, and give a unique adaptive response to any imposed load, can always be reduced to the same general expression describing the output (1). This expression includes an arbitrary function of the load resistance $\mathbf{h}(R_L)$ satisfying certain limiting conditions. The expression may be regarded as the canonical equation of the regulator; it can be written as a relationship between X_1 and J_1 which contains, in addition, only $\mathbf{h}(R_L)$ and the working limits of the converter. For the simplest case, when $\mathbf{h}(R_L)$ is constant, the expression reduces to the Hill force-velocity relation for muscle.

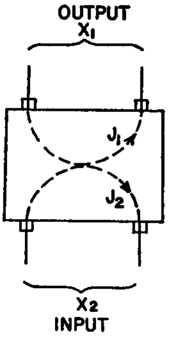

FIGURE 1 Diagrammatic representation of an energy converter as a "black box." J_1 and J_2 are the coupled output and input flows, X_1 and X_2 their respective conjugate forces.

The object of the present study is to derive and examine the corresponding input relation. It will be shown that for the simplest class of autonomic energy conversion, the input relation may be derived by two independent means. One of these involves a thermodynamic consideration of the *converter*, the other a mechanistic consideration of a model *regulator.*

We commence with a discussion of linear energy conversion, followed by two examples of electrochemical cells—one fully coupled, the other incompletely coupled. This is intended to clarify the point of view subsequently taken. A list of symbols is included at the end of Part II.

LINEAR ENERGY CONVERTERS

The characteristics of a linear energy converter have been discussed in the framework of nonequilibrium thermodynamics (2). The energy converter is considered as a stationary-state "black box" in which two coupled irreversible processes take place. If the system is isothermal its dissipation function or rate of free energy dissipation Φ, which is expressed in units of power, takes the form

$$\Phi = \underbrace{J_1X_1}_{\text{—output power}} + \underbrace{J_2X_2}_{\text{input power}} \tag{1}$$

where J_1 and J_2 are the two coupled flows, and X_1 and X_2 their conjugate *thermodynamic* forces. These are flows and forces in a generalized sense and include the velocities and affinities of chemical reactions. The output term is negative, since the output flow J_1 takes place *against* its conjugate force X_1 as a consequence of its coupling to the input flow J_2. The assumption of linear phenomenological equations relating the flows and the forces usually implies that the system is characterized by Onsager symmetry, but if this is not so the considerations to be outlined are unaffected. For the most general case two "degrees of coupling" are defined in terms of the phenomenological coefficients (2),

$$\begin{aligned} q_{12} &= L_{12}/\sqrt{L_{11}L_{22}} \\ q_{21} &= L_{21}/\sqrt{L_{11}L_{22}}\,. \end{aligned} \tag{2}$$

If the system is symmetrical in the Onsager sense

$$q_{12} = q_{21} = q \tag{3}$$

and the maximum efficiency attainable is given by

$$\eta_{\max} = -(J_1X_1/J_2X_2)_{\max} = q^2/(1+\sqrt{1-q^2})^2. \tag{4}$$

Two stationary states, in which the efficiency η is zero (except in the exceptional case $q^2 = 1$ which will be discussed presently), are of particular significance and are designated as follows:

(*a*) *Level Flow* ($X_1 = 0$, $J_1 = J_1{}^l$, $R_L = 0$). Examples are a short-circuited electrochemical cell, an unloaded muscle contraction, and the physiological transport of salt or water between isotonic solutions.

(*b*) *Static Head* ($X_1 = X_1^s$, $J_1 = 0$, $R_L = \infty$). Examples are an open-circuited electrochemical cell, an isometric muscle contraction, and the maintenance of concentration gradients across symmetrical plant and animal cell membranes by active transport. (Unless $q^2 = 1$, the input flow J_2 is not zero at static head.)

One method of measuring q is applicable to systems in which the driving force is either fixed or known to have the same value both at level flow and at static head. All that is required is to determine the input flow (i.e. the fuel consumption) in the two stationary states, since under these conditions

$$q^2 = 1 - (J_2^s/J_2{}^l)\ (X_2 \text{ constant}). \tag{5}$$

Another method depends on the relation[2]

$$q^2 = (\partial J_1/\partial J_2)_{X_1}(\partial J_2/\partial J_1)_{X_2}\,. \tag{6}$$

ELECTROCHEMICAL CELLS AS EXAMPLES OF ENERGY CONVERSION BY COUPLED PROCESSES

The electrochemical cell is perhaps the clearest example of coupling between chemical reaction and transport of material, in this case electrons. At static head an electrochemical potential difference is maintained between two "reservoirs" of electrons, the terminals; when both terminals are of the same metal (e.g. copper wires) this difference is thermodynamically well-defined. At level flow the difference is zero, but since most electrochemical cells tend to become polarized under such circumstances, the phenomenological coefficients may change, in which case equation 5 cannot be used for the determination of *q*. If no side reactions occur the dissipation function for the processes occurring in the cell takes the form (2)

$$\Phi = IE + vA, \tag{7}$$

where the quantities correspond directly to those in equation 1. The two coupled flows are *I* and *v*, representing electric current and reaction velocity respectively, while their conjugate forces *E* and *A* represent the potential difference between the terminals and the affinity of the reaction.

Consider the well-known Weston standard cell:

$$\mathrm{Pt}\;\Big|\;12.5\%\ \mathrm{Cd\ in\ Hg}\;\Big|\;\begin{array}{c}(3CdSO_4\cdot 8H_2O)(s),\qquad Hg_2SO_4(s)\\ \text{saturated solution}\end{array}\;\Big|\;\mathrm{Hg}\;\Big|\;\mathrm{Pt}.$$

The only chemical reaction possible here is

$$3Cd\ (\text{amalgam}) + 3Hg_2SO_4(s) + 8H_2O \rightleftharpoons (3CdSO_4\cdot 8H_2O)(s) + 6Hg, \tag{8}$$

but net reaction cannot occur unless it is accompanied by the passage of electrons between the platinum terminals. At static head, i.e. when the cell is either open-circuited or opposed by an emf such that the current is zero, net reaction is halted.

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[2] In biological energy converters the determination of J_2 may be complicated by the presence of basal metabolism. If the basal component is constant, it can be determined and the degree of coupling obtained (3), providing *some* linearly independent variation occurs in X_2 when X_1 is varied.

When current flows it is in a *fixed ratio* to the velocity of reaction, 1 faraday per equivalent of cadmium consumed, from which it follows that the degree of coupling q is unity. From equation 4 we conclude that the *maximum* efficiency of the Weston cell is also unity. It is readily shown (2) that this maximum can only be reached at static head, when the current is zero and indeed no processes take place at all. Although this seems contradictory, it is of course an essential characteristic of reversible equilibrium. We can approach unit efficiency as closely as we like by increasing the load and thus reducing the rates of the processes until they become infinitesimally small, *providing the system is completely coupled.* This is true of all types of energy converters.

The driving force or affinity of the reaction, a concept introduced by De Donder, is defined by (4)

$$A = -\sum_i \nu_i \mu_i \tag{9}$$

where μ_i is the chemical potential of the ith species and ν_i its stoichiometric coefficient in the reaction, taken as positive if it is a product and negative if a reactant. This should be distinguished from the Gibbs free energy of the system, which is given by

$$G = \sum_i n_i \mu_i \tag{10}$$

where n_i is the number of moles of the ith species present.[3] The velocity of the reaction must be expressed as follows in order to be conjugate to A (i.e., vA should represent the rate of free energy expenditure):

$$v = (1/\nu_i) \cdot (dn_i/dt). \tag{11}$$

Obviously v is unique for a given reaction and thus the same for all species taking part in the reaction. However, if the stoichiometric coefficients for the Weston cell reaction are taken from equation 8, v will represent the rate of production of the hydrate ($3CdSO_4 \cdot 8H_2O$) in moles per second since this is the only species for which ν_i is unity. Likewise A will be obtained in terms of calories per mole of the hydrate. It may be more convenient to base v and A on an equivalent of Cd consumed (or

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[3] The affinity, which is well-defined at each instant of time and characteristic of the reaction, is related to the Gibbs free energy change resulting from the reaction. If temperature and pressure are constant, and if the reaction proceeds to an extent small enough for the chemical potentials of all species to remain essentially constant, then the change in Gibbs free energy *per equivalent of* Cd *reacted*, $-\Delta G$, is evidently equal to A. In other words

$$-(\Delta G)_{T,p,\mu_i} = A.$$

If the chemical potentials do not remain constant (μ_{Cd} can vary in the Weston cell), then $-(\Delta G)_{T,p}$ represents an average value of A during the change (4).

a mole of Hg produced) by dividing the stoichiometric coefficients of equation 8 by 6 to obtain the ν_i's for equations 9 and 11. The product νA, however, is entirely independent of any arbitrary multiplicative factor in the coefficients. It is the correct form for the input in all conversions of chemical energy.

Now from the linear phenomenological equations, assuming symmetry, we have in general

$$(X_2^s/X_1^s) = (\partial X_2/\partial X_1)_{J_1} = -(1/q^2)(J_1^l/J_2^l)$$
$$= -(1/q^2)(\partial J_1/\partial J_2)_{X_1} = -(\partial J_1/\partial J_2)_{X_2}. \quad (12)$$

From equations 5 and 12 it is seen that if the driving force X_2 is constant it may be determined by measuring the reaction velocity as well as the output force and flow at static head and level flow. If level flow measurements are impracticable, the variation of J_1 with J_2 (brought about by varying the load resistance R_L) in the neighborhood of static head may be measured instead. Translating some of the relations (equation 12) into electrochemical terms, we introduce the emf $\mathcal{E}$ (defined as the negative of the externally-imposed potential which brings the current to zero), i.e.

$$\mathcal{E} = -E_{I=0}, \quad (13)$$

and assuming A is fixed we obtain

$$A = (1/q^2)(I/v)_{E=0}\mathcal{E} = (\partial I/\partial v)_A \mathcal{E}. \quad (14)$$

For the Weston cell, as we have seen, $q^2 = 1$. If v and A are in terms of equivalents of Cd, then for this case

$$(I/v)_{E=0} = (\partial I/\partial v)_A = \mathfrak{F}, \quad (15)$$

where $\mathfrak{F}$ denotes the Faraday constant. Consequently,

$$\mathcal{E} = A/\mathfrak{F}. \quad (16)$$

In contrast to the Weston cell, electrochemical cells involving liquid junctions, such as the Daniell cell, are not fully coupled (although their degree of coupling may be very close to unity) since on open circuit irreversible mixing and reaction continue to take place—albeit very slowly. An illuminating example of an incompletely coupled cell which does not involve a liquid junction is the following enzymatic "fuel cell" (5):

$$\begin{array}{c|cc|c|c|c|cc|c}
 & & & - & + & - & - & & \\
 & & \mathrm{RCONH_2} & \mathrm{RCONH_2} & \mathrm{PAPAIN} & \mathrm{RCONH_2} & \mathrm{RCONH_2} & & \\
\mathrm{Ag} & \mathrm{AgCl(s)} & \mathrm{NH_4Cl} & \mathrm{RCOONH_4} & \mathrm{RCONH_2} & \mathrm{RCOONH_4} & \mathrm{NH_4Cl} & \mathrm{AgCl(s)} & \mathrm{Ag} \\
 & & & & \mathrm{RCOONH_4} & & & &
\end{array}$$

The vertical bars with signs represent ion-exchange membranes having fixed charges as shown. Here the "black box" or working element may be identified with the *central* compartment, which is in essence a composite membrane consisting of two oppositely-charged ion-exchange membranes with a thin layer of papain solution in between. In all other respects the system is completely symmetrical. The *outer* two cation-exchange membranes constitute reversible ammonium electrodes. However, the chemical reaction responsible for the emf of this cell is not an electrode reaction. A low molecular weight neutral substrate, $RCONH_2$, which passes through all the membranes, is hydrolyzed in the presence of papain to an ammonium salt:

$$RCONH_2 + H_2O \xrightleftharpoons{\text{PAPAIN}} RCOO^- + NH_4^+. \tag{17}$$

As before, this is the only spontaneous reaction possible—but net reaction cannot halt on open circuit, or when the cell is opposed by an emf such that the current is zero, unless the central two ion-exchange membranes are ideally permselective. In general this is not the case, and the degree of coupling attained depends on the selectivities of these two membranes. The affinity of the reaction can be adjusted by varying the concentrations of amide and salt in the "fuel reservoirs," or compartments flanking the enzyme compartment, which due to their size are kept essentially identical in composition. The dissipation function is given by equation 7, and since it was shown experimentally that the system obeys Onsager symmetry, equations 12 apply. We have, therefore,

$$(\partial A/\partial E)_I = -(1/q^2)(\partial I/\partial v)_E = -(\partial I/\partial v)_A, \tag{18}$$

so that in this case, where the degree of coupling is not unity,

$$(\partial I/\partial v)_E \neq (\partial I/\partial v)_A \neq \mathfrak{F}.$$

With one model of this system it was found that $(\partial I/\partial v)_A = 2\mathfrak{F}$, and that on open circuit measurements $\mathcal{E} = A/2\mathfrak{F}$ (cf. equations 14). Further studies showed that this particular membrane combination was characterized by a degree of coupling $q = 0.79$, and hence according to equation 4 by an η_{max} of 25%.

It is well-known that in general the linear phenomenological relations hold for chemical reactions only when the condition

$$A \ll \mathbf{R}T \tag{19}$$

is satisfied, i.e. very close to equilibrium. Simple kinetic schemes lead to the relations (in which $v = v_{\text{forward}} - v_{\text{reverse}}$)

$$v = v_{\text{reverse}}\{\exp(A/\mathbf{R}T) - 1\} = v_{\text{forward}}\{1 - \exp(-A/\mathbf{R}T)\} \tag{20}$$

(for example, see reference 6, p. 205). A kinetic analysis of the papain cell when operated *outside* the linear region (5) gave an expression for the reaction velocity of the form

$$v = k_1\{\exp(A/\mathrm{R}T) - 1\} + k_2 I \tag{21}$$

where k_1 and k_2 contain rate constants of the reaction as well as transport coefficients of the membranes. From equation 21

$$(v/I)_{A=0} = (\partial v/\partial I)_A \tag{22}$$

as is the case for linear behavior in the vicinity of equilibrium. Furthermore it was shown experimentally that

$$(\partial I/\partial v)_A = 1/k_2 = -(A/E)_{I=0} \tag{23}$$

just as would be predicted from the Onsager symmetry relation for a linear system. The reaction rate at constant affinity was found to be a linear function of the current, and the open circuit potential a linear function of the affinity, despite the absence both of complete coupling (v and I are not related stoichiometrically) and linear kinetics. Whether or not this result has more general validity is as yet unknown. However, it is clear that nonlinear kinetics are not *necessarily* incompatible with linear phenomenological behavior.

AUTONOMIC ENERGY CONVERSION AND THE "INVERSE" HILL EQUATION

The canonical equation for a regulator controlling a linear energy converter of degree of coupling *less than unity* is given by (1)

$$(X_1/X_1^s\mathbf{h}(R_L)) + (J_1\mathbf{h}(R_L)/J_1{}^l) = 1 + (J_1X_1/J_2^sX_2{}^l). \tag{24}$$

The phenomenological equations of the converter involve four variables, X_1, X_2, J_1, and J_2, of which any given two may, in principle, be fixed independently. The equation of the regulator reduces the number of independent variables to one—either J_1 or X_1. The function $\mathbf{h}(R_L)$ is dimensionless and has a limiting value of unity when R_L is zero or infinity, i.e. at level flow or static head. Furthermore $\mathbf{h}(R_L)$ itself cannot become zero or infinity. If it is a constant, therefore, it must be unity for all R_L, whereas if it is not constant it must be "modulated" about the value unity. This suggests that $\mathbf{h}(R_L)$ contains *information* relating to the function of the regulator, although obviously it does not contain the entire information. Generally a self-adaptive mechanism requires programming according to an arbitrary criterion, since an element of choice is left in the design of the regulator after the operational limits have been specified. The element of choice appears in equation

24 as $\mathbf{h}(R_L)$. But there is a constraint which compels $\mathbf{h}(R_L)$ to be unity when constant, so the informational content of an "unmodulated" $\mathbf{h}(R_L)$ is zero. This corresponds to the canonically simplest class of autonomic energy converters mentioned in the Introduction, programmed only with the operational limits (at static head and level flow) and the degree of coupling. It is even redundant to add the degree of coupling to the operational limits in describing this program: q does not appear explicitly in equation 24, although it may be introduced by rewriting the equation entirely in terms of output limits using the identity (1)

$$J_2^s X_2^l \equiv -J_1^l X_1^s (1 - q^2)/q^2. \tag{25}$$

(A similar relation exists for q_{12} and q_{21} in the asymmetric case (1).) It will be shown presently that the regulator equation can also be written entirely in terms of input quantities without specifying q, since a knowledge of the input operating limits determines the degree of coupling if the converter is linear.

By defining two constants in terms of the operational limits,

$$\begin{aligned} a &= J_2^s X_2^l / J_1^l \\ b &= J_2^s X_2^l / (-X_1^s), \end{aligned} \tag{26}$$

and introducing them into the canonical equation 24, *restricting ourselves to the case of minimal programmed information* $\mathbf{h}(R_L) = 1$, we obtain

$$(-X_1 + a)(J_1 + b) = (-X_1^s + a)b = (J_1^l + b)a. \tag{27}$$

This equation is identical to the Hill force-velocity relation for muscle.[4] It may be normalized by introducing the quantities

$$\begin{aligned} \xi_1 &= X_1/X_1^s \\ \gamma_1 &= J_1/J_1^l \\ \theta &= a/(-X_1^s) = b/J_1^l = (1 - q^2)/q^2 \end{aligned} \tag{28}$$

where equation 25 has been used. Note that $ab = \theta J_2^s X_2^l$. (If the converter does not obey Onsager symmetry, the quantity $q_{12}q_{21}$ appears in place of q^2 in the definition of θ.) Then equation 27 reduces to

$$(\xi_1 + \theta)(\gamma_1 + \theta) = (1 + \theta)\theta \; (q^2 < 1). \tag{29}$$

The adjustable parameter in equation 29 is essentially the degree of coupling.

A transformation of equation 24 leads to a particularly interesting relationship containing only *input* parameters, with the exception of $\mathbf{h}(R_L)$. This transformation

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[4] The sign convention here is opposite to one used previously (1).

can be made straightforwardly with the linear phenomenological relations. The assumption of Onsager symmetry simplifies the calculation but does not influence the result, which is

$$\left\{\left(\frac{X_2}{X_2^l} - \frac{J_2}{J_2^l}\right)\cdot\frac{1}{\mathbf{h}(R_L)} + \frac{J_2^s}{J_2^l}\right\}\left\{\left(\frac{J_2}{J_2^s} - \frac{X_2}{X_2^s}\right)\cdot\mathbf{h}(R_L) + \frac{X_2^l}{X_2^s}\right\} = 1. \qquad (30)$$

In the Hill case equation 30 takes a simpler form if we define two new variables as follows:

$$\begin{aligned} \Delta X_2 &= X_2 - X_2^l \\ \Delta J_2 &= J_2 - J_2^s. \end{aligned} \qquad (31)$$

Substituting equations 31 into equation 30 and setting $\mathbf{h}(R_L)$ equal to unity, we obtain the inverse Hill equation:

$$\{(\Delta X_2/X_2^l) - (\Delta J_2/J_2^l) + 1\}\{(\Delta J_2/J_2^s) - (\Delta X_2/X_2^s) + 1\} = 1. \qquad (32)$$

This expression may readily be normalized in a fashion similar to the normalization of equation 27. The following quantities must be introduced:

$$\begin{aligned} \xi_2 &= X_2/X_2^s \\ \gamma_2 &= J_2/J_2^l \end{aligned} \qquad (33)$$

(cf. equations 28). In addition two constants are required:

$$\begin{aligned} \xi_2^l &= X_2^l/X_2^s \\ \gamma_2^s &= J_2^s/J_2^l. \end{aligned} \qquad (34)$$

Equation 32 then takes the normalized form

$$\{(\xi_2/\xi_2^l) - \gamma_2 + \gamma_2^s\}\{(\gamma_2/\gamma_2^s) - \xi_2 + \xi_2^l\} = 1. \qquad (35)$$

As mentioned earlier, the degree of coupling does not appear explicitly in the inverse Hill equation. But it is implicit, since the two constants defined by equations 34 are related to each other through q^2:

$$\xi_2^l\gamma_2^s \equiv 1 - q^2. \qquad (36)$$

It will be seen that the input equation (35) has the same kind of symmetry between forces and flows as the output equation (29), i.e. interchainging ξ_2 and γ_2 and *at the same time* interchanging ξ_2^l and γ_2^s leaves the expression unchanged. This symmetry principle may be used to obtain additional information from computations based on these equations.

MECHANISTIC TREATMENT OF AN AUTONOMIC ENERGY CONVERTER

The ideas discussed above stem from an abstract thermodynamic treatment of a machine. The mechanism of energy conversion is of no consequence provided that linear equations describe its behavior. To the thermodynamics has been added a cybernetic argument: the machine is controlled by a hypothetical regulator, which in the Hill case is concerned only with the limits of operation. Again the mechanism by which the regulator operates is of no consequence. It is of considerable interest, therefore, to examine some simple physical arrangement consistent with the thermodynamic and other requirements, in order to gain insight as to how the behavior predicted could arise. In particular, one would like to know in what sense the Hill case is the simplest in terms of such a model.

It should be emphasized that the example described below is not necessarily intended as an analog for any particular self-regulatory system. Many other devices could be conceived of, and the one chosen merely reflects the author's interest in membrane processes. However, it has the advantage of giving, in its own terms, a physical meaning to the quantities in the inverse Hill equation. The arrangement is shown in Fig. 2. Imagine a very large salt-water reservoir or lake situated at a considerable height. For simplicity the lake may be assumed to contain a solution of pure sodium chloride. It is intended to design a hydroelectric power station which will generate direct current by means of a battery of "reverse electroosmosis" cells, one of which appears in the diagram. It consists of two compartments separated by a cation-exchange membrane, i.e. a membrane bearing negative fixed charges, and each compartment contains a reversible chloride electrode. If the membrane is sufficiently porous, the "downstream" compartment will not differ appreciably from the "upstream" compartment in concentration under steady flow conditions. The dissipation function for the cell is then

$$\Phi = IE + J_v \Delta p \tag{37}$$

where J_v represents the volume flow across the membrane, driven by the hydrostatic pressure Δp. The first term in Φ has the same meaning here as in equation 7. Once again we have a dissipation function of the form of equation 1. It is convenient now to revert to the more general symbolism for ready comparison with the previous equations.

A special requirement of the power station is that it should furnish a high and more or less constant power output over a wide range of external resistance. Consequently both voltage and current must alter according to the load. Upper limits are set for the voltage on open circuit and for the current on short circuit so that the cells cannot be damaged. The regulator adopted to govern power output consists primarily of a small auxiliary reservoir incorporating certain control mechanisms. It will be appreciated that no separate feedback loop from an output-sensing device is necessary, since any change in the external load is immediately

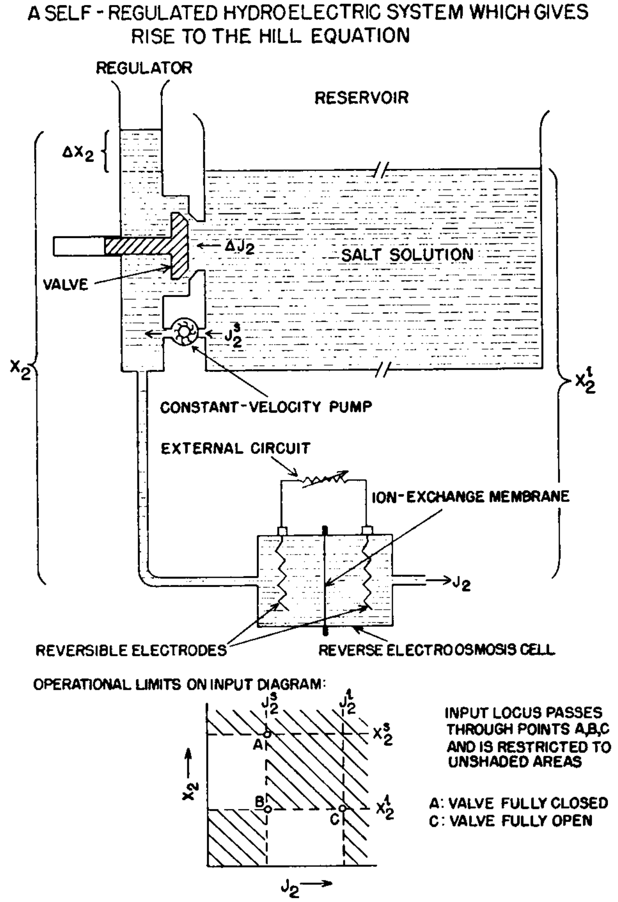

FIGURE 2 An autonomic hydroelectric energy converter and its input diagram (see text). The direction in which flow is regarded as positive is indicated by arrows. Note that the constant-velocity pump may be replaced by a direct line from the regulator to an additional "primary" reservoir situated at a considerably higher level, which may also serve to replenish the reservoir shown.

reflected in a change in the hydrodynamic "input resistance" seen by the regulator. The regulator has an additional power requirement, which we may assume to be provided by another lake in the neighborhood. This supplies sufficient pressure to drive a constant-velocity turbine pump, which maintains a steady flow J_2^s from the main reservoir to the regulator under all circumstances.[5] The other regulator mechanism is a valve, automatically controlled by an unspecified adaptive system, which

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[5] Alternatively, the constant-velocity turbine pump may be replaced by a pipe of suitable bore connecting the regulator directly to an additional "primary" salt-water reservoir situated at a considerably higher level. Variations in the level in the regulator would then have negligible effect on the flow J_2^s, which now comes from the primary reservoir. In this case the "secondary" reservoir which appears in Fig. 2 need not be so large, since it can be replenished separately by the primary reservoir and maintained at constant level.

gives rise to virtually zero resistance to flow between the reservoir and the regulator when fully open. The flow from reservoir to regulator through the valve will be called ΔJ_2. The pressure head available from the reservoir is X_2^l; any excess head developed in the regulator is ΔX_2. Thus the total force at the input of a cell is $X_2 = X_2^l + \Delta X_2$, and the total input flow is $J_2 = J_2^s + \Delta J_2$.

The control system of the valve is constructed so that any external change which tends to raise the level in the regulator, and thus reduce flow from reservoir to regulator, causes the valve to become more closed, and vice versa. At the high resistance limit it is closed completely and X_2 reaches the value X_2^s, which is determined therefore by J_2^s. The value of J_2^s has been chosen in accordance with the maximum allowable open-circuit voltage. At the low resistance limit the valve is completely open, and consequently the level in the regulator is negligibly different from that in the reservoir, which was denoted X_2^l accordingly (the difference in levels can be made arbitrarily close to zero). The total input flow is then J_2^l. It is seen that X_2^l determines the short-circuit current. The boundary conditions satisfied by the valve are:

$$\Delta X_2 = X_2^s - X_2^l \equiv \Delta X_2^s\colon \Delta J_2 = 0$$
$$\Delta J_2 = J_2^l - J_2^s \equiv \Delta J_2^l\colon \Delta X_2 = 0. \tag{38}$$

However, it is clear that the physical situation dictates certain other conditions of operation:

$$\Delta X_2 > 0\colon \Delta J_2 \leqq 0$$
$$\Delta J_2 > 0\colon \Delta X_2 \leqq 0. \tag{39}$$

Consequently, on grounds of continuity there must exist a particular state of the regulator in which the valve is neither completely open nor completely closed, such that

$$\Delta X_2 = \Delta J_2 = 0. \tag{40}$$

This is readily seen on examination of the "input diagram" (1) for the system given in Fig. 2, where A refers to static head, C to level flow, and B to the state represented by equation 40. The equation of the regulator describes a curve passing through points A, B, and C, and restricted to the unshaded areas.

It is evident that the equation of the regulator is essentially the equation of the valve in this case, and may be written as a relationship between ΔX_2 and ΔJ_2 which fulfills the above conditions. Any such relation will of necessity also have the following obvious property:

$$\text{At static head and level flow,} \qquad dX_2/dJ_2 \geqq 0. \tag{41}$$

$$\text{At the point } \Delta X_2 = \Delta J_2 = 0, \qquad dX_2/dJ_2 \leqq 0. \tag{42}$$

We are now ready to conduct a search for relations which, in increasing order of mathematical complexity, fit the conditions of the problem. They will be of the general form

$$\mathrm{f}(\Delta X_2, \Delta J_2) = 0, \tag{43}$$

where the function $\mathrm{f}(\Delta X_2, \Delta J_2)$ may be expressed as a polynomial in the variables ΔX_2 and ΔJ_2. Can $\mathrm{f}(\Delta X_2, \Delta J_2)$ be a polynomial of first degree? The answer is clearly no—a linear relation is excluded by the conditions, as is readily seen by inspection of the input diagram. Can $\mathrm{f}(\Delta X_2, \Delta J_2)$ be a polynomial of second degree? The answer to this is yes, i.e. a solution can be found for the coefficients in the quadratic expression

$$\mathrm{A}\Delta X_2^2 + \mathrm{B}\Delta X_2\Delta J_2 + \mathrm{C}\Delta J_2^2 + \mathrm{D}\Delta X_2 + \mathrm{E}\Delta J_2 + \mathrm{F} = 0 \tag{44}$$

which satisfies all the conditions, so that solutions involving polynomials of higher degree are also possible. It is shown in the Appendix that by requiring equation 44 to fit the conditions 38–42, four of the coefficients are determined, but B and C remain undetermined. Thus no unique second degree solution exists. But a further question arises: Can $\mathrm{f}(\Delta X_2, \Delta J_2)$ be a *reducible* polynomial of second degree? In other words, can any of the solutions to equation 44 be reduced to a product of two linear factors? Cases in which an expression of the form of 44 can be factorized are exceptional, and the resolution into factors is unique (7). It turns out, as shown in the Appendix, that $\mathrm{f}(\Delta X_2, \Delta J_2)$ cannot be a reducible polynomial of second degree. One more possibility deserves exploring, however, which stems from the fact that the zero on the right-hand side of equations 43 and 44 is merely a convenient constant. Let us define a new polynomial $\mathrm{g}(\Delta X_2, \Delta J_2)$ as follows:

$$\mathrm{g}(\Delta X_2, \Delta J_2) = \mathrm{f}(\Delta X_2, \Delta J_2) + \mathrm{Z} \tag{45}$$

where Z is an arbitrary constant. Then equation 43 becomes

$$\mathrm{g}(\Delta X_2, \Delta J_2) = \mathrm{Z}. \tag{46}$$

If $\mathrm{g}(\Delta X_2, \Delta J_2)$ is now required to be a reducible second degree polynomial, then there is indeed a unique solution for equation 46 which fits the conditions. *This solution is the inverse Hill equation, equation 32.* An outline of the proof is given in the Appendix.

Thus the equation of the regulator, which cannot be written in terms of a single linear expression, can be written in terms of a product of two linear expressions—but in just one way! This is the sense in which the Hill case is the simplest for this model. No further insight is gained by attempting to devise a specific mechanism for the valve: obviously both ΔX_2 and ΔJ_2 must be sensed and evaluated, for example by placing a spring behind the valve stem and vanes around the periphery of the valve head to cause it to rotate. The product of two linear combinations of the "signals" is to be constant, which can be arranged, presumably, by the cooperative action of two linear processes.

DISCUSSION

It is to be observed that both from a generalized thermodynamic argument and from a mechanistic argument based on a model we arrive at the identical equation for the regulator, or input. A remarkable aspect of the calculation for the model is that we do not need to postulate linearity of the energy converter, but obtain the input relation, the inverse Hill equation, just by considering a specific control system. This system, however, conforms to a description obtained from prior nonmechanistic arguments: the "program" of the valve is based entirely on the operational limits. On the other hand the output from a reverse electroosmosis cell regulated in this way will only obey the Hill equation (in this case a voltage-current relation) if the cell *is* a linear energy converter.

In the remainder of the discussion emphasis will be placed on mechanochemical energy conversion such as in muscle. The normalized inverse Hill equation (equation 35) has two adjustable parameters, unlike the normalized Hill equation (equation 29) which has only one, the degree of coupling. Equation 36 can be used to eliminate one of the constants of equation 35, but not both. Therefore, in plotting equation 35 and other derived relations, we need to select values for either ξ_2^l (the normalized affinity in unloaded contraction) or γ_2^s (the normalized reaction velocity in isometric contraction). For intuitive reasons ξ_2^l has been chosen as the adjustable parameter in addition to q. This parameter gives the relation between the affinities in an isometric and an unloaded contraction, although at high degrees of coupling it does *not* reflect the range over which the affinity varies. Actually nothing in the foregoing analysis precludes the possibility that ξ_2^l or γ_2^s may exceed unity. On physical grounds this is improbable, but for the sake of interest a value of ξ_2^l greater than unity is included. It should be borne in mind that in all plots of the equations we may interchange normalized forces and normalized flows by application of the symmetry principle mentioned earlier. The normalized input and output quantities may be related by a series of equations of which a typical one is

$$\gamma_2 = \frac{(1 - q^2)^2}{\xi_2^l\{(1 - \gamma_1)^{-1} - q^2\}} + \gamma_1, \tag{47}$$

a result derived in the same general way as equation 35. Equations such as 47 represent testable relations.

Some illustrative curves showing the relationships obtained are given in Figs. 3 and 4. In Fig. 3 the independent variable is γ_2, plotted against the dependent vari-

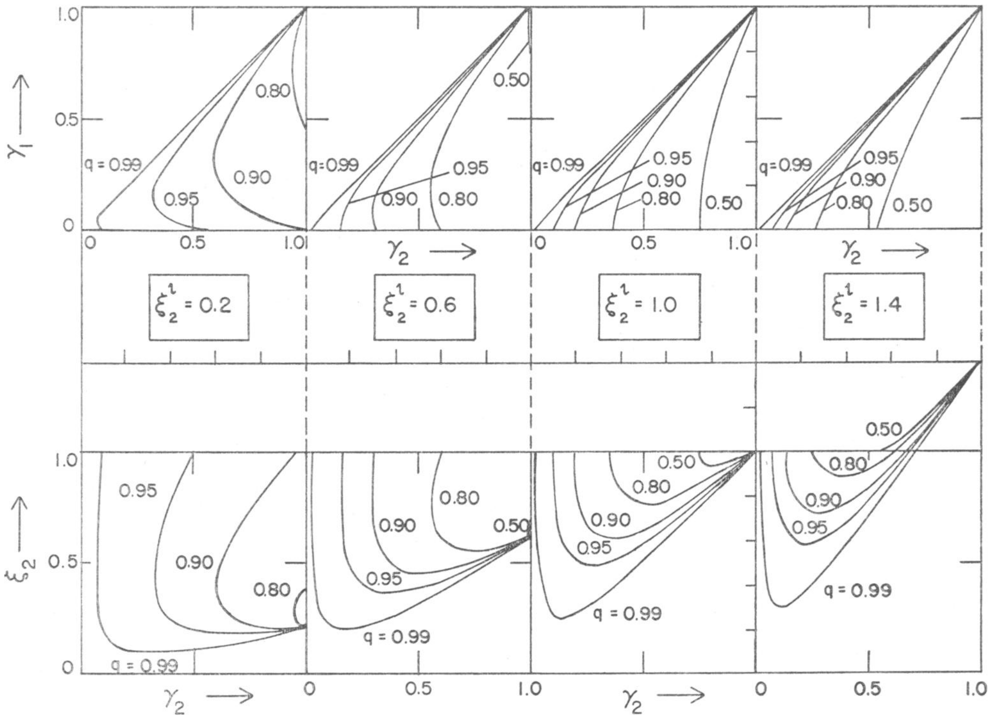

FIGURE 3 Normalized plots of contraction velocity (γ_1) and reaction affinity (ξ_2) vs. reaction velocity (γ_2) for several degrees of coupling q, at different values of the normalized reaction affinity in an unloaded contraction ($\xi_2{}^l$). The lower set of curves represents the "inverse" Hill equation.

ables γ_1 and ξ_2. In the latter case we have a series of straightforward "input diagrams," showing the behavior of the normalized inverse Hill equation directly. Each curve traces a path from static head (isometric contraction) to level flow (unloaded contraction) in a counterclockwise direction. Focusing attention on $q = 0.9$ and $\xi_2{}^l = 1.0$, i.e. assuming that the affinity of the driving reaction at level flow is not too different from its value at static head, we see that it passes through a minimum, dropping to 60% of its static head value when $\gamma_1 \approx 0.3$. Beyond this point γ_1, the contraction velocity, is very nearly proportional to γ_2, the reaction velocity. At $q = 0.9$ and $\xi_2{}^l = 0.6$ the general picture is not greatly changed, but now a barely perceptible minimum occurs in γ_2 as well. In Fig. 4 the independent variable is ξ_1, and the dependent variables are γ_2 and ξ_2. These curves trace the path from static head to level flow when read from right to left. Again choosing $q = 0.9$ it is seen that reaction velocity does not vary markedly with load at high loads, but increases rapidly with decreasing load at low loads, both at $\xi_2{}^l = 1.0$ and $\xi_2{}^l = 0.6$. The affinity passes through a much shallower minimum at $\xi_2{}^l = 0.6$ than at $\xi_2{}^l = 1.0$, as is also evident from Fig. 3.

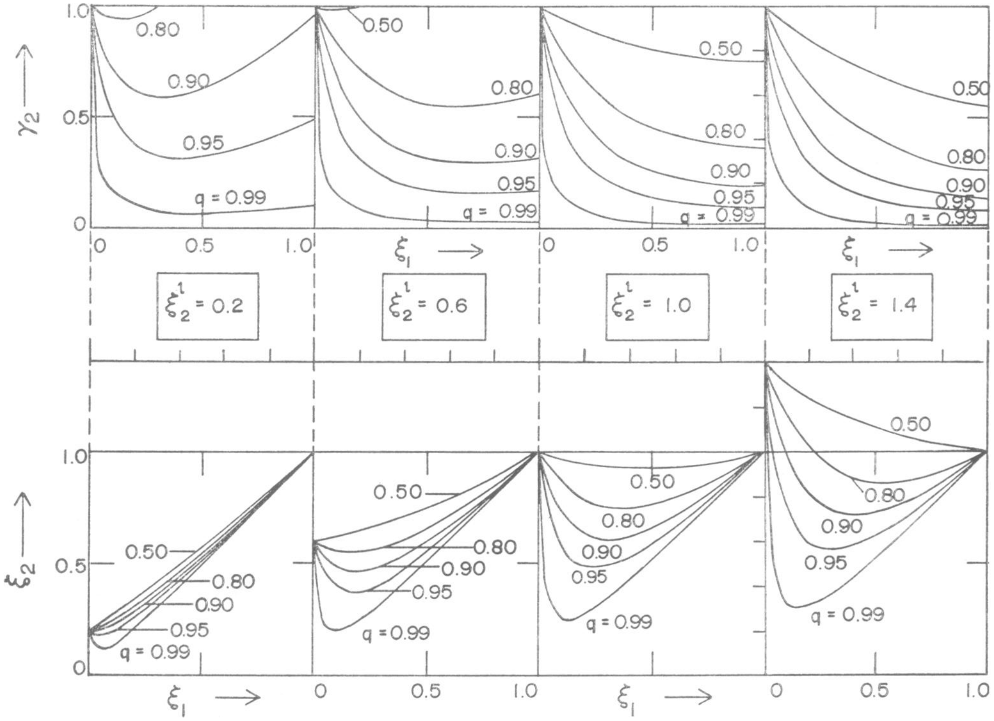

FIGURE 4 Normalized plots of reaction velocity (γ_2) and reaction affinity (ξ_2) vs. tension (ξ_1) for several degrees of coupling q, at different values of the normalized reaction affinity in an unloaded contraction (ξ_2^l).

The tendency for the ratio γ_2/γ_1 (reaction velocity/contraction velocity) to reach a constant value at high γ_1 in rather tightly coupled autonomic systems of this kind is illustrated more clearly in Fig. 5. The curves all refer to $q = 0.9$, and it is seen that even if ξ_2^l is as low as 0.6, the variation in γ_2/γ_1 when γ_1 exceeds 0.4 is less than 20%.

Teleologically speaking, the object of regulation seems to be, in the case of the Hill equation, to maintain power output as nearly maximal as possible over a considerable range of load resistance, with efficiency reasonably high. If so it can be shown that unless the coupling is virtually complete ξ_2^l should neither exceed unity nor be very small in comparison with unity. This has an important bearing on computed curves such as Figs. 3 and 4. When $\xi_2^l > 1$ a uniformly high output is generally confined to load resistances which are low compared with the value which maximizes efficiency, and when $\xi_2^l \ll 1$ a uniformly high output is similarly confined to high R_L.[6] One would not *expect* the driving force to be maximal in an unloaded

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[6] Introducing the reduced load resistance (1) $\rho_L = \xi_1/\gamma_1$, and denoting its value when efficiency is maximal by $\rho_L{}^0$, one finds that $\rho_L{}^0 = \xi_2^l/\sqrt{1 - q^2}$. The quantity $\rho_L{}^0$ is the ratio of the load resistance at maximum efficiency to that at maximum output for systems following the Hill equation. Maximum output is reached at a load resistance in the center of the range corresponding to uniformly high output power (see ref. 1, Fig. 6).

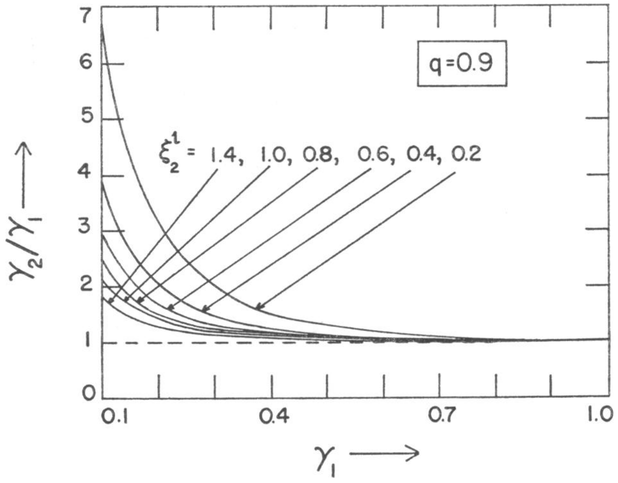

FIGURE 5 Normalized plot of the ratio of reaction velocity to contraction velocity (γ_2/γ_1) vs. contraction velocity (γ_1) for a series of values of the normalized reaction affinity in an unloaded contraction (ξ_2^l). The degree of coupling is 0.9.

contraction, or the reaction velocity to be maximal in an isometric contraction. In either of these cases the input would be much larger in one limiting state than in the other, particularly at higher degrees of coupling, as is readily seen by making use of "input-output" diagrams (1). For optimal regulation the input at static head should be commensurate with that at level flow (see the comment on symmetrical operational limits following equation A2 in the Appendix), which means that the relative increase in affinity in going from unloaded to isometric contractions should be commensurate with the relative decrease in reaction velocity. For $q = 0.9$ this would be approximately true for example when $\xi_2^l = 0.6$, the maximum variation in the affinity then being about 2:1 and that of the reaction velocity being about 3:1.

CONCLUSIONS

Linear phenomenological behavior is not necessarily incompatible with nonlinear kinetics.

The output equation for the canonically simplest class of self-regulated linear energy converters (the Hill equation) may be transformed into an input equation through the phenomenological relations of the converter. The assumption of Onsager symmetry is not necessary for this calculation. The constants appearing in the "inverse" Hill equation are the operational limits on the input to the converter (which contain, implicitly, its degree of coupling).

The inverse Hill equation may be derived independently by considering a model regulator mechanism, designed to depend on the operational limits of the converter. In terms of this physical model it is clear that the Hill behavior is the simplest case, in the sense that the regulatory action depends on linear combinations of "signals."

The two forms of the Hill equation give rise to a series of interesting and testable relations between input and output. In particular, it is seen that in a rather tightly coupled autonomic mechanochemical energy converter (such as the muscle may be) the ratio of reaction velocity to contraction velocity tends to reach a constant value with increasing velocity of contraction. For optimal regulation of output power the relative increase in reaction affinity in going from unloaded to isometric contractions should be commensurate with the relative decrease in reaction velocity.

APPENDIX

Equation 44 loses no generality by setting A = 1, and from condition 40 F = 0. Applying the boundary conditions (38) we obtain

$$f(\Delta X_2, \Delta J_2) \equiv \Delta X_2^2 + \mathrm{B}\Delta X_2 \Delta J_2 + \mathrm{C}\Delta J_2^2 - \Delta X_2^s \Delta X_2 - \mathrm{C}\Delta J_2^l \Delta J_2 = 0. \quad \text{(A1)}$$

Consider the case of "symmetrical operational limits" defined by

$$J_2^s X_2^s = J_2^l X_2^l. \quad \text{(A2)}$$

Thus input power at static head is identical to input power at level flow. (This is the condition for maximum output power to coincide with maximum efficiency in a system following the Hill equation.) The normalized input diagram for this case (we are considering limits only) is symmetrical about the diagonal passing through the origin. Referring to the input diagram in Fig. 2, and supposing it to be normalized, then if the operational limits are symmetrical we would expect the slope of the input locus at the point $\Delta X_2 = \Delta J_2 = 0$ to be given by

$$d\xi_2/d\gamma_2 = -1, \quad \text{(A3)}$$

since there is no a priori reason why the normalized input locus itself should not be symmetrical in such a diagram. Differentiating equation A1 and introducing equation 40 we obtain

$$dX_2/dJ_2 = -\mathrm{C}(\Delta J_2^l/\Delta X_2^s) \qquad (X_2 = X_2^l,\ J_2 = J_2^s) \quad \text{(A4)}$$

and hence, using equation A3 we find *for this case*

$$\mathrm{C} = (X_2^s/J_2^l)^2 = (X_2^l/J_2^s)^2 = (X_2^s X_2^l/J_2^s J_2^l). \quad \text{(A5)}$$

These three expressions are identical when the operational limits are symmetrical, but not otherwise. Consequently C would be expected to equal one of them in the general case, but on grounds of symmetry it is not possible to say which. Nor, on grounds of symmetry, is it possible to determine B.

It is proved in textbooks of algebra (7) that the necessary and sufficient condition for the quadratic function

$$\mathrm{S} \equiv \mathrm{a}x^2 + 2\mathrm{h}xy + \mathrm{b}y^2 + 2\mathrm{g}x + 2\mathrm{f}y + \mathrm{c} \quad \text{(A6)}$$

to be expressible as the product of two linear factors is that its discriminant should vanish, i.e.

$$\begin{vmatrix} \mathrm{a} & \mathrm{h} & \mathrm{g} \\ \mathrm{h} & \mathrm{b} & \mathrm{f} \\ \mathrm{g} & \mathrm{f} & \mathrm{c} \end{vmatrix} = 0. \quad \text{(A7)}$$

If the two linear factors have real coefficients, all three principal minors in the discriminant must be negative. Now, it may readily be shown that if ($y = 0, x \neq 0$) and ($x = 0, y \neq 0$) are real points within the field of S, then the negatives of the three principal minors must be perfect squares. This is the essential point on which the demonstration below hinges. Comparing equations A1 and A6, we have

$$\begin{aligned} \mathrm{a} &= 1 & \mathrm{f} &= -\mathrm{C}\Delta J_2^l/2 \\ \mathrm{b} &= \mathrm{C} & \mathrm{g} &= -\Delta X_2^s/2 \\ \mathrm{c} &= 0 & \mathrm{h} &= \mathrm{B}/2. \end{aligned} \tag{A8}$$

Introducing these quantities into equation A7 and expanding, we obtain a relation between B and C:

$$\mathrm{B} = \mathrm{C}(\Delta J_2^l/\Delta X_2^s) + (\Delta X_2^s/\Delta J_2^l). \tag{A9}$$

Differentiating equation A1 and taking values for the derivative at static head and level flow, we find

$$\begin{aligned} dX_2/dJ_2 &= \mathrm{C}(\Delta J_2^l/\Delta X_2^s) - \mathrm{B} & &\text{(static head)} \\ dX_2/dJ_2 &= \mathrm{C}/\{(\Delta X_2^s/\Delta J_2^l) - \mathrm{B}\} & &\text{(level flow).} \end{aligned} \tag{A10}$$

Combining equations A9 and A10,

$$dX_2/dJ_2 = -(\Delta X_2^s/\Delta J_2^l) \qquad \text{(static head and level flow)} \tag{A11}$$

and consequently this quantity is negative, since ΔX_2^s and ΔJ_2^l are both positive in the model. Therefore equation A11 conflicts with condition 41, and no reducible polynomial of the form appearing in equation A1 satisfies all our conditions.

Consider instead

$$\begin{aligned} \mathrm{g}(\Delta X_2, \Delta J_2) \equiv \Delta X_2^2 + \mathrm{B}\Delta X_2 \Delta J_2 + \mathrm{C}\Delta J_2^2 - \Delta X_2^s \Delta X_2 \\ - \mathrm{C}\Delta J_2^l \Delta J_2 + \mathrm{Z} = \mathrm{Z}. \end{aligned} \tag{A12}$$

Equations A8 remain valid, with the exception that

$$\mathrm{c} = \mathrm{Z}. \tag{A13}$$

The negative values of the three principal minors of $\mathrm{g}(\Delta X_2, \Delta J_2)$ are:

$$(\tfrac{1}{4})\{\mathrm{B}^2 - 4\mathrm{C}\}, \qquad (\tfrac{1}{4})\{(\Delta X_2^s)^2 - 4\mathrm{Z}\}, \qquad (\mathrm{C}^2/4)\{(\Delta J_2^l)^2 - 4(\mathrm{Z}/\mathrm{C})\}.$$

By expanding the difference terms in the second and third expressions above, and remembering that the limiting values of X_2 and J_2 may all be arbitrarily chosen, it is seen that the only possible values of Z and C which ensure that the two expressions will be perfect squares are given by

$$\begin{aligned} \mathrm{Z} &= -X_2^s X_2^l \\ \mathrm{C} &= X_2^s X_2^l / J_2^s J_2^l. \end{aligned} \tag{A14}$$

This value for C coincides with one of the values found from symmetry considerations. Introducing these quantities into equation A7 with the aid of equations A8 and A13, we may solve for B, with the result that either

$$B = (X_2^s/J_2^l) + (X_2^l/J_2^s) \tag{A15}$$

or

$$B = -\{(X_2^s/J_2^s) + (X_2^l/J_2^l)\}. \tag{A16}$$

Both of these values convert ($B^2 - 4C$) into a perfect square. If we make use of equation A15 in evaluating equations A10, we find

$$\begin{aligned} dX_2/dJ_2 &= \{(X_2^l)^2J_2^l - (X_2^s)^2J_2^s\}/J_2^sJ_2^l\Delta X_2^s \qquad \text{(static head)} \\ dX_2/dJ_2 &= X_2^sX_2^l\Delta J_2^l/\{(J_2^s)^2X_2^s - (J_2^l)^2X_2^l\} \qquad \text{(level flow).} \end{aligned} \tag{A17}$$

The signs of the derivatives depend on the numerator of the first and the denominator of the second. It is readily established that these two quantities cannot *simultaneously* be positive, and therefore equations A17 and A15 conflict with condition 41. We are left with equation A16, which satisfies all the conditions. Equation A12 then reduces to equation 32.

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