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H.C. Mel and P.S. Geissler

October 1986

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GLOBAL THERMODYNAMIC POTENTIAL FUNCTION FOR
NONEQUILIBRIUM, OPEN CHEMICAL REACTION SYSTEMS

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October 1986

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I. INTRODUCTION

Complex, dynamical systems can be investigated at various hierarchical levels of description. One of these entails focussing on the details of the individual interactions--the differential equations comprising the "parts" of the system. Another is a global view emphasizing "system" properties--the endpoints, their distributions and stabilities--and variational principles guiding the evolution of the system towards the endpoints. This latter is the global-thermodynamic-potential approach to the analysis and characterization of the system.

The primordial thermodynamic potential function is, of course, the total entropy (i.e. the entropy of a system plus that of its surroundings). Its thermodynamic potential character is expressed as a variational principle, in terms of its orderly, monotonic increase to its "evolutionary extremum" (maximum), achieved for endpoints of thermodynamic equilibrium--the second law of thermodynamics. In practice it is usually more convenient to work with thermodynamic functions of the system alone, such as the Gibbs free energy, which under particular sets of circumstances become surrogates for the total entropy.

Valuable as the total entropy and its surrogates are, they cannot serve as thermodynamic potentials for processes which evolve to endpoints even slightly displaced from equilibrium. A successful extension of this kind of global variational principle was made for the near-to-equilibrium domain or so-called "linear domain" of non-equilibrium steady state systems, in the form of the system's entropy

production per unit time, $\frac{d_i S}{dt} = \mathcal{P}$, (more simply the "entropy production"), and Prigogine's "minimum entropy production theorem (1-3). As is well known, this function evolves monotonically both in time and in configuration space (e.g. activity space) for chemically reacting species, from initial values determined by arbitrary initial conditions, reaching its extremum-minimum value at the final stationary state.

Given the inherently nonlinear or far-from-equilibrium nature of many complex dynamical systems, especially biological systems, different approaches have been taken in attempts to generalize the variational-principle concept to embrace the realistic non-linear kinetics of such systems. One approach, taken by Prigogine and co-workers (4-7), has been to abandon the search for a global thermodynamic potential function in favor of "local potentials" based on the local stability criterion: $\sum_i J_i \cdot \delta X_i \geq 0$. This approach does not generally lead to thermodynamic (state) functions, and its utility is, hence, limited to the analysis of local kinetic behavior.

Finding this "local potential" constituted a theoretical advance; it has not, however, obviated or lessened the value of thermodynamic potentials possessing global or state-function character, if such functions could be found. Their existence may be suspected from the responses and dynamics of many complex systems. For biological systems, in particular, despite their multifaceted nature, (and often far-from-equilibrium endpoints), in the manifestation of their many homeostatically-controlled metabolic and other subsystems, they

typically behave as if they are describable (if not actually guided) by such an evolutionary/variational principle. Such "self-restoration" to an other-than-equilibrium endpoint has sometimes been referred to as an "extended Le Chatelier-Braun Principle" (1,p.58; 4,p.64).

A contribution towards a more general, global thermodynamic potential theory for open systems of chemical reactions, constrained far away from equilibrium, led to the "affinity squared minimum function", or $\mathcal{M}$ function, by nature a "kinetically-weighted system-free-energy" quantity (8). This function was shown quite generally to have its extremum--minimum values in the steady state, irrespective of how far away from equilibrium a system was constrained to operate. Furthermore, for a variety of kinds of "kinetically connected" reaction networks, including, as well, straight-line, autocatalytic and disproportionation reactions, a well-behaved time-evolution character could be demonstrated, i.e. the property of $\frac{d\mathcal{M}}{dt} \leq 0$, where the equality applied only to the stationary state. All but one of the kinetic systems which were previously studied using the $\mathcal{M}$ function possessed only a single, stable stationary state. A summary of some of the essential features of the $\mathcal{M}$ function is included as Appendix A.

In subsequently considering a "more demanding" test of the $\mathcal{M}$ function, analysis was made of a system possessing 3 steady states--2 stable plus one unstable (9). Though by the nature of the construction of the $\mathcal{M}$ function, the variational property of $\mathcal{M}_{\text{steady state}} = \mathcal{M}_{\text{minimum}}$ remained valid for all three of the stationary states, and furthermore, for most of the full domain of "concentration space" the property

$\frac{dM}{dt} \leq 0$ held as well, in a few small regions this latter property became no longer valid. That is, for short times during the system's evolution, the value of M increased, prior to decreasing once again to its final minimum value.*

It was during the course of analyzing the nature of this "failure" of M to retain everywhere all of its global thermodynamic potential qualities for this multi-steady state system, and in considering means of circumventing this limitation, that we arrived at the present ϕ function. While still retaining the desired variational properties, the function ϕ does not suffer this same limitation with respect to the sign of its time derivative. Moreover, its thermodynamic potential (state function) character is seen to be of considerable interest and generality because it enables thermodynamic analysis of a system's global features and characteristics rather than merely its local stability properties. As will be seen, ϕ also is mathematically and conceptually closely related to M , hence as well to P and to S_{total} -- functions for which the elements are simple and well known, and with which there is much "physical" experience.#

* This statement refers to behavior in regions of the two stable stationary states. In the reference frame of the unstable steady state, comparable occasional violations were found, i.e. where $\frac{dM}{dt} > 0$.

Another approach to generalized questions of stability and evolutionary tendency has been presented in a body of work by Biot (10). Founded in mechanics as an extension of d'Alembert's principle, it employs the concepts of virtual work and virtual and generalized dissipation, and also extends their application to chemical thermodynamic systems. Though formally familiar, the equations are developed in terms of functions somewhat removed from the standard thermodynamic and kinetic quantities underlying S , P , M , and ϕ , (and even involve something of a redefinition of chemical potential, entropy, etc.). It is thus not a simple matter to relate Biot's results to those of more traditional irreversible thermodynamics.

II. GENERAL PROPERTIES OF THE ϕ FUNCTION

A. DEFINING RELATIONS

For any open, chemical reaction system, there is a function $\phi(x,y,...)$ of the concentration* variables $(x,y,...)$ defined by:

$$\frac{d\phi}{dt} = - (M - M^{ss}); \quad (\text{Eqn 1})$$

and

$$\phi = - \int (M - M^{ss}) dt. \quad (\text{Eqn 2})$$

In the following sections, several properties of $\phi(x,y,...)$ are examined to evaluate ϕ as a thermodynamic potential function, for open chemical reaction systems operating far-from-equilibrium, i.e., systems exhibiting "non-linear" phenomenological laws.

For all "molecularly acceptable" chemical reaction networks, ϕ is shown to have the following properties:

1. ϕ is a global state function;
2. $(\phi - \phi^{ss})$ is positive-definite;
3. ϕ exhibits extrema at stationary states;
4. for stable stationary states, the extrema are minima;
5. for non-stable stationary states, the extrema have a cusp-like character.
6. $\frac{d\phi}{dt}$ is negative definite.

Following the general demonstration of these properties, ϕ is examined in some detail for two example reaction systems, including one exhibiting multistable and unstable stationary state behavior.

* For purposes of this paper we take all concentrations equal to their respective activities.

In this manner, both from the six general properties, and as illustrated in three specific systems, ϕ , as defined by Equations (1) and (2), is seen to be a global thermodynamic potential function for the evolution of a system towards far-from-equilibrium as well as near-to-equilibrium steady states.

B. STATE FUNCTION PROPERTY

For chemical reaction systems at constant temperature and pressure in a homogeneous medium, the set of concentration variables $(x, y, \dots)$ provides a complete specification of the state of the system. These variables apply to any reaction network described by its corresponding set of chemical kinetic equations. These equations describe the system's evolution in time, starting from any arbitrary initial condition $(x, y, \dots)$ at $t = 0$. They allow one to calculate the subsequent values of the concentration variables as they change due to (i) chemical reactions within the system, and (ii) flows in and out of the system. The kinetic equations are first-order in time and thus reflect the time-forward, irreversible character of nonequilibrium systems.

For any chemical reaction network the set of chemical kinetic equations describing the system's evolution will have the form:

$$\frac{dx}{dt} = f(x, y, \dots) \quad (\text{Eqn 3})$$

$$\frac{dy}{dt} = g(x, y, \dots) \quad (\text{Eqn 4})$$

where f and g are single valued functions of the concentrations.

The set of stationary states of the system, $(x^{ss}, y^{ss}, \dots)$, also referred to mathematically as critical points of the system, are given by the algebraic equations:

$$f(x^{ss}, y^{ss}, \dots) = 0 \quad (\text{Eqn 5})$$

$$g(x^{ss}, y^{ss}, \dots) = 0 \quad (\text{Eqn 6})$$

The stationary states represent the end points of the system's evolution in time and the system's ultimate locus in $(x, y, \dots)$ space (in the limit as time goes to infinity).

Thus, once the initial conditions are specified for a system, its evolution or "trajectory" in $(x, y, \dots)$ space is completely specified. Because of the single-valued and first order character of the kinetic equations, each state $(x, y, \dots)$ has associated with it only one unique value of $\frac{dx}{dt}$ and $\frac{dy}{dt}$. Therefore, except for the stationary states, there can be no "branch points" or intersecting trajectories in $(x, y, \dots)$ space. Moreover, the entire $(x, y, \dots)$ space is "dense with trajectories"--every point lies on a trajectory, each trajectory ends at a single stationary state, and all trajectories converge to one or another stationary state of the system.

The value of the function $\phi(x, y, \dots)$ at any point is found by evaluating the integral in Equation 2:

$$\phi(x, y, \dots) = \int_0^{\infty} (M - M^{ss}) dt + \phi(x^{ss}, y^{ss}, \dots), \quad (\text{Eqn 7})$$

where the path of integration is the trajectory connecting the point $(x,y,...)$ with the steady state point as determined by the kinetic equations. This procedure leads to a unique value of ϕ for every point $(x,y,...)$, independent of the previous history of the system. The function $\phi(x,y,...)$ is therefore a global state function, a "thermodynamic function", a function having a perfect differential.

C. POSITIVE-DEFINITE CHARACTER OF ϕ

From the defining relation, Equation 2, we see that:

$$\phi(x^{ss}, y^{ss}, ...) - \phi(x, y, ...) = - \int_0^{\infty} (M - M^{ss}) dt. \quad (\text{Eqn 8})$$

The integration, here, is taken in the "time-forward" direction, $dt > 0$, along the irreversible path of the system's evolution, from any arbitrary initial condition at $(x,y,...)$ along the trajectory in $(x,y,...)$ space to its corresponding final steady state. The integrand, $(M - M^{ss})$, is always positive-definite (8), so the right hand side of Equation 8, above, must be negative-definite for any position $(x,y,...)$ away from a stationary state.

It therefore follows that:

$$\phi(x, y, ...) - \phi(x^{ss}, y^{ss}, ...) \geq 0, \quad (\text{Eqn 9})$$

where the equality holds only at the stationary state.

D. TOPOLOGICAL FEATURES OF THE ϕ SURFACE

This section is concerned with the topology of the ϕ surface associated with chemical reaction systems. Such systems may have more than one stationary state, both stable and unstable in character. Though a more detailed treatment of both stable and unstable steady states is presented later, it is useful here to categorize, by preliminary definition, these two kinds of states according to the system's response to perturbations away from the steady state:

Stable stationary state: when the system is slightly perturbed away, it always returns;

Nonstable stationary state: when the system is slightly perturbed away it does not always return.

The demonstration that $\phi(x,y)$ exhibits a topological extremum at each of the (stable or unstable) stationary states of any open chemical reaction system is founded upon the positive-definite character of the $\mathcal{M}$ function and upon the restrictions inherent in the form of all kinetic equations, when homogeneous-phase reactions are correctly written in their most elementary molecular form. These restrictions on the kinetics will first be developed here. We then examine the $\phi(x,y)$ topology and demonstrate the extremum properties in the vicinity of stable stationary states, and follow this by extending the treatment to nonstable stationary states. We are further able to show that the extrema are true minima for stable stationary states, whereas the extrema for nonstable stationary states are cusp-like in character. Finally, we end this section with a uniqueness theorem, demonstrating that

there is a one-to-one correspondence between extrema of the $\phi(x,y)$ surface and stationary states of the chemical reaction system, and that true minima of $\phi(x,y)$ are found only at the stable stationary states.

1. Elementary Chemical Reaction Kinetics

Systems of chemical reactions, no matter how complex overall, can ultimately be "decomposed" into sequences of individual steps involving, at most, collisions between two reactants. (This is because under any reasonable biological conditions, simultaneous 3-body collisions of chemically interacting solutes can be considered sufficiently improbable so as to be ignored.) Thus, at the elementary molecular level, reaction steps can only be monomolecular--dependent upon the concentration of only a single species (example: a simple chemical isomerization), or bimolecular--dependent upon the concentrations of two reacting species. In addition, considerations of "microscopic reversibility" require that both forward and reverse pathways exist for any actual reaction, even if one of the unidirectional rates is very small. Thus, the kinetics of any complex reaction network can be written in the form of a sequence of first-order and/or second-order rate equations. Furthermore, from the standpoint of any given reacting species, x , the kinetic equation for each reaction step, i , must be of the form:

$$\left(\frac{dx}{dt}\right)_i = a_i x^2 + b_i x + c_i, \quad (\text{Eqn } 10)$$

where one of the coefficients must be zero. This restricted form of Equation 10 follows directly from the monomolecular, bimolecular, reverse-pathway restrictions/limitations/conditions listed above, as readily seen by examining the complete set of "permitted" (i.e. mono- or bi-molecular) elementary reactions for x in the following Table.

Table 1. ELEMENTARY REACTIONS

<u>Reaction Type</u>		Equation of the Form:			
		$\frac{dx}{dt} =$	$a_i x^2$	$+ b_i x$	$+ c_i$
1.	$x \xrightleftharpoons[k']{k} y$	$\frac{dx}{dt} =$	0	- kx	+ (k'y)
2.	$x \xrightleftharpoons[k']{k} y + y$	$\frac{dx}{dt} =$	0	- kx	+ (k'y ²)
3.	$x \xrightleftharpoons[k']{k} y + z$	$\frac{dx}{dt} =$	0	- kx	+ (k'y z)
4.	$x + y \xrightleftharpoons[k']{k} y + z$	$\frac{dx}{dt} =$	0	- (ky)x	+ (k'y z)
5.	$x + x \xrightleftharpoons[k']{k} y$	$\frac{dx}{dt} =$	-kx ²	+ 0	+ (k'y)
6.	$x + x \xrightleftharpoons[k']{k} y + y$	$\frac{dx}{dt} =$	-kx ²	+ 0	+ (k'y ²)

Table 1 (continued)

<u>Reaction Type</u>	Equation of the Form:
	$\frac{dx}{dt} = a_i x^2 + b_i x + c_i$
7. $x + x \xrightleftharpoons[k']{} y + z$	$\frac{dx}{dt} = -kx^2 + 0 + (k'yz)$
8. $x + y \xrightleftharpoons[k']{} y + y$	$\frac{dx}{dt} = 0 - (ky)x + \underline{(k'y^2)}$
9. $x + y \xrightleftharpoons[k']{} z$	$\frac{dx}{dt} = 0 - (ky)x + (k'z)$
10. $x + y \xrightleftharpoons[k']{} x + x$	$\frac{dx}{dt} = -k'x^2 + (ky)x + 0$
11. $x + y \xrightleftharpoons[k']{} y + y$	$\frac{dx}{dt} = 0 - (ky)x + (k'y^2)$
12. $x + y \xrightleftharpoons[k']{} z + z$	$\frac{dx}{dt} = 0 - (ky)x + (k'z^2)$
13. $x + y \xrightleftharpoons[k']{} y + z$	$\frac{dx}{dt} = 0 - (ky)x + (k'yz)$
14. $x + y \xrightleftharpoons[k']{} z + u$	$\frac{dx}{dt} = 0 - (ky)x + (k'u)$

Evidently the overall expression for $\frac{dx}{dt}$ for any reaction network (the sum of any number of such individual reaction steps) must necessarily retain the general quadratic form of Equation 10. That is,

$$\frac{dx}{dt} = \sum_i \left(\frac{dx}{dt}\right)_i = ax^2 + bx + c, \quad (\text{Eqn 11})$$

where b and c (but not a) may be functions of the concentrations of any species in the reaction system, other than x .

It will be noted from Table 1, above, that the coefficient a_i of Equation 10 is never positive: whenever x combines with another x in an elementary reaction step, it necessarily results in a depletion of x from the system. Likewise, the coefficient c_i (Equation 10) is never negative: to affect the concentration of x , by a reaction in which x is not a reactant, x must be a product of the reaction. Furthermore, all of the equations contain just two of the three terms from the right-hand side of Equation 10.

In summary,

$$\left. \begin{array}{l} a_i \leq 0 \\ c_i \geq 0 \end{array} \right\} \quad \text{for all } i. \quad (\text{Eqn 12})$$

a. Second Order Case Restrictions. When the kinetic equation (Equation 11) is second order in x , it may also be written:

$$\left(\frac{dx}{dt}\right)_i = a (x - x_1^{ss}) (x - x_2^{ss}), \quad (\text{Eqn 13})$$

where

$$x_1^{ss} = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (\text{Eqn 14})$$

and

$$x_2^{ss} = \frac{-b - \sqrt{b^2 - 4ac}}{2a} \quad (\text{Eqn 15})$$

When c is nonzero (hence positive), and given that, $a < 0$, we see that:

$$b^2 - 4ac > 0, \text{ and } > b. \quad (\text{Eqn 16})$$

These conditions require both that the roots be unequal, and that x_2^{ss} be positive (physically acceptable) and x_1^{ss} negative (physically unacceptable). Furthermore, we see from Equation 11 that:

$$\left[\frac{\partial}{\partial x} \left(\frac{dx}{dt} \right) \right]_y = 2ax + b. \quad (\text{Eqn 17})$$

Evaluating the expression at the stationary state, x_2^{ss} :

$$\left[\frac{\partial}{\partial x} \left(\frac{dx}{dt} \right) \right]_y^{ss} = 2a \left[\frac{-b - \sqrt{b^2 - 4ac}}{2a} \right] + b \quad (\text{Eqn 18})$$

$$= -\sqrt{b^2 - 4ac}. \quad (\text{Eqn 19})$$

Since $a < 0$ and $c > 0$, we see that:

$$b^2 - 4ac > 0, \quad (\text{Eqn 20})$$

and that therefore

$$\left[\frac{\partial}{\partial x} \left(\frac{dx}{dt} \right) \right]_y^{ss} = -\sqrt{b^2 - 4ac} \neq 0. \quad (\text{Eqn 21})$$

For the specific case of $c = 0$ (reaction 10 in Table 1), which requires $b > 0$ (note: the requirement for the existence of both a forward and back reaction precludes having both $b = 0$ and $c = 0$), x_1^{ss} of Equation 14 equals 0. Therefore, at x_1^{ss} , Equation 21 holds. In addition, from Equation 15, $x_2^{ss} = -b/a$. From Equation 19 it is evident that Equation 21 continues to be valid.

b. First Order Case Restrictions. When the kinetic equation, Equation 11, is merely first order in x , it may also be written:

$$\left(\frac{dx}{dt}\right)_y = b(x - x^{ss}) \quad (\text{Eqn 22})$$

where

$$x^{ss} = -\frac{c}{b}. \quad (\text{Eqn 23})$$

Furthermore, we see from Equation 22 that:

$$\left[\frac{\partial}{\partial x}\left(\frac{dx}{dt}\right)\right]_y^{ss} = b. \quad (\text{Eqn 24})$$

Since b is never zero (and in fact from Equation 23 must be negative) for reactions that are first order in x (reactions 1, 2, 3, 4, 8, 9, 11, 12, 13, 14 of Table 1), it follows that Equation 21 holds for all first order reactions as well. It has thus been shown to be valid for the set of all acceptable reactions (Table 1).

2. Extremum Property: Stable Stationary States

The restrictions to the set of "permitted" kinetics have important consequences for the thermodynamic functions that describe the steady state behavior and the approach to the steady state. These properties of the set of kinetic equations make it possible to demonstrate the

extrema of $\phi(x,y)$ in any reaction system through their effect on the various partial derivatives of ϕ evaluated at stationary states.

There are two ways of evaluating such partial derivatives. In both we start by perturbing the system away from the stationary state in the x direction by an infinitesimal displacement, dx . The change of ϕ is thus simply expressed as:

$$d\phi = \left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss} dx \quad . \quad (\text{Eqn 25})$$

The system is then allowed to relax after such a displacement, as required by stability, along a single trajectory that leads back to the stationary state. From Equation 25, the associated rate of change of ϕ will be:

$$\frac{d\phi}{dt} = \left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss} \frac{dx}{dt} \quad . \quad (\text{Eqn 26})$$

The expression $\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss}$ is evaluated directly from Equation 26, then using the defining relation, Equation 1, and noting explicitly that the trajectory is at constant y :

$$\begin{aligned} \left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss} &= \text{Limit}_{x \rightarrow x^{ss}} \left\{ \left(\frac{d\phi}{dx} \right) \right\} \text{ along a trajectory with } y = \text{constant}; \\ &= \text{Limit}_{x \rightarrow x^{ss}} \left\{ \frac{\left(\frac{d\phi}{dt} \right)}{\left(\frac{dx}{dt} \right)} \right\} \\ &= \text{Limit}_{x \rightarrow x^{ss}} \left\{ \frac{-(M - M^{ss})}{\left(\frac{dx}{dt} \right)} \right\} \end{aligned} \quad (\text{Eqn 27})$$

From this point we can evaluate $\left[\left(\frac{\partial \phi}{\partial x}\right)_y\right]^{ss}$ in two independent ways.

a. Method A - l'Hospital's Rule. We proceed directly, using l'Hospital's rule, applicable to the evaluation of such a limit where both the numerator and denominator are identically zero at the stationary state. The extremum properties of $(M - M^{ss})$ at the stationary states of the system (8) require that:

$$\lim_{x \rightarrow x^{ss}} \left\{ \frac{\partial}{\partial x} (M - M^{ss})_y \right\} = 0 \quad (\text{Eqn 28})$$

along the trajectory $y = y^{ss}$ in the neighborhood of the stationary state. We have already seen from Equation 21 that:

$$\lim_{x \rightarrow x^{ss}} \left\{ \frac{\partial}{\partial x} \left(\frac{dx}{dt} \right)_y \right\} \neq 0 \quad (\text{Eqn 29})$$

for all reactions in Table 1.

Thus, from Equation 27 and invoking l'Hospital's Rule, we find that:

$$\left[\left(\frac{\partial \phi}{\partial x}\right)_y\right]^{ss} = \lim_{x \rightarrow x^{ss}} \left\{ \frac{\frac{\partial}{\partial x} (M - M^{ss})_y}{\frac{\partial}{\partial x} \left(\frac{dx}{dt} \right)_y} \right\} \quad (\text{Eqn 30})$$

$$= \frac{\text{zero}}{\text{nonzero}} = 0. \quad (\text{Eqn 31})$$

The other partial derivatives of ϕ may be similarly evaluated at the stationary state, and by symmetry they must also vanish. Thus, $\phi(x, y)$ exhibits an extremum at a stable stationary state.

b. Method B - The "Zero Over Zero" Gambit. In this method we evaluate the expression by indirect argument, without invoking L'Hospital's rule. We start by noting some fundamental mathematical properties of a simple ratio. Any expression of the form $0/a$ must equal zero unless $a = 0$. Conversely, if such an expression does not equal zero, " a " necessarily must equal zero.

For reasons which will subsequently become obvious, our $0/a$ "test ratio" is taken in the form:

$$\frac{\left[\left(\frac{\partial M}{\partial x} \right)_y \right]^{ss}}{\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss}}, \quad (\text{Eqn 32})$$

where the numerator is necessarily zero, in view of the proven extremum properties of M in the steady state (8). In this context $\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss}$ would be zero if and only if:

$$\frac{\left[\left(\frac{\partial M}{\partial x} \right)_y \right]^{ss}}{\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss}} \neq 0. \quad (\text{Eqn 33})$$

Following our argument, we demonstrate the extremum property, $\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss} = 0$, by showing that the test ratio, Equation 32, is nonzero.

We now proceed to evaluate this ratio by first expressing the extremum property of M in its equivalent form as a limit:

$$\left[\left(\frac{\partial M}{\partial x} \right)_y \right]^{ss} = \lim_{x \rightarrow x^{ss}} \left\{ \frac{(M - M^{ss})}{(x - x^{ss})} \right\} = 0 . \quad (\text{Eqn 34})$$

We now consider movement along the particular trajectory $y = y^{ss}$ in the neighborhood of the steady state. Replacing the numerator of Equation 33 by its equivalent from Equation 34 and expressing the denominator as in Equation 27, our test ratio becomes:

$$\frac{\left[\left(\frac{\partial M}{\partial x} \right)_y \right]^{ss}}{\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss}} = \frac{\lim_{x \rightarrow x^{ss}} \left\{ \frac{(M - M^{ss})}{x - x^{ss}} \right\}}{\lim_{x \rightarrow x^{ss}} \left\{ \frac{\left(\frac{d\phi}{dt} \right)}{\left(\frac{dx}{dt} \right)} \right\}} . \quad (\text{Eqn 35})$$

By the cancellation afforded by the defining relation, Equation 1, the right hand side of Equation 35 becomes:

$$= \lim_{x \rightarrow x^{ss}} \left\{ \frac{\left(\frac{dx}{dt} \right)}{-(x - x^{ss})} \right\} . \quad (\text{Eqn 36})$$

This expression is most clearly evaluated by considering, as before, the two separate cases.

(i) Quadratic Case. We first substitute into the numerator of Equation 36 the general kinetic equation in the form of Equation 13. We then evaluate this limit for the single, physically acceptable root, x_2^{ss} . Expression 36 thus becomes:

$$= \lim_{x \rightarrow x_2^{ss}} \left\{ \frac{a(x - x_1^{ss})(x - x_2^{ss})}{-(x - x_2^{ss})} \right\} \quad (\text{Eqn 37})$$

$$= \lim_{x \rightarrow x_2^{ss}} \left\{ -a(x - x_1^{ss}) \right\} \quad (\text{Eqn 38})$$

$$= -a(x_2^{ss} - x_1^{ss}) > 0. \quad (\text{Eqn 39})$$

The inequality holds because of the intrinsic signs of a , x_1^{ss} , and x_2^{ss} as discussed above. Therefore, from Equation 33:

$$\left[\left(\frac{\partial \phi}{\partial x} \right)_y \right]^{ss} = 0. \quad (\text{Eqn 40})$$

By symmetry, the other partial derivatives must also vanish at the stationary states of any reaction system.

(ii) Linear Case. for this case we substitute the linear form of the kinetic equation, Equation 22, into the numerator of Equation 36 and evaluate the limit at the single stationary state. Equation 36 thus becomes:

$$= \lim_{x \rightarrow x^{ss}} \left\{ \frac{b(x - x^{ss})}{-(x - x^{ss})} \right\} \quad (\text{Eqn 41})$$

$$= -b \neq 0. \quad (\text{Eqn 42})$$

(Since this is by definition the linear case, the coefficient b , from Equation 11, must be nonzero.) Once again, from Equation 33 and the symmetry argument, we have the vanishing of all partial derivatives of ϕ at the stable stationary state.

3. Minimum Property: Stable Stationary States

As the system approaches a stationary state within its "territory," it is evident from the defining relation, Equation 1, that the value of ϕ is always decreasing in time. Therefore, ϕ also decreases continually in a spatial sense as the system progresses towards its steady state end point, following a determined trajectory. For stable stationary states, these features, together with the vanishing of all partial derivatives, require that the extremum value of ϕ at the stationary state must be a minimum.

4. Nonexistence of Other Minima: Uniqueness

It remains to show that these stationary states are the only points at which the minimum or even true extremum conditions hold, i.e., the various partial derivatives, $(\frac{\partial \phi}{\partial x})_y$ $(\frac{\partial \phi}{\partial y})_x$ vanish simultaneously only at such a stationary state. To accomplish this we introduce a new spatial coordinate, $\tilde{r}$, and then examine the variations of ϕ with respect to this new variable.

Let us denote by $\tilde{r}$ the scalar distance along a trajectory between any point (x,y) and the stationary state at the end of its evolving trajectory, viz.:

$$\tilde{r} = \int_{x,y}^{x^{ss},y^{ss}} d\vec{r} .$$

(Eqn 43)

This line integral is taken in the time-forward direction of the trajectory that passes through the point (x,y) en route to the stationary state (x^{ss}, y^{ss}) . The quantity $\vec{r}(x,y)$ is the unit vector at each point in the (x,y) plane, pointing along this trajectory.

For any system, we can see by inspection of Equation 43 that:
at steady states:

$$\frac{d\vec{r}}{dt} = 0; \quad (\text{Eqn 44})$$

away from steady states:

$$\frac{d\vec{r}}{dt} < 0. \quad (\text{Eqn 45})$$

(Note: Equation 45 must hold rigorously since the integrand in Equation 43 as a unit vector cannot be zero.)

For an infinitesimal displacement along a kinetic trajectory:

$$d\phi = \left(\frac{d\phi}{d\vec{r}}\right) d\vec{r}. \quad (\text{Eqn 46})$$

Let us consider any point (x,y) which is not a stationary state of the system. The time rate of change of ϕ is:

$$\frac{d\phi}{dt} = \frac{d\phi}{d\vec{r}} \cdot \frac{d\vec{r}}{dt}. \quad (\text{Eqn 47})$$

Solving for $\frac{d\phi}{d\vec{r}}$ and also using the defining relation, Equation 1, we have:

$$\frac{d\phi}{d\vec{r}} = \frac{\frac{d\phi}{dt}}{\frac{d\vec{r}}{dt}} \quad (\text{Eqn 48})$$

and

$$\frac{d\phi}{d\tilde{r}} = \frac{-(M - M^{SS})}{\frac{d\tilde{r}}{dt}} \quad . \quad (\text{Eqn 49})$$

For an extremum of ϕ to exist at any point, $\frac{d\phi}{d\tilde{r}}$ must be zero at that point. For any point (x,y) which is not a stationary state of the system, this expression can never be zero since both the numerator (8) and the denominator (by Equation 45) must be nonzero. With the vanishing of $\frac{d\phi}{d\tilde{r}}$ thus excluded, any such point which is not a steady state cannot be the locus of an extremum of ϕ .

5. Stability and Instability: An Enlarged View

Previous sections have dealt with steady states, and the behavior of ϕ in a relation to these, from several points of view: extremum property, minimum property, and time-dependent behavior. To demonstrate the extremum property, we employed a technique of infinitesimally displacing the system away from the steady state; then allowing it to relax back to that stationary state, as described by the kinetic equations. This kind of behavior is inherently that of a system exhibiting stability. But other behavior is possible; a system may be unstable and thus not return to that steady state once displaced away from it. Except for the very unlikely instance that such a perturbed state is, itself, a new steady state, or that the perturbation is exactly along a separatrix (see p. 26), an unstable system will continue to move away from its initial position, towards some entirely new end point. One approach to questions of instability is that of

catastrophe theory (11), originally created by Rene Thom to provide a theoretical framework for dealing with the phenomena of embryological development in biology. Our dual approach, below, is founded on more traditional branches of physical chemistry.

a. Kinetic Definitions. The most common means of assessing a system's stability properties is by examination of the kinetic equations themselves, focusing on their local properties in the vicinity of a stationary state. This is a purely mathematical approach (4,p.62). A given steady state is termed stable if all points in its vicinity "belong" to that steady state region (i.e., as stated above, that all such points lie on trajectories that lead to that particular steady state). Contrarywise, if (any of) the near-vicinity points of the given steady state do not belong kinetically to that steady state region, the given steady state is termed unstable or nonstable.

Our two kinetic definitions are chosen because they conform closely to the generally perceived intuitive and fundamental notions of stability, and to what it means to "belong kinetically to a steady state region." The notion of a steady state region is not merely a local concept, however. No matter how close or far away a point (x,y) may be from a given steady state, if it lies on a trajectory leading to that steady state, it is within that steady state region. Evidently, all points in the (x,y) plane belong to one or another steady state region.

b. Thermodynamic View of Stability. For a thermodynamic view of stability, we return to the enlarged dimensionality, e.g. $x, y, \phi(x,y)$, inherent in the potential function approach of previous

sections. It is the "topographical" features of the ϕ surface that we will look to, to be in one-to-one correspondence with the kinetic stability behavior described above. In effect, we have already accomplished parts of this task by demonstrating for (kinetically defined) stable stationary states, the correspondence between the topographical feature, the minimum of ϕ , and the system's stability. That is, the demonstration of the extremum property, $(\frac{\partial \phi}{\partial x})_y = 0$, utilizes our kinetic definition of stability, as does the minimum-property demonstration. The characteristic topographical feature of the stable stationary state is that it has a lower value of ϕ than for all nearby points. The system always moves spontaneously towards regions of lower ϕ , and the stable stationary state is sought out as the point of minimum ϕ . This topographical feature of ϕ allows the stable stationary state to be readily identified by inspection.

c. Thermodynamic View of Instability. Having just shown how the topology of a ϕ surface - the minimum feature - reflects stability in the vicinity of a stable stationary state, we now ask, what topological features might characterize an unstable stationary state. Clearly, there is more than one type of surface geometry which could be compatible with the fundamental requirement, $\frac{d\phi}{dt} \leq 0$, and also be in one-to-one correspondence with kinetic instability. However, they would all have this in common: some nearby points would lie below the stationary state, i.e., the steady state would have a higher value of ϕ than those for some nearby points.

In view of the fundamental requirement, $\frac{d\phi}{dt} \leq 0$, under all conditions, a system displaced from the (unstable) steady state to such a point

having a lower ϕ value could not return. In fact, it would have to continue to move to positions of even lower values of ϕ , towards some other endpoint. Hence, the ϕ surface cannot display a true minimum at an unstable stationary state: the surface must have the form of some other kind of extremum. Whether the extremum would be a maximum, a saddle point or other, one cannot say simply from these general considerations. Nevertheless, the topographical features of an unstable stationary state, namely, that some of its nearby points lie lower than it, would be immediately evident upon viewing the ϕ surface.

In summary, the above visible topographical features of the mathematically defined ϕ function thus provide the desired thermodynamic criteria of stability and instability, criteria not requiring the solutions of the kinetic differential equations. We shall see in Section IV how this thermodynamic treatment of stability is applied to a specific multistationary state system. In the next section we shall take a more detailed "thermodynamic" look at ϕ - surface topology in the vicinity of instabilities.

6. Extremum Properties in the Vicinity of Nonstable Stationary States

In a multistationary state kinetic system, the set of all points whose trajectories lead to a given stationary state (we have called the locus of such a set of points a "kinetic region") must have a boundary. This boundary fits the mathematical definition of a separatrix: the dividing line(s) between two regions whose trajectories lead to different final endpoints (7,p.82). A separatrix then "separates" these adjacent kinetic regions in (x,y) space and is a curve consisting of two curvilinear trajectories that lead to the nonstable endpoint. The separatrix is, itself, a kinetic region which includes this endpoint.

The principal detailed features of the ϕ surface in the vicinity of such a nonstable stationary state may be deduced by employing the perturbation technique suggested in our preliminary definition of a nonstable stationary state (c.f. page 9), namely by considering the subsequent behavior of the system following particular infinitesimal perturbations away from the nonstable stationary state:

Away from the Separatrix: By the very definition of a separatrix, the system follows a trajectory towards one of the stable stationary states, with $\phi(x,y)$ continually decreasing;

Along the Separatrix: The system returns to the nonstable stationary state along the separatrix-trajectory, with $\phi(x,y)$ continually decreasing as the stationary state is approached (Eqn 1).

a. Cusp-Like Character Near the Separatrix. The topographical character of the $\phi(x,y)$ surface in the vicinity of the nonstable stationary state is not that of a normal saddle point: along the separatrix, we show, below, that ϕ exhibits a true minimum at the stationary state, but that on either side of the separatrix it exhibits a cusp-like maximum, with infinite slope.

The analytical demonstration of this cusp-like singular character of the $\phi(x,y)$ surface follows from the analysis of particular

infinitesimal perturbations away from the nonstable stationary state. These are chosen so as to cause the system to move to positions in (x,y) space within a stable region (i.e., to points not on the separatrix) on one or the other of the curves:

$$\frac{dx}{dt} = f(x,y) = 0 \quad (\text{Eqn 50})$$

$$\frac{dy}{dt} = g(x,y) = 0. \quad (\text{Eqn 51})$$

The functions $f(x,y)$ and $g(x,y)$ are given by the kinetic equations, Equations 3 and 4.

The time-derivative of $\phi(x,y)$ along any trajectory may be generally written as follows:

$$\frac{d\phi}{dt} = \left(\frac{\partial\phi}{\partial x}\right)_y \frac{dx}{dt} + \left(\frac{\partial\phi}{\partial y}\right)_x \frac{dy}{dt} . \quad (\text{Eqn 52})$$

Along the curve $\frac{dx}{dt} = f(x,y) = 0$, the expression for this time-derivative simplifies to:

$$\frac{d\phi}{dt} = \left(\frac{\partial\phi}{\partial y}\right)_x \frac{dy}{dt} . \quad (\text{Eqn 53})$$

By substituting the defining relation, Equation 1, into Equation 53, above, and solving for the partial derivative, we obtain an expression whose limiting behavior may be evaluated as the nonstable stationary state is approached:

$$\left(\frac{\partial\phi}{\partial y}\right)_x = - \frac{(M - M^{SS})}{\frac{dy}{dt}} . \quad (\text{Eqn 54})$$

In the limit of smaller and smaller perturbations away from the nonstable stationary state, by inspection of Equations 13 and 22, the trajectory velocity, $\frac{dy}{dt}$, in the denominator of Equation 54 becomes vanishingly small. However, the numerator of Equation 54 remains finite because the expression $(M-M^{SS})$ is evaluated using the parameters for the stable kinetic region appropriate for the system's subsequent evolution ending at a new, stable stationary state.

Therefore, the partial derivative $(\frac{\partial \phi}{\partial y})_x$ must become infinite as the nonstable stationary state is approached along the curve $f(x,y) = 0$.

In a similar fashion, along the curve $\frac{dy}{dt} = g(x,y)$, the expression for the time-derivative of $\phi(x,y)$ simplifies to:

$$\frac{d\phi}{dt} = (\frac{\partial \phi}{\partial x})_y \frac{dx}{dt} \quad (\text{Eqn 55})$$

By an identical argument to that just given, it follows that $(\frac{\partial \phi}{\partial x})_y$ also becomes infinite.

Thus, the infinite steepness and cusp-like character of the $\phi(x,y)$ surface has thus been established for representative, nearby points off of the separatrix. It remains only to show that along the separatrix $\phi(x,y)$ exhibits a true minimum.

To do this, we will again employ the spatial coordinate, $\tilde{r}$, to follow the system as it moves toward the nonstable stationary state along the separatrix. We will then utilize L'Hospital's rule to evaluate $\frac{d\phi}{d\tilde{r}}$ along the separatrix, thereby demonstrating the minimum property.

b. Minimum of ϕ Along the Separatrix. As the nonstable stationary state is approached along the separatrix, the expression for $\frac{d\phi}{dr}$ given in Equation 49 is indeterminate because both the numerator and denominator vanish at the steady state. Differentiating the numerator and denominator with respect to the spatial coordinate, $\tilde{r}$, yields an expression for $\frac{d\phi}{dr}$ which may be readily evaluated in the steady state limit:

$$\text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{d\phi}{dr} \right\} = \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{- \frac{d}{dr} (M - M^{ss})}{\frac{d}{dr} \left(\frac{dr}{dt} \right)} \right\}. \quad (\text{Eqn } 56)$$

The kinetic region associated with a nonstable stationary state consists of only two trajectories in the x, y plane, namely, the separatrix. In general, displacements along this curve are describable as increments of $\tilde{r}$. For such a limited domain, the general extremum properties of the M function (c.f. Appendix A) can be expressed as a vanishing of M with respect to the single spatial coordinate, $\tilde{r}$, rather than as the vanishing of the partial derivatives with respect to x and y . Thus, Equation 56 may be written as follows:

$$\text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{d\phi}{dr} \right\} = \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{\text{zero}}{\frac{d}{dr} \left(\frac{dr}{dt} \right)} \right\}. \quad (\text{Eqn } 57)$$

The instantaneous velocity at any point along such a linear segment of the separatrix can be written explicitly as follows:

$$\frac{d\tilde{r}}{dt} = \cos \tilde{a} \frac{dx}{dt} + \sin \tilde{a} \frac{dy}{dt} \quad , \quad (\text{Eqn 58})$$

where $\tilde{a}$ is the smaller of the two angles between the separatrix segment and the x axis.

Next, we examine the special cases when the separatrix is parallel to either the x or y axis and the general case when it is not.

(i) Special Cases. In the event that the segment is parallel to either the x or y axis (i.e. $\sin \tilde{a} = 0$, or $\cos \tilde{a} = 0$), the velocity along the separatrix segment is given directly by $\frac{dx}{dt}$ or $\frac{dy}{dt}$, respectively. It then follows that $\frac{d}{dr}(\frac{d\tilde{r}}{dt})$, the denominator of Equation 57, maps into $\frac{d}{dx}(\frac{dx}{dt})$ or $\frac{d}{dy}(\frac{dy}{dt})$. But from the general form of the kinetic equations we have already shown such expressions to be nonzero (c.f. Eqn 21 and Eqn 24). Therefore the right hand side of Equation 57 must become zero, thus demonstrating the extremum property of ϕ along the separatrix for both these two special cases. These extrema must be minima since ϕ is continually decreasing during the approach to the nonstable stationary state.

(ii) General Case. For nonzero values of $\sin \tilde{a}$ or $\cos \tilde{a}$, Equation 56 can be simplified in another fashion, eliminating the variable y:

$$\frac{d\tilde{r}}{dt} = (\cos \tilde{a} + \sin \tilde{a} \tan \tilde{a}) \frac{dx}{dt}. \quad (\text{Eqn 59})$$

Note: this follows from the fact that $\tan \tilde{a} = \frac{(\frac{dy}{dt})}{(\frac{dx}{dt})}$.

From Equation 59 we can write:

$$\frac{dx}{d\tilde{r}} = 1/(\cos \tilde{a} + \sin \tilde{a}). \quad (\text{Eqn 60})$$

This equation enables us to evaluate $\frac{d}{d\tilde{r}} \left(\frac{d\tilde{r}}{dt} \right)$ by its equivalent (using the chain rule):

$$\frac{d}{d\tilde{r}} \left(\frac{d\tilde{r}}{dt} \right) = \frac{d}{dx} \left(\frac{d\tilde{r}}{dt} \right) \cdot \frac{dx}{d\tilde{r}} \quad (\text{Eqn 61})$$

$$= \left(\frac{d}{dx} (\cos \tilde{a} + \sin \tilde{a} \tan \tilde{a}) \right) \frac{dx}{d\tilde{r}} / (\cos \tilde{a} + \sin \tilde{a} \tan \tilde{a}) \quad (\text{Eqn 62})$$

As the stationary state is approached, the curvature of the separatrix in the x-y plane may be neglected and $\tilde{a}$ takes on a value that is independent of x. Then the term $(\cos \tilde{a} + \sin \tilde{a} \tan \tilde{a})$ may be factored out of Equation 62, yielding the result:

$$\frac{d}{d\tilde{r}} \left(\frac{d\tilde{r}}{dt} \right) = \frac{d}{dx} \left(\frac{dx}{dt} \right) \quad (\text{Eqn 63})$$

This result indicates that even for the general case (i.e., for any slope of the local separatrix-trajectory), $\frac{d}{d\tilde{r}} \left(\frac{d\tilde{r}}{dt} \right)$ maps into the simpler expression, $\frac{d}{dx} \left(\frac{dx}{dt} \right)$, which we have already shown to be nonzero in Equations 21 and 24. The fact that $\frac{d}{d\tilde{r}} \left(\frac{d\tilde{r}}{dt} \right) \neq 0$ is a vectorial consequence of the fact that $\frac{d}{dx} \left(\frac{dx}{dt} \right) \neq 0$ and $\frac{d}{dy} \left(\frac{dy}{dt} \right) \neq 0$. Therefore, just as for the special cases, above, the separatrix-trajectory exhibits an extremum and a minimum at the nonstable stationary state.

These general features of the ϕ surface are shown for an example system in Chapter IV. Note that in Figure 3, the stable stationary states are clearly seen as minima of the ϕ surface and the cusp-like topographical feature is associated with the separatrix.

7. Uniqueness of Extremal Cusps to Nonstable Stationary States

We have just shown in the previous section two properties of the ϕ surface for a nonstable stationary state:

- (i) an extremal property along the trajectory (trajectories) leading to the nonstable stationary state, i.e. $\frac{d\phi}{dr} = 0$, at the steady state;
- (ii) a steepness property on trajectories leading away from the steady state (towards some other stationary state), i.e. $\frac{d\phi}{dr}$ takes on the limiting value of minus infinity at the nonstable steady state.

We arrive at our desired uniqueness result by excluding the possibility of these properties, taken together, occurring anywhere else (i.e. anywhere other than at a nonstable stationary state).

First, we note from the section on "Nonexistence of Other Minima: Uniqueness" (p. 21) that the vanishing of $\frac{d\phi}{dr}$, given by Equation 49, can only occur at a stationary state. This part of the uniqueness argument applies equally well to any stationary state. Secondly, we note that a stable stationary state does not exhibit the steepness property. That is, the minima-extrema shown for all stable stationary states (p. 15-21) perforce do not have any such steepness property, nor any trajectories leading away from them. Thus, if $\frac{d\phi}{dr}$ fails to vanish at some kind of stationary state, but this stationary state cannot be a stable one, it must necessarily be a nonstable one--ergo, "uniqueness".

E. THE TIME DERIVATIVE

The function, $\mathcal{M}$, is positive-definite for all values of the concentration variables and takes on a minimum value at a stationary state (8; also shown in Appendix A). Thus, the quantity $-(\mathcal{M} - \mathcal{M}^{ss})$ must always be negative at positions away from the steady state. Therefore, from the defining relations for ϕ , Equations 1 and 2, it is required that for any irreversible process,

$$\frac{d\phi}{dt} \leq 0. \quad (\text{Eqn 64})$$

The equality holds only at a stationary state.

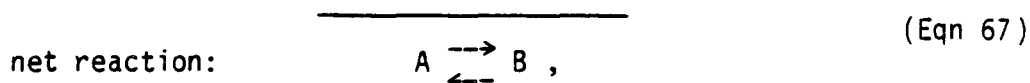
Thus, ϕ serves as "time's arrow" for irreversible processes.

III. EXAMPLE SYSTEMS

Up to this point our treatment of the thermodynamic potential character of ϕ has been general--independent of particular applications. It is, however, also instructive to treat (some) specific examples, both as illustrations of the ways that the general properties manifest themselves, and for displaying analytical and computational means that can be employed to evaluate the ϕ function numerically. Two such examples are presented herein--the first one as the simplest reaction network having a far-from-equilibrium steady state, the second to illustrate a multistationary-state control system, exhibiting instability and bifurcation. Since for both of these examples the well-behaved, negative-definite, time-evolutionary character of ϕ follows so self-evidently from the basic definition, Equation 1, it is not worthwhile to present specific calculations on their point-by-point trajectories in time. Hence, in the following examples we show calculations only for the variational behavior of ϕ , in "concentration space".

A. A STRAIGHT-LINE ISOMERIZATION SEQUENCE

There are two general methods for finding ϕ , one requiring a solution to the kinetic (differential) equations, the other requiring a knowledge only of the form of the kinetic equations. Both methods are shown in detail for the following 2-step sequence of elementary, monomolecular (e.g. isomerization) reactions:



where A and B are held constant by a reservoir or "chemostat" or a buffer system. The respective velocities and affinities of each of these elementary reactions are:

$$v_1 = \frac{d_1}{dt} = \left(\frac{dx}{dt}\right)_1 = k_1 A - k_1' x \quad ; \quad \mathcal{A}_1 = RT \ln \frac{k_1 A}{k_1' x} \quad (\text{Eqn 68})$$

$$v_2 = \frac{d_2}{dt} = -\left(\frac{dx}{dt}\right)_2 = k_2 x - k_2' B \quad ; \quad \mathcal{A}_2 = RT \ln \frac{k_2 x}{k_2' B} \quad (\text{Eqn 69})$$

$$\text{overall affinity:} \quad \mathcal{A} = \mathcal{A}_1 + \mathcal{A}_2 = RT \ln \left[K_1 K_2 \left(\frac{A}{B} \right) \right] \quad . \quad (\text{Eqn 70})$$

The fixed concentrations of species A and B, as well as the initial value of the single concentration variable, x, may be chosen arbitrarily. The system may thus be constrained to operate away from equilibrium in any desired manner simply by appropriate choice of these parameters. Therefore, without loss of generality, we may set all the forward and reverse rate constants, k, (hence, also, both equilibrium constants $K = k/k'$) equal to unity and still enable the

system to exhibit irreversibility to any desired extent. We choose to do so because of the mathematical simplicity thereby afforded.

By inspection of Equations 68 and 69 it is seen that the concentration of x varies according to the kinetic equation, expressed as an algebraic function in terms of x or, alternatively, in terms of a reduced variable, $z = \frac{x}{x^{ss}}$, as follows:

<u>Concentration Variable</u>	<u>Reduced Variable</u>	
$\frac{dx}{dt} = v_1 - v_2 = (A-x) - (x-B)$ $= A + B - 2x;$	$\frac{dz}{dt} = 2(1-z) .$	(Eqn 71)

The single, stable, stationary state of the system is evidently given by:

$$\frac{dx}{dt} = 0 = A + B - 2x^{ss} ; \quad \frac{dz}{dt} = 0 = 2(1-z^{ss}); \quad (\text{Eqn 72})$$

$$x^{ss} = \frac{A + B}{2} ; \quad z^{ss} = 1 . \quad (\text{Eqn 73})$$

The first method of calculating ϕ requires direct integration of the kinetic equation, Equation 71, above. If x° represents the initial value of the concentration variable at $t = 0$, and x^{ss} is the steady state value, as given by Equation 73, above, then integration of Equation 71 yields the expression for $x(t)$:

$$x(t) = (x^\circ - x^{ss})e^{-2t} + x^{ss} . \quad (\text{Eqn 74})$$

This parametric representation of x will be used shortly.

Proceeding directly from the defining relation, Equation 2, we have:

$$\phi(x^\circ) - \phi(x^{ss}) = + \int_0^\infty (M - M^{ss}) dt. \quad (\text{Eqn 75})$$

(Note that calculation of $\phi(x^\circ)$ is simply a device for calculating $\phi(x)$; for any value, x , can be considered equally well to be an "initial value" x° , the start of a trajectory in chemical reaction systems which "lack inertia". For this reason, we simplify the notation by henceforth dropping the x° and z° in favor of x and z , respectively.) To evaluate the integral in Equation 75, we use the definition of M (c.f. Appendix A):

$$M = \frac{1}{T} (\alpha_1 A_1^2 + \alpha_2 A_2^2) \quad (\text{Eqn 76})$$

$$\text{where } \alpha_1 = \frac{v_1^{ss}}{A_1^{ss}} > 0, \quad (\text{Eqn 77})$$

$$\alpha_2 = \frac{v_2^{ss}}{A_2^{ss}} > 0, \quad (\text{Eqn 78})$$

and A_1 and A_2 are the simplified ($k=k'=1$) forms of the affinities from Equations 68 and 69. We also employ the reduced variable z , and recall that $M^{ss} = \phi^{ss} = (v^{ss} \cdot A^{ss})/T$ (this follows from the steady state condition applied to Equation 71: $v_1^{ss} = v_2^{ss} = v^{ss}$, plus Equation 70). Thereby:

$$(M-M^{SS}) = \frac{1}{T} (\alpha_1 A_1^2 + \alpha_2 A_2^2 - v^{SS} A^{SS}) \quad (\text{Eqn 79})$$

$$= \frac{1}{T} [\alpha_1 (A_1^{SS} + RT \ln z)^2 + \alpha_2 (A_2^{SS} - RT \ln z)^2 - v^{SS} A^{SS}] \quad (\text{Eqn 80})$$

$$= \frac{1}{T} [\alpha_1 R^2 T^2 + \alpha_2 R^2 T^2] \ln^2 z \quad (\text{Eqn 81})$$

For purposes of our first method we express Equation 81 in terms of our original variable x , whereby Equation 75 becomes:

$$\phi(x) - \phi(x^{SS}) = [\alpha_1 R^2 T + \alpha_2 R^2 T] \int_0^\infty \ln^2 \left(\frac{x(t)}{x^{SS}} \right) dt \quad (\text{Eqn 82})$$

Using Equations 73 and 74, the integral (variable) portion of Equation 82, has been calculated for several values of $z = x/x^{SS}$, for the particular nonequilibrium case of $A = 1$, $B = 10$, using numerical integration based upon the method of Gaussian quadratures. The results are tabulated in Table 2, column 2 below, and plotted in Figure 1. The ϕ function is clearly seen to take on its minimum value at the steady state. Furthermore, it is everywhere concave upwards.

For comparison, the corresponding variable portions of the M function and the entropy production function, are calculated for this same system, tabulated in Table 2, Columns 3 and 4, and plotted in Figures 2 and 3, respectively. As must be the case for the M function, its extremum occurs precisely at the steady state position. By contrast, the entropy production minimum is seen to be clearly displaced from the steady state position. This is a graphical demonstration of the well-known fact that the entropy production function (or the dissipation function) cannot serve as a thermodynamic potential function for a far-from-equilibrium, "nonlinear" system.

Table 2. THERMODYNAMIC FUNCTIONS EVALUATED FOR THE SYSTEM $A \rightleftharpoons x \rightleftharpoons B$

x/x^{ss}	$\frac{\phi(x) - \phi(x^{ss})}{[\alpha_1 R^2 T + \alpha_2 R^2 T]}$	$T (M(x) - M^{ss})$	$T P(x)$
0	1.06		
0.1	0.58	5.301898	27.678015
0.2	0.368	2.590290	19.654278
0.5	0.095	0.480453	11.129937
0.9	0.00268	0.011101	9.868728
1.0	-0-	-0-	10.361633
1.1	0.00234	0.009084	11.075275
1.5	0.0469	0.164402	15.635697
2	0.150	0.480453	24.074263
3	0.427	1.206949	46.707125
4	0.739	1.921812	74.373380
5	1.06	2.590290	105.528945
6	1.38	3.210402	139.348459
10	2.61	5.301898	

The second method of finding ϕ is an analytical method and requires only the differential form of the kinetic equation, Equation 71. We commence with the defining equation, Equation 2:

$$\phi(x) - \phi(x^{ss}) = \int_0^{\infty} (M - M^{ss}) dt \quad ; \quad (\text{Eqn 83})$$

and proceed using Equation 83:

$$\phi(x) - \phi(x^{ss}) = \frac{1}{T} [\alpha_1 R^2 T^2 + \alpha_2 R^2 T^2] \int_0^{\infty} \ln^2(z) dt. \quad (\text{Eqn 84})$$

Using the differential form of the kinetic equation, Equation 71:

$$\frac{1}{2} \frac{dz}{(1-z)} = dt \quad , \quad (\text{Eqn 85})$$

Equation 84 takes the form:

$$\phi(x) - \phi(x^{ss}) = \frac{1}{2T} [\alpha_1 R^2 T^2 + \alpha_2 R^2 T^2] \int_z^1 \frac{\ln^2 z}{1-z} dz \quad . \quad (\text{Eqn 86})$$

$$= [\alpha_1 R^2 T + \alpha_2 R^2 T] \frac{I(z)}{2} \quad . \quad (\text{Eqn 87})$$

where $I(z)$ is the integral of Equation 86.

Because the integrand in Equation 86 exhibits a strong singularity at $z = 1$, the evaluation of the integral must be performed in two parts, first, along the positive real axis from $z = 0$ to $z = 1$, and, secondly, along the positive real axis from $z = \infty$ to $z = 1$. (There is no contribution to the integral for $z = 1$, since both the left and right hand sides of Equation 86 vanish for $x = x^{ss}$, i.e. $z = 1$.)

The integral, $I(z)$, may be expressed in terms of little-used, special functions, polylogarithms (12;p.274,Eq.6; p.244,Eq.6; p.258,Eq.6):

For $z < 1$,

$$I(z) = \ln(1-z)\ln^2(z) + 2\ln(z) \text{Li}_2(z) - 2\text{Li}_3(z) + 2\text{Li}_3(1) ; \quad (\text{Eqn 88})$$

For $z > 1$,

$$I(z) = \ln(z-1)\ln^2(z) - \frac{2}{3} \ln^3(z) - 2\ln(z)\text{Li}_2\left(\frac{1}{z}\right) - 2\text{Li}_3\left(\frac{1}{z}\right) + 2\text{Li}_3(1), \quad (\text{Eqn 89})$$

where Li_2 and Li_3 are the dilogarithm and trilogarithm functions, respectively. This allows us to evaluate the expression $I(z)$ over the entire domain $0 \leq z \leq \infty$, and hence evaluate $[\phi(x) - \phi(x^{ss})]/[\alpha_1 R^2 T + \alpha_2 R^2 T]$, for $0 \leq x \leq \infty$, using the series definitions for these special functions, given below in terms of the dummy variable, $\tilde{z}$. (We have also included the series expansion for the logarithm function in order to display the simple, family relationship between all of the (poly)logarithm functions.)

$$\ln(\tilde{z}) \text{ is the logarithm of } \tilde{z}, \quad = \sum_{n=1}^{\infty} \frac{\tilde{z}^n}{n} ; \quad (\text{Eqn 90})$$

$$\text{Li}_2(\tilde{z}) \text{ is the dilogarithm of } \tilde{z}, \quad = \sum_{n=1}^{\infty} \frac{\tilde{z}^n}{n^2} ; \quad (\text{Eqn 91})$$

$$\text{Li}_3(\tilde{z}) \text{ is the trilogarithm of } \tilde{z}, \quad = \sum_{n=1}^{\infty} \frac{\tilde{z}^n}{n^3} . \quad (\text{Eqn 92})$$

Two comments are in order. First, these series converge only for $\tilde{z} \leq 1$. Second, this condition presents no restriction on the domain over which $I(\tilde{z})$ can be calculated, because of its two-part form as given in Equations 88 and 89: in both of these expressions, the arguments of the polylogarithms are, indeed, always less than unity.

Numerical calculations using tabulated values of these special functions, (12;p.275), show that $[\phi(x) - \phi(x^{ss})]/[\alpha_1 R^2 T + \alpha_2 R^2 T]$ calculated by this method using Equation 86 is precisely the same as when evaluated by the first method, Equation 82. Hence, the numerical values given in Table 2, column 2, and Figure 1 apply to this calculation as well.

B. AN AUTOCATALYTIC REACTION NETWORK

In order to examine the ϕ surface and to confirm its general properties for a reaction system exhibiting qualitatively different features of interest, numerical calculations were carried out for the following multistationary state, open, chemical reaction system:



where x , e , and c are concentration variables, and A and B are held constant by a reservoir, or "chemostat" or a buffer system. It is also evident by inspection of Equations 94 and 95 that the sum of $e + c = E$, must also remain constant. The respective velocities and affinities of each of these elementary reactions are:

$$v_1 = k_1 Ax - k_1' x^2 \quad ; \quad \mathcal{A}_1 = RT \ln \frac{k_1 A}{k_1' x} \quad (\text{Eqn 97})$$

$$v_2 = k_2 xe - k_2' c \quad ; \quad \mathcal{A}_2 = RT \ln \frac{k_2 xe}{k_2' c} \quad (\text{Eqn 98})$$

$$v_3 = k_3 c - k_3' eB \quad ; \quad \mathcal{A}_3 = RT \ln \frac{k_3 c}{k_3' eB} \quad (\text{Eqn 99})$$

$$\text{overall affinity} \quad \mathcal{A} = \mathcal{A}_1 + \mathcal{A}_2 + \mathcal{A}_3 = RT \ln [K_1 K_2 K_3 \left(\frac{A}{B}\right)] \quad (\text{Eqn 100})$$

The condition, $e + c = E$ (constant), reduces the number of independent concentration variables from three to two, which we take as x and e . Again setting all rate constants equal to unity, the rates of change of x and e are given by the kinetic equations:

$$\frac{dx}{dt} = v_1 - v_2 = -x^2 + Ax - xe + (E - e) \quad (\text{Eqn 101})$$

$$\frac{de}{dt} = -v_2 + v_3 = -xe - Be + 2(E - e) \quad (\text{Eqn 102})$$

The solutions of these equations, plotted as trajectories in the x, e phase-plane, are given in Figure 4, for the boundary conditions $A = 8.44$, $B = 0.20$, $E = 30.0$, and a representative set of initial conditions.

This system, first studied by Edelstein in 1970 (13,4p.274), has been shown to exhibit either a single, stable stationary state, or three stationary states (2-stable, 1-unstable), depending upon the values for the boundary conditions, A , B and E . The values we selected for A , B and E ensure the system's multistable stationary-state behavior (9). This stability/instability feature of the reaction network depends upon the autocatalytic character of the first reaction of the network.

The individual trajectories of Figure 4 do not reveal any knowledge of either the system's rate of approach to the stationary states, or of possible instabilities exhibited by the system. However, the family of all such trajectories does indicate system-stability properties. The two stable stationary states of the system (stationary states I and III), as is clearly indicated on the phase-plane map, Figure 4, are the

respective end-points of virtually all possible trajectories. Sandwiched between trajectories leading to stationary states I and III, lies the separatrix, which "separates" kinetic regions I and III, and consists of a pair of trajectories leading to the unstable stationary state, II. From examination of Figure 4, the separatrix (dashed line) is seen to lie somewhere in the narrow region for which no trajectories are plotted, between the kinetic regions I and III. However, only the approximate location of the separatrix can be inferred from the phase-plane trajectories. In fact, no general mathematical method apparently exists for finding the separatrix for an arbitrary system of differential equations, even for such a simple system as Equations 101 and 102.

The location of the unstable stationary state II, can also be inferred only approximately by inspection of the phase-plane trajectories. It lies on the separatrix, at its intersection with what may be called the "inverse separatrix" (the latter obtained by integrating the kinetic equations with respect to negative time). Of course the exact location of stationary state II can be obtained directly from the kinetic equations; it is simply calculated as one of the three solutions to the algebraic steady-state form of Equations 101 and 102.

Figure 4 consists of curves which are strictly kinetic in nature. By contrast, Figures 5-9 exhibit the thermodynamics of the system. They contain the results of calculations of the ϕ function for this system, carried out numerically starting from 10,000 different points,

equally dividing the same region of the x, e plane as in Figure 4. The time-integration of $(J - J^{SS})$ according to Equation 2 was carried out along the trajectories of regions I and III using the steady state values of reaction velocity and affinity appropriate to each region (inherent to the J function). Because the velocities decrease to zero as any steady state is approached, it was necessary to perform more than 100,000 iterative steps along each trajectory to evaluate the family of integrals, ϕ . The absolute convergence of $\phi(x, e)$, as was predicted from the general demonstration based upon ℓ' Hospital's Rule, was verified by numerical calculations at the two stable stationary states.

The singular character of $\phi(x, e)$, in the near vicinity of the trajectories which lead to the unstable stationary state was also verified by numerical calculations. The unusual cusp-like structure of the ϕ surface in this region was predicted and derived in Section II-D from very general considerations: the nonzero character of the integrand, $(J - J^{SS})$, and the semi-infinite limits of the integration indicated that ϕ would become unbounded as the unstable stationary was approached. Furthermore, the numerical calculations brought out an added feature—namely, that analytic continuation can be employed to find the limits of a kinetic region. It is readily seen in Figures 5-8 that ϕ exhibits singular character along the separatrix, yet is an analytic function in the near vicinity of the separatrix. Thus, ϕ diverges as the separatrix is approached in the x, e plane, but does so smoothly. The smooth and continuous character of ϕ can, in fact, be

employed to find the location of the separatrix to any desired degree of precision.

The three-dimensional $\phi(x,e)$ surface is most readily visualized in Figures 6-9. In these figures, many general features of the ϕ surface which were mathematically proven in Section II may be verified by inspection, including: (a) $(\phi - \phi^{SS})$ is positive-definite; (b) stable stationary state extrema are minima; (c) unstable stationary state extrema are cusp-like saddle points; and (d) extrema are unique to stationary states of the system. Overall we can say that there is a one-to-one correspondence between the topographical features of the ϕ surface and the kinetic behavior of the system.

For purposes of comparison with the ϕ topology, we include two additional contour maps of closely related thermodynamic functions: the TM function and TP function as Figures 10 and 11, respectively. The extent to which each of these can and cannot serve as a thermodynamic potential function for the multi-steady state, far-from-equilibrium "Edelstein" system is indicated in Figures 10 and 11 and their captions.

IV. DISCUSSION

A principal point of departure for this paper was the identification of a limit of validity for a previously-studied function, the $\mathcal{M}$ function, that is, its imperfection to serve as a general purpose far-from-equilibrium thermodynamic potential for a more complex and more interesting (multi-stationary-state) system than had previously been investigated. This led to the ϕ function which was able to "cure" this "defect" without otherwise sacrificing the remaining, desirable properties of $\mathcal{M}$. Curiously, the ϕ function is closely related to $\mathcal{M}$, indeed, directly constructed upon $\mathcal{M}$. It is therefore appropriate to open this discussion section by first examining a direct comparison of the explicit forms of $\mathcal{M}$ and ϕ in the context of the examples we have analyzed herein. We subsequently consider, briefly, the physical/biological significance of the two examples, themselves, then focus on the conceptual linkages and interrelationships existing within an enlarged set of global thermodynamic potential functions covering the full domain from equilibrium systems to far-from-equilibrium systems. We conclude by touching briefly on future directions for this work.

A. COMPARATIVE FORMS OF $\mathcal{M}$ AND ϕ

For the first of our two examples, III-A, it is possible without too much complexity, and therefore it is instructive, to present in overview format a comparison of the specific forms of $\mathcal{M}$ and its principal derivative functions, with those of ϕ and its corresponding derivative functions, expressed at several levels of increasing algebraic

detail. This comparison serves two specific purposes: (1) it facilitates making (virtually all) the most significant and useful intra- and interfunction comparisons; and (2) it enables the most straightforward demonstration of each of the central properties of ϕ and M , taking advantage of the best form in each case (i.e., the most appropriate level of expression) to make the validity of that property most readily self-evident. (For the benefit of those not familiar with the analytical properties of the M function, we have included a general demonstration of the extremum property as Appendix A.)

The general properties to be demonstrated in each case, as presented in Table 3 are: positive definiteness, extremum-in-steady-state, and time-dependent variation. Together with an identification-reference to the "best" form for the demonstration, these are given in the right-most two columns of Table 3. The forms of closest correspondence for the M (lines 1-3) and ϕ (lines 4-6) functions are within a given vertical column, for example [b]-1 with [b]-4, [b]-2 with [b]-5, [b]-3 with [b]-6, (and similarly for columns [c] and [d]). The left-most column, [a], contains entries only for the ϕ function forms, which accents the differing-level relationship between the defining forms of ϕ and M : integral (for ϕ) to differential (for M).

We omit a comparable table for our second example, III-B, since the nature of this autocatalytic kinetic system would render the table, as a whole, unwieldy--some of the algebraic forms are much too complex to permit drawing simple conclusions by mere inspection. Suffice it to say that in such a table a number of the properties would still be

simply self-evident in the corresponding positions as for Table 3, others would not be self evident, and one would not even be true (i.e. as indicated previously, $\frac{dT_M}{dt}$ is not always negative definite). It is evident from Table 3 that our success at finding global thermodynamic potentials hinges on our explicit use of the expressions for the velocity and affinity in terms of the concentration variables. Thus, it is for a particular class of nonlinearity (e.g. linear-logarithm type) that our theory applies. Fortunately, this class of behavior encompasses the whole of normal chemical kinetics.

B. SIGNIFICANCE OF THE TWO EXAMPLES STUDIED IN THIS PAPER

1. Example III-A, the Linear Network. As the simplest possible non-trivial open chemical reaction system that can be constrained to operate in a non-equilibrium (including far-from-equilibrium) fashion, this system is too elementary to model the dynamics of a system of real, interesting complexity. The 2-step monomolecular reaction sequence (and multi-variable straight-line extensions) are representative, rather, of processes such as a series of successive molecular de-excitations, or of isomerizations, or of sequential isotopic decays.

2. Example III-B, the Autocatalytic Network (13,9). Even with such a relatively simple 3-reaction (2-independent-variable) bimolecular sequence as this, an impressive degree of dynamic ("control-system") complexity is inherent in it: three stationary states; an unstable stationary state; a separatrix. In a global mechanistic

TABLE 3 SUMMARY OF IMPORTANT ALGEBRAIC FORMS FOR THE SYSTEM $A \rightleftharpoons x \rightleftharpoons B$ (SETTING RATE CONSTANTS = 1 AND $RT = 1$)

FUNCTION	[a]	[b]	[c]	[d]
1. T_M		$= \left[a_1 A_1^2 + a_2 A_2^2 \right]$	$= v^{ss} \left[\frac{A_1^2}{A_1^{ss}} + \frac{A_2^2}{A_2^{ss}} \right]$	$= \frac{(A-B)}{2} \left[\frac{\ln^2 \frac{A}{x}}{\ln \frac{A}{x^{ss}}} - \frac{\ln^2 \frac{x}{B}}{\ln \frac{x}{B^{ss}}} \right]$
2. $\frac{dT_M}{dx}$		$= 2 \left[a_1 A_1 \frac{dA_1}{dx} + a_2 A_2 \frac{dA_2}{dx} \right]$	$= 2 v^{ss} \frac{dA_1}{dx} \left[\frac{A_1}{A_1^{ss}} - \frac{A_2}{A_2^{ss}} \right]$	$= - \frac{(A-B)}{x} \left[\frac{\ln \frac{A}{x}}{\ln \frac{A}{x^{ss}}} - \frac{\ln \frac{x}{B}}{\ln \frac{x}{B^{ss}}} \right]$
3. $\frac{dT_M}{dt}$		$= 2 \frac{dx}{dt} \left[a_1 A_1 \frac{dA_1}{dx} + a_2 A_2 \frac{dA_2}{dx} \right]$	$= 2 v^{ss} \frac{dx}{dt} \frac{dA_1}{dx} \left[\frac{A_1}{A_1^{ss}} - \frac{A_2}{A_2^{ss}} \right]$	$= - \frac{2(A-B)}{x} (x^{ss} - x) \left[\frac{\ln \frac{A}{x}}{\ln \frac{A}{x^{ss}}} - \frac{\ln \frac{x}{B}}{\ln \frac{x}{B^{ss}}} \right]$
4. $T(\phi - \phi^{ss})$	$= T \int (M - M^{ss}) dt$	$= \int_0^\infty \left[a_1 (A_1^2 - A_1^{ss2}) + a_2 (A_2^2 - A_2^{ss2}) \right] dt$	$= v^{ss} \int_0^\infty \left[\frac{A_1^2}{A_1^{ss2}} - 1 + \frac{A_2^2}{A_2^{ss2}} - 1 \right] dt$	$= \frac{(A-B)}{2} \left(\frac{1}{\ln \frac{A}{(A+B)/2}} + \frac{1}{\ln \frac{(A+B)/2}{B}} \right) \int_0^\infty \frac{\ln^2 (x/x^{ss})}{1 - (x/x^{ss})} d(x/x^{ss})$
5. $\frac{dT\phi}{dx}$	$= \frac{-T}{(\frac{dx}{dt})} (M - M^{ss})$	$= - \frac{1}{(\frac{dx}{dt})} \left[a_1 (A_1^2 - A_1^{ss2}) + a_2 (A_2^2 - A_2^{ss2}) \right]$	$= - \frac{v^{ss}}{(\frac{dx}{dt})} \left[\frac{A_1^2}{A_1^{ss2}} - 1 + \frac{A_2^2}{A_2^{ss2}} - 1 \right]$	$= - \frac{(A-B)}{4(x^{ss}-x)} \left[\ln \frac{A}{x^{ss}} \left(\frac{\ln^2 \frac{A}{x}}{\ln^2 \frac{A}{x^{ss}}} - 1 \right) + \ln \frac{x^{ss}}{B} \left(\frac{\ln^2 \frac{x}{B}}{\ln^2 \frac{x}{B^{ss}}} - 1 \right) \right]$
6. $\frac{dT\phi}{dt}$	$= -T (M - M^{ss})$	$= - \left[a_1 (A_1^2 - A_1^{ss2}) + a_2 (A_2^2 - A_2^{ss2}) \right]$	$= - v^{ss} \left[\frac{A_1^2}{A_1^{ss2}} - 1 + \frac{A_2^2}{A_2^{ss2}} - 1 \right]$	$= - \frac{(A-B)}{2} \left[\ln \frac{A}{x^{ss}} \left(\frac{\ln^2 \frac{A}{x}}{\ln^2 \frac{A}{x^{ss}}} - 1 \right) + \ln \frac{x^{ss}}{B} \left(\frac{\ln^2 \frac{x}{B}}{\ln^2 \frac{x}{B^{ss}}} - 1 \right) \right]$

* For the nonequilibrium case, where $A \neq B$, (and where we take $(A-B) > 0$ without loss of generality), expression 3[d] takes the form:

$$\frac{dT_M}{dt} = - \left[\frac{2(A-B)}{x} \right] \left[\frac{A+B}{2} - x \right] \left[\frac{\ln \frac{A}{x}}{\ln \frac{2A}{A+B}} - \frac{\ln \frac{x}{B}}{\ln \frac{2B}{A+B}} \right]. \text{ By inspection, we can now evaluate the sign of } \frac{dT_M}{dt} \text{ by considering the sign}$$

of each of the latter two bracketed terms only (since the first bracketed term is inherently positive). For the three possible domains:

(i) $\left[\frac{A+B}{2} - x \right] > 0$; (ii) $\left[\frac{A+B}{2} - x \right] = 0$; and (iii) $\left[\frac{A+B}{2} - x \right] < 0$, the latter two terms have the signs:

(i) + and +; (ii) 0 and 0; (iii) - and -, respectively. Hence, in all three cases, $\frac{dT_M}{dt} \leq 0$.

** For the equilibrium case, $A = B (= x^{ss})$, expression 3[b] takes the form: $\frac{dT_M}{dt} = -4 \left[\frac{1}{x} \right] [a_1 + a_2] [(A-x) \ln \frac{A}{x}]$.

(i) For $x \neq x^{ss}$, each bracketed term is clearly positive, so $\frac{dT_M}{dt} < 0$.

(ii) For $x = x^{ss} (= A)$, the last term vanishes, hence $\frac{dT_M}{dt} = 0$.

sense the behavior of this network is that of a "two-position" switch (e.g., a "toggle" switch). In point of fact, such a switch, examined more closely, actually represents a 3-steady state device (where the steady-states are actually equilibrium states): two stable, and one (intermediate position) unstable state.

A biological analogue of such control-system behavior would be the differentiation of a "bi-potential" stem cell into two alternative end-cell or progeny lines. In this model the stem-cell state represents the unstable steady state (in which the cell can and must be able to remain while it reproduces, but which if "perturbed" slightly will lead to the cells irreversibly departing for one or the other stable end points). Other biological models of dynamic similarity include anabolic enzyme induction, e.g., lac operon of *E. coli* (14), and the Krebs cycle/glycolytic cycle "bifurcation" process.

C. ϕ IN LARGER CONTEXT

The significance of the ϕ function will be examined primarily in relation to a set of four state functions which possess global thermodynamic potential character, and in terms of its dimensionality. The other 3 functions are: total entropy (S_{tot}); "entropy production" ($\dot{P} = \frac{d_i S}{dt}$); and the "affinity squared minimum function" ($\mathcal{M}$). The domains of applicability of their respective thermodynamic potential character evidently span the range from strictly-equilibrium, through near-to-equilibrium, to far-from-equilibrium, as shown in Table 4, below.

Table 4. THERMODYNAMIC POTENTIALS AND THEIR DOMAINS

$\mathcal{P}$ (near-equilibrium)	S_{tot} (equilibrium endpoint)
$\mathcal{M}$ (far-from-equilibrium) (not all systems)	ϕ (far-from-equilibrium)

To emphasize the relationships explicitly we can expand Table 4 in the form of Table 5. (Where no subscript is given, the connotation system is implied.)

Table 5. INTEGRAL-DIFFERENTIAL RELATIONSHIPS

$$\mathcal{P} = \frac{d_i S}{dt} = \frac{dS_{\text{tot}}}{dt} \qquad \int \mathcal{P} dt = S_{\text{tot}}$$

$$-(\mathcal{M} - \mathcal{M}^{\text{SS}}) = \frac{d\phi}{dt} \qquad -\int (\mathcal{M} - \mathcal{M}^{\text{SS}}) dt = \phi$$

This table is configured (left to right) with each left-column item being the differential of its corresponding right-column (integral) item, taken with respect to the same variable--time. Furthermore, since $\mathcal{P}$ and $\mathcal{M}$ both have the same dimensions (of entropy production per unit time; recall that $\mathcal{M}^{\text{SS}} = \mathcal{P}^{\text{SS}}$), so must the expressions in the right-hand column also have the same dimensions, i.e. the dimensions of the new function ϕ must be simply those of entropy.

Another "structural" feature of Tables 4 and 5 is that, proceeding counterclockwise from the entropy function, each succeeding function in turn is applicable as a thermodynamic potential for systems of increasing generality (and/or "farness-from-equilibrium").

Conceptually, introduction of the function $\mathcal{P}$ broke new ground: for the first time there was a global thermodynamic function, and one of simple physical interpretation, which could "model" or "guide" the evolution of a chemical system to a point removed (even if slightly so) from equilibrium. That is, the evolution brought the system through successive states of ever-lower entropy production to the final minimum value at the steady state. The advance brought to thermodynamic analysis by the advent of the $\mathcal{P}$ function is evident in light of the fact that even the slightest constraint (imposed by boundary conditions) forcing the endpoint of an evolving system to be displaced from the equilibrium position, utterly eliminates the (total) entropy from consideration as the evolutionary "guiding principle" of the kinetic processes. In that sense, the function S_{tot} with its "constraintless" domain is qualitatively different from the other three functions, operating in their variously constrained domains.

From one point of view, that might seem to make S_{tot} of less general applicability than the other functions, at least with respect to "interesting" systems such as living systems. Another perspective, however, is that the domain of S_{tot} places it at a different level, and in fact "over" the domains of the other 3 functions. That is

because, regardless of the constrained-system behavior they model, all their respective systems are also ultimately subjected to the power of entropy--with its tendency to drive them toward the final fate of equilibrium. In defense of the three nonequilibrium functions, however, it should be noted that their domains penetrate into that of the entropy: these functions will continue to serve as thermodynamic potentials as their respective constraints would be successively relaxed, down to and including the equilibrium domain of the entropy.

These ideas may be summarized in a list of strengths and weakness, as follows:

S_{total}

- Strengths: ● applicable to all systems of any kinetic complexity;
- applicable within the complete domain, near-to and far-from the endpoint;
 - applicable on an overall "supervisory" level, also, to systems being guided by "restricted-domain" thermodynamic potentials.
- Weaknesses: ● Strictly limited to systems evolving towards the sole endpoint of equilibrium.

P

- Strengths: ● applicable to systems evolving to an enlarged and whole new class of endpoints--nonequilibrium endpoints--as well as to equilibrium-endpoint systems;
- applicable to systems of any formal kinetic complexity;
 - provides a principle of simple physical interpretation for spontaneous ordering (as opposed to the disordering principle of entropy).

- Weaknesses: ● severely restricted, in-toto, to near-to-equilibrium, or the "linear" domain;
- the permitted, general formal complexity of kinetics is illusory, since all "interesting" kinetic/control-system behavior is lost when the usual nonlinear relationships of real chemical kinetics are "collapsed" into the linear domain.

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- Strengths: ● extends the formal, global thermodynamic potential approach to the far-from-equilibrium domain, for many types of realistic chemical kinetics (and remains applicable down to equilibrium).
- Weaknesses: ● fails to retain all of its thermodynamic potential character for all realistic chemical kinetic systems of wide/biological interest.

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- Strengths: ● retains global thermodynamic potential character for far-from-equilibrium steady state systems of considerable biological interest (multi-steady-state, unstable-steady-state character);
- provides an unexpected payoff in the form of an important kinetic parameter, the "separatrix";
 - has physically simple character, and the astonishingly simple dimensions of entropy units.
- Weaknesses: ● ?

Some additional comments on Tables 4 and 5 are in order.

With respect to integral-differential relationships, customarily, entropy production, $\dot{P}$, is thought of as the differential of (an) entropy, rather than entropy being viewed as an integral of the $\dot{P}$ function. Such thinking, which carries the implication that the entropy is "more fundamental" than $\dot{P}$, is rooted in the classical thermodynamical focus on reversible systems and their evolution toward

the equilibrium endpoint. It may be argued that more fundamental is the notion of evolution to general endpoints, virtually all of which are nonequilibrium in character. In this view, dynamic, irreversible systems become the natural starting point, and reversible or equilibrium-bound systems only a special, limiting case. Indeed, as already mentioned, this more general view is the proper one for modeling the evolutionary (and stability) properties of living systems from a thermodynamic-potential perspective. Thus, S_{tot} might better be considered to be founded on ϕ (in the form of its integral), than the reverse.

In that spirit, the "integral definition" of ϕ in terms of a dynamic quantity, $\mathcal{M}$, is most natural, perhaps providing a measure of "independent validity" for ϕ , by noting that its origins are entirely analogous in kind to those of the entropy itself.* At the very least, by virtue of the nature of its origins as well as the identity of its dimensionality with entropy, one can say that ϕ is conceptually in very good company.

D. STEADY STATE VALUES OF THE POTENTIAL FUNCTIONS

Another difference which exists between ϕ and the other thermodynamic potential functions of Tables 4 and 5 which has not previously been commented on is one which relates to their steady state values. The functions S , ϕ , and $\mathcal{M}$ are all absolute functions in the sense that they possess defined, nonzero values in their respective steady state

* This is speaking within the present macroscopic rather than probabilistic context, of course.

endpoints. The entropy (whether in its steady state, i.e. equilibrium, state or not) derives its absolute value from the third law of thermodynamics. The function ρ^{SS} , expressed as $\sum_i A_i^{SS} \cdot v_i^{SS}$, is likewise defined absolutely since all A_i^{SS} and v_i^{SS} have absolute values calculable from the particular steady state concentrations. Given its identity with ρ^{SS} , J^{SS} likewise has no indeterminacy.*

Given the origins of ϕ solely in terms of an integral, without additional information it must be considered defined only in a relative sense. That is, its definition in terms of $(J - J^{SS})$ —as an "integrated relative J "—assures its vanishing in the steady state, but provides no information as to an absolute value which would differ from one steady state to another. Thus, with respect to numerical values for ϕ , these always measure a system's "distance" from its endpoint, but do not allow going beyond this to compare different endpoints. (Note that had the entropy been given its macroscopic origins as the integral of the ρ function, as discussed above, additional information would have been required for it, as well, to evaluate the constant of integration, and to enable the definition of S to be more than a relative one.) For J and ρ in multiple steady state systems, the different absolute values of $J^{SS} = \rho^{SS}$ do allow ordering the steady states themselves in terms of the levels of their respective dissipations.

* In systems with more than one steady state, both ρ^{SS} and J^{SS} evidently have values which depend on the particular steady state from which the parameters are derived.

A possible approach to arriving at an absolute value for ϕ may be found by considering the form taken by functions in Table 5, in the case of simplified example-systems. For instance, consider chemical reaction systems of the following character: (a) evolving toward an equilibrium endpoint; (b) a-thermal as well as isolated, whereby $dS_{\text{syst}} = dS_{\text{tot}} \geq 0$; (c) chemical reaction systems (properly written in their phenomenologically uncoupled form) operating solely within the linear-law dynamic region. Under these circumstances several simplifications apply to the functions and expressions of Table 5:

$$M^{ss} = M^{eq} = P^{eq} = 0 \quad (\text{Eqn 103})$$

and

$$M = P \quad (\text{Eqn 104})$$

Substituting Equation 103 and 104 as well as condition (b) in the paragraph above, into the two left-hand expressions of Table 5, adding the two expressions, then integrating, yields:

$$\phi_{\text{system}} + S_{\text{system}} = \phi_{\text{system}}^{\text{equil}} + S_{\text{system}}^{\text{equil}} \quad (\text{Eqn 105})$$

A simple and obvious choice for the constant of integration, $\phi_{\text{system}}^{\text{equil}}$, in this special situation is:

$$\phi_{\text{system}}^{\text{equil}} = S_{\text{system}}^{\text{equil}} \quad . \quad (\text{Eqn } 106)$$

Such a choice would further strengthen the "interface" between ϕ and S : these two functions would become identical in content as well as in units, at the equilibrium endpoint.

What about the general situation, in the nonlinear domain and with far-from-equilibrium endpoints. Generalizing Equation 108, again in the simplest and most natural way, would lead to:

$$\phi_{\text{system}}^{\text{ss}} = S_{\text{system}}^{\text{ss}} \quad . \quad (\text{Eqn } 107)$$

This choice would also provide an additional feature of comparability, a pair wise comparability of $\phi - S$ with $M - P$ vis a vis their steady states. That is, the relationship $\phi^{\text{ss}} = S^{\text{ss}}$ is formally equivalent to the general relationship, $M^{\text{ss}} = P^{\text{ss}}$. (Note that this latter arises in a nonarbitrary fashion since the definition of M does not carry with it any indeterminacy.)

If there is no inherent impediment to making an arbitrary choice of ϕ^{ss} , then a choice according to Equation 109 could be viewed as completing the definition of ϕ , beyond the original differential definition provided by Equation 1. At this point it remains to be seen whether some other nonarbitrary basis or relation exists for arriving at a different value and choice for ϕ^{ss} , thereby otherwise recasting our relative ϕ in the form of an absolute ϕ . Whether or not this can

be accomplished, however, is not central to the utility of the ϕ function, any more than it is to the normal uses of the usual functions of reversible thermodynamics (internal energy and its derivative free energies, etc.): in general it is only ΔE , ΔG , etc. that are of interest.

E. FUTURE DIRECTIONS

Having presented in this paper the theoretical development of the ϕ function, plus a detailed examination of its application to two kinds of chemical reaction systems, it is in order to glance briefly at priority items for future work. Four of these stand out, three by way of different classes of example-systems to be addressed, the fourth a parallel development of a different (but closely related) theoretical function, the " Π " function.

Diffusion-Reaction System. The reaction systems treated herein (Table 1), though of broad generality and validity, are still limited to homogeneous systems, purely chemical in nature. An obvious, extended class of far-from-equilibrium systems to investigate with respect to its ϕ properties is that involving both the transport process of diffusion, and chemical reaction. To proceed requires only a slight generalization of the definition of the J and ϕ functions, whereby we would write:

$$TJ = \sum_i \alpha_i X_i^2, \quad (\text{Eqn } 108)$$

where the X_i are the generalized thermodynamic driving forces (including the chemical affinities, for pure reactions, and the negative chemical potential differences/gradients for the diffusional processes). The calculation of ϕ and evaluation of its extremum and other properties would then proceed from Equation 2 as before, but now using the enlarged definition of J from Equation 108.

Limit Cycles. The second class of example is still one founded on open-system, homogeneous reaction kinetics of purely chemical systems,

but a class exhibiting a kind of nonequilibrium endpoint that has not yet been addressed--a limit cycle (7). As for the diffusion-reaction example, a simple generalization of the formalism is also required, in this case one dealing with the nature of the steady state. Though a limit cycle endpoint is clearly not "steady" (in the sense of maintaining the time-invariance of all concentrations/activities) it still represents an identical kinetic limiting condition on the dynamic equations, the condition corresponding to $t \rightarrow \infty$. Thus, the generalization of $\mathcal{M}$ in this case is one that is applicable only to the term $\mathcal{M}^{ss}$, namely:

$$\mathcal{M}^{ss} \rightarrow \mathcal{M}^{t \rightarrow \infty} . \quad (\text{Eqn 109})$$

With this generalization we again can proceed with the evaluation of ϕ using Equation 2. It remains to be seen whether the integrand of Equation 2 vanishes sufficiently rapidly, as the limit-cycle endpoint is approached, so that the integral remains finite and well-behaved.

Chaos. Another class of endpoints serving the evolution of nonequilibrium systems, one attracting much attention in recent times, is the condition referred to as chaos (15). To the extent that limit cycles may be considered to be the step beyond steady states, chaotic endpoints, with their irregular and unpredictable cyclings, may be viewed as the step beyond limit cycles. The path toward chaos may include bifurcation-instabilities (15) not unlike the one we have analyzed in this paper. Still an open question: what kind of behavior would/should an ideal thermodynamic potential exhibit in tracking (the evolution toward) such an endpoint?

The Π Function. A great deal of attention has been paid in the past to the inexact-differential character of the two partial differentials of the entropy production, $\mathcal{P}$, the so-called $d_X \mathcal{P}$ and $d_J \mathcal{P}$ terms for chemical reaction systems (7). This character renders either of these terms, individually, unsuitable for integration to yield a global thermodynamic potential function. (The validity of the $d_X \mathcal{P}$ term as a test and indicator of stability--Prigogine's "universal stability criterion"--has been well-established, however (7).)

It happens that by only a "modest" transformation, the incomplete differential $d_X \mathcal{P}$ can, in fact, be converted to an integral form which defines Π --another "candidate global thermodynamic potential function." The transformation is simply:

$$d_X \mathcal{P} \rightarrow \frac{d_X \mathcal{P}}{dt} \quad (\text{Eqn 110})$$

(It might even be argued that this transformation is not so much a change as an interpretation of the reasonable meaning of $d_X \mathcal{P}$, in the same sense that a common, reasonable meaning of the expression dS is that it refers to entropy changes in time.)

A start has been made on the development and analysis of this Π function, and some of the results to date have been summarized in Appendix B. Three particular points are worth noting here: 1) this function possesses the same far-from-equilibrium domain of validity as does ϕ ; 2) with Π , it offers no particular simplification, and therefore it is not necessary, to restrict the kinetic equations to those of just 2-body interactions. These equations are therefore left

in the form of more general n -body interactions, which might permit treating of more exotic processes, such as those occurring in highly condensed states of matter, for example; and 3) the units of $\mathbb{A}$ are the same as those of $\mathcal{P}$ and $\mathcal{M}$; in this sense and in its form (founded on the same basic components as are the $\mathcal{P}$ and $\mathcal{M}$ functions--reaction velocities and affinities) it is a function closely linked, conceptually, to the other functions of Table 5. Further work is necessary to clarify these relationships, and the ultimate status as a generalized thermodynamic potential function.

V. APPENDIX A: THE JM FUNCTION

The "affinity squared minimum function," JM , is defined for a system of i chemical reactions as follows:

$$JM = \sum_i \alpha_i A_i^2, \quad (\text{Eqn 111})$$

where T is the absolute temperature of the isothermal system, and

where A_i is the affinity of the i^{th} reaction, given by:

$$A_i = - \sum_Y \nu_{Y,i} \mu_Y. \quad (\text{Eqn 112})$$

The $\nu_{Y,i}$ are the stoichiometric coefficients for the i^{th} reaction,

and the μ_Y are the chemical potentials, both applicable to the species, Y . For what follows, we assume two independent concentration (activity) variables, x and y .

The choice of the constants, α_i , derives from two requirements: first that JM is a state function, i.e. that $\frac{\partial}{\partial x}(\frac{\partial(JM)}{\partial y})_x = \frac{\partial}{\partial y}(\frac{\partial(JM)}{\partial x})_y$; and second that $(\frac{\partial(JM)}{\partial x})_y = 0$ and $(\frac{\partial(JM)}{\partial y})_x = 0$ at (and only at) all steady states of the system. The algebraic forms of the various partial derivatives of JM follow from Equation 111:

$$(\frac{\partial(JM)}{\partial x})_y = 2 \sum_i \alpha_i A_i (\frac{\partial A_i}{\partial x})_y \quad (\text{Eqn 113})$$

$$(\frac{\partial(JM)}{\partial y})_x = 2 \sum_i \alpha_i A_i (\frac{\partial A_i}{\partial y})_x. \quad (\text{Eqn 114})$$

From Equation 112, we see that:

$$\left(\frac{\partial A_i}{\partial x}\right)_y = - v_{x,i} \frac{d\mu_x}{dx} \quad (\text{Eqn 115})$$

and

$$\left(\frac{\partial A_i}{\partial y}\right)_x = - v_{y,i} \frac{d\mu_y}{dy} \quad (\text{Eqn 116})$$

where:

$$v_{x,i} = \begin{cases} n, & \text{if } n \text{ x's are produced by reaction } i \\ 0, & \text{if no net x is produced or consumed } \\ -n, & \text{if } n \text{ x's are consumed by reaction } i \end{cases} \quad (\text{Eqn 117})$$

and similarly for $v_{y,i}$.

We note that Equations 115, 116 and 117, taken collectively, summarize in a slightly different form the formal algebra of the intrinsic network "flow-through" relation:

$$\left(\frac{\partial A_i}{\partial x}\right)_y = - \left(\frac{\partial A_{i+1}}{\partial x}\right)_y \quad (\text{Eqn 118})$$

where x is "produced" by the single reaction i , and "consumed" by a single subsequent reaction $i + 1$ (8). We choose to introduce the alternative forms (Equations 115-117) of this (local) "flow through" connectivity relation, because these afford ease of algebraic manipulation as well as generalization to arbitrary networks in what follows.

Upon substitution of Equations 115 and 116 into Equations 113 and 114 we obtain the intermediate result:

$$\left(\frac{\partial (TM)}{\partial x}\right)_y = - 2 \frac{d\mu_x}{dx} \sum_i a_i A_i v_{x,i} \quad (\text{Eqn 119})$$

$$\left(\frac{\partial(T_M)}{\partial y}\right)_x = - 2 \frac{d\mu_y}{dy} \sum_i \alpha_i A_i v_{y,i} \quad (\text{Eqn 120})$$

The vanishing of the various partial derivatives of T_M at all steady states may be assured mathematically by expressing them in terms of any quantities that vanish identically in the stationary state. Since the fundamental, kinetic feature of the steady state is the time-invariance of the intensive (here: activity) variables of the system, obvious choices for such vanishing quantities are the $\frac{dx}{dt}$ and $\frac{dy}{dt}$ of the system. In this sense we can write:

$$\begin{aligned} \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \left(\frac{\partial(T_M)}{\partial x}\right)_y \right\} &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{dx}{dt} \right\} \\ &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i \left(\frac{dx}{dt}\right)_i \right\} \\ &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i v_{x,i} v_i \right\}; (\text{Eqn 121}) \end{aligned}$$

and:

$$\begin{aligned} \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \left(\frac{\partial(T_M)}{\partial y}\right)_x \right\} &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \frac{dy}{dt} \right\} \\ &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i \left(\frac{dy}{dt}\right)_i \right\} \\ &= \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i v_{y,i} v_i \right\}; (\text{Eqn 122}) \end{aligned}$$

where $v_i = \frac{1}{v_{x,i}} \left(\frac{dx}{dt} \right)_i = \frac{1}{v_{y,i}} \left(\frac{dy}{dt} \right)_i$ is the reaction (net velocity) of the i^{th} reaction in an arbitrary network.

Substituting Equations 119 and 120 into Equations 121 and 122 leads to:

$$\text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ -2 \frac{d\mu}{dx} \sum_i \alpha_i A_i v_{x,i} \right\} = \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i v_{x,i} v_i \right\} \quad (\text{Eqn 123})$$

and

$$\text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ -2 \frac{d\mu}{dy} \sum_i \alpha_i A_i v_{y,i} \right\} = \text{Limit}_{x,y \rightarrow x^{ss}, y^{ss}} \left\{ \sum_i v_{y,i} v_i \right\} \quad (\text{Eqn 124})$$

The simplest means of assuring the validity of Equations 123 and 124 in the steady state, is by equating their left and right "summons" on a term-by-term basis. This yields for the α_i :

$$\alpha_i = \frac{v_i^{ss}}{A_i^{ss}} \quad . \quad (\text{Eqn 125})$$

Such a choice for the α_i guarantees the vanishing of the various partials of $\mathcal{T}\mathcal{M}$ at (and only at) the steady states of the system. Together with the De Donder inequality, $A v \geq 0$, (1), this also assures that all $\alpha_i > 0$ for all elementary chemical reactions of the network (such reactions are inherently uncoupled, in a phenomenological sense). This sign restriction on the α_i renders $\mathcal{T}\mathcal{M}$ from Equation 111 a positive-definite quadratic form, which in turn requires that all extrema are minima. This choice of the α_i leads to the simplest possible interface between $\mathcal{M}$ and $\mathcal{P}$ in the steady state, namely:

$$\mathcal{M}^{ss} = \mathcal{P}^{ss}.$$

VI. APPENDIX B: THE $\mathcal{A}$ FUNCTION

For any open, chemical reaction system, the $\mathcal{A}$ function is defined from its time derivative form, in terms of the velocities, v_i , and affinities, A_i , of the i chemical reactions, as follows:

$$\frac{d\mathcal{A}}{dt} = \sum_i v_i \frac{dA_i}{dt} , \quad (\text{Eqn 126})$$

and

$$\mathcal{A}(x) - \mathcal{A}(x^{ss}) = - \int_0^\infty \sum_i v_i \frac{dA_i}{dt} dt , \quad (\text{Eqn 127})$$

where the v_i are the velocities and A_i are the affinities of the $i = 1$ to n reactions in the system.

To illustrate the analytical properties of $\mathcal{A}$, we consider an open, chemical reaction network system involving the intermediate concentration variables x and y along with the fixed concentrations A and B of the reactants and products, these latter two held constant so as to prevent the system from attaining equilibrium. Such chemical reaction network systems could involve any number of individual reactions arranged with arbitrary network connectivity.

The time derivative of $\mathcal{A}$ is given directly by the defining relation, Equation 126 and may be evaluated by noting the following three facts.

First, from the state function character of the affinity we can write:

$$dA = \left(\frac{\partial A}{\partial x} \right)_y dx + \left(\frac{\partial A}{\partial y} \right)_x dy ; \quad (\text{Eqn 128})$$

this implies that:

$$\frac{dA}{dt} = \left(\frac{\partial A_i}{\partial x}\right)_y \frac{dx}{dt} + \left(\frac{\partial A_i}{\partial y}\right)_x \frac{dy}{dt} \quad , \quad (\text{Eqn 129})$$

which allows $\frac{d\eta}{dt}$ in Equation (126) to be written in the expanded form:

$$\frac{d\eta}{dt} = \sum_i v_i \left[\left(\frac{\partial A_i}{\partial x}\right)_y \frac{dx}{dt} + \left(\frac{\partial A_i}{\partial y}\right)_x \frac{dy}{dt} \right] \quad . \quad (\text{Eqn 130})$$

Second, the form of the affinity (Equation 112) assures that the various partial derivatives have the form given in Equations 115 and 116, i.e.:

$$\left(\frac{\partial A_i}{\partial x}\right)_y = - v_{x,i} \frac{d\mu_x}{dx} \quad , \quad (\text{Eqn 131})$$

and

$$\left(\frac{\partial A_i}{\partial y}\right)_x = - v_{y,i} \frac{d\mu_y}{dy} \quad . \quad (\text{Eqn 132})$$

Third, $\frac{dx}{dt}$ and $\frac{dy}{dt}$ may be written (from Equations 121 and 122) as:

$$\frac{dx}{dt} = \sum_i \left(\frac{dx}{dt}\right)_i = \sum_i v_{x,i} v_i \quad , \quad (\text{Eqn 133})$$

and

$$\frac{dy}{dt} = \sum_i \left(\frac{dy}{dt}\right)_i = \sum_i v_{y,i} v_i \quad . \quad (\text{Eqn 134})$$

Substituting Equations 131 and 132 into Equation 130, gives the result:

$$\frac{d\pi}{dt} = - \frac{d\mu_x}{dx} \frac{dx}{dt} \sum_i v_{x,i} v_i - \frac{d\mu_y}{dy} \frac{dy}{dt} \sum_i v_{y,i} v_i \quad (\text{Eqn 135})$$

Substitution of Equations 133 and 134 into Equation 135 yields:

$$\frac{d\pi}{dt} = - \frac{d\mu_x}{dx} \left(\frac{dx}{dt}\right)^2 - \frac{d\mu_y}{dy} \left(\frac{dy}{dt}\right)^2 \quad (\text{Eqn 136})$$

By inspection, this function is seen to vanish at all steady states of the system. Furthermore, since the chemical potential is always an increasing function of activity, $\frac{d\pi}{dt}$ must be negative for all other values of (x,y) . Thus, $\frac{d\pi}{dt}$ is negative-definite, and π , itself, is seen to be a decreasing function of time for all $t \geq 0$.

The analytical demonstration of the extremum properties of the $\pi(x,y)$ surface is similar to that presented for the ϕ function. It follows from an analysis of particular, infinitesimal perturbations away from a stationary state, to nearby positions in (x,y) space, along one or the other of the general curves: $\frac{dx}{dt} = 0$, or $\frac{dy}{dt} = 0$.

The time derivative, $\frac{d\pi}{dt}$, along the curve $\frac{dx}{dt} = 0$ is given by:

$$\frac{d\pi}{dt} = \left(\frac{\partial \pi}{\partial y}\right)_x \frac{dy}{dt} \quad (\text{Eqn 137})$$

Along this same curve, $\frac{d\pi}{dt}$ in Equation 136 simplifies to:

$$\frac{d\pi}{dt} = - \frac{d\mu_y}{dy} \left(\frac{dy}{dt}\right)^2 \quad (\text{Eqn 138})$$

enabling us to write:

$$\left(\frac{\partial \Pi}{\partial y}\right)_x = - \frac{d\mu_y}{dy} \frac{dy}{dt} . \quad (\text{Eqn 139})$$

Similarly, along the curve, $\frac{dy}{dt} = 0$, we have:

$$\left(\frac{\partial \Pi}{\partial x}\right)_y = - \frac{d\mu_x}{dx} \frac{dx}{dt} . \quad (\text{Eqn 140})$$

The vanishing of both the partial derivatives of $\Pi(x,y)$ at all steady states of the system, thus establishes the extremum principle. By a similar argument to that presented in Section II.D3, these extrema (for stable stationary states) are true minima.

VII. ACKNOWLEDGMENTS

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VIII. BIBLIOGRAPHY

1. Prigogine, I.: Etude Thermodynamique des Phenomenes Irreversible, Editions Desoer, Liege, 1947, Chapter 5.
2. Prigogine, I.: Introduction to Thermodynamics of Irreversible Processes, 3rd Edition, John Wiley/Interscience, New York 1967, Chapter 6.
3. Prigogine, I. and I. Stengers: Order Out of Chaos, Bantam Books, New York, 1984, pp. 138-141. (Based on the authors' "La Nouvelle Alliance", Editions Gallimard, Paris, 1979.)
4. Glansdorff, P. and I. Prigogine: Thermodynamic Theory of Structure, Stability and Fluctuations, John Wiley/Interscience, New York, 1971, Chapter 10.
5. Prigogine, I., G. Nicolis and A. Babloyantz: Thermodynamics of Evolution, Physics Today, 25, No. 11, 23-28 (1972).
6. idem, 25, No. 12, 38-44 (1972).
7. Nicolis, G. and I. Prigogine: Self Organization in Nonequilibrium Systems, Wiley/Interscience, New York, 1977, p. 50.
8. Mel, H. C. and D. A. Ewald: Thermodynamic Potentials and Evolution Towards the Stationary State in Open Systems of Far-from-equilibrium Chemical Reactions: The Affinity Squared Minimum Function, J. Mathematical Biology 1, 133-151 (1974).
9. Bash, P. A.: Analysis of the "Edelstein" Chemical Reaction System Using the Affinity Squared Minimum Function. Senior Honors Thesis, University of California, Berkeley, Department of Biophysics and Medical Physics, 1974.

10. Biot, M. A.: New Variational-Lagrangian Irreversible Thermodynamics with Application to Viscous Flow, Reaction-Diffusion, and Solid Mechanics, in Advances in Applied Mechanics, J. W. Hutchinson and T. Y. Wu, Editors, Vol. 24, Academic Press, Inc., New York, 1984, pp. 1-89.
11. Thom, R.: Structural Stability and Morphogenesis, Benjamin/Cummings Publishing Co., Reading MA. (1975).
12. Lewin, L.: Dilogarithms and Associated Functions, Macdonald, London, 1958.
13. Edelstein, B. B.: Biochemical Model with Multiple Steady States and Hysteresis, J. Theoretical Biology 29, 57-62 (1970).
14. Edelstein, B. B.: "The Dynamics of Cellular Differentiation and Associated Pattern Formation, J. Theoretical Biology 37, 221-243 (1972).
15. Olsen, L. F. and H. Degn: Chaos in Biological Systems, Quarterly Review of Biophysics 18, 165-225 (1984).

IX. FIGURES

Figure 1. The integral (variable) portion of the thermodynamic potential, $\phi(x) - \phi(x^{ss})$, from Equation 82, plotted as a function of $z = \frac{x}{x^{ss}}$, for the reaction system $A \xrightleftharpoons{x} B$.

(See note page 38 regarding the equivalence of x and x° , z and z° .)

Figure 1

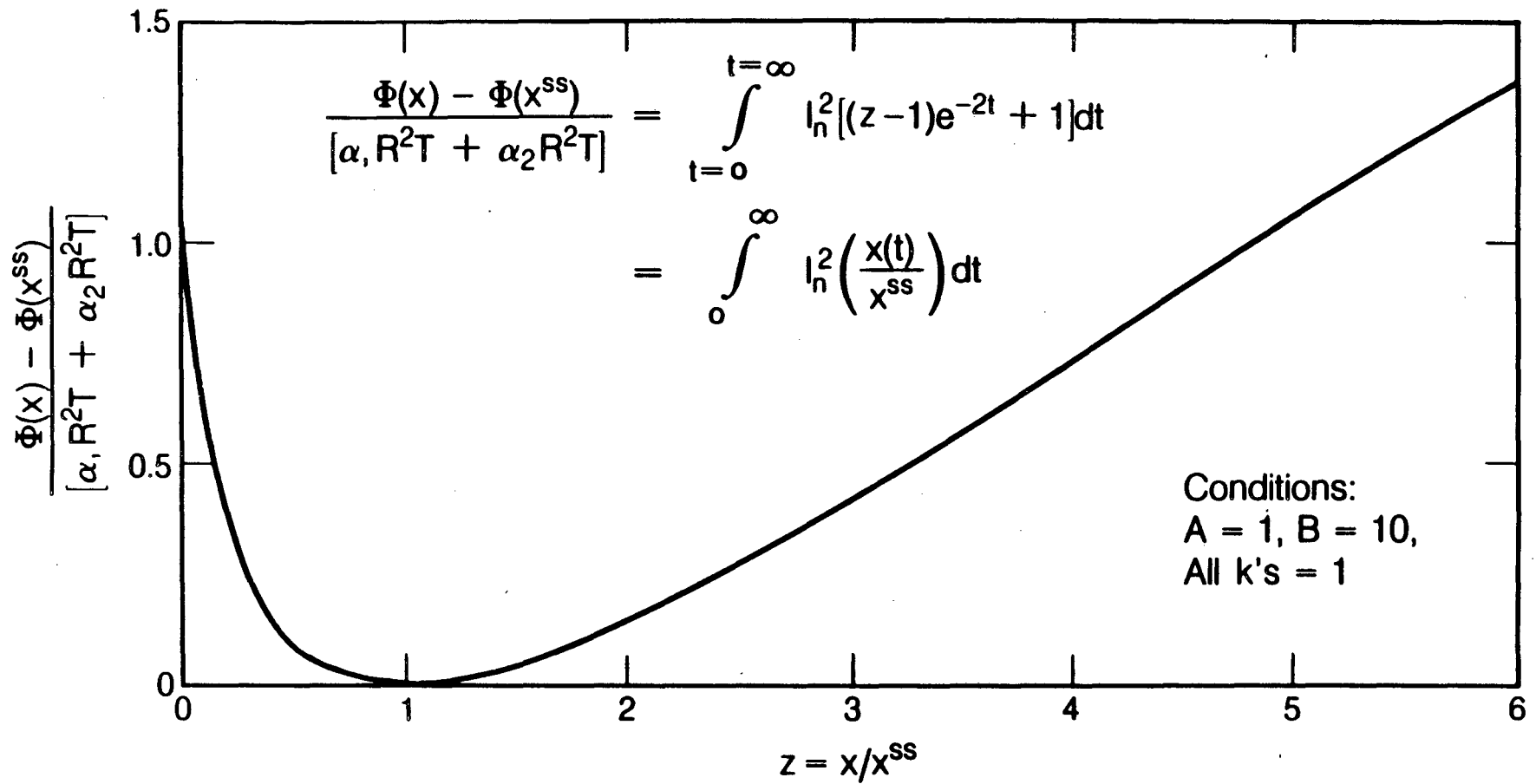
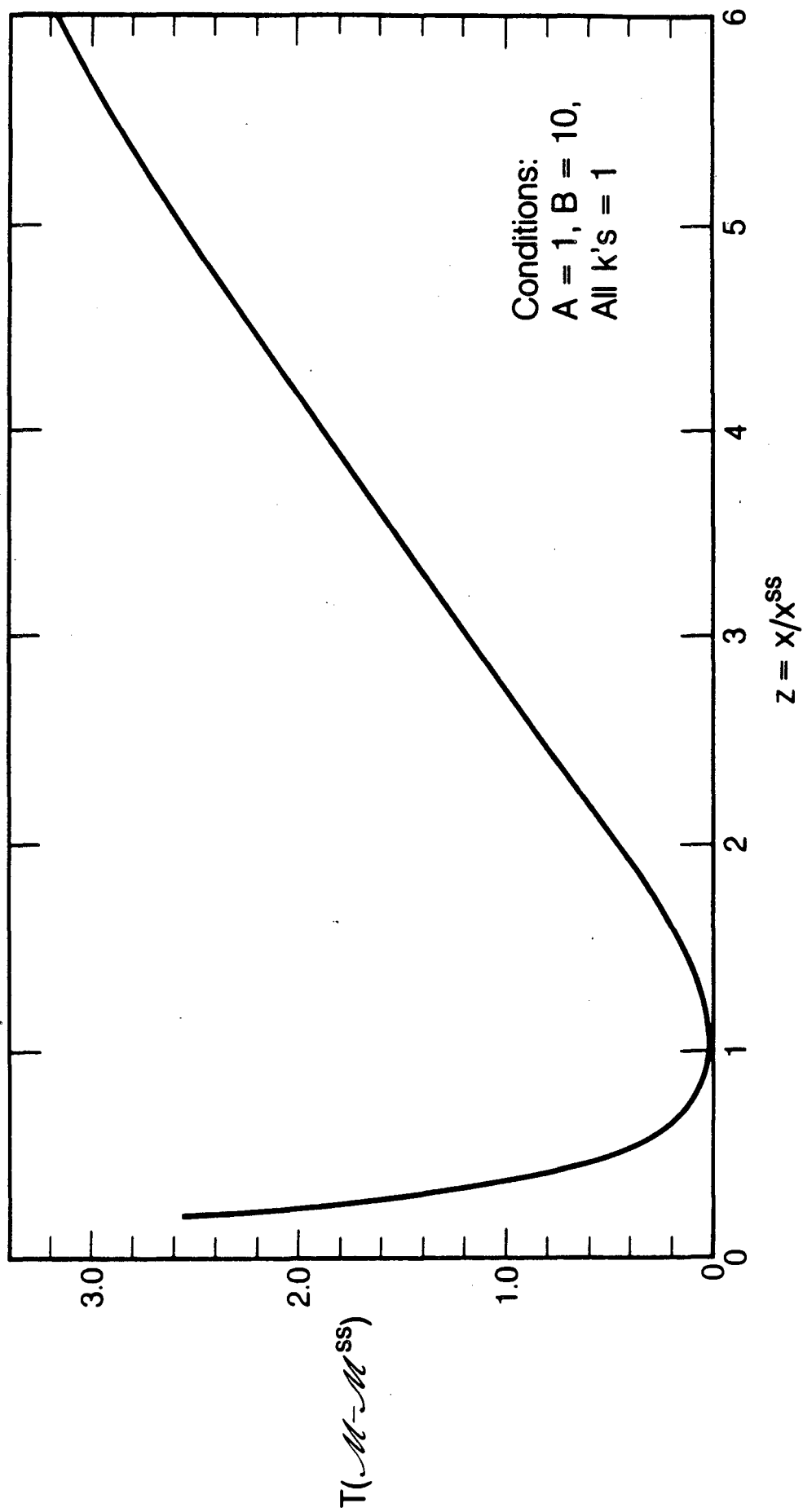


Figure 2. The "kinetically-weighted system-free-energy" quantity,

$T(M_{ss})$, as a function of $\frac{x}{x_{ss}}$ for the reaction system $A \xrightleftharpoons[k_{-1}]{k_1} x \xrightleftharpoons[k_{-2}]{k_2} B$.

Figure 2



XBL 848-7846

Figure 3. The dissipation function, $\mathcal{TP}$, plotted versus $\frac{x}{x_{ss}}$, for the reaction system $A \xrightleftharpoons[k_{-1}]{k_1} x \xrightleftharpoons[k_{-2}]{k_2} B$, for the same nonequilibrium conditions as for Figures 1 and 2 (solid curve). For comparison we have also plotted this function for "equilibrium conditions" (dashed curve), for which $\mathcal{TP}$ regains its thermodynamic potential character.

Figure 3

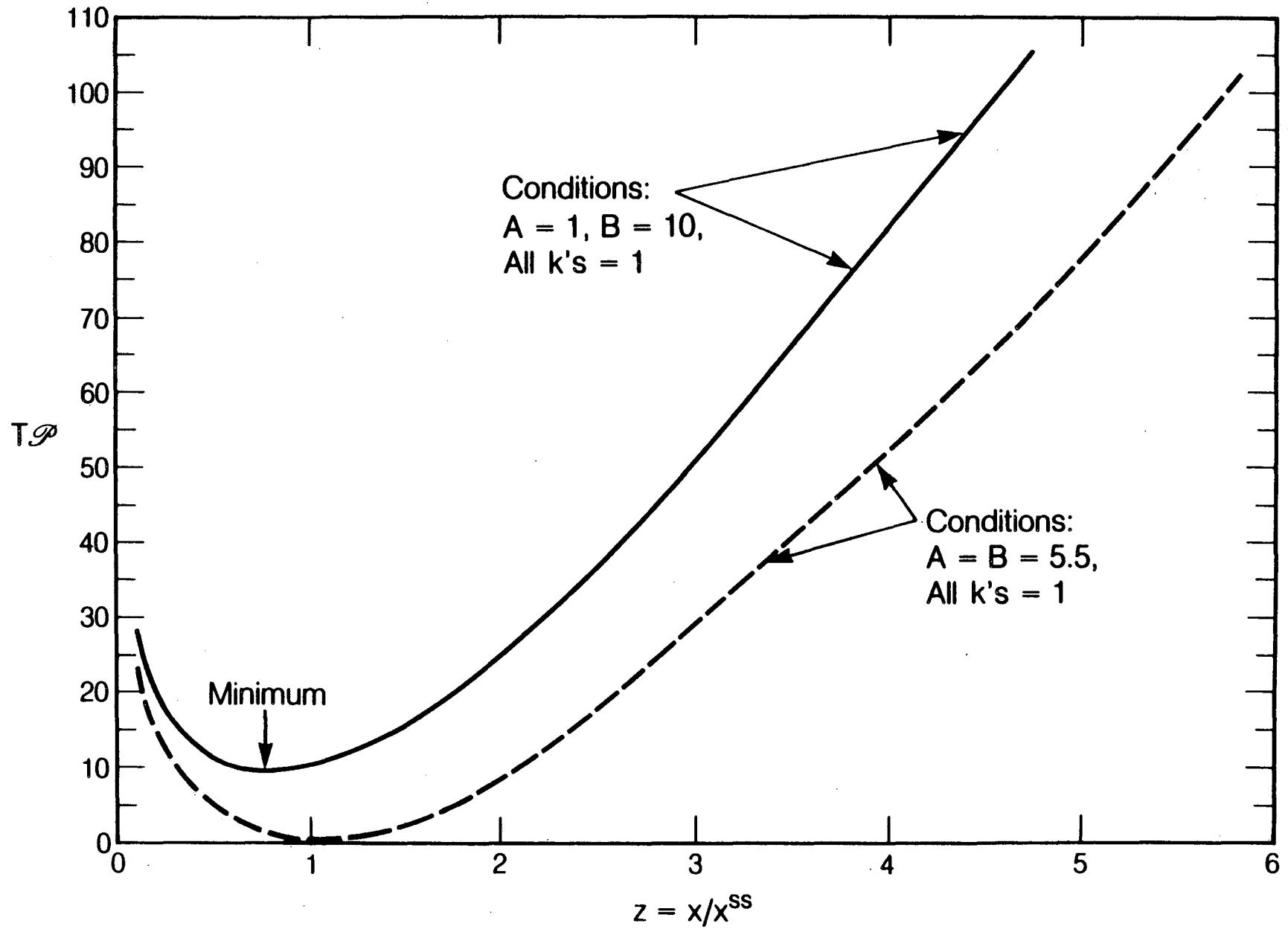
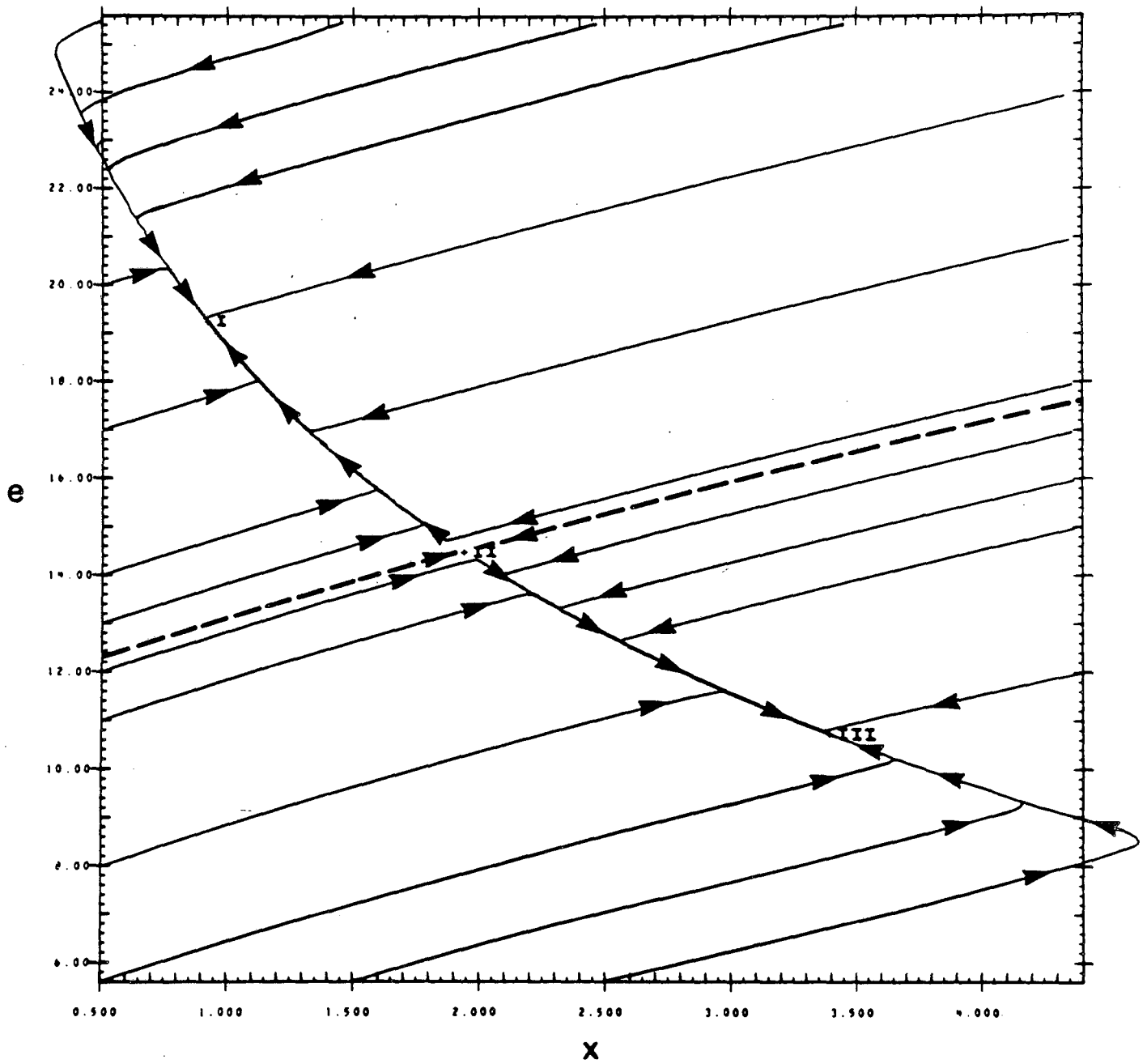


Figure 4. Kinetic trajectories in the x, e phase plane for the "Edelstein" system (Equations 101--2), for the boundary conditions which give rise to two stable steady state end points (I, III), and one unstable steady state endpoint (II). The dashed line depicts the position of the separatrix, which separates the two kinetic regions of stability. (A duplicate of this figure for overlay purposes, in the form of a transparency, Figure 4T, is to be found in the back-cover pocket.)

Figure 4

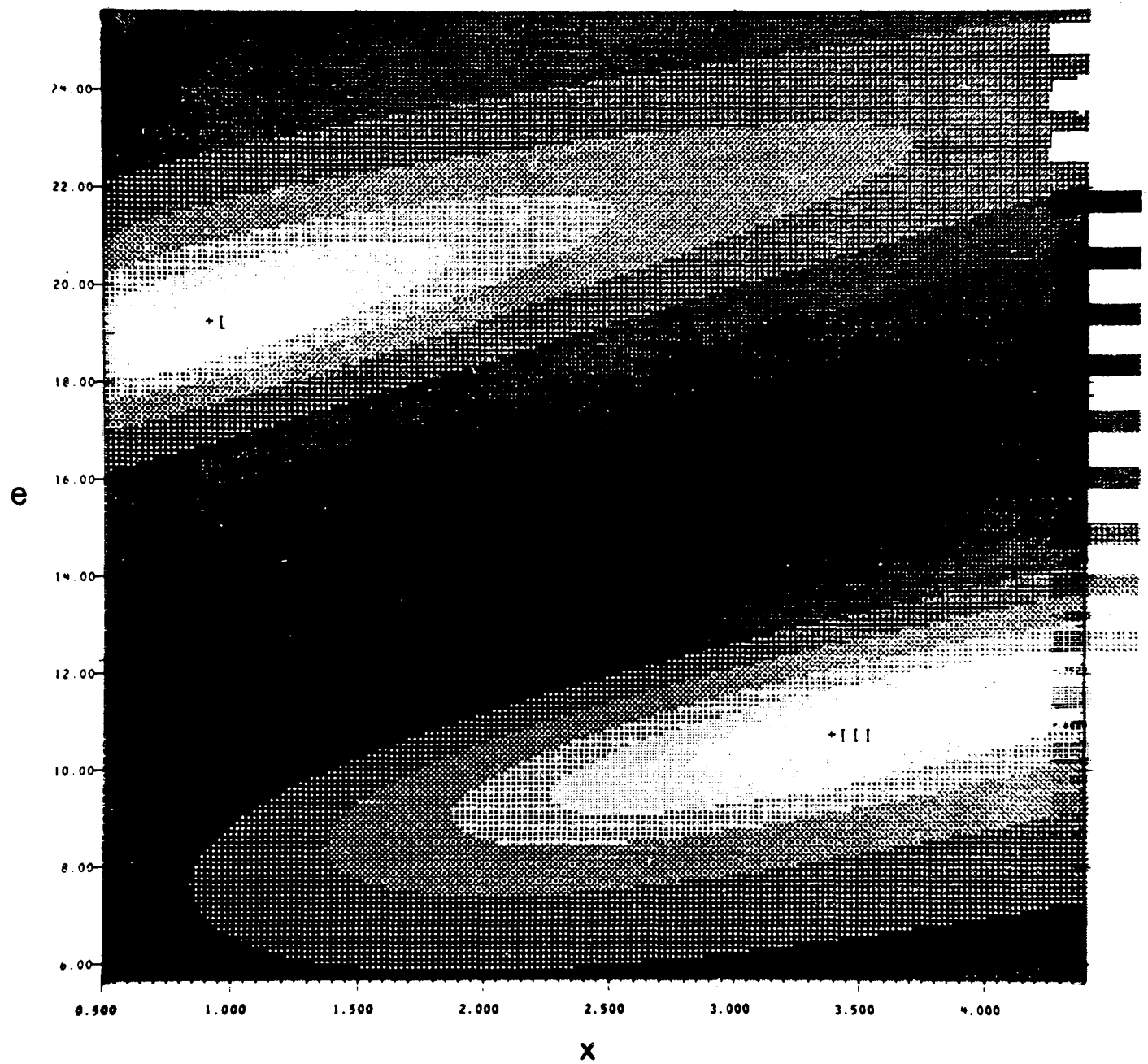
EDELSTEIN, GLOBAL



XBL 866-8813

Figure 5. Shaded contour map of the variable portion of the ϕ -function surface, calculated from Equation 2, for the autocatalytic "Edelstein" reaction system of Equations 93-95, under the same boundary conditions as for Figure 4. The separatrix has been emphasized by the dashed line. (Note that the transparency, Figure 4T, can serve as an overlay for Figures 5 and 6.)

Figure 5

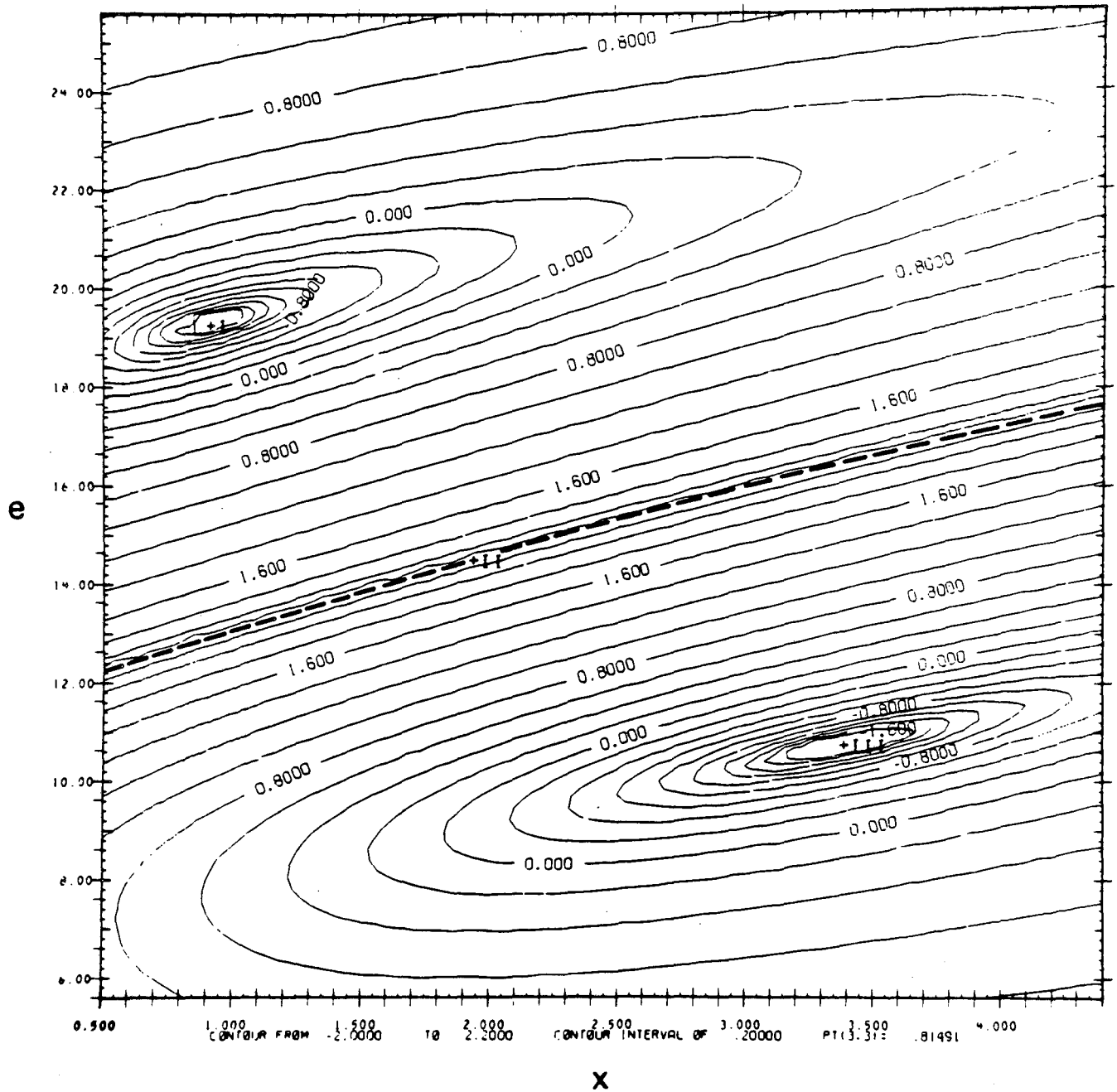


XBL 866-8814

Figure 6. Selected contours of the variable portion of the ϕ -function surface corresponding to the shaded-contour map of Figure 5.

Figure 6

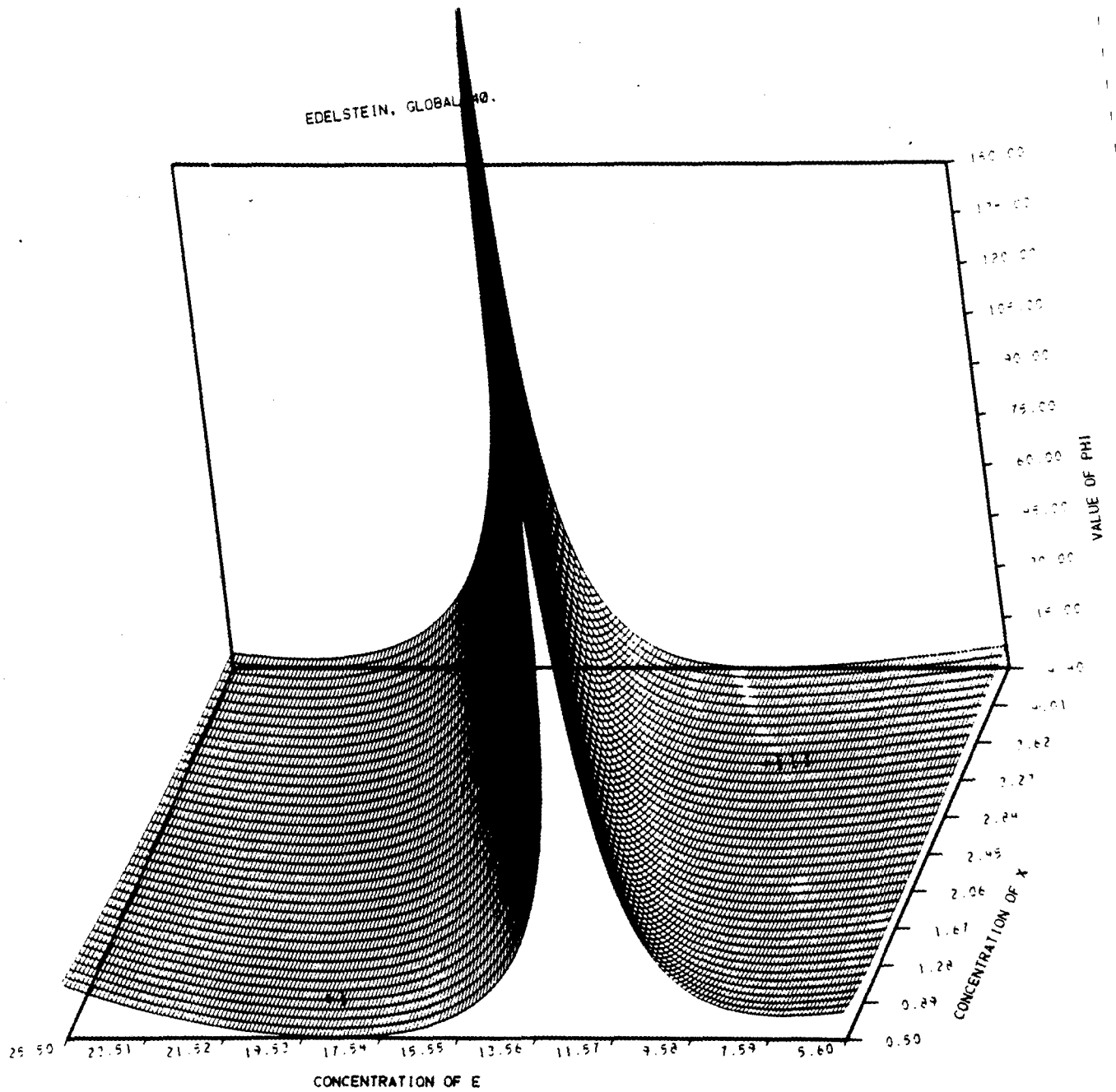
EDELSTEIN, GLOBAL



XBL 866-8815

Figure 7. Three-dimensional Cal-Comp plot of the variable portion of the ϕ -function surface for the multistationary state "Edelstein" reaction system of Figure 5. This viewing angle and coordinate scaling were chosen to best illustrate the cusp-like character of the surface in the vicinity of the separatrix. The minimum-extremum nature of the two stable stationary states (I and II) is best seen in Figures 6 and 5.

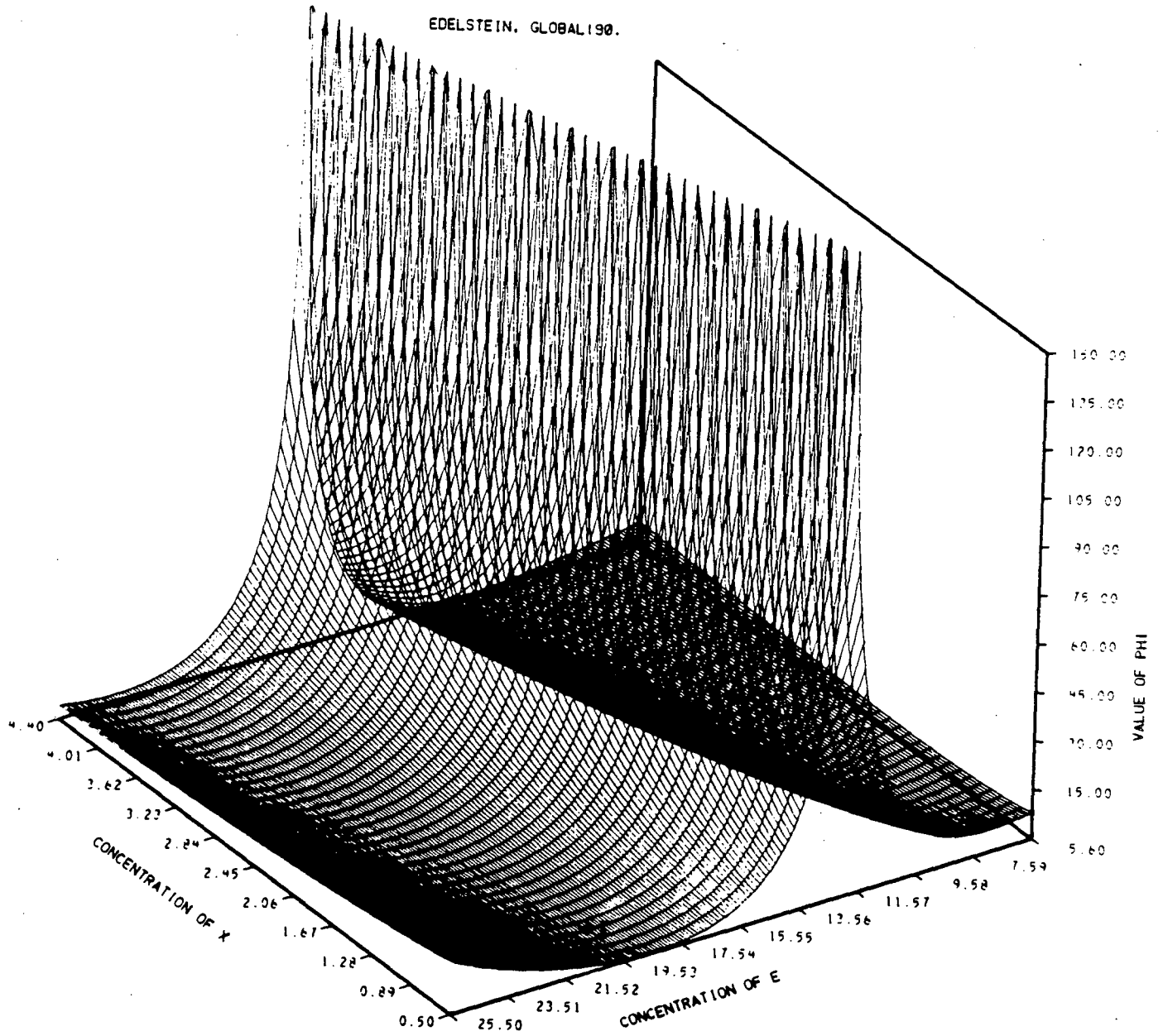
Figure 7



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Figure 8. Another three-dimensional view of the variable portion of the ϕ -function surface for the "Edelstein" reaction system.

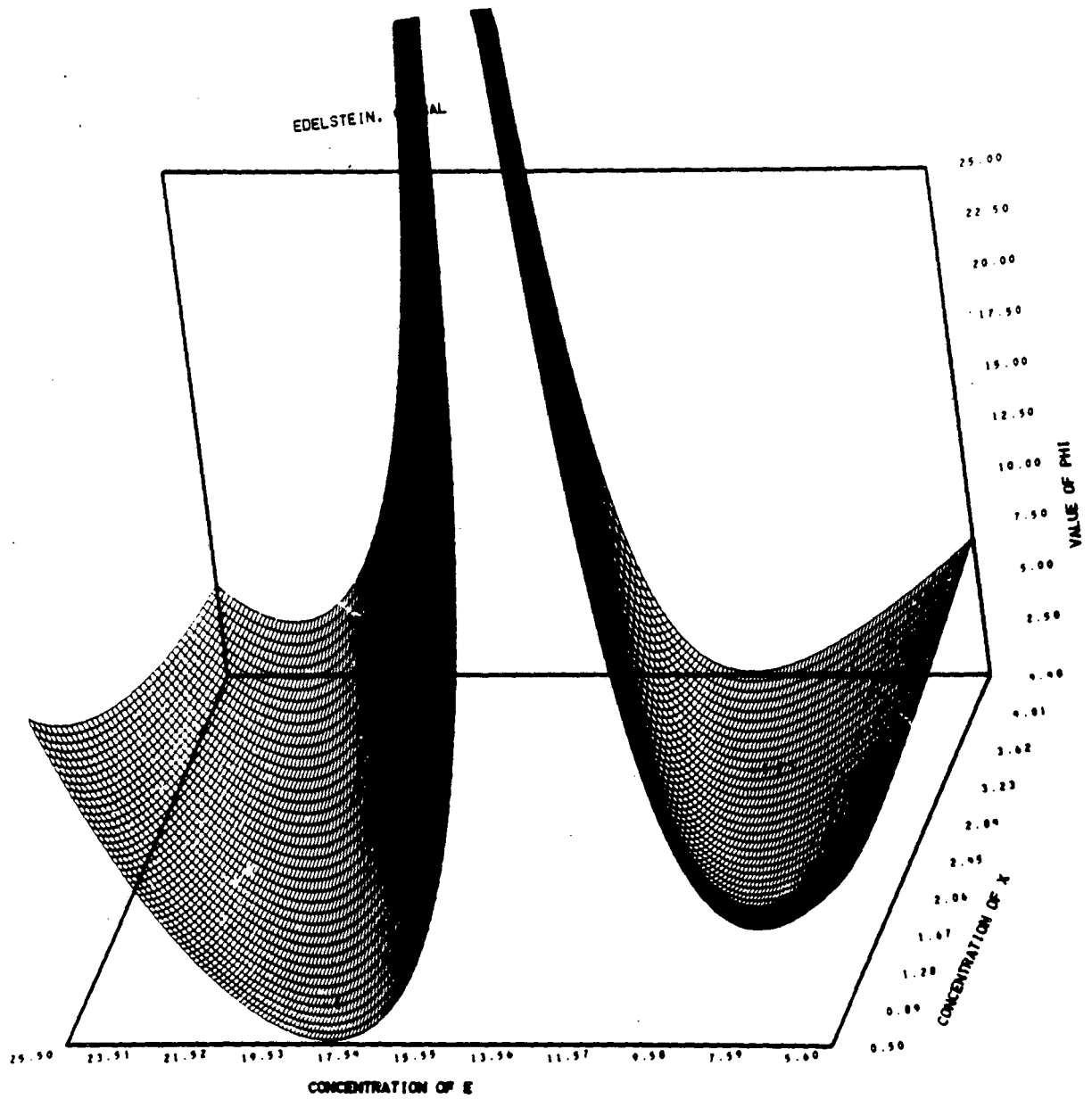
Figure 8



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Figure 9. Additional three-dimensional view of the variable portion of the ϕ -function surface for the "Edelstein" reaction system.

Figure 9



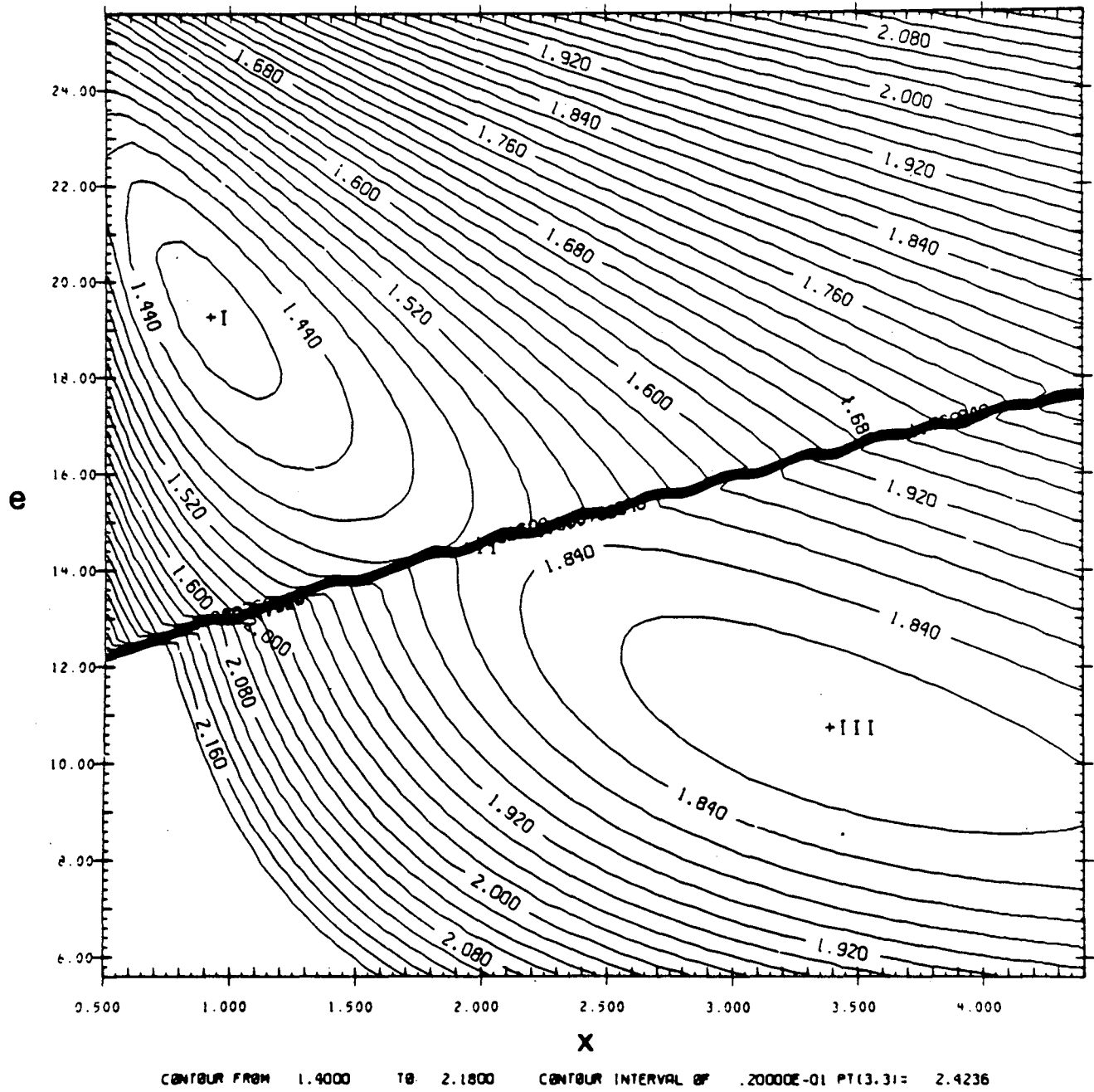
XBL 866-8818

Figure 10. Contour maps of portions of the $\mathcal{M}$ -function surfaces for the "Edelstein" reaction, calculated from Equations 103 and 116 in Appendix A, for steady-state regions I and III, under the same boundary conditions as for Figure 4. The black line results from the superposition of contour lines which (by computer instruction) discontinuously connect the contours of regions I and III at the separatrix. Note that for the ϕ surface, Figures 5-9, the separatrix results naturally as the region I - region III intersection-interface. For the $\mathcal{M}$ function there is a comparable "natural" intersection-interface (dotted line). Though the 3-dimensional concavities of the $\mathcal{M}$ surface components are qualitatively similar to those of the ϕ surface (extrema at all steady states) in the case of $\mathcal{M}$, the region I - region III intersection appears to have no theoretical significance; in any case, it does not correspond to the separatrix.

The "failure" of a key thermodynamic potential requirement for this chemical reaction network--the ability to serve as "time's arrow" for the system--can be visualized by overlaying on this Figure the kinetic trajectories (Figure 4T). Close examination shows that the trajectories which abruptly change direction by more than 90° go "up-hill" for a time, before dropping to their final steady-state minimum endpoints.

Figure 10

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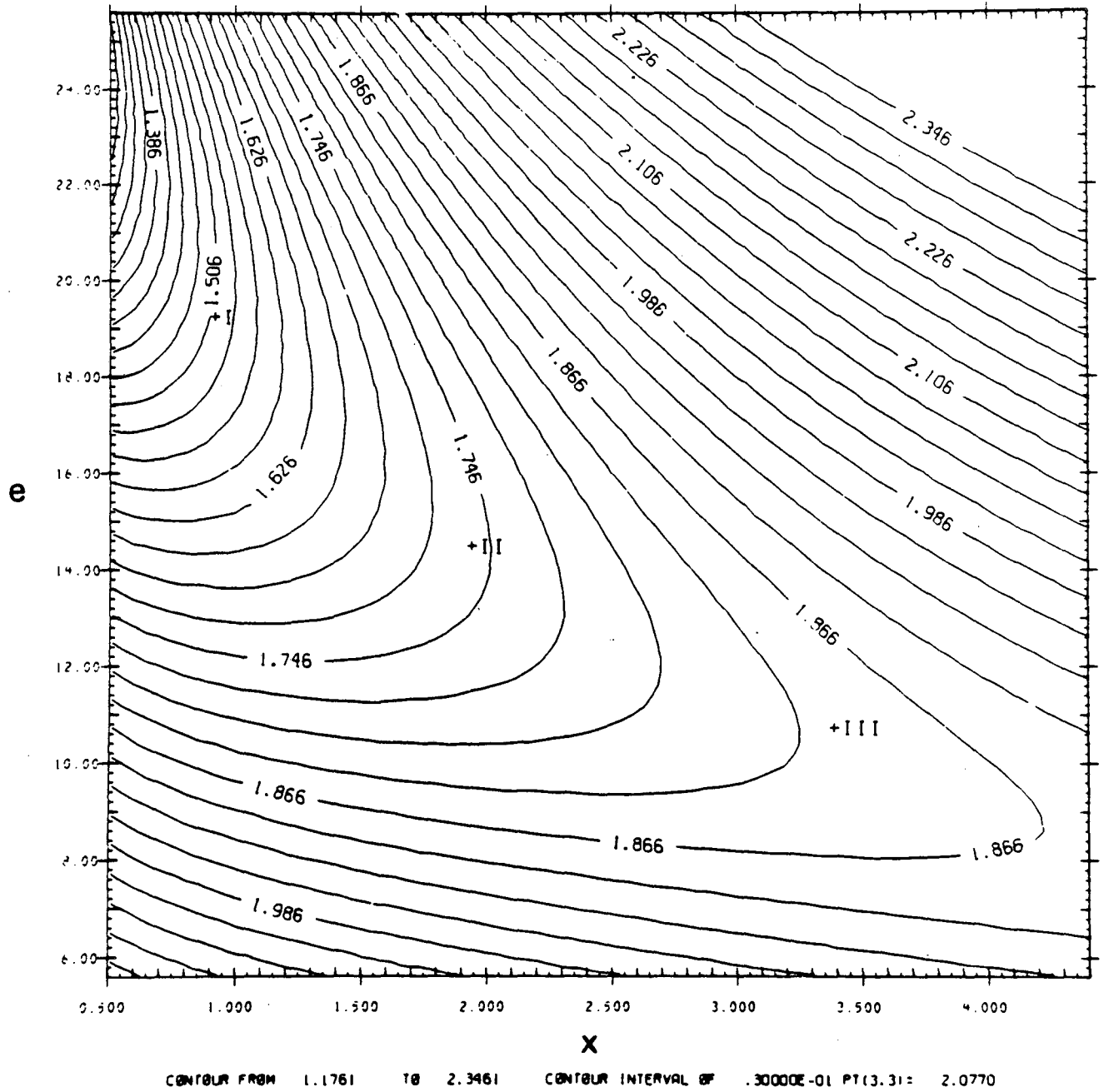


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Figure 11. Contour map of the variable portion of the entropy production function ($\mathcal{P} = \mathcal{A}_1 v_1 + \mathcal{A}_2 v_2 + \mathcal{A}_3 v_3$) for the "Edelstein" reaction (Equations 97-99) under the same boundary conditions as for Figure 4. The $\mathcal{P}$ function is seen to lack both of the key properties crucial to its serving as a thermodynamic potential for this far-from-equilibrium system: 1) extrema at the steady states; and 2) well-behaved correspondence between the topography of Figure 10 and the kinetic trajectories of Figure 4.

Figure 11

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