



REVIEW

Thermodynamics and Evolution

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The science of thermodynamics is concerned with understanding the properties of inanimate matter in so far as they are determined by changes in temperature. The Second Law asserts that in irreversible processes there is a uni-directional increase in thermodynamic entropy, a measure of the degree of uncertainty in the thermal energy state of a randomly chosen particle in the aggregate. The science of evolution is concerned with understanding the properties of populations of living matter in so far as they are regulated by changes in generation time. Directionality theory, a mathematical model of the evolutionary process, establishes that in populations subject to bounded growth constraints, there is a uni-directional increase in evolutionary entropy, a measure of the degree of uncertainty in the age of the immediate ancestor of a randomly chosen newborn. This article reviews the mathematical basis of directionality theory and analyses the relation between directionality theory and statistical thermodynamics. We exploit an analytic relation between temperature, and generation time, to show that the directionality principle for evolutionary entropy is a non-equilibrium extension of the principle of a uni-directional increase of thermodynamic entropy. The analytic relation between these directionality principles is consistent with the hypothesis of the equivalence of fundamental laws as one moves up the hierarchy, from a molecular ensemble where the thermodynamic laws apply, to a population of replicating entities (molecules, cells, higher organisms), where evolutionary principles prevail.

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Introduction

Evolutionary theory and thermodynamic theory represent two domains whose mathematical structures embody a principle describing a uni-directional increase of an operationally measurable property. This article will delineate the relation between these two mathematical structures and exploit this relation to derive an analytical correspondence between the thermodynamic laws, which pertain to aggregates of inanimate matter, and evolutionary principles, which refer to aggregates of living matter.

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EVOLUTIONARY PROCESSES

Directionality in evolutionary theory is characterized by the observation that species in any phyletic lineage are in general better adapted to the local environment than the ones they replaced. The term adaptedness in this context refers to the morphological, behavioral, and physiological attributes of a species that permit it to compete successfully with other members of its own species or with individuals of other species. Darwin (1859) proposed a mechanistic explanation of adaptation by appealing to the principle of natural selection. In Darwin's

model, adaptation is the result of a gradual dynamic process which arises from the continual production of new variation, and competition between the new variants and the incumbent types for the existing resources. Directionality is described in terms of an increase in fitness, a qualitative measure of adaptation, as one population replaces another under the selective process.

The concept Darwinian fitness has a range of specific meanings depending on the situation being examined. It embodies, according to context, features such as keenness of vision, swiftness of reflexes, muscular strength. These attributes, which confer an ability to survive and reproduce, were supposed to improve over generations under the force of selection. Fitness in Darwin's theory is thus a phenomenological concept; accordingly, its explanatory and predictive power is purely qualitative.

The issue of finding an operational measure of fitness, the first step in any quantitative theory of evolution, has been addressed by several generations of theoreticians. The current dominant approach, proposed by Fisher (1930), characterizes fitness as the number of offspring that a typical individual of a given genotype is expected to bring up to reproductive age. Directionality in the context of these models is described in terms of an increase in mean fitness, an assertion about the *relative* fitness of individuals in the population but of scant relevance to the *absolute* survival and reproduction of the population. The Fisherian models, with their emphasis on the relative fitness of genotypes, essentially ignored the impact of ecological factors on evolutionary change, and furthermore assumed that individual differences in fecundity and mortality due to differences in age, size or any physiological condition—a feature which is intrinsic to any genetically homogeneous population—can be neglected in explaining adaptation.

A new analytical theory of the evolutionary process, introduced in Demetrius (1974), resolved the problems generated by the Fisherian model by considering the variability in demographic parameters within a population, and the response of this heterogeneity to ecological conditions, as the critical factors in explaining adaptive changes. The analysis appealed to a demographic model which goes back to Lotka (1939), where

individuals in the population were parameterized in terms of their age-specific fecundity and mortality. The question addressed in the analysis was: What function of this set of fecundity and mortality components best characterizes Darwinian fitness, the ability of a population to survive and persist under given environmental conditions?

By exploiting studies in the ergodic theory of dynamical systems, I showed that Darwinian fitness is completely described by evolutionary entropy, a demographic variable which measures the heterogeneity in the age of reproducing individuals in the population. Entropy is a function of the age-specific fecundity and mortality, and is given by $H = \tilde{S}/\tilde{T}$, where

$$\tilde{S} = - \sum_j \tilde{p}_j \log \tilde{p}_j, \quad \tilde{T} = \sum_j j \tilde{p}_j. \quad (1)$$

Here \tilde{p}_j represents the probability that the immediate ancestor of a randomly chosen newborn belongs to age-class j . The parameter \tilde{S} , which we will also call evolutionary entropy (the distinction between \tilde{S} and H will be evident from the context) is a dimensionless quantity: it describes the uncertainty in the age of the immediate ancestor of a randomly chosen newborn. The quantity \tilde{T} is called the generation time. It represents the mean age of mothers at the birth of their offspring. Evolutionary entropy, as described by H , thus has the dimension of inverse time.

The work developed in Demetrius (1992) for constant environmental models, and in Arnold *et al.* (1994), Demetrius & Gundlach (1999) for random environment models, called Directionality theory, derived for different ecological conditions a set of theorems describing changes in H , and invoked these theorems to infer equivalent changes in \tilde{S} , as the population evolves from one equilibrium state to the next. In this model, two modes of population growth as a response to ecological constraints were distinguished (i) *bounded* growth, characterized by the condition of stationary size or fluctuations around a stationary size, a situation which typically occurs when resources are limited; (ii) *unbounded* growth, described by extended episodes of exponential growth, a condition which typically results when resources are abundant. Directional

changes in \tilde{S} in response to different ecological forces can be delineated as follows.

E(1) *A uni-directional increase in \tilde{S}* : bounded population growth.

E(2) *A uni-directional decrease in \tilde{S}* : unbounded population growth, large population size.

E(3) *Random, non-directional change in \tilde{S}* : unbounded population growth, small population size.

Now a population which is exponentially increasing throughout a long period of its evolutionary history will ultimately cause an exhaustion of available resources. Accordingly, the condition of unbounded growth cannot persist over extended periods of evolutionary time, and hence a state of bounded growth will characterize the typical demographic condition. Directionality theory thus predicts that, generically, evolution will be described by a uni-directional increase in entropy.

Evolutionary entropy, as defined by eqn (1) is a statistical property which describes the variability in the ages of reproducing individuals in a population. The age of an organism is correlated with its metabolic energy, hence, entropy can also be described as the heterogeneity in the metabolic energy state of reproducing individuals in the population. Evolutionary entropy also admits a macroscopic representation (Demetrius, 1997, 1999). Up to additive constants, the microscopically defined evolutionary entropy \tilde{S} can be expressed as the product of the metabolic rate of the organism, \tilde{Q} , and the generation time \tilde{T} . Accordingly, under constraints of stationary growth, the infinitesimal change in entropy $d\tilde{S}$ is given by the relation

$$d\tilde{S} = \tilde{T} d\tilde{Q}. \quad (2)$$

There exist allometric relations between body size, W , a morphometric variable, and the parameters metabolic rate and generation time. We have (see Peters, 1983; Calder, 1984), $\tilde{Q} \sim W^{3/4}$; $\tilde{T} = W^{1/4}$. These relations imply that $\tilde{Q}\tilde{T} = \alpha W$, a condition which entails that evolutionary entropy \tilde{S} is isometric to body size, $\tilde{S} = \alpha W$. This isometry between entropy and body size can be exploited to predict the following correspondence between trends in body size and the

ecological constraints the population experiences during its evolutionary history.

E(1)* *A uni-directional increase in body size*: bounded population growth.

E(2)* *A uni-directional decrease in body size*: unbounded population growth, large population size.

E(3)* *Random, non-directional change in body size*: unbounded population growth, small population size.

As we observed, the condition of unbounded growth over extended periods is atypical, hence, directionality theory predicts that generically, evolution will be described by a uni-directional increase in body size.

THERMODYNAMIC PROCESSES

In thermodynamic theory, directionality derives from the empirical observation that heat flows from high to low temperatures. Clausius (1870) proposed a mathematical representation of this principle by showing that the constraints on the direction of heat flow imply the existence of a function S_C , called thermodynamic entropy, whose infinitesimal change is given by

$$dS_C = dQ/T, \quad (3)$$

where Q denotes the quantity of heat, and T the absolute temperature. Clausius invoked this quantity to establish an analytic description of the Second Law. In this description, two types of processes were recognized: (i) an *irreversible* process, characterized by the condition where some of the energy introduced to drive the system is lost to friction and turbulence, and (ii) a *reversible* process, an idealized situation described by the absence of friction or turbulence due to the relatively slow progression of the interactions that define the system. Clausius formalized changes in S_C , as the system moves from one equilibrium state to the next, according to the following relations:

T(1) *A uni-directional increase in S_C* : irreversible processes.

T(2) *A constant value for S_C* : reversible processes.

The intuitive meaning of reversibility is that the interactions are proceeding very slowly relative to the time it takes the system to reach its equilibrium state. Thus, in reversible processes, the states of the system are approximately equilibrium states for all time—an atypical situation. Hence, generically, thermodynamic processes are characterized by a unidirectional increase in thermodynamic entropy.

Clausius' entropy is a macroscopically defined property: it makes no reference to the state of the individual particles that define the system and thus provides no mechanistic explanation of the Second Law. The model that established the link between atomic theory and directional trends in heat flow was proposed by Boltzmann (1896) and is based on a statistically defined quantity. This new parameter associates to each equilibrium macrostate M of the system, and thus to each microstate X which gives rise to M , a Boltzmann entropy, which we denote by $S_B(X)$, given (up to multiplicative constants) by

$$S_B(X) = \log P_{M(X)}, \quad (4)$$

where $P_{M(X)}$ is the phase-space volume associated with the macrostate M .

Boltzmann considered the change in entropy as a system evolves to a final equilibrium state when a macroscopic constraint is lifted in the system initially at equilibrium, and showed that $S_B(X_2) \geq S_B(X_1)$ where X_1 and X_2 denote the initial and final states, respectively. A crucial observation made by Boltzmann was that when X corresponds to an equilibrium state, then $S_B(X)$ agrees (up to terms negligible in the size of the system) with the thermodynamic entropy of Clausius, consequently the directional change in $S_B(X)$ provided a mechanistic explanation of the Second Law.

It was further observed that at equilibrium the Boltzmann entropy $S_B(X)$ coincides (up to multiplicative constants) with the Gibbs entropy $S_G(\rho)$,

$$S_G(\rho) = - \int \rho(x) \log \rho(x) dx, \quad (5)$$

which is defined not for individual microstates but for statistical ensembles ρ . Hence, directional changes can also be parameterized in terms of the

statistical quantity $S_G(\rho)$. We write

T(1)* *A uni-directional increase in S_G : irreversible process.*

T(2)* *A constant value for S_G : reversible process.*

EVOLUTIONARY AND THERMODYNAMIC PROCESSES: A RAPPROCHEMENT

The circle of directionality theorems for evolutionary entropy E(1)–E(3); E(1)*–E(3)* and thermodynamic entropy T(1), T(2); T(1)*, T(2)* indicate a formal correspondence between the thermodynamic and evolutionary models which we now delineate.

The science of evolution in its widest sense is concerned with understanding the properties of populations of replicating organisms in so far as they are determined by generation time. The evolutionary properties of organisms, are determined by their capacity to transform resources from the environment into maintenance and reproductive activity—a condition which depends on the metabolic energy of the organism. Directionality theory, a mathematical model of the evolutionary process, is thus concerned with the rules determining the transformation of metabolic energy between populations of replicating entities competing for the same resources. The central parameters in this theory are the generation time, and evolutionary entropy. The latter concept has both a statistical representation, as given by eqn (1), and a macroscopic description as expressed by eqn (2).

The science of thermodynamics in its widest sense is concerned with understanding the properties of aggregates of matter in so far as they are determined by changes in temperature. The capacity of a material aggregate to perform work is determined by the quantity of heat energy it contains. Thermodynamic theory is thus concerned with the rules governing the transfer of heat energy between aggregates of matter subject to various kinds of external constraints. The main parameters of the theory are temperature, and thermodynamic entropy. The latter concept also has both a statistical description, as given by eqns (4) and (5), and a macroscopic representation, as given by eqn (3). The family of parameters that define the two theories were shown (see

TABLE 1
Relation between thermodynamic and evolutionary properties

Properties	Thermodynamic theory	Directionality theory
Manifestation of energy	Heat	Metabolic
Intensity factor	Temperature, T	Reciprocal generation time, \tilde{T}
Entropy		
<i>Statistical</i>	Uncertainty in the thermal energy state of a randomly chosen particle	Uncertainty in the age of the mother of a randomly chosen newborn
<i>Macroscopic</i>	$dS = (1/T) dQ$, where Q is the heat energy	$d\tilde{S} = \tilde{T} d\tilde{Q}$, where \tilde{Q} is the metabolic energy

Table 1), to be formally related (Demetrius, 1983; Arnold *et al.*, 1994).

This article reviews the mathematical basis for the formal correspondence given in Table 1, and analyses the relationship between directionality theory and thermodynamic theory. In elucidating this connection we will appeal to an analytic relation between generation time \tilde{T} , and temperature T , which is valid for populations of replicating organisms whose birth and death rates are determined by the temperature of the external environment. We have (Demetrius, 1997)

$$\tilde{T} = \left(\frac{ch}{\rho k} \right) \frac{1}{T}. \quad (6)$$

Here h denotes Planck's constant, and k , the Boltzmann constant. The parameter $\rho = \exp(-\Delta F^\ddagger/RT)$ where ΔF^\ddagger is an effective activation energy, and R the gas constant. The parameter c is a function of the concentration of enzymes and substrates in the different cells in the population.

We will exploit eqn (6) to show that the principle of evolutionary entropy increases as the system evolves from one stationary state to the next under bounded growth constraints, is a non-equilibrium extension of the principle of thermodynamic entropy increase for irreversible processes. This proposition is consistent with the general tenet regarding the equivalence of

fundamental laws as one moves up the hierarchy, from an aggregate of inanimate matter whose organization is determined by temperature, to an ensemble of replicating entities whose organization is generated by cycle time.

RELATED STUDIES

The problem of parameterizing the state of evolutionary processes (at the level of molecules, cells, higher organisms), so that its change ascribes a temporal direction analogous to the increase in thermodynamic entropy has occupied the attention of several generations of scientists. Fisher (1930) addressed the problem at the organismic level and proposed the concept mean fitness as the evolutionary analog of the Gibbs-Boltzmann entropy. Fisher indeed claimed that his theorem, which asserts an increase in the mean fitness under natural selection, is an evolutionary analog of the Second Law. This observation has stimulated several efforts to exploit Fisher's theorem to analytically relate population variables with thermodynamic concepts such as energy and entropy (cf. Weber *et al.*, 1988). It is now generally conceded, however, that Fisher's theorem pertains uniquely to *local* changes in population properties (see Karlin, 1992; Levins & Lewontin, 1985; Maynard Smith, 1988) and is thus conceptually distinct from the Second Law which refers to *global* changes in thermodynamic variables. More recent efforts to provide a parameterization of the evolutionary process at the organismic level are described in Brooks & Wiley (1986) and Wicken (1987). (See also the articles in Weber *et al.*, 1988.) These studies are based on the formalism of phenomenological thermodynamics. Analyses at the molecular level, in terms of Eigen's quasi-species model, see Eigen *et al.* (1988), are developed within the formalism of statistical, mechanical and dynamical systems theory. Studies of the quasi-species model exploit the Ising spin system to delineate certain correspondences between concepts in molecular evolution and thermodynamic variables. The development reviewed in this article (see Demetrius, 1997) is based on some recent developments in the ergodic theory of dynamical systems (Sinai, 1972; Bowen, 1975; Bowen & Ruelle, 1975). This

body of work provides the basis for relating evolutionary entropy, which is the entropy of a dynamical system associated with the evolutionary process, with the Gibbs–Boltzmann entropy of thermodynamic theory.

Evolutionary Dynamics

The Darwinian theory of evolution by natural selection was intended to provide a mechanistic model, based on interactions at the individual level, of the adaptation of populations of organisms to their environment. In modern language, Darwin’s model postulates that the dynamical system which describes the replacement of one population by another within a lineage is the outcome of the combined action of two processes which operate on two distinct time-scales. The first process, the mutation event, acts on a short time-scale, and is the mechanism whereby new types are introduced in the population. This process is random in the sense that it is not caused by, and is unrelated to, the current needs of the organism or the nature of the environment. The second process, the selection event, acts on a much longer time-scale: it is the mechanism that screens the new types according to their capacity to survive and reproduce in competition with ancestral types. This process is deterministic, in the sense that its outcome, the invasion or extinction of the new type is modulated by the response of the organism to the environmental factors. During the unfolding of this process, the fitness of the population, the term Darwin invoked to describe the capacity of individual organisms to survive and reproduce, will undergo change: the less fit, that is, the less well adapted to the environmental condition, ultimately being replaced by the more fit. The unfolding of this process eventually drives the population to a state where the fitness is optimal and the population is in a state of adaptation to the environmental conditions.

Darwin’s theory was developed within the empirical tradition of 19th century biology, a milieu which apart from the statistical work of Mendel (which was not appreciated in its time) was devoid of any mathematical constructs. The issue of providing a mathematical representation of the theory gradually achieved prominence

with the rediscovery of Mendel’s laws which embodied a set of quantitative rules for the transmission of inheritance. One of the most sustained efforts to translate the Darwinian program into an analytic framework was made by Fisher (1930), who immediately recognized certain formal analogies between the mechanistic models introduced by Boltzmann (1896) to analyse physical systems, and the selection models proposed by Darwin (1859) to explain adaptation in biological systems. By considering the dynamical system which describes the changes in gene frequency of the population which occurs under natural selection, Fisher proved a directionality theorem, which he called the fundamental theorem of natural selection, and which states: the rate of increase in the mean fitness at any time is equal to the genetic variance in fitness. Analytically, the theorem is often written in the form

$$\frac{d\bar{m}}{dt} = Vg(\bar{m}), \quad (7)$$

where \bar{m} describes the average Malthusian parameter of the genotype, and $Vg(m)$ refers to the additive genetic variance.

Fisher claimed that the theorem was an analog of Boltzmann’s principle of entropy increase, and thus considered eqn (7) to be an analog of the Second Law. These claims have now been re-evaluated. It is now generally admitted that the directional change in mean fitness is only a statement about the relative viability of individuals within the population and makes no prediction about the absolute survival and reproduction of populations. Fisher’s theorem thus has little relevance in understanding macroevolutionary changes in adaptation.

The issue of developing a quantitative theory which would explain the adaptation of populations in terms of a mechanistic model based on interaction at the level of the organism, was addressed by Demetrius (1974, 1977), in a new perspective which drew extensively from developments in the ergodic theory of dynamical systems. These new population models, in sharp contrast to the development proposed by Fisher (1930), considered the evolutionary process as a two-stage event, involving mutation and

selection, and analysed changes in population composition as the process evolved from one state to the next. According to the Darwinian model, mutation provides a continuous source of variation, whereas selection, which monitors this variation, will result in the less fit, that is, the less well adapted to the environmental condition, being replaced by the more fit or the better adapted. Consequently, Darwinian fitness, a concept whose analytical representation is critical for any quantitative theory of evolution, should be characterized by properties which reflect features of adaptation, namely: (i) stability—the persistence of population numbers to small perturbations in the individual fecundity and mortality variables; (ii) competitive ability—the invulnerability of a genotype to invasion by rare mutants, and (iii) directionality—the temporal asymmetry of the evolutionary process as one population replaces another under the combined effects of mutation and selection.

The work developed in Demetrius (1974) considered a model of a population of individuals structured in terms of the ages at which they reproduce and die. The microscopic variables in this model are the age-specific fecundity and mortality of the individuals.

In this model, the transition between the different age-classes according to the birth and death process, can be represented by the life cycle graph as in Fig. 1.

In this figure, n denotes the number of age-classes: b_i , the proportion of individuals surviving from age-class (i) to age-class ($i + 1$); and m_i , the mean number of offspring produced by individuals in the i -th age-class.

The quantity $l_j = b_1 b_2 \cdots b_{j-1}$ represents the probability that an individual born in age-class

(1) survives to the j -th age-class, and $w_j = l_j m_j$ denote the net-offspring production of individuals in age-class (j). The probability \tilde{p}_j that the immediate ancestor of a randomly chosen newborn belongs to age-class (j) can be expressed in terms of the net-offspring production w_j and the population growth rate r . We have

$$\tilde{p}_j = w_j \exp(-rj). \quad (8)$$

We showed that evolutionary entropy, as defined by the variable $H = \tilde{S}/\tilde{T}$, where $\tilde{S} = -\sum \tilde{p}_j \log \tilde{p}_j$ and $\tilde{T} = \sum j \tilde{p}_j$, characterizes the following features which we now annotate qualitatively.

(a) *Demographic stability.* The concept demographic stability refers to the invulnerability of a population to small perturbations in the birth and death rates: entropy determines the rate of decay of fluctuations in population numbers due to small perturbations in the age-specific fecundity and mortality. In populations subject to bounded growth constraints, demographically stable states are described by the condition of maximal entropy; in populations with unbounded growth, demographically stable states are described by the condition of minimal entropy (Demetrius, 1977; Demetrius & Gundlach, 1999).

(b) *Evolutionary stability.* This notion pertains to the invulnerability of a genotype to invasion by rare mutants: entropy determines the conditions for invasion of a mutant allele in a population. In bounded growth populations, evolutionarily stable states are described by the state of maximal entropy; under conditions of unbounded growth, evolutionarily stable states are characterized by minimal entropy (Demetrius & Gundlach, 1999).

(c) *Directionality.* The changes in entropy parameterize the genotypic and phenotypic changes in population composition as one population replaces another under mutation and selection. Under bounded growth conditions, entropy increases; under unbounded growth conditions, *large* population size, entropy decreases; under unbounded growth conditions, *small* population size, the change in entropy is random and non-directional (Demetrius, 1992).

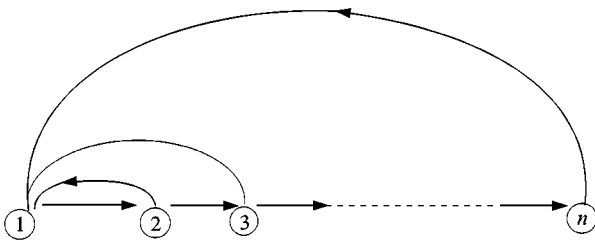


FIG. 1. Life cycle graph of a population.

We now give an outline of the mathematical basis for the above three properties.

DIRECTIONALITY THEORY

The directionality principle for evolutionary entropy is based on a model which considers biological evolution as involving two complementary processes: mutation and selection. A population will under the force of certain ecological constraints attain a state of demographic equilibrium, characterized by the condition in which the proportion of individuals in the different age-classes remain constant in time. Random mutation will perturb this equilibrium state by introducing new types in the population. Competition between the ancestral and mutant types will ensue and selection will ultimately drive the population to a new equilibrium state. The mathematical representation of this evolutionary process was initially developed in terms of continuous age-structured models (Demetrius, 1992). In this article, we will adopt, for expository convenience, the formulation in discrete time given in Arnold *et al.* (1994).

The Population Dynamics

The state of the population at time t is given by the vector $\bar{u}(t) = [u_1(t), \dots, u_n(t)]$, where $u_i(t)$ denotes the number of individuals in age-class (i) at time t . The changes in the age-distribution are given by

$$\bar{u}(t+1) = A(t)\bar{u}(t),$$

where $A(t)$ is the population matrix with age-specific fecundity rates (m_j) in the top row, and age-specific survival probabilities (b_j) along the sub-diagonal, and zero elsewhere. It is known that when certain natural conditions on the age-specific fecundity and mortality rates obtain, the system will converge to the equilibrium state described by a stable age-distribution, with a population growth rate $r = 0$, when birth and death rates are density-dependent, and $r > 0$ when density-independent conditions prevail (Liu & Cohen, 1987).

The population growth rate is known to satisfy a variational principle analogous to the principle of the minimization of free energy in statistical

mechanics. This variational principle is defined in terms of a new configuration space Ω , the set of all paths of the life cycle graph given by Fig. 1.

To characterize the variational principle, we consider the shift operator τ on Ω ; and we let M denote the set of all τ -invariant probability measures on Ω . Also let $H_\mu(\tau)$ denote the dynamical entropy (the Kolmogorov-Sinai invariant) for the shift τ with respect to μ .

By appealing to the ergodic theory of dynamical systems, we showed that the growth rate r satisfies the following extremal principle (Demetrius, 1974):

$$r = \sup_{\mu} \left[H_\mu(\tau) + \int \varphi d\mu \right], \quad (9)$$

where $\varphi: \Omega \rightarrow R$ is given by $\varphi(x) = \log a_{x_1, x_0}$, with (a_{ij}) the (i, j) entry of the matrix A which describes the population at demographic equilibrium.

The supremum in (9) is achieved at a unique μ which we denote by $\hat{\mu}$. The probability measure $\hat{\mu}$ can be explicitly described in terms of the elements of the stochastic matrix $P = (p_{ij})$ obtained by the canonical normalization of the population matrix A . The terms $H_{\hat{\mu}}(\tau)$ and $\int \log a_{x_1, x_0} d\hat{\mu}$ can be explicitly computed. These two terms, denoted H and Φ , are given by

$$H = - \frac{\sum \tilde{p}_j \log \tilde{p}_j}{\sum j \tilde{p}_j} \equiv \frac{\tilde{S}}{\tilde{T}},$$

$$\Phi = \frac{\sum \tilde{p}_j \log w_j}{\sum j \tilde{p}_j} \equiv \frac{\tilde{E}}{\tilde{T}}, \quad (10)$$

where \tilde{p}_j is given in eqn (8).

The quantity \tilde{S} describes the uncertainty in the age of the mother of a randomly chosen newborn; \tilde{E} represents the net-offspring production averaged over all age-classes. \tilde{T} denotes the generation time, the mean age of mothers at the birth of their offspring. We have from eqn (10) the identity

$$r = H + \Phi. \quad (11)$$

In view of the variational characterization of the growth rate, it follows that a population at demographic equilibrium can be represented by the mathematical object $(\Omega, \hat{\mu}, \varphi)$, where φ denote

the potential on the configuration space Ω , defined by $\varphi(x) = \log a_{x,x_0}$.

We observe from the preceding identity that the following implications hold:

$$\Phi < 0 \Rightarrow r < H, \quad \Phi > 0 \Rightarrow r > H. \quad (12)$$

This leads to a natural classification of populations in terms of their growth rate. The property $\Phi < 0$ (bounded growth), describes a population whose growth rate is limited by the entropy. This circumstance includes populations with constant size and populations which spend the greater part of their evolutionary history with size fluctuating around some constant value. The property $\Phi > 0$ (unbounded growth), defines populations whose growth rate exceeds entropy. This situation includes populations which spend an extended part of their evolutionary history in the exponential growth phase.

The Mutation Event

The model postulates that random mutations occur in a small subset of the ancestral population. A mutation in this subset is analytically represented by a perturbation of φ , a situation which gives rise to a new potential function

$$\varphi^* = \varphi + \delta\psi.$$

The magnitude δ of the perturbation is assumed to be small, and the potential functions φ and ψ are assumed to satisfy $\int \varphi \, d\mu = \int \psi \, d\mu$.

Let Δr and ΔH denote changes in the demographic variables which result from the mutation event. We have shown that for small absolute values δ , the following relations hold (Demetrius, 1992, Arnold *et al.*, 1994):

$$\Delta r = \Phi\delta, \quad \Delta H = -\sigma^2\delta,$$

where Φ is given as in eqn (10), and σ^2 , the demographic variance, is given by

$$\sigma^2 = \frac{\sum_j (W_j)^2 \tilde{p}_j}{\bar{T}}, \quad (13)$$

where $W_j = -j\Phi + \log w_j$.

The above perturbation conditions imply, since $\sigma^2 > 0$, the following set of mutation

relations,

$$\begin{aligned} \Phi < 0 &\Rightarrow \Delta r \Delta H > 0, \\ \Phi > 0 &\Rightarrow \Delta r \Delta H < 0. \end{aligned} \quad (14)$$

The perturbation methods also show that the change $\Delta\sigma^2$ in the demographic variance is given by $\Delta\sigma^2 = \gamma\delta$, where γ , called the correlation index, is given by

$$\gamma = 2\sigma^2 - \frac{3\sigma^2}{\bar{T}} \sum_j j p_j W_j + \frac{1}{\bar{T}} \sum_j p_j W_j^3.$$

We now have the following implications:

$$\begin{aligned} \gamma < 0 &\Rightarrow \Delta H \Delta\sigma^2 > 0, \\ \gamma > 0 &\Rightarrow \Delta H \Delta\sigma^2 < 0. \end{aligned} \quad (15)$$

INVASION-EXTINCTION

The invasion-extinction dynamics of the mutant gene, that is, the condition for its ultimate establishment in the population, can be analysed in terms of diffusion processes (cf. Feller, 1951). The analysis described in Demetrius & Gundlach (1999) integrated the techniques of diffusion processes and the ergodic theory of age-structured populations to show that the outcome of competition between the incumbent allele and the mutant type is determined by the parameter s , where

$$s = \Delta r - \frac{1}{N} \Delta\sigma^2.$$

Let $P(y)$ denote the probability that a mutant with initial frequency y invades the population. As shown, Demetrius (1997), Demetrius & Gundlach (1999), the function $P(y)$ can be expressed explicitly in terms of the parameters s , Δr , $\Delta\sigma^2$ and the population size N . Moreover, the geometry of the function $P(y)$ is determined by the sign of s . We have:

$$s > 0 \Rightarrow P(y) \text{ convex}; \quad s < 0 \Rightarrow P(y) \text{ concave}$$

The preceding observation can be exploited to express the conditions for invasion in terms of the parameters Δr and $\Delta\sigma^2$. We have:

- (i) $\Delta r > 0$, $\Delta\sigma^2 < 0$: invasion occurs almost surely (a.s.);

TABLE 2
Invasion–extinction dynamics of mutants

Ecological constraint	Demographic state	Selective outcome
I. Bounded growth	$\Delta H > 0$ $\Delta H < 0$	Mutant invades almost surely (a.s) Mutant becomes extinct (a.s)
II. Unbounded growth; Unbounded population size	$\Delta H < 0$ $\Delta H < 0$	Mutant invades (a.s) Mutant becomes extinct (a.s)
III. Unbounded growth; Bounded population size	$\Delta H > 0$ $\Delta H < 0$	Mutant invades with a probability which is a decreasing function of size Mutant invades with a probability which is an increasing function of size

- (ii) $\Delta r < 0$, $\Delta\sigma^2 > 0$: extinction occurs (a.s.);
 (iii) $\Delta r < 0$, $\Delta\sigma^2 < 0$:
 (a) $N > \frac{\Delta\sigma^2}{\Delta r}$: extinction occurs (a.s.)
 (b) $N < \frac{\Delta\sigma^2}{\Delta r}$: invasion occurs with a probability which increases as the population size decreases;
 (iv) $\Delta r > 0$, $\Delta\sigma^2 > 0$:
 (a) $N > \frac{\Delta\sigma^2}{\Delta r}$: invasion occurs (a.s.)
 (b) $N < \frac{\Delta\sigma^2}{\Delta r}$: extinction occurs with a probability which increases as the population size decreases.

Now, the parameters Δr and $\Delta\sigma^2$, as (14) and (15) indicate, are correlated with ΔH . Accordingly, the conditions for invasion can be expressed uniquely in terms of ΔH , together with the parameters Φ and γ which define ecological constraints. These constraints define (a) limits on the population growth rate, which we describe as bounded, when $\Phi < 0$, and unbounded, when $\Phi > 0$; (b) limits on the population size, which we describe as bounded when $N < \gamma/\Phi$, and unbounded when $N > \gamma/\Phi$.

Table 2 describes the selective outcome of competition between mutant allele and incumbent type, in terms of the entropy, and the constraints on population growth rate and population size.

THE DYNAMICS OF SELECTION

The mutation event introduces new genotypes in the population. These new types will mate with the ancestral types according to the Mendelian laws to generate new types. During the selection process which proceeds on a time-scale that is much longer than the invasion process, ecological

factors will regulate the population dynamics and the number of these genotypes will vary in response to the ecological effects. This process can be described in terms of the interaction between the three dynamical systems induced by the genotype. As shown in Demetrius (1992), this coupled dynamical system will converge to a new steady state described by a new entropy.

The expression $\tilde{\Delta H}$, which denotes the change in entropy as the population evolves from one demographic equilibrium state to the next, and ΔH , which denotes the change in entropy which characterizes the invading mutant, can be shown to satisfy (Demetrius, 1992),

$$\Delta H \tilde{\Delta H} > 0. \quad (16)$$

This relation asserts that the *global* directional change in entropy as one population replaces another under the action of mutation and selection is positively correlated with the *local* directional changes in entropy induced by the invading mutant itself.

The integration of the mutation relations as described by eqn (14), the invasion–extinction

TABLE 3
Relation between ecological conditions and evolutionary trends in entropy

Ecological constraints	Directional trends
Bounded growth	Increase in \tilde{S}
Unbounded growth	
(i) Large population size	Decrease in \tilde{S}
(ii) Small population size	Random, non-directional changes in \tilde{S}

criteria, as described in Table 2, and the selection event, as represented by eqn (16) provide a means of relating demographic and ecological conditions with global directional trends in entropy. The directional trends in \tilde{S} and the corresponding ecological constraints are summarized in Table 3.

There exist intrinsic limits to the directional changes in entropy owing to constraints on the ability of new mutants to become established in the population. The degree of genetic polymorphism at a given locus can be shown to increase for the mutation–selection process when ecological conditions that generate directional changes in entropy obtain. However, a limit will ultimately be attained described by the state where the genome becomes invulnerable to the invasion of new alleles. The limiting condition derives from a result due to Kingman (1980) which asserts that the expectation ρ , that a new mutant takes its place in a new equilibrium population, scales according to the relation, $\rho \sim \exp(-\alpha k)$, where α is a parameter that depends on the fitness of the different alleles, and k denotes the number of alleles at the locus. The expression for ρ implies that large polymorphisms once established are highly resistant to invasion by a new mutant; moreover, this resistance increases exponentially with the number of alleles. In view of this property, we can assert, for example, that in populations evolving under stationary growth constraints, the entropy \tilde{S} will increase to some upper limit which may be inferior to the mathematically defined maximum condition.

Molecular Models

The results described in the preceding section pertain to a wide class of models. Directionality principles for evolutionary entropy have been shown to hold for dynamical systems described by products of random matrices, Arnold *et al.* (1994). These dynamical systems include the Leslie matrices, models of cellular populations, and also discrete analogs of the quasi-species models developed by Eigen (1971) and Eigen & Schuster (1979).

The quasi-species model is concerned with the dynamics of different polynucleotide sequences that may be mutually interconverted through replication and mutation. The statistical mechanics

formalism can also be applied to this model. In the studies by Demetrius (1987), we exploited a variational principle to derive thermodynamic analogs of the population parameters in the quasi-species model. Leuthausser (1987) has also explored the connection between population variables and thermodynamic parameters by characterizing the quasi-species model in terms of Ising spin lattice systems. These complementary analyses, reviewed in Eigen *et al.* (1988), underscore the significance of statistical mechanics in the analysis of evolutionary processes at different levels of biological organization.

Thermodynamics and Evolution: Formal Relations

Thermodynamic theory in its widest sense is concerned with explaining and interpreting the properties of matter insofar as they are determined by changes of temperature. The three central parameters in the theory are the temperature, T , thermodynamic entropy S , and energy E , the mean kinetic and potential energy of the molecules in the aggregate.

The three quantities are known to be related: the temperature can be described by the amount of heat that must be added to the system to increase its entropy by one unit. We write

$$\frac{1}{T} = \frac{\Delta S}{\Delta E}.$$

The above expression can also be written

$$\Delta E = \Delta S \times T. \quad (17)$$

Equation (17) expresses the heat energy present in a substance at a particular temperature T as the product of two factors. The net transmittable motion, represented by the temperature T , is the intensity factor because it is independent of the amount of substance in the system under consideration. The capacity property ΔS of the heat energy is an extensive factor since it is proportional to the amount of substance in the system.

Irreversibility in thermodynamic processes is expressed in terms of the Second Law: a system subject to adiabatic constraints is characterized by a uni-directional increase in entropy. This

principle is illustrated by the following model. Consider, as our thermodynamic process, a bar in an adiabatic enclosure. We assume that the bar is in a non-equilibrium state—in the thermodynamic sense. This condition entails that one end of the bar is hotter than the other. The Second Law asserts that the hot end of the bar will cool and the cold end will warm so that the initial temperature gradient disappears and a state of uniform temperature is attained. During this process the thermodynamic entropy of the bar will increase until, as the state of thermal equilibrium is attained, it ceases to increase and reaches its maximum.

Evolutionary theory in its widest sense is concerned with understanding the properties of populations of replicating entities in so far as they are affected by changes in the mean cycle time, that is, the mean age at which replication occurs. The central parameters in the theory are the generation time, \tilde{T} , evolutionary entropy \tilde{S} and reproductive potential, Φ .

These three quantities are related. A perturbation analysis of eqn (11) shows that the generation time \tilde{T} can be described as the amount of reproductive potential that must be added to the population to reduce its entropy by one unit. We write

$$\tilde{T} = \frac{\Delta\tilde{S}}{-\Delta\Phi}.$$

The above expression can be written in the form

$$\Delta\Phi = -\frac{1}{\tilde{T}} \Delta\tilde{S}. \quad (18)$$

Now the reproductive process involves the conversion of energy assimilated by the organism to the production of new tissues, seed, eggs and embryos. This process of reproduction (generation of new gametes), and survivorship (maintenance and growth of the organism) involves expenditure of metabolic energy. Equation (18) can be interpreted as expressing the metabolic energy present in a population with a given cycle time \tilde{T} as a product of two factors. The quantity $1/\tilde{T}$ is an intensity factor: it is the same in every part of the population and is not dependent on the structure of a given subset of the population. The quantity $\Delta\tilde{S}$ represents the extensive or capacity factor of the metabolic energy.

Irreversibility in evolutionary processes is embodied in terms of the directionality principle for \tilde{S} : as a population subject to bounded growth constraints evolves from one demographic equilibrium state to the next, the entropy \tilde{S} increases. This principle can be illustrated by the following model. Consider a population in an environment with limited resources so that the population growth is stationary. We assume that the population is in a non-equilibrium state—in the evolutionary sense. This means that the population is vulnerable to the invasion of new mutants—a condition which entails that the generation time of the resident population is greater than the generation time of mutant populations. The directionality principle for evolutionary entropy asserts that new mutants will arise and continue to invade the population until a state of evolutionary equilibrium is attained. During the transition towards evolutionary equilibrium, the evolutionary entropy will increase until the population becomes invulnerable to the invasion by new mutants and the condition of maximal entropy is reached.

The observations I have described point to a formal correspondence between thermodynamic variables and evolutionary parameters which can be elucidated as follows. We first observe that the free energy in a thermodynamic system is given by the relation

$$F = E - ST. \quad (19)$$

whereas the population growth rate in evolutionary systems is expressed, using eqn (11), by

$$r = \Phi + \tilde{S}/\tilde{T}. \quad (20)$$

The contrast between the pair of expressions (17), (18) and (19), (20), indicates the existence of a formal correspondence between the thermodynamic variables and the population parameters, namely: free energy—growth rate; inverse temperature—generation time; thermodynamic entropy—evolutionary entropy.

Thermodynamics and Evolution: Analytic Relations

The arguments we have described indicate a formal correspondence between the parameters

that define thermodynamic and evolutionary processes, and entail a formal analogy between thermodynamic entropy and evolutionary entropy. The problem we now address is: does this formal analogy have an analytic basis? We will show that an analytic relation exists in the case of populations of cells: organisms whose birth and death rates are determined by the temperature of the external environment. We will establish for cellular populations that, as the absolute temperature tends to zero, thermodynamic entropy and evolutionary entropy coincide. This limiting condition is based on analytic relations between two pairs of variables: (a) thermodynamic entropy and temperature, intrinsic properties of aggregates of inanimate matter, (b) evolutionary entropy and generation time, intrinsic properties of replicating organisms.

THERMODYNAMIC ENTROPY AND TEMPERATURE

Expression (3) indicates that thermodynamic entropy is a function of temperature. The relation between changes in entropy S as the absolute temperature T tends to zero is expressed in terms of the principle

$$S \rightarrow 0 \quad \text{as} \quad T \rightarrow 0. \quad (21)$$

This tenet, known as the third law of thermodynamics was postulated by Nernst based on the observation that in chemical reactions, the change ΔS in entropy vanishes as the absolute temperature tends to zero. The principle can be derived from considerations of statistical mechanics. The essential features of the model are: (i) the energy levels of the system are quantized; and (ii) the ground state is non-degenerate. Given these premises it follows that at a sufficiently low temperature all the particles will be forced down into the lowest possible levels and the entropy will be zero.

EVOLUTIONARY ENTROPY AND GENERATION TIME

Expression (2) shows that evolutionary entropy is a function of the generation time. The relation between changes in entropy \tilde{S} as the generation time increases to infinity can be

derived from statistical mechanics considerations (Demetrius, 1983). In the case of stationary populations, we have

$$\tilde{S} \rightarrow 0 \quad \text{as} \quad \tilde{T} \rightarrow \infty. \quad (22)$$

The derivation of eqn (22) rests on a discretization of the population into an infinite number of age-classes. The changes in the age-distribution can be represented, without loss of generality, by the infinite Leslie matrix

$$\begin{bmatrix} 0 & b_0 & b_0 & \cdots & \cdots \\ b_1 & 0 & 0 & \cdots & \cdots \\ 0 & b_2 & 0 & \cdots & \cdots \\ 0 & 0 & b_3 & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots \end{bmatrix}.$$

The population growth rate r satisfies an extremal principle of the form (9) where the potential φ is now a many-body potential (see Demetrius, 1983). The net-reproductive function at age k is given by $V_k = b_0 l_k$, where $l_k = b_1 \cdots b_{k-1}$. We assume that $\sum_k V_k = 1$, that is, the population has stationary size. Demographic equilibrium states of the population are described by probability measures, defined on the space of genealogies, which maximize the sum of the entropy and the reproductive potential, see eqn (7). It was shown (Demetrius, 1983) that if $\sum (k+1)V_k = \infty$, then the population has a unique equilibrium state. This state is ergodic and is the Dirac measure, which implies that the entropy $\tilde{S} = 0$. Now the generation time $\tilde{T} = \sum_k k V_k$. We conclude that when stationary growth constraints obtain, $\tilde{T} \rightarrow \infty$ implies that $\tilde{S} \rightarrow 0$.

THERMODYNAMIC ENTROPY AND EVOLUTIONARY ENTROPY

We can exploit eqns (21) and (22) to derive an analytic relation, under certain limiting conditions, between S and \tilde{S} . We showed, Demetrius (1997), that in the case of populations of replicating cells, an analytic relation between temperature and generation time exists, as given

by eqn (6). We conclude from eqn (6), (21) and (22) that in the limiting case $T = 0$, the entropies S and \tilde{S} coincide, and assume the limiting value zero.

A population of cells can be considered both as a thermodynamic system, defined by a temperature T and an entropy S ; and as an evolutionary system, described by a generation time \tilde{T} and an entropy \tilde{S} . The analytic relations between: (a) generation time and temperature, as given by eqn (6), and (b) thermodynamic entropy and evolutionary entropy in the limit $T = 0$, indicate that the correspondence between the directionality principles for thermodynamic and evolutionary processes is more than a formal analogy. At a certain level of abstraction, both principles describe the existence of equivalent constraints on the flow of energy. The increase in thermodynamic entropy is a consequence of the fact that heat energy always flows spontaneously from systems at high to systems at low temperatures; whereas, the increase in evolutionary entropy derives from the fact that, in populations competing for limited resources, the conversion of resource energy into metabolic energy is achieved more efficiently by populations with shorter generation times.

Now thermodynamic entropy is a measure of the uncertainty in the thermal energy state of a randomly chosen particle in an aggregate of inanimate matter. In view of the correlation between an organism's age and its metabolic energy, evolutionary entropy can be considered to be a measure of the uncertainty in the metabolic energy state of the mother of a randomly chosen newborn in a population of replicating organisms. When $T = 0$, these two measures of uncertainty coincide. When $T > 0$, we can appeal to equations (2), (3) and the analytical relation between generation time \hat{T} and temperature T given by (6), to infer the following condition: the principle that asserts a uni-directional increase in evolutionary entropy for systems subject to bounded growth constraints constitutes a non-equilibrium extension of the principle that posits a unidirectional increase in thermodynamic entropy for irreversible processes.

Conclusion

Directionality in aggregates of inanimate matter can be described in terms of the Second

Law of Thermodynamics: the increase in thermodynamic entropy for irreversible processes. The significance of the Second law derives from the fact that it embodies a universal property of physical systems—and thus constitutes a law of Nature. The theory proposed by Boltzmann owes its importance to the fact that it provides a statistical interpretation of the Clausius' entropy, thus giving an explanation of the Second Law in terms of the laws of Newtonian mechanics.

Directionality in populations of replicating organisms can be described in terms of an increase in evolutionary entropy in populations with bounded growth. Evolutionary entropy is a statistical quantity: it is a measure of the uncertainty in the age of the mother of a randomly chosen newborn in a population of replicating organisms. The directionality principle for evolutionary entropy is derived from a mathematical model of mutation and selection in a population process, hence, the status of this principle as a universal law will depend on its empirical validity. The empirical significance of the principle is currently being addressed, and preliminary investigations, both at the level of cells and higher organisms, provide support. We now comment briefly on these studies.

Changes in the composition of populations of cells can be parameterized in terms of the heterogeneity in cycle time, a variable which is correlated with evolutionary entropy. The changes in this measure of heterogeneity using diploid human cells evolving under quasi-stationary conditions (Macieira-Coelho *et al.*, 1996), indicate a uni-directional increase, which concords with our predictions. Changes in the composition of human populations can be parameterized in terms of the heterogeneity in the age of reproducing individuals in the population, a property measured by evolutionary entropy. Over relatively short periods of time, say 200 years, these changes in entropy will be due mainly to cultural rather than genetic factors. However, the theory, as observed in Demetrius & Ziehe (1984) is also applicable to changes induced primarily by cultural mechanisms. The analysis in Demetrius & Ziehe (1984), and Demongeot & Demetrius (1989) based on Swedish and French demographic data during the last two centuries, indicates an increase in entropy, except in France

during the war years, when exogenous forces prevail. These increases are also consistent with the predictions of directionality theory.

Indirect evaluation of the theory can be made by studying trends in the morphometric variable body size, a parameter which we have shown is allometrically related to entropy. The theory predicts: (a) a uni-directional increase in body size, under slow or stationary growth constraints; (b) a uni-directional decrease in body size, in exponentially increasing populations with large population size; and (c) random non-directional changes in body size, in rapidly increasing populations with small population size. There exists an extensive literature regarding trends in body size within phyletic lineages (Bonner, 1965; Newell, 1949; Stanley, 1973). These empirical studies point to a uni-directional increase as the typical condition for mammalian lineages—a property known as Cope's rule. Most mammals can be considered as evolving under ecological conditions which induce slow or stationary population growth; hence, this pattern of entropy increase accords with our predictions. These observations indicate that the increase in evolutionary entropy under bounded growth constraints have both strong explanatory and predictive properties and constitute a unifying principle for understanding the patterns generated by mutation and natural selection over evolutionary time.

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REFERENCES

- ARNOLD, L., DEMETRIUS, L. & GUNDLACH, M. (1994). Evolutionary formalism for products of positive random matrices. *Ann. Appl. Probab.* **4**, 859–901.
- BOLTZMANN, L. (1896). *Vorlesungen über Gas Theorie*. Leipzig, Germany: Barth.
- BONNER, J. T. (1965). *Size and Cycle: an Essay on the Structure of Biology*. Princeton: Princeton University Press.
- BOWEN, R. (1975). *Equilibrium States and the Ergodic theory of Anosov Diffeomorphisms*. New York: Springer-Verlag.
- BOWEN, R. & RUELLE, D. (1975). The ergodic theory of Axiom A flows. *Invent. Math.* **29**, 181–202.
- BROOKS, D. & WILEY, E. (1986). *Evolution as Entropy: Towards a Unified Theory of Biology*. Chicago: University of Chicago Press.
- CALDER, W. (1984). *Size, Function and Life-history*. Cambridge, MA: Harvard University Press.
- CLAUSIUS, R. (1870). *Mechanical Theory of Heat*. London: John van Voorst.
- DARWIN, C. (1859). *On the origin of species*. London: Murray.
- DEMETRIUS, L. (1974). Demographic parameters and natural selection. *Proc. Natl Acad. Sci. U.S.A.* **71**, 4645–4647.
- DEMETRIUS, L. (1977). Measures of fitness and demographic stability. *Proc. Natl Acad. Sci. U.S.A.* **74**, 384–386.
- DEMETRIUS, L. (1983). Statistical mechanics and population biology. *J. Statist. Phys.* **30**, 709–753.
- DEMETRIUS, L. (1987). An extremal principle of macro-molecular evolution. *Phys. Scr.* **36**, 693–901.
- DEMETRIUS, L. (1992). Growth rate, population entropy and evolutionary dynamics. *Theor. Pop. Biol.* **41**, 208–223.
- DEMETRIUS, L. (1997). Directionality principle in thermodynamics and evolution. *Proc. Natl. Acad. Sci. U.S.A.* **94**, 3491–3498.
- DEMETRIUS, L. (2000). Population genetics and life history evolution. In: *Evolutionary genetics from molecules to morphology* (Singh, R. & Krimbas, P. eds). Cambridge University Press, Cambridge, pp. 275–311.
- DEMETRIUS, L. & GUNDLACH, M. (1999). Evolutionary dynamics in random environments. In: *Random Dynamical Systems* (Crauel, H. & Gundlach, M., eds), pp. 371–394. Berlin: Springer.
- DEMETRIUS, L. & ZIEHE, M. (1984). The measurement of Darwinian fitness in human populations. *Proc. Roy. Soc. London. Series B.* **222**, 33–50.
- DEMONGEOT, J. & DEMETRIUS, L. (1989). Les facteurs endogenes et exogenes dans l'évolution démographique de la France—une étude empirique. *Population* **1**, 109–134.
- EIGEN, M. (1971). Self-organization of matter and the evolution of biological macromolecules. *Naturwissenschaften* **58**, 465–523.
- EIGEN, M., MCCASKILL, J. & SCHUSTER, P. (1988). Molecular quasi-species. *J. Phys. Chem.* **92**, 6881–6891.
- EIGEN, M. & SCHUSTER, R. (1979). *The Hypercycle—A Principle of Natural Self-organization*. Berlin: Springer.
- FELLER, W. (1951). Diffusion processes in genetics. In: *Proceedings 2nd Berkeley Symposium on Mathematical Statistics and Probability* (Neyman, J., ed.). University of California Press, Berkeley, pp. 227–246.
- FISHER, R. A. (1930). *The Genetical Theory of Natural Selection*. New York: Dover.
- KARLIN, S. (1992). R. A. Fisher and evolutionary theory. *Statist. Sci.* **7**, 13–33.
- KINGMAN, J. F. C. (1980). *The Mathematics of Genetic Diversity*. Philadelphia: Society of Industrial and Applied Mathematics.
- LEUTHÄUSSER, I. (1987). Statistical mechanics of Eigen's evolution model. *J. Statist. Phys.* **48**, 343–360.
- LEVINS, R. & LEWONTIN, R. (1985). *The Dialectical Biologist*, pp. 14–17. Cambridge, MA: Harvard University Press.
- LIU, L. & COHEN, J. E. (1987). Equilibrium and local stability in a logistic matrix model for age-structured populations. *J. Math. Biol.* **25**, 73–88.
- LOTKA, A. (1939). On an integral equation in population analysis. *Ann. Math. Stat.* **10**, 144–161.
- MACIEIRA-COELHO, A., PONTEN, J. & PHILIPSON, L. (1966). *Exp. Cell Res.* **42**, 673–684.
- MAYNARD SMITH, J. (1988). In: *Evolutionary Progress* (Nitecki, M., ed.) Chicago: pp. 219–230. University of Chicago Press.
- NEWELL, N. D. (1949). Phyletic size increase: an important trend illustrated by fossil invertebrates. *Evolution* **3**, 103–124.

- PETERS, R. H. (1983). *The Ecological Implications of Body Size*. Cambridge, U.K.: Cambridge University Press.
- SINAI YA, G. (1972). Gibbs measures in ergodic theory. *Russ. Math. Surv.* **27**, 21–69.
- STANLEY, S. M. (1973). An explanation of Cope's rule. *Evolution* **27**, 1–26.
- WEBER, B. H., DEPEW, D. J. & SMITH, J. D. 1988. *Entropy, Information and Evolution*. Cambridge, MA: The MIT Press.
- WICKEN, J. S. (1987). *Evolution, Information and Thermodynamics: Extending the Darwinian Program*. Oxford: Oxford University Press.