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Thermodynamics of natural selection II: Chemical Carnot cycles

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Abstract

This is the second in a series of three papers devoted to energy flow and entropy changes in chemical and biological processes, and to their relations to the thermodynamics of computation. In the first paper of the series, it was shown that a general-form dimensional argument from the second law of thermodynamics captures a number of scaling relations governing growth and development across many domains of life. It was also argued that models of physiology based on reversible transformations provide sensible approximations within which the second-law scaling is realized. This paper provides a formal basis for decomposing general cyclic, fixed-temperature chemical reactions, in terms of the chemical equivalent of Carnot's cycle for heat engines. It is shown that the second law relates the minimal chemical work required to perform a cycle to the Kullback–Leibler divergence produced in its chemical output ensemble from that of a Gibbs equilibrium. Reversible models of physiology are used to create reversible models of natural selection, which relate metabolic energy requirements to information gain under optimal conditions. When dissipation is added to models of selection, the second-law constraint is generalized to a relation between metabolic work and the combined energies of growth and maintenance.

Keywords: Carnot cycle; Landauer's principle; Thermodynamics; Natural selection

1. Introduction: from the second law to physiology and natural selection

This is the second in a series of three papers, which jointly construct a framework for understanding the energetic constraints on metabolism and natural selection, and for relating chemical entropy reduction in biology to the information gain in computational processes. The first paper (Smith, 2008a) (hereafter called Paper I) introduced the fundamental relation between energy and information suggested by the second law of thermodynamics

$$\mathrm{d}W = k_B T \, \mathrm{d}\mathcal{I}, \tag{1}$$

in which $\mathrm{d}W$ is the increment of work required in a reversible process at absolute temperature T, and $\mathrm{d}\mathcal{I}$ is the information gained about a system through that process, measured as a reduction brought about in the system's entropy. (k_B is Boltzmann's constant.)

Paper I reviewed physiological evidence from bacterial growth (Morowitz, 1955) and allometric regularities in metazoan development (West et al., 2002; West and Brown, 2005), which suggest that the energy used in organismal growth and development, across a range of sizes, scales with the entropy reduction to form its biomass as some multiple of Eq. (1). The constant of proportionality varies somewhat with taxon, but its total variation is much less than the biomass variation in the organisms considered (picograms to metric tons), and the proportionality constant does not seem to depend on body size, temperature, or the temporal rate of growth within a taxon. In other words, the energetics of individual growth and development seems indexed to a metabolic measure of information, even though growth is not carried out reversibly.

The current paper performs three tasks not undertaken in Paper I: introduction of a particular model of physiological growth through reversible transformations, explicit definition of chemical work, and derivation of a measure of information appropriate to biochemical organization. The main observation of the paper is that

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reversible metabolic processes at fixed temperature are naturally decomposed into chemical cycles analogous to the Carnot cycle for reversible heat engines (Fermi, 1956), with the substitution of particle number for heat, and chemical potential for temperature, in the Carnot diagram. Just as infinitesimal thermal Carnot cycles provide a basis for decomposing arbitrary reversible thermal cycles, the infinitesimal chemical Carnot cycles provide a basis for decomposing arbitrary reversible fixed-temperature chemical cycles. The chemical work required to carry out a reversible chemical cycle is then a lower bound on the work required for *any* cycle that rejects the same entropy from the chemical medium—in this case, the growth medium that is being converted to biological matter (hereafter "biomatter").[1]

A Carnot-like decomposition of physiology provides a basis, on one hand, for embedding physiology in a context of natural selection, and on the other hand, for relating chemical organization to computation. The scaling of growth energetics in proportion to Eq. (1) suggests that reversible physiology can serve as a foundation for a reversible limit of natural selection, in which differential fitness is introduced but all degradative as well as synthetic reactions are lossless. Mutation, decay, and other irreversible effects may then be introduced as departures from reversible selection, to establish relations between the entropy reduction of biomatter and the ongoing metabolic power required to maintain it.

The comparison to computation is the domain of the third paper (Smith, 2008b) (hereafter, Paper III). The projection of the chemical Carnot cycle onto a larger space in which total entropy is conserved between the system and its environment yields a non-closed path, whose net effect is the transfer of entropy between the chemical milieu and a heat bath. This path, here called a *Landauer cycle*, maps in detail onto the classical Landauer description of computation (Landauer, 1961; Bennett, 1982) as a composition of reversible logic operations and irreversible erasure steps. The entropy reduction of chemistry corresponds directly to the data entropy reduction inherent in computation, clarifying the sense in which physiology directed by natural selection is a computational process.

1.1. Scope of the results

For the sake of definiteness, the mapping onto a chemical Carnot cycle and the derivation of energetic bounds on information will be performed for a toy model of physiology, drawn from the polymerization and hydrolysis of oligomers. The idealization is similar to one used by Bennett (1982), who was also concerned with the mapping of physiology and selection onto Landauer's principle. The thermodynamic disaggregation of reversible cycles is more explicit in this paper than in Bennett (1982), and provides an underpinning for the idealized treatment of aggregate transformations in Bennett's work.

The relations between energy and information will be derived in this paper, however, in a way that makes clear how they extend to more general processes in physiology. The major function of the toy model is to bridge the abstract constraint from the second law of thermodynamics and the explicit physiological mechanisms by which that constraint may be realized. To illustrate that the results are not limited either to the physiological domain of oligomer sequencing, or even to cyclic transformations, the same equations will be interpreted also for the problem of molecular recognition by non-covalent assemblies (Schneider et al., 1986; Schneider, 1991a, b, 1997), where a related mapping onto the problem of channel encoding has been derived. Paper III will complete the analysis of this case, relating encoding to the more general process of computation.

The remainder of the introduction considers the choice of a toy model intended to capture the interaction between physiology and selection, and the interpretation of such a model within the more complex hierarchy and information flow of real physiology. Section 2 introduces the chemistry of the formal model and the device of the van't Hoff reaction box to make explicit the idealization of infinite separation of timescales in a complex reaction sequence. The main results for chemical efficiency, heat transfer, and the second-law relation between chemical work and heat, are derived in this section, and the extension to more general chemistry including the problem of molecular recognition is discussed. Section 3 extends the toy model of physiology to an equivalent toy model of natural selection, first in the idealization of reversibility and then with the addition of dissipation. The physiological bound for the energetic creation of ordered chemical states (Eq. (22)) is extended to an expression for the evolutionary creation and maintenance of such states in this section (Eq. (36)). Finally, Section 4 provides summary comments and discussion.

1.2. Choosing a model system

Because the conceptual contribution of this paper is the *decomposition* of idealized chemical cycling into a standard basis of primitive transformations, it is more desirable to concretely model a subset of physiology for which this decomposition is fairly literal and intuitive, than to try to capture all of cell physiology in an abstract model. Physiology includes, as broad categories of processes, (1) the metabolic network of small-molecular substrates, (2) the chemi-osmotic energy system for transducing redox couples to phosphate esters, (3) a diverse array of oligomerization reactions acting on a selected subset of the small metabolites, (4) physical processes of folding, self-assembly, complex formation, vesicularization, etc., and (5) diverse energy-intensive but non-biosynthetic processes

[1]In these three papers, *biomatter* is used to refer to the compositional state of the constituents of living systems, while *biomass* is used as a measure referring to the mass of some collection of biomatter.

associated with signaling, regulation, and transport. The chemical and physical interactions, and levels of structure participating in these transformations vary widely among physiological processes, while the catalytic nature of interactions across levels of structure causes information to be redundantly represented in different physical substrates (Smith, 2007).

The major distinctions of interest for this paper, between small-molecule metabolism and the oligomerization reactions, are that the synthesis of the small collection of universal (Smith and Morowitz, 2004), low molecular-weight core metabolites accounts for most metabolic energy (McCollom and Amend, 2005), but pathways themselves are not directly inherited, mutated, or selected; rather the metabolic network is selected only indirectly through selection on the genome, through the filters of development and regulation. Small-molecule metabolism also involves somewhat heterogeneous organic chemistry of functional groups, which is cumbersome to capture in a general notation that also captures the constraints from catalysis. In contrast, oligomerization—specifically of RNA, DNA, polypeptides, and some oligosaccharides—occurs uniformly through phosphate-mediated dehydration, with ATP the usual phosphoryl donor and coupler between polymerization and the chemi-osmotic energy system. Because polymerization accounts for less energy than primary organosynthesis, and because the polymer bonds in an oligomer are identical at the level of local chemistry, the information in oligomers is primarily represented by their monomer sequences (or branching structures in the case of glycans), making oligomers the most obviously informational component of biomatter.

Among the oligomers, the most exclusively informational are RNA—which retains some catalytic and regulatory functions (Huang et al., 2000), but has given over to proteins most enzymatic functions it is proposed to have had in an earlier RNA-dominated phase of life—and DNA, which probably never had such functions. The subset of heterotrophic physiology devoted to hydrolysis of oligomers and repolymerization of their monomers in new sequences is the foundation of trophic ecology. For RNA and DNA in particular, specific oligomer sequences have so many defining properties of species that they are sometimes held to have been the first substrate for Darwinian selection (Gesteland et al., 2006). The chemistry of oligomerization therefore provides a simple model for use in this paper, onto which Darwinian selection may be imposed with minimal need to explicitly model control flow or informational redundancy within cells.

Bennett (1982) emphasized that the processes of oligomerization *could be* carried out reversibly, consistent with the functioning of real polymerases, so that a model of reversible oligomerization violates no underlying cellular mechanisms, even though polymerization and hydrolysis in living cells do not take place reversibly. Furthermore, because the relations between work and information derived for this model simply reflect the second law of thermodynamics and the structure of the Gibbs free energy, their generalization to arbitrary reversible chemical reactions is straightforward, even if the associated decomposition into chemical Carnot cycles may not be. The oligomer model should not, therefore, be understood as a representation of most energy flow in cells, or as a simplification of information flow along the lines of a naïve interpretation of the central dogma, but rather as a fortuitous case for which minimal deviations from real processes are required to bring together physiology, selection, thermodynamics, and computation.

2. Formalizing chemical cycles in metabolism and evolution

The two major components of a reversible oligomerization model are the chemistry of polymerization and hydrolysis, and the regeneration of ATP. The latter may be captured in a simplified model of the chemi-osmotic system. The similarity to Carnot cycling in thermodynamics begins with the recognition that the chemi-osmotic system is the origin of chemical *work* for polymerization, while the monomers, oligomers, and ATP are the chemical counterparts to a *working fluid*. The fact that most cellular ATP synthesis is performed by a mechanical enzyme, the ATP synthase, permits the further simplification of omitting explicit reference to the respiratory system and proton transport, and modeling the ATP synthase as a source of entropy-free enthalpy in the conversion of ATP to AMP and orthophosphate. The ATP synthase—approximately reversible in real cells—becomes the piston of the Carnot analysis, decoupling the polymerization process from whatever chemical engine cycles drive the synthase. It is interesting that nature appears to have favored such a mechanical coupling between redox energy and the most prevalent biosynthetic reaction (phosphate-driven polymerization) so strongly that the ATP synthase is an invariant feature of all domains of life (Martin and Russell, 2006), which not even cellular lipids or DNA replicase systems are (Koonin and Martin, 2005).

To further idealize the separation between sequence information of oligomers and the energetics of monomer formation, it is convenient to consider sequences of some fixed length N. It is not necessary to assume that different sequences have the same free energies of formation; indeed it clarifies the later generalization to metabolism to suppose sequence-specific free energy. It will, however, be convenient for the abstraction of idealized cycles to consider hydrolysis and polymerization only among sequences with the same monomeric composition.[2]

Rather than abstract polymerization as a single reversible process, as in Bennett (1982), reversibility will be made explicit and decomposed into legs analogous to the legs of the Carnot cycle with the device of the van't Hoff

[2]The generalization of this constraint to metabolism is a requirement of flux balance, which is cyclical for organic molecules only at the level of the autotrophic organism or ecosystem.

reaction box (Fermi, 1956). The constraints provided by the van't Hoff box represent the idealized separation of timescales by the polymerase enzymes, which are regarded as external to the polymerization reaction they catalyze, but which could be made endogenous with population-level models of multiple sequences constituting a hypercycle (Eigen and Schuster, 1977, 1978).

Introduce an alphabet of Z monomers with chemical symbols $\mathrm{M}_z, z \in 1,\ldots,Z$, and vectors of ordered components $\vec{\alpha} \equiv (\alpha_1,\ldots,\alpha_{N+1})$, with $\alpha_i \in 1,\ldots,Z$ for each i, to index polymers of length $N+1$ made from the monomers. (Length $N+1$ is chosen so that N phosphate ester linkages are formed, as a notational convenience.) Take $\Pi_{\vec{\alpha}}$ as the chemical symbol for a polymer with sequence $\vec{\alpha}$.

To entail reversibility, suppose that polymerization is in equilibrium with ATP hydrolysis in the reaction

$$N\mathrm{ATP} + \sum_{i=1}^{N+1} \mathrm{M}_{\alpha_i} \rightleftharpoons N\mathrm{AMP} + 2N\mathrm{P}_i + \Pi_{\vec{\alpha}}. \tag{2}$$

(P_i denotes orthophosphate.) This may be understood as merely an assumption about rates relative to diffusion and regeneration of ATP, since the value of the equilibrium constant need not be near unity. Reaction (2) may be interpreted in terms of polymerization activated by pyrophosphate transfer from ATP (onto the other nucleoside monophosphates by nucleoside monophosphate kinases, Stryer, 1981, p. 747), or adenylate transfer (as in polypeptide synthesis, Stryer, 1981, p. 880, or the action of DNA ligase if the "monomeric" units are thought of as pre-formed strands of DNA, Stryer, 1981, p. 793).[3] In all such cases either the activation or polymerization step is coupled to pyrophosphate hydrolysis, and the other to release of AMP. Introducing

$$v_z^{\vec{\alpha}} \equiv \sum_{i=1}^{N+1} \delta_{\alpha_i,z}$$

(the number of occurrences of monomer z in $\Pi_{\vec{\alpha}}$), Eq. (2) may be recast in canonical form as

$$N\mathrm{ATP} + \sum_{z=1}^{Z} v_z^{\vec{\alpha}} \mathrm{M}_z \rightleftharpoons N\mathrm{AMP} + 2N\mathrm{P}_i + \Pi_{\vec{\alpha}}. \tag{3}$$

Denoting by [X] the molar concentration of any species X, and supposing that activities are proportional to concentrations for simplicity, the equilibrium condition for reaction (3) may be written as

$$\left(\frac{[\mathrm{ATP}]}{[\mathrm{AMP}][\mathrm{P}_i]^2}\right)^N = \frac{[\Pi_{\vec{\alpha}}]}{\prod_{z=1}^{Z}[\mathrm{M}_z]^{v_z^{\vec{\alpha}}}} K_{\vec{\alpha}}(T). \tag{4}$$

If the polymers are chemically degenerate, all sequences are combinatorially neutral. This case corresponds to taking the equilibrium constant $K_{\vec{\alpha}}(T)$ to be the same function of temperature for all $\vec{\alpha}$ of length N. Except where this special case leads to some feature of interest below, the various $K_{\vec{\alpha}}(T)$ will be assumed to be distinguishable functions.

The ATP synthase reaction for interconverting ATP and AMP is

$$\mathrm{AMP} + 2\mathrm{P}_i \rightleftharpoons \mathrm{ATP}. \tag{5}$$

If metabolic enzymes are idealized as providing an infinite separation of timescales, ATP/AMP interconversion happens only through the synthase or in conjunction with polymerization/depolymerization, and the reaction (5) need not be in chemical equilibrium at any time.

A minimal idealized *metabolic cycle* within this system is the combined catabolism of one polymer $\Pi_{\vec{\beta}}$ to monomers and ATP, followed by anabolism of those monomers to some (generally different) polymer $\Pi_{\vec{\alpha}}$. Catabolism and anabolism correspond, respectively, to death and reproduction if we choose to regard the polymer produced as a molecular equivalent of an "individual". The way in which different metabolic cycles will be endowed with different relative rates below, to create a model of natural selection, respects such an interpretation but does not require it.

2.1. Serial catalysis and the metabolic cycle

Catalyst/substrate complex formation allows catalysts to act serially, so that the subset of reactions participating in a chemical equilibrium (with all other reactions forbidden) can change through time. Complex formation provides the equivalent of valves that decouple particular molecular species from the main reactions in a chemical counterpart to the classical Carnot cycle. *Aggregate* metabolic processes can operate reversibly as long as coupling and decoupling are alternated with changes in the chemical potentials for ATP versus AMP in the main reaction domain.

"Biomatter" in this description comprises a collection of reservoirs for the polymers of different sequences, which will be supposed here to be large enough that their concentrations and chemical potentials are not changed by the addition of finite numbers of molecules. Metabolism changes the entropy of biomatter by changing individual polymer sequences and so altering the numbers of molecules and hence the entropy in different reservoirs, consuming or delivering chemical work as required to do so reversibly. An ideal cyclic metabolism preserves the total number of polymers and returns the monomer and ATP/AMP systems to their original states at the end of each cycle.

A single pathway in such an idealized reversible metabolism can be analyzed with the van't Hoff reaction box (Fermi, 1956) of Fig. 1. A reaction chamber filled with a solution of all the monomers $\{\mathrm{M}_z\}$ is serially coupled or uncoupled by valves from diffusive contact with reservoirs of two species of polymers $\Pi_{\vec{\alpha}}$ and $\Pi_{\vec{\beta}}$. The reactor is continuously in diffusive contact with reservoirs for ATP, AMP, and P_i, and these are injected with the stoichiometry of Eq. (5) by a system of pistons whose displacement is a

[3] A somewhat more complex process involving two ATP and various phosphate and adenylate transfers is involved in polysaccharide formation (Metzler, 2003, p. 994), which would require a slightly different model reaction but not different principles.

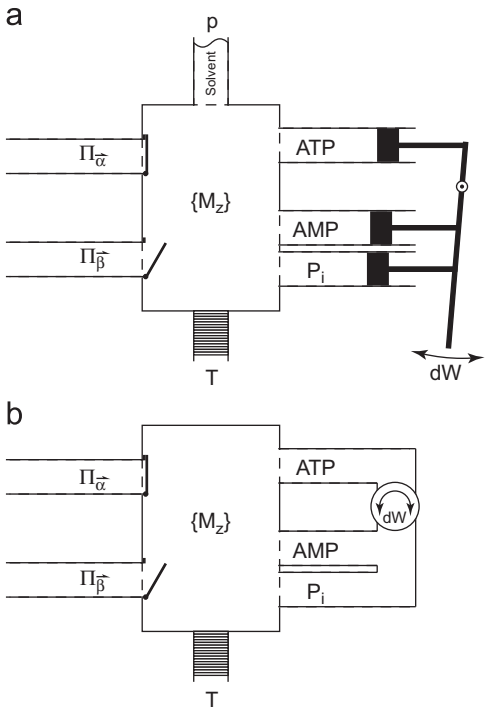

Fig. 1. (a) Metabolism idealized with a van't Hoff reaction box. Cylinders containing solutions of the indicated solutes are in diffusive contact with a reaction chamber through windows permeable only to the solvent and the solutes particular to each cylinder. Cylinders with polymers $\Pi_{\vec{\alpha}}$ and $\Pi_{\vec{\beta}}$ are infinite reservoirs, which may be decoupled from the reaction chamber by valves. The reaction chamber contains the inventory of monomers M_z and any solutes drawn from the other cylinders. The solvent reservoir is in equilibrium at a pressure p, and coupled to the reaction chamber through a window permeable only to solvent. A thermal reservoir maintains temperature T in the whole system. The action of ATP synthase is achieved in the van't Hoff picture with some linkages that deliver concentrations of ATP, AMP, and P_i consistent with Eq. (5). (b) The ATP synthase performs the transformation of Eq. (5) directly on the solutes.

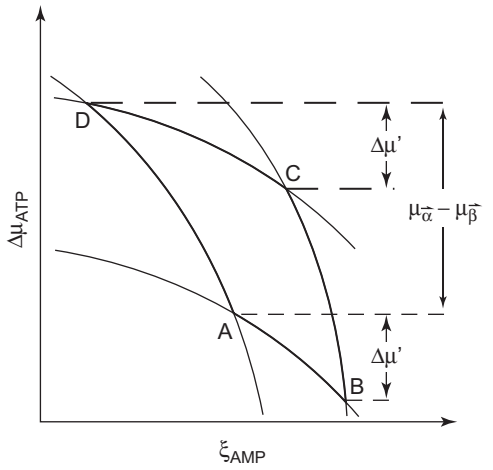

Fig. 2. A chemical refrigeration cycle $ABCDA$ (or engine cycle $ADCBA$), performed by the van't Hoff box of Fig. 1. Individual arcs are described in the text. ξ_{AMP} is the number of moles of ATP converted to AMP by the pistons as the cycle progresses, and $\Delta\mu_{ATP} \equiv \mu_{ATP} - \mu_{AMP} - 2\mu_{P_i}$. If we assume chemical equivalence of $\Pi_{\vec{\alpha}}$ and $\Pi_{\vec{\beta}}$, arcs AB and CD will lie on identical curves translated by $\mu_{\vec{\alpha}} - \mu_{\vec{\beta}} = \log([\Pi_{\vec{\alpha}}]/[\Pi_{\vec{\beta}}])$ in the polymer reservoirs. Because the same number of monomers is generated along AB as is consumed along CD, the same change in chemical potential $\Delta\mu'$ occurs along arc AB and arc DC. The total chemical work $\oint dW \equiv -\oint \Delta\mu_{ATP}\, d\xi_{AMP}$ done on the system is the area inside the dark boundary, positive for refrigeration and negative for the engine cycle.

pure work variable. The reactor and all reservoirs are kept at pressure p through the solvent, and temperature T through contact with a heat bath.

A reversible metabolic cycle consuming polymer $\Pi_{\vec{\beta}}$ and producing $\Pi_{\vec{\alpha}}$ is shown in Fig. 2. It is the chemical analogue to the Carnot cycle for thermal engines or refrigerators, with particle number (in this case, ATP) taking the place of entropy and chemical potential taking the place of temperature in a Carnot state diagram. The cycle of Fig. 2 describes a chemical engine in the direction $ADCBA$, and a "refrigerator" in direction $ABCDA$, if the chemical potential of $\Pi_{\vec{\alpha}}$ is assumed to be higher than that of $\Pi_{\vec{\beta}}$. The four arcs of the cycle (in the refrigerating direction) are specified as follows:

1. Arc AB is performed with the reservoir for polymers $\Pi_{\vec{\beta}}$ open to the reaction chamber. The concentration (hence chemical potential) of ATP is lowered with the pistons, driving reaction (3) toward the left and consuming $\Pi_{\vec{\beta}}$ to produce monomers. Because catabolism generates ATP, the pistons must remove this and more to reduce the ATP concentration.
2. Arc BC is performed with the reaction chamber isolated from both polymer reservoirs, using AMP → ATP conversion to raise the reactor chemical potential from equilibrium with $\mu_{\vec{\beta}}$ to equilibrium with $\mu_{\vec{\alpha}}$.
3. Arc CD is performed in contact with the reservoir for $\Pi_{\vec{\alpha}}$. Now ATP is generated to drive reaction (3) to the right, producing $\Pi_{\vec{\alpha}}$ and returning the monomer concentration to its original value. More ATP must be produced on arc CD than was consumed on arc AB, because $\mu_{\vec{\alpha}} > \mu_{\vec{\beta}}$.
4. Finally arc DA is performed in isolation from both polymer reservoirs, using ATP → AMP conversion to restore the chemical potential to equilibrium with $\mu_{\vec{\beta}}$. More ATP is consumed by the pistons on arc DA than was produced on arc BC, because the average ATP concentration is higher in equilibrium with lower concentrations of monomers, and more moles are consumed to effect the same change in concentration.

2.2. Heat transfer in the metabolic cycle

To analyze the entropic consequences of the cycle in Fig. 2, we consider the flows of particles, enthalpy and entropy, making use of the strict cyclicity of this model of metabolism. A few standard definitions are provided in Appendix A to establish notation, and also to present the point of view from which Legendre duality will be considered throughout the paper. Temperature will be measured in energy units, $\tau \equiv k_B T$, and entropy $\sigma \equiv S_{Gibbs}/k_B$ will be measured in units of the natural logarithm (nats).

Since it is conventional to work with molar concentrations rather than particle numbers, for each molecular species X, the particle number is expressed in terms of the concentration by $N_X = VN_A[\mathrm{X}]$, and the Gibbs free energy (A.7) as

$$G_X = VN_A[\mathrm{X}]\mu_X, \tag{6}$$

where V is the containing volume, N_A is Avagadro's number, and μ_X is the chemical potential of X. All species changed over whole metabolic cycles are in separate solutions in Fig. 1, and entropies of mixing in common reaction volumes will be omitted from the notation here for simplicity.

Under the simplifying assumption that activities can be replaced with concentrations, μ_X at any concentration [X] is related to its value $\bar{\mu}_X$ at reference concentration [$\bar{\mathrm{X}}$] as

$$\mu_X = \bar{\mu}_X + \tau \log\left(\frac{[\mathrm{X}]}{[\bar{\mathrm{X}}]}\right). \tag{7}$$

If [$\bar{\mathrm{X}}$] is simply a reference scale for concentrations, independent of species, we may recognize $\bar{\mu}_X \equiv G^0_X$, the standard free energy of formation per particle of species X, up to a constant that can be absorbed in the zero of chemical potential. For instance, under a thermodynamic equilibrium among the polymer species, the relative concentrations are related by

$$\mu_{eq} = G^0_{\Pi_{\vec{\alpha}}} + \tau \log\left(\frac{[\Pi_{\vec{\alpha}}]_{eq}}{[\bar{\mathrm{X}}]}\right), \tag{8}$$

for all $\Pi_{\vec{\alpha}}$. It is useful to keep the notation for $G^0_{\Pi_{\vec{\alpha}}}$ from Eq. (8), even if the polymers are chemically equivalent, because it clarifies the role of chemical work in producing deviations of the polymer distribution from equilibrium.

Using the relation (6) that, for any species, $VN_A[\mathrm{X}]\mu_X = G_X = H_X - \tau\sigma_X$, the entropy under the same conditions can be written as

$$\sigma_X = \frac{1}{\tau}(H_X - VN_A[\mathrm{X}]G^0_X) - VN_A[\mathrm{X}]\log\left(\frac{[\mathrm{X}]}{[\bar{\mathrm{X}}]}\right). \tag{9}$$

In Eq. (9), $\sigma^0_X \equiv (H_X/(VN_A[\mathrm{X}]) - G^0_X)/\tau$ is an entropy of formation per particle for species X at standard conditions, including entropies of solvation and internal degrees of freedom. Likewise we may introduce the notation $h^0_X \equiv H_X/(VN_A[\mathrm{X}])$ for the enthalpy of formation per particle, which is not dependent on the concentration. For polymers the entropy may be referenced to a chemical equilibrium by rewriting Eq. (9) as

$$\sigma_{\Pi_{\vec{\alpha}}} = \frac{1}{\tau}(H_{\Pi_{\vec{\alpha}}} - VN_A[\Pi_{\vec{\alpha}}]\mu_{eq}) - VN_A[\Pi_{\vec{\alpha}}]\log\left(\frac{[\Pi_{\vec{\alpha}}]}{[\Pi_{\vec{\alpha}}]_{eq}}\right). \tag{10}$$

The reaction (3) (proceeding to the left) converts polymers to monomers and AMP to ATP, while the reaction (5) (proceeding to the left) consumes ATP to produce AMP and chemical work. Denote the extent of the former reaction of polymer $\Pi_{\vec{\alpha}}$ by $\xi_{\vec{\alpha}}$, and the extent of the latter by ξ_{AMP}. These reactions take initial concentrations $[\mathrm{X}]_0$ for species X to concentrations [X] in the course of the reaction according to

$$\begin{aligned}
&[\Pi_{\vec{\alpha}}] \to [\Pi_{\vec{\alpha}}]_0 - \xi_{\vec{\alpha}},\\
&[\mathrm{M}_z] \to [\mathrm{M}_z]_0 + \nu^{\vec{\alpha}}_z \xi_{\vec{\alpha}}, \quad \forall z,\\
&[\mathrm{ATP}] \to [\mathrm{ATP}]_0 + N\xi_{\vec{\alpha}} - \xi_{AMP},\\
&[\mathrm{AMP}] \to [\mathrm{AMP}]_0 - N\xi_{\vec{\alpha}} + \xi_{AMP},\\
&[\mathrm{P}_i] \to [\mathrm{P}_i]_0 - 2N\xi_{\vec{\alpha}} + 2\xi_{AMP}.
\end{aligned} \tag{11}$$

The equilibrium equation (4) arises from the more general equation of chemical potentials

$$\mu_{\Pi_{\vec{\alpha}}} - \sum_{z=1}^{Z} \nu^{\vec{\alpha}}_z \mu_{\mathrm{M}_z} = N(\mu_{ATP} - \mu_{AMP} - 2\mu_{\mathrm{P}_i}) \tag{12}$$

under the assumption (7). Suppose also that the initial concentrations $[\mathrm{X}]_0$ are in equilibrium with each other (for consideration of a single metabolic cycle, the polymer concentrations $[\Pi_{\vec{\alpha}}]_0$ need not be in chemical equilibrium with each other at values $[\Pi_{\vec{\alpha}}]_{eq}$), and denote the chemical potential coupled to the ATP synthase (the pistons in Fig. 1) by $\Delta\mu_{ATP} \equiv \mu_{ATP} - \mu_{AMP} - 2\mu_{\mathrm{P}_i}$. The chemical work done on the system, formally the sum

$$\mathrm{d}W \equiv \sum_X \mathrm{d}G_X = \sum_X \mu_X \,\mathrm{d}N_X \tag{13}$$

over all species, reduces by Eq. (12) to

$$\mathrm{d}W = -\Delta\mu_{ATP}\,\mathrm{d}\xi_{AMP}, \tag{14}$$

which by Eq. (A.6) may also be written $\mathrm{d}W = \mathrm{d}H - \tau\,\mathrm{d}\sigma$ for total enthalpy H and entropy σ. Over a complete metabolic cycle therefore

$$\oint \mathrm{d}W = \oint \mathrm{d}H - \oint \tau\,\mathrm{d}\sigma. \tag{15}$$

If we were to assume that $K_{\vec{\alpha}}(\tau)$ is the same function of τ for all $\vec{\alpha}$, the further simplification would result that

$$\oint \mathrm{d}H = 0, \tag{16}$$

though the results below are derived more generally.

In this idealization of metabolism the internal components of the reactor return to their original conditions over complete cycles

$$\oint \left(\mathrm{d}G_{ATP} + \mathrm{d}G_{AMP} + \mathrm{d}G_{\mathrm{P}_i} + \sum_{z=1}^{Z} \mathrm{d}G_{\mathrm{M}_z}\right) = 0, \tag{17}$$

and as many polymers are consumed as are produced

$$\Delta N_{\Pi_{\vec{\alpha}}} = -\Delta N_{\Pi_{\vec{\beta}}}. \tag{18}$$

Therefore from the definition (13) of chemical work and Eq. (17), we also have

$$\oint \mathrm{d}W = \mu_{\Pi_{\vec{\alpha}}} \Delta N_{\Pi_{\vec{\alpha}}} + \mu_{\Pi_{\vec{\beta}}} \Delta N_{\Pi_{\vec{\beta}}} = \Delta G^{CD}_{\Pi_{\vec{\alpha}}} + \Delta G^{AB}_{\Pi_{\vec{\beta}}}, \tag{19}$$

in which superscripts serve as a reminder over which arc of the cycle a given polymer number changes. With Eq. (18), Eq. (19) becomes the chemical equivalent of Carnot's theorem (Fermi, 1956) for the cycle of Fig. 2

$$\oint \mathrm{d}W = \left(1 - \frac{\mu_{\Pi_{\vec{\beta}}}}{\mu_{\Pi_{\vec{\alpha}}}}\right) \Delta G^{CD}_{\Pi_{\vec{\alpha}}}. \tag{20}$$

For a Carnot engine, the reference energy on the right-hand side would be the heat rejected to the hot reservoir. For the chemical cycle it is the change $\Delta G^{CD}_{\Pi_{\vec{\alpha}}}$ in Gibbs free energy of the polymer reservoir at higher chemical potential. The number $\eta_{\vec{\alpha}\vec{\beta}} \equiv (1 - \mu_{\Pi_{\vec{\beta}}}/\mu_{\Pi_{\vec{\alpha}}})$ is the chemical counterpart to the Carnot efficiency, and $\gamma_{\vec{\alpha}\vec{\beta}} \equiv \eta_{\vec{\alpha}\vec{\beta}}/(1 - \eta_{\vec{\alpha}\vec{\beta}})$ is called the coefficient of performance when the cycle is being run as a refrigerator.

Sequence information is conventionally expressed in terms of Shannon entropies of normalized distributions, while chemical entropy is normalized by particle number. To convert from chemical to Shannon entropies for a fixed number of particles, and so to extract the distributional consequences of work flux, introduce a probability distribution p (now for any number of polymer types), with components $p_{\vec{\alpha}}$ that are the fractions of polymers in each sequence state $\vec{\alpha}$. Supposing for convenience that the volume is the same in each polymer reservoir, and denoting by

$$N_\Pi \equiv \sum_{\vec{\alpha}} N_{\Pi_{\vec{\alpha}}}$$

the total number of polymers, the probability components may be expressed also in terms of concentrations

$$p_{\vec{\alpha}} \equiv \frac{N_{\Pi_{\vec{\alpha}}}}{N_\Pi} = \frac{[\Pi_{\vec{\alpha}}]}{\sum_{\vec{\alpha}} [\Pi_{\vec{\alpha}}]}. \tag{21}$$

Denote by π the value of the distribution p when the polymers are in chemical equilibrium at concentrations $[\Pi_{\vec{\alpha}}]_{eq}$ (recalling that always

$$\sum_{\vec{\alpha}} [\Pi_{\vec{\alpha}}] = \sum_{\vec{\alpha}} [\Pi_{\vec{\alpha}}]_{eq}$$

by Eq. (18)).

Then combining Eq. (15) for the chemical work with the equilibrium-referenced form (10) for the entropy

$$\oint \mathrm{d}W = N_\Pi \tau \sum_{\vec{\alpha}} \oint \mathrm{d}p_{\vec{\alpha}} \log \frac{p_{\vec{\alpha}}}{\pi_{\vec{\alpha}}} = N_\Pi \tau \oint \mathrm{d}D(p\|\pi), \tag{22}$$

where

$$D(p\|\pi) \equiv \sum_{\vec{\alpha}} p_{\vec{\alpha}} \log \frac{p_{\vec{\alpha}}}{\pi_{\vec{\alpha}}} \tag{23}$$

is the Kullback–Leibler divergence of the distribution p from the chemical equilibrium distribution π and we have used the fact that

$$\sum_{\vec{\alpha}} \oint \mathrm{d}p_{\vec{\alpha}} = 0.$$

(See Cover and Thomas, 1991, Section 2.3 for a discussion of the Kullback–Leibler divergence and its interpretation.) The explicit enthalpy terms cancel in Eq. (22), and the contribution to the Gibbs free energy from μ_{eq} vanishes by conservation of polymer number, with the only remaining contribution represented in the equilibrium distribution π. This relation is therefore valid whether or not $K_{\vec{\alpha}}(\tau)$ is the same function for all $\vec{\alpha}$. Note also that it applies, whether only two indices $\vec{\alpha}$ and $\vec{\beta}$ are affected by a single metabolic cycle, or the work flux is summed over an arbitrary collection of reversible cycles acting collectively on a larger distribution.

The Kullback–Leibler divergence (23) is positive-semi-definite and vanishes only on $p = \pi$. In the literal form of Eq. (1), $N_\Pi \oint \mathrm{d}D(p\|\pi)$ would serve at non-zero $\oint \mathrm{d}W$ as the correct measure of "information written into" the distribution of polymers by the sequence of metabolic reactions. $D(p\|\pi)$ is not generally a pure difference of entropies, so if it is desirable to preserve the interpretation of $\mathrm{d}\mathscr{I}$ as an entropy reduction, the literal chemical work $\mathrm{d}W$ must be augmented by an enthalpy term in Eq. (1), as discussed in Section 2.3.

In the special case that metabolism has the effect of introducing new constraints on p but *respecting* all of the constraints on the equilibrium distribution, the Kullback–Leibler divergence does reduce to a pure entropy difference. Formally, the condition is that the equilibrium distribution π be a *coarse-graining* of the distribution p (defined and discussed at length in Gell-Mann and Lloyd, 1996), in which case

$$S(\pi) - S(p) = D(p\|\pi), \tag{24}$$

and the Shannon entropy is defined as

$$S(p) \equiv -\sum_{\vec{\alpha}} p_{\vec{\alpha}} \log p_{\vec{\alpha}}. \tag{25}$$

Then any integral of the form (22), starting from the equilibrium distribution, is directly an entropy reduction, which can be regarded as a mutual information about the way chemical work was input, by the arguments from Adami (2002) reviewed in Paper I. Such an entropy reduction also admits the interpretation of an instance of effective complexity. In the language of Gell-Mann and Lloyd (1996), we may regard $S(\pi)$ as a *total information*, or the entropy reduction possible upon sampling one molecule of type $\vec{\alpha}$ from the equilibrium distribution. The entropy $S(p)$ measures the residual information available upon

sampling one molecule of type $\vec{\alpha}$ if it is already known that the samples are being drawn from the evolved distribution. Their difference (24) therefore measures the information needed to specify the evolved ensemble relative to equilibrium, which is the difference between the average lengths of the shortest codes for members of the equilibrium and evolved ensembles. The difference in code length between two ensembles with the same elements is the message length needed to specify the compression algorithm for encoding the lower-entropy relative to the higher-entropy ensemble, thus a description of the regularities in the lower-entropy ensemble, which defines effective complexity. (We will return in Section 3.5 to the terms by which the coarse-graining relation (24) may be violated, but it remains an interesting empirical question to what degree metabolism refines the distributional structure of abiotic matter but mostly respects the ordering of compounds according to free energy of formation.)

2.3. Self-powering cycles

Net external work need not be provided to power the metabolic cycle, if the enthalpy of reaction is sufficient to reject the necessary entropy as heat. This is just the condition that the net free energy of reaction be negative, although in the van't Hoff schema for reversibility it is assumed that a mechanism is available to distribute the energy among the legs of the cycle as needed. To generalize from the model notation of Eq. (22) to an aggregate representation suitable for other processes, such as molecular recognition (Schneider et al., 1986; Schneider, 1991a, b) or more general small-molecule metabolism, it is helpful to revert to the explicit enthalpy/entropy decomposition of Eq. (15).

Recognizing that

$$D(p\|\pi) = \sum_{\vec{\alpha}} p_{\vec{\alpha}} \log\left(\frac{1}{\pi_{\vec{\alpha}}}\right) - S(p), \tag{26}$$

making use of the relation (8) between standard free energies and Gibbs equilibrium, and the decomposition of the standard free energy per particle $G^0_{\Pi_{\vec{\alpha}}} \equiv h^0_{\Pi_{\vec{\alpha}}} - \tau\sigma^0_{\Pi_{\vec{\alpha}}}$ defined following Eq. (9), we may express

$$N_\Pi \tau\, \mathrm{d}D(p\|\pi) = \sum_{\vec{\alpha}} N_\Pi\, \mathrm{d}p_{\vec{\alpha}} h^0_{\Pi_{\vec{\alpha}}} - N_\Pi \tau \left(\mathrm{d}S(p) + \sum_{\vec{\alpha}} \mathrm{d}p_{\vec{\alpha}} \sigma^0_{\Pi_{\vec{\alpha}}}\right). \tag{27}$$

(The constant terms dropped by using

$$\sum_{\vec{\alpha}} \mathrm{d}p_{\vec{\alpha}} = 0$$

are the opposite of those dropped in arriving originally at Eq. (22).) The sum involving $h^0_{\Pi_{\vec{\alpha}}}$ is the polymer representation of $\mathrm{d}H$ in Eq. (15), while the remaining term on the right-hand side is the representation of $\tau\,\mathrm{d}\sigma$. (Thus we check that entropies of formation per particle and entropies of distribution are additive, as required by the chain rule, Cover and Thomas, 1991.)

In the problem of molecular recognition, rather than create and destroy sequences by polymerization, proteins form non-covalent complexes with regions of DNA or RNA, and the specificity problem is to convert an initial ensemble of diverse protein-sequence complexes into a final ensemble in which any protein is paired with its target sequence exclusively (Schneider, 1997). In this context the number N_Π corresponds to the number of bound proteins (which in the simplest model may be taken as conserved), and the initial enthalpy of the (non-cyclic) recognition process is provided by "priming" the protein. If relaxation is free, no external work is provided after priming. For optimally efficient recognition, the enthalpy converted to rejected heat as the bound protein relaxes toward the target sequence equals τ times the sequence entropy removed from the population of possible complexes, with the thermal entropy $\sigma^0_{\Pi_{\vec{\alpha}}}$ of the complexes regarded as roughly constant and determined only by the number of non-covalently interacting degrees of freedom. The problem of maximizing the Shannon entropy rejected for a given priming enthalpy has been mapped onto the computational problem of optimal encoding for a noisy channel (Schneider et al., 1986; Schneider, 1991a, b). Its equivalent formulation as a problem of reversible computation will be considered in Paper III.

2.4. Chemical cycles on the entropy plaquette

The cyclic integral of the internal free energies (the term depending on the equilibrium distribution π) in Eq. (22) vanishes if the polymers are chemically identical. In such a case of symmetric particles Eq. (22) reduces to

$$\frac{1}{N_\Pi} \oint \mathrm{d}W = -\tau \oint \mathrm{d}S(p), \tag{28}$$

where N_Π now counts the total number of polymers over any collection of sequences $\vec{\alpha}$. Case (28) is appropriate for comparison to computation on a combinatorial data stream of physically interchangeable components, and is the appropriate form of Eq. (1) for processes decomposable into complete metabolic cycles.

From the chemical work relation (19), and the relation between work and both heat (15) (with $\oint \mathrm{d}H = 0$) and information (28), we could refer to the cycle of Fig. 2 as a *Landauer cycle* (the connection with the classical Landauer construction in computer science will be developed in Paper III.) A Landauer cycle is any reversible cycle isomorphic to the Carnot cycle in some *other* state variable pair than (τ, σ), which for metabolism is (μ, N). Instead of entropy flux conservation between reservoirs as in the Carnot cycle, it conserves the other extensive quantity (N), which identifies the coefficient of performance and the relevant free energy. Because it is reversible, however, it *also* conserves total entropy if the heat bath is taken into account. If we plot the same pathway on the simplex of

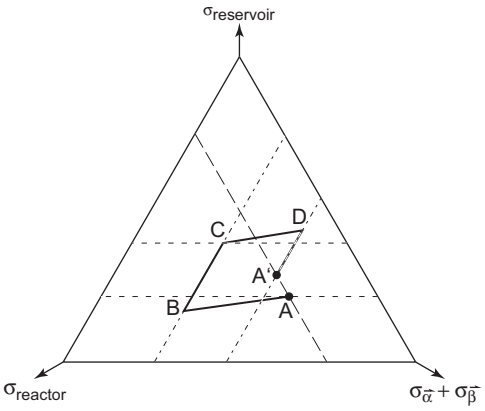

Fig. 3. The chemical refrigeration cycle on the simplex of conserved total entropy $\sigma_{reservoir} + \sigma_{reactor} + \sigma_{\vec{\alpha}} + \sigma_{\vec{\beta}}$, for the case of chemically identical polymers. The catabolic arc AB could be endothermic (shown) or exothermic, depending on the assumed reactions, and likewise for the inverse anabolic arc CD. Arcs BC and DA' are performed in isolation from the polymers $\Pi_{\vec{\alpha}}$ and $\Pi_{\vec{\beta}}$, and exchange heat solely between reactor and reservoir. The path that is cyclic in Fig. 2 makes a non-closed plaquette here, whose net effect is to transfer an amount of entropy $\oint \mathrm{d}W/\tau$ from the polymer system to the reservoir.

constant total entropy, we obtain the non-closing plaquette of Fig. 3.

Here $\sigma_{reservoir}$ is the entropy only of the heat bath,

$$\sigma_{reactor} \equiv \sigma_{ATP} + \sigma_{AMP} + \sigma_{\mathrm{P}_i} + \sum_{z=1}^{Z} \sigma_{\mathrm{M}_z}$$

is the entropy of all those components that return to their original states after each cycle, and $\sigma_{\vec{\alpha}} + \sigma_{\vec{\beta}}$ is the entropy of the chemical system on which metabolism has acted. The input of non-zero work $\oint \mathrm{d}W$, together with the assumption that the enthalpy of the chemical reservoirs has not changed, requires that an amount of entropy $\oint \mathrm{d}W/\tau$ be rejected to the thermal reservoir, equal to the entropy reduction in the chemical system, distinguishing the end of the pathway A' from the beginning A. Paper III develops the argument that the transfer of entropy from some non-thermal form of ensemble uncertainty to a heat bath is the essence of computation, and the conservation law demonstrated in Fig. 3 is the familiar Landauer's theorem for computation. Landauer entropy transfer is not the same as thermal refrigeration, in the sense that the system and heat bath are at the same temperature, and the coefficient of performance of a cycle is determined by its chemical parameters.

By repeating a Landauer cycle we can reduce the entropy of a polymer distribution arbitrarily. We achieve a particular structure in the ordered distribution if we act on it with a collection of metabolic cycles with different rates, instantiating a process of evolutionary adaptation. For reversible cycles, no further details matter about how the rates are biased or how cycles are sampled to act on the distribution.

3. From physiology to natural selection

The most basic question that arises in any attempt to relate physiological processes to natural selection is whether the energy requirements for new growth, or some other inputs associated with maintenance of the biotic state, are the primary energetic constraints on organism replacement. Beyond this basic category distinction between growth and maintenance, the question remains whether the Landauer bound (22) is informative even about the energy of new growth. Paper I reviewed two results, from bacterial growth and metazoan life histories, showing a striking relation between metabolic energy use and the entropy of formation of biomatter, but no strong connection with either physical time or temperature.

For bacterial growth into new medium, it was found (Morowitz, 1955) that the enthalpy converted to rejected heat up to any time was proportional (by a factor of about three) to the Landauer estimate for idealized growth of the biomass formed by that time. Bacterial growth into new medium is exponential, meaning that colonies of any size within this regime increase in mass by the same geometric factor per unit time, and there is no scale factor associated with the "lifetime" of individual cells except the division time.

For metazoans—which develop, age, and die—the suite of macroscopic observables is richer, but the observation again was that basic life stages as well as total lifetime are associated with approximately invariant multiples of the idealized energy required to create the body mass at each stage. For both bacteria and metazoans, the existence of such scaling regularities expresses only energetic constraints proportional to the informational *state* of biomatter, and does not reflect constraints from its maintenance through time.

The surprise from these observations is that individual development should appear to be free from any constraints of maintenance *not linked explicitly to the extent of growth*, and that inherently thermal or temporal effects are relegated at leading order to the population structure as it becomes limited by environmental carrying capacity.[4] The separation between individual and population dynamics suggests that the model of reversible physiology may be used as a basis for introducing structured natural selection, with irreversible effects added afterward to parametrize costs of maintenance. In such a model, polymers provide the energetic link as they transition from

[4]The surprise can be illustrated with the metazoan allometric observation (West et al., 2002; West and Brown, 2005) that the mass-specific adult metabolic rate of an organism scales as $M^{-1/4}$, where M is the asymptotic adult body mass. If there were no upper limit on the sizes of organisms, this relation would assert that biomatter could be maintained with arbitrarily little metabolic power per gram. No systematic deviation from the allometric constraint is observed even for the largest known organisms, to suggest that an intrinsic energy of maintenance has surpassed the energetic requirements associated with growth as the constraint on body size or lifetime.

physiological roles as metabolites to evolutionary roles as individuals.

The metabolic model represents only which polymer is consumed and which produced in a given cycle. We may elevate "production" to "re-production" if we imagine that the molecule produced is of the same type as some "parent" molecule in the population, which remains unaltered in the process. At the level of metabolism, the basis for natural selection is that some types of molecules (pores, enzymes, or the DNA that code for them) prepare a cell to carry out energy-yielding reactions on the species actually present in its environment, keeping it alive or allowing it to reproduce, while other molecules either provide no function or prepare the cell for situations that never arise in its actual environment, and are hence maladaptive. Where the environmental molecules also represent other individuals, metabolic competence and behavioral competence are not distinguished.

3.1. "Reversible" selection

We can model an ecology of molecular species with a distribution of polymers, and consider binary interactions through metabolic cycles, whose probabilities to be sampled depend on the input and output molecules. For reversible cycles the unit of time does not matter, so by Eq. (28) we may pass directly from single-particle cycles to a representation of their action on the distribution. The lowest-order polynomial for which the rate of production of species $\Pi_{\vec{\alpha}}$ from species $\Pi_{\vec{\beta}}$ is proportional to the probability of binary collision between $\Pi_{\vec{\alpha}}$ (parents) and $\Pi_{\vec{\beta}}$ (food) is

$$\left.\frac{\mathrm{d}p_{\vec{\alpha}}}{\mathrm{d}t}\right|_{rev} = \sum_{\vec{\beta}} p_{\vec{\alpha}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}. \tag{29}$$

The requirement that the total number of polymers be conserved[5] is

$$0 = \sum_{\vec{\alpha}} \left.\frac{\mathrm{d}p_{\vec{\alpha}}}{\mathrm{d}t}\right|_{rev} = \sum_{\vec{\alpha},\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\alpha}} p_{\vec{\beta}}; \tag{30}$$

thus we must choose the rate matrix $r_{\vec{\alpha}\vec{\beta}}$ antisymmetric. In the domain of reversible metabolic cycles, there is no energetic or entropic consequence to simultaneous fluxes $\Pi_{\vec{\alpha}} \leftrightarrow \Pi_{\vec{\beta}}$, so the antisymmetric rate matrix governing the evolution of probabilities also governs work and heat flows, per Eq. (28).

Under "reversible" evolution, differential "fitness" results from differential rates of survival and reproduction for each type of individual. Here the net of the two effects is given by the appropriate column (or row) of $r_{\vec{\alpha}\vec{\beta}}$. The excess probability of death (being catabolized) over replacement per polymer $\Pi_{\vec{\beta}}$ is

$$\sum_{\vec{\alpha}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\alpha}},$$

or alternatively, the excess probability of reproduction over death per polymer $\Pi_{\vec{\alpha}}$ is

$$\sum_{\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}.$$[6]

The well-studied replicator dynamic (29) can produce attractive fixed points (on the boundary of the probability simplex) limit cycles, or even chaotic orbits (Hofbauer and Sigmund, 1998), depending on the dimension and the spectrum of $r_{\vec{\alpha}\vec{\beta}}$. In the first case a well-defined entropy of the asymptotic distribution exists; in other cases the best we may be able to do is define an average entropy over the stationary distribution on the attractor. Some amount of persistent dynamical variation in the entropy of an ecological distribution may be realistic in appropriate models (where irreversible driving may be taken as a primitive of the dynamics), but within the context of these models, where we are concerned with the consumption of work to generate heat, persistent dynamics arises as an artifact of the idealization of reversibility, as will be shown below. The organism distribution in this model gains entropy by extracting heat and offering work to the environment, allowing repeated switching among types to persist indefinitely.

Differential survival and reproduction are incorporated in Eq. (29), but not the third canonical element of natural selection: mutation. Mutation could be incorporated by expanding $r_{\vec{\alpha}\vec{\beta}}$ to a three-index matrix $r_{\vec{\alpha}'\vec{\alpha}\vec{\beta}}$, to produce $\Pi_{\vec{\alpha}'}$ (offspring) from $\Pi_{\vec{\alpha}}$ (parent) and $\Pi_{\vec{\beta}}$ (food). However, genetic mutations arise from error mechanisms related to those that cause decay and entropy production, and the rates of the two types of processes will generally be quantitatively related. Therefore it is more natural to incorporate mutation and decay together.

3.2. "Irreversible" selection due to noise

Presumably energetic limits on the maintenance of biomatter are reached whenever the metabolic energy devoted to growth structured by selection goes entirely toward counteracting randomizing effects that impact the population structure. The introduction of random events to the model of the last section adds a steady-state maintenance power to the Landauer energy for the creation of new biomatter, thus introducing an explicit physical timescale. We will continue to use the model of biomatter as the deviation of a polymer ensemble from its equilibrium

[5]Such a constraint might be generalized to complete metabolism at the ecosystem level by proposing a material carrying capacity that reflects the energetic maintenance constraints on core anabolism (McCollom and Amend, 2005), even if the origin of those constraints is not understood.

[6]If symmetric rate terms for $\Pi_{\vec{\alpha}} \leftrightarrow \Pi_{\vec{\beta}}$ were added to these excesses, separate gross rates for death and reproduction could be modeled, and in terms of them the expected fecundity as the reproduction rate times the expected lifetime for a given polymer species. In $r_{\vec{\alpha}\vec{\beta}}$ only the excess rates can be represented.

distribution, and both the creation energy and the maintenance power will be proportional to the number of polymers. Scaling per-polymer is the model's representation of mass-specific creation energy and maintenance power in a more general chemical ecology with closed matter cycles.

As the replicator dynamic (29) is the lowest-order polynomial incorporating binary interactions, general noise may be added with the lowest-order consistent term, which is linear. The resulting dynamical system is defined by

$$\left.\frac{\mathrm{d}p_{\vec{\alpha}}}{\mathrm{d}t}\right|_{irrev} = \sum_{\vec{\beta}} (d_{\vec{\alpha}\vec{\beta}} + p_{\vec{\alpha}} r_{\vec{\alpha}\vec{\beta}}) p_{\vec{\beta}} \equiv f_{\vec{\alpha}}(p). \tag{31}$$

The only mathematical requirement on the matrix d is probability conservation, ensured if

$$\sum_{\vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} = 0, \quad \forall \vec{\beta}.$$

Physically, if we suppose that all consequences of driving are treated with the reversible bound represented in r, the remaining dissipative process must have the equilibrium distribution π as the stationary $r \equiv 0$ solution. Thus

$$\sum_{\vec{\beta}} d_{\vec{\alpha}\vec{\beta}} \pi_{\vec{\beta}} = 0, \quad \forall \vec{\alpha}.$$

The stationary solution is stable if $d_{\vec{\alpha}\vec{\beta}} \geqslant 0$ for $\vec{\alpha} \neq \vec{\beta}$, and it describes a microscopically reversible process if detailed balance holds: $d_{\vec{\alpha}\vec{\beta}} \pi_{\vec{\beta}} = d_{\vec{\beta}\vec{\alpha}} \pi_{\vec{\alpha}}$, for all pairs $\vec{\alpha}, \vec{\beta}$.

We may thus define a matrix $\hat{d}$ with components $\hat{d}_{\vec{\alpha}\vec{\beta}} \equiv d_{\vec{\alpha}\vec{\beta}} \pi_{\vec{\beta}}$, which is symmetric and has the vector of all ones as its (left or right) null eigenvector. $\hat{d}_{\vec{\alpha}\vec{\beta}}$ gives the (equal and opposite) current leaving $\vec{\alpha}$ and $\vec{\beta}$, respectively, along link $\vec{\alpha}\vec{\beta}$ in the equilibrium state.

Under these assumptions it is not hard to show that as long as all off-diagonal $d_{\vec{\alpha}\vec{\beta}} > 0$, boundary solutions are ruled out, and that if there is an interior fixed point of Eq. (31), it is a stable attractor. To prove the first claim, suppose that there is a boundary solution with component $p_{\vec{\alpha}} = 0$. The driven current out of index $\vec{\alpha}$ is proportional to $p_{\vec{\alpha}}$, thus zero, while the inward current equals

$$\sum_{\vec{\beta}} d_{\vec{\alpha}\vec{\beta}} \pi_{\vec{\beta}} > 0.$$

Hence $p_{\vec{\alpha}} = 0$ cannot characterize a steady state.

To prove the second claim, note that $f_{\vec{\alpha}}(p) = 0$ implies

$$\sum_{\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}} = -\left(\frac{1}{p_{\vec{\alpha}}}\right) \sum_{\vec{\beta}} d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}} = -d_{\vec{\alpha}\vec{\alpha}} - \left(\frac{1}{p_{\vec{\alpha}}}\right) \sum_{\vec{\beta} \neq \vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}},$$

as long as we can divide by $p_{\vec{\alpha}}$ (interior assumption). But for $r_{\vec{\alpha}\vec{\alpha}} = 0, \forall \alpha$ (implied if r is antisymmetric)

$$\frac{\partial f_{\vec{\alpha}}(p)}{\partial p_{\vec{\alpha}}} = d_{\vec{\alpha}\vec{\alpha}} + \sum_{\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}} = -\sum_{\vec{\beta} \neq \vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} (p_{\vec{\beta}}/p_{\vec{\alpha}}) \leqslant 0$$

for each $\vec{\alpha}$, by the assumption that all $d_{\vec{\alpha}\vec{\beta}}$ in the sum are non-negative. Thus $Div(f) \leqslant 0$, with strict inequality unless the matrix $d \equiv 0$. In the generic case any polymer will be subject to decay, so that within this simplified model of decay as sequence permutation, each component $\partial f_{\vec{\alpha}}(p)/\partial p_{\vec{\alpha}} < 0$ independently. Then there cannot be interior saddle points, and any interior fixed point must be unique and have the whole probability simplex as its basin of attraction.

3.3. Work fluxes

Stationary solutions to Eq. (31) satisfy

$$p_{\vec{\alpha}} = \frac{\sum_{\vec{\beta} \neq \vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}}{(-d_{\vec{\alpha}\vec{\alpha}}) - \sum_{\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}} = \frac{\sum_{\vec{\beta} \neq \vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}}{(-d_{\vec{\alpha}\vec{\alpha}}) - (r \cdot p)_{\vec{\alpha}}}. \tag{32}$$

At a stationary solution, the particle flux driven into any index $\vec{\alpha}$ by metabolic consumption of work,

$$p_{\vec{\alpha}} \sum_{\vec{\beta}} r_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}},$$

equals the dissipative particle flux out,

$$-\sum_{\vec{\beta}} d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}} = \sum_{\vec{\beta} \neq \vec{\alpha}} (d_{\vec{\beta}\vec{\alpha}} p_{\vec{\alpha}} - d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}),$$

where we have used

$$\sum_{\vec{\alpha}} d_{\vec{\alpha}\vec{\beta}} = 0.$$

The metabolic work flux that maintains a steady state against dissipation is not distinguished from a work flux that changes a distribution in a dissipationless world, so we may express the work flux $\dot{W}$ (defined as an average over times longer than the cycle time) from Eq. (22), using only the metabolic component of $\mathrm{d}p_{\vec{\alpha}}/\mathrm{d}t$ (which in steady state equals the dissipative component)

$$\frac{\dot{W}}{N_\Pi \tau} = \sum_{\vec{\alpha},\vec{\beta}} (d_{\vec{\beta}\vec{\alpha}} p_{\vec{\alpha}} - d_{\vec{\alpha}\vec{\beta}} p_{\vec{\beta}}) \log \frac{p_{\vec{\alpha}}}{\pi_{\vec{\alpha}}}. \tag{33}$$

Eqs. (32) and (33) can be clarified by working with the matrix $\hat{d}$, similarly defining a matrix $\hat{r}$ of rates of metabolism evaluated at the equilibrium state, with components $\hat{r}_{\vec{\alpha}\vec{\beta}} \equiv \pi_{\vec{\alpha}} r_{\vec{\alpha}\vec{\beta}} \pi_{\vec{\beta}}$, and finally working with the probability relative to equilibrium, defined as $\hat{p}_{\vec{\alpha}} \equiv p_{\vec{\alpha}}/\pi_{\vec{\alpha}}$.

Then Eq. (32) becomes

$$\hat{p}_{\vec{\alpha}} = \frac{\sum_{\vec{\beta} \neq \vec{\alpha}} \hat{d}_{\vec{\alpha}\vec{\beta}} \hat{p}_{\vec{\beta}}}{(-\hat{d}_{\vec{\alpha}\vec{\alpha}}) - (\hat{r} \cdot \hat{p})_{\vec{\alpha}}}, \tag{34}$$

and Eq. (33) becomes

$$\frac{\dot{W}}{N_\Pi \tau} = \sum_{\vec{\alpha},\vec{\beta}} (\hat{d}_{\vec{\beta}\vec{\alpha}}\hat{p}_{\vec{\alpha}} - \hat{d}_{\vec{\alpha}\vec{\beta}}\hat{p}_{\vec{\beta}}) \log \hat{p}_{\vec{\alpha}} = \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} \hat{d}_{\vec{\alpha}\vec{\beta}}(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log \frac{\hat{p}_{\vec{\alpha}}}{\hat{p}_{\vec{\beta}}}, \tag{35}$$

where symmetry of $\hat{d}$ is used in the second line.

For each pair $(\vec{\alpha},\vec{\beta})$ in Eq. (35) the product $(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log(\hat{p}_{\vec{\alpha}}/\hat{p}_{\vec{\beta}})$ is non-negative and symmetric under exchange of $\vec{\alpha}$ and $\vec{\beta}$, and vanishes only when $\hat{p}_{\vec{\alpha}} = \hat{p}_{\vec{\beta}}$. As all $\hat{d}_{\vec{\alpha}\vec{\beta}}$ contributing to the sum are non-negative, $\dot{W} = 0$ only if $\hat{p}_{\vec{\alpha}} = \hat{p}_{\vec{\beta}}$ for all non-zero $\hat{d}_{\vec{\alpha}\vec{\beta}}$. In other words, $\dot{W} = 0$ only if the distribution $\hat{p}$ is uniform on all components connected by decay processes (which may effectively depend on timescale). Since both the $\pi_{\vec{\alpha}}$ the $p_{\vec{\alpha}} \equiv \hat{p}_{\vec{\alpha}}\pi_{\vec{\alpha}}$ sum to unity, uniform $\hat{p}_{\vec{\alpha}}$ over all $\vec{\alpha}$ is possible only at equilibrium, $p = \pi$.

Steady-state flux balance (35) is part of a more general relation for the evolution from the Gibbs equilibrium distribution at time 0 to p at any later time

$$\int_0^t \mathrm{d}t \frac{\dot{W}}{N_\Pi \tau} = D(p\|\pi) + \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} \hat{d}_{\vec{\alpha}\vec{\beta}} \int_0^t \mathrm{d}t (\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log \frac{\hat{p}_{\vec{\alpha}}}{\hat{p}_{\vec{\beta}}}, \tag{36}$$

wherein both integrals diverge as $t \to \infty$ while the difference converges to $D(p\|\pi)$ at the steady (evolved) state. The relation (36) is the generalization of the bound (22) for reversible creation of new order.

3.4. Cycle-free driving

Both the Kullback–Leibler measure (23) of information (and possibly internal free energy) in the ordered distribution, and the work (35) required to maintain it, depend only on the $n-1$ independent components of p, in relation to the probabilities π and diffusion barriers $\hat{d}$ of the equilibrium distribution. Thus the $n(n-1)/2$ independent real components of $\hat{r}$ are $(n/2)$-fold degenerate.

To understand the degeneracy, introduce the current over a link:

$$j_{\vec{\alpha}\vec{\beta}} \equiv \hat{p}_{\vec{\alpha}}\hat{r}_{\vec{\alpha}\vec{\beta}}\hat{p}_{\vec{\beta}} - \hat{d}_{\vec{\alpha}\vec{\beta}}(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \equiv j^M_{\vec{\alpha}\vec{\beta}} - j^D_{\vec{\alpha}\vec{\beta}}, \tag{37}$$

in which the $\hat{r}$ and $\hat{d}$ components are labeled *M*etabolic and *D*issipative, respectively. By antisymmetry there is no definition of a current from a node to itself ($j_{\vec{\alpha}\vec{\alpha}} \equiv 0$). Stationarity under Eq. (31) is simply the statement

$$\sum_{\vec{\beta}} j_{\vec{\alpha}\vec{\beta}} = 0, \quad \forall \vec{\alpha}. \tag{38}$$

We may write any $\hat{r}$ giving Eq. (38) at a given $\hat{p}$ as a sum of terms $\hat{r}_{\vec{\alpha}\vec{\beta}} \equiv \hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}} + \delta\hat{r}_{\vec{\alpha}\vec{\beta}}$, where the current arising from the particular ($\hat{d}$-dependent) solution $\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}}$ satisfies $j_{\vec{\alpha}\vec{\beta}} = 0$ independently on every link, and the remainder $\delta\hat{r}_{\vec{\alpha}\vec{\beta}}$ produces link currents at the distribution $\hat{p}$ that can be written as sums of cyclic currents around elementary plaquettes $\vec{\alpha}\vec{\beta}\vec{\gamma}$. The particular solution is immediately

$$\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}} = \hat{d}_{\vec{\alpha}\vec{\beta}}\left(\frac{1}{\hat{p}_{\vec{\beta}}} - \frac{1}{\hat{p}_{\vec{\alpha}}}\right). \tag{39}$$

The sum of cyclic currents created by $\delta\hat{r}$ is free because it automatically satisfies stationarity under Eq. (31), but has no effect on the work flux. $\log \hat{p}_{\vec{\alpha}}$ is a potential function on the positions $\vec{\alpha}$, so

$$\sum_{\vec{\alpha}\vec{\beta}\in\partial\mathscr{P}} j^{\mathscr{P}}(\log \hat{p}_{\vec{\alpha}} - \log \hat{p}_{\vec{\beta}}) \equiv 0, \tag{40}$$

where the sum is over directed links $\vec{\alpha}\vec{\beta}$ in the oriented boundary $\partial\mathscr{P}$ of some plaquette $\mathscr{P}$, and $j^{\mathscr{P}}$ is the contribution to the link current $j_{\vec{\alpha}\vec{\beta}}$ associated with cycling around that plaquette.

The form (39) for $\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}}$ is equivalent to a requirement of path-independence

$$\frac{\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}}}{\hat{d}_{\vec{\alpha}\vec{\beta}}} + \frac{\hat{r}^{(d)}_{\vec{\beta}\vec{\gamma}}}{\hat{d}_{\vec{\beta}\vec{\gamma}}} = \frac{\hat{r}^{(d)}_{\vec{\alpha}\vec{\gamma}}}{\hat{d}_{\vec{\alpha}\vec{\gamma}}} \tag{41}$$

together with the condition of no self-driving $\hat{r}^{(d)}_{\vec{\alpha}\vec{\alpha}} \equiv 0$. For $\vec{\alpha} = \vec{\gamma}$ these imply antisymmetry

$$\frac{\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}}}{\hat{d}_{\vec{\alpha}\vec{\beta}}} + \frac{\hat{r}^{(d)}_{\vec{\beta}\vec{\alpha}}}{\hat{d}_{\vec{\beta}\vec{\alpha}}} = 0, \tag{42}$$

and they imply closure around elementary plaquettes

$$\frac{\hat{r}^{(d)}_{\vec{\alpha}\vec{\beta}}}{\hat{d}_{\vec{\alpha}\vec{\beta}}} + \frac{\hat{r}^{(d)}_{\vec{\beta}\vec{\gamma}}}{\hat{d}_{\vec{\beta}\vec{\gamma}}} + \frac{\hat{r}^{(d)}_{\vec{\gamma}\vec{\alpha}}}{\hat{d}_{\vec{\gamma}\vec{\alpha}}} = 0. \tag{43}$$

An additional normalization requirement for $\hat{p}$ comes from π via $\pi \cdot \hat{p} = 1$.

A basis for the cyclic terms is $1/\hat{p}_{\vec{\alpha}}\hat{p}_{\vec{\beta}}$, so that general $\delta\hat{r}$ may be written as

$$\delta\hat{r}_{\vec{\alpha}\vec{\beta}} = \frac{1}{\hat{p}_{\vec{\alpha}}\hat{p}_{\vec{\beta}}}\sum_{\mathscr{P}} j^{\mathscr{P}}\sigma^{\mathscr{P}}_{\vec{\alpha}\vec{\beta}}, \tag{44}$$

where $\sum_{\mathscr{P}}$ is over plaquettes, $j^{\mathscr{P}}$ is the cycle current associated with plaquette $\mathscr{P}$, and $\sigma^{\mathscr{P}}_{\vec{\alpha}\vec{\beta}} = 1$ if link $\vec{\alpha}\vec{\beta}$ appears with positive sense in the boundary of $\mathscr{P}$, $\sigma^{\mathscr{P}}_{\vec{\alpha}\vec{\beta}} = -1$ if it appears with negative sense, and $\sigma^{\mathscr{P}}_{\vec{\alpha}\vec{\beta}} = 0$ if the link is not in the boundary of $\mathscr{P}$.

3.5. Ergodic decay

We can gain some understanding of the work flux (35), and consider an interesting special case, by noting that the Shannon entropy (25) for any distribution p can be rotated into a component along the distribution π, and the orthogonal remainder, as

$$-S(p) = \sum_{\vec{\alpha}} \pi_{\vec{\alpha}} \log p_{\vec{\alpha}} + \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} (p_{\vec{\alpha}}\pi_{\vec{\beta}} - p_{\vec{\beta}}\pi_{\vec{\alpha}}) \log \frac{p_{\vec{\alpha}}}{p_{\vec{\beta}}}. \tag{45}$$

Eq. (45) and a symmetric expression for $S(\pi)$ then allow us to write

$$S(\pi) - S(p) = D(p\|\pi) + \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} \pi_{\vec{\alpha}}\pi_{\vec{\beta}}(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log \frac{\pi_{\vec{\alpha}}}{\pi_{\vec{\beta}}}$$
$$= -D(\pi\|p) + \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} \pi_{\vec{\alpha}}\pi_{\vec{\beta}}(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log \frac{p_{\vec{\alpha}}}{p_{\vec{\beta}}}, \tag{46}$$

here we have made use of the definition (23) for the Kullback–Leibler divergences. From Eq. (46) we identify

$$D(p\|\pi) + D(\pi\|p) = \frac{1}{2}\sum_{\vec{\alpha},\vec{\beta}} \pi_{\vec{\alpha}}\pi_{\vec{\beta}}(\hat{p}_{\vec{\alpha}} - \hat{p}_{\vec{\beta}}) \log \frac{\hat{p}_{\vec{\alpha}}}{\hat{p}_{\vec{\beta}}}. \tag{47}$$

The sum of Kullback–Leibler divergences is a symmetric (under exchange of p and π), positive-semidefinite function vanishing only on $p = \pi$. Each term in the right-hand side of Eq. (47) is symmetric under exchange of both p with π, and $\vec{\alpha}$ with $\vec{\beta}$. Moreover, the terms in $\hat{p}$ in the right-hand sum are those appearing in the work flux (35).

Now note that there is a matrix $d^{(0)}$ for which

$$\hat{d}^{(0)}_{\vec{\alpha}\vec{\beta}} \equiv \pi_{\vec{\alpha}}\pi_{\vec{\beta}} - \delta_{\vec{\alpha}\vec{\beta}}\pi_{\vec{\beta}}$$
$$= (\pi_{\vec{\alpha}} - \delta_{\vec{\alpha}\vec{\beta}})\pi_{\vec{\beta}} \equiv d^{(0)}_{\vec{\alpha}\vec{\beta}}\pi_{\vec{\beta}}. \tag{48}$$

$d^{(0)}$ has π as its null eigenvector, and the off-diagonal elements of $\hat{d}^{(0)}$ are exactly $\pi_{\vec{\alpha}}\pi_{\vec{\beta}}$. For a large number of indices $\vec{\alpha}$ and small values of any single $\pi_{\vec{\alpha}}$, all the diagonal elements $d^{(0)}_{\vec{\alpha}\vec{\alpha}} \approx -1$. $d^{(0)}$ is a "canonical" dissipation matrix consistent with the chemical equilibrium distribution, with roughly equal probability to decay *from* any $\vec{\beta}$, and a probability per unit time to decay *into* any $\vec{\alpha}$ equal to its occupancy at equilibrium. Decay under $d^{(0)}$ is thus ergodic in some fairly strong sense.

If we happen to have $d = \gamma d^{(0)}$, then Eq. (34) reduces to

$$p_{\vec{\alpha}} = \pi_{\vec{\alpha}} \frac{\gamma}{\gamma - (r \cdot p)_{\vec{\alpha}}}, \tag{49}$$

and we can combine Eq. (47) with Eq. (35) as

$$D(p\|\pi) + D(\pi\|p) = \frac{\dot{W}}{\gamma N_\Pi \tau}. \tag{50}$$

The associated cycle-free rate matrix is then given by

$$r^{(\gamma)}_{\vec{\alpha}\vec{\beta}} = \gamma\left(\frac{\pi_{\vec{\beta}}}{p_{\vec{\beta}}} - \frac{\pi_{\vec{\alpha}}}{p_{\vec{\alpha}}}\right). \tag{51}$$

It is appealing to think that some universal rate constant associated with dissipation establishes a limit like Eq. (50), between work flux and the information it can maintain in a distribution of molecules. For instance, it was shown in McCollom and Amend (2005) that almost 10 times as much energy is required to create new biomatter in an oxidizing environment as in a reducing environment, and then suggested that the disparate creation costs lead to corresponding, disparate maintenance costs, which may explain why anaerobic organisms can colonize environments where the energy available from catabolism is very low. On the other hand, given the wide range of energy barriers that exist for organic reactions, a chemical model of ergodic dissipation seems at first implausible. If, however, we are trying to relate the entire entropy of biomatter to the aggregate metabolic flux on earth, we should somehow average over all possible processes, including the evolution of catalysts by organisms to digest molecules in other organisms. Whether an aggregate process approximating ergodic decay arises in such an average, and what would set the resulting timescale γ, are left as open questions.

4. Conclusions

This paper refines and significantly clarifies some arguments of Bennett (1982), based on the second law of thermodynamics, about necessary relations between energy and information in reversible polymerization. The major refinement is the decomposition of joint processes of oligomer hydrolysis and repolymerization into a chemical cycle with the same structure as the Carnot cycle of thermodynamics. This decomposition, and the projection of the chemical Carnot cycle onto the plaquette of conserved total entropy, will make it possible to map chemical information cycles onto the classical Landauer construction of computation, in Paper III of this series. The device of the van't Hoff reaction box formalizes the constraints of separation of timescales assumed by such complex aggregate chemical cycles, and provides a formal definition of chemical work.

The main result of the paper, the model relation (22) between chemical work and the Kullback–Leibler divergence of the polymer distribution from an equilibrium Gibbs distribution, links sequence information measures to the general statement (15) of conservation of energy. The model relation (22) immediately extends to more general chemical reactions, while the explicit Landauer decomposition of the chemical work cycle provides a formal model for the conversion of either externally supplied work or enthalpy of reaction into rejected heat, subject to Eq. (15). The substitution of enthalpy of reaction for the formal work variable in the Landauer formulation (1) of the second law makes possible the application of the same results to irreversible processes such as molecular recognition (Schneider, 1991a, b).

The embedding of a reversible model of physiology within an ecological context, justified by some empirical results on the energetics of growth and development, provides an explicitly energetic model of natural selection under capacity constraints. A minimal model for selective fitness differences was introduced, and then augmented with a minimal model of perturbations by noise, extending the physiological bounds on the energy required for growth to a phenomenological representation of the energy required for maintenance.

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Appendix A. Notation and Legendre duality

The basic measurable extensive state variables for any component of the reactor are U (internal energy), V (system volume), and N (particle number of the solute). The extensive entropy function of these variables $\sigma(U, V, N)$ defines the surface of state for a classical thermodynamic system. The following constructions from the surface of state can all be found in Kittel and Kroemer (1980).

Intensive state variables are most symmetrically defined as the derivatives of the entropy by its extensive arguments. Inverse temperature

$$\left.\frac{\partial\sigma}{\partial U}\right|_{V,N} = \frac{1}{\tau}, \tag{A.1}$$

pressure relative to temperature

$$\left.\frac{\partial\sigma}{\partial V}\right|_{U,N} = \frac{p}{\tau}, \tag{A.2}$$

and chemical potential relative to temperature

$$\left.\frac{\partial\sigma}{\partial N}\right|_{U,V} = -\frac{\mu}{\tau}. \tag{A.3}$$

The equation for conservation of energy within the surface of state is then a definition:

$$\mathrm{d}U = -p\,\mathrm{d}V + \mu\,\mathrm{d}N + \tau\,\mathrm{d}\sigma. \tag{A.4}$$

The Gibbs potential G off the surface of state is a function of the extensive variables *parametrized* by the intensive variables, which are regarded as properties of the system boundaries. Written as the Legendre dual to the entropy

$$\frac{1}{\tau}G \equiv \frac{1}{\tau}U + \frac{p}{\tau}V - \sigma. \tag{A.5}$$

G is minimized at U and V for which the derivatives of the entropy (A.1), (A.2) equal the imposed boundary conditions $(1/\tau, p/\tau)$. Within the resulting surface of state as a function of p, τ, we have from Eq. (A.4) both that

$$\mathrm{d}G = \mu\,\mathrm{d}N = \mathrm{d}H - \tau\,\mathrm{d}\sigma, \tag{A.6}$$

where $H \equiv U + pV$ is the enthalpy, and by integration (as N is the only remaining extensive argument of G), that

$$G = \mu N, \tag{A.7}$$

where $\mu(p, \tau)$ is a function only of pressure and temperature. We also recover the more usual energetic-dual definition of the chemical potential

$$\left.\frac{\partial G}{\partial N}\right|_{p,\tau} = \mu. \tag{A.8}$$

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