



## Natural process – Natural selection

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### Abstract

Life is supported by a myriad of chemical reactions. To describe the overall process we have formulated entropy for an open system undergoing chemical reactions. The entropy formula allows us to recognize various ways for the system to move towards more probable states. These correspond to the basic processes of life i.e. proliferation, differentiation, expansion, energy intake, adaptation and maturation. We propose that the rate of entropy production by various mechanisms is the fitness criterion of natural selection. The quest for more probable states results in organization of matter in functional hierarchies.

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“Life is chemistry” is a cliché but it is one that deserves a re-inspection. For a long time, it has been understood that chemical reactions lead to chemical equilibrium. Gibbs was first to realize that this stationary state, where chemical potentials  $\mu$  on both sides of a reaction formula are equal, corresponds to the maximum entropy [1]. Chemical reactions as well as other processes, e.g. diffusion, heat flow from hot to cold and ion currents in electric fields that evolve towards increasing entropy are all called natural processes [2]. Does this mean that life is a natural process towards high-entropy states?

The question has remained open despite many studies [3–8]. Since high-entropy states are often associated with high disorder and ordered structures are distinctive features of life, it is customarily thought that living processes work to reduce entropy rather than to increase it [9]. However, no firm proof has been given and it has remained obscure what prevents us from deriving characteristics of living matter from the fundamental principles. Is it a missing concept or a misconception or something else?

Nevertheless, one open question is easy to define. Even if the condition for maximum entropy i.e.  $dS \Leftrightarrow \sum \mu_j = 0$  is known, the formula of  $S$  itself has remained unknown. This state-of-affairs is peculiar particularly because the rate of entropy

change  $dS/dt = \sum v_j A_j / T$  due to reaction velocities  $v_j$  and affinities  $A_j = \sum \mu_j$  is known as well [2]. Here we derive the formula of entropy to describe evolution of an open system undergoing numerous chemical reactions.

### 1. Entropy of an open system

The relationship between a state of a system and its probability  $P$  was formulated by Boltzmann already some 140 years ago [10]. For a homogeneous system entropy is [11]

$$S = R \ln P \approx R \sum_{i=1}^N n_i [\ln(g_i/n_i) + 1] \quad (1)$$

where identical particles in the total numbers  $N = \sum n_i$  are distributed among levels of (kinetic) energy  $E_i$  relative to thermal energy  $RT$  e.g. given per mole. The indistinguishable particles  $n_i$  are often considered non-interacting or only weakly interacting, i.e. the occupancy of each level  $g_i$  is assumed to be a constant.

This must be the restriction why the formalism cannot account for an evolution of a homogeneous system to an open heterogeneous system via chemical reactions. It is important to notice that when various chemical reactions are running simultaneously substrates used in one reaction are away from other reactions. These dynamic bounds correspond to probabilities and should be included in the total probability of the

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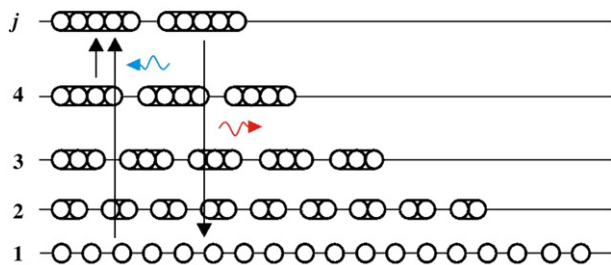


Fig. 1. Diagram presenting a distribution of matter among compounds in numbers  $N_j$  in classes  $j$  of increasing Gibbs free energy along vertical axis. The distribution will change in chemical reactions, i.e. synthesis and degradation (arrows) that deliver (red) or absorb (blue) energy (wavy arrows) as illustrated for an endothermic reaction  $N_1 + N_4 \rightleftharpoons N_5$  and for an exothermic reaction  $N_5 \rightleftharpoons 5N_1$ .

system as will be shown below in analogy to the basic derivation of classical statistics [11] for ideal gas.

From here on we work to reveal the general principles that govern living matter. We understand that living matter is complex and our statistical description is only a starting point that will require further elaboration to account fully for any specific case. Nevertheless knowledge of underlying principles is valuable. In essence we ask how numerous chemical reactions will distribute matter among various chemical compounds.

The probability  $P$  for a distribution of elemental constituents, e.g. atoms in total numbers  $N = \sum n_j$  among various classes  $j$  of compounds  $N_j$ , is obtained by inspecting the level diagram of Gibbs free energy (Fig. 1). The first level holds stable elemental constituents in numbers  $n_1$ . The associated probability is the familiar binomial  $P_{1b} = N! / n_1! (N - n_1)!$ , since all  $n_1$  are identical the order of compounds at the level is immaterial. Second level houses metastable compounds that are composed of two elemental constituents. These compounds are referred to as metastable because they keep spontaneously degrading to the stable compounds. The associated probability is  $P_{2b} = (N - n_1)! / (n_2/2)! (N - n_1 - n_2)!$ . The factorial  $(n_2/2)!$  gives the number of combinations associated with the number of compounds  $N_2$ . The probabilities of subsequent levels are expressed accordingly

$$P_{jb} = \frac{(N - n_1 - \dots - n_{j-1})!}{(n_j/j)! (N - n_1 - n_2 - \dots - n_j)!} \quad (2)$$

The notation by including the term  $n_j/j$  for the compound stoichiometry, i.e. assembly rules of an entity, opens the way from homogeneity to heterogeneity. In analogy to the derivation of classical statistics for indistinguishable particles [11] the factor  $N!$  will cancel since all elemental constituents are identical, e.g. all carbon atoms are alike.

Obviously living matter comprises many different atoms and not only one type of constituents as outlined above. The partition of matter among compounds in a many-constituent system is obtained analogously to the single-constituent system when the stoichiometry of an entity with respect to the basic constituents is denoted. For example, the probability  $P_{321l}$  for a

partition of compounds made of three elemental constituents  $h$ ,  $k$  and  $l$  is

$$P_{321l} = \frac{(H - h_{100} - \dots - h_{320})!}{\left(\frac{h_{321}}{3} + \frac{k_{321}}{2} + \frac{l_{321}}{1}\right)! (H - h_{100} - \dots - h_{321})!} \times \frac{(K - k_{100} - \dots - k_{320})!}{(K - k_{100} - \dots - k_{321})!} \times \frac{(L - l_{100} - \dots - l_{320})!}{(L - l_{100} - \dots - l_{321})!} \quad (3)$$

where  $H$ ,  $K$  and  $L$  denote the total numbers of constituents. The term  $(h_{321}/3 + k_{321}/2 + l_{321}/1) = HKL_{321} = N_{321}$  is equal to the numbers of particular entities. Similarly to the single constituent system, the factor  $H!K!L!$  for each indistinguishable class of basic constituents will cancel. In general the resulting distribution of entities is multinomial with respect to its various basic constituents.

Next, we consider probabilities that depend on the availability of substrates  $N_k$ , the Gibbs free energy difference between the substrates and products  $\Delta G_{jk} = G_j - \sum G_k$  as well as external energy  $\Delta Q_{jk}$  that may couple to the reactions

$$P_{ja} = \left[ \prod_k N_k \exp \frac{\Delta Q_{jk} - \Delta G_{jk}}{RT} \right]^{N_j} \equiv \Gamma_j^{N_j} \quad (4)$$

where we assume constant temperature  $T$ . Motions of substrates are considered statistically independent from each other, e.g. in a solution, thus denoted by the product  $\prod_k$  and the energy contributions that expressed relative to thermal energy  $RT$  are regarded as reactants as well. The bracket is raised to the power of the number of products  $N_j$  because the substrates and associated energy differences may incorporate in any of the possible products. We rename  $P_{ja}$  as  $\Gamma_j^{N_j}$  to have a concise notation in analogy to Eq. (1).

The overall probability is obtained as the product of probabilities over all levels, i.e. for all compounds that participate in reactions of the system

$$P = P_{1a} P_{1b} P_{2a} P_{1b} P_{3a} P_{3b} \dots \\ = \prod_{j=1} \frac{\Gamma_j^{N_j}}{N_j!} = \prod_{j=1} \frac{1}{N_j!} \left[ \prod_k N_k \exp \frac{\Delta Q_{jk} - \Delta G_{jk}}{RT} \right]^{N_j} \quad (5)$$

Finally, entropy  $S$  per mole is obtained by taking logarithm for  $S = R \ln P$  and applying Stirling's approximation

$$S \approx R \sum_{j=1} N_j [\ln(\Gamma_j / N_j) + 1] \\ = R \sum_{j=1} N_j \left[ \ln \left( \prod_k N_k \exp \frac{\Delta Q_{jk} - \Delta G_{jk}}{RT} / N_j \right) + 1 \right] \\ = \frac{1}{T} \sum_{j=1} N_j \left( \sum_k \mu_k + \Delta Q_{jk} - \mu_j + RT \right) \\ = \frac{1}{T} \sum_{j=1} N_j (A_j + RT). \quad (6)$$

where the affinity  $A_j = \sum \mu_k + \Delta Q_{jk} - \mu_j$  includes also external energy when it couples to reaction. The Eq. (6) designates all

available  $jk$ -reaction pathways for synthesis and degradation for all compounds in numbers  $N_j$  including also transition states when present. These mechanisms are considered to distribute effectively all matter and energy to make the system. When a  $jk$ -reaction pathway is open matter will flow from substrates in numbers  $N_k$  to products in numbers  $N_j$  when the potential [12]  $\mu_k = RT \ln[N_k \exp(G_k/RT)]$  is higher than  $\mu_j = RT \ln[N_j \exp(G_j/RT)]$  including external energy when it couples to the reaction. Then the system is in motion towards more probable states. Any matter or energy that does not involve in reactions is not considered to be a part of the system.

Since the assembly rules, i.e. stoichiometries of compounds, are inherently contained in the expression of entropy we may examine systems at various levels of details. In other words an entity can be regarded as a system itself consisting of its interacting entities. For example an organism can be considered as a system of cells, a cell can be considered as a system of molecules and molecules as a system of atoms. Relevant interactions that characterize a particular system are contained in Gibbs free energies. Furthermore, our notation implies an ideal dilute system and  $N_j$  should be understood as active concentrations when relevant. We emphasize that the study aims to explain principles that could be developed further to account for specific cases and their characteristics.

We stress the meaning of entropy as a logarithmic probability measure for a state of a system. The entropy formula applies for a system where constituents interact with each other, not for a collection of non-interacting compounds incapable of progression. At any given moment the system comprises its constituents in matter and energy as well as interactions. From time to time the system may open to take in energy as radiation or as matter from its surroundings or to expel it. Typically the surroundings of a system comprises of other open systems. For example an ecosystem houses a myriad of hierarchically nested subsystems that bathe in mutual fluxes of energy and matter. The open system description allows us to include, similar to  $\Delta G_{jk}$ , an external energy  $\Delta Q_{jk}$  that couples to endothermic  $jk$ -reactions, as well as to exclude, i.e. dissipate, energy from the system arising from exothermic reactions. Indeed it is in the very nature of chemical reactions not to conserve energy within the system. Energy may also come as high chemical potential matter (food) and leave the system as low chemical potential matter (excrement). The open system formalism is central for statistics of systems undergoing chemical reactions.

## 2. Equation of motion

We will proceed to differentiate Eq. (5) or alternatively Eq. (6), i.e.  $\partial(\ln P)/\partial t = (1/P)(\partial P/\partial t)$ , with respect to time to obtain the equation of motion for a system undergoing chemical reactions

$$\frac{\partial P}{\partial t} = LP, L \approx \sum_{j=1} \frac{dN_j}{dt} \frac{A_j}{RT} \quad (7)$$

where Stirling's approximation has been used. The Liouvillian  $L$  for chemical reactions allows us to identify affinities  $A_j$  as the

generator of the motive force. The system will move when there are mechanisms for flows of matter via chemical reactions from compounds to compounds. Obviously the statistical description that is based only on probabilities does not contain any specific knowledge about mechanisms. Thus the formalism may only reveal statistical consequences when reaction pathways are open.

Naturally the flow rate  $dN_j/dt$  from  $N_k$  to  $N_j$  must exactly balance the flow rates  $\sum dN_k/dt$  from  $N_j$  to  $N_k$  not to lose any matter in the process. The condition holds when

$$\frac{dN_j}{dt} = r_j \frac{A_j}{RT} = - \sum_k \frac{dN_k}{dt} \quad (8)$$

where rates  $r_j$  depend on mechanisms, e.g. structures that catalyze reactions. Consequently we may rewrite

$$L \approx \frac{1}{(RT)^2} \prod_{j=1} r_j A_j^2. \quad (9)$$

The quadratic form of affinities reminds us from Onsager reciprocal relations [2] that are valid near stationary non-equilibrium and equilibrium states of entropy production. The equation of motion is more general in describing a system on its way to equilibrium or non-equilibrium stationary states.

## 3. Dissipative evolution

The equation of motion appears similar to the Liouville equation of a classical system containing kinetic and potential energy terms. However, we fail to find a transformation to separate affinities  $A_j$  from entities  $N_j$  to find invariants of motion. According to Noether's theorem this implies a lack of symmetry and associated conserved current. Thus we suspect that the equation of motion is non-integrable [13,14]. Intuitively the non-associative algebra beyond Hilbert space results from time-ordered operations when various reaction pathways draw on same constituents affecting each other's paths of motions. When the system is moving also potentials keep changing that in turn to affect the motion itself. The motion is chaotic in the sense of Poincaré, i.e. for any non-trivial system the detailed trajectory of motion cannot be obtained.

The obvious question is what might be the non-conserved quantity? On the basis of Eq. (9) we are not left much else but to suspect but the driving forces. Affinities are under no transformation constants of motion. We note that for matter to flow in chemical reactions total energy of the open system is not conserved. Indeed on this basis chemical reactions are classified as endo- ( $\Delta Q_{jk} > 0$ ) and exothermic. A steady flow of external energy to or from the system will displace the system from the equilibrium partition  $P_{eq}$  given by law of mass-action [15] to a non-equilibrium stationary partition  $P_{ss}$ .

$$\ln P_{ss} = \sum_{j=1} N_j \left[ \ln \left( \frac{\prod_k N_k}{N_j} \exp \frac{-\Delta G_{jk}}{RT} \right) + 1 + \frac{\Delta Q_{jk}}{RT} \right] \quad (10)$$

Thus a passage from an initial state  $P(0)$  to a final state  $P(t)$  is given by the dissipation. Evolution is inherently coupled with structural changes in states caused by absorption or emission of energy. This conceives the idea of time [16]. Energy within the open system is not conserved in transitions towards the stationary state. The motion of a macroscopic system via reactions means irreversible destructions of embedded microscopic systems either by repeated mergers to larger and larger subsystems or by break downs to smaller and smaller subsystems. This is of course exactly what chemistry is.

#### 4. Stationary state

At a steady state the net flow of energy in and out of the open system vanishes. Then the system has become macroscopically reversible as there is no net dissipation of energy. The stationary state may though exhibit random fluctuations or cyclic motions as structures sporadically disintegrate and reintegrate. This can be understood so that the system, often perceived as one closed system, is in fact composed of several open systems that bathe in mutual sporadic or periodic fluxes from each other. The stationary state with random fluctuations is usually pictured as thermodynamic equilibrium and the one with periodic oscillations as a heat engine.

The knowledge of  $S$  allows us to obtain the time derivative, i.e. the rate of entropy production due to various reactions

$$\begin{aligned} \frac{dS}{dt} &= \sum_{j=1} \frac{dS}{dN_j} \frac{dN_j}{dt} = \frac{1}{T} \sum_{j=1} \frac{dN_j}{dt} \left( \sum_k \mu_k + \Delta Q_{jk} - \mu_j \right) \\ &= \frac{1}{T} \sum_{j=1} v_j A_j \geq 0 \end{aligned} \quad (11)$$

The well-known last form [2] contains in the affinity  $A_j = \sum_k \mu_k + \Delta Q_{jk} - \mu_j$  also the external energy that couples in

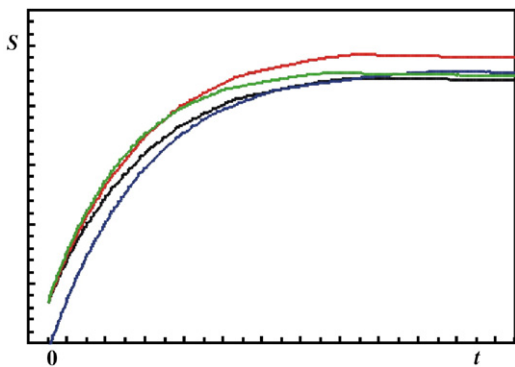


Fig. 2. Simulation of entropy given by Eq. (6) vs. time. A model system evolves from homogeneity of basic constituents to heterogeneity of compounds by non-catalyzed endothermic polymerization reactions i.e.  $N_1 + N_{j-1} \rightleftharpoons N_j$  and by degrading exothermic reactions  $N_j \rightleftharpoons jN_1$ . The syntheses couple external energy to system whereas the degradations expel energy from the system. For comparisons  $S$  vs.  $t$  is shown when 20% more matter in terms of  $N_1$  is available (blue), when reactions happen 20% faster (green) and when 20% more energy couples to the transitions (red) than in the original system (black). The time series is produced by a for-loop where at every time increment synthesis and degradation operations are performed according to Eq. (8).

synthesis. The steady-state non-equilibrium partition of reactants is obtained from Eq. (11) at the condition

$$\begin{aligned} dS = 0 &\Leftrightarrow \mu_j = \sum_k \mu_k + \Delta Q_{jk} \\ &\Leftrightarrow N_j = \prod_k N_k \exp \frac{\Delta Q_{jk} - \Delta G_{jk}}{RT}. \end{aligned} \quad (12)$$

The stationary-state condition applies when entropy does not change any more, i.e. fluxes of energy to and from the open system are equal. The form of the law of mass action shows that the external energy will raise the stationary population of high- $j$  compounds from the ground state equilibrium. These energy-powered metastable states are referred to as dissipative structures [2]. In other words the external energy supports high-entropy states containing complex compounds. The open system will respond changes in flux by evolving towards a new stationary state dictated by the new flux. We emphasize that the flow of external energy to the open system will *increase* entropy. In the following we will reveal characteristics of the high-entropy non-equilibrium states. Most importantly we will show that the high-entropy states will contain matter in functional structures, i.e. also order. This is obviously in contrast with the common but unfounded belief that the highest entropy state equates with the state of least order.

#### 5. Evolution to diversity

Next we will examine Eqs. (6) and (11) analytically to identify various ways of entropy production. The reasoning is also illustrated by simulations (Fig. 2).

Entropy will increase when increasing numbers of compounds emerge from reactions as long as the system has not reached the stationary-state equilibrium given by Eq. (12). Thus already at the molecular level there is a spontaneous drive for *proliferation* when using the vocabulary of biology. Entropy will also increase when various kinds of compounds emerge from syntheses, i.e. the sum over  $j$  extends to new classes. Thus there is a spontaneous drive for *differentiation* and motion towards molecular diversity. (At this point we postpone the explanation why new classes of compounds may appear later during the evolution.) Entropy will also increase when the system acquires more compounds to its processes from surroundings. This conclusion is obvious as the numbers  $N_j$  will become larger. Thus there is a spontaneous drive for *expansion*. Entropy will increase when more and more  $jk$ -reaction pathways open to involve more and more matter to processes. Entropy will increase when more external energy couples to increasing number of reactions and when energy is used more and more efficiently to power various reactions. This is consistent with the notion that energy is also a reactant. Thus there is a spontaneous drive for greater intake of energy and matter to the system. The set of processes to maximize the entropy production we refer to as *adaptation*. The energy consumption will level off at the state of maturity [17], i.e. the



steady-state, when no more matter or energy can be recruited to the system or when no new or faster reaction pathways appear.

Importantly the metastable entities may only participate to reactions that they will reach within their lifetimes. Thus the system is limited in its evolution by the range of interactions in space and time. Further increase of  $S$  may take place at a higher hierarchical level where the system itself becomes a constituent of a larger system. A system is composed of interacting entities that themselves are systems. The Eq. (6) describes by nature the nested organization at various scales because the system description contains stoichiometries, i.e. assembly rules, as substrates and energy. Therefore knowledge of constituents is available to change the level of inspection. Obviously entities will organize to a higher hierarchical structure only when the resulting system will produce more entropy than independent entity systems. All the aforementioned entropy producing processes are strikingly familiar to us as the processes of life yet they were exposed only by a trivial inspection of Eqs. (6) and (11). Therefore we arrive to the conclusion that life is a natural process.

## 6. The selection criterion

When several systems access a common but limited pool of matter and energy, the associated rates of entropy production, the terms  $(dS/dN_j)(dN_j/dt)$  of Eq. (11), are important. Those systems that produce entropy more rapidly will involve in their processes more matter and energy than those that are slower in their entropy production (Fig. 3). The competition for matter and energy is incessant because the high-entropy states are metastable, i.e. entities  $j > 1$  are bound by lifetimes and degrade continuously to more basic constituents. The living systems are continually and rapidly regenerating themselves to attain and maintain high entropy states. Under these conditions the rate of

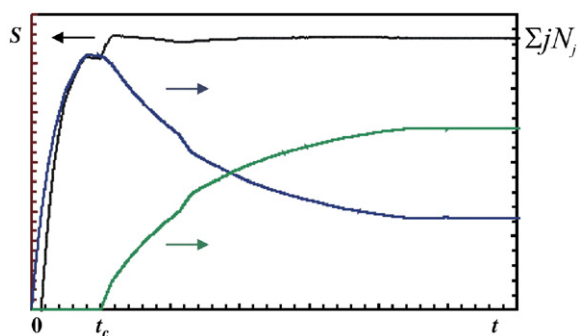


Fig. 3. Competition for matter obtained from simulation of Eq. (6) for polymerization reactions  $N_1 + N_{j-1} \rightleftharpoons N_j$  and for degradation  $N_j \rightleftharpoons jN_1$ . The total amount of matter in compounds  $N_{j>1}$  is shown at the right hand scale. A model system initially evolved to a non-equilibrium steady state until time  $t_c$  when another system emerged and began to draw matter from the common pool of basic stable constituents  $N_1$  at a 1.5 times faster rate  $dN_j/dt$ . Consequently, the amount of matter in compounds of the original  $N_{j>1}$  system began to decline (blue) and the amount in compounds of the invader system started to rise (green). After a redistribution of matter the overall entropy  $S$  (black) at the left hand scale of the final dual-system reached a higher level than that of the original system. For simplicity no catalytic activity was included in the simulation.

production is very important, since the products themselves may act as substrates for subsequent reactions. Entropy will increase when simple compounds, i.e. low- $j$  entities, react to form more complex compounds, i.e. high- $j$  entities as long as the equilibrium is not yet reached. The emerging complexity is functional. The process is biased for products that facilitate the motion towards more probable states. Therefore, we propose that the rate of entropy production is the fitness criterion of natural selection [18].

The association of natural selection with the rate of entropy production may at first appear only a conceptual connection and perhaps only valid in a simple system. Mechanisms of entropy production are many in contemporary biota, thus also targets for natural selection are many. The spontaneous rise of diversity is inherently biased for functional structures i.e. catalytic mechanisms that produce entropy rapidly. Even slight and gradual improvements in reaction rates will with time give significant contributions to  $S$ . Catalysis is ubiquitous. All biological structures can be regarded as catalysts or parts of them to generate flow of matter towards high entropy states. Indeed rapid growth and expansion are characteristics of living processes. When new mechanisms appear a gradual evolution may be punctuated by rapid growth phase (Fig. 3).

The knowledge of  $S$  allows us for the first time to inspect the stability of a heterogeneous non-equilibrium stationary state by Lyapunov criterion [2]. The variation with respect to  $\delta N_j$  reveals that  $-\delta^2 S > 0$  and  $d(-\delta^2 S)/dt < 0$ , i.e. the steady state is stable. However when products are autocatalytic, i.e.  $dN_j/dt \propto N_j$ , then  $d(-\delta^2 S)/dt > 0$  and oscillations are expected. Such a system will easily over-deplete  $N_k$  in the production of  $N_j$ . Indeed autocatalytic, i.e.  $r_j(N_j)$  in Eq. (8), chemical reactions are known to fluctuate about the equilibrium [19]. On the other hand hypercycles [20] and systems with catalytic networks, e.g. cells and ecosystems are mostly stable. Obviously the open systems may also suffer time to time from perturbations when there are changes in external or internal flows.

## 7. Discussion

The formula of entropy for an open system is mathematically simple. However, the description is profoundly new in comparison with the traditional view of a closed weakly or non-interacting system. Entropy of Eq. (6) does not only enumerate particles but also includes energies, i.e. Gibbs free energy differences and external energy, required for transitions. The formula of  $S$  describes the inter-exchange of energy and matter. In endothermic reactions energy is bound to compounds and in exothermic reactions released from the system. Incoming high-energy radiation may couple e.g. to photosynthesis or incoming high-chemical potential matter may be consumed in catabolic reactions. Subsequently the system may dissipate low-energy, i.e. thermal energy, or discard low-chemical potential matter.

It should be mentioned that the well-known partition of ideal gas particles  $n_i$  that is customarily deduced from Eq. (1) is also obtained analogously to Eq. (12) when retaining only kinetic energy term  $E_i$ . Obviously gaseous particles collide with each

other when the system evolves towards equilibrium, whereas chemical reactions proceed via specific reaction pathways.

When interactions are included in the system description, entities  $N_j$  acquire properties also. To be specific, entities obtain their characteristics through mutual interactions and those that do not differ from each other in interactions are identical. This view is consistent with modern physics and modern biology. Interactions can be considered to maintain or “power” metastable entities, i.e. living systems. Obviously when two classes of entities draw from common resources, the one that can generate a higher rate of entropy production has an advantage over the other. We expect that the rate of entropy production, even though it is a simple concept, to account for many complex phenomena attributed to natural selection. Mechanisms for entropy production of present-day biota are many and thus obscuring the common underlying principle. The rate of entropy production is a more general criterion than what is customarily attributed to natural selection. The rate of entropy production as the fitness criterion resolves the circular argument “survival of the fittest — the criterion for fitness is survival”.

Our conclusion of life as a natural process is consistent with the remark by Boltzmann that the existence of animate beings is a struggle *for* entropy, not *against* as it is often thought. The common misconception arises when biological entities are only considered as disconnected from their environments. A biological entity without its supportive interactions and external energy is clearly improbable and will decay to basic stable constituents. The entropy formula allows us to include in the description flows of matter and energy to the open system that will make the biological entity in fact probable. Thus there is no need to recruit ad hoc assumptions about *decreasing* entropy but the same principle of *increasing* entropy valid for chemical reactions holds also for a complex set of reactions, the natural process known commonly as life.

An open system is hardly ever at a stationary state. From time to time a biological system connects to flows energy in the form of radiation from the Sun or to high- $\mu$  matter usually referred to as food. Since we have not specifically addressed time dependent fluxes our view is a time averaged statistical description. Of course the fluxes and flows could be analyzed in detailed time increments. An open system subject to steady fluxes evolves towards a stationary state corresponding to maximum entropy. However the system may become unstable when newly assembled or acquired structures open new routes of interactions to entropy production. It may also happen that reductions in external fluxes of energy or matter compel the system to retract back to a stationary state of reduced entropy.

The open system statistics is consistent with thermodynamics yielding known formula of entropy production and chemical equilibrium at the stationary state. We expect the natural statistics to give understanding to questions such as why life emerged, why handedness of proteins and nucleic acids is ubiquitous, why our genomes are fragmented and swollen with non-coding segments. We hope to inspire by this work many more applied and fundamental studies of open systems.

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