

Time Arrows and Determinism in Biology

Bartolomé Sabater

Department of Plant Biology
University of Alcalá
Alcalá de Henares
Madrid, Spain
bartolome.sabater@uah.es

Abstract

I propose that, in addition to the commonly recognized increase of entropy, two more time arrows influence living beings. The increase of damage reactions, which produce aging and genetic variation, and the decrease of the rate of entropy production involved in natural selection are neglected arrows of time. Although based on the statistical theory of the arrow of time, they are distinguishable from the general arrow of the increase of entropy. Physiology under healthy conditions only obeys the increase of entropy arrow. But aging, death, and evolution are determined by the other time arrows as well. Paradoxes emerge from conflicts among the specific determinisms associated with each arrow. These conflicts, along with uncertainties intrinsic to the low-number statistics of the arrows of damage reactions and decrease of the rate of production of entropy, highlight the limits of determinism at different levels of biology and its dependence on time span and number of organisms. The recognition of the three time arrows opens new perspectives for the problem of compatibility of the flow of time in physics and psychology.

Keywords

aging, entropy, ergodic principle, evolution, paradoxes, time arrow

Within the framework of the statistical theory of the arrow of time, the irreversible increase of entropy is usually assumed as the time arrow of all physicochemical processes (Bishop 2004; Esfeld 2006). In our personal experience, time also has a definite direction toward what we conventionally call the future (Eddington 1931), and a fundamental question is whether the physicochemical bases of our physiology determine this psychological time arrow. Far removed still from a molecular understanding of our mental activities, I discuss whether the thermodynamic arrow of time is sufficient to explain processes such as death and evolution that we share with most other organisms.

Differences between the variables of time in physics and biology have been discussed by Smith (2003), who proposed to characterize as biological those systems that are sufficiently complex to be able to isolate the spacetimes of certain of their components; physical systems, on the other hand, would be those in which all the components are coupled to universal time. In this context, the interesting possibility emerges that the spacetimes of different biological components may have different arrows of time. The different arrows of time could be associated with conflicting determinisms in biology.

Although the functioning of living beings is in agreement with the second law of thermodynamics (Schrödinger 1944), we cannot exclude that additional time arrows must be taken into account to explain certain specific processes of biology.

The increase of entropy confers a time arrow to the functioning of organisms as it does for other nonequilibrium systems (Schrödinger 1944; Prigogine 1978). Entropy is a measure of the statistical probability of the allocation of energy. When exchanges among different forms of energy are possible, the energy of the system will be converted into the form with the most probable distribution—the one of highest entropy (Coveney 1988; Ksenzhek and Volkov 1998). Heat is by far the most probable allocation of energy, because multiple vibration, rotation, and translation levels allow a high number of combinations for the distribution of total energy. The transformations of, e.g., radiant and chemical energies into heat are irreversible, and the associated increase of entropy confers a time arrow to the physiological processes in photosynthetic and non-photosynthetic organisms alike (Brooks et al. 1989).

Although entropy also increases during aging and evolution, I hypothesize that (1) the irreversible effects on organisms of age, death, and evolution depend on time arrows other than entropy increase, and (2) based on the relationship between arrow of time and determinism (arrow of causation), conflicts among different time arrows mark the limit of a comprehensive determinism in biology. I will first review key concepts implicit in the statistical background of the time arrow linked to entropy increase. Second, I shall demonstrate that different, also statistical, backgrounds are inherent in the models emerging from the investigations of aging, death, and evolution, and

that these backgrounds are associated with specific arrows of time, which have not been considered previously.

Statistical Bases of the Entropy-Associated Time Arrow

Speculations about time are frequent in philosophy and experimental science. Since Aristotle, traditional thinking (Saint Augustine, Kant, etc.) associated time with change and the related question whether time has a beginning. When thermodynamics inquired about what changes are possible, a new magnitude, entropy, was recognized that could only increase when time goes forward (time arrow). This resonates with a deeply rooted psychological perception that was not considered in Newtonian mechanics, whose equations are time-reversible. The statistical approach was first developed by Boltzmann to base thermodynamics as well as the irreversibility of time on mechanics—an approach that was strongly contested by Poincaré. The statistical grounds of the time arrow were recognized by Eddington (1931) and received new input by Prigogine (1968). Subsequent developments led to a wide debate in the second half of the 20th century that persists today and extends to philosophy, physics, biology, and psychology (for the main issues and recent references see, e.g., Coveney 1988; Price 1996; Uzan 2000; Edens 2001; Primas 2002; Smith 2003; Bishop 2004; Giulini 2005; Dorato 2006; Esfeld 2006). Here I will not dwell upon issues such as whether “arrow” is inherent to time, radiation and entropy time arrows, a quantum time arrow, and so on. Instead, I will focus on the widely accepted energetic and molecular basis of the statistical thermodynamic interpretation of the arrow of time that can be applied and compared to biological systems.

Statistical thermodynamics provides the molecular explanation of the irreversible increase of entropy (S) of a system in terms of probability, which, for a high number of molecules, makes unlikely the reverse steps associated with the decrease of entropy. The Boltzmann–Shannon equation (Shannon 1948), first formulated by Boltzmann and later interpreted against the background of information theory, defines the entropy as the product of the Boltzmann constant (k , $1,381 \times 10^{-23} \text{ J K}^{-1}$) by the sum of the products of the probability (p_i) of each energy configuration (or in general of every state) by the respective natural logarithm: $S = -k \times \sum p_i \times \ln p_i$. The higher the number of energy configurations (i) and the more similar the values of the respective probabilities (p_i), the lower is the certainty about the actual distribution of energy among the different molecules and about the energy configuration of each individual molecule. Similarly, according to the Boltzmann–Shannon equation, the higher the number of energy configurations (i) and the more similar the values of the respective probabilities (p_i), the higher is the entropy S of the system. Therefore, the entropy of a

system is a measure of the uncertainty of the distribution of energy among and within the molecules of the system, because the probability value of an energy distribution increases with the number (or multiplicity) of *undistinguishable* energy configurations in the system. In this regard, it must be noted that the less distinguishable are the energy configurations, the lower is the certainty about what is the actual configuration. The thermodynamic principle of time-irreversible entropy increase is equivalent to the increase of uncertainty, because the two imply transition to the more probable energy configurations. At the focus of Popper's criticism of the statistical foundation of the time arrow (see Popper 1957, 1965) is that probability is a time forward-linked concept (expectance), which makes the arguments relating the arrow of time with probability circular.

Statistical explanations are easily stated for gases. In a gas, the heat energy is distributed among different molecules, and within each molecule through different combinations of possible levels of translation, rotation, vibration, and electronic excitation. The diversity of these combinations, within a molecule and among molecules, produces a multiplicity of energy configurations that are not static; they reversibly and rapidly change from one to another. The total energy of the gas is distributed dynamically (not statically) among molecules, and within molecules results in the most probable (lowest information) overall steady-state configuration. Lack to appreciate that conversions among different energy distributions are rapid and reversible is probably at the basis of many misunderstandings about the meaning of thermodynamic statistical irreversibility and its alleged incompatibility with mechanics (classical, quantum, or relativistic) (Coveney 1988). Reversibility among energy forms is common in mechanics (e.g., between kinetic and potential energy in a pendulum); obviously, it does not imply time irreversibility. Reversibility among elemental energy configurations in a molecule lies at the basis of the principle of microscopic reversibility (Tolman 1925), with the added feature that transitions are far quicker than in macroscopic systems. For example, the coming back to the ground state of an electron excited by light, with the conversion of the excitation energy to vibration, rotation, and translation energies of the molecule would last for some 10^{-16} second (Osborne and Yeston 2007). Compared to the rates of macroscopic processes for which thermodynamics is valid, transitions among energy configurations of molecules are essentially instantaneous, and the different configurations are assumed as simultaneous (as different resonant structures of the benzene molecule are considered simultaneous). In fact, multiplicity is not necessarily the same as simultaneity, and irreversibility arises as the necessary consequence of the kinetic approaches required to systems consisting of dynamic (Coveney 1988), freely reversible energy configurations, where most of them are rapidly interconverted. Elementary calculus predicts that a singular configuration (cf. the former example of a molecule

with an excited electron) is essentially substituted by rapidly exchangeable, undistinguishable (but different) combinations of vibration, rotation, and translation energies in the molecule. By applying the classic principle of microscopic reversibility (Tolman 1925) to the distribution of energy within a system, the kinetic approach leads to the conclusion of the irreversible transition from a single configuration to a multiplicity of configurations based on undistinguishable, very rapidly interchangeable states of energy distribution.

As a consequence of collisions, molecules interchange energy in amounts and forms that depend on the energy configuration of the molecules at the precise moment of collision, and new multiple configurations rapidly inter-convert after collision. The configurations obtained immediately after interaction are not retained and, as a consequence, the collision event becomes essentially irreversible, even more so when the large number of molecular interactions in a gas guarantees further collisions. Therefore, in contrast to the deterministic classical mechanics of macroscopic bodies, the dynamics of molecular collisions is irreversible. As pointed out by Schlater (2007), the fundamental randomness of the quantum-mechanical realm makes possible intuitive time and its flow; and randomness is present when the energy is allocated among different configurations that are indistinguishable and essentially instantaneously interchangeable.

Irrespective of whether the supporting dynamic-kinetic arguments are accepted or not, the statistical foundation of thermodynamic time irreversibility is commonly assumed in metabolic processes. Heat is the highest entropy (low information) form of energy because of the high multiplicity or large number of interchangeable energy-level combinations in which molecules can accommodate their actual energy with almost similar probability. Therefore, the irreversibility of exothermic reactions is explained by the transformation of low-entropy chemical energy to high-entropy heat energy. By extension to metabolic reactions, Albert Szent-Györgi's funny definition of life, "Life is nothing but an electron looking for a place to rest," could be pertinent to the extent that the best rest is reached by the highest entropy or the most probable state (see also Trefil et al. 2009). However, as I discuss below, life displays other aspects in addition to the healthy metabolic reactions as well. The hypothetical reversion of an exothermic reaction would require the very improbable collision of the products and solvent molecules, which are heat-excited in the same energy configuration, as they are immediately produced after the forward reaction. Therefore, the irreversibility of chemical reactions has the same microscopic statistical basis as conventional (nonchemical) physical processes: The multiplicity of energy configurations among and within the molecules of the system is higher at the final state than at the initial state.

Metabolic reactions are conventional chemical reactions, and most of them are enzyme-catalyzed. Therefore, their

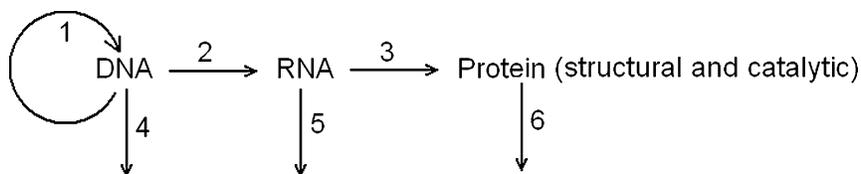


Figure 1.

Failures in the functioning of the cell. Normal cell processes are affected by different failures: wrong base pairing in DNA replication (1) and transcription (2), and wrong amino acid charge in tRNA and erroneous base pairing for translation (3). In addition, attack by highly reactive molecules modifies bases and breaks base chains of DNA (4) and RNA (5) and modifies amino acids collapsing the structural and functional properties of proteins (6).

irreversibility is also based on the higher multiplicity of energy configurations of the product than that of the reacting molecules (including the nontransformed solvent molecules that receive heat energy).

Time Arrows Associated With Organism Aging and Biological Evolution

Let us consider a fully differentiated animal or plant cell converting sources of carbon and energy to CO_2 to maintain its structure, composition, and functional activities. Despite its continuous metabolic activity, the cell composition does not change; the cell receives as much mass as it delivers to surroundings. Thermodynamically, the cell is an open system that receives low-entropy energy sources, generates entropy, and delivers outside energy and compounds carrying the generated entropy (Ksenzhek and Volkov 1998). This ideal dynamic cell system maintains constant its entropy and composition, although the entropy increases in the whole cell-surrounding system, which consequently shows an obvious time arrow. The cell itself has no time arrow, just as there is no time arrow in the mechanical system of an oscillating pendulum or at the core of a gold coin. According to both the Aristotle–Saint Augustine tradition and the statistical interpretation, conventional cell physiology has no time arrow. Moreover, the whole adult multicellular organism or a stabilized population of any biological species has no time arrow; only external references would provide them with a time arrow. Its spacetime is isolated from the surrounding physical and universal spacetime (Smith 2003).

However, although they are widely recognized as a genuine manifestation of life, conventional cell and organism metabolisms do not last forever. Sooner or later, aging and senescence preceding death (or mutation and/or competition with other biological species) alter the intraorganism system that thus acquires a history and displays a time arrow. Hazardous reactions leading to mutation, death, and natural selection are inevitable; they provide a time arrow for the latter biological processes. The occurrence of nonconventional side reactions is statistical but, as we will see, this statistic is significantly different from the one determining the irreversibility of conventional metabolic reactions.

Modern theories of aging and senescence (Martin 2002; Zapata et al. 2005; Rocchi 2006; Hayflick 2007) take into

account some basic mechanisms that include statistical components. Aging results from cell failures that are due to nonenzyme-catalyzed reactions, which, although equally irreversible, are different from healthy metabolic reactions destroying cell components like protein and/or modifying the genetic message by hazardously changing nucleotides of DNA and RNA (Figure 1).

Not all DNA changes lead to aging and death; some of them are not lethal and determine an increase of the genetic variability of organisms. In the absence of competition for resources, there is no selection and the biological changes are random (Ross 2006). The term “population entropy” has been coined (Demetrius 1997) for the genetic variability that results from the fixation of nonlethal changes in DNA. Organisms use enzyme and nonenzyme protections against damage reactions to delay aging (Orr and Sohal 1994; Dufour and Larsson 2004; Zapata et al. 2005; Hayflick 2007). As a secondary effect, protective reactions also diminish the frequency of changes in DNA, thus slowing down the increase in genetic variability.

Full protection against damages is not realistic because it would require infinite consumption of resources and would prevent the genetic variability necessary for biological evolution in both constant and changing environments to occur. Therefore, as a consequence of enzyme and nonenzyme reactions, aging leading to death and genetic variability is unavoidable and consequently associated to an arrow of time: death and genetic variability are bound to happen sooner or later. Obviously, when no factor limits the growth of a population, there are no selective conditions, and genetic variability—being also a time arrow—irreversibly increases. When enough time is provided, the possibility of the occurrence of low-probability events becomes comparable to the possibility of an increase of entropy after short times. Entropy increases in healthy metabolic reactions, aging, and genetic changes, but the occurrence of the last two is not related to their associated entropy increase; it follows from the self-evident assertion that, sooner or later, low-probability events will take place—what is potential will become fact. Aging and genetic variation will fatally take place (Rocchi 2006) and, sometimes, the degradation of the cellular machinery will surpass the healthy metabolic processes. The increase of entropy is a necessary but insufficient condition for aging and genetic variation; and, as has

been pointed out by Berry (1995), the irreversibility of evolution is not a consequence of thermodynamic irreversibility. The key issue is that sometimes low-probability events substitute health by damage reactions. This transition requires time flow and, therefore, the process is in fact a time arrow.

Randomness in the sense of mathematical probability theory is nothing but a generalization of determinism with its corollary of time arrow and distinction between cause and effect (Primas 2002). If enough time is provided, the low number (low probability) statistic associated with the occurrence of a damage reaction is as deterministic as the high-number statistic associated to entropy increase. Randomness and its associated determinism were recognized long ago in the mutational origin of genetic variability (de Vries [1901] 1903; Monod 1971). What I want to emphasize here is that the damage reactions compel biology to accept a new time arrow, based on statistical grounds that differ from those of entropy increase (and sometimes conflicting with it).

The reason why, sooner or later, damage and genetic variation survive to correction reactions is statistical, but unrelated to the amount of entropy production of the competing health and damage-variation reactions. The decay of unstable radioactive atoms, such as tritium, is also a low-probability entropy-production process that is associated with the arrow of time. However, tritium has no alternative to radioactive decay, which will happen sooner or later because it is an energy-dissipation process. Biological systems are distinct from this because the time arrows of cell damage and genetic variation have alternative processes in the form of health metabolism and correction entropy-production reactions that, because they provide a time arrow for the whole organism–environment system, maintain the organism within the system but away from the universal physical time arrow. In some differentiation processes, deactivation of correction reactions leads to programmed cell death (Dufour and Larsson 2004; Zapata et al. 2005; Hayflick 2007); but in most cases highly active correction reactions make aging a low-probability, though unavoidable event. In contrast to isolated systems in equilibrium, such as hydrogen gas in a sealed bottle, organisms are open systems that require continuous metabolic processes, which expose them to damage. Like health reactions, aging and genetic-variation reactions are themselves irreversible entropy-linked time arrow processes, and no thermodynamic rule predicts which of them will be the fastest. The transition of overall reactions from healthy to aging is linked to a critical level of damage. The increase of cell damage and the fixation of nucleotide changes in DNA are unavoidable, but their rates do not depend on the linked increase of entropy. They are statistical processes whose probabilities depend on the rates of damage and correction reactions.

Biological evolution is the result of, successively, the increase of population entropy (Demetrius 1997) and the natural

selection of the fitness variant (Sabater 2006; Whitfield 2007). Natural selection is also an irreversible time arrow-associated event that is not determined by the increase of entropy. The fittest organisms are selected because they save more resources per unit of biomass generated during their functioning than other organisms or, in more general terms, because they have the lowest rate of entropy production (Sabater 2006; Sharma and Annala 2007; Annala and Kuismanen 2009), which is usually linked to the increased self-organization (Hoelzer et al. 2006; Pulselli et al. 2009). Accordingly, the tendency to lower the rates of entropy production is another biological time arrow, which is responsible for natural selection and is evidently different from the arrow of entropy increase.

The time intervals required to detect low-probability events in aging and genetic variability, and low rates of entropy production in evolution—typically of the order of 10^6 and 10^{12} seconds, respectively—are far longer than those that depend on the increase of entropy in metabolic processes (around 1 second). Therefore, conflicting outcomes of the three time arrows are frequent and hardly reducible to deterministic physical explanations. As an example, high mutation rates will sooner or later be “rewarded” by reaching the optimal gene sequence and organization, in agreement with the time arrow to lower the rates of entropy production. However, high mutation rates (associated to a low level of protection reactions) lead to increased aging and death rates and, consequently, high risk of extinction of the species. In this respect, organisms are confronted with a dilemma similar to the Saint Petersburg paradox: How much resources should be paid to play the coin game that rewards $2^{(n-1)}$ if face appears after n throws? Probability laws (based on an infinite number of throws) conclude that any huge payment will get surplus rewarding. Similarly, probability laws (based on unlimited time and mutations) conclude that any arbitrarily high mutation rate will be rewarded by reaching the fittest genome. However, as Daniel Bernouilli acknowledged for the response of humans to the Saint Petersburg paradox (Daston 1983), organisms that are time limited should not adjust their evolutionary behavior to strict statistical rationality. Otherwise, very probably, living beings would not exist.

Limited time (imposed by the time arrow associated to low-probable damage reactions) introduces a casuistic that makes biological evolution (imposed by the time arrow to lower the rate of entropy production) hardly reducible to deterministic physical explanations. In the above example, the large difference (six orders of magnitude) in the response time of the two time arrows strongly exposes evolution to the hazardous events involved in aging and death. In contrast to the entropy increase arrow, whose effects result from probability rules applied to large numbers, the aging arrow results from low-probability events, and its short-time observable effects have an intrinsic hazardous component similar to the DNA mutations (Monod 1971) involved (or not) in aging.

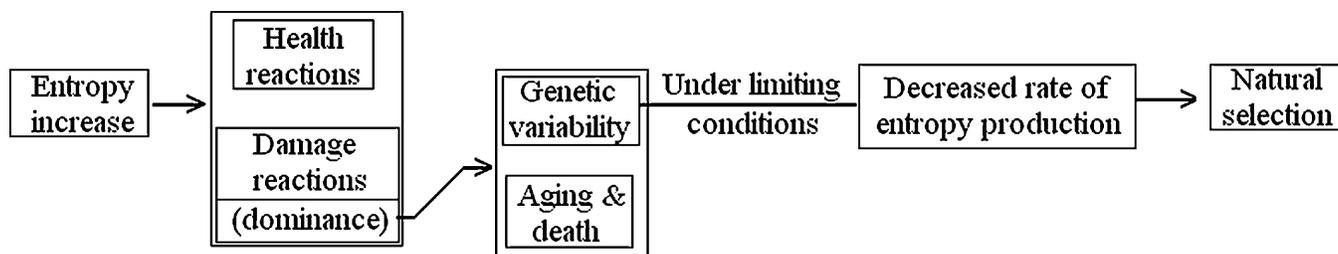


Figure 2.
Time arrows in biology and their main effects.

Determinisms in Biology as Related to the Arrows of Time

In biology—as in physics in general—causality is closely related to the time arrow, minimally because the effect cannot precede the cause (Rohrlich 2000). The arrow of becoming is a necessary condition for the possibility that event *a* causally influences event *b* (Dorato 2006). As discussed by Primas (2002), statistical necessity on the basis of the mathematical theory of probability is a type of determinism with its corollary of time arrow and distinction between cause and effect. Therefore, the recognition of time arrows different from entropy increase, yet statistically based on them, opens new perspectives to discuss the old questions of time flow in general as well as determinism in biology. In addition, the analysis of reductionism (Delehanty 2005) in biology could benefit from considering the previously neglected time arrows associated with low-probability events and trends to lower the rates of entropy production, respectively. However, the complex relationships among the concepts of reductionism, causality, determinism, time arrow, and emergent properties require a deeper analysis that is beyond my present purpose. First, I shall discuss how the hazardous components of low-probability events impose a limit to reductionism.

Most, if not all, of the arrows of time of biology may be derived from the three primaries—increase of entropy, dominance of damage reactions, and decrease in the rate of entropy production—as represented in Figure 2.

The first arrow—the increase of entropy—is based on large-number statistics; it allows for healthy metabolic reactions necessary for life but, inevitably, at the same time, also for damage reactions. No biological system is possible with health reactions free of damage reactions. The second arrow—the dominance of damage reactions—is based on low-number statistics; it allows genetic variability with the inevitable side effect of aging and senescence. The third arrow—the decrease of the rate of entropy production—is based on the linearity near the equilibrium under limiting conditions, and leads to the natural selection of species that save more resources and, hence, produce entropy at the lowest rate (Sabater 2006; Sharma and Annala 2007; Annala and Kuismanen 2009). In the scheme

of Figure 2, the increase of genetic variability and aging and senescence processes are considered as secondary arrows derived from the dominance of the arrow of damage reactions. Similarly, natural selection is a secondary arrow derived from the arrow of the decrease of the rate of entropy production.

It must be noted that the whole process of evolution by selecting organisms that produce entropy at the lowest rate is also accompanied by an increase of entropy due to the elimination of organisms producing entropy at higher rates. Therefore, every selection–extinction step has the limitation that the entropy saved by the selected species must be surpassed by the entropy produced by the extinct species during the time interval when it changes from life to death (i.e., the entropy change accompanying death). Natural selection implies the elimination of competing, genetically different organisms, and the whole selection–elimination process is obviously in agreement with the second law of thermodynamics, although the selection component of the process allows the survival of organisms that have lower rates of entropy production.

Although they share the trend to increase entropy, the three time arrows I have described are independent. Therefore, their associated determinisms are different and sometimes enter into conflict. Their independence could produce observable processes in biology (as the one concerning optimal rates of mutation described before) that are influenced by casuistic factors and cannot be reduced to a single arrow. The large difference in the observable response time to each of the three time arrows makes it hard to find a common paradigm for the different processes in biology. Hence, the increase of entropy arrow is a keystone of physiology and provides precise explanations and predictions of the metabolic responses of an organism to a large variety of conditions. However, the increase of entropy associated to damage reaction does not provide explanations or predictions of the damage reaction that will be produced. Only considering possible changes and damages in DNA, their number is essentially infinite. Within the entire time span conceivable for life, the universe will never reach the high number of potential DNA sequences (4^n , where *n* is the number of nucleotides in the genome), and the new sequence resulting from a single hazardous mutation (Monod 1971) is not predictable although conditioned by the previously existing sequence—it

has a history (Beatty and Desjardins 2009), it only slightly differs from the parent sequence, and is not hazardously chosen among the 4^n possibilities. Physical backgrounds only predict frequencies of lethal and genetic variants whose observation requires a large number of mutational events in a large number of individuals. In contrast to the laws derived from the arrow of increase of entropy, which are valid for the functioning of each single organism, most laws derived from the damage reaction arrow are only applicable to a large number of individuals and over long times. As an example, when considering the case of aging-death, the damage reaction arrow, although determining the fatal need of death, by no means determines when and how death will arrive (Dufour and Larsson 2004; Hayflick 2007). In contrast to the precise determinism of health metabolic processes depending on high-number statistics, the hidden determinism of the low-number statistics of aging and genetic variation only allow precise predictions at long time span and/or for a high number of organisms. One must take into account that although entropy increase provides a clear determinism for health metabolic processes, one cannot predict, say, how many, if any, molecules of glucose a specific *Escherichia coli* cell will consume in 1 picosecond.

The requirements of longer times and larger number of individuals are even more patent to observe deterministic laws associated with the third arrow (decrease of the rate of entropy production). The fitness of organisms during evolution is the progressive reduction of the entropy production rate of their global reaction, and the Boltzmann's ergodic principle allows us to consider organisms as chemical entities for the analysis of evolution (Sabater 2006). Accordingly, the time-average state of a single individual over a long period (as in evolutionary time) coincides with the average state of a sufficiently large number of individuals for shorter times. When compared with the high number of molecules in current chemical reactions, the number of individuals of any biological species is always very low, and the selection of specific individuals, dependent on the decrease of the rate of entropy production, would only be patent after long periods of time. Meanwhile, statistical uncertainties intrinsic to the behavior of a low number of elements are added to the statistical uncertainties of the damage reactions. In effect, looking, e.g., to point mutation, the concrete nucleotide that is muted results from the hazardous selection by the mutagenic agent (ultraviolet light or aggressive chemical) among the n (millions or billions) nucleotides of the organism's DNA that have, at the moment of interaction, the appropriate energy configuration among the multiple possible reactions as discussed under the section of "Statistical basis of the entropy-associated time arrow."

The statistical foundation of the three time arrows of biology implies that each has an associated weak determinism. As indicated earlier, the determinism is patent for the increase of entropy in the physiology of each organism. However, aging

and evolution of organisms can hardly be explained on exclusive physiological bases. The hidden determinism associated with the arrows of dominance of damage reactions and decrease in the rate of entropy production is only uncovered for progressively larger numbers of individuals and after longer times it lacks meaning for the single individual. Therefore, the ergodic principle emerges as a powerful tool to generalize physical laws, yet successful at the metabolic level, to the higher biological levels of aging and evolution whose time arrows reveal a strong determinism for large numbers of individuals and/or long times (Sabater 2006). But that generalization is precisely based on the recognition of the randomness (very weak determinism) of many events at the time scale of the life span of the individual.

The compatibility of the psychological arrow of time with the thermodynamic arrow was yet suggested by Boltzmann and its grounds are still disputed (Schulman 1997; Smith 2003; Zeh 2006). We cannot still explain the psychological arrow of time on molecular bases but the recognition of time arrows in biology not previously considered in thermodynamics could be a useful step for further understanding of the psychological time arrow and its compatibility or conflict with the thermodynamic time arrow. We have explained how, under some aspects, the three time arrows discussed for biology are compatible: all are entropy-increasing processes and, therefore, they share (or reflect) a universal time arrow. However, the determinism associated with each time arrow can lead to opposite issues, which could explain why the occurrence of living beings is sometimes as hardly reducible to rational rules as is the Saint Petersburg paradox.

Conflict between determinisms related to the second and third arrows of time of biology is also evident in the paradox of the impossibility of the organism to reach the functional optimum. The paradox has implications for the sociocultural evolution of humankind, which according to Cavalli-Sforza (2001) and Crozier (2008) is also subject to natural selection. For organisms, the paradox may be described by highlighting that the optimum organism must not waste energy (or produce entropy) in reactions and protect it from damages, which has the consequence that it cannot endure. The insoluble dilemma for organisms and societies is how much resources to invest in protection as long as low investment implies vulnerability to hazardous agents and high investment leads to extinction in the competition with more efficient organisms, societies, or cultures. The highly different time scales of the two opposite determinants are manifested in the double appearance of the evolution of organisms and societies: erratic history paths where we can grasp some regularity rules.

Biological determinism is frequently identified with genetic determinism, where biological factors (genes) modulated by environmental factors determine how the organisms behave and change over time (Rose 1998) according to universal

physical laws. In strict reductionism, genetic and environmental factors and their interactions are themselves the necessary consequences of universal physical laws. As alternatives to reductionistic–deterministic explanations, random changes such as mutations (Monod 1971; Ross 2006) and the emerging complexity of biological systems (Emmeche 1997; Delehanty 2005; Mazzocchi 2008) have been invoked. By recognizing the time arrows and determinisms associated with low-probability events, like cell damage, and in order to decrease the rate of entropy production, key aspects of the determinism–indeterminism discussion could be focused with reference to conflicting determinisms acting on different time scales. In this regard, the capacity of our mind to focus its reference time on very different scales could explain the possibility of alternative responses that suggest a nonstrict deterministic behavior in humans.

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