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THE RELIABILITY THEORETICAL ASPECTS OF THE BIOLOGICAL CONTINUITY PRINCIPLES

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Continuity requirements ensure the unbroken dynamics of evolution. Continuity principles describe the conditions for the origin, maintenance and transitions of the organizational units and their networks. It can be shown that the empirical foundations of the continuity principles are based on the reliability theoretical aspects of the living entities.

Key words: reliability, evolution, continuity, organization

THE PROBLEMS

Evolutionary processes can be described in terms of heredity, reproduction and variation. A main problem in ecology and evolutionary biology is that this simplified evolutionary picture does not tell us the sufficient criteria of a dynamically satisfactory description of evolution (see LEWONTIN 1974 for details). A second problem is the object of this paper. Specifically, we shall analyse here the main conditions that keep evolution in motion. We follow FISHER (1930), whose first statement in his classic book, *The genetical theory of natural selection* is that "Natural selection is not evolution."

To anticipate an answer to the problems raised above, there exist a number of conditions or requirements, which must be satisfied for keeping evolution in motion. Briefly, we shall refer to the description of these conditions as continuity principles. We intend to point out the connections of the continuity principles and the reliability of biological objects.

THE CONCEPT OF A CONTINUITY PRINCIPLE

The structure of a continuity principle

The structure of a continuity principle is the following type of statement: 'If a specific set of condition is satisfied, then the evolutionary continuity by descent with modifications is satisfied'. Two classical types of these continuity principles are MENDEL's laws and WEISMANN continuity of germ plasm doctrine. Both of these concern with the evolutionary continuity of heredity. These principles ex-

press regularities of hereditary transmission of genetic properties occurring in the germ line and the non-heritable, mortal character of the soma. In other words, these statements express the evolutionary behaviour of the separated soma and germ in genetic terms. It can be shown, however, that these hereditary principles do not exhaust completely even the concept of genetic continuity [see CAVALIER-SMITH's (1991, 2001) discussion of the membrane inheritance or the concept of dual inheritance (JABLONKA & LAMB 1995, MOLNÁR 1990)].

The principles of heredity refer to rules of the transmission of genetic information. The term 'principle' is associated with other important genetic, developmental and evolutionary concepts, like rule and constraint. The principal importance of the continuity principles is that they describe the couplings and the separations of organizational levels or units in organisms and their groups, moreover the transitions between organizational levels or units. Therefore, the dynamical coexistence of the organizational levels or their parts obey continuity principles. For instance, the origins of cells by symbiosis and autogenesis was generated by fusion and separation of organizational levels, as explained clearly by CAVALIER-SMITH (1987), in terms of symbiosis between membranes, catalysts and genes. Symbiosis is an example for a continuity principle. The generation of the evolutionary novelty by symbiosis, however, has limits. There are other related principles, such as the 'mix-match' principle.

The aim of this paper is to summarize the existing knowledge about continuity principles and to make some steps towards the explorations of their nature, relations, relevance and further methodical explorations. The area of continuity principles is capable of generating efficient integration in evolutionary biology, creating more consistency and awareness in evolutionary practice and theory. A typical structure of a continuity principle can be described in the following form:

*i*th unit of organization transmission *i*th or *j*th unit of organization.

In other words, a continuity principle describes the origin, maintenance and the transmission of various units of biological organization under internal and external living conditions. As we shall see later, the theoretical basis of such problems can suitably be treated by the tools and the concepts of the theory of reliability, where the concept of continuity is of central importance. The reason is simple. In general, reliability is the precondition of the successful operation of a system, an organizational unit or their networks.

A classification of the continuity principles

As a first step, it is plausible to separate continuity principles into three classes, as genetic, developmental and ecological continuity principles. Then, later on, it would be useful to look at their combinations.

Continuity of genetic systems. We can mention several genetic continuity principles, such as the operation of autocatalytic systems, the complementarity of base pairing according to the CHARGAFF's rules, MENDEL's rules, WEISMANN's continuity of germ and the germ-soma separation, and finally the membrane inheritance without genes.

Continuity in phenotypes and development. The phenomenon of phenotypic or developmental continuity can be observed both in unicellular and multicellular organisms. In ciliates, the surface or cortical structures are perpetuating, apparently without detectable genetic control, from generation to generation (see JABLONKA & LAMB 1995 for an overview). This means that there exists at least one case, where the unbroken chain of the propagating developing structures and their transformations can be transmitted between generations by seemingly purely developmental mechanisms. The cortical inheritance is a clear case of Lamarckian inheritance of acquired characters. JABLONKA & LAMB (1995) argue that the clonal propagation of cortical structures in ciliates affects the symmetry, pattern and form of these organisms.

An important phenomenon in the development of multicellular organisms is the embryonic induction. This is an interaction between two cell populations. The inducing cells transform the qualitative properties of the induced, competent cells. A major element of the multicellular development consists of a network or cascade of inductive effects. An essential requirement of the inductive chains is their continuous, unbroken propagation. When the inductive chain is broken, the development stops. This important requirement is expressed as a continuity principle of multicellular development (HORDER 1983). As HORDER (1983, p. 339.) says: 'This proposal satisfies an essential requirement which should be met by any hypothetical evolutionary sequence; a continuous sequence of morphogenetic events in an embryo is a repetition of a continuous sequence of morphological steps built up through the preceding evolving series of embryos, each stage of which must have been functionally advantageous in the transitional organism. This will be referred to as the continuity principle.' HORDER considered the evolution of the eyes in vertebrates. He showed that the specific components of the vertebrate eyes were acquired in a gradual way. Firstly, the photoreceptive element evolved. Secondly, these elements localized under the surface of the body. Thirdly, this system was complemented by the lens and the cornea, constituting the image projecting elements, seemingly step-by-step.

Because of the 'functional advantage' of the developmental stages, the continuity requirement is neither tautological, nor easy to explore. In the light of a more explicitly dynamical view of the developmental sequence concept (e.g., ALBERCH 1985) discontinuous developmental dynamics or bifurcations of developmental programs and developmental continuities can be easily reconcilable, if the underlying developmental control parameters vary continuously. In such cases, developmental outcomes can show discontinuities, as in the case of generation of skin organs (OSTER & ALBERCH 1982). Therefore, continuity and discontinuity are not necessarily mutually exclusive views in the phenotypic organization and its evolution.

A set of discontinuous biological shapes [e.g., self-reproducing primeval cells, gastrula, spatially periodical structures, obcell (primeval cell) membrane (cf. CAVALIER-SMITH 1987)] can be generated on the basis of a variation principle (CIANCHO *et al.* 1996). The essence of this 'curvature' model is the minimization of the curvature energy, generating various anisotropic bilayers. There are at least three evolutionary implications of this model. First, the organisms and their parts can be regarded as an infolding of dynamically interacting shell/membrane systems. Secondly, not only genes, but also generative mechanisms can exhibit evolutionary conservation or continuity with manifold, apheliotropic effects, as in the case of the origins of blastulae and gastrulae (WOLPERT 1990). The real number of the germ layers (endo-meso-ectoderm) seems to be an unsolved problem in the light of the hierarchical shell/membrane infolding picture of the organisms. Finally, the simplest forms of the self-reproduction originated from morphogenetic processes.

Ecological continuity

We are aware of only two important aspects of the continuity of ecological systems. The first is concerned with the connection of adaptation and population demography. The second is about the matching between phenotypic and environmental patterns.

LEWONTIN (1978) realized the evolutionary importance of two characteristics of the selection, existing between character states and reproductive fitness. These characteristics are continuity and quasi-independence. 'Continuity means that small changes in a characteristic must result in only small changes in ecological relations; a very slight change in fish shape cannot cause a dramatic change in sexual recognition or make the organism suddenly attractive to new predators. Quasi-independence means that there is a great variety of alternative paths by which a given characteristic may change, so that some of them will allow selection

to act on the characteristics of the organism in a countervailing fashion; pleiotropic and allometric relations must be changeable. Continuity and quasi-independence are the most fundamental characteristics of the evolutionary process. Without them organisms as we know them could not exist because adaptive evolution would have been impossible.' (p. 169). We can only agree. LEWONTIN expressed in a transitive way that reliability belongs to the most fundamental evolutionary organizational principles, on which continuity and quasi-independence are based. It is fair to say that some aspects of LEWONTINS' principles were formulated in a vaguer style by RONALD FISHER in 1930 (see MOLNÁR 1995).

The other important aspect of the continuity of ecological relations is connected to the dynamical phenotype-environmental pattern matchings and its recognitions (DETHIER 1986, JERMY *et al.* 1990, JERMY 1993, MOLNÁR 1990, SCHOONHOVEN *et al.* 1998, CHAPMAN 1999). Reaction norms may also change continuously or show various bifurcations.

Combinations of genetic, phenotypic and ecological continuity

The complex combinations of genetic, developmental and ecological continuity can be simplified first using pairwise connections: 1. genetic-phenotypic, 2. genetic-ecological, and 3. phenotypic-ecological relations of continuity.

A useful way of analysing genetic and developmental connections is the embedding of locally acting specific genetic elements or systems into typical or generic, globally and/or locally acting physicochemical pattern and form generating mechanisms (MITTENTHAL 1989, NEWMAN & COMPER 1990, MOLNÁR 1986). The essential continuity requirement for the existence of coupled genetic-generic effect combinations is to fulfil or obey a matching principle (MITTENTHAL 1989, MOLNÁR 1986). This matching principle claims that short-range and long-range genetic and generic physicochemical mechanisms and their effects should meet. This principle implies that the continuity of development and evolution depend on the interactions between genes and the physicochemical mechanisms of developmental dynamics, generating ecologically relevant or competent phenotypes. Our view differs from the rest. The (often dually heritable) genetic-generic effect combinations operate within the internal and external ecology of organisms (cf. BUSS 1987), consisting of dynamical coexistence of competitive and cooperative selective factors (such as cell death, cell and cell lineage competitions and/or cooperations). To put more simply, our suggestion is that generic-genetic effect pairs or combinations and dynamically coexisting cooperative and competitive organism parts (multilevel parasitism, predation, mutualism, etc.) reciprocally drive

each other through a set of mediators during development, in its evolution, and in life cycle evolution, and in their coevolution.

A RELIABILITY THEORETICAL BASIS OF CONTINUITY PRINCIPLES

The argument for creating a reliability theoretical basis of the biological continuity principles

As mentioned previously, reliability can play a fundamental role in the generation of continuous operations in biological entities. Here we outline the elements of this conviction. A technique for incorporating reliability theoretical foundations into continuity principles is to connect the essential reliability shaping factors with the following scheme:

*i*th unit of organization transmission *i*th or *j*th unit of organization.

For this reason, we determine specific connections between reliability modifying factors with organizational units or their networks, such as genes, genomes, phenotypes, and ecological or social structures. The two fundamental classes of reliability determining factors are (1) error production and error reduction, and (2) generation of so called composite structures, the couplings of which can be series, parallel or their combined designs. Such a work is in progress, extending the status quo described in this paper. First, let us summarize briefly the elements of reliability theory.

The concepts of reliability

In this part of the paper, we show that a convenient way to treat the biological continuity principles is the theory of reliability.

The "reliability" of a system has several meanings. We present two of them in terms of measures of reliability. The reliability of a system is the probability of successful operations during given time, in a given environment (reviewed in ALEXANDER 1981, BARLOW & PROCHAIN 1965, MOLNÁR 1995). Reliability can also be expressed (ALEXANDER 1981) in terms of safety factors (SF) (SF = Capacity/Demand).

It is sometimes assumed (DAWKINS 1995) that safety factors are evenly distributed in an organism, because natural selection fine-tunes the costly safety factors. However, data show that vital organs can loose components or capacity in a variable manner; safety is unevenly distributed within a given range (ALEXANDER 1981, DIAMOND 1994, WEISS *et al.* 1998, NIKLAS & SPECK 2001), and the safety

factors can numerically differ among the parts of an organism, ranging from one to eight in the case of bones and tendons (ALEXANDER 1981) or between one and 2.7 in metabolic systems (WEISS *et al.* 1998), depending on loads. Highly unpredictable loads imply high, more predictable loads imply low safety factor (ALEXANDER 1981). (Un)Predictability can characterize the environment, which influences reliability.

The exact measurement of reliability in organisms is a difficult problem. Therefore, we discuss organismic reliability in terms of reliability decreasing errors, typical or generic reliability enhancing factors (REFs) and their effects. A reliability enhancing factor, or more simply a reliability enhancer, is a determinant that ensures the propagation of information, matter and energy within and between organisms. Alternatively, to put more generally, within and among organizational units, such as selective or evolutionary units, as we shall see later. These REFs include redundancies, repair mechanisms, storage materials and mechanisms, feedbacks, activators, inhibitors, replacements and combinations of series or parallel structures. There exists proof for direct or indirect relationship between reliability and its enhancers in the engineering and in the biological literature (ALEXANDER 1981, BARLOW & PROSCHAN 1965, MOLNÁR & VÖRÖS 1994, MOLNÁR 1995, NOWAK *et al.* 1997, JORDÁN & MOLNÁR 1999, JORDÁN *et al.* 1999), except for the case of selective processes. It is intuitively clear, however, that by removing erroneous parts from organisms by internal selective processes, the number of errors or the error rate can be decreased (see later), and consequently, the reliability can indirectly be increased. The same is true for the effects of other reliability enhancers as well, when reliability enhancers act after the formation of errors, as in the case of repair, feedback or replacement. Redundancy, storage and certain combinations of parallel and series structures tend to prevent error formation. A further confirmation of the connection between reliability enhancers and reliability would be the removal of reliability enhancers from organisms, and to evaluate their effects on reliability. There will be further concrete examples showing the action of reliability enhancers later in this paper. Error (or failure) is a factor, that inhibits or blocks the propagation of matter, energy and information, or capable of causing various other defects.

We now introduce a classification of various reliability enhancers, which helps to put all these factors in perspective. In the next three parts of this paper the reliability increasing and decreasing components will be outlined: first, the noise and/or errors, secondly, the reliability increasing factors, thirdly the composite structures.

The meaning, variation and classification of biological errors

The genesis of genomes and phenotypes include dynamic molecular, cellular, organismal, populational or higher phenomena. These events constitute patterns (ordered inhomogeneity) with characteristic shape, or more simply, with morphogenesis. Morphogenesis is the birth of biological forms. The major genotypic, phenotypic or ecological systems change in evolution. In addition, these systems have been associated with balanced changes between several error increasing and error reducing factors. We are aware that errors represent a fraction of the variation. Variation, however, is necessary for evolution, but errors are not. By error (or more generally speaking, by failure) we shall mean such effects, which decrease the reliability of the units of selection.

The variation of failures is associated with patterns, rates and with dynamic, evolving genotypic, phenotypic or ecological structures, functions, processes, evolving modes of heredity, variation generation, reproduction, evolutionary lineages or else.

An elementary classification of the diversity of failures can be organized according to the following properties of failures. A. According to their appearance, failures can behave continuously (i.e., accumulative), sudden (catastrophic, lethal, sublethal). B. According to connectivity or distance of interaction, failures can be classified as independent or local, moderately or highly connective, dependent, global failure groups, with varying interaction strength. C. According to spatial, temporal or spatiotemporal behaviour, failures can be classified as temporary, repetitive or constant failures. Certain failures can cause other failures, propagating in series, parallel or in combined ways. D. According to failure localisation in composite structures, we can make distinctions between failures emerging in series, parallel systems or in their combinations, e.g., in bridge structures. E. According to origins, failures can be dependent upon genotypic, phenotypic or environmental factors, or they can reflect their independencies on them or on their combinations.

Error production and error propagation in evolution

We do not know the quantitative measure of error rates in the separate or the joint evolution of heredity, variation and of reproduction. What we do know, however, is the fact that these evolutionary properties are prone to failures. Traditionally, studies on the evolution of error patterns or error rates focus on the heritable mutations. We would like to know, however, not only the failures of hereditary information, but the sources, patterns and rates of failures in the generation of genotypic, phenotypic or environmental variation, and the failures observed in the various modes of evolution of reproduction or the failures of the invasion of

genotypic or phenotypic variants. Now we will refer to some representative investigations studying the evolutionary patterns and rates of heritable, variation generating or reproductive failures and their possible evolutionary interactions.

Mutations do not constitute unambiguous error sources, because a subset of mutations has evolutionary advantage. EIGEN (1971), DRAKE *et al.* (1998), NINIO (1997) have described quantitative measures of mutation rates and their evolution.

We have a very rich evolutionary literature on the origins of erroneous genetic and phenotypic variation. Some of them include GOLDSCHMIDT's (1940) book on the hopeful monsters capable of spreading under favourable conditions. GRUNEBERG (1963) wrote a whole book on the pathology of development. As for the erroneous genetic variants, a number of monographs have published largely inconclusive information about the real distribution on the various patterns and rates of genetic errors.

What can we say briefly about the evolutionary interaction of the heritable variation generating and spreading of the successful variants? Perhaps the best example is the concept of ESS (MAYNARD SMITH & PARKER 1973), which defines the condition of the spread of a potential, new variant, and its failure to spread. Accordingly, evolutionary game theory cannot explain the origins of novel variants; it just assumes their existence in its strategical reasonings. The views of the origins of variants, however, cannot take into account the generative mechanisms of the variation generation. Finally, it is safe to say that there must be an equilibrium in the production of successful and in the erroneous variants in preventing or avoiding extinction.

Classification of genotypic, phenotypic and ecological reliability enhancing factors

In many cases, we cannot determine the level of the exact quantitative value of reliability, neither safety factors, nor transition probabilities. In such cases, we can still qualitatively detect if a factor decreases or increases the value of reliability.

We propose (MOLNÁR & VÖRÖS 1994, MOLNÁR 1995, MOLNÁR unpubl.) that all reliability-enhancing factors fall into the following categories, which are illuminated in each case by typical examples.

1. Repair. Examples include: Recombinational repair during which elimination of genetic errors can take place (EISEN & HANAWALT 1999, AARAVIND *et al.* 1999). Cellular detoxification of poisons. Wound-healing and regeneration (KIRKWOOD 1981).

2. Replacement. The replacement of lost cells and tissues in the epithelium of the intestine by means of stem cells or the replacements of immune or sperm cells.

3. Feedback. Feedback regulation is well known in the neural or hormonal control. According to MEINHARDT (1995), the reliability of development is mainly based on autocatalytic self-activation, cross reactions and feedback of gene products. But as WOLPERT (1994) realized, embryonic development cannot be stabilised by negative feedback alone, because embryos would get into "frozen" or stabilised states instead of going through their successive developmental pathways. Self-stabilising genetic, cellular and other redundancies seen in intracellular and intercellular processes can contribute to the stabilisation of developmental pathways (see MOLNÁR & VÖRÖS 1994, MOLNÁR 1995, NOWAK *et al.* 1997, TAUTZ 1992, THOMAS 1993, WOLPERT 1992).

4. Storage. Good examples for variation of storage are plant storage proteins (SHEWRY 1995), especially starch, which is controlled by a single gene, and the yolk in animal eggs (BERRIL 1948). The role of storages can be important in fluctuating environments in averaging fluctuating resource density, for instance. The evolutionary success of the *Volvox* can in part be regarded as the success of large extracellular matrix, which is capable of buffering uneven resource level (BELL & KOUFOPANOU 1991, KIRK 1998). Storages represent excess or reserve materials that can be mobilized.

5. Redundancy. Genetic information can contain variable amount of genetic redundancy (OHNO 1970, ANDERSON & ROTH 1977, TAUTZ, 1992, THOMAS, 1993, BROOKFIELD 1997, NÁDORI *et al.* 1996, NOWAK *et al.* 1997).

6. Combination of series and parallel structures. A representative example is the bridge structure, which is a parallel organized structure which contains one or more crosslinks (BARLOW & PROSCHAN 1965, JORDÁN & MOLNÁR 1999, MOLNÁR unpubl.). Bridge structures are ubiquitous in nature; they can be observed in molecular networks, such as gene regulatory networks, signal transduction pathways, cellular networks, such as cytoplasmic bridge structures of *Volvox*, anatomical networks, such as venation or blood vessel patterns, or even in ecological networks, such as food webs (BARLOW & PROSCHAN 1965, BELL & KOUFOPANOU 1991, INGBER 1993, JORDÁN & MOLNÁR 1999, JORDÁN *et al.* 1999, KIRK 1998, MOLNÁR & JORDÁN unpubl. results).

As we have demonstrated elsewhere by using graph theoretical models of specific molecular, cellular, supracellular and ecological networks, these models possess predictive features in the reliability theoretical analysis and synthesis of biologically important networks (MOLNÁR & JORDÁN, unpubl. results). The relevance of these models is the quantitative prediction and demonstration of the existence of certain preferred biological structures.

7. Activation and inhibition. These actions are well known in the operation of the nervous systems.

8. Multilevel selection. The various sources of multilevel selection (LEWONTIN 1970) can also be regarded as reliability enhancing factor, because their function is the reduction of genetic, phenotypic or developmental errors. Spontaneous abortion in human pregnancy belongs to this category.

Balance between the error formation and the error reduction in the main stages of evolution

We propose a hypothesis for describing alterations in reliability enhancers in evolution. The core of this hypothesis is that it is likely that there exists a balance between errors and their controls. The origin of genotypic or phenotypic variability seems to involve coevolution between novel error possibilities and their novel controls.

The assumption that there exists a balance between the level of errors (or more correctly error rates) and the rates of generating reliability enhancing factors in evolution requires a justification. The errors are unavoidable factors in organisms. When the error level is high, the continuity of the biological processes can break down. This phenomenon can be observed in aging (KIRKWOOD 1981), in developmental defects caused by lethal factors, and in the dynamic of the heart caused by failures, for instance.

The most clearly known example of the control of error rate by reliability enhancing factors is the origin and maintenance of the error level in DNA molecules (DRAKE *et al.* 1998, NINIO 1991, REANNEY 1987, REANNEY *et al.* 1983). The evolution of mutation rate of DNA can be taken as an example for demonstrating the evolutionarily changing balance between error formation and error reduction. It is assumed, (REANNEY 1987) that in an initial stage of DNA evolution, the error rate was high, 10^{-2}/nucleotide/generation. Later, antimutator and repair or proofreading genes and catalysts, furthermore suppressors were capable of reducing the error rate to 10^{-9}/nucleotide/generation, in DNA molecules. So the errors cannot be eliminated, but their occurrence can be reduced to a certain level (DRAKE *et al.* 1998, NINIO 1997, REANNEY 1987). Similar events can be observed in protein synthesis. We propose that the principle of balanced error producing and error reducing processes occurring at genetic level can be extended to phenotypic organizational levels as well. Important initial steps towards such a direction have been made at molecular level, for instance (NINIO 1991, 1997, DRAKE *et al.* 1998).

We do not know exactly the level of balance of error producing and error reducing factors above the molecular level. We do know, however, that novel, variable errors must have come into existence at different organizational levels, such as damage of membrane or cytoskeletal elements in cells, and errors in cell divi-

sion, cell assembly or cell replacement, and so on. All these phenomena have been convincingly demonstrated by the huge databases of the pathological molecular, cellular and developmental processes. As we have seen, the error reducing reliability enhancers changed through the main steps of evolution in concert with the appearance of novel sources of errors. Since the maintenance of reliability enhancing factors is costly, their levels must be constrained within maintainable ranges (ALEXANDER 1981, DIAMOND & HAMMOND 1992, MOLNÁR & VÖRÖS, 1994, NÁDORI *et al.* 1996). If the level of reliability enhancers were low, saving energetic or other cost of their maintenance, biological processes would be more vulnerable or would break down. We need a quantitative theory for describing the balance of errors and their controls at phenotypic level. But even some trivial questions still were missing at the beginning of a more systematic analysis of the role of reliability in morphogenesis, development and evolution (MOLNÁR & VÖRÖS 1994, MOLNÁR 1995).

It is likely that reliability enhancers possess multifunctional properties, i.e., that they have been involved in several functions, in parallel or sequentially. It seems plausible to consider the origins of reliability enhancing factors as evolutionary novelties, which reappeared at the birth of novel organisational levels. This view raises an important problem. Reliability enhancing factors show specificity sometimes, as in the case of recombinational repair, and multifunctionality in many other cases. It seems that the degree of their specificity might tell us whether the REFs have specialized for error correction or not. We need not know exactly all the possible functions of structures or mechanisms to recognize cases when a structure or a mechanism plays a role – among other roles – in error correction.

The concept, the variation and the behaviour of the composite structures in evolution

A composite structure consists of more than one serially or parallel coupled elements. Composite structures consisting of more than two components have high relevance of their topologic coupling from reliability theoretical point of view. The various patterns and processes in the living world can be represented by composite structures.

Reliability of composite systems change according to their architecture. We propose the following view in this paper: The characteristic patterns and processes in life cycles or evolution can be regarded as composite structures with their respective reliability. Hence, the principal processes of evolution, such as microevolution, macroevolution, speciation, body plan evolution, coevolution are considered to be various composite structures. A reinterpretation of the patterns and

processes in nature may lead us to a novel grandeur of the history of life. The continuity of living patterns and processes can be discussed in terms of evolutionary genomics and phenomics.

Now let us discuss the concept, the variation and the behaviour of the *k*-out-of-*n* structures in evolution, as a special class of the composite structures. Imagine a system consisting of *n* components of subsystems. A system with *k*-out-of-*n* structure works, if at least *k* elements work, and $k \quad n$.

In this part of this paper, we describe an hypothesis for the evolutionary origins of genomes (NÁDORI *et al.* 1996). A basic character of the genetic systems is that their composition allows the loss of certain genes. We propose that this property or the dispensability of a specific set of elements corresponds to the *k*-out-of-*n*-like structure class of the reliability theory (BARLOW & PROSCHAN 1965). Knockout experiments or gene targeting show (TAUTZ 1992) that a number of genetic elements can be lost or inactivated without visible phenotypic effects. The case of the regulation of the Krüppel gene by four other genes in *Drosophila*, and its intact function when its 1, 2 and 3 regulators were knocked-out (TAUTZ 1992), is a nice illustration of a *k*-out-of-*n*-like behaviour. The minimal genome concept (the fact, that nearly 256 genes or even less operate in a given bacterial cell, living on optimal resource without competition) reviewed by KOONIN (2000) also provides a good example for the operation of minimal genetic systems reduced to indispensable genes. Since there exist many similar examples for the genetic phenomenon at different phylogenetic positions, we think that this is an evolutionarily conserved property. We assume that the evolutionary origins of the genomes may have emerged from coupled islands of *k*-out-of-*n*-like genetic elements. The result of this effect is the existence of genetic systems with multiple channels. The mechanisms of the coupling of genetic elements may have been the same, as in the case of the scenario. This is a clear case of the nontrivial, but probably widespread, unavoidable recapitulation. (Recapitulation is the repetition of evolutionary events in development.) We also remark that several constraints may act on the value of *k*.

Our approach can be applied to the treatment of other phenomena as well, occurring at different organizational levels. The potential role of *k*-out-of-*n* structures has been discussed by MOLNÁR (1995) at different organizational levels, as in the case of cell lineages, replacements of stem cells or other organismic devices (see DIAMOND 1994, for further examples of the reducibility of various phenotypic structures, the loss of which until a threshold level is still compatible with survival and reproduction).

OSTER & WILSON (1978) have applied this idea for describing the *k*-out-of-*n* behaviour in the organization of behavioural sequences in animal societies. OSTER

& WILSON (1978) described the evolutionary transition from a solitary to a colonial animal in terms of a reliability theoretical model. They regarded the steeper reliability relation between the component animals and the social group as a key selective advantage in the transition.

The evolutionary effects of reliability enhancing factors

An obvious way to point out these effects is to show their potential fitness consequences. We do not understand clearly the control (or proximate or ultimate causes) of the quantitative aspects of REFs. The simplest form of the problem is the following: If a high level of overdetermination or reliability enhancing factors is useful, why do not exist more of them? More explicitly, if two kidneys are better than one, why not have three (DIAMOND 1994). The simplest explanation is that reliability enhancers require cost and limited, organised packing (see ALEXANDER 1981, and DIAMOND 1994 for cost consideration in the maintenance of reliability).

In this regard, the same hypothesis connects the various data sets. As we have seen above, this requirement is satisfied. We are, however, aware of the incompleteness of our data, but the multiplication of the various data would not affect the essence of our two central organizing principles. A second type of evolutionary hypothesis testing is to ask whether the traits in question can propagate or invade efficiently under certain conditions. The tool of studying of this second strategic or ecological aspect of reliability enhancers can in principle be determined in terms of their fitness consequences. We describe first two direct and then one indirect relationships connecting reliability enhancing factors and fitness.

1. The influential paper of ALEXANDER (1981) describes the fitness cost of safety.

2. We have developed a mathematical method for the treatment of the joint actions of reliability determinants on fitness elsewhere (MOLNÁR & VÖRÖS 1994, and MOLNÁR & VÖRÖS unpubl. results, for a novel view of the evolution of aging). We have pointed out in a model that the coupling between various REF combinations and selection can describe the evolution of aging and longevity. (Description of aging is a prototype of the description of deterioration or its control in biological systems.) Unfortunately, our approach has not yet been applied for describing phenotypic properties under the effects of changing reliability enhancers.

3. An important possible step in connecting reliability to its ecological consequences has been put forward by VERMEIJ in his hypothesis of escalation (VERMEIJ 1994). Briefly, VERMEIJ's central thesis is that the main devices of the competition for various resources between enemies (predators, competitors and dangerous preys) are defensive or offensive means, which can be escalated in arms

races by positive feedback. For illustrating the similarity between VERMEIJ's view and ours, it is useful to quote him: "Individuals often fail to acquire or retain resources during encounters with other individuals. Insofar as failure reduces the probability of survival or opportunities for reproduction, there is room for adaptive improvement. The potential for improvement can be roughly gauged by the frequency and cost of failure." (VERMEIJ 1994, p. 221.) The main difference between VERMEIJ's and our views is that we think that various combinations of reliability enhancing factors can be an underlying basis for escalating defences and offensive weaponry. Furthermore, we study the connections of reliability enhancers in the context of the major morphogenetic transitions, and so neglect the fascinating topic of defences and offences. Finally, we think that the escalation of defences and offences were preceded by an escalation of several reliability enhancers.

The acquisition of reliability decreasing and increasing factors in the main steps of evolution

In this part of the paper, we present a pattern of evolution: an association between error possibilities in the novel ways of genotypic, phenotypic, ecological or social systems and error control exerted by REFs. In a very popular sense, our approach reflects the fight between good and evil forces. This mythical sense is being projected into the structure and the operation of biological objects. The outline of this evolutionary scenario is shown in Table 1, which presents the successive evolutionary origins of different types of REFs. These REFs might have played potential error reducing or other roles in the major stages of evolution.

CONCLUSIONS

In this paper, we have briefly outlined reliability theoretical foundations of the biological continuity principles. Finally, we summarize the main points of the paper.

1. As WOLPERT remarked, "Selection on developmental processes acts primarily on reliability and this requires consideration of buffering and redundancy in developmental processes." (WOLPERT 1992). If so, the various evolutionary views should be compatible with the reliability theoretical approach to evolving hereditary systems, phenotypes and ecological or social design generating processes.

2. The various reliability enhancers can be regarded as evolutionary novelties, which could have reappeared at various evolutionary stages in evolutionarily changing ways. Accordingly, evolution repetitively invented similar construc-

tional devices at various organizational levels in an iterated way. Using this evolutionary "trick", natural selection is capable of preserving the successful units of organization more efficiently.

3. Reliability enhancers often have dual or even multiple functions (MOLNÁR & VÖRÖS 1994, MOLNÁR 1995). Dual function means that reliability enhancers are capable of conserving genetic, phenotypic, cellular, developmental, ecological

Table 1. Associations between the main steps of evolution and their acquired reliability enhancing factors, such as repair, replacement, storage, redundancy, feedback, series and parallel structures. T1–4 indicates the main steps between evolutionary stages. References are in part given in the text or can be obtained from the author.

1. PROTOCELLS
unknown reliability enhancing factors
T1
↓
2. PROKARYOTES
holoenzyme (autolysine+ transpeptidase) redundancy in wall stress regulation,
repair, genetic redundancy, *k*-out-of-*n* behaviour of bacterial colonies
(every clone behaves in *k*-out-of-*n* manner, D. KAISER, pers. comm.),
feedback in metabolic networks, partial redundancy in autocatalytic cycle.
T2
↓
3. PROTOZOA
self-regulating local and global positional information,
repair, genetic redundancy, bridge structures in cytoskeleton,
redundancy in signal transduction,
feedback in metabolic network, partial redundancy in autocatalytic cycle.
T3
↓
4. MULTICELLULAR ORGANISMS (ANIMALS, FUNGI, PLANTS, CHROMISTA)
k-out-of-*n*-like behaviour in cell populations,
bridge structures in molecular and cellular networks *Volvox*,
crosslinks between ECM molecules enhancing mechanical reliability,
cell replacement, e.g. stem cell activity,
storages, such as Volvox ECM, (better starvation tolerance in fluctuating
environment) ontogenetic buffer mechanisms,
elastic energy storage in tendons for animal movement,
feedback in embryonic induction or in neuroendocrine control,
multiple assurance in intercellular signal propagation, e.g. in induction,
genetic, cellular or modular redundancy.
T4
↓
5. PHENOTYPIC PATTERNS OF ANIMAL COLONIES
feedback in caste determination, storages, such as pollen or honeycomb,
redundancy in the number of colony members.

or social characters, as the buffering role of the redundant genes indicates in the case of canalisation. At the same time, these factors are capable of generating novel genetic, morphogenetic, ecological and evolutionary possibilities, as in the case of heterochrony (MOLNÁR & VÖRÖS 1994, MOLNÁR 1995). Because of their dual or multiple effects, reliability enhancers constitute a specific set of factors governing evolvability (GERHART & KIRSCHNER 1997, WAGNER & ALTENBERG 1996) since reliability enhancers are capable of generating and preserving evolutionary potentials.

4. What problem does all this create for evolutionary theory? First, it seems reasonable to think that error formation and error control play a fundamental role in the "struggle for existence", which should be explored more explicitly. According to DARWIN, the term "struggle for existence" refers to two notions: "dependency of one being on another" and to "success in leaving progeny" (DARWIN 1859). Reliability of the organisms affects both properties. The view presented here overlaps with and complements DARWIN's evolutionary vision by emphasizing an important class of internal factors of evolution and their potential connections with ecologically important defensive and offensive characters (VERMEIJ 1994). Second, the relationships between the view of evolution presented in this paper and other evolutionary scenarios, such as the conflict-based view of evolution, should be formulated more exactly, because they describe different aspects of the evolving biological organization. For example, parent-offspring conflict, genetic conflicts, sexual selection or predator-prey arms races represent typical conflicts driving evolution. Third, reliability-related errors and error controls reflect mainly self-organisation within and among organisms resulting in both chance and ordered evolutionary consequences, in many cases even before the action of natural selection. Finally, errors or failures represent a fundamental aspect of historical contingency (cf. GOULD 1989, CONWAY MORRIS 1998, LAWTON 1999). Therefore, any fundamental view of the evolutionary history of biological processes should contain a description of errors and the safety techniques of the organisms, or more generally, the various units of biological organization and of their networks.

*

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