Revista Chilena de Historia Natural
80: 109-116, 2007

COMMENTARY

Within selection

Dentro de la selección

CARLOS Y. VALENZUELA

Programa de Genética Humana, ICBM, Facultad de Medicina, Universidad de Chile,
Independencia 1027, Casilla 70061, Independencia, Chile
e-mail for correspondence: cvalenzu@med.uchile.cl

ABSTRACT

The synthetic theory of evolution proposes that biotic variations generated by mutation are mostly fixed, lost or maintained polymorphic by natural selection, with a marginal effect due to genetic drift. Based on the theory of autopoiesis some authors have proposed that selection is unable to explain most evolutionary changes, and natural or phenotype drift and epigenesis are the mechanisms that explain most of evolution. This view misunderstands basic evolutionary notions. Selection is a natural process that occurs with or without evolution; it does not explain evolution, it is a factor of the evolutionary process. The concept of autopoiesis implies an invariant condition of living beings, thus, it cannot explain and even less produce evolution conceived as ontogeny and phylogeny (highly variable processes). Natural drift does not solve this conceptual insufficiency; random drift is not a directional process; its expected evolutionary effect is zero.

Key words: autopoiesis, evolution, natural drift, neutral evolution, selection, synthetic theory.

RESUMEN

La teoría sintética de la evolución postula que la variabilidad biótica generada por las mutaciones es mayoritariamente fijada, eliminada o mantenida polimórfica por la selección natural, con algún efecto marginal debido a la deriva genética. Basado en la autopoiesis algunos autores han propuesto que la selección no puede explicar la mayor parte de los cambios evolutivos y la deriva natural o fenotípica, más la epigénesis son los mecanismos que explican la mayor parte de la evolución. Este planteamiento incluye errores conceptuales de las nociones básicas sobre evolución. La selección es un proceso natural que ocurre con o sin evolución y no es explicativa de la evolución, sino que es un factor incluido en el proceso evolutivo. La autopoiesis es una condición invariante de los seres vivos que no puede explicar y menos producir evolución concebida como la ontogenia y filogenia (procesos muy variables). La deriva natural no corrige esta insuficiencia conceptual ya que la deriva al azar no es un proceso direccional y su efecto evolutivo esperado es cero.

Palabras clave: autopoyesis, deriva natural, evolución, evolución neutral, selección, teoría sintética.

INTRODUCTION

The synthetic theory of evolution, known also as the neo-Darwinian theory, integrated Mendelian inheritance and mutation to the Darwin-Wallace view of evolution as a inherited variation-selection process. Population genetics gave the mathematical basis for the synthetic theory (Simpson et al. 1957, Futuyma 1998). This version was the main evolutionary paradigm (disciplinary matrix) until 1970. Shortly, it proposes that organic variation emerges by mutation and its fixation, extinction or polymorphic maintenance is mostly due to natural selection; genetic drift, as a factor of evolution, acts in a lesser extent. Genetic drift was known since the early works on population genetic equilibrium (Hardy-Weinberg equilibrium, Simpson et al. 1957) and was dealt with extensively by Wright (1931). Kimura (1968) and King & Jukes (1969) proposed that evolution (fixations, extinctions and

polymorphisms) might be better explained by mutation and genetic drift, instead of selection that acts in a lesser extent, founding what is known as the Neutral Theory of evolution. Neither neo-Darwinists nor neutralists ever quantified the extent or importance of selection or drift in evolution. Nearly neutralists are neutralists that accept selection with coefficients similar to the mutation rate. The present accepted notion of biotic evolution is the process of variation and maintenance of inter-related (mostly by descent) population distributions of genomes. Independently of these scientific developments, theories of life (living beings) were also developed (Valenzuela 1997, 2002a). Mainly two theories have been proposed: (i) living beings are order-generating structures (Bertalanffy 1963, Elsheikh 1988), and (ii) living beings are autopoietic (self-producers of their organization) systems (Maturana & Varela 1972). Living beings as anagenetic beings (a system of organizational relays that maintain and produce similar organizations) has been preliminarily presented (Valenzuela 1997, 2002a). The intersection of evolutionary and life theories was unavoidable and occurred mainly around the idea or process of adaptation. According to the synthetic theory adaptation is a result of natural selection. For the autopoiesis theory, living beings are autopoietic beings that are always adapted (they are alive); they cannot be a result of natural selection that implies degrees of adaptation (fitness). Thus, in this theory, evolution should be conceived as the change among equally adapted living beings. This viewpoint is more compatible not with genetic drift, but with phenotypic or natural drift (Camus 1997, 2000, Maturana & Mpodosis 2000). In relation with these hypotheses, another important element present in the current evolutionary paradigm came from paleontology: the controversial hypothesis of punctuated equilibrium (Gould & Eldredge 1977, Gould 2002). The pattern of evolution would include small or gradual phenotypic changes that occurred during long time periods (equilibrium or stasis), interrupted (punctuated) by fast species transformation, of which no or few fossils are left (Futuyma 1998). The similarity of this hypothesis with the structure of science proposed by Kuhn (1970) is remarkable: "normal science", performed within the same paradigm, grows for long periods, but it is interrupted by "paradigmatic science" (paradigm changes). Vargas (2005) invited us to go beyond selection and proposes that natural drift explains most evolutionary processes better than selection, and that the present population genetics theory is unable to deal with advances on phylogenetic analysis, developmental evolution and paleontology. Epistemological and basic conceptual differences do not allow one to follow his arguments. I invite you to walk along within selection.

AN EPISTEMOLOGICAL NOTE

Science is not primarily involved with explanations, but with knowing or understanding natural or universal processes that existed, exist and shall exist, regardless the human mind. Explanations, theories, hypotheses or models are transitory tools. To confuse the process of evolution with evolutionary explanations is a regrettable gnoso-ontic confusion. Evolution did and does give rise to humans and their mind; the mind did not and does not create evolutionary processes (Valenzuela 2001a, 2001b, 2002a). Natural selection is not an explanation, but a central process of the living world and evolution. Mendel's genetic particles (factors) and regularities are not explanations, but, traits of biotic inheritance. I agree with reductionism, as the evaluation or explanation of processes of a discipline (biology) by the elements of another discipline (physics), without (I add) semantic homogeneity (physicalism). Not less erroneous and dangerous is the refusal (anti-reductionist integrism) of members of a discipline (paleontology) to confront their hypotheses with the well-demonstrated facts of another discipline (population genetics). Inter- and trans-disciplinary analyses of the same process, with a common semantics, are compulsory in science to maintain consistency. Science has a purpose: to understand happenings objectively (a positive correlate among different subjectivities).

LIVING BEINGS ARE NOT AUTOPOIETIC SYSTEMS

Vargas (2005), based on the conception of life as a form of autopoeisis, proposes evolution by natural drift instead of selection. As life may be an ideologically biased concept and may not

exist (Valenzuela 2002a), let us consider living beings as autopoietic beings. Autopoiesis is "a network of processes of production (transformation and destruction) of components that produces the components that: (i) through their interactions and transformations continuously regenerate the network of processes (relations) that produced them; and (ii) constitute it (the machine) as a concrete unity in the space in which they (the components) exist by specifying the topological domain of its realizations as such a network (http://www.imprint.co.uk/thesaurus/autopoiesis.htm). If we equate organization to the network of processes of production of components, an autopoietic system is a self-producing organization. No living being self-organizes, it receives its organization from its ancestors. The zygote organization results from the sperm-ovule fusion and does not exist before; moreover, its network of processes lead not to re-produce the zygote, but to produce a two-cells embryo. Also, when in a (unicellular) bacterium the network of processes of production of components produces its genome (a component), the bacterium does not re-produce the original net of processes, but it produces (after other concatenated processes) two new bacteria and makes the ancient network disappear. Then cells are rather allopoietic (the process whereby an organization produces something other than the organization itself; http:// pespmc1.vub.ac.be/ASC/ ALLOPOIESIS.html) and not autopoietic organisms. This is a general condition of uni- or multi-cellular organisms. They inexorably develop, age, suffer genetic (organizational) diseases (disorganizations) and die. Thus, the network of processes of the ontogenetic stage OGS_1 does not produce OGS_1, but OGS_2 which is at a time mostly similar but a little different from OGS_1. Living beings present us as auto-allo-poietic systems. A caterpillar organization auto-organizes to a larger caterpillar organization or pupa organization, and pupa organization in a butterfly organization. In an absolute and complete autopoietic organism metamorphosis or ontogeny are impossible. So, autopoiesis as a process of maintenance of the organization is also false. According to autopoiesis caterpillars, pupas and butterflies, are equally autopoeitic, but have different organizations (networks of processes), that cannot proceed from autopoiesis. These auto-allo-poietic beings, connected historically by a process of organizational relays, has been named anagenetic beings (Valenzuela 1997, 2002a). The anagenetic organization implies processes of maintenance, repair and regulated changes (homeostasis, ontogenesis, phylogenesis, mutation) of the components or the network of (intra and inter-individual) processes; but they are insufficient to maintain this organization invariant. Variation of the living organization is a fundamental property of living beings. Autopoiesis is an idealistic (non-real) conception based on the abstraction of the population variation of the network of processes. For every adult animal that reproduces, many do not, due to genetic or accidental death or to reproductive impairment. At least 40 % of human zygotes, embryos, fetuses or children die due to known abnormal genetic conditions. Before dying they were alive (thus, autopoietic?) but not autopoietic (because they died by traits of their self-organization). Moreover, the organization of unicellular organisms includes the organization of their self-death or apoptosis (a sub-network of processes, included in its genomic norm of reaction, that destroys the whole network of processes). Suicide does occur. Furthermore, living beings are polymorphic, especially sexually dimorphic. Males are just as autopoietic as females. Why the difference? If we abstract from living beings their nature of historical population processes, polymorphisms, sex, ontogeny, phylogeny, aging, death, genetic diseases, reproductive impairment, mutations, genetically different susceptibility to diseases, and we think in the condition of this being that still remains, we shall conceive autopoeisis as the invariant condition of this ideal, but biased living being. When, after doing so, we want to understand (explain), with this invariance of invariants (autopoiesis), the production of the variance in ontogeny, phylogeny and populations, we find that this is impossible. An invariant cannot explain and less produce a variant. Prof. R. Berríos has favored autopoiesis by proposing that variants among invariant autopoietic organisms could arise by phenotypic drift. Prof. H. Maturana called this natural drift (Maturana & Varela 1984). Random environment fluctuations, interacting with phenetic factors

could select, trigger structural changes, stabilize or fixate genomic configurations (Lamarckism?). It is evident that the "ad hoc" hypothesis of natural drift has been created to fill in the insufficiency of autopoiesis; a negative heuristic protective belt proposed to save the theory.

THE POPULATION GENETIC STRUCTURE IS THE FRAME OF EVOLUTION

Individual living beings with their genome pass away; the dynamic population genetic structure remains; so, evolution cannot occur, nor be explained and less understood, outside the process of the dynamic population genetic structure. This is not a simple concept, but it is the dynamic genomic process that includes the historical genetic relations among individuals and generations, their reproductive and mating (sexual species) structures, their kinships and interactions with the environment. Species are a particular class of genetic population structure (or organization). Evolution is a change in the genetic structure of populations; within a species it is microevolution, over this biotic level it is macroevolution. Species have different genetic composition, as Dobzhansky proposed, without any confusion. The denial of this proposition: species do not have genome differences is scientifically untenable.

NATURAL SELECTION IS A FUNDAMENTAL PROCESS OF EVOLUTION

Natural selection is a true process and the second most important component of evolution. We know thousands of lethal and semi-lethal mutations and others with impaired fitness that persist at low frequencies in most species due to the mutation–selection equilibrium. Chromosomes, genome structures and genetic code are also maintained by this mechanism. Spontaneous abortions are often due to chromosome aberrations. Natural selection is a process of genetic differential reproducibility (of individuals and population genetic structures), universally documented not only in field and laboratory studies, but also in the daily life. In reality, it is not exactly the contribution to the next generation (reproducibility), but the probability to remain and contribute to remain in the future generations. There is no term to express this (remainability?). In the article (Vargas 2005), this well documented universal presence of selective processes in evolution is not mentioned. The demand to population genetics to explain the transformation of the jaw to the middle ear, without knowing genes, epigenetic factors and environmental changes that are involved in this evolutionary step is non sense. With these restrictions, population genetics cannot say anything, but, that there is nothing against this change. The assumption (hypothesis) that, the genetic population structures (alleles frequencies, their regulators and systems of gene expression) of the particular genes for the development of this portion of branchial arches and neural crest are exactly the same for reptiles and mammals is simply wrong.

EPIGENESIS

Vargas (2005) proposed that epigenetic processes could be good candidates as mechanism of phenotype drift. Let us choose editing (adding bases to mRNAs), genome imprinting (methylation of gene regulator zones) and hormones. These three well-known epigenetic processes need enzymes, proteins, receptors, and DNA segments to be recognized besides other molecules that are produced by genomic information. However, it seems that Vargas (2005) used another semantics for epigenetic effects. One of the most important traits of living beings is to be in a constant turnover process of their components or elements (Valenzuela 1997, 2002a). Any environmental (phenocopy) or epigenetic effect is lost or diluted in one, two or a few individual or cell cycle generations. The only known manner to conserve a function during several generations is within the genome. The condition for having epigenetic processes "epigeneticity" must be genomically conserved. The same occurs with the proposed natural drift triggered by the environment. "Triggerability" (included in the norm of reaction of formal genetics) must be conserved in the genome. Genome action organizes the internal milieu to make epigeneticity and triggerability possible.

HERITABILITY

The article (Vargas 2005) fiercely attacks heritability to explain evolution, without considering that heritability is a population-biased conceptualization that can only be applied to characters that vary within a population. Formally, it is the quotient between additive genotypic variance and phenotypic variance. Genome studies show us that monomorphisms and not polymorphisms (variations) are the rule. Most nucleotide sites and genome segments remain fixed for thousand million cell cycles or generations. For monomorphic traits heritability is undetermined (denominator 0). Let us denote by genomicity the condition: to be mostly determined by the genome or genomic derived functions (epigenesis). Most traits of living beings are monomorphic (genomicity equal or close to 100 %). Humans are living beings, eucaryotes, animals, chordates, vertebrates, mammals, primates, homo sapiens, have genome and cells, specific nuclear and mitochondrial genetic codes, two legs, the nose between the eyes, develop from an unicellular to a multicellular being, and so on. Heritability cannot apply to these traits whose genomicity is near 100 %. All these traits and taxonomical traits were not only acquired, but also maintained by positive selection. Evolution is not only change, but maintenance. The concepts of population dynamic changes (population genetics) among polymorphisms and monomorphisms (fixation and loss) are essential for understanding evolution.

THE FALLACY AND ILLUSION OF DRIFT IN EVOLUTION

Drift is random motion. So much so that neutralists took the diffusion equation used to study Brownian motion for founding the theory of neutral evolution (Kimura 1957, 1968, 1993). Neutral evolution is therefore the Brownian or random motion of alleles or bases in genomes. Randomness implies definite and categorical expectancies. If the four bases A, T, G and C are selectively neutral, the expectancies for them to be found in a nucleotide site are $^1/_4$ A, $^1/_4$ T, $^1/_4$ G, $^1/_4$ C. This expected distribution has never been found, not even in bacteria populations in oceans, but the neutral theory has not been considered refuted and left. Phenotypic drift implies finding a distribution in which any possible character has the same probability to appear. No one has found this. For example, humans have the nose below and between the eyes, but human teratology describes cyclopia with one eye usually below the nose (proboscis). Phenotypic drift would imply finding cyclopia and normality with the same probability (no more comments). Genes for cyclopia are known and cyclopia is seldom seen because of natural selection. Neutralists and defenders of drift quickly caught another negative heuristic protective belt to maintain neutralism: there are constraints. They do not dare say: there are selective constraints. Drift also implies reversibility or transitivity among all the possibilities. The chance does not have memory. The transformation of the jaw into the middle ear should occur with equal probability as the reverse transformation. This does not occur. Drift cannot drive evolution and destroys fixation. The random motion of sand may build but not maintain a sand castle. Drift, randomness, Brownian motion is part of the thermodynamic tendency of nature known as entropy (second principle). The only expectancy of drift, for living beings, is their death or extinction. This is not reductionism. Living beings are material beings; they cannot escape to entropy or physics.

MUTATION, ADAPTATION AND FITNESS

The article (Vargas 2005) includes 14 pages on evolution without mentioning the most important process in evolution: mutation (and epigenetic mutations). Mutation (a transmissible change) is the source of variation and the foundation of evolution (necessary condition). Once a mutant appears in a population, its evolution is fixation, extinction or its polymorphic maintenance. Evolution can also be seen as the change in the population structure of the state of genome nucleotide sites. The hypotheses on the causes of these changes or stabilities (their dynamic fixation, extinction or polymorphisms) divide evolutionists as we described in the Introduction.

Adaptation has at least two meanings. Physiological and population adaptation. Physiological adaptation implies the maintenance of individual morpho-functional (organization) parameters, within a range compatible with life, in spite of environmental variations (morpho-functional homeostasis). Endogenous (mutation) or exogenous (environment) changes deviate the inner conditions of a living being from their parameters. Homeostasis is the capacity of the system to return these conditions to the normal parameters. Resilience is the resistance to deviations or the capability to maintain homeostasis in spite of changes; thus it allows the conservation of adaptation. Even though living beings are equally adapted (autopoietic), they are differently resilient. If all the other conditions are equal (ceteris paribus condition), individuals with a stronger resilience shall live longer, leave more descendants and have a higher fitness. Resilience gives the probability that a living being maintains its adaptation (autopoiesis) during a definite period and is mostly determined by the individual genome. The theory of autopoiesis does not include this probability of maintenance. Mutations can increase, decrease or maintain resilience. However, an individual with a high genetic resilience (large physiological adaptation) may not have reproductive advantage (population adaptation) and its genome contribution (lineage) to the next generations could be small or zero (small population adaptation or fitness). Uni- and multi-cellular organisms are in continuous transformation and turn over of their elements, genomes and organizations. DNA, RNA and chromosomes mutate inexorably especially during replication. As we noted, living beings are neither autopoietic nor adapted; they are permanently adapting to endo- or exo-genous variations; they inexorably age and die; their endogenous general resilience always decreases, even though experience and knowledge may increase it until a definite limit or time period. Also, the theory of autopoiesis does not include thermodynamics; the living non-random organization need energy to be maintained far from randomness, and the structured processes to obtain and use energy to maintain this organization is mostly determined by the genome. Life is a permanent struggle against entropy (randomness). Equally autopoietic organisms have different genetic strategies for this struggle and are differentially favored or disfavored with mutations or environmental changes, and this is and important part of their fitness. Multicellular organisms are mosaics of cell populations. Sometimes these mutations lead to cancer, aging or genetic disease of the mutated cell lineage, and often to the individual's death. Cells are continuously selected within an organism. A cell with a load of uncorrected mutations usually initiates apoptosis, a process that is part of its organization (genome). DNA is a dynamic molecule (really a process). The only process by which an individual can contribute to evolution (excepting extinction) is leaving fertile descendants, with or without mutations. The absolute fitness of the individual is the number of its offspring. Fitness is a quantitative phenotype determined by genotype-environment interactions; it includes the environment and its changes. We can assign fitness to genes, genotypes, phenotypes, genomes, couples and populations. There is no controversy about fitness. A widespread misunderstanding of fitness is the survival of survivors. This is a cartoon of fitness that destroys the scientific and operational definition of fitness and avoid testing non-selective hypotheses. Fitness is measurable and goes from 0 to any number. The non-survivors (fitness 0) are as important as survivors for population genetics and evolution. The study of evolution with living beings whose rests remained (fossils) and remains (present living beings) is greatly biased. The organization of fossils persists regardless of the cataclysms that extinguished the living beings that generated them. Thus, fossils are better adapted than living beings. They represent no more than the 1 % of all the living beings that have existed and exist, and they have had and have the highest fitness, but not as living beings. If we analyze these equally highly selected individuals, and dismiss others that cannot and could not arrive to our knowledge, our conclusion is obvious: selection is unnecessary either for their existence or for their condition of being adapted or autopoietic. Population adaptation implies the maintenance of populations in spite of environmental variations. The existence of polymorphisms is crucial for the maintenance of the population when the environment changes; this cannot occur with an

individual. Not only diseases, but accidents, predator-pray relations, chemical or physical factors kill some individuals and leave others alive due to their genome differences. Which of them is autopoietic or adapted? Adaptation is relative to their genomes and environments. Sexual processes are mostly responsible for creation of variability; they accelerate the death of individuals, thus decreasing their fitness, but increase the population fitness. The first step of transformation of the jaw into the ear had to occur first in one individual (male or female?). The diffusion of this new character in the population necessarily followed a genetically structured population dynamics.

FACTORS IN EVOLUTION, IMPOSSIBILITY OF NEUTRAL FIXATION

The evolution of a population mostly depends of the rate of mutation and the selection coefficients or fitness of its different genetic forms. These two factors determine the direction of evolution, the equilibrium conditions and the number of generations to reach the equilibrium (fixation, extinction or polymorphism). There is a widespread error when thinking that drift can drive evolution. Drift is a non-directional factor. Drift makes the population genetic structure determined by mutation and selection fluctuate to and fro, up and down, but its evolutionary effect is (due to the nature of drift), as an average, zero. Recurrent forward and backward mutations and drift make fixation by drift alone impossible, even in a population with one bacterium (Valenzuela & Santos 1996, Valenzuela 2000, 2002b). This widespread error arose when substitution (continuous turn over of bases) was taken as synonymous of fixation; nevertheless, they are contradictory processes. Kimura (1968) showed that the substitution rate is equal to the mutation rate. King & Jukes (1969) misunderstood this as the equivalence between the fixation and mutation rates. Both articles demonstrated that the rate of neutral substitution is independent of population size (N); but these authors did not conclude that neutral evolution is independent of drift, because drift is dependent on N (logic laws of transitivity). The error was extended to the bottleneck effect. If we observe few generations, in a population of small N, we may observe pseudo-fixation (really substitution). But this is not true for several generations, where fixation is impossible. Only selective evolution can produce and maintain fixation.

THE CATHOLIC SOUL AND MIND

Vargas (2005), quoting an assumed catholic author, pointed out that the catholic thought on soul and mind is that both cannot be generated by evolution. Christians, Muslims or Jews believe that animals do not have a soul, but they do have a mind. The Catholic Church believes that the human zygote and early embryo are full human beings; they have a soul, but not a mind. If evolution is a process of matter and energy (a matter-energy process), then spiritual beings (souls) cannot be generated by evolution. But, what is the nature of the mind? Is it only a matter-energy process? Is there a spiritual mind? Is moral consciousness lost with anesthesia? We can say that the matter-energy mind of neurosciences was originated by the matter-energy process of evolution, but nothing else. Now, if we introduce the Hindu or Buddhist notion of soul, where animal do have a soul, the problem may be more complex. We can not reduce philosophy or theology to neuroscience, if we do not want to be reductionist, as Vargas (2005) demanded.

ACKNOWLEDGEMENTS

I am grateful to Prof. R Berríos-Loyola, who introduced the concept of phenotype drift, for his valuable precisions and discussion. I developed the ideas of living beings as a net system of organizational self-repair and reproductive relays, with the late Prof. D. Brncic, who named living beings as anagenetic beings. Prof. S. Koref read critically the article and improved it.

LITERATURE CITED

CAMUS PA (1997) Evolución darwiniana y no darwiniana: ¿hacia una antisíntesis moderna? Revista Chilena de Historia Natural 70: 459-464.

CAMUS PA (2000) Evolution in Chile: natural drift versus natural selection, or the preservation of favored theories in the struggle for knowledge. Revista Chilena de Historia Natural 73: 215-219.

ELSHEIKH EM (1988) Evolution of unicellular organisms in terms of vitality function. Trilogía (Chile). Número especial, Junio: 86-94.

GOULD SJ (2002) The structure of evolutionary theory. The Belknap Press of Harvard University, Cambridge, Massachusetts, USA. 741 pp.

GOULD SJ & N ELDREDGE (1977) Punctuated equilibria: the tempo and mode of evolution reconsidered. Paleobiology 3: 115-151.

FUTUYMA DJ (1998) Evolutionary biology. Third edition. Sinauer, Sunderland, Massachusetts, USA. 231 pp.

KIMURA M (1957) Some problems of stochastic processes in genetics. Annals of Mathematic Statistics 28: 882-901.

KIMURA M (1968) Evolutionary rate at the molecular level. Nature 217: 624-626.

KIMURA M (1993) Retrospective of the last quarter century of the neutral theory. Japanese Journal of Genetics 68: 521-528.

KING JL & TH JUKES (1969) Non-Darwinian evolution. Science 64: 788-164.

KUHN TS (1970) The structure of scientific revolutions. University of Chicago Press, Chicago, Illinois, USA.

MATURANA-ROMECÍN H & J MPODOSIS (2000) The origin of species by mean of natural drift. Revista Chilena de Historia Natural 73: 261-310.

MATURANA H & F VARELA (1972) De máquinas y seres vivos. Editorial Universitaria, Santiago, Chile. 69 pp.

MATURANA H & F VARELA (1984) El árbol del conocimiento. Editorial Universitaria, Santiago, Chile. 172 pp.

SIMPSON GG, PITTENDRIGH CS & TIFFANY LH (1957) Life: an introduction to biology. Hartcourt, Brace and Co., New York, New Cork. USA. 395 pp.

VALENZUELA CY (1997) Ética científica del origen humano. Revista Médica de Chile 125: 701-705.

VALENZUELA CY (2001a) Comienzo ontogenético del individuo humano desde su genoma. Revista Médica de Chile 129: 441-446.

VALENZUELA CY (2001b) Respuesta a comentarios sobre ética biomédica. Revista Médica de Chile 129: 963-967.

VALENZUELA CY (2000) Misconceptions and false expectations in neutral evolution. Biological Research 33: 187-195.

VALENZUELA CY (2002a) Does biotic life exist? In: Palyi G, Zvechi C, (eds) Fundamentals of life: 331-334. Elsevier, Paris, France.

VALENZUELA CY (2002b) A biotic Big-Bang. In: Palyi G, Caglioti L (eds) Fundamentals of life: 197-202. Elsevier, Paris, France.

VALENZUELA CY & JL SANTOS (1996) A model of complete random molecular evolution by recurrent mutation. Biological Research 29: 203-212.

VARGAS A (2005) Beyond selection. Revista Chilena de Historia Natural 78: 739-752.

VON BERTALANFFY L (1963) Concepción biológica del cosmos. Comisión Central de Publicaciones de la Universidad de Chile, Santiago, Chile.

WRIGHT S (1931) Evolution in Mendelian populations. Genetics 16: 97-159.

Associate Editor: Patricio Camus
Received March 31, 2006; accepted September 25, 2006