

# Genetic control mechanisms and Genetic regulatory systems

## Abstract

The concepts of Genetic Control Mechanisms (GCMs) and Genetic Regulation Systems (GRSs) are discussed, and the nature and significance of their efficient functioning is made explicit. These GRSs, in interaction with the environment, and as a result of their high degree of functional efficiency, give rise to a biological system (organism) while at the same time they establish and maintain, at all its levels of organization, the genetic steady-state (GSS) or genetic homeostasis, presented as a technical interpretation of life. The relevance of some aspects of the genome, development, birth, genetic individuality, the life cycle and the life span, evolution and biocollapse (death), with the consequent detachment of the bioenergetic (BEG) is historically elaborated upon. The Spanish version of this article was written in 1970 and published in 1972, and it is detailed 50 years later for its English version, updated in some bioenergetic (BEL) aspects.

**Keywords:** genetic steady-state, genetic regulation systems, genetic control mechanisms, desoxyribonucleic acid, ribonucleic acid, biological system, ecosystem, biomaterial-biointerfacial-bioenergetic universes, bioenergetic communication, unit universe, bioenergetic, intuitions, intuitive

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**Alejandro Cuevas-Sosa**

Managing director, Center for the Prevention and Treatment of Sexual and Interfamily Violence, Mexico

**Correspondence:** Dr. Alejandro Cuevas-Sosa, Ce Managing director, Center for the Prevention and Treatment of Sexual and Interfamily Violence, Mexico, Tel +52 55 55751111, Email [commentstoneuno@gmail.com](mailto:commentstoneuno@gmail.com)

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**Abbreviations:** GSS, genetic steady-state; GRSs, genetic regulation systems; GCMs, genetic control mechanisms; BML, biomaterial; BEL, bioenergetic; BIFL, biointerfacial; BEG, bioenergetic; BELC, bioenergetic communication

## Genetic control mechanisms and Genetic regulatory systems

It is now necessary to establish a working concept of what is called Genetic Control Mechanisms and Genetic Regulation Systems — concepts about which there is no general consensus in the scientific literature. I will talk about Genetic Control Mechanisms (GCMs) when it comes to the control of a single step in a complex genetic process. Examples of steps governed by genetic control mechanisms are: a) the identification by RNA (ribonucleic acid) polymerase of the DNA (deoxyribonucleic acid) chain that serves as a template during the transcription or reading of that DNA region;<sup>1-7</sup> b) the direction of messenger RNA (mRNA)<sup>8</sup> synthesis from 5' to 3' carbon atom; c) the identification that the Sigma factor makes of the transcription start point;<sup>9</sup> d) the identification that the Rho factor makes of the transcription interruption point;<sup>10,11</sup> and e) the binding of the repressor to the operator in an Operon type system.<sup>12,13</sup> Regarding the issue of genetic control mechanisms, James D. Watson<sup>14</sup> has written "...a control mechanism must decide whether the separated DNA strands will function as a template for a complementary DNA strand or a complementary RNA strand."

However, from the operational point of view, the GCMs are closely interrelated, in such a way that they are combined to form working groups related to the direction of a process that pursues a single result. I refer to these working groups as Genetic Regulation Systems (GRSs). In turn, these GRSs do not remain in an organism as isolated functional units, that is, series of GRSs are activated during the different life stages of an organism and their activation has specific functional consequences. The GRSs determine, for example: a) DNA replication. DNA duplication occurs when its two strands separate, thus allowing the strands to serve as templates for the formation of complementary strands;<sup>15,16</sup> b) protein synthesis. This occurs in two basic steps: transcription and translation of mRNA. Its GRSs are made up of known GCMs and others remain to be discovered;<sup>17</sup> c)

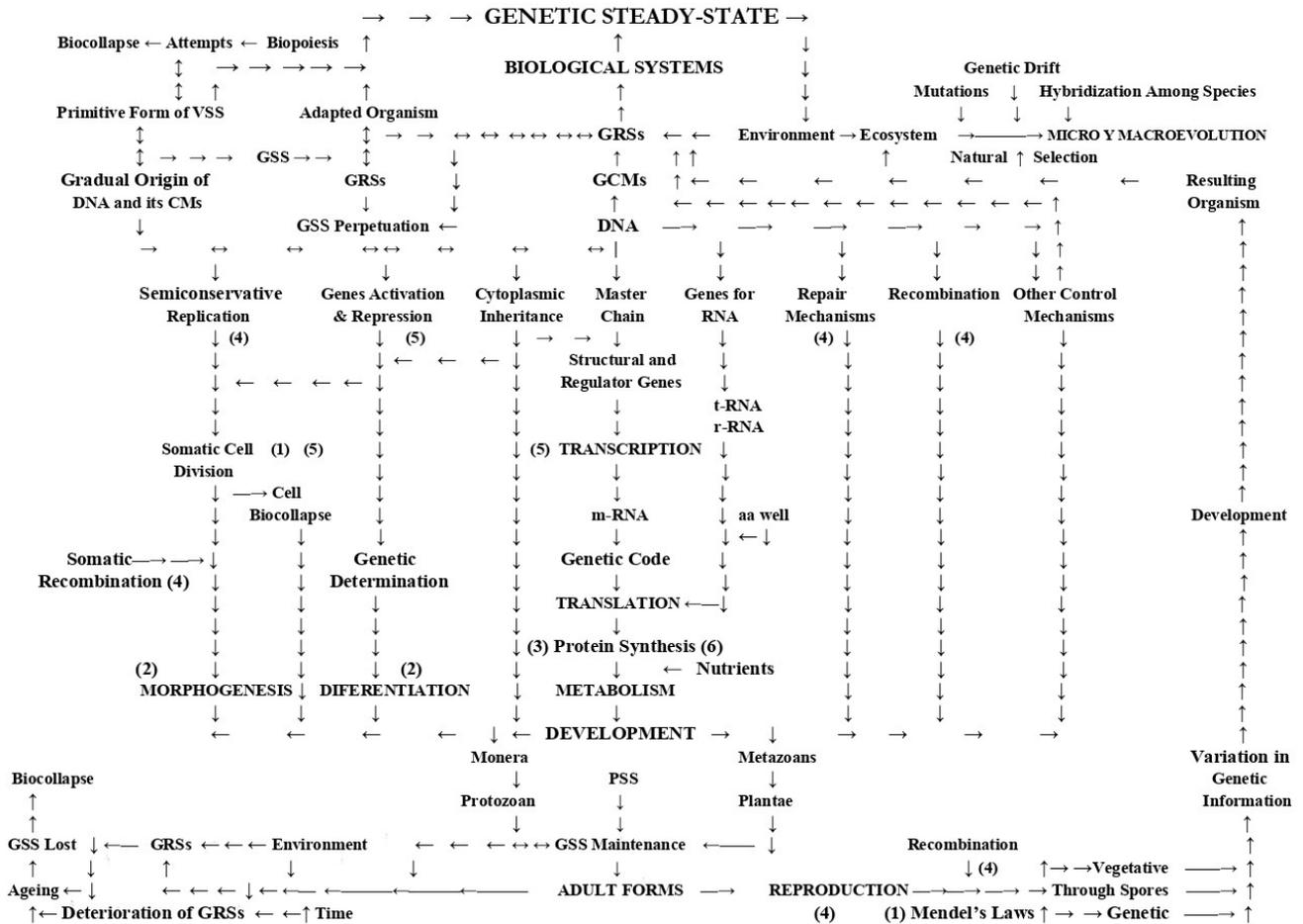
differentiation of the ribosome structure, according to Kurland: "The salient impression is that the ribosome is far from being a primitive organelle. Rather, it appears to be a highly developed and complicated entity, containing a much larger number of components than could be inferred from current understanding of protein synthesis;"<sup>18</sup> d) the formation of a mitochondria. Which, according to Schatz: "...requires the intracellular cooperation of two separate genetic systems and presumably involves as yet unknown mechanisms of cooperation;"<sup>19</sup> e) the structural differentiation of chromosomes in cells with a true nucleus (eukaryotes). The physical state that chromatin assumes during cell division is the result of interactions between DNA strands, histones, and other components of the nucleus;<sup>20</sup> f) cell division, for Mueller: "The spectacular achievement of this process is that both active and inactive chromatin are precisely replicated and distributed to daughter cells, thus ensuring genetic and phenotypic continuity;"<sup>21</sup> g) in general, morphogenesis and differentiation, which presuppose the formation of all tissues and organs to give rise to an organism as a whole (Figure 1). Shapiro says that: "Important advances in the understanding of cell differentiation could be achieved by studying interacting systems of regulatory genes involved in the programmed expression of well-defined characteristics;"<sup>22</sup> h) the immune response in mammals. Two general theories have been proposed: 1. The somatic theory positing that antibody genes are formed by hypermutation from a few genes in early germ cell lines during somatic differentiation; and, 2. The theory of germ cell lines, which postulates that vertebrates have, from their germinal origin, genes for each of the polypeptide chains of the antibodies that the subject is capable of producing;<sup>23</sup> and, i) photosynthesis, according to Levine: "...photosynthesis in higher plants and algae comprises the action of two photochemical systems and these systems are linked by series of electron carriers."<sup>24</sup>

Examples of GRSs proper are: a) The genetic code. Universal code, without overlapping, degenerate (because several triplets or codons specify the same amino acid), without commas and formed by triplets;<sup>25,26</sup> b) The complementarity between guanine and cytosine, and thymine and adenine in the DNA molecule;<sup>15</sup> and c) The lactose operon, about which Watson<sup>14</sup> has written that it is: "...the most important system developed to date to understand the control of protein synthesis in bacteria."

### The genetic steady-state

When considering the nature of GCMs and GRSs, it is evident that for their function to have any vital meaning, they must be guided by the principle of efficiency. In such a way that the concept of functional efficiency, as used in this article, refers to the events that constitute the GCMs and the GRSs, events that, through their

integration, coordination and dynamic nature, favor the adequate achievement of their functional objective. The GRSs, in interrelation with the environment and as a result of their high degree of functional efficiency, give rise to a biological system (organism) at the same time that they establish and maintain, at all levels of its organization, its genetic steady-state (Figure 1).



**Figure 1** Role of the genetic steady-state (GSS) based on current biological concepts. VSS: vital steady state; CMs: Control mechanisms; GCMs: genetic control mechanisms; GRSs: genetic regulation systems; PSS: physiological steady-state; aa:amino acids; m-RNA: ribosomal ribonucleic acid; DNA:deoxyribonucleic acid. Deviation from normal: (1) chromosomal non disjunction; (2) chromosomal malformations; (3) inborn errors of metabolism; (4) mutations and structural chromosomal abnormalities; (5) cancer; (6) uncontrolled protien synthesis (myeloma).

This biological system, according to Miller, is “made of matter and energy organized by information.”<sup>27</sup> On the other hand, the genetic steady-state or genetic homeostasis is the condition of lasting equilibrium of the processes that result from the GRSs of the biological system itself and as a result of the functional efficiency of the same GRSs; as well as the genetic steady-state represents an essential condition for the GRSs to express their phenotypic potentialities. “The organisms —in Strauss’s opinion— that exist on earth at a given moment are the result of the action of natural forces that act in the first instance on inanimate matter. So instead of seeing elements of life everywhere in the natural world, let us think of life as just one aspect of the possible arrangements of inanimate matter. It is in this sense that the biologist speaks of the secrets of life. At this level, the question, what is life? is a technical question because it refers to the arrangements of inanimate matter that result in growth and regulation, mobility and metabolism, the properties that we recognize as characteristic of life.”<sup>25</sup>

### The genome

It was not until conclusive experimental evidence in support of the role of DNA as the carrier of genetic information was obtained that it became possible to postulate GRSs other than those that could be inferred from Mendel’s laws and the chromosome theory of heredity.<sup>28</sup> Segregation of chromatids during mitosis or cell division of human diploid (eukaryotic) cells in vitro is also random.<sup>67</sup> In this sense, the work on Pneumococcus on transformation,<sup>29,30</sup> thanks to which DNA was definitively demonstrated as genetic material (Figure 1), allowed directing research towards a deeper understanding of the genome. The studies carried out by James Watson and Francis Crick<sup>15</sup> that resulted in the determination of the structure of DNA and the postulation of a model for its semi-conservative replication, pointed the way to an era in which the GCMs and the GRSs began to be known with increasing certainty. The first step in this direction occurred when, as a result of the brilliant work of François Jacob and Jacques Monod, the concept

of the Operon was born.<sup>31</sup> And although it was originally conceived as a model of genetic regulation system for understanding protein synthesis in bacteria, it soon proved to be of basic importance for a better understanding of GRSs in general.

The genotype resides in the DNA. More specifically, it is found in the characteristic linear sequence of the four bases (adenine, guanine, cytosine and thymine) of the DNA chains, information that can be transcribed into complementary sequences according to the following rule: the four bases only form two pairs complementary between the two chains: guanine-cytosine and adenine-thymine. These base pairs are used as the basis for DNA replication, gene transcription, ribosomal and transfer RNA synthesis—in which thymine is substituted for uracil, the same in mRNA—and in the regulation of the typical helical structure of the double chain of the DNA molecule. The sequence of bases on one of the complementary strands (master strand) of DNA can be transcribed into mRNA. The one that later, when translated, determines the sequence of amino acids in the polypeptide chains, a translation that follows the rules of the genetic code.<sup>2</sup>

On the other hand, as a result of the coordination of its genes “by means—Kauffman emphasizes—of precisely constructed control circuits,”<sup>32</sup> the genome establishes a complex series of genetic regulation systems (GRSs) whose interrelation gives rise to morphogenesis, differentiation, and metabolism (Figure 1). At the molecular level, the explanation is clear: the structure of a gene determines the primary structure of the corresponding polypeptide, while the interaction of the gene with GRSs, which respond to environmental stimuli, determines the number of polypeptide chains to be synthesized.<sup>33</sup> This statement agrees with what is known about cellular metabolism; that exceptionally more material is synthesized or destroyed than is required for anabolism and growth. Therefore, all major metabolic systems possess the inherent capacity for autoregulation, which ultimately depends on the regulation of enzyme activity. And, broadly speaking, enzymes are regulated in two ways: through GRSs and through direct control of cells.<sup>34</sup>

Consequently, after considering the nature of the genome, it is clear that the functions it gives rise to—through the establishment of GCMs and GRSs—must be highly efficient, so that, as a result, the genome is capable of give rise to a biological system at the same time that it achieves and maintains at the genetic level a condition characterized by the presence of stable and coordinated events, that is, the genetic steady-state or genetic homeostasis.

## Development

Perhaps the most complex biological event—and apparently the most promising in the field of genetic research—is that of embryonic development, that is, the period in the life of organisms characterized by the greatest activity of GRSs.<sup>35,36</sup> However, according to Weisz, “... the scope of development is universal; all types of change, occurring at any level of vital organization and encompassing moments of natural history, have meaning in development. Developmental changes can be structural or functional, quantitative or qualitative, progressive or regressive, normal or abnormal. Actually, ...development always encompasses all these moments simultaneously... Development is universal also in relation to the living unit in which the change occurs and with respect to time. A molecule develops no less than a cell or a tissue, a whole organism no less than an entire species... Development occurs throughout the history of life.”<sup>37</sup>

A preliminary requirement for embryonic development to take place consists of the simultaneous establishment, and functional integration, of the GRS series for morphogenesis, differentiation, and metabolism (Figure 1).<sup>37</sup> However, it should be emphasized that

embryonic development occurs primarily through differentiation processes. For Barry Pierce, these include “relatively stable changes in cellular properties that progressively concentrate the activities and structure of the cell, or portions of it, in particular directions at the expense of others.”<sup>38</sup> The end result takes shape in a specialized cell capable of to manifest the structural and functional peculiarities that give it the specific activity of genes.

It is known that the series of GRSs that control gene activity and repression are of primary importance among the different GRSs that determine cell type and function in specialized tissues of higher organisms. During development, regions of total chromosomal DNA are transcribed into RNA in different cell lines, at different times, and in the same cell at different stages.<sup>39,40</sup> This fractional use of the gene seems to have arisen as a necessary adaptation to the presence in each diploid somatic cell of the complete chromosomal complement and therefore of sufficient DNA to guide the development of a complete organism, “which—Gelehrter summarizes—has been demonstrated in [the fruit fly] *Drosophila [melanogaster]*, in the transplantation of frog intestinal cell nuclei, and in the ectopic production of protein hormones in certain human tumors.”<sup>34</sup> For this reason, individual cells must possess GRSs to repress most of the DNA they contain, and also to selectively activate a relatively small number of genes for RNA synthesis.<sup>20</sup>

Among the functional and structural properties offered to a eukaryotic cell by the differential or specific activity of certain genes, we have:

1. Changes in the physical structure, and thus in the composition and function of the template of chromatin during gene activation. These changes involve both acidic and basic proteins associated with the chromatin DNA molecule. “As examples—Allfrey assures—, we have the acetylation of lysine residues in arginine-rich histones and the phosphorylation of serine residues in core phosphoproteins. These structural modifications of pre-existing proteins occur at a very early stage during the gene activation process in lymphocytes ‘transformed’ by phytohemagglutinin, and in liver parenchymal cells during the regenerative response after partial hepatectomy.”<sup>20</sup>
2. The ability to acquire new biochemical properties while losing existing ones. One of the biggest problems that researchers of the series of GRSs for cell differentiation have faced, is understanding how it is that the cells of a tissue combine morphological development with the biochemical specificities that they gradually acquire, since, in effect, one of the most important functional aspects of GRSs related to morphogenesis is the degree of coupling or uncoupling of the synthesis of specific proteins.<sup>40</sup>
3. Progressive cell diversification and specialization, characterized morphologically by specific cell structures, and biochemically by the synthesis of equally specific proteins. The form of morphological and biochemical cell specialization can be seen in the muscle cell, in the erythrocyte and in the lens cells. They synthesize tissue-specific proteins in the form of myosin, hemoglobin, and crystalline, respectively.<sup>40</sup> Morphologically, they have well-defined characteristics present in the cytoplasm in the form of typical accumulations of organelles and macromolecules.<sup>38</sup>

Therefore, it can be seen that, in general, during cell differentiation, an event of basic importance is the gradual and predetermined transformation of the existing GRSs, as well as the activation of others according to the functional needs of the specialized cell. Each

adult organism has GRSs that are peculiar to it and that were present, albeit potentially, from the early stages of its embryonic development. Based on what is known about the enzymatic control of metabolism and the nature of the genome, it can be inferred that the phenotype ultimately depends for its specification on the structure dictated by mRNA for protein synthesis specific to the species.

In conclusion, during the embryonic development of mammals, we find a stage characterized by incessant and complex activity by the GRSs, which at that time are concentrated in the metabolic, morphological and differentiation changes that lead to the gradual structuring of a phenotype (biological system) predetermined by the genotype. In addition, embryonic development represents one of the most outstanding biological phenomena in the fact that despite being a complex process, the efficiency of its GRSs is maintained to such a degree of effectiveness that, commonly, the genetic steady-state is preserved both to unicellular and multicellular level.

## Birth

In humans, Nelson reports, "...fetal life, unlike embryonic life, begins with the completion of organogenesis, which occurs around the twelfth week, the end of the third month, of gestation. Without forgetting that genetic and environmental influences are already operating before fertilization that will influence the fetus... The genetic material carried by the chromosomes of each of the parents plays an important role not only in fetal development but also in survival of the fetus... Many of the physical, physiological or biochemical problems found in the newborn are related to the interference or failure of biochemical and physiological adjustments, as in the premature newborn, by adverse environmental influences or anatomical abnormalities, whether become apparent during intrauterine life, during or after birth."<sup>41</sup> This is what happens when the mother has folic acid (vitamin B12) deficiency before and during pregnancy, the newborn could suffer from neural tube abnormalities, such as spina bifida, spinal cord or brain abnormalities, and even biocollapse (death).<sup>68,70</sup>

In mammals, an organism passes through and survives birth when it has reached a suitable stage of phenotypic development, and this in turn suggests that the organism possesses equally suitable GRSs. Therefore, at birth, in those cases in which adverse environmental factors are not involved, the body's GRSs will be tested for their ability to maintain a genetic steady-state autonomously and in relation to the extrauterine environmental conditions. Under these circumstances, the newborn: a) may have GRSs within the normal limits for the species and, accordingly, will also be phenotypically normal; or b) in the event that it has some alteration in its GRSs and does not prevent survival, then phenotypically it will also manifest some alteration, such as the case of phenylketonuria or trisomy 21 in humans (Figure 1).<sup>35</sup>

It is also possible to consider the situation in which, due to intrinsic alterations of the GRSs, they cannot carry out their function within the normal qualitative and/or quantitative limits for the species. This, over time, will result in the loss of the precariously maintained genetic steady-state of the organism or biocollapse (death).<sup>68</sup> Examples of this situation in humans are found in trisomy D or E, anencephaly or hydrocephalus.<sup>42,43</sup>

The birth, then, makes it clear whether the new organism, when confronted with the extrauterine environment, its GRSs will have the capacity to autonomously maintain the genetic steady-state. Which is in agreement with an opinion expressed by Claude Bernard in 1870: "Life is the result of a conflict, that is, of a close and harmonious relationship between external conditions and the pre-established constitution of the organism" (quoted by Breathnach).<sup>44</sup>

## Genetic individuality

Each one of the members of a species possesses biological individuality resulting from the combination of genes that the organism inherited from its parents, genes that, according to Davis, "contribute to determining a certain potential of characteristics."<sup>33</sup> This series of genes received from the parents make each organism sufficiently similar to the rest of the members of the species, identifying with them from the physiological, biochemical, morphological and behavioral point of view, but at the same time they also give the organism enough phenotypic individuality.<sup>45-47</sup> In human anatomy we find many specific examples, Williams describes them as follows: "Normal stomachs vary considerably in their shape and size. The transverse colon varies widely in the position in which it crosses the abdomen; the patterns of the pelvic colon also vary frequently. Two, three, four, and sometimes up to five or six arterial branches arise from the aortic arch; the aorta itself often varies in size, and the heart differs morphologically and physiologically in such a way that cardiac output shows wide variation among normal young subjects. The size of the arteries and their branches are such that in each subject the various organs and tissues receive blood unequally, which results in an individual pattern regarding the distribution of blood in the body."<sup>48</sup> Similarly, to say of Breathnach, in the field of human physiology: "The precise way in which the various homeostatic mechanisms work is to some extent an individual characteristic, probably determined by the genome. Individuals use similar regulatory mechanisms to achieve equivalent adaptive responses, but mobilize their systems in quantitatively different ways to achieve a final organization."<sup>44</sup> Indeed, it must be emphasized that physiological homeostasis represents a phenotypic manifestation of the individual's genome (Figure 1). Of course, with the permanent influence of the bioenergetics, which provides stability and harmony in every organism.<sup>68</sup>

Likewise, the specific degree of complexity in development represents an example of genetic individuality at the species level. In sum, the exact degree of physiological, biochemical, morphological, and behavioral complexity achieved by a species reflects, in general, the variety and specific degree of complexity of its GRSs. Besides, the perpetuation of the most diverse types of organisms—more than 8.7 million species have been identified, plus or minus 2.7 million—<sup>71</sup> is possible due to the high degree of functional efficiency of the GRSs that are their own, independently, say, the degree of complexity of the organism in question. A virus, for example, has a genome that stores a minimum of genetic material, enough to specify its morphological characteristics and express its functional properties—as long as the genetically favorable environment of a more complex uni- or multicellular organism is within its reach.<sup>49</sup> Furthermore, as we ascend the scale of genetic complexity, the more complex unicellular or multicellular organisms are of course the result of more varied and complex genomes, and the consequent greater number of GRSs and their efficient functional integration within the corresponding biological system. This gives it the capacity for development and self-perpetuation, and also allows the organism better adaptive responses in the ecosystem (Figure 1). In conclusion, the variety of genes and the particular combination of them are unlimited. However, only those genotypes capable, within a given ecosystem, of adequately establishing and maintaining the genetic steady-state are biologically admissible.

## The life cycle and life span

All organisms have a typical life span for the species to which they belong. For Essam Fikry: "In some cases the life span is drastically short, for example, 17 years for some cases of carob trees. But we think of life span as an average value—a few minutes for a bacterium,

a few days for certain insects, a few months for an annual plant, a few decades for humans, a few hundred years for some giant trees.”<sup>50</sup> Sometimes, the duration of the life span is influenced by biological adaptation mechanisms that make possible a type of latent life in response to environmental circumstances particularly unfavorable for survival, such is the case of spores in microorganisms.<sup>51</sup> Other adaptive mechanisms allow the organism to go into a dormant state, as occurs with hibernation in some mammals.<sup>37</sup> Although in some cases the metabolic processes are considerably diminished, the genetic steady-state is maintained.

The length of the life span is a genetically conditioned event. Therefore, it can be considered that the GRSs have an average life span during which they retain their activity and functional efficacy. The progressive decrease in the degree of activity and functional efficacy of the GRSs that occurs during aging could be an event under genetic control, as is the case of the regulation systems for the synthesis of hemoglobin in humans.<sup>52,53</sup> While the cumulative deterioration of GRSs may be the primary result of the deleterious effects of the environment over time.<sup>54,55</sup> One factor can potentiate the other, and sooner or later, either together or separately, will lead to the cessation of the activity of the GRSs of a given biological system (Figure 1). So, according to Bullough, “the pathological changes of adult life and old age may rather represent impaired efficiency of repair mechanisms, rather than the time-dependent accumulation of cellular damage.”<sup>56</sup> It is in this way that mammalian organs and tissues follow a standard pattern over time: growth to adult size associated with full functional development, gradual deterioration of the functional efficiency of their GRSs with aging, and loss of that functional efficiency. until biocollapse (death).<sup>54</sup> At that point, however, a distinction must be made between the age of the cell at the molecular level and the age of the cell as a whole.<sup>54,57</sup> Although there is a difference between the group of cells that age slowly, such as neurons, and the group of cells that renew frequently, such as the crypt cells of Lieberkühn in the small intestine,<sup>56,58</sup> this distinction is valid only at the cellular level. At the molecular level, the characteristic event is the variation in the rate of turnover of the different cellular and extracellular components that ranges from minutes (mRNA) to years (DNA, collagen).<sup>8,13,57</sup> Thus, the gradual deterioration that results in the aging process, and which inevitably leads to the biocollapse of the organism, is a phenomenon intrinsic to the structure and function of the genome, which is perhaps favored by specific unfavorable environmental influences.

In all organisms, the GRSs have reached a genetic steady-state preserved within a framework peculiar to each species and which in biology is known as the life cycle. For some species, their life cycle is very restricted and susceptible to the slightest change in certain environmental conditions (temperature, water, sunlight, etc.), changes that can lead to the loss of their genetic steady-state. This means that the GRSs have achieved a stable genetic state with great commitment to the survival of the species; in such a way that its members are very limited in their ability to adapt and as a result will have little chance of perpetuating themselves as a species. In contrast, the fewer the constraints inherent in a particular life cycle, that is the greater the capacity that the GRSs confer on the organism to enjoy the advantages of the ecosystem, the more efficient and favorable will be its genetic steady-state and consequently the greater the chances of survival both at the individual and species level. “What actually distinguishes higher organisms from lower forms is their greater ability to maintain their existence and ensure their future by facing contingencies, often adverse, that fluctuations in the environment present, making use of better adaptive resources, regulatory, coordination and integration” (Sommerhoff, quoted by Miller).<sup>27</sup> Therefore, it is understood that the events that constitute the life cycle of a unicellular organism are the

result of the adaptive response that its GRSs have to the demands presented by the ecosystem, an adaptation that allows preserving and strengthening the genetic steady-state of the organism. The life cycle of a multicellular organism includes the previous situation, but also results from the integration of the life cycles inherent to each of its cell lines and from the solidity of its genetic steady-state.

## Evolution

In recent decades, knowledge of the genetics of microorganisms has been possible thanks to a very efficient experimental methodology. When this methodology was applied to multicellular forms, it allowed the arrival of a basic biological conclusion: that the principles on which GRSs are founded are substantially the same regardless of the biological species under consideration (Figure 1). That is, the nature and activity of DNA, its replication, the genetic code, and the basic mechanisms for protein synthesis are essentially the same in all organisms.<sup>17</sup> On the contrary, there must be characteristic GRSs for each of the known species, and whose variety and resulting functional interrelation have served to determine the degree of complexity in the specific development of the species.<sup>59,60</sup> In this sense, the high degree of intrinsic stability that has a level of genetic complexity already established, is the main obstacle to overcome for evolution to occur, while the possibility of its occurrence depends basically on the specific degree of potential variation (mutability) intrinsic to DNA.<sup>59,61,62</sup> Stebbins wrote: “One of the most important characteristics of all living organisms, from bacteria to man, is the high adaptive value that, the conservation of complex structures and organizational patterns has acquired. In most organisms this conservation decreases progressively during evolution. However, by preventing or greatly reducing the chance of genetic changes of a degenerative nature taking hold, it actually increases the likelihood that it will actually progress to more complex levels of biological organization.”<sup>63</sup>

We can then reach a relevant conclusion: each of the known biological species is the result not only of the great variety of evolutionary attempts made to integrate common GRSs into pre-existing biological species, but also of the establishment and concomitant functional assimilation of new and efficient GRSs. The result in each case has been the acquisition of new phenotypic characteristics. Those evolutionary attempts to functionally integrate a biological system and that for some reason failed and did not lead to the establishment of a new genetic steady-state, therefore, did not give rise to an adapted organism of a new species. And what happened can be considered as a failed biological attempt.<sup>64</sup> The genetic steady-state refers, therefore, to the condition of stability and integration caused by the GRSs of a biological system (organism), and that allows its own integration and the possibility of successfully manifesting, within its ecosystem, all its genetically conditioned properties. In other words, the genetic steady-state is the morphofunctional condition necessary to, together with the bioenergetics, result in an organism with life in a given ecosystem on Earth and, in fact, in any other ecosystem of the biomaterial universe (Figure 1).<sup>68</sup>

This leads us to consider that the life condition could have first originated only after certain control mechanisms, then put to the test (Figure 1),<sup>64</sup> have had the functional capacity to guarantee the existence of an original vital steady state. This in turn opened up the possibility of developing primitive GRSs: “...codons of the genetic code —Thomas posits— probably first appeared in a pre-code system for polypeptide synthesis, as components of a site at which amino acids were linked to ribose residues via adenosine monophosphate derivatives.”<sup>65</sup> Furthermore, Lesk theorizes, “...as protein aminoacids sequences emerged, a mechanism that introduced modest amounts of variation could be helpful, or at least not disadvantageous. On the other

hand, it may clearly have been efficient to have precise adaptation and replication systems after the ‘proteins’ produced reached a reasonable catalytic capacity.”<sup>66</sup> After the gradual functional integration of the then established genetic control mechanisms [GCMs], DNA as its key constituent in efficient GRSSs, it became possible to establish and maintain the incipient genetic steady-state and thus integrate a biological system with more and more possibilities. of success (Figure 1). Finally, for Davidson: “...by controlling metabolism and self-perpetuation, DNA governs the structure, function and development of the cell. And by controlling cells, DNA governs the life of all organisms, and thus the survival of the entire living world. Genes started life, genes still carry it on, and by their absence or failure, genes ultimately end it.”<sup>36</sup>

## Homeostasis and genetic steady-state

Claude Bernard introduced the concept of milieu intérieur in 1865. Walter B. Cannon extended the concept to physiological homeostasis in 1926.<sup>67,68</sup> In parallel, A. V. Bock et al in 1928 introduced the concept of steady-state from their studies in lung physiology.<sup>69</sup> To specify the concepts, it must be pointed out that a system in equilibrium refers to the fact that it is more stable when its level of free energy is lower given the conditions in which it finds itself. Energy does not enter or leave the system. In contrast, homeostasis refers to the relatively constant maintenance of system conditions, and thus the concept is applied to unicellular organisms, plants and animals and their components, or to regional or worldwide ecosystems. For homeostasis to be maintained, it is key that the internal mechanisms within the system remain constant, within its own dynamics. It is often said that an organism is in steady-state, in which case this concept is interchangeable with that of homeostasis. However, while homeostasis refers forcefully to the entire internal environment, the concept of steady-state could be forcefully restricted to talking about specific mechanisms. According to this, a unicellular organism would be in homeostasis as long as each and every one of its internal mechanisms is in steady-state. In addition, steady-state requires that the system receive frequent inputs of free energy, such as food or oxygen. In this article we will use both concepts—steady-state and homeostasis—interchangeably.<sup>70,71</sup>

Of primary importance in biology is the increasingly better understanding not only of how organisms are constituted and how their organization and property of life emerge, but also what this condition of life actually represents. It is my purpose to offer a general analysis of the basic role that genetic processes and some known biological principles play in sustaining the condition that is commonly known as life,<sup>1-6,66</sup> a condition that I interpret and suggest to be designated as the Genetic Steady-state (GSS).<sup>71-74</sup> It remains to add the contributions that bioenergemal research (BEL) has made during its thirty years of duration, such as the three-shared existence, temporarily biomaterial (BML), transiently biointerfacemal (BIFL) and permanently bioenergemal. Stages that are complemented by the Unit Universe Model, made up of the BML (three-dimensional space-time), biointerfacemal (possible fourth dimension) and BEL (possible fifth dimension) universes.<sup>73</sup>

## Conclusions

I have analyzed the genetic steady-state as the essential condition of stability, exclusive of those systems that possess information in the form of genetic material, and that simultaneously results from, and is maintained by, the phenotypic expression of that information. Implicit in the concept of the genetic steady-state, therefore, is the continued existence, in time and space, of a specific genetic functional order. Therefore, I have proposed the genetic steady-state as a technical interpretation of what life is. I must admit, however, that this way

of understanding what the genetic steady-state represents is only an indicator of what is possible to conclude based on the extent to which the methods of study can delve into the nature of the process called life.

After 50 years, these reflections have broadened considerably with the findings of the bioenergemal research that I have been carrying out for more than 30 years and in which I have noted that the human and every terrestrial organism, and in fact of the entire biomaterial universe, carries with it a specific component of organized bioenergemal energy that I have named as bioenergeme. Which, when the body biocollapses, detaches and passes into the bioenergemal universe to lead a presumably indefinite existence. This being so, the BEG is not only indispensable to give life, but it is likely that the BEG provides and sustains it through a permanent and cohesive participation in all the macro and micro components of any organism, and at all scales of complexity and size of organisms.

In addition, through the BEG we anticipate events, we dream and have intuitions, which is why I have suggested the existence of an intuitional language or Intuilish, and the existence of an intuitional energy that surely plays a fundamental role in events such as quantum entanglement and interaction between all the components of the biomaterial universe and at all scales, from the photoneutronic to the cosmic. Intuitional interaction that also takes place with the BEGs that are already in the BEL universe and of these with the BEGs located in the BML universe, always with the intermediary of a possible biointerfacemal (BIFL) function of the brain, as occurs during dreams or in the BEL communication, typical of BEL research using any common relaxation technique.<sup>73,74</sup>

For BEL research, it is very relevant that in the field of physics there is also talk of steady state in relation to physical events when the properties of a system do not change over time. When speaking of equilibrium, it refers to thermal equilibrium, and non-equilibrium states can be in steady state if an energy source favors that imbalance. If an electrical conductor, for example copper, reaches a state in which the copper or steel bar no longer captures any more heat and the temperature remains stable, it can also be in steady state.<sup>67,68,78</sup>

ACS: On the morning of Saturday, July 26, 2008, shortly before waking up, I dreamed a first bioscene in which I saw a medium-grown plant, very healthy and strong, with a semi-dark whitish green color and rhomboid leaves whose edges were coupled with each other forming a uniform surface formed by the leaves. Then I saw another bioscene with two plants grown like bushes. One of darker green color and also rhomboid leaves –or perhaps polygonal– that were also coupled together forming a surface that on the proximal edge had a not very pronounced but evident undulation, which at the end was continued with another plant equally grown and equal to the plant in the first bioscene, possibly the same, but grown. Between the two plants or bushes they formed an undulating surface towards the front and two shades of dull green. I showed the plants and their characteristics to two or three young people, but I couldn’t tell who they were. The surface on its periphery showed that, in addition to the undulation between the plants, it was also convex, made up of uniform leaves with attractive veins (it reminds me of the leaves of the phytonia). –I woke up with the intuition that new biospecies of plants were represented or bioproduced in the BEL sleep or biosleep. The bioimage that the plants gave was one of harmony and plenitude, since in addition to the fact that the rhomboid leaves of both fit very well, they did not leave any gap between them. The puzzle of the BEL experience, both in the BML universe and in the BEL universe, with bioscenes and bioimages from the BIFL universe, is becoming more and more complex. In this case, we would be talking about homeostasis

between the BML, BIFL and BEL universes of the unit universe, at all scales, from nanoscopic to macrocosmic dimensions.<sup>77,78</sup>

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## Conflicts of interest

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