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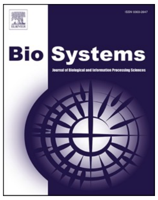

Overview of the fourth special issue in code biology

1. Introduction

After the discovery of the genetic code, in the 1960s, a second code (the *metabolic code*) was described by Gordon Tomkins (1975), and a third code (the *Hox code*) was announced by Paul Hunt (1991) and by Kessel and Gruss (1991). Between 1987 and 1999 Edward Trifonov (1987, 1989, 1999) announced a fourth class (the *sequence codes*) and in 1996 Redies and Takeichi (1996) described a fifth one (the *adhesion codes*). In 2000, Strahl and Allis (2000) and Turner (2000) proposed a sixth code (the *histone code*) whereas Gabius (2000) published the *sugar code* and Jessel (2000) announced the eight family of codes, the *transcriptional codes*.

In 2002, in other words, the number of known biological codes was 8 but then it rapidly increased: in 2012 it was 22 and in 2022 it shot up to 237 codes, a number documented by more than 1500 papers published in peer-reviewed journals and all cited in the database of the Code Biology Society.

In front of such a novelty a question comes immediately to mind: are they *real* codes or processes that have been given the *name* of codes but codes are not?

A code is real if it is not determined by the laws of physics and chemistry, i.e., if it is made of *arbitrary* rules, and the rules are arbitrary if they have been chosen from a potentially unlimited number of possibilities. The rules of the Morse code, for example, are arbitrary because any letter of the alphabet could have been associated with any combination of dots and dashes.

The rules of the genetic code are arbitrary because many laboratory experiments have shown that the transfer-RNAs – the molecular adaptors that actually implement the code – can be modified in countless different ways. This means that at the beginning of the evolution of the genetic code there were a potentially unlimited number of adaptors and therefore a potentially unlimited number of coding rules and a potentially unlimited number of rules means that the rules are arbitrary.

To the best of our knowledge, the biological codes that have been discovered so far have adaptors that can be modified in countless different ways and are therefore real codes. This may not be true in all cases – mistakes are always possible – but it is true in most of them, and this means that the existence of hundreds of codes in living systems is an experimental reality.

This special issue was announced when the number of codes in the database of the Code Biology Society went beyond one hundred, and most of its papers are about the problems that arose from that unexpected discovery. To this purpose, the issue has been divided into four parts and its manuscripts are summarized in the rest of this editorial with short descriptions of their contents.

1.1. PART 1 – Codes and Biology (Prinz, 2023; Jurková and Zámečník, 2023; Farnsworth, 2023; Rodríguez, 2023; Farina and Villa, 2023)

1.1.1. – Robert Prinz

1.1.1.1. Nothing in Evolution Makes Sense Except in the light of Code Biology. In 1973, Theodosius Dobzhansky made a public praise of Darwin's theory with the statement that "*Nothing in Biology Makes Sense Except in the Light of Evolution*" (Dobzhansky, 1973). In 2021, Reiskind and colleagues underlined that it is biological systems that undergo evolution and argued that Dobzhansky's statement should be reversed: "*Nothing in Evolution Makes Sense Except in the Light of Biology*" (Reiskind et al., 2021). This is also the title of the present paper except that '*Biology*' is replaced by '*Code Biology*': "*Nothing in Evolution Makes Sense Except in the Light of Code Biology*". The reason is that life as we know it would not exist without codes. Without the genetic code, for example, the genes would not be translated into specific proteins. But there is another reason for that title. Modern Biology claims that life is based on the laws of physics and chemistry, whereas Code Biology states that living systems *obey* those laws but are based on the arbitrary rules of codes. The change is from deterministic laws to arbitrary rules, and this is a completely new approach to life. At the moment, however, such approach is a *qualitative* one and the author argues that it should be turned into a fully *quantitative* field. This can be achieved by expressing key concepts like '*complexity*' and '*modularity*' in mathematical terms and the paper offers a few examples which show that such quantification is possible.

1.1.2. – Barbora Jurková and Lukáš Zámečník

1.1.2.1. Turing and von Neumann machines: Completing the new mechanism. The goal of Code Biology is to introduce in science not only the concepts of energy and information, but also the concept of *meaning* because the genetic code is at the heart of life, and a code is a set of rules that generate meaning. In the Morse code, for example, the rule that 'dot-dash' corresponds to letter 'A', is equivalent to saying that letter 'A' is the meaning of 'dot-dash'. In the same way, the rule that a codon corresponds to an amino acid is equivalent to saying that amino acid is the *meaning* of that codon. More precisely, the goal of Code Biology is to describe not only the mechanisms that produce energy and the mechanisms that produce information, but also the mechanisms that produce meaning in living systems, mechanisms that have been referred to as *extended* mechanisms. In the original version of Code Biology it was implicitly assumed that these new mechanisms are different from those that have been investigated so far, but the authors argue that this is not

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the case. They show that the mechanisms proposed by Alan Turing and John von Neumann were already based on the concept of code and were therefore in line with the idea that codes and meaning are fundamental components of life.

1.1.3. – Keith Farnsworth

1.1.3.1. How biological codes break causal chains to enable autonomy for organisms. This paper argues that there are two main reasons which explain why biological codes are essential to life. The first is that the autonomy of living systems requires freedom from exogenous controls, and this is achieved by using biological transducers at the organism's boundary (e.g. cell receptors) that add arbitrary rules to the physical forces of the incoming signals. The second reason is that the reproduction of any living system requires a separate information store (in Von Neumann's sense) and this store must be isolated from the rest of the replicating system. This is achieved by storing the information in a form that does not correlate with the rest of the system and requires therefore a translation process in order to become effective. The paper describes the function of biological codes in concrete terms, and argues that template-based reproduction, signal transduction and other key biological processes work in parallel with the laws of physics and the principles of information theory. This gives a physical grounding to the semiotic processes of life and shows that codes have a central role in the generation and in the evolution of all living systems.

1.1.4. – Claudio Rodríguez

1.1.4.1. Is meaning commensurable in scientific theories? From arbitrariness to non-nomological relations in meaning-making. We give *names* to *objects* because in this way we can talk about them even when they are not present. The word *apple*, for example, indicates a specific fruit and we say that the *fruit* apple is the *meaning* of that word. The same objects, on the other hand, are given different names in different languages, and this is because there is no necessary link between them and the rules that give names to objects are *arbitrary*. This appears to show that meaning is a *cultural* entity, something that requires an agreement between the members of a community. If this were true we could not extend the concept of meaning to all living systems and in particular we could not say that the genetic code is a set of rules where codons give meaning to amino acids. This is why the author argues that meaning should not be associated only with *arbitrary* relationships but with all *non-nomological* relationships because the term '*arbitrary*' strictly applies only to cultural relationships whereas the term '*non-nomological*' is more general and applies to all relationships that are not dictated by the laws of physics and chemistry and yet exist in living systems.

1.1.5. – Almo Farina and Alessandro Villa

1.1.5.1. On the semantics of ecoacoustic codes. When animals eat, the proteins of the ingested food are dismantled into amino acids and these are put together to form the specific proteins of the individual animals according to the rules of the genetic code. Something similar takes place when animals hear something; an external sound is dismantled in its components and these are sent to the intermediate brain that puts them together in a specific sound according to the rules of the *acoustic code*. The acoustic code, in other words, is not just a *transmission* code that delivers sounds from the ear to the brain; it is a *manufacturing* code because it is a set of rules that the brain employs to manufacture a specific sound from its acoustic components. In some cases, furthermore, evolution has allowed some acoustic codes to incorporate environmental factors and this association has given origin to *ecoacoustic* codes. The ecoacoustic codes, in other words, are the result of the evolution of some acoustic codes. Ecological evolution, on the other hand, has worked on many other biological codes and has given origin to a third type of codes that have been referred to as *ecological codes*. The present paper (Farina, 2023a) shows that these three types of codes – acoustic, ecoacoustic and ecological codes – are an integral part of the world in which animals live and their study is a major project of Code Biology.

1.2. PART 2 – Emergent Codes (Kobylkov et al., 2023; Robuschi, 2023; Marconi, 2023; Vedor, 2023; Farina, 2023)

1.2.1. – Dmitry Kobylkov, Mirko Zanon, Matilde Perrino and Giorgio Vallortigara

1.2.1.1. Neural coding of numerousness. In many occasions animals need to make a quick approximate estimate of the number of items in a set ("how many fruits on a tree?", "how many predators in the environment?"). This operation has been called '*numerousness*' and is a widely diffused form of cognition. Insects, fishes, reptiles, birds and mammals have very different brains and yet they all seem to possess a 'number sense'. So far, however, the actual identification of '*number neurons*' has been obtained only in primates and in birds, which suggests that these neurons have been the result of a particular evolutionary processes. In primates, furthermore, the fronto-parietal network plays a crucial role in number cognition, but number neurons do not seem to be localized in specific areas and appear to be distributed throughout the network. More precisely, the information about numerousness goes through a first preprocessing at the subcortical level and then it is further processed at the cortical level and in the end it appears to involve the whole brain. It is still not clear how neurons can retrieve the meaning of the neural codes from the activities of the neurons, and this problem – universally known as *the symbol grounding problem* – arises also in the case of the neural code for numerousness. An unexpected limitation of this paper is the statement that the study of numerousness has been conducted within the framework of Shannon's theory. In this framework information is a computable entity which is linked to probabilities, whereas genetic information is a non-computable sequence of nucleotides. Most neural codes cannot be reduced to the transmission codes of Shannon's theory and this suggests that the study of the neural codes of numerousness would benefit from a wider theoretical framework.

1.2.2. – Camilla Robuschi

1.2.2.1. Code Biology and Aesthetics. Aesthetics is usually regarded either as the analysis of beauty or as the critique of the works of art, but the author points out that in 1750 the founder of the discipline, Alexander Gottlieb Baumgarten, defined aesthetics as "*the science of sense cognition*", i.e., the science of the *biological* processes that produce our sense of beauty. The author proposes to go back to this original definition and to investigate aesthetics with the tools of modern biology, and in particular with the concepts of Code Biology and the proposals made by Juri Lotman, Max Bense, Giorgio Prodi and Thomas Sebeok. More precisely, it is underlined that there are three cognitive systems in our species. The first is the system that transforms the signals from the sense organs into models of the outside and of the inside world (Umwelt and Innenwelt); the second system allows many animals to interpret what goes on in the world with the processes of abduction introduced by Charles Peirce; the third cognitive system is language, the system that allowed our species to build the entirely new word of culture. It is these three cognitive systems that allow us to recognize the aesthetic faculties that we have in common with other animals and those that are unique to our species.

1.2.3. – Valerio Marconi

1.2.3.1. The flower of the desert and a migrant experience: two examples of personal codes. Culture is made of codes. The commandments of religion, the laws of government, the value of money, the rules of chess and the highway regulations are all based on coding rules and it is the arbitrariness of these rules that makes culture fundamentally different from physics and chemistry. This paper adds something else. It states that there are two types of cultural codes: the *collective* codes and the *personal* ones. The collective codes are those that are adopted by a community whereas the personal codes are restricted to a single person or to a few individuals. The paper discusses two examples of personal codes. The first comes from the flower of the desert that grows on Mount Vesuvius and whose destiny to be annihilated by the lava of the volcano, a destiny that to the poet Giacomo Leopardi reminds that of our species which is also condemned to extinction. The second example is that of a migrant who must combine the codes of his original country with those of the new country. The author underlines that the concept of personal code is fully compatible with Code Biology and goes all the way back to Plato, who in the *Sophist* argued that every man contains a part with which he talks to himself and a part with which he communicates with all others.

1.2.4. – João Ereiras Vedor

1.2.4.1. Revisiting Carl Jung's archetype theory: a psychobiological approach. Carl Gustav Jung generalized the concept of unconscious introduced by Freud and argued that in addition to the '*individual*' unconscious there is also a '*collective*' unconscious that influences our behavior. More precisely Jung argued that the collective unconscious is the source of inborn ideas to which he gave the name of '*archetypes*'. Similar proposals have been made by other authors with different names. Claude Lévi-Strauss, for example, used the term '*unconscious infrastructures*', Noam Chomsky spoke of '*deep structures*', Antonio Damasio adopted the name '*proto-self*', and Gerald Edelman used the term '*primary consciousness*' to indicate the deep entities that control our behavior. The problem, however, is not the names that are given to these entities but the *mechanism* that generates them. The author underlines that coding is a mechanism that has operated in living systems throughout the history of life and has the ability to generate novelties by establishing arbitrary associations between objects. The author underlines in particular the idea that "*mental states like perceptions and feelings are manufactured from neural components just as proteins are manufactured from amino acids*". This is why he proposes that archetypes are manufactured by codes, i.e., that coding is the mechanism that the brain is using to produce countless neural objects, including its archetypes.

1.2.5. – Almo Farina

1.2.5.1. Discovering ecoacoustic codes in beehives: first evidence and perspectives. We have all been fascinated by the discovery of the 'waggle dance' of the bees, the movements by which a bee communicates to the other members of the hive the direction and the distance of a patch of flowers. Ethologists, on the other hand, have long suspected that the waggle dance is not the sole communication tool of the bees – such a conclusion would be like saying that language is the tool that humans employ to communicate the positions of the restaurants in a city. There is much more than that to human language and this suggests that there is much more than the waggle dance to the language of the bees. The problem, of course, is to find the experimental evidence of this larger communication systems, and that is what this paper is about. More precisely, the author argues that the acoustic patters that enter the beehive are divided by the bees into three different classes (uniform, random and regular) and represent an acoustic habitat where ecoacoustic codes are developed to coordinate the activity of the whole bee colony.

1.3. PART 3 – Extended Theories (Igamberdiev, 2023; Igamberdiev and Gordon, 2023; Heng and Heng, 2023; Petoukhov, 2023; Faria, 2024)

1.3.1. – Abir Igamberdiev

1.3.1.1. Reflexive structure of the conscious subject and the origin of language codes. This paper begins with the statement that "*The code paradigm in biological and social sciences arises from Aristotle*". More precisely, "*The concept of life as a system of codes is explicitly presented in the second part of 'De Anima' and also in 'Metaphysica'*". According to Aristotle, life is made of systems that have different degrees of complexities and the increase in their complexity is regarded as an increase in *knowing power*, an increase that Heraclitus described as "*self-growing Logos*". According to the author, in other words, the ancient 'logos' is what today we call 'codes'. One of the most important differences in life is that between conscious and unconscious creatures, and according to Aristotle the origin of consciousness was due to the origin of "*the reflexive capacity of sensing one's own senses*", an event that today can be referred to as "*the origin of new reflexive codes*". The paper suggests that these codes appeared first as a common signaling system and then split into two systems, one leading to language and the other to music. It is underlined furthermore that Aristotle's ideas on the nature of cognition have also been expressed in similar terms by Spinoza. Another key point is that any new code corresponds to a new internal computation system and a mathematical code is also present in the proof of incompleteness proposed by Gödel. According to the author, in conclusion, codes have been present for a long time in philosophy and today we are finally discovering the experimental proofs of their existence.

1.3.2. – Abir Igamberdiev and Richard Gordon

1.3.2.1. Macroevolution, differentiation trees, and the growth of coding systems. There are hundreds of different tissues in eukaryotic organisms and they come into being during embryonic development in a sequence of steps that has been referred to as the *differentiation tree*. This tree can be described as a network of choices between the digits 0 and 1, and in 2019 Richard and Natalie Gordon proposed that these choices are the result of a *differentiation code* (Gordon and Gordon, 2019). The key point is the mechanism of the differentiation steps, and on this point the authors embrace the idea that these steps are produced by signals emitted by the cytoskeleton. These signals were first described by Alexander Gurwitsch in 1925 in the form of '*mitogenetic rays*', and other variants have been proposed ever since, either in the form of '*mechanical waves*' or in the form of '*electromagnetic waves*'. The consequence of these proposals is the idea that in the long run the differentiation trees of embryonic development give origin to the phylogenetic trees of evolution. More precisely, the authors propose that changes of the differentiation tree that preserve the topology of the tree give origin to microevolution whereas the changes that modify the topology of the tree give origin to the great events of macroevolution.

1.3.3. – Julie Heng and Henry Heng

1.3.3.1. Karyotype as code of codes: an inheritance platform to shape the pattern and scale of evolution. The evolution of cancer takes place with transitions from a benign to a malignant condition, from a local to a diffuse state, from a drug-sensitive to a drug-resistant population of cells, and these transitions are characterized by whole-genome transformations that have been referred to as *karyotype* changes. These macro-changes in the genome, on the other hand, are accompanied by micro-changes in individual genes and the result is a two-phase phenomenon that takes place simultaneously at the macroscopic level of the genome and at the microscopic level of its genes. The proposal of the authors is that a similar two-phase mechanism is responsible for the evolution of life. The great events of macroevolution are caused by karyotype changes whereas the ordinary events of microevolution are the result of genetic mutations. This is why they conclude that "*karyotype change – and by extension macroevolution – occurs whenever the karyotype's coding is sufficiently changed*". In the original theory of Code Biology, the code-generating system, or '*codemaker*', was the '*ribotype*', the ribonucleoprotein system of the cell, whereas in this paper the codemaker is either the whole genome or the individual genes. This implies that the theory described in this paper is a new proposal about the components that gave origin to the codes of life.

1.3.4. – Sergey Petoukhov

1.3.4.1. The principle 'like begets like' in algebra-matrix genetics and code biology. The classical model of the double helix has revealed that DNA is a sequence of complementary couples of nucleotide bases (A and T or C and G), or, more precisely, a sequence of complementary couples of purines and pyrimidines. According to the author, the complementary of those bases is an example of the principle that '*like begets like*', a principle that can be expressed in mathematical form with matrices where the two complementary parts are represented by the numbers 0 and 1. The same matrices can be used to represent countless other forms of complementary associations that exist in biological systems, from those that we find at the molecular level to those that are present in the brain in the form of complementary mental images or complementary mirror neurons. The author maintains that the complementarities that we find in the mirror neurons and in the genes are just a few examples of the principle that '*like begets like*', a principle that can be regarded as a "holistic bio-algebraic" theory of the living systems.

1.3.5. – Marcella Faria

1.3.5.1. Endless forms of endless formation – The morphogenesis of organisms and scientific objects. This paper starts with the quotation that Darwin put at the end of his seminal book on the origin of species: "*… from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved*". The author points out that Darwin's concept of '*endless forms*' applies not only to physical objects but also to ideas and proposes a parallel between the world of life and the world of art. Biological objects come into being and evolve, art concepts come into being and evolve, and in both cases we find the general properties of the signs systems, namely the fact that "*… signs are polysemic, codes are degenerate and meanings are selective*". The author, furthermore, argues that the different proposals of past thinkers – the evolution by natural selection of Darwin, the true-to-nature method of Goethe and the experimental physiology of Claude Bernard – have opened the way to approaches that came later, such as Cognitive Sciences, Systems Biology, Biosemiotics, Relational Biology and Code Biology. There is diversity and unity in the world of life and in the world of art, and the state of endless becoming is at the heart of both of them.

1.4. PART 4 – The Genetic Code (Štambuk et al., 2023a, 2023b; Fimmel and Strüngmann, 2023; Zolyan, 2023; Spirov, 2023)

1.4.1. – Nikola Štambuk, Paško Konjevoda, Albert Štambuk

1.4.1.1. How ambiguity codes specify molecular descriptors and information flow in Code Biology. The standard table of the genetic code was formalized in 1970 by the International Union of Pure and Applied Chemistry (IUPAC) and contains eleven characters that can be associated with any combination of the four bases (A, T, C, G), and for this reason have been referred to as "*ambiguity codes*". The authors, furthermore, have proposed a version of the genetic code that is different from the standard one because it describes that code not with a single table of 64 characters but with four tables of 16 characters each. This version is called the '*relational model*' and its main advantage is that it requires only 45 tRNAs, which is the number that is actually found in most species whereas the standard model requires 64 tRNAs and needs to resort to additional processes, like the wobble effect, in order to account for the number that is present in living systems. The ambiguity codes and the relational model give us new tools for the study of the genetic code and are particularly useful in Code Biology because they help us to understand the process of '*codepoiesis*', the mechanism that generates and conserves the biological codes in living systems.

1.4.2. – Nikola Štambuk, Paško Konjevoda, Krunoslav Brčić-Kostić, Josip Baković, Albert Štambuk

1.4.2.1. New algorithm for the analysis of nucleotide and amino acid evolutionary relationships based on Klein four-group. The building of phylogenetic trees is one of the major tools that scientists employ for the reconstruction of the history of life and any improvement in these techniques is potentially a great help to our reconstruction of the past. The authors of the present paper have adopted a new approach to the phylogenetic studies by adopting the '*relational model*' of the genetic code, a model that describes that code not with a single table of 64 characters but with four tables of 16 characters each. In this paper they describe another innovation by presenting a new algorithm for the analysis of nucleotide and amino acid sequences, an algorithm that is based on the matrices of the Klein four-group. The combination of the relational model with the distance matrices of new Klein four-group allow the authors to evaluate differences in transition and in transversion within the observed sequences and give us new phylogenetic information for the study of the history of molecular life on the primitive Earth.

1.4.3. – Elena Fimmel and Lutz Strüngmann

1.4.3.1. The spiderweb of error-detecting codes in the genetic information. In protein synthesis any mistake in identifying the beginning of translation (a frame-shift error) would cause a different sequence of amino acids and therefore a totally different protein. In order to avoid these fatal mistakes the cell must have evolved mechanisms that avoid the frame-shifts, and the identification of these mechanisms has been actively investigated for many years. An important step forward in this field has been the discovery of the *circular codes* whose main characteristic is precisely the ability to detect a frame-shift of one or two positions. These codes can be regarded as additional rules that have been evolved with the specific purpose of preserving the proper reading frame in protein synthesis. In a previous study the authors identified a total of 216 circular codes grouped into 27 equivalence classes with eight codes in each class. In this paper they show that a set of 27 winner codes can be derived with a natural algorithm and each winner code represents an equivalence class. The authors also show that the circular codes can be moved from one equivalence class to another by removing a codon/anticodon pair and adding a different one. This result is a new significant step forward in the search of the mechanisms that the ancestral cells invented in order to avoid the frame-shift errors in protein synthesis.

1.4.4. – Suren Zolyan

1.4.4.1. On the minimal elements of the genetic code and their semiotic functions. Francis Crick described the genetic code as "*the small dictionary which relates the four-letter language of nucleic acids to the twenty-letter language of the proteins*", and since then it has become commonplace to say that the nucleotides are equivalent to the *letters* of a language. In this paper it is argued instead that they are equivalent not to the letters but to the *phonemes* of a language. This idea was first proposed by Roman Jakobson and then by François Jacob but it has never become popular and the present paper is a new attempt to reviving it. Language has evolved as an *acoustic* activity, a form of communication based on sounds, and Ferdinand de Saussure underlined that it is made of an abstract part that he called *langue* and a concrete part that he called *parole*. The same is true for the components of language: the phonemes are the abstract components and the sounds are their concrete expressions. A phoneme is identified by the various features that distinguish it from all the other phonemes, and is therefore a set of properties not a single one. The key point is that this composite structure is also present in the nucleotides of the genetic code. Any nucleotides has two features that separate it from all the others: the first is the number of carbon rings, the second is the number of hydrogen bonds, all of which means that it has the complex composition of a phoneme, not the elementary composition of a letter.

1.4.5. – Alexander Spirov

1.4.5.1. Evolution of the RNA world: from signals to codes. The divide between chemistry and life is due to the fact that the molecules of chemistry are produced *spontaneously* whereas the molecules of life are *manufactured* by molecular machines. This amounts to saying that life begun when the first molecular machines appeared on the primitive Earth and started populating it with manufactured molecules, i.e., with molecular *artifacts*. The old controversy between the protein-first and the gene-first models on the origin of life has been abandoned when it became clear that some RNAs can function like proteins and others like genes, which strongly suggests that life originated in a world dominated by the RNAs, the so called '*RNA world*'. The present paper suggests that the transition from ancestral to modern life consisted in three major events: the first was the evolution of the adaptors that implement the rules of the genetic code; the second was the development of signalling RNAs that evolved into the modern riboswitches of the cell; the third was the evolution of ancestral networks that became the precursors of the modern gene regulatory networks. The result of these multiple events is that the complexity of the modern cells can be traced all the way back to the achievements of the RNA world.

References

Dobzhansky, T., 1973. Nothing in biology makes sense except in the light of evolution. Am. Biol. Teach. 35 (3), 125–129. https://doi.org/10.2307/4444260.

Faria, M., 2024. Endless forms of endless formation – The morphogenesis of organisms and scientific objects. Biosystems 235, 105068.

Farina, A., Villa, A., 2023. On the semantics of the ecoacoustic codes. Biosystems 232, 105002. https://doi.org/10.1016/j.biosystems.2023.105002.

Farina, A., 2023. Discovering ecoacoustic codes in beehives: first evidence and perspectives. Biosystems 234, 105041. https://doi.org/10.1016/j.biosystems.2023.105041.

Farnsworth, K., 2023. How biological codes break causal chains to enable autonomy for organisms. Biosystems 232, 105013. https://doi.org/10.1016/j.biosystems.2023.105013.

Fimmel, E., Strüngmann, L., 2023. The spiderweb of error-detecting codes in the genetic information. Biosystems 233, 105009. https://doi.org/10.1016/j.biosystems.2023.105009.

Gabius, H.-J., 2000. Biological information transfer beyond the genetic code: the sugar code. Naturwissenschaften 87 (3), 108–121. https://doi.org/10.1007/s001140050687.

Gordon, R., Gordon, N.K., 2019. The differentiation code. Biosystems 184, 104013. https://doi.org/10.1016/j.biosystems.2019.104013.

Heng, J., Heng, H.H., 2023. Karyotype as code of codes: an inheritance platform to shape the pattern and scale of evolution. Biosystems 233, 105016. https://doi.org/10.1016/j.biosystems.2023.105016.

Hunt, P., Whiting, J., Nonchev, S., Sham, M.-H., Marshall, H., Graham, A., Cook, M., Alleman, R., Rigby, P.W., Gulisano, M., 1991. The branchial *Hox* code and its implications for gene regulation, patterning of the nervous system and head evolution. Development 2, 63–77.

Igamberdiev, A.U., 2023. Reflexive structure of the conscious subject and the origin of language codes. Biosystems 231, 104983. https://doi.org/10.1016/j.biosystems.2023.104983.

Igamberdiev, A.U., Gordon, R., 2023. Macroevolution, differentiation trees, and the growth of coding systems. Biosystems 234, 105044. https://doi.org/10.1016/j.biosystems.2023.105044.

Jessell, T.M., 2000. Neuronal specification in the spinal cord: inductive signals and transcriptional codes. Nat. Rev. Genet. 1 (1), 20–29. https://doi.org/10.1038/35049541.

Jurková, B., Zámečník, L., 2023. Turing and von Neumann machines: completing the new mechanism. Biosystems 234, 105046. https://doi.org/10.1016/j.biosystems.2023.105046.

Kessel, M., Gruss, P., 1991. Homeotic transformation of murine vertebrae and concomitant alteration of *hox* codes induced by retinoic acid. Cell 67 (1), 89–104. https://doi.org/10.1016/0092-8674(91)90574-i.

Kobylkov, D., Zanon, M., Perrino, M., Vallortigara, G., 2023. Neural coding of numerousness. Biosystems 232, 104999. https://doi.org/10.1016/j.biosystems.2023.104999.

Marconi, V., 2023. The flower of the desert and a migrant experience: two examples of personal codes. Biosystems 233, 105040. https://doi.org/10.1016/j.biosystems.2023.105040.

Petoukhov, S.V., 2023. The principle 'like begets like' in algebra-matrix genetics and code biology. Biosystems 233, 105019. https://doi.org/10.1016/j.biosystems.2023.105019.

Prinz, R., 2023. Nothing in evolution makes sense except in the light of code biology. Biosystems 229, 104907. https://doi.org/10.1016/j.biosystems.2023.104907.

Reiskind, M.O.B., Moody, M.L., Bolnick, D.I., Hanifin, C.T., Farrior, C.E., 2021. Nothing in evolution makes sense except in the light of biology. Bioscience 71 (4), 370–382. https://doi.org/10.1093/biosci/biaa170.

Robuschi, C., 2023. Code biology and aesthetic process. Some points of reflection. Biosystems 234, 105065. https://doi.org/10.1016/j.biosystems.2023.105065.

Rodríguez, C., 2023. Is meaning commensurable in scientific theories? From arbitrariness to non-nomological relations in meaning-making. Biosystems 234, 105042. https://doi.org/10.1016/j.biosystems.2023.105042.

Redies, C., Takeichi, M., 1996. Cadherins in the developing central nervous system: an adhesive code for segmental and functional subdivisions. Dev. Biol. 180 (2), 413–423. https://doi.org/10.1006/dbio.1996.0315.

Spirov, A., 2023. Evolution of the RNA world: from signals to codes. Biosystems 234, 105043. https://doi.org/10.1016/j.biosystems.2023.105043.

Štambuk, N., Konjevoda, P., Štambuk, A., 2023a. How ambiguity codes specify molecular descriptors and information flow in Code Biology. Biosystems 233, 105034. https://doi.org/10.1016/j.biosystems.2023.105034.

Štambuk, N., Konjevoda, P., Brčić-Kostić, K., Baković, J., Štambuk, A., 2023b. New algorithm for the analysis of nucleotide and amino acid evolutionary relationships based on Klein four-group. Biosystems 233, 105030. https://doi.org/10.1016/j.biosystems.2023.105030.

Strahl, B.D., Allis, D., 2000. The language of covalent histone modifications. Nature 403 (6765), 41–45. https://doi.org/10.1038/47412.

Tomkins, M.G., 1975. The metabolic code. Science 189 (4205), 760–763. https://doi.org/10.1126/science.169570.

Trifonov, E.N., 1987. Translation framing code and frame-monitoring mechanism as suggested by the analysis of mRNA and 16s rRNA nucleotide sequence. J. Mol. Biol. 194 (4), 643–652. https://doi.org/10.1016/0022-2836(87)90241-5.

Trifonov, E.N., 1989. The multiple codes of nucleotide sequences. Bull. Math. Biol. 51 (4), 417–432. https://doi.org/10.1007/BF02460081.

Trifonov, E.N., 1999. Elucidating sequence codes: three codes for evolution. Ann. N. Y. Acad. Sci. 870, 330–338. https://doi.org/10.1111/j.1749-6632.1999.tb08894.x.

Turner, B.M., 2000. Histone acetylation and an epigenetic code. Bioessays 22 (9), 836–845. https://doi.org/10.1002/1521-1878(200009)22:9<836::AID-BIES9>3.0.CO;2-X.

Vedor, J.E., 2023. Revisiting Carl Jung's archetype theory a psychobiological approach. Biosystems 234, 105059. https://doi.org/10.1016/j.biosystems.2023.105059.

Zolyan, S., 2023. On the minimal elements of the genetic code and their semiotic functions (degeneracy, complementarity, wobbling). Biosystems 231, 104962. https://doi.org/10.1016/j.biosystems.2023.104962.

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