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Biocommunication and natural genome editing

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Abstract

The biocommunicative approach investigates communication processes within and among cells, tissues, organs and organisms as sign-mediated interactions, and nucleotide sequences as code, i.e. language-like text, which follows in parallel three kinds of rules: combinatorial (syntactic), context-sensitive (pragmatic), and content-specific (semantic). Natural genome editing from a biocommunicative perspective is competent agent-driven generation and integration of meaningful nucleotide sequences into pre-existing genomic content arrangements and the ability to (re-)combine and (re-)regulate them according to context-dependent (i.e. adaptational) purposes of the host organism.

Key words: Biotic agents; Signs; Molecular syntax; Communication; Nucleotide sequence editing

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INTRODUCTION AND EDUCATIONAL EXPERIENCE

From 1987 to 1990, I (Figure 1) developed a Theory of Communicative Nature. Living nature is structured and organized by language and communication within and among organisms. This means that, besides human language and communication, every organism within its population is competent to use signs with which organisms can differentiate between self and non-self, and can exchange information about common coordinations and organizations of single and group behavior. These sign-mediated interactions are termed biocommunication.

The starting point for me to develop a pragmatic philosophy of biology was a sailing trip in 1986 in the upper Adriatic Sea in the boat of my friend, Helmut Gruber. Initially, it was an intuition about the possibility of rule-governed, sign-mediated interactions in non-human nature. Annemarie Pieper encouraged me to renew this thought and introduced me to Hermann Krings. From his two essays "Kann man die Natur verstehen" (Is nature understandable) and "Natur als Subjekt" (Nature as subject)[1,2], I discovered crucial philosophical questions to which a pragmatic philosophy of biology tries to give answers. My study of numerous reports from different biological disciplines was parallel to this consideration. It

showed that different biological disciplines used linguistic or communication-theoretical vocabulary to describe their observations, and as the case may be, writing that provides theoretical substantiation of empirical data. From the study of Karl Otto Apel's works, it quickly became clear to me that the whole field that I was reading about engaged in uncritical usage of communication-theoretical vocabulary.

ACADEMIC ACHIEVEMENTS

Application of a three-leveled semiotics to all sectors of biology

The exciting part in the development of the pragmatic philosophy of biology[3,4] was my application of a three-leveled semiotics to all sectors of biology, i.e. to processes: (1) in organisms (intraorganismic); (2) between organisms of the same species (interorganismic); and (3) between organisms of different species (metaorganismic). Accordingly, Natur der Sprache - Sprache der Natur. Sprachpragmatische Philosophie der Biologie[3] first published in 1993, examined language and communication between bees, within and between cells, and as communicative dysfunction in organs and organisms and its consequences. I took Manfred Eigen's example of molecular syntax and showed that while the semiotic perception in his model is basically right, his reduction of the principally irreducible three-leveled semiotics to a (universal) syntax cannot be sufficiently substantiated. I applied a pragmatic philosophy of biology to all realms of organisms and followed the separation of the realms of organisms from each other using Nicolai Hartman's theory of layers. Finally, the application of a pragmatic philosophy of biology to evolution theory led me to posit evolution according to semiotic aspects; a position, that was incompatible with "chance mutations" as a central element of genesis of new species.

Continued presentation of a new transdisciplinary theory

In 1989, I was able to present the first results of my theory at the First International Schelling Congress in Bad Leonberg, and in 1990, at the Deutscher Kongress für Philosophie (German Philosophy Congress) in Hamburg. In 1992, Rupert Riedl, director of Konrad Lorenz Institute gave me the opportunity to present and discuss my theses in Altenberg a.d. Donau. Roland Posner's invitation to write an article for the Zeitschrift für Semiotik (1992), and my acquaintanceship and many decisive conversations with Thure von Uexküll (1993) opened up semiotics and biosemiotics to me. From 1994 to 2010, I received invitations for presentations at semiotics congresses (Berkeley, 1994 and Dresden, 1999), at symposia held by the Akademie für Integrierte Medizin (Academy for Integrated Medicine), which was founded by Thure von Uexküll (Munich, 1996; Wiesbaden, 1996, 1997; and Bad Glotterbad, 1998), at the Second World Congress for Contructivism in Heidelberg (1998), the Congress of the International Society for History, Philosophy and Social Studies in Vienna (2003), the Gatherings in Biosemiotics (Prague, 2004; Urbino, 2005; Salzburg, 2006; and Braga, 2010), as well as at the First International Symposium on Plant Neurobiology (Florence, 2005) and Cold Spring Harbor Laboratory, 2007. All of this allowed a presentation and further development of the pragmatic philosophy of biology.

Beyond Neo-Darwinism and Neo-Lamarckism: Evolution by genome editing

The English translation of my book appeared in 2000 under the title "Life: The Communicative Structure"[4] and has been updated to that year of publication. In Chapter 9 of the translation, I present an initial thesis that suggests that the genesis of new species, genera, and realms of organisms does not occur in any neo-Darwinistic sense *via* "chance mutations" and their "selections", but *via* a kind of innovation code (evolution code, creation code, text-generating code), which is capable of DNA/RNA text editing.

The English translation of 2000 further develops the thesis about the overcoming of Neo-Darwinism and Neo-Lamarckism as do the supplementary commentaries to my 1993 core thesis. It turns out that the genetic code that encodes proteins - practically the sole subject of current bioengineering - is only a kind of structuring vocabulary, and not a complete structure in itself, and is subject to a higher-order regulatory code that lies hidden in the non-protein-coding regions of the DNA, which have been identified as RNA agents many years later[5].

The fact that such meta-DNA characteristics - together with a DNA text-editing function that can code for influences on organisms such as stress (hormonal, neuronal, viral, bacterial, or inflammatory) - could exist was (and still is) barely imaginable for most scientists, who still believed in the central dogma of molecular biology: DNA/RNA/proteins/anything else. However, with the rise of epigenetics, it has become understandable how completely different reading processes of one and the same genetic data set can produce completely different "protein meanings".

Every organism is involved in intra-, inter- and transorganismic communication

The pragmatic philosophy of biology that I developed between 1987 and 1990 had a central thesis that living nature is structured and organized linguistically and communicatively. This theory of communicating living nature postulates: (1) that every living being is involved in intra-, inter- and transorganismic communication processes without which any living being would not be able to live; and (2) evolution in its decisive steps is regulated and constituted by a higher order genome function. The pragmatic philosophy of biology was first published in 1993[3]. At that time, its theses were - with the exception of Rupert Riedl, Thure von Uexküll and Wilhelm Vossenkuhl - rejected by both philosophers and biologists. One philosopher muttered "He probably heard bacteria talking to one another." In the meantime, the course of development has proven this thesis correct on all counts. "Using (…) ad-

vanced linguistic capabilities, bacteria can lead rich social lives for the group benefit. They can develop collective memory, use and generate common knowledge, develop group identity, recognize the identity of other colonies, learn from experience to improve themselves, and engage in group decision-making, an additional surprising social conduct that amounts to what should most appropriately be dubbed as social intelligence"[6].

In the framework of a linguistically and communicatively structured and organized living nature, evolution cannot be a process of chance mutations that are then selected; the evolutionary process is not subject to the strict mechanics of natural laws. Rather, it is a process that follows linguistic and communicative rules, to which organisms have developed or can develop a relationship of adherence or non-adherence. The key steps of evolution - as the SET (Serial Endosymbiotic Theory of Lynn Margulis)[7] has demonstrated - are a union process of formerly independent gene bearers into integrated genomes. However, this does not involve "merging", "fusion", "incorporation" of genetic material, but it is only explainable through numerous enzyme proteins that are sufficiently competent to conduct highly complex text-processing, and RNAs that have similar abilities.

After innovation of eukaryotic protoctists, the constitution of a genetic higher order dataset in the phenotypic frame of a multicellular eukaryotic superkingdom was regulated and constituted through the abilities of non-protein-coding regions of DNA, such as self splicing ribozymes.

Questions: Meta-DNA? Do codes code themselves? What and where are coding agents?

This hidden "meta-DNA" has been predicted as being necessary to explain higher order functions such as combination, recombination, control and integration of large-scale structures of the chromosome[8-13].

This changes our perception about the function and sense of evolution dramatically: no longer are small steps that involve chance mutations that are responsible for differentiating eukaryotic organismic kingdoms, whose phenotypes are then subject to selection pressure. What numerous researchers have always surmised, i.e. that chance mutations could not have brought about the enormous complexity of intracellular processes or this astounding diversity of organisms, has been proven. The arguments of neo-Darwinism, that have vehemently defended this monistic (mutation/selection-) evolution over more than half a century, have lost their validity.

Mutations do occur, but they do not lead to a higher evolution of organisms, but rather to adaptational variants. They are fine-tunings and not originating factors for *de novo* evolution. Through the union processes of genes of bacterial origin in the sense of SET, entire blocks of genes, and therefore, phenotypically effective characters also become components of such integration processes. Even the thesis - developed in the pragmatic philosophy of biology - of normal- and revolutionary-evolutive phases[4], which attempts to explain the relatively saltatory development of new species, and that attempts to explain phenomena such as the Cambrian explosion or the absence of a large number of missing links, can be further developed. The innovation code that have I proposed, which is assumed to lie in the non-coding DNA, whose reading leads - as we know today - to active microRNAs, a variety of small non-coding RNAs and other ribozymatic structures that have RNA/DNA-text-editing capabilities, gains a new interpretational basis in the framework of the SET. Accordingly, the meta-DNA that codes only for active miRNAs has (three-leveled) semiotic competences to incorporate entire blocks of DNA of foreign organisms (non-self-recognition) into its own DNA. It achieves this: (1) at the correct location; (2) in the correct relation to the existing genome ratio; and (3) in correct relation to the DNA-skeletal/non-coding DNA ratio.

New reports have suggested that the capabilities of non-coding DNA with higher order regulatory functions have descended from ancestral viral genome editing competences that have been integrated by endogenous viruses, e.g. retroviruses. There are also strong reasons to consider that the eukaryotic nucleus is of viral origin. DNA viruses are held to be competent to create new genes in large numbers; both complex and simple ones[14-19].

Persistent viruses and virus-like agents do natural genome editing

Within the last decade views on natural genetic engineering and natural genome editing have changed dramatically[20]. In particular, research in virology[21-26] has opened perspectives on early evolution of life, as well as on viruses as essential agents within the roots and stem of the tree of life[27,28]. The early meta-DNA thesis and the genome editing MetaCode I have predicted and met their empirical counterparts in an astonishing assembly of viral competences, as outlined in detail by Villarreal[19], such as:

From the early RNA-world perspective, the whole diversity of processes within and between evolutionarily later-derived cellular life depends on various RNAs.

The pre-cellular RNA world must have been dominated by quasi-species consortia-based evolution, as are current RNA viruses.

Viruses can parasitize almost any replication system - even prebiotic ones.

RNA viruses store crucial and dynamic information.

Based on this and the results of phylogenetic analyses and comparative genomics, it is possible to establish viral lines of ancestral origin.

These lines of origin can also be non-linear because different parts of viruses contain different evolutionary histories.

Since viruses with RNA genomes are the only living beings that use RNA as a storage medium, they are considered to be witnesses of an earlier RNA world.

Current negatively stranded RNA viruses have genome structures and replication patterns that are dissimilar to all known cell types.

No similarity between RNA-viral replicases and those of any known cell types has been identified.

DNA viruses, too, do not give any reference to a cellular origin. DNA-repair proteins of DNA viruses do not have any counterparts in cells.

One milliliter of seawater contains one million bacteria and 10 times more viral sequences. 10^{31} bacteriophages infect 10^{24} bacteria/s.

The enormous viral genetic diversity in the ocean has established pathways for the integration of complete and complex genetic data sets into host genomes, e.g. acquisition of complex new phenotypes.

A prophage can provide the acquisition of > 100 new genes in a single genome editing event.

Today, it is assumed that the gene word order in bacterial genomes is determined by viral settlers of bacterial host genomes.

Not only bacterial life is determined by non-lytic viral settlements, but also the evolution of eukaryotes has strongly depended on viral properties.

In contrast to mitochondria and other eukaryotic parts of bacterial descent, the eukaryotic nucleus was formerly a large double-stranded DNA virus.

All properties of the eukaryotic nucleus are lacking in bacterial life forms but are typical features of DNA viruses.

Even lethally irradiated viruses can often repair themselves.

They are competent to recombine combinations of defective viral genomes in order to assemble intact viruses.

Therefore, viruses are the only living agents capable of meaningfully recombining text fragments of a damaged genome into a fully functional viral genome that is capable of self-replication.

Lytic diseases that are caused by viral infections are the exception in viral life strategies, although they might have epidemic and pandemic and therefore catastrophic consequences for infected populations.

The most dominant viral life strategy is the non-lytic but persistent viral settlement of cytoplasm of cellular hosts and even more of cellular host genomes.

Addiction modules are the result of integration of former competing viral infections.

As symbiotic neutralization and counterpart regulation, they represent new host phenotypic features.

One feature is regulated exactly by the antagonist according to developmental stages in the cell cycle, replication, and tissue growth.

Should this suppressor function become unbalanced, then the normally downregulated part might become lytic again.

We can identify viral-derived addiction modules in every toxin/antitoxin, restriction/modification or insertion/deletion modules in which former competing viral clouds are now immunologically balanced.

If a balanced status is reached this means a changed genetic identity of the host organism, and in consequence, a changing genetic identity of the viral settler.

Current knowledge indicates that most evolutionarily novel derived species are the result of changed and expanded genomic identities caused by persistent viral colonization.

Research results in virology[19,29] have led to the assumption that, besides communicative competences of cellular organisms, which are involved in coordinating behavior, there are "linguistic" competences of viruses and virus-derived viral parts (e.g. env, gag, pol), which not only regulate all cellular processes, but edit the genetic content of living organisms[5]. This viral genetic text-editing competence depends on living organisms that are different from each other, and it therefore needs a biotic matrix to expand this competence. Without living and interacting organisms and cells, genomic creativity would only be a possibility that is restricted to mere RNA combinatorial events (in an early pre-cellular RNA world), which has no relevance to the generation of a biosphere.

CONCLUSION

Most of the processes that evolve, constitute, conserve, and rearrange the genetic storage medium of DNA are described by terms that were originally used in linguistics, such as coding, copying, transcription, translation, signaling, and signal transduction. Meanwhile, the linguistic approach has also lost its metaphorical character, and the similarity between linguistic languages/codes and genetic storage media are not only accepted, but are fully adapted in bioinformatics, biolinguistics, protein linguistics, biohermeneutics and biosemiotics. The advantage of methodological adaptation of communication and linguistic terminology is the availability of appropriate tools for differentiation at specific levels that are difficult to describe in the language of physics and chemistry alone. No semiotic rules (syntax, semantics, pragmatics) are involved if water freezes to ice, but without semiotic rules, biotic signaling does not work.

The biocommunicative approach investigates communication processes within and among cells, tissues, organs and organisms as sign-mediated interactions, and nucleotide sequences as code, i.e. language-like text, which follows in parallel three types of rules: combinatorial (syntactic), context-sensitive (pragmatic), and content-specific (semantic).

Natural genome editing from a biocommunicative perspective is competent agent-driven generation and integration of meaningful nucleotide sequences into pre-existing genomic arrangements, and the ability to (re-)combine and (re-)regulate them according to context-dependent (i.e. adaptational) purposes of the host organism.

The original theoretical concepts in "Theory of Communicative Nature" have been adapted to recent empirical data in the concept of biocommunication and natural genome editing, to replace the mechanistic biology of the 20th century with a non-reductionistic but integrative biology in the 21st century.

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